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UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

ORTHO-McNEIL PHARMACEUTICAL, INC., Plaintiff, v. COBALT PHARMACEUTICALS INC., Defendant.	Civil Action No. _____ **COMPLAINT FOR PATENT INFRINGEMENT**

Plaintiff Ortho-McNeil Pharmaceutical, Inc. ("Ortho-McNeil"), by its attorneys, brings this action against defendant Cobalt Pharmaceuticals Inc. ("Cobalt") for patent infringement and alleges as follows:

Parties

1. Plaintiff Ortho-McNeil is a corporation organized and existing under the laws of the State of Delaware, with its principal place of business at 1000 U.S. Route 202, Raritan, New Jersey 08869. Ortho-McNeil is engaged in the business of marketing prescription pharmaceutical products in the United States.

2. On information and belief, defendant Cobalt is a corporation organized and existing under the laws of Canada having its principal place of business at 6500 Kitimat

Road, Mississauga, Ontario, Canada L5N 2B8. Cobalt manufactures and distributes generic versions of branded pharmaceutical drugs.

Jurisdiction and Venue

3. This action for patent infringement arises under the patent laws of the United States, Title 35, United States Code, Section 271(e)(2), and Title 21, United States Code, Section 355. Subject matter jurisdiction is based on Title 28, United States Code, Sections 1331 and 1338(a).

4. Cobalt has consented to personal jurisdiction in this district and further has consented to service of this action by service on James E. Cecchi, Carella, Byrne, Bain, Gilfillan, Cecchi, Stewart & Olstein, 5 Becker Farm Road, Roseland, New Jersey 07068.

5. Venue is proper in this Court pursuant to Title 28, United States Code, Sections 1391(c) and (d).

Ortho-McNeil's Patent

6. On April 23, 1985, the United States Patent and Trademark Office ("USPTO") duly and lawfully issued United States Patent No. 4,513,006 ("the '006 patent," a copy of which is attached as Exhibit A), entitled ANTICONVULSANT SULFAMATE DERIVATIVES, to McNeilab, Inc., as assignee of the inventors Bruce E. Maryanoff and Joseph F. Gardocki. McNeilab, Inc. is a corporate predecessor of plaintiff Ortho-McNeil. Ortho-McNeil is the owner of the entire right, title and interest in and to the '006 patent, including the right to sue and recover for infringement. At all times subsequent to issuance of the '006 patent, Ortho-McNeil or its corporate predecessors have been the owner of such right, title and interest.

7. Ortho-McNeil is the holder of approved New Drug Applications ("NDAs") under Section 505(a) of the Federal Food Drug and Cosmetic Act ("FFDCA"),

21 U.S.C. § 335(a), for topiramate tablets (NDA 20-505) and topiramate sprinkle capsules (NDA 20-844), both of which are marketed in the United States under the trade name TOPAMAX®. The claims of the '006 patent cover the drug topiramate, pharmaceutical compositions containing topiramate, and a method of using topiramate for treatment of convulsions in a mammal.

8. Pursuant to 21 U.S.C. § 355, the '006 patent is identified in the Food and Drug Administration publication entitled "Approved Drug Products with Therapeutic Equivalence Evaluations" ("the Orange Book") as covering TOPAMAX® products.

9. The '006 patent was the subject of an application under 35 U.S.C. § 156, requesting a patent term restoration of five years, or until September 26, 2008. On March 11, 2003, the USPTO issued an Order Granting Interim Extension, indicating that the '006 patent was eligible for restoration of the patent term and extending the original expiration date of the '006 patent for one year, until September 26, 2004. On July 23, 2004, the USPTO granted for the '006 patent a term restoration of five years. Accordingly, the term of the '006 patent expires in September 2008.

Cobalt's Actions

10. Pursuant to Section 505 of the FFDCA, Cobalt filed an Abbreviated New Drug Application ("ANDA") for topiramate sprinkle capsules, 15 mg and 25 mg ("ANDA product"), seeking approval to engage in the commercial manufacture, use, offer for sale and sale of the ANDA product before the '006 patent expires. The number of the Cobalt ANDA is 77-868.

11. As part of its ANDA filing, Cobalt has provided written certification to the Food and Drug Administration, as called for by § 505 of the FFDCA, which certification alleges

that the claims of the '006 patent are invalid, unenforceable, and/or will not be infringed by the activities described in Cobalt's ANDA. Thus, Cobalt has alleged that no valid claim of the '006 patent will be infringed by the ANDA product it proposes to manufacture, use, offer for sale and sell.

12. Cobalt sent written notice of its filing to Ortho-McNeil, which notice was received by Ortho-McNeil. The notice alleged that the claims of the '006 patents are invalid, unenforceable, and/or will not be infringed by Cobalt and further alleged that, as a result, no valid claim of the '006 patent will be infringed by Cobalt's proposed manufacture, use, offer for sale and sale of the ANDA product. Cobalt's notice also informed Ortho-McNeil that Cobalt seeks approval to market the ANDA product before the '006 patent expires. This action is being filed within 45 days after Ortho-McNeil received Cobalt's notice.

Claim For Relief

13. Ortho-McNeil restates and incorporates by reference the allegations of the foregoing paragraphs 1-12 as though fully set forth herein.

14. Because Cobalt seeks approval of its ANDA to engage in the commercial manufacture, use or sale of a drug or drug formulation claimed in the '006 patent before it expires, Cobalt has infringed the '006 patent pursuant to 35 U.S.C. § 271(e)(2)(A).

15. Ortho-McNeil is entitled to relief provided by 35 U.S.C. § 271(e)(4), including an order of this Court that the effective date of the approval of Cobalt's ANDA be a date that is not earlier than the present expiration date of the '006 patent, or any later expiration of exclusivity to which Ortho-McNeil is or becomes entitled.

16. Upon information and belief, Cobalt was aware of the existence of the '006 patent and was aware that the filing of its ANDA and certification with respect to the '006 patent constituted an act of infringement of that patent.

17. Cobalt's statement of the factual and legal bases for its opinion regarding the alleged invalidity of the '006 patent is devoid of an objective good faith basis in either the facts or the law.

18. Ortho-McNeil will be irreparably harmed if Cobalt is not enjoined from infringing or actively inducing or contributing to infringement of the '006 patent.

19. Ortho-McNeil does not have an adequate remedy at law.

20. This case is an exceptional one, and Ortho-McNeil is entitled to an award of its reasonable attorneys' fees under 35 U.S.C. § 285.

PRAYER FOR RELIEF

WHEREFORE, plaintiff Ortho-McNeil respectfully requests that:

a. Judgment be entered that defendant Cobalt has infringed the '006 patent by submitting the aforesaid ANDA;

b. Judgment be entered that Ortho-McNeil is entitled to its reasonable attorneys' fees pursuant to 35 U.S.C. § 285;

c. To the extent Cobalt has committed any acts with respect to the compounds claimed in the '006 patent, other than those acts expressly exempted by 35 U.S.C. § 271(e)(l), Ortho-McNeil be awarded damages for such acts, which this Court should treble pursuant to 35 U.S.C. § 284;

d. A permanent injunction be issued, pursuant to 35 U.S.C. § 271(e)(4)(B), restraining and enjoining Cobalt, its officers, agents, attorneys and employees, and those acting in privity or concert with them, from engaging in the commercial manufacture,

use, offer for sale, or sale within the United States, or importation into the United States, of drug compounds or formulations as claimed in the '006 patent, or from practicing any method of treatment as claimed in the '006 patent, or from actively inducing or contributing to infringement of the '006 patent;

e. An order be issued pursuant to 35 U.S.C. § 271(e)(4)(A) that the effective date of any approval of ANDA No. 77-868 be a date which is not earlier than the present expiration date for the '006 patent, or any later expiration of exclusivity to which the '006 patent is or becomes entitled to; and

f. An order be issued for such other and further relief as the Court may deem just and proper under the circumstances.

ORTHO-McNEIL
PHARMACEUTICAL, INC.,

By: Jason E Halper
Douglas S. Eakeley
Jason E. Halper

Dated: December 22, 2005

OF COUNSEL:

JENNER & BLOCK LLP
Harry J. Roper
Aaron A. Barlow
Eric L. Lohrenz
Marshall J. Schmitt
One IBM Plaza
Chicago, IL 60611-7603
312.222.9350

LOCAL CIVIL RULE 11.2 CERTIFICATION

I hereby certify that plaintiff Ortho-McNeil Pharmaceutical Inc. has filed two related patent infringement actions, which are pending, in the United States District Court for the District of New Jersey.

The first such action is titled *Ortho-McNeil Pharmaceutical, Inc. v. Mylan Laboratories Inc. and Mylan Pharmaceuticals Inc.*, Civil Action No. 04 CV 1689 (SRC) (TJB) (Trenton vicinage) ("the *Mylan* action"). The complaint in the *Mylan* action alleges in part that defendants Mylan Laboratories Inc. and Mylan Pharmaceuticals Inc. infringed United States Patent No. 4,513,006 ("the '006 patent") by filing Abbreviated New Drug Application ("ANDA") No. 76-314. The second such action is titled *Ortho-McNeil Pharmaceutical, Inc. v. Cobalt Pharmaceuticals Inc.*, Civil Action No. No. 05-4961 (SRC) (TJB) (Trenton vicinage) ("the *Cobalt I* action"). The complaint in the *Cobalt I* action alleges in part that defendant Cobalt Pharmaceuticals Inc. infringed the '006 patent by filing Abbreviated New Drug Application ("ANDA") No. 77-643. Both ANDA No. 76-314 and ANDA No. 77-643 relate to the same active drug ingredient as ANDA 77-868, topiramate, which gave rise to the foregoing Complaint for Patent Infringement.

The *Mylan* action, the *Cobalt I* action and the present action all involve the validity, enforceability, and infringement of the '006 patent.

By _____
Jason E. Halper

Dated: December 22, 2005

EXHIBIT A

United States Patent [19]

Maryanoff et al.

[11] **Patent Number: 4,513,006**

[45] **Date of Patent: Apr. 23, 1985**

[54] **ANTICONVULSANT SULFAMATE DERIVATIVES**

[75] Inventors: **Bruce E. Maryanoff**, New Hope; **Joseph F. Gardocki**, Doylestown, both of Pa.

[73] Assignee: **McNeil Lab., Inc.**, Fort Washington, Pa.

[21] Appl. No.: **535,475**

[22] Filed: **Sep. 26, 1983**

[51] **Int. Cl.**[3] **A61K 31/35**; C07D 311/78; C07D 311/94; C07D 309/06

[52] **U.S. Cl.** ..... **514/23**; 549/426; 549/396; 549/387; 549/338; 549/337; 549/336; 549/427; 536/54; 260/456 A; 514/459; 514/517

[58] **Field of Search** ..... 549/387, 396, 426, 337, 549/338; 260/456 A; 424/283, 303; 536/54

[56] **References Cited**

U.S. PATENT DOCUMENTS

4,075,351 2/1978 Hirsch 424/303

OTHER PUBLICATIONS

N. K. Kochetkov, et al., in Zhurnal Obshchei Khimii, vol. 41, No. 8, pp. 1866–1871, (1971).

N. K. Kochetkov, et al., in Journal of General Chemistry of the USSR 42 (12) 2755–2757 (1972).

N. K. Kochetkov, et al., in Journal of General Chemistry of the USSR 44 (4) 871–875 (1974).

N. K. Kochetkov, et al., in Doklady Akademii Nauk SSSR, vol. 216, No. 1, pp. 97–100, (1974).

Tetrahedron Letters No. 36, pp. 3365–3368, Pergamon Press Ltd. (1978) by T. Tsuchiya.

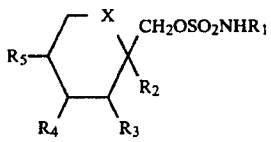
J. Med. Chem. 1981, 24, 901–903, A. F. Hirsch.

Primary Examiner—Nicky Chan

Attorney, Agent, or Firm—David J. Levy

[57] **ABSTRACT**

Sulfamates of the following formula (I):



(I)

wherein X is O or CH_2 and R_1, R_2, R_3, R_4 and R_5 are as herein defined have been found to exhibit anticonvulsant activity and are thus useful in the treatment of conditions such as epilepsy. Further, pharmaceutical compositions containing a compound of formula (I) as well as methods for their use and intermediates form part of the present invention.

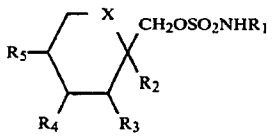
12 Claims, No Drawings

ANTICONVULSANT SULFAMATE DERIVATIVES

Sulfamates of various structures, including those derived from monosaccharides are described in references such as N. K. Kochetkov et al in Zhurnal Obshchei Kimii, Vol. 41, No. 8, 1866 to 1871 (1971), Vol. 42, No. 12, 2755 to 2757 (1972) and Vol. 44, No. 4, 871 to 875 (1974) and in Doklady Akademii Nauk SSR, Vol. 216, No. 1, 97 to 100 (1974); T. Tsuchiya et al., in Tetrahedron Letters, No. 36, 3365 to 3368 (1978); and A. F. Hirsch in Journal of Medicinal Chemistry, 24, 901 to 903 (1981) and U.S. Pat. No. 4,075,351.

SUMMARY OF THE INVENTION

It has been found that sulfamates of the following formula (I):

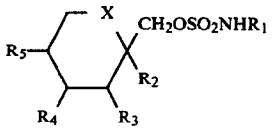


(I)

wherein X is O or CH_2 and R_1, R_2, R_3, R_4 and R_5 are as hereinafter defined, possess anticonvulsant activity in mammals and are thus useful in treating disease states such as epilepsy and glaucoma. Also part of the present invention are pharmaceutical compositions containing one or more sulfamates of formula (I) as well as methods for the treatment e.g., prevention, of convulsions using such compositions.

DETAILED DESCRIPTION OF THE INVENTION

The sulfamates of the invention are of the following formula (I):



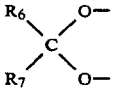
(I)

wherein

X is CH_2 or oxygen;

R_1 is hydrogen or alkyl; and

R_2, R_3, R_4 and R_5 are independently hydrogen or lower alkyl and, when X is CH_2, R_4 and R_5 may be alkene groups joined to form a benzene ring and, when X is oxygen, R_2 and R_3 and/or R_4 and R_5 together may be a methylenedioxy group of the following formula (II):



(II)

wherein

R_6 and R_7 are the same or different and are hydrogen, lower alkyl or are alkyl and are joined to form a cyclopentyl or cyclohexyl ring.

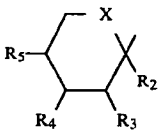
R_1 in particular is hydrogen or alkyl of about 1 to 4 carbons, such as methyl, ethyl and iso-propyl. Alkyl throughout this specification includes straight and

branched chain alkyl. Alkyl groups for R_2, R_3, R_4, R_5, R_6 and R_7 are of about 1 to 3 carbons and include methyl, ethyl, iso-propyl and n-propyl. When X is CH_2, R_4 and R_5 may combine to form a benzene ring fused to the 6-membered X-containing ring, i.e., R_4 and R_5 are defined by the alkatrienyl group =CH—CH=CH—CH=.

A particular group of compounds of formula (I) is that wherein X is oxygen and both R_2 and R_3 and R_4 and R_5 together are methylenedioxy groups of the formula (II) wherein R_6 and R_7 are both hydrogen, both alkyl or combine to form a spiro cyclopentyl or cyclohexyl ring, in particular where R_6 and R_7 are both alkyl such as methyl. A second group of compounds is that wherein X is CH_2 and R_4 and R_5 are joined to form a benzene ring. A third group of compounds of formula (I) is that wherein both R_2 and R_3 are hydrogen.

The compounds of formula (I) may be synthesized by the following methods:

(a) Reaction of an alcohol of the formula RCH_2OH with a chlorosulfamate of the formula $ClSO_2NH_2$ or $ClSO_2NHR_1$ in the presence of a base such as potassium t-butoxide or sodium hydride at a temperature of about −20° to 25° C. and in a solvent such as toluene, THF or dimethylformamide wherein R is a moiety of the following formula (III):



(III)

(b) Reaction of an alcohol of the formula RCH_2OH with sulfurylchloride of the formula SO_2Cl_2 in the presence of a base such as triethylamine or pyridine at a temperature of about −40° to 25° C. in a solvent such as diethyl ether or methylene chloride to produce a chlorosulfate of the formula RCH_2OSO_2Cl.

The chlorosulfate of the formula RCH_2OSO_2Cl may then be reacted with an amine of the formula R_1NH_2 at a temperature of about −40° to 25° C. in a solvent such as methylene chloride or acetonitrile to produce a compound of formula (I). The reaction conditions for (b) are also described by T. Tsuchiya et al in Tet. Letters, No. 36, p. 3365 to 3368 (1978).

(c) Reaction of the chlorosulfate RCH_2OSO_2Cl with a metal azide such as sodium azide in a solvent such as methylene chloride or acetonitrile yields an azidosulfate of the formula $RCH_2OSO_2N_3$ as described by M. Hedayatullah in Tet. Lett. p. 2455-2458 (1975). The azidosulfate is then reduced to a compound of formula (I) wherein R_1 is hydrogen by catalytic hydrogenation, e.g. with a noble metal and H_2 or by heating with copper metal in a solvent such as methanol.

The starting materials of the formula RCH_2OH may be obtained commercially or as known in the art. For example, starting materials of the formula RCH_2OH wherein both R_2 and R_3 and R_4 and R_5 are idential and are of the formula (II) may be obtained by the method of R. F. Brady in Carbohydrate Research, Vol. 15, p. 35 to 40 (1970) or by reaction of the trimethylsilyl enol ether of a R_6COR_7 ketone or aldehyde with fructose at a temperature of about 25° C. in a solvent such as a halocarbon, e.g. methylene chloride in the presence of a protic acid such as hydrochloric acid or a Lewis Acid

such as zinc chloride. The trimethylsilyl enol ether reaction is described by G. L. Larson et al in J. Org. Chem. Vol. 38, No. 22, p. 3935 (1973).

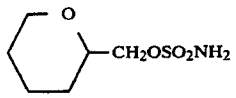
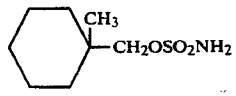
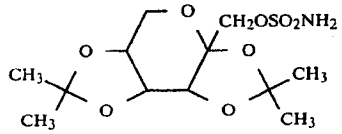
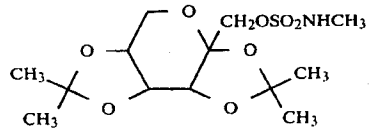
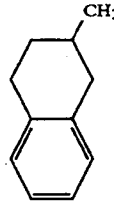
Further, carboxylic acids and aldehydes of the formulae RCOOH and RCHO may be reduced to compounds of the formula RCH_2OH by standard reduction techniques, e.g. reaction with lithium aluminum hydride, sodium borohydride or borane-THF complex in an inert solvent such as diglyme, THF or toluene at a temperature of about 0° to 100° C., e.g., as described by H. O. House in "Modern Synthetic Reactions", 2nd Ed., pages 45 to 144 (1972).

The compounds of the invention include the various individual isomers as well as the racemates thereof, e.g., the various alpha and beta attachments, i.e., below and above the plane of the drawing, of R_2, R_3, R_4 and R_5 on the 6-membered ring. Preferably, the oxygens of the methylenedioxy group (II) are attached on the same side of the 6-membered ring.

The compounds of formula (I) are useful as anticonvulsant agents. The anticonvulsant activity of the subject compounds was determined using a standard "maximal electroshock test" (MES). In this test, activity is indicated by a block of the toxic extensor seizure caused by application of an electric shock to mice via corneal electrodes, as described by Swinyard et al in J. Pharmacol. Exptl. Therap. 106, 319 (1952), and recorded as % block. A more recent description of current anticonvulsant drug screening is given in Swinyard et al in Epilepsia 19, 409 (1978).

The anticonvulsant activity of compounds of this invention tested according to the Swinyard (1952) method is shown in the following Table I:

TABLE I

Example	Compound	MES test ED_{50}* (mg/kg, i.p.)
1		195
2		270
3		26
4		70% block at 200 mg/kg, i.p.
5		55

*Unless otherwise noted.

For treating epilepsy, a compound of formula (I) may be employed at a daily dosage in the range of about 30 to 2000 mg, usually in 2 to 4 divided doses, for an average adult human. A unit dose would contain about 10 to 500 mg of the active ingredient.

In general, compounds of formula (I) may be used in treating epilepsy in a manner similar to that used for phenytoin. Medical aspects of the treatment of epilepsy are described by L. S. Goodman et al in "The Pharmacological Basis of Therapeutics", 5th Ed. pages 201 to 226, Macmillan (1975).

Further, compounds of formula (I) are inhibitors of carbonic anhydrase, as determined by the methods described by S. J. Dodgson et al in the Proc. Natl. Acad. Sci., U.S.A., 77, pages 5562 to 5566 (1980) or by N. Itada et al in the Journal Biol. Chem., 252, pages 3881 to 3890 (1977) and as such, are useful in the treatment of glaucoma. The relationship between the treatment of glaucoma and carbonic anhydrase inhibition is described by A. Stein et al in the American Journal of Opthalmology, 95:222–228 (1983). For the treatment of glaucoma, a compound of formula (I) may be administered systemically, e.g. by oral or parenteral routes as described below, or topically in the eye in a mineral oil solution or suspension, or aqueous suspension. When used systemically, the compound would be administered in an amount of about 50 to 500 mg per day for an average adult human, while the topical dosage would be about 1 to 3 drops (per eye) of a solution or suspension containing about 1 to 5% by weight of a compound of formula (I) with the dosage being administered about 1 to 4 times per day.

To prepare the pharmaceutical compositions of this invention, one or more sulfamate compounds of formula (I) are intimately admixed with a pharmaceutical carrier according to conventional pharmaceutical compounding techniques, which carrier may take a wide variety of forms depending on the form of preparation desired for administration, e.g., oral, by suppository, or parenteral. In preparing the compositions in oral dosage form, any of the usual pharmaceutical media may be employed. Thus, for liquid oral preparations, such as, for example, suspensions, elixirs and solutions, suitable carriers and additives include water, glycols, oils, alcohols, flavoring agents, preservatives, coloring agents and the like; for solid oral preparations such as, for example, powders, capsules and tablets, suitable carriers and additives include starches, sugars, diluents, granulating agents, lubricants, binders, disintegrating agents and the like. Because of their ease in administration, tablets and capsules represent the most advantageous oral dosage unit form, in which case solid pharmaceutical carriers are obviously employed. If desired, tablets may be sugar

coated or enteric coated by standard techniques. Suppositories may be prepared, in which case cocoa butter could be used as the carrier. For parenterals, the carrier will usually comprise sterile water, though other ingredients, for example, for purposes such as aiding solubility or for preservation, may be included. Injectable suspensions may also be prepared, in which case appropriate liquid carriers, suspending agents and the like may be employed.

The pharmaceutical compositions herein will contain, per dosage unit, e.g., tablet, capsule, powder, injection, teaspoonful, suppository and the like, from about 10 to about 500 mg of the active ingredient.

The foregoing compositions are particularly suitable for use in the treatment of epilepsy or the symptoms of epilepsy by a method comprising internally administering to a subject suffering from the symptoms of epilepsy compositions comprising an effective epilepsy inhibiting amount of a compound of formula (I).

Also part of the present invention are intermediates of the formulae RCH_2OSO_2Cl and $RCH_2OSO_2N_3$.

In the following Examples and throughout the specification the following abbreviations may be used: g (grams); ml (milliliters); min (minutes); hr (hours); mol (moles); cm (centimeters); v/v (volume to volume); mp (melting point); TLC (thin layer chromatography); NMR (nuclear magnetic resonance); IR (infrared); DMF (dimethylformamide); THF (tetrahydrofuran); and C, H, N, etc. (the chemical symbols for the elements).

EXAMPLE 1

(Tetrahydro-2H-pyran-2-yl)methane sulfamate

To a cold solution (−5° C.) of tetrahydropyran-2-methanol (2.33 g, 0.02 mol) in DMF (40 ml) was added 50% oily sodium hydride (1.17 g, 0.024 mol as NaH). After stirring for 45 min, sulfamoyl chloride (3.42 g, 0.03 mol) was added and the stirring continued for an additional 45 min, at −5° C. The reaction mixture was poured into cold water and extracted with chloroform. The organic layer was dried (Na_2SO_4) and the solvents were removed under vacuum to give a syrup which was dry column chromatographed (eluted with ethyl acetate:hexane, 4:1 v/v) to give pure (tetrahydro-2H-pyran-2-yl) methanesulfamate as a pale yellow syrup, IR:($CHCl_3$) 1180 cm^{-1} and 1370 cm^{-1} (OSO_2NH_2).

EXAMPLE 2

(1-Methylcyclohexyl)methane sulfamate

To a cold solution (−4° C.) of (1-methylcyclohexyl)-methanol (6.2 g, 0.048 mol) in DMF (90 ml) was added 50% oily sodium hydride (2.81 g, 0.059 mol as NaH). After stirring for 1 hr, sulfamoyl chloride (7.82 g, 0.062 mol) was added and the stirring was continued for an additional 30 min at −4° C. The reaction mixture was poured into cold water and extracted with toluene. The organic layer was dried (Na_2SO_4) and the solvents were removed under vacuum to give a syrup which crystallized upon cooling. Recrystallization from chloroform-/hexane gave pure (1-methylcyclohexyl)methane sulfamate, mp 40°–42° C.

EXAMPLE 3

2,3:4,5-Bis-O-(1-methylethylidene)-β-D-fructopyranose sulfamate

To a cold solution (−4° C.) of 2,3:4,5-di-O-isopropylidene-β-fructopyranose (75 g, 0.29 mol) in DMF (725 ml) was added 50% oily sodium hydride (16.34 g, 0.34 mol as NaH). After stirring for 90 min, sulfamoyl chloride (54.9 g, 0.48 mol) was added and the stirring continued for an additional 3.5 hr at that temperature. The reaction mixture was poured into cold water and extracted with toluene. The organic layer was dried (Na_2SO_4) and the solvents removed under vacuum to give a syrup which crystallized immediately. Recrystallization from ethylacetate/hexane gave pure 2,3:4,5-bis-O-(1-methylethylidene)-β-D-fructopyranose sulfamate, mp 125°–126° C.

EXAMPLE 4

2,3:4,5-Bis-O-(1-methylethylidene)-β-D-fructopyranose methyl sulfamate

A solution of sulfonyl chloride (93 ml, 1.15 mol) in methylene chloride (100 ml) was added dropwise to a cold solution (−35° C.) of 2,3:4,5-di-O-isopropylidene-β-D-fructopyranose (150 g, 0.58 mol) in methylene chloride (400 ml) and pyridine (150 ml). The reaction mixture was allowed to stir and warm to room temperature (25° C.); it was stirred for an additional 2 hr. Solvents were removed under vacuum. The resulting semi-solid was dissolved in anhydrous acetonitrile (35 g, 150 ml) and methyl amine was bubbled in. The reaction mixture was tightly stoppered and solvents removed under vacuum. The resulting syrup was subjected to liquid chromatography (dry column ethyl acetate:hexane, 4:1) yielding a light yellow syrup, 2,3:4,5-bis-O-(1-methylethylidene)-β-D-fructopyranose methylsulfamate, which was homogeneous by TLC and ^{1}HNMR.

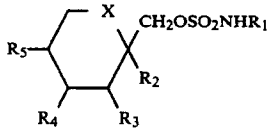
EXAMPLE 5

(1,2,3,4-Tetrahydro-2-naphthalenyl)methyl sulfamic acid ester

To a cold solution (−5°) of (1,2,3,4-tetrahydro-2-naphthalenyl)methanol (7.1 g, 0.044 mol) in DMF (80 ml) was added 50% oily sodium hydride (2.56 g, 0.054 mol as NaH). After stirring for 45 min, sulfamoyl chloride (6.6 g, 0.057 mol) was added and the stirring continued for an additional 95 min at −5° C. The reaction mixture was poured into cold water and extracted with toluene. The organic layer was dried (Na_2SO_4) and the solvents removed under vacuum to give a syrup which crystallized immediately. Recrystallization from chloroform/hexane gave pure (1,2,3,4-tetrahydro-2-naphthalenyl)methyl sulfamic acid ester, mp 108°–109° C., as a white solid.

What is claimed is:

1. A sulfamate of the following formula (I):



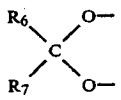
(I)

wherein

X is oxygen;

R_1 is hydrogen or alkyl; and

R_2, R_3, R_4 and R_5 are independently hydrogen or lower alkyl and R_2 and R_3 and/or R_4 and R_5 together may be a group of the following formula (II):



(II)

wherein

R_6 and R_7 are the same or different and are hydrogen, lower alkyl or are alkyl and are joined to form a cyclopentyl or cyclohexyl ring.

2. The sulfamate of claim 1, wherein

R_2 and R_3 and R_4 and R_5 together are groups of the formula (II).

3. The sulfamate of claim 1, wherein said alkyl group for R_1 is alkyl of about 1 to 4 carbons; said lower alkyl group for R_2, R_3, R_4 and R_5 is alkyl of about 1 to 3 carbons; and said lower alkyl for R_6 and R_7 is alkyl of about 1 to 3 carbons.

4. The sulfamate of claim 1, wherein said sulfamate of formula (I) is selected from the group consisting of:

(tetrahydro-2H-pyran-2-yl)methane sulfamate;

2,3:4,5-bis-O-(1-methylethylidene)-β-D-fructopyranose sulfamate;

2,3:4,5-bis-O-(1-methylethylidene)-β-D-fructopyranose methylsulfamate.

5. The sulfamate of claim 4, wherein said sulfamate is 2,3:4,5-bis-O-(1-methylethylidene)-β-D-fructopyranose sulfamate.

6. A pharmaceutical composition effective for the treatment of convulsions comprising an anticonvulsantly effective amount of a sulfamate of claim 1 and a pharmaceutically-acceptable carrier.

7. The pharmaceutical composition of claim 6, wherein said sulfamate is present in a unit dosage amount of about 10 to 500 milligrams of the sulfamate.

8. A method for the treatment of convulsions in a mammal which comprises administering to the mammal, the pharmaceutical composition of claim 6.

9. The sulfamate of claim 4, wherein said sulfamate is 2,3:4,5-bis-O-(1-methylethylidene)-β-D-fructopyranose methylsulfamate.

10. The sulfamate of claim 1, wherein the two oxygen atoms of the group of formula (II) are attached on the same side of the six-membered ring depicted in formula (I).

11. The sulfamate of claim 1, wherein the sulfamate of formula (I) is a fructopyranose.

12. The sulfamate of claim 1, wherein in formula (I), R_1 is hydrogen.

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