

COMMONWEALTH OF AUSTRALIA
PATENTS ACT 1952
APPLICATION FOR A STANDARD PATENT

Chemisch Pharmazeutische Forschungsgesellschaft m.b.H., of St.Peter-Strasse
25, A-4021 Linz, AUSTRIA, hereby apply for the grant of a standard patent for
an invention entitled:

Novel Sulphamoylthiophenes, A Process for their Preparation
and their Use

which is described in the accompanying complete specification.

Details of basic application(s):-

<u>Basic Applic. No:</u>	<u>Country:</u>	<u>Application Date:</u>
A 1639/89	AT	5 July 1989

The address for service is:-

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DATED this TWENTY SEVENTH day of JUNE 1990

Chemisch Pharmazeutische Forschungsgesellschaft m.b.H.

By:



Registered Patent Attorney

TO: THE COMMISSIONER OF PATENTS
OUR REF: 133240
S&F CODE: 52605

SPRUSON & FERGUSON

COMMONWEALTH OF AUSTRALIA

PATENTS ACT 1952

DECLARATION IN SUPPORT OF A CONVENTION
APPLICATION FOR A PATENT

In support of the convention application made for a patent for an invention entitled:

Novel Sulphamoylthiophenes, A Process for their Preparation and their Use

I/we, Trond Jacobsen
[full name of declarant(s)]
care of Chemisch Pharmazeutische Forschungsgesellschaft m.b.H.,
St. Peter-Strasse 25, A-4021 Linz, Austria
[full address of declarant(s) - not post office box]

do solemnly and sincerely declare as follows:

1. I am/~~w~~ authorized by Chemisch Pharmazeutische Forschungsgesellschaft m.b.H, the applicant for the patent to make this declaration on its behalf.
2. The basic application as defined by Section 141 of the Act was made in Austria on 5 July 1989 by Dieter Binder.
3. Dieter Binder, Franz Rovenszky, Norman Brunner and Hubert Peter Ferber, of Sieveringerstrasse 207, A-1190 Wien; Lagerhausstrasse 5/8, A-2460 Bruck a.d.Leitha; Bergstrasse 66, A-2102 Hagenbrunn and Ahornweg 24, A-4021 Ansfelden all in Austria, respectively, are the actual inventors of the invention and the facts upon which the applicant is entitled to make the application are as follows:-

Dieter Binder made the basic application as assignee of his co-inventors Franz Rovenszky, Norman Brunner and Hubert Peter Ferber and the Chemisch Pharmazeutische Forschungsgesellschaft m.b.H. is the assignee by virtue of the Assignment dated October 16, 1989 from the actual inventors including the priority rights accruing from said basic application.
4. The basic application referred to in paragraph 2 of this Declaration was the first application made in a Convention country in respect of the invention the subject of the application.

DECLARED at Linz, this 16th day of August 1990

Chemisch Pharmazeutische Forschungsgesellschaft m.b.H.

..... Trond Jacobsen
Signature of Declarant(s)

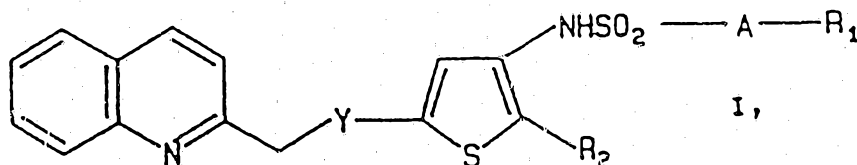
TO: THE COMMISSIONER OF PATENTS
AUSTRALIA

Ref: S&F 133240
SBR/JS/6998D

(12) PATENT ABRIDGMENT (11) Document No. AU-B-57993/90
(19) AUSTRALIAN PATENT OFFICE (10) Acceptance No. 623025

- (54) Title
NOVEL SULPHAMOYLTHIOPHENES, A PROCESS FOR THEIR PREPARATION AND THEIR USE
- (51)⁵ International Patent Classification(s)
C07D 409/12 A61K 031/47
- (21) Application No. : 57993/90 (22) Application Date : 28.06.90
- (30) Priority Data
- (31) Number (32) Date (33) Country
1639/89 05.07.89 AT AUSTRIA
- (43) Publication Date : 10.01.91
- (44) Publication Date of Accepted Application : 30.04.92
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- (74) Attorney or Agent
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- (56) Prior Art Documents
AU 28748/89 C07D 215/04 C07D 409/12
AU 588960 67638/87 C07D 409/12 A61K 031/38
- (57) Claim

1. Sulphamoylthiophenes of the general formula



in which

Y denotes O or S,
A denotes a single bond or a straight-chain or branched alkylene group having 1 - 5 carbon atoms,
R₁ denotes methyl or trifluoromethyl and
R₂ denotes hydrogen or a group COOH or COOR₃, in which
R₃ represents (C₁-C₄)-alkyl,
and, in the case in which R₂ denotes a group COOH, their pharmaceutically tolerable salts.

10. A method for the treatment or prophylaxis of diseases which can be alleviated or cured by leukotriene antagonists in a patient requiring said treatment or prophylaxis, which method comprises administering to said patient an effective amount of at least one compound according to any one of claims 1 to 5 or 8, or of a preparation according to claim 7.

FORM 10

623025

Ref: 133240

COMMONWEALTH OF AUSTRALIA

PATENTS ACT 1952

COMPLETE SPECIFICATION

(ORIGINAL)

FOR OFFICE USE:

Class Int Class

Complete Specification Lodged:

Accepted:

Published:

Priority:

Related Art:

Name and Address
of Applicant:

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Complete Specification for the invention entitled:

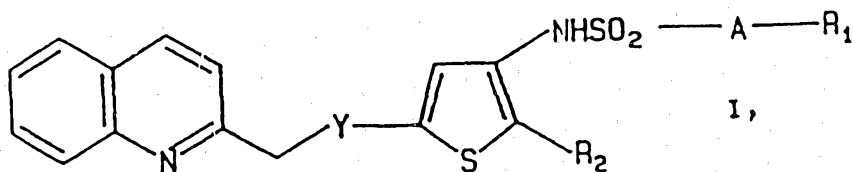
Novel Sulphamoylthiophenes, A Process for their Preparation
and their Use

The following statement is a full description of this invention, including the
best method of performing it known to me/us

5845/4

Abstract

Sulphamoylthiophenes of the general formula



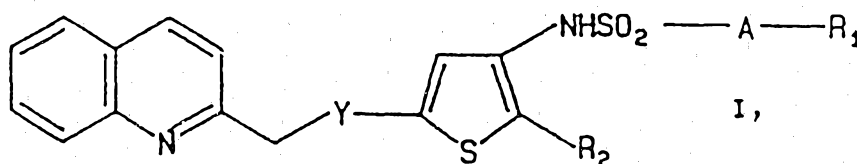
in which

- 5 Y denotes O or S,
A denotes a single bond or a straight-chain or
 branched alkylene group having 1 - 5 carbon atoms,
R₁ denotes methyl or trifluoromethyl and
R₂ denotes hydrogen or a group COOH or COOR₃, in which
10 R₃ represents (C₁-C₄)-alkyl,
and, in the case in which R₂ denotes a group COOH, their
 pharmaceutically tolerable salts, a process for their
 preparation, pharmaceutical preparations which contain
15 these compounds and their use in medicaments as leuko-
 triene antagonists for the treatment of asthma and
 allergies.

Novel sulphamoylthiophenes, a process for their preparation and their use

The invention relates to novel sulphamoylthiophenes, to a process for their preparation, to pharmaceutical preparations which contain these compounds and to their use in medicaments as leukotriene antagonists.

The invention relates to novel sulphamoylthiophenes of the general formula



10 in which

Y denotes O or S,

A denotes a single bond or a straight-chain or branched alkylene group having 1 - 5 carbon atoms,

R₁ denotes methyl or trifluoromethyl and

15 R₂ denotes hydrogen or a group COOH or CCOR₃, in which R₃ represents (C₁-C₄)-alkyl,

and, in the case in which R₂ denotes a group COOH, to their pharmaceutically tolerable salts, to a process for their preparation, to pharmaceutical preparations which contain these compounds and to their use in medicaments as leukotriene antagonists.

A preferred class of compounds of the general formula I contains those compounds in which A denotes a single bond and R₁ denotes trifluoromethyl.

25 Particularly preferred individual compounds are: methyl 5-(2-quinolinylmethoxy)-3-(1,1,1-trifluoromethylsulphamoyl)-2-thiophenecarboxylate.

5-(2-quinolinylmethoxy)-3-(1,1,1-trifluoromethylsulphamoyl)-2-thiophenecarboxylic acid.

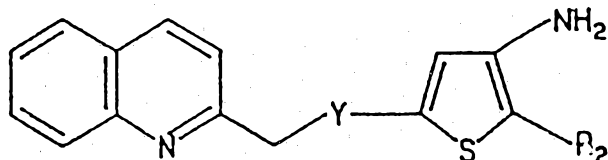
30 1,1,1-trifluoro-N-[5-(2-quinolinylmethoxy)-3-thienyl]-methanesulphonamide.

The expression (C₁-C₄)-alkyl used in this description indicates straight-chain or branched saturated

hydrocarbon radicals having 1 to 4 carbon atoms, such as, for example, methyl, ethyl, propyl, isopropyl, butyl, isobutyl and tert. butyl.

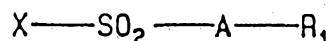
5 The compounds of the general formula I are prepared by a process in which

a) a compound of the general formula



II

10 in which Y denotes O or S and R₂ denotes a group COOR₃, where R₃ represents (C₁-C₄)-alkyl, is reacted with a compound of the general formula



III

15 in which A and R₁ have the above meaning and X represents chlorine or a group -O-SO₂-A-R₁, where A and R₁ have the above meaning, in an inert organic solvent,

b) if desired, an ester of the general formula I, obtained in process step a), in which Y, A and R₁ have the above meaning and R₂ represents a radical COOR₃, where R₃ denotes (C₁-C₄)-alkyl, is hydrolysed to give a free acid of the general formula I in which R₂ denotes a group COOH, and, if desired, converted into a pharmaceutically tolerable salt using inorganic or organic bases and

20 c) if desired, a free acid of the general formula I, obtained in process step b), in which R₂ represents a group COOH and Y, A and R₁ have the above meaning, is decarboxylated to give a compound of the formula I in which R₂ denotes hydrogen.

25 The reaction according to process step a) is best carried out by dissolving or suspending a compound of the formula II in an inert organic solvent, such as a halogenated organic solvent, for example methylene chloride or chloroform or an ether, for example diethyl ether, adding at least two equivalents of an inorganic or

30

5 organic base such as triethylamine, pyridine, N-methyl-
morpholine or trimethylsilylanolate, preferably triethyl-
amine or pyridine, and adding dropwise a solution of a
compound of the general formula III in the same solvent
at a temperature between -80 and 30°C, preferably between
-20 and 20°C. The reaction time is then between 30 min-
utes and 4 hours, preferably between 30 and 90 minutes.

10 The esters of the general formula I thus obtained
can be hydrolysed in a customary manner with alcoholic
aqueous alkali according to process step b) to give the
free carboxylic acids of the formula I. For this purpose,
the ester is dissolved in a mixture of a lower aliphatic
alcohol and water and 2 to 6 equivalents of alkali are
added, preferably 2 to 4 equivalents. The mixture is then
15 stirred at a temperature between 30 and 100°C. The
reaction time in this case is between 2 and 24 hours, the
higher temperatures being associated with the shorter
reaction times.

20 The compounds of the formula I obtained, in which
 R_2 denotes a group COOH, can be converted with inorganic
or organic bases into their pharmaceutically utilizable
salts. The salt formation can be carried out, for
example, by dissolving the compounds of the formula I
mentioned in a suitable solvent, for example water or a
25 lower aliphatic alcohol, adding an equivalent amount of
the desired base, providing for thorough mixing and
removing the solvent by distillation in vacuo after salt
formation is complete. If desired, the salts can be
recrystallized after isolation.

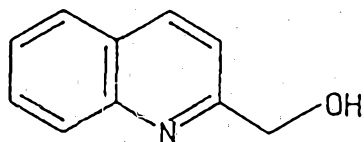
30 Pharmaceutically utilizable salts are, for
example, metal salts, in particular alkali metal or
alkaline earth metal salts, such as sodium, potassium,
magnesium or calcium salts. Other pharmaceutically
utilizable salts are, for example, also easily crystal-
35 lizing ammonium salts. The latter are derived from
ammonia or organic amines, for example mono-, di- or tri-
lower (alkyl, cycloalkyl or hydroxyalkyl)amines, lower
alkylenediamines or (hydroxy lower alkyl or aryl lower
alkyl) lower alkylammonium bases, for example

methylamine, diethylamine, triethylamine, dicyclohexylamine, triethanolamine, ethylenediamine, tris(hydroxymethyl)aminomethane, benzyltrimethylammonium hydroxide and the like.

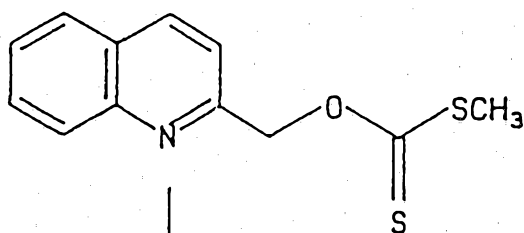
5 The free acids obtained by process step b) or their salts can be decarboxylated to give compounds of the general formula I in which R_2 denotes hydrogen. For this purpose, the starting material is dissolved or suspended in a suitable solvent, such as in cyclic or
10 aliphatic ethers or in pyridine, aqueous ammonia solution or in a lower aliphatic alcohol and heated for between 15 minutes and 8 hours, preferably between 10 and 60 min, at a temperature between 40 and 90°C, preferably between 60 and 80°C, with thorough mixing.

15 The compounds obtained are worked up by methods which are customary and familiar to any person skilled in the art such as, for example, extraction, precipitation or recrystallization.

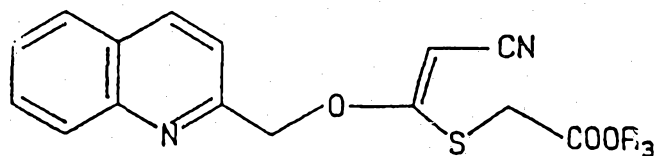
20 The compounds of the general formula II can be prepared according to the following equation and the special instructions in the examples.



- 1.) NaOCH₃
- 2.) CS₂
- 3.) CH₃I



- 1.) -CH₂CN
- 2.) BrCH₂COOR₃



Base

II

The sulphonyl chlorides or anhydrides of the general formula III are known from the literature or commercially available.

5 The novel compounds of the formula I and, if R₂ denotes a group COOH, their pharmaceutically utilizable salts show an excellent inhibitory action on leukotrienes in in vivo and in vitro models. In addition, they inhibit the inflammatory processes in chronic disorders of the gastrointestinal tract, for example Crohn's disease, with



lower side effects than known leukotriene antagonists.

5 On the basis of these pharmacological properties, the novel compounds can be used alone or in a mixture with other active substances in the form of customary pharmaceutical preparations for the treatment of diseases which are caused by an excess of leukotrienes, such as, for example, in asthma and allergies.

10 The compounds of the formula I are intended for use in humans and can be administered in a customary manner, such as, for example, orally, parenterally or by inhalation. They are preferably administered by inhalation, the daily dose being about 10 mcg to 10 mg/kg of body weight, preferably 50 to 500 mcg/kg of body weight. The treating physician may, however, depending on the
15 general condition and the age of the patient, the appropriate substance of the formula I, the nature of the disease and the manner of the formulation, also prescribe doses above or below this.

20 If the substances according to the invention are used for prophylaxis, the dose varies in approximately the same bounds as in the treatment case. Administration by inhalation is also preferred in the case of prophylaxis.

25 The compounds of the formula I can be administered in medicaments alone or in combination with other pharmaceutically active substances, the content of the compounds of the formula I being between 0.1 and 99 %. In general, the pharmaceutically active compounds are present in a mixture with suitable inert auxiliaries and/or excipients or diluents, such as, for example,
30 pharmaceutically acceptable solvents, gelatin, gum arabic, lactose, starch, magnesium stearate, talc, vegetable oils, polyalkylene glycol, petroleum jelly and the like.

35 The pharmaceutical preparations may be present in solid form, for example as tablets, coated tablets, suppositories, capsules and the like, in liquid form, for example as solutions, suspensions or emulsions, in compositions with sustained release of the active

compound, or in formulations for inhalation. If desired, they are sterilized and contain auxiliaries, such as preservatives, stabilizers or emulsifiers, salts for changing the osmotic pressure and the like. Formulations in spray containers contain propellants such as CO₂, nitrogen or halogenated hydrocarbons in addition to the abovementioned substances.

Pharmaceutical preparations may in particular contain the compounds according to the invention in combination with other therapeutically useful substances. Using these, the compounds according to the invention can be formulated, for example, together with the abovementioned auxiliaries and/or excipients or diluents to give combination preparations.

Example 1:

Methyl 5-(2-quinolinylmethoxy)-3-(1,1,1-trifluoromethylsulphamoyl)-2-thiophenecarboxylate

30.0 g (0.095 mol) of methyl 3-amino-5-(2-quinolinylmethoxy)thiophene-2-carboxylate are suspended in 400 ml of abs. methylene chloride at room temperature and 19.3 g (0.191 mol) of abs. triethylamine are added with stirring. The clear solution is cooled to 0°C. 47.1 g (0.167 mol) of trifluoromethanesulphonic anhydride dissolved in 50 ml of abs. methylene chloride are added dropwise at 0°C in the course of 50 minutes. After completion of the addition, the reaction mixture is stirred at 0°C for 30 minutes and then allowed to warm to room temperature. The brown reaction solution is diluted with 200 ml of methylene chloride and extracted by shaking twice with 100 ml of saturated sodium bicarbonate solution each time. The methylene chloride phase is extracted twice with 100 ml of 0.5 N hydrochloric acid each time and then extracted by shaking with 50 ml of saturated sodium bicarbonate solution. The combined organic phases are dried over sodium sulphate/active carbon, filtered and evaporated. The crude product (40.5 g) is crystallized from 75 ml of ethanol.

Yield: 23.3 g of brown crystals (55 % of theory, salt-free)

M.p.: 108-110°C (ethanol)

The starting material can be prepared as follows:

O-(2-Quinolinylmethyl) S-methyl dithiocarbonate

80.0 g (0.503 mol) of 2-quinolinemethanol

5 [V. Bockelheide and W.J. Linn; J. Am. Chem. Soc. 76, 1286
(1954)] are dissolved in 800 ml of absolute methanol and
94 ml of 5.4 M (0.506 mol) sodium methoxide solution are
added. The clear solution is evaporated and dried under
10 high vacuum. 600 ml of acetone are added to the grey
crystalline product (89.5 g), the suspension is cooled to
0°C with stirring and 80.0 g (1.051 mol) of carbon
disulphide are added in one portion. The mixture is
stirred for a further 30 minutes at room temperature, a
clear solution being formed. 85.8 g (0.602 mol) of methyl
15 iodide are added to this solution in one portion. The
mixture is stirred at 40°C for 20 minutes, then 15.0 g of
sodium sulphite are added to the reaction solution and it
is evaporated. The residue is partitioned between 700 ml
of saturated sodium sulphite solution and 500 ml of ether
20 and the aqueous phase is extracted twice more using
300 ml of ether each time. The combined organic phases
are washed once with 400 ml of water, dried over sodium
sulphate/active carbon and evaporated. The crude product
(118.6 g) is dissolved in 500 ml of diisopropyl ether at
25 room temperature, active carbon is added, and the mixture
is filtered and allowed to precipitate at -20°C. The
product is filtered off with suction, digested twice with
50 ml of ice-cold diisopropyl ether each time and dried
at 25°C/1 mbar for three hours.

30 Yield: 103.2 g of ochre-coloured crystals (82 % of
theory)

M.p.: 42-43°C (diisopropyl ether)

Methyl 3-amino-5-(2-quinolinylmethoxy)-2-thiophene-
carboxylate

35 231 ml (0.578 mol) of 2.5 M butyllithium solution
in n-hexane is cooled to -80°C with stirring and 300 ml
of absolute tetrahydrofuran are added in the course of
25 minutes. 22.2 g (0.539 mol) of dry acetonitrile,
dissolved in 100 ml of abs. tetrahydrofuran, are then

added dropwise to the BuLi solution such that the temperature does not exceed -75°C (30 minutes). The mixture is stirred further at -80°C for 45 minutes. 133.6 g (0.536 mol) of O-(2-quinolinylmethyl) S-methyl dithiocarbonate, dissolved in 300 ml of absolute tetrahydrofuran, are then added dropwise to the reaction solution in the course of 35 minutes such that the temperature does not exceed -80°C . The reaction mixture is stirred further at -80°C for one hour, then allowed to warm to 0°C and evaporated. The remaining orange-red oil is dissolved in 300 ml of abs. tetrahydrofuran, cooled to -30°C with stirring and 84.9 g (0.555 mol) of methyl bromoacetate, dissolved in 150 ml of absolute tetrahydrofuran, are added in one portion, the temperature rising to 5°C . The reaction mixture is subsequently heated under reflux for 150 minutes and then evaporated. The oily crude product is partitioned between 500 ml of saturated sodium carbonate solution and 800 ml of methylene chloride. The methylene chloride phase is extracted three times with 60 ml of 0.5 N hydrochloric acid each time, dried over sodium sulphate/active carbon and cooled to 0°C . While stirring, the final product is precipitated as the hydrochloride using gaseous hydrogen chloride. The precipitate is filtered off with suction and washed twice with 100 ml of cold methylene chloride each time (75.4 g). The hydrochloride is suspended in 500 ml of ethyl acetate and extracted twice with 500 ml of ethyl acetate. The combined organic phases are dried over sodium sulphate/active carbon, filtered and evaporated. The residue (57.2 g) is recrystallized from 250 ml of ethanol, using active carbon.

Yield: 48.6 g of pale brown crystals (29 % of theory)

M.p.: $143 - 145^{\circ}\text{C}$ (diisopropyl ether)

Example 2

5-(2-Quinolinylmethoxy)-3-(1,1,1-trifluoromethylsulphamoyl)-2-thiophenecarboxylic acid

38.0 g (0.085 mol) of methyl 5-(2-quinolinylmethoxy)-3-(1,1,1-trifluoromethylsulphamoyl)-2-thiophenecarboxylate are dissolved in 350 ml of methanol and about

100 ml of 2 N sodium hydroxide solution are added. The reaction mixture is heated under reflux and with stirring for 7 hours. The reaction solution is concentrated to 20 % of its volume and diluted with 500 ml of water. The aqueous phase is extracted four times with a total of 500 ml of ether. The aqueous phase is cooled to 0°C with stirring and acidified with 0.5 N hydrochloric acid. The product precipitated in this way is filtered off with suction, digested twice with 50 ml of ice-cold ether each time and dried at 60°C/1 mbar.

Yield: 25.7 g of pale brown crystals (70 % of theory)

M.p.: 101-102°C (dec.)

Example 3

1,1,1-Trifluoro-N-[5-(2-quinolinylmethoxy)-3-thienyl]-methanesulphonamide

22.0 g (0.051 mol) of 5-(2-quinolinylmethoxy)-3-(1,1,1-trifluoromethylsulphamoyl)thiophene-2-carboxylic acid are suspended in 220 ml of water and 22 ml of conc. ammonia are added. Active carbon is added to the clear solution, and it is filtered, heated to 75°C for 15 minutes with stirring and then allowed to cool to 35°C. The solution is acidified with 2 N hydrochloric acid with vigorous stirring and immediately covered with 250 ml of ether. The aqueous phase is thoroughly stirred a further three times with 200 ml of ether each time, and the combined ether phases are dried over sodium sulphate/active carbon, filtered and evaporated. The crude product (15.8 g) is dissolved in 620 ml of diisopropyl ether at room temperature, active carbon is added, and the solution is filtered and allowed to crystallize at -20°C in a deep-freeze. The product is filtered off with suction and digested twice with a little ice-cold diisopropyl ether. The final product is dried at 60°C/1 mbar.

Yield: 10.3 g of colourless crystals (52 % of theory)

M.p.: 115.5 - 116.5°C (diisopropyl ether, dec.)

Example 4

Guinea-pigs were anaesthetized with urethane (1.4 g/kg i.p.). A cannula was tied into the trachea and connected to a pneumotachograph (Messrs. Fleisch) which

was connected to a Validyn differential pressure transducer (model DP 45-16) to measure the respiratory flow. The intrapleural pressure was measured continuously using a water-filled catheter which was tied into the intrapleural cavity and connected to a Validyn pressure transducer (model MPX-11 DP).

The data were recorded and evaluated in a Buxco Pulmonary Mechanics Analyzer (model 6) in order to obtain values for respiratory volume and resistance and compliance of the lungs.

In order to administer the substances, catheters were tied into the jugular vein and into the duodenum.

LTD₄ (leukotriene D₄, 0.6 mcg/kg i.v.) was administered 10 minutes after the intravenous administration or 20 minutes after the intraduodenal administration of the test substances. As a control, animals were used which received the solvent without substances. All animals were pretreated with indomethacin (10 mg/kg i.v.) and propranolol (0.5 mg/kg i.v.) 20 and 15 minutes before administration of the test substances. The test substances were dissolved in a mixture of DMSO and 0.15 mol/l of NaHCO₃ (1:1).

4 experiments were carried out per concentration value and the values were indicated as changes in the starting value in %. The results are presented in Table 1.

Table 1:

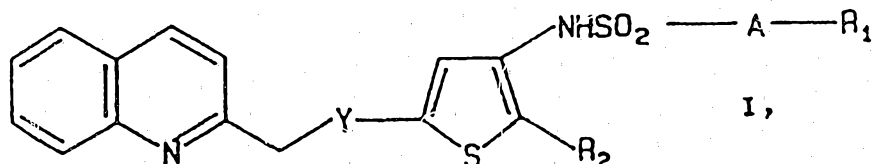
	Resistance	Compliance
Control	+ 1,018 % (± 525)	- 68 % (± 22)
30 3 mg/kg i.v.	+ 74 % (± 31)	- 23 % (± 7)
5 mg/kg i.v.	+ 27 % (± 9)	- 9 % (± 3)
1 mg/kg i.d.	+ 450 % (± 132.3)	- 43 % (± 17)
3 mg/kg i.d.	+ 172 % (± 96)	- 31 % (± 12)
10 mg/kg i.d.	+ 20 % (± 8)	- 18 % (± 9)

i.v.: intravenous

i.d.: intraduodenal

~~Patent Claims~~ The claims defining the invention are as follows:

1. Sulphamoylthiophenes of the general formula



in which

Y denotes O or S.

5 A denotes a single bond or a straight-chain or branched alkylene group having 1 - 5 carbon atoms,

R₁ denotes methyl or trifluoromethyl and

R₂ denotes hydrogen or a group COOH or COOR₃, in which

R₃ represents (C₁-C₄)-alkyl,

10 and, in the case in which R₂ denotes a group COOH, their pharmaceutically tolerable salts.

2. Compounds of the general formula I defined in Claim 1, in which A denotes a single bond and R₁ denotes trifluoromethyl.

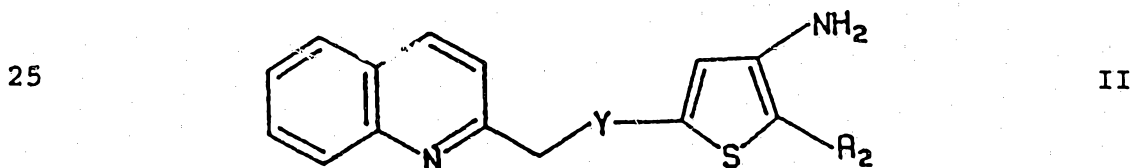
15 3. Methyl 5-(2-quinolinylmethoxy)-3-(1,1,1-trifluoromethylsulphamoyl)-2-thiophenecarboxylate.

4. 5-(2-Quinolinylmethoxy)-3-(1,1,1-trifluoromethylsulphamoyl)-2-thiophenecarboxylic acid.

20 5. 1,1,1-Trifluoro-N-[5-(2-quinolinylmethoxy)-3-thienyl]methanesulphonamide.

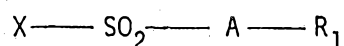
6. Process for the preparation of compounds of the general formula I according to Claim 1, characterized in that

a) a compound of the general formula



25 in which Y denotes O or S and R₂ denotes a group COOR₃, where R₃ represents (C₁-C₄)-alkyl, is reacted with a

compound of the general formula



III

5

in which A and R₁ have the above meaning and X represents chlorine or a group -O-SO₂-A-R₁, where A and R₁ have the above meaning, in an inert organic solvent,

b) if desired, an ester of the general formula I, obtained in process 10 step a), in which Y, A and R₁ have the above meaning and R₂ represents a radical COOR₃, where R₃ denotes (C₁-C₄)-alkyl, is hydrolysed to give a free acid of the general formula I in which R₂ denotes a group COOH, and, if desired, converted into a pharmaceutically tolerable salt using inorganic or organic bases and

15 c) if desired, a free acid of the general formula I, obtained in process step b), in which R₂ represents a group COOH and Y, A and R₁ have the above meaning, is decarboxylated to give a compound of the formula I in which R₂ denotes hydrogen.

7. Pharmaceutical preparations containing any one or more of compounds 20 of the general formula I according to Claim 1 or, in the case in which R₂ represents a group COOH, their pharmaceutically tolerable salts, in combination with customary pharmaceutical auxiliaries and/or excipients or diluents.

8. 5-(2-quinolinylmethoxy)- or 5-(2-quinolinylmethyl-thio)- 25 sulfamoylthiophenes substantially as hereinbefore described with reference to any one of the Examples.

9. A process for the preparation of 5-(2-quinolinylmethoxy)- or 5-(2-quinolinylmethyl-thio)-sulfamoylthiophenes substantially as hereinbefore described with reference to any one of the Examples.

30 10. A method for the treatment or prophylaxis of diseases which can be alleviated or cured by leukotriene antagonists in a patient requiring said treatment or prophylaxis, which method comprises administering to said patient an effective amount of at least one compound according to any one of claims 1 to 5 or 8, or of a preparation according to claim 7.

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DATED this THIRD day of FEBRUARY 1992

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