APPLICATION FOR A STANDARD PATENT

I/We, BYK GULDEN LOMBERG CHEMISCHE FABRIK GMBH

of Byk-Gulden-Strasse 2,
D-7750 Konstanz,
Federal Republic of Germany

hereby apply for the grant of a standard patent for an invention entitled "Substituted tricyclic thieno compounds, processes for their preparation, their use and medicament containing them."

which is described in the accompanying complete specification.

Details of basic application(s):

<table>
<thead>
<tr>
<th>Number of basic application</th>
<th>Name of Convention country in which basic application was filed</th>
<th>Date of basic application</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 581/80-0</td>
<td>Switzerland</td>
<td>May 7, 1980</td>
</tr>
<tr>
<td>652/81-0</td>
<td>Switzerland</td>
<td>February 2, 1981</td>
</tr>
</tbody>
</table>

My/our address for service is care of CLEMENT HACK & CO., Patent Attorneys, 140 William Street, Melbourne, Victoria, 3000, Australia.

DATED this 6th day of May, 1981

BYK GULDEN LOMBERG CHEMISCHE FABRIK GMBH

CLEMENT HACK & CO.

The Commissioner of Patents.

[Signature]
DECLARATION IN SUPPORT OF A CONVENTION OR NON-CONVENTION APPLICATION FOR A PATENT OR PATENT OF ADDITION

In support of the application made by Byk Gulden Lomberg Chemische Fabrik GmbH

for a patent for an invention entitled Substituted tricyclic thieno compounds, processes for their preparation, their use and medicament containing them

I/We, Dr. Günther Cordes and Dr. Herbert Suchy
c/o Byk Gulden Lomberg Chemische Fabrik GmbH
Byk-Gulden-Straße 2, D-7750 Konstanz
Federal Republic of Germany

do solemnly and sincerely declare as follows:-

1. I/We are authorised by the abovementioned applicant to make this declaration on its behalf.

2. The basic application(s) as defined by Section 141 of the Act was/were made in the following country or countries on the following date(s) by the following applicant(s) namely:-

   Country, filing date and name of Applicant(s)
   in Switzerland on 7th May, 1980
   by Byk Gulden Lomberg Chemische Fabrik GmbH
   in Switzerland on 2nd February, 1981
   by Byk Gulden Lomberg Chemische Fabrik GmbH

3. The said basic application(s) was/were the first application(s) made in a Convention country in respect of the invention the subject of the application.

4. The actual inventor(s) of the said invention is/are Dr. Volker Figala, Am Hochfürst 2, D-7753 Allensbach 4
   Dr. Richard Riedel, Selmannswellergasse 36, D-7750 Konstanz
   Dr. Georg Rainer, Josef-Anton-Feuchtmayer-Straße 7, D-7750 Konstanz
   Prof. Dr. Kurt Klemm, Im Weinberg 2, D-7753 Allensbach*

5. The facts upon which the application(s) is/are entitled to make this application are as follows:- *all Federal Republic of Germany

   All rights in connection with the invention have passed to the applicant by virtue of a claim of the applicant (=employer) according to Section 6 of the German Law relating to Inventions of Employees.

DECLARED at Konstanz this 11th day of March 1981

Byk Gulden Lomberg Chemische Fabrik GmbH

(Dr. Günther Cordes) (c/o Dr. Herbert Suchy)

This form may be completed and filed after the filing of a patent
Compounds have protective action on the digestive tract.

Claim 1. Substituted thienobenzodiazepinones of the general formula I

\[
\begin{align*}
\text{R}^1 & \text{ denotes a hydrogen atom or an alkyl radical with 1 to 4 carbon atoms,} \\
\text{R}^2 & \text{ represents a halogen atom or has one of the meanings of } \text{R}^1, \\
\text{R}^3 & \text{ denotes a halogen atom or the group } -\text{N}(\text{R}^4)\text{R}^5 \\
\text{R}^4 & \text{ denotes an alkyl radical with 1 to 4 carbon atoms or an alkenyl radical with 3 to 5 carbon atoms,} \\
\text{R}^5 & \text{ has one of the meanings of } \text{R}^4 \text{ or represents the group } -(\text{CH}_2)_m-\text{N}(\text{R}^6)\text{R}^7 \text{ or }
\end{align*}
\]

Embodiments of the medicaments are those which...
R⁴ and R⁵ together, and with the inclusion of the nitrogen atom to which they are bonded, denote a morpholino group, a pyrrolidino group, a piperidino group, a hexahydroazepin-1-yl group, a piperazin-1-yl group which is optionally sub-
SHORT TITLE: INT.

INT. CI: 701 98/81

APPLICATION NUMBER: LODGED:

COMPLETE SPECIFICATION—LOADED:

ACCEPTED:

LAPSED:

PUBLISHED:

PRIORITY:

RELATED ART:

TO BE COMPLETED BY APPLICANT

NAME OF APPLICANT: BYK GULDEN LOMBERG CHEMISCHE FABRIK GMBH

ADDRESS OF APPLICANT: Byk-Gulden-Strasse 2,
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ACTUAL INVENTOR: Volker FIGALA,
Richard RIEDEL
Georg RAINER
Kurt KLEMM

ADDRESS FOR SERVICE: CLEMENT HACK & CO.,
140 William Street,
Melbourne, Vic. 3000.
Australia.

COMPLETE SPECIFICATION FOR THE INVENTION ENTITLED:
SUBSTITUTED TRICYCLIC THIENO COMPOUNDS, PROCESSES FOR
THEIR PREPARATION, THEIR USE AND MEDICAMENTS CONTAINING
THEM.

THE FOLLOWING STATEMENT IS A FULL DESCRIPTION OF THIS INVENTION, INCLUDING THE BEST METHOD OF PERFORMING IT KNOWN TO ME:

PF/CPIF/2/80
The invention relates to substituted tricyclic thieno compounds, processes for their preparation, their use and medicaments containing them.

The compounds according to the invention are used in the pharmaceutical industry as intermediate products and for the preparation of medicaments.

Ulcer and secretion inhibiting actions are ascribed to certain dibenzodiazepinones in German unexamined Patent Specification DE-OS 1,795,176. Substituted benzodiazepinones with an antidepressant and analgesic action are known from U.S. Patent Specification US-PS 3,953,430. Substituted thienobenzodiazepines with an analgesic action are described in US-PS 4,168,269. Thienobenzodiazepinones which have new interesting pharmacological actions have now been conceived.

The invention relates to substituted thienobenzodiazepinones of the general formula I

\[
\begin{align*}
R^1 & \text{ denotes a hydrogen atom or an alkyl radical with 1 to 4 carbon atoms,} \\
R^2 & \text{ represents a halogen atom or has one of the meanings of } R^1, \\
R^3 & \text{ denotes a halogen atom or the group } -N(R^4)R^5, \\
\end{align*}
\]

\[
\text{CO-A-R}^3
\]

wherein

\[
R^1 \text{ denotes a halogen atom or the group } -N(R^4)R^5
\]
R\textsuperscript{4} denotes an alkyl radical with 1 to 4 carbon atoms or an alkenyl radical with 3 to 5 carbon atoms, R\textsuperscript{5} has one of the meanings of R\textsuperscript{4} or represents the group -(CH\textsubscript{2})\texttextsuperscript{m}-N(R\textsuperscript{6})R\textsuperscript{7}, or R\textsuperscript{4} and R\textsuperscript{5} together, and with the inclusion of the nitrogen atom to which they are bonded, denote a morpholino group, a pyrrolidino group, a piperidino group, a hexahydroazepin-1-yl group, a piperazin-1-yl group which is optionally substituted in the 4-position by a methyl, ethyl or benzyl group, a 2,4-dimethyl-piperazin-1-yl group, or a hexahydro-1H-1,4-diazepin-1-yl group which is substituted in the 4-position by a methyl or ethyl group, R\textsuperscript{6} denotes an alkyl group with 1 to 4 carbon atoms, R\textsuperscript{7} denotes an alkyl group with 1 to 4 carbon atoms, A denotes a straight-chain or branched alkylene group with 1 to 5 carbon atoms, m denotes 2 or 3, and their acid addition salts.

Alkyl radicals with 1 to 4 carbon atoms are the methyl, ethyl, propyl, isopropyl, n-butyl, isobutyl, sec.-butyl and tert.-butyl radical. Of the alkyl radicals, the methyl radical and ethyl radical are preferred in the case of R\textsuperscript{1}, R\textsuperscript{2}, R\textsuperscript{4}, R\textsuperscript{5}, R\textsuperscript{6} and R\textsuperscript{7}.

The methyl radical is particularly preferred as the alkyl radical in the case of R\textsuperscript{1} and R\textsuperscript{2}.

The allyl radical and the 2-methallyl radical may be mentioned as alkenyl radicals with 3 to 5 carbon atoms.

The process is characterised in that thieno-
Halogen atoms $R^2$ are the bromine atom and, in particu-
lar, the chlorine atom. Halogen atoms $R^3$ (Hal) are the
iodine atom, the bromine atom and, in particular, the
chlorine atom.

Alkylene groups with 1 to 5 carbon atoms are the
trimethylene, tetramethylene, pentamethylene, propylene
and ethylmethylene group, preferably the ethylene group
and in particular the methylene group.

Suitable salts include any acid addition salt. The
pharmacologically acceptable salts of the inorganic and
organic acids customarily used galenically may be mentioned
in particular. Pharmaceutically unacceptable salts are
converted into pharmacologically acceptable salts by pro-
cesses which are known to the expert. Examples of such
pharmacologically acceptable salts which may be mentioned
are water-soluble or water-insoluble acid addition salts,
such as the hydrobromide, hydriodide, nitrate, acetate,
benzoate, hibenzate [2-(4-hydroxy-benzoyl)-benzoate],
fendizoate (2-[(2'-hydroxy-4-biphenylyl)-carbonyl]-benzoate),
propionate, butyrate, sulphasalicylate, laurate, oxalate,
amsonate (4,4'-diaminostilbene-2,2'-disulphonate), embonate
[4,4'-methylene-bis-(3-hydroxy-2-naphthoate)], metembonate
[4,4'-methylene-bis-(3-methoxy-2-naphthoate)], stearate,
2-hydroxy-3-naphthoate and 3-hydroxy-2-naphthoate, and in
particular the hydrochloride, phosphate, sulphate, citrate,
gluconate, maleate, malate, fumarate, succinate, tartrate,
tosylate (p-toluenesulphonate), mesylate (methanesulphonate)

vent, if appropriate in the presence of an auxiliary base
Substituted thienobenzodiazepinones of the general formula I*

wherein

- $R^1*$ denotes a hydrogen atom or a methyl or ethyl radical,
- $R^2*$ represents a chlorine atom or has one of the meanings of $R^1*$,
- $R^3*$ denotes a chlorine atom,
- $A^*$ denotes a straight-chain or branched alkylene group with 1 or 2 carbon atoms,

form an embodiment of the invention.

Preferred representatives of embodiment I* are those in which $R^1*$ denotes a hydrogen atom or a methyl radical, $R^2*$ denotes a hydrogen atom or a methyl radical and $A^*$ denotes a methylene group.

Particularly preferred representatives of embodiment I* are those in which $R^1*$ and $R^2*$ denotes a hydrogen atom and $A^*$ denotes a methylene group.

Substituted thienobenzodiazepinones of the general formula I**

To prepare the substituted thienobenzodiazepinones
wherein

R\(^{1**}\) denotes a hydrogen atom or a methyl or ethyl radical,

R\(^{2**}\) represents a chlorine atom or has one of the meanings of R\(^{1**}\),

R\(^{3**}\) denotes the group \(-N(R^{4**})R^{5**}\),

R\(^{4**}\) denotes an alkyl radical with 1 to 4 carbon atoms or an alkenyl radical with 3 or 4 carbon atoms,

R\(^{5**}\) has the meaning of R\(^{4**}\) or represents the group \(-(CH_2)_m**-N(R^{6**})R^{7**}\), or R\(^{4**}\) and R\(^{5**}\) together, with the inclusion of the nitrogen atom to which they are bonded, denote a morpholino group, a pyrrolidino group, a piperidino group, a hexahydroazepin-1-yl group, a piperazin-1-yl group which is optionally substituted in the 4-position by a methyl, ethyl or benzyl group, a 2,4-dimethyl-piperazin-1-yl group or a hexahydro-1H-1,4-diazepin-1-yl group which is substituted in the 4-position by a methyl or ethyl group, and R\(^{6**}\) denotes a methyl or ethyl group,

R\(^{7**}\) denotes a methyl or ethyl group,

and 80 hours, depending on the amount and nature of the...
m** denotes 2 or 3 and
A** denotes a straight-chain or branched alkylene
group with 1 or 2 carbon atoms,

and their acid addition salts form a further embodiment
of the invention.

A group of representatives of embodiment I** are
those in which R** denotes a hydrogen atom or a methyl
or ethyl radical, R** represents a chlorine atom or has
one of the meanings of R'; R** denotes a methyl or
ethyl radical and R** has the meaning of R** or repre-
sents the group -(CH_{2})_{m**}-N(R^{6**})R^{7**}, or R** and R**
together, with the inclusion of the nitrogen atom, denote
a pyrrolidino, piperidino or hexahydroazepin-1-yl radi-
cal, R^{6**} and R^{7**} denote a methyl or ethyl radical, m**
denotes 2 and A** denotes a methylene group, and their
pharmacologically acceptable acid addition salts.

Another group of representatives of embodiment I**
are those in which R** denotes a hydrogen atom or a
methyl or ethyl radical, R** represents a chlorine atom
or has one of the meanings of R**; R** and R** together,
with the inclusion of the nitrogen atom, denote a pipera-
zin-1-yl which is substituted in the 4-position by a methyl,
ethyl or benzyl group, a 2,4-dimethylpipazin-1-yl group
or a hexahydro-1H-1,4-diazepin-1-yl group which is substi-
tuted in the 4-position by a methyl or ethyl group and A**
denotes a methylene group, and their pharmacologically
acceptable acid addition salts.

acid anhydrides, such as are formed from salts of the
Preferred representatives of embodiment I** are those in which $R^1$ denotes a hydrogen atom or a methyl radical, $R^2$ denotes a hydrogen atom or a methyl radical, $R^3$ and $R^4$ together, with inclusion of the nitrogen atom, denote a piperazin-1-yl group which is substituted in the 4-position by a methyl group and $A^*$ denotes a methylene group, and their pharmacologically acceptable acid addition salts.

Examples which may be mentioned of representatives of the compounds according to the invention are:

9,10-dihydro-4-[(2-di-n-propylamino)-propionyl]-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, 4-[4-(di-n-butylamino)-butyryl]-9,10-dihydro-4H-thieno[3,4-b][1,5]-benzodiazepin-10-one, 4-[2-(diethylamino)-propionyl]-9,10-dihydro-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, 4-[5-(diisopropylamino)-valeryl]-9,10-dihydro-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, 4-[diisobutylaminoacetil]-9,10-dihydro-3-methyl-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, 4-[N-n-butyl-tert-butylaminoacetil]-9,10-dihydro-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, 4-[4-(diallylamino)-butyryl]-9,10-dihydro-1,3-dimethyl-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, 4-[di-sec.-butylaminoacetil]-9,10-dihydro-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, 4-[2-(N-ethyl-n-butyramino)-propionyl]-9,10-dihydro-4H-thieno[3,4-b][1,5]-benzodiazepin-10-one, 9,10-dihydro-3-methyl-4-[N-methyl-sec.-butylaminoacetil]-4H-thieno[3,4-b][1,5]benzodia-
9,10-dihydro-4-[5-(N-methyl-tert.-butylamino)-valeryl]-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, 9,10-dihydro-4-[2-piperidinopropionyl]-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, 4-[4-(hexahydroazepin-1-yl)-butyryl]-9,10-dihydro-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, 4-[3-(di-n-butylamino)-propionyl]-9,10-dihydro-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, 4-[3-(diallylamino)-propionyl]-9,10-dihydro-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, 4-[3-(di-sec.-butylamino)-propionyl]-9,10-dihydro-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, 4-[3-(N-ethyl-n-butylamino)-propionyl]-9,10-dihydro-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, 9,10-dihydro-4-[3-(N-methyl-sec.-butylamino)-propionyl]-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, 9,10-dihydro-4-[3-piperidinopropionyl]-4H-thieno[3,4-b][1,5]benzodiazepin-10-one and preferably 9,10-dihydro-4-[(4-methylpiperazin-1-yl)-acetyl]-4H-thieno[3,4-b][1,5]benzodiazepin-10-one and their pharmacologically acceptable acid addition salts.
The substituted thieno-benzodiazepinones of the general formula I and their acid addition salts and embodiments I* and I** have valuable properties which render them commercially useful. The substituted thieno-benzodiazepinones of the general formula I in which $R_3$ denotes the group $\text{-N}(R_4)R_5$ and $R_4$ and $R_5$ have the abovementioned meanings, and those of embodiment I** are characterised by an excellent protective action on the stomach and intestines of warm-blooded animals, for example they inhibit the development of gastric ulcers. Furthermore, as a result of their low toxicity and the absence of substantial side effects, they have an advantageous therapeutic range. The substituted thieno-benzodiazepinones of the general formula I in which $R_3$ denotes a halogen atom (Hal) and Hal has the abovementioned meaning, and those of embodiment I* are valuable intermediate products in the preparation of the pharmacologically active and therapeutically useful compounds according to the invention.

The excellent activity of the pharmacologically active substitute, thieno-benzodiazepinones and their pharmacologically, that is to say biologically, acceptable acid addition salts enables them to be employed in human medicine and also in veterinary medicine, where they are used for the treatment and prophylaxis of illnesses based on disorders in the stomach or intestine.

The salts are isolated by filtration, precipitation with
For example, acute and chronic ulcus ventriculi and ulcus duodeni, gastritis or hyperacid gastric irritation in humans or animals are treated.

The compounds according to the invention thus are used in the treatment of mammals suffering from one of the abovementioned illnesses. In that treatment a therapeutically effective and pharmacologically acceptable amount of one or more compounds of the general formulae I or I**, preferred representatives thereof and/or salts thereof is administered to the sick mammal.

The invention also relates to the compounds according to the invention for use in combating the abovementioned illnesses. The invention furthermore comprises the use of compounds according to the invention in the preparation of medicaments which are employed for combating the illnesses mentioned.

The invention also relates to medicaments which contain one or more thieno-benzodiazepinones of the general formula Ia

![Diagram](image)

Phenylenediamine (VI) is reacted with the tetra-
wherein

$R^1$ denotes a hydrogen atom or an alkyl radical with 1 to 4 carbon atoms,

$R^2$ represents a halogen atom or has one of the meanings of $R^1$,

$R^{3a}$ denotes the group $-N(R^4)R^5$,

$R^4$ denotes an alkyl radical with 1 to 4 carbon atoms or an alkenyl radical with 3 to 5 carbon atoms,

$R^5$ has one of the meanings of $R^4$ or represents the group $-(CH_2)_m-N(R^6)R^7$, or $R^5$ and $R^6$ together, and with the inclusion of the nitrogen atom to which they are bonded, denote a morpholino group, a pyrrolidino group, a piperidino group, a hexahydroazepin-1-yl group, a piperazin-1-yl group which is optionally substituted in the 4-position by a methyl, ethyl or benzyl group, a 2,4-dimethylpiperazin-1-yl group, or a hexahydro-1H-1,4-diazepin-1-yl group which is substituted in the 4-position by a methyl or ethyl group,

$R^6$ denotes an alkyl group with 1 to 4 carbon atoms,

$R^7$ denotes an alkyl group with 1 to 4 carbon atoms,

$A$ denotes a straight-chain or branched alkylene group with 1 to 5 carbon atoms and

$m$ denotes 2 or 3,

and/or their pharmacologically acceptable acid addition salts.
Embodiments of the medicaments are those which contain thieno-benzodiazepinones of the formula I** or their preferred representatives and/or their pharmaceutically acceptable acid addition salts.

The medicaments are prepared by processes which are in themselves known. As medicaments, the compounds according to the invention are employed either on their own or, preferably, in combination with suitable pharmaceutical excipients. If the new pharmaceutical formulations contain pharmaceutical excipients in addition to the compounds according to the invention, the content of active compound in these mixtures is 0.5 to 95, preferably 15 to 75, per cent by weight of the total mixture.

The medicaments are formulated, for example, for oral, rectal or parenteral (intravenous, intramuscular, subcutaneous) administration in suitable doses, e.g. in the form of a tablet, a dragee, a capsule, a suppository or a measured volume of a powder, of a granular material, of a solution, of an emulsion or of a suspension.

In general, the daily dose of active compound or compounds, when given orally, is between 0.01 and 5, preferably 0.05 and 2.5 and in particular 0.1 and 1.5, mg/kg of body weight, if appropriate in the form of several, preferably 1 to 3, individual administrations, in order to achieve the desired results.
The pharmaceutical formulations preferably consist of the active compounds according to the invention and non-toxic, pharmaceutically acceptable medicinal excipients, which are used as an admixture or diluent in solid, semi-solid or liquid form, or as a means of encasing, for example in the form of a capsule, a tablet coating, a sachet or some other container for the therapeutically active ingredient. An excipient can, for example, serve as a promoter of the resorption of the medicament by the body, as a formulating auxiliary, as a sweetener, as a flavour correctant, as a colourant or as a preservative.

If the substituted thienobenzodiazepinones according to the invention and/or their pharmacologically acceptable acid addition salts are to be employed for treatment of the illnesses mentioned, the pharmaceutical formulations can also contain one or more pharmacologically active ingredients from other groups of medicaments, such as antacids, for example aluminium hydroxide and magnesium aluminate; secretion inhibitors, such as H₂-blockers, for example cimetidine; gastric and intestinal therapeutics, for example metoclopramide, bromopride and tiapride; tranquillisers, such as benzodiazepines, for example diazepam; spasmolytic agents, for example bietamiverine and camylofin; anticholinergic
agents, for example oxyphencyclimine and phencarbamide; glucocorticoids, such as prednisolone, flucortolone and betamethasone; non-steroidal antiphlogistic agents, such as arylacetic acids and arylpropionic acids and hetero-arylacetic acids and hetero-arylpropionic acids, benzothiazinecarboxamide dioxides, pyrazolidinediones and quinazolinones, for example ibuprofen, naproxen, diclofenac, fenbufen, indomethacin, lonazolac, sudoxicam, piroxicam, phenylbutazone, bumadizone calcium and proquazone; and local anaesthetics, for example tetra- caine and procaine; and if appropriate also enzymes, vitamins and aminoacids.

The invention furthermore relates to a process for the preparation of the substituted thienobenzodiazepinones of the general formula

\[
\begin{align*}
\text{H} & \text{N} \\
\text{S} & \text{(I ),}
\end{align*}
\]

wherein

1. \( R^1 \) denotes a hydrogen atom or an alkyl radical with 1 to 4 carbon atoms,
2. \( R^2 \) represents a halogen atom or has one of the meanings of \( R^1 \),
R² represents a halogen atom or has one of the meanings of R¹,
R³ denotes a halogen atom or the group -N(R⁴)R⁵,

R³ denotes a halogen atom or the group -N(R⁴)R⁵
and
R⁴ denotes an alkyl radical with 1 to 4 carbon atoms or an alkenyl radical with 3 to 5 carbon atoms and
R⁵ has one of the meanings of R⁴ or represents the group -(CH₂)m-N(R⁶)R⁷, or R⁴ and R⁵ together, and with the inclusion of the nitrogen atom to which they are bonded, denote a morpholino group, a pyrrolidino group, a piperidino group, a hexahydroazepin-1-yl group, a piperazin-1-yl group which is optionally substituted in the 4-position by a methyl or ethyl group or by a benzyl group, a 2,4-dimethylpiperazin-1-yl group, or a hexahydro-1H,4-diazepin-1-yl group which is substituted in the 4-position by a methyl or ethyl group, and R⁶ denotes an alkyl group with 1 to 4 carbon atoms,
R⁷ denotes an alkyl group with 1 to 4 carbon atoms,
A denotes a straight-chain or branched alkylene group with 1 to 5 carbon atoms and m denotes 2 or 3,
and their acid addition salts.
alkyl radical in the case of $R^1$ and $R^2$.

The allyl radical and the 2-methallyl radical may be mentioned as alkenyl radicals with 3 to 5 carbon atoms.

The process is characterised in that thienobenzodiazepinones of the general formula II

$$
\begin{array}{c}
\text{R}^1 \\
\text{H} \\
\text{S} \\
\text{R}^2 \\
\text{H} \\
\text{N} \\
\text{O}
\end{array}
$$

wherein

$R^1$ and $R^2$ have the abovementioned meaning, are acylated and, if appropriate, are then aminated, and/or resulting bases are converted into the acid addition salts, or resulting acid addition salts are converted into the free base or into pharmacologically acceptable acid addition salts.

The acylation and the subsequent optional amination are carried out by methods which are known per se.

To prepare the thienobenzodiazepinones of the general formula I in which $R^3$ denotes Hal, the starting compounds of the formula II wherein $R^1$ and $R^2$ have the abovementioned meanings, or their acid addition salts, are reacted with compounds of the general formulae III: Hal-A-CO-Hal' (III) or IV: [Hal-A-CO]$_2$0 (IV), wherein Hal and Hal' denote a halogen atom and A denotes an alkylene group with 1 to 5 carbon atoms. This acylation is carried out without a solvent or, preferably, in an inert solvent at room temperature or elevated temperature, the maximum temperature being the boiling point of the sol-
vent, if appropriate in the presence of an auxiliary base and/or an acylation catalyst. The acid halides III are preferable to the acid anhydrides IV. Chloroacetyl chloride is the preferred acid halide III and chloroacetic anhydride is the preferred acid anhydride IV. Examples of solvents which may be mentioned are aromatic hydrocarbons, such as toluene, xylene or chlorobenzene; open-chain or cyclic ethers, such as diisopropyl ether or dioxane; chlorinated hydrocarbons, such as dichloroethane, and other solvents, such as pyridine, acetonitrile or dimethylformamide. Auxiliary bases which may be mentioned are, for example, tertiary organic bases, such as triethylamine and ethyl diisopropylamine, or pyridine; or inorganic bases, such as anhydrous alkali metal carbonates or bicarbonates or alkaline earth metal carbonates or bicarbonates or alkaline earth metal oxides. Examples of possible acylation catalysts are imidazole, pyridine or 4-dimethylaminopyridine.

The process for the preparation of the intermediate products of the general formula I is thus characterised in that a thienobenzodiazepinone of the general formula II is acylated with compounds of the general formulae III or IV. Appropriate starting substances are employed for the preparation of the intermediate products of the general formula I*.
To prepare the substituted thienobenzodiazepinones of the general formula I in which \( R^1, R^2 \) and \( A \) have the abovementioned meaning and \( R^3 \) denotes a group \(-N(R^4)R^5\), the resulting reaction product of the formula I wherein \( R^3 \) denotes \( \text{Hal} \) is reacted with secondary amines of the general formula \( \text{V}: \text{HN}(R^4)R^5 \) (V), wherein \( R^4, R^5 \) and \( \text{Hal} \) have the above meaning.

The amination is carried out in an inert solvent at temperatures between \( 0^\circ \) and the boiling point of the solvent, either with at least 2 mols of secondary amine \( \text{V} \) or with 1 to 2 mols of secondary amine \( \text{V} \) and an auxiliary base. Examples of possible solvents are chlorinated hydrocarbons, such as methylene chloride, chloroform or dichloroethane; open-chain or cyclic ethers, such as diethyl ether, tetrahydrofuran or dioxane; aromatic hydrocarbons, such as benzene, toluene, xylene, chlorobenzene or pyridine; alcohols, such as ethanol or isopropanol; ketones, such as acetone; acetonitrile or dimethylformamide. Examples of auxiliary bases which may be mentioned are tertiary organic bases, such as triethylamine, \( N \)-methylpiperidine, diethylaniline or pyridine, or inorganic bases, such as alkali metal carbonates or bicarbonates or alkaline earth metal carbonates or bicarbonates or alkaline earth metal hydroxides or oxides. If appropriate, the reaction can be accelerated by adding alkali metal iodides. The reaction times are between 15 minutes
and 80 hours, depending on the amount and nature of the amine V employed. When starting compounds in which A represents an alkylene group with 2 to 5 carbon atoms are reacted, the reaction can also proceed with H-Hal being split off; the intermediately formed alkenyl compound, which can optionally be isolated, reacts with the secondary amine V to give the same end product.

To prepare the substituted thienobenzodiazepinones of the general formula I in which \( R^1, R^2 \) and \( A \) have the abovementioned meaning and \( R^3 \) denotes a group \( -N(R^4)R^5 \), thienobenzodiazepinones of the general formula II are acylated alternatively with compounds of the general formula IX

\[
Z - CO - A - N(R^4)R^5 \quad (IX),
\]

wherein

\( A, R^4 \) und \( R^5 \) have the abovementioned meaning and

\( Z \) denotes a leaving group,

and, if desired, the products are then converted into the acid addition salts.

The reaction of compounds II with the acid derivatives IX is carried out in a manner which is known per se. The leaving group \( Z \) is a group which, together with the carbonyl group to which it is bonded, forms a reactive carboxylic acid derivative. Examples of reactive carboxylic acid derivatives which may be mentioned are acid halides, esters and anhydrides and mixed
denotes a methylene group, and their pharmacologically acceptable acid addition salts.

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acid anhydrides, such as are formed from salts of the corresponding acid (Z = OH) and acid chlorides, such as phosphorus oxychloride, or chloroformates. The reaction is preferably carried out with the mixed anhydrides of IX and strong mineral acids, in particular chlorophosphoric acid. Where relevant, the reaction is carried out in the presence of an acid-binding agent (proton acceptor). Examples of suitable proton acceptors which may be mentioned are alkali metal carbonates or bicarbonates, such as sodium carbonate or potassium bicarbonate; tertiary organic amines, such as pyridine, triethylamine or ethyldiisopropylamine; or sodium hydride. The reaction is carried out at temperatures between \(-25^\circ\) and \(50^\circ\), in an inert solvent, preferably in dimethylformamide.

To prepare the substituted thienobenzodiazepinones of the general formula I, wherein \(R^1\), \(R^2\) and A have the above-mentioned meaning and \(R^3\) denotes a group \(-N(R^4)R^5\) in which \(R^4\) and \(R^5\), including the nitrogen atom to which they are bonded, denote a piperazin-1-yl group which is substituted in the 4-position by a methyl or ethyl group, or a hexahydro-1H-1,4-diazepin-1-yl group which is substituted in the 4-position by a methyl or ethyl group, obtained piperazinylthienobenzodiazepinones of the general formula X.
9,10-dihydro-3-methyl-4-[N-methyl-sec.-butylaminoacetyl]-4H-thieno[3,4-b]1,5]benzodia-

\[
\begin{align*}
\text{H} & \quad \text{R}^1 \\
\text{O} & \quad \text{CO-A-N} \\
\text{N} & \quad \text{NH} \\
\text{S} & \quad \text{R}^2 \\
\end{align*}
\]

(X),

wherein \( R^1 \), \( R^2 \) and \( A \) have the abovementioned meaning and \( n \) denotes 2 or 3, are alternatively methylated or ethylated.

The methylation or ethylation are carried out in a manner which is known per se. Examples of methylation or ethylation agents which may be mentioned are: methyl and ethyl esters of strong acids, such as sulphuric acid, phosphoric acid or p-toluenesulphonic acid, or methyl or ethyl halides, which are reacted in a hydrous or a nonhydrous medium at temperatures between 0°C and 50°C optionally in the presence of an acid-binding agent (proton acceptor), as described e.g. in Houben-Weyl Volume XI/1 pages 24 ff. and 205 ff., Georg Thieme-Verlag, Stuttgart (1957); mixtures of formaldehyde or acetaldehyde with a reducing agent (method of reductive alkylation), examples of reducing agents which may be mentioned are hydrogen in statu nascendi (e.g. from zinc and hydrochloric acid), hydrogen in the presence of a hydrogenation catalyst, such as platinum or Raney nickel, formic acid or complex metal hydrides, such as sodium borohydride or sodium cyanoborohydride. Methods of reduction alkylation are described, for example, in
and their pharmacologically acceptable acid addition salts.


The process for the preparation of the pharmacologically active thienobenzodiazepinones of the general formula I is thus characterised in that compounds of the formula I wherein $R^3$ denotes Hal are reacted with compounds of the general formula V or that thienobenzodiazepinones of the general formula II are acylated with acid derivatives IX or that compounds X are methylated or ethylated and, if appropriate, the resulting base is then converted into a pharmacologically acceptable acid addition salt, or a resulting acid addition salt is converted into the free base or into a pharmacologically acceptable acid addition salt.

Acid addition salts are obtained by dissolving the resulting free base in a suitable solvent, for example water, acetone, an alkanol, such as ethanol or isopropanol, or an open-chain or cyclic ether, such as diethyl ether or tetrahydrofuran, which contains the desired acid or to which the desired acid is then added.
The salts are isolated by filtration, precipitation with a non-solvent for the acid addition salt or by evaporation of the solvent. Salts can also be converted into other salts, for example pharmacologically acceptable acid addition salts, by converting them into the base and then reacting the base further with another acid.

Resulting salts can be converted into the free base, for example by alkalisation with aqueous sodium hydroxide or potassium hydroxide, and the free base is then isolated by suitable measures, for example solvent extraction with a water-immiscible solvent, such as chloroform, diethyl ether or toluene.

The preparation of the starting compounds of the general formula II is carried out according to or analogously to the preparation in US-PS 3,953,430, in accordance with the following reaction scheme:

\[
\begin{align*}
\text{VI} & \quad \text{VII} \\
& \quad \text{VIII}
\end{align*}
\]
Phenylenediamine (VI) is reacted with the tetrahydrothiophenecarboxylic acid derivatives VII, in which $R^1$ has the abovementioned meaning, $R^{2a}$ denotes a hydrogen atom or an alkyl group with 1 to 4 carbon atoms and $R^8$ denotes a hydrogen atom or an alkyl group with 1 to 5 carbon atoms, in inert solvents, for example toluene, whilst heating, to form the tetrahydrothienobenzodiazepinones VIII. The compounds VIII are dehydrogenated with a suitable dehydrogenating agent, for example N-bromosuccinimide in dimethylformamide, to give the dihydrothienobenzodiazepinones IIa. The representatives IIa, in which $R^{2a}$ denotes a hydrogen atom, are converted into the halogen derivatives IIb, in which $R^{2b}$ denotes a chlorine or bromine atom, by chlorination or bromination with suitable halogenating agents.

The compounds IX are known or are prepared, optionally in situ, according to known processes. The piperazinothienobenzodiazepinones X are prepared by reacting compounds of formula I, wherein $R^3$ denotes -Hal, with appropriate amines V, i.e. piperazine or homopiperazine, according to the procedure described above for the amination.

Appropriate starting compounds II*, III* and IV*, respectively,
m denotes 2 or 3,
and/or their pharmacologically acceptable acid addition salts.

\[ \text{Hal}^* - A^* - \text{CO} - \text{Hal}'^* \quad (\text{III}^*) \]
\[ (\text{II}^*) \quad [\text{Hal}^* - A^* - \text{CO}]_2 \text{O} \quad (\text{IV}^*) \]

wherein

- \( R_1^* \) denotes a hydrogen atom or a methyl or ethyl radical,
- \( R_2^* \) represents a chlorine atom or has one of the meanings of \( R_1^* \),
- \( \text{Hal}^* \) and \( \text{Hal}'^* \) denote a chlorine atom and
- \( A^* \) denotes a straight-chain or branched alkylene group with 1 or 2 carbon atoms,

and \( \text{II}^{**} \), \( \text{III}^{**} \), \( \text{IV}^{**} \), \( \text{V}^{**} \), \( \text{IX}^{**} \) and \( \text{X}^{**} \), respectively,

\[ \text{Hal}^{***} - A^{***} - \text{CO} - \text{Hal}'^{***} \quad (\text{III}^{***}) \]
\[ (\text{II}^{***}) \quad [\text{Hal}^{***} - A^{***} - \text{CO}]_2 \text{O} \quad (\text{IV}^{***}) \]

\[ \text{HN}(R_4^{***})S^{**} \quad (\text{V}^{**}) \quad Z^{**} - \text{CO} - A^{**} - N(R_4^{***})S^{**} \quad (\text{IX}^{**}) \]

\[ \text{CO} - A^{**} - N(\text{CH}_2)_n \quad (\text{X}^{**}) \]
wherein

\( R^1 \) denotes a hydrogen atom or a methyl or ethyl radical,
\( R^2 \) represents a chlorine atom or has one of the meanings of \( R^1 \),
\( \text{Hal}^2 \) and \( \text{Hal}^4 \) denote a chlorine atom,
\( R^4 \) denotes an alkyl radical with 1 to 4 carbon atoms or an alkenyl radical with 3 or 4 carbon atoms,
\( R^5 \) has the meaning of \( R^4 \) or represents the group \(-(CH_2)_m-N(R^6)^7\) or \( R^4 \) and \( R^5 \) together, with the inclusion of the nitrogen atom to which they are bonded, denote a morpholino group, a pyrrolidino group, a piperidino group, a hexahydroazepin-1-yl group, a piperazin-1-yl group which is optionally substituted in the 4-position by a methyl, ethyl or benzyl group, a 2,4-dimethyl-piperazin-1-yl group or a hexahydro-1H-1,4-diazepin-1-yl group which is substituted in the 4-position by a methyl or ethyl group,
\( R^6 \) denotes a methyl or ethyl group,
\( R^7 \) denotes a methyl or ethyl group,
\( m \) denotes 2 or 3,
\( n \) denotes 2 or 3,
\( A \) denotes a straight-chain or branched alkylene group with 1 or 2 carbon atoms,
\( Z \) denotes a leaving group,

are employed for the preparation of the compounds \( I^* \) and \( I^{**} \).
The following examples serve to illustrate the invention in more detail. "m." denotes "melting point".

**Example 1**

3.5 g of 4-chloroacetyl-9,10-dihydro-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, 8.1 g of N-methylpiperazine and 50 ml of toluene are stirred at 80°C for 2 hours. 60 ml of dilute sodium hydroxide solution are added, the layers are separated and the aqueous phase is extracted again several times by shaking with toluene and concentrated to dryness in vacuo. The residue is made to crystallise with a little acetone. 4.2 g of 9,10-dihydro-4-[(4-methyl-piperazin-1-yl)acetyl]-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, m. 177-178°C (acetone), are obtained.

9,10-Dihydro-3-methyl-4-[(4-methyl-piperazin-1-yl)acetyl]-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, m. 263-264°C (ethanol), 3-chloro-9,10-dihydro-4-[(4-methyl-piperazin-1-yl)acetyl]-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, m. 239°C, and 9,10-dihydro-1,3-dimethyl-4-[(4-methyl-piperazin-1-yl)-acetyl]-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, m. 204-205°C, are obtained analogously by reaction of 4-chloroacetyl-9,10-dihydro-3-methyl-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, 3-chloro-4-chloroacetyl-9,10-dihydro-4H-thieno[3,4-b][1,5]benzodiazepin-10-one or 4-chloroacetyl-9,10-dihydro-1,3-dimethyl-4H-thieno[3,4-b][1,5]benzodiazepin-10-one with N-methylpiperazine.
Example 2

14.9 g of 4-chloroacetyl-9,10-dihydro-4H-thieno-3,4-b][1,5]benzodiazepin-10-one, 21 g of N-methylpiperazine and 70 ml of dioxane are stirred at 80°C for 1 hour and the solution is concentrated to dryness in vacuo. 150 ml of isopropanol and 40 ml of water are added to the residue, 25 ml of concentrated hydrochloric acid are added dropwise, the mixture is cooled in an ice-bath and 9,10-dihydro-4-[(4-methylpiperazin-1-yl)-acetyl]-4H-thieno[3,4-b][1,5]benzodiazepin-10-one dihydrochloride is obtained as a mixture with N-methylpiperazine hydrochloride. The hydrochlorides are dissolved in water and chloroform, the pH is adjusted to 8.2 with 2N sodium hydroxide solution, the aqueous phase is extracted exhaustively by shaking with chloroform and the organic solution is dried and concentrated to dryness in vacuo. 16 g of 9,10-dihydro-4-[(4-methyl-piperazin-1-yl)acetyl]-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, m. 177-179°C (from acetone), are obtained.

9,10-Dihydro-4-(morpholinoacetyl)-4H-thieno[3,4-b]-1,5]benzodiazepin-10-one, 4-[(4-benzylpiperazin-1-yl)-acetyl]-9,10-dihydro-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, 4-[(4-ethylpiperazin-1-yl)-acetyl]-9,10-dihydro-4H-thieno[3,4-b][1,5]benzodiazepin-10-one and 4-[(2,4-dimethyl-piperazin-1-yl)acetyl]-9,10-dihydro-4H-thieno-
[3,4-b][1,5]benzodiazepin-10-one are obtained analogously by reaction of 4-chloroacetyl-9,10-dihydro-4H-thieno-[3,4-b][1,5]benzodiazepin-10-one with morpholine, N-benzylpiperazine, N-ethylpiperazine and 1,3-dimethylpiperazine respectively.

**Example 3**

1.9 g of 4-chloroacetyl-9,10-dihydro-4H-thieno-[3,4-b][1,5]benzodiazepin-10-one, 0.55 g of pyrrolidine, 0.85 g of ground sodium carbonate and 15 ml of absolute ethanol are heated at the boil for 2 hours and the hot solution is filtered and concentrated in vacuo. The residue is dissolved in methylene chloride, the organic solution is washed at pH 7 with water and concentrated and 1.4 g of 9,10-dihydro-4-(pyrrolidinoacetyl)-4H-thieno[3,4-b][1,5]benzodiazepin-10-one are obtained.

**Example 4**

1.9 g of 4-chloroacetyl-9,10-dihydro-4H-thieno-[3,4-b][1,5]benzodiazepin-10-one, 3.7 g of piperidine and 15 ml of dioxane are stirred at 80°C for 1 hour, the mixture is concentrated in vacuo and the residue is recrystallised from isopropanol/water. 2.0 g of 9,10-dihydro-4-(piperidinoacetyl)-4H-thieno[3,4-b][1,5]benzodiazepin-10-one are obtained. 9,10-Dihydro-3-methyl-4-(piperazin-1-yl-acetyl)-4H-thieno[3,4-b][1,5]benzodiazepin-10-one (m. 225-228°C, dec.), 9,10-dihydro-1,3-dimethyl, 4-(morpholin-4-yl-acetyl)-4H-thieno[3,4-b][1,5]benzodiazepin-10-one (m. 188-190°C) and 9,10-dihydro-1,3-dimethyl-4-
(piperidin-1-yl-acetyl)-4H-thieno[3,4-b][1,5]benzodiazepin-10-one (m. 162-164°C) are obtained analogously by reaction of 4-chloroacetyl-9,10-dihydro-3-methyl-4H-thieno[3,4-b]-[1,5]benzodiazepin-10-one with piperazine, of 4-chloroacetyl-9,10-dihydro-1,3-dimethyl-4H-thieno[3,4-b][1,5]-benzodiazepin-10-one with morpholine and of 4-chloroacetyl-9,10-dihydro-1,3-dimethyl-4H-thieno[3,4-b][1,5]benzodiazepin-10-one with piperidine.

**Example 5**

2.0 g of 4-chloroacetyl-9,10-dihydro-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, 6 ml of 40% strength aqueous dimethylamine solution and 10 ml of methylene chloride are stirred at 35°C for 2 hours, 0.35 g of sodium carbonate are added and the mixture is concentrated to dryness in vacuo. A little water is added, the solution is extracted repeatedly by shaking with chloroform and the organic solution is dried with sodium sulphate and concentrated to dryness. 1.9 g of 4-(dimethylaminoacetyl)-9,10-dihydro-4H-thieno[3,4-b][1,5]-benzodiazepin-10-one are obtained. 4-(Diethylaminoacetyl)-9,10-dihydro-3-methyl-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, m. 196-197°C (toluene), and 4-(diethylaminoacetyl)-9,10-dihydro-1,3-dimethyl-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, m. 186-187°C (toluene) are obtained analogously by reaction of 4-chloroacetyl-9,10-dihydro-3-methyl-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, and 4-chloroacetyl-9,10-dihydro-1,3-dimethyl-4H-thieno-
[3,4-b][1,5]benzodiazepin-10-one, respectively, with diethylamine.

**Example 6**

9,10-Dihydro-3-methyl-4- (pyrrolidinoacetyl)-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, 3-chloro-9,10-dihydro-4- (pyrrolidinoacetyl)-4H-thieno[3,4-b][1,5]benzodiazepin-10-one and 9,10-dihydro-1,3-dimethyl-4- (pyrrolidinoacetyl)-4H-thieno[3,4-b][1,5]benzodiazepin-10-one are obtained analogously to Example 4 by reaction of 4-chloroacetyl-9,10-dihydro-3-methyl-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, 3-chloro-4-chloroacetyl-9,10-dihydro-4H-thieno[3,4-b][1,5]benzodiazepin-10-one and, respectively, 4-chloroacetyl-9,10-dihydro-1,3-dimethyl-4H-thieno[3,4-b][1,5]benzodiazepin-10-one with pyrrolidine.

**Example 7**

4-(Dimethylaminoacetyl)-9,10-dihydro-3-methyl-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, 3-chloro-4-(dimethylaminoacetyl)-9,10-dihydro-4H-thieno[3,4-b][1,5]benzodiazepin-10-one and 4-(dimethylaminoacetyl)-9,10-dihydro-1,3-dimethyl-4H-thieno[3,4-b][1,5]benzodiazepin-10-one are obtained analogously to Example 5 by reaction of 4-chloroacetyl-9,10-dihydro-3-methyl-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, 3-chloro-4-chloroacetyl-9,10-dihydro-4H-thieno[3,4-b][1,5]benzodiazepin-10-one and, respectively, 4-chloroacetyl-9,10-dihydro-1,3-dimethyl-4H-thieno[3,4-b][1,5]benzodiazepin-10-one with dimethylamine.
Example 8

8 g of 9,10-dihydro-3-methyl-4H-thieno[3,4-b][1,5]-benzodiazepin-10-one and 5.6 ml of chloroacetyl chloride in 160 ml of dioxane are boiled under reflux in the presence of 8 g of ground potassium carbonate for 8 hours. The solution is concentrated to dryness, the residue is taken up in toluene, the toluene mixture is washed with sodium bicarbonate solution and then with water and the toluene solution is dried over sodium sulphate. Concentration of the solution gives 4-chloroacetyl-9,10-dihydro-3-methyl-4H-thieno[3,4-b][1,5]-benzodiazepin-10-one, m. 156-158°C.

3-Chloro-4-chloroacetyl-9,10-dihydro-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, m. 214-216°C, and 4-chloroacetyl-9,10-dihydro-1,3-dimethyl-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, m. 192-195°C, are obtained analogously by reaction of 3-chloro-9,10-dihydro-4H-thieno[3,4-b][1,5]benzodiazepin-10-one and, respectively, 9,10-dihydro-1,3-dimethyl-4H-thieno[3,4-b]-[1,5]benzodiazepin-10-one with chloroacetyl chloride.

Example 9

10.4 ml of chloroacetyl chloride are added dropwise at room temperature to a suspension of 18.8 g of 9,10-dihydro-4H-thieno[3,4-b][1,5]benzodiazepin-10-one in 500 ml of dioxane, whereupon a clear solution is formed. The solution is left to stand for 3 hours and is concentrated
to dryness, the residue is taken up in toluene, the toluene mixture is washed with sodium bicarbonate solution and then with water and the toluene solution is dried over sodium sulphate. Concentration of the solution gives 4-chloroacetyl-9,10-dihydro-4H-thieno[3,4-b][1,5]benzodiazepin-10-one in the form of an oil, which crystallizes slowly, m. 220°C.

4-Chloroacetyl-9,10-dihydro-1-methyl-4H-thieno[3,4-b]-[1,5]benzodiazepin-10-one and 4-chloroacetyl-9,10-dihydro-3-methyl-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, m. 156-158°C, are obtained analogously by reaction of 9,10-dihydro-1-methyl-4H-thieno[3,4-b][1,5]benzodiazepin-10-one and 9,10-dihydro-3-methyl-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, respectively, with chloroacetyl chloride.

Example 10

2.2 g of chloroacetyl chloride and 2 ml of triethylamine are simultaneously added dropwise to a boiling solution of 2.2 g of 9,10-dihydro-4H-thieno[3,4-b][1,5]benzodiazepin-10-one in 30 ml of absolute dioxane in the course of 40 minutes and the mixture is stirred for a further 3 hours. It is allowed to cool and is filtered, the filtrate is concentrated to dryness, the residue is chromatographed over a silica gel column by means of a mixture of petroleum ether/ethyl acetate (1:1) and the product is recrystallised from toluene to give 2.0 g of 4-chloroacetyl-9,10-dihydro-4H-thieno[3,4-b][1,5]benzodiazepin-10-one as an oil, which crystallizes.
Example 11

5 ml of sulfuryl chloride in 100 ml methylene chloride are added dropwise to a solution of 12 g of 4-chloroacetyl-9,10-dihydro-4H-thieno[3,4-b][1,5]-benzodiazepin-10-one in 300 ml of methylene chloride at 20°C. The mixture is left to stand at room temperature for a further 12 hours and is then extracted by shaking it with sodium bicarbonate solution and washing it with water; the organic phase is dried and concentrated. The residue is made to crystallise with a little methanol. 7 g of 3-chloro-4-chloroacetyl-9,10-dihydro-thieno[3,4-b][1,5]benzodiazepin-10-one is thus obtained, m. 214-216°C (acetonitril).

Example 12

A mixture of 1.00 g of (4-methylpiperazin-1-yl)-acetic acid and 0.20 g of 75 per cent sodium hydride (in paraffin oil) in 16 ml of dimethylformamide is warmed at 50-80°C until the evolution of hydrogen has ended (2 to 3 hours). 1.35 g of 9,10-dihydro-4H-thieno[3,4-b][1,5]benzodiazepin-10-one are added to the sodium salt formed from the acid, and 0.99 g of 98% pure phosphorus oxychloride are added dropwise at -10°C in the course of 10 minutes. The batch is stirred at -10°C for 4 hours, at 0°C for 4 hours and at room temperature for 20 minutes. It is poured onto ice, adjusted to pH 3.5 with sodium hydroxide solution and extracted by shaking with methylene
chloride, and the aqueous phase is adjusted to pH 9 
and extracted by shaking again with methylene chloride.

The organic phase is washed with water and con-
centrated in vacuo. 0.6 g of 9,10-dihydro-4-[(4-methyl-
piperazin-1-yl)-acetyl]-4H-thieno[3,4-b][1,5]benzodiazepin-
10-one, m. 177-178°C (from acetone) are obtained.

9,10-Dihydro-3-methyl-4-[(4-methylpiperazin-1-yl)-
acetyl]-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, 
m. 263-264°C, and 9,10-dihydro-1,3-dimethyl-4-[(4-methyl-
piperazin-1-yl)acetyl]-4H-thieno[3,4-b][1,5]benzodiazepin-
10-one, m. 204-205°C, are obtained analogously by reaction 
of (4-methylpiperazin-1-yl)acetic acid with sodium hydride,
9,10-dihydro-3-methyl-4H-thieno[3,4-b][1,5]benzodiazepin-
10-one, respectively, 9,10-dihydro-1,3-dimethyl-4H-thieno-
[3,4-b][1,5]benzodiazepin-10-one and phosphorous oxy-
chloride.

Example 13

1.1 g of ethyl chloroformate are added dropwise at 
0°C to a suspension of 1.58 g of (4-methylpiperazin-1-yl)-
acetic acid in 20 ml of tetrahydrofuran.
2.18 g of 9,10-dihydro-4H-thieno[3,4-b][1,5]benzodiazepin-
10-one are added to the suspension obtained. The mixture 
is stirred 1 hour at 0°C and further 4 hours at room 
temperature. It is poured onto 2 N sodium hydroxide 
solution and extracted with toluene. The organic phase 
is concentrated to dryness. The residue is chromatographed 
over a silica gel column by means of a mixture of dioxane/
methanol (1:1) to give 9,10-dihydro-4-[(4-methylpiperazin-1-yl)acetyl]-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, m. 177-179°C.

9,10-Dihydro-3-methyl-4-[(4-methylpiperazin-1-yl)acetyl]-4H-thieno[3,4-b][1,5]benzodiazepin-10-one (m. 263-264°C) is obtained analogously by reaction of 9,10-dihydro-3-methyl-4H-thieno[3,4-b][1,5]benzodiazepin-10-one with (4-methylpiperazin-1-yl)acetic acid and ethyl chloroformate.

Example 14

2.0 g of 9,10-dihydro-3-methyl-4-[(piperazin-1-yl-acetyl)-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, 1.3 g of 98 per cent formic acid and 0.3 g of 35 per cent aqueous formaldehyde solution are warmed at 100-105°C for 2 hours. The mixture liquefies under evolution of gas. It is concentrated in vacuo, diluted with water, adjusted to pH 3.5 with diluted hydrochloric acid and extracted by shaking with dichloromethane. The aqueous phase is adjusted to pH 9 and extracted with dichloromethane. The organic phase is washed, dried and concentrated. Recrystallization of the residue from methanol yields 9,10-dihydro-3-methyl-4-[(4-methylpiperazin-1-yl)acetyl]-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, m. 263-264°C.

The starting compounds are obtained in the following manner:

Example A: 13.5 g of sulphuryl chloride in 100 ml of methylene chloride are added dropwise to a solution of
21.6 g of 9,10-dihydro-4H-thieno[3,4-b][1,5]benzodiazepin-10-one in 300 ml of methylene chloride at -40°C. The mixture is left to stand at room temperature for a further hour and is extracted by shaking with sodium bicarbonate solution and washed with water, and the organic phase is dried and concentrated. The residue is made to crystallise with a little methanol. 3-Chloro-9,10-dihydro-4H-thieno[3,4-b][1,5]benzodiazepin-10-one is obtained.

Example B: 10 g of 1,3,9,10-tetrahydro-3-methyl-4H-thieno[3,4-b][1,5]benzodiazepin-10-one and 8.2 g of N-bromosuccinimide are dissolved in 250 ml of dimethylformamide. After one hour, the solution is poured into 2 l of water. The precipitate is filtered off and dissolved in hot toluene and the solution is clarified with Tonsil®. On cooling, 9,10-dihydro-3-methyl-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, m. 228-230°C (methanol), is obtained as a precipitate.

9,10-Dihydro-1-methyl-4H-thieno[3,4-b][1,5]benzodiazepin-10-one and 9,10-dihydro-1,3-dimethyl-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, m. 195-196°C, are obtained analogously by dehydrogenation of 1,3,9,10-tetrahydro-1-methyl-4H-thieno[3,4-b][1,5]benzodiazepin-10-one or 1,3,9,10-tetrahydro-1,3-dimethyl-4H-thieno-[3,4-b][1,5]benzodiazepin-10-one with N-bromosuccinimide.
Example C: 49.9 g of o-phenylenediamine and 80 g of 5-methyl-tetrahydro-4-oxo-3-thiophenecarboxylic acid in 4.5 l of toluene are boiled. The water formed is distilled off azeotropically with 2 l of the solvent in the course of 7 hours. The solvent is removed. 1,3,9,10-Tetrahydro-3-methyl-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, m. 195-197°C (isopropanol) is obtained.

1,3,9,10-Tetrahydro-1-methyl-4H-thieno[3,4-b][1,5]-benzodiazepin-10-one and 1,3,9,10-tetrahydro-1,3-dimethyl-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, m. 148-150°C, are obtained analogously by reaction of tetrahydro-2-methyl-4-oxo-3-thiophenecarboxylic acid or tetrahydro-2,5-dimethyl-4-oxo-3-thiophenecarboxylic acid with o-phenylenediamine.

The following examples describe the formulation of a compound according to the invention to give medicaments.

Example 1

10,000 tablets with an active compound content of 20 mg are prepared from the following constituents:

200 g of 9,10-dihydro-4-[(4-methyl-piperazin-1-yl)acetyl]-4H-thieno[3,4-b][1,5]benzodiazepin-10-one, 900 g of maize starch, 500 g of lactose, 30 g of amorphous silicic acid and 40 g of sodium lauryl-sulphate are mixed and the mixture is sieved. This mixture is moistened with a solution of 50 g of polyvinylpyrrolidone (average molecular weight: 25,000) in 320 ml of alcohol and is granu-
lated through a sieve of mesh width 1.25 mm. The granules are dried at 40° and mixed with 160 g of pectin, 100 g of talc and 20 g of magnesium stearate. This mixture is compressed to 200 mg tablets with a diameter of 8 mm.

Example 16

100,000 capsules with an active compound content of 30 mg are prepared from the following constituents:
3,000 g of 9,10-dihydro-4-[(4-methyl-piperazin-1-yl)acetyl]-4H-thieno[3,4-b][1,5]benzodiazepin-10-one are mixed with 5,000 g of neutral oil (Miglyol® 812) and the mixture is filled into soft gelatin capsules.

Example 17

100,000 capsules with an active compound content of 15 mg are prepared from the following constituents:
1,500 g of 9,10-dihydro-4-[(4-methyl-piperazin-1-yl)acetyl]-4H-thieno[3,4-b][1,5]benzodiazepin-10-one and 1,500 g of magnesium trisilicate are mixed with 5,000 g of neutral oil (Miglyol® 812) and the mixture is filled into soft gelatin capsules.

Medicaments containing 9,10-dihydro-3-methyl-4-[(4-methylpiperazin-1-yl)acetyl]-4H-thieno[3,4-b][1,5]benzodiazepin-10-one and, respectively, 9,10-dihydro-1,3-dimethyl-4-[(4-methylpiperazin-1-yl)acetyl]-4H-thieno[3,4-b][1,5]benzodiazepin-10-one are obtained analogously by replacing 9,10-dihydro-4-[(4-methylpiperazin-1-yl)acetyl]-4H-thieno[3,4-b][1,5]benzodiazepin-10-one in Examples 15 to 17 by the above mentioned compounds.
Pharmacology

The excellent protective action on the stomach shown by the pharmacologically active substituted thienobenzodiazepinones can be demonstrated using as a model the so-called Shay rat. The compounds according to the invention prove to have a protective action on the stomach and a therapeutic range which are clearly superior to those of the known commercial product carbadoxolone (1), as can be shown, for example, by comparing (1) with 9,10-dihydro-4-[ (4-methyl-piperazin-1-yl) acetyl]-4H-thieno[3,4-b][1,5]benzodiazepin-10-one (2), 3-Chloro-9,10-dihydro-4-[ (4-methylpiperazin-1-yl) acetyl]-4H-thieno[3,4-b][1,5]benzodiazepin-10-one (3), 9,10-dihydro-3-methyl-4-[ (4-methyl-piperazin-1-yl) acetyl]-4H-thieno[3,4-b][1,5]benzodiazepin-10-one (4) and 9,10-dihydro-1,3-dimethyl-4-[ (4-methyl-piperazin-1-yl) acetyl]-4H-thieno[3,4-b][1,5]benzodiazepin-10-one (5).

Table I: Antiulcerogenic action and toxicity of thienobenzo-
diazepinones

<table>
<thead>
<tr>
<th>Serial No.</th>
<th>Toxicity LD$_{50}$[mg/kg], intravenous administration to mice</th>
<th>Protective action on the stomach ED$_{50}$[mg/kg], per oral administration to rats</th>
<th>TQ LD$<em>{50}$/ED$</em>{50}$</th>
<th>Gastric secretion* % inhibition in rats</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>290</td>
<td>~70</td>
<td>4.1</td>
<td>7</td>
</tr>
<tr>
<td>2</td>
<td>190</td>
<td>2.5</td>
<td>76</td>
<td>35</td>
</tr>
<tr>
<td>3</td>
<td>75</td>
<td>~1</td>
<td>75</td>
<td>28</td>
</tr>
<tr>
<td>4</td>
<td>130</td>
<td>~0.3</td>
<td>~433</td>
<td>20</td>
</tr>
<tr>
<td>5</td>
<td>180</td>
<td>1.3</td>
<td>139</td>
<td>17</td>
</tr>
</tbody>
</table>
**ED<sub>50</sub>** = dose which reduces the ulcer index by 50% in the treated group compared with the control group

**LD<sub>50</sub>** = dose at which 50% of the animals die

**TQ** = therapeutic quotient **LD<sub>50</sub>/ED<sub>50</sub>**

+ **% inhibition** = inhibition of the gastric secretion

(5) **4 hours after administration of the antiulcerogenic**

**ED<sub>50</sub>**

It should be particularly emphasised that an **ED<sub>50</sub>** can indeed still be determined in the case of compound 1, but the dose/action curve is then very severely flattened, so that no substantial increase in the ulcerogenic action can be achieved even at 300 mg/kg. In contrast, the action of compounds 2 to 5 is strictly dependent on the dose; inhibition effects of up to 95% can be achieved.

The antiulcerogenic action was tested in accordance with the method using the so-called Shay rat:

Rats (female, 180 - 200 g, 4 animals per cage on a high grid) which had been fasted for 24 hours were subjected to ulcer provocation by pylorus ligature (under diethyl ether anaesthetic) and oral administration of 100 mg/10 ml/kg of acetylsalicylic acid. The substances to be tested are administered orally (10 ml/kg) 1 hour before the pylorus ligature. The wound was closed by means of Michel clamps. 4 hours thereafter, the animals are killed under an ether anaesthetic by atlas
dislocation and the stomach is removed. The stomach is opened longitudinally and fixed to a cork tile, after the amount of gastric juice secreted (volume) has been determined; the number and size (= diameter) of ulcers present are determined with a stereomicroscope with 10-fold magnification. The product of the degree of severity (according to the following rating scale) and the number of ulcers serves as the individual ulcer index.

Scale of points:

<table>
<thead>
<tr>
<th>Ulcer Diameter</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>no ulcers</td>
<td>0</td>
</tr>
<tr>
<td>ulcer diameter 0.1 - 1.4 mm</td>
<td>1</td>
</tr>
<tr>
<td>1.5 - 2.4 mm</td>
<td>2</td>
</tr>
<tr>
<td>2.5 - 3.4 mm</td>
<td>3</td>
</tr>
<tr>
<td>3.5 - 4.4 mm</td>
<td>4</td>
</tr>
<tr>
<td>4.5 - 5.4 mm</td>
<td>5</td>
</tr>
<tr>
<td>&gt; 5.5 mm</td>
<td>6</td>
</tr>
</tbody>
</table>

The reduction in the average ulcer index of each treated group compared with that of the control group (= 100%) serves as a measure of the antiulcerogenic effect. The ED$_{50}$ designates the dose which reduces the average ulcer index by 50%.

**Determination of the toxicity**

The toxicity investigations are carried out on female NMRI mice (body weight: 22 - 26 g). The animals (5 animals per dose) receive feed and water ad libitum.
Various doses of the substances are administered intravenously (injection time: 1 minute). The observation period is 7 days. The LD$_{50}$, that is to say the dose at which 50% of the animals die, is determined by means of linear regression.
THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. Substituted thienobenzodiazepinones of the general formula I

\[
\begin{array}{c}
\text{N} \\
\text{CO-A} -R^3 \\
\text{R}^2 \\
\text{H} \\
\text{O} \\
\text{R}^1 \\
\end{array}
\]

wherein

- \( R^1 \) denotes a hydrogen atom or an alkyl radical with 1 to 4 carbon atoms,
- \( R^2 \) represents a halogen atom or has one of the meanings of \( R^1 \),
- \( R^3 \) denotes a halogen atom or the group \(-N(R^4)R^5\),
- \( R^4 \) denotes an alkyl radical with 1 to 4 carbon atoms or an alkenyl radical with 3 to 5 carbon atoms,
- \( R^5 \) has one of the meanings of \( R^4 \) or represents the group \(-(\text{CH}_2)_m-N(R^6)R^7\), or
- \( R^4 \) and \( R^5 \) together, and with the inclusion of the nitrogen atom to which they are bonded, denote a morpholino group, a pyrrolidino group, a piperidino group, a hexahydroazepin-1-yl group, a piperazin-1-yl group which is optionally sub-
stituted in the 4-position by a methyl, ethyl or benzyl group, a 2,4-dimethyl-piperazin-1-yl group, or a hexahydro-1H-1,4-diazepin-1-yl group which is substituted in the 4-position by a methyl or ethyl group,

\[ R^6 \] denotes an alkyl group with 1 to 4 carbon atoms,

\[ R^7 \] denotes an alkyl group with 1 to 4 carbon atoms,

\( A \) denotes a straight-chain or branched alkylene group with 1 to 5 carbon atoms and \( m \) denotes 2 or 3, and their acid addition salts.

2. Substituted thienobenzodiazepinones according to Claim 1, characterised by the general formula I*

\[
\begin{align*}
\text{H} & \quad \text{N} \\
& \quad \text{S} \\
& \quad \text{N} \\
& \quad \text{O} \\
& \quad \text{R}^1 \star \\
& \quad \text{R}^2 \star \\
& \quad \text{A} \star \text{-R}^3 \star \\
& \quad \text{CO} \\
\end{align*}
\]

(I*)

wherein

\[ R^1 \star \] denotes a hydrogen atom or a methyl or ethyl radical,

\[ R^2 \star \] represents a chlorine atom or has one of the meanings of \[ R^1 \star \],
R^3* denotes a chlorine atom and
A* denotes a straight-chain or branched alkylene
group with 1 or 2 carbon atoms.

3. Substituted thienobenzodiazepinones according to
Claim 1, characterised by the general formula I**

\[
R^1** \quad R^2** \quad R^3**
\]

wherein
R^1** denotes a hydrogen atom or a methyl or
ethyl radical,
R^2** represents a chlorine atom or has one of
the meanings of R^1**,
R^3** denotes the group \(-N(R^4**\)R^5**\)
R^4** denotes an alkyl radical with 1 to 4 carbon
atoms or an alkenyl radical with 3 to 4 carbon
atoms,
R^5** has the meaning of R^4** or represents the
group \(-\text{CH}_2\text{N}(R^6**)\text{R}^7**\), or
R^4** and R^5** together, with the inclusion of the
nitrogen atom to which they are bonded, denote
a morpholino group, a pyrrolidino group, a
piperidino group, a hexahydroazepin-1-yl group,
a piperazin-1-yl group which is optionally substituted
in the 4-position by a methyl, ethyl or benzyl
group, a 2,4-dimethyl-piperazin-1-yl group or
a hexahydro-1H-1,4-diazepin-1-yl group which is
substituted in the 4-position by a methyl or
ethyl group,
R^6** denotes a methyl or ethyl group,
R^7** denotes a methyl or ethyl group,
m** denotes 2 or 3 and
A** denotes a straight-chain or branched alkylene
group with 1 or 2 carbon atoms,
and their acid addition salts.

4. Compounds according to Claim 3, in which R^1**
denotes a hydrogen atom or a methyl or ethyl radical, R^2**
represents a chlorine atom or has one of the meanings of
R^1**; R^3** denotes the group -N(R^4**)_m**-N(R^6**)R^7**, or R^1** and
R^5** together, with the inclusion of the nitrogen atom,
denote a pyrrolidino, piperidino or hexahydroazepin-1-yl
radical, R^6** and R^7** denote a methyl or ethyl radical,
m** denotes 2 and A** denotes a methylene group, and their
pharmacologically acceptable acid addition salts.

5. Compounds according to Claim 3, in which R^1**
denotes a hydrogen atom or a methyl or ethyl radical,
R^2** represents a chlorine atom or has one of the meanings
of $R_1^{**}$; $R_3^{**}$ denotes the group $-N(R_4^{**})R_5^{**}$, $R_4^{**}$ and $R_5^{**}$ together, with the inclusion of the nitrogen atom, denote a piperazin-1-yl which is substituted in the 4-position by a methyl, ethyl or benzyl group, a 2,4-dimethylpiperazin-1-yl group or a hexahydro-1H-1,4-diazepin-1-yl group which is substituted in the 4-position by a methyl or ethyl group and $A^{**}$ denotes a methylene group, and their pharmacologically acceptable acid addition salts.

6. Compounds according to Claim 3, in which $R_1^{**}$ denotes a hydrogen atom or a methyl radical, $R_2^{**}$ denotes a hydrogen atom or a methyl radical, $R_3^{**}$ denotes the group $-N(R_4^{**})R_5^{**}$, $R_4^{**}$ and $R_5^{**}$ together, with inclusion of the nitrogen atom, denote a piperazin-1-yl group which is substituted in the 4-position by a methyl group and $A^{**}$ denotes a methylene group, and their pharmacologically acceptable acid addition salts.

7. Medicaments which contain as active ingredient one or more thienobenzodiazepinones of the general formula Ia

\[
\text{Ia)
}
\]

wherein

$R_1^1$ denotes a hydrogen atom or an alkyl radical with 1 to 4 carbon atoms,
R^2 represents a halogen atom or has one of the meanings of R^1,
R^3a denotes the group -N(R^4)R^5.
R^4 denotes an alkyl radical with 1 to 4 carbon atoms or an alkenyl radical with 3 to 5 carbon atoms and
R^5 has one of the meanings of R^4 or represents the group -(CH_2)_m-N(R^6)R^7 or R^4 and R^5 together, and with the inclusion of the nitrogen atom to which they are bonded, denote a morpholino group, a pyrrolidino group, a piperidino group, a hexahydroazepin-1-yl group, a piperazin-1-yl group which is optionally substituted in the 4-position by a methyl, ethyl or benzyl group, a 2,4-dimethyl-piperazin-1-yl group, or a hexahydro-1H-1,4-diazepin-1-yl group which is substituted in the 4-position by a methyl or ethyl group,
R^6 denotes an alkyl group with 1 to 4 carbon atoms,
R^7 denotes an alkyl group with 1 to 4 carbon atoms,
A denotes a straight-chain or branched alkylene group with 1 to 5 carbon atoms and
m denotes 2 or 3,
and/or their pharmacologically acceptable acid addition salts.

8. Process for the preparation of the substituted thienobenzodiazepinones of the general formula I

\[
\text{I)}
\]

wherein

- \(R^1\) denotes a hydrogen atom or an alkyl radical with 1 to 4 carbon atoms,
- \(R^2\) represents a halogen atom or has one of the meanings of \(R^1\),
- \(R^3\) denotes a halogen atom or the group \(-N(R^4)R^5\),
- \(R^4\) denotes an alkyl radical with 1 to 4 carbon atoms or an alkenyl radical with 3 to 5 carbon atoms,
- \(R^5\) has one of the meanings of \(R^4\) or represents the group \(-(CH_2)_m-N(R^6)R^7\), or \(R^4\) and \(R^5\) together, and with the inclusion of the nitrogen atom to which they are bonded, denote a morpholino group, a pyrrolidino group,
a piperidino group, a hexahydroazepin-1-yl group, a piperazin-1-yl group which is optionally substituted in the 4-position by a methyl, ethyl or benzyl group, a 2,4-dimethyl-piperazin-1-yl group, or a hexahydro-1H-1,4-diazepin-1-yl group which is substituted in the 4-position by a methyl or ethyl group, 

R denotes an alkyl group with 1 to 4 carbon atoms, 

R' denotes an alkyl group with 1 to 4 carbon atoms, 

A denotes a straight-chain or branched alkylene group with 1 to 5 carbon atoms and 

m denotes 2 or 3, 

and their acid addition salts, characterised in that thienobenzodiazepinones of the general formula II

![Formula II](image)

wherein 

R^1 and R^2 have the abovementioned meaning, are acylated and, if appropriate, are then aminated, and/or resulting bases are converted into the acid addition salts, or resulting acid addition salts are converted into the free base or into pharmacologically acceptable acid addition salts.
9. Process according to Claim 8, to prepare the thienobenzodiazepinones of the general formula I in which \( R^3 \) denotes -Hal, characterised in that the acylation is carried out with compounds of the general formulae
\[
\text{Hal-A-CO-Hal}' \quad \text{(III)} \quad \text{or} \quad \text{(Hal-A-CO)}_2 \text{O} \quad \text{(IV)},
\]
wherein Hal and Hal' denote a halogen atom and A denotes an alkylene group with 1 to 5 carbon atoms.

10. Process according to Claim 8, characterised in that compounds of the general formula I wherein \( R^3 \) represents a halogen atom, and secondary amines of the general formula \( \text{HN}(R^4)R^5 \) (V), wherein \( R^4 \) and \( R^5 \) have the meaning given in Claim 8, are employed in the optional subsequent amination.

11. Process according to Claim 10, characterised in that piperazine or homopiperazine are employed as secondary amines V and the obtained product of the general formula X
\[
\begin{align*}
\text{H} & \quad \text{O} \\
\text{N} & \quad \text{R}^1 \\
\text{N} & \quad \text{S} \\
\text{CO-A-N} & \quad \text{NH} \\
\text{CH}_2 & \quad \text{(CH}_2)_n \\
\end{align*}
\]

wherein \( R^1, R^2 \) and A have the meaning given in Claim 8 and \( n \) denotes 2 or 3, is methylated or ethylated.
12. Process according to Claim 8, characterised in that the acylation is carried out with compounds of the general formula \( Z-CO-A-N(R^4)R^5 \) (IX), wherein \( Z \) denotes a leaving group and \( A, R^4 \) and \( R^5 \) have the meaning given in Claim 8.

13. Process according to Claims 8 and 9, characterised in that substituted thienobenzodiazepinones of the general formula I*:

\[
\begin{align*}
&\text{S} \\
&\text{N} \\
&\text{CO-A*-R}^3
\end{align*}
\]

wherein

- \( R^1* \) denotes a hydrogen atom, a methyl or ethyl radical,
- \( R^2* \) denotes a chlorine atom or has one of the meanings of \( R^1* \),
- \( R^3* \) denotes a chlorine atom,
- \( A* \) denotes a straight-chain or branched alkylene group with 1 or 2 carbon atoms,

are prepared by reaction of thienobenzodiazepinones of the general formula II*:

\[
\begin{align*}
&\text{S} \\
&\text{N} \\
&\text{CO-A*-R}^3
\end{align*}
\]
wherein

\[ R_1^* \text{ and } R_2^* \text{ have the abovementioned meaning,} \]

with acid derivatives Cl-A*-CO-Cl (III*) or (Cl-A*-CO)_2O (IV*),

wherein A* has the abovementioned meaning.

14. Process according to Claims 8 and 10, characterised in that substituted thienobenzodiazepinones of the general formula I**

\[
\text{[Diagram]} \]

wherein

\[ R_1^{**} \text{ denotes a hydrogen atom, a methyl or ethyl radical,} \]

\[ R_2^{**} \text{ denotes a chlorine atom or has one of the meanings of } R_1^{**}, \]

\[ R_3^{**} \text{ denotes the group } -N(R_4^{**})R_5^{**}, \]

\[ R_4^{**} \text{ denotes an alkyl radical with 1 to 4 carbon atoms or an alkenyl radical with 3 to 4 carbon atoms,} \]

\[ R_5^{**} \text{ has the meaning of } R_4^{**} \text{ or represents the group } -(\text{CH}_2)_m^{**}N(R_6^{**})R_7^{**}, \text{ or} \]

\[ R_4^{**} \text{ and } R_5^{**} \text{ together, and with the inclusion of the nitrogen atom to which they are bonded, denote a morpholino group, a pyrrolidino group, a piperidino group, a hexahydroazepin-} \]
1-yl group, a piperazin-1-yl group which is optionally substituted in the 4-position by a methyl, ethyl or benzyl group, a 2,4-dimethylpiperazin-1-yl group, a hexahydro-1H-1,4-diazepin-1-yl group which is substituted in the 4-position by a methyl or ethyl group, 

\( R^6 ** \) denotes a methyl or ethyl group, 
\( R^7 ** \) denotes a methyl or ethyl group, 
\( A^{**} \) denotes a straight-chain or branched alkylene group with 1 or 2 carbon atoms and 
\( m^{**} \) denotes 2 or 3, 
and their acid addition salts are prepared by reaction of compounds of the general formula I**, wherein 
\( R^3 ** \) denotes a chlorine atom, with secondary amines 

\( \text{HN}(R^{4 **})R^{5 **}(V**) \), wherein \( R^{4 **} \) and \( R^{5 **} \) have the above-mentioned meaning.

15. Process according to Claim 14, characterised in that compounds of the general formula I** in which \( R^1 ** \) denotes a hydrogen atom, a methyl or ethyl radical, \( R^2 ** \) represents a chlorine atom or has one of the meanings of \( R^1 ** \); 
\( R^3 ** \) denotes the group \( -N(R^{4 **})R^{5 **} \), 
\( R^{4 **} \) denotes a methyl or ethyl radical and \( R^{5 **} \) has the meaning of \( R^{4 **} \) or represents the group \( -CH_2 \) \( _m^{**} \) \( -N(R^{6 **})R^{7 **} \), or \( R^{4 **} \) and \( R^{5 **} \) together, with the inclusion of the nitrogen atom, denote a pyrrolidino, piperidino or hexahydroazepin-1-yl radical, \( R^6 ** \) and \( R^7 ** \) denote a methyl or ethyl radical, 
\( m^{**} \) denotes 2 and \( A^{**} \) denotes a methylene group, and their pharmacologically acceptable acid addition salts are prepared.
16. Process according to Claim 14, characterised in that compounds of the general formula I**, in which \( R^{1**} \) denotes a hydrogen atom, a methyl or ethyl radical, \( R^{2**} \) represents a chlorine atom or has one of the meanings of \( R^{1**}; R^{3**} \) denotes the group \(-N(R^{4**})R^{5**}; R^{4**} \) and \( R^{5**} \) together, with the inclusion of the nitrogen atom, denote a piperazin-1-yl which is optionally substituted in the 4-position by a methyl, ethyl or benzyl group, a 2,4-dimethylpiperazin-1-yl group or a hexahydro-1H-1,4-diazepin-1-yl group which is substituted in the 4-position by a methyl or ethyl group and \( A^{**} \) denotes a methylene group, and their pharmacologically acceptable acid addition salts are prepared.

17. Process according to Claim 14, characterised in that compounds of the general formula I**, in which \( R^{1**} \) denotes a hydrogen atom or a methyl radical, \( R^{2**} \) denotes a hydrogen atom or a methyl radical, \( R^{3**} \) denotes the group \(-N(R^{4**})R^{5**}; R^{4**} \) and \( R^{5**} \) together, with inclusion of the nitrogen atom, denote a piperazin-1-yl group which is substituted in the 4-position by a methyl group and \( A^{**} \) denotes a methylene group, and their pharmacologically acceptable acid addition salts are prepared.

18. Process according to Claims 8 and 11, characterised in that substituted thienobenzodiazepinones of the general formula I**

\[
\text{(I**),}
\]
wherein

\[ R^{1\text{**}} \] denotes a hydrogen atom, a methyl or ethyl radical,
\[ R^{2\text{**}} \] represents a chlorine atom or has one of the meanings of \( R^{1\text{**}} \),
\[ R^{3\text{**}} \] denotes the group \( -N(R^{4\text{**}})R^{5\text{**}} \),
\[ R^{4\text{**}} \text{ and } R^{5\text{**}} \text{ together, with the inclusion of the nitrogen atom to which they are bonded, denote a piperazin-1-yl group which is substituted in the 4-position by a methyl or ethyl group, or a hexahydro-1H-1,4-diazepin-1-yl group which is substituted in the 4-position by a methyl or ethyl group,} \]
and their addition salts are prepared by reaction of compounds of the general formula \( I^{**} \), wherein
\[ R^{3\text{**}} \] denotes a chlorine atom, with piperazine or homopiperazine as secondary amines \( HN(R^{4\text{**}})R^{5\text{**}} (V^{**}) \) and subsequent methylation or ethylation of the obtained piperazinothienobenzodiazepinones of the general formula \( X^{**} \)

\[ (X^{**}) \]

wherein
\[ R^{1\text{**}}, R^{2\text{**}} \text{ and } A^{**} \text{ have the abovementioned meaning and } n^{**} \text{ denotes 2 or 3.} \]
19. Process according to Claim 18, characterised in that compounds of the general formula I**, wherein $R^{1**}$ denotes a hydrogen atom or a methyl radical, $R^{2**}$ has one of the meanings of $R^{1**}$, $R^{3**}$ denotes the group $-N(R^{4**})R^{5**}$, $R^{4**}$ and $R^{5**}$ together, with the inclusion of the nitrogen to which they are bonded, denote a piperazin-1-yl group which is substituted in the 4-position by a methyl group, and their pharmacologically acceptable acid addition salts are prepared.

20. Process according to Claim 8 and 12, characterised in that substituted thienobenzodiazepinones of the general formula I**

\[
\begin{align*}
\text{[Diagram: I**]} \\
\end{align*}
\]

wherein $R^{1**}$, $R^{2**}$, $R^{3**}$ and $A^{**}$ have the meaning given in Claim 14, are prepared by reaction of thienobenzodiazepinones of the general formula II**

\[
\begin{align*}
\text{[Diagram: II**]} \\
\end{align*}
\]

wherein $R^{1**}$ and $R^{2**}$ have the abovementioned meaning, with reactive acid derivatives of the general formula IX** $Z^{**}$-CO-$A^{**}$-N($R^{4**}$)R$^{5**}$ (IX**), wherein $Z^{**}$ denotes a leaving group and $A^{**}$, $R^{4**}$ and $R^{5**}$ have the meaning given in Claim 14.
21. Pharmaceutical preparations containing from 0.5 to 95% by weight of the total mixture of at least one compound according to claims 1 to 6 in admixture with one or more solid or liquid pharmaceutically acceptable carriers.

22. A process for the preparation of substituted thienobenzodiazepinones of the general formula I according to claim 1 substantially as described with reference to the specific examples hereinbefore set forth.

Dated this 6th day of May, 1981.

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