

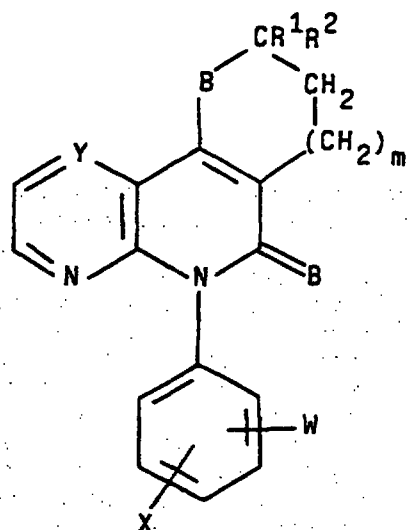
Description

The present invention relates to novel tricyclic compounds which possess anti-allergic, anti-inflammatory and cytoprotective activity.

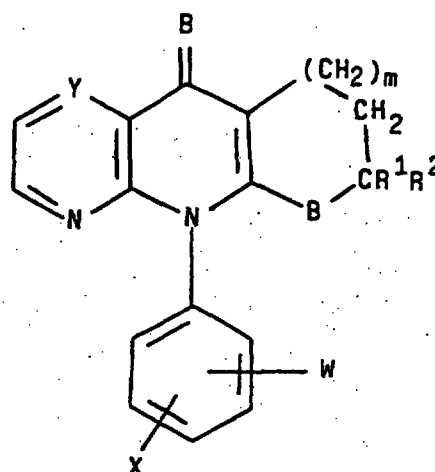
The preparation of the compound 2'-methylpyrano-5',6':3,4-(2-oxo-1,2-dihydroquinoline) and its N-phenyl derivative is described in Bull. Soc. Chim. Fr., pp. 364-9 (1968) (C.A. 68: 114419c).

Further, naphthyridinone derivatives having analgesic, anti-inflammatory, central nervous system depressing and diuretic actions are described in JP-A-7716495 (see also *Chem. Abs.* 88 (1978) 105298y. Naphthyridinone derivatives useful for treating allergic reactions in mammals are described in EP-0 092 786. The naphthyridinone derivatives described in these documents are bicyclic compounds, as compared to the fused tricyclic derivatives to which the present invention relates.

According to one aspect of the invention there are provided compounds having the structural formula A' or A''



A'



A''

wherein

B is independently oxygen or sulfur;

R¹ and R² may be the same or different and are hydrogen or alkyl having from 1 to 6 carbon atoms; m is 0, 1 or 2;

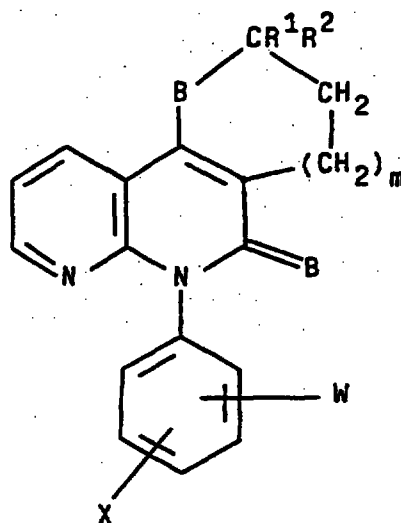
W and X may be the same or different and are hydrogen, hydroxy, alkyl having from 1 to 6 carbon atoms, halogen, nitro, alkoxy having from 1 to 6 carbon atoms, or NHR^a (wherein R^a is alkyl having from 1 to 6 carbon atoms); and

Y is CH or N.

A preferred subgenus of compounds is that wherein B is oxygen.

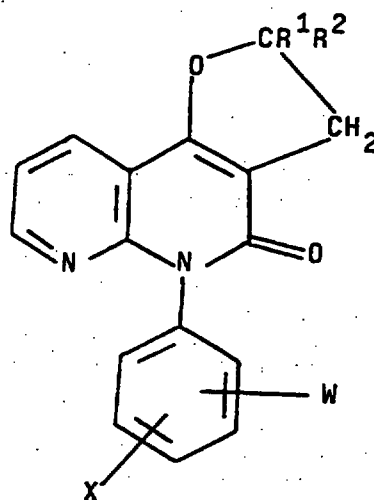
A more preferred subgenus of compounds comprises those of formula A' wherein B is oxygen.

Compounds of particular interest are those in which Y is CH. Such compounds include particularly those of formula

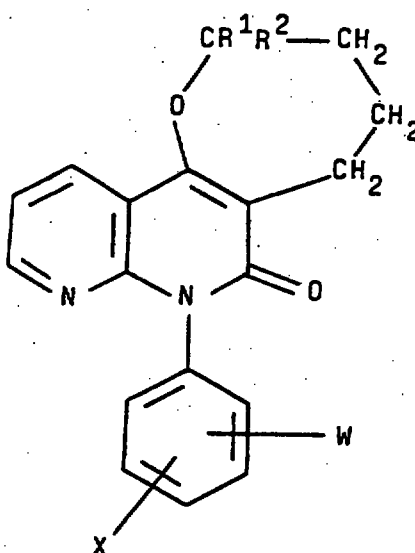


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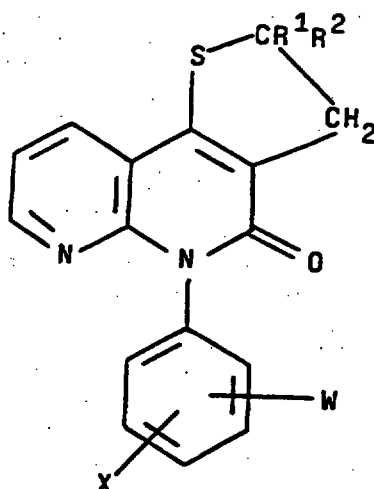
wherein B, W, X, R¹, R² and m are as defined above, especially those of formula



and those of formula



A further class of interest are compounds of formula



Of interest are compounds in which one of R¹ and R² is methyl and the other is hydrogen, compounds wherein W is 3-chloro and X is hydrogen, chlorine or fluorine; compounds in which W is 3-methoxy and X is hydrogen or fluorine and compounds in which W and X are both hydrogen.

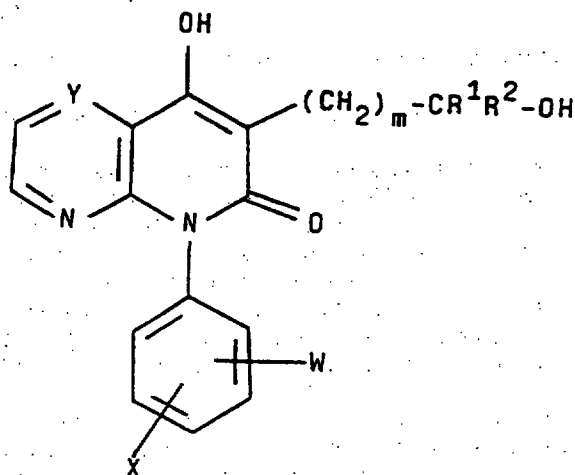
Preferred species are those having the names:

3,5-dihydro-5-phenyl-furo[3,2-c][1,8]naphthyridin-4[2H]-one;
 6-phenyl-2,3,4,6-tetrahydro-pyrano[3,2-c][1,8]naphthyridin-5-one;
 2-methyl-3,5-dihydro-5-phenyl-furo[3,2-c][1,8]naphthyridin-4[2H]-one;
 3,9-dihydro-9-phenyl-furo[2,3-b][1,8]naphthyridin-4[2H]-one;
 3,9-dihydro-9-(p-methylphenyl)-furo[2,3-b][1,8]naphthyridin-4[2H]-one;
 3,9-dihydro-2-methyl-9-phenyl-furo[2,3-b][1,8]naphthyridin-4[2H]-one;
 3,5-dihydro-5-(p-methylphenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-one;
 3,5-dihydro-5-(p-fluorophenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-one;
 3,5-dihydro-5-(m-methoxyphenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-one;
 3,9-dihydro-9-(p-fluorophenyl)-furo[2,3-b][1,8]naphthyridin-4[2H]-one;
 3,9-dihydro-9-(m-methoxyphenyl)-furo[2,3-b][1,8]naphthyridin-4[2H]-one;
 3,5-dihydro-5-(3,4-dichlorophenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-one;
 3,5-dihydro-5-(3,4-dichlorophenyl)-2-methyl-furo[3,2-c][1,8]naphthyridin-4[2H]-one;
 3,5-dihydro-5-(4-chlorophenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-one;
 3,5-dihydro-5-(3-chlorophenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-one;
 3,5-dihydro-5-(3-chlorophenyl)-2-methyl-furo[3,2-c][1,8]naphthyridin-4[2H]-one;
 3,5-dihydro-5-(4-fluorophenyl)-2-methyl-furo[3,2-c][1,8]naphthyridin-4[2H]-one;
 3,5-dihydro-5-(3-methoxyphenyl)-2-methyl-furo[3,2-c][1,8]naphthyridin-4[2H]-one;
 3,5-dihydro-5-(3,5-dichlorophenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-one;
 3,5-dihydro-5-(3,5-dichlorophenyl)-2-methyl-furo[3,2-c][1,8]naphthyridin-4[2H]-one;
 3,5-dihydro-5-phenyl-2,2-dimethyl-furo[3,2-c][1,8]naphthyridin-4[2H]-one;
 3,9-dihydro-9-(3,4-dichlorophenyl)-furo[2,3-b][1,8]naphthyridin-4[2H]-one;
 3,9-dihydro-9-(4-chlorophenyl)-furo[2,3-b][1,8]naphthyridin-4[2H]-one;
 3,9-dihydro-9-(3-chlorophenyl)-furo[2,3-b][1,8]naphthyridin-4[2H]-one;
 3,9-dihydro-9-(3-chlorophenyl)-2-methyl-furo[2,3-b][1,8]naphthyridin-4[2H]-one;
 3,9-dihydro-9-(4-fluorophenyl)-2-methyl-furo[2,3-b][1,8]naphthyridin-4[2H]-one;
 3,9-dihydro-9-(3-methoxyphenyl)-2-methyl-furo[2,3-b][1,8]naphthyridin-4[2H]-one;
 3,9-dihydro-9-(3,5-dichlorophenyl)-furo[2,3-b][1,8]naphthyridin-4[2H]-one;
 3,9-dihydro-9-(3,5-dichlorophenyl)-2-methyl-furo[2,3-b][1,8]naphthyridin-4[2H]-one;
 6-(4-Chlorophenyl)-2,3,4,6-tetrahydro-5H-pyrano[3,2-c][1,8]naphthyridin-5-one;
 6-(3,4-Dichlorophenyl)-2,3,4,6-tetrahydro-5H-pyrano[3,2-c][1,8]naphthyridin-5-one;
 6-(4-Methoxyphenyl)-2,3,4,6-tetrahydro-5H-pyrano[3,2-c][1,8]naphthyridin-5-one;
 6-(4-Methylphenyl)-2,3,4,6-tetrahydro-5H-pyrano[3,2-c][1,8]naphthyridin-5-one;
 10-(3,4-Dichlorophenyl)-2,3,4,10-tetrahydro-5H-pyrano[2,3-b][1,8]naphthyridin-5-one;
 10-(4-Methoxyphenyl)-2,3,4,10-tetrahydro-5H-pyrano[2,3-b][1,8]naphthyridin-5-one;
 10-(4-Chlorophenyl)-2,3,4,10-tetrahydro-5H-pyrano[2,3-b][1,8]naphthyridin-5-one;
 10-(4-Methylphenyl)-2,3,4,10-tetrahydro-5H-pyrano[2,3-b][1,8]naphthyridin-5-one;
 10-Phenyl-2,3,4,10-tetrahydro-5H-pyrano[2,3-b][1,8]naphthyridin-5-one;
 7-Phenyl-3,4,5,7-tetrahydro-oxepino[3,2-c][1,8]naphthyridin-6[2H]-one;
 7-(4-Chlorophenyl)-3,4,5,7-tetrahydro-oxepino[3,2-c][1,8]naphthyridin-6[2H]-one;
 7-(3-Chlorophenyl)-3,4,5,7-tetrahydro-oxepino[3,2-c][1,8]naphthyridin-6[2H]-one;
 7-(3-Methoxyphenyl)-3,4,5,7-tetrahydro-oxepino[3,2-c][1,8]naphthyridin-6[2H]-one;
 7-(3-Hydroxyphenyl)-3,4,5,7-tetrahydro-oxepino[3,2-c][1,8]naphthyridin-6[2H]-one;

The invention is also directed to pharmaceutical compositions which comprise a compound having structural formula I in combination with a pharmaceutically acceptable carrier.

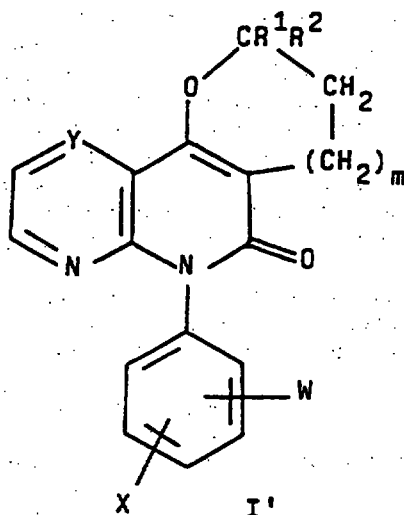
The compounds of the invention are useful for treating allergic reactions, inflammation and peptic ulcers in a mammal by administering an effective amount of the above defined pharmaceutical composition to said mammal.

The compounds of the invention may be prepared from a properly substituted 3-(hydroxyalkyl)-4-hydroxy-1-substituted-[quinolin; 1,5-naphthyridin; or 1,8-naphthyridin]-2(1H)-one, a 7-(hydroxyalkyl)-8-hydroxy-5-substituted-pyrido[2,3-b]pyrazin-6(5H)-one having the structural formula II



wherein W, X, Y, R¹, R² and m are as defined herein.

Compounds of the invention having formula A' wherein both Bs are oxygen and m is 0 or 1 i.e., compounds having structural formula I'

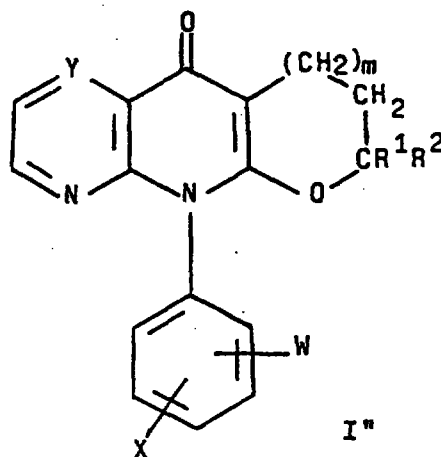


may be prepared by treating a correspondingly substituted compound having structural formula II with a strong aqueous acid solution. Useful acids include sulfuric acid, hydrobromic acid, perchloric acid, trifluoroacetic acid, phosphoric acid. A compatible non-reactive solvent may be utilized to aid solubility, if desired. The use of approximately 30% sulfuric acid without additional solvent is preferred.

In this procedure, the starting compound II is dissolved or suspended in the reaction medium and heated to reflux temperature over a period of about 1 hour. The mixture is maintained at reflux temperature until the reaction is substantially complete. The progress of the reaction may be monitored by standard means, for example thin layer chromatographic means, and is usually substantially completed after about 6 hours. The product may be recovered, for example, by adding the reaction mixture to an excess of cold dilute base solution such as sodium hydroxide or potassium carbonate and isolating the product by standard means such as extraction with an organic solvent or by filtration. Further purification, if desired, may be effected by recrystallization.

The thiated derivatives of I' may be prepared by procedures described below.

Compounds of the invention having formula A'' wherein both Bs are oxygen i.e., compounds having structural formula I''



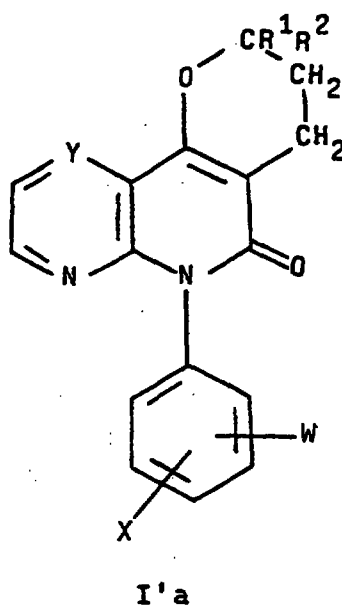
20 may be prepared by treating a corresponding substituted compound having structural formula II with a dehydrating reagent under anhydrous conditions. Suitable dehydrating reagents for this purpose are phosphorus pentoxide/methanesulfonic acid [known as Eaton's reagent, J. Org. Chem. 35, 4071 (1973)] and thionyl chloride/pyridine/methylene chloride, for example.

25 In the preferred method for preparing compounds having structural formula I'', a correspondingly substituted compound having structural formula II is dissolved or suspended in Eaton's reagent at elevated temperature until the reaction is substantially complete. Temperatures from 50° to 100°C are useful. At temperatures of from 60° to 80°C, the reaction has been observed to be substantially completed in 1 to 4 hours.

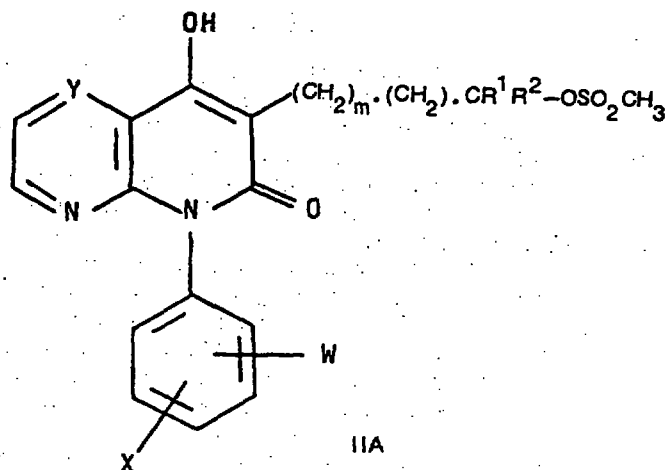
30 The progress of the reaction may be monitored by standard means. The product may be recovered, for example, by adding the reaction mixture to an excess of cold dilute base solution such as sodium hydroxide, potassium carbonate or the like and isolating the product by standard means such as extraction with an organic solvent or by filtration. Further purification, if desired, may be effected by recrystallization.

The thiated derivatives of I'' may be prepared by procedures described below.

35 Compounds of the invention having formula A' wherein both Bs are oxygen and m is 1, i.e. compounds having the structural formula I'a



65 may be prepared by the cyclization of a compound having structural formula IIA



This cyclization is preferably carried out by treating IIA with a base such as cesium carbonate in a convenient solvent such as N,N-dimethylformamide. The product may be isolated and purified by standard methods.

Other base/solvent pairs may be utilized for this cyclization such as sodium or potassium carbonate in N,N-dimethylformamide or N,N-dimethyl acetamide; potassium carbonate in acetone; tetra-*n*-butylammonium hydroxide, triethylamine or 1,8-diazabicyclo[5.4.0]undec-7-ene in methylene chloride or chloroform. In addition, the methanesulfonate leaving group of IIA may be replaced by other leaving groups known in the art such as bromine, chlorine and other sulfonic acid esters derived from acids such as benzenesulfonic acid, *p*-toluenesulfonic acid and *p*-bromobenzenesulfonic acid.

The compounds having structural formula II may be prepared by known methods from known starting materials. Exemplary of such starting materials are 2-anilino-3-pyrazine carboxylic acids prepared, for example, as described in United States Reissue Patent 26,655, and 2-phenylamino-3-pyrazine carboxylate esters which may be prepared substantially as exemplified herein starting with a 2-amino-3-pyrazine carboxylate ester. 2-Anilino-3-pyrazine carboxylic acid is a known compound, C.A., 75, 20154e (1971), which may be esterified by standard procedures.

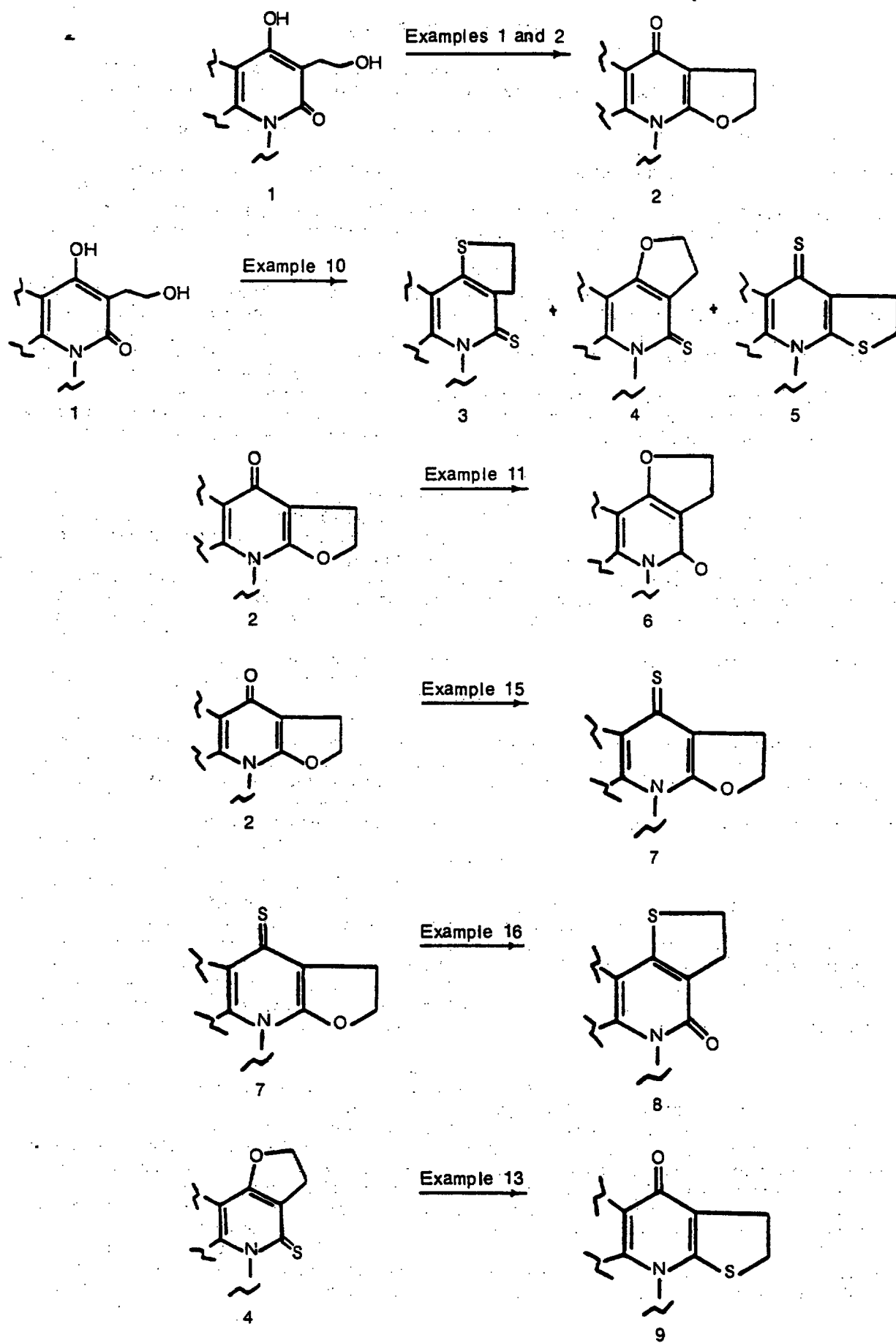
The compounds having structural formula IIA may be prepared from the corresponding substituted compound having structural formula II by known methods. For example, compound II may be treated with methanesulfonic acid in the presence of a dehydrating agent such as phosphorus pentoxide (Eaton's reagent).

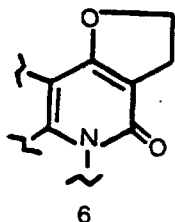
The compounds having structural formula I' may also be produced from a correspondingly substituted compound having structural formula I''. Thus for example, a compound having structural formula I'' may be treated with a nucleophile such as bromide or iodide anion under anhydrous conditions in a non-reactive solvent such as N,N-dimethylacetamide between 60°C and the mixture's reflux temperature for 2 to 12 hours to effect this conversion.

Certain compounds of the invention having structural formula I in which one or both of B are sulfur may be prepared from the correspondingly substituted compound having structural formula II by treatment with, for example, Lawesson's Reagent [2,4-bis(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane-2,4-disulfide] in hot toluene. Under these conditions both cyclization of II and thiation are found to occur. Also, reaction of Lawesson's Reagent with compounds I' yields mainly a singly thiated product, i.e. the product in which the carbonyl oxygen atom has been replaced by sulfur (a thioamide); whereas —O— is not replaced.

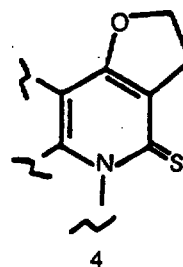
In addition, certain compounds wherein one of the B substituents is oxygen and one is sulfur may be rearranged by treatment with a nucleophile as described above. Thus, for example, a thioamide compound wherein the cyclic B atom is oxygen having structural formula I', may be rearranged to produce a compound having structural formula I'' wherein the cyclic B atom is sulfur and the doubly bonded B atom is oxygen.

The above-described thiation conversions and rearrangements are further described below by use of diagrams. For reasons of convenience and clarity, abbreviated structures are utilized in the diagrams. The references noted on the arrows refer to the procedures of the indicated working examples.





Example 12



When utilized herein and in the appended claims the below listed terms, unless specified otherwise, are defined as follows:

halogen — fluorine, chlorine, bromine and iodine;

alkyl and alkoxy — comprised of straight and branched carbon chains containing from 1 to 6 carbon atoms.

The compounds of the invention may possibly contain two different "B" substituents. It is intended that both may simultaneously be oxygen or sulfur, or that either may be oxygen or sulfur.

Certain compounds of the invention may exist in isomeric forms. The invention contemplates all such isomers both in pure form and in admixture, including racemic mixtures.

The compounds of this invention can be used to treat allergy caused diseases and their preferred use is for treating allergic chronic obstructive lung diseases. Chronic obstructive lung disease as used herein means disease conditions in which the passage of air through the lungs is obstructed or diminished such as is the case in asthma or bronchitis.

The anti-allergy method of this invention is identified by tests which measure a compound's inhibition of anaphylactic bronchospasm in sensitized guinea pigs having antigen induced bronchoconstriction. For example, the compound 3,5-dihydro-5-phenyl-furo[3,2-c][1,8]naphthyridin-4[2H]-one was found to inhibit anaphylactic bronchospasms in such test procedure when given at an oral dose of 3—5 mg/kg. Said compound was also found to inhibit allergen-induced histamine release from guinea pig and human sensitized tissue. The compounds are effective non-adrenergic, non-anticholinergic antianaphylactic agents. When administered orally they are active at doses from 0.1 to 10 mg/kg of body weight; when administered parenterally, e.g., intravenously, the compounds are active at dosages of from 0.05 to 5 mg/kg body weight; when administered by inhalation (aerosol or nebulizer) the compounds are active at dosages of 0.25 to 5 mg per puff, one to four puffs may be taken every 4 hours.

The compounds of this invention are also useful for the treatment of inflammation. The anti-inflammatory use of the compounds of the present invention may be demonstrated by the Reversed Passive Arthus Reaction (RPAR) Synovitis technique as set forth below using male Lewis rats (obtained from Charles River Breeding Laboratories) weighing 200—250 grams. The potency of the compounds is determined using indomethacin as the standard. On the basis of the test results, an oral dosage range of about 5 milligrams per kilogram of body weight per day to about 50 milligrams per kilogram of body weight per day in divided doses taken at about 4 hour intervals is recommended.

The dosage to be administered and the route of administration depends upon the particular compound used, the age and general health of the patient and the severity of the inflammatory condition. Thus, the dose ultimately decided upon must be left to the judgment of a trained health-care practitioner.

RPAR Synovitis Technique

A Lewis rat is dosed orally with drug or placebo one hour prior to intravenous administration of 2.28 mg of bovine serum albumin (BSA) in 0.2 cc of pyrogen-free saline followed by the intraperitoneal injection of 0.54 mg of rabbit anti-BSA antibody in 0.03 cc of pyrogen-free saline into one knee. The contralateral knee is injected with 0.03 cc of pyrogen-free saline. All injections are made with the rat under light ether anesthesia. Three hours later the rat is again dosed orally with drug or placebo. The doses are split. That is, one-half of the dose is administered before lesion induction and one-half is administered after lesion induction.

The following morning (about 17 hours after lesion induction) the rat is killed and both knee joints are exposed. The subpatellar areolar tissue with attendant synovium is excised and weighed. Differences between the weight of antibody and saline injected knees are considered to represent the inflammatory response for each animal (delta synovial weight). Differences in delta synovial weight between lesion controls and drug-treated rats are evaluated for statistical significance with an analysis of variance. Relative potencies are determined with a linear regression analysis.

The compounds of this invention are also useful in the treatment of peptic ulcers. They display chemotherapeutic activity which enables them to relieve the symptoms of peptic ulcer disease, stress ulceration, and promote healing of gastric and/or duodenal ulcers. The antiulcer activity of the compounds of this invention is identified by tests which measure the cytoprotective effects in rats. The compounds are also useful as conjunctive therapeutic agents for coadministration with such antiinflammatory/analgesic agents as aspirin, indomethacin, phenylbutazone, ibuprofen, naproxen, tolmetin and other agents. The

compounds of this invention prevent the untoward side effects of irritation and damage to the gastrointestinal tract caused by such agents.

The compounds of this invention are evaluated for their antiulcer activity characteristics by standard biological testing procedures.

5 In cytoprotective tests in rats in which ethanol is employed to induce gastrointestinal damage, the compounds of this invention are found to be effective at doses of 0.05—50 mg/kg of body weight per day. Preferably the total dosages are administered in 2—4 divided doses per day.

When administered parenterally, e.g. intravenously, the compounds are administered at a dosage range of 0.01—10 mg/kg of body weight in single or multiple daily doses.

10 To treat peptic ulcer disease, and prevent and treat drug-induced gastric ulceration, the active compounds of this invention can be administered in unit dosage forms such as tablets, capsules, pills, powders, granules, sterile parenteral solutions or suspensions, suppositories, mechanical delivery devices, e.g. transdermal.

The compounds of the invention of formula I can exist in unsolvated as well as solvated forms, 15 including hydrated forms. In general, the solvated forms, with pharmaceutically acceptable solvents such as water or ethanol are equivalent to the unsolvated forms for purposes of the invention.

For preparing pharmaceutical compositions from the compounds described by this invention, inert, pharmaceutically acceptable carriers can be either solid or liquid. Solid form preparations include powders, tablets, dispersible granules, capsules, cachets and suppositories. A solid carrier can be one or more 20 substances which may also act as diluents, flavoring agents, solubilizers, lubricants, suspending agents, binders or tablet disintegrating agents; it can also be an encapsulating material. In powders, the carrier is a finely divided solid which is in admixture with the finely divided active compound. In the tablet the active compound is mixed with carrier having the necessary binding properties in suitable proportions and compacted in the shape and size desired. The powders and tablets preferably contain from 5 or 10 to 70 25 percent of the active ingredient. Suitable solid carriers include magnesium carbonate, magnesium stearate, talc, sugar, lactose, pectin, dextrin, starch, gelatin, tragacanth, methylcellulose, sodium carboxymethylcellulose, a low melting wax or cocoa butter. The term "preparation" is intended to include the formulation of the active compound with encapsulating material as carrier providing a capsule in which the active component (with or without other carriers) is surrounded by carrier, which is thus in association with it. 30 Similarly, cachets are included. Tablets, powders, cachets and capsules can be used as solid dosage forms suitable for oral administration.

For preparing suppositories, a low melting wax such as a mixture of fatty acid glycerides or cocoa butter is first melted, and the active ingredient is dispersed homogeneously therein as by stirring. The molten homogeneous mixture is then poured into convenient sized molds, allowed to cool and thereby 35 solidify.

Liquid form preparations include solutions, suspensions and emulsions. As an example may be mentioned water or water-propylene glycol solutions for parenteral injection. Liquid preparations can also be formulated in solution in aqueous polyethylene glycol solution. Aqueous solutions suitable for oral use can be prepared by adding the active component in water and adding suitable colorants, flavors, 40 stabilizing, sweetening, solubilizing and thickening agents as desired. Aqueous suspensions suitable for oral use can be made by dispersing the finely divided active component in water with viscous material, i.e., natural or synthetic gums, resins, methylcellulose, sodium carboxymethylcellulose and other well-known suspending agents.

Also included are solid form preparations which are intended to be converted, shortly before use, to 45 liquid form preparations for either oral or parenteral administration. Such liquid forms include solutions, suspensions and emulsions. These particular solid form preparations are most conveniently provided in unit dose form and as such are used to provide a single liquid dosage unit. Alternately, sufficient solid may be provided so that after conversion to liquid form, multiple individual liquid doses may be obtained by measuring predetermined volumes of the liquid form preparation as with a syringe, teaspoon or other 50 volumetric container. When multiple liquid doses are so prepared, it is preferred to maintain the unused portion of said liquid doses at low temperature (i.e., under refrigeration) in order to retard possible decomposition. The solid form preparations intended to be converted to liquid form may contain, in addition to the active material, flavorants, colorants, stabilizers, buffers, artificial and natural sweeteners, dispersants, thickeners or solubilizing agents. The solvent utilized for preparing the liquid form preparation 55 may be water, isotonic water, ethanol, glycerine or propylene glycol as well as mixtures thereof. Naturally, the solvent utilized will be chosen with regard to the route of administration, for example, liquid preparations containing large amounts of ethanol are not suitable for parenteral use.

Preferably, the pharmaceutical preparation is in unit dosage form. In such form, the preparation is subdivided into unit doses containing appropriate quantities of the active component. The unit dosage 60 form can be a packaged preparation, the package containing discrete quantities of preparation, for example, packeted tablets, capsules and powders in vials or ampoules. The unit dosage form can also be a capsule, cachet or tablet itself or it can be the appropriate number of any of these in packaged form.

The quantity of active compound in a unit dose of preparation may be varied or adjusted from 1 mg to 100 mg according to the particular application and the potency of the active ingredient. The compositions 65 can, if desired, also contain other therapeutic agents.

The dosages may be varied depending upon the requirements of the patient, the severity of the condition being treated and the particular compound being employed. Determination of the proper dosage for a particular situation is within the skill of the art. Generally, treatment is initiated with smaller dosages which are less than the optimum dose of the compound. Thereafter, the dosage is increased by small increments until the optimum effect under the circumstances is reached. For convenience, the total daily dosage may be divided and administered in portions during the day if desired.

EXAMPLES

Example 1

3,9-Dihydro-9-(4-methylphenyl)-furo[2,3-b][1,8]-naphthyridin-4(2H)-one

A solution of 4-hydroxy-3-(2-hydroxyethyl)-1-(4-methylphenyl)-1,6-naphthyridin-2(1H)-one (2.2 g) in Eaton's Reagent (10% P₂O₅ in methane sulfonic acid; 40 ml) was stirred in an atmosphere of nitrogen and heated to 70°C for 2 hr. After cooling, the product was poured into water, adjusted to pH 4 with NaHCO₃, filtered, washed with water, air dried and was recrystallized from isopropanol with decolorization to yield the product, m.p. 246—248.5°C.

Example 2

9-(3,4-Dichlorophenyl)-3,9-dihydro-2-methyl-furo[2,3-b][1,8]-naphthyridin-4(2H)-one

A solution of 1-(3,4-dichlorophenyl)-4-hydroxy-3-(2-hydroxypropyl)-1,8-naphthyridin-2(1H)-one (5 g) in Eaton's Reagent (10% P₂O₅ in methanesulfonic acid; 100 ml), under an atmosphere of nitrogen, was heated at 70°C for 2 hr. The mixture was cooled and poured into water. The pH was adjusted to 7 with NaHCO₃. The product was filtered off, washed with water, dried in air, and recrystallized from isopropanol/charcoal to yield the product, m.p. 218—220.5°C.

The following compounds may be similarly prepared by substituting the appropriate starting material and using the method of Example 1 or 2.

3,9-Dihydro-9-phenyl-furo[2,3-b][1,8]-naphthyridin-4(2H)-one, m.p. 245—247°C

3,9-Dihydro-2-methyl-9-phenyl-furo[2,3-b][1,8]-naphthyridin-4(2H)-one, m.p. 207—209°C

3,9-Dihydro-2-(n-butyl)-9-phenyl-furo[2,3-b][1,8]-naphthyridin-4(2H)-one, m.p. 169—170°C

3,9-Dihydro-9-(4-fluorophenyl)-furo[2,3-b][1,8]-naphthyridin-4(2H)-one, m.p. 244—246°C

3,9-Dihydro-2-methyl-9-(4-fluorophenyl)-furo[2,3-b][1,8]-naphthyridin-4(2H)-one, m.p. 195—197.5°C

3,9-Dihydro-2-(n-butyl)-9-(4-fluorophenyl)-furo[2,3-b][1,8]-naphthyridin-4(2H)-one

3,9-Dihydro-9-(4-chlorophenyl)-furo[2,3-b][1,8]-naphthyridin-4(2H)-one, m.p. 243—245°C

3,9-Dihydro-2-methyl-9-(4-chlorophenyl)-furo[2,3-b][1,8]-naphthyridin-4(2H)-one

3,9-Dihydro-9-(4-methoxyphenyl)-furo[2,3-b][1,8]-naphthyridin-4(2H)-one, m.p. 227—228°C

3,9-Dihydro-2-methyl-9-(4-methoxyphenyl)-furo[2,3-b][1,8]-naphthyridin-4(2H)-one

3,9-Dihydro-9-(3-methoxyphenyl)-furo[2,3-b][1,8]-naphthyridin-4(2H)-one

3,9-Dihydro-2-methyl-9-(3-methoxyphenyl)-furo[2,3-b][1,8]-naphthyridin-4(2H)-one, m.p. 194—196°C

3,9-Dihydro-9-(3-chlorophenyl)-furo[2,3-b][1,8]-naphthyridin-4(2H)-one, m.p. >260°C

3,9-Dihydro-9-(3,5-dichlorophenyl)-furo[2,3-b][1,8]-naphthyridin-4(2H)-one, m.p. 279—281°C (dec.)

3,9-Dihydro-2-methyl-9-(3,5-dichlorophenyl)-furo[2,3-b][1,8]-naphthyridin-4(2H)-one, m.p. 230—233°C

3,9-Dihydro-9-(2,3-dichlorophenyl)-furo[2,3-b][1,8]-naphthyridin-4(2H)-one

3,9-Dihydro-2-methyl-9-(2,3-dichlorophenyl)-furo[2,3-b][1,8]-naphthyridin-4(2H)-one

3,9-Dihydro-9-(2,5-dichlorophenyl)-furo[2,3-b][1,8]-naphthyridin-4(2H)-one

3,9-Dihydro-9-(3-chloro-4-fluorophenyl)-furo[2,3-b][1,8]-naphthyridin-4(2H)-one

3,9-Dihydro-2-methyl-9-(3-chloro-4-fluorophenyl)-furo[2,3-b][1,8]-naphthyridin-4(2H)-one

3,9-Dihydro-9-(3,4-dichlorophenyl)-furo[2,3-b][1,8]-naphthyridin-4(2H)-one, m.p. >260°C

2,3,4,10-Tetrahydro-10-phenyl-pyrano[2,3-b][1,8]-naphthyridin-5-one, m.p. 288—290°C (dec)

2,3,4,10-Tetrahydro-2-methyl-10-phenyl-pyrano[2,3-b][1,8]-naphthyridin-5-one

2,3,4,10-Tetrahydro-10-(4-fluorophenyl)-pyrano[2,3-b][1,8]-naphthyridin-5-one

2,3,4,10-Tetrahydro-10-(4-chlorophenyl)-pyrano[2,3-b][1,8]-naphthyridin-5-one, m.p. 268—270°C

2,3,4,10-Tetrahydro-10-(3,4-dichlorophenyl)-pyrano[2,3-b][1,8]-naphthyridin-5-one, m.p. >265°C

2,3,4,10-Tetrahydro-10-(4-methylphenyl)-pyrano[2,3-b][1,8]-naphthyridin-5-one, m.p. 276—279°C

2,3,4,10-Tetrahydro-10-(4-methoxyphenyl)-pyrano[2,3-b][1,8]-naphthyridin-5-one, m.p. 256—258°C

2,3,4,10-Tetrahydro-10-(3-methoxyphenyl)-pyrano[2,3-b][1,8]-naphthyridin-5-one

2,3,4,10-Tetrahydro-10-(3-chlorophenyl)-pyrano[2,3-b][1,8]-naphthyridin-5-one

2,3,4,10-Tetrahydro-10-(3-methoxyphenyl)-pyrano[2,3-b][1,8]-naphthyridin-5-one

7,8-Dihydro-5-phenyl-furo[3',2':5,6]pyrido[2,3-b]pyrazin-9(5H)-one

7,8-Dihydro-5-(4-fluorophenyl)-furo[3',2':5,6]pyrido[2,3-b]pyrazin-9(5H)-one

7,8-Dihydro-5-(4-chlorophenyl)-furo[3',2':5,6]pyrido[2,3-b]pyrazin-9(5H)-one

7,8-Dihydro-5-(4-methylphenyl)-furo[3',2':5,6]pyrido[2,3-b]pyrazin-9(5H)-one

7,8-Dihydro-5-(4-methoxyphenyl)-furo[3',2':5,6]pyrido[2,3-b]pyrazin-9(5H)-one

7,8-Dihydro-5-(3-methoxyphenyl)-furo[3',2':5,6]pyrido[2,3-b]pyrazin-9(5H)-one

7,8-Dihydro-5-(3-chlorophenyl)-furo[3',2':5,6]pyrido[2,3-b]pyrazin-9(5H)-one

5,7,8,9-Tetrahydro-5-phenyl-10H-pyrano[3',2':5,6]pyrido[2,3-b]pyrazin-10-one

5,7,8,9-Tetrahydro-7-methyl-5-phenyl-10H-pyrano[3',2':5,6]pyrido[2,3-b]pyrazin-10-one

5,7,8,9-Tetrahydro-5-(4-fluorophenyl)-10H-pyrano[3',2':5,6]pyrido[2,3-b]pyrazin-10-one

5,7,8,9-Tetrahydro-7-methyl-5-(4-fluorophenyl)-10H-pyrano[3',2':5,6]pyrido[2,3-b]pyrazin-10-one
 5,7,8,9-Tetrahydro-5-(3-methoxyphenyl)-10H-pyrano[3',2':5,6]pyrido[2,3-b]pyrazin-10-one
 5,7,8,9-Tetrahydro-5-(3-chlorophenyl)-10H-pyrano[3',2':5,6]pyrido[2,3-b]pyrazin-10-one
 5,7,8,9-Tetrahydro-7-methyl-5-(3-methoxyphenyl)-10H-pyrano[3',2':5,6]pyrido[2,3-b]pyrazin-10-one
 5,7,8,9-Tetrahydro-7-methyl-5-(3-chlorophenyl)-10H-pyrano[3',2':5,6]pyrido[2,3-b]pyrazin-10-one

Example 3

3,9-Dihydro-2-methyl-9-phenyl-furo[2,3-b][1,8]naphthyridin-4(2H)-one

A suspension of 4-hydroxy-3-(2-hydroxyphenyl)-1-phenyl-1,8-naphthyridin-2(1H)-one (1 g) in CH₂Cl₂ was stirred in an atmosphere of nitrogen. To this was added pyridine (1.5 ml). To this mixture was added a solution of SOCl₂ (1.5 ml) in CH₂Cl₂ (10 ml) dropwise over a period of 15 minutes. The mixture was stirred overnight at room temperature then water was added. The CH₂Cl₂ layer was separated, dried and evaporated. Recrystallization from isopropanol yielded the product, m.p. 207—209°C.

Example 4

5-(3,4-Dichlorophenyl)-3,5-dihydro-2-methyl-furo[3,2-c][1,8]naphthyridin-4(2H)-one

A solution of p-toluene sulfonic acid (5 g) in toluene (100 ml) was prepared. To this was added 1-(3,4-dichlorophenyl)-4-hydroxy-3-(2-hydroxypropyl)-1,8-naphthyridin-2(1H)-one (5 g) and the mixture was stirred and heated to reflux in an atmosphere of nitrogen. The mixture was refluxed for 18 hrs. The resulting solution was poured into water (200 ml), stirred for ½ hour then filtered. The solids were recrystallized from isopropanol to yield the product, m.p. 273—274°C.

Example 5

2-n-Butyl-3,5-dihydro-5-phenyl-furo[3,2-c][1,8]naphthyridin-4(2H)-one

A solution of 4-hydroxy-3-(2-hydroxyhexyl)-1-phenyl-1,8-naphthyridin-2(1H)-one (2 g) in 47% HBr was stirred in an atmosphere of nitrogen and heated to 80°C for 4½ hrs after which time it was cooled and poured into water. The precipitate was filtered off, washed with water, dried in air, recrystallized from ethanol/charcoal to yield the product m.p. 179—180°C.

Example 6

2-Methyl-3,5-dihydro-5-phenyl-furo[3,2-c][1,8]naphthyridin-4(2H)-one

A solution of 4-hydroxy-3-(2-hydroxypropyl)-1-phenyl-1,8-naphthyridin-2(1H)-one (8.9 g; 0.03 mole) in 47% HBr (90 ml) was stirred in an atmosphere of nitrogen. The solution was heated to 90°C for 4½ hrs then was allowed to cool, poured into water and was adjusted to pH 4.5 with sodium acetate. The product was filtered off, washed with water, dried in air and recrystallized from CHCl₃/isopropanol to yield the product, m.p. 223—224°C.

Example 7

6-Phenyl-2,3,4,6-tetrahydro-pyrano[3,2-c][1,8]naphthyridin-5-one

A suspension of 4-hydroxy-3-(3-hydroxypropyl)-1-phenyl-1,8-naphthyridin-2(1H)-one (5.67 g) in 47% HBr (50 ml) was stirred in an atmosphere of nitrogen and was heated to 90°C for 5 hrs. After cooling, the product was poured into water, and the pH was adjusted to 4.5 with potassium acetate. Chromatographic purification of the product on silica gel eluting with CH₂Cl₂: 5% ether and subsequent recrystallization of the product from the relevant fractions yielded the product, m.p. 253—255°C.

Example 8

3,5-Dihydro-5-phenyl-furo[3,2-c][1,8]naphthyridin-4(2H)-one

A solution of 4-hydroxy-3-(2-hydroxyethyl)-1-phenyl-1,8-naphthyridin-2(1H)-one (10 g) in 30% (v/v) sulfuric acid (200 ml) was heated to reflux, in an atmosphere of nitrogen, and was held at reflux until no further reaction occurred (ca. 5—8 hrs). After cooling, the solution was added slowly and carefully to an ice-cooled solution of sodium hydroxide (50% solution; 200 ml). The mixture was allowed to stand overnight and was then filtered. The product was washed with water, dried in air and recrystallized from dimethyl-formamide/water, with charcoal treatment, to yield the product, m.p. 276—277.5°C.

The following compounds may be similarly prepared by substituting the appropriate starting material and using the method of Examples 5, 6, 7 or 8.

3,5-Dihydro-5-(4-chlorophenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one, m.p. >260°C
 3,5-Dihydro-2-methyl-5-(4-chlorophenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one
 3,5-Dihydro-2-ethyl-5-(4-chlorophenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one
 3,5-Dihydro-2-(n-propyl)-5-(4-chlorophenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one
 3,5-Dihydro-2-(n-butyl)-5-(4-chlorophenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one
 3,5-Dihydro-2-ethyl-5-phenyl-furo[3,2-c][1,8]naphthyridin-4(2H)-one
 3,5-Dihydro-2-(n-propyl)-5-phenyl-furo[3,2-c][1,8]naphthyridin-4(2H)-one
 3,5-Dihydro-2-(iso-butyl)-5-phenyl-furo[3,2-c][1,8]naphthyridin-4(2H)-one
 3,5-Dihydro-2,2-dimethyl-5-phenyl-furo[3,2-c][1,8]naphthyridin-4(2H)-one, m.p. 216—217.5°C
 3,5-Dihydro-5-(4-fluorophenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one, m.p. >260°C
 3,5-Dihydro-2-methyl-5-(4-fluorophenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one, m.p. 252—254°C

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- 3,5-Dihydro-2-ethyl-5-(4-fluorophenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one
- 3,5-Dihydro-2-(n-propyl)-5-(4-fluorophenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one
- 3,5-Dihydro-2-(n-butyl)-5-(4-fluorophenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one
- 3,5-Dihydro-5-(4-methylphenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one, m.p. 258.5—260°C
- 3,5-Dihydro-2-methyl-5-(4-methylphenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one
- 3,5-Dihydro-2-(n-butyl)-5-(4-methylphenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one
- 3,5-Dihydro-5-(4-methoxyphenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one, m.p. 282—284°C
- 3,5-Dihydro-2-methyl-5-(4-methoxyphenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one
- 3,5-Dihydro-2-(n-butyl)-5-(4-methoxyphenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one
- 3,5-Dihydro-5-(3,4-dichlorophenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one, m.p. 256.5—258°C
- 3,5-Dihydro-2-methyl-5-(3,4-dichlorophenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one, m.p. 273—274°C
- 3,5-Dihydro-2-(n-butyl)-5-(3,4-dichlorophenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one
- 3,5-Dihydro-5-(3-methoxyphenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one
- 3,5-Dihydro-2-methyl-5-(3-methoxyphenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one, m.p. >260°C
- 3,5-Dihydro-2-(n-butyl)-5-(3-methoxyphenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one
- 3,5-Dihydro-5-(3,5-dichlorophenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one, m.p. 283—284°C
- 3,5-Dihydro-2-methyl-5-(3,5-dichlorophenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one, m.p. 254—256°C
- 3,5-Dihydro-5-(2,3-dichlorophenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one
- 3,5-Dihydro-2-methyl-5-(2,3-dichlorophenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one
- 3,5-Dihydro-5-(2,5-dichlorophenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one
- 3,5-Dihydro-2-methyl-5-(2,5-dichlorophenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one
- 3,5-Dihydro-5-(3-chloro-4-fluorophenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one
- 3,5-Dihydro-2-methyl-5-(3-chloro-4-fluorophenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one
- 3,5-Dihydro-5-(3-chlorophenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one, m.p. 205—207°C
- 3,5-Dihydro-2-methyl-5-(3-chlorophenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one, m.p. 254—256°C
- 3,5-Dihydro-2-methyl-5-(3-methylsulfonylaminophenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one, m.p. 258—260°C
- 3,5-Dihydro-5-(3-methylsulfonylaminophenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one, m.p. >260°C
- 2,3,4,6-Tetrahydro-6-phenyl-pyrano[3,2-c][1,8]naphthyridin-5-one, m.p. 253—255°C
- 2,3,4,6-Tetrahydro-2-methyl-6-phenyl-pyrano[3,2-c][1,8]naphthyridin-5-one
- 2,3,4,6-Tetrahydro-6-(4-fluorophenyl)-pyrano[3,2-c][1,8]naphthyridin-5-one
- 2,3,4,6-Tetrahydro-6-(4-chlorophenyl)-pyrano[3,2-c][1,8]naphthyridin-5-one, m.p. 236—237°C
- 2,3,4,6-Tetrahydro-6-(3,4-dichlorophenyl)-pyrano[3,2-c][1,8]naphthyridin-5-one, m.p. >265°C
- 2,3,4,6-Tetrahydro-6-(4-methylphenyl)-pyrano[3,2-c][1,8]naphthyridin-5-one, m.p. >280°C
- 2,3,4,6-Tetrahydro-6-(4-methoxyphenyl)-pyrano[3,2-c][1,8]naphthyridin-5-one, m.p. >270°C
- 2,3,4,6-Tetrahydro-6-(3-methoxyphenyl)-pyrano[3,2-c][1,8]naphthyridin-5-one
- 2,3,4,6-Tetrahydro-6-(3-chlorophenyl)-pyrano[3,2-c][1,8]naphthyridin-5-one
- 2,3,4,6-Tetrahydro-6-(3,5-dichlorophenyl)-pyrano[3,2-c][1,8]naphthyridin-5-one
- 2,3,4,6-Tetrahydro-6-(2,3-dichlorophenyl)-pyrano[3,2-c][1,8]naphthyridin-5-one
- 2,3,4,6-Tetrahydro-6-(2,5-dichlorophenyl)-pyrano[3,2-c][1,8]naphthyridin-5-one
- 2,3,4,6-Tetrahydro-6-(3-chloro-4-fluorophenyl)-pyrano[3,2-c][1,8]naphthyridin-5-one
- 7,8-Dihydro-5-phenyl-furo[2',3':4,5]pyrido[2,3-b]pyrazin-6(5H)-one
- 7,8-Dihydro-8-methyl-5-phenyl-furo[2',3':4,5]pyrido[2,3-b]pyrazin-6(5H)-one
- 7,8-Dihydro-8-(n-butyl)-5-phenyl-furo[2',3':4,5]pyrido[2,3-b]pyrazin-6(5H)-one
- 7,8-Dihydro-5-(4-fluorophenyl)-furo[2',3':4,5]pyrido[2,3-b]pyrazin-6(5H)-one
- 7,8-Dihydro-8-methyl-5-(4-fluorophenyl)-furo[2',3':4,5]pyrido[2,3-b]pyrazin-6(5H)-one
- 7,8-Dihydro-5-(4-chlorophenyl)-furo[2',3':4,5]pyrido[2,3-b]pyrazin-6(5H)-one
- 7,8-Dihydro-5-(4-methylphenyl)-furo[2',3':4,5]pyrido[2,3-b]pyrazin-6(5H)-one
- 7,8-Dihydro-5-(4-methoxyphenyl)-furo[2',3':4,5]pyrido[2,3-b]pyrazin-6(5H)-one
- 7,8-Dihydro-5-(3-methoxyphenyl)-furo[2',3':4,5]pyrido[2,3-b]pyrazin-6(5H)-one
- 7,8-Dihydro-8-methyl-5-(3-methoxyphenyl)-furo[2',3':4,5]pyrido[2,3-b]pyrazin-6(5H)-one

Example 9

5-(3,4-Dichlorophenyl)-3,5-dihydro-2-methyl-furo[3,2-c][1,8]naphthyridin-4(2H)-one
To a solution of 9-(3,4-dichlorophenyl)-3,9-dihydro-2-methyl-furo[2,3-b][1,8]naphthyridin-4(2H)-one (125 mg) (prepared as in example 2) in dimethylacetamide (20 ml) in an atmosphere of nitrogen was added sodium iodide (250 mg). The solution was refluxed for 4 hrs, and it was poured over ice-water, filtered, dried and recrystallized from isopropanol to yield the desired product, m.p. 273—274°C.

Example 10

A mixture of 4-hydroxy-3-(2'-hydroxyethyl) 1-phenyl-1,8-naphthyridin-2(1H)-one (3 g) and 2,4-bis (4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane-2,4-disulfide (also known as Lawesson's Reagent) (4.3 g) in toluene (100 ml) was stirred in an atmosphere of nitrogen and heated to reflux. The mixture was refluxed for 20 hr after which it was cooled, evaporated, dissolved in CH₂Cl₂, washed with water, dried, and chromatographed over silica gel, eluting with increasing concentrations of ethyl acetate (0—5%) in CH₂Cl₂.

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Three products were isolated and characterised as follows:

1st compound eluted: 3,5-Dihydro-5-phenyl-thieno[3,2-c][1,8]naphthyridin-4(2H)-thione, m.p. 275—276.5°C.

2nd compound eluted: 3,5-Dihydro-5-phenyl-furo[3,2-c][1,8]naphthyridin-4(2H)-thione, m.p. 243—245.5°C.

3rd compound eluted: 3,9-Dihydro-9-phenyl-thieno[2,3-b][1,8]naphthyridin-4(2H)-thione, m.p. 264—266°C (dec).

In a similar manner, application of this procedure to other compounds having structural formula II would lead to the preparation of analogous products to those described in this Example.

Example 11

3,5-Dihydro-5-(4-methoxyphenyl)-furo[3,2-c][1,8]naphthyridin-4(2H)-one

A solution of 3,9-dihydro-9-(4-methoxyphenyl)-furo[2,3-b][1,8]naphthyridin-4(2H)-one (1 g) and sodium iodide (1 g) in dry dimethylacetamide (10 ml) was heated to 70°C for 4 hr in a nitrogen atmosphere. The product was cooled, poured over ice-water, filtered, dried and recrystallized from CH₂Cl₂ to yield the desired product, m.p. 282—284°C.

Essentially any of the products, prepared according to the procedures of Examples 1 and 2, and in which a methylene group is next to the ring oxygen atom may be converted by this process into the products which may otherwise be prepared according to the procedures of Examples 5, 6, 7 and 8.

Example 12

3,5-Dihydro-5-phenyl-furo[3,2-c][1,8]naphthyridin-4(2H)-thione

A suspension of 3,5-dihydro-5-phenyl-furo[3,2-c][1,8]naphthyridin-4(2H)-one (3 g) and 2,4-bis-(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane-2,4-disulfide (Lawesson's Reagent; 5 g) in dry toluene (100 ml) was stirred in an atmosphere of nitrogen and heated to reflux for 6 hrs. After cooling, the organic layer was washed with water, dried and evaporated. The product was purified by chromatography over silica gel in CH₂Cl₂ containing increasing amounts of ethyl acetate (0—5%). The fractions containing pure product were combined, evaporated, suspended in ethanol, filtered and dried to yield the desired product, m.p. 242—244.5°C.

In a similar manner, other compounds produced according to Examples 5, 6, 7 or 8 may be converted to their thione analogs by this process.

Example 13

3,9-Dihydro-9-phenyl-thieno[2,3-b][1,8]naphthyridin-4(2H)-one

A solution of 3,5-dihydro-5-phenyl-furo[3,2-c][1,8]naphthyridin-4(2H)-thione (500 mg) and sodium iodide (500 mg) in dry dimethylacetamide (5 ml) was stirred in an atmosphere of nitrogen and heated at 125° for 2 hr. After cooling, the solution was poured into ice-water, filtered, washed with water and dried to yield the desired product, m.p. 260—261°C.

Similarly may be prepared other such derivatives from the corresponding starting materials prepared according to the method of Example 12.

Example 14

5-Phenyl-furo[3,2-c][1,8]naphthyridin-4(5H)-one

A mixture of 3,5-dihydro-5-phenyl-furo[3,2-c][1,8]naphthyridin-4(2H)-one (2 g) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ; 2 g) in dry toluene (50 ml) was stirred in an atmosphere of nitrogen and heated to reflux. Refluxing was continued for 20 hrs. After cooling somewhat the mixture was evaporated, dissolved in CH₂Cl₂, filtered and chromatographed on silica gel eluting with increasing concentrations of ethyl acetate in CH₂Cl₂ (0—10%). Evaporation of the relevant fractions and recrystallization from acetonitrile yielded the desired product, m.p. 245—247°C.

In a similar manner, any of the tricyclic-dihydro-furo derivatives may be oxidized to the corresponding furo-derivative.

Example 15

3,9-Dihydro-9-phenyl-furo[2,3-b][1,8]naphthyridin-4(2H)-thione

To a stirred suspension of 3,9-dihydro-9-phenyl-furo[2,3-b][1,8]naphthyridin-4(2H)-one (1 g) in dry toluene (40 ml) at 55°C, under an atmosphere of dry nitrogen, was added a suspension of 2,4-bis-(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane-2,4-disulfide (Lawesson's Reagent; 0.8 g) in dry toluene (10 ml). The reaction was followed by t.l.c. (silica gel/CH₂Cl₂: 5% Methanol) and warming was continued until no starting material remained (ca. 2½ hr). Toluene was removed under reduced pressure and the product was dissolved in CH₂Cl₂. The solution was separated by chromatography on silica gel eluting with increasing concentrations of ethyl acetate in CH₂Cl₂ (2%—5%). The desired product was obtained as an orange-yellow solid, m.p. ca. 273—275°C (dec.).

Similarly, application of this procedure to other compounds having structural formula I'', prepared according to the procedures of Examples 1 or 2, will produce the thione analogs of compounds described in those examples.

Example 16

3,5-Dihydro-5-phenyl-thieno[3,2-c][1,8]naphthyridin-4(2H)-one

A solution of 3,5-dihydro-9-phenyl-furo[2,3-b][1,8]naphthyridin-4(2H)-thione (500 mg) and sodium

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iodide (500 mg) in dry dimethylacetamide (5 ml) was stirred in an atmosphere of nitrogen and heated to 100°C for 2 hrs. After cooling, the solution was poured into ice water, filtered, washed with water, dried and recrystallized from isopropanol to yield the desired product, m.p. 277—279°C.

In a similar manner may be prepared other such derivatives from the corresponding starting materials prepared according to the method of Example 15.

Examples of such compounds are:

- 3,5-Dihydro-2-methyl-5-phenyl-thieno[3,2-c][1,8]-naphthyridin-4(2H)-one
- 3,5-Dihydro-5-(4-fluorophenyl)-thieno[3,2-c][1,8]-naphthyridin-4(2H)-one
- 3,5-Dihydro-2-methyl-5-(4-fluorophenyl)-thieno[3,2-c][1,8]-naphthyridin-4(2H)-one
- 3,5-Dihydro-5-(3-chlorophenyl)-thieno[3,2-c][1,8]-naphthyridin-4(2H)-one
- 3,5-Dihydro-2-methyl-5-(3-chlorophenyl)-thieno[3,2-c][1,8]-naphthyridin-4(2H)-one
- 3,5-Dihydro-5-(3-methoxyphenyl)-thieno[3,2-c][1,8]-naphthyridin-4(2H)-one
- 3,5-Dihydro-2-methyl-5-(3-methoxyphenyl)-thieno[3,2-c][1,8]-naphthyridin-4(2H)-one
- 3,5-Dihydro-5-(3-methylthiophenyl)-thieno[3,2-c][1,8]-naphthyridin-4(2H)-one
- 3,5-Dihydro-5-(3,5-dichlorophenyl)-thieno[3,2-c][1,8]-naphthyridin-4(2H)-one
- 3,5-Dihydro-2-methyl-5-(3,5-dichlorophenyl)-thieno[3,2-c][1,8]-naphthyridin-4(2H)-one
- 3,5-Dihydro-5-(3-chloro-4-fluorophenyl)-thieno[3,2-c][1,8]-naphthyridin-4(2H)-one
- 3,5-Dihydro-2-methyl-5-(3-chloro-4-fluorophenyl)-thieno[3,2-c][1,8]-naphthyridin-4(2H)-one
- 3,5-Dihydro-5-(4-chlorophenyl)-thieno[3,2-c][1,8]-naphthyridin-4(2H)-one
- 3,5-Dihydro-5-(4-methylphenyl)-thieno[3,2-c][1,8]-naphthyridin-4(2H)-one
- 3,5-Dihydro-5-(4-methoxyphenyl)-thieno[3,2-c][1,8]-naphthyridin-4(2H)-one
- 3,5-Dihydro-5-(3,4-dichlorophenyl)-thieno[3,2-c][1,8]-naphthyridin-4(2H)-one

Example 17

7-Phenyl-3,4,5,7-tetrahydro-oxepino[3,2-c][1,8]-naphthyridin-6(2H)-one
The mono-mesylate (1 g) from Preparative Example 7 was dissolved in DMF (20 ml) at R.T. and cesium carbonate (2 g) was added. The reaction was followed by HPLC or TLC until essentially no starting material remained (ca. 1 hr). A mixture of two products was formed. The total product was poured into ice-water and the product was filtered off. The two products were separated by column chromatography [Whatman LPS-2 silica gel; CH₂Cl₂ + 0—5% MeOH] or by preparative reversed-phase HPLC [Whatman Partisil 40; ODS-3; Magnum 40 column] and the desired fractions isolated. Evaporation yielded 7-phenyl-3,4,5,7-tetrahydro-oxepino[3,2-c][1,8]naphthyridin-6(2H)-one m.p. 180—181°C.

The following compounds may be prepared similarly by substituting the appropriate starting material from Preparative Example 6.

- 7-(4-Chlorophenyl)-3,4,5,7-tetrahydro-oxepino[3,2-c][1,8]naphthyridin-6(2H)-one, m.p. 241—243°C;
- 7-(3-Chlorophenyl)-3,4,5,7-tetrahydro-oxepino[3,2-c][1,8]naphthyridin-6(2H)-one, m.p. 151—153°C;
- 7-(3-Methoxyphenyl)-3,4,5,7-tetrahydro-oxepino[3,2-c][1,8]naphthyridin-6(2H)-one, m.p. 223—224.5°C;
- and
- 7-(3-Hydroxyphenyl)-3,4,5,7-tetrahydro-oxepino[3,2-c][1,8]naphthyridin-6(2H)-one, m.p. >260°C

PREPARATIVE EXAMPLES

Preparative Example 1

3-(2-Hydroxyethyl)-4-hydroxy-1-phenyl-1,8-naphthyridin-2(1H)-one
To a solution of 6.8 g of methyl 2-phenylamino-3-pyridine carboxylate in 60 ml of gamma-butyrolactone there was added, under nitrogen, 13.4 g of potassium tertiary butoxide. The reaction mixture was heated and stirred for one hour at 95°C, poured on ice and stirred overnight. The mixture was extracted with ether, the aqueous layer acidified with acetic acid to pH 4.5 and the product was collected by filtration. Recrystallization from chloroform, acetone, isopropanol yielded the product of this example as a colorless solid; m.p. 235—236°C.

According to this procedure, or an art-recognized modification thereof, any of the 2-hydroxyethyl side-chain materials used as starting materials in the reactions described in Examples 1—8 may be prepared.

Preparative Example 2

Methyl-2-phenylamino-3-pyrazine carboxylate

(A) Methyl 2-bromo-3-pyrazine carboxylate:

To a stirred mixture of 12.7 g of methyl 2-amino pyrazine carboxylate and 47 ml of 48% hydrobromic acid there was added, dropwise, 12.6 ml of bromine keeping the temperature at 0°. A solution of 14.4 g of sodium nitrite in 60 ml of water was then added, dropwise, at 0° and the reaction mixture stirred for 15 minutes. The reaction mixture was basified to pH 8 with sodium bicarbonate and extracted with ethyl acetate and again with chloroform. The organic layers were dried over magnesium sulfate, filtered and concentrated to a yellow oil. Recrystallization from ether-hexane yielded the product, m.p. 43—45°C.

(B) Methyl 2-phenylamino-3-pyrazine carboxylate:

A mixture of 9.5 g of methyl 2-bromo-3-pyrazine carboxylate, 8.2 g of aniline, 0.5 g of p-toluene sulfonic acid and 100 ml of water was stirred and refluxed for two hours. The reaction mixture was poured

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on ice, extracted with ethyl acetate, the organic extracts were dried and concentrated to yield an oil. The crude residue was eluted on a silica gel column with ethyl acetate-hexane (1:2) yielding the product of this example as a yellow solid, m.p. 72—75°C.

Preparative Example 3

4-Hydroxy-3-(3-hydroxypropyl)-1-(4-methoxyphenyl)-1,8-naphthyridin-2(1H)-one

A mixture of delta-valerolactone (120 ml), ethyl 2-(4-methoxyphenylamino)nicotinate (12 g) and potassium *t*-butoxide (24 g) was stirred and heated in an atmosphere of nitrogen to 100°C for 2 hrs. After cooling, the mixture was poured into 1000 ml of 5% KOH solution and stirred overnight. The aqueous solution was extracted with ether (2 × 250 ml) which was discarded. The aqueous solution was then acidified to pH 4.5 with conc. HCl. The product was filtered off, washed with water, dried in air and recrystallized from CHCl₃/isopropanol to yield the desired product, m.p. 229—231°C.

According to this procedure, or an art-recognized modification thereof, any of the 3-hydroxypropyl side-chain materials used as starting materials in the reactions described in Examples 1—8 may be prepared.

Preparative Example 4

1-(3,4-Dichlorophenyl)-4-hydroxy-3-(2-hydroxypropyl)-1,8-naphthyridin-2(1H)-one

A stirred mixture of gamma-valerolactone (40 g), ethyl 2-(3,4-dichlorophenylamino)-nicotinate (20 g) and potassium *t*-butoxide (30 g) was warmed in an atmosphere of nitrogen to 110°C and kept there for 5 hr. After cooling somewhat the product was poured into 1000 ml of 5% KOH solution and was allowed to stir overnight. The basic solution was extracted with ether (2 × 500 ml) and the aqueous solution was acidified to pH 5 with conc. HCl. The solid was filtered off, washed with water, dried in air then recrystallized from methanol/charcoal to yield the desired product, m.p. 232—234°C.

This procedure or an art-recognized modification thereof may be used to prepare any of the 2-hydroxy-propyl side-chain starting materials for use in Examples 1—8.

Preparative Example 5

4-Hydroxy-3-(2-hydroxyhexyl)-1-phenyl-1,8-naphthyridin-2(1H)-one

A mixture of methyl 2-phenylaminonicotinate (5 g), gamma-octanoic lactone (10 g) and potassium *t*-butoxide (7.5 g) was stirred in a nitrogen atmosphere and heated to 95°C where it was held for 6 hrs. After cooling, the mixture was poured into 5% NaOH (200 ml) and stirred overnight. Acidification to pH 4.6 yielded an oil, which was extracted with ether, washed with water, dried (Na₂SO₄), filtered, and evaporated to a small volume. Hexane was added until turbidity was noticed, and the mixture was allowed to stand for about 5 hrs. The solid was filtered off and recrystallized from CH₂Cl₂/isopropanol/isopropyl ether to produce the desired product, m.p. 184—186°C.

This process, or an art-recognized modification thereof may be used to prepare any of the 2-hydroxy-hexyl side-chain starting materials for use in Examples 1—8.

In general, by following the procedures described in Preparative Examples 1, 4, 5 or 6, or an art-recognized modification thereof, using lactones with desired substituents, other intermediates, II (B = O), useful for conversion to the products of the invention according to one of the methods described in Examples 1—8 and 10 may be prepared.

Preparative Example 6

4-Hydroxy-3-(4-hydroxybutyl)-1-phenyl-1,8-naphthyridin-2(1H)-one

A mixture of methyl 2-phenylamino-nicotinate (100 g), epsilon-caprolactone (1000 g) and potassium *t*-butoxide (200 g) was stirred at room temperature, in a nitrogen atmosphere, for ½ hr. It was heated at 45°C for 1 hr then at 85°C for 2 hr and finally at 105°C for 3 hr.

The hot mixture was poured carefully into 8 L of 5% KOH solution and was stirred overnight.

The mixture was extracted with 2 L of ether and the aqueous phase was retained. It was extracted again with a fresh 2 L of ether. The clear aqueous phase was adjusted to pH 4.5 with conc. HCl to yield a white solid which was filtered off, washed with water and dried to yield 4-hydroxy-3-(4-hydroxybutyl)-1-phenyl-1,8-naphthyridin-2(1H)-one, m.p. 205.5—206°C (from isopropanol).

By substituting the relevant ester and lactone in this preparative example intermediates to many other compounds of the invention may be prepared.

Preparative Example 7

4-Hydroxy-3-(4-methanesulfonyloxybutyl)-1-phenyl-1,8-naphthyridin-2(1H)-one

4-Hydroxy-3-(4-hydroxybutyl)-1-phenyl-1,8-naphthyridin-2(1H)-one (10 g) was dissolved, with stirring, in Eaton's Reagent (10% P₂O₅ in methanesulfonic acid; 50 ml) under a nitrogen atmosphere. The solution was heated to 55°C where it was held for 3½ hr. It was then cooled and poured into a water/ice mixture. After stirring for several hours, the aqueous mixture was extracted (3x) with ethyl acetate (250 ml each). The organic extract was separated, dried (Na₂SO₄), filtered and evaporated. The residue was stirred with a small volume of cold isopropanol and filtered to yield a brown solid, the mono-mesylate, which was used without further purification in Example 7.

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Preparative Example 8

2-(2-Chloro-3-nicotinoyl)-gamma-butyrolactone

A 1 M solution of lithium bis(trimethylsilyl)amide (260 ml; in hexane) was cooled to below -60°C in a nitrogen atmosphere. To this was added a solution of gamma-butyrolactone (25.8 g) in tetrahydrofuran (40 ml) keeping the temperature below -60°C . The mixture was stirred for 1 hr, then to it was added a solution of ethyl 2-chloro-nicotinate (37.2 g) in tetrahydrofuran (60 ml) keeping the reaction temperature below -60°C . After stirring for 2 hrs, the reaction mixture was allowed to warm to room temperature and it was kept there overnight. Most of the solvent was removed then 500 g of ice was added to the residue. The aqueous layer was adjusted to pH 5 and was then extracted with methylene chloride (3×500 ml). The dried methylene chloride extract was evaporated to an oil which was purified by preparative high pressure liquid chromatography separation (Whatman Magnum 40 column; Partisil 40, ODS-3; $\text{CH}_3\text{CN}(25): \text{H}_2\text{O}(75): \text{CH}_3\text{CO}_2\text{H}(1)$) to yield the desired product, m.p. $50-52^{\circ}\text{C}$.

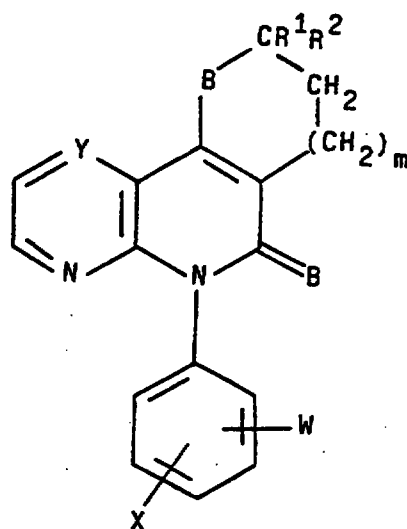
Preparative Example 9

4-Hydroxy-3-(2-hydroxyethyl)-1-(3-nitrophenyl)-1,8-naphthyridin-2(1H)-one

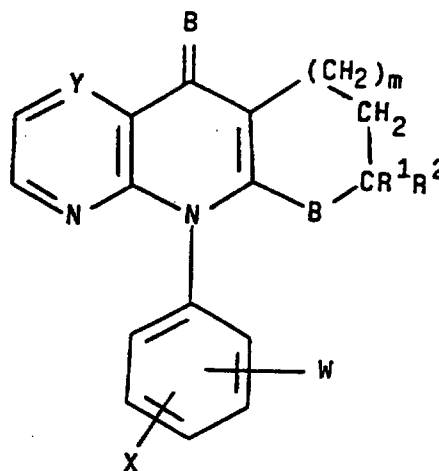
A mixture of 2-(2-chloro-3-nicotinoyl)-gamma-butyrolactone (Preparative Example 8) (3 g) and m-nitroaniline (3.67 g) in methanol (50 ml) was stirred in a nitrogen atmosphere and heated to an oil bath temperature of 130°C . The methanol was allowed to distil off. After $1\frac{1}{2}-2$ hr, the mixture was allowed to cool. To the product was added 10% potassium hydroxide solution (200 ml) and the mixture was stirred overnight. After adjusting the pH to 5.5, the solid product was filtered off, washed with water, dried, and recrystallized from isopropanol to yield the desired product, m.p. $244-245^{\circ}\text{C}$. Conversion of this material to compounds of the invention may be accomplished by utilizing the procedures described in the Examples.

Claims for the Contracting States: BE CH DE FR GB IT LI LU NL SE

1. A compound having the structural formula A' or A''



A'



A''

wherein

B is independently oxygen or sulfur;

R^1 and R^2 may be the same or different and are hydrogen or alkyl having from 1 to 6 carbon atoms;

m is 0, 1 or 2;

W and X may be the same or different and are hydrogen, hydroxy, alkyl having from 1 to 6 carbon atoms, halogen, nitro, alkoxy having from 1 to 6 carbon atoms, or NHR^a (wherein R^a is alkyl having from 1 to 6 carbon atoms); and

Y is CH or N.

2. The compounds defined in claim 1 wherein Y is CH.

3. The compounds defined in claim 2 having the structural formula:

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Preparative Example 8

2-(2-Chloro-3-nicotinoyl)-gamma-butyrolactone

A 1 M solution of lithium bis(trimethylsilyl)amide (260 ml; in hexane) was cooled to below -60°C in a nitrogen atmosphere. To this was added a solution of gamma-butyrolactone (25.8 g) in tetrahydrofuran (40 ml) keeping the temperature below -60°C . The mixture was stirred for 1 hr, then to it was added a solution of ethyl 2-chloro-nicotinate (37.2 g) in tetrahydrofuran (60 ml) keeping the reaction temperature below -60°C . After stirring for 2 hrs, the reaction mixture was allowed to warm to room temperature and it was kept there overnight. Most of the solvent was removed then 500 g of ice was added to the residue. The aqueous layer was adjusted to pH 5 and was then extracted with methylene chloride (3×500 ml). The dried methylene chloride extract was evaporated to an oil which was purified by preparative high pressure liquid chromatography separation (Whatman Magnum 40 column; Partisil 40, ODS-3; $\text{CH}_3\text{CN}(25): \text{H}_2\text{O}(75): \text{CH}_3\text{CO}_2\text{H}(1)$) to yield the desired product, m.p. $50-52^{\circ}\text{C}$.

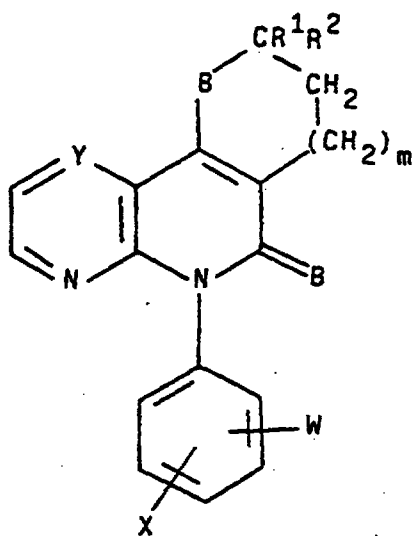
Preparative Example 9

4-Hydroxy-3-(2-hydroxyethyl)-1-(3-nitrophenyl)-1,8-naphthyridin-2(1H)-one

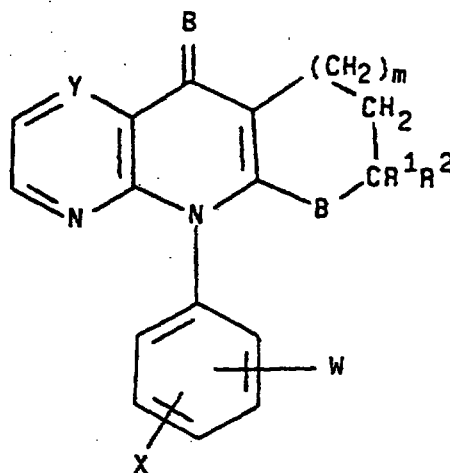
A mixture of 2-(2-chloro-3-nicotinoyl)-gamma-butyrolactone (Preparative Example 8) (3 g) and m-nitroaniline (3.67 g) in methanol (50 ml) was stirred in a nitrogen atmosphere and heated to an oil bath temperature of 130°C . The methanol was allowed to distil off. After $1\frac{1}{2}-2$ hr, the mixture was allowed to cool. To the product was added 10% potassium hydroxide solution (200 ml) and the mixture was stirred overnight. After adjusting the pH to 5.5, the solid product was filtered off, washed with water, dried, and re-crystallized from isopropanol to yield the desired product, m.p. $244-245^{\circ}\text{C}$. Conversion of this material to compounds of the invention may be accomplished by utilizing the procedures described in the Examples.

Claims for the Contracting States: BE CH DE FR GB IT LI LU NL SE

1. A compound having the structural formula A' or A''



A'



A''

wherein

B is independently oxygen or sulfur;

R¹ and R² may be the same or different and are hydrogen or alkyl having from 1 to 6 carbon atoms; m is 0, 1 or 2;

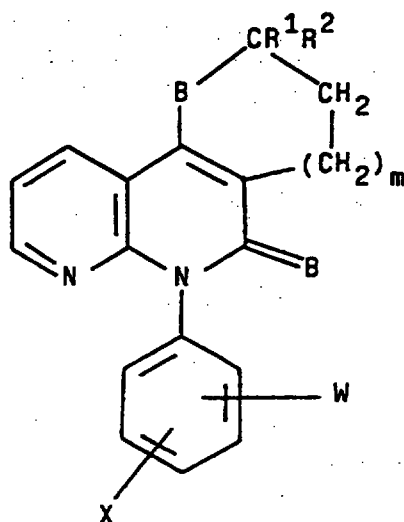
W and X may be the same or different and are hydrogen, hydroxy, alkyl having from 1 to 6 carbon atoms, halogen, nitro, alkoxy having from 1 to 6 carbon atoms, or NHR^a (wherein R^a is alkyl having from 1 to 6 carbon atoms); and

Y is CH or N.

2. The compounds defined in claim 1 wherein Y is CH.

3. The compounds defined in claim 2 having the structural formula:



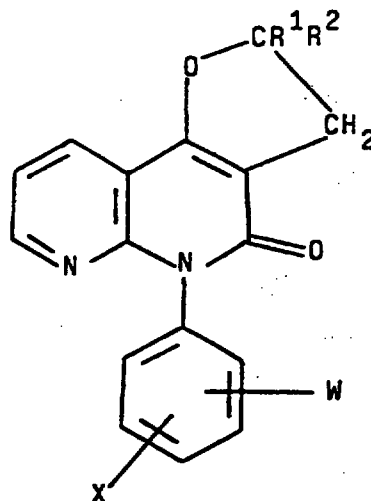


wherein B, W, X, R¹, R² and m are as defined in claim 1.

4. The compounds defined in claim 3 wherein m is 0 or 2.

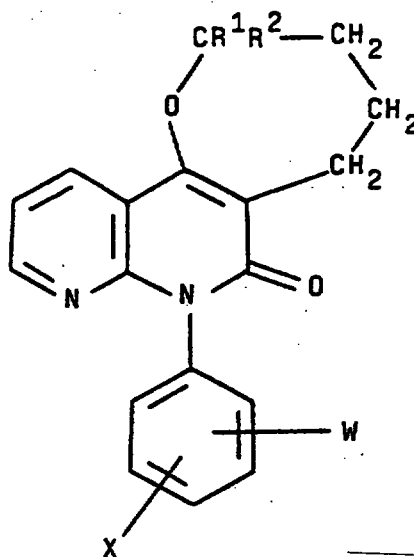
5. The compounds defined in claim 4 wherein B is oxygen.

6. The compounds defined in claim 5 having the structural formula:



wherein W, X, R¹ and R² are as defined in claim 1.

7. The compounds defined in claim 5 having the structural formula:



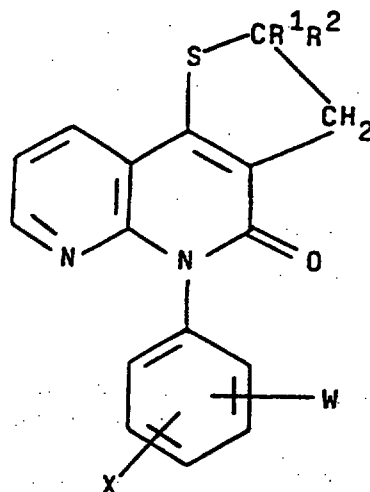
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wherein W, X, R¹ and R² are as defined in claim 1.

8. The compounds defined in claim 6 or 7 wherein R¹ and R² are hydrogen or methyl.

9. The compounds defined in claim 8 wherein R¹ is methyl and R² is hydrogen.

10. The compounds defined in claim 4 having the structural formula:



wherein X and W are as defined in claim 1.

11. The compounds defined in claim 10 wherein W is 3-chloro and X is hydrogen, chlorine or fluorine.

12. The compounds defined in claim 10 wherein W is 3-methoxy and X is hydrogen or fluorine.

13. The compounds defined in claim 10 wherein W and X are both hydrogen.

14. The compounds defined in claim 1 having the names:

3,5-dihydro-5-phenyl-furo[3,2-c][1,8]naphthyridin-4[2H]-one;

2-methyl-3,5-dihydro-5-phenyl-furo[3,2-c][1,8]naphthyridin-4[2H]-one;

3,5-dihydro-5-(p-methylphenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-one;

3,5-dihydro-5-(p-fluorophenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-one;

3,5-dihydro-5-(m-methoxyphenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-one;

3,5-dihydro-5-(3,4-dichlorophenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-one;

3,5-dihydro-5-(3,4-dichlorophenyl)-2-methyl-furo[3,2-c][1,8]naphthyridin-4[2H]-one;

3,5-dihydro-5-(4-chlorophenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-one;

3,5-dihydro-5-(3-chlorophenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-one;

3,5-dihydro-5-(3-chlorophenyl)-2-methyl-furo[3,2-c][1,8]naphthyridin-4[2H]-one;

3,5-dihydro-5-(4-fluorophenyl)-2-methyl-furo[3,2-c][1,8]naphthyridin-4[2H]-one;

3,5-dihydro-5-(3-methoxyphenyl)-2-methyl-furo[3,2-c][1,8]naphthyridin-4[2H]-one;

3,5-dihydro-5-(3,5-dichlorophenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-one; and

3,5-dihydro-5-(3,5-dichlorophenyl)-2-methyl-furo[3,2-c][1,8]naphthyridin-4[2H]-one.

15. The compounds defined in claim 1 having the names:

6-phenyl-2,3,4,6-tetrahydro-pyrano[3,2-c][1,8]naphthyridin-5-one;

6-(4-Chlorophenyl)-2,3,4,6-tetrahydro-5H-pyrano[3,2-c][1,8]naphthyridin-5-one;

6-(4-Methoxyphenyl)-2,3,4,6-tetrahydro-5H-pyrano[3,2-c][1,8]naphthyridin-5-one; and

6-(4-Methylphenyl)-2,3,4,6-tetrahydro-5H-pyrano[3,2-c][1,8]naphthyridin-5-one.

16. The compounds defined in claim 1 having the names:

3,9-dihydro-9-phenyl-furo[2,3-b][1,8]naphthyridin-4[2H]-one;

3,9-dihydro-9-(p-methylphenyl)-furo[2,3-b][1,8]naphthyridin-4[2H]-one;

3,9-dihydro-9-(p-fluorophenyl)-furo[2,3-b][1,8]naphthyridin-4[2H]-one;

3,9-dihydro-9-(m-methoxyphenyl)-furo[2,3-b][1,8]naphthyridin-4[2H]-one;

3,9-dihydro-9-(4-chlorophenyl)-furo[2,3-b][1,8]naphthyridin-4[2H]-one;

3,9-dihydro-9-(3-chlorophenyl)-furo[2,3-b][1,8]naphthyridin-4[2H]-one;

3,9-dihydro-9-(4-fluorophenyl)-2-methyl-furo[2,3-b][1,8]naphthyridin-4[2H]-one;

3,9-dihydro-9-(3-methoxyphenyl)-2-methyl-furo[2,3-b][1,8]naphthyridin-4[2H]-one;

3,9-dihydro-9-(3,5-dichlorophenyl)-furo[2,3-b][1,8]naphthyridin-4[2H]-one; and

3,9-dihydro-9-(3,5-dichlorophenyl)-2-methyl-furo[2,3-b][1,8]naphthyridin-4[2H]-one.

17. The compounds defined in claim 1 having the names:

10-(3,4-Dichlorophenyl)-2,3,4,10-tetrahydro-5H-pyrano[2,3-b][1,8]naphthyridin-5-one;

10-(4-Methoxyphenyl)-2,3,4,10-tetrahydro-5H-pyrano[2,3-b][1,8]naphthyridin-5-one;

10-(4-Chlorophenyl)-2,3,4,10-tetrahydro-5H-pyrano[2,3-b][1,8]naphthyridin-5-one;

10-(4-Methylphenyl)-2,3,4,10-tetrahydro-5H-pyrano[2,3-b][1,8]naphthyridin-5-one; and



40-Phenyl-2,3,4,10-tetrahydro-5H-pyrano[2,3-b][1,8]naphthyridin-5-one.

18. The compounds defined in claim 1 having the names:

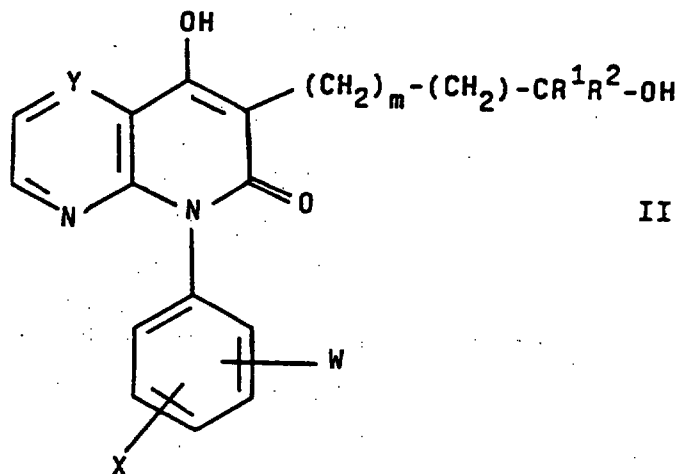
7-Phenyl-3,4,5,7-tetrahydro-oxepino[3,2-c][1,8]naphthyridin-6[2H]-one;

7-(4-Chlorophenyl)-3,4,5,7-tetrahydro-oxepino[3,2-c][1,8]naphthyridin-6[2H]-one;

7-(3-Chlorophenyl)-3,4,5,7-tetrahydro-oxepino[3,2-c][1,8]naphthyridin-6[2H]-one; and

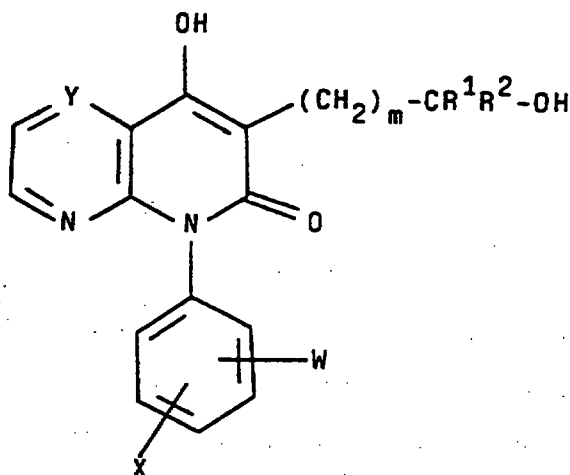
7-(3-Methoxyphenyl)-3,4,5,7-tetrahydro-oxepino[3,2-c][1,8]naphthyridin-6[2H]-one.

19. A process for the preparation of a compound of formula A' as defined in claim 1 in which both Bs are oxygen, which is characterized by treating a compound of the general formula II



in which m, W, X, Y, R¹ and R² are as defined in claim 1, with a dehydrating agent under anhydrous conditions to produce a compound of formula A' in which both Bs are oxygen.

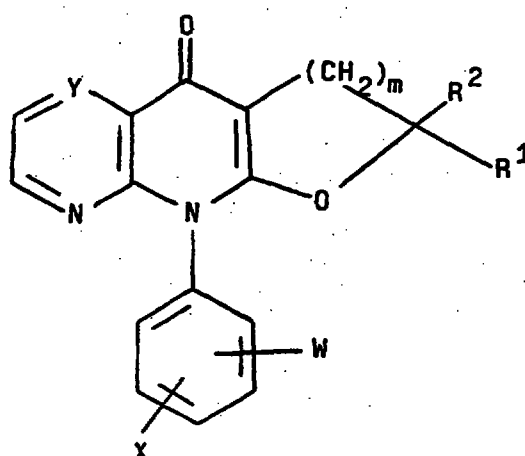
20. A process for the preparation of a compound of formula A' as defined in claim 1 which is characterized by treating a compound having the general formula



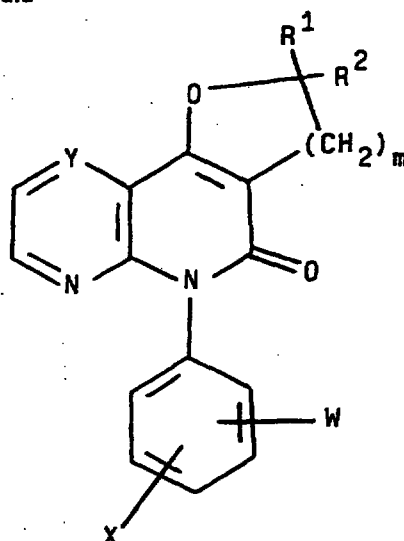
in which m, W, X, Y, R¹ and R² are as defined in claim 1, with a strong aqueous acid solution to produce a compound of formula A' wherein both Bs are oxygen; or subjecting a compound having the general formula



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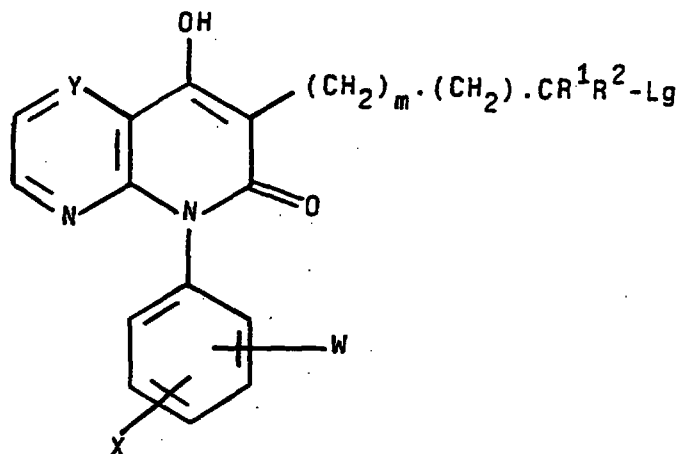


in which m , W , X , Y , R^1 and R^2 are as defined in claim 1, to intramolecular rearrangement, so as to produce a compound of formula A' in which both Bs are oxygen; followed if desired by treating a resulting compound having the general formula



in which m , W , X , Y , R^1 and R^2 are as defined in claim 1, under thiating conditions so as to produce a compound of formula A' wherein m is zero, the B atom in the ring is oxygen and the other B atom is sulphur.

21. A process for the preparation of a compound of formula A' as defined in claim 1 in which both Bs are oxygen, which is characterized by cyclizing a compound of the general formula



in which Lg is a leaving group, and m , W , X , Y , R^1 and R^2 are as defined in claim 1, to produce a compound of formula A' in which both Bs are oxygen.

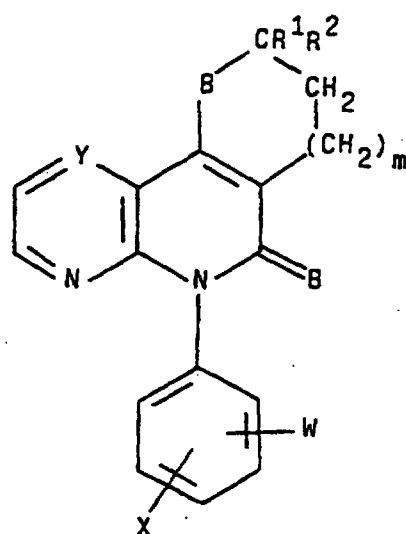


22. A process for the preparation of a compound of formula A' or A'' as defined in claim 1 which is characterized by treating a compound of general formula II as defined in claim 19 under cyclising and thiating conditions so as to produce a compound of formula A' or A'' or mixture thereof in which one or both Bs are sulfur and, if desired, separating a compound of formula A' or A'' from a mixture so produced; and if desired subjecting a resulting compound of the general formula A' or A'' in which one of the B atoms is oxygen and the other is sulphur to intramolecular rearrangement whereby compounds of formulae A' or A'' are converted respectively to the compounds of formulae A'' or A' such that a cyclic oxygen atom or sulphur atom becomes a doubly bonded oxygen atom or sulphur atom and the doubly bonded oxygen atom or sulphur atom becomes the ring oxygen atom or sulphur atom.

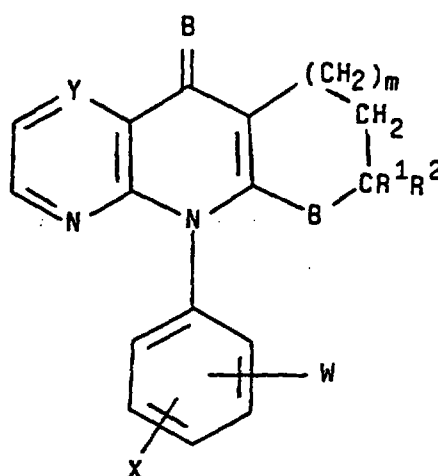
23. A pharmaceutical composition which comprises a compound having structural formula A' or A'' as defined in claim 1, in combination with a pharmaceutically acceptable carrier.

Claims for the Contracting State: AT

1. A process for the preparation of a compound having the structural formula A' or A''



A'



A''

wherein

B is independently oxygen or sulfur;

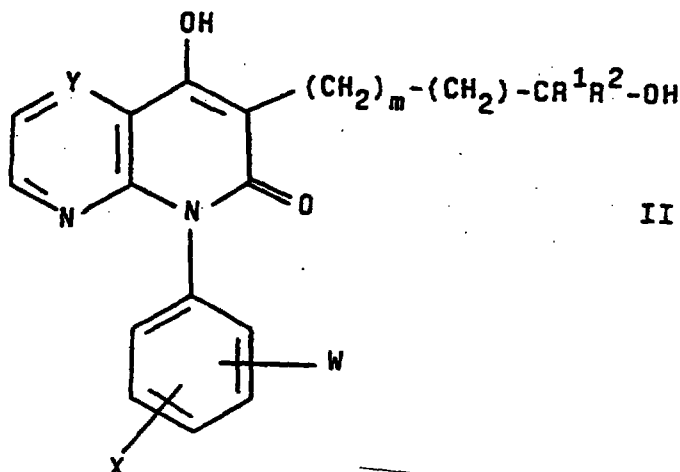
R¹ and R² may be the same or different and are hydrogen or alkyl having from 1 to 6 carbon atoms;

m is 0, 1 or 2;

W and X may be the same or different and are hydrogen, hydroxy, alkyl having from 1 to 6 carbon atoms, halogen, nitro, alkoxy having from 1 to 6 carbon atoms, or NHR^a (wherein R^a is alkyl having from 1 to 6 carbon atoms); and

Y is CH or N characterized by:

a) treating a compound of the general formula II



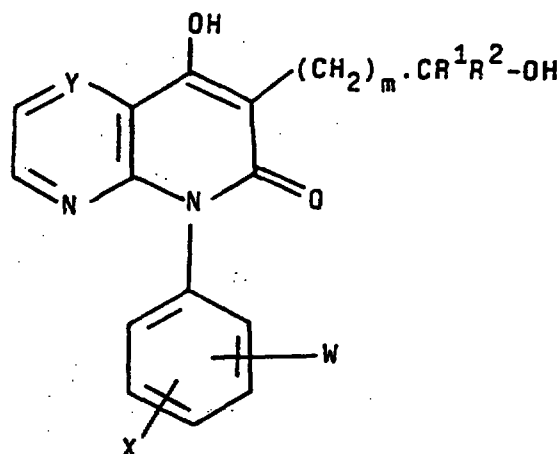
II



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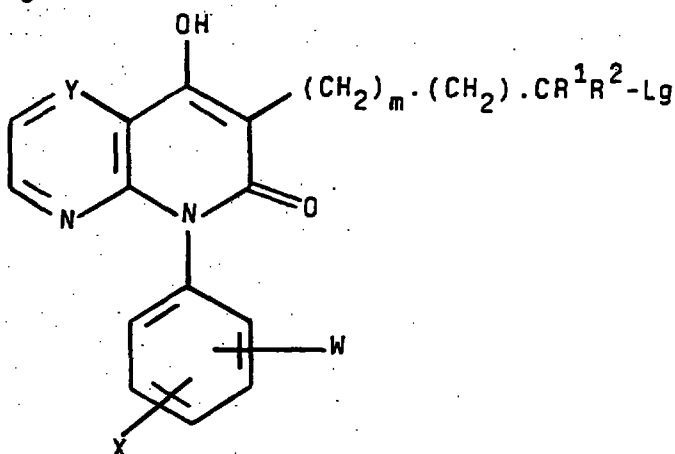
in which m, W, X, Y, R¹ and R² are as defined above, with a dehydrating agent under anhydrous conditions to produce a compound of formula A'' in which both Bs are oxygen;

b) treating a compound having the general formula



in which m, W, X, Y, R¹ and R² are as defined above, with a strong aqueous acid solution to produce a compound of formula A' in which both Bs are oxygen;

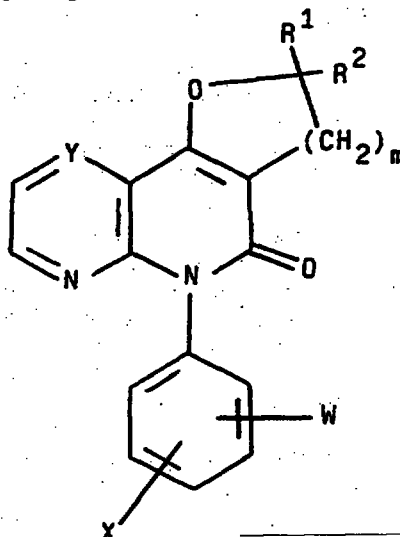
c) cyclising a compound of the general formula



in which Lg is a leaving group and m, W, X, Y, R¹ and R² are as defined above, to produce a compound of formula A', in which both Bs are oxygen.

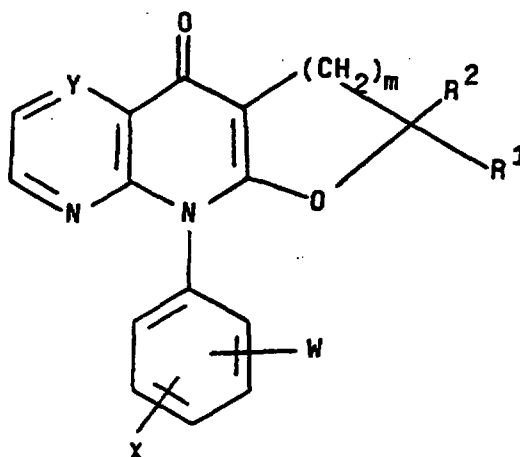
d) treating a compound of general formula II as defined in process a) above, under cyclising and thiating conditions so as to produce a compound of formula A', A'' or a mixture thereof in which one or both Bs are sulfur and, if desired, separating a compound of formula A' or A'' from a mixture so produced;

e) treating a compound having the general formula



in which m, W, X, Y, R¹ and R² are as defined above under thiating conditions so as to produce a compound of formula A' in which m is zero, the B atom in the ring is oxygen and the other B atom is sulphur.

f) subjecting a compound having the general formula

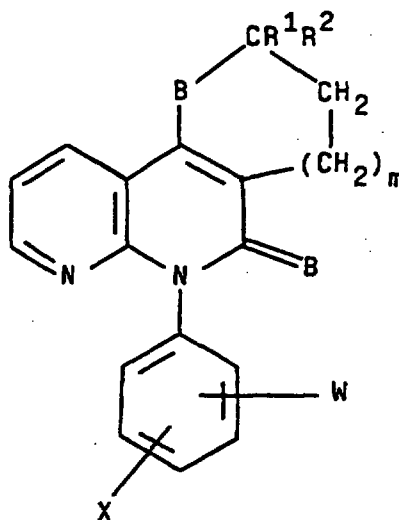


in which m, W, X, Y, R¹ and R² are as defined above, to intramolecular rearrangement, so as to produce a compound of formula A' as defined above in which both Bs are oxygen,

g) subjecting a compound of the general formula A' or A'' in which one of the B atoms is oxygen and the other is sulphur, to intramolecular rearrangement whereby said compound of formula A' or A'' is converted respectively to a compound of formula A'' or A' such that a cyclic oxygen atom or sulphur atom becomes a doubly bonded oxygen atom or sulphur atom and the doubly bonded oxygen atom or sulphur atom becomes the ring oxygen atom or sulphur atom; and thereafter, if desired, transforming a compound of formula A' or A'' so obtained by a process a), b), c), d), e), f) or g) into another compound of formula A' or A''.

2. A process as defined in Claim 1 characterised in that a compound of formula A' or A'' is produced in which Y is CH.

3. A process as defined in Claim 2 characterised in that a compound is produced having the structural formula:



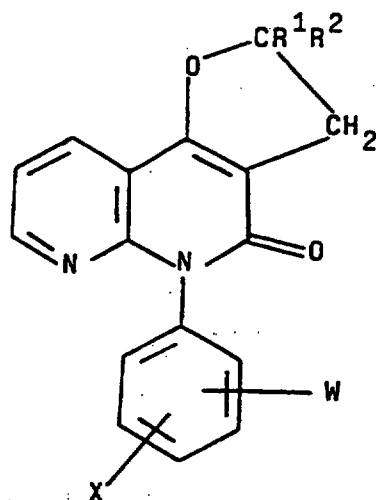
wherein B, W, X, Y, R¹ and R² and m are as defined in Claim 1.

4. A process as defined in Claim 3 characterised in that a compound is produced wherein m is 0 or 2.

5. A process as defined in Claim 4 characterised in that a compound is produced wherein B is oxygen.

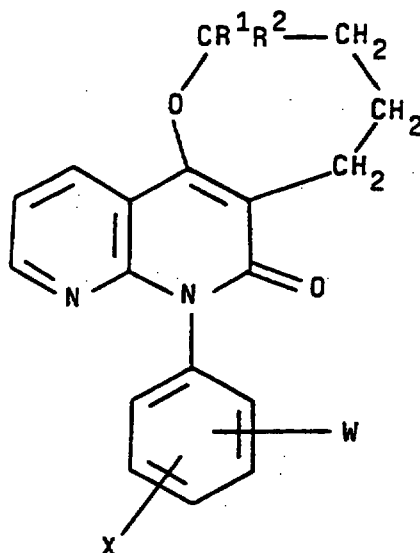
6. A process as defined in Claim 5 characterised in that a compound is produced having the structural formula:





wherein W, X, R¹ and R² are as defined in Claim 1.

7. A process as defined in Claim 5 characterised in that a compound is produced having the structural formula:

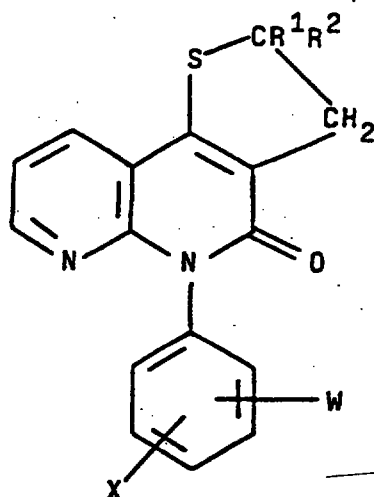


wherein W, X, R¹ and R² are as defined in Claim 1.

8. A process as defined in Claim 6 or Claim 7 characterised in that a compound is produced wherein R¹ and R² are hydrogen or methyl.

9. A process as defined in Claim 8 characterised in that a compound is produced wherein R¹ is methyl and R² is hydrogen.

10. A process as defined in Claim 4 characterised in that a compound is produced having the structural formula:



wherein X and W are as defined in Claim 1.

11. A process as defined in Claim 10 characterised in that a compound is produced wherein W is 3-chloro and X is hydrogen, chlorine or fluorine.

12. A process as defined in Claim 10 characterised in that a compound is produced wherein W is 3-methoxy and X is hydrogen or fluorine.

13. A process as defined in Claim 10 characterised in that a compound is produced wherein W and X are both hydrogen.

14. A process as defined in Claim 1 characterised in that one of the following compounds is produced:

- 3,5-dihydro-5-phenyl-furo[3,2-c][1,8]naphthyridin-4[2H]-one;
- 2-methyl-3,5-dihydro-5-phenyl-furo[3,2-c][1,8]naphthyridin-4[2H]-one;
- 3,5-dihydro-5-(p-methylphenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-one;
- 3,5-dihydro-5-(p-fluorophenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-one;
- 3,5-dihydro-5-(m-methoxyphenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-one;
- 3,5-dihydro-5-(3,4-dichlorophenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-one;
- 3,5-dihydro-5-(3,4-dichlorophenyl)-2-methyl-furo[3,2-c][1,8]naphthyridin-4[2H]-one;
- 3,5-dihydro-5-(4-chlorophenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-one;
- 3,5-dihydro-5-(3-chlorophenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-one;
- 3,5-dihydro-5-(3-chlorophenyl)-2-methyl-furo[3,2-c][1,8]naphthyridin-4[2H]-one;
- 3,5-dihydro-5-(4-fluorophenyl)-2-methyl-furo[3,2-c][1,8]naphthyridin-4[2H]-one;
- 3,5-dihydro-5-(3-methoxyphenyl)-2-methyl-furo[3,2-c][1,8]naphthyridin-4[2H]-one;
- 3,5-dihydro-5-(3,5-dichlorophenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-one; and
- 3,5-dihydro-5-(3,5-dichlorophenyl)-2-methyl-furo[3,2-c][1,8]naphthyridin-4[2H]-one.

15. A process as defined in Claim 1 characterised in that one of the following compounds is produced:

- 6-phenyl-2,3,4,6-tetrahydro-pyrano[3,2-c][1,8]naphthyridin-5-one;
- 6-(4-Chlorophenyl)-2,3,4,6-tetrahydro-5H-pyrano[3,2-c][1,8]naphthyridin-5-one;
- 6-(4-Methoxyphenyl)-2,3,4,6-tetrahydro-5H-pyrano[3,2-c][1,8]naphthyridin-5-one; and
- 6-(4-Methylphenyl)-2,3,4,6-tetrahydro-5H-pyrano[3,2-c][1,8]naphthyridin-5-one.

16. A process as defined in Claim 1 characterised in that one of the following compounds is produced:

- 3,9-dihydro-9-phenyl-furo[2,3-b][1,8]naphthyridin-4[2H]-one;
- 3,9-dihydro-9-(p-methylphenyl)-furo[2,3-b][1,8]naphthyridin-4[2H]-one;
- 3,9-dihydro-2-methyl-9-phenyl-furo[2,3-b][1,8]naphthyridin-4[2H]-one;
- 3,9-dihydro-9-(p-fluorophenyl)-furo[2,3-b][1,8]naphthyridin-4[2H]-one;
- 3,9-dihydro-9-(m-methoxyphenyl)-furo[2,3-b][1,8]naphthyridin-4[2H]-one;
- 3,9-Dihydro-9-(4-chlorophenyl)-furo[2,3-b][1,8]naphthyridin-4[2H]-one;
- 3,9-Dihydro-9-(3-chlorophenyl)-furo[2,3-b][1,8]naphthyridin-4[2H]-one;
- 3,9-Dihydro-9-(4-fluorophenyl)-2-methyl-furo[2,3-b][1,8]naphthyridin-4[2H]-one;
- 3,9-Dihydro-9-(3-methoxyphenyl)-2-methyl-furo[2,3-b][1,8]naphthyridin-4[2H]-one;
- 3,9-Dihydro-9-(3,5-dichlorophenyl)-furo[2,3-b][1,8]naphthyridin-4[2H]-one; and
- 3,9-Dihydro-9-(3,5-dichlorophenyl)-2-methyl-furo[2,3-b][1,8]naphthyridin-4[2H]-one.

17. The process as defined in Claim 1 characterised in that one of the following compounds is produced:

- 10-(3,4-Dichlorophenyl)-2,3,4,10-tetrahydro-5H-pyrano[2,3-b][1,8]naphthyridin-5-one;
- 10-(4-Methoxyphenyl)-2,3,4,10-tetrahydro-5H-pyrano[2,3-b][1,8]naphthyridin-5-one;
- 10-(4-Chlorophenyl)-2,3,4,10-tetrahydro-5H-pyrano[2,3-b][1,8]naphthyridin-5-one;
- 10-(4-Methylphenyl)-2,3,4,10-tetrahydro-5H-pyrano[2,3-b][1,8]naphthyridin-5-one; and
- 10-Phenyl-2,3,4,10-tetrahydro-5H-pyrano[2,3-b][1,8]naphthyridin-5-one.

18. The process as defined in Claim 1 characterised in that one of the following compounds is produced:

- 7-Phenyl-3,4,5,7-tetrahydro-oxepino[3,2-c][1,8]naphthyridin-6[2H]-one;
- 7-(4-Chlorophenyl)-3,4,5,7-tetrahydro-oxepino[3,2-c][1,8]naphthyridin-6[2H]-one;
- 7-(3-Chlorophenyl)-3,4,5,7-tetrahydro-oxepino[3,2-c][1,8]naphthyridin-6[2H]-one;
- 7-(3-Methoxyphenyl)-3,4,5,7-tetrahydro-oxepino[3,2-c][1,8]naphthyridin-6[2H]-one; and
- 7-(3-Hydroxyphenyl)-3,4,5,7-tetrahydro-oxepino[3,2-c][1,8]naphthyridin-6[2H]-one.

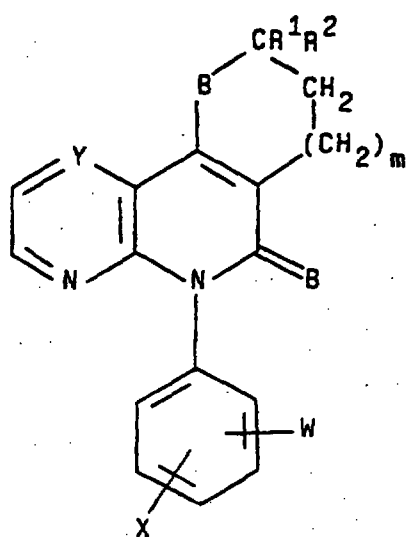
19. A method of preparing a pharmaceutical composition which comprises combining a compound of formula A' or A'' as defined in Claim 1, with a pharmaceutically acceptable carrier.

20. A method of preparing a pharmaceutical composition which comprises combining a compound of formula A' or A'' as defined in Claim 1, prepared by the process of any one of Claims 1 to 18, with a pharmaceutically acceptable carrier.

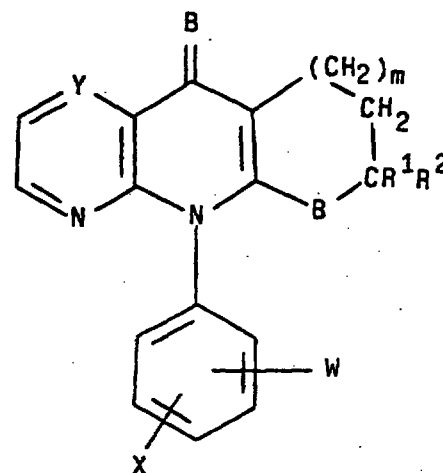
21. A compound of formula A' or A'' as defined in Claim 1, whenever produced by the process of any one of Claims 1 to 18 or equivalent thereof.

22. A compound having the structural formula A' or A''





A'



A''

wherein

B is independently oxygen or sulfur;

R¹ and R² may be the same or different and are hydrogen or alkyl having from 1 to 6 carbon atoms;

m is 0, 1 or 2;

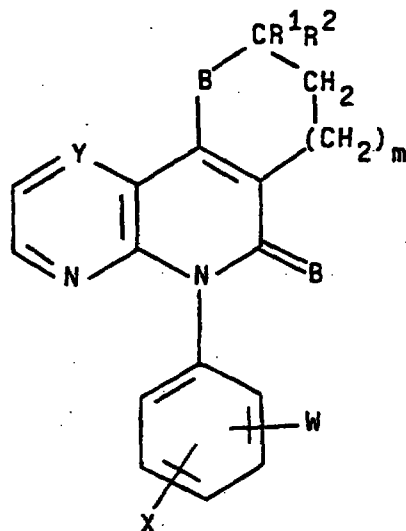
W and X may be the same or different and are hydrogen, hydroxy, alkyl having from 1 to 6 carbon atoms, halogen, nitro, alkoxy having from 1 to 6 carbon atoms, or NHR^a (wherein R^a is alkyl having from 1 to 6 carbon atoms); and

Y is CH or N.

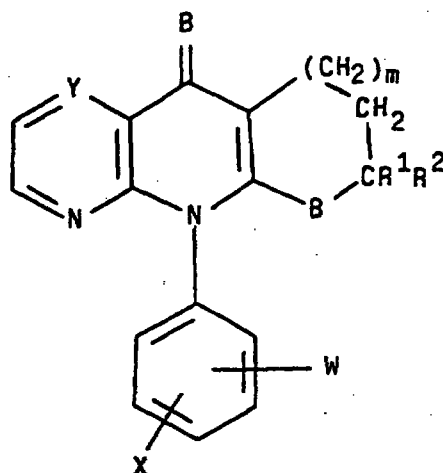
23. A compound according to Claim 22, having a structure as defined in any of Claims 2 to 18 for a produced compound.

Patentansprüche für die Vertragsstaaten: BE CH DE FR GB IT LI LU NL SE

1. Verbindung der Strukturformel A' oder A''



A'



A''

worin

B unabhängig Sauerstoff oder Schwefel ist,

R¹ und R² gleich oder verschieden sein können und Wasserstoff oder Alkyl mit 1 bis 6 Kohlenstoff-Atomen sind,

m 0, 1 oder 2 ist,

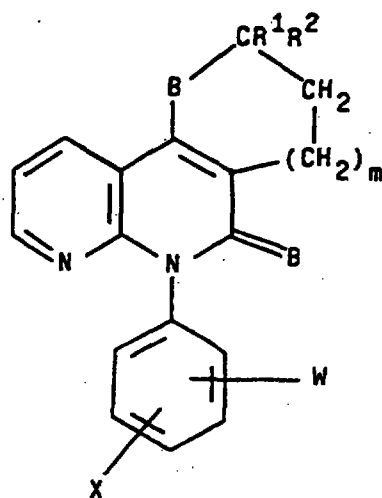
W und X gleich oder verschieden sein können und Wasserstoff, Hydroxy, Alkyl mit 1 bis 6 Kohlenstoff-Atomen, Halogen, Nitro, Alkoxy mit 1 bis 6 Kohlenstoff-Atomen oder NHR^a (worin R^a Alkyl mit 1 bis 6 Kohlenstoff-Atomen ist) sind und



Y CH oder N ist.

2. Verbindungen nach Anspruch 1, worin Y CH ist.

3. Verbindungen nach Anspruch 2 mit der Strukturformel

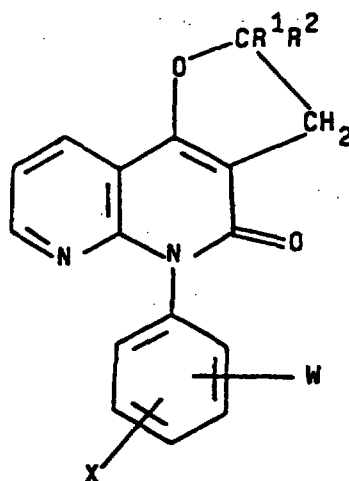


in der B, W, X, R¹, R² und m die in Anspruch 1 angegebenen Bedeutungen haben.

4. Verbindungen nach Anspruch 3, worin m 0 oder 2 ist.

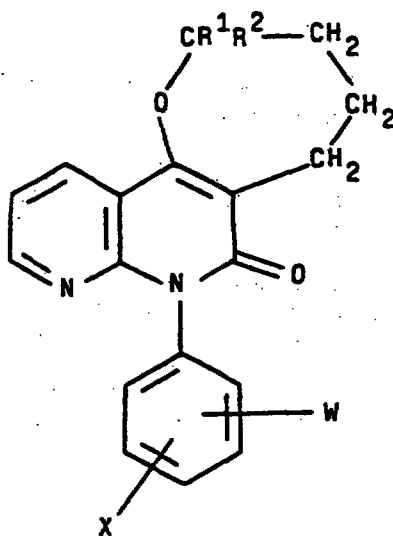
5. Verbindungen nach Anspruch 4, worin B Sauerstoff ist.

6. Verbindungen nach Anspruch 5 mit der Strukturformel



in der W, X, R¹ und R² die in Anspruch 1 angegebenen Bedeutungen haben.

7. Verbindungen nach Anspruch 5 mit der Strukturformel





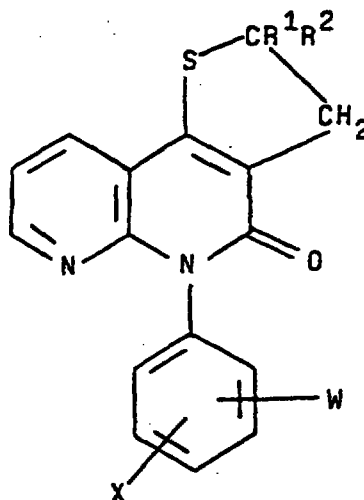
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in der W, X, R¹ und R² die in Anspruch 1 angegebenen Bedeutungen haben.

8. Verbindungen nach Anspruch 6 oder 7, worin R¹ und R² Wasserstoff oder Methyl sind.

9. Verbindungen nach Anspruch 8, worin R¹ Methyl ist und R² Wasserstoff ist.

10. Verbindungen nach Anspruch 4 mit der Strukturformel



in der W und X die in Anspruch 1 angegebenen Bedeutungen haben.

11. Verbindung nach Anspruch 10, worin W 3-Chloro ist und X Wasserstoff, Chlor oder Fluor ist.

12. Verbindung nach Anspruch 10, worin W 3-Methoxy ist und X Wasserstoff oder Fluor ist.

13. Verbindung nach Anspruch 10, worin W und X beide Wasserstoff sind.

14. Verbindung nach Anspruch 1 mit den Namen

3,5-Dihydro-5-phenyl-furo[3,2-c][1,8]naphthyridin-4[2H]-on;

2-Methyl-3,5-dihydro-5-phenyl-furo[3,2-c][1,8]naphthyridin-4[2H]-on;

3,5-Dihydro-5-(p-methylphenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-on;

3,5-Dihydro-5-(p-fluorophenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-on;

3,5-Dihydro-5-(m-methoxyphenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-on;

3,5-Dihydro-5-(3,4-dichlorophenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-on;

3,5-Dihydro-5-(3,4-dichlorophenyl)-2-methyl-furo[3,2-c][1,8]naphthyridin-4[2H]-on;

3,5-Dihydro-5-(4-chlorophenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-on;

3,5-Dihydro-5-(3-chlorophenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-on;

3,5-Dihydro-5-(3-chlorophenyl)-2-methyl-furo[3,2-c][1,8]naphthyridin-4[2H]-on;

3,5-Dihydro-5-(4-fluorophenyl)-2-methyl-furo[3,2-c][1,8]naphthyridin-4[2H]-on;

3,5-Dihydro-5-(3-methoxyphenyl)-2-methyl-furo[3,2-c][1,8]naphthyridin-4[2H]-on;

3,5-Dihydro-5-(3,5-dichlorophenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-on; und

3,5-Dihydro-5-(3,5-dichlorophenyl)-2-methyl-furo[3,2-c][1,8]naphthyridin-4[2H]-on.

15. Verbindungen nach Anspruch 1 mit den Namen

6-Phenyl-2,3,4,6-tetrahydro-pyrano[3,2-c][1,8]naphthyridin-5-on;

6-(4-Chlorophenyl)-2,3,4,6-tetrahydro-5H-pyrano[3,2-c][1,8]naphthyridin-5-on;

6-(4-Methoxyphenyl)-2,3,4,6-tetrahydro-5H-pyrano[3,2-c][1,8]naphthyridin-5-on und

6-(4-Methylphenyl)-2,3,4,6-tetrahydro-5H-pyrano[3,2-c][1,8]naphthyridin-5-on.

16. Verbindung nach Anspruch 1 mit den Namen

3,9-Dihydro-9-phenyl-furo[2,3-b][1,8]naphthyridin-4[2H]-on;

3,9-Dihydro-9-(p-methylphenyl)-furo[2,3-b][1,8]naphthyridin-4[2H]-on;

3,9-Dihydro-2-methyl-9-phenyl-furo[2,3-b][1,8]naphthyridin-4[2H]-on;

3,9-Dihydro-9-(p-fluorophenyl)-furo[2,3-b][1,8]naphthyridin-4[2H]-on;

3,9-Dihydro-9-(m-methoxyphenyl)-furo[2,3-b][1,8]naphthyridin-4[2H]-on;

3,9-Dihydro-9-(4-chlorophenyl)-furo[2,3-b][1,8]naphthyridin-4[2H]-on;

3,9-Dihydro-9-(3-chlorophenyl)-furo[2,3-b][1,8]naphthyridin-4[2H]-on;

3,9-Dihydro-9-(4-fluorophenyl)-2-methyl-furo[2,3-b][1,8]naphthyridin-4[2H]-on;

3,9-Dihydro-9-(3-methoxyphenyl)-2-methyl-furo[2,3-b][1,8]naphthyridin-4[2H]-on;

3,9-Dihydro-9-(3,5-dichlorophenyl)-furo[2,3-b][1,8]naphthyridin-4[2H]-on und

3,9-Dihydro-9-(3,5-dichlorophenyl)-2-methyl-furo[2,3-b][1,8]naphthyridin-4[2H]-on.

17. Verbindungen nach Anspruch 1 mit den Namen

10-(3,4-Dichlorophenyl)-2,3,4,10-tetrahydro-5H-pyrano[2,3-b][1,8]naphthyridin-5-on;

10-(4-Methoxyphenyl)-2,3,4,10-tetrahydro-5H-pyrano[2,3-b][1,8]naphthyridin-5-on;

10-(4-Chlorophenyl)-2,3,4,10-tetrahydro-5H-pyrano[2,3-b][1,8]naphthyridin-5-on;

10-(4-Methylphenyl)-2,3,4,10-tetrahydro-5H-pyrano[2,3-b][1,8]naphthyridin-5-on und

10-Phenyl-2,3,4,10-tetrahydro-5H-pyrano[2,3-b][1,8]naphthyridin-5-on.

18. Verbindungen nach Anspruch 1 mit den Namen

7-Phenyl-3,4,5,7-tetrahydro-oxepino[3,2-c][1,8]naphthyridin-6[2H]-on;

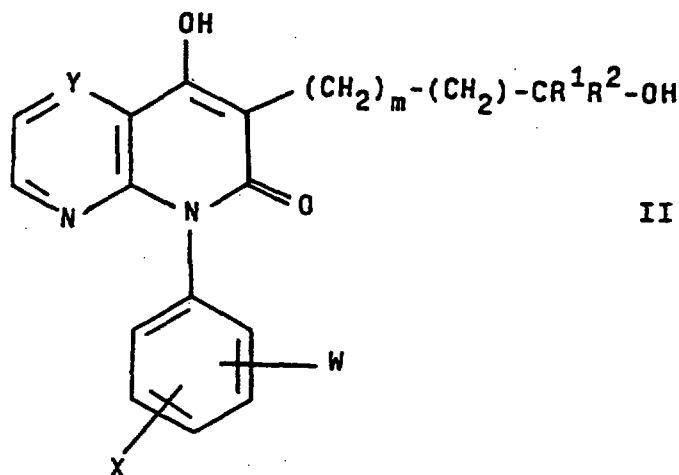
7-(4-Chlorophenyl)-3,4,5,7-tetrahydro-oxepino[3,2-c][1,8]naphthyridin-6[2H]-on;

7-(3-Chlorophenyl)-3,4,5,7-tetrahydro-oxepino[3,2-c][1,8]naphthyridin-6[2H]-on;

7-(3-Methoxyphenyl)-3,4,5,7-tetrahydro-oxepino[3,2-c][1,8]naphthyridin-6[2H]-on und

7-(3-Hydroxyphenyl)-3,4,5,7-tetrahydro-oxepino[3,2-c][1,8]naphthyridin-6[2H]-on.

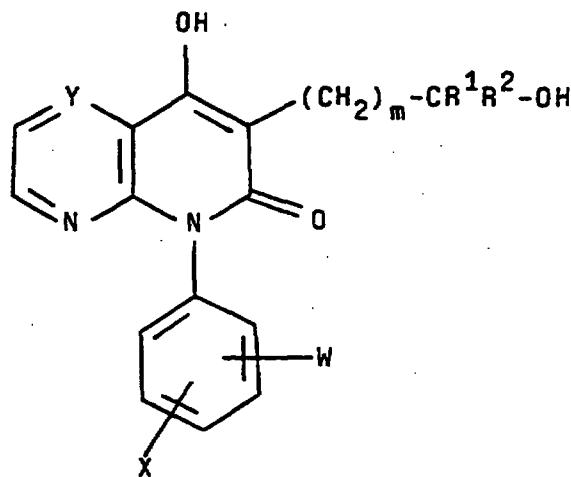
19. Verfahren zur Herstellung einer Verbindung der Formel A'' gemäß Anspruch 1, worin beide B's Sauerstoff sind, dadurch gekennzeichnet, daß eine Verbindung der allgemeinen Formel II



II

in der m, W, X, Y, R¹ und R² die in Anspruch 1 angegebenen Bedeutungen haben, mit einem wasser-
absplattendenden Mittel unter wasserfreien Bedingungen umgesetzt wird, wodurch eine Verbindung der
Formel A'' erzeugt wird, in der beide B's Sauerstoff sind.

20. Verfahren zur Herstellung einer Verbindung der Formel A' gemäß Anspruch 1, dadurch
gekennzeichnet, daß eine Verbindung der allgemeinen Formel

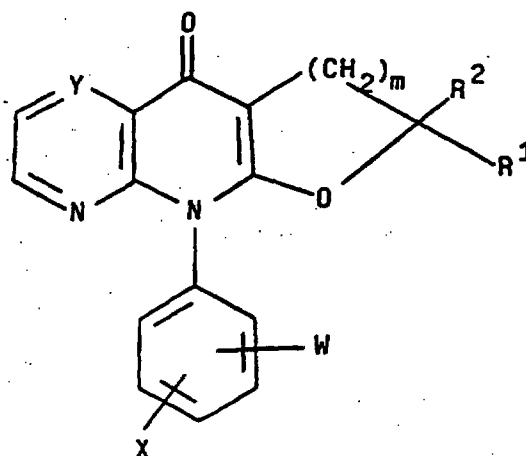


in der m, W, X, Y, R¹ und R² die in Anspruch 1 angegebenen Bedeutungen haben, mit einer starken
wäßrigen Säure-Lösung umgesetzt wird, wodurch eine Verbindung der Formel A' erzeugt wird, in der
beide B's Sauerstoff sind, oder eine Verbindung der allgemeinen Formel

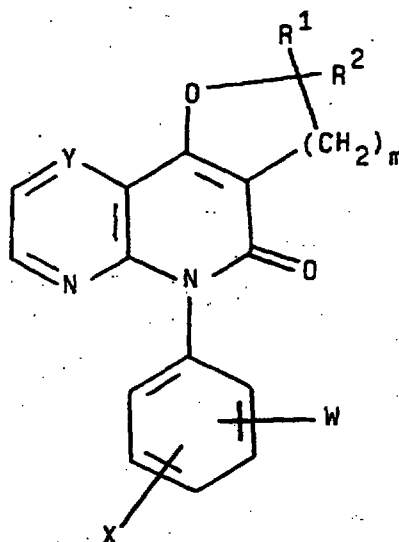




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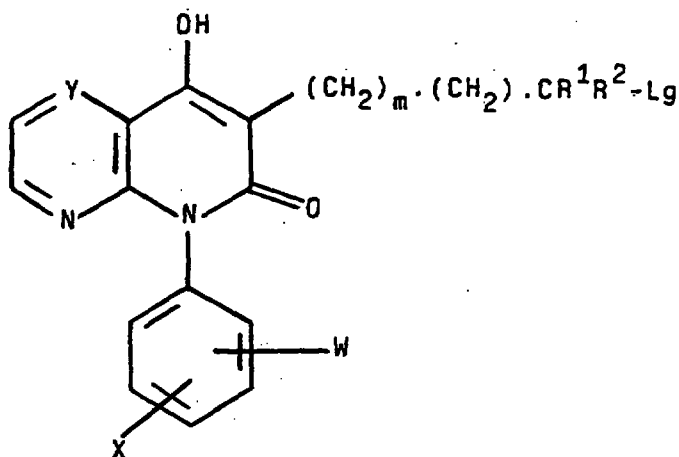


20 in der m, W, X, Y, R¹ und R² die in Anspruch 1 angegebenen Bedeutungen haben, einer intramolekularen Umlagerung unterworfen wird, wodurch eine Verbindung der Formel A' erzeugt wird, in der beide B's Sauerstoff sind, und gewünschtenfalls anschließend eine resultierende Verbindung der allgemeinen Formel



45 in der m, W, X, Y, R¹ und R² die in Anspruch 1 angegebenen Bedeutungen haben, unter sulfidierenden Bedingungen behandelt wird, wodurch eine Verbindung der Formel A' erzeugt wird, in der m Null ist, das B-Atom im Ring Sauerstoff ist und das andere B-Atom Schwefel ist.

21. Verfahren zur Herstellung einer Verbindung der Formel A' gemäß Anspruch 1, worin beide B's Sauerstoff sind, dadurch gekennzeichnet, daß eine Verbindung der allgemeinen Formel



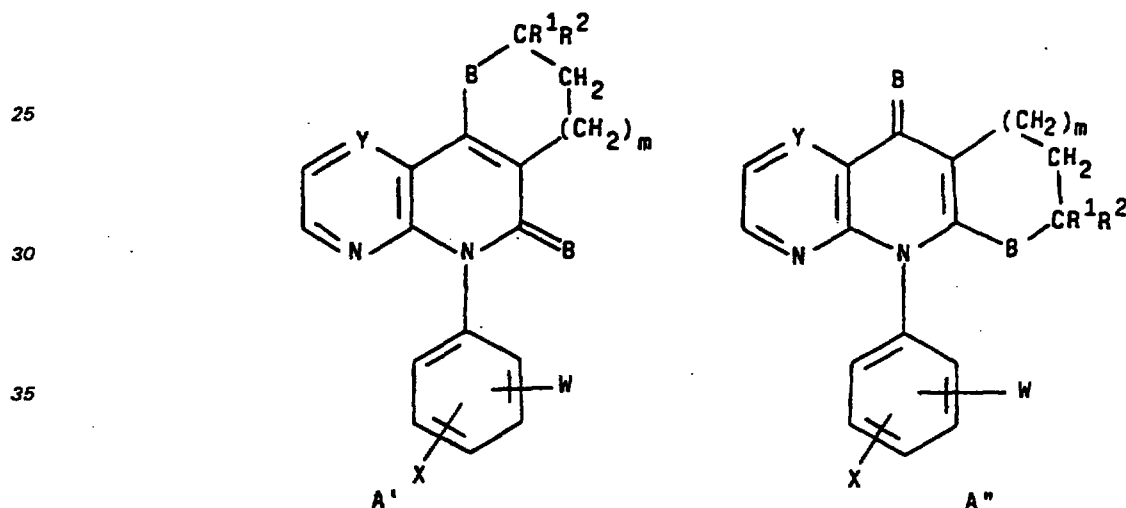
in der Lg eine abspaltbare Gruppe ist und m, W, X, Y, R¹ und R² die in Anspruch 1 angegebenen Bedeutungen haben, cyclisiert wird, wodurch eine Verbindung der Formel A' erzeugt wird, in der beide B's Sauerstoff sind.

22. Verfahren zur Herstellung einer Verbindung der Formel I gemäß Anspruch 1, dadurch gekennzeichnet, daß eine Verbindung der allgemeinen Formel II gemäß Anspruch 19 unter cyclisierenden und sulfidierenden Bedingungen behandelt wird, wodurch eine Verbindung der Formel I oder ein Gemisch solcher Verbindungen erzeugt wird, in der ein oder beide B's Schwefel sind, und gewünschtenfalls eine Verbindung der Formel I aus einem solchen Gemisch abgetrennt wird, und gewünschtenfalls eine resultierende Verbindung der allgemeinen Formel I, in der eines der B-Atome Sauerstoff ist und das andere Schwefel ist, einer intramolekularen Umlagerung unterworfen wird, wodurch Verbindungen der Formeln A' oder A'' jeweils in solcher Weise in die Verbindungen der Formeln A' oder A'' überführt werden, daß ein cyclisches Sauerstoff-Atom oder Schwefel-Atom ein doppelt gebundenes Sauerstoff-Atom oder Schwefel-Atom wird und das doppelt gebundene Sauerstoff-Atom oder Schwefel-Atom zu dem Ring-Sauerstoff- oder -Schwefel-Atom wird.

23. Pharmazeutische Zusammensetzung, umfassend eine Verbindung mit der Strukturformel A' oder A'' gemäß Anspruch 1 in Verbindung mit einem pharmazeutisch annehmbaren Träger.

Patentansprüche für den Vertragsstaat: AT

1. Verfahren zur Herstellung einer Verbindung der Strukturformel A' oder A''



40 worin

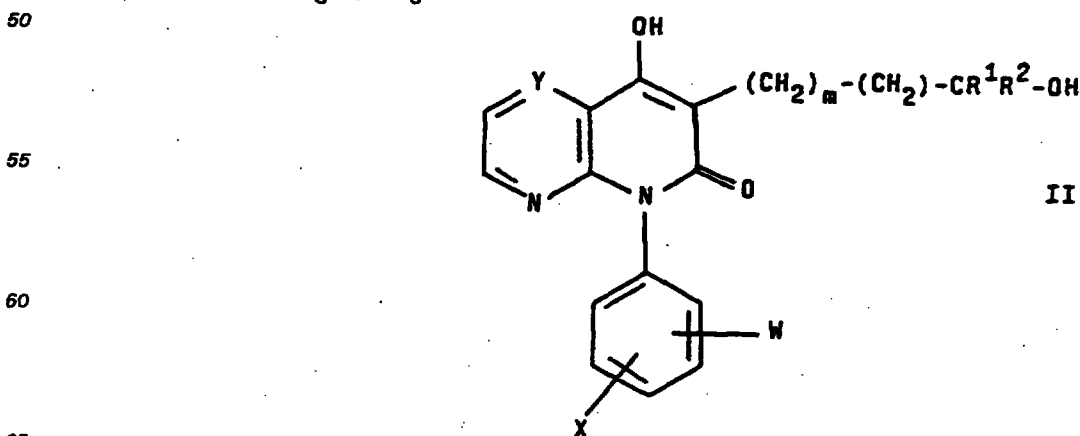
B unabhängig Sauerstoff oder Schwefel ist,
R¹ und R² gleich oder verschieden sein können und Wasserstoff oder Alkyl mit 1 bis 6 Kohlenstoff-Atomen sind,

m 0, 1 oder 2 ist,

45 W und X gleich oder verschieden sein können und Wasserstoff, Hydroxy, Alkyl mit 1 bis 6 Kohlenstoff-Atomen, Halogen, Nitro, Alkoxy mit 1 bis 6 Kohlenstoff-Atomen oder NHR^a (worin R^a Alkyl mit 1 bis 6 Kohlenstoff-Atomen ist) sind und

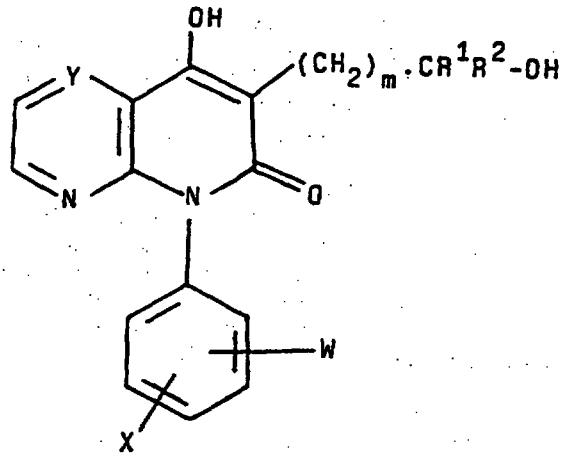
Y CH oder N ist, dadurch gekennzeichnet, daß

a) eine Verbindung der allgemeinen Formel II



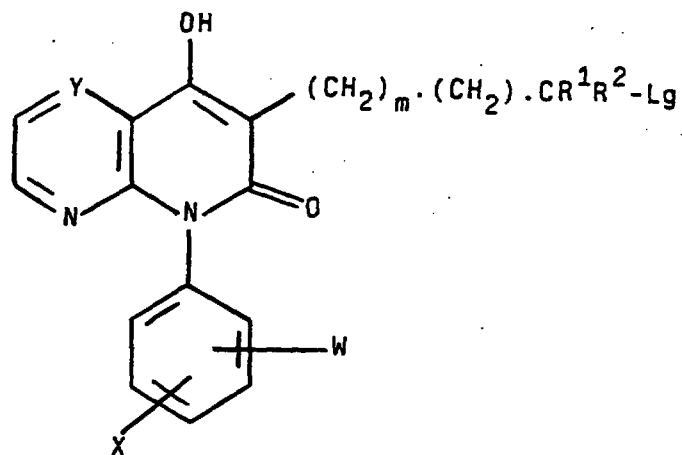
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in der m, W, X, Y, R¹ und R² die im Vorstehenden angegebenen Bedeutungen haben, mit einem wasser-
abspaltenden Mittel unter wasserfreien Bedingungen umgesetzt wird, wodurch eine Verbindung der
Formel A'' erzeugt wird, in der beide B's Sauerstoff sind,
b) eine Verbindung der allgemeinen Formel



in der m, W, X, Y, R¹ und R² die im Vorstehenden angegebenen Bedeutungen haben, mit einer starken
wäßrigen Säure-Lösung umgesetzt wird, wodurch eine Verbindung der Formel A' erzeugt wird, in der
beide B's Sauerstoff sind,

c) eine Verbindung der allgemeinen Formel



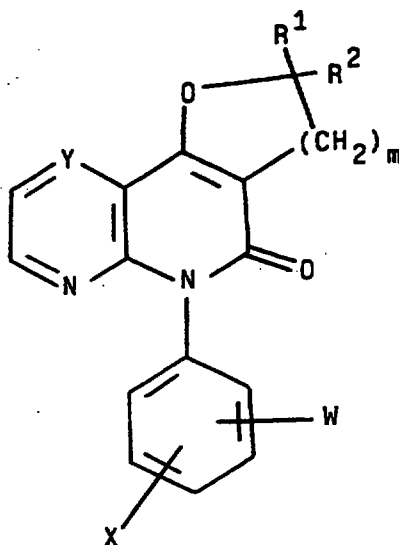
in der Lg eine abspaltbare Gruppe ist und m, W, X, Y, R¹ und R² die im Vorstehenden angegebenen
Bedeutungen haben, cyclisiert wird, wodurch eine Verbindung der Formel A' erzeugt wird, in der beide B's
Sauerstoff sind,

d) eine Verbindung der allgemeinen Formel II gemäß dem vorstehenden Verfahren a) unter
cyclisierenden und sulfidierenden Bedingungen behandelt wird, wodurch eine Verbindung der Formel A',
A'' oder ein Gemisch solcher Verbindungen erzeugt wird, in der ein oder beide B's Schwefel sind, und
gewünschtenfalls eine Verbindung der Formel A' oder A'' aus einem so erzeugten Gemisch abgetrennt
wird,

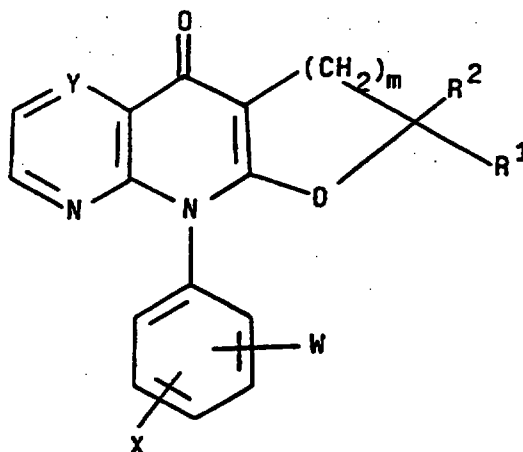


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e) eine Verbindung der allgemeinen Formel



in der m, W, X, Y, R¹ und R² die im Vorstehenden angegebenen Bedeutungen haben, unter sulfidierenden Bedingungen behandelt wird, wodurch eine Verbindung der Formel A' erzeugt wird, in der m Null ist, das B-Atom im Ring Sauerstoff ist und das andere B-Atom Schwefel ist,
f) eine Verbindung der allgemeinen Formel



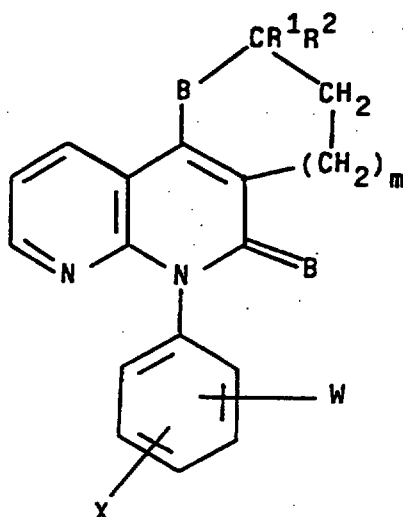
in der m, W, X, Y, R¹ und R² die im Vorstehenden angegebenen Bedeutungen haben, einer intramolekularen Umlagerung unterworfen wird, wodurch eine Verbindung der Formel A' erzeugt wird, in der beide B's Sauerstoff sind,

g) eine Verbindung der allgemeinen Formel A' oder A'', in der eines der B-Atome Sauerstoff ist und das andere Schwefel ist, einer intramolekularen Umlagerung unterworfen wird, wodurch die Verbindung der Formel A' oder A'' jeweils in solcher Weise in eine Verbindungen der Formeln A' bzw. A' überführt wird daß ein cyclisches Sauerstoff-Atom oder Schwefel-Atom ein doppelt gebundenes Sauerstoff-Atom oder Schwefel-Atom wird und das doppelt gebundene Sauerstoff-Atom oder Schwefel-Atom zu dem Ring-Sauerstoff- oder -Schwefel-Atom wird, und danach gewünschtenfalls eine so erhaltene Verbindung A' oder A'' durch ein Verfahren a), b), c), d), e), f) oder g) in eine andere Verbindung der Formel A' oder A' umgewandelt wird.

2. Verfahren nach Anspruch 1, dadurch gekennzeichnet, daß Y CH ist.

3. Verfahren nach Anspruch 2, dadurch gekennzeichnet, daß eine Verbindung mit der Strukturformel



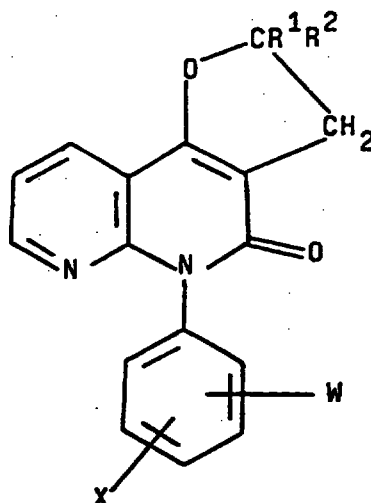


hergestellt wird, in der B, W, X, R¹, R² und m die in Anspruch 1 angegebenen Bedeutungen haben.

4. Verfahren nach Anspruch 3, dadurch gekennzeichnet, daß eine Verbindung hergestellt wird, in der m 0 oder 2 ist.

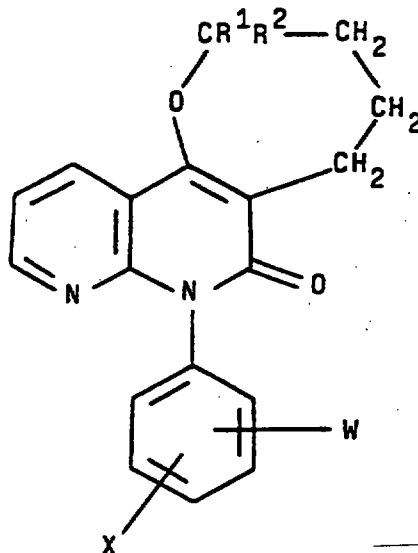
5. Verfahren nach Anspruch 4, dadurch gekennzeichnet, daß eine Verbindung hergestellt wird, in der B Sauerstoff ist.

6. Verfahren nach Anspruch 5, dadurch gekennzeichnet, daß eine Verbindung mit der Strukturformel



hergestellt wird, in der W, X, R¹ und R² die in Anspruch 1 angegebenen Bedeutungen haben.

7. Verfahren nach Anspruch 5, dadurch gekennzeichnet, daß eine Verbindung mit der Strukturformel

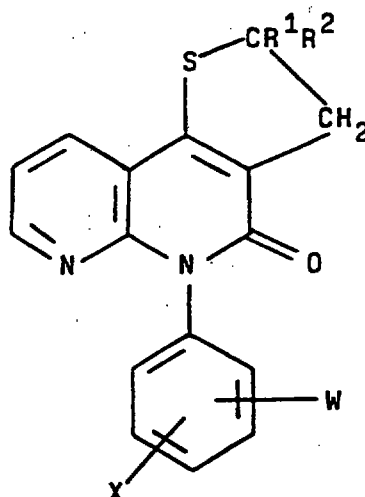


hergestellt wird, in der W, X, R¹ und R² die in Anspruch 1 angegebenen Bedeutungen haben.

8. Verfahren nach Anspruch 6 oder 7, dadurch gekennzeichnet, daß eine Verbindung hergestellt wird, in der R¹ und R² Wasserstoff oder Methyl sind.

9. Verfahren nach Anspruch 8, dadurch gekennzeichnet, daß eine Verbindung hergestellt wird, in der R¹ Methyl ist und R² Wasserstoff ist.

10. Verfahren nach Anspruch 4, dadurch gekennzeichnet, daß eine Verbindung mit der Strukturformel



hergestellt wird, in der W und X die in Anspruch 1 angegebenen Bedeutungen haben.

11. Verfahren nach Anspruch 10, dadurch gekennzeichnet, daß eine Verbindung hergestellt wird, in der W 3-Chloro ist und X Wasserstoff, Chlor oder Fluor ist.

12. Verfahren nach Anspruch 10, dadurch gekennzeichnet, daß eine Verbindung hergestellt wird, in der W 3-Methoxy ist und X Wasserstoff oder Fluor ist.

13. Verfahren nach Anspruch 10, dadurch gekennzeichnet, daß eine Verbindung hergestellt wird, in der W und X beide Wasserstoff sind.

14. Verfahren nach Anspruch 1 dadurch gekennzeichnet, daß eine der folgenden Verbindungen hergestellt wird:

- 3,5-Dihydro-5-phenyl-furo[3,2-c][1,8]naphthyridin-4[2H]-on;
- 2-Methyl-3,5-dihydro-5-phenyl-furo[3,2-c][1,8]naphthyridin-4[2H]-on;
- 3,5-Dihydro-5-(p-methylphenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-on;
- 3,5-Dihydro-5-(p-fluorophenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-on;
- 3,5-Dihydro-5-(m-methoxyphenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-on;
- 3,5-Dihydro-5-(3,4-dichlorophenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-on;
- 3,5-Dihydro-5-(3,4-dichlorophenyl)-2-methyl-furo[3,2-c][1,8]naphthyridin-4[2H]-on;
- 3,5-Dihydro-5-(4-chlorophenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-on;
- 3,5-Dihydro-5-(3-chlorophenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-on;
- 3,5-Dihydro-5-(3-chlorophenyl)-2-methyl-furo[3,2-c][1,8]naphthyridin-4[2H]-on;
- 3,5-Dihydro-5-(p-fluorophenyl)-2-methyl-furo[3,2-c][1,8]naphthyridin-4[2H]-on;
- 3,5-Dihydro-5-(3-methoxyphenyl)-2-methyl-furo[3,2-c][1,8]naphthyridin-4[2H]-on;
- 3,5-Dihydro-5-(3,5-dichlorophenyl)-furo[3,2-c][1,8]naphthyridin-4[2H]-on; und
- 3,5-Dihydro-5-(3,5-dichlorophenyl)-2-methyl-furo[3,2-c][1,8]naphthyridin-4[2H]-on.

15. Verfahren nach Anspruch 1 dadurch gekennzeichnet, daß eine der folgenden Verbindungen hergestellt wird:

- 6-Phenyl-2,3,4,6-tetrahydro-pyrano[3,2-c][1,8]naphthyridin-5-on;
- 6-(4-Chlorophenyl)-2,3,4,6-tetrahydro-5H-pyrano[3,2-c][1,8]naphthyridin-5-on;
- 6-(4-Methoxyphenyl)-2,3,4,6-tetrahydro-5H-pyrano[3,2-c][1,8]naphthyridin-5-on und
- 6-(4-Methylphenyl)-2,3,4,6-tetrahydro-5H-pyrano[3,2-c][1,8]naphthyridin-5-on.

16. Verfahren nach Anspruch 1 dadurch gekennzeichnet, daß eine der folgenden Verbindungen hergestellt wird:

- 3,9-Dihydro-9-phenyl-furo[2,3-b][1,8]naphthyridin-4[2H]-on;
- 3,9-Dihydro-9-(p-methylphenyl)-furo[2,3-b][1,8]naphthyridin-4[2H]-on;
- 3,9-Dihydro-2-methyl-9-phenyl-furo[2,3-b][1,8]naphthyridin-4[2H]-on;
- 3,9-Dihydro-9-(p-fluorophenyl)-furo[2,3-b][1,8]naphthyridin-4[2H]-on;
- 3,9-Dihydro-9-(m-methoxyphenyl)-furo[2,3-b][1,8]naphthyridin-4[2H]-on;
- 3,9-Dihydro-9-(4-chlorophenyl)-furo[2,3-b][1,8]naphthyridin-4[2H]-on;
- 3,9-Dihydro-9-(3-chlorophenyl)-furo[2,3-b][1,8]naphthyridin-4[2H]-on;
- 3,9-Dihydro-9-(4-fluorophenyl)-2-methyl-furo[2,3-b][1,8]naphthyridin-4[2H]-on;



3,9-Dihydro-9-(3-methoxyphenyl)-2-methyl-furo[2,3-b][1,8]naphthyridin-4[2H]-on;
 3,9-Dihydro-9-(3,5-dichlorophenyl)-furo[2,3-b][1,8]naphthyridin-4[2H]-on und
 3,9-Dihydro-9-(3,5-dichlorophenyl)-2-methyl-furo[2,3-b][1,8]naphthyridin-4[2H]-on.

17. Verfahren nach Anspruch 1 dadurch gekennzeichnet, daß eine der folgenden Verbindungen hergestellt wird:

10-(3,4-Dichlorophenyl)-2,3,4,10-tetrahydro-5H-pyrano[2,3-b][1,8]naphthyridin-5-on;
 10-(4-Methoxyphenyl)-2,3,4,10-tetrahydro-5H-pyrano[2,3-b][1,8]naphthyridin-5-on;
 10-(4-Chlorophenyl)-2,3,4,10-tetrahydro-5H-pyrano[2,3-b][1,8]naphthyridin-5-on;
 10-(4-Methylphenyl)-2,3,4,10-tetrahydro-5H-pyrano[2,3-b][1,8]naphthyridin-5-on und
 10-Phenyl-2,3,4,10-tetrahydro-5H-pyrano[2,3-b][1,8]naphthyridin-5-on.

18. Verfahren nach Anspruch 1 dadurch gekennzeichnet, daß eine der folgenden Verbindungen hergestellt wird:

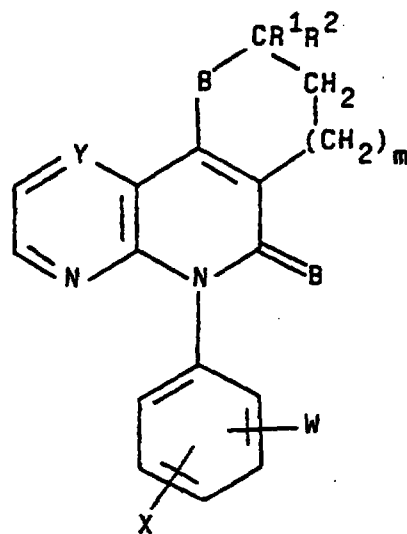
7-Phenyl-3,4,5,7-tetrahydro-oxepino[3,2-c][1,8]naphthyridin-6[2H]-on;
 7-(4-Chlorophenyl)-3,4,5,7-tetrahydro-oxepino[3,2-c][1,8]naphthyridin-6[2H]-on;
 7-(3-Chlorophenyl)-3,4,5,7-tetrahydro-oxepino[3,2-c][1,8]naphthyridin-6[2H]-on;
 7-(3-Methoxyphenyl)-3,4,5,7-tetrahydro-oxepino[3,2-c][1,8]naphthyridin-6[2H]-on und
 7-(3-Hydroxyphenyl)-3,4,5,7-tetrahydro-oxepino[3,2-c][1,8]naphthyridin-6[2H]-on.

19. Verfahren zur Herstellung einer pharmazeutischen Zusammensetzung, umfassend die Vereinigung einer Verbindung mit der Formel A' oder A'' gemäß Anspruch 1 mit einem pharmazeutisch annehmbaren Träger.

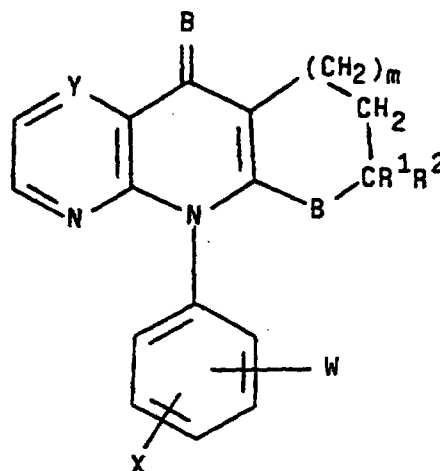
20. Verfahren zur Herstellung einer pharmazeutischen Zusammensetzung, umfassend die Vereinigung einer Verbindung mit der Formel A' oder A'' gemäß Anspruch 1, hergestellt mittels des Verfahrens nach irgendeinem der Ansprüche 1 bis 18, mit einem pharmazeutisch annehmbaren Träger.

21. Verbindung der Formel A' oder A'' gemäß Anspruch 1, sofern sie mittels des Verfahrens nach irgendeinem der Ansprüche 1 bis 18 oder einem Äquivalent derselben hergestellt ist.

22. Verbindung der Strukturformel A' oder A''



A'



A''

worin

B unabhängig Sauerstoff oder Schwefel ist,
 R¹ und R² gleich oder verschieden sein können und Wasserstoff oder Alkyl mit 1 bis 6 Kohlenstoff-Atomen sind,

m 0, 1 oder 2 ist,

W und X gleich oder verschieden sein können und Wasserstoff, Hydroxy, Alkyl mit 1 bis 6 Kohlenstoff-Atomen, Halogen, Nitro, Alkoxy mit 1 bis 6 Kohlenstoff-Atomen oder NHR^a (worin R^a Alkyl mit 1 bis 6 Kohlenstoff-Atomen ist) sind und

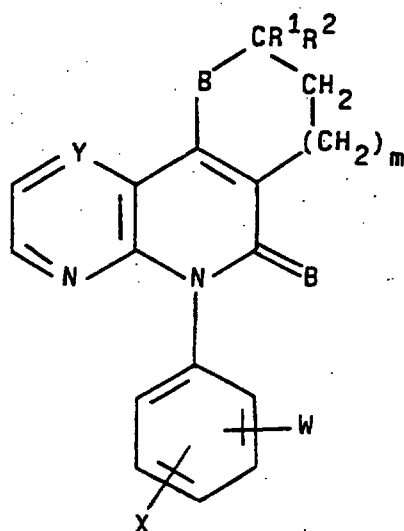
Y CH oder N ist.

23. Verbindung nach Anspruch 22 mit einer Struktur, wie sie in irgendeinem der Ansprüche 2 bis 18 für eine erzeugte Verbindung angegeben ist.

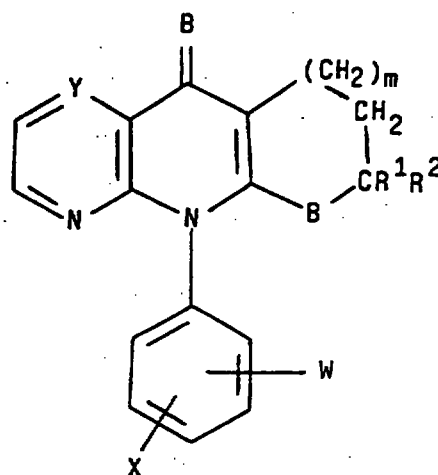


Revendications pour les Etats contractants: BE CH DE FR GB IT LI LU NL SE

1. Composé ayant la formule de structure A' ou A''



A'



A''

où

B est indépendamment oxygène ou soufre;

R¹ et R² peuvent être identiques ou différents et sont hydrogène ou alkyle ayant de 1 à 6 atomes de carbone;

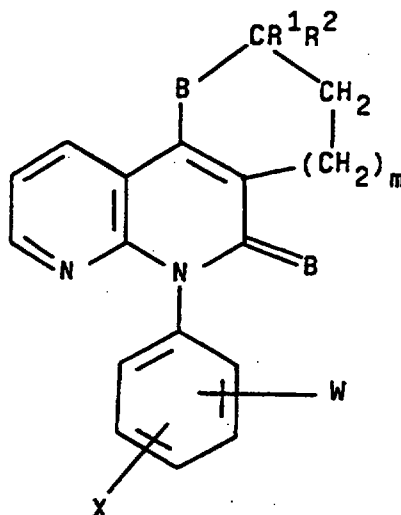
m est 0, 1 ou 2;

W et X peuvent être identiques ou différents et sont hydrogène, hydroxy, alkyle ayant de 1 à 6 atomes de carbone, halogène, nitro, alcoxy ayant de 1 à 6 atomes de carbone, ou bien NHR^a (où R^a est alkyle ayant de 1 à 6 atomes de carbone) et

Y est CH ou N.

2. Composés définis à la revendication 1 où Y est CH.

3. Composés définis à la revendication 2 ayant la formule de structure:

où B, W, X, R¹, R² et m sont tels que définis à la revendication 1.

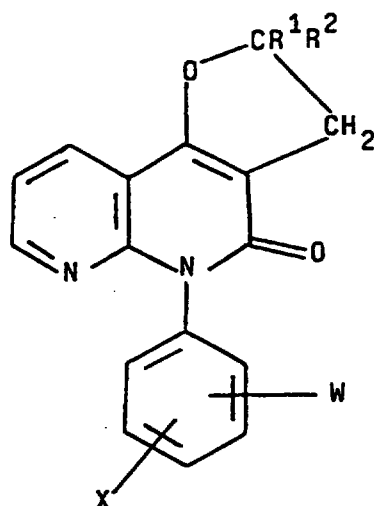
4. Composés définis à la revendication 3 où m est 0 ou 2.

5. Composés définis à la revendication 4 où B est oxygène.

6. Composés définis à la revendication 5 ayant la formule de structure:

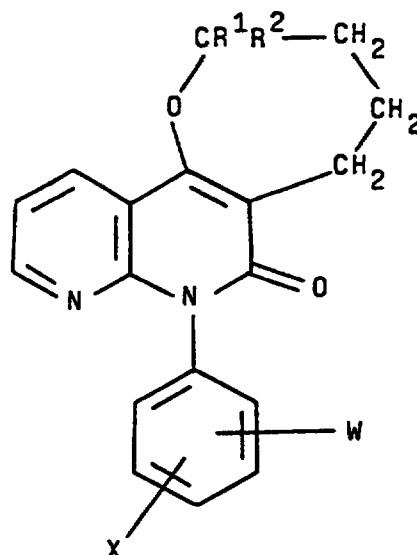


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20 où W, X, R¹ et R² sont tels que définis à la revendication 1.

7. Composés définis à la revendication 5 ayant la formule de structure:

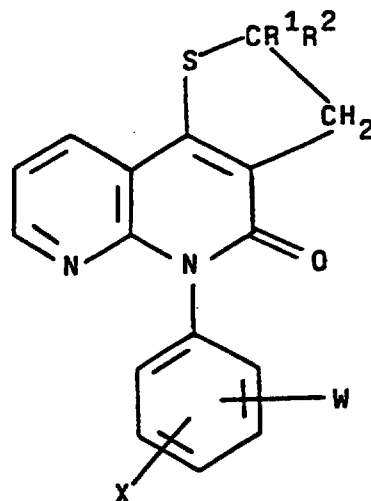


où W, X, R¹ et R² sont tels que définis à la revendication 1.

8. Composés définis à la revendication 6 ou 7 où R¹ et R² sont hydrogène ou méthyle.

9. Composés définis à la revendication 8 où R¹ est méthyle et R² est hydrogène.

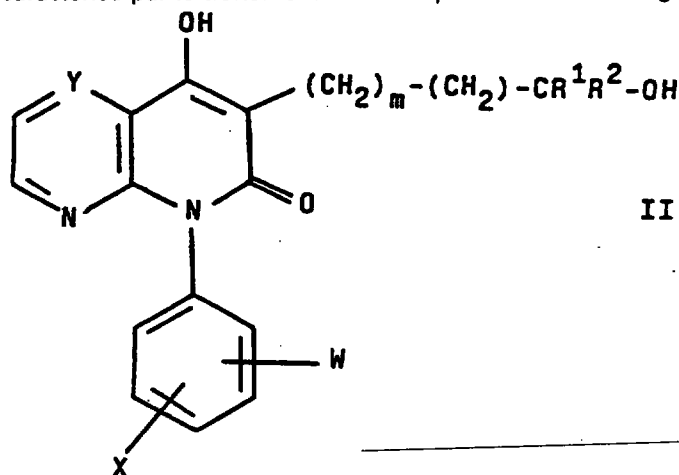
10. Composés définis à la revendication 4 ayant la formule de structure:



65 où X et W sont tels que définis à la revendication 1.



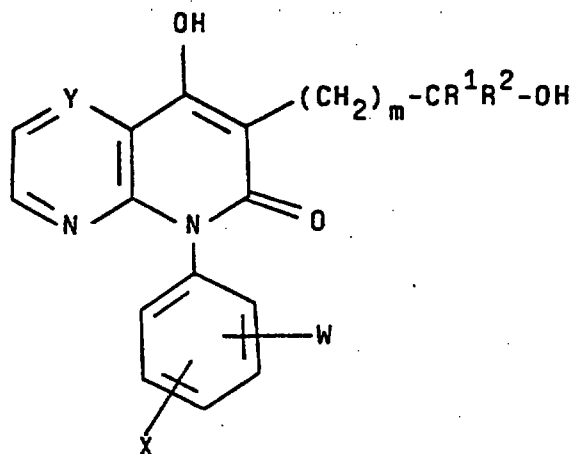
11. Composés définis à la revendication 10 où W est 3-chloro et X est hydrogène, chlore ou fluor.
 12. Composés définis à la revendication 10 où W est 3-méthoxy et X est hydrogène ou fluor.
 13. Composés définis à la revendication 10 où W et X sont tous deux hydrogène.
 14. Composés définis à la revendication 1 ayant pour noms:
 3,5-dihydro-5-phényl-furo[3,2-c][1,8]naphtyridin-4-[2H]-one;
 2-méthyl-3,5-dihydro-5-phényl-furo[3,2-c][1,8]naphtyridin-4[2H]-one;
 3,5-dihydro-5-(p-méthylphényl)-furo[3,2-c][1,8]naphtyridin-4[2H]-one;
 3,5-dihydro-5-(p-fluorophényl)-furo[3,2-c][1,8]naphtyridin-4[2H]-one;
 3,5-dihydro-5-(m-méthoxyphényl)-furo[3,2-c][1,8]naphtyridin-4[2H]-one;
 3,5-dihydro-5-(3,4-dichlorophényl)-furo[3,2-c][1,8]naphtyridin-4[2H]-one;
 3,5-dihydro-5-(3,4-dichlorophényl)-2-méthyl-furo[3,2-c][1,8]naphtyridin-4[2H]-one;
 3,5-dihydro-5-(4-chlorophényl)-furo[3,2-c][1,8]naphtyridin-4[2H]-one;
 3,5-dihydro-5-(3-chlorophényl)-furo[3,2-c][1,8]naphtyridin-4[2H]-one;
 3,5-dihydro-5-(3-chlorophényl)-2-méthyl-furo[3,2-c][1,8]naphtyridin-4[2H]-one;
 3,5-dihydro-5-(4-fluorophényl)-2-méthyl-furo[3,2-c][1,8]naphtyridin-4[2H]-one;
 3,5-dihydro-5-(3-méthoxyphényl)-2-méthyl-furo[3,2-c][1,8]naphtyridin-4[2H]-one;
 3,5-dihydro-5-(3,5-dichlorophényl)-furo[3,2-c][1,8]naphtyridin-4[2H]-one; et
 3,5-dihydro-5-(3,5-dichlorophényl)-2-méthyl-furo[3,2-c][1,8]naphtyridin-4[2H]-one.
 15. Composés définis à la revendication 1 ayant pour noms:
 6-phényl-2,3,4,6-tétrahydro-pyrano[3,2-c][1,8]naphtyridin-5-one;
 6-(4-chlorophényl)-2,3,4,6-tétrahydro-5H-pyrano[3,2-c][1,8]naphtyridin-5-one;
 6-(4-méthoxyphényl)-2,3,4,6-tétrahydro-5H-pyrano[3,2-c][1,8]naphtyridin-5-one; et
 6-(4-méthylphényl)-2,3,4,6-tétrahydro-5H-pyrano[3,2-c][1,8]naphtyridin-5-one.
 16. Composés définis à la revendication 1 ayant pour noms:
 3,9-dihydro-9-phényl-furo[2,3-b][1,8]naphtyridin-4[2H]-one;
 3,9-dihydro-9-(p-méthylphényl)-furo[2,3-b][1,8]naphtyridin-4[2H]-one;
 3,9-dihydro-2-méthyl-9-phényl-furo[2,3-b][1,8]naphtyridin-4[2H]-one;
 3,9-dihydro-9-(p-fluorophényl)-furo[2,3-b][1,8]naphtyridin-4[2H]-one;
 3,9-dihydro-9-(m-méthoxyphényl)-furo[2,3-b][1,8]naphtyridin-4[2H]-one;
 3,9-dihydro-9-(4-chlorophényl)-furo[2,3-b][1,8]naphtyridin-4[2H]-one;
 3,9-dihydro-9-(3-chlorophényl)-furo[2,3-b][1,8]naphtyridin-4[2H]-one;
 3,9-dihydro-9-(4-fluorophényl)-2-méthyl-furo[2,3-b][1,8]naphtyridin-4[2H]-one;
 3,9-dihydro-9-(3-méthoxyphényl)-2-méthyl-furo[2,3-b][1,8]naphtyridin-4[2H]-one;
 3,9-dihydro-9-(3,5-dichlorophényl)-furo[2,3-b][1,8]naphtyridin-4[2H]-one; et
 3,9-dihydro-9-(3,5-dichlorophényl)-2-méthyl-furo[2,3-b][1,8]naphtyridin-4[2H]-one.
 17. Composés définis à la revendication 1 ayant pour noms:
 10-(3,4-dichlorophényl)-2,3,4,10-tétrahydro-5H-pyrano[2,3-b][1,8]naphtyridin-5-one;
 10-(4-méthoxyphényl)-2,3,4,10-tétrahydro-5H-pyrano[2,3-b][1,8]naphtyridin-5-one;
 10-(4-chlorophényl)-2,3,4,10-tétrahydro-5H-pyrano[2,3-b][1,8]naphtyridin-5-one;
 10-(4-méthylphényl)-2,3,4,10-tétrahydro-5H-pyrano[2,3-b][1,8]naphtyridin-5-one; et
 10-phényl-2,3,4,10-tétrahydro-5H-pyrano[2,3-b][1,8]naphtyridin-5-one.
 18. Composés définis à la revendication 1 ayant pour noms:
 7-phényl-3,4,5,7-tétrahydro-oxépino[3,2-c][1,8]naphtyridin-6[2H]-one;
 7-(4-chlorophényl)-3,4,5,7-tétrahydro-oxépino[3,2-c][1,8]naphtyridin-6[2H]-one;
 7-(3-chlorophényl)-3,4,5,7-tétrahydro-oxépino[3,2-c][1,8]naphtyridin-6[2H]-one;
 7-(3-méthoxyphényl)-3,4,5,7-tétrahydro-oxépino[3,2-c][1,8]naphtyridin-6[2H]-one; et
 7-(3-hydroxyphényl)-3,4,5,7-tétrahydro-oxépino[3,2-c][1,8]naphtyridin-6[2H]-one.
 19. Procédé pour la préparation d'un composé de formule A'' tel que défini à la revendication 1 où les
 deux B sont de l'oxygène, qui est caractérisé par le traitement d'un composé de la formule générale II



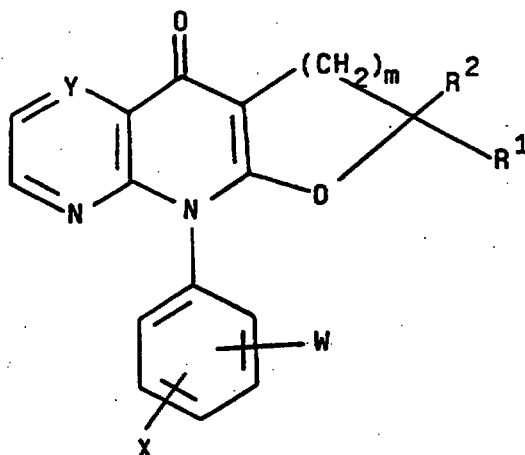
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où m, W, X, Y, R¹ et R² sont tels que définis à la revendication 1, avec un agent déshydratant en conditions anhydres pour produire un composé de formule A'' où les deux B sont de l'oxygène.

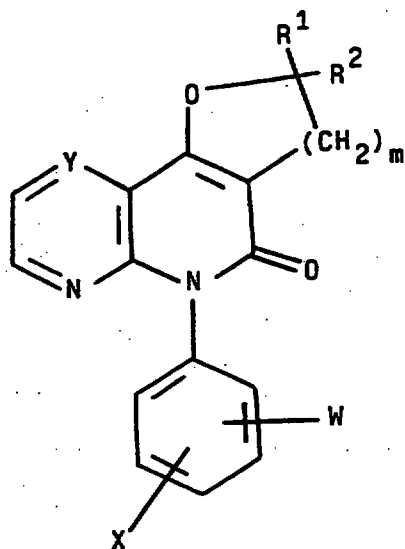
20. Procédé pour la préparation d'un composé de formule A' tel que défini à la revendication 1 qui est caractérisé par le traitement d'un composé ayant la formule générale



où m, W, X, Y, R¹ et R² sont tels que définis à la revendication 1, avec une solution acide aqueuse forte pour produire un composé de formule A' où les deux B sont oxygène; ou en soumettant un composé ayant la formule générale



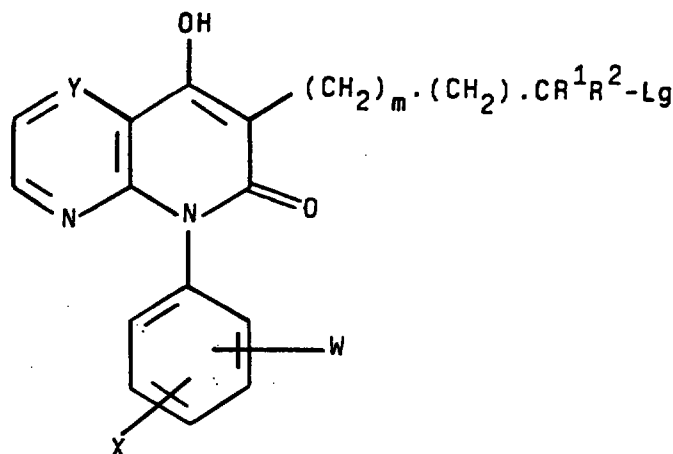
où m, W, X, Y, R¹ et R² sont tels que définis à la revendication 1, à un réarrangement intramoléculaire afin de produire un composé de formule A' dans lequel les deux B sont de l'oxygène; avec ensuite, si on le souhaite, le traitement d'un composé résultant ayant la formule générale



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où m, W, X, Y, R¹ et R² sont tels que définis à la revendication 1, en conditions de thiation afin de produire un composé de formule A' où m est zéro, l'atome B dans le noyau est oxygène et l'autre atome B est soufre.

21. Procédé pour la préparation d'un composé de formule A' tel que défini à la revendication 1 où les deux B sont oxygène, qui est caractérisé par la cyclisation d'un composé de la formule générale



où Lg est un groupe partant, et m, W, X, Y, R¹ et R² sont tels que définis à la revendication 1, pour produire un composé de formule A' où les deux B sont oxygène.

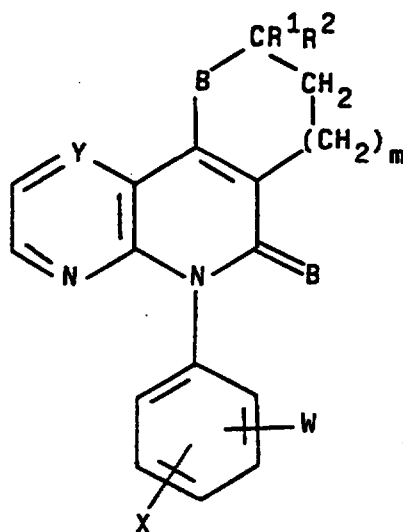
22. Procédé pour la préparation d'un composé de formule A' ou A'' tel que défini à la revendication 1, qui est caractérisé par le traitement d'un composé de formule générale II tel que défini à la revendication 19 en conditions de cyclisation et de thiation afin de produire un composé de formule A' ou A'' ou mélange où l'un ou les deux B sont soufre et si on le souhaite la séparation d'un composé de formule A' ou A'' d'un mélange ainsi prouduit;

et si on le souhaite, on soumet un composé résultant de la formule générale A' ou A'' où l'un des atomes de B est oxygène et l'autre est soufre à un réarrangement intramoléculaire où les composés des formules A' ou A'' sont convertis respectivement en composés de formules A'' ou A' de manière qu'un atome d'oxygène ou atome de soufre cyclique devienne un atome d'oxygène ou atome de soufre doublement lié et que l'atome d'oxygène ou atome de soufre doublement lié devienne l'atome d'oxygène ou atome de soufre cyclique.

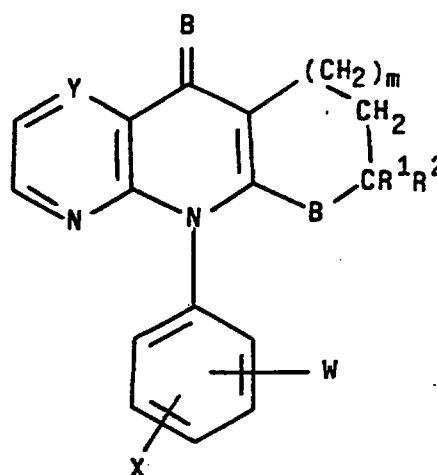
23. Composition pharmaceutique qui comprend un composé ayant la formule de structure A' ou A'' tel que défini à la revendication 1 en combinaison avec un véhicule acceptable en pharmacie.

Revendications pour l'Etat contractant: AT

1. Procédé pour la préparation d'un composé ayant la formule de structure A' ou A''



A'



A''

où

B est indépendamment oxygène ou soufre;



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R¹ et R² peuvent être identiques ou différents et sont hydrogène ou alkyle ayant de 1 à 6 atomes de carbone;

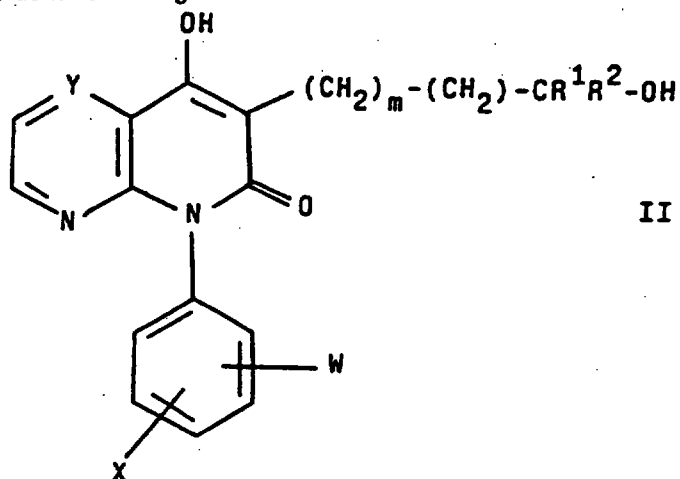
m est 0, 1 ou 2;

W et X peuvent être identiques ou différents et sont hydrogène, hydroxy, alkyle ayant de 1 à 6 atomes de carbone, halogène, nitro, alcoxy ayant de 1 à 6 atomes de carbone, ou bien NHR^a (où R^a est alkyle ayant de 1 à 6 atomes de carbone); et

Y est CH ou N;

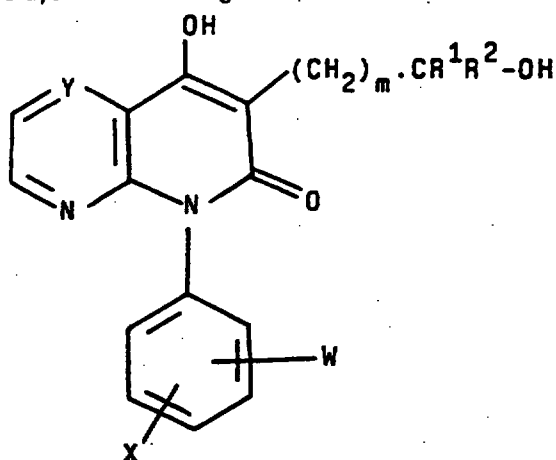
caractérisé par:

a) le traitement d'un composé de la formule générale II



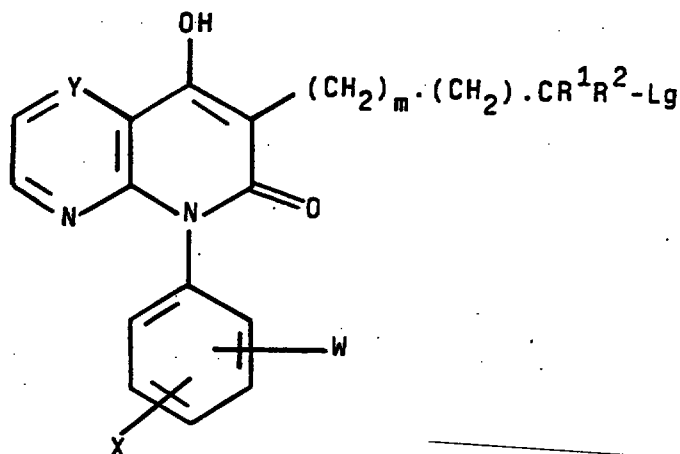
où m, W, X, Y, R¹ et R² sont tels que définis ci-dessus, avec un agent déshydratant en conditions anhydres pour produire un composé de formule A'' dans lequel les deux B sont oxygène;

b) le traitement d'un composé ayant la formule générale



où m, W, X, Y, R¹ et R² sont tels que définis ci-dessus, avec une solution acide aqueuse forte pour produire un composé de formule A' dans lequel les deux B sont oxygène;

c) la cyclisation d'un composé de formule générale

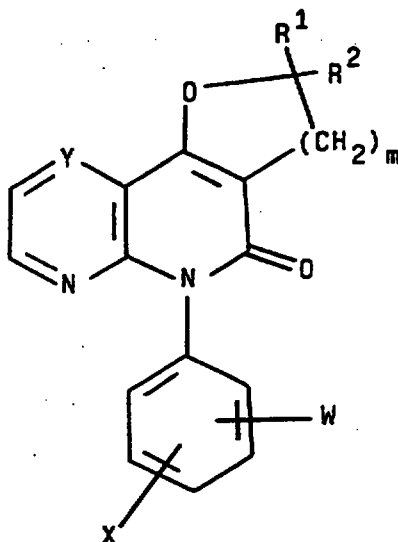


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où Lg est un groupe partant et m, W, X, Y, R¹ et R² sont tels que définis ci-dessus, pour produire un composé de formule A', où les deux B sont oxygène;

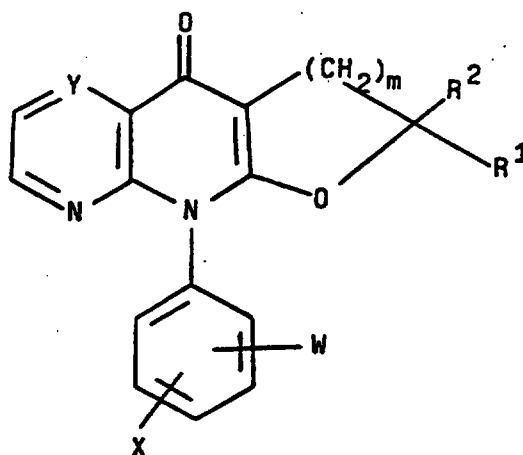
d) le traitement d'un composé de formule générale II tel que défini au procédé c) ci-dessus en conditions de cyclisation et de thiation afin de produire un composé de formule A', A'' ou un mélange où l'un ou les deux B sont soufre et, si on le souhaite, la séparation d'un composé de formule A' ou A'' d'un mélange ainsi produit;

e) le traitement d'un composé ayant pour formule générale



où m, W, X, Y, R¹ et R² sont tels que définis ci-dessus, en conditions de thiation afin de produire un composé de formule A' où m est zéro, l'atome B dans le noyau est oxygène et l'autre atome B est du soufre.

f) la soumission d'un composé ayant la formule générale



où m, W, X, Y, R¹ et R² sont tels que définis ci-dessus, à un réarrangement intramoléculaire afin de produire un composé de formule A' tel que défini ci-dessus où les deux B sont oxygène,

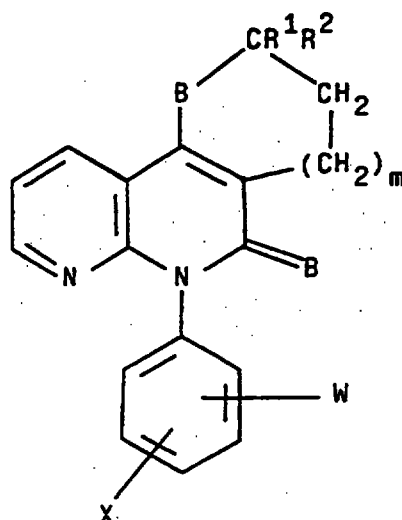
g) la soumission d'un composé de la formule générale A' ou A'' où l'un des atomes B est oxygène et l'autre est soufre, à un réarrangement intramoléculaire pour qu'ainsi ledit composé de formule A' ou A'' soit converti respectivement en un composé de formule A'' ou A' tel qu'un atome d'oxygène ou atome de soufre cyclique devienne un atome d'oxygène ou atome de soufre doublement lié et que l'atome d'oxygène ou atome de soufre doublement lié devienne l'atome d'oxygène ou atome de soufre cyclique;

et ensuite, si on le souhaite, la transformation d'un composé de formule A' ou A'' ainsi obtenu par un procédé a), b), c), d), e), f) ou g) en un autre composé de formule A' ou A''.

2. Procédé tel que défini à la revendication 1 caractérisé en ce qu'un composé de formule A' ou A'' est produit où Y est CH.

3. Procédé tel que défini à la revendication 2 caractérisé en ce qu'un composé est produit ayant la formule de structure:



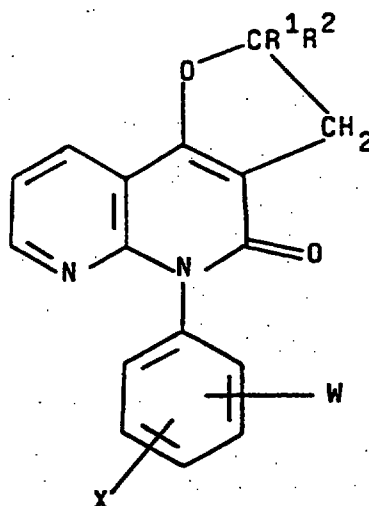


où B, W, X, Y, R¹ et R² et m sont tels que définis à la revendication 1.

4. Procédé tel que défini à la revendication 3 caractérisé en ce qu'un composé est produit où m est 0 ou 2.

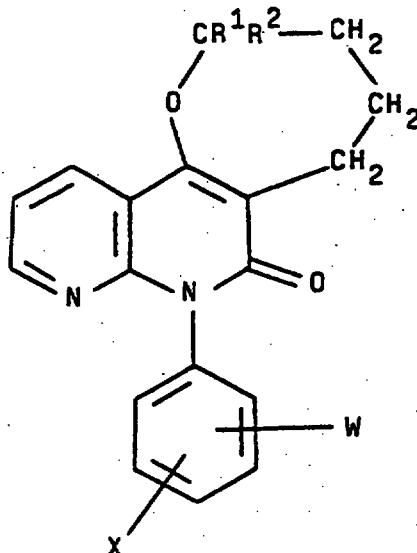
5. Procédé tel que défini à la revendication 4 caractérisé en ce qu'un composé est produit où B est oxygène.

6. Procédé tel que défini à la revendication 5 caractérisé en ce qu'un composé est produit ayant la formule de structure:



où W, R¹ et R² sont tels que définis à la revendication 1.

7. Procédé tel que défini à la revendication 5 caractérisé en ce qu'un composé est produit ayant la formule de structure:



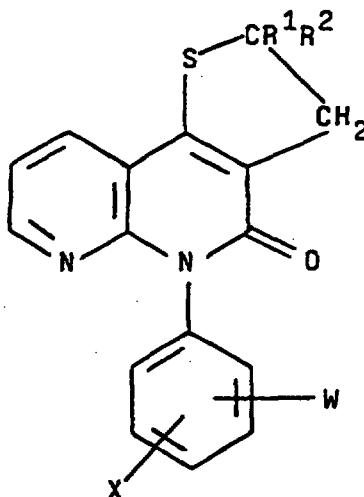


où W, X, R¹ et R² sont tels que définis à la revendication 1.

8. Procédé tel que défini à la revendication 6 ou à la revendication 7 caractérisé en ce qu'un composé est produit où R¹ et R² sont hydrogène ou méthyle.

9. Procédé tel que défini à la revendication 8 caractérisé en ce qu'un composé est produit où R¹ est méthyle et R² est hydrogène.

10. Procédé tel que défini à la revendication 4 caractérisé en ce qu'un composé est produit ayant la formule de structure:



où X et W sont tels que définis à la revendication 1.

11. Procédé tel que défini à la revendication 10 caractérisé en ce qu'un composé est produit où W est 3-chloro et X est hydrogène, chlore ou fluor.

12. Procédé tel que défini à la revendication 10 caractérisé en ce qu'un composé est produit où W est 3-méthoxy et X est hydrogène ou fluor.

13. Procédé tel que défini à la revendication 10 caractérisé en ce qu'un composé est produit où W et X sont tous deux de l'hydrogène.

14. Procédé tel que défini à la revendication 1 caractérisé en ce que l'un des composés suivants est produit:

- 3,5-dihydro-5-phényl-furo[3,2-c][1,8]naphtyridin-4[2H]-one;
- 2-méthyl-3,5-dihydro-5-phényl-furo[3,2-c][1,8]naphtyridin-4[2H]-one;
- 3,5-dihydro-5-(p-méthylphényl)-furo[3,2-c][1,8]naphtyridin-4[2H]-one;
- 3,5-dihydro-5-(p-fluorophényl)-furo[3,2-c][1,8]naphtyridin-4[2H]-one;
- 3,5-dihydro-5-(m-méthoxyphényl)-furo[3,2-c][1,8]naphtyridin-4[2H]-one;
- 3,5-dihydro-5-(3,4-dichlorophényl)-furo[3,2-c][1,8]naphtyridin-4[2H]-one;
- 3,5-dihydro-5-(3,4-dichlorophényl)-2-méthyl-furo[3,2-c][1,8]naphtyridin-4[2H]-one;
- 3,5-dihydro-5-(4-chlorophényl)-furo[3,2-c][1,8]naphtyridin-4[2H]-one;
- 3,5-dihydro-5-(3-chlorophényl)-furo[3,2-c][1,8]naphtyridin-4[2H]-one;
- 3,5-dihydro-5-(3-chlorophényl)-2-méthyl-furo[3,2-c][1,8]naphtyridin-4[2H]-one;
- 3,5-dihydro-5-(4-fluorophényl)-2-méthyl-furo[3,2-c][1,8]naphtyridin-4[2H]-one;
- 3,5-dihydro-5-(3-méthoxyphényl)-2-méthyl-furo[3,2-c][1,8]naphtyridin-4[2H]-one;
- 3,5-dihydro-5-(3,5-dichlorophényl)-furo[3,2-c][1,8]naphtyridin-4[2H]-one; et
- 3,5-dihydro-5-(3,5-dichlorophényl)-2-méthyl-furo[3,2-c][1,8]naphtyridin-4[2H]-one.

15. Procédé tel que défini à la revendication 1 caractérisé en ce que l'un des composés suivants est produit:

- 6-phényl-2,3,4,6-tétrahydro-pyrano[3,2-c][1,8]naphtyridin-5-one;
- 6-(4-chlorophényl)-2,3,4,6-tétrahydro-5H-pyrano[3,2-c][1,8]naphtyridin-5-one;
- 6-(4-méthoxyphényl)-2,3,4,6-tétrahydro-5H-pyrano[3,2-c][1,8]naphtyridin-5-one; et
- 6-(4-méthylphényl)-2,3,4,6-tétrahydro-5H-pyrano[3,2-c][1,8]naphtyridin-5-one.

16. Procédé tel que défini à la revendication 1 caractérisé en ce que l'un des composés suivants est produit:

- 3,9-dihydro-9-phényl-furo[2,3-b][1,8]naphtyridin-4[2H]-one;
- 3,9-dihydro-9-(p-méthylphényl)-furo[2,3-b][1,8]naphtyridin-4[2H]-one;
- 3,9-dihydro-2-méthyl-9-phényl-furo[2,3-b][1,8]naphtyridin-4[2H]-one;
- 3,9-dihydro-9-(p-fluorophényl)-furo[2,3-b][1,8]naphtyridin-4[2H]-one;
- 3,9-dihydro-9-(m-méthoxyphényl)-furo[2,3-b][1,8]naphtyridin-4[2H]-one;
- 3,9-dihydro-9-(4-chlorophényl)-furo[2,3-b][1,8]naphtyridin-4[2H]-one;
- 3,9-dihydro-9-(3-chlorophényl)-furo[2,3-b][1,8]naphtyridin-4[2H]-one;
- 3,9-dihydro-9-(4-fluorophényl)-2-méthyl-furo[2,3-b][1,8]naphtyridin-4[2H]-one;
- 3,9-dihydro-9-(3-méthoxyphényl)-2-méthyl-furo[2,3-b][1,8]naphtyridin-4[2H]-one;

3,9-dihydro-9-(3,5-dichlorophényl)-furo[2,3-b][1,8]naphtyridin-4[2H]-one; et
3,9-dihydro-9-(3,5-dichlorophényl)-2-méthyl-furo[2,3-b][1,8]naphtyridin-4[2H]-one.

17. Procédé tel que défini à la revendication 1 caractérisé en ce que l'un des composés suivants est produit:

- 5 10-(3,4-dichlorophényl)-2,3,4,10-tétrahydro-5H-pyrano[2,3-b][1,8]naphtyridin-5-one;
10-(4-méthoxyphényl)-2,3,4,10-tétrahydro-5H-pyrano[2,3-b][1,8]naphtyridin-5-one;
10-(4-chlorophényl)-2,3,4,10-tétrahydro-5H-pyrano[2,3-b][1,8]naphtyridin-5-one;
10-(4-méthylphényl)-2,3,4,10-tétrahydro-5H-pyrano[2,3-b][1,8]naphtyridin-5-one; et
10-phényl-2,3,4,10-tétrahydro-5H-pyrano[2,3-b][1,8]naphtyridin-5-one.

18. Procédé tel que défini à la revendication 1 caractérisé en ce que l'un des composés suivants est produit:

- 7-phényl-3,4,5,7-tétrahydro-oxépino[3,2-c][1,8]naphtyridin-6[2H]-one;
7-(4-chlorophényl)-3,4,5,7-tétrahydro-oxépino[3,2-c][1,8]naphtyridin-6[2H]-one;
7-(3-chlorophényl)-3,4,5,7-tétrahydro-oxépino[3,2-c][1,8]naphtyridin-6[2H]-one;
15 7-(3-méthoxyphényl)-3,4,5,7-tétrahydro-oxépino[3,2-c][1,8]naphtyridin-6[2H]-one; et
7-(3-hydroxyphényl)-3,4,5,7-tétrahydro-oxépino[3,2-c][1,8]naphtyridin-6[2H]-one.

19. Méthode de préparation d'une composition pharmaceutique qui consiste à combiner un composé de formule A' ou A'' tel que défini à la revendication 1 avec un véhicule acceptable en pharmacie.

20. Méthode de préparation d'une composition pharmaceutique qui consiste à combiner un composé de formule A' ou A'' tel que défini à la revendication 1, préparé par le procédé selon l'une des revendications 1 à 18, avec un véhicule acceptable en pharmacie.

21. Composé de formule A' ou A'' tel que défini à la revendication 1 produit par le procédé selon l'une des revendications 1 à 18 ou son équivalent.

22. Composé ayant la formule de structure A' ou A''

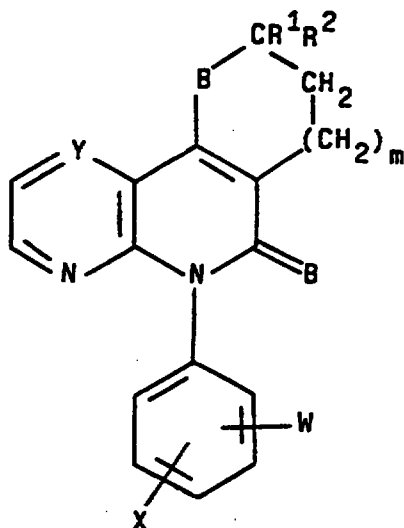
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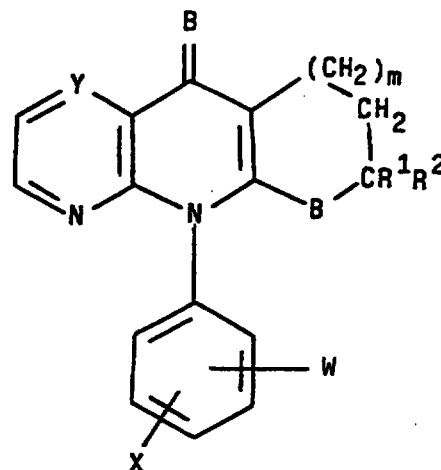
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A'



A''

où

B est indépendamment oxygène ou soufre;
50 R¹ et R² peuvent être identiques ou différents et sont hydrogène ou alkyle ayant de 1 à 6 atomes de carbone;

m est 0, 1 ou 2;

W et X peuvent être identiques ou différents et sont hydrogène, hydroxy, alkyle ayant de 1 à 6 atomes de carbone, halogène, nitro, alcoxy ayant de 1 à 6 atomes de carbone, ou NHR^a (où R^a est alkyle ayant de 1 à 6 atomes de carbone); et

55 Y est CH ou N.

23. Composé selon la revendication 22, ayant une structure telle que définie selon l'une des revendications 2 à 18 pour un composé produit.

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