# United States Patent [19]

**Hoyle et al.**

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[45] **Aug. 28, 1973**


[54] **3-(5-NITRO-2-FURYL)-1H-PYRAZOLO[3,4]PYRIMIDINS-4(5H)-ONES**


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[30] **Foreign Application Priority Data**

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[52] **U.S. Cl.** ... **260/256.4 F,** 260/310 R, 260/347.3, 260/347.7, 424/251

[51] **Int. Cl.** ..... **C07d 51/46**

[58] **Field of Search** ..... 260/256.4 F



[56] **References Cited**

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[57] **ABSTRACT**

Compounds of the class of 3-(5-nitro-2-furyl)- 1H-pyrazolo[3,4-d]pyrimidin-4(5H)-one have antimicrobial properties and are active ingredients in pharmaceutical compositions and animal feedstuff compositions, an illustrative example is 1,6-dimethyl-3-(5-nitro-2-furyl)-1H-pyrazolo[3,4-d]pyrimidin-4(5H)-one.

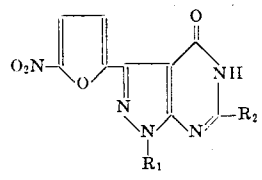

**6 Claims, No Drawings**

# 3-(5-NITRO-2-FURYL)-1H-PYRAZOLO[3,4]PYRIMIDINS-4(5H)-ONES

## DETAILED DESCRIPTION

The present invention relates to nitrofuryl derivatives, in particular, to derivatives of 3-(5-nitro-2-furyl)-1H-pyrazolo[3,4-d]pyrimidin-4(5H)-one which compounds have antimicrobial properties. It further relates to pharmaceutical and animal feedstuff compositions containing these compounds and to methods for the treatment of mammals suffering from microbial infections, particularly of urinary tract infections, comprising administering to said mammals an effective amount of such compound. The invention also provides methods for protecting organic material susceptible to microbial attack with an effective amount of a compound according to the invention.

More particularly, the present invention relates to compounds of the formula I



(I)

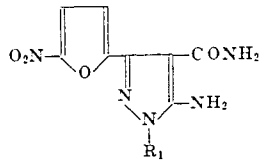
wherein

$R_1$ is alkyl having from one to five carbon atoms or carbalkoxy having from one to five carbon atoms in the alkyl moiety, and

$R_2$ is hydrogen, alkyl having from one to five carbon atoms which may be unsubstituted or substituted partially or completely by chloro or bromo; cycloalkyl having from five to seven carbon atoms in the carbocyclic ring, aralkyl having up to 12 carbon atoms, or alkenyl having from two to four carbon atoms.

Examples of alkyl groups having from one to five carbon atoms are methyl, ethyl, n-propyl, isopropyl, n-butyl, tertiarybutyl and n-pentyl groups. Preferably, $R_1$ as an alkyl group contains from one to three carbon atoms. Cycloalkyl of from five to seven carbon atoms embraces cyclopentyl, cyclohexyl and cycloheptyl groups, whereby the cyclohexyl group is preferred. By the term aralkyl is meant for example the benzyl group and other groups consisting of an aryl and an alkyl moiety, such as phenylethyl, naphthylmethyl and the like. Alkenyl containing from two to four carbon atoms embraces the vinyl, allyl, 2-methallyl, but-2-enyl and but-3-enyl group.

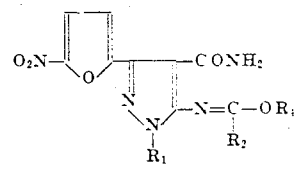
Compounds of formula I are produced by treating a compound of the formula II



(II)



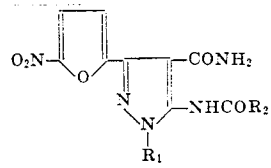
in which $R_1$ has the meaning as given under formula I, with a reagent $R_2C(OR_4)_3$ where $R_4$ is an alkyl group containing from one to three carbon atoms, with or without a reaction promotor such as a carboxylic acid anhydride, to give an intermediate of formula III



(III)

wherein $R_1$, $R_2$ and $R_4$ are as herein before defined, which is cyclised without isolation.

This reaction may be carried out directly between the compound II and the selected reagent, or may be carried out in the presence of an inert solvent, such as for example dimethylsulphoxide or dimethylformamide. The presence of an inert solvent is of course desirable if the compound II is a solid. In all cases, the reaction will preferably be carried out at a temperature of from 20°C. to the reflux temperature of the reaction mixture. Alternatively, a compound of the general formula II may be reacted with a carboxylic acid derivative $R_2COX$ or $(R_2CO)_2O$ where $R_2$ is as previously defined and X is hydroxyl, halogen (preferably chlorine or bromine), amino, or the grouping $-OR_3$ where $R_3$ is an alkyl or alkenyl group containing from one to three carbon atoms, to given an intermediate of formula IV

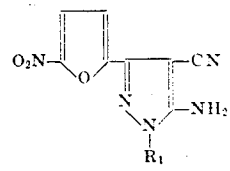


(IV)

wherein

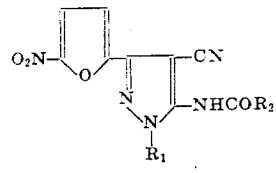
$R_1$ and $R_2$ are as previously defined. The compounds of formula IV are cyclised without isolation.

In a further process, compounds of general formula V



(V)

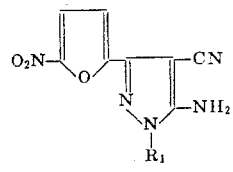
wherein $R_1$ is as herein before defined, may be reacted with formic acid or with carboxylic acid derivative $R_2COX$ or $(R_2CO)_2O$, where $R_1$, $R_2$ and X have their previous significance [except that X may not be hydroxyl] to give an intermediate of general formula VI



(VI)

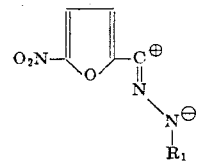
the reaction being carried out in the presence of an acid or basic catalyst and the intermediate then isolated or immediately cyclised without isolation. Compounds of general formula VI are novel per se, and have antimicrobial activity.

The starting compounds of formula II can be prepared by hydrolysing the corresponding nitrofuryl-pyrazole derivative having the formulae V



(V)

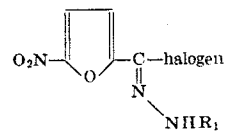
wherein $R_1$ has the previous significance. The compounds of formula V are themselves prepared by reacting the corresponding nitrofuryl-nitrilimine which in one of its canonical forms may be represented by the formula X



(X)

with malononitrile, where $R_1$ has its previous significance.

The nitrofuryl-nitrilimine of formula X may conveniently be generated, as required, during the course of the reaction with malononitrile, by treating with a base the corresponding nitrofuryl-α-halo-hydrazone having the formula XI



(XI)

The process may, if desired, be effected in the presence of a conventional base or other hydrogen halide acceptor. The halogen present in the halohydrazone of formula XI is preferably chlorine or bromine.



The compounds of the invention have valuable antimicrobial properties, and in particular have antibacterial, antimycoplasmal, anthelminthic, antiprotozoal, coccidiostatic, trypanocidal and antimalarial activity of value in human or veterinary medicine. The compounds are particularly valuable in the treatment of infections of the intestinal and urinary tracts.

Their antimicrobial activity is demonstrated in a number of conventional pharmacological tests. Thus it is shown that, for example, 1-methyl-3-(5-nitro-2-furyl)-1H-pyrazolo[3,4-d]pyrimidin-4(5H)-one and 1,6-dimethyl-3-(5-nitro-2-furyl)-1H-pyrazolo[3,4-d]pyrimidin-4(5H)-one have in vitro an excellent growth inhibiting effect against staphylococcus aureus, Escherichia coli, Klebsiella pneumonia, Salmonella typhi and others if added in amounts of about 1 to about 10 γ/ml to the bacterial culture.

The toxicity of the compounds of the invention as demonstrated for example in mice is of favourable low order.

For their intended internal use, for example for the treatment of intestinal and urinary tract infections, the active compounds are administered in dosages depending on the kind of infection, the species and the age, weight and particular condition of the individual being treated. In general the daily dosage upon oral application will vary from about 1 to 100 mg/kg for mammals. The compounds may also be used to protect a high molecular weight hydrophobic or other organic material susceptible to bacterial or other microbial deterioration by contacting the organic material with, impregnating in or otherwise treating with, the compounds in amounts up to about 5 percent by weight. The compounds also find application as growth-promoting additives to animal feedstuffs, to which they may be added in proportion of from 5 to 500 parts per million.

Accordingly, the invention also provides a pharmaceutical composition comprising an antimicrobially effective proportion of an active compound of the invention and a pharmacologically acceptable solid carrier or liquid diluent.

The pharmaceutical compositions according to the invention contain at least one active compound of the invention as active substance together with a conventional pharmaceutical carrier. The type of carrier actually used depends to a great extent on the intended application, for external use, for example in disinfecting healthy skin, disinfecting wounds and in treating dermatoses and affections of the mucous membranes caused by bacteria, ointments, powders and tinctures are used in particular. The ointment bases may be anhydrous, for instance they can consist of mixtures of wool fat and soft paraffin, or they can consist of aqueous emulsions in which the active substance is suspended. Suitable carriers for powders are, for instance, rice starch and other starches; the bulk weight of the carriers may be made lighter, if desired, for example by adding highly dispersed silicic acid, or may be made heavier by adding talcum. The tinctures may contain at least one active ingredient in aqueous ethanol, in particular 45 to 75 percent ethanol, to which 10 to 20 percent of glycerol may be added, if desired. Solutions prepared from polyethylene glycol and other conventional solubility promoters, and also, optionally, from emulsifying agents, may be used with particular advantage in disinfecting healthy skin. The content of active ingredient in pharmaceutical compositions for external appli-

cation is preferably in the range of from 0.1 to 5 percent.

Gargles or concentrates for their preparation, and tablets for slow dissolution in the mouth, are suitable for the disinfection of the mouth and throat. The former are preferably prepared from alcoholic solutions containing 1 to 5 percent of active substance to which glycerol or flavourings may be added. Lozenges, that is solid dosage units, preferably have a relatively high content of sugar or similar substances and a relatively low content of active substance, for instance 0.2 to 20 percent by weight, as well as the usual convential additives such as binding agents and flavourings.

Solid dosage units, in particular tablets, dragees (sugar coated tablets) and capsules, are convenient for use in intestinal disinfection and for the oral treatment of urinary tract infections. These units preferably contain from 10 to 90 percent of the active compound to enable the administration of daily doses of from 0.1 to 2.5 grams to adults, or of suitable reduced doses to children to be made. Tablets and dragee cores are produced by combining the active compounds with solid, pulverulent carriers such as lactose, saccharose, sorbitol, maize starch, potato starch or amylopectin, cellulose derivatives or gelatines, preferably with the addition of lubricants such as magnesium or calcium stearate or polyethylene glycols of suitable molecular weight. Dragee cores may then be coated, for example with concentrated sugar solutions which can also contain gum arabic, talcum and/or titanium dioxide, or they may be coated with a lacquer dissolved in volatile organic solvents or mixture of solvents. Dyestuffs can be added to these coatings, for instance to differentiate between varying dosages. Soft gelatine capsules and other closed capsules consist, for example, of a mixture of gelatines and glycerol and may contain, for example, mixtures of the active compound with polyethylene glycol. Hard gelatine capsules contain, for example, granulates of an active substance with solid pulverulent carriers, for instance lactose, saccharose, sorbitol, mannitol, starches (such as potato starch, maize starch or amylopectin), cellulose derivatives of gelatines, and magnesium stearate or stearic acid.

In all forms for administration the active compounds can be present as solo active ingredients or they can also be combined with other known pharmacologically active, and especially antibacterial and/or antimycotically or other anti-microbially active substances, for example to broaden the range of application. They can be combined for example, with 5,7-dichloro-2-methyl-8-quinolinol or other derivatives of 8-quinolinol, with sulfamerazine or sulfafurazole or other derivatives of sulfanilamide, with chloramphenicol or tetracycline or other antibiotics, with 3,4',5-tribromosalicylanilide or other halogenated salicylanilides, with halogenated carbanilides, with halogenated benzoxazoles or benzoxazolones, with polychloro-hydroxy-diphenylmethanes, with halogen-di-hydroxy-diphenyl sulphides, with 4,4'-dichloro-2-hydroxydiphenylether or 2',4,4'-trichloro-2-hydroxydiphenylether or other polyhalogenhydroxydiphenylethers, or with bactericidal quaternary compounds or with certain dithiocarbamic acid derivatives such as tetramethylthiuram disulphide. Also, carriers which themselves have favourable pharmacological properaties may be used, for instance sulphur as a powder base or zine stearate as a component of ointment bases.

The invention also provides a method of protecting an organic material susceptible to bacterial or other microbial attack which comprises treating the material with an active compound of the invention. The organic material may be, for instance, a natural or synthetic polymeric material, a proteinaceous or carbohydrate substance, or a natural or synthetic fibre or textile material formed therefrom.

The invention also provides an animal feedstuff composition comprising an active compound of the invention in an amount sufficient to promote the growth of the animal fed with the composition.

The following examples will serve to further illustrate the nature of the present invention, however, they should not be construed as a limitation on the scope thereof.

## EXAMPLE 1

A mixture of 10 grams of 5-amino-4-cyano-1-methyl-3-(5-nitro-2-furyl)-pyrazole and 100 millilitres of 90 percent formic acid was heated under reflux for 1 hour and cooled. The crystalline solid was collected, washed with water and recrystallised from dimethylformamide. The product was 1-methyl-3-(5-nitro-2-furyl)-1H-pyrazolo[3,4-d]pyrimidin-4(5H)-one, having melting point >300°C.

## EXAMPLE 2

The procedure described in Example 1 was carried out using 5-amino-4-carbamoyl-1-methyl-3-(5-nitro-2-furyl)-pyrazole as starting material instead of 5-amino-4-cyano-1-methyl-3-(5-nitro-2-furyl)-pyrazole, the reaction conditions being the same.

The product was 1-methyl-3-(5-nitro-2-furyl)-1H-pyrazolo[3,4-d]pyrimidin-4(5H)-one, having melting point >300°C., identical with the product obtained in Example 1.

## EXAMPLE 3

A mixture of 0.2 grams of 5-amino-4-carbamoyl-1-methyl-3-(5-nitro-2-furyl)-pyrazole and 5.0 millilitres of triethylorthoformate was heated under reflux for 3 hours and cooled. The crystalline solid was collected, washed with ethanol and dried. The product was 1-methyl-3-(5-nitro-2-furyl)-1H-pyrazolo[3,4-d]pyrimidin-4(5H)-one having melting point >300°C.

## EXAMPLE 4

The procedure described in Example 1 was carried out using 5-amino-4-cyano-1-isopropyl-3-(5-nitro-2-furyl)-pyrazole as starting material instead of 5-amino-4-cyano-1-methyl-3-(5-nitro-2-furyl)-pyrazole, the reaction conditions being the same.

The product was 1-isopropyl-3-(5-nitro-2-furyl)-1H-pyrazolo[3,4-d]pyrimidin-4(5H)-one.

## EXAMPLE 5

The procedure described in Example 1 was carried out using 5-amino-4-cyano-3-(5-nitro-2-furyl)-1-n-pentyl-pyrazole as starting material instead of 5-amino-4-cyano-1-methyl-3-(5-nitro-2-furyl)-pyrazole, the reaction conditions being the same.

The product was 3-(5-nitro-2-furyl)-1-n-pentyl-1H-pyrazolo[3,4-d]pyrimidin-4(5H)-one.

## EXAMPLE 6

A mixture of 10 grams of 5-amino-4-carbamoyl-1-

methyl-3-(5-nitro-2-furyl)-pyrazole and 100 millilitres of acetic anhydride was heated under reflux for 6 hours and cooled. The crystalline solid was collected, washed with alcohol and recrystallised from dimethylformamide.

The product was 1,6-dimethyl-3-(5-nitro-2-furyl)-1H-pyrazolo[3,4-d]pyrimidin-4(5H)-one which has melting point >300°C.

EXAMPLE 7

The procedure described in Example 6 was carried out using crotonic anhydride as starting material instead of acetic anhydride, the reaction condition being the same.

The product was 1-methyl-6-(1-propenyl)-3-(5-nitro-2-furyl)-1H-pyrazolo[3,4-d]pyrimidin-4-(5H)-one, which has melting point >300°C.

EXAMPLE 8

The procedure described in Example 6 was carried out using chloro-acetic anhydride as starting material instead of acetic anhydride, the reaction conditions being the same.

The product was 6-chloromethyl-1-methyl-3-(5-nitro-2-furyl)-1H-pyrazolo[3,4-d]pyrimidin-4-(5H)-one, which has melting point >300°C. with decomposition.

EXAMPLE 9

The procedure described in Example 6 was carried out using cyclohexane carboxylic anhydride as starting material instead of acetic anhydride, the reaction conditions being the same.

The product was 6-cyclohexyl-1-methyl-3-(5-nitro-2-furyl)-1H-pyrazolo[3,4-d]pyrimidin-4-(5H)-one, which has melting point >300°C.

EXAMPLE 10

The procedure described in Example 6 was carried out using phenylacetic anhydride as starting material instead of acetic anhydride, the reaction conditions being the same.

The product was 6-benzyl-1-methyl-3-(5-nitro-2-furyl)-1H-pyrazolo[3,4-d]pyrimidin-4(5H)-one, which has melting point >300°C.

EXAMPLE 11

A mixture of 14.0 grams of 5-amino-4-cyano-1-methyl-3-(5-nitro-2-furyl)-pyrazole, 7.8 grams of propionic anhydride and 2.0 grams of concentrated sulphuric acid (S.G. 1.84) was heated at a reaction temperature of 100°–120°C. for 15 minutes and then cooled. The solid which crystallised was collected, washed with 100 millilitres of water and dried. Recrystallisation from dimethyl formamide gave 6-ethyl-1-methyl-3-(5-nitro-2-furyl)-1H-pyrazolo-[3,4-d]pyrimidin-4(5H)-one, having melting point >300°C.

EXAMPLE 12

The procedure described in Example 11 was carried out using crotonic anhydride as starting material instead of propionic anhydride, the reaction conditions being the same.

The product was 1-methyl-3-(5-nitro-2-furyl)-6-(1-propenyl)-1H-pyrazolo[3,4-d]pyrimidin-4(5H)-one, having melting point >300°C.

EXAMPLE 13

The procedure described in Example 11 was carried out using butyric anhydride as starting material instead of propionic anhydride, the reaction conditions being the same.

The product was 1-methyl-3-(5-nitro-2-furyl)-6-propyl-1H-pyrazolo[3,4-d]pyrimidin-4(5H)-one, having melting point >300°C.

EXAMPLE –

A mixture of 14.0 grams of 5-amino-4-cyano-1-methyl-3-(5-nitro-2-furyl)-pyrazole, 9.5 grams isobutyric anhydride and 0.6 grams of concentrated sulphuric acid (S.G. 1.84) was heated at a reaction temperature of 100°–120°C. for 15 minutes and then cooled. The solid which crystallised was collected, washed with ether and dried. Recrystallisation from aqueous dimethylformamide gave 4-cyano-5-isobutyramido-1-methyl-3-(5-nitro-2-furyl)-pyrazole having melting point 225°C.

A mixture of 3.5 grams of 4-cyano-5-isobutyramido-1-methyl-3-(5-nitro-2-furyl)-pyrazole, 20 millilitres of dimethylformamide and 10 millilitres of concentrated sulphuric acid (S.G. 1.84) was heated under reflux for 1 hour and cooled. The mixture was then diluted with 50 millilitres of water and the solid which formed was collected, washed with water and dried. Recrystallisation from dimethylformamide gave 6-isopropyl-1-methyl-3-(5-nitro-2-furyl)-1H-pyrazolo[3,4-d]pyrimidin-4(5H)-one, having melting point >300°C.

EXAMPLE 15

A mixture of 11.6 grams of 5-amino-4-cyano-1-ethoxycarbonyl-3-(5-nitro-2-furyl)-pyrazole, 4.1 grams of acetic anhydride and 2.0 grams of concentrated sulphuric acid (S.G. 1.84) was heated under reflux for 3 hours. The solid product which formed during reaction was collected by filtration, washed with ether and dried. Recrystallisation from dimethylformamide gave 1-ethoxycarbonyl-6-methyl-3-(5-nitro-2-furyl)-1H-pyrazolo[3,4-d]pyrimidin-4(5H)-one, having decomposition point 296°C.

EXAMPLE 16

The procedure described in Example 11 was carried out using chloroacetic anhydride as starting material instead of propionic anhydride, the reaction conditions being otherwise essentially the same. The product was 6-chloromethyl-1-methyl-3-(5-nitro-2-furyl)-1H-pyrazolo[3,4-d]pyrimidin-4(5H)-one, having melting point 300°C. with decomposition.

EXAMPLE 17

A mixture of 2.3 grams of 5-amino-4-cyano-1-methyl-3-(5-nitro-2-furyl)-pyrazole, 15 millilitres of dimethylformamide, 15 millilitres of anhydrous pyridine and 0.8 grams of acetyl chloride was heated under reflux for 2 hours and cooled. The mixture was diluted with 50 millilitres of ice-water and the solid which precipitated was collected, washed with water and dried. Recrystallisation from aqueous dimethylformamide gave 5-acetamido-4-cyano-1-methyl-3-(5-nitro-2-furyl)-pyrazole having melting point 250°C.

EXAMPLE 18

a. The procedure described in Example 17 was car-

ried out using hexahydrobenzoyl chloride as starting material instead of acetyl chloride, the reaction conditions being the same.

The product was 4-cyano-5-hexahydrobenzamido-1-methyl-3-(5-nitro-2-furyl)-pyrazde, having melting point 234°C.

b. A mixture of 10.0 grams of 4-cyano-5-hexahydrobenzamido-1-methyl-3-(5-nitro-2-furyl)-pyrazole, 60 millilitres of ethanol and 40 millilitres of concentrated sulphuric acid (S.G. 1.84) was heated under reflux for 1 hour and cooled. The mixture was then diluted with 50 millilitres of water and the solid product which formed was collected, washed with ether and dried. Recrystallisation from glacial acetic acid gave 6-cyclohexyl-1-methyl-3-(5-nitro-2-furyl)-1H-pyrazolo[3,4-d]pyrimidin-4(4H)-one, having melting point >300°C.

## EXAMPLE 19

A mixture of 11.6 grams of 5-amino-4-cyano-1-methyl-3-(5-nitro-2-furyl)-pyrazole, 7.7 grams of phenylacetyl chloride, 50 millilitres of dimethylformamide and 30 millilitres of anhydrous pyridine was heated under reflux for 4 hours and cooled. The mixture was then diluted with 100 millilitres of ice-water and a crude solid was obtained. A mixture of this solid with 10 millilitres of dimethylformamide and 10 millilitres of concentrated sulphuric acid (S.G. 1.84) was heated under reflux for 30 minutes and cooled. Dilution of the mixture with 50 millilitres of ice-water yielded a product which on recrystallisation from dimethylformamide gave 6-benzyl-1-methyl-3-(5-nitro-2-furyl)-1H-pyrazolo-[3,4-d]pyrimidin-4(5H)-one, having melting point >300°C.

## EXAMPLE 20

The procedure described in Example 15 was carried out using 5-amino-4-cyano-1-n-propyl-3-(5-nitro-2-furyl)-pyrazole as starting material instead of 5-amino-4-cyano-1-ethoxycarbonyl-3-(5-nitro-2-furyl)-pyrazole.

The product was 6-methyl-1-n-propyl-3-(5-nitro-2-furyl)-1H-pyrazole[3,4-d]pyrimidin-4(5H)-one, having melting point 276°C.

## EXAMPLE 21

Preparation of Tablets

100 g of 1-methyl-3-(5-nitro-2-furyl)-1H-pyrazolo [3,4-d]pyrimidin-4(5H)-one are mixed with 60.0 g of maize starch and 35.0 g of lactose, the mixture is moistened with a solution of 5.0 g of gelatin and 3.0 g of glycerol in 70.0 g of water and granulated through a sieve. The granulate is mixed with a mixture of 15.0 g of talcum, 10.0 g of maize starch and 2.0 g of magnesium stearate. The resulting mixture is pressed into 1,000 tablets, each containing 100 mg of active substance. If desired, the tablets can be grooved for better adaption of the dosage.

## EXAMPLE 22

| | Preparation of Dragees<br>Composition | for 1,000 dragees |
|---|---|---|
| | 1,6-Dimethyl-3-(5-nitro-2-furyl)-1H-pyrazolo[3,4-d]pyrimidin-4(5H)-one | 100.0 g |
| | Maize starch | 27.0 g |
| | Gelatin | 8.0 g |
| II | Glycerol | 2.0 g |
| | Distilled water q.s. ad 100 ml | |
| | Maize starch | 10.0 g |
| III | Talcum | 7.0 g |
| | Magnesium stearate | 1.0 g |
| | | 155.0 g |
| IV | White dragee coating | |
| | Shellac | 2.0 g |
| | Sugar | 50.0 g |
| | Talcum | 38.0 g |
| | Gum arabic | 7.4 g |
| | Colloidal silicon dioxide | 2.2 g |
| | Titanium dioxide | 0.4 g |

Composition I is granulated in the heat with composition II through a sieve of 1.2 mm mesh diameter. The dried granulate is mixed with composition III and the resulting mixture is pressed into 1,000 dragee cores. These are then coated with composition IV and dried. The dragees obtained weigh 255.0 mg and contain 100 mg of active substance.

## EXAMPLE 23

| Preparation of a Syrup<br>Composition | for 1 liter |
|---|---|
| 1-Methyl-3-(5-nitro-2-furyl)-1H-pyrazolo[3,4-d]pyrimidin-4(5H)-one | 100.0 g |
| Colloidal silicone dioxide | 13.0 g |
| p-Hydroxybenzoic acid methyl ester | 1.4 g |
| p-Hydroxybenzoic acid propyl ester | 0.6 g |
| Citric acid | 1.0 g |
| Sodium cyclamate | 5.0 g |
| Distilled water | 610.0 g |
| Glycerol | 100.0 g |
| Sodium carboxymethyl cellulose | 4.0 g |
| Sugar | 320.0 g |
| | 1150.0 g |

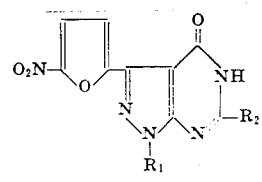
The active substance and the colloidal silicon dioxide are passed through a sieve of 1.2 mm mesh diameter (I).

The p-hydroxybenzoic acid esters, the citric acid and the sodium cyclamate are dissolved in the given amount of boiling distilled water; the glycerol is then added to this solution (II). The sodium carboxymethyl cellulose and the sugar are thoroughly mixed (III).

Composition III is then added at 75°C to Solution II under stirring until complete dissolution of III. The viscous, slightly turbid liquid is cooled to room temperature, filtered, if necessary, and mixed with composition I. Water is added to the resulting mixture up to the prescribed weight of 1,155.0 g and the syrup obtained is homogenized.

What is claimed is:

**1. A compound of the formula I**



(I)

wherein

$R_1$ is alkyl having from one to five carbon atoms or carbalkoxy having from one to five carbon atoms in the alkyl moiety; and

$R_2$ is hydrogen, alkyl having from one to five carbon atoms which may be unsubstituted or substituted by chloro or bromo; cycloalkyl having from five to seven carbon atoms in the carbocyclic ring, benzyl, phenylethyl, naphthylmethyl, or alkenyl having from two to four carbon atoms.

2. A compound according to claim 1 which is 1-methyl-3-(5-nitro-2-furyl)-1H-pyrazolo[3,4-d] pyrimidin-4(5H)-one.

3. A compound according to claim 1 which is 1-isopropyl-3-(5-nitro-2-furyl)-1H-pyrazolo[3,4-d]pyrimidin-4(5H)-one.

4. A compound according to claim 1 which is 3-(5-nitro-2-furyl)-1-n-pentyl-1H-pyrazolo[3,4-d]pyrimidin-4(5H)-one.

5. A compound according to claim 1 which is 1,6-dimethyl-3-(5-nitro-2-furyl)-1H-pyrazolo[3,4-d]pyrimidin-4(5H)-one.

6. A compound according to claim 1 which is 1-methyl-3-(5-nitro-2-furyl)-6-(1-propenyl)-1H-pyrazolo[3,4-d]pyrimidin-4(5H)-one.

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