4-Substituted alkylthio-1-\(\beta\)-D-ribofuransylpyrazole-(3,4-d) pyrimidines are active against coccidia in vivo and unlike the 4-methylthio analogue, are non-toxic. Methods for preparing and using the compounds, intermediates in the preparation and compositions of the compounds are also described.
PYRAZOLE PYRIMIDINE RIBOSIDE COMPOUNDS, PHARMACEUTICAL COMPOSITIONS AND METHOD OF USE

The present invention relates to 4-(substituted)thio-1-β-D-ribofuranosylpyrazolo[3,4-d]pyrimidine derivatives which are useful as antiprotozoal agents, especially for treating or preventing coccidiosis.

Coccidiosis is caused by protozoa of the genus Eimeria, which infect susceptible hosts by contact with feces of diseased animals. It is therefore particularly damaging when animals are kept in close contact, and is thus the most important disease of poultry. Various therapeutic and prophylactic agents are known for combating coccidiosis and are used with differing degrees of success. These are usually administrated throughout the life of animals and there is consequently a risk of the protozoa developing resistance to one or more of these agents.


The 4-methylthiopyrazolo[3,4-d]pyrimidine riboside has now been tested against coccidia and whilst it has good in vitro activity, it was found to be highly toxic, causing unacceptable fatalities in chickens.

It has now been found that 4-(substituted)thiopyrazolo[3,4-d]pyrimidine ribosides, in which the substituent on the sulphur atom of a group larger than a methyl group, are also active against protozoa of the genus Eimeria. In contrast with the known 4-methylthio derivative, these compounds have surprisingly low toxicity towards the host animal and are therefore suitable for treating or preventing coccidiosis in poultry.

According to the present invention there is a provided a compound of formula (I)

![Chemical Structure](image)

wherein n is an integer of 1 to 6 and R is a lower alkoxy or lower alkylthio group or a phenoxy or phenylthio group or an unsubstituted or mono-substituted phenyl group, or, when n is 1 a group —CO—CR2 wherein R2 is a mono-, di- or tri-substituted phenyl or an unsubstituted phenyl, substituents for the aforementioned phenyl groups being selected from halogen atoms and lower alkyl, lower alkoxy, trifluoromethyl, benzoyloxy, phenoxy, amino, mono- or di-lower alkyl amino and hydroxyl groups, and either R1, R2 and R3 are the same and are hydroxyl or acyloxy groups —O—CO—R4 wherein R4 is a hydrogen atom or a lower alkyl group or a substituted or unsubstituted phenyl group or R1 and R2 are hydroxyl or acyloxy groups as hereinbefore defined and R3 is a phosphate group, or a salt thereof.

When R4 is present as a phenyl group it may be optionally substituted with one or more of the substituents commonly known in the art and used as substituents for benzyl esters of nucleosides and nucleotides, such as amino, hydroxyl, nitro, lower alkyl and lower alkoxy groups and halogen atoms.

As used herein the terms “lower alkyl group” and “lower alkoxy group” refer to such groups having from 1 to 4 carbon atoms.

If R4 represents the salt of a phosphate group it is preferred that it is a pharmaceutically acceptable salt, such as the sodium or potassium salt in a mono or dibasic form. When R4, in a compound of formula (I), is a phenyl group it is preferred that n has the value 1 to 3.

Compounds are particularly preferred when they embody two or more of the preferred features outlined above.

The most preferred compounds are the free ribosides, their phosphate esters and salts thereof.

Compounds of formula (I) may be prepared either by modification of the 4-substituent of a 1-B-D-ribofuranosylpyrazolo[3,4-d]pyrimidine (the precursor), or by linking the ribose moiety to a pyrazolo[3,4-d]pyrimidine derivative already bearing the correct atom or group at the 4-position.

According to a second aspect of the present invention there is therefore provided a process for producing compounds of formula (I) comprising either

(a) The reaction between the precursor, a 4-(substituted)-1-β-D-ribofuranosylpyrazolo[3,4-d]pyrimidine derivative and a compound R(CH2)nx wherein n and R are as hereinbefore defined and either

(i) X is a halogen atom and the 4-substituent of the precursor is a thio group and the reaction is performed in the presence of an organic or inorganic base or a basic resin in an aqueous, a lower alcoholic or an aprotic solvent; or

(ii) X is an appropriate mercaptide radical and the 4-substituent of the precursor is a halogen atom or an alkylthio or aralkylthio group and the reaction is performed in the presence of an aprotic solvent; or

(b) the reaction of a compound of formula (II)

![Chemical Structure](image)

wherein R is as hereinbefore defined and Q is an appropriate leaving atom or group, with a riboside donor system by chemical, enzymatic or microbiological methods known in the art of nucleoside synthesis, and optionally thereafter forming appropriate organic or phosphate esters, and salts of the latter, by techniques known in the art.

As used herein in relation to the precursor of method (a) the term “4-(substituted)-1-β-D-ribofuranosylpyrazolo[3,4-d]pyrimidine derivative” includes such or-
ganic and phosphate esters, and salts of the latter, as are appropriate to the final product of the process.

In method (a) (i) the halogen atom may be a chloride, bromine or iodine atom. The base used in this method may be an alkali or alkaline earth metal hydroxide or alkoxide, quaternary ammonium hydroxide hydrogen carbonate or carbonate, or a basic resin such as Dowex 1-X8 (bicarbonate) (Dowex is a Registered Trade Mark) supplied by Bio-Rad Laboratories, California, U.S.A. The solvent may be water, a lower alcohol, such as methanol or ethanol or an aprotic solvent such as N,N-dimethylsulphoxide or hexamethylphosphoric triamide, although N,N-dimethylformamide is preferred.

When method (a) (ii) is employed, it is desirable to protect the hydroxyl groups of the ribosyl moiety of the precursor with blocking groups, that is with acyl groups, provided by the use of such acylating agents as acid anhydrides, e.g. acetic anhydride, or acid chlorides, e.g. benzoyl chloride. These blocking groups may subsequently be removed by conventional methods of deacylation such as treatment with alcoholic ammonia or an alkali metal alkoxide followed by neutralisation of the base.

Method (a) (ii) may be applied to any suitable 4-halogeno-, 4-alkylthio- or 4-alkylaminothio-substituted precur- sor and can thus be used to interconvert compounds of formula (I) by nuclophilic displacement of the 4-substituent. The radical X may conveniently be a sodium or potassium mercuryate, however other metal mercaptates are also suitable. In this particular method it is preferred that the 4-substituent of the precursor is a halogen atom or a lower alkylthio group, especially a methylthio group.

Chemical processes may be employed in method (b), using a compound of formula (II) in which Q is a hydro- gen or a metal atom, e.g. an alkali metal atom such as sodium or other leaving group, and the riboside donor system comprises a reactive ribose derivative such as a 1-chlororibose derivative, the reaction being performed in an appropriate solvent system such as an aprotic solvent, e.g. dimethyl formamide or acetonitrile. However, it is preferred that enzymatic or microbiological processes are used.

Such enzymatic processes include the preparation of compounds of formula (I) from the appropriate free base using phosphorylase type enzymes in a manner known in the art; see for instance T. A. Kreinetsky, G. B. Ellon, R. A. Strelitz, G. H. Hitchings, J. Biol. Chem., 242,2675-2682 (1967); U.K. Patent Application No. 45668/77 of European Patent Application No. 78 101 50 295.0 in which case, Q is hydrogen and the riboside donor system consists of appropriate purine and/or pyrimidine-1-β-D ribosides and/or ribose-1-phosphate and the appropriate enzyme or enzymes.

Alternatively the ribosidation may be accomplished by microbiological processes such as that disclosed in German Offenlegungsschrift No. 2 209 078 wherein Q is hydrogen and the riboside donor system comprises bacteria of the genera Brevibacterium, Arthrobacter, Corynebacterium or Micrococcus and the culture me- dium which includes glucose.

Whenever the compound of formula (I) is required to carry acyloxy groups for R1, R2, and R3, a correspond- ing starting compound having hydroxy groups in these positions is reacted with acylating agents such as acetic anhydride or benzoyl chloride according to conven- tional methods. Acylation may be effected before or after other synthetic steps except that when enzymatic or microbiological processes are to be used for the ribosidation of a compound of formula (II) the acylation must be performed after the ribosidation.

When R3 of the desired compound of formula (I) is to be a phosphate group, this may be introduced into the corresponding compound having a hydroxyl group in that position by phosphorylation using traditional phos- phorylating agents such as trialkyl phosphates, e.g. triethyl phosphate, with a phosphorus oxyhalide such as phosphoryl chloride. When this technique is used it is advantageous to block the 2' and 3' positions of the ribose moiety either by blocking only these two positions by using appropriate conditions or by blocking the 2', 3' and 5' positions and then selectively deblocking the 5' position. The latter course may be facilitated by first blocking the 5' position with a bulky group, such as a trityl group or a t-butylidemethylsilyl group, then block- ing the 2' and 3' positions by conventional means, and finally deblocking the 5' position. After phosphoryla- tion the 2' and 3' positions are then deblocked to afford the required compound.

Rather than block the 2' and 3' positions as described above, it is preferred to use phosphoryl chloride in the presence of a trialkylphosphate (preferably triethyl phos- phate) and a trace of water at a temperature of about 0°C or below. This forms the 5'-phosphoro dichloride which is then hydrolysed to the 5'-phosphate upon treatment with water at slightly basic pH.

Salts of phosphate-substituted compounds of formula (I) are obtained by conventional reactions between the phosphate derivative and an appropriate base in aque- ous media.

The precursors for use in method (a) may be well known compounds such as 4-hydroxy-4-thio or 4- methylthio-1-β-D-ribofuranosylpyrazolo[3,4-d]pyrimidine derivatives, or may be obtained therefrom by conventional techniques. These ribosides may have been prepared from the corresponding free pyrazo- lo[3,4-d]pyrimidine bases by ribosidation as described for method (b) above.

The 4-halogeno precursor can be derived by treating an acylated derivative of 4-hydroxy-pyrazolo[3,4-d] pyrimidine riboside with a phosphoryl halide, the corresponding Vilsmeier reagent or other known halog- enating reagents. Alternatively, treatment of the 4-thio analogue with chloride or bromine and the appropriate hydrogen halide in a lower alcohol at low temperature, affords the 4-halogeno precursor.

The 4-thio substituted precursor may be obtained from the acylated 4-halogeno-pyrazolo[3,4-d]pyrimi-idine riboside by treatment of the latter with thiourea or sodium hydroxysulphide.

The 4-alkylthio- and 4-alkylaminothio substituted precursors may be derived from other compounds of this class, from the 4-halogeno precursor or from the 4-thio pre-cursor by process (a), mutatis mutandis. Compounds of formula (II) for use in method (b), i.e. the 1-unsub- stituted analogues of compounds (I), may be produced by the techniques described above for the production of precursors and by method (a) above, mutatis mutandis.

Simple reagents of the formula R(CH2)2X for use in method (a) above or for producing compounds of formula (II) for use in method (b) may be available com- mercially (e.g. from Aldrich Chemical Co., Milwaukee, Wisconsin, U.S.A.). However all these reagents, R(CH2)2X may be produced by methods well known in the art. These reagents wherein R is a phenoxy, phy- nylthio, alkoxy or alkylthio group are produced by the
following methods from either the appropriate w-
halogenoalkyl alcohol or a,w-dihalogeno alkane.
The w-halogenated alcohols are generated by reducti-
on of the corresponding w-halogenoalkyl carboxylic
acid, chloride or ester using reducing agents such as
lithium aluminium hydride or sodium borohydride or
by catalytic hydrogenation using a catalyst such as
platinum oxide. The w-halogenoalkyl alcohol is then
reacted with the alkoxy, phenoxy, thiolate or phe-
nylthiolate corresponding to the R moiety, (which is
generated by the action of an alkali metal or its hydride,
carbonate or methoxide, on the appropriate alcohol or
thio) in an aprotic solvent such as N,N-dimethylforma-
mide, diglyme, ether or dimethylsulphoxide or in the
alcohol or thiol corresponding to R, at a temperature
between 20° C. and 150° C., preferably up to 100° C.
The w-hydroxyether or w-hydroxyxthioether so formed is
then halogenated by methods known in the art to
afford the required reagent R(CH₂)ₙX.

Alternatively an a,w-dihalogeno alkane is added, in
a greater than three fold excess, to a solution of
the metal alcoholate or thiolate (as described above) in
an aprotic solvent such as N,N-dimethylformamide,
diglyme, ether or dimethylsulphoxide or in the alcohol or
thiol corresponding to R and the reaction is allowed to
proceed, at a temperature of 20° C. to 150° C. preferably
up to 100° C., until the solution is no longer basic.
The w-halogenated ether or thioether of formula R(CH₂)ₙX
may then be used to produce compounds of formula (I)
or (II).

In a third aspect of the present invention there is
provided a 1-β-D-ribofuranosylpyrazolo[3,4-d]pyrimei-
dine derivative of general formula (III).

![Chemical structure](image)

wherein Y is a halogen atom,

In a fourth aspect of the present invention there is
provided a compound of general formula (IV)

wherein n, R and Q are as hereinbefore defined.

Compounds of formula (I) as hereinbefore defined are
useful for treating coccidial infections, or preventing
them, in livestock. The compounds may be adminis-
tered alone, or in association with carriers.

In a further aspect of the present invention there is
provided a pharmaceutical formulation comprising at
least a compound of formula (I) for administration to
livestock.

It may be convenient to administer the compounds in
association with various carriers and additives to facili-
tate that administration. In particular, the compounds
may be administered in the foodstuff or drinking water
provided for the livestock.
The present invention, in a further aspect, therefore
provides a pharmaceutical composition comprising a
compound of formula (I) in association with a carrier
therefor.

Carriers are materials which are useful for the pur-
pose of administering the compound while being other-
wise inert as regards interaction with the compound and
non-toxic to the recipient of the composition. It is par-
ticularly preferred that the carrier is the foodstuff or
drinking water provided for the livestock.

When incorporated into foodstuff or drinking water
the compounds may be administered at a concentration
of about 10 ppm to 400 ppm, preferably 50 ppm to 200
ppm and most preferably 100 ppm.

Some compounds of formula (I) are insufficiently
soluble for administration in drinking water. In this case
the phosphate ester, or more preferably, a salt thereof
can be employed.

In a further aspect of the present invention there is
provided a method for preventing or treating coccidial
infections of livestock comprising the administration of
an effective anticoccidial amount of a compound of
formula (I) or a formulation or composition thereof.
The invention will now be illustrated by the follow-
ing Examples, which should not be construed as limit-
ing the invention in any way.

**EXAMPLE 1**

Preparation of

4-(2-phenylethylthio)-1-B-D-ribofuranosyl-
pyrazolo[3,4-d] pyrimidine

Dowex (Registered Trade Mark) 1-X8 (bicarbonate)
(4.0g) was mixed with 4-mercapto-1-B-D-
ribofuranosylpyrazolo[3,4-d]pyrimidine (2.0g) and
methanol was added. The mixture was warmed and
stirred until no ultra-violet absorbing material remained
in solution. 2-Phenylethyl bromide (1.3g) was added
and the mixture stirred at ambient temperature for 3
days. The resin was removed by vacuum filtration and
washed with methanol. The filtrate and washings were
combined and the methanol evaporated in vacuo to
afford after trituration with warm diethyl ether a solid,
4-(2-phenylethylthio)-1-B-D ribofuranosylpyrazolo
(3,4-d)pyrimidine m.p. 85–87° C.

**EXAMPLE 2**

Preparation of

4-(3-phenylpropyldio)-1-B-D-ribofuranosylpyrozolo-
(3,4-d)pyrimidine

By a method exactly analogous to that of Example 1
the title compound, (mp 95–97° C.) was prepared.

**EXAMPLE 3**

Preparation of

4-(3-(4-methylphenyl)-propyldio)-1-B-D-
ribofuranosylpyrazolo(3,4-d)pyrimidine

4-Mercapto-1-B-D-ribofuranosylpyrazolo(3,4-
d)pyrimidine (2 g) was added to ethanol (0.11) contain-
ing aqueous sodium bicarbonate (0.6 g/ml). 3-(4-
 methylphenyl)-propyl chloride (1.19 g) in ethanol
(0.005 l) was added dropwise with stirring. The mixture
was warmed on a steam bath to effect solution then heated under reflux for 24 hours. The reaction mixture was evaporated to a syrup (in vacuo) which was triturated with hexane and warm petroleum ether to afford a syrup. The syrup was heated with water, cooled and the solid isolated. The solid was recrystallized twice from ethanol to give 4-(3-(4-methylphenyl)-propylthio)-1-B-D-ribofuranosylpyrazolo[3,4-d]-pyrimidine (m.p. 118°-120.5° C.) as the hemihydrate.

**EXAMPLE 4**

By a method exactly analogous to that of Example 3, the following were prepared.

<table>
<thead>
<tr>
<th>Example</th>
<th>Halide</th>
<th>Duration (hours)</th>
<th>product (1-B-D-ribofuranosylpyrazolo[3,4-d]-pyrimidine)</th>
<th>M.p. (°C.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4a</td>
<td>Cl</td>
<td>41</td>
<td>4-(3-(4-chlorophenyl)-propylthio)</td>
<td>129.5-130.5</td>
</tr>
<tr>
<td>4b</td>
<td>Cl</td>
<td>48</td>
<td>4-(2-(4-chlorophenyl)-ethylthio)</td>
<td>103-105</td>
</tr>
</tbody>
</table>

**EXAMPLE 5**

Preparation of 4-(2-phenoxyethylthio)-1-B-D-ribofuranosylpyrazolo[3,4-d]-pyrimidine

Crude 2-phenoxyethyl chloride (2.7 g) was added to a stirred solution of 4-mercapto-1-B-D-ribofuranosylpyrazolo[3,4-d]pyrimidine (2.0 g) and potassium carbonate (1.07 g) in N,N-dimethylformamide. The solution was heated (40° C. on an oil bath) for 24 hours. After cooling the reaction mixture was poured into water (20.0 l) and the resultant precipitate was collected.

The 4-(2-phenoxyethylthio)-1-B-D-ribofuranosylpyrazolo[3,4-d]pyrimidine so obtained was recrystallised from methanol, m.p. 125°-126° C.

**EXAMPLES 6 AND 7**

The compounds of Examples 6 and 7 were prepared by a method exactly analogous to that of Example 5 except that the reaction was conducted for the duration shown.

<table>
<thead>
<tr>
<th>Ex.</th>
<th>Halide</th>
<th>Duration (hours)</th>
<th>Product (1-B-D-ribofuranosylpyrazolo[3,4-d]-pyrimidine)</th>
<th>M.p. (°C.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>Cl</td>
<td>24</td>
<td>4-(2-(4-methylphenyl)-ethylthio)</td>
<td>96-97</td>
</tr>
<tr>
<td>7(a)</td>
<td>Cl</td>
<td>24</td>
<td>4-(2-(3-methylphenyl)ethylthio)</td>
<td>88-91</td>
</tr>
<tr>
<td>7(b)</td>
<td>Cl</td>
<td>3</td>
<td>4-(4-benzoxylbenzylthio)</td>
<td>181-185</td>
</tr>
<tr>
<td>7(c)</td>
<td>Cl</td>
<td>1</td>
<td>4-(3-phenyl-2-propylthio)</td>
<td>137</td>
</tr>
</tbody>
</table>

**EXAMPLES 8 TO 10**

The compounds of Example 8 to 10 were prepared using a method exactly analogous to that used in Example 3.

**EXAMPLE 11**

Preparation of 4-(5-phenylpentythio)-1-B-D-ribofuranosylpyrazolo[3,4-d]-pyrimidine

Crude 5-phenylpentyl chloride (1.3 g) was added to a stirred solution of 4-mercapto-1-B-D-ribofuranosylpyrazolo[3,4-d]pyrimidine (2.0 g) and potassium bicarbonate (0.7 g) in N,N-dimethylformamide. The reaction mixture was heated on a steam bath for 25 hours. An additional 0.7 g of potassium bicarbonate was added and after heating for 1 hour more, the mixture was poured into water. The cooled aqueous mixture was extracted with chloroform. The chloroform soluble material was chromatographed on a silica gel column. The fractions containing the compound were combined and evaporated. Trituration with ether gave 0.4 g of crude product. This was dissolved in ethyl acetate and washed with water. The dried ethyl acetate solution was evaporated and purified by reversed phase chromatography in methanol water (80:20 vol/vol) to give 0.28 g of product m.p. 72°-75° C. (indefinite).

Analysis Calc'd for C_{21}H_{26}N_{4}O_{6}: Theory: C: 58.58% H: 6.09% N: 13.01%. Found: C: 58.83% H: 6.15% N: 13.06%. S: 7.57%.

**EXAMPLE 12**

In order to assess the activity of compounds of formula (I) against coccidia, the compounds were administered to groups of 5 male Ross Ranger chicks (7 days old), at various dosages in the diet, for 6 days. The chicks were each infected with *Elmeria tenella* and *E. acervulina* one day after the beginning of the medication. The compounds had some effect on the *E. acervulina* and cleared chicks of *E. tenella* as indicated in Table 1 below. No obvious signs of toxicity were observed during this experiment.

**Table 1**

<table>
<thead>
<tr>
<th>Number of chicks cleared of <em>E. tenella</em> by administration of compounds of formula (I) at various dose levels.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compound of Example No. 200</td>
</tr>
<tr>
<td>----------------------------</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4(a)</td>
</tr>
<tr>
<td>4(b)</td>
</tr>
<tr>
<td>5</td>
</tr>
<tr>
<td>6</td>
</tr>
<tr>
<td>7(a)</td>
</tr>
<tr>
<td>7(b)</td>
</tr>
<tr>
<td>7(c)</td>
</tr>
<tr>
<td>8</td>
</tr>
<tr>
<td>9</td>
</tr>
<tr>
<td>10</td>
</tr>
<tr>
<td>11</td>
</tr>
</tbody>
</table>

We claim:

1. A compound of formula (I)
wherein n is an integer of 1 to 6 and R is lower alkoxy or lower alkylthio group or phenoxy or phenylthio group or an unsubstituted or mono-substituted phenyl group, or, when R has the value 1, a group —C==C—R, wherein R is a mono- di- or tri-substituted phenyl or an unsubstituted phenyl, substituents for the aforementioned phenyl groups being selected from halogen atoms and lower alkyl, lower alkoxy, trifluoromethyl, benzylxoy, phenoxy, amino, mono- or di-lower alkylylamino, and hydroxyl and either R1, R2 and R3 are the same and are hydroxyl or acyloxy groups —O—CO—R4 wherein R4 is a hydrogen atom or a lower alkyl group or a substituted or unsubstituted phenyl group wherein the substituents are selected from the group consisting of amino, hydroxyl, nitro, lower alkyl, lower alkoxy or halogen or R1 and R2 are hydroxyl or acyloxy groups as hereinbefore defined and R3 is a phosphate group, or a salt thereof.

2. A compound according to claim 1 wherein R1 and R2 are hydroxyl and R3 is hydroxyl or a phosphate group or a salt thereof.

3. A compound according to claim 1 wherein n has a value from 1 to 3 and R is a substituted or unsubstituted phenyl group.

4. A compound according to claim 3 wherein R is a substituted phenyl group, the substituents being selected from the group consisting of halogen and lower alkyl.

5. A compound of formula (III).

(III)

wherein Y is a halogen atom.

6. A compound of general formula (IV) wherein n is an integer of 1 to 6, R is lower alkoxy, lower alkylthio, phenoxy, phenylthio, phenyl or mono-substituted phenyl, or when n is 1, a group —C==C—R, wherein R is mono-, di- or tri-substituted phenyl, substituents for the aforementioned phenyl being selected from the group consisting of halogen, lower alkyl, lower alkoxy, trifluoromethyl, benzylxoy, phenoxy, amino, mono- or di-lower alkylylamino and hydroxyl groups and Q is hydrogen or an alkali metal atom.

7. A compound or salt of claim 1 which is 4-2-phenylethylthio)-1-β-D-ribofuranosylpyrazolo(3,4-d)pyrimidine or a pharmaceutically acceptable salt thereof.

8. A compound or salt of claim 1 which is 4-(3-phenylpropylthio)-1-β-D-ribofuranosylpyrazolo(3,4-d)pyrimidine or a pharmaceutically acceptable salt thereof.

9. A compound or salt of claim 1 which is 4-(3-(4-methylphenyl)propylthio)-1-β-D-ribofuranosylpyrazolo(3,4-d)pyrimidine or a pharmaceutically acceptable salt thereof.

10. A compound or salt of claim 1 which is 4-(4-benzylxoybenzylthio)-1-β-D-ribofuranosylpyrazolo(3,4-d)pyrimidine or a pharmaceutically acceptable salt thereof.

11. A compound or salt of claim 1 which is 4-(4-methylbenzylthio)-1-β-D-ribofuranosylpyrazolo(3,4-d)pyrimidine or a pharmaceutically acceptable salt thereof.

12. A compound or salt of claim 1 which is 4-(4-chlorobenzylthio)-1-β-D-ribofuranosylpyrazolo(3,4-d)pyrimidine or a pharmaceutically acceptable salt thereof.

13. A pharmaceutical composition for use in combating coccidiosis comprising an effective coccidiosis combatting amount of a composition or salt of claims 1, 7, 8, 9, 10, 11 or 12 in association with a carrier therefor.

14. A method for combating coccidial infections of livestock comprising the administration to the livestock of an effective, non-toxic coccidiosis combatting amount of the compound or salt of claims 1, 7, 8, 9, 10, 11 or 12.

15. A method for combating coccidial infections of livestock comprising the administration to the livestock of an effective, non-toxic coccidiosis combatting amount of the compound or salt of claims 1, 7, 8, 9, 10, 11 or 12 in foodstuff or drinking water in a concentration of from about 25 ppm to 400 ppm.