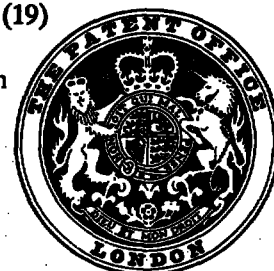


PATENT SPECIFICATION

(11) 1 571 368

1 571 368

- (21) Application No. 16267/78 (22) Filed 25 Apr. 1978 (19)
 (31) Convention Application Nos. 2718799 (32) Filed 27 Apr. 1977
 2718799 24 Jun. 1977 in
 (33) Fed. Rep of Germany (DE)
 (44) Complete Specification Published 16 Jul. 1980
 (51) INT. CL³ A61K 31/41 //
 C07D 251/38



(52) Index at Acceptance

A5B	180	332	333	33Y	38Y	394	39X	420
	422	42Y	466	46Y	480	482	484	485
	48X	48Y	503	504	50Y	541	542	544
	54Y	565	566	56Y	586	58Y	642	64Y
	660	66Y	H					
C2C	1652	215	220	22Y	250	252	25Y	
	305	311	313	31Y	338	351	352	364
	36Y	371	373	37Y	385	396	397	461
	464	465	510	51X	537	613	614	635
	645	662	695	699	761	768	802	80Y
	AA	QS	QT	SF				

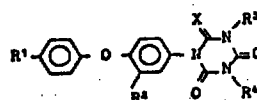
- (72) Inventors: AXEL HABERKORN
 MARTIN SCHEER
 JURGEN STOLTEFUSS

(54) GROWTH PROMOTING AGENT

(71) We, BAYER AKTIENGESELLSCHAFT, a body corporate organised under the laws of Germany, of Leverkusen, Germany, do hereby declare the invention, for which we pray that a Patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:-

The present invention relates to growth promoters, which contain 1-(4-phenoxy-phenyl)-1,3,5-triazine derivatives as active compounds.

It has been found that 1-(4-phenoxy-phenyl)-1,3,5-triazine derivatives of the formula



in which

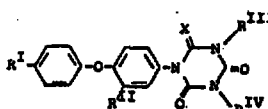
R¹ represents halogenoalkylthio, halogenoalkyl-sulphinyl or halogenoalkylsulphonyl, R² represents hydrogen, alkyl, alkoxy, alkoxyalkyl, alkylmercapto, halogen, halogenoalkyl or an optionally substituted sulphonyl radical (as hereinafter defined),

R³ and R⁴ can be identical or different and represent hydrogen, alkyl, alkenyl or alkynyl and

X can be O or S,

and their physiologically acceptable salts have a very highly pronounced growth promoting action.

Furthermore, it has been found that, in particular, the following compounds of the formula Ia and their physiologically acceptable salts have an excellent growth promoter action:



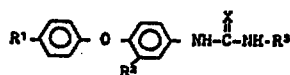
in which

R^I represents halogenoalkyl(C_1-C_4)-thio, halogenoalkyl(C_1-C_4)-sulphinyl or halogenoalkyl(C_1-C_4)-sulphonyl, R^{II} represents hydrogen, alkyl(C_1-C_4), alkoxy(C_1-C_4), alkoxy(C_1-C_4)alkyl(C_1-C_4), alkyl(C_1-C_4)-mercapto, halogen, dialkyl(C_1-C_4)aminosulphonyl or halogenoalkyl(C_1-C_4) and R^{III} and R^{IV} can be identical or different and represent hydrogen, alkyl(C_1-C_4) or alkenyl(C_2-C_4).

According to the present invention we provide a pharmaceutical composition for use in the promoting growth containing as an active ingredient a compound of the abovementioned formula (I) or (Ia) or its physiologically acceptable salt in admixture with a solid or liquified gaseous diluent or in admixture with a liquid diluent other than a solvent of molecular weight less than 200 except in the presence of a surface active agent.

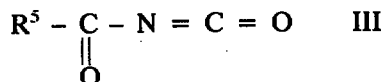
The pharmaceutical composition may be in the form of a sterile or isotonic aqueous solution and may contain 0.5 to 95% of the said active ingredient, by weight.

The compounds of the general formula (I) can be prepared by a process in which a) 1-(4-phenoxy-phenyl)-1,3,5-triazines of the formula I are obtained when compounds of the formula II



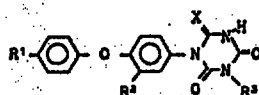
in which

R^I , R^2 , R^3 and X have the meaning indicated above, are reacted with a substituted carbonyl isocyanate of the formula III



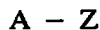
in which

R^5 represents a halogen atom, an alkoxy group or an aryloxy group, and the substituted 1,3,5-triazine derivatives, formed during this procedure, of the formula IV



in which

R^I , R^2 , R^3 and X have the meaning indicated above, are optionally isolated and optionally reacted with a compound of the formula V



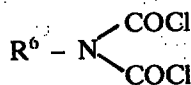
wherein

A represents alkyl, alkenyl or alkynyl and

Z represents halogen;

or that

b) 1-(4-phenoxy-phenyl)-1,3,5-triazine derivatives of the general formula I are obtained when compounds of the formula II, in which R^I , R^2 , R^3 and X have the meaning indicated above, are reacted with bis-(chlorocarbonyl)-amines of the formula VI



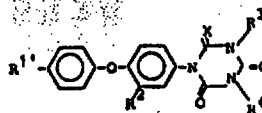
in which

R^6 represents alkyl,

optionally in the presence of acid acceptors, or that

c) in order to obtain compounds of the formula I in which the substituents R^2 , R^3 and R^4 as well as X have the meaning indicated above and R^I represents halogenoalkylsulphinyl or halogenoalkylsulphonyl,

compounds of the formula



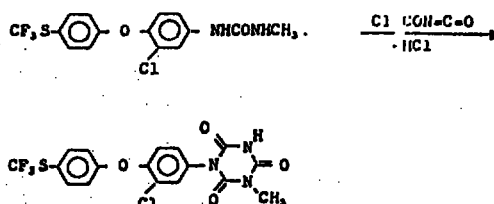
in which

R^2 , R^3 and R^4 have the meaning indicated above and R^1 represents halogenoalkylthio, are reacted with the appropriate amount of a suitable oxidising agent.

Some of the compounds of the general formula (I) are known from the disclosed documents of Hungarian Patent Application BA - 3,229. Surprisingly, the 1-(4-phenoxy-phenyl)-1,3,5-triazines according to the invention exhibit an excellent growth promoter action, in addition to an action against coccidiosis in poultry and mammals. With regard to the practical use, the combination of this type of action is extremely useful, especially since the commercially available substances known according to the state of the art, such as 3,5-dinitrotoluyamide, 1-[(4-amino-2-propyl-5-pyrimidinyl)-methyl]-2-picolinium chloride hydrochloride, 3,5-dichloro-2,6-dimethyl-4-pyridone and the complex of 4,4'-di-(nitrophenyl)-urea, 4,6-dimethyl-2-hydroxy-pyrimidine, Monensin and Lasalocid, do not exhibit this type of effect.

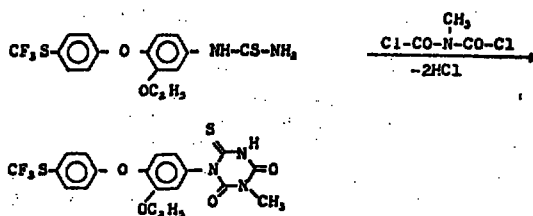
In addition, they are also distinguished by the fact that they have an action both against coccidiosis in poultry and against coccidiosis in mammals. This breadth of action is not known in the commercially available coccidiosis agents.

If N-[3-chloro-4-(4'-trifluoromethylthio-phenoxy)-phenyl]-N'-methyl-urea and chlorocarbonyl isocyanate are used in process variant a), the course of the reaction can be represented by the following equation:

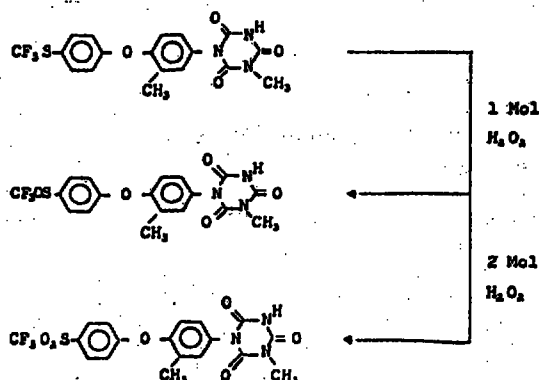


40

If N-[3-ethoxy-4-(4'-trifluoromethylthio-phenoxy)-phenyl]-thiourea and N-methyl-bis-(chlorocarbonyl)-amine are used as the starting materials in process variant b), the course of the reaction can be represented by the following equation:



The compounds of the general formula I, obtained according to process variant a) or b), in which R_1 = halogenoalkylthio and $X = O$ can be oxidised according to process variant c) to the corresponding halogenoalkylsulphinyl or halogenoalkylsulphonyl derivatives. If hydrogen peroxide is used as the oxidising agent, the course of the reaction can be represented by the following equation:



In the formulae I, II, IV, V, VI and VII, alkyl R^2 , R^3 , R^4 , R^6 or A is straight-chain or branched alkyl with preferably 1 to 6, in particular 1 to 4, carbon atoms. Examples which may be mentioned are optionally substituted methyl, ethyl, n- and i-propyl and n-, i- and t-butyl.

In the formulae I, II, IV, V and VII, alkenyl R^3 , R^4 or A is straight-chain or branched alkenyl with preferably 2 to 6, in particular 2 to 4, carbon atoms. Examples which may be mentioned are optionally substituted ethenyl, propen-1-yl, propen-2-yl and buten-3-yl.

In the formulae I, II, IV, V and VII, alkynyl R^3 , R^4 or A is straight-chain or branched alkynyl with preferably 2 to 6, in particular 2 to 4, carbon atoms. Examples which may be mentioned are optionally substituted ethynyl, propin-1-yl, propin-2-yl and butin-3-yl.

In the formulae I, II, III, IV and VII, alkoxy R^2 or R^5 is straight-chain or branched alkoxy with preferably 1 to 6, in particular 1 to 4, carbon atoms. Examples which may be mentioned are optionally substituted methoxy, ethoxy, n- and i-propoxy and n- and i-butoxy.

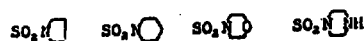
In the formulae I, II, III, IV, V and VII, halogen R^2 , R^5 or Z is preferably fluorine, chlorine, bromine and iodine, especially chlorine and bromine.

In the formulae I, II, IV and VII, halogenoalkylthio R^1 is halogenoalkylthio with preferably 1 to 4, in particular 1 or 2, carbon atoms and preferably 1 to 5, in particular 1 to 3, identical or different halogen atoms, halogen atoms preferably being fluorine, chlorine and bromine, especially fluorine and chlorine. Examples which may be mentioned are trifluoromethylthio, chloro-di-fluoromethylthio, bromomethylthio, 2,2,2-trifluoroethylthio and pentafluoroethylthio.

In the formulae I, II and IV, halogenoalkylsulphinyl R^1 is halogenoalkylsulphinyl with preferably 1 to 4, in particular 1 or 2, carbon atoms and preferably 1 to 5, in particular 1 to 3, identical or different halogen atoms, halogen atoms preferably being fluorine, chlorine and bromine, especially fluorine and chlorine. Examples which may be mentioned are trifluoromethylsulphuryl, chloro-di-fluoromethylsulphuryl, bromomethylsulphinyl, 2,2,2-trifluoroethylsulphinyl and pentafluoroethylsulphinyl.

In the formulae I, II and IV, halogenoalkylsulphonyl R^1 is halogenoalkylsulphonyl with preferably 1 to 4, in particular 1 or 2, carbon atoms and preferably 1 to 5, in particular 1 to 3, identical or different halogen atoms, halogen atoms preferably being fluorine, chlorine and bromine, especially fluorine and chlorine. Examples which may be mentioned are trifluoromethylsulphonyl, chloro-di-fluoromethylsulphonyl, bromomethylsulphonyl, 2,2,2-trifluoroethylsulphonyl and pentafluoroethylsulphonyl.

In the formulae I, II and IV, the term "optionally substituted sulphamoyl" R^2 means the sulphamoyl radical or one of the following radicals:



and $SO_2N(CH_3)-CH_3$

In the formulae III, aryloxy R⁵ is preferably phenoxy.

The substituted ureas or thioureas of the formula II which are used as starting materials can be easily prepared by methods which are in themselves known by a) either reacting substituted 4-aminodiphenyl ethers with the corresponding substituted isocyanates or isothiocyanates in an inert solvent at temperatures between 0°C and 100°C, or, reversing the sequence, b) reacting ammonia or substituted amines and the corresponding substituted 4-isocyanato or 4-isothiocyanato-diphenyl ethers with one another under the same conditions, or by c) subjecting substituted 4-hydroxyphenyl-ureas or -thioureas to a condensation reaction with activated halogenoaromatic compounds in aprotic solvents, such as dimethylsulphoxide, dimethylformamide or hexamethylphosphoric acid triamide, in the presence of bases, such as sodium hydride, potassium hydroxide, potassium carbonate at temperatures between 20°C and 150°C.

When the amount of solvent is appropriately chosen, the reaction products generally crystallise out on cooling the solution. Literature for the alternate preparation of ureas from amines and isocyanates is: Methoden der Org. Chemie (Methods of Organic Chemistry) (Houben-Weyl), IVth edition, Volume VIII, page 157-158.

Some of the bis-(chlorocarbonyl-amines) of the general formula VI which can be used according to the invention in process b) are already known (compare the article in Synthesis 1970, page 542-543) and, if they are not yet known, they can be prepared in an analogous manner from cyclic diacyldisulphides and chlorination in inert organic solvents, preferably in carbon tetrachloride.

Possible diluents for the reaction of the ureas or thioureas of the formula II both with carbonyl isocyanates of the formula III (process variant a) and with bis-(chloro-carbonyl)-amines of the formula VI (process variant b) as well as for the reaction of the 1,3,5-triazine derivatives of the formula IV with compounds of the formula A-Z are all the organic solvents which are inert in these reactions.

These include, in addition to pyridine, preferably, aromatic hydrocarbons, such as benzene, toluene and xylene, halogenated aromatic hydrocarbons, such as chlorobenzene and dichlorobenzene, and ethers, such as tetrahydrofuran and dioxane.

The hydrochloric acid which may form during the reaction escapes as a gas or can be bonded by organic or inorganic acid acceptors. The acid acceptors include, preferably, tertiary organic bases, such as triethylamine, pyridine and many others, or inorganic bases, such as alkali metal carbonates or alkaline earth metal carbonates.

The reaction temperatures for the abovementioned reaction stages can be varied within a wide range. In general, the reaction is carried out between about 0°C and about 150°C, preferably between 20°C and 100°C.

In the abovementioned reaction stages, the reaction can be carried out under normal pressure or under elevated pressure. In general, the reaction is carried out under normal pressure.

Possible oxidising agents for the conversion, according to process variant c) of the trifluoromethylthio compounds of the general formula I, in which Y represents oxygen, into the corresponding sulphonyl or sulphonyl compounds are, H₂O₂/glacial acetic acid; H₂O₂/acetic anhydride; H₂O₂/methanol; peracids, such as, for example, m-chloroperbenzoic acid, and chromic acid; potassium permanganate; sodium periodate, ceric ammonium nitrate; and nitric acid.

The active compounds of the formula (I), and their salts, exhibit a marked growth promoter action, that is to say they promote weight development in, for example, chickens, rabbits and pigs, with a simultaneously reduced feed consumption, compared with untreated controls. A considerable improvement in the feed utilisation is thereby achieved.

The feeding experiments were carried out in the following manner:

3 day old hybrids (broilers) sorted according to sex were used. 20 animals were employed per formulation and dose.

Pure chick feed, without the addition of antibiotics, commercially available coccidiostatic agents and stabilising auxiliaries, was given to animals kept in cages. The substances to be tested were intermixed with this feed. Feed and water were available ad libitum. The temperature was 28°C at the start of the experiment and about 23°C at the end of the experiment.

The animals were exposed to synthetic light 16 hours per day. At the start of the experiment, all the animals of one experimental group had the same starting weight. The duration of the experiment was over 14 days.

The weight increase rates and the feed consumption were used as evaluation criteria.

Administering the new active compounds as a feedstuff additive leads to accelerated growth, accelerated weight increase and better feed utilisation. The active compounds can be admixed to any desired feed and/or to the drinking water in the customary manner and thus be administered to the animals. They can, of course, also be admixed to feed

15

6

1 571 368

6

concentrate and the formulations containing vitamins and/or mineral substances. The compounds obtainable according to the invention are preferably added to the feed, to feed formulations or to the drinking water in amounts of about 1 to about 200 ppm, in particular 10 to 50 ppm. The dosage range applied amounts from about 0.1 to 100 mg per kg body weight per day. However, it can be appropriate to increase or to reduce the concentration of the active compound, depending on the species of animal, the age of the animals and the general conditions of keeping the animals. Particularly good successes in promoting the growth and in the feed utilisation are achieved in the rearing of young animals, such as, for example, calves and piglets, as well as poultry, such as, for example, chicks.

The good properties as a feedstuff additive can be seen from the feed experiments which follow (Table 1).

The experimental animals used were chicks which were kept in cages and which had feed (complete chick feed) and water available ad libitum.

The active compounds were mixed, in the finely divided form, into the feed using a mixing machine. The experiments were repeated several times and the duration of the experiment was 14 days.

TABLE 1

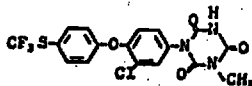
Weight development in chicks (average values of several experiments) after feeding with the active compound

Active compound	Number of the animals	Number of the experiments	Active compound concentration in the feed in ppm	Weight development in per cent	Feed consumption in per cent
untreated control	135	3	-	100	100
compound from Example 2	68	3	25	102.6	96.2
	68	3	50	100.5	93.3
compound from Example 1	48	2	25	109.9	95.4
	48	2	50	109.2	97.1

Preparation of compounds of the formula (I)

Preparation Example 1

5



5

2.64 g (7 mmols) of N-[3-chloro-4-(4'-trifluoromethylthio-phenoxy)-phenyl]-N'-methyl-urea of melting point 146° are suspended in 12.9 ml of absolute toluene, and a solution of 0.92 g (8.6 mmols) of chlorocarbonyl isocyanate in 1 ml of absolute toluene is added dropwise, whilst stirring. The mixture is stirred for 30 minutes at room temperature and the clear solution formed is heated to the boil for 2 hours. It is cooled to 10°C and the resulting crystals are filtered off, washed with toluene and petroleum ether and dried at 100° in vacuo. This gives 2.76 g (89% of theory) of 1-[3-chloro-4-(4'-trifluoromethylthio-phenoxy)-phenyl]-3-methyl-1,3,5-triazine-2,4,6(1H, 3H, 5H)-trione of melting point: 186°C.

The following compounds are obtained analogously:

20 Example No.

20

2 1-[3-Methyl-4-(4'-trifluoromethylthio-phenoxy)-phenyl]-3-methyl-1,3,5-triazine-2,4,6(1H,3H,5H)-trione, melting point: 194°C.

3 1-[3-Methyl-4-(4'-trifluoromethylsulphonyl-phenoxy)-phenyl]-3-methyl-1,3,5-triazine-2,4,6(1H,3H,5H)-trione, melting point: 242°C.

25 4 1-[3-Methoxy-4-(4'-trifluoromethylthio-phenoxy)-phenyl]-3-methyl-1,3,5-triazine-2,4,6(1H,3H,5H)-trione, melting point: 216°C.

25

5 1-[3-Chloro-4-(4'-trifluoromethylsulphonyl-phenoxy)-phenyl]-3-methyl-1,3,5-triazine-2,4,6(1H,3H,5H)-trione, melting point: 260°C.

30 6 1-[3-Methoxy-4-(4'-trifluoromethylsulphonyl-phenoxy)-phenyl]-3-methyl-1,3,5-triazine-2,4,6(1H,3H,5H)-trione, melting point: 255°C.

30

7 1-[3-Ethoxy-4-(4'-trifluoromethylsulphonyl-phenoxy)-phenyl]-3-methyl-1,3,5-triazine-2,4,6(1H,3H,5H)-trione, melting point: 247°C.

8 1-[3-Ethoxy-4-(4'-trifluoromethylthio-phenoxy)-phenyl]-3-methyl-1,3,5-triazine-2,4,6(1H,3H,5H)-trione, melting point: 227°C.

35 9 1-[3-Dimethylaminosulphonyl-4-(4'-trifluoromethylsulphonyl-phenoxy)-phenyl]-3-methyl-1,3,5-triazine-2,4,6(1H,3H,5H)-trione, melting point: >300°C.

35

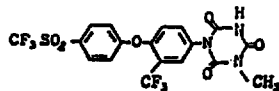
10 1-[3-Dimethylaminosulphonyl-4-(4'-trifluoromethylthio-phenoxy)-phenyl]-3-methyl-1,3,5-triazine-2,4,6(1H,3H,5H)-trione, melting point: >300°C.

40 11 1-[3-Trifluoromethyl-4-(4'-trifluoromethylthio-phenoxy)-phenyl]-3-methyl-1,3,5-triazine-2,4,6(1H,3H,5H)-trione, melting point: 170°C.

40

Example 12

45



45

50 5.2 g (45 mmols) of 30% strength hydrogen peroxide are added dropwise, at 20°, to a solution of 4.79 g (10 mmols) of 1-[3-trifluoromethyl-4-(4'-trifluoromethylthio-phenoxy)-phenyl]-3-methyl-1,3,5-triazine-2,4,6(1H,3H,5H)-trione, of melting point: 170°, in 30 ml of anhydrous acetic acid. The mixture is heated to the boil for 2 hours, whilst stirring, 3 ml of water are added and the mixture is cooled, whilst stirring. The crystals which have precipitated are filtered off, and washed with 50% strength acetic acid and then with water. This gives 4.1 g (82.5% of theory) of 1-[3-trifluoromethyl-4-(4'-trifluoromethylsulphonyl-phenoxy)-phenyl]-3-methyl-1,3,5-triazine-2,4,6(1H,3H,5H)-trione of melting point: 238°C.

50

55

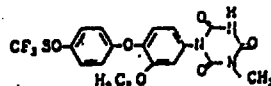
55

The following was prepared analogously

Example No.

13. 1-[3-Morpholinosulphonyl-4-(4'-trifluoromethylsulphonylphenoxy)-phenyl]-3-methyl-1,3,5-triazine-2,4,6(1H,3H,5H)-trione, melting point: 309°C.

Example 14



- 0.94 g (11 mmols) of 30% strength hydrogen peroxide is added to a solution of 4.55 g (10 mmols) of 1-[3-ethoxy-4-(4'-trifluoromethylthio-phenoxy)-phenyl]-3-methyl-1,3,5-triazine-2,4,6(1H,3H,5H)-trione of melting point: 227° in 140 ml of anhydrous acetic acid. The mixture is stirred for 3 days at 50°C and 140 ml of water are then added dropwise. The crystals which have precipitated are filtered off and recrystallised from isopropanol. This gives 2.4 g (51% of theory) of 1-[3-ethoxy-4-(4'-trifluoromethylsulphonyl-phenoxy)-phenyl]-3-methyl-1,3,5-triazine-2,4,6(1H,3H,5H)-trione of melting point: 225°C.

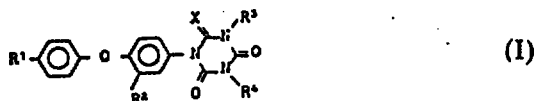
The following was obtained in an analogous manner:

Example No.

- 15 1-[3-Methyl-4-(4'-trifluoromethylsulphonyl-phenoxy)-phenyl]-3-methyl-1,3,5-triazine-2,4,6(1H,3H,5H)-trione, melting point: 130°C.

WHAT WE CLAIM IS:-

1. A pharmaceutical composition for use in promoting growth containing as an active ingredient a compound of the following general formula (I) or its physiologically acceptable salt

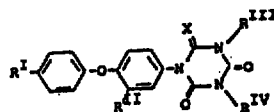


in which

- R¹ is halogenoalkylthio, halogenoalkylsulphonyl or halogenoalkylsulphonyl.
R² represents hydrogen, alkyl, alkoxy, alkoxyalkyl, alkylmercapto, halogen, halogenoalkyl or optionally substituted sulphonyl (as hereinbefore defined).

- R³ and R⁴ are the same or different and represent hydrogen, alkyl, alkenyl or alkynyl and X represents an oxygen atom or a sulphur atom, in admixture with a solid or liquefied gaseous diluent or in admixture with a liquid diluent other than a solvent of a molecular weight less than 200 except in the presence of a surface-active agent.

2. A composition according to claim 1 in which the active ingredient is a compound of the following formula or its physiologically acceptable salt



in which

- R^I is halogenoalkylthio, halogenoalkylsulphonyl or halogenoalkylsulphonyl.
R^{II} represents hydrogen, alkyl alkoxy, alkoxy alkyl, alkyl mercapto, dialkylaminosulphonyl, halogen or halogenoalkyl, wherein in each case the alkyl moiety or moieties has/have from 1 to 4 carbon atoms, and

- R^{III} and R^{IV} are the same or different and represent hydrogen, alkyl having 1 to 4 carbon atoms, or alkenyl having 2 to 4 carbon atoms.

3. A composition according to claim 2 wherein R^{II} is other than halogen.
4. A composition according to claim 1 in which the active ingredient is 1-[3-Methyl-4-(4'-trifluoromethylthio-phenoxy)-phenyl]-3-methyl-1,3,5-triazine-2,4,6-(1H,3H,5H)-trione or its physiologically acceptable salt.

5. A composition according to claim 1 in which the active ingredient is 1-[3-Chloro-4-(4'-trifluoromethylthio-phenoxy)-phenyl]-3-methyl-1,3,5-triazine-2,4,6-(1H,3H,5H)-trione or its physiologically acceptable salt.

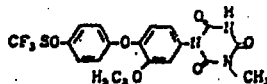


The following was prepared analogously

Example No.

13. 1-[3-Morpholinosulphonyl-4-(4'-trifluoromethylsulphonylphenoxy)-phenyl]-3-methyl-1,3,5-triazine-2,4,6(1H,3H,5H)-trione, melting point: 309°C.

Example 14



- 0.94 g (11 mmols) of 30% strength hydrogen peroxide is added to a solution of 4.55 g (10 mmols) of 1-[3-ethoxy-4-(4'-trifluoromethylthio-phenoxy)-phenyl]-3-methyl-1,3,5-triazine-2,4,6(1H,3H,5H)-trione of melting point: 227° in 140 ml of anhydrous acetic acid. The mixture is stirred for 3 days at 50°C and 140 ml of water are then added dropwise. The crystals which have precipitated are filtered off and recrystallised from isopropanol. This gives 2.4 g (51% of theory) of 1-[3-ethoxy-4-(4'-trifluoromethylsulphonyl-phenoxy)-phenyl]-3-methyl-1,3,5-triazine-2,4,6(1H,3H,5H)-trione of melting point: 225°C.

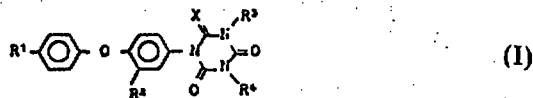
The following was obtained in an analogous manner:

Example No.

- 15 1-[3-Methyl-4-(4'-trifluoromethylsulphonyl-phenoxy)-phenyl]-3-methyl-1,3,5-triazine-2,4,6(1H,3H,5H)-trione, melting point: 130°C.

WHAT WE CLAIM IS:-

1. A pharmaceutical composition for use in promoting growth containing as an active ingredient a compound of the following general formula (I) or its physiologically acceptable salt



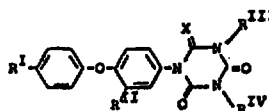
in which

R¹ is halogenoalkylthio, halogenoalkylsulphonyl or halogenoalkylsulphanyl.

R² represents hydrogen, alkyl, alkoxy, alkoxyalkyl, alkylmercapto, halogen, halogenoalkyl or optionally substituted sulphonyl (as hereinbefore defined).

R³ and R⁴ are the same or different and represent hydrogen, alkyl, alkenyl or alkynyl and X represents an oxygen atom or a sulphur atom, in admixture with a solid or liquefied gaseous diluent or in admixture with a liquid diluent other than a solvent of a molecular weight less than 200 except in the presence of a surface-active agent.

2. A composition according to claim 1 in which the active ingredient is a compound of the following formula or its physiologically acceptable salt



in which

R¹ is halogenoalkylthio, halogenoalkylsulphonyl or halogenoalkylsulphanyl.

R^{II} represents hydrogen, alkyl alkoxy, alkoxy alkyl, alkyl mercapto, dialkylaminosulphonyl, halogen or halogenoalkyl, wherein in each case the alkyl moiety or moieties has/have from 1 to 4 carbon atoms, and

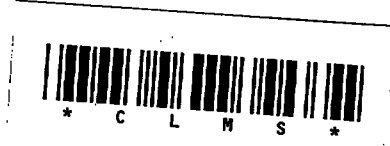
R^{III} and R^{IV} are the same or different and represent hydrogen, alkyl having 1 to 4 carbon atoms, or alkenyl having 2 to 4 carbon atoms.

3. A composition according to claim 2 wherein R^{II} is other than halogen.

4. A composition according to claim 1 in which the active ingredient is 1-[3-Methyl-4-(4'-trifluoromethylthio-phenoxy)-phenyl]-3-methyl-1,3,5-triazine-2,4,6-(1H,3H,5H)-trione or its physiologically acceptable salt.

5. A composition according to claim 1 in which the active ingredient is 1-[3-Chloro-4-(4'-trifluoromethylthio-phenoxy)-phenyl]-3-methyl-1,3,5-triazine-2,4,6-(1H,3H,5H)-trione or its physiologically acceptable salt.

19



10

1 571 368

10

6. A composition according to claim 1 in which the active ingredient is any compound as defined in claim 1 which is hereinbefore specifically mentioned in any of Examples 3 to 14.

7. A composition according to claim 1 in which the active ingredient is any compound as defined in claim 1 which is hereinbefore specifically mentioned other than those in claims 4 to 6.

8. A pharmaceutical composition containing as an active ingredient a compound as defined in any of claims 1 to 7 in the form of a sterile or isotonic aqueous solution.

9. A composition according to any of claims 1 to 8 containing from 0.5 to 95% of the said active ingredient, by weight.

10. A feedstuff additive, in dosage unit form comprising a compound as defined in any of claims 1 to 7.

11. A feedstuff additive in dosage unit form comprising a compound as defined in any of claims 1, 3 and 4 to 7.

12. An animal feed or drinking water containing as an active ingredient a compound as defined in any of claims 1, 3 and 4 to 7.

13. An animal feedstuff, feedstuff concentrate or drinking water containing as an active ingredient a compound as defined in any of claims 1 to 7.

14. An animal feedstuff, feedstuff concentrate or drinking water as claimed in claim 13 containing from 1 to 200 ppm of said compound.

15. An animal feedstuff, feedstuff concentrate or drinking water as claimed in claim 13 containing from 10 to 50 ppm of said compound.

16. A method of promoting growth in non-human animals which comprises administering to the animals a compound as defined in any of claims 1 to 7 either alone or in admixture with a diluent or in the form of a feedstuff additive according to claim 10 or 11, or an animal feedstuff, feedstuff concentrate or drinking water according to any of claims 13 to 15.

17. A method of promoting growth in non-human animals which comprises administering to the animals a compound as defined in any of claims 1, 3 and 4 to 7 either alone or in admixture with a diluent or in the form of an animal feed according to claim 12.

18. A method according to claim 16 or 17 in which the animals are mammals.

19. A method according to claim 16 or 17 in which the animals are avians.

20. A method according to any of claims 16 to 19 in which the active compound is administered orally.

21. A method of promoting growth in non-human animals substantially as described hereinbefore with particular reference to Table 1.

For the Applicants,
CARPMAELS & RANSFORD,
Chartered Patent Agents,
43, Bloomsbury Square,
London : WC1A 2RA.