

PATENT SPECIFICATION

(11) 1 547 842

- (21) Application No. 19880/78 (22) Filed 17 Sept. 1976
 (62) Divided out of No. 1547841
 (31) Convention Application No. 2541742
 (32) Filed 19 Sept. 1975 in
 (33) Federal Republic of Germany (DE)
 (44) Complete Specification published 27 June 1979
 (51) INT. CL² C07C 143/68 A61K 31/325
 (52) Index at acceptance
 C2C 220 227 22Y 30Y 311 313 314 31Y 321 326 32Y 332 338 364
 36Y 380 395 39Y 60X 620 660 661 694 699 73X 751 753
 75X 76Y 78Y 802 80Y RK RV SM

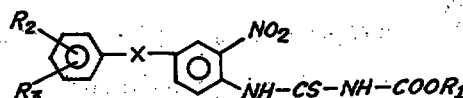


(54) PHENYLTHIONOCARBAMOYL
 ALKYL CARBAMINATE DERIVATIVES

(71) We, HOECHST AKTIENGESELLSCHAFT, a body corporate organised according to the laws of the Federal Republic of Germany, of 6230 Frankfurt (Main) 80, Postfach 80 03 20, Federal Republic of 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 phenylthionocarbamoyl alkylcarbaminate derivatives.

The present invention provides a compound of the general formula

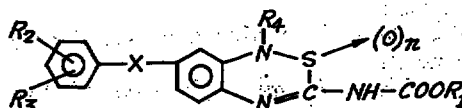


in which

R₁ represents an alkyl radical having from 1 to 4 carbon atoms, R₂ and R₃ each represent, independently from each other, a hydrogen or halogen atom, an alkoxy radical having from 1 to 4 carbon atoms, an alkyl radical having from 1 to 4 carbon atoms or a trifluoromethyl or cyano group, and

X represents the group —O—SO₂— or —SO₂—O—.

Compounds of the general formula (2) are anthelmintically active. They are also useful for the preparation of 3 - alkoxy carbonylamino - 1H - 2,1,4 - benzothiadiazine derivatives of the general formula



in which

R₁, R₂, R₃ and X have the meanings given above, and

R₄ represents a hydrogen atom, a saturated acyl radical having from 2 to 4 carbon atoms or a benzoyl radical, and

n represents the number 0 or 1. These compounds, their preparation and use as anthelmintics are described and claimed in application 38602/76, (Serial No. 1,547,841).

As alkyl radicals represented by R₁, R₂ and/or R₃ there may be mentioned, for example, methyl, ethyl, propyl, isopropyl, butyl, secondary butyl and tertiary butyl radicals. As alkoxy radicals represented by R₂ and/or R₃ there may be mentioned, for example, methoxy, ethoxy, propoxy, isopropoxy and butoxy radicals. As halogen atoms represented by R₂ and/or R₃ there may be mentioned, for example, fluorine, chlorine, bromine and iodine atoms.

Preference is given especially to those compounds in which R₁ represents a methyl, ethyl, propyl or butyl radical, R₂ represents a hydrogen atom and R₃ represents a hydrogen, chlorine or bromine atom or a trifluoromethyl, methyl, ethyl, meth-

oxy or ethoxy radical, R_3 preferably being in the 3-position of the phenyl ring, and to those in which R_1 represents a methyl radical, R_2 represents a hydrogen atom or trifluoromethyl radical and R_3 represents a hydrogen atom.

As *o*-nitrophenylthionocarbamoyl carbaminate of the formula (2) of the invention, the following compounds may be mentioned, for example:

- 5 2 - nitro - 4 - phenoxysulphonylphenylthionocarbamoyl methylcarbaminate,
- 2 - nitro - 4 - (4 - chlorophenoxysulphonyl) - phenylthionocarbamoyl methyl-
- carbamate,
- 10 2 - nitro - 4 - (3 - chlorophenoxysulphonyl) - phenylthionocarbamoyl methyl-
- carbamate,
- 2 - nitro - 4 - (2 - chlorophenoxysulphonyl) - phenylthionocarbamoyl methyl-
- carbamate,
- 2 - nitro - 4 - (2 - chlorophenoxysulphonyl) - phenylthionocarbamoyl methyl-
- carbamate,
- 15 2 - nitro - 4 - (3,5 - dichlorophenoxysulphonyl) - phenylthionocarbamoyl methyl-
- carbamate,
- 2 - nitro - 4 - (4 - bromophenoxysulphonyl) - phenylthionocarbamoyl methyl-
- carbamate,
- 2 - nitro - 4 - (3 - bromophenoxysulphonyl) - phenylthionocarbamoyl methyl-
- carbamate,
- 20 2 - nitro - 4 - (2 - bromophenoxysulphonyl) - phenylthionocarbamoyl methyl-
- carbamate,
- 2 - nitro - 4 - (4 - methylphenoxysulphonyl) - phenylthionocarbamoyl methyl-
- carbamate,
- 25 2 - nitro - 4 - (3 - methylphenoxysulphonyl) - phenylthionocarbamoyl methyl-
- carbamate,
- 2 - nitro - 4 - (2 - methylphenoxysulphonyl) - phenylthionocarbamoyl methyl-
- carbamate,
- 2 - nitro - (4 - *t*-butylphenoxysulphonyl) - phenylthionocarbamoylmethylcarb-
- 30 aminate,
- 2 - nitro - 4 - (2,4 - dimethylphenoxysulphonyl) - phenylthionocarbamoyl
- methylcarbaminate,
- 2 - nitro - 4 - (2 - chloro - 4 - methylphenoxysulphonyl) - phenylthionocarbamoyl
- methylcarbaminate,
- 35 2 - nitro - 4 - (2 - chloro - 6 - methylphenoxysulphonyl) - phenylthionocarbamoyl
- methylcarbaminate,
- 2 - nitro - 4 - (3 - chloro - 4 - methylphenoxysulphonyl) - phenylthionocarbamoyl
- methylcarbaminate,
- 2 - nitro - 4 - (3 - chloro - 6 - methylphenoxysulphonyl) - phenylthionocarbamoyl
- methylcarbaminate,
- 40 2 - nitro - 4 - (4 - chloro - 2 - methylphenoxysulphonyl) - phenylthionocarbamoyl
- methylcarbaminate,
- 2 - nitro - 4 - (4 - chloro - 2 - methylphenoxysulphonyl) - phenylthionocarbamoyl
- methylcarbaminate,
- 2 - nitro - 4 - (4 - chloro - 3 - methylphenoxysulphonyl) - phenylthionocarbamoyl
- methylcarbaminate,
- 45 2 - nitro - 4 - (3 - trifluoromethylphenoxysulphonyl) - phenylthionocarbamoyl
- methylcarbaminate,
- 2 - nitro - 4 - (4 - methoxyphenoxysulphonyl) - phenylthionocarbamoyl methyl-
- carbamate,
- 50 2 - nitro - 4 - (3 - methoxyphenoxysulphonyl) - phenylthionocarbamoyl methyl-
- carbamate,
- 2 - nitro - 4 - (2 - methoxyphenoxysulphonyl) - phenylthionocarbamoyl methyl-
- carbamate,
- 55 2 - nitro - 4 - (4 - propoxyphenoxysulphonyl) - phenylthionocarbamoyl methyl-
- carbamate,
- 2 - nitro - 4 - (4 - isopropoxyphenoxysulphonyl) - phenylthionocarbamoyl
- methylcarbaminate,
- 2 - nitro - 4 - (4 - butoxyphenoxysulphonyl) - phenylthionocarbamoyl methyl-
- carbamate,
- 60 2 - nitro - 4 - (4 - isobutoxyphenoxysulphonyl) - phenylthionocarbamoyl methyl-
- carbamate,
- 2 - nitro - 4 - (3 - cyanophenoxysulphonyl) - phenylthionocarbamoyl methyl-
- carbamate,

9

3

1,547,842

3

	2 - nitro - 4 - phenoxy sulphonyl phenylthionocarbonyl ethylcarbaminate,	
	2 - nitro - 4 - phenoxy sulphonyl phenylthionocarbonyl propylcarbaminate,	
	2 - nitro - 4 - phenoxy sulphonyl phenylthionocarbonyl isopropylcarbaminate,	
5	2 - nitro - 4 - phenoxy sulphonyl phenylthionocarbonyl butylcarbaminate,	5
	2 - nitro - 4 - phenoxy sulphonyl phenylthionocarbonyl isobutylcarbaminate,	
	2 - nitro - 4 - phenoxy sulphonyl phenylthionocarbonyl tert. butylcarbaminate,	
	2 - nitro - 4 - phenylsulphonyloxy phenylthionocarbonyl methylcarbaminate,	
	2 - nitro - 4 - (4 - chlorophenylsulphonyloxy) - phenylthionocarbonyl methyl-	
10	carbaminate,	10
	2 - nitro - 4 - (3 - chlorophenylsulphonyloxy) - phenylthionocarbonyl methyl-	
	carbaminate,	
	2 - nitro - 4 - (2 - chlorophenylsulphonyloxy) - phenylthionocarbonyl methyl-	
	carbaminate,	
15	2 - nitro - 4 - (2,5 - dichlorophenylsulphonyloxy) - phenylthionocarbonyl	15
	methylcarbaminate,	
	2 - nitro - 4 - (3,4 - dichlorophenylsulphonyloxy) - phenylthionocarbonyl	
	methylcarbaminate,	
	2 - nitro - 4 - (3,5 - dichlorophenylsulphonyloxy) - phenylthionocarbonyl	
20	methylcarbaminate,	20
	2 - nitro - 4 - (4 - bromophenylsulphonyloxy) - phenylthionocarbonyl methyl-	
	carbaminate,	
	2 - nitro - 4 - (3 - bromophenylsulphonyloxy) - phenylthionocarbonyl methyl-	
	carbaminate,	
25	2 - nitro - 4 - (2 - bromophenylsulphonyloxy) - phenylthionocarbonyl methyl-	25
	carbaminate,	
	2 - nitro - 4 - (4 - methylphenylsulphonyloxy) - phenylthionocarbonyl methyl-	
	carbaminate,	
	2 - nitro - 4 - (3 - methylphenylsulphonyloxy) - phenylthionocarbonyl methyl-	
30	carbaminate,	30
	2 - nitro - 4 - (2 - methylphenylsulphonyloxy) - phenylthionocarbonyl methyl-	
	carbaminate,	
	2 - nitro - 4 - (4 - tert. butylphenylsulphonyloxy) - phenylthionocarbonyl	
	methylcarbaminate,	
35	2 - nitro - 4 - (2 - chloro - 4 - methylphenylsulphonyloxy) - phenylthionocarb-	35
	onyl methylcarbaminate,	
	2 - nitro - 4 - (2 - chloro - 6 - methylphenylsulphonyloxy) - phenylthionocarb-	
	onyl methylcarbaminate,	
	2 - nitro - 4 - (3 - chloro - 4 - methylphenylsulphonyloxy) - phenylthionocarb-	
40	onyl methylcarbaminate,	40
	2 - nitro - 4 - (3 - chloro - 5 - methylphenylsulphonyloxy) - phenylthionocarb-	
	onyl methylcarbaminate,	
	2 - nitro - 4 - (4 - chloro - 2 - methylphenylsulphonyloxy) - phenylthionocarb-	
	onyl methylcarbaminate,	
45	2 - nitro - 4 - (4 - chloro - 3 - methylphenylsulphonyloxy) - phenylthionocarb-	45
	onyl methylcarbaminate,	
	2 - nitro - 4 - (3 - trifluoromethylphenylsulphonyloxy) - phenylthionocarbonyl	
	methylcarbaminate,	
	2 - nitro - 4 - (4 - methoxyphenylsulphonyloxy) - phenylthionocarbonyl methyl-	
	carbaminate,	
50	2 - nitro - 4 - (3 - methoxyphenylsulphonyloxy) - phenylthionocarbonyl methyl-	50
	carbaminate,	
	2 - nitro - 4 - (2 - methoxyphenylsulphonyloxy) - phenylthionocarbonyl methyl-	
	carbaminate,	
	2 - nitro - 4 - (4 - propoxyphenylsulphonyloxy) - phenylthionocarbonyl methyl-	
55	carbaminate,	55
	2 - nitro - 4 - (2 - isopropoxyphenylsulphonyloxy) - phenylthionocarbonyl	
	methylcarbaminate,	
	2 - nitro - 4 - (4 - butoxyphenylsulphonyloxy) - phenylthionocarbonyl methyl-	
	carbaminate,	
60	2 - nitro - 4 - (4 - isobutoxyphenylsulphonyloxy) - phenylthionocarbonyl	60
	methylcarbaminate,	
	2 - nitro - 4 - phenylsulphonyloxy phenylthionocarbonyl ethylcarbaminate,	
	2 - nitro - 4 - phenylsulphonyloxy phenylthionocarbonyl propylcarbaminate,	
	2 - nitro - 4 - phenylsulphonyloxy phenylthionocarbonyl isopropylcarbaminate,	
65	2 - nitro - 4 - phenylsulphonyloxy phenylthionocarbonyl butylcarbaminate,	65

(10)

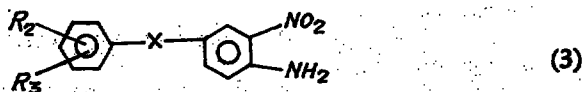
4

1,547,842

4

- 2 - nitro - 4 - phenylsulphonyloxyphenylthionocarbamoyl isobutylcarbaminate,
 2 - nitro - 4 - phenylsulphonyloxyphenylthionocarbamoyl tert.butylcarbaminate,
 2 - nitro - 4 - (3 - trifluoromethylphenylsulphonyloxy) - phenylthionocarbamoyl
 ethylcarbaminate,
 5 2 - nitro - 4 - (3 - trifluoromethylphenylsulphonyloxy) - phenylthionocarbamoyl
 isopropylcarbaminate,
 2 - nitro - 4 - (3 - trifluoromethylphenylsulphonyloxy) - phenylthionocarbamoyl
 isobutylcarbaminate.

10 The present invention provides a process for the preparation of a compound of
 general formula (2) which comprises reacting an o - nitro - aniline derivative of the
 general formula



in which R_2 , R_3 and X have the meanings given above, with an alkyl isothiocyanato-
 formate of the general formula



in which R_1 has the meaning given above.

Depending on the reactivity of the starting materials, the reaction may be carried
 out for one to several hours at a temperature in the range of from 20 to 120°C. The
 alkyl isothiocyanatoformate is suitably used in an excess amount, so that it serves also
 20 as a solvent. The reaction products may be isolated by evaporating the excess alkyl-
 isothiocyanatoformate, and the residue extracted with an inert solvent, for example
 ethyl acetate, diethyl ether, diisopropyl ether, methylene chloride, chloroform or
 benzene.

As o-nitraniline derivatives in accordance with the formula (3) there may be
 25 mentioned, for example,

- 2 - nitro - 4 - phenyloxysulphonylaniline,
 2 - nitro - 4 - (4 - chlorophenoxy sulphonyl) - aniline,
 2 - nitro - 4 - (3 - chlorophenoxy sulphonyl) - aniline,
 2 - nitro - 4 - (2 - chlorophenoxy sulphonyl) - aniline,
 30 2 - nitro - 4 - (2,5 - dichlorophenoxy sulphonyl) - aniline,
 2 - nitro - 4 - (3,5 - dichlorophenoxy sulphonyl) - aniline,
 2 - nitro - 4 - (4 - bromophenoxy sulphonyl) - aniline,
 2 - nitro - 4 - (3 - bromophenoxy sulphonyl) - aniline,
 2 - nitro - 4 - (2 - bromophenoxy sulphonyl) - aniline,
 35 2 - nitro - 4 - (4 - methylphenoxy sulphonyl) - aniline,
 2 - nitro - 4 - (3 - methylphenoxy sulphonyl) - aniline,
 2 - nitro - 4 - (2 - methylphenoxy sulphonyl) - aniline,
 2 - nitro - 4 - (4 - t.butylphenoxy sulphonyl) - aniline,
 2 - nitro - 4 - (2,4 - dimethylphenoxy sulphonyl) - aniline,
 40 2 - nitro - 4 - (2 - chloro - 4 - methylphenoxy sulphonyl) - aniline,
 2 - nitro - 4 - (2 - chloro - 6 - methylphenoxy sulphonyl) - aniline,
 2 - nitro - 4 - (3 - chloro - 4 - methylphenoxy sulphonyl) - aniline,
 2 - nitro - 4 - (3 - chloro - 6 - methylphenoxy sulphonyl) - aniline,
 2 - nitro - 4 - (4 - chloro - 2 - methylphenoxy sulphonyl) - aniline,
 45 2 - nitro - 4 - (4 - chloro - 3 - methylphenoxy sulphonyl) - aniline,
 2 - nitro - 4 - (3 - trifluoromethylphenoxy sulphonyl) - aniline,
 2 - nitro - 4 - (4 - methoxyphenoxy sulphonyl) - aniline,
 2 - nitro - 4 - (3 - methoxyphenoxy sulphonyl) - aniline,
 2 - nitro - 4 - (2 - methoxyphenoxy sulphonyl) - aniline,
 50 2 - nitro - 4 - (4 - propoxyphenoxy sulphonyl) - aniline,
 2 - nitro - 4 - (4 - isopropoxyphenoxy sulphonyl) - aniline,
 2 - nitro - 4 - (4 - butoxyphenoxy sulphonyl) - aniline,
 2 - nitro - 4 - (4 - isobutoxyphenoxy sulphonyl) - aniline,
 2 - nitro - 4 - phenylsulphonyloxyaniline,
 55 2 - nitro - 4 - (4 - chlorophenylsulphonyloxy) - aniline,
 2 - nitro - 4 - (3 - chlorophenylsulphonyloxy) - aniline,
 2 - nitro - 4 - (2 - chlorophenylsulphonyloxy) - aniline,

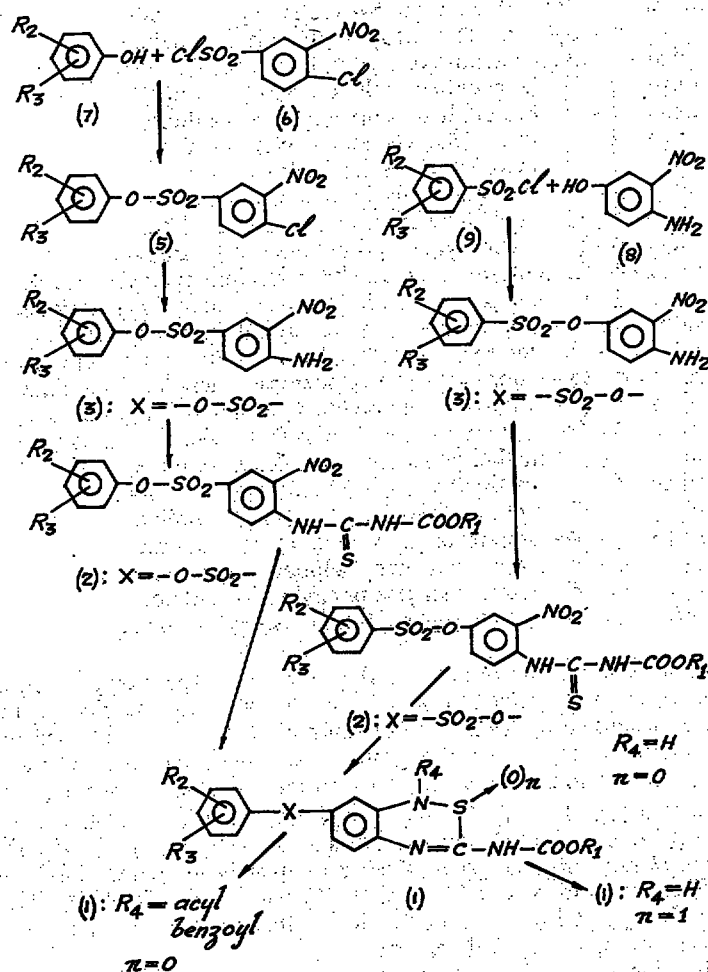
- 2 - nitro - 4 - (2,5 - dichlorophenylsulphonyloxy) - aniline,
2 - nitro - 4 - (3,4 - dichlorophenylsulphonyloxy) - aniline,
2 - nitro - 4 - (3,5 - dichlorophenylsulphonyloxy) - aniline,
2 - nitro - 4 - (4 - bromophenylsulphonyloxy) - aniline,
5 2 - nitro - 4 - (3 - bromophenylsulphonyloxy) - aniline, 5
2 - nitro - 4 - (2 - bromophenylsulphonyloxy) - aniline,
2 - nitro - 4 - (4 - methylphenylsulphonyloxy) - aniline,
2 - nitro - 4 - (3 - methylphenylsulphonyloxy) - aniline,
2 - nitro - 4 - (2 - methylphenylsulphonyloxy) - aniline,
10 2 - nitro - 4 - (4 - tert.butylphenylsulphonyloxy) - aniline, 10
2 - nitro - 4 - (2 - chloro - 4 - methylphenylsulphonyloxy) - aniline,
2 - nitro - 4 - (2 - chloro - 6 - methylphenylsulphonyloxy) - aniline,
2 - nitro - 4 - (3 - chloro - 3 - methylphenylsulphonyloxy) - aniline,
2 - nitro - 4 - (3 - chloro - 6 - methylphenylsulphonyloxy) - aniline,
15 2 - nitro - 4 - (4 - chloro - 2 - methylphenylsulphonyloxy) - aniline, 15
2 - nitro - 4 - (4 - chloro - 3 - methylphenylsulphonyloxy) - aniline,
2 - nitro - 4 - (3 - trifluoromethylphenylsulphonyloxy) - aniline,
2 - nitro - 4 - (4 - methoxyphenylsulphonyloxy) - aniline,
2 - nitro - 4 - (3 - methoxyphenylsulphonyloxy) - aniline,
20 2 - nitro - 4 - (2 - methoxyphenylsulphonyloxy) - aniline, 20
2 - nitro - 4 - (4 - propoxyphenylsulphonyloxy) - aniline,
2 - nitro - 4 - (4 - isopropoxyphenylsulphonyloxy) - aniline,
2 - nitro - 4 - (4 - butoxyphenylsulphonyloxy) - aniline,
2 - nitro - 4 - (4 - isobutoxyphenylsulphonyloxy) - aniline.

25 As alkylisothiocyanatoformates of the formula (4) there may be mentioned methyl, 25
ethyl, propyl, isopropyl, butyl, isobutyl, and tertiary butylisothiocyanatoformate.

30 The o-nitraniline derivatives of the formula (3) may be obtained in their turn, in
the case where X represents the group $-O-SO_2-$, by reacting the corresponding
chloro-nitro compounds of the following formula (4a), in which R_2 and R_3 have the
same meanings as in formula (2) above, with ammonia in a suitable solvent, e.g. dioxan
or methanol, at an elevated temperature and an increased pressure. The chloro-nitro
compounds of the formula (5) in their turn may be obtained by reacting 3 - nitro-
4 - chlorobenzenesulphonic acid chloride (6) with a phenol of the following formula
(7), in which R_2 and R_3 are defined as in the formula (2) above, in an inert solvent in
35 the presence of a base, e.g. triethylamine. 35

In the case where X represents the group $-SO_2-O-$, the corresponding o-nitr-
aniline derivatives of the formula (3) are obtained by reacting 3 - nitro - 4 - amino-
phenol (8) with a benzene-sulphonic acid chloride of the formula (9), in which R_2
and R_3 have the same meanings as in the formula (2), in an inert solvent in the pre-
40 sence of a base, e.g. triethylamine. 40

The development of the reactions is illustrated by the following scheme.



The o-nitrophenylthionocarbamoyl carbaminates of the general formula 2 are anthelmintically active.

The compounds are especially active against a great number of helminths, for example, *Haemonchus*, *Trichostrongylus*, *Ostertagia*, *Strongyloides*, *Cooperia*, *Chabertia*, *Oesophagostomum*, *Hyostrongylus*, *Ankylostoma*, *Ascaris*, and *Heterakis*. Their activity against gastro-intestinal *Strongylides*, which especially infest ruminants, is particularly marked. They also act against liver flukes.

The present invention also provides a pharmaceutical preparation which comprises a compound of the general formula 2 in admixture or conjunction with a pharmaceutically suitable carrier.

The pharmaceutical preparations are suitably in dosage unit form.

The present invention also provides a method for combating helminths which comprises treating a non-human animal with a compound of the general formula 2.

The active substances may be applied orally or subcutaneously, together with suitable pharmaceutical solvents and/or carriers, the form of application preferred depending on the circumstances of the case.

The active substances of the formula 2 may be administered, depending on the case, in a daily dosage of from 0.5 to 50 mg per kg of body weight for a period of from 1 to 14 days.

For an oral application there are suitable, for example, tablets, dragées, capsules, powders, granules, or pastes which contain the active substances in admixture or conjunction with common auxiliary or carrier substances, e.g. starch, cellulose powder, talcum, magnesium stearate, sugar, gelatin, calcium carbonate, finely divided silica, carboxymethyl cellulose, or similar substances.

The following Examples illustrate the invention.

EXAMPLES

1. 2 - Nitro - 4 - phenoxy sulphonyl phenylthionocarbamoyl methylcarbaminate

29.4 g of 2 - nitro - 4 - phenoxy sulphonyl aniline was heated in 30 ml of methyl isothiocyanatoformate for 1 hour to 100°C, while stirring. After cooling to 30°C, a total of 200 ml of diisopropyl ether was slowly added to the mixture, which was then cooled in an ice bath, and the precipitated 2 - nitro - 4 - phenoxy sulphonyl phenylthionocarbamoyl methylcarbaminate was filtered off. It was sufficiently pure for further processing. The yield was 25 g, melting point 137°C.

In order to prepare the 2 - nitro - 4 - phenoxy sulphonyl aniline, 54 g of 3 - nitro - 4 - chlorobenzenesulphonic acid phenyl ester in 500 ml of dioxan were maintained at 5 atmospheres gauge of gaseous ammonia for 5 hours at 50°C, and the solvent was subsequently removed *in vacuo*. The residue was mixed with 200 ml of a mixture of equal parts of methanol and water, in which process a solid precipitate formed after a short time and was filtered off. After a recrystallisation from methanol and from benzene, 28 g of 2 - nitro - 4 - phenoxy sulphonyl aniline were obtained which had a melting point of 104°C.

3 - Nitro - 4 - chlorobenzenesulphonic acid phenyl ester was obtained by mixing 51 g of 5 - nitro - 4 - chlorobenzenesulphonic acid chloride with 18.8 g of phenol in 120 ml of acetone, and by adding 28 ml of triethylamine dropwise, while cooling, at a temperature not exceeding 10°C. Stirring of the mixture was continued for several hours at room temperature, and then water was added, in which process an oil separated and was extracted with ether. After recrystallization of the residue from methanol, 54 g of 3 - nitro - 4 - chlorobenzenesulphonic acid phenyl ester were obtained which had a melting point of 71°C.

In an analogous manner the following compounds were prepared from starting materials which had been modified accordingly:

2. 2 - nitro - 4 - (4 - chlorophenoxy sulphonyl) - phenylthionocarbamoyl methylcarbaminate (from 3 - nitro - 4 - chlorobenzenesulphonic acid 4 - chlorophenyl ester via 2 - nitro - 4 - (4 - chlorophenoxy sulphonyl) - aniline);

3. 2 - nitro - 4 - (3 - chlorophenoxy sulphonyl) - phenylthionocarbamoyl methylcarbaminate (from 3 - nitro - 4 - chlorobenzenesulphonic acid 3 - chlorophenyl ester via 2 - nitro - 4 - (3 - chlorophenoxy sulphonyl) - aniline);

4. 2 - nitro - 4 - (3,5 - dichlorophenoxy sulphonyl) - phenylthionocarbamoyl methylcarbaminate (from 3 - nitro - 4 - chlorobenzenesulphonic acid 3,5 - dichlorophenyl ester via 2 - nitro - 4 - (3,5 - dichlorophenoxy sulphonyl) aniline);

5. 2 - nitro - 4 - (3 - bromophenoxy sulphonyl) - phenylthionocarbamoyl methylcarbaminate (from 3 - nitro - 4 - chlorobenzenesulphonic acid 3 - bromophenyl ester via 2 - nitro - 4 - (3 - bromophenoxy sulphonyl) - aniline);

6. 2 - nitro - 4 - (4 - methylphenoxy sulphonyl) - phenylthionocarbamoyl methylcarbaminate (from 3 - nitro - 4 - chlorobenzenesulphonic acid 4 - methylphenyl ester via 2 - nitro - 4 - (4 - methylphenoxy sulphonyl) - aniline);

7. 2 - nitro - 4 - (3 - methylphenoxy sulphonyl) - phenylthionocarbamoyl methylcarbaminate (from 3 - nitro - 4 - chlorobenzenesulphonic acid 3 - methylphenyl ester via 2 - nitro - 4 - (3 - methylphenoxy sulphonyl) - aniline);

8. 2 - nitro - 4 - (4 - methoxyphenoxy sulphonyl) - phenylthionocarbamoyl methylcarbaminate (from 3 - nitro - 4 - chlorobenzenesulphonic acid 4 - methoxyphenyl ester via 2 - nitro - 4 - (4 - methoxyphenoxy sulphonyl) - aniline);

9. 2 - nitro - 4 - (3 - methoxyphenoxy sulphonyl) - phenylthionocarbamoyl methylcarbaminate (from 3 - nitro - 4 - chlorobenzenesulphonic acid 3 - methoxyphenyl ester via 2 - nitro - 4 - (3 - methoxyphenoxy sulphonyl) - aniline);

10. 2 - nitro - 4 - (3 - ethoxyphenoxy sulphonyl) - phenylthionocarbamoyl methylcarbaminate (from 3 - nitro - 4 - chlorobenzenesulphonic acid 3 - ethoxyphenyl ester via 2 - nitro - 4 - (3 - ethoxyphenoxy sulphonyl) - aniline);

11. 2 - nitro - 4 - (3 - cyanophenoxy sulphonyl) - phenylthionocarbamoyl methylcarbaminate (from 3 - nitro - 4 - chlorobenzenesulphonic acid 3 - cyanophenyl ester via 2 - nitro - 4 - (3 - cyanophenoxy sulphonyl) - aniline);

12. 2 - nitro - 4 - (3 - trifluoromethylphenoxy sulphonyl) - phenylthionocarbamoyl methylcarbaminate (m.p. of 157°C) (from 3 - nitro - 4 - chlorobenzenesulphonic acid 3 - trifluoromethylphenyl ester having a melting point of 65°C via 2 - nitro - 4 - (3 - trifluoromethylphenoxy sulphonyl) - aniline (m.p. of 131°C)).

13. 2 - Nitro - 4 - phenylsulphonyloxyphenylthionocarbamoyl methylcarbaminate. 29.4 g of 2 - nitro - 4 - phenylsulphonyloxyaniline was heated in 30 ml of methyl isothiocyanatoformate for 1 hour at 100°C, while stirring. After cooling to 30°C, a total of 200 ml of diisopropyl ether was slowly added to the mixture, which was then cooled in an ice bath, and the precipitated 2 - nitro - 4 - phenylsulphonyloxyphenyl-

thionocarbamoyl methylcarbaminate was filtered off with suction. The product was recrystallised from a mixture of methylglycol and methanol, and 30 g. of the above-mentioned substance were obtained which had a melting point of 134°C.

In order to prepare 2 - nitro - 4 - phenylsulphonyloxyaniline, 15.4 g of 3 - nitro - 4 - aminophenol in 100 ml of acetone were mixed with 14 ml of triethylamine, and 17.6 g of benzenesulphonic acid chloride dissolved in 30 ml of acetone were added dropwise, while stirring, at an internal temperature not exceeding 20°C in an ice bath. Stirring was continued for another 3 hours at room temperature, the triethylamine hydrochloride was filtered off, and the filtrate was evaporated to dryness. The residue was then stirred with 50 ml of methanol and was filtered. After washing with methanol and drying, 18.2 g of 2 - nitrophenylsulphonyloxyaniline were obtained which had a melting point of 140°C.

In an analogous manner, the following compounds were prepared from starting materials which had been modified accordingly:

14. 2 - nitro - 4 - (4 - chlorophenylsulphonyloxy - phenylthionocarbamoyl methylcarbaminate (from 2 - nitro - 4 - (4 - chlorophenylsulphonyloxy) - aniline);

15. 2 - nitro - 4 - (3 - chlorophenylsulphonyloxy) - phenylthionocarbamoyl methylcarbaminate (from 2 - nitro - 4 - (3 - chlorophenylsulphonyloxy) - aniline);

16. 2 - nitro - 4 - (3,4 - dichlorophenylsulphonyloxy) - phenylthionocarbamoyl methylcarbaminate (from 2 - nitro - 4 - (3,4 - dichlorophenylsulphonyloxy) - aniline);

17. 2 - nitro - 4 - (3,5 - dichlorophenylsulphonyloxy) - phenylthionocarbamoyl methylcarbaminate (from 2 - nitro - 4 - (3,5 - dichlorophenylsulphonyloxy) - aniline);

18. 2 - nitro - 4 - (3 - bromophenylsulphonyloxy) - phenylthionocarbamoyl methylcarbaminate (from 2 - nitro - 4 - (3 - bromophenylsulphonyloxy) - aniline);

19. 2 - nitro - 4 - (4 - methylphenylsulphonyloxy) - phenylthionocarbamoyl methylcarbaminate (from 2 - nitro - 4 - (4 - methylphenylsulphonyloxy) - aniline);

20. 2 - nitro - 4 - (3 - methylphenylsulphonyloxy) - phenylthionocarbamoyl methylcarbaminate (from 2 - nitro - 4 - (3 - methylphenylsulphonyloxy) - aniline);

21. 2 - nitro - 4 - (3 - trifluoromethylphenylsulphonyloxy) - phenylthionocarbamoyl methylcarbaminate (m.p. of 126°C) (from 2 - nitro - 4 - (3 - trifluoromethylphenylsulphonyloxy)aniline (m.p. of 132°C);

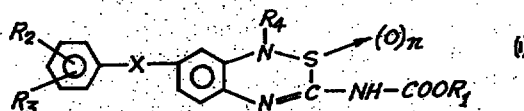
22. 2 - nitro - 4 - (3 - trifluoromethylphenylsulphonyloxy) - phenylthionocarbamoyl ethylcarbaminate (from 2 - nitro - 4 - (3 - trifluoromethylphenylsulphonyloxy)aniline);

23. 2 - nitro - 4 - (3 - trifluoromethylphenylsulphonyloxy) - phenylthionocarbamoyl isopropylcarbaminate (from 2 - nitro - 4 - (3 - trifluoromethylphenylsulphonyloxy)aniline);

24. 2 - nitro - 4 - (3 - trifluoromethylphenylsulphonyloxy) - phenylthionocarbamoyl isobutoxycarbaminato (from 2 - nitro - 4 - (3 - trifluoromethylphenylsulphonyloxy)aniline).

WHAT WE CLAIM IS:—

1. A compound of the general formula (2)



wherein R_1 represents an alkyl radical having from 1 to 4 carbon atoms, R_2 and R_3 each represent, independently from each other, a hydrogen or halogen atom, an alkoxy radical having from 1 to 4 carbon atoms, an alkyl radical having from 1 to 4 carbon atoms or a trifluoromethyl or cyano group, and X represents the group $-O-SO_2-$ or $-SO_2-O-$.

2. A compound as claimed in claim 1, wherein R_1 represents a methyl, ethyl, propyl, or butyl group.

3. A compound as claimed in claim 1 or claim 2, wherein R_2 represents a hydrogen atom.

4. A compound as claimed in any one of claims 1 to 3, wherein R_3 represents a hydrogen, chlorine or bromine atom or a trifluoromethyl, methyl, ethyl, methoxy or ethoxy group.

5. A compound as claimed in claim 1, wherein R_1 has the meaning given in claim 2, R_2 has the meaning given in claim 3 and R_3 has the meaning given in claim 4.

6. A compound as claimed in any one of claims 1 to 5, wherein R_4 is in the 3-position of the phenyl ring.



14

8

1,547,842

8

thionocarbamoyl methylcarbaminate was filtered off with suction. The product was recrystallised from a mixture of methylglycol and methanol, and 30 g of the above-mentioned substance were obtained which had a melting point of 134°C.

In order to prepare 2 - nitro - 4 - phenylsulphonyloxyaniline, 15.4 g of 3 - nitro - 4 - aminophenol in 100 ml of acetone were mixed with 14 ml of triethylamine, and 17.6 g of benzenesulphonic acid chloride dissolved in 30 ml of acetone were added dropwise, while stirring, at an internal temperature not exceeding 20°C in an ice bath. Stirring was continued for another 3 hours at room temperature, the triethylamine hydrochloride was filtered off, and the filtrate was evaporated to dryness. The residue was then stirred with 50 ml of methanol and was filtered. After washing with methanol and drying, 18.2 g of 2 - nitrophenylsulphonyloxyaniline were obtained which had a melting point of 140°C.

In an analogous manner, the following compounds were prepared from starting materials which had been modified accordingly:

14. 2 - nitro - 4 - (4 - chlorophenylsulphonyloxy) - phenylthionocarbamoyl methylcarbaminate (from 2 - nitro - 4 - (4 - chlorophenylsulphonyloxy) - aniline);

15. 2 - nitro - 4 - (3 - chlorophenylsulphonyloxy) - phenylthionocarbamoyl methylcarbaminate (from 2 - nitro - 4 - (3 - chlorophenylsulphonyloxy) - aniline);

16. 2 - nitro - 4 - (3,4 - dichlorophenylsulphonyloxy) - phenylthionocarbamoyl methylcarbaminate (from 2 - nitro - 4 - (3,4 - dichlorophenylsulphonyloxy) - aniline);

17. 2 - nitro - 4 - (3,5 - dichlorophenylsulphonyloxy) - phenylthionocarbamoyl methylcarbaminate (from 2 - nitro - 4 - (3,5 - dichlorophenylsulphonyloxy) - aniline);

18. 2 - nitro - 4 - (3 - bromophenylsulphonyloxy) - phenylthionocarbamoyl methylcarbaminate (from 2 - nitro - 4 - (3 - bromophenylsulphonyloxy) - aniline);

19. 2 - nitro - 4 - (4 - methylphenylsulphonyloxy) - phenylthionocarbamoyl methylcarbaminate (from 2 - nitro - 4 - (4 - methylphenylsulphonyloxy) - aniline);

20. 2 - nitro - 4 - (3 - methylphenylsulphonyloxy) - phenylthionocarbamoyl methylcarbaminate (from 2 - nitro - 4 - (3 - methylphenylsulphonyloxy) - aniline);

21. 2 - nitro - 4 - (3 - trifluoromethylphenylsulphonyloxy) - phenylthionocarbamoyl methylcarbaminate (m.p. of 126°C) (from 2 - nitro - 4 - (3 - trifluoromethylphenylsulphonyloxy)aniline (m.p. of 132°C));

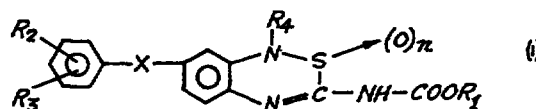
22. 2 - nitro - 4 - (3 - trifluoromethylphenylsulphonyloxy) - phenylthionocarbamoyl ethylcarbaminate (from 2 - nitro - 4 - (3 - trifluoromethylphenylsulphonyloxy)aniline);

23. 2 - nitro - 4 - (3 - trifluoromethylphenylsulphonyloxy) - phenylthionocarbamoyl isopropylcarbaminate (from 2 - nitro - 4 - (3 - trifluoromethylphenylsulphonyloxy)aniline);

24. 2 - nitro - 4 - (3 - trifluoromethylphenylsulphonyloxy) - phenylthionocarbamoyl isobutoxycarbaminato (from 2 - nitro - 4 - (3 - trifluoromethylphenylsulphonyloxy)aniline).

WHAT WE CLAIM IS:—

1. A compound of the general formula (2)



wherein R_1 represents an alkyl radical having from 1 to 4 carbon atoms, R_2 and R_3 each represent, independently from each other, a hydrogen or halogen atom, an alkoxy radical having from 1 to 4 carbon atoms, an alkyl radical having from 1 to 4 carbon atoms or a trifluoromethyl or cyano group, and X represents the group $-\text{O}-\text{SO}_2-$ or $-\text{SO}_2-\text{O}-$.

2. A compound as claimed in claim 1, wherein R_1 represents a methyl, ethyl, propyl, or butyl group.

3. A compound as claimed in claim 1 or claim 2, wherein R_2 represents a hydrogen atom.

4. A compound as claimed in any one of claims 1 to 3, wherein R_3 represents a hydrogen, chlorine or bromine atom or a trifluoromethyl, methyl, ethyl, methoxy or ethoxy group.

5. A compound as claimed in claim 1, wherein R_1 has the meaning given in claim 2, R_2 has the meaning given in claim 3 and R_3 has the meaning given in claim 4.

6. A compound as claimed in any one of claims 1 to 5, wherein R_3 is in the 3-position of the phenyl ring.



15

1,547,842

9

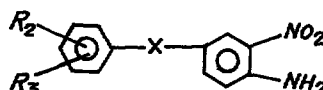
9

7. A compound as claimed in claim 1, wherein R_1 represents a methyl radical, R_2 represents a hydrogen atom or trifluoromethyl radical, and R_3 represents a hydrogen atom.

8. A compound as claimed in claim 1, which is 2-nitro-4-phenoxy-sulphonyl-phenylthionocarbonyl methylcarbaminate.

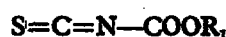
9. A compound as claimed in claim 1, which is specifically listed in the description or in any one of the Examples herein.

10. A process for the preparation of a compound claimed in claim 1, which comprises reacting an o-nitro-aniline derivative of the general formula (3).



(3)

in which R_2 , R_3 and X have the meanings given in claim 1, with an alkylisothiocyanatoformate of the formula (4)



(4)

in which R_1 is defined as in claim 1.

11. A process as claimed in claim 10, carried out substantially as described in any one of the Examples herein.

12. A compound as claimed in claim 1, whenever prepared by a process as claimed in claim 10 or claim 11.

13. A pharmaceutical preparation for combating helminths containing as the active ingredient a compound as claimed in any one of claims 1 to 9 and 12, in admixture or conjunction with a pharmaceutically suitable carrier.

14. A pharmaceutical preparation according to claim 13 being in dosage unit form for combating helminths with from 0.5 to 50 mg of active ingredient per kg body weight.

15. A method of combating helminths in non-human animals which comprises treating the animal with a compound as claimed in any one of claims 1 to 9 and 12 or with a pharmaceutical preparation as claimed in claim 13 or claim 14.

16. A method as claimed in claim 15, wherein the animal is a ruminant.

ABEL & IMRAY,
Chartered Patent Agents,
Northumberland House,
303-306 High Holborn,
London, WC1V 7LH.

Printed for Her Majesty's Stationery Office, by the Courier Press, Leamington Spa, 1979
Published by The Patent Office, 25 Southampton Buildings, London, WC2A 1AY, from which copies may be obtained.