

PATENT SPECIFICATION

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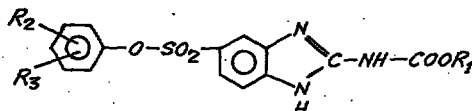
(54) ANTHELMINTICALLY ACTIVE 2-CARBALKOXYAMINO BENZIMIDAZOLYL-5(6) SULFONIC ACID PHENYL ESTERS AND PROCESS FOR THEIR MANUFACTURE

(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:—

This invention relates to anthelmintically active 2-carbalkoxyamino-benzimidazolyl-5(6)-sulfonic acid phenyl esters and to a process for their manufacture.

2-Carbalkoxy-amino-benzimidazolyl derivatives carrying alkyl, acyl, phenoxy and phenylthio groups in the 5(6)-position are known to possess anthelmintic properties (P. Actor et al., Nature 215, 321 (1967); German Offenlegungsschrift Nos. 2,029,637, 2,264,690 and 2,363,348).

The present invention provides anthelmintically active 2-carbalkoxyamino-benzimidazolyl-5(6)-sulfonic acid phenyl esters of the formula



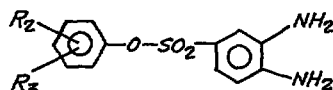
(1)

in which R₁ is an alkyl group having from 1 to 4 carbon atoms and each of R₂ and R₃ is a hydrogen atom, a hydroxy group, an alkoxy group having from 1 to 4 carbon atoms, a halogen atom, a trifluoromethyl group, an alkyl group having from 1 to 4 carbon atoms, a carbalkoxy group having from 1 to 4 carbon atoms in the alkoxy moiety, or a cyano group.

The alkyl groups represented by R₁, R₂ and R₃ are methyl, ethyl, propyl, isopropyl, butyl, secondary butyl and tertiary butyl groups. The alkoxy groups represented by R₂ and R₃ are methoxy, ethoxy, propoxy, isopropoxy and butoxy groups. The halogen atoms represented by R₂ and R₃ are fluorine, chlorine, bromine and iodine atoms. The carbalkoxy groups represented by R₂ and R₃ are carbomethoxy, carboethoxy, carbopropoxy or carbobutoxy groups.

Especially preferred compounds of formula (I) are those in which R₁ is a methyl group, R₂ is a hydrogen atom, and R₃ is a hydrogen, chlorine or bromine atom or a trifluoromethyl, methyl, ethyl, methoxy or ethoxy group, the especially preferred position of the substituents represented by R₃ being the 3-position of the phenyl ring.

The present invention also provides a process for the manufacture of the 2-carbalkoxyamino-benzimidazolyl-5(6)-sulfonic acid phenyl esters of the formula (1), which comprises condensing an *o*-phenylene diamine derivative of the formula



(2)

in which R₂ and R₃ have the meanings given above,

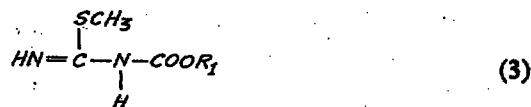
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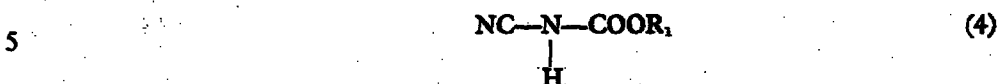
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(a) with an alkyl-S-methyl-thiourea carboxylate of the formula

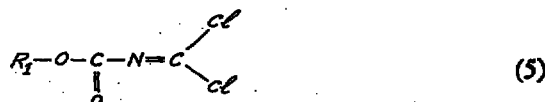


in which R₁ has the meaning given above, or
(b) with a cyanamide carboxylate of the formula



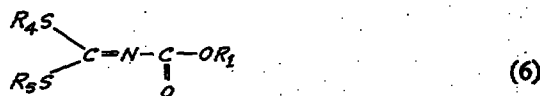
in which R₁ has the meaning given above, in both cases at a pH of from 1 to 6, preferably from 2 to 5, or

(c) with an N-dichloromethylene carbamic acid ester of the formula

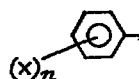


in which R₁ has the meaning given above, at a temperature of from -10° to +40°C in the presence of a base, or

(d) with a bis-alkyl or bis-aryl-thio-methylene-amino-formiate of the formula

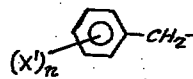


in which R₁ has the meaning given above, and each of R₄ and R₅ is an alkyl group having from 1 to 4 carbon atoms, an alkenyl group having from 3 to 5 carbon atoms, a cyclohexyl group, or an optionally substituted phenyl or benzyl group of the formula



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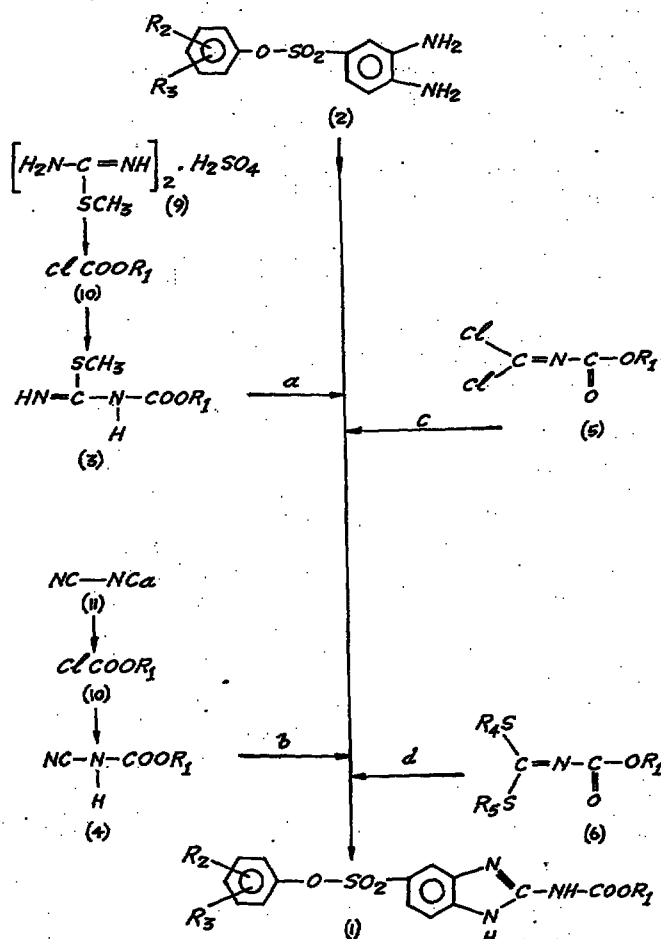
or



(8)

in which each of X and X' is a halogen atom or a methyl or nitro group, or R₄ and R₅ may be linked to form a ring containing 2 or 3 methylene groups, and in which n is zero, 1 or 2.

The reactions may also be illustrated by the following reaction schemes:



According to reaction (a), S-methyl-thiourea sulfate of the formula (9) is first mixed with a chloroformate of the formula (10) in water, and a strong base is then added dropwise, for example a 25% sodium hydroxide solution, while maintaining the temperature low, preferably at about 0°C. The alkyl-S-methyl-thiourea carboxylate of the formula (3) which is formed need not be isolated.

As chloroformates of the formula (10), there may be mentioned, for example,

methyl chloroformate,
ethyl chloroformate,
propyl chloroformate,
isopropyl chloroformate,
butyl chloroformate,
isobutyl chloroformate,
tert.butyl chloroformate.

The pH of the above reaction mixture is then advantageously adjusted to from 2 to 5, suitably by adding an organic acid, such as acetic acid or lactic acid. The o-phenylene diamine derivative of the formula (2) is then added, either in the form of a free base or of an acid addition salt, for example the hydrochloride. In this latter case, it may be advantageous to add an alkali metal salt of an organic acid as a buffer.

As o-phenylene diamine derivatives of the formula (2), there are mentioned, for example,

3,4-diamino-benzene sulfonic acid phenyl ester
3,4-diamino-benzene sulfonic acid-4-chloro-phenyl ester
3,4-diamino-benzene sulfonic acid-3-chloro-phenyl ester
3,4-diamino-benzene sulfonic acid-2-chloro-phenyl ester

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	3,4-diamino-benzene sulfonic acid-2,5-dichloro-phenyl ester	
	3,4-diamino-benzene sulfonic acid-3,5-dichloro-phenyl ester	
	3,4-diamino-benzene sulfonic acid-4-bromo-phenyl ester	
5	3,4-diamino-benzene sulfonic acid-3-bromo-phenyl ester	5
	3,4-diamino-benzene sulfonic acid-2-bromo-phenyl ester	
	3,4-diamino-benzene sulfonic acid-4-methyl-phenyl ester	
	3,4-diamino-benzene sulfonic acid-3-methyl-phenyl ester	
	3,4-diamino-benzene sulfonic acid-2-methyl-phenyl ester	
10	3,4-diamino-benzene sulfonic acid-4-tert.butyl-phenyl ester	10
	3,4-diamino-benzene sulfonic acid-2,4-dimethyl-phenyl ester	
	3,4-diamino-benzene sulfonic acid-2-chloro-4-methyl-phenyl ester	
	3,4-diamino-benzene sulfonic acid-2-chloro-6-methyl-phenyl ester	
	3,4-diamino-benzene sulfonic acid-3-chloro-4-methyl-phenyl ester	
	3,4-diamino-benzene sulfonic acid-3-chloro-6-methyl-phenyl ester	
15	3,4-diamino-benzene sulfonic acid-3-chloro-4-carbethoxy-phenyl ester	15
	3,4-diamino-benzene sulfonic acid-4-chloro-2-methyl-phenyl ester	
	3,4-diamino-benzene sulfonic acid-4-chloro-3-methyl-phenyl ester	
	3,4-diamino-benzene sulfonic acid-4-chloro-3,5-dimethyl-phenyl ester	
20	3,4-diamino-benzene sulfonic acid-3,5-bis(trifluoromethyl)-phenyl ester	20
	3,4-diamino-benzene sulfonic acid-4-methoxy-phenyl ester	
	3,4-diamino-benzene sulfonic acid-3-methoxy-phenyl ester	
	3,4-diamino-benzene sulfonic acid-2-methoxy-phenyl ester	
	3,4-diamino-benzene sulfonic acid-4-propoxy-phenyl ester	
25	3,4-diamino-benzene sulfonic acid-4-isopropoxy-phenyl ester	25
	3,4-diamino-benzene sulfonic acid-4-butoxy-phenyl ester	
	3,4-diamino-benzene sulfonic acid-4-isobutoxy-phenyl ester	

The reaction components are advantageously allowed to react at a temperature of from 30 to 100°C for a period of from 30 minutes to 10 hours. Methyl mercaptan is set free as a by-product. The 2-carbalkoxyamino-benzimidazolyl-5(6)-sulfonic acid phenyl esters of the formula (1) are isolated in the usual manner, for example by diluting the reaction mixture with water and separating the precipitated product by filtration.

In this manner, there are obtained

35	2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid phenyl ester	35
	2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-4-chloro-phenyl ester	
	2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3-chloro-phenyl ester	
	2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-2-chloro-phenyl ester	
40	2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-2,5-dichloro-phenyl ester	40
	2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3,5-dichloro-phenyl ester	
	2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-4-bromo-phenyl ester	
	2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3-bromo-phenyl ester	
	2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-2-bromo-phenyl ester	
45	2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-4-methyl-phenyl ester	45
	2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3-methyl-phenyl ester	
	2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-2-methyl-phenyl ester	
	2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-4-tert.butyl-phenyl ester	
	2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-2,4-dimethyl-phenyl ester	
50	2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-2-chloro-4-methyl-phenyl ester	50
	2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-2-chloro-6-methyl-phenyl ester	
	2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3-chloro-4-methyl-phenyl ester	
55	2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3-chloro-6-methyl-phenyl ester	55
	2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3-chloro-4-carbethoxy-phenyl ester	
	2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-4-chloro-2-methyl-phenyl ester	
60	2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-4-chloro-3-methyl-phenyl ester	60
	2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-4-chloro-3,5-dimethyl-phenyl ester	

2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3,5-bis-trifluoromethyl-phenyl ester

2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-4-methoxy-phenyl ester

2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3-methoxy-phenyl ester

2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-2-methoxy-phenyl ester

2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-4-propoxy-phenyl ester

2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-4-isopropoxy-phenyl ester

2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-4-butoxy-phenyl ester

2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-4-isobutoxy-phenyl ester

2-carb-ethoxyamino-5-benzimidazolyl-sulfonic acid-phenyl ester

2-carbopropoxyamino-5-benzimidazolyl-sulfonic acid-phenyl ester

2-carbisopropoxyamino-5-benzimidazolyl-sulfonic acid-phenyl ester

2-carbobutoxyamino-5-benzimidazolyl-sulfonic acid-phenyl ester

2-carbisobutoxyamino-5-benzimidazolyl-sulfonic acid-phenyl ester

2-carbo-tert.butoxyamino-5-benzimidazolyl-sulfonic acid-phenyl ester.

According to reaction (b), a chloroformate of the formula (10), as used for method (a), is first added to an aqueous suspension of cyanamide in the form of a salt, advantageously the calcium salt of the formula (11), while maintaining the temperature between 40 and 60°C by cooling.

After filtration of dark-coloured by-products which separate, the cyanamide carboxylate of the formula (4) is obtained in the filtrate.

The cyanamide carboxylate of the formula (4) thus obtained is combined with an *o*-phenylene diamine derivative of the formula (2), at a pH of from 1 to 6, preferably 2 to 4, by adding a mineral acid, for example concentrated hydrochloric acid. To complete the reaction, the reaction mixture is advantageously maintained at a temperature of from 30 to 100°C for a period of 30 minutes to 10 hours, depending on the reactivity of the *o*-phenylene diamine derivative used. After the reaction mixture has been cooled, the precipitated reaction product of the formula (1) is isolated by filtration and washing.

The *o*-phenylene diamine derivative of the formula (2) may be used either in the form of a free amine in the manner mentioned above with an alkyl-S-methyl thiourea carboxylate of the formula (3) or in the form of an acid addition salt with a suitable inorganic or organic acid, such as hydrochloric acid, sulfuric acid, acetic acid or oxalic acid.

According to the reaction (c), 1 mol of an *o*-phenylene-diamine derivative of the formula (2) is suitably reacted with 1 mol of an N-dichloromethylene carbamic acid ester of the formula (5) in the presence of 2 mols of a base.

As bases, there may be mentioned alkali metal or alkaline earth metal hydroxides, carbonates and hydrogen-carbonates, or tertiary organic bases, for example sodium hydroxide, sodium bicarbonate, sodium carbonate, potassium carbonate, potassium bicarbonate, triethylamine, pyridine and methylated pyridines.

The N-dichloromethylene carbamic acid esters of the formula (5) may be prepared according to the method described in German Offenlegungsschrift No. 1,932,297 by reacting dichloromethylene carbamic acid chloride with an alcohol in the presence of an inert organic solvent such as ether, dioxan, tetrahydrofuran, benzene or toluene, at a temperature of from 0° to 40°C.

As examples of N-dichloromethylenecarbamic acid esters of the formula (5), there may be mentioned N-dichloromethylene carbamic acid methyl ester, as well as the ethyl ester, isopropyl ester, propyl ester, n-butyl ester and sec.-butyl ester.

The reaction temperatures may be varied greatly, generally from -10° to +60°C, preferably from 0° to 30°C.

According to the reaction (d), 1 mol of the *o*-phenylene diamine derivative of the formula (2) is advantageously reacted with 1 mol of bis-alkyl or bis-aryl-thiomethylene-amino formate of the formula (6) in an inert solvent, such as tetrahydrofuran, dioxan, isopropyl ether or chloroform, at an elevated temperature, advantageously at the boiling temperature of the solvent used.

According to the present invention, it is also possible to prepare the bis-alkyl or bis-aryl-thiomethylene-amino-formate of the formula (6) in situ from the hydrochloride of imino-thiocarbonic acid ester by adding a chloroformate of the formula (10), as used for method (a).

In such a case, use must be made of an acid binder, for example an organic or inorganic base, such as sodium hydroxide, sodium bicarbonate or triethylamine. As reaction medium, polar and non polar solvents are suitable, for example ether,

acetone, dioxan, water, dimethylformamide, benzene or cyclohexane. during this reaction, the temperature should advantageously not exceed 20°C.

The bis-alkyl and bis-aryl-thiomethylene-amino-formates may be obtained by reacting the corresponding dithio-imino-carbonic acid esters with chloroformates of the formula (10) according to the method described in U.S. Patent No. 3,562,290.

As examples of bis-alkyl or bis-aryl-thiomethylene-amino-formates of the formula (6), there are mentioned:

bis-methylthio-methylene-amino-formic acid-methyl ester
bis-methylthio-methylene-amino-formic acid-ethyl ester
bis-methylthio-methylene-amino-formic acid-propyl ester
bis-methylthio-methylene-amino-formic acid-isopropyl ester
bis-methylthio-methylene-amino-formic acid-butyl ester
bis-methylthio-methylene-amino-formic acid-sec.butyl ester
bis-butylthio-methylene-amino-formic acid-methyl ester
methylthio-butylthio-methylene-amino-formic acid-methyl ester
allylthio-cyclohexylthio-methylene-amino-formic acid-methyl ester
methylthio-phenyl-thio-methylene-amino-formic acid-methyl ester
methylthio-(3,4-dichloro-benzyl-thio)-methylene-amino-formic acid-methyl ester
or
methylthio-(2-chloro-4-methylthio)-methylene-amino-formic acid-methyl ester.

The *o*-phenylene diamine derivative of the formula (2) used as a starting material for reactions (a) to (d) can be obtained by reduction of a corresponding amino-nitro derivative, for example in the manner described in our copending Application No. 52729/77 (Serial No. 1,516,509). The latter can be obtained from the corresponding chloro-nitro compound which can, in turn, be obtained from 3-nitro-4-chlorobenzene-sulfonyl chloride and an appropriate phenol.

The 2-carbalkoxyamino-benzimidazolyl-5(6)-sulfonic acid phenyl esters of the invention are valuable chemotherapeutic agents and are suitable for combating diseases caused by parasites in both humans and other animals, such as helminths and liver flukes.

They are especially active against a great number of helminths, for example *Haemonchus*, *Trichostrongylus*, *Ostertagia*, *Strongyloides*, *Cooperia*, *Chabertia*, *Oesophagostomum*, *Hyostrongylus*, *Ankylostoma*, *Ascaris* and *Heterakis*. They are most active against gastro-intestinal Strongylides, which most especially infest ruminants. The infestation of animals by these parasites causes great economical damage, so that the compounds of the present invention are mainly used in veterinary drugs.

The present invention therefore also provides pharmaceutical compositions containing as active ingredient a compound of the formula (1) in admixture or conjunction with a pharmaceutically suitable carrier, and a method for combating parasites which comprises administering to an infested organism other than a human being a compound of the formula (1).

The compounds of the formula (1) can be administered in doses of from 0.5 to 50 mg per kg of body weight for 1 to 14 days, depending on the individual case.

For oral administration, there may be used tablets, dragees, capsules, powder, granules or pastes, which contain the active substance in conjunction with the usual excipients and adjuvants, for example starch, cellulose powder, talcum, magnesium stearate, sugar, gelatin, calcium carbonate, finely divided silicic acid, carboxymethyl cellulose and similar substances.

For parenteral administration, there may be used solution, for example oily solutions prepared using sesame oil, castor oil or synthetic triglycerides, optionally with the addition of tocopherol as an antioxidant and/or surface-active substances, such as sorbitane fatty acid esters. In addition, there can be used aqueous suspensions which are prepared using ethoxylated sorbitane fatty acid esters, optionally with the addition of thickeners, such as polyethylene glycol or carboxymethyl cellulose.

The concentrations of the compounds of the present invention in the compositions are preferably in the range of from 2 to 20% by weight for veterinary drugs; for the use as medicaments for humans, the concentrations of the active substances are preferably in the range of from 20 to 80% by weight.

The activity of the compounds of the present invention was determined with the aid of chemotherapeutic investigations made on lambs, each having a weight of about 30 kg, which had been infested for test purposes with larvae of *Haemonchus contortus* and *Trichostrongylus colubriformis* respectively. The test animals were

kept in tiled boxes which were cleaned thoroughly every day. After the prepatence period (i.e. time between infestation and sexual maturity of the parasites, when secretion of eggs or larvae begins), the number of eggs per gram of excrement was determined by the modified McMaster method according to Wetzel (Tierärztliche Umschau, 6, 209—210 (1951)). Immediately after this, the treatment of the lambs was started (generally 4 to 8 animals, at least 2 animals, per active substance). The dosage units of the compounds of the invention were administered to the animals in the form of a suspension each in 10 ml of a 1% Tylose suspension ("Tylose" is a registered Trade Mark). On the 7th, 14th and 28th day after this treatment, the number of eggs per gram of excrement was again determined according to the above method, and the percentage decrease, compared to the initial value prior to the treatment, was calculated.

The products of the invention have an excellent activity not only when administered *per os* but also parenterally at doses as low as 2 mg/kg of body weight. Therefore, they are far superior to comparable benzimidazole derivatives, especially to all known 2-benzimidazolyl carbamates substituted in the 5(6)-position.

The following Examples illustrate the invention.

Process (a)

EXAMPLE 1

60 Grams of a 25% sodium hydroxide solution were added dropwise while cooling with ice at a temperature not exceeding 10°C to a thoroughly stirred mixture of 27.8 g of S-methylthiourea sulfate in 44 ml of water and 13 ml of methyl chloroformate. Stirring was continued for half an hour, and then a mixture of 10 ml of glacial acetic acid and 100 ml of water was added. Subsequently, 24.2 g of 3,4-diamino-benzene-sulfonic acid phenyl ester dissolved in 100 ml of isopropanol were added, and the mixture was refluxed for 2 hours, whereupon a solid began to precipitate. The solid was suction-filtered, carefully washed with methanol and then with water and, after drying, 19 g of 2-carbomethoxyamino-5-benzimidazolyl sulfonic acid phenyl ester were obtained. The crude product was purified by dissolving it in 250 ml of dioxan, filtering it with charcoal and adding 50 ml of water to the filtrate. The yield of the analytically pure product was 14 g, having a decomposition point of 242°C.

3,4-diamino-benzene-sulfonic acid phenyl ester was prepared by hydrogenating 27 g of 3-nitro-4-amino-benzene-sulfonic acid phenyl ester. The latter was prepared from 3-nitro-4-chloro-benzenesulfonic acid phenyl ester which itself was prepared from 3-nitro-4-chlorobenzenesulfonic acid chloride and phenol. This series of reactions is described in detail in our copending Application No. 52729/77 (Serial No. 1,516,509).

EXAMPLES 2—39

The following compounds were prepared in an analogous manner:

- 2) Via 3-nitro-4-chloro-benzenesulfonic acid-4-chloro-phenyl ester, m.p. 84°C and 3-nitro-4-amino-benzenesulfonic acid-4-chloro-phenyl ester, m.p. 156°C and 3,4-diamino-benzenesulfonic acid-4-chloro-phenyl ester the 2-carbomethoxyamino-5-benzimidazolylsulfonic acid-4-chloro-phenyl ester m.p. 250°C (decomp.).
- 3) Via 3-nitro-4-chloro-benzenesulfonic acid-3-chloro-phenyl ester, m.p. 68°C and 3-nitro-4-amino-benzenesulfonic acid-3-chloro-phenyl ester, m.p. 138°C and 3,4-diamino-benzenesulfonic acid-3-chloro-phenyl ester, m.p. 84°C, the 2-carbomethoxyamino-5-benzimidazolylsulfonic acid-3-chloro-phenyl ester, m.p. 234°C, (decomp.).
- 4) Via 3-nitro-4-chloro-benzenesulfonic acid-2-chloro-phenyl ester and 3-nitro-4-amino-benzenesulfonic acid-2-chloro-phenyl ester and 3,4-diamino-benzenesulfonic acid-2-chloro-phenyl ester, the 2-carbomethoxyamino-5-benzimidazolylsulfonic acid-2-chloro-phenyl ester.
- 5) Via 3-nitro-4-chloro-benzenesulfonic acid-2,5-dichloro-phenyl ester and 3-nitro-4-amino-benzenesulfonic acid-2,5-dichloro-phenyl ester and 3,4-diamino-benzenesulfonic acid-2,5-dichloro-phenyl ester, the 2-carbomethoxyamino-5-benzimidazolylsulfonic acid-2,5-dichloro-phenyl ester.
- 6) Via 3-nitro-4-chloro-benzenesulfonic acid-3,5-dichloro-phenyl ester, m.p. 104°C and 3-nitro-4-amino-benzenesulfonic acid-3,5-dichloro-phenyl ester, m.p. 164°C and 3,4-diamino-benzenesulfonic acid-3,5-dichloro-phenyl ester, m.p. 116°C, the 2-carbomethoxyamino-5-benzimidazolylsulfonic acid-3,5-dichloro-phenyl ester, m.p. 250°C (decomp.).

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- 7) Via 3-nitro-4-chloro-benzenesulfonic acid-4-bromo-phenyl ester and 3-nitro-4-amino-benzenesulfonic acid-4-bromo-phenyl ester and 3,4-diamino-benzenesulfonic acid-4-bromo-phenyl ester, the 2-carbomethoxyamino-5-benzimidazolylsulfonic acid-4-bromo-phenyl ester.
- 5 8) Via 3-nitro-4-chloro-benzenesulfonic acid-3-bromo-phenyl ester, m.p. 72°C and 3-nitro-4-amino-benzenesulfonic acid-3-bromo-phenyl ester, m.p. 141°C and 3,4-diamino-benzenesulfonic acid-3-bromo-phenyl ester, m.p. 94°C, the 2-carbomethoxyamino-5-benzimidazolylsulfonic acid-3-bromo-phenyl ester, m.p. 242°C (decomp.).
- 10 9) Via 3-nitro-4-chloro-benzenesulfonic acid-2-bromo-phenyl ester and 3-nitro-4-amino-benzenesulfonic acid-2-bromo-phenyl ester and 3,4-diamino-benzenesulfonic acid-2-bromo-phenyl ester, the 2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-2-bromo-phenyl ester.
- 15 10) Via 3-nitro-4-chloro-benzenesulfonic acid-4-methyl-phenyl ester, m.p. 68°C and 3-nitro-4-amino-benzenesulfonic acid-4-methyl-phenyl ester, m.p. 135°C and 3,4-diamino-benzenesulfonic acid-4-methyl-phenyl ester, the 2-carbomethoxyamino-5-benzimidazolylsulfonic acid-4-methyl-phenyl ester, m.p. 240°C₂ (decomp.).
- 20 11) Via 3-nitro-4-chloro-benzenesulfonic acid-3-methyl-phenyl-ester, m.p. 60°C and 3-nitro-4-amino-benzenesulfonic acid-3-methyl-phenyl ester, m.p. 138°C and 3,4-diamino-benzenesulfonic acid-3-methyl-phenyl ester, m.p. 84°C, the 2-carbomethoxyamino-5-benzimidazolylsulfonic acid-3-methyl-phenyl ester, m.p. 234°C (decomp.).
- 25 12) Via 3-nitro-4-chloro-benzenesulfonic acid-2-methyl-phenyl ester and 3-nitro-4-amino-benzenesulfonic acid-2-methyl-phenyl ester and 3,4-diamino-benzenesulfonic acid-2-methyl-phenyl ester, the 2-carbomethoxyamino-5-benzimidazolylsulfonic acid-2-methyl-phenyl ester.
- 30 13) Via 3-nitro-4-chloro-benzenesulfonic acid-4-tert.butyl-phenyl ester and 3-nitro-4-amino-benzenesulfonic acid-4-tert.butyl-phenyl ester and 3,4-diamino-benzenesulfonic acid-4-tert.butyl-phenyl ester, the 2-carbomethoxyamino-5-benzimidazolylsulfonic acid-tert.butyl-phenyl ester.
- 35 14) Via 3-nitro-4-chloro-benzenesulfonic acid-2,4-dimethyl-phenyl ester and 3-nitro-4-amino-benzenesulfonic acid-2,4-dimethyl-phenyl ester and 3,4-diamino-benzenesulfonic acid-2,4-dimethyl phenyl ester, the 2-carbomethoxyamino-5-benzimidazolylsulfonic acid-2,4-dimethyl-phenyl ester.
- 40 15) Via 3-nitro-4-chloro-benzenesulfonic acid-2-chloro-4-methyl-phenyl ester and 3-nitro-4-amino-benzenesulfonic acid-2-chloro-4-methyl-phenyl ester and 3,4-diamino-benzenesulfonic acid-2-chloro-4-methyl-phenyl ester, the 2-carbomethoxyamino-5-benzimidazolylsulfonic acid-2-chloro-4-methyl-phenyl ester.
- 45 16) Via 3-nitro-4-chloro-benzenesulfonic acid-2-chloro-6-methyl-phenyl ester and 3-nitro-4-amino-benzenesulfonic acid-2-chloro-6-methyl-phenyl ester and 3,4-diamino-benzenesulfonic acid-2-chloro-6-methyl-phenyl ester, the 2-carbomethoxyamino-5-benzimidazolylsulfonic acid-2-chloro-6-methyl-phenyl ester.
- 50 17) Via 3-nitro-4-chloro-benzenesulfonic acid-3-chloro-4-methyl-phenyl ester and 3-nitro-4-amino-benzenesulfonic acid-3-chloro-4-methyl-phenyl ester and 3,4-diamino-benzenesulfonic acid-3-chloro-4-methyl-phenyl ester, the 2-carbomethoxyamino-5-benzimidazolylsulfonic acid-3-chloro-4-methyl-phenyl ester.
- 55 18) Via 3-nitro-4-chloro-benzenesulfonic acid-3-chloro-6-methyl-phenyl ester and 3-nitro-4-amino-benzenesulfonic acid-3-chloro-6-methyl-phenyl ester and 3,4-diamino-benzenesulfonic acid-3-chloro-6-methyl-phenyl ester, the 2-carbomethoxyamino-5-benzimidazolylsulfonic acid-3-chloro-6-methyl-phenyl ester.
- 60 19) Via 3-nitro-4-chloro-benzenesulfonic acid-3-chloro-4-carbethoxy-phenyl ester and 3-nitro-4-amino-benzenesulfonic acid-3-chloro-4-carbethoxy-phenyl ester and 3,4-diamino-benzenesulfonic acid-3-chloro-4-carbethoxy-phenyl ester, the 2-carbomethoxyamino-5-benzimidazolylsulfonic acid-3-chloro-4-carbethoxy-phenyl ester.
- 20) Via 3-nitro-4-chloro-benzenesulfonic acid-4-chloro-2-methyl-phenyl ester and 3-nitro-4-amino-benzenesulfonic acid-4-chloro-2-methyl-phenyl ester and 3,4-diamino-benzenesulfonic acid-4-chloro-2-methyl-phenyl ester,

- the 2-carbomethoxyamino-5-benzimidazolylsulfonic acid-4-chloro-2-methyl-phenyl ester.
- 21) Via 3-nitro-4-chloro-benzenesulfonic acid-4-chloro-3-methyl-phenyl ester and 3-nitro-4-amino-benzenesulfonic acid-4-chloro-3-methyl-phenyl ester and 3,4-diamino-benzenesulfonic acid-4-chloro-3-methyl-phenyl ester, the 2-carbomethoxyamino-5-benzimidazolylsulfonic acid-4-chloro-3-methyl-phenyl ester. 5
- 22) Via 3-nitro-4-chloro-benzenesulfonic acid-4-chloro-3,5-dimethyl-phenyl ester and 3-nitro-4-amino-benzenesulfonic acid-4-chloro-3,5-dimethyl-phenyl ester and 3,4-diamino-benzenesulfonic acid-4-chloro-3,5-dimethyl-phenyl ester, the 2-carbomethoxyamino-5-benzimidazolylsulfonic acid-4-chloro-3,5-dimethyl-phenyl ester. 10
- 23) Via 3-nitro-4-chloro-benzenesulfonic acid-3,5-bistrifluoro-methyl-phenyl ester and 3-nitro-4-amino-benzenesulfonic acid-3,5-bistrifluoro-methyl-phenyl ester and 3,4-diamino-benzenesulfonic acid-3,5-bistrifluoro-methyl-phenyl ester, the 2-carbomethoxyamino-5-benzimidazolylsulfonic acid-3,5-bistrifluoro-methyl-phenyl ester. 15
- 24) Via 3-nitro-4-chloro-benzenesulfonic acid-4-methoxy-phenyl ester, m.p. 88°C and 3-nitro-4-amino-benzenesulfonic acid-4-methoxy-phenyl ester, m.p. 140°C and 3,4-diamino-benzenesulfonic acid-4-methoxy-phenyl ester, the 2-carbomethoxyamino-5-benzimidazolylsulfonic acid-4-methoxy-phenyl ester, m.p. 228°C, (decomp.). 20
- 25) Via 3-nitro-4-chloro-benzenesulfonic acid-3-methoxy-phenyl ester (oil) and 3-nitro-4-amino-benzenesulfonic acid-3-methoxy-phenyl ester, m.p. 116°C and 3,4-diamino-benzenesulfonic acid-3-methoxy-phenyl ester (oil), the 2-carbomethoxyamino-5-benzimidazolylsulfonic acid-3-methoxy-phenyl ester, m.p. 227°C (decomp.). 25
- 26) Via 3-nitro-4-chloro-benzenesulfonic acid-2-methoxy-phenyl ester and 3-nitro-4-amino-benzenesulfonic acid-2-methoxy-phenyl ester and 3,4-diamino-benzenesulfonic acid-2-methoxy-phenyl ester, the 2-carbomethoxyamino-5-benzimidazolylsulfonic acid-2-methoxy-phenyl ester. 30
- 27) Via 3-nitro-4-chloro-benzenesulfonic acid-4-propoxy-phenyl ester and 3-nitro-4-amino-benzenesulfonic acid-4-propoxy-phenyl ester and 3,4-diamino-benzenesulfonic acid-4-propoxy-phenyl ester, the 2-carbomethoxyamino-5-benzimidazolylsulfonic acid-4-propoxy-phenyl ester. 35
- 28) Via 3-nitro-4-chloro-benzenesulfonic acid-4-isopropoxy-phenyl ester and 3-nitro-4-amino-benzenesulfonic acid-4-isopropoxy-phenyl ester and 3,4-diamino-benzenesulfonic acid-4-isopropoxy-phenyl ester, the 2-carbomethoxyamino-5-benzimidazolylsulfonic acid-4-isopropoxy-phenyl ester. 40
- 29) Via 3-nitro-4-chloro-benzenesulfonic acid-4-butoxy-phenyl ester and 3-nitro-4-amino-benzenesulfonic acid-4-butoxy-phenyl ester and 3,4-diamino-benzenesulfonic acid-4-butoxy-phenyl ester, the 2-carbomethoxyamino-5-benzimidazolylsulfonic acid-4-butoxy-phenyl ester. 45
- 30) Via 3-nitro-4-chloro-benzenesulfonic acid-3-ethoxy-phenyl ester (oil) and 3-nitro-4-amino-benzenesulfonic acid-3-ethoxy-phenyl ester, m.p. 86°C and 3,4-diamino-benzenesulfonic acid-3-ethoxy-phenyl ester (oil), the 2-carbomethoxyamino-5-benzimidazolylsulfonic acid-3-ethoxy-phenyl ester, m.p. 212°C, (decomp.). 50
- 31) Via 3-nitro-4-chloro-benzenesulfonic acid-4-isobutoxy-phenyl ester and 3-nitro-4-amino-benzenesulfonic acid-4-isobutoxy-phenyl ester and 3,4-diamino-benzenesulfonic acid-4-isobutoxy-phenyl ester, the 2-carbomethoxyamino-5-benzimidazolylsulfonic acid-4-isobutoxy-phenyl ester. 55
- 32) Via 3-nitro-4-chloro-benzenesulfonic acid-3-cyano-phenyl ester, m.p. 118°C and 3-nitro-4-amino-benzenesulfonic acid-3-cyano-phenyl ester, m.p. 183°C and 3,4-diamino-benzenesulfonic acid-3-cyano-phenyl ester, the 2-carbomethoxyamino-5-benzimidazolylsulfonic acid-3-cyano-phenyl ester, m.p. 265°C, (decomp.). 60
- 33) Via 3-nitro-4-chloro-benzenesulfonic acid-phenyl ester and 3-nitro-4-amino-benzenesulfonic acid-phenyl ester and 3,4-diamino-benzenesulfonic acid-phenyl ester, the 2-carbomethoxyamino-5-benzimidazolylsulfonic acid phenyl ester. 65
- 34) Via 3-nitro-4-chloro-benzenesulfonic acid-phenyl ester and 3-nitro-4-amino-benzenesulfonic acid-phenyl ester 65

- and 3,4-diamino-benzenesulfonic acid-phenyl ester,
the 2-carbopropoxyamino-5-benzimidazolylsulfonic acid-phenyl ester.
- 35) Via 3-nitro-4-chloro-benzenesulfonic acid-phenyl ester
and 3-nitro-4-amino-benzenesulfonic acid-phenyl ester
and 3,4-diamino-benzenesulfonic acid-phenyl ester,
the 2-carboisopropoxyamino-5-benzimidazolylsulfonic acid-phenyl ester.
- 36) Via 3-nitro-4-chloro-benzenesulfonic acid-phenylester
and 3-nitro-4-amino-benzenesulfonic acid-phenyl ester
and 3,4-diamino-benzenesulfonic acid-phenyl ester,
the 2-carbobutoxyamino-5-benzimidazolylsulfonic acid-phenyl ester.
- 37) Via 3-nitro-4-chloro-benzenesulfonic acid-phenyl ester
and 3-nitro-4-amino-benzenesulfonic acid-phenyl ester
and 3,4-diamino-benzenesulfonic acid-phenyl ester,
the 2-carboisobutoxyamino-5-benzimidazolylsulfonic acid-phenyl ester.
- 38) Via 3-nitro-4-chloro-benzenesulfonic acid-phenyl ester
and 3-nitro-4-amino-benzenesulfonic acid-phenyl ester
and 3,4-diamino-benzenesulfonic acid-phenyl ester,
the 2-carbo-tert.butoxyamino-5-benzimidazolyl-sulfonic acid-phenyl ester.
- 39) Via 3-nitro-4-chloro-benzenesulfonic acid-3-trifluoro-methyl-phenyl ester, m.p.
65°C
and 3-nitro-4-amino-benzenesulfonic acid-3-trifluoromethyl-phenyl ester, m.p.
132°C
and 3,4-diamino-benzenesulfonic acid-3-trifluoromethyl-phenyl ester
the 2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3-trifluoromethyl-
phenyl ester, m.p. 250°C (with decomposition).

Process (b)

EXAMPLE 40

To a solution of 42 g of cyanamide in 210 ml of water, 90 g of chloroformic acid methyl ester and 218 g of a 33% sodium hydroxide solution were added. The mixture was stirred for 1.5 hours at a temperature of 30 to 35°C, then a solution of 213 g of 3,4-diamino-benzenesulfonic acid phenylester of 1 l of isopropanol was added, whereupon the temperature was raised to 80°C. After addition of 800 ml of glacial acetic acid, the reaction mixture was maintained at 90°C for another 3 to 4 hours. Then it was allowed to cool and stored overnight in a refrigerator. The precipitated 2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid phenyl ester was suction-filtered and washed with isopropanol and water. For purification the crude product was dissolved in dioxan, filtered with charcoal and combined with water. Yield: 80 g, decomposition point. 242°C.

3,4-Diamino-benzenesulfonic acid phenyl ester was obtained according to the method described in our copending application No. 52729/77 (Serial No. 1,516,509).

EXAMPLES 41-46

The following compounds were prepared in an analogous manner:

- 41) Via 3-nitro-4-chloro-benzene-sulfonic acid-3-chloro-phenyl ester, m.p. 68°C
and 3-nitro-4-amino-benzene-sulfonic acid-3-chloro-phenyl ester, m.p. 138°C
and 3,4-diamino-benzene-sulfonic acid-3-chloro-phenyl ester, m.p. 84°C
the 2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3-chlorophenyl ester
(identical with Example 3), m.p. 234°C (decomposition).
- 42) Via 3-nitro-4-chloro-benzene-sulfonic acid-3-bromo-phenyl ester, m.p. 72°C
and 3-nitro-4-amino-benzene-sulfonic acid-3-bromo-phenyl ester, m.p. 141°C
and 3,4-diamino-benzene-sulfonic acid-3-bromo-phenyl ester m.p. 94°C
the 2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3-bromo-phenyl ester
(identical with Example 8), m.p. 242°C (decomposition).
- 43) Via 3-nitro-4-chloro-benzene-sulfonic acid-3-methyl-phenyl ester, m.p. 60°C
and 3-nitro-4-amino-benzene-sulfonic acid-3-methyl-phenyl ester, m.p. 138°C
and 3,4-diamino-benzene-sulfonic acid-3-methyl-phenyl ester, m.p. 84°C
the 2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3-methyl-phenyl ester
(identical with Example 11, m.p. 234°C (decomposition).
- 44) Via 3-nitro-4-chloro-benzene-sulfonic acid-3-methoxy-phenyl ester (oil)
and 3-nitro-4-amino-benzene-sulfonic acid-3-methoxy-phenyl ester, m.p. 116°C
and 3,4-diamino-benzene-sulfonic acid-3-methoxy-phenyl ester (oil)
the 2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3-methoxy-phenyl
ester (identical with Example 25), m.p. 227°C (decomposition).

(19)

45) Via 3-nitro-4-chloro-benzene-sulfonic acid-3-ethoxy-phenyl ester (oil)
and 3-nitro-4-amino-benzene-sulfonic acid-3-ethoxy-phenyl ester, m.p. 86°C
and 3,4-diamino-benzene-sulfonic acid-3-ethoxy-phenyl ester (oil)
the 2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3-ethoxy-phenyl ester
(identical with Example 30), m.p. 212°C (decomposition).

46) Via 3-nitro-4-chloro-benzene-sulfonic acid-3-trifluoro-methyl-phenyl ester, m.p.
65°C
and 3-nitro-4-amino-benzene-sulfonic acid-3-trifluoro-methyl-phenyl ester, m.p.
132°C
and 3,4-diamino-benzene-sulfonic acid-3-trifluoromethyl-phenyl ester
the 2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3-trifluoromethyl-
phenyl ester, m.p. 250°C (decomposition).

Process (c)

EXAMPLE 47

26.4 Grams of 3,4-diamino-benzenesulfonic acid phenyl ester, 20.2 g of triethyl-
amine and 300 ml of chloroform were mixed and a solution of 15.6 g of N-dichloro-
methylene carbamic acid methyl ester in 50 ml of chloroform was slowly added
while stirring, the maximum temperature being 20°C. Stirring was continued for
1 hour, the precipitate formed was suction-filtered and washed with chloroform.

For purification, the crude product was dissolved in dioxan, filtered with char-
coal and combined with water. After suction-filtration, washing and drying, 5 g of
2-carbomethoxy-amino-5-benzimidazolyl-sulfonic acid phenyl ester having a decom-
position point of 242°C were obtained.

3,4-Diamino-benzenesulfonic acid phenyl ester was obtained in the manner
described in our copending Application No. 52729/77 (Serial No. 1,516,509).

EXAMPLES 48—53

The following compounds were prepared in an analogous manner:

48) Via 3-nitro-4-chloro-benzene-sulfonic acid-3-chloro-phenyl ester, m.p. 68°C
and 3-nitro-4-amino-benzene-sulfonic acid-3-chloro-phenyl ester, m.p. 138°C
and 3,4-diamino-benzene-sulfonic acid-3-chloro-phenyl ester, m.p. 84°C
the 2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3-chloro-phenyl ester
identical with Example 3), m.p. 234°C (decomposition).

49) Via 3-nitro-4-chloro-benzene-sulfonic acid-3-bromo-phenyl ester, m.p. 72°C
and 3-nitro-4-chloro-benzene-sulfonic acid-3-bromo-phenyl ester, m.p. 141°C
and 3,4-diamino-benzene-sulfonic acid-3-bromo-phenyl ester, m.p. 94°C
the 2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3-bromo-phenyl ester
(identical with Example 8), m.p. 242°C (decomposition).

50) Via 3-nitro-4-chloro-benzene-sulfonic acid-3-methyl phenyl ester, m.p. 60°C
and 3-nitro-4-amino-benzene-sulfonic acid-3-methyl-phenyl ester, m.p. 138°C
and 3,4-diamino-benzene-sulfonic acid-3-methyl-phenyl ester, m.p. 84°C
the 2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3-methyl-phenyl ester
(identical with Example 11), m.p. 234°C (decomposition).

51) Via 3-nitro-4-chloro-benzene-sulfonic acid-3-methoxy-phenyl ester (oil)
and 3-nitro-4-amino-benzene-sulfonic acid-3-methoxy-phenyl ester, m.p. 116°C
and 3,4-diamino-benzene-sulfonic acid-3-methoxy-phenyl ester (oil)
the 2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3-methoxy-phenyl
ester (identical with Example 25), m.p. 227°C (decomposition).

52) Via 3-nitro-4-chloro-benzene-sulfonic acid-3-ethoxy-phenyl ester (oil)
and 3-nitro-4-amino-benzene-sulfonic acid-3-ethoxy-phenyl ester, m.p. 86°C
and 3,4-diamino-benzene-sulfonic acid-3-ethoxy-phenyl ester (oil)
the 2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3-ethoxy-phenyl ester
(identical with Example 30), m.p. 212°C (decomposition).

53) Via 3-nitro-4-chloro-benzene-sulfonic acid-3-trifluoro-methyl-phenyl ester, m.p.
65°C
and 3-nitro-4-amino-benzene-sulfonic acid-3-trifluoro-methyl-phenyl ester, m.p.
132°C
and 3,4-diamino-benzene-sulfonic acid-3-trifluoromethyl-phenyl ester
the 2-carbomethoxyimino-5-benzimidazolyl-sulfonic acid-3-trifluoromethyl-phenyl
ester, m.p. 250°C (decomposition), (identical with Example 39).

Process (d)

EXAMPLE 54

17.9 Grams of bis-methylthio-methylene aminoformic acid methyl ester were added to 26.4 g of 3,4-diamino-benzenesulfonic acid phenyl ester in 200 ml of tetrahydrofuran, and the mixture was refluxed for 3 hours. It was then allowed to cool and the 2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid phenyl ester was suction-filtered, dissolved in dioxan, filtered with charcoal and precipitated with water to purify it. Yield: 12 g, decomposition point: 242°C.

3,4-Diamino-benzenesulfonic acid phenyl ester was obtained in the manner described in our copending Application No. 52729/77 (Serial No. 1,516,509).

EXAMPLE 55

To a cooled solution of 19.7 g of imino-dithiocarbonic acid methyl ester hydrochloride and 12.5 g of chloroformic acid methyl ester in 50 ml of water, a 10% sodium hydroxide solution was added dropwise, while taking care that the temperature did not exceed 10°C. As soon as the pH was adjusted to 7.5, 26.4 g of 3,4-diamino-benzenesulfonic acid phenyl ester in 50 ml of glacial acetic acid were added, and the mixture was refluxed for 2 hours while stirring. It was allowed to cool, and the 2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid phenyl ester formed was suction-filtered. It was identical in its properties with the reaction product disclosed in Example 54.

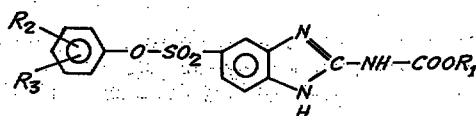
EXAMPLES 56—61

The following compounds were prepared in an analogous manner:

- 56) Via 3-nitro-4-chloro-benzene-sulfonic acid-3-chloro-phenyl ester, m.p. 68°C and 3-nitro-4-amino-benzene-sulfonic acid-3-chloro-phenyl ester, m.p. 138°C and 3,4-diamino-benzene-sulfonic acid-3-chloro-phenyl ester, m.p. 84°C the 2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3-chloro-phenyl ester (identical with Example 3) m.p. 234°C (decomposition).
- 57) Via 3-nitro-4-chloro-benzene-sulfonic acid-3-bromo-phenyl ester, m.p. 72°C and 3-nitro-4-amino-benzene-sulfonic acid-3-bromo-phenyl ester, m.p. 141°C and 3,4-diamino-benzene-sulfonic acid-3-bromo-phenyl ester, m.p. 94°C the 2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3-bromo-phenyl ester (identical with Example 8), m.p. 242°C (decomposition).
- 58) Via 3-nitro-4-chloro-benzene-sulfonic acid-3-methyl-phenyl ester, m.p. 60°C and 3-nitro-4-amino-benzene-sulfonic acid-3-methyl-phenyl ester, m.p. 138°C and 3,4-diamino-benzene-sulfonic acid-3-methyl-phenyl ester, m.p. 84°C the 2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3-methyl-phenyl ester (identical with Example 11), m.p. 234°C (decomposition).
- 59) Via 3-nitro-4-chloro-benzene-sulfonic acid-3-methoxy-phenyl ester (oil) and 3-nitro-4-amino-benzene-sulfonic acid-3-methoxy-phenyl ester, m.p. 116°C and 3,4-diamino-benzene-sulfonic acid-3-methoxy-phenyl ester (oil) the 2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3-methoxy-phenyl ester (identical with Example 25) m.p. 227°C (decomposition).
- 60) Via 3-nitro-4-chloro-benzene-sulfonic acid-3-ethoxy-phenyl ester (oil) and 3-nitro-4-amino-benzene-sulfonic acid-3-ethoxy-phenyl ester, m.p. 86°C and 3,4-diamino-benzene-sulfonic acid-3-ethoxy-phenyl ester (oil) the 2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3-ethoxy-phenyl ester (identical with Example 30) m.p. 212°C (decomposition).
- 61) Via 3-nitro-4-chloro-benzene-sulfonic acid-3-trifluoro-methyl-phenyl ester, m.p. 65°C and 3-nitro-4-amino-benzene-sulfonic acid-3-trifluoromethyl-phenyl ester, m.p. 132°C and 3,4-diamino-benzene-sulfonic acid-3-trifluoromethyl-phenyl ester the 2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3-trifluoromethyl-phenyl ester, m.p. 250°C (decomposition) (identical with Example 39).

WHAT WE CLAIM IS:—

1. A 2-carbalkoxyamino benzimidazolyl-5(6)-sulfonic acid phenyl ester of the formula





Process (d)

EXAMPLE 54

17.9 Grams of bis-methylthio-methylene aminoformic acid methyl ester were added to 26.4 g of 3,4-diamino-benzenesulfonic acid phenyl ester in 200 ml of tetrahydrofuran, and the mixture was refluxed for 3 hours. It was then allowed to cool and the 2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid phenyl ester was suction-filtered, dissolved in dioxan, filtered with charcoal and precipitated with water to purify it. Yield: 12 g, decomposition point: 242°C.

3,4-Diamino-benzenesulfonic acid phenyl ester was obtained in the manner described in our copending Application No. 52729/77 (Serial No. 1,516,509).

EXAMPLE 55

To a cooled solution of 19.7 g of imino-dithiocarbonic acid methyl ester hydrochloride and 12.5 g of chloroformic acid methyl ester in 50 ml of water, a 10% sodium hydroxide solution was added dropwise, while taking care that the temperature did not exceed 10°C. As soon as the pH was adjusted to 7.5, 26.4 g of 3,4-diamino-benzenesulfonic acid phenyl ester in 50 ml of glacial acetic acid were added, and the mixture was refluxed for 2 hours while stirring. It was allowed to cool, and the 2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid phenyl ester formed was suction-filtered. It was identical in its properties with the reaction product disclosed in Example 54.

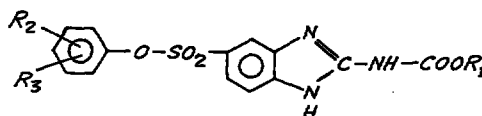
EXAMPLES 56—61

The following compounds were prepared in an analogous manner:

- 56) Via 3-nitro-4-chloro-benzene-sulfonic acid-3-chloro-phenyl ester, m.p. 68°C and 3-nitro-4-amino-benzene-sulfonic acid-3-chloro-phenyl ester, m.p. 138°C and 3,4-diamino-benzene-sulfonic acid-3-chloro-phenyl ester, m.p. 84°C the 2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3-chloro-phenyl ester (identical with Example 3) m.p. 234°C (decomposition).
- 57) Via 3-nitro-4-chloro-benzene-sulfonic acid-3-bromo-phenyl ester, m.p. 72°C and 3-nitro-4-amino-benzene-sulfonic acid-3-bromo-phenyl ester, m.p. 141°C and 3,4-diamino-benzene-sulfonic acid-3-bromo-phenyl ester, m.p. 94°C the 2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3-bromo-phenyl ester (identical with Example 8), m.p. 242°C (decomposition).
- 58) Via 3-nitro-4-chloro-benzene-sulfonic acid-3-methyl-phenyl ester, m.p. 60°C and 3-nitro-4-amino-benzene-sulfonic acid-3-methyl-phenyl ester, m.p. 138°C and 3,4-diamino-benzene-sulfonic acid-3-methyl-phenyl ester, m.p. 84°C the 2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3-methyl-phenyl ester (identical with Example 11), m.p. 234°C (decomposition).
- 59) Via 3-nitro-4-chloro-benzene-sulfonic acid-3-methoxy-phenyl ester (oil) and 3-nitro-4-amino-benzene-sulfonic acid-3-methoxy-phenyl ester, m.p. 116°C and 3,4-diamino-benzene-sulfonic acid-3-methoxy-phenyl ester (oil) the 2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3-methoxy-phenyl ester (identical with Example 25) m.p. 227°C (decomposition).
- 60) Via 3-nitro-4-chloro-benzene-sulfonic acid-3-ethoxy-phenyl ester (oil) and 3-nitro-4-amino-benzene-sulfonic acid-3-ethoxy-phenyl ester, m.p. 86°C and 3,4-diamino-benzene-sulfonic acid-3-ethoxy-phenyl ester (oil) the 2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3-ethoxy-phenyl ester (identical with Example 30) m.p. 212°C (decomposition).
- 61) Via 3-nitro-4-chloro-benzene-sulfonic acid-3-trifluoro-methyl-phenyl ester, m.p. 65°C and 3-nitro-4-amino-benzene-sulfonic acid-3-trifluoromethyl-phenyl ester, m.p. 132°C and 3,4-diamino-benzene-sulfonic acid-3-trifluoromethyl-phenyl ester the 2-carbomethoxyamino-5-benzimidazolyl-sulfonic acid-3-trifluoromethyl-phenyl ester, m.p. 250°C (decomposition) (identical with Example 39).

WHAT WE CLAIM IS:—

1. A 2-carbalkoxyamino benzimidazolyl-5(6)-sulfonic acid phenyl ester of the formula





in which R_1 is an alkyl group having from 1 to 4 carbon atoms, and each of R_2 and R_3 is a hydrogen atom, a hydroxy group, an alkoxy group having from 1 to 4 carbon atoms, a halogen atom, a trifluoromethyl group, an alkyl group having from 1 to 4 carbon atoms, a carbalkoxy group having from 1 to 4 carbon atoms in the alkoxy moiety, or a cyano group.

2. A compound as claimed in claim 1, in which R_1 is a methyl group, R_2 is a hydrogen atom, and R_3 is a hydrogen, chlorine or bromine atom or a trifluoromethyl, methyl, ethyl, methoxy or ethoxy group.

3. A compound as claimed in claim 1, in which R_1 is a methyl group, and R_2 and R_3 are hydrogen atoms.

4. A compound as claimed in claim 1, in which R_1 is a methyl group, R_2 is a hydrogen atom and R_3 is a chlorine atom.

5. A compound as claimed in claim 1, in which R_1 is a methyl group, R_2 is a hydrogen atom and R_3 is a bromine atom.

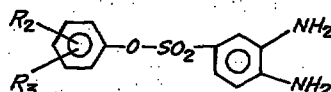
6. A compound as claimed in claim 1, in which R_1 is a methyl group, R_2 is a hydrogen atom and R_3 is a methyl group.

7. A compound as claimed in claim 1, in which R_1 is a methyl group, R_2 is a hydrogen atom and R_3 is a methoxy group.

8. A compound as claimed in claim 1, in which R_1 is a methyl group, R_2 is a hydrogen atom and R_3 is an ethoxy group.

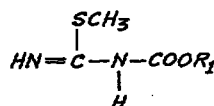
9. A compound as claimed in claim 1, in which R_1 is a methyl group, R_2 is a hydrogen atom and R_3 is a trifluoromethyl group.

10. A process for the manufacture of a compound as claimed in claim 1, which comprises condensing an *o*-phenylene derivative of the formula



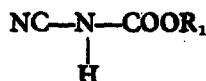
in which R_2 and R_3 have the meanings specified in claim 1,

(a) with an alkyl-S-methyl-thiourea carboxylate of the formula



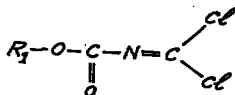
in which R_1 has the meaning specified in claim 1, or

(b) with a cyanamide carboxylate of the formula



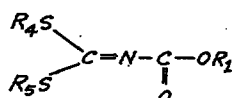
in which R_1 has the meaning specified in claim 1, in both cases at a pH of from 1 to 6, or

(c) with an N-dichloromethylene carbamic acid ester of the formula



in which R_1 has the meaning specified in claim 1, at a temperature of from -10° to $+40^\circ\text{C}$ in the presence of a base, or

(d) with a bis-alkyl or bis-aryl-thiomethylene-amino-formate of the formula



in which R_1 has the meaning specified in claim 1, and each of R_4 and R_5 is an alkyl group having from 1 to 4 carbon atoms, an alkenyl group having from 3 to 5

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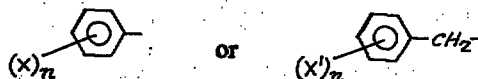
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carbon atoms, a cyclohexyl group or an optionally substituted phenyl or benzyl group of the formula



in which each of X and X' is a halogen atom or a methyl or nitro group, or in which R₁ and R₂ may be linked to form a ring containing 2 or 3 methylene groups, and in which n is zero, 1 or 2.

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 composition containing as active ingredient a compound as claimed in claim 1, in admixture or conjunction with a pharmaceutically suitable carrier.

14. A method for combating parasites which comprises administering to an infested organism other than a human being a compound as claimed in claim 1.

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