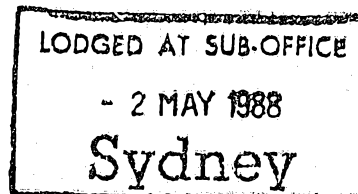


P 146027 JGS:GS 2582T/5

PATENT APPLICATION FORM
COMMONWEALTH OF AUSTRALIA

Patents Act 1952

Regulation 9



634 385 699/88

We, BAYER AKTIENGESELLSCHAFT of D-5090 Leverkusen, Bayerwerk, Germany hereby apply for the grant of a Standard Patent for an invention entitled NEW *Aminophenylethylamine derivatives, processes for their* PREPARATION AND THEIR USE AS YIELD PROMOTERS which is described in the accompanying complete specification.

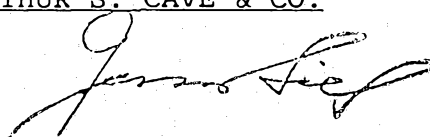
For a Convention application - details of basic application-

<u>Number</u>	<u>Country</u>	<u>Date of Application</u>
P 37 14 484.7	Germany	30 April 1987

Our address for service is ARTHUR S. CAVE & CO., Patent and Trade Mark Attorneys, Level 10, 10 Barrack Street, Sydney, New South Wales, Australia 2000.

Dated this 29th day of April, 1988.

BAYER AKTIENGESELLSCHAFT
By Its Patent Attorneys,
ARTHUR S. CAVE & CO.


J.G. SIELY F.I.P.A.A.

To:
Commissioner of Patents

APPLICATION ACCEPTED AND AMENDMENTS

ALLOWED.....7-9-90.....

ARTHUR S. CAVE & CO.
PATENT AND TRADE MARK ATTORNEYS
SYDNEY

ASC 1



PATENT DECLARATION FORM (CONVENTION)
COMMONWEALTH OF AUSTRALIA
Patents Act 1952

Regulation
12 (2)

DECLARATION IN SUPPORT OF A CONVENTION APPLICATION
FOR A PATENT

To be signed by the applicant(s) or in the case of a body corporate to be
signed by a person authorised by the body corporate.

(a) Insert title
of invention.

In support of the Convention application made for a patent for an invention entitled
New aminophenylethylamine derivatives, processes
(a)
for their preparation and their use as yield promoters
.....

(b) Insert full
name(s) of
declarant(s).

I/We (b)
Günter Schumacher and Joachim Gremm
.....

(c) Insert
address(es) of
declarant(s).

of (c)
Bayer Aktiengesellschaft, Leverkusen, Bayerwerk
.....
.....

do solemnly and sincerely declare as follows:—

1. I am/We are the applicant(s) for the patent

(OR, IN THE CASE OF AN APPLICATION BY A BODY CORPORATE.)

1. I am/We are authorised by Bayer Aktiengesellschaft.....
..... the applicant for the patent to make this declaration on its behalf.

2. The basic application(s) as defined by Section 141 of the Act was/were made in the following
country or countries on the following date(s) namely:—

(d) Insert
country in
which basic
application(s)
was/were
filed.

in (d) Germany on (c) April 30, 1987

(e) Insert date
of basic
application(s).

by (f) Bayer Aktiengesellschaft
in (d) on (c)

(f) Insert full
names of basic
applicant(s).

by (f)
in (d) on (c)

3. I am/We are the actual inventor(s) of the invention referred to in the basic application.

(OR, WHERE A PERSON OTHER THAN THE INVENTOR IS THE APPLICANT)

(g) Insert full
name(s) of
actual
inventor(s)

3. (g) 1) Hartmund Wollweber 2) Jürgen Stoltefuß
3) Friedrich Berschauer

(h) Insert
address(es) of
actual
inventor(s).

of (h) 1) In den Birken 73, D 5600 Wuppertal 1, Germany
2) Parkstrasse 20, D 5657 Haan 2, Germany
3) Claudiusweg 9, D 5600 Wuppertal 1, Germany

is/are the actual inventor(s) of the invention and the facts upon which the applicant(s) is/are entitled to
make the application are as follows:

(i) Set out how
applicant(s)
derive(s) title
from actual
inventor(s)
i.e., assignee of
the invention
from the actual
inventor(s).

(i) The company is the Assignee of the said invention
from the said inventors
.....

Attestation or
legalization
not required.

4. The basic application(s) referred to in paragraph 2 of this Declaration was/were the first
application(s) made in a Convention country in respect of the invention the subject of the application.

Declared at Leverkusen this 21st day of March 1988

To:

The Commissioner of Patents

ARTHUR S. CAVE & CO.
PATENT AND TRADE MARK ATTORNEYS
SYDNEY

A.S.C.-4

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Signature of Declarant(s)

(12) PATENT ABRIDGMENT (11) Document No. AU-B-15699/88
(19) AUSTRALIAN PATENT OFFICE (10) Acceptance No. 604885

(54) Title
 LIVESTOCK GROWTH PROMOTING COMPOUNDS, ESPECIALLY 5 PHENYL- 3U
 SUBSTITUTED OXAZOLIDINES

International Patent Classification(s)
 (51)⁴ C07C 093/14 A23K 001/16 C07C 093/04 C07C 093/12
 C07C 093/26 C07C 097/10 C07C 121/78 C07C 121/80
 C07C 149/24 C07D 263/06 C07D 263/24 C07D 305/06
 C07D 307/14 C07D 309/04
 (51)⁵ C07C 217/08 C07C 219/32 C07C 255/59 C07C 323/25
 C07F 007/18

(21) Application No. : 15699/88 (22) Application Date : 02.05.88

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 3714484 30.04.87 DE FEDERAL REPUBLIC OF GERMANY

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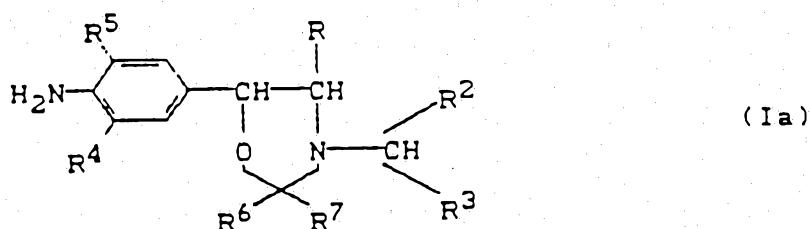
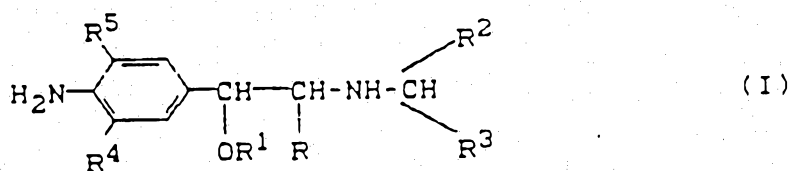
(71) Applicant(s)
 BAYER AKTIENGESELLSCHAFT

(72) Inventor(s)
 HARTMUND WOLLWEBER; JURGEN STOLTEFUSS; FRIEDRICH BERSCHAUER

(74) Attorney or Agent
 ARTHUR S CAVE & CO, GPO Box 3876, SYDNEY NSW 2001

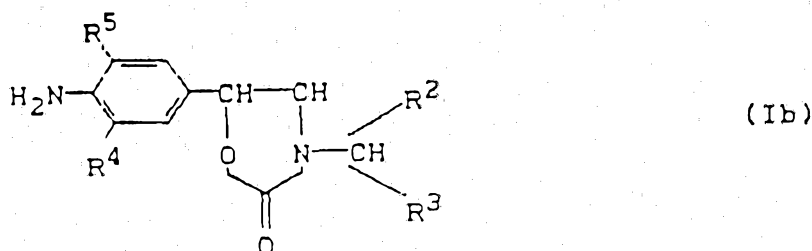
(57) Claim

1. Aminophenylethylamine derivatives of the general formulae



(11) AU-B-15699/88
(10) 604885

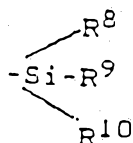
-2-



in which

R = H or alkyl,

R¹ = hydrogen, acyl, aroyl, arylacyl or



R² = methyl or ethyl,

R³ = straight-chain, branched or cyclic alkyl which is substituted by alkoxy or alkylthio or heterocyclyl which has 4-6 ring atoms and oxygen as the hetero atom and is optionally substituted by alkyl,

R⁴ = H, alkyl (C₁-C₃), halogen, trifluoromethyl or CN,

R⁵ = alkyl (C₁-C₃), halogen, trifluoromethyl, CN, alkoxy or alkylthio,

R⁶ = H or alkyl,

R⁷ = H, alkyl, phenyl or phenylalkyl and

R⁸, R⁹ and R¹⁰ = a straight-chain or branched alkyl radical.

4. Animal feeds, drinking water for animals and additives for animal feeds and drinking water for animals, characterized in that they contain aminophenylethylamine derivatives of the formulae I, Ia and Ib according to claim 1, in admixture with feedstuffs or drinking water.

AUSTRALIA

PATENTS ACT 1952

COMPLETE SPECIFICATION

(ORIGINAL)

FOR OFFICE USE

Application Number:
Lodged:

Complete Specification Lodged:
Accepted:
Published:

Priority:
Related Art:

This document contains the
amendments made under
Section 49 and is correct for
printing.

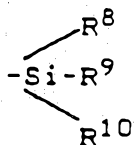
TO BE COMPLETED BY APPLICANT

Name of Applicant: BAYER AKTIENGESELLSCHAFT
Address of Applicant: D-5090 Leverkusen, Bayerwerk,
Germany
Actual Inventor: Dr. Hartmund Wollweber
Dr. Jurgen Stoltefusse
Dr. Friedrich Berschauer
Address for Service: ARTHUR S. CAVE & CO.
Patent & Trade Mark Attorneys
Level 10
10 Barrack Street
SYDNEY N.S.W. 2000
AUSTRALIA

Complete Specification for the invention entitled NEW *Aminophenylethylamine*
DERIVATIVES, PROCESSES FOR THEIR PREPARATION AND THEIR USE AS
YIELD PROMOTERS.

The following statement is a full description of this invention
including the best method of performing it known to me:-





R^2 = methyl or ethyl,

R^3 = straight-chain, branched or cyclic alkyl which is substituted by alkoxy or alkylthio or heterocyclyl which has 4-6 ring atoms and oxygen as the hetero atom and is optionally substituted by alkyl,

R^4 = H, alkyl (C_1-C_3), halogen, trifluoromethyl or CN,

R^5 = alkyl (C_1-C_3), halogen, trifluoromethyl, CN, alkoxy or alkylthio,

R^6 = H or alkyl,

R^7 = H, alkyl, phenyl or phenylalkyl and

R^8 , R^9 and R^{10} = a straight-chain or branched alkyl radical,

and their physiologically tolerated salts have been found. The compounds according to the invention can exist in the form of their racemates and their enantiomers or diastereomers.

They have an excellent yield-promoting, in particular growth-promoting, action on animals, for example they effect a shift in the meat/fat ratio in favour of meat.

Preferred compounds are phenylethylamine derivatives of the general formula (I) in which

R = hydrogen or methyl and

R^1 = hydrogen or the radicals

$-Si(CH_3)_2CH(CH_3)CH(CH_3)_2$ or

$Si(CH_3)_2C(CH_3)_3$,

R^2 = methyl,

R^3 represents the radical $(CR^{11}R^{12})_n-O-R^{13}$,

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wherein

R^{11} and R^{12} represent hydrogen or methyl or

R^3 represents C₅₋₆-cycloalkyl which is substituted by C₁₋₄-alkoxy,

5 n represents 1, 2 or 3 and

R^{13} represents C₁₋₄-alkyl or, together with one of the radicals R^{11} or R^{12} and the atoms to which they are bonded, forms a 4- to 6-membered ring which is interrupted by O and is optionally substituted by methyl.

10

Especially preferred compounds of the formula I

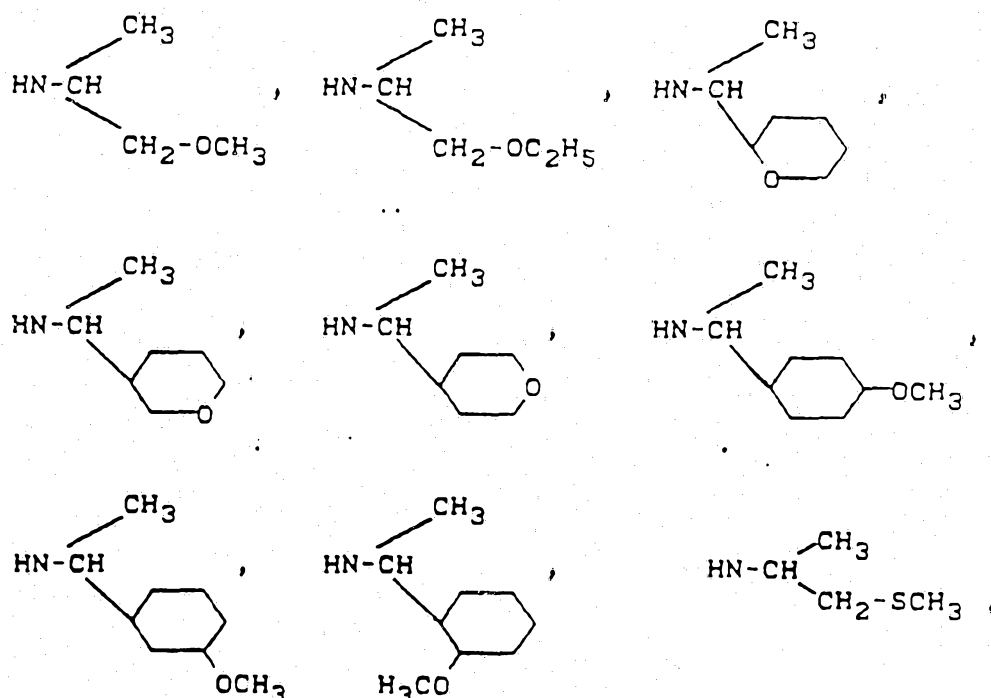
are those

in which

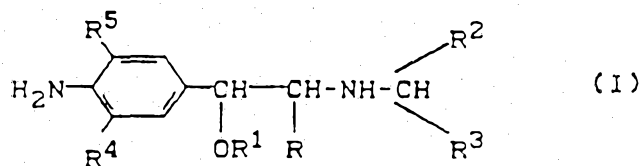
the radical $\text{NH}-\text{CH} \begin{matrix} \nearrow R^2 \\ \searrow R^3 \end{matrix}$ represents the following

15

radicals:



The new compounds of the formula (I)



in which

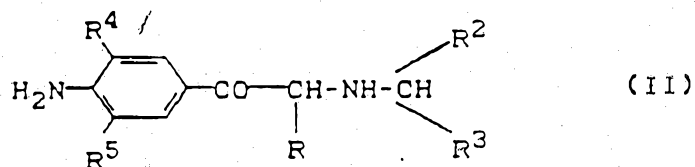
R and R² to R⁵ have the abovementioned meanings

and

R¹ represents hydrogen,

are obtained by a process in which

a) compounds of the formula (II)



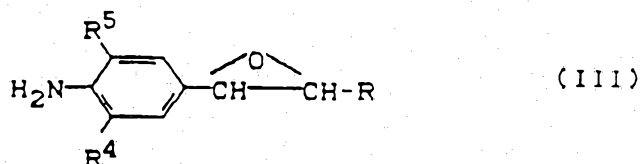
10 in which

R and R² to R⁵ have the abovementioned meanings,

are reduced catalytically or with suitable reducing

agents, such as, for example, sodium borohydride, sodium cyanoborohydride and the like, or

15 b) compounds of the formula (III)



in which

R, R⁴ and R⁵ have the abovementioned meanings,

are reacted with amines of the formula (IV)



20

in which

R , R^2 and R^3 have the abovementioned meanings,

or

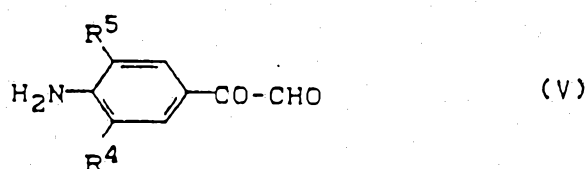
c) in the case of compounds of the formula (I)

5 in which

R represents hydrogen and

R^1 has the abovementioned meaning,

by a process in which compounds of the formula (V)



10 in which

R^4 and R^5 have the abovementioned meanings,

are reacted with an amine of the formula (IV) in the presence of a reducing agent, such as, for example, sodium borohydride.

15 d) The new compounds of the formula (I)

in which

R and $R^2 - R^5$ have the meanings given in the case of (I) and

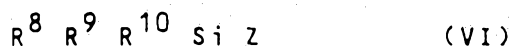
R^1 represents the radical $\begin{array}{c} R^8 \\ \diagup \\ -Si-R^9 \\ \diagdown \\ R^{10} \end{array}$ and

20 R^8 , R^9 and R^{10} have the abovementioned meanings, are obtained by a process in which compounds of the formula (I)

in which

R^1 represents hydrogen,

25 are reacted with suitable silylating substances of the formula (VI)



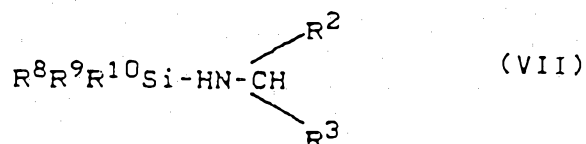
in which

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Z represents halogen, CN, OSO₂-CF₃,
 -O-Si-R²R³R⁴ or -O-SO₂-O-Si-R⁸R⁹R¹⁰ and
 R⁸, R⁹ and R¹⁰ have the abovementioned meanings,

or

- 5 e) the compound of the formula (III) (above) is reacted
 with a silylated amine of the formula (VII)



in which

R⁸, R⁹ and R¹⁰ have the abovementioned meanings.

- 10 f) The new compounds of the formula (I)

in which

R and R² - R⁵ have the meanings given in the case
 of (I) and

R¹ represents acyl, aroyl or arylacetyl,

- 15 are obtained by a process in which the compounds of the
 formula (I)

in which

R¹ represents hydrogen,

are reacted with suitable acylating agents, or

- 20 g) the compounds of the formula (Ia)

in which

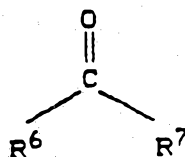
R² - R⁷ have the meanings given in the case of (I),

are obtained by a process in which the compounds of the
 formula (I)

- 25 in which

R¹ represents hydrogen,

are reacted with carbonyl compounds of the formula



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in which

R^6 and R^7 have the abovementioned meanings, if appropriate in the presence of acid catalysts, or h) compounds of the formula (Ib)

5 in which

$R^2 - R^5$ have the abovementioned meanings, are obtained by a process in which compounds of the formula (I)

in which

10 R^1 represents hydrogen, are cyclized with carbonic acid derivatives, if appropriate in the presence of bases.

The starting compounds of the formula (III) and (V) are already known (compare, for example, B.R.E. Lutz and co-workers, J. Org. Chem. 12, 617-703 and DAS (German Published Specification) 2,354,959). The compounds of the formula (II) are new (and may be prepared by known methods; compare J. Org. Chem. 12, 617-703). The amines of the formula (IV) are known or can be prepared by known
15 methods by amination of corresponding ketones.

Processes a) - h) are carried out analogously to known methods of organic chemistry.

Processes a) - h) according to the invention can be carried out in the presence of diluents. Possible
25 diluents are all the inert organic solvents. These include, in particular, aliphatic and aromatic, optionally halogenated hydrocarbons, such as pentane, hexane, heptane, cyclohexane, petroleum ether, benzine, ligroin, benzene, toluene, methylene chloride, ethylene chloride,
30 chloroform, carbon tetrachloride, chlorobenzene and o-dichlorobenzene, and furthermore ethers, such as diethyl ether, dibutyl ether, glycol dimethyl ether, diglycol dimethyl ether, tetrahydrofuran and dioxane, and moreover ketones, such as acetone, methyl ethyl ketone, methyl
35 isopropyl ketone and methyl isobutyl ketone, and also esters, such as methyl and ethyl acetate, and furthermore

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nitriles, such as, for example, acetonitrile, propionitrile, benzonitrile and glutaric acid dinitrile, and moreover amides, such as, for example, dimethylformamide, dimethylacetamide and N-methylpyrrolidone, as well as
5 dimethylsulphoxide, tetramethylenesulphone and hexamethylphosphoric acid triamide.

Process d) according to the invention can be carried out in the presence of catalysts. Catalysts which can preferably be used are: imidazole, triazole or
10 diisopropylethylamine.

The reaction temperature in processes a) - h) is kept between about 0°C and 130°C, preferably between about 20°C and 60°C. The processes are preferably carried out at atmospheric pressure.

15 In process e), the starting compounds of the formulae II and IV are in general employed in an approximately equimolar ratio, but an excess of up to 300% of the compounds of the formula IV can be employed.

In the other processes, the starting compounds
20 are in general employed in an approximately equimolar ratio. The reducing agents can be used in a 1- to 10-fold excess.

The active compounds have a favourable toxicity towards warm-blooded animals and are suitable as agents
25 for yield promotion in animals for breeding and stock animals. They are used here for promoting and accelerating growth and milk and wool production and for improving the feed utilization and meat quality and for shifting the meat-fat ratio in favour of meat.

30 The stock animals and animals for breeding include mammals, such as, for example, cattle, horses, sheep, pigs, goats, camels, water buffalo, asses, rabbits, fallow deer and reindeer, fur-bearing animals, such as, for example, mink, chinchillas and racoons,
35 birds, such as, for example, chickens, geese, turkeys and ducks, and freshwater and saltwater fish, such as, for

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example, trout, carp and eels.

The active compounds are used throughout all the growth and yield phases of the animals, regardless of the sex of the animals. The active compounds are preferably
5 used during the intensive growth and yield phase. The intensive growth and yield phase lasts from one month to 10 years, depending on the species of animal.

The compounds according to the invention moreover exhibit a good anti-inflammatory action on the carrageen-
10 an-induced paw oedema in rats.

They can therefore be used as anti-inflammatories and antirheumatics and for the treatment of inflammation and oedemas.

The active compounds have proved to be particu-
15 larly useful in the rearing and keeping of young animals and fattening animals.

The active compounds are used enterally or parenterally, directly or in the form of formulations suitable for animals. Enteral use of the active compounds is
20 effected, for example, orally in the form of powders, tablets, capsules, pastes, drinks or granules, solutions, emulsions or suspensions for oral administration, or boli, or via the feed or the drinking water. Parenteral use is effected, for example, in the form of injection
25 (intramuscular, subcutaneous, intravenous or by implants).

Formulations for administration via the feed or drinking water should be emphasized in particular. The active compounds can in this way be added to the feed directly or in the form of premixes or feed concentrates.

30 The feed includes individual feedstuffs of vegetable origin, such as hay, beet, cereals and cereal by-products, molasses and silage, individual feedstuffs of animal origin, such as meat, fats, milk products, bone-meal and fish products, and individual feedstuffs such as
35 vitamins, proteins, sugars, starch, flours, amino acids, for example DL-methionine, and salts, such as lime and

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sodium chloride. The feed also includes supplement, ready-made and mixed feedstuffs. These contain individual feedstuffs in a composition which guarantees balanced nutrition in respect of energy and protein supply and the
5 supply of vitamins, mineral salts and trace elements.

Premixes and feed concentrates are mixtures of the active compound with carriers and if appropriate other auxiliaries. The carriers include all the individual feedstuffs or mixtures thereof.

10 The active compounds can be present in the formulations by themselves or as a mixture with other yield-promoting active compounds, mineral feedstuffs, trace element compounds, vitamins, nitrogen-containing non-protein compounds, dyestuffs, antioxidants, aroma substances, emulsifiers, flow control auxiliaries, preserva-
15 tives and pressing auxiliaries.

Other yield-promoting active compounds are, for example, antibiotics, such as tylosin and virginiamycin.

Mineral feedstuffs are, for example, dicalcium
20 phosphate, magnesium oxide and sodium chloride.

Trace element compounds are, for example, iron fumarate, sodium iodide, cobalt chloride, copper sulphate, zinc oxide and selenium compounds.

Vitamins are, for example, vitamin A, vitamin D₃
25 and vitamin E.

Nitrogen-containing non-protein compounds are, for example, biuret and urea.

Dyestuffs are, for example, carotinoids, such as canthaxidine, zeaxanthine and capsanthine, or all dye-
30 stuffs which are permitted for colouring foodstuffs.

Antioxidants are, for example, ethoxyquin, butylhydroxy-toluene and ascorbic acid.

Aroma substances are, for example, vanillin.

Emulsifiers are, for example, esters of lactic
35 acid and lecithin.

Flow control auxiliaries are, for example, sodium

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stearate, calcium stearate, silicic acids, bentonites and lignin-sulphonates.

Preservatives are, for example, propionic acid, calcium propionate, sorbic acid and ascorbic acid.

5 Pressing auxiliaries are, for example, lignin-sulphonates and cellulose ethers.

The concentration of the active compounds in the feed is usually about 0.001-500 ppm, preferably 0.1-50 ppm.

10 The concentration of the active compounds in the premixes or feed concentrates is about 0.5 to 50 per cent by weight, preferably 1 to 20 per cent by weight.

The amount of active compounds administered to the animals for achieving the desired effect can be varied widely because of the favourable properties of the active compounds. It is preferably about 0.001 to 50 mg/kg, in particular 0.01 to 5 mg/kg of body weight per day. The appropriate amount of the active compound and the appropriate duration of administration depend, in particular, on the species, age, sex, state of health and nature of housing and feeding of the animals and can easily be determined by any expert.

20 The active compounds are administered to the animals by the customary methods. The nature of the administration depends, in particular, on the species, behaviour and state of health of the animals.

The active compounds can be administered once. However, the active compounds can also be administered temporarily or continuously during the entire or during part of the growth and yield phase. In the case of continuous administration, they can be used once or several times daily at regular or irregular intervals.

Example of the composition of a chick-rearing feed containing active compound according to the invention:

35 200 g of wheat, 340 g of maize, 361 g of shredded soya, 60 g of beef tallow, 15 g of dicalcium phosphate,

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10 g of calcium carbonate, 4 g of iodinated sodium chloride, 7.5 g of a vitamin-mineral mixture of the composition given below and 2.5 g of an active compound premix of the composition given below give, after thorough mixing, 1 kg of feed.

One kg of vitamin-mineral mixture contains:
600 I.U. of vitamin A, 100 I.U. of vitamin D₃, 10 mg of vitamin E, 1 mg of vitamin K₃, 3 mg of riboflavin, 2 mg of pyridoxine, 20 mcg of vitamin B₁₂, 5 mg of calcium pantothenate, 30 mg of nicotinic acid, 200 mg of choline chloride, 200 mg of MnSO₄ x H₂O, 140 mg of ZnSO₄ x 7 H₂O, 100 mg of FeSO₄ x 7 H₂O and 20 mg of CuSO₄ x 5 H₂O in cereal flour as the carrier.

1 kg of active compound premix contain 100 g of active compound and 900 g of wheat flour.

Example of the composition of a pig-rearing feed containing active compound according to the invention:
630 g of shredded cereal feed (composed of 200 g of maize, 150 g of shredded barley, 150 g of shredded oats and 130 g of shredded wheat), 80 g of fishmeal, 60 g of shredded soya, 60 g of tapioca flour, 38 g of brewer's yeast, 50 g of a vitamin-mineral mixture (composition as for the chick feed) 30 g of linseed cake, 30 g of maize gluten feed, 10 g of soya oil, 10 g of sugar cane molasses and 2 g of an active compound premix of the composition shown below give, after thorough mixing, 1 kg of feed.

1 kg of active compound premix contains 200 g of active compound, 20 g of vegetable oil and 780 g of calcium carbonate powder.

Example of the composition of a cattle feed containing the active compound according to the invention:
69.95% of shredded cereal feed, 10% of ground maize cobs, 8% of soya bean flour, 5% of lucerne flour, 5% of molasses, 0.6% of urea, 0.5% of calcium phosphate, 0.5% of calcium carbonate, 0.3% of sodium chloride, 0.15% of
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a vitamin-mineral mixture and 0.2 % of an active compound pre-mix of the composition as given for the pig feed. The vitamin-mineral mixture contains, per kg, 70,000 i.U. of vitamin A, 70,000 i.U. of vitamin D₃, 100 mg of vitamin E, 50 mg of MnSO₄ x H₂O and 30 mg of ZnSO₄ x 7H₂O in cereal flour as the carrier.

10 The active compound premix is admixed to the vitamin-mineral mixture in the required amount and this mixture is then mixed thoroughly with the remaining constituents.

Example A

Rat feeding experiment

15 Female laboratory rats weighing 90 - 110 g of the SPF Wistar type (bred by Hagemann) are fed ad libitum with standard rat food to which the desired amount of active compound is added. Each experimental set-up is carried out with food of an identical batch, so that differences in the composition of the food cannot impair the comparability of the results.

20 The rats are given water ad libitum.

Each experimental group is composed of 12 rats which are fed with food to which the desired amount of active compound is added. A control group receives food without active compound. The average body weight and the scatter in the body weights of the rats is the same in each experimental group, so that comparability of the experimental groups with one another is ensured.

The weight increase and amount of perirenal fatty tissue are determined during the 13-day experiment.

30 The results which can be seen from the table are obtained:

Table A

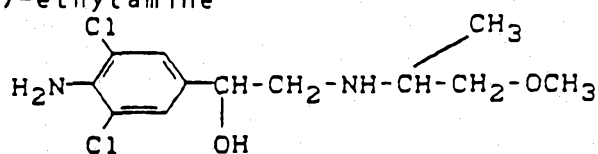
Rat feeding experiment

Active compound Example	Dose ppm	Number of animals	Additional growth (in relation to the control)
Control	25	12	100
Page 16 } Line 6 }	25	12	118
Page 14 } Line 15 }	25	12	126
Page 15 } Line 35 }	25	12	125
Page 14 } Line 30 }	25	12	132

Preparation Examples

Example 1

2-(3,5-Dichloro-4-amino-phenyl)-2-hydroxy-N-(1-methyl-2-methoxy-ethyl)-ethylamine



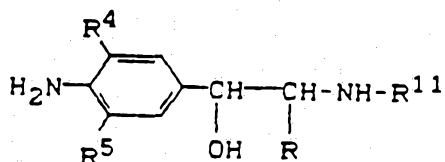
33 g of 4-amino-3,5-dichloro- ω -(1-methyl-2-methoxyethylamino)-acetophenone hydrochloride are dissolved in 180 ml of methanol and 83 ml of water, and a solution of 7.6 g of sodium borohydride in 30 ml of water is added dropwise, the pH being kept between 3 and 7 by addition of approximately 10% strength hydrochloric acid. When the reaction has ended, the mixture is rendered strongly acid and is concentrated. The concentrate is rendered basic with ammonia and extracted with ethyl acetate and the ethyl acetate phase is washed twice with water, dried and concentrated. The crystals obtained are stirred with heptane and filtered off with suction. 30.4 g of colourless crystals of melting point: 90-95°C are obtained. (Diastereomer mixture).

By redissolving and precipitating from ethyl acetate, the pure diastereomers A and B are obtained from the diastereomer mixture and are characterized with the aid of the signals of the methoxy groups in the $^1\text{H-NMR}$

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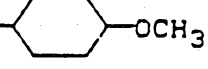
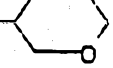
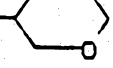
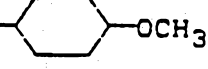
spectrum. The signals, which are concentration-dependent in chloroform, are at 3.3-3.4 ppm. The signal (at higher frequencies/lower field) is attributed to diastereomer A, melting point 111-112°C.

5 The following compounds were prepared analogously to Example 1:

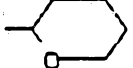
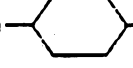
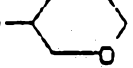
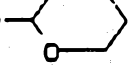
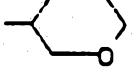


	R	R ⁴	R ⁵	R ¹¹	m.p. [°C]
10	H	Cl	Cl	CH(CH ₃)CH ₂ -OC ₂ H ₅	
15	H	Cl	Cl	CH(CH ₃)-	110-120
	H	Cl	Cl	CH(CH ₃)-	75- 80
20	H	Cl	Cl	CH(CH ₃)-	
	H	Cl	Cl	CH(CH ₃)-	
25	H	Cl	Cl	CH(CH ₃)-	
30	H	Cl	Cl	CH(CH ₃)-	
	H	Cl	Cl	CH(CH ₃)-	
35	H	Cl	Cl	CH(CH ₃)-	oil

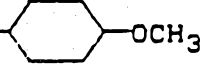
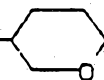
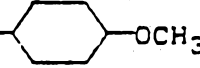
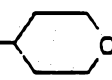
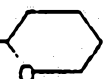
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	R	R ⁴	R ⁵	R ¹¹	m.p. [°C]
5	H	Cl	Cl	CH(CH ₃)— 	133
10	H	Cl	Cl	CH(CH ₃)— 	oil
	CH ₃	Cl	Cl	CH(CH ₃)CH ₂ -OCH ₃	
	H	Cl	CF ₃	CH(CH ₃)CH ₂ -OCH ₃	
15	H	Cl	CF ₃	CH(CH ₃)— 	
	H	Cl	CF ₃	CH(CH ₃)— 	
20	H	Cl	CF ₃	CH(CH ₃)— 	
	H	Cl	CF ₃	CH(CH ₃)— 	
25	H	Cl	H	CH(CH ₃)CH ₂ -OCH ₃	
	H	Cl	H	CH(CH ₃)— 	
30	H	Cl	H	CH(CH ₃)— 	
	H	Cl	H	CH(CH ₃)— 	
35	H	Cl	H	CH(CH ₃)— 	

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5	R	R ⁴	R ⁵	R ¹¹
	H	CN	H	CH(CH ₃)CH ₂ -OCH ₃
	H	CN	H	CH(CH ₃)- 
10	H	CN	H	CH(CH ₃)- 
	H	CN	H	CH(CH ₃)- 
15	H	CN	H	CH(CH ₃)- 
	H	Cl	CH ₃	CH(CH ₃)CH ₂ -OCH ₃
20	H	Cl	CH ₃	CH(CH ₃)- 
	H	Cl	CH ₃	CH(CH ₃)- 
25	H	Cl	CH ₃	CH(CH ₃)- 
	H	Cl	CH ₃	CH(CH ₃)- 
30	H	CH ₃	CH ₃	CH(CH ₃)CH ₂ -OCH ₃
	H	CH ₃	CH ₃	CH(CH ₃)- 
35	H	CH ₃	CH ₃	CH(CH ₃)- 

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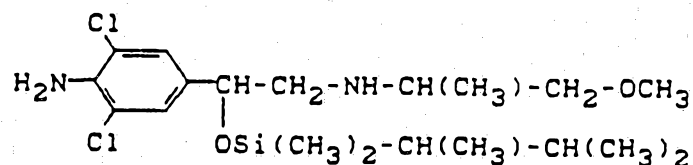
	R	R ⁴	R ⁵	R ¹¹	
5	H	CH ₃	CH ₃	CH(CH ₃)- 	
	H	CH ₃	CH ₃	CH(CH ₃)- 	
10	H	Cl	F	CH(CH ₃)CH ₂ -OCH ₃	
	H	Cl	F	CH(CH ₃)- 	
15	H	Cl	F	CH(CH ₃)- 	
	H	Cl	F	CH(CH ₃)- 	
20	H	Cl	F	CH(CH ₃)- 	
	H	CH ₃	H	CH(CH ₃)CH ₂ -OCH ₃	
	H	CH ₃	H	CH(CH ₃)- 	
25	H	Cl	Cl	CH(CH ₃)-C(CH ₃) ₂ -O-CH ₃	118-120° C
	H	CH ₃	H	CH(CH ₃)- 	
30	H	H ₃ CHO	CH ₃	CH(CH ₃)-CH ₂ -OCH ₃	
	H	H ₃ CO	H	CH(CH ₃)- 	
35	H	H ₃ CO	H	CH(CH ₃)- 	
	H	Cl	Cl	CH(CH ₃)-CH ₂ -SCH ₃	

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Example 2

2-(3,5-Dichloro-4-amino-phenyl)-2-(2,2-dimethylpropyl-dimethylsilyloxy)-N-(1-methyl-2-methoxyethylamine)-ethyl-amine

5



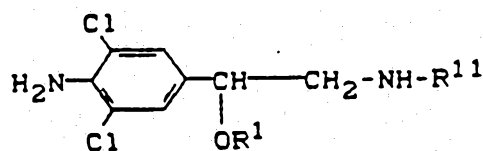
10

2.93 g (0.01 mol) of the compound of Example 1 are added to 1.36 g (0.02 mol) of imidazole in 15 ml of absolute dimethylformamide. 1.8 g of dimethyl-1,2-dimethyl-propyl-silyl chloride are now added at 0 to 5°C. The mixture is stirred for 2 hours, while cooling with ice, and is concentrated, the residue is taken up in toluene/water, the phases are separated, the toluene phase is washed 4 times with water, dried and concentrated and the residue is freed from residues of solvent using an oil pump. 4.3 g of an almost colourless oil are obtained.

15

The following silyloxy compounds are prepared by a corresponding procedure:

20



R¹

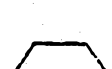
R¹¹

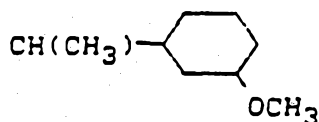
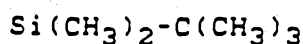
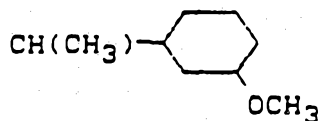
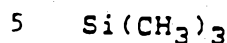
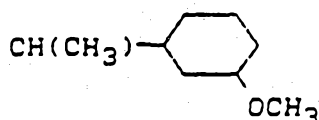
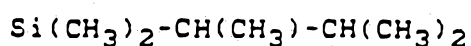
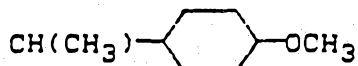
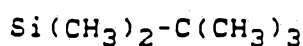
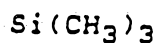
Si(CH₃)₃

CH(CH₃)CH₂OCH₃

Si(CH₃)₂-C(CH₃)₃

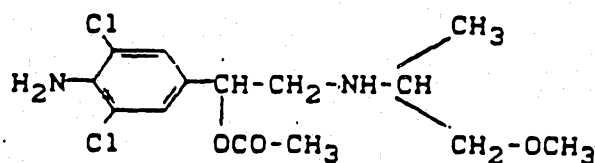
CH(CH₃)CH₂OCH₃

	R ¹⁰	R ¹¹	
5	Si(CH ₃) ₂ -CH(CH ₃)-CH(CH ₃) ₂	CH(CH ₃)CH ₂ OC ₂ H ₅	
	Si(CH ₃) ₃	CH(CH ₃)CH ₂ OC ₂ H ₅	
	Si(CH ₃) ₂ -C(CH ₃) ₃	CH(CH ₃)CH ₂ OC ₂ H ₅	
10	Si(CH ₃) ₂ -CH(CH ₃)-CH(CH ₃) ₂	CH(CH ₃)- 	
	Si(CH ₃) ₃	CH(CH ₃)- 	
15	Si(CH ₃) ₂ -C(CH ₃) ₃	CH(CH ₃)- 	
	Si(CH ₃) ₂ -CH(CH ₃)-CH(CH ₃) ₂	CH(CH ₃)- 	
20	Si(CH ₃) ₃	CH(CH ₃)- 	
	Si(CH ₃) ₂ -C(CH ₃) ₃	CH(CH ₃)- 	
25	Si(CH ₃) ₂ -CH(CH ₃)-CH(CH ₃) ₂	CH(CH ₃)- 	011
	Si(CH ₃) ₃	CH(CH ₃)- 	
30	Si(CH ₃) ₂ -C(CH ₃) ₃	CH(CH ₃)- 	
35	Si(CH ₃) ₂ -CH(CH ₃)-CH(CH ₃) ₂	CH(CH ₃)- 	

R¹⁰R¹¹Example 3

2-(3,5-Dichloro-4-amino-phenyl)-2-acetoxy-N-(1-methoxy-2-methoxy-ethyl)-ethylamine

10



15

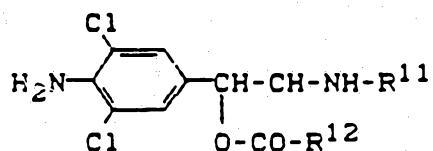
20

3 g of triethylamine are added to 2.93 g (0.01 mol) of 2-(3,5-dichloro-4-amino-phenyl)-2-hydroxy-N-(1-methoxy-ethyl)-ethylamine (Example 1), dissolved in 50 ml of CHCl_3 , 1.1 g (0.011 mol) of acetic anhydride are added dropwise at -5°C and the mixture is warmed to room temperature for 2 hours. When the reaction has ended (control by thin layer chromatography), the mixture is evaporated in vacuo, the residue is taken up in ethyl acetate, the solution is washed with sodium bicarbonate solution and then with saturated sodium chloride solution,

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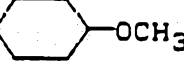
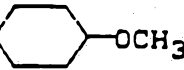
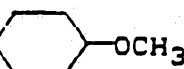
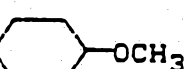
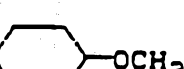
the organic phase is evaporated and the residue is chromatographed on a silica gel column (hexane/ethyl acetate = 2:1). Yield: 2.5 g.

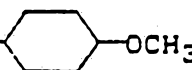
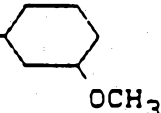
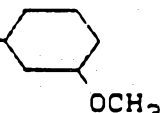
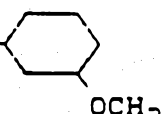
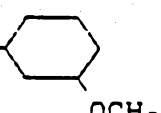
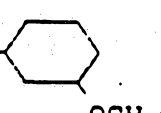
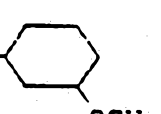
The following esters are obtained by a corresponding procedure:



	R ¹¹	R ¹²
	C ₂ H ₅	CH(CH ₃)CH ₂ OCH ₃
	CH(CH ₃) ₂	CH(CH ₃)CH ₂ OCH ₃
10	C ₄ H ₉	CH(CH ₃)CH ₂ OCH ₃
	C ₆ H ₅	CH(CH ₃)CH ₂ OCH ₃
	CH ₂ C ₆ H ₅	CH(CH ₃)CH ₂ OCH ₃
	CH ₃	CH(CH ₃)CH ₂ OC ₂ H ₅
	C ₂ H ₅	CH(CH ₃)CH ₂ OC ₂ H ₅
15	CH(CH ₃) ₂	CH(CH ₃)CH ₂ OC ₂ H ₅
	C ₄ H ₉	CH(CH ₃)CH ₂ OC ₂ H ₅
	C ₆ H ₅	CH(CH ₃)CH ₂ OC ₂ H ₅
	CH ₂ C ₆ H ₅	CH(CH ₃)CH ₂ OC ₂ H ₅
	CH ₃	CH(CH ₃)-

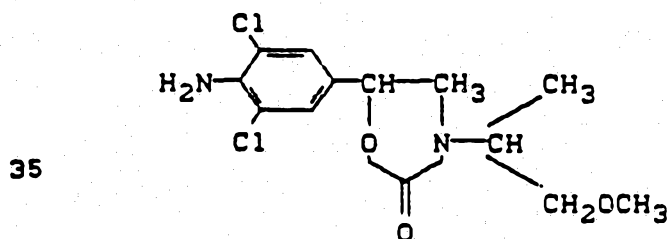
	R ¹¹	R ¹²
5	C ₂ H ₅	CH(CH ₃)- 
	CH(CH ₃) ₂	CH(CH ₃)- 
10	C ₄ H ₉	CH(CH ₃)- 
	C ₆ H ₅	CH(CH ₃)- 
15	CH ₂ C ₆ H ₅	CH(CH ₃)- 
	CH ₃	CH(CH ₃)- 
20	C ₂ H ₅	CH(CH ₃)- 
	CH(CH ₃) ₂	CH(CH ₃)- 
25	C ₄ H ₉	CH(CH ₃)- 
	C ₆ H ₅	CH(CH ₃)- 
30	CH ₂ C ₆ H ₅	CH(CH ₃)- 
35		

	R ¹¹	R ¹²
5		
	CH ₃	CH(CH ₃)— 
10	C ₂ H ₅	CH(CH ₃)— 
	CH(CH ₃) ₂	CH(CH ₃)— 
15	C ₄ H ₉	CH(CH ₃)— 
	C ₆ H ₅	CH(CH ₃)— 
20	CH ₂ C ₆ H ₅	CH(CH ₃)— 
	CH ₃	CH(CH ₃)— 
25	C ₂ H ₅	CH(CH ₃)— 
	CH(CH ₃) ₂	CH(CH ₃)— 
30	C ₄ H ₉	CH(CH ₃)— 
	C ₆ H ₅	CH(CH ₃)— 
35		

	R ¹¹	R ¹²
5	CH ₂ C ₆ H ₅	CH(CH ₃)- 
	CH ₃	CH(CH ₃)- 
10	C ₂ H ₅ H ₃) ₂	CH(CH ₃)- 
15	CH(CH ₃) ₂	CH(CH ₃)- 
	C ₄ H ₉	CH(CH ₃)- 
20	C ₆ H ₅	CH(CH ₃)- 
25	CH ₂ C ₆ H ₅	CH(CH ₃)- 

Example 4

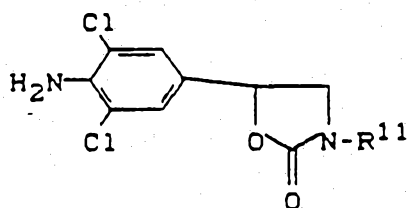
30 5-(3,5-Dichloro-4-amino-phenyl)-3-(1-methyl-2-methoxy-ethyl)-2-oxazolidinone



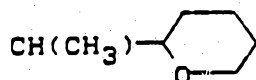
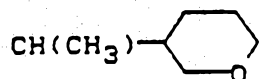
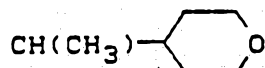
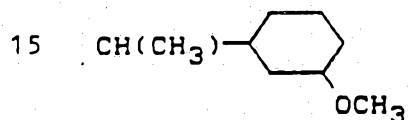
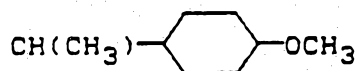
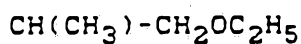
A solution of 1 g of COCl₂ in 20 ml of methylene
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chloride is added dropwise to 2.93 g (0.01 mol) of 2-(3-5-dichloro-4-amino-phenyl)-2-hydroxy-N-(1-methyl-2-methoxyethyl)-ethylamine, dissolved in 30 ml of methylene chloride and 3 g of triethylamine, at -5°C in the course of 20 minutes. The mixture is stirred at -5°C for 30 minutes and at room temperature for 1 hour and is evaporated in vacuo and the residue is chromatographed on a silica gel column with n-heptane/ $\text{CHCH}_2 = 1 : 1$. Yield: 1.3 g.

10 The following oxazolidinones are obtained in a corresponding manner:

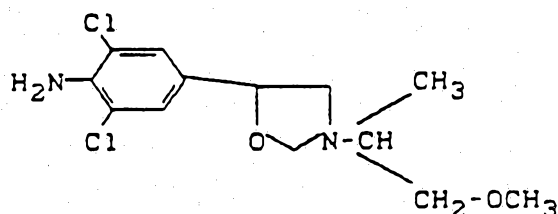


R₁₁



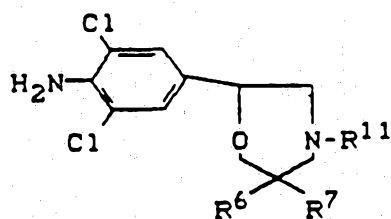
Example 5

2-(3,5-Dichloro-4-amino-phenyl)-3-(1-methyl-2-methoxy-ethyl)-2-oxazolidinone



- 5 2.93 g (0.01 mol) of 2-(3,5-dichloro-4-amino-phenyl)-2-hydroxy-N-(1-methyl-2-methoxy-ethyl)-ethylamine, dissolved in 60 ml of toluene, are heated with 100 ml of formaldehyde (38% strength), with the addition of 2 mg of p-toluenesulphonic acid, using a water separator, and
- 10 when no further water is separated off (after about 1 hour), the mixture is cooled, washed twice with 10% strength sodium hydroxide solution and then with water and dried over Na_2SO_4 . After evaporation, the residue is chromatographed on a silica gel column (hexane,
- 15 methylene chloride = 1 : 1) to give 2.4 g of an oil.

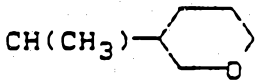
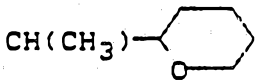
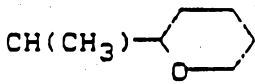
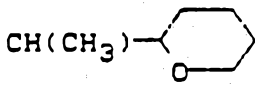
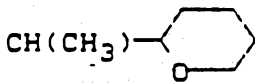
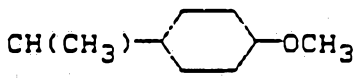
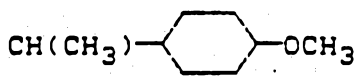
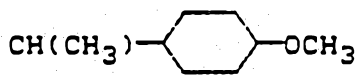
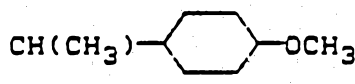
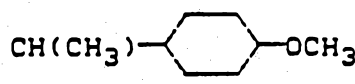
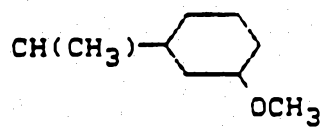
The following oxazolidines are obtained in a corresponding manner:



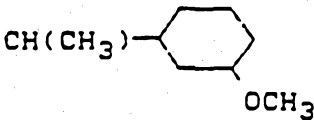
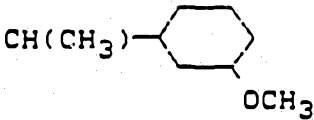
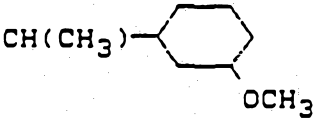
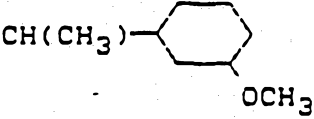
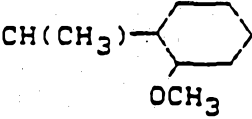
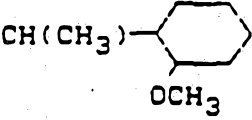
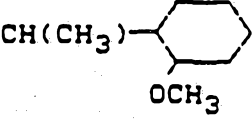
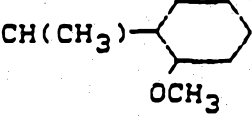
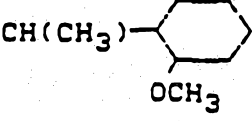
	R^{11}	R^6	R^7
20	$\text{CH}(\text{CH}_3)\text{CH}_2\text{OCH}_3$	H	CH_3
	$\text{CH}(\text{CH}_3)\text{CH}_3\text{OCH}_3$	H	C_6H_5

	R^{11}	R^6	R^7
5	$CH(CH_3)CH_2OCH_3$	CH_3	CH_3
	$CH(CH_3)CH_3OCH_3$	CH_3	C_6H_5
10	$CH(CH_3)-\text{C}_6\text{H}_4\text{O}$	H	H
	$CH(CH_3)-\text{C}_6\text{H}_4\text{O}$	H	CH_3
15	$CH(CH_3)-\text{C}_6\text{H}_4\text{O}$	H	C_6H_5
	$CH(CH_3)-\text{C}_6\text{H}_4\text{O}$	CH_3	CH_3
20	$CH(CH_3)-\text{C}_6\text{H}_4\text{O}$	CH_3	C_6H_5
	$CH(CH_3)-\text{C}_6\text{H}_4\text{O}$	H	H
25	$CH(CH_3)-\text{C}_6\text{H}_4\text{O}$	H	CH_3
	$CH(CH_3)-\text{C}_6\text{H}_4\text{O}$	H	C_6H_5
30	$CH(CH_3)-\text{C}_6\text{H}_4\text{O}$	CH_3	CH_3
	$CH(CH_3)-\text{C}_6\text{H}_4\text{O}$	CH_3	C_6H_5
35			

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	R^{11}	R^6	R^7
5		H	H
10		H	CH ₃
		H	C ₆ H ₅
15		CH ₃	CH ₃
		CH ₃	C ₆ H ₅
20		H	H
		H	CH ₃
25		H	C ₆ H ₅
		CH ₃	CH ₃
30		CH ₃	C ₆ H ₅
35		H	H

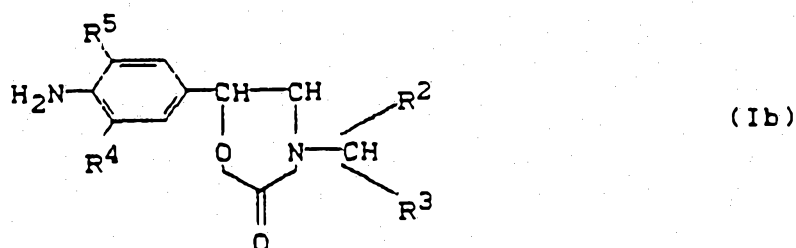
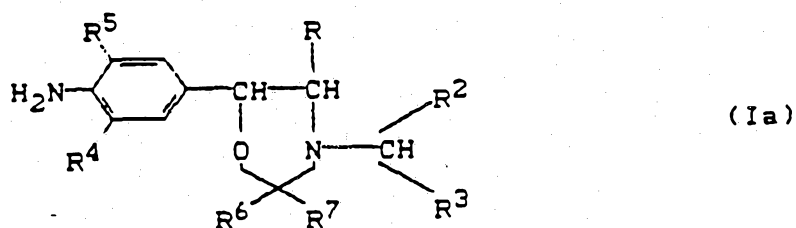
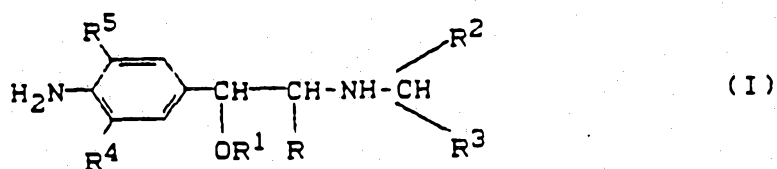
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	R^{11}	R^6	R^7
5		H	CH ₃
10		H	C ₆ H ₅
		CH ₃	CH ₃
15		CH ₃	C ₆ H ₅
20		H	H
		H	CH ₃
25		H	C ₆ H ₅
30		CH ₃	CH ₃
35		CH ₃	C ₆ H ₅

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The claims defining the invention are as follows:

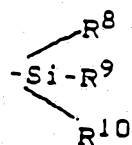
1. Aminophenylethylamine derivatives of the general formulae



in which

R = H or alkyl,

R¹ = hydrogen, acyl, aroyl, arylacyl or



R² = methyl or ethyl,

R³ = straight-chain, branched or cyclic alkyl which is substituted by alkoxy or alkylthio or heterocyclyl which has 4-6 ring atoms and oxygen as the hetero atom and is optionally substituted by alkyl,

R⁴ = H, alkyl (C₁-C₃), halogen, trifluoromethyl or CN,

R⁵ = alkyl (C₁-C₃), halogen, trifluoro-

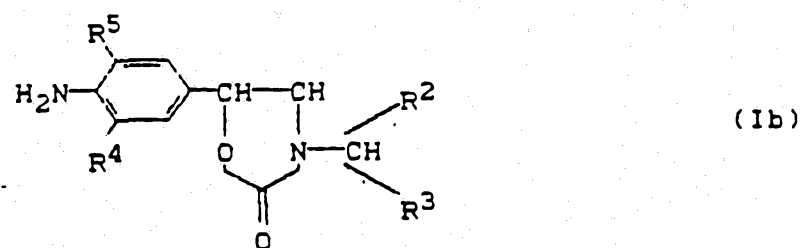
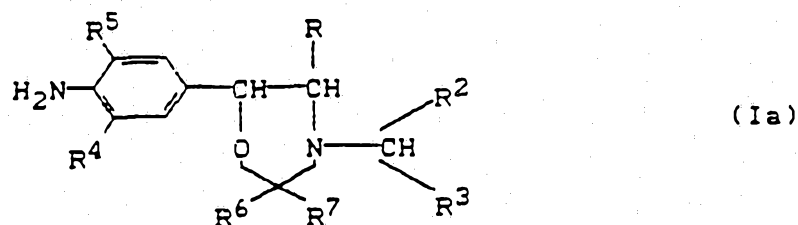
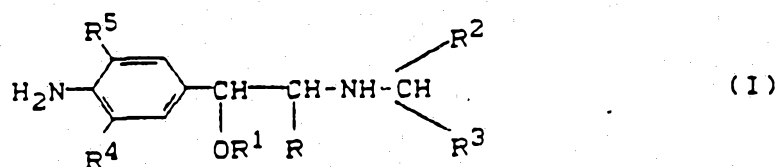
methyl, CN, alkoxy or alkylthio,

R^6 = H or alkyl,

R^7 = H, alkyl, phenyl or phenylalkyl and

R^8 , R^9 and R^{10} = a straight-chain or branched alkyl radical.

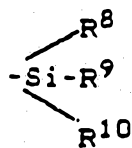
2. Process for the preparation of the aminophenyl-ethylamine derivatives of the general formulae



in which

R = H or alkyl,

R^1 = hydrogen, acyl, aroyl, arylacyl or



R^2 = methyl or ethyl,

R^3 = straight-chain, branched or cyclic

alkyl which is substituted by alkoxy or alkylthio

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or heterocyclyl which has 4-6 ring atoms and oxygen as the hetero atom and is optionally substituted by alkyl,

R^4 = H, alkyl (C_1 - C_3), halogen, trifluoromethyl or CN,

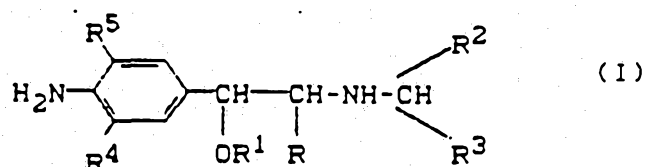
R^5 = alkyl (C_1 - C_3), halogen, trifluoromethyl, CN, alkoxy or alkylthio,

R^6 = H or alkyl,

R^7 = H, alkyl, phenyl or phenylalkyl and

R^8 , R^9 and R^{10} = a straight-chain or branched alkyl radical,

characterized in that, in the case of the compounds of the formula (I)

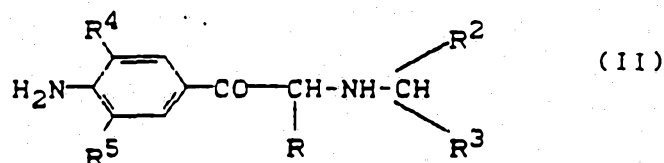


in which

R and R^2 to R^5 have the abovementioned meanings and

R^1 denotes hydrogen,

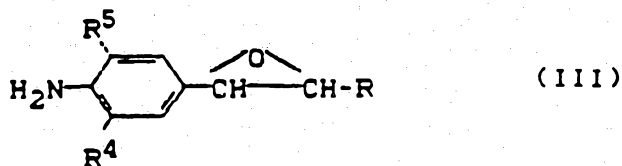
a) compounds of the formula (II)



in which

R and R^2 to R^5 have the abovementioned meanings, are reduced catalytically or with suitable reducing agents, or

b) compounds of the formula (III)



in which

R , R^4 and R^5 have the abovementioned meanings,

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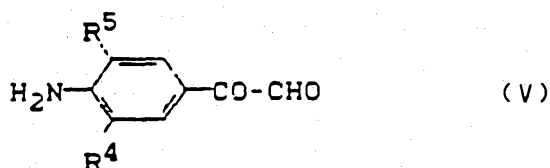
are reacted with amines of the formula (IV)



or

c) in the case of compounds of the formula (I)
in which

R represents hydrogen and
R¹ has the abovementioned meaning,
compounds of the formula (V)



are reacted with an amine of the formula (IV) (above) in
the presence of a reducing agent, such as, for example,
sodium borohydride, or

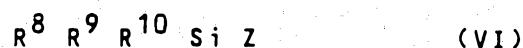
d) in the case of compounds of the formula (I)
in which

R and R² - R⁵ have the abovementioned meanings and

R¹ represents the radical $\begin{array}{c} \text{R}^8 \\ \diagup \\ -\text{Si}-\text{R}^9 \\ \diagdown \\ \text{R}^{10} \end{array}$ and

R⁸, R⁹ and R¹⁰ have the abovementioned meanings,
compounds of the formula (I)
in which

R¹ represents hydrogen,
are reacted with suitable silylating substances of the
formula (VI)



in which

Z denotes halogen, CN, OSO₂-CF₃,

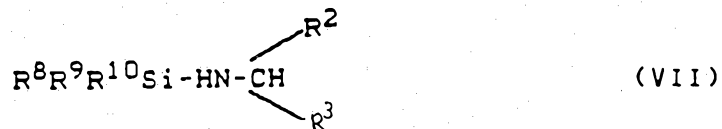
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$-O-Si-R^2R^3R^4$ or $-O-SO_2-O-Si-R^8R^9R^{10}$ and
 R^8, R^9 and R^{10} have the abovementioned meanings,

or

e) compounds of the formula (III) (above) are reacted
 with a silylated amine of the formula (VII)



in which

R^8, R^9 and R^{10} have the abovementioned meanings,

or

f) in the case of compounds of the formula (I)

in which

$R, R^2 - R^5$ have the meanings given in the
 case of (I) and

R^1 represents acyl, aroyl or arylacetyl,

compounds of the formula (I)

in which

R^1 represents hydrogen,

are reacted with acylating agents, or

g) in the case of compounds of the formula (Ia)

in which

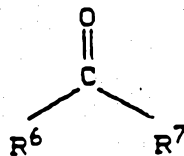
$R^2 - R^7$ have the abovementioned meanings,

compounds of the formula (I)

in which

R^1 represents hydrogen,

are reacted with carbonyl compounds of the formula



in which

R^6 and R^7 have the abovementioned meanings,

if appropriate in the presence of acid catalysts, or

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h) in the case of compounds of the formula (Ib)
in which

$R^2 - R^5$ have the abovementioned meanings,
compounds of the formula (I)
in which

R^1 represents hydrogen,
are cyclized with carbonic acid derivatives, if appropriate in the presence of bases.

3. Agents for yield promotion in animals, characterized in that they contain aminophenylethylamine derivatives of the formulae I, Ia and Ib according to Claim 1, *in admixture with extenders and/or diluents.*

4. Animal feeds, drinking water for animals and additives for animal feeds and drinking water for animals, characterized in that they contain aminophenylethylamine derivatives of the formulae I, Ia and Ib according to Claim 1, *in admixture with feedstuffs or drinking water.*

5. Use of aminophenylethylamine derivatives of the formulae I, Ia and Ib according to Claim 1 for yield promotion in animals.

6. Process for the preparation of agents for yield promotion in animals, characterized in that aminophenylethylamine derivatives of the formulae I, Ia and Ib according to Claim 1 are mixed with extenders and/or diluents.

7. Process for the preparation of animal feeds, drinking water for animals or additives for animal feeds and drinking water for animals, characterized in that aminophenylethylamine derivatives of the formula I, Ia and Ib according to claim 1 are mixed with feedstuffs or drinking water and if appropriate other auxiliaries.

8. Use of aminophenylethylamine derivatives of the formulae I, Ia and Ib according to Claim 1 for the preparation of agents for yield promotion in animals.



~~9. Any novel compound of the formula (II).~~

10. Any other novel compound, including starting and/or intermediate compounds, set forth herein, or any novel agent or feed or liquid or additive set forth herein, or any novel process or method or step thereof, set forth herein, the said compound, agent, feed, liquid, additive, process, method or ~~step being substantially as herein described.~~

DATED this 29th day of April, 1988.

BAYER AKTIENGESELLSCHAFT

By Its Patent Attorneys,

ARTHUR S. CAVE & CO.

