

PATENT SPECIFICATION

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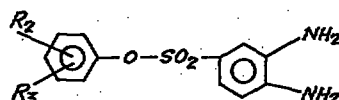


(54) *o*-PHENYLENEDIAMINE DERIVATIVES AND PROCESS FOR THEIR PREPARATION

(71) We, HOECHST AKTIENGESSELLSCHAFT, 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 *o*-phenylenediamine derivatives and to a process for their preparation.

The present invention provides compounds of the formula



(1)

in which 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, an alkoxycarbonyl group having from 1 to 4 carbon atoms in the alkoxy group, or a cyano group.

The alkyl groups represented by R_2 and R_3 are methyl, ethyl, propyl, isopropyl, butyl, secondary butyl and tertiary butyl groups. The alkoxy groups represented by R_2 and R_3 are methoxy, ethoxy, propoxy, isopropoxy and butoxy groups. The halogen atoms represented by R_2 and R_3 are fluorine, chlorine, bromine and iodine atoms. The alkoxycarbonyl groups represented by R_2 and R_3 are methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl and butoxycarbonyl groups.

Especially preferred compounds of formula (1) are those in which 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, the especially preferred position of the substituents represented by R_3 being the 3-position of the phenyl ring.

The present invention also provides addition salts of compounds of the formula (1) with inorganic and organic acids, for example hydrochloric acid, sulfuric acid, acetic acid and oxalic acid.

Compounds in accordance with the present invention are, for example:—

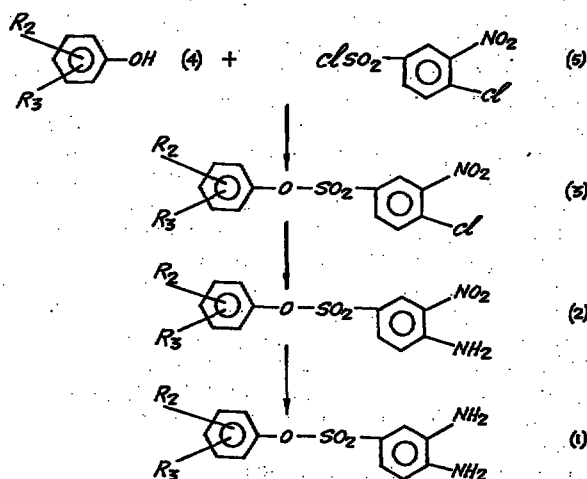
- phenyl 3,4-diamino-benzenesulfonate
- 4-chlorophenyl 3,4-diamino-benzenesulfonate
- 3-chlorophenyl 3,4-diamino-benzenesulfonate
- 2-chlorophenyl 3,4-diamino-benzenesulfonate
- 2,5-dichlorophenyl 3,4-diamino-benzenesulfonate
- 3,5-dichlorophenyl 3,4-diamino-benzenesulfonate
- 4-bromophenyl 3,4-diamino-benzenesulfonate
- 3-bromophenyl 3,4-diamino-benzenesulfonate
- 2-bromophenyl 3,4-diamino-benzenesulfonate
- 4-methylphenyl 3,4-diamino-benzenesulfonate
- 3-methylphenyl 3,4-diamino-benzenesulfonate
- 2-methylphenyl 3,4-diamino-benzenesulfonate

4-tert.butylphenyl 3,4-diamino-benzenesulfonate
 2,4-dimethylphenyl 3,4-diamino-benzenesulfonate
 2-chloro-4-methylphenyl 3,4-diamino-benzenesulfonate
 2-chloro-6-methylphenyl 3,4-diamino-benzenesulfonate
 3-chloro-4-methylphenyl 3,4-diamino-benzenesulfonate
 3-chloro-6-methylphenyl 3,4-diamino-benzenesulfonate
 3-chloro-4-ethoxycarbonylphenyl 3,4-diamino-benzenesulfonate
 4-chloro-2-methylphenyl 3,4-diamino-benzenesulfonate
 4-chloro-3-methylphenyl 3,4-diamino-benzenesulfonate
 4-chloro-3,5-dimethylphenyl 3,4-diamino-benzenesulfonate
 3,5-bistrifluoromethylphenyl 3,4-diamino-benzenesulfonate
 4-methoxyphenyl 3,4-diamino-benzenesulfonate
 3-methoxyphenyl 3,4-diamino-benzenesulfonate
 2-methoxyphenyl 3,4-diamino-benzenesulfonate
 4-propoxyphenyl 3,4-diamino-benzenesulfonate
 4-isopropoxyphenyl 3,4-diamino-benzenesulfonate
 4-butoxyphenyl 3,4-diamino-benzenesulfonate
 4-isobutoxyphenyl 3,4-diamino-benzenesulfonate.

The present invention also provides a process for preparing the *o*-phenylenediamine derivative of the formula (1) which comprises reducing the corresponding amino-nitro derivatives of the formula (2). The reduction may be carried out, for example by hydrogenation in the presence of Raney nickel and a solvent, such as methanol or dimethylformamide, at a temperature of from 20 to 60°C, or by a treatment with reducing agents, such as sodium dithionite.

The amino-nitro derivatives of the formula (2) can be obtained by reacting the corresponding chloro-nitro compounds of the formula (3) with ammonia in a suitable solvent, such as dioxan or methanol, at an elevated temperature and under elevated pressure. These chloro-nitro compounds of the formula (3) can, in turn, be obtained by reacting 3-nitro-4-chlorobenzenesulfonyl chloride of the formula (5) with an appropriate phenol of the formula (4) in an inert solvent in the presence of a base, such as triethylamine.

This series of reactions can be summarized as follows:—



The *o*-phenylenediamine derivatives of the present invention and acid addition salts thereof are valuable intermediates in the preparation of various anthelmintically active 2-alkoxycarbonylamino benzimidazoles as described in our copending Application No. 35217/75 (Serial No. 1,516,508).

The following Examples illustrate the invention.

Example 1

Phenyl 3,4-diaminobenzenesulfonate

27 g of phenyl 3-nitro-4-aminobenzenesulfonate were hydrogenated in 300 ml of methyl glycol with Raney nickel at atmospheric pressure and room temperature. The catalyst was separated by suction-filtration, and upon concentration, phenyl 3,4-diaminobenzenesulfonate was obtained in the form of 25 g of a dark-coloured oil.

(10)

To prepare phenyl 3-nitro-4-aminobenzenesulfonate, 54 g of phenyl 3-nitro-4-chlorobenzenesulfonate in 500 ml of dioxan were maintained at 50°C for 5 hours under an excess pressure of 5 atmospheres of gaseous ammonia, and the solvent was then removed *in vacuo*. The residue was combined with 200 ml of a mixture of equal parts of methanol and water, and the solid which precipitated after a short time was suction-filtered off. After repeated recrystallization from methanol and then from benzene, 28 g of phenyl 3-nitro-4-aminobenzenesulfonate were obtained, m.p. 104°C.

Phenyl 3-nitro-4-chlorobenzenesulfonate was obtained by mixing 51 g of 3-nitro-4-chlorobenzenesulfonyl chloride with 18.8 g of phenol in 120 ml of acetone, and adding dropwise 28 ml of triethylamine while cooling to a temperature not exceeding 10°C. Stirring was continued for some hours at room temperature, water was then added and an oil separated which was worked up with ether. Upon recrystallization from methanol, 54 g of phenyl 3-nitro-4-chlorobenzenesulfonate were obtained, m.p. 71°C.

Examples 2—34

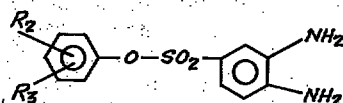
The following compounds were prepared in an analogous manner:

2. 4-chlorophenyl 3,4-diaminobenzenesulfonate
via 4-chlorophenyl 3-nitro-4-chlorobenzenesulfonate, m.p. 84°C
and 4-chlorophenyl 3-nitro-4-aminobenzenesulfonate, m.p. 156°C.
3. 3-chlorophenyl 3,4-diaminobenzenesulfonate, m.p. 84°C
via 3-chlorophenyl 3-nitro-4-chlorobenzenesulfonate, m.p. 68°C
and 3-chlorophenyl 3-nitro-4-aminobenzenesulfonate, m.p. 138°C.
4. 2-chlorophenyl 3,4-diaminobenzenesulfonate
via 2-chlorophenyl 3-nitro-4-chlorobenzenesulfonate
and 2-chlorophenyl 3-nitro-4-aminobenzenesulfonate.
5. 2,5-dichlorophenyl 3,4-diaminobenzenesulfonate
via 2,5-dichlorophenyl 3-nitro-4-chlorobenzenesulfonate
and 2,5-dichlorophenyl 3-nitro-4-aminobenzenesulfonate.
6. 3,5-dichlorophenyl 3,4-diaminobenzenesulfonate, m.p. 116°C
via 3,5-dichlorophenyl 3-nitro-4-chlorobenzenesulfonate, m.p. 104°C
and 3,5-dichlorophenyl 3-nitro-4-aminobenzenesulfonate, m.p. 164°C.
7. 4-bromophenyl 3,4-diaminobenzenesulfonate
via 4-bromophenyl 3-nitro-4-chlorobenzenesulfonate
and 4-bromophenyl 3-nitro-4-aminobenzenesulfonate.
8. 3-bromophenyl 3,4-diaminobenzenesulfonate, m.p. 94°C
via 3-bromophenyl 3-nitro-4-chlorobenzenesulfonate, m.p. 72°C
and 3-bromophenyl 3-nitro-4-aminobenzenesulfonate, m.p. 141°C.
9. 2-bromophenyl 3,4-diaminobenzenesulfonate
via 2-bromophenyl 3-nitro-4-chlorobenzenesulfonate
and 2-bromophenyl 3-nitro-4-aminobenzenesulfonate.
10. 4-methylphenyl 3,4-diaminobenzenesulfonate
via 4-methylphenyl 3-nitro-4-chlorobenzenesulfonate, m.p. 68°C
and 4-methylphenyl 3-nitro-4-aminobenzenesulfonate, m.p. 135°C.
11. 3-methylphenyl 3,4-diaminobenzenesulfonate, m.p. 84°C
via 3-methylphenyl 3-nitro-4-chlorobenzenesulfonate, m.p. 60°C
and 3-methylphenyl 3-nitro-4-aminobenzenesulfonate, m.p. 138°C.
12. 2-methylphenyl 3,4-diaminobenzenesulfonate
via 2-methylphenyl 3-nitro-4-chlorobenzenesulfonate
and 2-methylphenyl 3-nitro-4-aminobenzenesulfonate.
13. 4-tert.butylphenyl 3,4-diaminobenzenesulfonate
via 4-tert.butylphenyl 3-nitro-4-chlorobenzenesulfonate
and 4-tert.butylphenyl 3-nitro-4-aminobenzenesulfonate.
14. 2,4-dimethylphenyl 3,4-diaminobenzenesulfonate
via 2,4-dimethylphenyl 3-nitro-4-chlorobenzenesulfonate
and 2,4-dimethylphenyl 3-nitro-4-aminobenzenesulfonate.
15. 2-chloro-4-methylphenyl 3,4-diaminobenzenesulfonate
via 2-chloro-4-methylphenyl 3-nitro-4-chlorobenzenesulfonate
and 2-chloro-4-methylphenyl 3-nitro-4-aminobenzenesulfonate.
16. 2-chloro-6-methylphenyl 3,4-diaminobenzenesulfonate
via 2-chloro-6-methylphenyl 3-nitro-4-chlorobenzenesulfonate
and 2-chloro-6-methylphenyl 3-nitro-4-aminobenzenesulfonate.
17. 3-chloro-4-methylphenyl 3,4-diaminobenzenesulfonate

- via 3-chloro-4-methylphenyl 3-nitro-4-chlorobenzenesulfonate
and 3-chloro-4-methylphenyl 3-nitro-4-aminobenzenesulfonate.
18. 3-chloro-6-methylphenyl 3,4-diaminobenzenesulfonate
via 3-chloro-6-methylphenyl 3-nitro-4-chlorobenzenesulfonate
and 3-chloro-6-methylphenyl 3-nitro-4-aminobenzenesulfonate.
19. 3-chloro-4-ethoxycarbonylphenyl 3,4-diaminobenzenesulfonate
via 3-chloro-4-ethoxycarbonylphenyl 3-nitro-4-chlorobenzenesulfonate
and 3-chloro-4-ethoxycarbonylphenyl 3-nitro-4-aminobenzenesulfonate.
20. 4-chloro-2-methylphenyl 3,4-diaminobenzenesulfonate
via 4-chloro-2-methylphenyl 3-nitro-4-chlorobenzenesulfonate
and 4-chloro-2-methylphenyl 3-nitro-4-aminobenzenesulfonate.
21. 4-chloro-3-methylphenyl 3,4-diaminobenzenesulfonate
via 4-chloro-3-methylphenyl 3-nitro-4-chlorobenzenesulfonate
and 4-chloro-3-methylphenyl 3-nitro-4-aminobenzenesulfonate.
22. 4-chloro-3,5-dimethylphenyl 3,4-diaminobenzenesulfonate
via 4-chloro-3,5-dimethylphenyl 3-nitro-4-chlorobenzenesulfonate
and 4-chloro-3,5-dimethylphenyl 3-nitro-4-aminobenzenesulfonate.
23. 3,5-bistrifluoromethylphenyl 3,4-diaminobenzenesulfonate
via 3,5-bistrifluoromethylphenyl 3-nitro-4-chlorobenzenesulfonate
and 3,5-bistrifluoromethylphenyl 3-nitro-4-aminobenzenesulfonate.
24. 4-methoxyphenyl 3,4-diaminobenzenesulfonate
via 4-methoxyphenyl 3-nitro-4-chlorobenzenesulfonate, m.p. 88°C
and 4-methoxyphenyl 3-nitro-4-aminobenzenesulfonate, m.p. 140°C.
25. 3-methoxyphenyl 3,4-diaminobenzenesulfonate (oil)
via 3-methoxyphenyl 3-nitro-4-chlorobenzenesulfonate (oil)
and 3-methoxyphenyl 3-nitro-4-aminobenzenesulfonate, m.p. 116°C.
26. 2-methoxyphenyl 3,4-diaminobenzenesulfonate
via 2-methoxyphenyl 3-nitro-4-chlorobenzenesulfonate
and 2-methoxyphenyl 3-nitro-4-aminobenzenesulfonate.
27. 4-propoxyphenyl 3,4-diaminobenzenesulfonate
via 4-propoxyphenyl 3-nitro-4-chlorobenzenesulfonate
and 4-propoxyphenyl 3-nitro-4-aminobenzenesulfonate.
28. 4-isopropoxyphenyl 3,4-diaminobenzenesulfonate
via 4-isopropoxyphenyl 3-nitro-4-chlorobenzenesulfonate
and 4-isopropoxyphenyl 3-nitro-4-aminobenzenesulfonate.
29. 4-butoxyphenyl 3,4-diaminobenzenesulfonate
via 4-butoxyphenyl 3-nitro-4-chlorobenzenesulfonate
and 4-butoxyphenyl 3-nitro-4-aminobenzenesulfonate.
30. 3-ethoxyphenyl 3,4-diaminobenzenesulfonate (oil)
via 3-ethoxyphenyl 3-nitro-4-chlorobenzenesulfonate (oil)
and 3-ethoxyphenyl 3-nitro-4-aminobenzenesulfonate, m.p. 86°C.
31. 4-isobutoxy 3,4-diaminobenzenesulfonate
via 4-isobutoxy 3-nitro-4-chlorobenzenesulfonate
and 4-isobutoxy 3-nitro-4-aminobenzenesulfonate.
32. 3-cyanophenyl 3,4-diaminobenzenesulfonate
via 3-cyanophenyl 3-nitro-4-chlorobenzenesulfonate, m.p. 118°C
and 3-cyanophenyl 3-nitro-4-aminobenzenesulfonate, m.p. 183°C.
33. Phenyl 3,4-diaminobenzenesulfonate
via phenyl 3-nitro-4-chlorobenzenesulfonate
and phenyl 3-nitro-4-aminobenzenesulfonate.
34. 3-trifluoromethylphenyl 3,4-diaminobenzenesulfonate
via 3-trifluoromethylphenyl 3-nitro-4-chlorobenzenesulfonate, m.p. 65°C
and 3-trifluoromethylphenyl 3-nitro-4-aminobenzenesulfonate, m.p. 132°C.

WHAT WE CLAIM IS:—

1. A compound of the formula



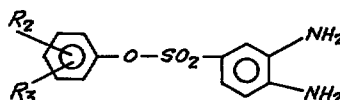
in which each of R_2 and R_3 is a hydrogen atom, a hydroxy group, an alkoxy group having from 1 to 4 carbon atoms, a halogen atom, a trifluoromethyl group, an alkyl group having from 1 to 4 carbon atoms, an alkoxycarbonyl group having from 1 to 4 carbon atoms in the alkoxy group, or a cyano group.



- via 3-chloro-4-methylphenyl 3-nitro-4-chlorobenzenesulfonate
and 3-chloro-4-methylphenyl 3-nitro-4-aminobenzenesulfonate.
18. 3-chloro-6-methylphenyl 3,4-diaminobenzenesulfonate
via 3-chloro-6-methylphenyl 3-nitro-4-chlorobenzenesulfonate
and 3-chloro-6-methylphenyl 3-nitro-4-aminobenzenesulfonate.
19. 3-chloro-4-ethoxycarbonylphenyl 3,4-diaminobenzenesulfonate
via 3-chloro-4-ethoxycarbonylphenyl 3-nitro-4-chlorobenzenesulfonate
and 3-chloro-4-ethoxycarbonylphenyl 3-nitro-4-aminobenzenesulfonate.
20. 4-chloro-2-methylphenyl 3,4-diaminobenzenesulfonate
via 4-chloro-2-methylphenyl 3-nitro-4-chlorobenzenesulfonate
and 4-chloro-2-methylphenyl 3-nitro-4-aminobenzenesulfonate.
21. 4-chloro-3-methylphenyl 3,4-diaminobenzenesulfonate
via 4-chloro-3-methylphenyl 3-nitro-4-chlorobenzenesulfonate
and 4-chloro-3-methylphenyl 3-nitro-4-aminobenzenesulfonate.
22. 4-chloro-3,5-dimethylphenyl 3,4-diaminobenzenesulfonate
via 4-chloro-3,5-dimethylphenyl 3-nitro-4-chlorobenzenesulfonate
and 4-chloro-3,5-dimethylphenyl 3-nitro-4-aminobenzenesulfonate.
23. 3,5-bistrifluoromethylphenyl 3,4-diaminobenzenesulfonate
via 3,5-bistrifluoromethylphenyl 3-nitro-4-chlorobenzenesulfonate
and 3,5-bistrifluoromethylphenyl 3-nitro-4-aminobenzenesulfonate.
24. 4-methoxyphenyl 3,4-diaminobenzenesulfonate
via 4-methoxyphenyl 3-nitro-4-chlorobenzenesulfonate, m.p. 88°C
and 4-methoxyphenyl 3-nitro-4-aminobenzenesulfonate, m.p. 140°C.
25. 3-methoxyphenyl 3,4-diaminobenzenesulfonate (oil)
via 3-methoxyphenyl 3-nitro-4-chlorobenzenesulfonate (oil)
and 3-methoxyphenyl 3-nitro-4-aminobenzenesulfonate, m.p. 116°C.
26. 2-methoxyphenyl 3,4-diaminobenzenesulfonate
via 2-methoxyphenyl 3-nitro-4-chlorobenzenesulfonate
and 2-methoxyphenyl 3-nitro-4-aminobenzenesulfonate.
27. 4-propoxyphenyl 3,4-diaminobenzenesulfonate
via 4-propoxyphenyl 3-nitro-4-chlorobenzenesulfonate
and 4-propoxyphenyl 3-nitro-4-aminobenzenesulfonate.
28. 4-isopropoxyphenyl 3,4-diaminobenzenesulfonate
via 4-isopropoxyphenyl 3-nitro-4-chlorobenzenesulfonate
and 4-isopropoxyphenyl 3-nitro-4-aminobenzenesulfonate.
29. 4-butoxyphenyl 3,4-diaminobenzenesulfonate
via 4-butoxyphenyl 3-nitro-4-chlorobenzenesulfonate
and 4-butoxyphenyl 3-nitro-4-aminobenzenesulfonate.
30. 3-ethoxyphenyl 3,4-diaminobenzenesulfonate (oil)
via 3-ethoxyphenyl 3-nitro-4-chlorobenzenesulfonate (oil)
and 3-ethoxyphenyl 3-nitro-4-aminobenzenesulfonate, m.p. 86°C.
31. 4-isobutoxy 3,4-diaminobenzenesulfonate
via 4-isobutoxy 3-nitro-4-chlorobenzenesulfonate
and 4-isobutoxy 3-nitro-4-aminobenzenesulfonate.
32. 3-cyanophenyl 3,4-diaminobenzenesulfonate
via 3-cyanophenyl 3-nitro-4-chlorobenzenesulfonate, m.p. 118°C
and 3-cyanophenyl 3-nitro-4-aminobenzenesulfonate, m.p. 183°C.
33. Phenyl 3,4-diaminobenzenesulfonate
via phenyl 3-nitro-4-chlorobenzenesulfonate
and phenyl 3-nitro-4-aminobenzenesulfonate.
34. 3-trifluoromethylphenyl 3,4-diaminobenzenesulfonate
via 3-trifluoromethylphenyl 3-nitro-4-chlorobenzenesulfonate, m.p. 65°C
and 3-trifluoromethylphenyl 3-nitro-4-aminobenzenesulfonate, m.p. 132°C.

WHAT WE CLAIM IS:—

1. A compound of the formula



in which 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, an alkoxy carbonyl group having from 1 to 4 carbon atoms in the alkoxy group, or a cyano group.



(12)

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2. A compound according to claim 1, wherein 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.

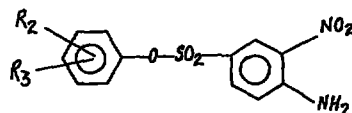
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3. A compound according to claim 2, wherein R_3 is in the 3-position.

4. An addition salt of a compound according to claim 1 with an inorganic or organic acid.

5

5. A process for preparing a compound according to claim 1, which comprises reducing a compound of the formula



10

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

10

6. A process according to claim 5 carried out substantially as described in any one of Examples 1 to 34 herein.

7. A compound according to claim 1 whenever prepared by a process according to claim 5 or claim 6.

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

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