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Phosphoric acid salt of aromatic diamine

The present invention relates to a new salt of N-methyl-o-phenylenediamine.

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Background of the invention

Aromatic amines are important intermediate compounds for the synthesis of dyes, antioxidants and particularly pharmaceuticals. Aromatic 1,2-diamines in particular are of great industrial importance for the manufacture of aromatic heterocycles, especially those with two heteronitrogen atoms such as benzimidazoles. These and the salts thereof are of great interest owing to their pharmacological versatility.

However, it is known that aromatic amines such as aniline are highly prone to oxidation. This makes it particularly difficult to store these compounds. This property is particularly noticeable with liquid aromatic amines or those dissolved in a liquid. Even in the presence of small traces of oxygen or light, these solutions turn deep black after only a short time. This high oxidation sensitivity of the aromatic amines means that they can only be used in further chemical reactions when freshly purified, usually freshly distilled. The oxidation sensitivity of these substances can be reduced by converting the aromatic amines into their salts. However, even the salts are usually still sufficiently prone to oxidation that they have to be stored in the absence of oxygen, for example. Such salts also have a tendency to hygroscopy. The most common salts are the hydrohalides, particularly the hydrochlorides.

The phenylenediamines are particularly oxidation-prone. Thus, in the Reports of the German Chemical Society, Volume 25, pages 2841–2842, O. Fischer states that the oily N-methyl-o-phenylenediamine "turns dark incredibly quickly and after just a short time becomes totally black even in dark, well-sealed bottles." According to O. Fischer even the dihydrochloride is a substance which is "relatively sensitive to air and light" (O. Fischer, loc. cit.). The same is true of other salts of N-methyl-o-phenylenediamine known from the prior art, salts of o-phenylenediamine itself and other salts of mono-, di- and tri-N-alkylated phenylenediamines.

In addition to their high sensitivity to oxidation and light and in some cases the marked hygroscopy of the hydrohalides of the above-mentioned phenylenediamines, these compounds have other serious disadvantages for use in large-scale industrial processes. Since the salts generally have to be converted into the free base *in situ* when they are reacted further, the corresponding halohydric acid is formed as a by-product. This is particularly detrimental when the reaction mixture is at a temperature at which hydrohalic acid is produced in gas form. Since these gases are corrosive, highly caustic and consequently toxic, they have to be carefully removed from the reaction. In some cases this can only be done with considerable technical input, which is accompanied by high costs.

However, not only the use but also the preparation of the salts of phenylenediamines with hydrohalic acids involves some problems on the industrial scale. It would be most convenient if the hydrogen halide were supplied in gas form to the corresponding phenylenediamine in order to minimise losses of yield. However, this is extremely laborious from a technical point of view, with the result that the salts have to be formed from the aqueous hydrohalic acids and high losses of yield have to be accepted.

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Description of the invention

It is an aim of the present invention to minimise the problems known from the prior art connected with the preparation, storage and use of N-methyl-o-phenylenediamine.

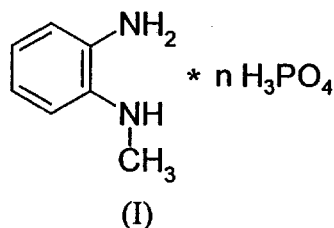
25 A further object of the invention is to convert N-methyl-o-phenylenediamine into a form which is easy to handle, with low sensitivity to oxidation and/or light and/or which is not hygroscopic and is easy to store, such that the free bases are rapidly available for subsequent reactions.

Detailed description of the invention

30 Surprisingly, it has been found that the salt of N-methyl-o-phenylenediamine and phosphoric acid does not have the disadvantages and consequent problems known

from the prior art for other salts of this kind or has them only to a significantly reduced extent.

Thus, the present invention solves the problem by converting N-methyl-o-phenylenediamine into a phosphoric acid salt according to Formula I



wherein n is a number between 0.5 and 1.0.

The term "phosphoric acid salt" denotes all salts of N-methyl-o-phenylenediamine with ortho-phosphoric acid (H_3PO_4). The ratio of one molecule of H_3PO_4 to one molecule of N-methyl-o-phenylenediamine according to Formula I is described as a statistical mean by the factor n.

A salt as described above wherein n is from 0.7 to 0.8 is preferred; most preferably, n equals 0.75 to 0.78.

In a particularly preferred embodiment, the phosphoric acid salt of N-methyl-o-phenylenediamine according to the invention is anhydrous or contains only slight traces of water. The water content of the salt is generally between 1.0 and 1.5 % by weight.

The advantages of the phosphoric acid salt of N-methyl-o-phenylenediamine according to the invention consists on the one hand in its resistance to oxidation, insensitivity to light and non-hygroscopic characteristics. As a result, it is easily stored without any major expense and can be used in further reactions without additional measures – with the optional exception of conversion into the free base. Moreover, it is surprisingly easy to manufacture on a large scale since the phosphoric acid used can be put in in the form of crystals. Moreover, when the phosphoric acid

salt itself is further used at elevated temperatures no caustic or corrosive gases are produced under the reaction conditions.

According to another aspect the present invention relates to the industrial-scale
5 manufacture of the N-methyl-o-phenylenediamine-phosphoric acid salt described above.

The salt is easily obtainable in high yields by dissolving N-methyl-o-phenylenediamine in a water- or alcohol- miscible solvent such as C₁ to C₅-alcohol,
10 preferably ethanol, propanol or isopropanol. This mixture is reacted with crystalline phosphoric acid or a phosphoric acid solution in amounts of from 75 – 100 Mol%. The phosphoric acid may be dissolved or suspended in water, a C₁- to C₅-alcohol such as methanol, ethanol, propanol, isopropanol or mixtures thereof. Preferably, ethanol, propanol or isopropanol are used as the solvents.

15 The N-methyl-o-phenylenediamine-phosphoric acid salt is either precipitated from the solvent or may optionally be precipitated by the addition of non-polar solvents such as aliphatic or aromatic hydrocarbons or ethers.

20 In a preferred process, anhydrous phosphoric acid is used.

An alternative embodiment of the invention relates to processes in which N-methyl-o-phenylenediamine is prepared *in situ* by reduction of the o-nitro-N-methylaniline.

25 The reduction of the o-nitro-N-methylaniline may be carried out using methods known from the prior art. The preferred reducing agent is hydrogen, using a hydrogenation catalyst in an alcohol as solvent, preferably ethanol, propanol or isopropanol. After the catalyst has been removed, the resulting solution can be reacted with phosphoric acid or a phosphoric acid solution. Preferably, a suspension of crystalline, anhydrous
30 phosphoric acid in the alcohol used for hydrogenation is used.

Example 1

A mixture of 190 kg of o-nitro-N-methylaniline, 0.95 kg of palladium/charcoal catalyst (10 % Pd) and 570 l of ethanol is hydrogenated in a 1200 l-VA-Hydrogenator at 60 – max. 85°C under a hydrogen pressure of 2 – 6 bar until the uptake of hydrogen
 5 has stopped. 99 kg of crystalline phosphoric acid and 238 l of ethanol are placed in another 1200 l apparatus and the contents of the hydrogenation apparatus are allowed to flow into it, with stirring, while the catalyst is filtered off.

The filter and the filtered catalyst are washed with 95 l of ethanol, cooled to 10 – 20°C and stirred for a further 30 – 60 minutes. The product is centrifuged, washed with 238
 10 l of ethanol and dried *in vacuo* at 40 – 60°C.

Yield : 230 kg of N-methylphenylenediamine, 0.77 phosphate (92 % of theory).

The product typically contains 1.0 – 1.5 % water.

According to titration a content of 61.0 % N-methylphenylenediamine and 37.7 % phosphoric acid is calculated.

15 Element analysis: C: 42.00 % H: 6.34 % N: 14.00 % P: 11.92 %

Example 2

A mixture of 190 kg of o-nitro-N-methylaniline, 0.95 kg of palladium/charcoal catalyst (10 % Pd) and 570 l of isopropanol is hydrogenated in a 1200 l-VA-
 20 Hydrogenator at 60 – max. 85°C under a hydrogen pressure of 2 – 6 bar until the uptake of hydrogen has stopped. 99 kg of crystalline phosphoric acid and 238 l of isopropanol are placed in another 1200 l apparatus and the contents of the hydrogenation apparatus are allowed to flow into it, with stirring, while the catalyst is filtered off.

25 The filter and the filtered catalyst are washed with 95 l of isopropanol, cooled to 10 – 20°C and stirred for a further 30 – 60 minutes. The product is centrifuged, washed with 238 l of isopropanol and dried *in vacuo* at 40 – 60°C.

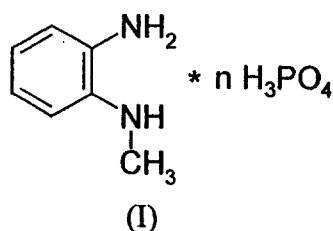
Yield : 225 kg of N-methylphenylenediamine, 0.77 phosphate (90 % of theory)

According to titration a content of 61.1 % N-methylphenylenediamine and
 30 37.6 % phosphoric acid is calculated.

Element analysis: C: 41.98 % H: 6.35 % N: 14.04 % P: 11.93 %

Patent Claims

1. Phosphoric acid salt of N-methyl-o-phenylenediamine.
- 5 2. Phosphoric acid salt of N-methyl-o-phenylenediamine according to claim 1, characterised by general formula I



wherein n is a number between 0.5 and 1.0.

- 10 3. Phosphoric acid salt of N-methyl-o-phenylenediamine according to claim 2, characterised in that n is between 0.7 and 0.8.
4. Phosphoric acid salt of N-methyl-o-phenylenediamine according to one of claims 2 and 3, characterised in that n is between 0.75 and 0.78.
- 15 5. Process for preparing a phosphoric acid salt of N-methyl-o-phenylenediamine according to one of the preceding claims 1 to 4, characterised in that N-methyl-o-phenylenediamine according to one of the preceding claims is dissolved in a solvent and mixed with crystalline or dissolved phosphoric acid.
- 20 6. Process according to claim 5 for preparing a phosphoric acid salt of N-methyl-o-phenylenediamine according to one of the preceding claims 1 to 4, characterised in that N-methyl-o-phenylenediamine is prepared *in situ*.
- 25 7. Process according to claim 6 for preparing a phosphoric acid salt of N-methyl-o-phenylenediamine according to one of the preceding claims 1 to 4, characterised in that the o-N-methylphenylenediamine is prepared *in situ* from o-nitro-N-methylaniline.

8. Process according to one of claims 5 to 7 for preparing a phosphoric acid salt of N-methyl-o-phenylenediamine according to one of the preceding claims 1 to 4, characterised in that the solvent is a C₁- to C₅-alcohol.

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9. Process according to claim 8 for preparing a phosphoric acid salt of N-methyl-o-phenylenediamine according to one of the preceding claims 1 to 4, characterised in that the solvent for N-methyl-o-phenylenediamine and for the phosphoric acid is ethanol, propanol or isopropanol.

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10. Process according to claim 9 for preparing a phosphoric acid salt of N-methyl-o-phenylenediamine according to one of the preceding claims 1 to 4, characterised in that the solvent for N-methyl-o-phenylenediamine and for the phosphoric acid is ethanol.