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MEDICINAL AZO COMPOUNDS

Raemer Rex Renshaw, New York, and Edmond T. Tisza and Bernard F. Duesel, Yonkers, N. Y., assignors to The Pyridium Corporation, Nepera Park, N. Y., a corporation of New York

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4 Claims. (Cl. 260—97)

This invention relates to medicinal preparations and also relates to processes for making the same.

Although many amino aromatic compounds and their derivatives are known to have physiological action, they are generally not used for medicinal or therapeutic purposes, because of their toxicity, and also because they are oxidizable in the human body to para-hydroxyl derivatives. These para-hydroxyl derivatives, even though of decreased toxicity, and even though they retain in large part the physiological action of the compounds from which they were derived, do not function satisfactorily because of the activity of the para-hydroxyl grouping. These phenolic hydroxyl groups readily enter into combinations including sulfonic or glucuronic acid groupings, which are inert and ineffective from a physiological viewpoint.

For example, it was early found that compounds such as aniline and acetanilide (Schmiedeberg, Archiv. fur experimentelle Pathologie and Pharmakologie, vol 8, page 1, 1878) are oxidized to para-amino phenols in the human system, which last-mentioned compounds are eliminated from the system in the form of inert and ineffective combinations.

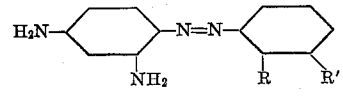
It has long been thought necessary, in order to decrease the toxicity and also to prevent the formation of such para-hydroxylated compounds, to insert a substituent group in the para-position in such amino-aromatic derivatives. According to this theory, phenacetin and a large number of other para compounds have been developed and have achieved wide-spread utilization in the field of medicine.

We have now found, however, that it is possible to obtain certain ortho- and/or meta-substituted azotized aromatic amines of markedly decreased toxicity and enhanced therapeutic value, without regard to whether or not the para-group was substituted.

These amines are preferably produced by the diazotization and coupling of a meta- and/or ortho-substituted aromatic amine with a diamino aromatic compound, such as meta-phenylenediamine. The preferred substituents include alkyl and an alkoxy or hydroxy group. It is desirable to exclude certain substituent groups such as the sulphonic acid group from these compounds.

These compounds are not particularly toxic; whether or not they are substituted in the para position; are not converted into inert compounds even though they may contain hydroxyl groups; and are particularly of value because of their enhanced bactericidal action, and because of their elimination in the urine.

The probable structural formula of the preferred type of the meta- and/or ortho-substituted azo compounds of the present invention is as follows:



in which one of the groups R and R' represents an alkyl group, as for example, CH_3 C_2H_5, C_4H_9, C_5H_{11}, and so forth, and the other represents an alkoxy group, as for example, OCH_3, OC_2H_5, OC_5H_{11}, or a hydroxy group.

The preferred method of obtaining these compounds is by diazotizing the corresponding ortho- and/or meta-substituted anilin and coupling the corresponding diazonium salt with m-phenylendiamine in acid solution.

The dyes obtained are of similar character, and form from yellow to dark brown crystals, faintly soluble in water, very soluble in organic solvents such as methanol, ether, acetone, carbon tetrachloride, and toluene. For purification, they may be recrystallized out of toluene.

With acids, they form salts, the hydrochlorides being dark red to bluish violet colored crystals. These salts are soluble in water, from which solution the bases may be precipitated with an alkali. The hydroxide, carbonate, or acetate of the alkali may be used as the alkali for this purpose.

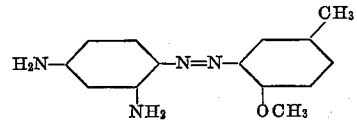
With concentrated hydrochloric acid they also form a dihydrochloride, which is usually darker than the corresponding mono-hydrochloride.

The following examples illustrate various methods of obtaining some representative medicinal preparations of the present invention. Equimolecular quantities were used of the compounds, which were coupled together to form the azo-derivative.

Example 1

2-methoxy-5-methylaniline (cresidine) when diazotized and coupled with m-phenylenediamine, forms a red-brown crystalline powder, which when purified by recrystallization out of toluene, has a melting point of about 44–46° C.

The probable structural formula of this compound is:



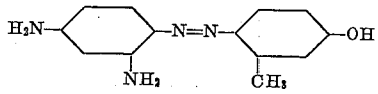
2-methoxy-5-methyl-2', 4'-diamino-azobenzene.

Example 2

3.9 g. of 2-methyl-4-hydroxyaniline were dissolved in 120 cc. of water and 7.5 of concentrated hydrochloric acid. The solution was cooled to 4° C. and then diazotized with a 10% solution of

sodium nitrite, using potassium iodide-starch paper as indicator to determine the end point. To this diazonium salt solution, a solution of 4.6 g. of m-phenylenediamine hydrochloride in 20 cc. of water was added. Upon making the solution almost neutral, copulation ensued. Upon the addition of a sodium alkali the sodium salt of the azo compound was precipitated. This compound was dissolved in dilute (about 10%) hydrochloric acid and precipitated with a saturated salt solution. The violet-black hydrochloride was recrystallized out of methanol. It decomposes at about 204° C. The base on account of its very high solubility in methanol, acetone or ether, could not be recrystallized from these solvents. On the other hand it was so slightly soluble in toluene, ligroin or chloroform that these solvents cannot readily be employed. Therefore it is most satisfactorily produced as the hydrochloride.

The probable structural formula of this compound is:—



2-methyl-4-hydroxy-2', 4'-diamino azobenzene.

What is claimed is:

1. As a new chemical monoazo compound useful for medicinal purposes, a di-amino-phenyl-azo-phenyl compound, the amino groups of the first phenyl group being unsubstituted and the second phenyl group being provided with two substituents, at least one of which is in ortho-position to the azo linkage, and at least one of which consists of a methyl group and the other of which is selected from the group consisting of methoxy and hydroxy.

2. A new chemical compound useful for medicinal purposes comprising an azo-benzene in which two nuclear hydrogen atoms are replaced by unsubstituted amino groups, another nuclear hydrogen atom is replaced by a lower alkyl group and still another is replaced by a lower alkoxy group, in which the lower alkoxy and the lower alky contain the same number of carbon atoms and are attached to one phenyl nucleus while the amino groups are attached to the other phenyl nucleus.

3. A new chemical compound useful for medicinal purposes comprising 2, 4-diamino, 2'-methoxy, 5' methyl-azo-benzene.

4. A new chemical compound useful for medicinal purposes comprising 2', 4'-diamino, 2-methyl, 4-hydroxy azobenozene.

RAEMER REX RENSHAW.
EDMOND T. TISZA.
BERNARD F. DUESEL.