[Second Edition]

# PATENT SPECIFICATION

**606,187**

*Convention Date (France): Sept. 9, 1943.*

*Application Date (In United Kingdom): May 17, 1945.* *No. 20194/45.*
*(Divided out of No. 606,181).*

*Complete Specification Accepted: Aug. 10, 1948.*

*(Under Section 91, sub-sections (2) and (4) of the Patents and Designs Acts, 1907 to 1942, and Section 6 (1) (a) of the Patents &c. (Emergency) Act, 1939, a single Complete Specification was left in respect of this Application and of Application No. 20193/45, and was laid open to inspection on Aug. 2, 1945.*

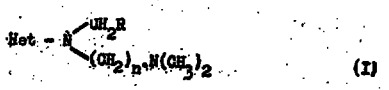
Index at acceptance:—**Class 2(iii)**, C2a, C2b(3: 18: 37).

COMPLETE SPECIFICATION

## Improvements in or relating to Substituted Diamines

We, SOCIETE DES USINES CHIMIQUES RHONE POULENC, a French body corporate, of 21 Rue Jean-Goujon, Paris, 8e, France, do hereby declare the nature of this invention and in what manner the same is to be performed, to be particularly described and ascertained in and by the following statement:—

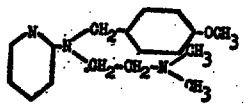
In the Specification of co-pending Application Nos. 12486—7/45 (Serial No. 606,181), of which the present application is a division, there are claimed processes for the preparation of new therapeutically valuable ditertiary diamines of the general formula:



(I)

(where "Het" represents a monocyclic heterocyclic nucleus (e.g. pyridine, thiazole or pyrimidine); R represents an alkyl, aralkyl or aryl group (the aryl nucleus in the aralkyl group may be substituted by alkyl or by alkoxy groups) or a monocyclic, heterocyclic group; and *n* represents a whole number equal to or greater than 2).

According to the present invention, it has been found now that the new tertiary diamine conforming to the formula:

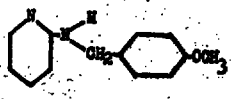


(II)

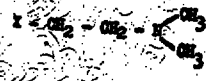
shows an exceptionally powerful antihistaminic action.

The present invention consists in the preparation of this new compound by either of the following methods:

(*a*)—Condensing the secondary amine



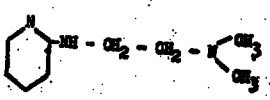
or its sodio derivative with a tertiary amine containing a reactive group X of the formula:



(III)

in which X may be a halogen atom, an hydroxyl group or a sulphuric or sulphonic acid ester radical or

(*b*)—Condensation of the heterocyclic amine:



or its sodio derivative with a *p*-methoxybenzyl-halide or alcohol, or with sulphuric or sulphonic esters of such alcohol.

The present invention is illustrated by the following non-limitative Examples:

EXAMPLE I.

43 g. of -p-methoxybenzylaminopyridine are heated in 60 ccs. of toluene to 95—100° C. and there is added, little by little, 18 g. of sodamine (85%). After evolution of ammonia the major part of the toluene is stilled off and 110 ccs. of a 40% solution of 1-dimethyl-amino-2-chloroethane are added in small amounts with shaking; the addition takes an hour. The mixture is heated to 140° C., first at

normal pressure, then under a reduced pressure of 150 mm. of mercury. The mass is taken up with dilute hydrochloric acid and ether. After separation of the ethereal layer, the hydrochloric solution is neutralised at pH7, and the α-*p*-methoxybenzyl-aminopyridine which separates is eliminated. After making the solution strongly alkaline, using excess of caustic potash, the product is extracted with benzene, dried and distilled. The product thereby obtained, N-β¹-dimethylaminoethyl - N - *p* - methoxybenzyl - α - aminopyridine boils at 185—190° C./2 mm. The monohydrochloride melts at 135° C. (Maquenne block).

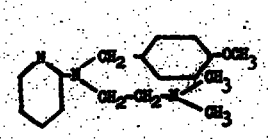
EXAMPLE II.

16.5 g. of N-β¹-dimethylaminoethyl-α-aminopyridine are allowed to react in 40 ccs. of xylene with 4.5 g. of 85% sodamide, then over a period of a quarter-of-an-hour there are added, at 115° C., 15.7 g. of para-methoxy benzyl-chloride. The whole is then heated for one hour at 140° C. It is then treated with 5% caustic potash and with benzene, decanted and rectified. There is thereby obtained the same product as in Example I.

The N-β¹-dimethylaminoethyl-α-aminopyridine is obtained by condensing α-aminopyridine with 1-dimethylamino-2-chlorethane in the presence of sodamide.

Having now particularly described and ascertained the nature of our said invention and in what manner the same is to be performed, we declare that what we claim is:—

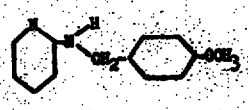
1. Process for the production of a new tertiary diamine conforming to the formula:



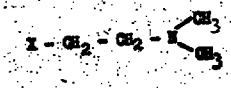
(II)

which shows a powerful anti-histaminic action, which comprises either of the following methods:

(a) condensing the secondary amine:



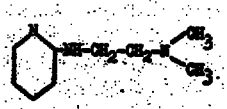
or its sodio derivative with a tertiary amine containing a reactive group X of the formula:



(III)

in which X may be a halogen atom, an hydroxyl group or a sulphuric or sulphonic acid ester radical or

(b) condensing the heterocyclic amine:



or its sodio derivative with a *p*-methoxy-benzyl-halide or alcohol, or with sulphuric or sulphonic esters of such alcohol.

2. Processes for the preparation of a new tertiary diamine of formula II, substantially as set forth in either of the foregoing specific Examples I and II.

3. The tertiary diamine of formula II when prepared by the process claimed in any one of the preceding claims.

Dated this 7th day of August, 1945.

For the Applicants,
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Bank Chambers, 329, High Holborn,
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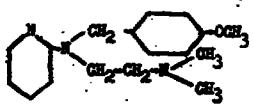
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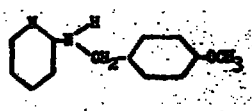
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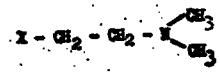
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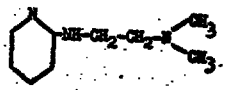
or its sodio derivative with a tertiary amine containing a reactive group X of the formula:



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