

L 153.103



PATENT SPECIFICATION

NO DRAWINGS

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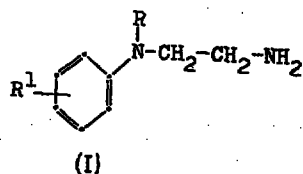
COMPLETE SPECIFICATION

Novel N,N-Disubstituted-Ethylenediamines

We, F. HOFFMANN-LA ROCHE & Co., AKTIENGESELLSCHAFT, a Swiss Company of 124—184 Grenzacherstrasse, Basle, Switzerland, 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:—

The present invention is concerned with novel N,N - disubstituted - ethylenediamines.

The novel N,N - disubstituted - ethylenediamines provided by the invention can be generically formulated thus:



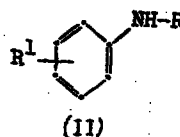
wherein R represents a lower-alkyl group and R¹ represents a chlorine or bromine atom or the nitro or trifluoromethyl group. They are useful as starting materials for the preparation of the ethylenediamine derivatives which from the subject of our copending Application for Letters Patent No. 29740/68 (now Serial No. 1,153,102) and which, in turn, are useful in that they can be converted into valuable benzodiaz[1,4]epine derivatives in accordance with the process described and claimed in the specification of our copending Application for Letters Patent No. 25272/67 (now Serial No. 1,153,101).

It will be appreciated that the term 'lower alkyl' is used in this description and in the claims appended hereto to mean a straight-chain or branched-chain alkyl group containing from 1 to 7 carbon atoms such as methyl, ethyl, propyl, isopropyl, butyl and isobutyl. The preferred lower-alkyl groups are those containing from 1 to 4 carbon atoms.

[Price 4s. 6d.]

An especially valuable class of novel N,N-disubstituted - ethylenediamines provided by the invention comprises compounds of formula I in which R¹ represents a chlorine or bromine atom. An especially preferred N,N-disubstituted - ethylenediamine of formula I is that in which R represents the methyl group and R¹ is in the 4-position and represents a chlorine atom; that is to say, N-(4 - chloro - phenyl) - N - methyl - ethylenediamine.

The novel N,N - disubstituted - ethylenediamines provided by the invention can be prepared by treating an N-(lower alkyl)-aniline of the general formula



, wherein R and R¹ have the significance given earlier, with ethyleneimine in the presence of an aprotic LEWIS acid (e.g. boron trifluoride, titanium tetrachloride and aluminium chloride, but preferably aluminium chloride), and an inert organic solvent (e.g. a hydrocarbon such as benzene or toluene).

The temperature at which the foregoing treatment of an N-(lower alkyl)-aniline with ethyleneimine is carried out is not critical, although it is preferred to operate at an elevated temperature, preferably at about the reflux temperature of the medium.

The following Example illustrates the manner in which the novel N,N - disubstituted-ethylenediamines provided by the invention can be prepared:

EXAMPLE

A mixture of 63.8 g (0.5 mol) of 4-chloro-

aniline and 114 g. (0.6 mol) of *paratoluene*-sulphonyl chloride in 400 ml of pyridine was stirred at room temperature overnight. Most of the pyridine was then removed *in vacuo*.
 5 The residue was poured into 2 litres of ice water and the tosylate extracted with ether. The ether was extracted with 1-*N* sodium hydroxide, aqueous hydrochloric acid and water, dried over magnesium sulphate and concentrated. The resulting oil was crystallized from ether to yield 1 - tosylamino - 4-chloro - benzene of melting point 119.5°—120.5°C.

A mixture of 70.4 g (0.25 mol) of 1-tosylamino - 4 - chloro - benzene, 700 ml toluene and 0.3 mol of sodium methoxide in 200 ml of methanol was stirred and heated under reflux for 1 hour. After distilling off most of the methanol, 47.3 ml (0.5 mol) of dimethyl sulphate were added. The stirring and heating under reflux was then continued for a further 5 hours. The precipitated sodium salt disappeared slowly. Excess dimethyl sulphate was destroyed by heating under reflux for an additional 1.5 hours with 400 ml of 3-*N* sodium hydroxide. The phases were separated and the toluene was distilled off to leave a white crystalline residue. Recrystallization from ethanol gave 1 - (N - methyl-tosylamino) - 4 - chloro - benzene of melting point 92°—93°C.

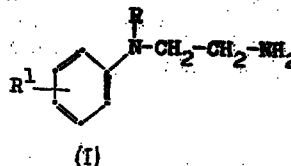
61.5 g (0.208 mol) of 1 - (N - methyl-tosylamino) - 4 - chloro - benzene were added to 580 ml of sulphuric acid (specific gravity 1.74) at 105°C. The mixture was stirred, heated up to 145°C. and kept at that temperature for 1 hour. After cooling, the solution was made strongly alkaline with 50% sodium hydroxide and the organic base extracted with ether. The organic extract was dried over potassium hydroxide pellets, concentrated and the residue distilled *in vacuo* to yield 4 - chloro - N - methyl-aniline of boiling point 74°—75°C/0.7 mm Hg.

14.1 g (0.1 mol) of 4 - chloro - N - methyl-aniline were added carefully and with cooling, to 13.3 g of aluminium chloride and 20 ml of dry benzene, in a 50 ml three-neck flask equipped with reflux condenser, dropping funnel and stirrer. After the addition

had been completed, the mixture was heated until reflux commenced and kept at that temperature for a short period. 4.3 g (0.1 mol) of freshly distilled ethylenimine were then slowly distilled into the reaction vessel from a small flask attached to the former with a gas inlet tube by heating the flask. After the addition had been completed, the reaction mixture was stirred for a further 0.5 hour and then poured on to 200 g of ice contained in a one-litre flask fitted with a condenser. 50 g of solid potassium hydroxide were added to the resulting solid in small portions and the material was seen to pass into solution. It was then cooled and extracted three times with benzene. The combined benzene extracts were dried over potassium hydroxide pellets and concentrated. The residue was distilled *in vacuo* through a 10 cm VIGREUX column to yield N - (4-chloro - phenyl) - N - methyl - ethylenediamine of boiling point 126°—127°C/0.05 mm Hg.

WHAT WE CLAIM IS:—

1. An N,N - disubstituted - ethylenediamine of the general formula



wherein R represents a lower-alkyl group and R¹ represents a chlorine or bromine atom or the nitro or trifluoromethyl group.

2. An N,N - disubstituted - ethylenediamine as formulated in claim 1, wherein R¹ represents a chlorine or bromine atom.

3. N - (4 - chloro - phenyl) - N - methyl-ethylenediamine.

W. D. WHITAKER,

— Patent Agent —

for F. Hoffmann-La Roche & Co.,
Aktiengesellschaft.

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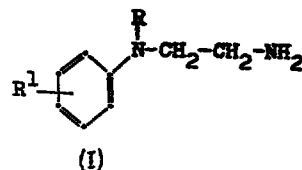
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