

1.153.102C

PATENT SPECIFICATION

NO DRAWINGS

1.153.102



Date of Application and filing Complete Specification: 1 June, 1967.

No. 29740/68.

Application made in United States of America (No. 554964) on 3 June, 1966.

(Divided out of No. 1153101)

Complete Specification Published: 21 May, 1969.

© Crown Copyright 1969.

Index at acceptance:—C2 C(KJ22Y, KJ220, KJ227, KJ31Y, KJ313, KJ32Y, KJ323, KJ338, KJ34Y, KJ342, KJ593, KJ62X, KJ660)

Int. Cl.:—C 07 c 103/82

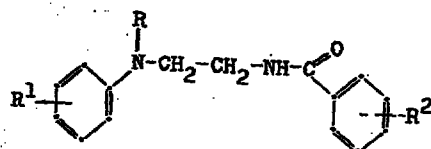
COMPLETE SPECIFICATION

Novel Ethylenediamine Derivatives

We, F. HOFFMANN-LA ROCHE & CO., AKTIENGESSELLSCHAFT, a Swiss Company of 124—184 Grenzachstrasse, 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 ethylenediamine derivatives.

The novel ethylenediamine derivatives provided by the invention can be generically formulated thus:



(I)

wherein R represents a lower-alkyl group, R¹ represents a chlorine or bromine atom or the nitro or trifluoromethyl group and R² represents a halogen atom and wherein the broken line denotes that the atom attached thereby is optional. These novel ethylenediamine derivatives 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).

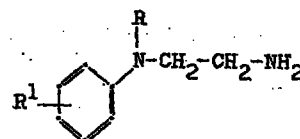
It will be appreciated that the term 'halogen' is used in this description and in the claims appended hereto to mean chlorine, bromine, iodine and fluorine. The term

[Price 4s. 6d.]

'lower alkyl' is used 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.

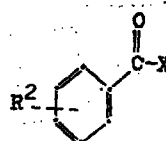
An especially valuable class of ethylenediamine derivatives provided by the invention comprises those in which R¹ represents a chlorine or bromine atom and R² is absent. An especially preferred derivative is that in which R represents the methyl group, R¹ is in the 4-position and represents a chlorine atom and R² is absent; that is to say, N-(4-chloro-phenyl)-N-methyl-N'-benzoyl-ethylenediamine.

The novel ethylenediamine derivatives provided by the invention can be prepared by reacting a compound of the general formula



(II)

, wherein R and R¹ have the significance given earlier, with a benzoic acid derivative of the general formula



(III)

, wherein R² and the broken line have the significance given earlier and X represents

any suitable leaving atom or group, in the presence of an inert organic solvent.

The leaving atom or group X in formula III can be any suitable leaving atom or group which will function efficaciously in the reaction. Advantageously, X represents a bromine or chlorine atom. However, X can represent any other appropriate leaving atom or group such as other halogen atoms or acyl groups. The benzoic acid derivatives of formula III can be generated *in situ* from benzoic acid or a halo-benzoic acid and an agent such as a dialkyl-carbodiimide or a *paratoluene*-sulphonyl halide. As will be evident from the foregoing all that is required of the leaving atom or group is that it be suitable for the purposes of the reaction; that is to say, that it permit formation of the ethylene diamine derivatives of formula I. The reaction may be carried out in the presence of an acid acceptor and in this case, an excess of the acid acceptor can be provided whereby it can also serve as the reaction medium. By this simple expedient, there can thus be provided to the reaction zone a single substance which can serve a two-fold purpose, namely, as acid acceptor and reaction medium. Any suitable acid acceptor which will function efficaciously in the reaction can be used. Especially preferred acid acceptors are tertiary amines (e.g. pyridine). However, the reaction is preferably carried out in an inert organic solvent without the addition of an acid acceptor. Examples of inert organic solvents which can be used in this preferred embodiment are aromatic hydrocarbons such as benzene and toluene, halogenated aromatic hydrocarbons such as chloro-benzene or any other suitable inert organic solvent. While temperature and pressure are not critical, it is preferred to carry out the reaction at about room temperature.

The compounds of formula II hereinbefore are claimed *per se* in the specification of our copending Application for Letters Patent No. 29741/68 (now Serial No. 1,153,103) and may be prepared as described therein.

The following Example illustrates the manner in which the novel ethylenediamine derivatives provided by the invention can be prepared:

EXAMPLE

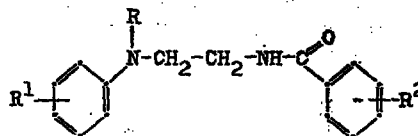
A mixture of 3.69 g. (20 mmol) of N-(4-chloro-phenyl)-N-methyl-ethy-

lenediamine [prepared as described in the specification of our copending Application No. 29741/68 (now Serial No. 1,153,103)] and 2.18 ml of benzoyl chloride in 10 ml of dry pyridine was allowed to stand at room temperature overnight. The reaction mixture was dissolved in ether and extracted once with 3-N sodium hydroxide and then three times with water. The organic phase was dried with sodium sulphate, concentrated and most of the pyridine removed *in vacuo*. Recrystallization of the reddish-brown residue from ethanol/water gave N-(4-chloro-phenyl)-N-methyl-N'-benzoyl-ethylenediamine of melting point 102°-103°C.

Further experiments showed that the last-mentioned compound was more suitably prepared by heating benzoyl chloride and N-(4-chloro-phenyl)-N-methyl-ethylenediamine at reflux in benzene. The isolated crude N-(4-chloro-phenyl)-N-methyl-N'-benzoyl-ethylenediamine was found to be pure enough to be used directly in preparing 7-chloro-1-methyl-5-phenyl-2,3-dihydro-1H-benzodiaz[1,4]epine in accordance with the process described and claimed in the specification of our copending Application No. 25272/67 (now Serial No. 1,153,101).

WHAT WE CLAIM IS:—

1. An ethylenediamine derivative of the general formula



wherein R represents a lower-alkyl group, R¹ represents a chlorine or bromine atom or the nitro or trifluoromethyl group and R² represents a halogen atom and wherein the broken line denotes that the atom attached thereby is optional.

2. An ethylenediamine derivative as formulated in claim 1, wherein R¹ represents a chlorine or bromine atom and R² is absent.

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

W. D. WHITAKER,

— Patent Agent —

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



any suitable leaving atom or group, in the presence of an inert organic solvent.

The leaving atom or group X in formula III can be any suitable leaving atom or group which will function efficaciously in the reaction. Advantageously, X represents a bromine or chlorine atom. However, X can represent any other appropriate leaving atom or group such as other halogen atoms or acyl groups. The benzoic acid derivatives of formula III can be generated *in situ* from benzoic acid or a halo-benzoic acid and an agent such as a dialkyl-carbodiimide or a *paratoluene*-sulphonyl halide. As will be evident from the foregoing all that is required of the leaving atom or group is that it be suitable for the purposes of the reaction; that is to say, that it permit formation of the ethylene diamine derivatives of formula I. The reaction may be carried out in the presence of an acid acceptor and in this case, an excess of the acid acceptor can be provided whereby it can also serve as the reaction medium. By this simple expedient, there can thus be provided to the reaction zone a single substance which can serve a two-fold purpose, namely, as acid acceptor and reaction medium. Any suitable acid acceptor which will function efficaciously in the reaction can be used. Especially preferred acid acceptors are tertiary amines (e.g. pyridine). However, the reaction is preferably carried out in an inert organic solvent without the addition of an acid acceptor. Examples of inert organic solvents which can be used in this preferred embodiment are aromatic hydrocarbons such as benzene and toluene, halogenated aromatic hydrocarbons such as chloro-benzene or any other suitable inert organic solvent. While temperature and pressure are not critical, it is preferred to carry out the reaction at about room temperature.

The compounds of formula II hereinbefore are claimed *per se* in the specification of our copending Application for Letters Patent No. 29741/68 (now Serial No. 1,153,103) and may be prepared as described therein.

The following Example illustrates the manner in which the novel ethylenediamine derivatives provided by the invention can be prepared:

EXAMPLE

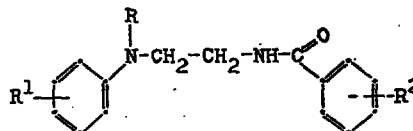
A mixture of 3.69 g. (20 mmol) of N-(4-chloro-phenyl)-N-methyl-ethy-

lenediamine [prepared as described in the specification of our copending Application No. 29741/68 (now Serial No. 1,153,103)] and 2.18 ml of benzoyl chloride in 10 ml of dry pyridine was allowed to stand at room temperature overnight. The reaction mixture was dissolved in ether and extracted once with 3-N sodium hydroxide and then three times with water. The organic phase was dried with sodium sulphate, concentrated and most of the pyridine removed *in vacuo*. Recrystallization of the reddish-brown residue from ethanol/water gave N-(4-chloro-phenyl)-N-methyl-N'-benzoyl-ethylenediamine of melting point 102°-103°C.

Further experiments showed that the last-mentioned compound was more suitably prepared by heating benzoyl chloride and N-(4-chloro-phenyl)-N-methyl-ethylenediamine at reflux in benzene. The isolated crude N-(4-chloro-phenyl)-N-methyl-N'-benzoyl-ethylenediamine was found to be pure enough to be used directly in preparing 7-chloro-1-methyl-5-phenyl-2,3-dihydro-1H-benzodiaz[1,4]epine in accordance with the process described and claimed in the specification of our copending Application No. 25272/67 (now Serial No. 1,153,101).

WHAT WE CLAIM IS:—

1. An ethylenediamine derivative of the general formula



wherein R represents a lower-alkyl group, R¹ represents a chlorine or bromine atom or the nitro or trifluoromethyl group and R² represents a halogen atom and wherein the broken line denotes that the atom attached thereby is optional.

2. An ethylenediamine derivative as formulated in claim 1, wherein R¹ represents a chlorine or bromine atom and R² is absent.

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

W. D. WHITAKER,

— Patent Agent —

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