

PATENT SPECIFICATION

NO DRAWINGS

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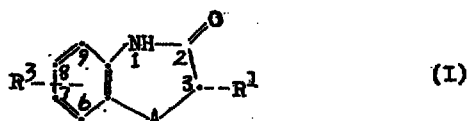
Int. Cl.:—C 07 d 53/06; 57/00

COMPLETE SPECIFICATION

A Process for the Manufacture of Benzdiaz[1,4]Epines

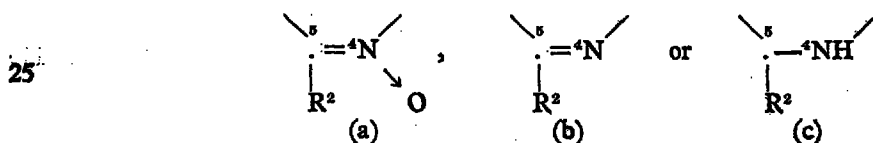
We, F. HOFFMANN-LA ROCHE & Co., AKTIENGESellschaft, a Swiss Company of 124—184 Grenzacherstrasse, Basle, Switzerland, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

Both benzdiaz[1,4]epinone-(2)s of the 15 general formula

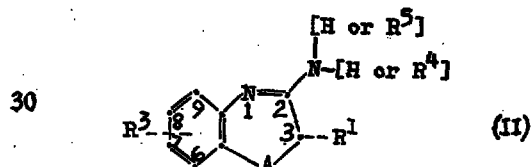


wherein R¹ represents a lower-alkyl or (lower alkoxy) - (lower alkyl) group, R² represents a halogen atom or the nitro or trifluoromethyl group or a lower-alkyl group, the broken lines denote that the substituents attached thereby are optional and A represents a grouping of the formula

The present invention relates to a process for the manufacture of benzdiaz[1,4]epine derivatives. More particularly, the invention is concerned with a process for the manufacture of 2 - amino - benzdiaz[1,4]epines from benzdiaz[1,4]epinone-(2)s.



in which R² represents the phenyl group or a (lower alkyl)-phenyl, nitro-phenyl, halo-phenyl or pyridyl group, and 2 - amino-benzdiaz[1,4]epines of the general formula



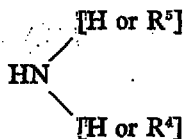
wherein R¹, R², A and the broken lines have the significance given earlier and R⁴ and R⁵ each represent a lower-alkyl group or, taken together with the nitrogen atom to which they

are attached, represent a five-membered or six-membered heterocyclic ring, are well known as being useful as sedatives, muscle relaxants and anticonvulsants. However, up until the present time, the benzdiaz[1,4]epinone-(2)s of formula I and 2-amino-benzdiaz[1,4]epines of formula II have been manufactured by separate synthetic routes using different reactants. Therefore it has long been desired to provide a process whereby benzdiaz[1,4]epinone-(2)s of formula I can be converted into the 2-amino-benzdiaz[1,4]epines of formula II, thereby eliminating the necessity of carrying out separate synthetic routes for the manufacture of these benzdiaz[1,4]epines.

[Price 4s. 6d.]

SEE ERRATA SLIP ATTACHED

It has now been found in accordance with the present invention that the benzdiaz[1,4]-epinone-(2)s of formula I can be directly converted into the 2-amino-benzdiaz[1,4]-epines of formula II by reaction with a compound of the general formula



(III)

(wherein R⁴ and R⁵ have the significance given earlier); the reaction being carried out in the presence of an acid catalyst where a benzdiaz[1,4]epinone-(2) starting material is used in which A represents a grouping of formula (a) hereinbefore and/or R³ is present and represents the nitro group.

Accordingly, the process of the present invention comprises reacting a benzdiaz[1,4]epinone-(2) of formula I hereinbefore with a compound of formula III hereinbefore to yield a 2-amino-benzdiaz[1,4]epine of formula II hereinbefore; the reaction being carried out in the presence of an acid catalyst where a benzdiaz[1,4]epinone-(2) starting material is used in which A represents a grouping of formula (a) hereinbefore and/or R³ is present and represents the nitro group.

Thus, it will be seen from the foregoing that the present process eliminates the necessity of providing two separate reaction routes for the manufacture of the benzdiaz[1,4]epinone-(2)s of formula I and the 2-amino-benzdiaz[1,4]epines of formula II. Furthermore, it has been found that yields as high as 70 per cent by weight of theoretical or higher can be obtained by the present process.

Where a benzdiaz[1,4]epinone-(2) of formula I in which A represents a grouping of formula (b) or (c) hereinbefore and R³ (when present) represents a halogen atom, the trifluoromethyl group or a lower-alkyl group is used as the starting material, the reaction can be simply carried out without the necessity of using an acid catalyst. However, an acid catalyst can also be used in this embodiment of the present process if desired.

It will be appreciated that the term 'lower alkyl' is used in this description and in the claims appended hereto to mean both straight-chain and branched-chain alkyl groups containing from 1 to 7 carbon atoms (e.g. methyl, ethyl, propyl, isopropyl and the like). The term 'lower alkoxy' is used to mean alkoxy groups containing from 1 to 7 carbon atoms (e.g. methoxy, ethoxy, propoxy, isopropoxy, isobutoxy, etc). The term 'halogen' includes all four halogens, namely iodine,

bromine, chlorine and fluorine, with chlorine, fluorine and bromine being preferred.

The preferred benzdiaz[1,4]epinone-(2) starting materials of formula I are those in which R¹ (when present) represents the methyl group and R² represents the phenyl or pyridyl-(2) group or a 2-halo-phenyl group (e.g. the 2-chloro-phenyl or 2-fluoro-phenyl group). Further, R³ is preferably present and represents a halogen such as chlorine or fluorine or the trifluoromethyl or nitro group, and is attached to the 7-position of the molecule. Where A represents a grouping of formula (b) or (c) hereinbefore R³ is preferably present and represents a chlorine or bromine atom attached to the 7-position of the molecule.

The preferred compounds of formula III which are used in carrying out the present process are primary amines such as methyl amine, ethyl amine, isopropyl amine, propyl amine, butyl amine, etc. While it is preferred to use primary amines in the process of this invention, secondary amines can also be used. Any conventional lower-alkyl secondary amine can be used in the process. Among the conventional secondary amines which can be used are diethyl amine, dimethyl amine, N-propyl-N-butyl amine, pyrrolidine, piperidine, etc.

In accordance with one embodiment of the present process, the benzdiaz[1,4]epinone-(2) starting materials of formula I can be converted into the 2-amino-benzdiaz[1,4]epines of formula II by treatment with a compound of formula III such as pyrrolidine, ammonia or any of the aforementioned primary or secondary lower-alkyl amines in the presence of an acid catalyst. In carrying out this embodiment, any conventional acid catalyst can be used. Typical acid catalysts which may be used include *para*-toluene-sulphonic acid, LEWIS acids such as titanium tetrachloride, aluminium trichloride, stannic tetrafluoride, ferric chloride, arsenic trichloride, antimony trichloride, boron trifluoride, etc. The preferred acid catalysts are *para*-toluene-sulphonic acid and titanium tetrachloride. The reaction is preferably carried out in the presence of an inert organic solvent. Any conventional inert organic solvent can be used; for example, diethyl ether, tetrahydro-furan, benzene, hexane, pentane, ethyl propyl ether and mixtures thereof. In carrying out the reaction, temperature and pressure are not critical and it can be carried out at room temperature or below, and at atmospheric pressure or at elevated temperatures and/or elevated pressure. Generally, it is preferred to carry out the reaction at a temperature of from about 0°C to 25°C. While it is generally preferable to use these low temperatures, temperatures as high as the reflux temperature of the solvent can be used.

Where a benzdiaz[1,4]epinone-(2) starting

material of formula I is converted into a 2-amino-benzdiaz[1,4]epine of formula II in the absence of an acid catalyst, the reaction is conveniently carried out at elevated temperatures and pressures in the presence of an inert organic solvent. Any of the conventional inert organic solvents such as those mentioned hereinbefore can be used in carrying out this embodiment. However, the preferred organic solvents are N,N-dimethylformamide and dimethyl sulphoxide. In carrying out this embodiment, it is generally preferred to use temperatures of from about 100°C to 175°C and pressures of from about 50 atmospheres to 75 atmospheres. While this reaction can advantageously proceed without the use of an acid catalyst such as one of those mentioned hereinbefore, an acid catalyst can be used if desired. However, since no additional beneficial results are achieved by using an acid catalyst, it is seldom necessary to use such.

Where a 2-amino-benzdiaz[1,4]epine of formula II is obtained in which A represents a grouping of formula (c) hereinbefore, it can be transformed readily into a 2-amino-benzdiaz[1,4]epine of formula II in which A represents a grouping of formula (b) hereinbefore by treatment with an oxidizing agent. The oxidation can be carried out using any conventional oxidizing agent, typical examples of which are manganese dioxide, selenium dioxide, silver oxide, an azodicarboxylic acid ester, etc. Generally, it is preferred to carry out this oxidation in a suitable organic solvent. Typical organic solvents which can be used include benzene, toluene, acetic acid, butanol, pyridine, etc. In carrying out the oxidation, temperature and pressure are not critical and it can be carried out at room temperature or at elevated or reduced temperatures. Generally, it is preferred to carry out the oxidation at a temperature of from 10°C to about 40°C. The concentration of the reactants in the oxidation is not critical, but the oxidizing agent should preferably be used in stoichiometric excess of the 2-amino-benzdiaz[1,4]epine which is being oxidized. The expression 'stoichiometric excess' means an amount of oxidizing agent in excess of the stoichiometric equivalent but less than two stoichiometric equivalents.

The benzdiaz[1,4]epinone-(2)s of formula I in which R¹ (when present) represents a lower-alkyl group, R³ (when present) represents a halogen atom or the nitro group and A represents grouping (b) in which R² represents a pyridyl group are claimed *per se* in the specification of our Letters Patent No. 948,888. The benzdiaz[1,4]epinone-(2)s of formula I in which A represents grouping (a), (b) or (c) wherein R² represents the phenyl group or a (lower alkyl)-phenyl or halo-phenyl group are claimed *per se* in the specification of our Letters Patent No. 972,968.

The benzdiaz[1,4]epinone-(2)s of formula I in which R¹ (when present) represents a lower-alkyl group, R³ (when present) represents a nitro group in the 7-position and A represents grouping (b) in which R² represents a 2-nitro-phenyl group are claimed *per se* in the specification of our Letters Patent No. 1,000,507. The benzdiaz[1,4]epinone-(2) of formula I in which R¹ is absent, R³ is present in the 7-position and represents the nitro group and A represents grouping (b) in which R² represents a 2-fluoro-phenyl group is claimed *per se* in the specification of our Letters Patent No. 1,039,372. The benzdiaz[1,4]epinone-(2)s of formula I in which R¹ (when present) represents a lower-alkyl group, R³ is present in the 7-position and represents the trifluoromethyl group and A represents grouping (b) in which R² represents a pyridyl group are claimed *per se* in the specification of our Letters Patent No. 1,100,675.

The 2-amino-benzdiaz[1,4]epines of formula II in which R¹ (when present) represents a lower-alkyl group, R³ (when present) represents a halogen atom or a lower-alkyl group, R⁴ is absent, and A represents grouping (a) in which R² represents the phenyl group or a nitro-phenyl or halo-phenyl group are claimed *per se* in the specification of our Letters Patent No. 864,824. The 2-amino-benzdiaz[1,4]epines of formula II in which R¹ (when present) represents a lower-alkyl group, R³ is present in the 7- or 8-position and represents the trifluoromethyl group, R⁴ is absent and A represents grouping (a) in which R² represents the phenyl group are claimed *per se* in the specification of our Letters Patent No. 972,969. The 2-amino-benzdiaz[1,4]epines of formula II in which R¹ is absent, R³ is present in the 7-position and represents grouping (a) in which R² represents the phenyl group or a halo-phenyl group are claimed *per se* in the specification of our Letters Patent No. 986,903. The 2-amino-benzdiaz[1,4]epines of formula II in which R¹ (when present) represents a lower-alkyl group, R³ (when present) represents a halogen atom or the trifluoromethyl group, R⁴ and R⁵ are both present and, together with the nitrogen atom to which they are attached, represents a five-membered or six-membered heterocyclic ring and A represents grouping (b) in which R² represents the phenyl group or a halo-phenyl group are claimed *per se* in the specification of our Letters Patent No. 1,023,793. The 2-amino-benzdiaz[1,4]epines of formula II in which R¹ is absent, R³ (when present) is in the 7-position and represents a halogen atom or the trifluoromethyl group, R⁴ and R⁵ are both present and, together with the nitrogen atom to which they are attached, represent a pyrrolidino group and A represents grouping (a) in which R² represents the phenyl group or a

halo-phenyl group are claimed *per se* in the specification of our Letters Patent No. 1,025,577.

5 The following Examples illustrate the invention:

EXAMPLE 1

10 A solution of 75 g of 7-chloro-5-phenyl-1,3-dihydro-2H-benzdiaz[1,4]epinone-(2) in 250 ml of N,N-dimethyl-formamide at 10°C was saturated with methyl amine. The resulting mixture was placed in a pressure vessel which was then charged with nitrogen to 67 atmospheres. The pressure vessel was then heated at 150°C for 24 hours, cooled and vented to the atmosphere. The solution was poured into 4 litres of water. The resulting aqueous mixture was adjusted to pH 6 with hydrochloric acid and filtered. The precipitate was dissolved in 1 litre of dichloro-methane and the resulting solution was extracted with three 250 ml portions of 3-N hydrochloric acid. The acid extracts were combined, washed with one 250 ml portion of dichloro-methane, made basic with ammonium hydroxide and extracted with three 250 ml portions of dichloro-methane. The organic layers were combined, washed with water, dried over anhydrous sodium sulphate, filtered and evaporated. The residue was boiled with three 150 ml portions of benzene. The hot benzene fractions were combined and concentrated to give, on cooling, crude 7-chloro-2-methylamino-5-phenyl-3H-benzdiaz[1,4]epine. Recrystallizations of the product from a mixture of dichloro-methane and methanol gave 7-chloro-2-methylamino-5-phenyl-3H-benzdiaz[1,4]epine as pale yellow prisms of melting point 248°-249°C.

EXAMPLE 2

40 A solution of 5 g (0.0184 mol) of 7-chloro-5-phenyl-1,3-dihydro-2H-benzdiaz[1,4]epinone-(2) in 125 ml of dry tetrahydro-furan was added to a solution of 15 g of methyl amine in 100 ml of dry tetrahydrofuran; the mixture was contained in a three-neck round-bottom flask fitted with a stirrer, dropping funnel and 'dry ice' condenser, the flask being externally cooled in an ice-bath and the mixture being kept under nitrogen. A tetrahydro-furan/(titanium tetrachloride) complex prepared by adding 1.8 g (0.01 mol) of titanium tetrachloride to 60 ml of tetrahydro-furan was added slowly over a period of 20 minutes to the mixture. The resulting mixture was continually stirred and allowed to reach room temperature. After 4 hours, thin layer chromatography indicated that the reaction was complete. The mixture was allowed to stand overnight and then filtered. The filtrates were evaporated to dryness and the residue was dissolved in 500 ml of dichloro-methane. The organic solution

was washed with one 100 ml portion of dilute ammonium hydroxide and two 100 ml portions of saturated brine, dried over anhydrous sodium sulphate, filtered and evaporated. The residue was recrystallized from a mixture of tetrahydro-furan and hexane to give 7-chloro-2-methylamino-5-phenyl-3H-benzdiaz[1,4]epine.

EXAMPLE 3

A solution of 5 g of 7-chloro-5-phenyl-1,3-dihydro-2H-benzdiaz[1,4]epinone-(2), 30 ml of pyrrolidine and 0.1 g of *para*-toluene-sulphonic acid monohydrate in 100 ml of toluene was stirred and heated at reflux using a water-remover and a drying tube. After 22.5 hours, the distillate was discarded and the residual solution in the reaction flask was evaporated *in vacuo*. The residue was extracted with a mixture of ether and 3-N acetic acid. The acid layer was filtered and the filtrate was made basic with dilute sodium hydroxide solution to give crude 7-chloro-5-phenyl-2-pyrrolidino-3H-benzdiaz[1,4]epine. This crude product was recrystallized from isopropanol to yield pure 7-chloro-5-phenyl-2-pyrrolidino-3H-benzdiaz[1,4]epine.

EXAMPLE 4

A solution of 5 g (0.0178 mol) of 7-nitro-5-phenyl-1,3-dihydro-2H-benzdiaz[1,4]epinone-(2) in 150 ml of dry tetrahydro-furan was added to a solution of 10 g of methyl amine in 100 ml of dry tetrahydro-furan. The resulting solution was cooled as described in Example 2 hereinbefore and treated with a solution of 2.4 g (0.013 mol) of titanium tetrachloride in 50 ml of dry benzene. The resulting mixture was warmed to room temperature and stirred overnight. Approximately 10 ml of water were added to decompose excess titanium tetrachloride and the solution was filtered. After the solvent had been removed, the residue was treated with 50 ml of ethanol, then filtered to remove solids. After filtration, the remaining liquor was concentrated to yield 2-methylamino-7-nitro-5-phenyl-3H-benzdiaz[1,4]epine.

EXAMPLE 5

A solution of 10 g (0.0348 mol) of 7-chloro-5-phenyl-1,3-dihydro-2H-benzdiaz[1,4]epinone-(2) 4-oxide in 400 ml of dry tetrahydro-furan was added to a solution of 20 g of methyl amine in 200 ml of dry tetrahydro-furan. The resulting mixture was cooled as described in Example 2 hereinbefore and then treated with a tetrahydro-furan/(titanium tetrachloride) complex prepared from 4.8 g (0.025 mol) of titanium tetrachloride and 100 ml of dry tetrahydro-furan (addition time 20 minutes). The resulting mixture was allowed to warm to room

temperature, then was allowed to stand overnight and was subsequently filtered. The filtrates were evaporated to dryness and the residue recrystallized from methanol to give 7 - chloro - 2 - methylamino - 5 - phenyl - 3H - benzdiaz[1,4]epine 4-oxide as pale yellow prisms.

EXAMPLE 6

A solution of 10 g (0.0348 mol) of 7-chloro - 5 - phenyl - 1,3 - dihydro - 2H-benzdiaz[1,4]epinone - (2) 4-oxide in 400 ml of dry tetrahydro-furan was added to a solution of 20 g of dimethyl amine in 200 ml of dry tetrahydro-furan. The resulting solution was cooled as described in Example 2 hereinbefore and then treated with a solution of 4.8 g (0.025 mol) of titanium tetrachloride in 100 ml of dry benzene (addition time 20 minutes). The resulting mixture was allowed to reach room temperature and then was stirred for 3 hours, when 10 ml of water were added. The solution was filtered and the solvent was removed under reduced pressure. The residue was stirred in 50 ml of ethanol and then shaken vigorously with 100 ml of 0.5-N sodium hydroxide solution to remove starting material. The mixture was diluted with 400 ml of water and then filtered. The precipitate was washed with water and recrystallized from ethanol to give 7 - chloro - 2 - dimethylamino - 5 - phenyl - 3H - benzdiaz[1,4]epine 4-oxide.

EXAMPLE 7

A solution of 10 g (0.0348 mol) of 7-chloro - 5 - phenyl - 1,3 - dihydro - 2H-benzdiaz[1,4]epinone - (2) 4-oxide in 400 ml of dry tetrahydro-furan was treated at 0°—10°C first with 15 ml of isopropyl amine and then with a solution of 4.8 g (0.025 mol) of titanium tetrachloride in 100 ml of dry benzene (addition time 20 minutes). The resulting mixture was allowed to warm to room temperature and then stirred overnight. 10 ml of water were added and the solution was filtered and then evaporated. The residue was stirred in 50 ml of ethanol and shaken well with 100 ml of 0.5-N sodium hydroxide solution to remove starting material. The mixture was diluted with 400 ml of water and filtered. The insoluble product was washed on the filter with water and was then recrystallized from ethanol to give 7 - chloro - 2 - isopropylamino - 5 - phenyl - 3H - benzdiaz[1,4]epine 4-oxide.

EXAMPLE 8

A mixture of 10 g (0.348 mol) of 7-chloro - 5 - phenyl - 1,3 - dihydro - 2H-benzdiaz[1,4]epinone - (2) 4-oxide and 15 ml of piperidine in 400 ml of dry tetrahydro-furan was cooled as in Example 2 hereinbefore and then treated with a solution of 4.8 g (0.025 mol) of titanium tetrachloride in

100 ml of dry benzene (addition time 20 minutes). The mixture was allowed to warm to room temperature and stirred overnight. 10 ml of water were added and the mixture was filtered. Solvents were removed and the residue was stirred in 50 ml of ethanol and then shaken thoroughly with 100 ml of 0.5-N sodium hydroxide solution. The mixture was filtered and the precipitate was washed with water. Recrystallization from a mixture of dichloro-methane and hexane gave 7-chloro-5 - phenyl - 2 - piperidino - 3H - benzdiaz[1,4]epine 4-oxide as pale yellow prisms.

EXAMPLE 9

A solution of 10 g (0.0348 mol) of 7-chloro - 5 - phenyl - 1,3 - dihydro - 2H-benzdiaz[1,4]epinone - (2) 4-oxide in 400 ml of dry tetrahydro-furan was stirred in a three-neck round-bottom flask fitted with a 'dry ice' condenser and dropping funnel. The flask was cooled externally with an ice-bath. Ammonia gas was bubbled into the solution until liquid ammonia was rapidly condensing on the 'dry ice' finger. A solution of 4.8 g (0.025 mol) of titanium tetrachloride in 100 ml of benzene was next added dropwise (addition time 20 minutes). The cooling bath was removed and the mixture was allowed to reach room temperature. After stirring overnight, 10 ml of water were added and the solution was filtered. Removal of solvents gave a residue which was slurried with 50 ml of ethanol and then shaken vigorously with 100 ml of 0.5-N sodium hydroxide solution. The resulting mixture was diluted with 400 ml of water and the precipitate was removed by filtration and washed with water. Recrystallization from methanol gave 2-amino - 7 - chloro - 5 - phenyl - 3H - benzdiaz[1,4]epine 4-oxide.

EXAMPLE 10

To a suspension of 25 g (0.0916 mol) of 7 - chloro - 5 - phenyl - 1,3,4,5 - tetrahydro - 2H - benzdiaz[1,4]epinone - (2) in 300 ml of dry tetrahydro-furan (under a nitrogen atmosphere) was added a solution of 30 g of methyl amine in 300 ml of dry tetrahydro-furan. The resulting mixture was cooled in an ice-bath, and a solution of 12 g (0.0632 mol) of titanium tetrachloride in 100 ml of benzene was added thereto with stirring over a period of 10 minutes. The ice-bath was removed and after 4 hours 20 ml of water were added. The solution was filtered, the precipitate was washed with tetrahydro-furan and the combined filtrates were evaporated to dryness. The oil was crystallized from methanol/ether to yield solid 7 - chloro - 2 - methylamino - 5 - phenyl - 4,5 - dihydro - 3H - benzdiaz[1,4]epine as white plates of melting point and mixed melting point 175°—180°C.

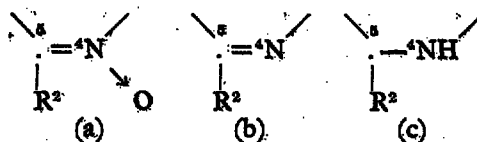
The foregoing 7 - chloro - 2 - methylamino-

5 - phenyl - 4,5 - dihydro - 3H - benzdiaz[1,4]epine was converted into 7 - chloro - 2 - methylamino - 5 - phenyl - 3H - benzdiaz[1,4]epine as follows:

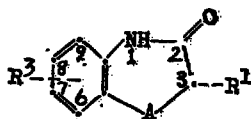
- 5 To a solution of 2.0 g (0.007 mol) of 7-chloro - 2 - methylamino - 5 - phenyl - 4,5-dihydro - 3H - benzdiaz[1,4]epine in 50 ml of dry benzene was added a solution of 1.2 g (0.007 mol) of diethyl azodicarboxylate in 10 ml of dry benzene. The resulting solution was heated at reflux for 1 hour, cooled, extracted with 50 ml of dilute ammonium hydroxide and filtered to give 7 - chloro - 2 - methylamino - 5 - phenyl - 3H - benzdiaz[1,4]epine as white prisms.

WHAT WE CLAIM IS:—

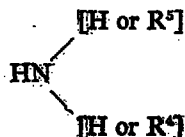
1. A process for the manufacture of 2-amino - benzdiaz[1,4]epines of the general formula



in which R² represents the phenyl group or a (lower alkyl)-phenyl, nitro-phenyl, halo-phenyl or pyridyl group, which process comprises reacting a benzdiaz[1,4]epinone - (2) of the general formula

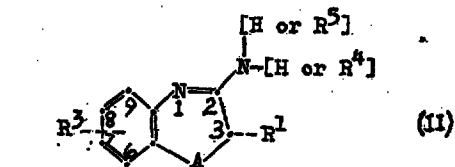


(wherein R¹, R³, A and the broken lines have the significance given earlier in this claim) with a compound of the general formula



(wherein R⁴ and R⁵ have the significance given earlier in this claim); the reaction being carried out in the presence of an acid catalyst where a benzdiaz[1,4]epinone - (2) starting material is used in which A represents a grouping of formula (a) given earlier in this claim and/or R³ is present and represents the nitro group.

2. A process as set forth in claim 1, wherein a benzdiaz[1,4]epinone - (2) starting material is used in which A represents a grouping of formula (b) or (c) given in claim 1 and R³ (when present) represents a halogen atom or the trifluoromethyl group or a lower-alkyl group and wherein the reaction is carried out in the presence of an acid catalyst.



, wherein R¹ represents a lower-alkyl or (lower alkoxy)-(lower alkyl group, R³ represents a halogen atom or the nitro or trifluoromethyl group or a lower-alkyl group, R⁴ and R⁵ each represent a lower-alkyl group or, taken together with the nitrogen atom to which they are attached represent a five-membered or six-membered heterocyclic ring, the broken lines denote that the substituents attached thereby are optional and A represents a grouping of the formula

ried out in the presence of an acid catalyst.

3. A process as set forth in claim 1 or claim 2, wherein said acid catalyst is *para*-toluene-sulphonic acid.

4. A process as set forth in claim 1 or claim 2 wherein said acid catalyst is titanium tetrachloride.

5. A process as set forth in claim 1 or claim 2, wherein said acid catalyst is aluminium chloride.

6. A process as set forth in any one of claims 1 to 5 inclusive, wherein the reaction is carried out in an inert organic solvent.

7. A process as set forth in claim 6, wherein said inert organic solvent is tetrahydrofuran.

8. A process as set forth in claim 1, wherein the reaction is carried out in N,N-dimethylformamide in the absence of an acid catalyst.

9. A process as set forth in claim 1, wherein the reaction is carried out at a temperature of from about 100°C to 175°C and at a pressure of from 50 to 75 atmospheres in the absence of an acid catalyst.

10. A process as set forth in any one of claims 1 to 9 inclusive, wherein a benzdiaz[1,4]epinone - (2) starting material is used in which R¹ is absent and R³ is present and represents a chlorine atom in the 7-position of the molecule.

11. A process as set forth in claim 10, wherein the grouping A in said benzdiaz[1,4]epinone - (2) has the formula (a) given in claim 1 in which R² represents the phenyl group.

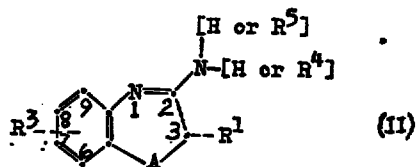
12. A process as set forth in any one of

5 - phenyl - 4,5 - dihydro - 3H - benzdia-
[1,4]epine was converted into 7 - chloro-
2 - methylamino - 5 - phenyl - 3H - benz-
diaz[1,4]epine as follows:

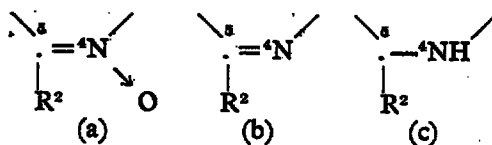
- 5 To a solution of 2.0 g (0.007 mol) of 7-
chloro - 2 - methylamino - 5 - phenyl - 4,5-
dihydro - 3H - benzdia[1,4]epine in 50 ml
10 of dry benzene was added a solution of 1.2
g (0.007 mol) of diethyl azodicarboxylate in
10 ml of dry benzene. The resulting solu-
tion was heated at reflux for 1 hour, cooled,
extracted with 50 ml of dilute ammonium
hydroxide and filtered to give 7 - chloro-
2 - methylamino - 5 - phenyl - 3H - benz-
15 diaz[1,4]epine as white prisms.

WHAT WE CLAIM IS:—

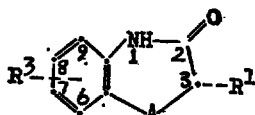
1. A process for the manufacture of 2-
amino - benzdia[1,4]epines of the general
formula



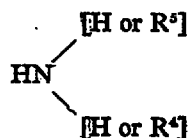
, wherein R¹ represents a lower-alkyl or
(lower alkoxy)-(lower alkyl group, R³ repre-
sents a halogen atom or the nitro or trifluoro-
methyl group or a lower-alkyl group, R⁴ and
R⁵ each represent a lower-alkyl group or,
taken together with the nitrogen atom to
which they are attached represent a five-
membered or six-membered heterocyclic ring,
the broken lines denote that the substituents
attached thereby are optional and A represents
a grouping of the formula



- 35 in which R² represents the phenyl group or a
(lower alkyl)-phenyl, nitro-phenyl, halo-
phenyl or pyridyl group, which process com-
prises reacting a benzdia[1,4]epinone - (2)
of the general formula



- 40 (wherein R¹, R², A and the broken lines have
the significance given earlier in this claim)
with a compound of the general formula



- 45 (wherein R⁴ and R⁵ have the significance
given earlier in this claim); the reaction being
carried out in the presence of an acid catalyst
where a benzdia[1,4]epinone - (2) starting
material is used in which A represents a
grouping of formula (a) given earlier in this
claim and/or R³ is present and represents the
50 nitro group.

2. A process as set forth in claim 1, where-
in a benzdia[1,4]epinone - (2) starting
material is used in which A represents a
grouping of formula (b) or (c) given in claim
1 and R³ (when present) represents a halogen
55 atom or the trifluoromethyl group or a lower-
alkyl group and wherein the reaction is car-

ried out in the presence of an acid catalyst.

3. A process as set forth in claim 1 or
claim 2, wherein said acid catalyst is *para*-
60 toluene-sulphonic acid.

4. A process as set forth in claim 1 or
claim 2 wherein said acid catalyst is titanium
tetrachloride.

5. A process as set forth in claim 1 or
claim 2, wherein said acid catalyst is alumi-
65 nium chloride.

6. A process as set forth in any one of
claims 1 to 5 inclusive, wherein the reaction
is carried out in an inert organic solvent.

7. A process as set forth in claim 6, where-
in said inert organic solvent is tetrahydro-
furan.

8. A process as set forth in claim 1, where-
in the reaction is carried out in N,N-dimethyl-
formamide in the absence of an acid catalyst.

9. A process as set forth in claim 1, wherein
the reaction is carried out at a temperature of
from about 100°C to 175°C and at a pres-
sure of from 50 to 75 atmospheres in the
absence of an acid catalyst.

10. A process as set forth in any one of
claims 1 to 9 inclusive, wherein a benzdia-
[1,4]epinone - (2) starting material is used
in which R¹ is absent and R³ is present and
represents a chlorine atom in the 7-position
of the molecule.

11. A process as set forth in claim 10,
wherein the grouping A in said benzdia-
[1,4]epinone - (2) has the formula (a) given
in claim 1 in which R² represents the phenyl
90 group.

12. A process as set forth in any one of



claims 1 to 11 inclusive, wherein the benz-
diaz[1,4]epinone - (2) starting material is
reacted with methyl amine.

5 13. A process as set forth in any one of
claims 1 to 11 inclusive, wherein the benz-
diaz[1,4]epinone - (2) starting material is
reacted with pyrrolidine or piperidine.

10 14. A process as set forth in claim 1, sub-
stantially as described with reference to the
foregoing Examples.

15. 2 - Amino - benzdiaz[1,4]epines as
formulated in claim 1, when manufactured
by the process claimed in any one of the
preceding claims.

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