

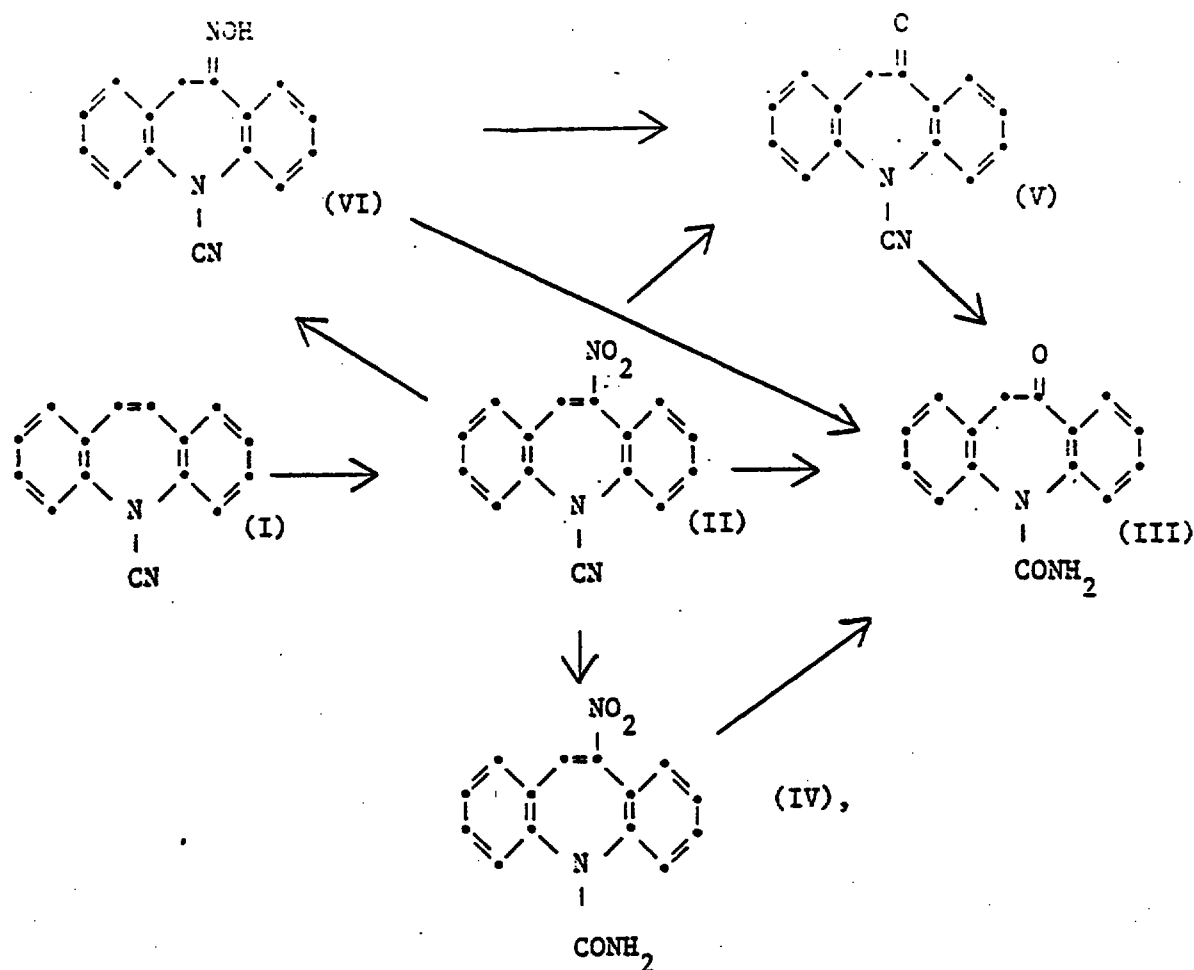
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Process for the preparation of an oxo compound and novel
intermediates required therefor

The invention relates to a novel and technically progressive process for the preparation of 5-carbamyl-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine of the formula III, which is characterized in that 5-cyano-5H-dibenzo[b,f]azepine of the formula I is nitrated, the resulting 5-cyano-10-nitro-5H-dibenzo[b,f]azepine of the formula II is hydrolysed to 5-carbamyl-10-nitro-5H-dibenzo[b,f]azepine of the formula IV, the 10-nitro group in the latter is reduced, the reduction product is hydrolysed and the resulting end product of the formula III is isolated in the pure form.

The process according to the invention is illustrated by the reaction scheme which follows:



German Offenlegungsschrift 2,011,087 has disclosed a process for the preparation of 5-carbamyl-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine by hydrolysis of 10-methoxy-5H-dibenzo[b,f]azepine-5-carboxamide by means of aqueous mineral acids. The accessibility of this starting material is indicated in Belgian Patent Specification No. 597,793, according to which, for example, 5-acetyl-5H-dibenzo[b,f]azepine is brominated to 5-acetyl-10,11-dihydro-10,11-dibromo-5H-dibenzo[b,f]azepine, the latter is converted to 5-acetyl-10-bromo-5H-dibenzo[b,f]azepine and, from the latter, 10-methoxy-5H-dibenzo[b,f]azepine is prepared. This is then converted by treatment with phosgene to the corresponding carbonyl chloride, from which 10-methoxy-5H-dibenzo[b,f]azepine-5-carboxamide is obtained by reaction with ammonia. Compared with this preparation process which is complicated to carry out because of its relatively large number of

intermediate stages and, moreover, is disadvantageous because of its high consumption of bromine, which serves only for the temporary conversion of intermediates, the process according to the invention comprises only a few process steps, which can be carried out in a simple and clear manner while avoiding expensive reagents and, moreover, lead in high yields to the end product of the formula III, which is obtained in excellent purity.

The nitration, according to the invention, of the compound I to give the compound of the formula II is carried out by means of conventional nitrating agents, for example dinitrogen trioxide (N_2O_3), if appropriate mixed with oxygen, for example air, or by means of dinitrogen tetroxide (N_2O_4) or mixtures of such compounds, or also, in addition, by means of nitric acid. The reaction is carried out in a suitable solvent, especially a solvent which remains stable under the nitration conditions and does not lead to undesired reactions with the nitrating agent. These are especially lower alkanecarboxylic or halogenated lower alkanecarboxylic acids each having up to 4 carbon atoms, for example acetic acid, propionic acid, n-butyric acid or isobutyric acid, and also, for example, trifluoroacetic or trichloroacetic acid, if appropriate mixed with water, or their anhydrides, for example acetic, propionic, n-butyric, isobutyric or trifluoroacetic anhydride, or mixtures of such carboxylic acids with the corresponding anhydrides. According to a preferred embodiment of the process according to the invention, the anhydrides of the said lower alkanecarboxylic acids, for example acetic anhydride, if appropriate mixed with a lower alkanecarboxylic acid, for example acetic acid, are used as the solvent.

The ratio of starting material to the quantity of solvent used (weight/volume) can vary within wide limits. Advantageously, a starting material/solvent ratio within the range from 1:3 to 1:30 is used. The reaction temperature is in the range of about 0-120°, especially 40-80°.

According to Chemical Reviews 36, (1945) pages 211-212, the reaction of styrene with nitrogen trioxide gives a

mixture of nitroso and nitro compounds. Moreover, the reaction product of styrene with nitrogen trioxide is said to give 1-nitro-2-phenylethylene, if the reaction product is subjected to steam distillation. It is also stated there that the reaction of stilbene with nitrogen tetroxide leads to 1,2-dinitro-1,2-diphenyl ether. According to page 218 of the same literature reference, the reaction of cyclohexene with dry nitrogen tetroxide in cold petroleum ether gives the corresponding bis-nitroso-nitro derivative and oily by-products.

In J.Org.Chem. 28, (1963), pages 125-129, it is stated that the reaction product of an olefin with dinitrogen tetroxide essentially contains nitro and nitroso groups, the conversion into a nitro-olefin compound requiring an addition of triethylamine. Thus, for example, cyclooctene is reacted with dinitrogen tetroxide and the reaction product is then treated with triethylamine, whereupon 1-nitrocyclooctene is obtained.

By contrast, it has been found, surprisingly, that additional operations, for example steam distillation or treatment of the reaction mixture with triethylamine, are unnecessary in the nitration according to the invention, and the working-up, which can be carried out in an extremely simple manner, always leads to good yields of the nitro compound of the formula II. This compound is novel and has not been described in the literature.

According to the invention, this is followed by the conversion of the compound of the formula II into the compound of the formula III. For this purpose, the cyano group is first converted by hydrolysis into the carboxamide group. Only those hydrolysis methods can be used for this conversion which do not adversely affect the 10-nitro group on the double bond. Advantageously, the hydrolysis is carried out by means of acidic agents, for example mineral acids, such as sulfuric acid, hydrochloric acid and, if appropriate, also formic acid. Preferably, boron trifluoride is used in an equimolar amount or in a small excess as a solution in a lower alkanecarboxylic or halogenated lower alkanecarboxylic



acid, for example such an acid of the above mentioned type, such as acetic acid or trifluoroacetic acid, it also being possible to use defined compounds of boron trifluoride with one of the said carboxylic acids such as acetic acid, for example of the formula $\text{BF}_3 \cdot 2\text{CH}_3\text{COOH}$. If necessary for carrying out the hydrolysis, a further inert solvent, for example a solvent of aromatic character, such as e.g. chlorobenzene, is added to the reaction mixture. This is followed by a treatment of the reaction mixture, or of the resulting addition compound, isolated in the pure form if desired, of the compound of the formula IV with BF_3 , with hydrolysing agents, for example water, whereupon 5-carbamyl-10-nitro-5H-dibenzo-[b,f]azepine of the formula IV is obtained in the pure form.

The hydrolysis of a nitrile group to the carboxamide group by means of boron trifluoride in the presence of acetic acid is known from J.org.Chemistry 20, (1955), 1448. The procedure described there requires high temperatures, a large excess of boron trifluoride and the use of aqueous acetic acid which, together with boron trifluoride, forms extremely corrosive solutions, so that its industrial use, especially at high temperatures, is restricted and is applicable only under special conditions in industrial equipment.

By contrast, the process according to the invention allows the use of boron trifluoride in only equimolar quantities, or a slight excess, in anhydrous solvents at room temperature. A further advantage is that a defined addition compound of boron trifluoride with the hydrolysis product of the formula IV can be isolated in high purity and almost quantitative yield even from severely contaminated reaction mixtures and can be converted by treatment with water into the pure hydrolysis product of the formula IV.

According to the invention, this is followed by the conversion of the resulting intermediate of the formula IV, if appropriate without isolation of the latter in the pure form, into the end product of the formula III. For this purpose, the compound of the formula IV is subjected to reducing conditions, e.g. the action of catalytically activated hydrogen, such as hydrogen in the presence of a hydrogenation

catalyst, e.g. a nickel or noble metal catalyst, for example Raney nickel or a palladium-on-carbon catalyst, in a suitable solvent, e.g. a lower alkanol having up to 4 carbon atoms, such as methanol or ethanol, or of nascent hydrogen, for example by means of a suitable metal, such as zinc which may be amalgamated, and especially iron, in an acid, for example a mineral acid, such as dilute sulfuric acid, or a carboxylic acid, such as a lower alkanecarboxylic acid, for example one of those mentioned above, such as acetic acid, or of a chemical reducing agent, for example tin(II) chloride. $2\text{H}_2\text{O}$, the reduction product obtained is hydrolysed in the same reaction batch, for example by means of water, and the end product of the formula III is isolated in the pure form. This product is obtained sometimes in very good yield and excellent purity.

However, the procedure can also be such that the compound of the formula II is hydrolysed by means of acidic agents, for example as indicated, such as, for example, boron trifluoride in acetic acid, if appropriate in the presence of a further inert solvent, e.g. a solvent of aromatic character, such as chlorobenzene, in the presence of water and the compound of the formula IV contained in the reaction mixture is then reduced, without isolation, e.g. as indicated, for example by means of catalytically activated hydrogen, such as hydrogen in the presence of a hydrogenation catalyst, such as a nickel or noble metal catalyst, for example Raney nickel, or a palladium-on-carbon catalyst, or by means of nascent hydrogen, e.g. as indicated, for example iron in an acid, e.g. a mineral acid, for example aqueous hydrochloric acid, or a lower alkanecarboxylic or halogenated lower alkanecarboxylic acid, e.g. as indicated, for example acetic acid, or the BF_3 /acetic acid/water mixture already present in the reaction batch. The reduction product present in the reaction mixture, without being isolated, is hydrolysed subsequently, or even simultaneously, by means of an acidic agent, e.g. as indicated, for example by means of an aqueous acid, e.g. the BF_3 /acetic acid/water mixture present in the reaction mixture, and the resulting end product of the formula III is isolated in the pure form.

The compound of the formula IV and its adduct with boron trifluoride is novel and has not been described in the literature.

A modification of the process according to the invention for the preparation of the end product of the formula III is characterized in that the 10-nitro group in the compound of the formula II is reduced, the reduction product is hydrolysed, the resulting 5-cyano-10-oxo-10,11-dihydro-5H-dibenzo[b,f]-azepine of the formula V is hydrolysed and the resulting end product of the formula III is isolated in the pure form. This variant of the process according to the invention comprises converting the compound of the formula II into that of the formula V and preparing the end product of the formula III from the latter. Accordingly, the nitro group in the 5-cyano-10-nitro-5H-dibenzo[b,f]azepine of the formula II is reduced by one of the methods described above and the intermediate formed in the reaction mixture is converted by hydrolysis into the compound of the formula V. The reduction can be carried out, as stated above, for example by means of catalytically activated hydrogen, such as hydrogen in the presence of a hydrogenation catalyst, e.g. a nickel or noble metal catalyst, for example Raney nickel or a palladium-on-carbon catalyst, in a suitable solvent, for example a lower alkanol having up to 4 carbon atoms, for example methanol or ethanol, or by means of nascent hydrogen, e.g. by means of a suitable metal, such as zinc which may be amalgamated, or especially iron, in an acid, for example a mineral acid, such as dilute sulfuric acid or concentrated hydrochloric acid, or a lower alkanecarboxylic acid, e.g. one of those mentioned above, for example acetic acid, or by means of a chemical reducing agent, such as e.g. tin(II) chloride. $2H_2O$. In this case, additional solvents, e.g. a lower alkanol having 1 to 4 carbon atoms, for example ethanol, or a lower alkoxy-lower alkanol having up to 4 carbon atoms in each case in the lower alkoxy and lower alkanol moieties, for example 2-methoxy- or 2-ethoxy-ethanol, and/or a solvent of aromatic character, for example a benzene which may be lower-alkylated, such as methylated, or halogenated,

such as chlorinated, such as benzene, toluene or chlorobenzene, may be used. The reaction temperature is in a range from 10 to 100°, preferably from 30-70°. Appropriately after removal of insoluble matter, the reaction mixture is then subjected to hydrolysis, for example the action of water, and, after working up, 5-cyano-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine of the formula V is isolated in the pure form, being obtained in good yields and excellent purity. This compound is novel and has not been described in the literature. In a preferred embodiment of the conversion of the compound of the formula II into that of the formula V, as described, the solvent used for the reduction by means of a metal, for example iron, as described above, holds the metal salts formed, for example iron salts, in solution and thus largely prevents the formation of a precipitate, say in the form of a sludge, which is difficult to filter. Examples of such solvents are highly polar organic solvents, e.g. lower alkyl ethers of ethylene glycol, wherein lower alkyl has up to 4 carbon atoms and represents, for example, methyl or ethyl, and is accordingly, for example, ethylene glycol monoethyl ester (sic).

This is followed by the conversion of the cyano group in the compound of the formula V by hydrolysis into the carboxamide group of the end product of the formula III. This conversion can be effected by means of basic or acidic agents. Basic agents for this purpose are, for example, the oxides or hydroxides of alkaline earth or alkali metals, for example magnesium or calcium hydroxide, and also, for example, sodium hydroxide, if appropriate in the presence of a peroxide, such as hydrogen peroxide, or an alkali metal bicarbonate, such as sodium bicarbonate, mixed with hydrogen peroxide, whereas acidic agents are, for example, mineral acids, such as sulfuric acid or polyphosphoric acid, and also lower alkanecarboxylic or halogenated lower alkanecarboxylic acids having up to 4 carbon atoms, for example formic or acetic acid and trichloroacetic or trifluoroacetic acid mixed with mineral acids, for example concentrated sulfuric acid. Further acidic agents are Lewis acids, for example boron

trifluoride, which can be present as a solution in a lower alkanecarboxylic acid of the type described above, such as acetic acid, or as a defined compound, for example of the formula $\text{BF}_3 \cdot 2 \text{CH}_3\text{COOH}$. If necessary, a further solvent is also added to the reaction mixture, for example a solvent of aromatic character, such as e.g. chlorobenzene. The reaction temperatures are in the range from -5 to $+150^\circ$, preferably $0-40^\circ$.

In a variant of this process, for preparing the intermediate of the formula V, the 10-nitro group in the compound of the formula II is reduced, the resulting 5-cyano-10-isonitroso-10,11-dihydro-5H-dibenzo[b,f]azepine of the formula VI is isolated in the pure form, the latter is hydrolysed to 5-cyano-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine of the formula V and the latter is isolated in the pure form. This process variant is characterized in that the nitro group in the compound of the formula II, is reduced to the 10-isonitroso compound corresponding to the formula VI, e.g. as indicated, for example by means of zinc dust in an acid, e.g. a lower alkanecarboxylic acid of the type indicated, such as acetic acid, if appropriate in the presence of an inert solvent, such as a lower alkanol of the type indicated, for example ethanol, or by means of hydrogen in the presence of a hydrogenation catalyst, such as a noble metal catalyst, for example a palladium-on-carbon catalyst in a suitable solvent, e.g. a solvent of aromatic character, for example pyridine, and the resulting 5-cyano-10-isonitroso-10,11-dihydro-5H-dibenzo[b,f]azepine of the formula VI is isolated in the pure form. The latter is obtained in a good yield and excellent purity. The compound is novel and has not been described in the literature. The compound of the formula VI is then converted by hydrolysis into the compound of the formula V by hydrolysing it, especially by means of acidic agents, e.g. as indicated, such as an acid, e.g. a mineral acid, for example hydrochloric acid or sulfuric acid, or a lower alkanecarboxylic or halogenated lower alkanecarboxylic acid, for example acetic acid or trifluoroacetic acid in the presence of water. If appropriate, an additional solvent is

also added to the reaction mixture, for example a solvent of aromatic character such as, for example, a benzene which may be substituted by lower alkyl having up to 4 carbon atoms, such as e.g. methyl, or by halogen, such as chlorine, such as benzene, toluene or chlorobenzene, or a lower alkanecarboxylic acid, e.g. of the type indicated, such as, for example, acetic acid, or a lower alkanol having up to 4 carbon atoms, for example ethanol, or mixtures of such solvents are used. The compound of the formula V is isolated in the pure form from the reaction mixture and is then converted, as indicated above, into the end product of the formula III.

A further modification of the process according to the invention for the preparation of the end product of the formula III is characterized in that the compound of the formula VI is hydrolysed and the resulting end product of the formula III is isolated in the pure form. According to this process variant, the 5-cyano group as well as the 10-isonitroso group in the compound of the formula VI are hydrolysed in the same reaction batch. Thus, for example, the 10-isonitroso group in the compound of the formula VI can be converted into the 10-oxo group by means of acidic agents, e.g. as indicated, for example by means of a mineral acid, such as hydrochloric acid, and the reaction mixture can then be hydrolysed, for example as described, with an acid, for example a mineral acid, such as sulfuric acid or polyphosphoric acid, or a carboxylic acid, for example a lower alkanecarboxylic or halogenated lower alkanecarboxylic acid, such as acetic acid or trifluoroacetic acid, or a Lewis acid, such as boron trifluoride in the presence of a carboxylic acid, for example acetic acid, or mixtures of such acids, if appropriate in the presence of a further inert solvent, such as a lower alkanol having up to 5 carbon atoms, such as methanol or ethanol, in the presence of water and the end product of the formula III can be isolated in the pure form.

The invention relates specifically to the process described in the examples.

Novel intermediates, in particular those of the formulae II, IV, V and VI also represent a subject of the

invention. The examples which follow serve to illustrate the invention; temperatures are given in degrees Celsius.

Example 1: 6.0 g (0.027 mol) of 5-cyano-5H-dibenzo[b,f]azepine are dissolved in a mixture of 80 ml of acetic anhydride and 20 ml of acetic acid. The mixture is heated to 50°, and the solution of 5.6 g (0.08 mol) of sodium nitrite in 10 ml of water is added dropwise in the course of 1 1/2 hours, the temperature not being allowed to exceed 55°.

The mixture is held for a further 2 hours at 50° and the solvent is then distilled off under a reduced pressure and at a bath temperature of 50°.

The residue is digested with twice 100 ml of ice water and taken up in 80 ml of ethanol.

After standing for several hours at 0°, the precipitated yellow crystals are filtered off with suction and washed with a little ethanol.

The 5-cyano-10-nitro-5H-dibenzo[b,f]azepine obtained melts at 175-176° with decomposition.

Yield: 5.2 g, 72% of theory.

The analytical and spectroscopic data are consistent with the assumed structure.

Example 2: 6.5 g (0.03 mol) of 5-cyano-5H-dibenzo[b,f]azepine are dissolved in a mixture of 100 ml of acetic acid and 100 ml of acetic anhydride. The mixture is heated to 40° and 6.2 g (0.09 mol) of sodium nitrite are added in the course of 45 minutes, a slow air stream being passed through the solution. The temperature rises to 55° without further heating and is held at 55° for a further hour after the end of the nitrite addition.

The solvent is distilled off in vacuo at a bath temperature of 50°, the residue is taken up in 300 ml of toluene, the mixture is extracted several times by shaking with water in order to remove the inorganic constituents, and the toluene is distilled off in vacuo down to 40 ml.

The precipitated yellow product is filtered off with suction and washed with a little toluene; it is identical to 5-cyano-10-nitro-5H-dibenzo[b,f]azepine according to Example 1. Yield: 6.1 g; 77.5% of theory.

Example 3: 19.6 g (0.09 mol) of 5-cyano-5H-dibenzo[b,f]azepine are reacted, as in Example 2, in 300 ml of acetic acid and 300 ml of acetic anhydride with 18.6 g (0.27 mol) of sodium nitrite. The red-yellow syrup remaining after evaporation of the solvent is thoroughly stirred with 300 ml of water until it has completely solidified. The solid is filtered off with suction, washed with water until the filtrate shows a neutral reaction, and dried in vacuo.

The same crude product is obtained when the above reaction is carried out at a temperature of 80-85°.

The crude product obtained is suitable for further reactions, but it can also be purified as follows:

1. 23.7 g of crude product are recrystallized from isopropanol and give a yellow crystalline material which is identical to 5-cyano-10-nitro-5H-dibenzo[b,f]azepine according to Example 1. Yield: 18.0 g, 76.2% of theory.
2. An end product identical with respect to yield and quality is obtained by digesting the crude product with acetic acid.

Example 4: Nitrous gases (N_2O_3) are generated in a flask by slow dropwise addition of 20% sulfuric acid to a concentrated aqueous solution of 40.0 g (0.58 mol) of sodium nitrite and passed by means of a slow air stream into the solution, heated to 55°, of 10.9 g (0.05 mol) of 5-cyano-5H-dibenzo[b,f]azepine in 100 ml of toluene. The atmospheric oxygen introduced is here kept so low that no explosive toluene vapour/oxygen mixtures can form. The introduction is continued until the starting material has been fully converted (DC check), the N_2O_3 excess is expelled by a vigorous nitrogen stream and the toluene is evaporated under a reduced pressure at a temperature of 40°. The remaining red syrup is taken up in 100 ml of isopropanol. After standing for several hours at 5°, the crystals are filtered off with suction and washed with a little isopropanol. The 5-cyano-10-nitro-5H-dibenzo[b,f]azepine obtained is identical to the product according to Example 1.

Yield: 9.4 g, 71.7% of theory.

Example 5: Analogously to the procedure described in Example

4, nitrous gases are generated in a flask from 55.0 g (0.8 mol) of sodium nitrite and are transferred by means of a slow air stream into the solution, held at 50°, of 10.9 g (0.05 mol) of 5-cyano-5H-dibenzo[b,f]azepine in 110 ml of acetic acid and 110 ml of acetic anhydride. The conversion is complete after 3 hours; the solvent is then distilled off in vacuo at a bath temperature of 50°, the residue is taken up in 50 ml of isopropanol and the material which has crystallized out is filtered off with suction after standing for several hours at 20°. This gives 5-cyano-10-nitro-5H-dibenzo[b,f]azepine which is identical to the product obtained according to Example 1.

Yield: 9.5 g, 72.5% of theory.

Example 6: Analogously to the procedure described in Example 4, nitrous gases are generated in a flask from 30.0 g (0.43 mol) of sodium nitrite and transferred by means of a slow air stream into the solution, held at 55°, of 10.9 g (0.05 mol) of 5-cyano-5H-dibenzo[b,f]azepine in 110 ml of acetic anhydride. After complete conversion (DC check), the reaction mixture is evaporated in vacuo at a bath temperature of 50° and the residue is taken up in 20 ml of acetic acid. The mixture is left to stand for 2 hours at 20°, the crystals are filtered off with suction and washed with a little acetic acid. This gives 5-cyano-10-nitro-5H-dibenzo[b,f]azepine which is identical to the product obtained according to Example 1.

Yield: 9.1 g, 69.4% of theory.

Example 7: 10.0 g (0.046 mol) of 5-cyano-5H-dibenzo[b,f]azepine are dissolved in 100 ml of toluene at 55°. 5.0 g (0.054 mol) of N₂O₄ from a cylinder are slowly passed with stirring into the solution, the temperature rising up to 60°, and the reaction mixture is then held at this temperature until all starting material has been converted (DC check), then cooled to 20° and the toluene phase is dried over sodium sulfate. After evaporation in vacuo, a red oil is obtained which is taken up in 50 ml of isopropanol. After standing for several hours at 20°, the crystals are filtered off with suction and washed with a little isopropanol. The resulting 5-cyano-10-nitro

5H-dibenzo[b,f]azepine is identical to the product obtained according to Example 1.

Yield: 6.7 g, 56% of theory.

Example 8: 43.6 g (0.2 mol) of 5-cyano-5H-dibenzo[b,f]azepine are dissolved in 250 ml of acetic acid at 55° and N₂O₄ from a cylinder is passed for 2 1/2 hours with stirring into the solution, the temperature being maintained at 55° by occasional cooling. The end of the reaction is detected by a green coloration of the solution (excess N₂O₄) and by a DC check. The mixture is allowed to cool, stirred at room temperature for several further hours, and the precipitate which has deposited is then filtered off and washed with a little acetic acid. By concentrating the filtrate and taking up in acetonitrile, a second lot of crystals of 5-cyano-10-nitro-5H-dibenzo[b,f]azepine is obtained, which is identical to the product obtained according to Example 1.

Total yield: 19.5 g, 37% of theory.

Example 9: 43.6 g (0.2 mol) of 5-cyano-5H-dibenzo[b,f]azepine are dissolved in 250 ml of acetic acid at 55°. 60 ml of water are added dropwise to the solution until it starts to turn cloudy, and N₂O₄ from a cylinder is then passed in slowly until starting material is no longer detectable by DC. The mixture is cooled to 5° and stirred for 2 hours at this temperature, and the crystals are then filtered off and washed with 80% acetic acid. This gives 5-cyano-10-nitro-5H-dibenzo[b,f]azepine which is identical to the product obtained according to Example 1.

Yield: 42.1 g, 80% of theory.

Example 10: 43.6 g (0.2 mol) of 5-cyano-5H-dibenzo[b,f]azepine are dissolved in 175 ml of acetic acid at 55°. At this temperature, N₂O₄ from a cylinder is passed into the solution until all the starting material has been converted (DC check) and the product precipitates. 16.4 g (0.2 mol) of sodium acetate are then added in portions with occasional cooling and the temperature is maintained at 50-55°. The mixture is then stirred for 3 hours at room temperature and filtered, and the crystals are rinsed with acetic acid and water. This gives 5-cyano-10-nitro-5H-dibenzo[b,f]azepine

which is identical to the product obtained according to Example 1.

Yield: 36.1 g, 68.6% of theory.

Example 11: 21.8 g (0.1 mol) of 5-cyano-5H-dibenzo[b,f]azepine are dissolved in 110 ml of acetic anhydride at 55°. 10.0 g (0.1 mol) of N₂O₄ from a cylinder are passed into this solution so slowly that no dark brown gases escape, and the temperature is maintained at 55° by occasional cooling. After the end of the reaction, a vigorous stream of nitrogen is passed through for one hour, and the mixture is then cooled to -20° and held for 2 hours at this temperature. The yellow crystals are then filtered off with suction and rinsed with a little acetonitrile, whereupon 5-cyano-10-nitro-5H-dibenzo[b,f]azepine which is identical to the product obtained according to Example 1 is obtained. The filtrate is evaporated in vacuo at a bath temperature of 50° to give a red oil. This is taken up in 10 ml of acetonitrile, the mixture is left to stand for 2 hours at 5° and the second lot of crystals is filtered off with suction.

Total yield: 19.5 g, 74.1% of theory.

Example 12: 21.8 g (0.1 mol) of 5-cyano-5H-dibenzo[b,f]azepine are dissolved in 140 ml of acetic anhydride at 50°. 12.0 g (0.13 mol) of N₂O₄ from a cylinder are slowly passed into this solution with stirring, the temperature being maintained between 50 and 55° by cooling. The reaction is allowed to continue for one hour, a vigorous stream of nitrogen is then passed through and 60 ml of water are added slowly, the temperature being maintained at 50 to 55° by cooling. The mixture is then cooled to 5°, crystallization is allowed to proceed for one hour and the crystals are filtered off. This gives 5-cyano-10-nitro-5H-dibenzo[b,f]azepine which is identical to the product obtained according to Example 1. The filtrate is evaporated in vacuo and, after taking up the residue in 40 ml of 80% acetic acid, affords a second lot of crystals.

Total yield: 21.5 g, 81.7% of theory.

Example 13: 43.6 (0.2 mol) of 5-cyano-5H-dibenzo[b,f]azepine are dissolved in 430 ml of acetic anhydride. 19.0 g

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(0.206 mol) of N_2O_4 from a cylinder are passed into this solution, with stirring and occasional cooling, so slowly that the temperature does not rise above 25° . After the end of the reaction, the solution takes on a green colour and the product precipitates in a crystalline form. The mixture is stirred for one hour while cooling with ice and passing a vigorous nitrogen stream through and is then filtered and the solid is washed with a little ethyl acetate. This gives 5-cyano-10-nitro-5H-dibenzo[b,f]azepine which is identical to the product obtained according to Example 1. After evaporation in vacuo and taking up with ethyl acetate, a second lot of crystals is obtained from the filtrate.

Total yield: 42.3 g, 80.4% of theory.

Example 14: 35.0 g (0.16 mol) of 5-cyano-5H-dibenzo[b,f]azepine are suspended in 160 ml of acetic anhydride at 20° . A solution of 14.7 g (0.16 mol) of N_2O_4 in 160 ml of acetic anhydride is added dropwise slowly in the course of 5 hours to the solution with stirring, the temperature being maintained between 20 and 25° . After complete conversion of the starting material (DC check), the mixture is cooled to $0-5^\circ$ while passing through a vigorous nitrogen stream for one hour, and the crystalline product is filtered off with suction. This gives 5-cyano-10-nitro-5H-dibenzo[b,f]azepine which is identical to the product obtained according to Example 1.

After evaporation in vacuo to 50 ml, a second lot of crystals is obtained from the filtrate.

Total yield: 34.6 g, 80% of theory.

Example 15: 43.6 g (0.2 mol) of 5-cyano-5H-dibenzo[b,f]azepine are dissolved in 175 ml of acetic anhydride at 50° .

Such a quantity of N_2O_4 from a cylinder is passed into this solution in the course of two hours that the starting material is completely converted and a slight excess of N_2O_4 becomes detectable in the off-gas. The product is allowed to crystallize out at 50° , and 16.5 g (0.2 mol) of sodium acetate are then added in portions. After the evolution of heat has subsided, the mixture is stirred for a further 30 minutes at 50° and then for several hours at room temperature. After filtration

and washing of the crystals with acetic acid and water, this gives 5-cyano-10-nitro-5H-dibenzo[b,f]azepine which is identical to the product obtained according to Example 1. A further 3 g of the compound can be obtained by working up the mother liquor.

Total yield: 44.1 g, 83.8% of theory.

Example 16: 5 ml of concentrated nitric acid (about 64%) are added dropwise at 20° with stirring to a solution of 2.0 g of 5-cyano-5H-dibenzo[b,f]azepine in 20 ml of acetic anhydride, an exothermic reaction proceeding with a colour change to deep yellow. The reaction is allowed to continue for one hour at 20°, 40 ml of water are then added dropwise at 50° and the resinous products precipitated are taken up in ethyl acetate. The residue remaining after washing and evaporation of the organic phase gives, on prolonged standing with acetonitrile, 0.6 g of yellow crystals which contain 78% of 5-cyano-10-nitro-5H-dibenzo[b,f]azepine according to a check by liquid chromatography.

Example 17: 50 ml of a solution of 15% by weight BF₃ in acetic acid (= 0.11 mol) are added at room temperature to a suspension of 26.3 g (0.1 mol) of 5-cyano-10-nitro-5H-dibenzo[b,f]azepine in 100 ml of acetic acid. During the addition, the temperature rises slowly to 34° with complete dissolution of the starting material. 30 ml of water are added at 30° in the course of 5 minutes, which leads to a renewed temperature rise to 37°. At this temperature, 40 g of iron powder are introduced in portions in the course of 20 minutes, the temperature being maintained at 65-70° by occasional cooling. After the exothermic reaction has subsided, stirring is continued for 15 minutes and inorganic material is then filtered off and rinsed three times with a little acetic acid. The total filtrate is added dropwise with good stirring to 1 1/2 l of water, the resulting precipitation is filtered off after stirring for 2 hours and washed with water until neutral. After drying in vacuo at 60°, this gives 5-carbamyl-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine which is identical to authentic material according to the IR spectrum.

Yield: 23.0 g, 91.2% of theory.

Example 18: 50 ml of a solution of 15% by weight of BF_3 in acetic acid are added rapidly to a suspension of 26.3 g (0.1 mol) of 5-cyano-10-nitro-5H-dibenzo[b,f]azepine in a mixture of 260 ml of chlorobenzene and 130 ml of acetic acid, a clear yellow solution being formed with slight warming. The reaction mixture is stirred for 10 minutes and 40 g of iron powder are then added in one portion. With good stirring, 100 ml of water are added dropwise in the course of 30 minutes, the temperature rising to 65° . The temperature is maintained for 2 hours at $60-65^\circ$ by external heating, and the inorganic part is filtered off and rinsed with chlorobenzene and acetic acid. After the chlorobenzene phase has been separated off, it is washed with water until crystallization of the product starts. The mixture is concentrated in vacuo and the residue is taken up in 100 ml of methanol. After filtration with suction and washing with a little methanol, this gives 5-carbamyl-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine which is identical to authentic material according to the IR spectrum.

Yield: 21.4 g, 85% of theory.

Example 19: 50 ml of a solution of 15% by weight BF_3 in acetic acid are allowed to flow rapidly into a suspension of 26.3 g (0.1 mol) of 5-cyano-10-nitro-5H-dibenzo[b,f]azepine in 200 ml of acetic acid. The mixture is stirred for 45 minutes, until dissolution is complete and the moderately exothermic reaction has subsided. 40 g of iron powder are then added at 30° and 100 ml of water are added dropwise slowly in the course of 30 minutes, the temperature rising to 65° . The mixture is stirred for 15 hours at room temperature and heated once more to 60° , and insoluble matter is filtered off and rinsed three times with acetic acid. The filtrate is evaporated in vacuo to a volume of about 100 ml, and 400 ml of water are added dropwise. The mixture is stirred for a further 2 hours and filtered, and the filter cake is washed with water until neutral. After drying in vacuo at 50° , this gives 23.8 g (94.4 % (sic) of theory) of crude product which is recrystallized from 200 ml of 8:2 acetic acid/water. This gives pure 5-carbamyl-10-oxo-10,11-

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dihydro-5H-dibenzo[b,f]azepine which is identical to authentic material according to the IR spectrum.

Yield: 19.7 g, 78% of theory.

Example 20: 31.5 g (0.12 mol) of 5-cyano-10-nitro-5H-dibenzo[b,f]azepine are suspended in 340 ml of chlorobenzene, and 98 ml of a solution of 10% by weight BF_3 in acetic acid are added rapidly. Dissolution takes place with warming to 30° , and shortly afterwards the BF_3 adduct of 5-carbamyl-10-nitro-5H-dibenzo[b,f]azepine starts to precipitate. The product is allowed to crystallize for 2 hours in an ice bath, and the crystals are filtered off with suction and rinsed with petroleum ether. The dry intermediate is dissolved in a mixture of 200 ml of acetic acid and 35 ml of water. In the course of 30 minutes, 50 g of iron powder are added in portions and the temperature is maintained at about 60° by cooling. The mixture is stirred for a further hour at 50° and filtered, and the solid is rinsed with acetic acid. The filtrate is evaporated in vacuo and the residue is taken up in 500 ml of water. The precipitated product is filtered off with suction, washed with water until neutral and dried in vacuo at 50° . This gives 5-carbamyl-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine which is identical to authentic material according to the IR spectrum.

Yield: 26.0 g, 86% of theory.

Example 21: 2 ml of concentrated sulfuric acid are added dropwise to a suspension of 4.0 g (0.015 mol) of 5-cyano-10-nitro-5H-dibenzo[b,f]azepine in 40 ml of acetic acid, and the mixture is stirred for a further 15 hours at room temperature. 100 ml of water are added gradually to the clear solution, the precipitated material is taken up in chloroform, and the chloroform layer is washed with water and evaporated to dryness. After recrystallization of the residue from isopropanol, this gives pure 5-carbamyl-10-nitro-5H-dibenzo[b,f]azepine; melting point $208-212^\circ$, yield 2.2 g, 52.4% of theory. The analytical and spectroscopic data are consistent with the indicated structure.

Example 22: 10 g (0.038 mol) of 5-cyano-10-nitro-5H-dibenzo[b,f]azepine are heated in 100 ml of 98% formic acid for 5



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hours to 90-100°. The mixture is allowed to cool to room temperature and 90 ml of water are then added until the solution starts to turn cloudy, crystallization is allowed to proceed for 15 hours, and the crystals are filtered off, rinsed with water and dried in vacuo at 40°. This gives 5-carbamyl-10-nitro-5H-dibenzo[b,f]azepine which is identical to the product obtained according to Example 21.

Yield: 9.1 g, 85% of theory.

Example 23: 25 ml of a solution of 15% by weight BF₃ in acetic acid are allowed to run rapidly with stirring into a suspension of 13.1 g (0.05 mol) of 5-cyano-10-nitro-5H-dibenzo[b,f]azepine in 130 ml of chlorobenzene, giving a clear brownish solution, the temperature of which rises to 35°. The crystallization which starts after a few minutes is completed by stirring for one hour in an ice bath. The product is filtered off with suction, washed with chlorobenzene and dried in vacuo at 40°, whereupon 19.2 g of 5-carbamyl-10-nitro-5H-dibenzo[b,f]azepine as a BF₃ adduct are obtained. To set the end product free, the BF₃ adduct is slurried in 150 ml of water, the mixture is stirred for 15 hours and filtered with suction, and the filter cake is washed with water until neutral. After drying, this gives 5-carbamyl-10-nitro-5H-dibenzo[b,f]azepine which is identical to the product obtained according to Example 21.

Yield: 13.5 g, 95.7% of theory.

Example 24: 50 ml of a solution of 15% by weight BF₃ in acetic acid are allowed to run into a suspension of 26.3 g (0.1 mol) of 5-cyano-10-nitro-5H-dibenzo[b,f]azepine in 40 ml of acetic acid, and the mixture is stirred until complete dissolution has taken place with self-heating to 40°. 10 ml of water are then added dropwise in the course of 10 minutes, the solution heating to 50°, this temperature is maintained for 10 minutes and a further 300 ml of water are then slowly added dropwise. The resulting crystal suspension is stirred for 1 hour at room temperature and filtered with suction, and the crystals are washed with water until neutral. After drying in vacuo at 60°, this gives 5-carbamyl-10-nitro-5H-dibenzo[b,f]azepine which is identical to the product obtained

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according to Example 21.

Yield 27.4 g, 97.5% of theory.

Example 25: 10.0 g (0.035 mol) of 5-carbamyl-10-nitro-5H-dibenzo[b,f]azepine are dissolved in a mixture of 100 ml of acetic acid and 50 ml of concentrated hydrochloric acid and, after addition of 1.0 g of palladium carbon (5%), hydrogenated at room temperature and normal pressure. After 1,700 ml (109% of theory) of hydrogen have been absorbed, the hydrogenation is stopped, the catalyst is filtered off and the filtrate is concentrated in vacuo to about 1/4 of the volume. After the addition of 400 ml of water, crystallization is allowed to proceed at 5° for a few hours, and the crystals are filtered off with suction and washed with water until neutral, which gives 5-carbamyl-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine which is identical to authentic material according to the IR spectrum.

Yield: 7.0 g, 78.6% of theory.

A similar result is obtained when platinum carbon (5%) is used as the catalyst.

Example 26: 7.0 g (0.025 mol) of 5-carbamyl-10-nitro-5H-dibenzo[b,f]azepine are dissolved in a mixture of 100 ml of acetic acid and 50 ml of concentrated hydrochloric acid. 12 g of iron powder are added with stirring in the course of 15 minutes at a temperature of 30-40°, stirring is continued for one further hour at 40°, undissolved matter is filtered off warm and rinsed three times with acetic acid. The filtrate is completely evaporated in vacuo, and the residue is taken up in 100 ml of water and stirred for several hours. The product is filtered off, washed with water until neutral and dried in vacuo at 60°. This gives 5-carbamyl-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine which is ... (sic) to authentic material according to the IR spectrum.

Yield: 5.5 g, 88.6% of theory.

Example 27: 7.9 g (0.03 mol) of 5-cyano-10-nitro-5H-dibenzo[b,f]azepine are suspended in 150 ml of ethanol, and 50 ml of concentrated hydrochloric acid are added. 15 g of iron powder are added in the course of 15 minutes with vigorous stirring at a temperature of 40°, the temperature rising to 55°.



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The mixture is stirred for one further hour at 55°, undissolved material is filtered off warm and rinsed with three times 25 ml of ethanol. The filtrate is evaporated to a volume of 80 ml, and 400 ml of ice water are slowly added with stirring. The grey-white precipitate is filtered off with suction, washed with water until neutral and dried in vacuo at 80°. This gives 5-cyano-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine which, after reprecipitation from ethanol, melts at 154-156°.

Yield: 4.8 g, 68.4% of theory.

The analytical and spectroscopic data are consistent with the assumed structure.

Example 28: 52.6 g (sic) (0.2 mol) of 5-cyano-10-nitro-5H-dibenzo[b,f]azepine are suspended in a mixture of 400 ml of toluene and 200 ml of ethanol. On addition of 130 ml of hydrochloric acid (concentrated), the material goes into solution with slight warming. The mixture is heated to 40°, and a solution of 113 g (0.5 mol) of $\text{SnCl}_2 \cdot 2 \text{H}_2\text{O}$ in 90 ml of concentrated hydrochloric acid is then added in the course of 10 minutes. The temperature rises to 55° and is then maintained at 55° for a further 20 minutes. The mixture is allowed to cool, the organic phase is separated off and the aqueous phase is extracted several times more with toluene. The combined toluene extracts are washed with water until neutral, dried over sodium sulfate and evaporated in vacuo. The remaining crude product is slurried with 100 ml of isopropanol, filtered off with suction and washed with a little cold isopropanol. This gives 5-cyano-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine which is identical to the product obtained according to Example 27.

Yield: 29.0 g, 62% of theory.

Example 29: 5.0 g (0.02 mol) of 5-cyano-10-nitro-5H-dibenzo[b,f]azepine are dissolved at 60° in a mixture of 80 ml of ethanol and 80 ml of acetic acid. 10 g of zinc dust are added in portions in the course of 10 minutes with stirring, the temperature rising to 80°. After the reaction has subsided, 40 ml of concentrated hydrochloric acid are added at room temperature. The reaction mixture is stirred for 5

hours, undissolved matter is filtered off, the filtrate is evaporated to dryness and the residue is taken up in 50 ml of water. After several recrystallizations of the precipitated crude product, pure 5-cyano-10-oxo-10,11-dihydro-5H-dibenzo-[b,f]azepine is obtained, which is identical to the product obtained according to Example 27.

Yield: 2.3 g, 50% of theory.

Example 30: 26.3 g (0.1 mol) of 5-cyano-10-nitro-5H-dibenzo-[b,f]azepine are suspended in a mixture of 150 ml of acetic acid and 100 ml of concentrated hydrochloric acid. 40 g of iron powder are added in portions in the course of 30 minutes at 30° with stirring, and the temperature is maintained at 60° by cooling. Stirring is continued for 30 minutes at 50-60°, and undissolved matter is filtered off and rinsed with acetic acid. Twice the volume of water is added to the filtrate and the mixture is extracted with three times 100 ml of methylene chloride. The combined organic phases are washed with water, dried over sodium sulfate and evaporated. The crystalline residue is slurried in 100 ml of isopropanol and the product is filtered off with suction. The 5-cyano-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine thus obtained is identical to the product obtained according to Example 27.

Yield: 21.8 g, 93.2% of theory.

Example 31: 5.2 g (0.02 mol) of 5-cyano-10-nitro-5H-dibenzo-[b,f]azepine are suspended in a mixture of 100 ml of chlorobenzene and 50 ml of ethanol. When 50 ml of concentrated hydrochloric acid are then added, the mixture warms to 35°. 20 g of iron powder are added in portions in the course of 5 minutes at this temperature with vigorous stirring, the reaction mixture warming to 60° within a few minutes. The mixture is then stirred for a further 3 hours and allowed to cool to 25° during this period, and the iron sludge is filtered off and rinsed several times with ethanol and water. The organic phase of the filtrate gives, after washing with water, drying and evaporation, a crystalline crude product which is recrystallized from isopropanol. The 5-cyano-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine thus obtained is

identical to the product obtained according to Example 27.
Yield: 3.8 g, 81% of theory.

A reaction batch carried out analogously with toluene instead of chlorobenzene as the solvent, gave an 84% yield of the said end product.

Example 32: 26.3 g (0.1 mol) of 5-cyano-10-nitro-5H-dibenzo[b,f]azepine are suspended together with 40 g of iron powder in a mixture of 250 ml of toluene and 125 ml of ethanol. 100 ml of concentrated hydrochloric acid are added dropwise in the course of 75 minutes with intensive stirring, the temperature rising up to 60°. After stirring for 10 hours at room temperature, the reaction mixture is worked up analogously to Example 31, which gives 5-cyano-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine which is identical to the product obtained according to Example 27.
Yield: 19.8 g, 84.6% of theory.

Example 33: 2.0 g (0.0085 mol) of 5-cyano-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine are dissolved in 10 ml of concentrated sulfuric acid while cooling with ice, and the solution is left to stand for 30 minutes at 0-5° and then added dropwise to 200 ml of ice water. The flocculent precipitate is filtered off with suction, washed with water until neutral, dried and recrystallized from isopropanol. This gives 5-carbamyl-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine which is identical to authentic material according to the IR spectrum.

Yield: 1.4 g, 65% of theory.

Example 34: A mixture of 1.0 g (0.0043 mol) of 5-cyano-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine, 8 ml of acetic acid and 2 ml of concentrated sulfuric acid is stirred for 48 hours until complete dissolution has occurred. The solution obtained is added dropwise with stirring to 100 ml of ice water, the flocculent precipitate is filtered off, washed with water until neutral and dried in vacuo at 50°, which gives 5-carbamyl-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine which is identical to authentic material according to the IR spectrum.

Yield: 0.9 g, 84% of theory.

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Example 35: The solution of 2.0 g (0.0085 mol) of 5-cyano-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine in 20 ml of 98% formic acid is heated for 8 hours in a bath at 110-120°.

The solution is then introduced into 100 ml of ice water, the mixture is filtered and the solid is washed with water until neutral and dried in vacuo at 50°. The resulting 5-carbamyl-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine is identical to authentic material according to the IR spectrum.

Yield: 1.8 g, 84% of theory.

Example 36: 1.0 g (0.0043 mol) of 5-cyano-10(11)-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine is triturated with 20 g of polyphosphoric acid, and the mixture is left to stand for several days at room temperature, until complete dissolution has occurred. Excess water is then added in small portions, and the yellowish-white precipitate is filtered off with suction and washed with water until neutral. After recrystallization from chlorobenzene, this gives 5-carbamyl-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine which is identical to authentic material according to the IR spectrum.

Yield: 0.75 g, 70% of theory.

Example 37: 5.0 ml of H₂O₂ (30%) are allowed to run at room temperature with stirring into a suspension of 1.0 g (0.0043 mol) of 5-cyano-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine in 20 ml of methanol and 5.0 g of sodium hydrogen carbonate are added after 30 minutes. After stirring for three hours, undissolved matter is filtered off and washed once with methanol and several times with water, whereupon 5-carbamyl-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine is obtained which is identical to authentic material according to the IR spectrum.

Yield: 0.6 g, 55% of theory.

Example 38: BF₃ gas is passed with stirring into a suspension of 3.0 g (0.013 mol) of 5-cyano-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine in a mixture of 30 ml of acetic acid and 3 ml of water until the initially highly exothermic reaction subsides, and the temperature is maintained at 50° by external cooling. The clear reaction solution is allowed to cool and 100 ml of water are added dropwise while cooling

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with ice, the colourless precipitate is filtered off, and the filter residue is washed with water until neutral and recrystallized from acetonitrile. The 5-carbamyl-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine obtained is identical to authentic material according to the IR spectrum.

Yield: 2.3 g, 71% of theory.

Example 39: 2.0 g (0.0085 mol) of 5-cyano-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine are introduced in portions into 40 ml of a solution of 10% by weight of BF_3 in acetic acid with stirring, a clear solution then being obtained at 20° in the course of 15 minutes. After standing for three hours, 100 ml of water are added while cooling with ice, and the solution is adjusted to pH 6 by adding sodium hydroxide solution. The precipitated crude 5-carbamyl-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine is filtered off with suction, washed with water and dried. According to the IR spectrum, it is identical to authentic material.

Yield: 1.6 g, 74.8% of theory.

Example 40: 10.3 g (0.055 mol) of $\text{BF}_3 \cdot 2 \text{CH}_3\text{COOH}$ complex are added to a suspension of 11.7 g (0.05 mol) of 5-cyano-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine in 60 ml of acetic acid and the temperature is allowed to rise to 35° without external cooling, the starting material dissolving slowly. After about 1 hour, a BF_3 adduct starts to crystallize out. The mixture is stirred at room temperature for 4 hours, and the solid is filtered off and rinsed with acetic acid. The intermediate is slurried in 100 ml of water and, after buffering with sodium acetate to pH 6, the mixture is stirred for one hour. After filtration with suction and washing with water, this gives 9.0 g of 5-carbamyl-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine which is identical to authentic material according to the IR spectrum. After evaporation, a further 1.2 g of product can be obtained from the filtrate of the intermediate by fractional crystallization from methanol/water.

Total yield: 10.2 g, 81% of theory.

Example 41: 50 ml of a solution of 15% by weight BF_3 in acetic acid are added to a suspension of 23.4 g (0.1 mol) of

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5-cyano-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine in 40 ml of acetic acid, and the mixture is stirred until the slight evolution of heat subsides. Dropwise addition of 15 ml of water gives a clear, deep blue solution, the temperature rising to 40-45°. The mixture is held for 15 minutes at 40°, and a further 135 ml of water are then added slowly. The resulting crystalline precipitate is stirred for several hours at room temperature, then filtered off with suction and washed with water until neutral. After drying in vacuo at 50°, this gives 5-carbamyl-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine which is identical to authentic material according to the IR spectrum.

Yield: 24.2 g, 96.0% of theory.

Example 42: A mixture of 15.4 ml (0.11 mol) of $\text{BF}_3 \cdot 2 \text{CH}_3\text{COOH}$ complex with 38 ml of acetic acid is allowed to run rapidly at room temperature with stirring into a suspension of 23.4 g (0.1 mol) of 5-cyano-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine in 230 ml of chlorobenzene. A clear brownish solution is formed with slight warming, from which a crystalline BF_3 adduct precipitates after about 10 minutes. The mixture is held at 5° for 30 minutes, and the solid is filtered and the solid is rinsed with chlorobenzene. The dry intermediate is slurried in 200 ml of water, stirred for 30 minutes, filtered off with suction and washed with water until neutral. After drying in vacuo at 60°, this gives 5-carbamyl-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine which is identical to authentic material according to the IR spectrum.

Yield 24.1 g, 95.6% of theory.

Example 43: 1.0 g (0.004 mol) of 5-cyano-10-nitro-5H-dibenzo[b,f]azepine is dissolved at 60° in a mixture of 40 ml of ethanol and 20 ml of acetic acid, and 2.0 g of zinc dust are added with vigorous stirring in the course of 10 minutes. The mixture is stirred for a further 15 minutes, undissolved matter is filtered off warm and rinsed with ethanol and water. The filtrate is evaporated to dryness and taken up in 50 ml of water. After filtration with suction, washing with water

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and drying, this gives crude 5-cyano-10-isonitroso-10,11-dihydro-5H-dibenzo[b,f]azepine which, after recrystallization from ethanol, melts at 185° with decomposition. The analytical and spectroscopic data are consistent with the assumed structure.

Yield: 0.9 g, 95% of theory.

Example 44: 50 g (0.19 mol) of 5-cyano-10-nitro-5H-dibenzo[b,f]azepine are dissolved in 500 ml of pyridine and, after the addition of 10 g of palladium-on-carbon (5%), hydrogenated at room temperature and normal pressure. After 2 hours, 7,960 ml (93% of theory) of hydrogen have been absorbed, and the hydrogenation stops. The catalyst is filtered off, the solvent is evaporated in vacuo and the remaining crude product is recrystallized from methanol/water, which gives 5-cyano-10-isonitroso-10,11-dihydro-5H-dibenzo[b,f]azepine which is identical to the product obtained according to Example 43.

Yield: 35.6 g, 75.2% of theory.

Example 45: 2.5 g (0.01 mol) of 5-cyano-10-isonitroso-10,11-dihydro-5H-dibenzo[b,f]azepine are suspended in a mixture of 25 ml of toluene, 15 ml of ethanol and 10 ml of hydrochloric acid (concentrated). The suspension is stirred for 30 minutes at 50°, and the toluene phase is separated off and evaporated to dryness in vacuo. The crystalline residue is slurried in 10 ml of isopropanol, and the crystals are filtered off with suction and washed twice with isopropanol, which gives 5-cyano-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine, which is identical to the product obtained according to Example 27.

Yield: 0.8 g, 35% of theory.

Example 46: 26.3 g (... (sic) mol) of 5-cyano-10-nitro-5H-dibenzo[b,f]azepine are suspended in a mixture of 265 ml of ethylene glycol monoethyl ether and 75 ml of concentrated hydrochloric acid. 40 g of iron powder are added in small portions at 40° in the course of 40 minutes, and the temperature is maintained at 40° by external cooling. Stirring is continued for 2 hours at room temperature, and the mixture is then heated to 80°, the precipitated product redissolving,

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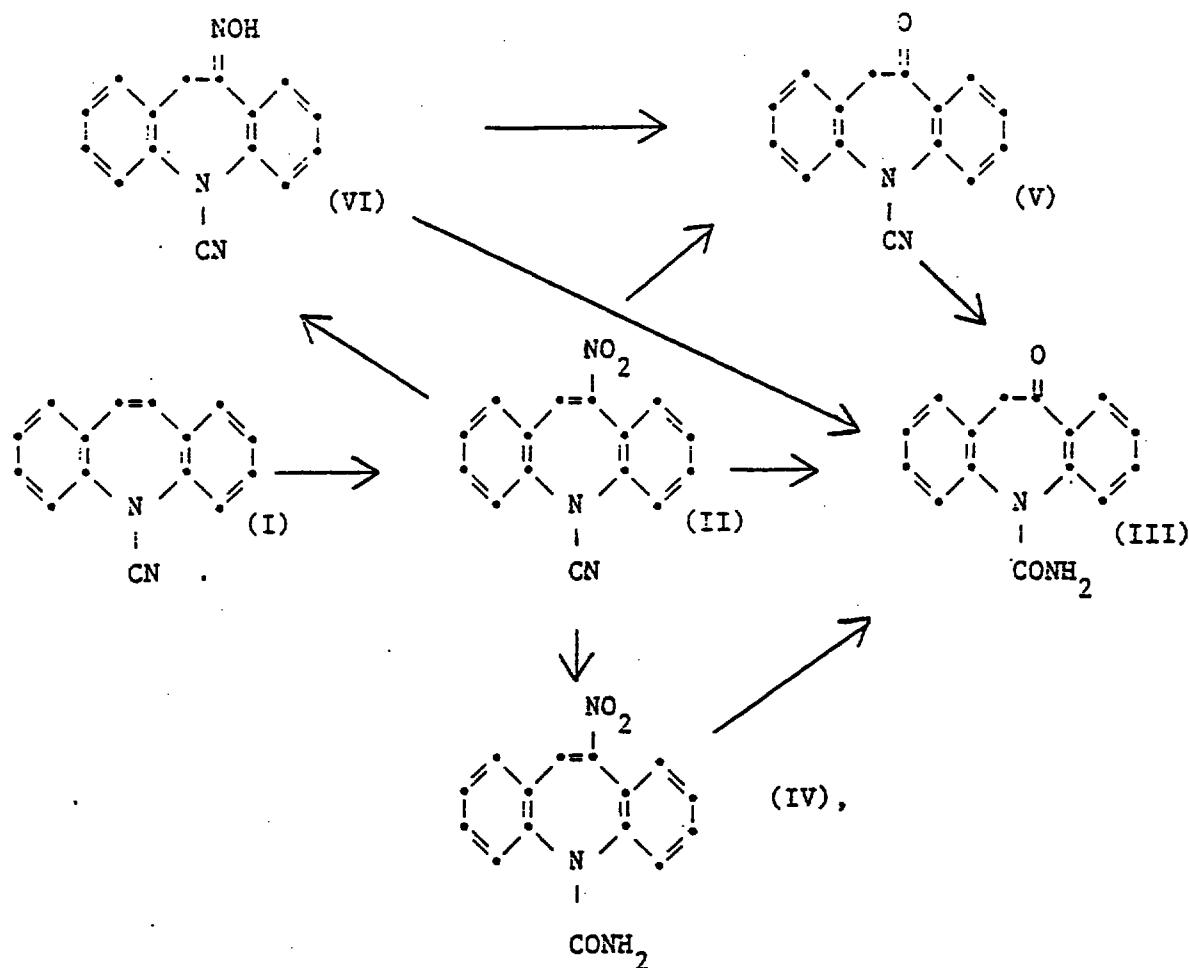
and filtered through a heated suction filter which is rinsed with ethylene glycol monoethyl ether. The crystallization which starts in the filtrate is completed by adding 200 ml of water. After cooling for one hour in an ice bath, the product is filtered off and rinsed with a mixture of ethylene glycol monoethyl ether and water in a 1:1 ratio. This gives 5-cyano-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine, which is identified by comparison of the IR spectrum with that of material from Example 27.

Yield: 19.0 g, 81.2% of theory.



Patent Claims:

1. Process for the preparation of 5-carbamyl-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine of the formula III,



characterized in that 5-cyano-5H-dibenzo[b,f]azepine of the formula I is nitrated, the resulting 5-cyano-10-nitro-5H-dibenzo[b,f]azepine of the formula II is hydrolysed to the 5-carbamyl-10-nitro-5H-dibenzo[b,f]azepine of the formula IV, the 10-nitro group in the latter is reduced and the reduction product is hydrolysed.

2. Process according to claim 1, characterized in that 5-cyano-5H-dibenzo[b,f]azepine is nitrated by means of dinitrogen trioxide, if appropriate mixed with oxygen, or by means of dinitrogen tetroxide or mixtures of such compounds or by means of nitric acid, to give the compound of the



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formula II.

3. Process according to claim 2, characterized in that the nitration is carried out in a suitable solvent which is stable under the reaction conditions.
4. Process according to claim 3, characterized in that lower alkanecarboxylic or halogenated lower alkanecarboxylic acids each having up to 4 carbon atoms, or their anhydrides, or mixtures of such carboxylic acids with the corresponding anhydrides are used as the solvent.
5. Process according to claim 4, characterized in that acetic acid, acetic anhydride or mixtures thereof are used as the solvent.
6. Process according to one of claims 1 - 5, characterized in that a starting material/solvent ratio (weight/volume) from 1:3 to 1:30 is used.
7. Process according to one of claims 1 - 6, characterized in that the nitration is carried out in a temperature range of about 0 - 120°, especially 40 - 80°.
8. Process according to claim 1, characterized in that the compound of the formula II is hydrolysed to the compound of the formula IV by means of acidic agents.
9. Process according to claim 8, characterized in that the hydrolysis is carried out by means of mineral acids or formic acid and water.
10. Process according to claim 8, characterized in that the hydrolysis is carried out by means of boron trifluoride in an equimolar amount or in a slight excess as a solution in a lower alkanecarboxylic or halogenated lower alkanecarboxylic acid each having up to 4 carbon atoms, and subsequent treatment with water.
11. Process according to claim 10, characterized in that the hydrolysis is carried out by means of a solution of BF₃ in acetic acid and subsequent treatment with water.
12. Process according to claim 11, characterized in that the resulting defined BF₃ addition compound with the hydrolysis product is isolated in the pure form and converted by treatment with water into the compound of the formula IV.
13. Process according to one of claims 8 - 12, characterized



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- in that the hydrolysis is carried out in the presence of a further inert solvent.
14. Process according to claim 13, characterized in that a solvent of aromatic character is used.
15. Process according to claim 14, characterized in that chlorobenzene is used as the further solvent.
16. Process according to claim 1, characterized in that the nitro group in the compound of the formula IV is reduced by means of catalytically activated hydrogen and the reduction product is hydrolysed to the compound of the formula III by means of water.
17. Process according to claim 16, characterized in that the reduction is carried out by means of hydrogen in the presence of a noble metal catalyst.
18. Process according to claim 17, characterized in that a palladium-on-carbon catalyst is used.
19. Process according to claim 16, characterized in that the nitro group in the compound of the formula IV is reduced by means of nascent hydrogen.
20. Process according to claim 19, characterized in that the reduction is carried out by means of a suitable metal in an acid.
21. Process according to claim 20, characterized in that the reduction is carried out by means of iron in a mineral acid or lower alkanecarboxylic acid having up to 4 carbon atoms or mixtures thereof.
22. Process according to claim 21, characterized in that the reduction is carried out by means of iron in a mixture of acetic acid and hydrochloric acid.
23. Process according to one of claims 16 - 22, characterized in that the reduction and hydrolysis measures required for converting the compound of the formula II into that of the formula III are carried out in the same reaction batch without isolation of the intermediate of the formula IV.
24. Modification of the process according to claim 1, characterized in that the 10-nitro group in the compound of the formula II is reduced, the reduction product is hydrolysed and the resulting 5-cyano-10-oxo-10,11-dihydro-5H-



dibenzo[b,f]azepine of the formula V is hydrolysed to 5-carbamyl-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine of the formula III.

25. Process according to claim 24, characterized in that the 10-nitro group is reduced by means of nascent hydrogen.

26. Process according to claim 25, characterized in that the reduction is carried out by means of a suitable metal in an acid.

27. Process according to claim 26, characterized in that the reduction is carried out by means of iron or zinc in a mineral acid.

28. Process according to claim 24, characterized in that the 10-nitro group is reduced by means of a chemical reducing agent.

29. Process according to claim 28, characterized in that the reduction is carried out by means of $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$.

30. Process according to one of claims 24 - 29, characterized in that the reduction is carried out in the presence of a lower alkanol having 1 to 4 carbon atoms, a lower alkoxy-lower alkanol having up to four carbon atoms in each of the lower alkoxy and lower alkanol moieties and/or a solvent of aromatic character as additional solvents.

31. Process according to one of claims 24 - 30, characterized in that the reduction is carried out in the presence of a lower alkyl ether of ethylene glycol, wherein lower alkyl has up to 4 carbon atoms.

32. Process according to one of claims 24 - 31, characterized in that the reduction is carried out in a temperature range from 10 - 100°C, preferably from 30 - 70°C.

33. Process according to claim 24, characterized in that the reduction product is hydrolysed with water to the compound of the formula V.

34. Process according to claim 24, characterized in that the 5-cyano group in 5-cyano-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine of the formula V is hydrolysed to the 5-carboxamide group by means of basic or acidic agents.

35. Process according to claim 34, characterized in that the hydrolysis is carried out by means of an oxide or



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hydroxide of alkaline earth or alkali metals or an alkali metal bicarbonate, if appropriate in the presence of a peroxide.

36. Process according to claim 35, characterized in that the hydrolysis is carried out by means of sodium bicarbonate in the presence of hydrogen peroxide.

37. Process according to claim 34, characterized in that the hydrolysis is carried out by means of mineral acids, lower alkanecarboxylic or halogenated lower alkanecarboxylic acids having up to 4 carbon atoms or their mixtures with mineral acids, or, if appropriate, Lewis acids present as a solution in a lower alkanecarboxylic acid and subsequent treatment with water.

38. Process according to claim 37, characterized in that the hydrolysis is carried out by means of hydrochloric acid, sulfuric acid, polyphosphoric acid, formic acid, acetic acid, boron trifluoride or a defined addition compound of boron trifluoride with acetic acid and subsequent treatment with water.

39. Process according to one of claims 34 - 38, characterized in that the hydrolysis is carried out in the presence of a further solvent.

40. Process according to claim 39, characterized in that a solvent of aromatic character is used as the further solvent.

41. Process according to one of claims 34 - 40, characterized in that the hydrolysis is carried out in a temperature range from -5 to $+150^{\circ}\text{C}$, preferably from 0 to 40°C .

42. Modification of the process according to claim 24, characterized in that the 10-nitro group in the compound of the formula II is reduced by means of zinc dust in an acid or by means of hydrogen in the presence of a hydrogenation catalyst, and the resulting 5-cyano-10-isonitroso-10,11-dihydro-5H-dibenzo[b,f]azepine of the formula V is hydrolysed.

43. Process according to claim 42, characterized in that the 10-nitro group is reduced by means of hydrogen in the presence of a palladium-on-carbon catalyst in a suitable solvent.



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44. Process according to claim 43, characterized in that a solvent of aromatic character is used as the solvent.
45. Process according to claim 44, characterized in that pyridine is used as the solvent.
46. Process according to claim 42, characterized in that the compound of the formula VI is hydrolysed to the compound of the formula V by means of a mineral acid.
47. Process according to claim 46, characterized in that the hydrolysis is carried out by means of hydrochloric acid.
48. Process according to one of claims 42 and 46 - 47, characterized in that the hydrolysis is carried out in the presence of an aromatic solvent or a lower alkanol having up to 4 carbon atoms or mixtures thereof.
49. Process according to claim 47, characterized in that the hydrolysis is carried out in the presence of a toluene/ethanol mixture.
50. Modification of the process according to claim 1, characterized in that the 5-cyano group as well as the 10-isonitroso group in 5-cyano-10-isonitroso-10,11-dihydro-5H-dibenzo[b,f]azepine of the formula VI are hydrolysed in the same reaction batch to give 5-carbamyl-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine of the formula III.
51. Process according to claim 50, characterized in that the hydrolysis is carried out by means of acidic agents.
52. Process according to claim 51, characterized in that the hydrolysis is carried out by means of a mineral acid, a lower alkanecarboxylic or halogenated lower alkanecarboxylic acid or a Lewis acid in the presence of water.
53. Process according to claim 52, characterized in that the hydrolysis is carried out by means of boron trifluoride in acetic acid and subsequent treatment with water.
54. Process according to one of claims 50 - 53, characterized in that the hydrolysis is carried out in the presence of a further inert solvent.
55. Process according to claim 54, characterized in that a lower alkanol having up to 5 carbon atoms is used as the further inert solvent.
56. 5-Cyano-10-nitro-5H-dibenzo[b,f]azepine.



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- 57. 5-Carbamyl-10-nitro-5H-dibenzo[b,f]azepine.
- 58. 5-Cyano-10-oxo-10,11-dihydro-5H-dibenzo[b,f]azepine.
- 59. 5-Cyano-10-isonitroso-10,11-dihydro-5H-dibenzo[b,f]-
azepine.