

PROCESS FOR PREPARING BIPYRIDYLS

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This invention relates to the manufacture of organic bases, and more particularly to the manufacture of bipyridyls.

It is known that bipyridyls can be prepared by oxidation of sodium-pyridine interaction products, and copending application, Serial No. 194,723, filed May 14, 1962 describes particular conditions for this reaction which improve the yield of bipyridyls, and especially of the 4:4'-isomer. In our copending applications, Serial No. 193,627, filed May 9, 1962 and Serial No. 221,899, filed September 6, 1962 there are also described processes for the manufacture of bipyridyls by oxidation of magnesium/pyridine and aluminium/pyridine interaction products respectively.

We have now found that the conventional oxidation step used for the conversion of metal-pyridine interaction products to bipyridyls can be dispensed with, and replaced by a treatment with water, in the substantial absence of an oxidising agent such as air or oxygen. This process provides bipyridyls in substantially undiminished yield compared with the earlier route, and avoids the lengthy air oxidation procedure and the use of conventional oxidising agents.

It is known to treat a sodium-pyridine interaction product with moist ether (Emmert: Ber. 1917, 50, 31). The product so treated was made by interacting sodium with excess pyridine and then removing excess pyridine (both operations at substantially room temperature) and then heating the residual sodium-pyridine interaction product under reduced pressure to convert it into a second sodium-pyridine interaction product. In this procedure, the product obtained is not a bipyridyl but a tetrahydrobipyridyl. We have found that bipyridyls can be obtained as the product has been heated to an elevated temperature with free pyridine before the water treatment is carried out.

Thus according to our invention we provide a process for the manufacture of bipyridyls which comprises treating with water a metal-pyridine interaction product which has been heated to an elevated temperature in the presence of a free pyridine.

The elevated temperature to which the mixture of metal-pyridine interaction product and the pyridine is heated before the water treatment should be at least 70° C. An upper limit is usually set by the boiling point of the mixture, though this may be increased if desired by heating under pressure or adding higher-boiling diluents. In the case of a very reactive metal such as sodium which can react with a pyridine below this temperature, heat should be applied if necessary to raise the temperature of the mixture appropriately. This heating may be during or after interaction. In the case of less reactive metals such as aluminium and magnesium, the necessary elevated temperature is usually achieved during the metal-pyridine interaction stage. The period of heating and the proportions of pyridine used may be those more fully-described in copending applications, Serial No. 194,723, Serial No. 193,627 and Serial No. 221,899 for the production of metal-pyridine interaction products.

The free pyridine may be in particular an excess of the

pyridine used in forming the metal-pyridine interaction product.

The pyridine is preferably pyridine itself, but any other pyridine reactive towards the selected metal may be used if desired, for example alkylpyridines. In general, alkylpyridines are less reactive than pyridine in this process.

The metal-pyridine interaction product may be in particular a sodium-pyridine, a magnesium-pyridine or an aluminium-pyridine interaction product though interaction products derived from other metals reactive towards the pyridine may be used if desired, for example those derived from other alkali metals. These interaction products may be produced by interacting the metal and pyridine with heating and optionally in the presence of a diluent (which may be an excess of the pyridine and for an inert organic liquid for example trimethyl benzene, as is more fully described in copending applications, Serial No. 193,627, Serial No. 194,723 and Serial No. 221,899. respectively. The metals used for this purpose may be pure or contain alloying metals. The interaction of magnesium with pyridine may be slow to start and may be initiated by addition of a small proportion of an initiator, particularly a material which can induce the formation of free radicals in the mixture, for example sodium, potassium, bromine or iodine; likewise the interaction of aluminium and pyridine may be initiated by a compound which can break down the surface oxide film on the metal, for example a mercury compound, particularly mercuric chloride, optionally in conjunction with an initiator capable of forming free radicals in the mixture.

We prefer to carry out the process of our invention using a metal-pyridine interaction product from which the excess of the pyridine used in its production is not removed before the treatment with water. In this way, problems arising from the isolation of the metal-pyridine interaction product are avoided. In the case of sodium-pyridine interaction products, which are violently explosive in contact with air, this avoidance of isolation is especially valuable from the safety aspect.

The treatment of the metal-pyridine interaction product with water is preferably carried out at an elevated temperature which is at least 40° C., and especially is in the range 80° C. to 120° C. The upper temperature limit is usually defined by the boiling point of the reaction mixture, and this boiling point may be raised above 120° C., for example by addition of higher boiling diluents such as dimethylaniline or by use of superatmospheric pressures. Accordingly the process of our invention can be carried out at temperatures above 120° C. if desired, but no additional overall advantage is usually achieved by doing so. Below 40° C. there is a tendency for the reaction mixture to become thick and lumpy, so that satisfactory completion of the reaction is difficult to achieve.

The treatment of the metal-pyridine interaction product with water may be carried out by simple mixing at the desired elevated temperature. Alternatively, the metal-pyridine interaction product and water may be mixed at a lower temperature and subsequently or simultaneously heated to the desired elevated temperature. This heating may be carried out in a subsequent operation, for example a distillation operation, and not necessarily during the treatment stage, although the vigorous reaction which takes place during the water treatment is a convenient source of heat. Conveniently, the process is carried out by adding cold water slowly with stirring to the metal-pyridine interaction product at such a rate that the mixture is maintained at the desired temperature without overheating; cooling may be applied if desired in order to assist this.

If desired, the metal pyridine interaction product (or the mixture containing this with excess pyridine) may be

diluted with an inert liquid before treatment with water. Suitable inert liquids for this purpose include hydrocarbons, for example trimethylbenzenes.

The proportion of water to be used should be at least 1 mole, and is preferably between 1.75 and 2.5 moles, for each equivalent of metal in the metal-pyridine interaction product. Larger proportions may be used if desired, but excessive dilution may make subsequent isolation of the product more difficult. Smaller proportions tend to give less complete reaction and to make the reaction mixture thicker and less easy to handle.

In the case of treatment of a sodium-pyridine interaction product, we find it especially advantageous to use a proportion of water which is substantially 2.2 moles for each equivalent of sodium used. With this proportion of water, the sodium hydroxide formed during the treatment separates out as a liquid aqueous phase which contains substantially all the water and leaves the liquid organic phase (containing the bipyridyls and excess pyridine) substantially dry. If the proportion of water is reduced there is a tendency for the sodium hydroxide to separate in solid form, and if the proportion of water is increased the organic phase will retain more water. This form of our process is especially advantageous as it provides a very simple and efficient method for separating the sodium hydroxide which avoids chemical treatment and wasteful filtration techniques, and also avoids the need for a separate drying operation before further treatment of the crude bipyridyl/pyridine mixture, for example by distillation. In this case, the mixture produced by treatment of the metal-pyridine interaction product with water may conveniently be maintained at a temperature above 80° C. but below its boiling point, and preferably at about 100° C., and then allowed to settle into two liquid phases and the aqueous sodium hydroxide layer separated and removed. The mixture is preferably kept hot, as indicated, to reduce the possibility of solidification of the aqueous sodium hydroxide phase, and the organic phase thus obtained may contain as little as 0.1% to 0.2% of water by weight.

The exclusion of air or oxygen may be effected to a satisfactory degree by carrying out the process in a vessel which has been purged with nitrogen and, preferably, by passing a slow stream of nitrogen through the vessel during the addition of the water. It is not necessary to take precautions to exclude the air or oxygen absolutely, and the presence of small traces in the nitrogen, or dissolved in the water is not detrimental.

The course of the reaction is obscure, but reaction is rapid and is usually completed within about an hour.

The isolation of the bipyridyls may be carried out in known manner, for example by fractional distillation and/or crystallisation of the product. An especially convenient method is that more fully described in copending application, Serial No. 260,883, filed February 25, 1963, now U.S. Patent 3,195,642, wherein the crude product containing bipyridyls is first dissolved in aqueous acid and any insoluble matter discarded, and the resulting aqueous acid solution is neutralised and extracted with a water-immiscible organic solvent, preferably at an elevated temperature. The bipyridyls are thus obtained as a solution in the water-immiscible organic solvent, and can be recovered by evaporation of the solvent. The 4:4'-bipyridyl can be recovered in the form of its hydrate, as is more fully described in copending application, Serial No. 260,882, filed February 25, 1963, now U.S. Patent 3,159,641, for example by adding water to a cold solution of the mixed bipyridyls in a water-immiscible organic solvent, as may for example be obtained by the extraction process mentioned above.

The process of the present invention has the advantage of simplifying the conversion of pyridine to bipyridyls by providing generally greater ease of working than the prior art methods. Moreover, we avoid many of the disadvantages and hazards associated with the earlier processes,

and in particular we avoid the necessity for a long oxidation stage, the risk of forming explosive pyridine/oxygen mixtures, the loss of pyridine and products by volatilisation in a stream of gaseous oxidising agent, and we minimise the requirements for streams of inert gas through the apparatus and the formation of by-products.

The crude mixture of bipyridyls produced by the process of the present invention in some cases contains a higher proportion of the 4:4'-isomer than the crude bipyridyls made by conventional oxidation techniques.

The invention is illustrated but not limited by the following examples in which the parts and percentages are by weight.

Example 1

Sodium metal (46 parts, 2 equivalents) in the form of a dispersion in trimethylbenzene (92 parts) was added during 45 minutes to pyridine (632 parts, 8 moles), stirred in an atmosphere of nitrogen, with cooling so that the temperature was maintained at 90° C. After addition of sodium was complete the temperature of the mixture was maintained at 90° C. for 15 minutes with continued stirring, and then water (80 parts, 2.2 moles per equivalent of sodium) was added continuously, the initial vigorous heat of reaction being removed by cooling so that the temperature of the mixture remained between 85° and 90° C. The addition of water was made over a period of 15 minutes, after which time stirring was maintained for a further 15 minutes. The colour of the reaction product turned from black to brown during the addition of water. The product was then heated to 100° C. and held at this temperature without stirring for one hour, after which time the upper organic layer (740 parts) was separated from the lower aqueous layer (125 parts). Less than 1 part of the 80 parts of caustic soda formed in the reaction remained in the upper layer after the separation and less than 1 part of pyridine was drawn off with the lower aqueous layer.

The organic layer was then fractionally distilled and from it was recovered pyridine (476 parts) and a mixture consisting of 2:2'-bipyridyl (0.2 part), 2:4'-bipyridyl (5 parts) and 4:4'-bipyridyl (49 parts).

Example 2

The procedure of Example 1 was repeated except that the interaction of the sodium and pyridine, and the subsequent addition of water, were carried out at 100° C. The products recovered were pyridine (471 parts) and a mixture consisting of 2:2'-bipyridyl (0.2 part), 2:4'-bipyridyl (4 parts) and 4:4'-bipyridyl (42 parts).

Example 3

A mixture of 12 parts of magnesium turnings and 395 parts of pyridine was heated under reflux conditions, interaction was initiated by addition of 2 parts of a 33% dispersion of sodium metal in trimethyl benzene, and then interaction was continued for 2 hours while a stream of nitrogen was passed through the reaction vessel. 35 parts of water (2 moles per equivalent of magnesium) were then added with stirring during 15 minutes, and the resulting mixture was stirred for a further 15 minutes and then fractionally distilled. There were thus recovered pyridine (288 parts) and a mixture consisting of 2:2'-bipyridyl (1 part), 2:4'-bipyridyl (3 parts), and 4:4'-bipyridyl (41 parts). This yield of 4:4'-bipyridyl corresponded to 38% of theory, based on the pyridine consumed.

Example 4

A mixture of 36.4 parts of magnesium turnings and 1264 parts of pyridine was heated under reflux conditions, interaction was initiated by addition of 3 parts of a 33% dispersion of sodium metal in trimethyl benzene, and then interaction was continued for 6 hours at 105° C. to 110° C. while a stream of nitrogen was passed through the reaction vessel. 120 parts of water (2.2 moles per

equivalent of magnesium metal) were then added with stirring during 30 minutes while the temperature of the mixture was maintained at 105° to 110° C. A portion of the reaction product (one half, i.e. 710 parts) was fractionally distilled, and the products thereby obtained were pyridine (419 parts) and a mixture consisting of 2:2'-bipyridyl (4 parts), 2:4'-bipyridyl (12 parts) and 4:4'-bipyridyl (63 parts). The yield of 4:4'-bipyridyl corresponded to 30% of theory, based on the pyridine consumed.

Example 5

A mixture of 132 gms. of dry pyridine (water content estimated as 0.01% by Karl Fischer method) and 4 gms. of magnesium turnings was stirred and heated to reflux in an atmosphere of nitrogen and treated with 2 ml. of a 25% dispersion of sodium in trimethyl benzene. The refluxing was continued for 1 hour 25 minutes, and then the reaction mixture was cooled to 90° C. and 25 ml. of water were added during 10 minutes. Analysis of the product showed the present of 14.3 gms. of 4:4'-bipyridyl. There were also recovered 100 gms. of unchanged pyridine.

Example 6

The procedure of Example 5 was repeated except that 200 ml. of dry oxygen-free trimethyl benzene (a commercial mixture of isomers) were added to the hot reaction mixture, which was then cooled with stirring to ambient temperature (about 20° C.) and treated with 25 ml. of water. The amount of 4:4'-bipyridyl formed was found to be 14.6 gms., and 100 gms. of unchanged pyridine were recovered.

Example 7

The procedure of Example 5 was repeated up to the completion of the refluxing, and then the reaction mixture was distilled at reduced pressure up to a temperature of 80° C. to remove unchanged pyridine while 200 ml. of dry oxygen-free trimethylbenzene were added. The resulting mixture was cooled to ambient temperature with stirring and 25 ml. of water were added at that temperature. The amount of 4:4'-bipyridyl thus formed was found to be 14.6 gms., and 98 gms. of unchanged pyridine were recovered.

Example 8

Interaction of a mixture of 10 gms. of aluminium powder and 399 gms. of dry pyridine was initiated by 3 gms. of mercuric chloride and continued for 3.75 hours at 116° C. To the resulting mixture were then added 25 gms. of water. The amount of 4:4'-bipyridyl formed was 14.3 gms. (corresponding to an efficiency of 16% of theory on the aluminium or 17.4% on the pyridine consumed).

Example 9

Interaction of a mixture of aluminium powder (10 gms.) and dry pyridine (150 gms.) was initiated by 3 gm. of mercuric chloride, followed by addition of 150 gms. of N:N-dimethylaniline and continued refluxing for 3.75 hours at 116° C. The mixture was then treated with 25 gm. of water. The amount of 4:4'-bipyridyl thus formed was found to be 1.7 gm. (2% efficiency on the aluminium used and 7% on the pyridine consumed).

Example 10

Interaction of mixture of aluminium powder (10 gm.), dry pyridine (150 gm.) and N:N-dimethylaniline (250 gm.) was initiated by mercuric chloride (3 gm.) and the mixture was refluxed for 3.75 hours at 116° C. The resulting mixture was treated with water (25 gm.). The amount of 4:4'-bipyridyl thus formed was found to be 2.9 gm. (corresponding to 3% efficiency on the aluminium or 5% on the pyridine consumed).

Example 11

Interaction of a mixture of aluminium powder (10 gm.) and dry pyridine (528 gm.) was initiated by mercuric chloride (3 gm.) followed by sodium (2 gm.). The mixture was the refluxed for 2.5 hours and then treated with water (15 gm.). The amount of 4:4'-bipyridyl thus formed was found to be 14.3 gms., corresponding to 16% of theory based on the aluminium or 18% of theory based on the pyridine consumed.

What we claim is:

1. A process for preparing a bipyridyl which comprises interacting a pyridine-reactive metal with a compound selected from the group consisting of pyridine and alkyl derivatives thereof in the presence of an excess amount of said compound to provide a metal-pyridine interaction product, thereafter heating said metal-pyridine interaction product to an elevated temperature and treating the same with water to convert said metal-pyridine interaction product to the desired bipyridyl product.

2. The process of claim 1 wherein the reactive metal is interacted with said compound at a temperature of at least 70° C.

3. The process of claim 1 wherein the excess amount of said compound is present when said metal-pyridine interaction product is treated with water.

4. The process of claim 1 wherein the treatment with water is carried out at a temperature of at least 40° C.

5. The process of claim 1 wherein the treatment of said metal-pyridine interaction product with water is carried out at a temperature between 80° C. and 120° C.

6. The process of claim 1 wherein at least one mol of water is used for each equivalent of metal in the metal-pyridine interaction product.

7. The process of claim 1 wherein between 1.75 and 2.5 moles of water are used for each equivalent of metal in said metal-pyridine interaction product.

8. A process for preparing 4:4'-bipyridyl which comprises the steps of interacting magnesium with a compound selected from the group consisting of pyridine and alkyl derivatives thereof at a temperature of at least 70° C. in the presence of an excess amount of said compound to provide a magnesium-pyridine interaction product, and thereafter heating to a temperature of at least 40° C. and treating said magnesium-pyridine interproduct with at least an equimolar amount of water to convert said magnesium-pyridine interaction product to a bipyridyl product consisting primarily of 4:4'-bipyridyl, and thereafter recovering the 4:4'-bipyridyl from said bipyridyl product.

9. A process for preparing 4:4'-bipyridyl which comprises the steps of interacting aluminium with a compound selected from the group consisting of pyridine and alkyl derivatives thereof at a temperature of at least 70° C. in the presence of an excess amount of said compound to provide an aluminium-pyridine interaction product, and thereafter heating to a temperature of at least 40° C. and treating said aluminium-pyridine interaction product with at least an equimolar amount of water to convert said aluminium-pyridine interaction product to a bipyridyl product consisting primarily of 4:4'-bipyridyl, and thereafter recovering the 4:4'-bipyridyl from said bipyridyl product.

10. A process for preparing 4:4'-bipyridyl which comprises the steps of interacting sodium with a compound selected from the group consisting of pyridine and alkyl derivatives thereof at a temperature of at least 70° C. in the presence of an excess amount of said compound to provide a sodium-pyridine interaction product, and thereafter heating to a temperature of at least 40° C. and treating said sodium-pyridine interaction product with at least an equimolar amount of water to convert said sodium-pyridine interaction product to a bipyridyl product consisting primarily of 4:4'-bipyridyl, and thereafter recovering the 4:4'-bipyridyl from said bipyridyl product.

11. Process as claimed in claim 10 wherein the proportion of water used is substantially 2.2 moles for each equivalent of sodium in the sodium-pyridine interaction product.

12. The process of claim 11 wherein a liquid organic phase containing the bipyridyl product is recovered by separation of the water-treated product at a temperature of at least 80° C. into two liquid phases, followed by removing the aqueous sodium hydroxide phase.

13. The process of claim 12 wherein the separation temperature is about 100° C.

14. The process of claim 1 wherein the compound is pyridine.

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