

**Chemistry.** — *On some derivatives of di-(2-pyridyl)-amine, and on tri-(2-pyridyl)-amine.* By J. P. WIBAUT and G. L. C. LA BASTIDE. (Communicated by Prof. A. F. HOLLEMAN.)

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1. *Introduction.* Of diphenylamine  $(C_6H_5)_2NH$  several derivatives are known in which nitro groups or halogen atoms are substituted for one or more hydrogen atoms of the benzene nuclei. Nitroderivatives of diphenylamine may, in general, be prepared by bringing halogen-nitrobenzenes in reaction with aniline, in which a diphenylamine derivative is formed and hydrogen halide is split off. Also the nitration of diphenylamine is possible.

The analogue of diphenylamine in the pyridine series, di-(2-pyridyl)-amine  $(C_5H_4N)_2NH$  is now also known. Our purpose was to prepare substitution products for this substance, and if possible, to find the constitution of the substances obtained. We have examined the nitration and bromination of dipyridylamine, and have obtained a dinitro- and a dibromo-derivative. Accordingly the hydrogen atoms of the pyridine nuclei in dipyridylamine may be readily substituted, just as this is the case in 2-amino-pyridine itself.

The determination of the constitution of these substances has not succeeded, as unexpected difficulties presented themselves. Our researches in this direction have led, however, to the synthesis of the hitherto unknown tri-(2-pyridyl)-amine,  $(C_5H_4N)_3N$ .

2-dipyridylamine was prepared for the first time by TSCHITSCHIBABIN, who for this purpose heated 2-aminopyridine and 2-chloropyridine in the presence of chloride of zinc <sup>1)</sup>. STEINHAUSER and DIEPOLDER <sup>2)</sup> carry out this reaction by heating with barium oxide. TSCHITSCHIBABIN has also prepared dipyridylamine by heating 2-aminopyridine at 240—250° for a long time with an equivalent quantity of the hydrochloric acid salt of this base, a method which is quite analogous to the preparation of diphenylamine.

According to our experience this last method is best adapted to the preparation of dipyridylamine, though we have not succeeded in raising the yield above 25 %. We have also heated the sodium compound of 2-aminopyridine at 170—180° with 2-chloropyridine and parafin oil as diluent; the yield of dipyridylamine then amounts to 40 %, but this method of preparation is more laborious, as first the sodium compound has to be made. For the melting point of the dipyridylamine purified by recrystallisation from diluted alcohol, we found 95.5—96°.

<sup>1)</sup> J. Soc. Phys. Chem. Russe, **46**, 1216 (1914).

<sup>2)</sup> J. prakt. Chem., (2) **93**, 392 (1916).

*Nitration of dipyridylamine.*

If this base is dissolved in strong sulphuric acid, and if at 0° C. nitric acid of density 1.4 is added, no reaction takes place. We have not been able to detect any formation of a nitramine, which is formed from 2-aminopyridine under these circumstances. The nitration, however, proceeds smoothly, if the mixture of dipyridylamine, concentrated sulphuric acid and nitric acid is heated on the water bath.

It appeared from the analysis of the nitration product that this substance contained two nitro groups. After repeated crystallisation from toluene the dinitrodipyridylamine was obtained in the form of yellow-brown needles of a melting-point of 195—196°.

This substance has a very feebly basic character; it dissolves in strong acids, but is again precipitated on dilution with water. It is very sparingly soluble in alcohol and water.

Analysis:

Found C 45.74%; H 2.80%; N 26.98%.

Calculated for C<sub>10</sub>H<sub>7</sub>N<sub>5</sub>O<sub>4</sub> C 45.96%; H 2.70%; N 26.82%.

*Bromination of Dipyridylamine.*

To a diluted solution of this base in glacial acetic acid a solution of bromine in glacial acetic was added gradually, care being taken that it was properly cooled. The quantity of bromine added was calculated for the introduction of two bromine atoms. From the reaction product a substance was isolated, which appeared to be a salt with hydrogen bromide and which was obtained after repeated recrystallisation from alcohol in the form of yellow orange needles melting at 253—254°.

Analysis:

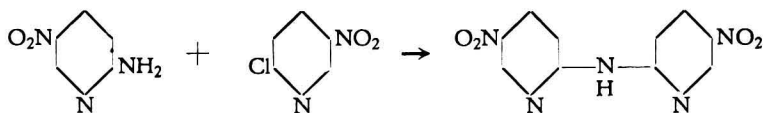
Found 64.99% Br; 8.47% N.

Calculated for C<sub>10</sub>H<sub>7</sub>N<sub>3</sub>Br<sub>2</sub>·2HBr 65.37% Br; 8.56% N.

Accordingly this substance is a salt of dibromodipyridylamine with two molecules of hydrobromic-acid. The alcoholic solution of this salt was made alkaline, whereby the free base was obtained, which after recrystallisation from alcohol melts at 191°; white needles.

Analysis: Br found 48.27% Calculated for C<sub>10</sub>H<sub>7</sub>N<sub>3</sub>Br<sub>2</sub> 48.63%.

In order to determine the positions which the nitro-groups, respectively the bromine atoms, occupy in these substances, we have tried to prepare these compounds in another way, i.e. by bringing substituted 2-aminopyridines in reaction with 2-halogenopyridines. From 2-amino-5-nitropyridine and 2-chloro-5-nitropyridine 5,5'-dinitrodipyridylamine might be formed:



The synthesis of monosubstitution products of dipyridylamine or of other disubstitution products might be tried in a similar way. We have, therefore, prepared the substituted pyridines suitable for our purpose, and tried to transform them in dipyridylamine-derivatives in the sense of the above-mentioned formula.

The following mixtures of substances were heated with barium oxide, in analogy to DIEPOLDER's method of preparation for dipyridylamine itself:

2-amino-5-nitropyridine	with 2-chloropyridine
„	„ 2-bromopyridine
„	„ 2-iodopyridine
2-amino-5-bromopyridine	„ 2-chloropyridine
„	„ 2-bromopyridine
„	„ 2-iodopyridine
2-amino-5-bromopyridine	„ 2-iodo-5-bromopyridine <sup>1)</sup>
2-amino-3,5-dibromopyridine	„ 2-chloropyridine

All these experiments gave negative results. If the temperature was raised to about 150°, no reaction took place, but if the temperature was carried up to 200°, the substances were quite decomposed, only a charry residue being obtained. Nor did TSCHITSCHIBABIN's method for the preparation of dipyridylamine, heating of aminopyridine with an equivalent quantity of the hydrochloric acid salt of this base, give any result for the substituted aminopyridines. Experiments were made with 2-amino-5-nitropyridine and 2-amino-3,5-dibromopyridine, which were each heated with an equivalent quantity of the hydrochloric acid salt. At 150° no reaction took place, at higher temperature again total decomposition.

It appeared, therefore, from these experiments that for the synthesis of substituted dipyridylamines high temperatures are to be avoided, as the substituted aminopyridines are decomposed at increased temperature. Since diphenylamine derivatives may be obtained in many cases from halogennitrobenzenes and aniline by boiling a mixture of these substances in alcoholic solution with addition of sodium acetate, we have tried this method with the following substances :

2-amino-3,5-dibromopyridine	with 2-chloropyridine
2-amino-5-bromopyridine	„ 2-chloropyridine
2-amino-5-nitropyridine	„ 2-chloro-5-nitropyridine
2-amino-5-nitropyridine	„ 2-chloropyridine

The substances, however, do not react under the circumstances of the experiment.

From these experiments we get the impression that a halogen atom bound in the pyridine nucleus in position 2, is difficult to bring in reaction, also

<sup>1)</sup> Instead of with barium oxide we have also heated the substances with potash and copper powder (ULLMANN), likewise however with a negative result.

in those cases where in this pyridine nucleus other halogen atoms or a nitro group have been substituted in position 5.

For these synthetic attempts a number of substituted pyridines had to be prepared, some of which were not yet known. These new compounds will be briefly described here.

*2-iodo-5-bromopyridine.*

This substance was obtained by adding 2-amino-5-bromopyridine dissolved in 50 % acetic acid gradually to a boiling solution of potassium iodide and sodium nitrite, hence the same method being used as for the preparation of 2-iodo-pyridine according to TSCHITSCHIBABIN. 2-iodo-5-bromopyridine crystallizes from alcohol in white plates melting at 117°.

*5-iodo-2-bromopyridine.*

This substance was prepared by treating 2-amino-5-iodopyridine dissolved in strong hydrobromic acid with sodium nitrite. The 2-bromo-5-iodopyridine crystallized from alcohol in shiny plates melting at 122°.5.

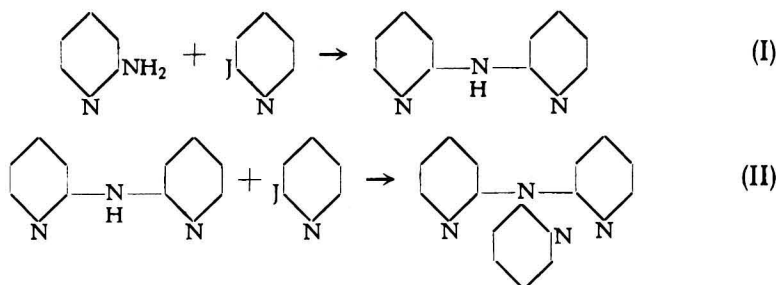
*2-5-di-iodopyridine.*

This substance was obtained in an analogous way from 2-amino-3,5-dibromopyridine. The 2-iodo-3,5-dibromopyridine is obtained from alcohol in white crystal plates, which melt at 70°.5. In appearance and in smell the substance resembles the dihalogenopyridines which have just been described. Experimental details of these experiments and analytical data will be published elsewhere.

3. *Preparation of tri-(2-pyridyl)-amine.*

We have undertaken the synthesis of the still unknown tri-pyridylamine by analogous methods as that tried for dipyridyl derivatives, and have succeeded in preparing this substance in two ways.

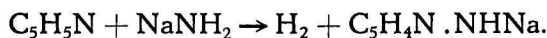
A mixture of 2-aminopyridine (0.1 mols.) and 2-iodopyridine (0.2 mols.) dissolved in mesitylene was heated with anhydrous potash, some copper powder and a little potassium during 14 hours at 150—160°; it is found that tripyridylamine had been formed in a yield of 10—20 % of the theoretically calculated quantity. This experiment shows that the method, which was found by ULLMANN for the synthesis of diphenylamine derivatives, may be applied in the pyridine series. The reaction takes place in two stages:



The second reaction proceeds, however, more rapidly than the first, for if only 1 mol. of 2-iodopyridine is brought in reaction with 1 mol. of

aminopyridine in the way just mentioned, only tripyridylamine is formed, and no dipyridylamine can be detected. A good yield of tripyridylamine is obtained when a mixture of dipyridylamine and 2-iodopyridine dissolved in mesitylene is heated with potash and some copper powder and potassium iodide.

On the other hand the sodium compound of dipyridylamine:  $(C_5H_4N)_2N.Na$  does not react with chloropyridine. This result seems plausible, as in sodium amide it are the hydrogen atoms, and not the sodium atom which are reactive, as TITHERLEY has pointed out <sup>1)</sup>. This investigator found in his researches on reactions with sodium amide that this substance does not react with alkylhaloids to form primary amines. From hexachloroethane and sodiumamide was formed among other substances the sodium compound of cyanamide  $CN.N.Na_2$ , in which the sodium atoms are, still present. In TSCHITSCHIBABIN's amidation reaction it is again the hydrogen atom of the sodiumamide which is reactive:



We already mentioned that the sodium compound of aminopyridine  $C_5H_4N.NHNa$  reacts on chloropyridine with formation of dipyridylamine. It is probable that here primarily the sodium compound of dipyridylamine is formed, from which after decomposition with diluted hydrochloric acid, the dipyridylamine itself is obtained. In the sodium compound of dipyridylamine however, no reactive hydrogen atom is available, so that a reaction with chloropyridine cannot take place.

*Tri(2-pyridyl)-amine  $(C_5H_4N)_3N$ .*

This substance may be obtained from diluted alcohol or from a mixture of benzene and ligroin in the form of long colourless needles, which melt at  $132.5^\circ$ .

Analysis:

Found: C 72.51 %; 72.40 %; H 5.08 %; 4.71 %; N 22.67 %; 22.62 %.

Calculated for:  $C_{15}H_{12}N_4$ : C 72.58 %; H 4.88 %; N 22.58 %.

Molecular weight found cryoscopically in benzene solution: 234 and 237, calculated 248.

The picrate of this base crystallises from alcohol in yellow needles, which melt at  $149^\circ$ . Nitrogen content found 20.74 %, calculated for  $C_{15}H_{12}N_4 + C_6H_2OH(NO_2)_3$ : 20.54 %. In the picrate 1 mol. of picric acid is, therefore, bound to 1 mol. of tripyridylamine.

The double salt with mercury chloride crystallises from diluted hydrochloric acid in white needles, which melt at  $180^\circ$ .

N found: 10.16 % and 10.21 %

Calculated for  $C_{15}H_{12}N_4.HCl.HgCl_2$  10.07 % N.

Tripyridylamine appeared to be a very feeble base, which is little soluble in water. This aqueous solution is scarcely basic to litmus. The compound

<sup>1)</sup> Journ. Chem. Soc., 71, 460.

is readily soluble in diluted mineral acids. The slight basicity of this pyridine base is surprising. Pyridine itself is a basic substance, it might be expected that on substitution of the hydrogen atoms of ammonia by pyridyl groups a base would be formed, which would be comparable in strength to the aliphatic amines. This is, however, not the case. To get an idea of the difference in basicity between 2-aminopyridine, di(2-pyridyl)-amine, and tri(2-pyridyl)-amine we have measured the electric conductivity of 0.01 normal solutions of these bases in a mixture of water and 10 % alcohol. It appeared that dipyridylamine has a greater conductivity than aminopyridine, tripyridylamine, however, shows a smaller conductive power than aminopyridine. This result was confirmed by measurement of the concentration of the hydrogen ions in 0.01 normal solutions in 15 % alcohol, by the aid of the chinhydrone electrode <sup>1</sup>).

The values found are :

2-aminopyridine  $P_H = 9.07$ .

di(2-pyridyl)amine  $P_H = 9.41$ .

tri(2-pyridyl)amine  $P_H = 7.40$ .

It appears, therefore, that the basicity of aminopyridine slightly increases when a second pyridyl group is attached to the nitrogen atom of the ammonia rest as might be expected, but that the basicity appreciably decreases if the third hydrogen atom of the ammonia rest is substituted by a pyridyl group.

More detailed experimental data of this investigation here will be published elsewhere.

*Organic Chemical Laboratory  
of the University.*

*Amsterdam, May 1927.*

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<sup>1</sup>) The measurements of the conductivity have been made by one of us (LA BASTIDE) in the Electrochemical Laboratory of the University of Amsterdam under the direction of Prof. Dr. A. H. W. ATEN, the  $P_H$  measurements in the Physiological Laboratory of the State University of Groningen, under the direction of Dr. BRINKMAN. We gladly express our indebtedness to both gentlemen.