

LXXXI.—*The Chlorination of Methyl Derivatives of Pyridine. Part I. 2-Methylpyridine.*

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FEW changes among analogues show a greater difference and exemplify better the influence of the nitrogen atom than the direct action of chlorine on benzene and toluene as contrasted with its effect on pyridine and picoline. In the former series, as is well known, no great difficulty is experienced in obtaining fairly regular chlorination and good yields, whilst in the latter the molecule for the most part breaks down and the products form a tar-like mass, from which mere traces of a mixture of chlorinated derivatives can be isolated. Moreover, 2-methylpyridine, unlike pyridine, blackens at once when heated with phosphorus pentachloride either with or without phosphorus oxychloride, and further experiments with this reagent were abandoned.

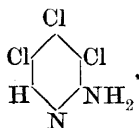
In these circumstances, recourse was had to the process found successful in the case of pyridine (Trans., 1899, 75, 979), namely, the direct chlorination of 2-methylpyridine hydrochloride saturated with hydrochloric acid, the product thus formed remaining liquid at the ordinary temperature of the laboratory. According to Ramsay (*Phil. Mag.*, 1876, II, [iv], 2), "picoline hydrochloride is not acted on by chlorine even when heated with it," but whilst this statement was found to be true at the ordinary temperature, it ceases to be so as the temperature rises, and at 105–110° the hydrogen is rapidly replaced without darkening and substitution derivatives are readily produced. How far this difference is due to the fact that in the work here recorded the 2-methylpyridine hydrochloride was saturated with hydrochloric acid remains to be seen.

It is hoped that conditions may be found under which the hydrogen of the side-chain and nucleus may be separately replaced, but so far the experiments have in the main been confined to the study of a more complete displacement in which both the hydrogen of the methyl group and the nucleus has been involved. So far, the only solid substance isolated as the result of the chlorination is hexachloropicoline, melting at 102–103°, the composition of which is represented by the formula C_6HCl_6N . This compound readily yields successively trichloropicolinic acid and trichloropyridine. The hexachloropicoline is isomeric with the substance (m. p. 60°) obtained by Ost (*J. pr. Chem.*, 1893, [ii], 27, 257) by the action of phosphorus pentachloride on comenamic acid. In addition to the foregoing compound, there is a liquid product consisting of less highly chlorinated compounds, the work on which, although

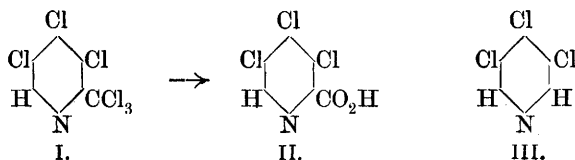
advanced, is still incomplete and will form the subject of a further communication.

It is worthy of remark that there is a total absence of the dipyridyl derivative, of which such a large quantity was produced in the chlorination of pyridine hydrochloride (Trans., 1899, **75**, 979 ; 1901, **79**, 899). This, of course, was expected, seeing that the 2-position—to which the second pyridine nucleus is attached—is in this instance occupied by the methyl group. The solid compound (m. p. 102—103°) already mentioned, when gently heated with approximately eighty per cent. sulphuric acid, gives a nearly quantitative yield of trichloropicolinic acid, $C_5HNC l_3 \cdot CO_2H$, showing that three of the six atoms of chlorine in the original compound belong to the side-chain. This trichloropicolinic acid, when distilled with glycerol, breaks down giving a quantitative yield of a trichloropyridine (m. p. 72—73°) identical with the compound erroneously described by Keiser (*Amer. Chem. J.*, 1886, **8**, 310) as the hydrochloride of a dichloropyridine and subsequently proved by Sell and Dootson (Trans., 1898, **73**, 442) to be a trichloropyridine. This substance is produced, not only by the direct chlorination of pyridine, but also by the action of phosphorus pentachloride on that substance (Sell and Dootson, Trans., 1898, **73**, 437). From the general properties and particularly the highly basic character of this trichloropyridine, it was suspected that the chlorine atoms occupied the positions 3, 4, and 5, and the experimental verification of this assumption should be possible when based on the following considerations.

We may take for comparison the substance 3 : 4 : 5-trichloro-2-aminopyridine, the formula of which may be thus depicted :



This compound, the preparation and orientation of which were described by Sell and Dootson (Trans., 1899, **75**, 980 ; 1900, **77**, 771), should also be obtainable from the trichloropicolinic acid mentioned above by converting it into its amide, and the latter by the Hofmann reaction into the foregoing 3 : 4 : 5-trichloro-2-aminopyridine. The reactions were carried out and resulted in a substance indistinguishable from, and therefore identical with, the compound having the above graphic formula. It may therefore be definitely concluded that in the compounds here described the chlorine atoms in the nucleus occupy the positions 3, 4, and 5, and that in compound I the hydrogen of the methyl group is entirely replaced by chlorine :



EXPERIMENTAL.

The 2-methylpyridine used in this work was in the main obtained from Schuchardt, and was subsequently carefully purified by means of its mercurichloride, a process involving much time and labour. The base was recovered from the double salt (m. p. 154°) by caustic soda, and fractionated after drying over caustic potash. Another specimen of the base was purchased from Kahlbaum.

The hydrochloride was made by saturating the 2-methylpyridine with hydrogen chloride, in which process it absorbs nearly double the theoretical amount of the gas and gives an oily liquid with no tendency to crystallise at the ordinary temperature of the laboratory.

After preliminary trials of small quantities of the hydrochloride under various conditions, it was found that chlorine had no action at the ordinary temperature either in the dark or in bright sunshine, or even in presence of such chlorine carriers as iodine or ferric chloride. When, however, the temperature of the hydrochloride was raised to 100°, fumes of hydrogen chloride were abundantly formed, and the flask containing the substance rapidly increased in weight. In the early stages of the work, several portions were chlorinated at 100°, but it was subsequently found that at 105–110° the absorption of chlorine was still more rapid, and the later experiments were carried out at this temperature.

As the chlorination proceeded, as in the similar work with pyridine hydrochloride, a heavy layer was formed in the liquid which increased in quantity until finally the upper layer disappeared and no increase in weight occurred. During the chlorination, the tube conveying the chlorine was kept as much as possible in the upper layer. The product was cooled by ice and a slow current of air aspirated through for several hours to remove free chlorine, during which operation a copious white, crystalline deposit separated. This was filtered off, and after thorough draining from the liquid product crystallised from alcohol. The crystals are prismatic in form, and dissolve in alcohol and most organic solvents but are insoluble in water. The substance melts at 102–103° without decomposition. The average yield of the re-crystallised substance was over 52 per cent. of the 2-methylpyridine taken.

0.2500 gave 0.2195 CO_2 and 0.0116 H_2O . $\text{C} = 23.94$; $\text{H} = 0.51$.

0.2195 „ 0.630 AgCl . $\text{Cl} = 71.0$.

$\text{C}_6\text{HNC}_3\text{Cl}_3$ requires $\text{C} = 24.00$; $\text{H} = 0.33$; $\text{Cl} = 71.0$ per cent.

Conversion of Hexachloropicoline into 3 : 4 : 5-Trichloropicolinic Acid.

After preliminary trials, fifty grams of the preceding compound were dissolved in 150 c.c. of 80 per cent. sulphuric acid and heated at $120\text{--}130^\circ$ in a reflux apparatus for from $1\frac{1}{2}$ —2 hours, the heating being discontinued when fumes of hydrogen chloride ceased. If the temperature is allowed to rise much higher than 130° , a good deal of the trichloropicolinic acid is decomposed into trichloropyridine, which remains in solution in sulphuric acid. When the temperature of the mixture is carefully kept within the above limit, a nearly theoretical yield of the acid is obtained by pouring the mixture into water, collecting the precipitated acid, and recrystallising from boiling water or alcohol. The substance separates from these menstrua in small, white, anhydrous, short, pointed needles or in filamentous rosettes of needles, according to the temperature of deposition; it melts at $164\text{--}165^\circ$ (uncorr.) with effervescence. The compound dissolves to a moderate extent in boiling, and very sparingly in cold, water and in acetic acid; it is fairly soluble in boiling alcohol and in most organic solvents.

0.2038 gave 0.388 AgCl . $\text{Cl} = 47.09$.

$\text{C}_6\text{HNC}_3\text{Cl}_3 \cdot \text{CO}_2\text{H}$ requires $\text{Cl} = 47.02$ per cent.

A solution of the acid gives the following reactions :

(1) With silver nitrate, a white, gelatinous silver salt which is sparingly soluble in boiling water, from which it separates in filamentous needles.

(2) When a soluble copper salt is added to a hot solution of the acid, a light blue, crystalline (apparently rhombohedral) precipitate of the copper salt is produced, which is very sparingly soluble in either hot or cold water.

(3) Ferrous sulphate produces at first a yellowish-brown colour, but after a short time the solution deposits microscopic rosettes of dark red prisms.

(4) The lead and mercuric salts separate in the form of white rosettes of very sparingly soluble needles or prisms.

Formation of 3 : 4 : 5-Trichloropyridine from 3 : 4 : 5-Trichloropicolinic Acid.

A sample of the pure acid weighing five grams was mixed with 20 c.c. of glycerol, and the mixture rapidly distilled from a small retort until nothing more in the nature of an oil was visible in the

flask used as a condenser. The oily portion of the distillate solidified in the flask to a crystalline mass which, when washed and dried, weighed 3.9 grams, the calculated yield being 4.02 grams. The substance separates from solution in hot alcohol in long, colourless needles melting at 72—73° (uncorr.). The melting point here given is 1° higher than that recorded by Keiser (*Amer. Chem. J.*, 1886, **8**, 310) and by Sell and Dootson (*Trans.*, 1898, **73**, 438), and is not materially affected when the compound is mixed with samples from different sources.

0.1736 gave 0.411 AgCl. Cl = 58.5.

$C_5HNC l_3$ requires Cl = 58.4 per cent.

The compound from other sources, as shown (*loc. cit.*), gives a platinum salt having the formula $(C_5H_2Cl_3N)_2PtCl_4$, containing 27.66 per cent. of platinum. A specimen prepared from the trichloropyridine from trichloropicolinic acid furnished the following numbers:

0.1635 gave 0.0445 Pt. Pt = 27.21 per cent.

As a further confirmation, samples of the double salt with mercuric chloride from the different sources were compared, and found to be practically identical in melting point and general characters.

Formation of Methyl 3 : 4 : 5-Trichloropicolinate.

Methyl 3 : 4 : 5-trichloropicolinate was prepared by saturating a mixture of the acid and methyl alcohol with hydrogen chloride. On leading the gas into the cold mixture, the acid gradually dissolved, and on passing in a further quantity of this reagent a crystalline precipitate of the ester separated. This was removed by filtration and more gas passed into the filtrate until complete saturation was effected. After standing for twelve hours, the excess of hydrogen chloride was removed by a current of dry air, and the excess of alcohol by distillation in a partial vacuum. The deposited ester was recrystallised from methyl alcohol, from which it separates in colourless plates, having a pearly lustre and melting at 84—85° (uncorr.). The ester is freely soluble in organic solvents and moderately so in boiling water, from which it separates in plates, the melting point being unaltered.

Formation of 3 : 4 : 5-Trichloropicolinamide from Methyl 3 : 4 : 5-Trichloropicolinate.

When the methyl ester was dissolved in hot methyl alcohol and an excess of strong aqueous ammonia added, the amide rapidly separated as a crystalline magma of fine needles; this substance, when collected and recrystallised from spirit, formed long, colourless, flat needles

melting at $184-185^{\circ}$ (uncorr.); it is freely soluble in most organic solvents, and moderately so in boiling water, from which it separates on cooling ($184-185^{\circ}$, uncorr.).

0.1860 gave 0.3529 AgCl. Cl = 47.02.

0.2445 „ 0.4628 „ Cl = 46.86.

$C_5HNCI_3 \cdot CONH_2$ requires Cl = 47.22 per cent.

Formation of 3:4:5-Trichloro-2-aminopyridine from 3:4:5-Trichloro-picolinamide.

The Hofmann reaction was carried out on 4.5 grams of the picolinamide, using the theoretical amounts of bromine and caustic potash. The only deviation from the usual procedure was the filtration of the crystalline compound from the cooled alkaline solution and its purification by distillation in a current of steam, to avoid the risk of any possible decomposition by distillation from the strongly alkaline liquid. All but mere traces of the crystalline product came over during the steam-distillation, and when collected and recrystallised from alcohol formed a mass of fine needles melting at $160-161^{\circ}$ (uncorr.).

0.2870 gave 35 c.c. nitrogen at 24° and 767 mm. N = 13.78.

Trichloroaminopyridine, $C_5H_2N_2Cl_3$, requires N = 14.17 per cent.

Trichloropicolinamide, $C_5HNCI_3CONH_2$, requires N = 12.41 per cent.

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