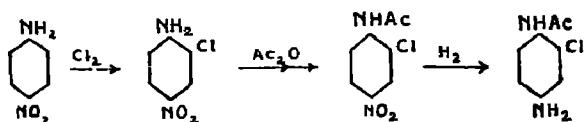


A New Method for the Preparation of 4-Acetylamino-3-chloro-aniline.

BY SUDHIR CHANDRA NIYOGY.

4-Acetylamino-3-chloro-aniline, which is used in preparing substances that are of value in medicine, was prepared by Cain (*J. Chem. Soc.*, 1909, 95, 716). As his method was found to be imperfect it was decided to ascertain the necessary details.

The starting point in the preparation of the substance is *p*-nitraniline. The first step is the chlorination of *p*-nitraniline so as to obtain 2-chloro-4-nitraniline, which is then acetylated and subsequently reduced.



There are many methods for the preparation of 2-chloro-4-nitraniline (*Annalen*, 1876, 182, 108; *Ber.*, 1894, 27, 377; *J. Chem. Soc.*, 1908, 93, 1773; *Chem. Zents*, 1900, II, 360). All these may be broadly divided into two classes: (1) Chlorination in concentrated mineral acid solution; (2) chlorination in dilute mineral acid solution. The chlorinating agent employed are (1) chlorine gas, (2) sodium hypochlorite, and (3) bleaching powder.

Careful repetition of Flurschein's method for the preparation of 2-chloro-4-nitraniline (*J. Chem. Soc.*, 1908, 93, 1773) showed that the author's claims are exaggerated, as the formation of tarry matter is very considerable. On following the specification of Casse¹la and Co's Patent (D. R. P., 109189) the product obtained was invariably 2:6-dichloro-4-nitraniline even when only half the required quantity of chlorine was used.

Sodium hypochlorite, and bleaching powder containing a known weight of available chlorine, were next employed without any better result. The corresponding bromo-derivative is very easily prepared by the addition of the required quantity of bromine in acetic acid

solution to an acetic acid solution of *p*-nitraniline at ordinary temperature. But when the experiment was repeated using acetic acid containing a known weight of chlorine, the result was indifferent. As the result of this series of experiments it may be safely concluded that all common methods of preparing 2-chloro-4-nitraniline are either faulty or misleading.

In one experiment *p*-nitro-acetanilide was boiled with hydrochloric acid to hydrolyse the anilide, and the acid solution was cooled with ice and treated with chlorine. A yellowish brown product separated which, on purification, had m.p. 103—4°, the m.p. of 2-chloro-4-nitraniline being 104·5°. So this was the required compound. The main difference in this experiment is the presence of acetic acid and assuming that this is somehow favourable to the formation of 2-chloro-4-nitraniline, a series of experiments was made using varying proportions of acetic acid, hydrochloric acid and water, till the experimental conditions were so adjusted as to give a yield of 8·5 g. of 2-chloro-4-nitraniline from 10 g. *p*-nitraniline.

The failure of the previous experiments may be accounted for as follows:—If during the chlorination, a solvent (like hydrochloric acid, sulphuric acid or a mixture of hydrochloric acid and acetic acid) is employed in which *p*-nitraniline as well as 2-chloro-4-nitraniline is soluble, the resulting product is invariably the dichloro compound. But if a solvent is employed in which *p*-nitraniline is soluble but not the 2-chloro-4-nitraniline, the latter separates as soon as it is produced and escapes further chlorination. The best yield obtained amounted to about 70% of the theory. Some decomposition invariably takes place and some of the dichloro-compound is invariably formed.

The reduction of 4-acetylamino-3-chloro-1-nitrobenzene was effected by Cain (*loc. cit.*) using acetic acid and iron filings. The reduction product obtained by me was different from Cain's product. Cain's sample was yellow needles, m.p. 111°, and was moderately soluble in water. The product (empirical formula, C_8H_8ONCl) obtained by me had a very faint pink colour (which darkened on exposure to sunlight) and melted at 134·35°. It was very soluble in water and gave the following reactions:—

- (1) It gave the diazo reaction and therefore contains a free amino group.
- (2) When dissolved in dilute hydrochloric acid, it does not give the indamine test for *p*-diamines; when it is

heated for some time with concentrated hydrochloric acid, it gives this test.

Thus one is led to conclude that the compound having a m.p. 134—35° is 4-acetylamino-3-chloraniline. Cain must have been misled by some experimental error.

EXPERIMENTAL.

2-Chloro-4-nitraniline.

p-Nitraniline (10 g.) was dissolved in water (860 c.c.) containing hydrochloric acid (50 c.c. 37%) and glacial acetic acid (25 c.c.). The solution was cooled to a temperature of 10—15° and a slow current of chlorine was passed through the liquid with constant stirring. (If the current of chlorine is rapid, the quantity of tarry matter formed is considerable.) A yellow precipitate separated which was filtered off from time to time. The end of the reaction is very easily ascertained: when all the nitraniline had been used up, chlorine begins to escape. The combined solid product was boiled with water when a tarry mass settled down. Rectified spirit was then added in small quantities at a time to the boiling liquid, till the residue had a granular appearance. The whole was then filtered rapidly and the filtrate was largely diluted with water when 2-chloro-4-nitraniline separated as a yellow flocculent precipitate. As the compound is somewhat soluble both in water and in dilute alcohol, the filtrate was cooled in ice water. The precipitate was collected and dried; m.p. 103-4°. Yield 8.5 g.

Acetylation of 2-Chloro-4-nitraniline.

2-Chloro-4-nitraniline (10 g.) was dissolved in glacial acetic acid (80 c.c.) and acetic anhydride (45 c.c.) was added. Sulphuric acid (20 drops) was added to it with shaking. After an hour the solution was poured into boiling water (600 c.c.). On cooling, light brown crystals separated, m. p. 139—40°. Yield 9 g. In the absence of sulphuric acid the acetylation is far from being complete (*cf.* however, Orton, *J. Chem. Soc.*, 1908, 93, 1242).

1-Amino-4-acetylamino-3-chlorobenzene.

Iron dust (5 g.), glacial acetic acid (2 c.c.) and water (50 c.c.) were placed in a round bottom flask, 4-Acetylamino-3-chloro-1-

nitro-benzene (5 g.) was taken and half of it was at once added to the contents of the flask and thoroughly mixed by shaking. The mixture became warm but in no case did the temperature rise higher than 50°. Further quantities of the nitro-compound were added gradually to this warm mixture. After all the nitro compound had been added, the mixture was shaken till it reached its initial temperature. The mixture was then gently boiled with a solution of sodium carbonate (2 g.) in water (10 c.c.) and filtered hot at the pump. The residue was twice extracted with small quantities of water and filtered hot. The combined filtrates, on cooling, gave a light pink precipitate, m. p. 125-28°. It was recrystallised from benzene, m.p. 134-35°. Yield 3.2 g. (Found: N, 15.21; Cl, 19.74; C, 52.1; H, 5.2. $C_8H_8ON_2Cl$ requires N, 15.18; Cl, 19.24; C, 52.03; H, 4.8 per cent.).

My thanks are due to Prof. H. K. Sen for the kind interest he has taken in this work.

UNIVERSITY COLLEGE OF SCIENCE AND TECHNOLOGY,
DEPARTMENT OF APPLIED CHEMISTRY,
CALCUTTA.

Received June 14, 1926.