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SANDMEYER REACTIONS OF MONOACYL ARYLENEDIAMINES

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Fluorinated aromatic amines can be prepared by an application of the Schiemann reaction to half-acylated diamines (*m*- and *p*-acetamidoarylamines, *o*-phthalimidoarylamines), followed by removal of the acyl group (1). From the viewpoint of preparative organic chemistry, it seemed of interest to investigate whether this method is applicable to the synthesis of fluoro amines only, or whether other halogeno amines and aminonitriles also could be prepared by extension of this simple method. It could be demonstrated that the half-acylated diamines give sufficiently stable diazonium salts to make a variety of Sandmeyer reactions possible. From monophthaloyl-*o*-phenylenediamine N-phthaloyl-*o*-aminobenzonitrile has been obtained in 83% yield, and from N^1-phthaloyl-4-methoxy-1,2-phenylenediamine there was obtained 2-amino-5-methoxybenzonitrile in 63% yield (2 steps). From N-acetyl-1,4-phenylenediamine *p*-iodo-, *p*-bromo- and *p*-cyano-acetanilide were prepared in 51, 47, and 64% yield, respectively. Analogously, 41 and 72% yields of 3-bromo- and 3-cyano-acetanilide have been secured.

It is recalled that N-acetyl-*m*-phenylenediamine has been used for the preparation of azo-dyes (2), and the diazotization of N-acetyl-*p*-phenylenediamine and its use for the synthesis of such dyes has been described repeatedly (3–8).

The substances obtained in this study have been identified by means of their physical constants or by conversion into known transformation products.

EXPERIMENTAL PART

N-Phthalyl-o-aminobenzonitrile. To the hydrochloride of N^1-phthaloyl-1,2-phenylenediamine prepared by brief heating of 4.8 g. of the substance (1) with 25 ml. of concentrated hydrochloric acid, was added 50 g. of ice and the substance was diazotized at 0° with 1.5 g. of sodium nitrite in 20 ml. of water. The diazonium solution was added slowly with stirring and at a temperature not exceeding 5° to a solution of cuprous cyanide (prepared from 5.6 g. of potassium cyanide in 10 ml. of water and 5 g. of cupric sulfate in 15 ml. of water) which was covered with a layer of toluene. Stirring was continued for two hours at room temperature, and the temperature was raised gradually to 50°. The toluene layer was separated, washed with water and dried over sodium sulfate. Concentration gave a pink crystalline product of m.p. 144–145° after recrystallization from benzene; yield, 4.2 g. (83%).

Anal. Calc'd for $C_{15}H_8N_2O_2$: N, 11.3. Found; N, 11.5; 11.5.

o-Aminobenzonitrile. To a suspension of 3.7 g. of the foregoing compound in 50 ml. of ethanol, 8 ml. of hydrazine hydrate was added, and the mixture was refluxed for two hours. Then the solvent was removed, the residue warmed with 50 ml. of hydrochloric acid, the phthalyl hydrazide filtered, and the filtrate made alkaline and extracted with ether. The brown oil so obtained crystallized upon scratching; m.p. 43°. Recrystallization from a mixture of equal volumes of ether and petroleum ether raised the m.p. to 47° [Literature: 47° (9); 50° (10); 51° (11)]. Yield, 1.2 g. (68%).

2-Amino-5-methoxybenzonitrile. The diazonium solution prepared from 4 g. of N^1-phthaloyl-4-methoxy-1,2-phenylenediamine (1), 40 ml. of concentrated hydrochloric acid, 30 g. of ice, and 1.4 g. of sodium nitrite in 20 ml. of water, was added slowly, as above, to a cuprous cyanide solution (from 5.6 g. of potassium cyanide and 5 g. of cupric sulfate) which was covered with a layer of benzene. The reaction mixture was worked up as above and the crude product in a little benzene was refluxed for two hours with 6 ml. of hydrazine hydrate. The benzene was removed and the residue was heated with 40 ml. of hydrochloric acid; after removal of the phthalyl hydrazide the solution was made alkaline and extracted with ether. The pink crystalline product so obtained was recrystallized from benzene and melted at 130°. Yield, 1.4 g. (63%).

Anal. Calc'd for $C_8H_8N_2O$: N, 18.9. Found: N, 18.8.

2-Amino-5-methoxybenzoic acid. The foregoing compound (1.4 g.) was heated with potassium hydroxide in aqueous-alcoholic solution until ammonia was no longer evolved. The alcohol was removed by distillation, and the remaining solution was extracted with ether, to remove unchanged starting material, and acidified. The precipitate was filtered and recrystallized from alcohol. Plates of m.p. 170–171° (dec.) [Lit. 179–180° (12); 149–150° (13, 14)]. Yield, 0.9 g. (51%).

4-Iodoacetanilide. To the diazonium solution prepared from 6 g. of N^1-acetyl-1,4-phenylenediamine (1), 20 ml. of conc'd hydrochloric acid, 60 ml. of water, and 3.2 g. of sodium nitrite in 10 ml. of water, a concentrated solution of 8 g. of potassium iodide was added. The evolution of nitrogen which started immediately was allowed to subside and the mixture heated for a few minutes at 50°. The oily product was extracted with toluene, and the solution was washed several times with a sodium carbonate solution and water and dried over sodium sulfate. On concentration, a solid product was obtained which was recrystallized from alcohol. M.p. 183° [Lit. 181.5° (15); 183° (16); 184° (17)]. Yield, 5.3 g. (51%).

4-Bromoacetanilide. In presence of some pieces of ice, 9 g. of N^1-acetyl-1,4-phenylenediamine was triturated in a mortar with 36 ml. of 40% hydrobromic acid and the mixture was diazotized with 4.8 g. of sodium nitrite in 15 ml. of water at 0°. After addition of 1 g. of copper powder, the clear solution was stirred for three hours at room temperature and filtered. The filtrate was extracted with ether, and the extract was washed with sodium carbonate solution and water and dried over sodium sulfate. On removal of the ether, a slightly pink crystalline product was obtained which was recrystallized from dilute alcohol. M.p. 167° [Lit. 165° (18); 167–168° (19)]. Yield, 6 g. (47%).

4-Cyanoacetanilide. N^1-Acetyl-1,4-phenylenediamine (7.5 g.) was triturated in a mortar with a few pieces of ice and 25 ml. of 2 *N*-hydrochloric acid. After addition of 37.5 ml. of the same acid, diazotization was carried out at 0° with 50 ml. of *N* sodium nitrite solution. The clear solution was added to a solution of cuprous cyanide (from 14 g. of potassium cyanide and 12.5 g. of cupric sulfate) which was covered with a layer of benzene. After two hours at room temperature, the benzene layer was separated, washed with sodium carbonate solution and water, and dried over sodium sulfate. The melting point (198°) of the crystalline product was raised by recrystallization from water to 204°. [Lit. 200° (20); 205.5° (21)]. Yield, 5.1 g. (64%).

3-Cyanoacetanilide. N^1-Acetyl-1,3-phenylenediamine (1) (7.5 g.) was treated as in the foregoing example. The reaction product was filtered, and the precipitate was washed with benzene. The combined benzene solutions were washed with sodium carbonate solution and water, dried over sodium sulfate, and concentrated. The orange crystalline product was recrystallized from water, and had m.p. 130° [Lit. 130.5–131° (22)]. Yield, 5.8 g. (72%).

3-Bromoacetanilide. N^1-Acetyl-1,3-phenylenediamine was treated as described for the *para*-isomer. The solution obtained was filtered and extracted with ether, and the ethereal solution was washed and dried over sodium sulfate. On removal of the ether, an orange crystalline product remained which was recrystallized from chloroform. Needles of m.p. 87° [Lit.: 87.5° (23)]. Yield, 5.8 g. (41%).

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