[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF TEMPLE UNIVERSITY]

A Further Study of the Bromination of *p*-Acetaminodiphenyl

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In a search for a readily available source of 3,4-dibromodiphenyl,[1] consideration was given to the possibility of obtaining it by the bromination of *p*-acetaminodiphenyl followed by hydrolysis and conversion of the resulting 4-amino-3-bromo compound to the desired dibromo compound. It was stated by Scarborough and Waters[2] that on monobromination, *p*-acetaminodiphenyl yields a mixture of brominated products which by fractional crystallization was separated into 3,4′-dibromo-4-acetaminodiphenyl, 4-bromo-4′-acetaminodiphenyl and a product melting at 145°, which he believed to be 4-bromo-4′-aminodiphenyl (assuming that the free base had been liberated by hydrolysis). Kenyon and Robinson[3] repeating this bromination observed the formation of 4-bromo-4′-acetaminodiphenyl (30%) and of the product melting at 145° (50%). From the latter they obtained by hydrolysis, fractional crystallization, and reacetylation pure 3-bromo-4-acetaminodiphenyl, m. p. 161°. They regarded the 145° melting product as essentially 3-bromo-4-acetaminodiphenyl with "admixed 4-bromo-4′-acetaminodiphenyl, unchanged 4-acetaminodiphenyl, and some dibrominated material."

Experiments have been conducted in this Laboratory with a view to determining the exact composition of this mixture whose melting point remains unchanged by repeated crystallization. It was first found that bromination in the presence of anhydrous sodium acetate nevertheless yields the same product, thus eliminating the possibility of a free base (the result of hydrolysis by hydrobromic acid) being present as an impurity. Furthermore, the product was unchanged by acetylation. An analysis indicated 31.1% bromine. Monobromoacetaminodiphenyl contains 27.6% Br. Since no free base is present, the high bromine analysis was considered to be due to the presence of a dibromoacetaminodiphenyl. This requires 43.3% Br. On this assumption the 145° melting mixture should contain 22% of the dibromo compound. It was observed that on dibromination *p*-acetaminodiphenyl yields large amounts of 3,4′-dibromo-4-acetaminodiphenyl (m. p. 195°) and some of the 145° product. The former compound was hydrolyzed to the free base which previously has not been characterized.

The base resulting from the hydrolysis of the 145° compound was separated by fractional distillation in a vacuum into two portions, one of which after recrystallization and acetylation yielded 4-acetamino-3-bromodiphenyl, m. p. 161–162°, and the other 3,4′-dibromo-4-aminodiphenyl, which on acetylation melted at 195°. The two compounds when mixed together in the proportions of 78/22, respectively, and recrystallized from alcohol yielded the mixture melting constantly at 145°.

The structure of the base 3-bromo-4-aminodiphenyl was established by Kenyon and Robinson by converting it to the known 3,5-dibromo-4-aminodiphenyl. We have synthesized 3-bromo-4-acetaminodiphenyl by an independent method and found it to melt unchanged with that obtained by direct bromination. In this synthesis *m*-bromoacetanilide was nitrated and hydrolyzed to yield 4-nitro-3-bromoaniline. This was converted to 4-nitro-3-bromodiphenyl by the reaction of Gomberg and Pernert,[4] then reduced and acetylated.

A study of the dibromination of *p*-acetaminodiphenyl shows that in the presence of sodium acetate the chief product is 3,4′-dibromo-4-acetaminodiphenyl, while some of the "145 degree" product is also formed. In the absence of sodium acetate, however, using the same amount of bromine, extensive hydrolysis results, the principal product being 3,5,4′-tribromo-4-aminodiphenyl. Other products isolated were the acetyl derivative of this base, 4-bromo-4′-acetaminodiphenyl, and the "145 degree" product.

Experimental Part

Separation of the 145° Melting Mixture into its Components.—The above mixture (33 g.) was hydrolyzed by refluxing with 300 cc. of alcohol and 120 g. of constant boiling hydrobromic acid. The liberated crude base was distilled in a vacuum and separated into two fractions (A) 20 g., b. p. 195–200° (5 mm.); (B) 7 g., b. p. 200–220° (5 mm.). Fraction A on crystallization from an ether-petroleum ether mixture yielded 13 g., m. p. 62–63°. This on acetylation yielded a derivative melting at 161–

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[1] Case, THIS JOURNAL, **58**, 1249 (1936).

[2] Scarborough and Waters, *J. Chem. Soc.*, 557 (1926).

[3] Kenyon and Robinson, *ibid.*, 3050 (1926).

[4] Gomberg and Pernert, THIS JOURNAL, **48**, 1372 (1926).

162°, and unchanged when mixed with 3-bromo-4-acetaminodiphenyl obtained by the synthetic method described later. Fraction B after two crystallizations from ether–petroleum ether yielded 1.5 g. melting at 102° and not depressed in melting point when mixed with 3,4'-dibromo-4-aminodiphenyl. On acetylation this base yielded a product melting at 195° and identical with 3,4'-dibromo-4-acetaminodiphenyl.

Dibromination of *p*-Acetaminodiphenyl. (A) In Absence of Sodium Acetate.—To 35 g. of *p*-acetaminodiphenyl in 400 cc. of glacial acetic acid was added 55 g. of bromine (2 moles) in 60 cc. of acetic acid. The mixture was allowed to stand overnight and then warmed on the steam-bath until decolorized. After cooling, the precipitate was filtered, washed with water and dried. On recrystallization from alcohol, 7 g. of pure 3,5,4'-tribromo-4-aminodiphenyl melting at 149–150° was obtained. The alcoholic filtrate, after evaporation to dryness, was extracted with benzene. From the benzene-insoluble part was obtained 1.5 g. of 4-bromo-4'-acetaminodiphenyl, m. p. 248°, identified by mixed melting point. The benzene soluble part yielded an additional 3 g. of 3,5,4'-tribromo-4-aminodiphenyl.

The acetic acid filtrate from the first filtration was poured into ice water, and the precipitate crystallized from alcohol, yielding 1.5 g. of 3,5,4'-tribromo-4-acetaminodiphenyl, identified by mixed melting point with the product obtained by acetylating the corresponding base. The alcoholic filtrate, on evaporation and crystallization of the residue, yielded 1 g. of material melting at 143–144° and shown by mixed melting point to be the "145° melting mixture."

B. In Presence of Sodium Acetate.—The same proportions and directions were used as in A, except that 38 g. of fused sodium acetate was added to the mixture. The precipitate separating from the acetic acid was recrystallized from alcohol, yielding 27 g. of 3,4'-dibromo-4-acetaminodiphenyl, m. p. 194–195°.

The acetic acid filtrate was poured into ice water and recrystallized from alcohol, yielding an additional 2 g. of the above acetamino compound. The alcoholic filtrate on evaporation to dryness and recrystallization of the residue yielded 4 g. of the "145° melting mixture."

3,4'-Dibromo-4-aminodiphenyl.—This was obtained by the hydrolysis of the corresponding acetamino compound (m. p. 195°) in alcoholic hydrobromic acid. The base was crystallized from benzene–petroleum ether, m. p. 107–108°.

Anal. Calcd. for $C_{12}H_9NBr_2$: Br, 48.89. Found: Br, 49.20.

3-Bromo-4-nitroaniline.—The following procedure was found to be superior to those given in the literature:[5] 50 g. of *m*-bromoacetanilide was dissolved in a minimum quantity of glacial acetic acid and cooled with ice and salt; 280 cc. of concentrated sulfuric acid was added. When the temperature fell below 5°, a previously cooled solution of 25 g. of potassium nitrate in a minimum amount of concentrated sulfuric acid was added drop by drop, with stirring, the temperature being kept below 5°. Stirring was continued for one hour after the addition was complete, the container being kept cool. The mixture was then poured onto ice in a thin stream. The precipitate was filtered off, washed with water and then steam-distilled after adding to the water in the flask a weight of concentrated sulfuric acid equal to the weight of the precipitate. 3-Bromo-6-nitroaniline distilled over while the desired product, 3-bromo-4-nitroaniline, remained in the flask. It was necessary to distil over about four liters of water before all the isomer was removed. The contents of the flask was made alkaline with concentrated sodium hydroxide, cooled, and the yellow precipitate was filtered off. This was then recrystallized from alcohol: m. p. 177°; yield, 22 g. (43%).

3-Bromo-4-nitrodiphenyl.—To 30 g. of 3-bromo-4-nitroaniline was added 35 cc. of concentrated hydrochloric acid and 13 cc. of water. The mixture was cooled to 5° and diazotized with a solution of 12 g. of sodium nitrite. One hundred cc. of cold thiophene-free benzene was added and then 60 cc. of 5 *N* sodium hydroxide, drop by drop with stirring, the temperature being kept below 5°. The mixture was allowed to stand overnight and then filtered from a considerable amount of tarry matter. The benzene was removed from the benzene layer, and the residue distilled *in vacuo*. It boiled at 252–254° (7 mm.). It was not further purified; yield 12 g.

3-Bromo-4-acetaminodiphenyl.—Ten grams of stannous chloride ($SnCl_2 \cdot 2H_2O$) was dissolved in 67 cc. of absolute alcohol; 10 g. of 3-bromo-4-nitrodiphenyl was added and the mixture warmed gently on the steam-bath for ten hours. The alcohol was then evaporated off, ice water added and then concentrated sodium hydroxide until the contents of the flask was strongly alkaline. The mixture was then extracted with ether. After removal of the ether an oil remained to which was added 75 cc. of glacial acetic acid and 10 cc. of acetic anhydride. The mixture was refluxed for six hours. The contents of the flask was poured into ice water and the precipitate filtered off. It was recrystallized from methyl alcohol: m. p. 161°; yield 7 g.

Anal. Calcd. for $C_{14}H_{12}ONBr$: Br, 27.58. Found: Br, 27.36.

Summary

1. The composition of the constant-melting (145°) mixture, which is the chief product of the bromination of *p*-acetaminodiphenyl, has been determined.

2. 3-Bromo-4-acetaminodiphenyl has been synthesized by an independent method.

3. A study has been made of the dibromination of *p*-acetaminodiphenyl.

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[5] Claus and Scheulen, *J. prakt. Chem.*, [2] **43**, 201 (1891); Lukěs and Fragner, *Chem. Listy*, **22**, 321 (1928); Orton, *J. Chem. Soc.*, **81**, 495 (1902).