

reagents, cinnamyl diacetate may be reduced to cinnamyl acetate by means of iron and acetic acid, in 60.7% yield.

4. Pure cinnamic aldehyde and cassia oil may likewise be reduced to cinnamyl acetate with good yields.

5. The addition of copper or nickel salts to the iron and acetic acid reducing medium does not catalyze the formation of cinnamyl acetate.

6. Aluminum amalgam, zinc-copper couple, zinc-nickel couple, or zinc and acetic acid with cinnamyl diacetate give *glycols*, and not *cinnamyl acetate*.

7. Cinnamyl acetate is hydrolyzed in 98% yield by 5% alcoholic sodium hydroxide.

8. Cinnamyl alcohol forms an addition compound with calcium chloride which may be used for the purification of the crude alcohol.

9. Cinnamyl alcohol reacts with *p*-nitrobenzoyl chloride to form the characteristic ester, cinnamyl *p*-nitrobenzoate.

NEW HAVEN, CONNECTICUT

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[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE STATE  
UNIVERSITY OF IOWA]

## STERIC HINDRANCE IN THE MIGRATION OF ACYL FROM NITROGEN TO OXYGEN

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Previous work published from this Laboratory<sup>1</sup> has shown that the migration of acetyl from nitrogen to oxygen, which occurs when an *o*-acetylaminophenol is benzoylated by the Schotten-Baumann method, is not prevented by the presence of acid-forming (halogen) or certain other substituents attached to the phenol nucleus. In view of the fact, however, that many well-known reactions are hindered to a greater or less degree, depending apparently on the weight and space occupied by the radicals adjacent to the reacting groups,<sup>2</sup> it became a matter of interest to us to study the behavior of acetyl-benzoyl derivatives of aminophenols in which the positions *ortho* to both amino and hydroxyl groups were occupied by heavy radicals. For this purpose the bromine derivatives of *o*-amino-*p*-cresol and *o*-amino-*o*-cresol (OH=1) were selected. 2-Amino-3,6-dibromo-4-methylphenol, obtained by reduction of the corresponding nitro compound which, in turn, was prepared by nitration of 2,3,6-tribromo-*p*-cresol,<sup>3</sup> was acetylated in the usual way. Though hydrolysis of this

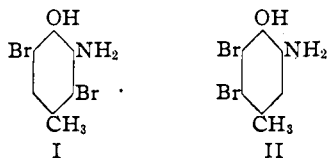
<sup>1</sup> THIS JOURNAL, 45, 1738 (1923), gives a list of papers.

<sup>2</sup> For a bibliography of the subject see Stewart, "Stereochemistry," Longmans, Green and Co., 1907, p. 261.

<sup>3</sup> (a) Zincke, *J. prakt. Chem.*, [2] 61, 564 (1900). (b) Zincke and Emmerich, *Ann.*, 341, 312 (1905).

product with dil. sodium hydroxide solution went more slowly than in some other cases due, possibly, to steric hindrance, it gave an acetylaminophenol that melted at  $158^{\circ}$ . Benzoylation of this product gave a diacyl derivative, melting at  $232^{\circ}$ , and this upon hydrolysis lost acetyl and left a phenolic substance melting at  $154^{\circ}$ , which was shown by analysis to contain a benzoyl radical. The structure of this compound was further established through synthesis by Ransom's method<sup>4</sup> from benzoyl chloride and the free base indicated above. Acetylation of each of these products gave the same substance, m. p.  $232^{\circ}$ , and this was found to be identical with that obtained by the action of benzoyl chloride on 2-acetylamino-3,6-dibromo-4-methylphenol. In the reaction last indicated, therefore, the benzoyl radical went to nitrogen while acetyl migrated to oxygen.

In these experiments no attempt was made to decide whether the base here used was 2-amino-3,6-dibromo-4-methylphenol (I) or its isomer 2-amino-4-methyl-5,6-dibromophenol (II).



In the second configuration it is, of course, clear that the amino group is not protected, and it was held that results obtained from the base in hand were not entirely conclusive. To meet objections that might be raised on this score it was proposed to study the behavior of a base in which all benzene hydrogen had been substituted. One of these was obtained through nitration of tetrabromo-*p*-cresol,<sup>3a</sup> and reduction of the nitro compound in the usual way. The diacyl compound obtained in this instance was, as indicated in the case described above, hydrolyzed slowly, but a mono-acetyl derivative melting at  $189^{\circ}$  and containing a phenolic hydroxyl was obtained. Benzoylation of this product gave a diacyl derivative that melted at  $177^{\circ}$ , which upon hydrolysis gave an N-benzoyl compound that melted at  $195^{\circ}$ , and a small portion of what appeared to be the N-acetyl derivative. Whether the benzoylation had been incomplete or the migration of acetyl only partial was left undetermined because of the small amount of material available.<sup>5</sup> Proof of the structure of the N-benzoyl product was obtained by synthesizing it from the corresponding free base by Ransom's method. A phenolic compound melting at  $195^{\circ}$  and showing the other properties of the one that was found upon hydrolysis of the acetyl-benzoyl derivative, melting at  $177^{\circ}$ , was

<sup>4</sup> Ransom, *Am. Chem. J.*, **23**, 17 (1900).

<sup>5</sup> The bearing of these observations will be considered more fully in a subsequent communication in which it will be shown that in certain cases migration may occur during hydrolysis.

obtained. A mixture of the two phenolic products melted still at 195°, and acetylation of each gave the same compound, which melted at 177°. Evidently the presence of the bromine atoms had not prevented the migration.

To test the question further, the behavior of the diacyl derivatives of the isomeric base 2-amino-3,4,5-tribromo-6-methylphenol were studied. This base was secured by reduction of the *o*-nitro compound obtained by nitration of tetrabromo-*o*-cresol in accordance with Zincke's<sup>3a</sup> general directions. In addition to the observations of this author, who found that nitration of the bromine derivative gave only one product, 2-nitro-3,4,5-tribromo-6-methylphenol, it is shown below that the isomeric compound 4-nitro-2,3,5-tribromo-6-methylphenol is also formed in the same reaction.<sup>6</sup>

An attempt to separate the isomers by steam distillation was unsuccessful owing to the slight volatility of the *ortho* compound. Fractional crystallization gave two products—one melting with apparent decomposition at 177°,<sup>7</sup> and which is shown below to be a *para* compound, and a second one, melting at 159°, which is doubtless identical with the product Zincke and Hedenström isolated from the nitration mixture, for which they recorded a melting point of 156°, and which they regarded as having the *ortho* relationship, though they furnished no direct proof of its structure.

From the aminophenol obtained by reducing in the usual way the product melting at 159°, the corresponding diacetyl derivative was prepared. Hydrolysis of this material gave an acetyl-aminophenol that melted at 186°, and the latter upon treatment with benzoyl chloride gave an acetyl-benzoyl derivative melting at 234°. When this product was hydrolyzed it lost the acetyl radical and left a phenolic compound that melted at 133°, and which was shown by synthesis from the corresponding base by Ransom's method to have benzoyl attached to nitrogen. Both of these phenolic products gave, when acetylated, an acetyl-benzoyl derivative that melted

<sup>6</sup> It is of interest to note here that Zincke reported the replacement of halogen by the nitro group by this method of nitration in 1900 [*J. prakt. Chem.*, [2] 61, 561 (1900)], on the basis of work done by his students [Foster, *Dissertation*, Marburg, 1898, and Wagner, *Dissertation*, Marburg, 1899], and that he conducted studies in this field for fifteen years thereafter [*Ann.*, 398, 343 (1913)]. He has summarized the work done by himself and students on the bromine derivatives of *o*-, *m*- and *p*-cresols, and has reached the conclusion that in the *meta* series this method of nitration gives products in which the halogen atom *para* to hydroxyl is replaced by the nitro group, while in the *ortho* and *para* series the atom *ortho* to hydroxyl is replaced. In no case, however, so far as we are aware, has he recorded the formation of isomeric compounds as the result of a single nitration. The pair of isomers obtained in the present work adds another to the list already reported [Raiford, *THIS JOURNAL*, 44, 158 (1922)] in which it has been shown that isomeric nitro compounds may be obtained from both *ortho* and *meta* cresol derivatives, as well as from those of phenol, when the halogen atom is other than chlorine.

<sup>7</sup> This agrees with the record of Zincke and Klostermann [(a) *Ber.*, 40, 683 (1907)] who obtained this product by treatment of tetrabromo-*o*-methyl-quinol with caustic alkali.

at 234° and was proved to be identical with that obtained by benzoylation of 2-acetylamino-3,4,5-tribromo-6-methylphenol. In the last-named reaction, therefore, benzoyl must have attached itself to nitrogen while acetyl migrated to oxygen, from which it follows that the presence of atoms of high atomic weight adjacent to the reacting groups does not prevent this migration. These results are indicated in Table I.

TABLE I  
COMPOSITION AND BEHAVIOR OF DIACYL DERIVATIVES

Acyl radicals used	Aminophenols	Diacyl derivatives	Hydrolysis products
Acetyl and benzoyl	2-Amino-3,6-dibromo-4-methylphenol	Identical	Benzoyl on nitrogen
Acetyl and benzoyl	2-Amino-3,5,6-tribromo-4-methylphenol	Identical	Benzoyl on nitrogen
Acetyl and benzoyl	2-Amino-3,4,5-tribromo-6-methylphenol	Identical	Benzoyl on nitrogen

### Experimental Part

#### A. Bases Obtained from Para-Cresol

**2-Amino-3,6-dibromo-4-methylphenol** (or **2-Amino-4-methyl-5,6-dibromophenol**).—The starting material used in preparing this compound was *p*-cresol. The purest obtainable commercial sample was fractionated and the portion boiling at 199–200° (uncorr.) was reserved for this work. One-half a molecular proportion (54 g.) was converted into the tribromo derivative by the use of 245 g. of bromine as directed by Zincke and Wiederhold.<sup>8</sup> The crude product was freed from iron compounds by treatment of the material with dil. sodium hydroxide solution, filtration of the mixture, and addition of acid to the clear filtrate. A yield of 146 g. or 86% was obtained. The substance was crystallized from ligroin (100–110°) and was obtained in colorless needles that melted sharply at 99°. Zincke and Wiederhold recorded 102°.

Fifty g. of this product was dissolved in ten times its weight of glacial acetic acid, the liquid cooled to 12–15°, and 11 g. (10% more than the calculated amount) of sodium nitrite added during half an hour, while the mixture was frequently shaken. After an hour the solution was poured with stirring into five volumes of water, and the solid allowed to settle. The material obtained by filtration and drying weighed 41 g.; yield, 83%. Crystallization from ligroin gave yellow needles that melted at 123°.<sup>9</sup>

Eight g. of the nitro compound described above was dissolved in the smallest possible amount of hot alcohol and reduced<sup>10</sup> to the corresponding amino compound. The hydrochloride that separated weighed 6.8 g.; yield, 84%.

To obtain the free base, 3 g. of the hydrochloride was ground with water to a thin paste and treated with the required amount of ammonium carbonate solution. When effervescence ceased, the remaining solid was quickly removed by filtration and washed

<sup>8</sup> Zincke and Wiederhold, *Ann.*, **320**, 202 (1902).

<sup>9</sup> Zincke and Emmerich, [Ref. 3 b, p. 311] found 124°.

<sup>10</sup> Raiford, *Am. Chem. J.*, **46**, 419 (1911).

free from ammonium salt. The product was very soluble in alcohol, ether, benzene, ligroin, chloroform, toluene, ethyl acetate and carbon disulfide. From dil. alcohol it crystallized in cerise-colored, flat-surfaced plates which turned brown on standing. It melted at 122°. Its composition was confirmed by analysis for bromine.

*Anal.* Subs., 0.1232: AgBr, 0.1686. Calc. for  $C_7H_7ONBr_2$ : Br, 56.94. Found: 57.19.

**2-Acetylamino-3,6-dibromo-4-methylphenyl Acetate.**—The diacetyl derivative of the above-mentioned base was prepared by heating a mixture of 5 g. of the hydrochloride and an equal weight of finely powdered sodium acetate with 5 g. ( $2\frac{1}{2}$  molecular proportions) of acetic anhydride. Upon cooling, the mass was extracted with water to remove sodium salts, and the residue removed and dried. This was soluble in cold alcohol, ligroin, chloroform, ethyl acetate, ether, carbon tetrachloride and carbon disulfide; it dissolved easily in hot toluene and benzene, from both of which it crystallized in white needles that in masses resembled cotton. It was noticed that solvents containing the hydroxide group tend to hydrolyze it at high temperatures. Analysis for bromine indicated the presence of two acetyl radicals.

*Anal.* Subs., 0.1321: AgBr, 0.1338. Calc. for  $C_{11}H_{11}O_3NBr_2$ : Br, 43.83. Found: 44.10.

**2-Acetylamino-3,6-dibromo-4-methylphenol.**—Four g. of the diacetyl compound described above was mixed with a solution of sodium hydroxide containing 1 g. of alkali in 10 cc. of water, and the mixture shaken frequently during a period of two hours. The traces of undissolved material remaining were removed by filtration, and the clear filtrate was acidified. The solid was collected as usual and dried; yield, 2.7 g., or 78%. The substance was soluble in the ordinary organic solvents, and was best crystallized from 50% alcohol, from which it separated in light brown needles that melted at 158°. It was readily soluble in caustic alkali solution, and was reprecipitated unchanged by acids. Analysis for bromine indicated the presence of but one acetyl radical.

*Anal.* Subs., 0.1526: AgBr, 0.1772. Calc. for  $C_9H_9O_2NBr_2$ : Br, 49.53. Found: 49.41.

**Benzoylation of 2-Acetylamino-3,6-dibromo-4-methylphenol.**—One g. of the mono-acetyl derivative just described was dissolved in 30 cc. of water containing 2 g. of sodium hydroxide. Slightly more than the calculated quantity of benzoyl chloride was added and the mixture shaken until no odor of the chloride was evident. After separation in the usual way, the solid weighed 1 g., a yield of 77%. Crystallization from ethyl acetate and from a mixture of alcohol and acetone, respectively, gave clusters of fine, white needles that radiated from common centers. The compound is soluble in the usual organic solvents, but could be crystallized satisfactorily only from those mentioned. It melted at 232°. Analysis for bromine indicated the presence of both acetyl and benzoyl radicals.

*Anal.* Subs., 0.1361: AgBr, 0.1206. Calc. for  $C_{16}H_{13}O_3NBr_2$ : Br, 37.47. Found: 37.70.

**Proof of the Structure of 2-Benzoylamino-3,6-dibromo-4-methylphenyl Acetate.**—An attempt to hydrolyze the above-mentioned acetyl-benzoyl derivative with a water solution of sodium hydroxide was unsatisfactory, but a dil. methyl alcoholic solution of the alkali rapidly gave the desired result. After separation in the usual way, the product gave, when crystallized from 30% alcohol, clusters of short, white needles that melted with decomposition at 154°. The solubility of the compound in alkali solution indicated a phenolic structure, while analysis for bromine indicated the presence of the benzoyl radical.

*Anal.* Subs., 0.1412: AgBr, 0.1367. Calc. for  $C_{14}H_{11}O_2NBr_2$ : Br, 41.55. Found: 41.19.

To prepare the *N*-benzoyl compound of the base under consideration, 5 g. of the latter was dissolved in ether, and the solution treated with benzoyl chloride as directed by Ransom. The crystalline mass was shaken with a cold solution of sodium hydroxide, the mixture filtered and the filtrate acidified.<sup>11</sup> The precipitate was removed by filtration, washed with water and dried; yield, 2.4 g., or 35%. After crystallization from 30% alcohol, this product was found to have the same melting point, 154°, and other properties as those of the substance obtained by hydrolysis of the acetyl-benzoyl derivative described above. A mixture of the two melted without depression of the melting point.

The *N*-benzoyl compound here in question was further characterized by conversion into the acetyl derivative. A mixture of 2 g. of the substance and an equal weight of anhydrous sodium acetate was warmed for ten minutes with 1 g. of acetic anhydride. After the product had cooled it was freed from sodium salt and crystallized from ethyl acetate, from which it separated as colorless needles that melted at 232–233°. A mixture of this product and that obtained by benzoilation of 2-acetyl-amino-3,6-dibromo-4-methylphenol melted at 232°, showing identity of the two products.

**Tetrabromo-*p*-cresol.**—Two attempts to prepare this product by Zincke's directions<sup>12</sup> gave poor yields. The most satisfactory method was as follows. Fifty-four g. of cresol was dissolved in ten times its weight of chloroform, and a few grams of powdered iron added as a carrier. Into this was slowly run the calculated amount of bromine dissolved in twice its weight of chloroform, and the mixture allowed to stand for three days at room temperature. The chloroform was then distilled, the residue shaken with dil. sodium hydroxide solution, the mixture filtered and the product precipitated from the filtrate by the addition of acid. The solid was collected on a filter, washed and dried; yield, 172 g., or 81%. Crystallization from benzene gave long, colorless needles that melted at 196°, which agrees with the melting point given in the literature.

**2-Nitro-3,5,6-tribromo-4-methylphenol.**—Ten g. of the tetrabromo product was suspended in 100 g. of glacial acetic acid and while the mixture was shaken at room temperature, 1.9 g. ( $\frac{1}{4}$  more than the calculated amount) of sodium nitrite added during half an hour, after which the resulting liquid was worked up as previously described; 7.3 g. of solid, or a yield of 78%, was obtained. It was purified by crystallization from ligroin (100–110°), and was found to melt at 160° as described by Zincke.

**2-Amino-3,5,6-tribromo-4-methylphenol.**—Eight g. of the nitro product described above was dissolved in hot alcohol, and reduced by means of stannous chloride in the usual way. A yield of 6.8 g., or 80%, of the corresponding hydrochloride was isolated. This was rubbed into a thin paste with water, and the calculated amount of ammonium carbonate solution added. When effervescence ceased, the mixture was filtered and the residue washed thoroughly with water. The product was soluble in ether, chloroform, benzene, ethyl acetate, acetone and toluene at ordinary temperature, and in warm carbon disulfide, ligroin and carbon tetrachloride. It was best purified by crystallization from 50% alcohol from which it was deposited in clusters of thick, straw-colored needles. Analysis for bromine agreed with the formula assigned.

*Anal.* Subs., 0.1283; AgBr, 0.2015. Calc. for  $C_7H_6ONBr_3$ : Br, 66.66. Found: 66.83.

**2-Acetyl-amino-3,5,6-tribromo-4-methylphenyl Acetate.**—A mixture of 5 g. of the hydrochloride described above and an equal weight of freshly fused sodium acetate was warmed for ten minutes with 2.5 molecular proportions of acetic anhydride, and the cooled mass extracted with 50 cc. of water. The residue was separated and dried in the

<sup>11</sup> We have found that Ransom's method of acylation gives a mixture of mono- and dibenzoyl derivatives with certain bases.

<sup>12</sup> Ref. 8, p. 205.

usual way. A yield of 5.2 g. or 92%, was obtained. Owing to its extreme solubility in most organic solvents the product was difficult to purify. The method finally used was to precipitate it from glacial acetic acid solution by the addition of water. A small portion which was crystallized with difficulty from xylene was obtained in the form of colorless needles that melted at 171°. Analysis for bromine indicated that the compound was not quite pure, but showed clearly that it was a diacetyl derivative.

*Anal.* Subs., 0.1481: AgBr, 0.1862. Calc. for  $C_{11}H_{10}O_3NBr_3$ : Br, 54.05. Found: 53.50.

**2-Acetyl-amino-3,5,6-tribromo-4-methylphenol.**—Four g. of the crude diacetyl derivative described above was mixed with 50 cc. of water containing 0.5 g. of sodium hydroxide, and the whole shaken until nearly all had dissolved. The clear liquid obtained by filtering the mixture was acidified by hydrochloric acid, and the precipitate collected and dried. A yield of 2.3 g., or 63%, was obtained. It was readily soluble in most organic solvents except petroleum ether, from which it was crystallized as long, fibrous, colorless needles that melted at 189°. It was readily soluble in solutions of caustic alkali, and was precipitated unchanged by acids, which indicated a phenolic character. Analysis for bromine was in accord with this behavior.

*Anal.* Subs., 0.1081: AgBr, 0.1512. Calc. for  $C_9H_8O_2NBr_3$ : Br, 59.70. Found: 59.52.

**Action of Benzoyl Chloride on 2-Acetyl-amino-3,5,6-tribromo-4-methylphenol.**—Two g. of the mono-acetyl derivative described above was dissolved in 30 cc. of water containing 1.25 molecular proportions of sodium hydroxide, 0.9 g. of benzoyl chloride was added, and the whole shaken until no odor of the acid chloride was evident. The light brown solid that formed very rapidly was collected in the usual way and dried. It was found to be very soluble in the usual organic solvents, but could be crystallized from dil. butyl alcohol. In this way it was obtained as long, silvery white prisms that melted with blackening at 177°. The yield of pure product was 1.8 g., or 72%.<sup>13</sup>

*Anal.* Subs., 0.1311: AgBr, 0.1469. Calc. for  $C_{16}H_{12}O_3NBr_3$ : Br, 47.43. Found: 47.68.

**Proof of the Structure of 2-Benzoylamino-3,5,6-tribromo-4-methylphenyl Acetate.**—One-half g. of the acetyl-benzoyl compound was hydrolyzed by treatment with a water-alcoholic solution of caustic alkali containing one-fourth more than the calculated amount. When the mixture was worked up in the usual way a solid was obtained which could be crystallized from ligroin (100–110°); m. p., 195°. Its solubility in caustic alkali solution and its reprecipitation unchanged by acids showed that it was phenolic in character. Analysis for bromine indicated that the acetyl radical had been lost by hydrolysis.

*Anal.* Subs., 0.1101: AgBr, 0.1331. Calc. for  $C_{14}H_{10}O_2NBr_3$ : Br, 51.72. Found: 51.44.

<sup>13</sup> Attention is here called to the fact that two further attempts to benzoylate 2-acetyl-amino-3,5,6-tribromo-4-methylphenol, which were made with the hope of improving the yield and purity of the product, gave what appeared to be mixtures that melted at 168–174°. When the material was subjected to the action of an alcoholic solution of potassium hydroxide, a product was obtained that melted at 189° and had other properties of 2-acetyl-amino-3,5,6-tribromo-4-methylphenol described above. A mixture of the two products melted without depression which, taken in connection with the low yield of N-benzoyl-O-acetyl derivative, appears to indicate that benzoylation was incomplete or that migration was only partial. Either or both of these results might be due to steric hindrance caused by the presence of the three bromine atoms. Analysis for bromine agreed with a formula requiring both an acetyl and a benzoyl radical.

To show that the product just described had benzoyl on nitrogen, a small portion of 2-amino-3,5,6-tribromo-4-methylphenol was acylated with benzoyl chloride according to Ransom's method. The product here obtained showed the same melting point, 195°, and other properties found for that obtained by hydrolysis of the acetyl-benzoyl derivative specified above. A mixture of the two melted still at 195°. The N-benzoyl derivative was further characterized by acetylation. Five-tenths g. was mixed with an equal weight of sodium acetate, and warmed with 0.3 cc. of acetic anhydride, and the product worked up in the usual way; yield, 0.4 g., or 80%. Crystallization from butyl alcohol gave colorless prisms that melted at 177° and, when mixed with the product obtained by the action of benzoyl chloride on 2-acetylamino-3,5,6-tribromo-4-methylphenol, did not depress its melting point.

### B. A Base Obtained from *o*-Cresol

The starting material was tetrabromo-*o*-cresol which was prepared by a slight modification of Zincke's method,<sup>14</sup> in which the product first obtained was extracted with caustic alkali solution, filtered from insoluble matter, and the desired compound precipitated by acid. A yield of 84% was obtained, and the product after crystallization from benzene melted at 204°. Zincke and Hedenström found 205° for the melting point, but recorded no yield.

**Nitration of Tetrabromo-*o*-cresol.**—Ten g. of the product just described was powdered and suspended in 100 cc. of glacial acetic acid, after which 1.6 g. of sodium nitrite was added during half an hour while the mixture was shaken. When the action was complete the mixture was poured with stirring into four volumes of water which precipitated a yellow solid. After standing for some hours this was collected on a filter, washed and dried; yield, 8 g., or 85%. The product began to melt at 152° and was liquid at 174°, which suggested the presence of two substances.

**Separation of the Isomers.**—The solid was dissolved in the smallest possible quantity of hot carbon tetrachloride, and ligroin (b. p., 80–90°) was added, while the liquid was stirred, until precipitation started. The mixture was then heated until all solid had dissolved, after which it was allowed to cool. The crystals that separated were removed by filtration and recrystallized from ligroin (b. p., 100–110°). They melted at 177° with apparent decomposition.<sup>15</sup> Evaporation of the filtrate gave a yellow solid

<sup>14</sup> Zincke and Hedenström, *Ann.*, **350**, 273 (1906).

<sup>15</sup> Zincke and Klostermann, Ref. 7 a. Our product was further characterized by reduction to the amino derivative and oxidation of the latter to the corresponding quinone. Ten g. of the nitro product was dissolved in hot alcohol and reduced by stannous chloride in the usual way. A yield of 8.1 g. of pure hydrochloride, or 79%, was obtained. Three g. of this finely divided material was suspended in 25 cc. of water, and the mixture cooled to about 0°. During 25 minutes a mixture of 3 g. of sodium dichromate, 10 g. of sulfuric acid and 40 cc. of water was added while the whole was well shaken, and the temperature kept down. The yellow solid that resulted was filtered off and dried. From alcohol it was obtained as yellow, laminated crystals, m. p., 235–236°, which agrees with the melting point found by Canzoneri and Spica [*Gazz. chim. ital.*, **12**, 470 (1882)] for the product obtained by oxidation of commercial cresol with a mixture of manganese dioxide, sulfuric acid and potassium bromide. Auwers and Ziegler [*Ber.*, **29**, 2350 (1896)] reported 234–236°, for the product obtained by oxidation of 2,3,6-tribromo-5-methyl-4-hydroxybenzyl alcohol with dil. nitric acid. Our product was further identified by conversion into the hydroquinone. One g. was dissolved in 50% alcohol, the liquid



that upon crystallization from dil. alcohol was deposited in clusters of long, yellow needles that melted sharply at 159°.<sup>16</sup>

**The Hydrochloride of 2-Amino-3,4,5-tribromo-6-methylphenol.**—Ten g. of the product melting at 159° was dissolved in boiling alcohol and reduced with hydrochloric acid solution of stannous chloride in the usual way. The pure amine salt was obtained by saturating a dil. alcoholic solution of the crude product with gaseous hydrogen chloride; yield, 7.9 g., or 74%.

**2-Amino-3,4,5-tribromo-6-methylphenol.**—A thin paste made by grinding with water 5 g. of the hydrochloride described above was treated with a solution of ammonium carbonate until effervescence ceased, the mixture filtered at once and the residue washed with water. The yield was almost quantitative. The dried substance was readily soluble in most organic solvents, and was crystallized from ligroin (100–110°) from which it separated as pinkish-yellow needles that melted at 167°. The substance was readily soluble in alkali solution.

*Anal.* Subs., 0.1138: AgBr, 0.2054. Calc. for C<sub>7</sub>H<sub>6</sub>ONBr<sub>3</sub>: Br, 66.66. Found: 66.31.

**2-Acetylamino-3,4,5-tribromo-6-methylphenyl Acetate.**—A mixture of 5 g. of the hydrochloride of the base described above and an equal weight of anhydrous sodium acetate was warmed for ten minutes with a slight excess of acetic anhydride. After the mass had cooled it was extracted with water and the insoluble portion dried; yield, 4.9 g., or 86%. The compound was readily soluble in most organic solvents, and could be crystallized satisfactorily only from dil. acetic acid, from which it was deposited in short glistening needles that melted at 146°.

*Anal.* Subs., 0.1506: AgBr, 0.1918. Calc. for C<sub>11</sub>H<sub>10</sub>O<sub>2</sub>NBr<sub>3</sub>: Br, 54.05. Found: 54.19.

**2-Acetylamino-3,4,5-tribromo-6-methylphenol.**—Attempts to hydrolyze with aqueous solution of sodium hydroxide the diacetyl derivative described above gave very poor results. A dil. (about 50%) alcoholic solution of the alkali was shaken with 5 g. of the acetate until practically all had dissolved, the liquid filtered and the filtrate acidified. When dry the precipitate weighed 3.7 g., a yield of 82%. From ligroin (80–90°) it was crystallized in colorless, downy needles that melted at 186°.

*Anal.* Subs., 0.1177: AgBr, 0.1646. Calc. for C<sub>9</sub>H<sub>8</sub>O<sub>2</sub>NBr<sub>3</sub>: Br, 59.70. Found: 59.51.

**Benzoylation of 2-Acetylamino-3,4,5-tribromo-6-methylphenol.**—Three g. of the phenol was dissolved in 30 cc. of water containing 1.25 molecular proportions of sodium hydroxide, and the solution shaken with slightly more than the calculated quantity of benzoyl chloride until no odor of the latter was evident. A gummy solid separated. After some hours the clear liquid was decanted, and the residue crystallized from ethyl acetate which gave nearly colorless, fluffy needles. A yield of 2.7 g. or 72% of pure material was

saturated with sulfur dioxide, one volume of water added, and the mixture allowed to stand. The product that was deposited weighed 1 g., or a yield of 98%. Crystallization from dil. alcohol gave colorless needles that melted at 202°, which agrees with the literature [Canzoneri and Spica, *loc. cit.*]. In view of the fact, however, that it is unusual to find a hydroquinone that melts lower than the corresponding quinone, this one was analyzed.

*Anal.* Subs., 0.1072: AgBr, 0.1678. Calc. for C<sub>7</sub>H<sub>2</sub>O<sub>2</sub>Br<sub>3</sub>: Br, 66.48. Found: 66.61.

<sup>16</sup> Zincke and Hedenström (Ref. 7 a) found 156° as the melting point of this product.

obtained; m. p., 234°. The substance was very soluble in acetone, alcohol and chloroform, and less readily so in benzene, ethyl acetate and ligroin.

*Anal.* Subs., 0.1658: AgBr, 0.1846. Calc. for  $C_{16}H_{12}O_3NBr_3$ : Br, 47.43. Found: 47.38.

**Proof of the Structure of 2-Benzoylamino-3,4,5-tribromo-6-methylphenyl Acetate.**—Five g. of 2-amino-3,4,5-tribromo-6-methylphenol was dissolved in 40 cc. of ether, and the solution treated with benzoyl chloride as described by Ransom. After removal of the precipitated amino hydrochloride the ether was evaporated and the residue was extracted with an alkaline solution containing 1 g. of sodium hydroxide dissolved in 45 cc. of water,<sup>17</sup> the mixture filtered and the filtrate acidified with hydrochloric acid. A faintly colored solid that weighed 1.9 g. (a yield of 29%) was obtained. The compound was crystallized from dil. alcohol, and separated as nearly colorless needles that melted at 133°.

*Anal.* Subs., 0.1218: AgBr, 0.1473. Calc. for  $C_{14}H_{10}O_2NBr_3$ : Br, 51.72. Found: 51.46.

A mixture of 3 g. of the benzoyl-aminocresol described above and an equal weight of anhydrous sodium acetate was heated with the calculated amount of acetic anhydride for 10 minutes. When cool the mass was extracted with cold water and the insoluble residue crystallized from ethyl acetate. The appearance of this product was exactly like that obtained by benzoylation of 2-acetylamino-3,4,5-tribromo-6-methylphenol. The substance melted, also, at 234°, and a mixture of the two melted at the same temperature.

### Summary

1. Acetyl-benzoyl derivatives have been prepared from three aminocresols, namely, 2-amino-3,6-dibromo-4-methylphenol, 2-amino-3,5,6-tribromo-4-methylphenol, and 2-amino-3,4,5-tribromo-6-methylphenol, and in each case the benzoyl radical was found attached to nitrogen, regardless of the order in which the radicals were introduced, which shows that a rearrangement must have occurred during the benzoylation in each instance.

2. The presence of bromine atoms adjacent to the reacting groups does not prevent the migration of the lighter acyl from nitrogen to oxygen.

3. When tetrabromo-*o*-cresol was nitrated in accordance with Zincke's method, two isomeric tribromomono-nitrocresols, instead of one, as reported by Zincke, were obtained. The relative positions of the hydroxyl and nitro radicals in these compounds were shown to be *ortho* and *para*, respectively.

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<sup>17</sup> This precaution was found necessary because our experience has shown that some dibenzoyl derivative is often obtained.