

These compounds are remarkably stable to acids in comparison with other mercury salt-olefin compounds.

3. The mercurated dihydrobenzofurans formed from mercuric acetate or mercuric chloride and *o*-allyl-phenol, upon treatment with potassium iodide, yield the corresponding iodide. This iodide, on treatment with iodine, yields 1-iodomethyl-1,2-dihydrobenzofuran which in turn is readily reduced to 1-methyl-1,2-dihydrobenzofuran.

4. The mercurated dihydrobenzofurans, by treatment with sodium amalgam, give compounds of the general type  $\text{R}_2\text{Hg}$ .

5. No reasonable molecular formula for the mercurated dihydrobenzofurans can be written which will explain the structure and the chemical reactions of these compounds. The addition formula allows for a simple explanation of all the experimental facts.

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

## THE MIGRATION OF ACYL FROM NITROGEN TO OXYGEN

BY L. CHAS. RAIFORD AND JOHN R. COUTURE

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In a previous communication from this laboratory<sup>1</sup> it was pointed out that when certain aminophenols were acylated in such a way as to introduce both the acetyl and the benzoyl radicals into the same molecule, the heavier of these groups was found attached to nitrogen, regardless of the order in which they were introduced. In one case acetyl must have migrated from nitrogen to oxygen, while benzoyl may have shifted in the opposite direction. It was recognized at that time, however, that the cases studied might have been isolated ones, and that much more work would be necessary to show that the behavior of these substances represented a general reaction. Attention was drawn also to the possibility that this rearrangement might be determined by factors other than that which was emphasized in the first observations, namely, the difference in weight of the acyl radicals.

To answer the question whether the behavior reported for the three bases already studied is general for the group, it seemed important, first of all, to show that aminophenols isomeric with one of those previously studied and differing from it only in the relative positions of the radicals present, with the exception that the hydroxyl and amino groups must

<sup>1</sup> THIS JOURNAL, 41, 2068 (1919).

be adjacent to each other, will give acetyl-benzoyl derivatives in which benzoyl always attaches itself to nitrogen. The first observations were made with a base obtained from *p*-cresol, 3-amino-4-hydroxy-5-bromotoluene, while the work now reported was carried out with the corresponding substances prepared from *ortho* and *meta* cresols, 2-hydroxy-3-amino-5-bromotoluene and 3-hydroxy-4-amino-6-bromotoluene, respectively. A careful examination of the diacyl (acetylbenzoyl) derivatives obtained from these bases shows that in these cases, also, the heaviest of these radicals goes to nitrogen. Work is in progress with compounds containing fatty acyl radicals that have higher molecular weights than that of the acetyl radical; the results will be given in a future report.

### Experimental Part

#### I. Derivatives of the Base from *o*-Cresol

**2-Hydroxy-3-nitro-5-bromotoluene.**—The starting point in the preparation of this compound was pure *o*-cresol obtained by fractionation of the purest commercial product obtainable. This was brominated according to the method used by Claus and Jackson.<sup>2</sup> The product, which is 2-hydroxy-5-bromotoluene, has a pale lavender color and melts at 62.5° (Claus and Jackson record 64°). The nitration of this compound was done by the method of Zincke,<sup>3</sup> modified with respect to the temperature of the reaction mixture and the time it was allowed to stand. Twenty-six g. of the phenol was dissolved in 300 cc. of glacial acetic acid and 1.25 times the theoretical quantity of sodium nitrite was added during half an hour, the solution being stirred constantly and the temperature kept between 14° and 15°. When the reaction was complete the solution was allowed to stand for half an hour and then poured with vigorous stirring into 2 liters of water. The yellow flocculent precipitate which formed was filtered off after standing overnight. When dry the product weighed 21.5 g., a yield of 68.2%. Another nitration of a 20g. sample produced 19 g. of the crude product, a yield of 76.5%.

An attempt was made to fractionate this material because of the fact that studies now going on in this laboratory<sup>4</sup> have shown that the nitration of 2-hydroxy-3,5-dibromotoluene by means of sodium nitrite in acetic acid solution gives two isomeric mononitro-bromo derivatives, one of which is identical with the product here obtained (see below). The crude material was dissolved in 22 cc. of warm chloroform and, after filtering, twice the volume of ligroin (b. p. 80–90°) was added. After standing for some time, yellow prisms having a melting point of 85–88° were deposited. Repeated crystallization from alcohol raised the melting point of the compound to 90.5°. Zincke<sup>3</sup> records 88° as the melting point of this compound. Although the chloroform-ligroin solvent liquor was carefully worked up no evidence of the presence of another product was found. Other than the melting point, this compound shows the properties described by Zincke.

**Hydrochloride of 2-Hydroxy-3-amino-5-bromotoluene.**—This compound was prepared by reducing an alcoholic solution of the nitro compound specified above, according to the method described by Raiford.<sup>5</sup> Subsequent crystallization as directed, using 50% alcohol, gave a product free from tin salt, and otherwise pure, as shown by analysis for halogen.

<sup>2</sup> Claus and Jackson, *J. prakt. Chem.*, [2] **38**, 326 (1888).

<sup>3</sup> Zincke, *Ann.*, **350**, 277 (1906).

<sup>4</sup> THIS JOURNAL, **44**, 158 (1922).

<sup>5</sup> Raiford, *Am. Chem. J.*, **46**, 419 (1911).

*Analysis.* Subs., 0.2396; AgHal, 0.3349. Calc. for  $C_7H_5ONClBr$ : Hal, 48.40. Found: 48.70.

**2-Hydroxy-3-amino-5-bromotoluene.**—A base having this composition and probably this structure was isolated by Claus and Jackson<sup>6</sup> who, however, studied none of its derivatives and made no attempt to establish its structure, though they regarded it as an *ortho* compound. Our product was made by grinding the corresponding hydrochloride to a thin paste with water, adding the calculated quantity of ammonium carbonate in solution and mixing thoroughly. As soon as action had ceased the mixture was filtered and the residue washed with several small portions of cold water.

*Analysis.* Subs., 0.1793; AgBr, 0.1675. Calc. for  $C_7H_5ONBr$ : Br, 39.56. Found: 39.75.

**2-Acetylamino-4-bromo-6-methylphenyl Acetate.**—This compound was made by treating a mixture of 4.7 g. of the hydrochloride of the base and 4 g. of freshly fused and powdered sodium acetate with 10 g. of acetic anhydride. The mixture was kept liquid by refluxing for 15 minutes. When cool the solid mass was ground in a mortar with sufficient water to dissolve the sodium chloride and sodium acetate present, after which the residue was filtered off, washed with a little cold water, dried and weighed;<sup>7</sup> 5.6 g. was obtained, a yield of 84.1%. The compound crystallizes from alcohol in pale-brown, silky needles melting at 200°. It is readily soluble in other organic solvents. It is not instantly soluble in cold solution of caustic alkali, but dissolves slowly due to saponification at the O-connection (see below). This behavior characterizes it as a diacetyl derivative, which is in agreement with the results of analysis for halogen.

*Analysis.* Subs., 0.1474; AgBr, 0.0979. Calc. for  $C_{11}H_{12}O_3NBr$ : Br, 27.94. Found: 28.26.

**2-Acetylamino-4-bromo-6-methylphenol.**—This compound was obtained by saponification of the diacetyl derivative just described; 4.5 g. of the latter was shaken until completely dissolved with a solution of 2 g. of sodium hydroxide in 50 cc. of water. This required about half an hour. At the end of this time the solution was filtered and the filtrate acidified. A white precipitate was formed which became reddish-brown on

<sup>6</sup> Ref. 2, p. 324.

<sup>7</sup> Attention is here called to the fact that in this work the preparation of O-acetyl-N-acetyl derivatives of aminophenols was carried out much more easily and quickly than has been done by previous workers. Thus, Ladenburg [*Ber.*, 9, 1524 (1876)] refluxed a mixture of the base and an excess of acetic anhydride for a long time; Philip and Calm [*ibid.*, 17, 2436 (1884)] heated a mixture of the aminophenol and dry sodium acetate with the theoretical amount of acetic anhydride for 2 hours at 140°; Ikuta [*Am. Chem. J.*, 15, 42 (1893)] heated the aminophenol with excess of acetic anhydride for 2 or 3 hours at 150–160°; Meldola, Woolcott and Wray [*J. Chem. Soc.*, 69, 1324 (1896)] boiled a mixture of the dry amino hydrochloride and sodium acetate with excess of acetic anhydride for some hours; Bamberger [*Ber.*, 36, 2050 (1903)] obtained the product by boiling the starting material, mixed with the required amount of acetic anhydride dissolved in about 20 times its weight of acetic ether, for 2 hours, while Auwers and Eisenlohr [*Ann.*, 369, 224 (1909)] state that the simplest and most rapid way to obtain such a compound (they were studying the diacetyl derivative of 3-amino-4-hydroxytoluene) is to boil the base, mixed with some dry sodium acetate, with an excess of acetic anhydride for 3 hours. To test the time requirement of this acylation in as many cases as possible, we prepared, in addition to the new products here reported, the diacetyl derivative of the base specified by Auwers and Eisenlohr, and obtained within 15 minutes a product which, after one crystallization from ethyl acetate, melted at the temperature (145°) recorded by these authors.

standing. This material was crystallized from dil. alcohol, from which it separated in the form of colorless needles that melted at 119°. Samples crystallized from benzene melted at the same temperature. The compound is readily soluble in alkali, and from this solution the unchanged substance is precipitated by acids, all of which indicate its phenolic character. Analysis for halogen gave figures that agree with a formula requiring a single acetyl radical.

*Analysis.* Subs., 0.1686; AgBr, 0.1307. Calc. for  $C_9H_{10}O_2NBr$ : Br, 32.75. Found: 32.99.

**Benzoylation of 2-Acetylamino-4-bromo-6-methylphenol.**—The benzoylation of this compound was carried out by dissolving 1.2 g. in a solution of 0.25 g. (1.25 mols) of sodium hydroxide in 50 cc. of water and adding 1 g. (1.25 mols) of benzoyl chloride. The mixture was shaken until the odor of the chloride had disappeared. A solid formed immediately, gathering in small lumps. After standing overnight the solid material was filtered off, washed with water, and dried. A quantitative yield was obtained. The compound was crystallized from benzene from which it separated in fine white needles that in bulk and texture had the appearance of masses of cotton. It melted at 168° after repeated crystallization. Analysis for halogen gave figures that agree with a formula requiring one acetyl and one benzoyl radical.

*Analysis.* Subs., 0.1436; AgBr, 0.0782. Calc. for  $C_{16}H_{14}O_3NBr$ : Br, 22.90. Found: 23.16.

#### Proof of the Structure of the Benzoyl-acetyl Derivative

**A. Saponification of the Derivative.**—Ninety-three hundredths g. of the compound just described was shaken with a solution of 0.5 g. of sodium hydroxide in 50 cc. of water. A somewhat longer time was required for saponification than in the case of the diacetyl derivative, but solution was complete after the mixture had stood for 24 hours. Upon acidifying the solution a dark-colored solid was obtained which yielded beautiful rose-colored needles by crystallization from alcohol. The melting point of this compound was found to be 194.5°. The fact that this substance is soluble in alkali and from such a solution is precipitated unchanged by acids, indicates that the hydroxyl group is free. Analysis for halogen (see below) shows that it contains a benzoyl rather than an acetyl radical. Consideration of these facts leads to the conclusion that benzoyl is here bound to nitrogen and that rearrangement must have occurred during the introduction of benzoyl or when the diacylated compound was saponified. The substance was shown to be 2-benzoylamino-4-bromo-6-methylphenol by preparing it from the base by the action of benzoyl chloride.

*Analyses.* Subs., 0.1123, 0.1184; AgBr, 0.0687, 0.0728. Calc. for  $C_{14}H_{12}O_2NBr$ : Br, 26.12. Found: 26.02, 26.16.

**B. Preparation of 2-Benzoylamino-4-bromo-6-methylphenol by Benzoylation of the Base.**—To secure further identification of the compound just described a sample was prepared from the corresponding free base according to the method of Ransom;<sup>8</sup> 6.4 g. (2 mols) of the base was dissolved in ether and 2.3 g. (1 mol) of benzoyl chloride, also in ether solution, was allowed to drop in slowly, the mixture being shaken continuously during the addition. After standing for some time to allow for the complete precipitation of the hydrochloride which is formed in the reaction, the latter compound was filtered off and the ether solution allowed to evaporate spontaneously. The residue was crystallized from alcohol and gave pale rose-colored needles that melted at 194°. The compound prepared in this way melted together with the product of saponification of the benzoyl-acetyl derivative described above without depression of the melting point, which indicates that they are identical.

<sup>8</sup> Ransom, *Am. Chem. J.*, **23**, 17 (1900).

C. Acetylation of 2-Benzoylamino-4-bromo-6-methylphenol.—One and four-tenths g. of the benzoylamino derivative just described, and an equal weight of sodium acetate were warmed with an excess of acetic anhydride. When water was added on completion of the reaction the entire mass went into solution. This solution was extracted with ether. The solvent was evaporated and the dry residue taken up in warm benzene from which, on cooling, was deposited a mass of very fine white needles having the general appearance of cotton and melting at 167°. A mixture of this substance and the product obtained by benzylation of 2-acetylamino-4-bromo-6-methylphenol (m. p. 168°) melted without depression of the melting point. The latter compound is, therefore, also 2-benzoylamino-4-bromo-6-methylphenylacetate and must have resulted from a molecular rearrangement during the benzylation of 2-acetylamino-4-bromo-6-methylphenol.

## II. The Base Derived from *m*-Cresol

2-Acetylamino-4-bromo-5-methylphenyl Acetate.—The starting point in the preparation of this product was 4-nitro-6-bromo-*m*-cresol, prepared according to the directions of Raiford and Leavell<sup>9</sup> modified to the extent of decreasing the amount of solvent used which, in accordance with the experience of one of us (Couture), to be described in a future communication, caused a marked increase in the yield; 15.3 g. of 4-nitro-*m*-cresol,<sup>10</sup> m. p. 56°, was dissolved in 50 cc. of glacial acetic acid, and into this there was dropped 10.3 cc. (2 mols) of bromine which had previously been mixed with 5 cc. of acetic acid. Crystals began to separate before all the bromine had been added. After the mixture had stood overnight, the solid that had separated was removed by filtration, washed free from mother liquor with a small portion of acetic acid, and dried on a clay plate. Twenty g. was obtained, which is a yield of 86.2% calculated on the basis of the formation of a monobromo derivative. After crystallization from alcohol it showed the melting point and other properties recorded in the literature.

Five and nine-tenths g. of the hydrochloride of the base, obtained by reducing the above nitro compound in the usual way, was intimately mixed with an equal weight of anhydrous sodium acetate and warmed for 10 minutes with a slight excess of acetic anhydride. After cooling, the solid was extracted with water to remove sodium salts, and the residue filtered off at the pump and dried. A yield of 84% was obtained. In this condition the product softened at 182° and was completely melted at 188°. It is soluble in most organic solvents, but was best crystallized from alcohol, from which it separated in colorless leaflets that melted sharply at 188°. Its failure to dissolve quickly in caustic alkali solution (it dissolved slowly owing to hydrolysis at the O-connection) and the results of analysis for bromine show that it is a diacetyl derivative.

*Analysis.* Subs., 0.1730; AgBr, 0.1128. Calc. for C<sub>11</sub>H<sub>12</sub>O<sub>2</sub>NBr: Br, 27.94. Found: 27.63.

3-Hydroxy-4-acetylamino-6-bromotoluene.—One molecular proportion (2.86 g.) of the diacetyl derivative described above was shaken with 50 cc. of cold water containing 2 equivalents (0.9 g.) of sodium hydroxide until complete solution took place, which required about 15 minutes. The liquid, which was slightly yellowish, was filtered, the clear filtrate acidified with hydrochloric acid, and the precipitate that formed immediately collected on a filter, washed with water and dried. A quantitative yield was obtained. In this condition the product melted at 198–199° with apparent decomposition, and was nearly pure. Portions crystallized from methyl alcohol, ethyl alcohol and acetone, respectively, melted at 199° with decomposition. From ethyl alcohol the crystals separated in the form of nearly colorless needles. It is but slightly soluble in

<sup>9</sup> Raiford and Leavell, *THIS JOURNAL*, **36**, 1498 (1914).

<sup>10</sup> Staedel and Orth, *Ann.*, **217**, 51 (1883).

ligroin. Caustic alkali solutions dissolve it readily, and from such a liquid the unchanged substance is precipitated by acids. This behavior and the results of analysis for bromine are in agreement with a formula requiring a free hydroxide group and an acetyl radical.

*Analysis.* Subs., 0.2076; AgBr, 0.1594. Calc. for  $C_9H_{10}O_2NBr$ : Br, 32.75. Found: 32.66.

Action of Benzoyl Chloride on 3-Hydroxy-4-acetylamino-6-bromotoluene.—One and twenty-two hundredths g. of the mono-acetyl derivative described above was dissolved in 30 cc. of cold water containing 0.25 g. (1.25 mol) of sodium hydroxide, after which 0.88 g. of benzoyl chloride (1.25 mol) was added, and the whole shaken until the odor of the chloride had disappeared. The colorless solid that began to precipitate at once was finally removed by filtration at the pump, washed with several small portions of water and dried. Practically a quantitative yield was obtained. The crude product softened at  $143^\circ$  and melted at  $149$ – $150^\circ$ . It is soluble in the usual organic solvents, and samples crystallized from alcohol and from benzene, respectively, from which it separated as colorless, fine needles, melted at  $157$ – $158^\circ$ . It did not dissolve in a solution of sodium hydroxide except on long standing (hydrolysis at the O-connection). Analysis for bromine indicates the presence of both an acetyl and a benzoyl radical.

*Analysis.* Subs., 0.1967; AgBr, 0.1066. Calc. for  $C_{16}H_{14}O_3NBr$ : Br, 22.90. Found: 23.05.

A portion (0.35 g.) of the acetylbenzoyl derivative just described was shaken with 40 cc. of water containing 2 equivalents of sodium hydroxide. Solution took place very slowly and after 48 hours the greater portion of the solid remained undissolved. Filtration of this mixture, and treatment of the filtrate with acid gave too small a portion of material for further study. The residue that did not dissolve in the alkali was found to melt still at the same temperature ( $157$ – $158^\circ$ ) as the acetylbenzoyl derivative described above, and a mixture of it and the untreated portion melted without depression at the same temperature.

Proof of the Structure of 2-Benzoylamino-4-bromo-5-methylphenyl Acetate.—A portion of 3-hydroxy-4-amino-6-bromotoluene<sup>11</sup> weighing 2.0 g. (2 mols) was dissolved in dry ether, and to this was slowly added 0.7 g. (1 mol) of benzoyl chloride while the flask was continually shaken, as directed by Ransom.<sup>8</sup> After the precipitated hydrochloride had been removed, the ether was allowed to evaporate spontaneously, and the solid that remained was collected and shaken with a solution of sodium bicarbonate to remove benzoic acid. The residue was crystallized from alcohol from which it separated as nearly colorless leaflets that melted with blackening and apparent decomposition at  $223^\circ$ . Analysis for bromine, taken in connection with the behavior described below, shows that the benzoyl radical is attached to nitrogen.

*Analysis.* Subs., 0.0973; AgBr, 0.0606. Calc. for  $C_{14}H_{12}O_2NBr$ : Br, 26.12. Found: 26.49.

This compound is readily soluble in caustic alkali solution, and from this liquid hydrochloric acid precipitated material that was so finely divided it could not readily be collected by filtration. Extraction with ether, drying the extract with anhydrous sodium sulfate, and evaporation of the solvent left a solid that was slightly yellowish in color, but evidently the original material slightly contaminated. It melted at about  $212^\circ$  with blackening and apparent decomposition. Since the amount available at this stage was too small to permit of complete purification it was converted into an acetyl derivative by heating it with anhydrous sodium acetate and acetic anhydride. The product here obtained was washed with water and crystallized from alcohol. It melted

<sup>11</sup> Ref. 9, p. 1505.

at 156-7° (a second crystallization would doubtless have raised the melting point) and a mixture of this product and 2-benzoylamino-4-bromo-5-methylphenylacetate (m. p. 157-8°) described above melts between 156° and 158°, which indicates that they are identical, and that in the benzoylation of 2-acetylamino-4-bromo-5-methylphenol the benzoyl radical attached itself to nitrogen while the acetyl migrated to oxygen.

### Summary

When the acetyl and benzoyl radicals are introduced into the *o*-aminophenols obtained from *o*- and *m*-cresols, respectively, the benzoyl radical is found attached to nitrogen in each case, regardless of the order of introduction. This confirms the observations previously reported.

The work was done while the junior author held the Du Pont scholarship in chemistry at the State University of Iowa, and our thanks are due to E. I. Du Pont de Nemours and Company for this assistance in our work.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

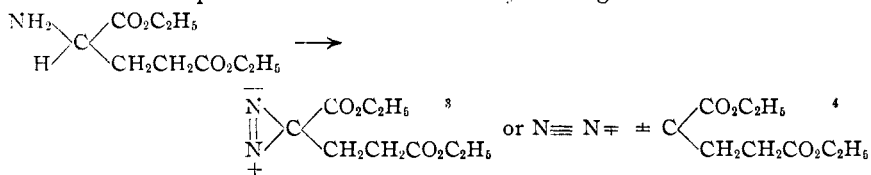
## OPTICALLY ACTIVE DIAZO COMPOUNDS. II

By H. M. CHILES WITH W. A. NOYES

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In a previous paper C. S. Marvel<sup>1</sup> with one of us has given an account of unsuccessful experiments undertaken in the hope of preparing optically active aliphatic diazo compounds in which the only asymmetric carbon atom is combined with the two nitrogen atoms. After that paper was published Levene and Mikeska<sup>2</sup> reported that they had obtained diethyl-diazosuccinate in an active form. We have now succeeded in preparing 6 such active compounds. The failure of the former experiments was due to the fact that such compounds racemize very easily. It is necessary to carry through all operations very carefully and to distil the compounds under a very low pressure.

The first compound obtained was diethyl-diazoglutarate.



It seems to be impossible to reconcile the Curtius formula for these active compounds with the ideas of atomic structure and of non-polar valence proposed by G. N. Lewis and Irving Langmuir. The Angeli-

<sup>1</sup> C. S. Marvel with W. A. Noyes, *THIS JOURNAL*, 42, 2259 (1920).

<sup>2</sup> Levene and Mikeska, *J. Biol. Chem.*, 45, 593 (1921); 52, 485 (1922).

<sup>3</sup> The Curtius formula.

<sup>4</sup> The Angeli-Thiele formula.