2. In the methylation of benzoylene urea, results have been obtained differing from those of Abt.

3. Dichloro- and dimethoxy-quinazoline have been prepared in purer form than hitherto.

4. Our knowledge of *o*-uramino benzoic acid and of its dinitro derivative has been extended.

5. 5-Nitro-anthranilic acid and its acetyl derivative have been studied and some of the existing confusion in the literature cleared up.

6. The structure of 6-nitro-4-quinazolone has been proven by its synthesis from 5-nitro-anthranilic acid.

7. The serviceability of certain quinazolines as indicators has been tested.

8. The following new compounds have been prepared: methyl-*o*-uramino benzoate, the sodium salt of 6-nitro-benzoylene urea, the potassium and ammonium salts of 6,8-dinitro-benzoylene urea, methyl-dinitro-*o*-uramino benzoate, various salts of 5-nitro-acetanthranilic acid and of 5-nitro-anthranilic acid, and the methyl ester of the latter.

NEW YORK, N. Y.

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

MOLECULAR REARRANGEMENT IN THE ACYLATION OF CERTAIN AMINOPHENOLS.

BY L. CHAS. RAIFORD.

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During the course of a research now in progress in this laboratory, the purpose of which is the study of the steric relations involved in the acylation of aminophenols, it became necessary in the identification of one of the products isolated to prepare a diacylated derivative of an *o*-aminophenol in which the acyl radicals bound to oxygen and to nitrogen, respectively, were different. In the case under consideration the two radicals were acetyl and benzoyl. It may be stated at the outset that further examination of the product showed that the heavier of these radicals, benzoyl in this case, was always found attached to nitrogen, regardless of the order in which they were introduced, which indicates that a rearrangement must have occurred in one case.

As will appear below, the rearrangement in this case involved the migration of acetyl from nitrogen to oxygen, and possibly the shift of benzoyl in the opposite direction, though the mechanism of the reaction has not yet been satisfactorily determined. The migration of acyl from oxygen to nitrogen has previously been observed in several different cases, following the work of Böttcher[1] on 2-benzoyl-aminophenol.[2] The replacement of

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[1] *Ber.*, 16, 629 (1883).

[2] For a bibliography of the subject see Weyl, "Die Methoden der Organischen Chemie," II, p. 1281; Leipzig, 1911 (Thieme).

a lighter acyl radical (acetyl) by a heavier one (*m*-nitrobenzoyl) was recorded by Torrey and Kipper[1] and the migration of acyl from nitrogen to oxygen has been observed by Willstätter and Veraguth[2] and by Auwers;[3] but, so far as the writer is aware, the exact behavior described in the present research has not hitherto been reported. Ransom,[4] it is true, has prepared diacylated *o*-aminophenols in which the acyl groups are different, and Ransom and Nelson[5] as a result of further study of the reactions involved, state "that when two carboxyl radicals (COOR and $COOR_1$) are introduced into the molecule of *o*-aminophenol the lighter one becomes attached to nitrogen, the position not being influenced by the order in which the groups are introduced; and that to accomplish this, a molecular rearrangement occurs in one case. This is also true when both of the radicals are carbonyls (COR and COR_1)." In the light of these statements the results obtained in the research described below were unexpected, and this made it a matter of much interest to determine whether the present observation represented merely an isolated case or was an example of a more general reaction.

The base employed in the first experiments was 2-amino-4-methyl-6-bromophenol.[6] When this was warmed with anhydrous sodium acetate and the necessary amount of acetic anhydride, in the usual way, it was converted into a diacetyl derivative. Treatment of the latter with a cold dilute solution of sodium hydroxide caused saponification to take place rapidly at the *o*-connection, giving 2-acetylamino-4-methyl-6-bromophenol. When this phenol was subjected to the Schotten-Baumann reaction with benzoyl chloride, the reaction proceeded smoothly and rapidly to give an acetyl-benzoyl derivative. Saponification of the latter product with alkali took place somewhat more slowly than was the case with the diacetyl derivative, and the phenolic substance that resulted was not the 2-acetylamino-4-methyl-6-bromophenol which was used in preparing the acetyl-benzoyl derivative, and which one might expect to obtain if saponification again took place at the *o*-connection and no rearrangement had occurred, but 2-benzoylamino-4-methyl-6-bromophenol. The identity of the last named product was established by synthesizing it in a wholly different way, *viz.*, by treatment of an ethereal solution of the free aminophenol with benzoyl chloride as described by Ransom,[7] and by showing that the benzoyl derivative thus obtained could readily be converted, by acetylation in the usual way, into the acetyl-benzoyl derivative whose structure was in

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[1] THIS JOURNAL, **30**, 859 (1908).

[2] *Ber.*, **40**, 1432 (1907).

[3] *Ibid.*, **40**, 2154 (1907).

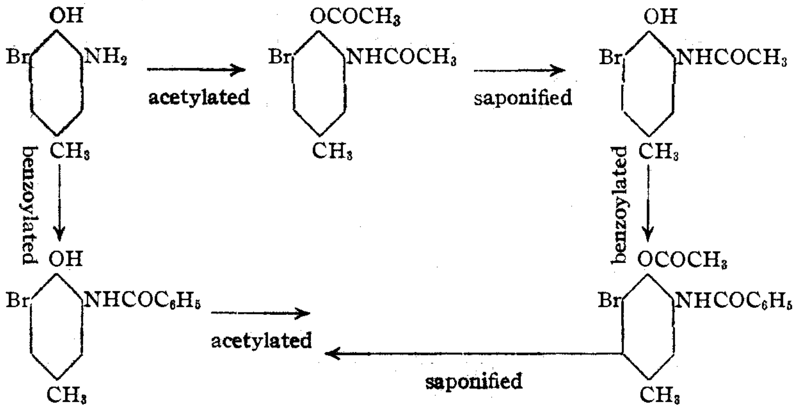
[4] *Am. Chem. J.*, **23**, 1 (1900).

[5] THIS JOURNAL, **36**, 390 (1914).

[6] *Ann.*, **311**, 375 (1900).

[7] *Loc. cit.*

question. From these reactions it appears that the rearrangement occurred during the introduction of the benzoyl radical into 2-acetylamino-4-methyl-6-bromophenol, and not during the saponification of the resulting acetyl-benzoyl compound. Similar results were obtained when these experiments were repeated, using 2-amino-4,6-dibromophenol as the starting base (see experimental part). The reactions involved with the first of these bases may be briefly summarized as follows:



The suggestion[1] that the behavior of the compounds here described might be explained by the possibility that both acyl radicals were bound to nitrogen, and that the substances belong in the class known as alkali-insoluble phenols, does not seem to be in agreement with the facts. In the first place, the compounds are not insoluble in alkali solution, although the ease with which solution takes place is not the same for all cases. The fact that a diacetyl derivative dissolves (through saponification) more rapidly than the corresponding acetyl-benzoyl compound, and an unsubstituted diacyl derivative dissolves more quickly than a substituted one, could possibly be explained by steric hindrance. It should be noted, also, that the concentration of the alkali solution here used did not exceed 1% and that the reactions took place at room temperature, while that employed by Torrey and collaborators[2] and by Adams[3] in testing the solubility of alkali-insoluble phenols had a concentration of 10% and was often used at the boiling point. Moreover, Adams has shown that the insolubility in alkali of the class of so-called alkali-insoluble phenols represented by the phenylhydrazones of *o*-hydroxyaldehydes and ketones depends chiefly upon (1) the tendency of the sodium salts of these phenols to hydrolyze, (2) the extreme insolubility of the free phenols in

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[1] Made during the discussion at the time this paper was presented in abstract at the Philadelphia meeting of the American Chemical Society, September 5, 1919.

[2] *Loc. cit.*

[3] THIS JOURNAL, 41, 247 (1919).

water, (3) the temperature of the alkali solution, and (4) the increase in molecular weight brought about by the introduction of any atom or group of atoms into any part of the molecule, and not upon the structure of the compound, except in the case of the nitro derivatives. In addition to these differences, many of the alkali-insoluble phenols are highly colored, while only a few of the compounds here investigated had even a slight color and most of them were colorless. Finally, no diacylated aminophenols having both acyl radicals attached to nitrogen seem to have been recorded in the literature, and specific attempts by Tingle and Williams[1] to prepare them were unsuccessful.

As has been noted above, Ransom[2] found, in the diacylated aminophenols prepared in his work, that the lighter acyl radical was always attached to nitrogen, and that in the work here reported the heavier of the two acyls went to nitrogen. In comparing these results, and in trying to account for the differences, it seemed necessary to consider the fact that Ransom's work was done with *o*-aminophenol in which there were no acid-forming substituents, while two of the bases employed in my work had a part of the benzene hydrogen replaced by bromine. Recent work[3] in this laboratory, as well as the results of work done elsewhere, indicates that the reactions of a phenolic hydroxyl, or of an amino group attached to a benzene ring, may be very appreciably modified by the presence of acid-forming substituents in the ring. On this account it seemed desirable to repeat, with *o*-aminophenol, all the experiments that had been carried out with the substituted bases specified above. This was done, care being taken to duplicate conditions as far as possible in all cases. The results, however, show that the same type of migration occurred in both instances, from which it appears that the acid-forming substituents are not alone responsible for the rearrangement.

Work is in progress with bases containing other substituents, in which an attempt will be made to determine whether the rearrangement observed is dependent on the differences in weight of the radicals used, their chemical characteristics, or upon the relative positions of the hydroxyl and amino groups.

Experimental.

2-Benzoylamino-4-methyl-6-bromophenyl Acetate, $C_6H_2(OCOCH_3)(NHCOC_6H_5)CH_3.Br$.—The starting point in the preparation of this

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[1] *Am. Chem. J.*, 37, 51 (1907).

[2] *Loc. cit.*

[3] Unpublished research. Mr. R. L. Howard has found that the amount of phenolic ether formed by several different methods, and the extent to which such ethers can be decomposed by heating them with ammonia under pressure, may depend, to a very considerable extent, on the presence of acid-forming substituents, while Mr. R. Taft has shown that the formation of diacetanilides is accelerated by the presence of such substituents in certain positions. In both cases the ortho position seems to exert the greatest influence.

compound was *m*-nitro-*p*-cresol,[1] which was first brominated according to the method used by Thiele and Eichwede.[2] A much better yield of a purer product was obtained by a modification of Zincke and Wiederhold's method.[3] The bromination was carried out in chloroform solution, using a slight excess of bromine, in the presence of iron filings, and after allowing the mixture to stand for 48 hours the chloroform was removed by distillation. At this point Zincke and Wiederhold purified their bromine derivatives by distillation or by crystallization, according to the volatility of the product in question. In the present case it was found more satisfactory to boil the residue with ammonia water and filter, which removed the nitrobromocresol in the form of its ammonium salt and left the iron compounds in the flask. The ammonium salt was next decomposed by hydrochloric acid and the free nitro compound that separated was further purified by repeated crystallization from alcohol, from which it separated in the form of orange-colored leaflets that melted at 69°, in agreement with the observations of Thiele and Eichwede.[4] The yield of pure material was about 65%, but this may be increased very much by working up the mother liquors.

2-Amino-4-methyl-6-bromophenol, $C_6H_2OH.NH_2.CH_3.Br$.—To prepare the hydrochloride of this aminophenol, Thiele and Eichwede reduced the nitro compound mentioned above by means of stannous chloride and hydrochloric acid dissolved in glacial acetic acid, and removed the tin salt with hydrogen sulfide. In my work the reduction was carried out very quickly and the separation from tin salt effected by much less labor by following the method described by Raiford.[5] From the hydrochloride thus obtained, dissolved in water, the free base was prepared by adding a solution of ammonium carbonate. The precipitated base was filtered off at once, washed with several portions of water, and dried on clay plate, in which condition it melted at 92–3°. Crystallization from alcohol did not change the melting point.

2-Acetylamino-4-methyl-6-bromophenyl Acetate, $C_6H_2(OCOCH_3)(NHCOCH_3)CH_3.Br$.—One molecular proportion (2.5 g.) of the base described above was mixed with an equal weight of anhydrous sodium acetate and about 3 cc. (two mols.) of acetic anhydride. The mixture, which became very warm at once, was further heated over a direct flame until the whole was fluid, after which it was allowed to stand until it reached the room temperature. The crystalline solid was next triturated with enough water to dissolve the sodium acetate present, and the mixture

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[1] *Ber.*, **24**, 1960 (1891).

[2] *Ann.*, **311**, 375 (1900).

[3] *Ibid.*, **320**, 202 (1902).

[4] *Loc. cit.*

[5] *Am. Chem. J.*, **46**, 419 (1911).

filtered. The dried residue began to shrink at about 155° and was entirely melted at 166°. Two crystallizations from alcohol gave a product that softened at 160° and melted at 169°. A second portion was purified as follows: A hot concentrated chloroform solution of the substance in a suitable flask was placed under a reflux condenser, and the liquid raised to the boiling point. Through the condenser tube ligroin (b. p. 80–90°) was slowly dropped until the solution began to deposit crystals, after which the flask was removed and allowed to cool. This treatment gave beautiful, colorless, feathery crystals that showed signs of softening at 160° and melted sharply at 169°. This compound is soluble in other organic solvents but none gave as satisfactory crystals as the mixture named above. It dissolves readily in cold solution of sodium hydroxide[1] which saponifies it at the *o*-connection. Analysis[2] for halogen indicated a diacetyl compound.

Subs., 0.2014; AgBr, 0.1331.
Calc. for $C_{11}H_{12}O_3NBr$: Br, 27.95. Found: 28.12.

2-Acetylamino-4-methyl-6-bromophenol, $C_6H_2OH(NHCOCH_3)CH_3$.-Br.—2.86 g. of the above-described diacetyl compound was shaken with 75 cc. of cold water containing 1.0 g. of sodium hydroxide until practically all solid had disappeared and the liqud had a pale yellow color. The mixture was then filtered, the clear filtrate acidified with hydrochloric acid, and the precipitate that formed immediately was filtered off, washed with water and dried. The precipitate weighed 2.17 g., which corresponded to a yield of about 89% calculated on the basis of a monoacetyl compound as the product. The crude material melts at 127–8°, and is soluble in solutions of caustic alkalies from which it is precipitated unchanged by acids, indicating the phenolic character of the substance. It is soluble in the usual organic solvents, but was best crystallized from water out of which it was deposited in long, colorless, silky needles that melted at 129°. Analysis for bromine gave the following figures, which agree with the formula for a monoacetylated compound.

Subs., 0.0889; AgBr, 0.0687.
Calc. for $C_9H_{10}O_2NBr$: Br, 32.76. Found: 32.88.

Action of Benzoyl Chloride on 2-Acetylamino-4-methyl-6-bromophenol.—0.73 g. of the monoacetylated compound described above was dissolved in a solution made up of 50 cc. of cold water and 0.15 g. (1.25 mols) of sodium hydroxide. 0.6 g. of benzoyl chloride was next added and the whole shaken until the odor of the chloride had disappeared. The colorless solid which began to precipitate immediately was finally filtered out, washed with several portions of water and dried. A quantitative yield

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[1] The significance of this behavior will be discussed, along with other cases, in a future communication.

[2] I am indebted to Mr. R. L. Howard for the analysis of this and the compound next described.

was obtained. In this condition the product began to shrink at about 160° and was melted at 168°. Repeated crystallization from alcohol gave colorless fibrous-looking masses made up of very short prisms that melted at 172°. Analysis for bromine gave results that are in agreement with a formula that requires both a benzoyl and an acetyl radical and the other reactions of the compound (see below) support this view.

Subs., 0.2457; AgBr, 0.1338.
Calc. for $C_{16}H_{14}O_3NBr$: Br, 22.97. Found: 23.17.

Proof of the Structure of 2-Benzoylamino-4-methyl-6-bromophenyl Acetate.—0.7 g. of the benzoyl-acetyl compound described above was mixed with 25 cc. of water containing 0.2 g. (2.5 equivalents) of sodium hydroxide, and shaken for some minutes. It was noted that solution took place much more slowly than in the case (see above) where both acyl radicals were acetyl, and on this account the mixture was allowed to stand overnight. The slight amount of unchanged material was removed by filtration, and the clear filtrate, which was yellow in color, was acidified by hydrochloric acid. A yellowish solid that appeared much like sand upon standing was precipitated. The melting point of the crude product was about 165°, but was not sharp. The substance is readily soluble in solutions of caustic alkali, from which acids precipitate it in the unchanged condition. It is soluble also in chloroform, ether, and alcohol, but was best crystallized from 70% alcohol, from which it separated in the form of slender fawn-colored needles that melted at 185°. This melting point, together with the other properties and the analysis given below, show that the compound under consideration cannot possibly be 2-acetylamino-4-methyl-6-bromophenol (m. p. 129°) described on page 2073. The results of the analysis for bromine are in accordance with the requirements of the formula for 2-benzoylamino-4-methyl-6-bromophenol.

Subs., 0.2002; AgBr, 0.1242.
Calc. for $C_{14}H_{12}O_2NBr$: Br, 26.12. Found: 26.39.

In order to identify further the compound just described, and to prove that the benzoyl radical in it was attached to nitrogen, a portion of 2-benzoylamino-4-methyl-6-bromophenol was prepared in accordance with the method used by Ransom[1] in which one molecule of benzoyl chloride was slowly added to an ether solution of two molecules of the aminophenol melting at 92–3° (p. 2072). After the hydrochloride of the base, which was rapidly precipitate, was filtered off, the remaining solution was allowed to evaporate spontaneously. The residue, which melted at 182–3°, was dissolved in sodium hydroxide solution, the liquid filtered and the clear filtrate acidified with hydrochloric acid. The precipitated phenol was collected on a filter, washed several times and dried. It melted sharply at 185°, and a mixture of this product and the phenolic compound obtained

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[1] *Am. Chem. J.*, 23, 17 (1900).

by saponifying the benzoyl-acetyl derivative described on page 2074 melted at the same temperature as either of them separately, 185°. In the saponified product, therefore, the benzoyl radical is bound to nitrogen.

Further proof of the relationship of the product obtained by benzoylating 2-amino-4-methy-6-bromophenol and that produced by benzoylating 2-acetylamino-4-methyl-6-bromophenol was secured by acetylating the compound that resulted in the first case. 0.25 g. of the phenol prepared by Ransom's method was mixed with an equal weight of anhydrous sodium acetate and the requisite quantity of acetic anhydride, and warmed until the whole was fluid. After cooling, the product was freed from sodium acetate and crystallized from alcohol until the melting point was constant. The substance obtained melted at 170–1°, and a mixture of this and the benzoyl-acetyl derivative described on page 2074 showed no depression. This behavior shows that in the benzoylation of 2-acetylamino-4-methyl-6-bromophenol the acetyl radical migrates to oxygen while the benzoyl radical attaches itself to nitrogen.

To test further the rearrangement shown above it was thought desirable to examine the behavior of a closely related base having two bromine atoms present. Accordingly, 4,6-dibromo-*o*-aminophenol was carried through the series of experiments specified for the base already studied.

2-Acetylamino-4,6-dibromophenyl Acetate, $C_6H_2(OCOCH_3)(NHCOCH_3)Br_2$.—The starting point in the preparation of this compound was *o*-nitrophenol, which was first converted into 4,6-dibromo-*o*-nitrophenol[1] by a method which is more convenient than any heretofore published. The nitrophenol was dissolved in 5 to 6 times its weight of glacial acetic acid, after which the calculated amount (two mols.) of bromine was added at once. The mixture was allowed to stand for 48 hours, and then poured slowly, with stirring, into 7 or 8 volumes of cold water, which precipitated the brominated product. After standing for some hours the precipitated material was removed by filtration, washed with water, and dried. Crystallization from alcohol will give a pure product, but the substance employed in this work was purified in the form of its potassium salt, which was twice crystallized from water. The free nitrobromophenol, which was obtained by decomposition of the salt by hydrochloric acid, was finally crystallized from alcohol. It melted sharply at 117°, which is in agreement with the literature.

The preparation of the free base was carried out by reduction of the nitro compound and purification of the resulting aminohydrochloride as described by Raiford[2] after which the aminophenol was obtained by treatment of the water solution of the hydrochloride with solution of ammonium carbonate. The precipitated base was further purified by crystallization

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[1] Korner, *Ann.*, 137, 207 (1866).

[2] *Loc. cit.*

from dilute alcohol, and was found to melt at 91–2°, and to have the other properties specified by Holz.[1]

5.3 g. of the dibromo-aminophenol mentioned above was mixed with an equal weight of anhydrous sodium acetate, and the mixture warmed with slightly more than the calculated amount of acetic anhydride necessary to acylate both the amino and the hydroxyl groups. When cold the resulting mass was extracted with enough water to dissolve the sodium acetate present, and the residue dried. The product is soluble in alcohol, chloroform, and benzene, but was best crystallized from chloroform, out of which it separated in the form of colorless, fibrous-looking masses made up of fine, hair-like needles. It shrinks slightly between 190 and 195° and melts at 199°. It dissolves readily in cold solution of sodium hydroxide on account of being saponified at the *o*-connection. Analysis for halogen gave the following results, which are in accord with a diacylated compound:

Subs., 0.2136; AgBr, 0.2304.
Calc. for $C_{10}H_9O_3NBr_2$: Br, 45.56. Found: 45.90.

2-Acetylamino-4,6-dibromophenol, $C_6H_2OH(NHCOCH_3)Br_2$.—3.5 g. of the diacylated compound just described was shaken with 25 cc. of cold water containing two equivalents of sodium hydroxide until complete solution had taken place, after which the clear liquid was acidified with hydrochloric acid. A precipitate was formed immediately. After standing for some minutes this was collected on a filter, washed with several portions of water, and dried. It is soluble in alcohol and other organic solvents, and slightly soluble in water. Samples were crystallized both from water and from 75% alcohol, but best from the latter, from which it was deposited in tufts made up of short needles radiating from a common center, and melting at 174–5° with apparent decomposition. This compound is soluble in solution of caustic alkali, from which it is precipitated in unchanged form by acids. Holz[2] prepared a monoacetyl derivative from the base used in this work, and assigned to it the structure of my product, though he found 186° to be the melting point.

Subs., 0.2815; AgBr, 0.3410.
Calc. for $C_8H_7O_2NBr_2$: Br, 51.75. Found: 51.55.

Action of Benzoyl Chloride on 2-Acetylamino-4,6-dibromophenol.—1.5 g. of the monoacetyl compound described above was dissolved in about 50 cc. of water containing 0.25 g. (1.25 mols) of sodium hydroxide, and to this was then added 0.87 g. of benzoyl chloride, after which the whole was shaken until the odor of the chloride had disappeared. A solid which tended to collect in little balls was formed at once. After standing for some time it was filtered off, washed and dried. A quantitative yield was obtained. This compound is but slightly soluble in ligroin or ether,

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[1] *J. prakt. Chem.*, [2] **32**, 69 (1885).

[2] *Loc. cit.*

and could not be crystallized satisfactorily from either of them. It is more soluble in chloroform or in alcohol, and was best crystallized from the latter, from which it was deposited in short, silky needles that tended to cling together in star-like masses. After several crystallizations it melted at 195–6°. A mixture of this substance and 2-acetylamino-4,6-dibromophenyl acetate, m. p. 199°, page 2075, melts at 167–71°.[1] Analysis for bromine is in agreement with a formula that requires both an acetyl and a benzoyl radical.

Subs., 0.2379; AgBr, 0.2163.
Calc. for $C_{15}H_{11}O_3NBr_2$: Br, 38.71. Found: 38.69.

Proof of the Structure of 2-Benzoylamino-4,6-dibromophenyl Acetate.—0.62 g. of the benzoyl-acetyl compound indicated above was mixed with 30 cc. of water containing 0.15 g. of sodium hydroxide, and the mixture shaken for some time. Saponification took place very slowly, consequently the mixture was allowed to stand overnight. Since the reaction was not completed during this period, the mixture was filtered and the unchanged material added to a fresh portion of alkali. After 24 hours practically all solid had disappeared. This portion was filtered, and the combined filtrate, which was yellow in color, was acidified with hydrochloric acid. The phenolic compound that was precipitated was collected on a filter, washed well with several portions of water, and dried. The crude material melted between 170 and 175°. It was twice crystallized from alcohol, from which it was deposited in clusters of short, very pointed needles that radiated from a common center. These melted at 198° with apparent decomposition. The behavior indicated above shows that the hydroxyl group is free, and the analysis for bromine agrees with a formula requiring the presence of a benzoyl radical. These facts, together with the behavior of a mixture of the substance under consideration and 2-acetylamino-4,6-dibromophenol (melting point 174–5°), from which the benzoyl derivative was prepared when heated, shows that the products cannot be identical. The mixture melts with decomposition at 160–2°.

Subs., 0.2012; AgBr, 0.2038.
Calc. for $C_{13}H_9O_2NBr_2$: Br, 43.10. Found: 43.10.

In order to characterize further the hydroxyl compound described above and to prove that in it the benzoyl radical is bound to nitrogen, a small quantity of the benzoylamino compound of the base under consideration was prepared according to Ransom's[2] method. 2.66 g. of 4,6-dibromo-*o*-aminophenol was dissolved in about 25 cc. dry ether, and to this

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[1] It is worth while to note this behavior in passing, because in preparing the benzoyl derivative in quantity it is unnecessary to isolate 2-acetylamino-4,6-dibromophenol, as was done in this case; the benzoyl derivative can be obtained by adding benzoyl chloride directly to the solution obtained by dissolving the diacetyl compound in sodium hydroxide solution.

[2] *Loc. cit.*

was added 0.7 g. ($^1/_2$ mol) of benzoyl chloride, and the mixture allowed to stand until the odor of the chloride had nearly disappeared. The hydrochloride of the base which had meanwhile precipitated was filtered off, and the clear ether solution allowed to evaporate spontaneously. The residue melted at 193–5°, and was probably contaminated with traces of the hydrochloride only, for dissolving it in solution of sodium hydroxide and reprecipitating it with hydrochloric acid gave a product that melted quite sharply at 198°, which is the melting point of the product obtained by saponifying the acetyl-benzoyl derivative described on page 2076. A mixture of the two products melts at 198°, which indicates identity.

The relationship of the phenolic product prepared by Ransom's method to 2-benzoylamino-4,6-dibromophenyl acetate was still further established by preparing some of the latter from the phenol. 0.2 g. of the phenol was mixed with an equal weight of anhydrous sodium acetate and the required amount of acetic anhydride, and warmed until the whole became liquid. After cooling it was separated from sodium acetate and crystallized from alcohol until the melting point was constant. In this condition it did not depress the melting point of 2-benzoylamino-4,6-dibromophenylacetate, which shows that in the benzoylation of 2-acetylamino 4,6-dibromophenol the benzoyl radical goes to nitrogen, while the acetyl radical migrates to oxygen.

In view of the fact that the results reported above are not in accord with the observations of Ransom and Ransom, and Nelson[1] it was at first thought that possibly the character of the aminophenols used might have a bearing on the case. The results recorded by the observers mentioned were all obtained through the use of an aminophenol that was unsubstituted while the first observations in my work were made with aminophenols that contained acid-forming substituents. On account of these differences it became at once a matter of interest to repeat the experiments, using the unsubstituted aminophenol employed by Ransom. It may be stated at once that the results so far obtained are the same in type for both substituted and unsubstituted bases, although the saponification of the acyl derivatives of the substituted compounds is less rapid, due, possibly to steric hindrance.

2-Benzoylaminophenyl Acetate, $C_6H_4(OCOCH_3)(NHCOC_6H_5)$.—The starting point in the preparation of this compound was 2-acetylaminophenol, first prepared by Ladenburg[2] and which was obtained for my work

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[1] *Loc. cit.*

[2] *Ber.*, **9**, 1524 (1876). It will be shown later that this compound can be obtained by a method which is much more easily carried out than that used by Ladenburg, and that the diacetyl derivative (which was overlooked by Ladenburg) from which it was here obtained can be prepared with much less difficulty than has been done by any previous worker. The saponification of the diacetyl compound, its homologs and certain of its derivatives will form the subject of a future report.

by the saponification of the corresponding diacetyl derivative. The product melted at 201°, and had the other properties recorded in the literature. 4.5 g. of this material was mixed with about 50 cc. of water and 1.25 molecular proportions of sodium hydroxide, and the resulting solution shaken with 25% more than the calculated quantity of benzoyl chloride until the odor of the latter had disappeared. After standing for some hours the solid that had separated was collected on a filter, washed with several portions of water, and dried. The yield was nearly quantitative. In this form the substance melted at 134–5°. Crystallization from alcohol, benzene or ligroin gave slightly pinkish colored needles that melted at 138° if heated rapidly, or at 135° if heated more slowly. The compound is practically insoluble in water, but is slowly dissolved, on account of being saponified at the *o*-connection, when allowed to stand in the cold with sodium hydroxide solution. It is interesting in this connection to note that Tingle and Williams[1] subjected 2-acetylaminophenol to benzoylation by the Schotten-Baumann method, using potassium hydroxide instead of sodium hydroxide, and mixing the substances in a different order than that specified above, and obtained a good yield of dibenzoyl-*o*-aminophenol. In this work they prepared 4 diacylated aminophenols in which the acyl radicals were different, but observed no rearrangements. The reactions of my product are confirmed by analysis[2] for nitrogen.

Subs., 0.6208; N (Kjeldahl), 0.0312 g.
Calc. for $C_{15}H_{13}O_3N$: N, 5.49. Found: 5.03.

A portion of the purified material specified above was mixed with a solution of sodium hydroxide containing 2.5 equivalents of the alkali and was allowed to stand in the cold overnight or until practically all solid had passed into solution. The mixture was then filtered and the clear filtrate acidified with hydrochloric acid, whereupon a practically colorless crystalline precipitate was thrown down. This was removed, washed well with water, and when dried on clay plate melted without further purification at 165–7°. The product was readily soluble in solution of sodium hydroxide from which it could be precipitated in unchanged form by the addition of acids, indicating its phenolic character. To show that the product in question could not be an impure specimen of the acetylaminophenol (m. p. 201°) with which the experiment was started, portions of the two products were mixed and melted. The mass began to melt at 148° and was entirely liquid at 187°. A second portion of the product obtained by saponification of the benzoyl-acetyl derivative was further purified by repeated crystallization, after which it melted sharply at 167°. This, together with the behavior already noted, showed that the product in question could not be identical with the acetylaminophenol melting at 201°.

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[1] *Loc. cit.*

[2] I am indebted to Mr. J. L. Clark for this analysis.

To determine whether it was benzoyl-*o*-aminophenol, described by Hubner[1] and by Ransom,[2] a portion of that compound was prepared according to the directions given by Ransom, and its properties carefully compared with those of my product. They agreed in every particular, and a mixture of the products melted at the same temperature as either of them separately, 167°.

The identity of the two products was still further established by converting them into acetyl derivatives. Each was mixed with an equal weight of anhydrous sodium acetate and the requisite amount of acetic anhydride, and heated for a few minutes. After purification in the usual way, the product in each case had the melting point 134° or 138° (depending on the rate of heating) and other properties given above under 2-benzoylaminophenyl acetate. Each of the products melting at 167° was benzoylated in accordance with the Schotten-Baumann method, and each gave a product which, after crystallization from alcohol, melted at 182°. These products were melted together without depressing each other's melting point, and were found to be identical with 2-benzoylaminophenyl benzoate, reported by Kalckhoff.[3]

Summary.

1. When certain *o*-aminophenols were acylated in such a way as to introduce acetyl and benzoyl groups into the same molecule, the heavier of these radicals was found attached to nitrogen, regardless of the order in which the radicals were introduced. In one case a molecular rearrangement must have occurred.

2. So far as the work has been carried, no differences have been observed between the behavior, in this respect, of substituted and unsubstituted aminophenols, which indicates that acid-forming substituents are not responsible for the rearrangement.

3. It is recognized that factors other than the weight of the acyl radicals may determine the behavior observed in this work, and these are now under consideration.

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[1] *Ann.*, **210**, 387 (1881).

[2] *Am. Chem. J.*, **23**, 17 (1900).

[3] *Ber.*, **16**, 1828 (1883).