

the measurements of densities and vapor pressures, and automatically to 0.005° or better in the determination of the viscosities.

### Summary

Assuming the atoms of phenyl isocyanate and of diazobenzene-imide to be arranged as indicated in the formulas,  $C_6H_5NCO$  and  $C_6H_5NNN$ , application of the octet theory leads to the conclusion that they are isosteric. They should, therefore, be very similar in their physical properties. Their densities, vapor pressures and viscosities have been measured at various temperatures, and this prediction confirmed. These results also confirm the straight-chain structure for triazo compounds.

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[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE STATE  
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## DIACYL DERIVATIVES OF ORTHO-HYDROXYBENZYLAMINE

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Previous work in this Laboratory has shown (a) that when 2-acetylaminophenol is subjected to the action of benzoyl chloride (Schotten-Baumann reaction), the benzoyl radical is attached to nitrogen while acetyl migrates to oxygen;<sup>1</sup> (b) that this migration is not prevented by the presence of acid-forming substituents (halogen) attached to the nucleus of the aminophenol;<sup>2</sup> (c) that the acetyl-benzoyl derivatives of *p*-aminophenols do not suffer this rearrangement;<sup>3</sup> (d) that the presence of bromine and other heavy radicals adjacent to the reacting groups (amino and hydroxyl), which in many reactions causes marked retardation, does not prevent the migration;<sup>4</sup> and (e) that these observations seem to hold with bases derived from naphthalene, namely, 1-amino-2-naphthol and halogenated derivatives.<sup>5</sup> Since the acetyl-benzoyl derivatives of more than 15 *o*-amino-phenols, having various substituents at different positions in the molecule, have been tested in this way and all have been found to undergo this migration, it may be assumed that this behavior is general for this class of compounds when the acyl radicals are those specified.

Although the migration of this kind has thus far been observed to take place only in the derivatives of compounds in which both reacting groups

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

<sup>2</sup> Raiford and Couture, *ibid.*, **44**, 1793 (1922).

<sup>3</sup> Raiford and Iddles, *ibid.*, **45**, 469 (1923).

<sup>4</sup> Woolfolk, unpublished report.

<sup>5</sup> Armstrong, unpublished report.

(hydroxyl and amino) were attached directly to the benzene ring. Auwers and his students<sup>6</sup> have reported a rearrangement in which acyl wandered from oxygen to nitrogen when oxygen was attached to the ring and nitrogen was on a side chain. Thus, when an O-acyl derivative of *o*-hydroxybenzyl bromide was heated with aniline, the bromine atom was replaced by the phenylamino radical and at the same time the position of the acyl shifted from oxygen to nitrogen; while McConnan and Titherly<sup>7</sup> found that under certain conditions *o*-acylsalicylamide rearranged to N-acylsalicylamide, and that the change was reversible. The starting compounds in these cases were somewhat different from those heretofore employed in our work, in that in salicylamide not only was the amino radical on a side chain, but the carbon of this chain was in the form of a carbonyl group, while in the benzylamine used by Auwers and collaborators one of the amino hydrogen atoms was replaced by a hydrocarbon radical (phenyl or a homolog).<sup>8</sup> Auwers' results, too, differed from ours to the extent that, with only one of the benzylamine derivatives he prepared, apparently, did he observe the migration of acyl from nitrogen to oxygen. In that instance the product was not stable, but rearranged spontaneously to the N-acyl derivative, which would be expected when the amino radical is not already acylated. On account of these differences, and also because of the sharply defined behavior of the products studied by the above-mentioned authors, as well as the equally definite results of our own work, it became a matter of interest to study the behavior of acetyl-benzoyl derivatives prepared from a phenolic compound having an unsubstituted amino radical attached to a side chain adjacent to an hydroxyl group.

For this study *o*-hydroxybenzylamine, prepared as indicated below, was selected. With the exceptions noted in the Experimental Part, the preparation and hydrolysis of the derivatives of this base were carried out as described in previous papers. It may, however, be stated at once that benzoylation of *o*-hydroxybenzyl-acetamide did not cause the migration of the acetyl radical, and that the introduction of the acyl radicals in different orders gave isomeric acetyl-benzoyl derivatives; this is entirely

<sup>6</sup> Auwers and others, *Ber.*, **33**, 1923 (1900).

<sup>7</sup> McConnan and Titherly, *J. Chem. Soc.*, **89**, 1318 (1906).

<sup>8</sup> In this connection it is to be noted that certain well-known rearrangements involving the amino radical do not take place when this hydrogen has been substituted by an alkyl or aryl radical. Thus, Slosson [*Ber.*, **28**, 3266 (1895); *Am. Chem. J.*, **29**, 295 (1903)] found that "the presence of the hydrogen atom (H<sup>+</sup>) of the acylamine halides, RCONH-Hal is essential for the successful Beckmann rearrangement," while Ransom, [*Am. Chem. J.*, **23**, 26 (1900)] proved that in the diacyl derivatives of methyl-*o*-aminophenol that he studied there was no molecular rearrangement. Stieglitz [*Am. Chem. J.*, **29**, 52 (1903)] formulated a theory to account for this behavior and, in addition to the cases cited above, has called attention to the fact that chloro-imido esters, whose parent substances are acid halogen-amides, and hydroxylamine derivatives that can no longer lose water, have lost the tendency to undergo a Beckmann rearrangement.

different from the behavior of such compounds when both the reacting radicals are attached directly to the aromatic nucleus.

### Experimental Part

***o*-Hydroxybenzylamine.**—Salicylaldoxime, used in preparing this amine, was obtained in excellent yield by following the general method of Loch<sup>9</sup> modified by removing under reduced pressure practically all the alcohol used as solvent in the early part of the experiment, and mixing the residue with water before extraction with ether. The extract thus obtained was dried with anhydrous sodium sulfate, the greater part of the ether was distilled, and the residue allowed to crystallize. The product was purified by treatment of its chloroform solution with petroleum ether, which gave colorless crystals that melted at 57° as reported in the literature. Fifty g. of aldehyde gave 55 g. of oxime, a yield of 98%. Loch reported no yield.

To obtain the amine<sup>10</sup> 20 g. of the oxime, purified as indicated above, was dissolved in 300 cc. of 50% alcohol and reduced in the usual way with 2.5% sodium amalgam.<sup>11</sup> The temperature was kept below 55° and the excess of alkali continually neutralized by the addition of hydrochloric acid. However, the reaction mixture was kept slightly alkaline to litmus until reduction had been completed. This was indicated by a copious evolution of hydrogen. The solution was then made slightly acid, separated from the mercury and evaporated under reduced pressure until sodium chloride began to crystallize. The residue was diluted with water and concentrated as before, in order to remove as completely as possible the alcohol previously used as solvent. The mixture was again diluted with water to a volume of about 300 cc. and transferred to an Erlenmeyer flask containing about 25 cc. of ether. Ammonium hydroxide was added in small portions until a slight excess was present. The mixture was shaken vigorously after each addition. Upon continued shaking for a few minutes the amine began to crystallize on the sides of the flask. After a short time, the product was removed by filtration. Extraction of the mother liquor with ether and evaporation of the solvent gave more of the

<sup>9</sup> Loch, *Ber.*, **16**, 1782 (1883).

<sup>10</sup> This amine had previously been prepared by Goldschmidt and Ernst [*Ber.*, **23**, 2740 (1890)] in accordance with Salkowski's method [*Ber.*, **22**, 2142 (1889)] by heating *o*-anisamine with hydrochloric acid under pressure for several hours. These workers stated that only a poor yield of the base could be obtained by reduction of salicylaldoxime with sodium amalgam, although several different modifications of the method were tried. They recorded 121° as the melting point of their product. Tiemann [*Ber.*, **23**, 3016 (1890)], who obtained this base by the reduction of salicyl-*m*-hydrazone-benzoic acid with zinc dust and dil. sulfuric acid, reported no yield but recorded a melting point of 125°. Auwers and Walker [*Ber.*, **31**, 3038 (1898)], who prepared it from *o*-cyanophenol by the Mendius reaction, reported neither yield nor melting point.

<sup>11</sup> This was prepared in accordance with Nef's method [*Ann.*, **280**, 307 (1894)] modified as follows: 25 g. of sodium in small pieces was added to 975 g. of purified mercury covered by 400 cc. of toluene in a 1-liter beaker and the mixture stirred constantly. This was most easily done by placing the pieces of sodium on a sharp pointed glass stirring rod and, forcing them under the surface of the mercury; the reaction took place at once. The toluene reached the boiling point before all the sodium had been introduced, but the latter was added quite rapidly toward the end. Finally the toluene was decanted, and the solid amalgam was gently heated in a casserole until it melted and became homogeneous. It was next freed from slag by pouring it slowly upon a large piece of paper, the slag remaining in the casserole. As soon as the pure product thus obtained was sufficiently cool to be handled, it was broken up and placed in a well-stoppered container.

crystals. In this way 20 g. of oxime gave 15.5 g. of amine by direct crystallization and 1.7 g. from the mother liquor, a total of 17.2 g. or a yield of 96%.

It was best recrystallized by treatment of a solution in absolute alcohol with petroleum ether. Purified in this way, it began to soften at 126° and melted at 129° (uncorr.). Analysis (Kjeldahl) indicated that it was pure.

*Analysis.* Subs., 0.2513: 20.25 cc. of 0.1 *N* HCl. Calc. for  $C_7H_9ON$ : N, 11.37. Found: 11.29.

***o*-Acetyloxybenzyl-acetamide.**—Two g. of *o*-hydroxy-benzylamine was added slowly to a hot solution of 2 drops of concd. sulfuric acid in 8 g. of acetic anhydride, after which the mixture was boiled gently for 5 minutes and then allowed to stand for 2 hours. It was poured into water and neutralized with sodium hydrogen carbonate. The acetyl derivative was removed by extraction with chloroform, the solution dried and evaporated to a small volume, after which petroleum ether was added. The crystals weighed 2.8 g.; yield,<sup>12</sup> 83%. Recrystallization by the same method gave hexagonal plates; m. p., 102–103°. Analysis (Kjeldahl) indicated the presence of 2 acetyl radicals.

*Analysis.* Subs., 0.3041: 14.58 cc. of 0.1 *N* acid. Calc. for  $C_{11}H_{13}O_2N$ : N, 6.76. Found: 6.72.

***o*-Hydroxybenzyl-acetamide.**—This compound, previously prepared by Goldschmidt and Ernst<sup>10</sup> by direct acetylation, was obtained by hydrolysis of the diacetyl derivative described above. One g. of the latter was dissolved in 50 cc. of 95% alcohol containing slightly more than 2 molecular proportions of potassium hydroxide. The solution was allowed to stand for about 5 minutes, and then made acid to congo red with hydrochloric acid. Potassium chloride was removed, the filtrate evaporated under reduced pressure to a small volume, and 20 cc. of water added. This gave 0.59 g. of a crystalline product. The mother liquor was extracted with chloroform, the extract dried and reduced to a small volume, and petroleum ether added. A further quantity of substance, 0.21 g. was obtained; yield, 0.80 g. (quantitative). The combined product was recrystallized as just indicated, and gave thick rectangular plates that melted at 140°, as found by Goldschmidt and Ernst. Analysis (Kjeldahl) indicated the presence of only 1 acetyl radical.

*Analysis.* Subs., 0.3014: 18.10 cc. 0.1 *N* acid. Calc. for  $C_9H_{11}O_2N$ : N, 8.46. Found: 8.41.

***o*-Benzoyloxybenzyl-acetamide.**—A compound having apparently this composition and structure was obtained by Auwers and Eisenlohr,<sup>13</sup> but they gave neither yield nor analysis of their product; the melting point they recorded is 108–109°; that found by us is 116°; yield, 93%.

**Hydrolysis of the Acetyl-benzoyl Derivative.**—A solution of 1.8 g. of the diacetyl derivative just described, in 75 cc. of alcohol containing 0.85 g. (2.25 molecular equivalents) of potassium hydroxide, was allowed to stand for half an hour, after which it was made acid to congo red with hydrochloric acid. This caused the development of a pronounced odor of ethyl benzoate and a precipitation of potassium chloride. The salt was removed by filtration, the filtrate concentrated almost to dryness, and the residue

<sup>12</sup> Goldschmidt and Ernst tried to prepare this product by boiling the amine with acetic anhydride and anhydrous sodium acetate, but they obtained only the *N*-acetyl derivative and a small portion of an oily material having weak basic properties, which they assume may have been an anhydro base. We found that when a mixture of 1 part of base, 0.25 parts of dry sodium acetate and 4 parts of acetic anhydride, was treated as directed in our experiment described above, a yield of 74% of the diacetyl derivative was obtained.

<sup>13</sup> Auwers and Eisenlohr, *Ann.*, **369**, 236 (1909).

then mixed with 25 cc. of water containing sufficient potassium hydroxide to bring about solution. After filtration, hydrochloric acid was added until a Sørensen value of 6-7 was reached, which caused the precipitation of 0.82 g. of solid. Removal of this and extraction of the mother liquor with chloroform gave 0.17 g. additional, a total of 0.99 g., which corresponds to a yield of 89.5% on the basis of the *N*-acetyl derivative as the product. The crude material melted at 135°, but purification by treatment of its chloroform solution with petroleum ether gave colorless irregular plates that melted at 140-141°. A mixture of this product and the *N*-acetyl derivative previously described melted at the same temperature as either of them separately.

***o*-Hydroxybenzyl-benzamide.**—This compound was first obtained by treatment of 2.0 g. (2 molecular equivalents) of the free base suspended in 50 cc. of dry ether with 1 molecular proportion of benzoyl chloride dissolved in ether, according to Ransom's method.<sup>14</sup> The product weighed 0.8 g., corresponding to a yield of only 43.4%. After solution in chloroform and precipitation by the addition of petroleum ether, it melted at 110-115°.

Recrystallization by treatment of a solution in absolute alcohol with petroleum ether gave short, thick needles that softened at 140° and melted at 142°. Further crystallization caused no change in melting point. The low yield here obtained made it advisable to find some other way to obtain this product, and this was done by hydrolysis of the dibenzoyl derivative (see below).

***o*-Benzoyloxybenzyl-benzamide.**—To a solution of 3 g. of the free base in 300 cc. of water containing 2.1 molecular proportions of potassium hydroxide, was added 2.75 g. (2.15 molecular proportions) of benzoyl chloride, after which the material was shaken until the precipitation was complete; the liquid was still slightly acid to litmus. The solid, collected on a filter, washed and dried, weighed 8.5 g., which is more than the theoretical requirement. The excess may possibly be due to the formation of a tribenzoyl derivative.<sup>15</sup> When the substance was purified by dissolving it in absolute alcohol and adding petroleum ether it separated in masses of long, thin needles that with the unaided eye had the appearance of paper pulp. It softened at 137° and melted to a clear liquid at 142-143°. Four recrystallizations caused no change in melting point. Analysis of an air-dried sample (Kjeldahl) indicated the presence of 2 benzoyl radicals.

*Analysis.* Subs., 0.6013: 18.02 cc. of 0.1 *N* acid. Calc. for  $C_{21}H_{17}O_3N$ : N, 4.23. Found: 4.20.

**Preparation of *o*-Hydroxybenzyl-benzamide by Hydrolysis of the Dibenzoyl Derivative.**—A solution of 3 g. of the dibenzoyl derivative just described in 150 cc. of alcohol containing 1.2 g. (2.25 molecular proportions) of potassium hydroxide was allowed to stand for 20 minutes, after which it was made acid to congo red by the addition of hydrochloric acid. The potassium chloride was removed and the filtrate evaporated under reduced pressure almost to dryness, after which 40 cc. of water was added, containing enough potassium hydroxide to dissolve the benzoyl derivative present. The mixture was filtered, and the ethyl benzoate removed by distillation in a vacuum. The remaining liquid was diluted to a volume of about 50 cc. and hydrochloric acid was added until a Sørensen value of 6-7 was reached. The precipitated benzoyl derivative was collected on a filter, washed and dried; yield, quantitative. It softened at 139° and melted to a clear liquid at 142-143°. After purification by solution in chloroform and the addition of petroleum ether, it was obtained in the form of rhombohedral plates that softened at 140° and melted sharply at 142°.

This material was shown not to be an impure sample of the dibenzoyl derivative

<sup>14</sup> Ransom, *Am. Chem. J.*, **23**, 1 (1900).

<sup>15</sup> Auwers and Eisenlohr, Ref. 13, p. 228, reported such a product from *o*-amino-*p*-cresol.

(m. p., 142–143°) from which it was prepared, by (a) the determination of the melting point of a mixture of the 2 products, found to be 110–115°; (b) by melting a mixture of the product here in question and the monobenzoyl compound obtained by Ransom's method (see above), in which case no depression was observed, and (c) by analysis for nitrogen, which indicated the presence of one benzoyl radical.

*Analysis.* Subs., 0.4013: 17.51 cc. of 0.1 *N* acid. Calc. for  $C_{14}H_{13}O_2N$ : N, 6.17. Found: 6.11.

**Acetylation of the *N*-Benzoyl Derivative.**—A mixture of 2.8 g. of the monobenzoyl compound, 0.75 g. of dry sodium acetate and 12 g. of acetic anhydride was gently boiled for 10 minutes. After the product had cooled, 50 cc. of water was added and the greater part of the acid and anhydride was neutralized by the addition of sodium bicarbonate. This caused crystals of the acetyl-benzoyl derivative to separate almost completely within a few minutes; yield 3.2 g., or 97%. The crude product softened at 70° and melted to a milky liquid at 80–83°. Purification by solution in benzene and precipitation with petroleum ether gave irregular masses of poorly defined needles that softened at 80° and melted to a milky liquid at 85°. Recrystallization from several other solvents caused no change in melting point. This product was further identified by analysis (Kjeldahl), which indicated the presence of both acetyl and benzoyl radicals.

*Analysis.* Subs., 0.5005: 18.42 cc. of 0.1 *N* acid. Calc. for  $C_{16}H_{15}O_3N$ : N, 5.20. Found: 5.17.

Finally, the melting point of a mixture of this material and the acetyl-benzoyl derivative (m. p., 116°) obtained by benzoylation of *o*-hydroxybenzyl-acetamide, was found to be 70–75°. This together with the analyses and the fact that these compounds give different products when hydrolyzed, indicates that they are isomeric and not identical, and that in the benzoylation of a phenol containing an acetylamino group attached to a side chain the migration characteristic of a derivative of *o*-aminophenol does not take place.

**Hydrolysis of *o*-Acetyloxybenzyl-benzamide.**—A solution of 1 g. of the product in 50 cc. of alcohol containing 0.47 g. (2.25 molecular proportions) of potassium hydroxide, was allowed to stand for 30 minutes. Hydrochloric acid was then added until the mixture reacted acid to congo red. The potassium chloride that had been precipitated was removed by filtration, and the filtrate concentrated under reduced pressure almost to dryness. The residue was washed from the flask with about 50 cc. of water and dried. The product weighed 0.7 g.; yield, 91%. It softened at 140° and melted at 142°. A mixture of this material and the *N*-benzoyl derivative prepared by the two methods indicated above showed no depression in melting point, while a mixture of this substance and the product (m. p., 140–141°) obtained by hydrolysis of *o*-benzoyloxybenzyl-acetamide melted at 110–120°.

### Summary and Conclusions

1. An improvement of Nef's method for the preparation of sodium amalgam has been described.

2. It has been shown that, contrary to the results of Goldschmidt and Ernst, a very high yield of *o*-hydroxybenzylamine may be obtained by reduction of salicylaldoxime with sodium amalgam.

3. The observations here reported indicate that the migration of acyl previously shown to be characteristic of diacylated *o*-aminophenols does not occur when the amino radical is attached to a side chain.