

values are low, and Ost's high, as compared with the best available information. Landolt's equation is the result of converting Gubbe's formula for  $q$  into one for  $p$ . From Vosburgh's data for fructose, Tollens' for glucose, and from Vosburgh's rule concerning the rotation of sugar mixtures, the following equation is developed;  $[\alpha]_D^{20}$  of invert sugar =  $-(19.415 + 0.07065c - 0.00054c^2)$ .

Vosburgh's experimental figures agree well with this formula. The temperature-correction formula is found to be  $[\alpha]_D^t = [\alpha]_D^{20} + (0.283 + 0.0014c)(t - 20)$ . The first formula gives  $-5.554^\circ$  circular for the rotation of the inverted half-normal weight of sucrose in 100 ml. at  $20^\circ$ . By converting this into the negative constituent of the Clerget divisor for pure invert sugar by means of the general factor 0.34657, a value of 32.05 is obtained. Landolt's conversion factor for invert sugar, 0.3432, results in the extremely high value 32.37. In a redetermination of this conversion factor for invert sugar 0.34615 was found, from which 32.09 is obtained. It appears that the accepted value of 32.00 is slightly too low.

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

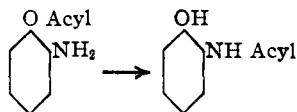
## THE EFFECT OF THE ACIDITY OF ACYL UPON THE MIGRATION FROM NITROGEN TO OXYGEN IN ORTHO-AMINOPHENOLS<sup>1</sup>

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The work of Böttcher,<sup>2</sup> Ransom,<sup>3</sup> Einhorn and Pfyl,<sup>4</sup> and Auwers<sup>5</sup> has shown that, in general, the *O*-esters of *o*-aminophenols are not capable of existence, and when formed rearrange to the corresponding *N*-acyl derivatives, in which case the acyl wanders from oxygen to nitrogen. In subse-



quent papers Auwers and collaborators<sup>6</sup> prepared mixed diacyl derivatives of 2-amino-4-methylphenol, and assumed that the radical last introduced

<sup>1</sup> Condensed from a thesis presented by H. P. Lankelma to the Graduate College of the State University of Iowa in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

<sup>2</sup> Böttcher, *Ber.*, **16**, 629 (1883).

<sup>3</sup> Ransom [*Ber.*, **31**, 1055 (1898); **33**, 199 (1900); *Am. Chem. J.*, **23**, 1 (1900)] found that under special conditions he could isolate the *O*-ester of carbonic acid.

<sup>4</sup> Einhorn and Pfyl, *Ann.*, **311**, 34 (1900).

<sup>5</sup> Auwers, *Ber.*, **33**, 1923 (1900).

<sup>6</sup> See Auwers and Eisenlohr, *Ann.*, **369**, 209 (1909).

went to oxygen, although the possibility of preparing the isomeric derivative by introduction of the radicals in the reverse order was not always tested. When rearrangement was observed, the effect was attributed to the alkali used in hydrolysis. Apparently they did not regard rearrangement as possible during acylation when two different acyl radicals are involved.

Work in this Laboratory<sup>7</sup> has shown (1) that when acetyl-benzoyl derivatives of *o*-aminophenols are prepared, the heaviest of these radicals is found on nitrogen, regardless of the order of introduction,<sup>8</sup> and (2) that with this particular pair of radicals rearrangement takes place during acylation. This work also showed that relative weight of acyl is an important factor in this rearrangement when other radicals are employed. In testing this question further with radicals heavier than benzoyl, it was found convenient to employ halogen- or nitro-substituted benzoyl chloride as one of the reagents. It was recognized when these experiments were planned that such substitutions would change both the weight and the acidity of the radical, and might modify the results to a considerable degree. As a matter of fact, derivatives obtained by the use of nine pairs of acyl radicals on three different *o*-aminophenols showed clearly that difference in weight of radical is not the only factor involved in the migration, and indicated that acidity should be considered. If the last-named were the chief factor, the more acidic of a given pair should always be found on nitrogen. The study here reported was undertaken to test that point.

The general methods of preparation and hydrolysis of these derivatives have been specified in previous papers, and will not be repeated here. In the present case, radicals from acids with known ionization constants were used when possible, and comparisons were based on the published values. Since the determination of these values involves the purity of the compound, the experimental method employed, etc., the values selected in any given comparison were those reported by the same author, and determined under the same conditions, when these could be found. When, as in the case of the naphthoyl radicals (see Table I), the results were not decisive, one member of the pair was modified by the introduction of a negative substituent which doubtless caused considerable difference in the acidity of the two. The base employed throughout was 2-amino-4-methyl-6-chlorophenol<sup>9</sup> and the derivatives studied were obtained by introduction of the radicals in both possible orders.

The study was begun with the acetyl and benzoyl radicals for several reasons. They were easily obtainable, they differ markedly in weight, structure and acidity and, in view of work already reported, it seemed desirable to test them on a base not previously studied. Benzoylation of

<sup>7</sup> For a bibliography see the previous papers.

<sup>8</sup> For an exception, see Raiford and Couture, (*a*) *THIS JOURNAL*, **46**, 2307 (1924).

<sup>9</sup> Zincke, *Ann.*, **328**, 313 (1903).

the *N*-acetylamino derivative of the above-mentioned phenol, and acetylation of the corresponding *N*-benzoylamino compound gave the same product, which indicated a rearrangement in one case and was, thus far, in agreement with previous experience. Hydrolysis of this product gave about 15% of the *N*-acetyl derivative, while the greater part was converted into the *N*-benzoyl compound. Evidently a complete rearrangement occurred during benzoylation, in which the more acidic radical went to nitrogen, while the migration during hydrolysis was only partial.

In previous work in several attempts to determine the influence of weight of acyl in this migration, and especially in the experiments with the  $\alpha$ -naphthoyl radical<sup>10</sup> it was shown with three different *o*-aminophenols that when acetyl and  $\alpha$ -naphthoyl were the radicals employed; the heaviest one was always found on nitrogen. In view, however, of the differences in acidity between these radicals and the influence of this factor suggested by work referred to above, it might be argued that the rearrangement which occurs when this pair is employed is due quite as largely to differences in acidity as to differences in weight. When the  $\beta$ -naphthoyl radical (which is less acidic than the  $\alpha$ -isomer) was used, complete rearrangement appeared to take place when the more acidic radical was the last to be introduced. Hydrolysis of the product gave nearly equimolecular proportions of the two possible *N*-acylamino phenols, which indicated partial rearrangement in the opposite direction.

The results obtained in previous work through the use of the acetyl and benzoyl radicals, particularly, were thought to depend mainly on the difference in weight of these groups. But they differ, also, in structure as well as in acidity. If structure were the determining factor, the fact that benzoyl was almost invariably found on nitrogen would lead one to expect that with a given pair of radicals, only one of which was aromatic, the latter would always go to nitrogen, regardless of the order of introduction or the method of acylation. Work previously reported shows conclusively that such a view is not in accord with the facts. But the use of isomeric radicals of different structures would eliminate the factor of weight, and leave the question between structure and acidity. The behavior of radicals exhibiting only the last-named differences was studied through the preparation and examination of diacyl derivatives obtained from several pairs of isomeric acid chlorides.

It seemed desirable here to start with acid radicals which showed but slight structural differences. The  $\alpha$ - and  $\beta$ -naphthoyl radicals represent such a pair. Treatment of a solution of the *N*- $\alpha$ -naphthoyl derivative of the phenol with  $\beta$ -naphthoyl chloride at room temperature gave a diacyl derivative that melted at 168–169°, while introduction of these radicals in the reverse order gave an isomeric product melting at 208°. Fur-

<sup>10</sup> Raiford and Greider, *THIS JOURNAL*, **46**, 430 (1924).

ther study showed that when in the first reaction the mixture was refluxed on the water-bath for a few minutes after addition of  $\beta$ -naphthoyl chloride, a mixture of the two diacyl derivatives resulted, in which the ratio of the lower- and the higher-melting products was about 3 to 1. A second repetition of the experiment at an elevated temperature showed that when chloroform<sup>11</sup> was omitted from the mixture, only the lower-melting isomer was obtained, which suggests that the solvent may exercise an influence on the course of the reaction.<sup>12</sup> Hydrolysis of these products gave only the N- $\alpha$ -naphthoylaminophenol and  $\beta$ -naphthoic acid. Evidently, 2- $\beta$ -naphthoylamino-4-methyl-6-chlorophenyl  $\alpha$ -naphthoate underwent complete rearrangement during hydrolysis, leaving the more acidic radical on nitrogen.

A second attempt to bring about rearrangement during acylation with these radicals was made by further increase of the difference in acidity between them by using a bromine derivative of  $\alpha$ -naphthoyl chloride.<sup>13</sup> As in the previous case, introduction of these radicals into the aminophenol in different orders gave different diacyl derivatives. Hydrolysis of these products gave the same substances, namely, 2-(5-bromo- $\alpha$ -naphthoylamino)-4-methyl-6-chlorophenol and  $\beta$ -naphthoic acid. Here, also, the more acidic of the pair was ultimately found on nitrogen, indicating rearrangement during hydrolysis.<sup>14</sup>

When the naphthoyl radicals did not give decisive results, it was proposed to use a pair in which the difference in structure was more pronounced and the difference in acidity less so. For this purpose the radicals of phenylacetic and *p*-toluic acids, respectively, were selected. When these were introduced, in different orders, into the base under consideration, they gave the same product. This was shown by hydrolysis to be 2-phenylacetyl-amino-4-methyl-6-chlorophenyl *p*-toluate, from which it appears that rearrangement took place during acylation, and that the most acidic radical went to nitrogen.

The behavior just noted suggested that more decisive results might be obtained through the use of benzoyl radicals into which acid-forming substituents had been introduced in different positions. To test this possibility, derivatives from the following pairs were studied: *o*-nitrobenzoyl and *p*-nitrobenzoyl; *o*-nitrobenzoyl and *m*-nitrobenzoyl; *o*-chlorobenzoyl and *p*-chlorobenzoyl; *o*-iodobenzoyl and *p*-iodobenzoyl.<sup>15</sup>

<sup>11</sup> The solvent previously employed was a mixture of pyridine and chloroform.

<sup>12</sup> Lack of time prevented further consideration of this point, which will be taken up later.

<sup>13</sup> 5-Bromo- $\alpha$ -naphthoic acid is doubtless more acidic than the unsubstituted acid.

<sup>14</sup> It may be a question in such cases as these whether the failure to rearrange during acylation might not depend on the space occupied by these radicals rather than on their acidic characters.

<sup>15</sup> Victor Meyer and Sudborough [*Ber.*, **27**, 1580 (1894)] found that *ortho*-substituted benzoic acids give low yields or no esters, when treated with alcohol and hydrogen

When diacyl derivatives were prepared in the usual way, it was found in the first three cases indicated above that from a given pair the same product was obtained, regardless of the order of introduction. Examination of the respective products showed that, in each case, the most acidic radical was on nitrogen. The substituted benzoic acid represented by the other radical was, in each instance, isolated and identified. Moreover, the amounts of these products recovered from the hydrolysis mixture (see experimental part) show that the reaction indicated is certainly the chief change that occurs. Evidently, in the first three of these cases the rearrangement took place during acylation, and the more acidic radical went to nitrogen.

With the fourth pair of these acyls different products were obtained when the radicals were introduced in the two orders, although the most acidic<sup>16</sup> one was found on nitrogen in the end. This behavior was interpreted to mean that the acylation went normally, without rearrangement, to give the two possible derivatives, 2-(*o*-iodobenzoylamino)-4-methyl-6-chlorophenyl *p*-iodobenzoate and 2-(*p*-iodobenzoylamino)-4-methyl-6-chlorophenyl *o*-iodobenzoate, and that during hydrolysis the second-named derivative rearranged. *p*-Iodobenzoic acid was recovered from each hydrolysis mixture.

In previous work,<sup>17</sup> carried out to test the effect of weight of acyl in this migration, it was a surprise to find that benzoyl displaced the heavier (and more acidic) *p*-nitrobenzoyl radical when the base 2-amino-4,6-dibromophenol was used. It was proposed to test the question further with the present base by using a still more acidic radical against benzoyl. 3,5-Dinitrobenzoyl was employed. The same diacyl derivative was obtained by introduction of the radicals in different orders, but hydrolysis of the product gave only 2-benzoylamino-4-methyl-6-chlorophenol and 3,5-dinitrobenzoic acid. This indicated rearrangement during acylation in one case, whereby the more acidic radical had migrated to oxygen.

The results thus far obtained with radicals containing the carbonyl

group,  $\begin{array}{c} \text{O} \\ || \\ -\text{C}-\text{R}(\text{Ph}) \end{array}$ , made it a matter of much interest to examine the

behavior of derivatives containing the sulfonyl group,  $\begin{array}{c} | \\ \text{O}=\text{S}=\text{O} \\ | \\ \text{Ph} \end{array}$ . Though

chloride gas, due, apparently to steric hindrance. Raiford and Woolfolk [THIS JOURNAL, 46, 2246 (1924)] showed that the rearrangement here in question is not prevented by the presence of heavy radicals adjacent to the reacting groups.

<sup>16</sup> While comparable data were not available for the *para* isomer, it is doubtless less acidic than the *ortho* compound.

<sup>17</sup> Ref. 8 a, p. 2305.

no satisfactory data concerning the ionization constant of benzene sulfonic acid are available, it is doubtless much more acidic than either acetic or benzoic acid, and therefore might be expected to displace either of them from nitrogen during acylation. Mixed diacyl derivatives containing the acetyl and benzenesulfonyl, and the benzoyl and benzenesulfonyl radicals, respectively, were prepared and hydrolyzed in the usual way; nevertheless, no rearrangement was observed. These facts seem to indicate a striking difference in the behavior of the two classes of radicals.

TABLE I  
COMPOSITIONS AND BEHAVIORS OF DIACYL DERIVATIVES OBTAINED FROM 2-AMINO-4-METHYL-6-CHLOROPHENOL

Pairs of acyl radicals used	Ionization constants	Character of derivatives	Hydrolysis products
Acetyl <sup>18</sup>	$1.85 \times 10^{-5}$ at 18°		
Benzoyl <sup>18</sup>	$7.2 \times 10^{-4}$ at 18°	Identical	Mixture
Acetyl <sup>19</sup>	$1.8 \times 10^{-5}$ at 25°		
$\alpha$ -Naphthoyl <sup>20</sup>	$2.0 \times 10^{-4}$ at 25°	Identical	$\alpha$ -Naphthoyl on nitrogen
Acetyl			
$\beta$ -Naphthoyl <sup>20</sup>	$6.8 \times 10^{-5}$ at 25°	Identical	Mixture
$\alpha$ -Naphthoyl			
$\beta$ -Naphthoyl		Different	$\alpha$ -Naphthoyl on nitrogen
$\beta$ -Naphthoyl			5-Bromo- $\alpha$ -naphthoyl on N
5-Bromo- $\alpha$ -naphthoyl	No data	Different	
<i>p</i> -Toluy <sup>21</sup>	$4.4 \times 10^{-5}$ at 25°		
Phenylacetyl <sup>22</sup>	$5.2 \times 10^{-5}$ at 25°	Identical	Phenylacetyl on nitrogen
<i>p</i> -Nitrobenzoyl <sup>23</sup>	$4.0 \times 10^{-4}$ at 18°		
<i>o</i> -Nitrobenzoyl <sup>23</sup>	$7.0 \times 10^{-3}$ at 18°	Identical	<i>o</i> -Nitrobenzoyl on nitrogen
<i>m</i> -Nitrobenzoyl <sup>23</sup>	$3.5 \times 10^{-4}$ at 18°		
<i>o</i> -Nitrobenzoyl		Identical	<i>o</i> -Nitrobenzoyl on nitrogen
<i>p</i> -Chlorobenzoyl <sup>23</sup>	$9.9 \times 10^{-5}$ at 18°		
<i>o</i> -Chlorobenzoyl <sup>23</sup>	$1.35 \times 10^{-3}$ at 18°	Identical	<i>o</i> -Chlorobenzoyl on nitrogen
<i>p</i> -Iodobenzoyl	Data not comparable		
<i>o</i> -Iodobenzoyl <sup>24</sup>	$1.37 \times 10^{-3}$ at 25°	Different	<i>o</i> -Iodobenzoyl on nitrogen
Benzoyl			
3,5-Dinitrobenzoyl	$1.6 \times 10^{-3}$ at 18°	Identical	Benzoyl on nitrogen
Acetyl			
Benzenesulfonyl	No data	Different	Normal
Benzoyl			
Benzenesulfonyl		Different	Normal

<sup>18</sup> Salm, *Z. physik. Chem.*, **63**, 94 (1908).

<sup>19</sup> Ostwald, *ibid.*, **3**, 174 (1889).

<sup>20</sup> Bethmann, *ibid.*, **5**, 399 (1890).

<sup>21</sup> White and Jones, *Am. Chem. J.*, **44**, 186 (1910).

<sup>22</sup> White and Jones, *ibid.*, **42**, 536 (1909).

<sup>23</sup> Ref. 18, p. 102.

<sup>24</sup> Schaller, *Z. physik. Chem.*, **25**, 522 (1898).

The results described above are summarized in Table I, in which the radicals used, the ionization constants of the corresponding acids, the character of diacyl derivatives, and the hydrolysis products are indicated.

### Experimental Part

**Methods of Work.**—The methods of acylation and hydrolysis used in this work have been described by Raiford and Couture.<sup>8a</sup> When any variation is employed it will be noted below.

#### Acetyl and Benzoyl

**2-Amino-4-methyl-6-chlorophenol.**—The purest commercial *p*-cresol obtainable was distilled, and the fraction boiling at 200–202° was chlorinated as directed by Zincke.<sup>25</sup> The product was nitrated by Zincke's method and the nitro compound purified by steam distillation; yield, 65–75%. The product was reduced by stannous chloride and hydrochloric acid, and the amino-hydrochloride recrystallized in the usual way; yield, 87–95%. Treatment of this salt with ammonium carbonate solution gave the free base; m. p., 88–90°. Zincke found 89–90° for the melting point.

**2-Acetylamino-4-methyl-6-chlorophenol.**—The corresponding diacetyl derivative, repeatedly crystallized until it melted sharply at 162° as recorded,<sup>25</sup> was hydrolyzed. Crystallization from water gave silky needles; m. p., 125–126°. The substance is phenolic.

*Anal.* Calcd. for C<sub>9</sub>H<sub>10</sub>O<sub>2</sub>NCl: Cl, 17.79. Found: 17.79.<sup>26</sup>

**2-Benzoylamino-4-methyl-6-chlorophenol.**—This product was obtained by hydrolysis of the *O*-benzoyl-*N*-benzoyl compound. Crystallization from alcohol gave colorless needles; m. p., 201–202°. Analysis indicated the presence of but one benzoyl radical.

*Anal.* Calcd. for C<sub>14</sub>H<sub>12</sub>O<sub>2</sub>NCl: Cl, 13.57. Found: 13.66.

**Benzoylation of 2-Acetylamino-4-methyl-6-chlorophenol.**—A yield of 67% of diacyl derivative was obtained by the Schotten-Baumann method. Crystallization from alcohol gave colorless needles that had the general appearance of cotton; m. p., 159–160°. The substance was not immediately soluble in alkali solution. The same compound was obtained by acetylation of the corresponding *N*-benzoylaminophenol.

*Anal.* Calcd. for C<sub>16</sub>H<sub>14</sub>O<sub>3</sub>NCl: Cl, 11.69. Found: 12.05.

#### Acetyl and $\alpha$ -Naphthoyl

**2-( $\alpha$ -Naphthoylamino)-4-methyl-6-chlorophenol.**—The aminophenol hydrochloride was converted into the di- $\alpha$ -naphthoyl derivative by treatment with 2.5 molecular proportions of  $\alpha$ -naphthoyl chloride.<sup>27</sup> This crude material was suspended in twice its weight of alcohol and hydrolyzed by potassium hydroxide; yield, 80%. When crystallized from alcohol the product formed colorless needles; m. p., 146°. It is soluble in aqueous alkali.

*Anal.* Calcd. for C<sub>18</sub>H<sub>14</sub>O<sub>2</sub>NCl: Cl, 11.39. Found: 11.61.

**Acetylation of 2-( $\alpha$ -Naphthoylamino)-4-methyl-6-chlorophenol.**—The *N*- $\alpha$ -naph-

<sup>25</sup> Zincke, *Ann.*, **328**, 277 (1903).

<sup>26</sup> The compounds that contained halogen but no sulfur were usually analyzed for the former by the Carius method. Sulfur determinations were made in accordance with Parr's instructions [THIS JOURNAL, **30**, 768 (1908)].

<sup>27</sup> Prepared by Hofmann's method [*Ber.*, **1**, 41 (1868)] from acid that was obtained from  $\alpha$ -bromonaphthalene by the Grignard synthesis [*Acree, Ber.*, **37**, 626 (1904)].

thoyl derivative was acetylated with acetyl chloride; yield, 74% of a product which from alcohol gave colorless crystals that melted at 188°.

*Anal.* Calcd. for  $C_{20}H_{16}O_3NCl$ : Cl, 10.04. Found: 10.32.

**Action of  $\alpha$ -Naphthoyl Chloride on 2-Acetylamino-4-methyl-6-chlorophenol.**—Conversion of the N-acetyl derivative into the diacylated compound by the usual method gave a yield of 90%. The product gave colorless needles from alcohol, m. p. 188°, and is identical with the acetyl- $\alpha$ -naphthoyl derivative previously described.

Treatment of this substance with cold aqueous alkali for 48 hours left some unchanged material. From the portion hydrolyzed the N- $\alpha$ -naphthoyl derivative, m. p. 145–146°, was recovered. The mother liquors contained neither  $\alpha$ -naphthoic acid nor the N-acetyl compound.

### Acetyl and $\beta$ -Naphthoyl

**2-( $\beta$ -Naphthoylamino)-4-methyl-6-chlorophenol.**—This product was obtained by hydrolysis of the corresponding di- $\beta$ -naphthoyl derivative, which latter was secured by treatment of the hydrochloride of the aminophenol with  $\beta$ -naphthoyl chloride;<sup>28</sup> yield, 90%, of colorless needles from alcohol; m. p., 169–170°.

*Anal.* Calcd. for  $C_{18}H_{14}O_2NCl$ : Cl, 11.39. Found: 11.47.

**Action of Acetyl Chloride on the 2- $\beta$ -Naphthoylamino-phenol.**—Acylation of this phenol gave a product that did not dissolve in aqueous alkali; yield, 80%. From alcohol it gave fine needles; m. p., 176–177°.

*Anal.* Calcd. for  $C_{20}H_{16}O_3NCl$ : Cl, 10.04. Found: 9.73.

The same substance was obtained by treatment of 2-acetylamino-4-methyl-6-chlorophenol with  $\beta$ -naphthoyl chloride.

Hydrolysis of the diacyl derivative gave three products. Approximately 53% of the material gave the N- $\beta$ -naphthoylamino-phenol and acetic acid, while the remainder gave  $\beta$ -naphthoic acid and 2-acetylamino-4-methyl-6-chlorophenol.

### $\alpha$ -Naphthoyl and $\beta$ -Naphthoyl

**2-( $\beta$ -Naphthoylamino)-4-methyl-6-chlorophenyl  $\alpha$ -Naphthoate.**—The action of the  $\alpha$ -naphthoyl chloride on the  $\beta$ -naphthoylamino-phenol gave a 90% yield of diacyl derivative. Treatment of a boiling chloroform solution of this compound with ligroin to the point of precipitation, and cooling, gave colorless, feathery crystals that were insoluble in aqueous alkali; m. p., 208°.

*Anal.* Calcd. for  $C_{28}H_{20}O_5NCl$ : Cl, 7.62. Found: 7.98.

**2-( $\alpha$ -Naphthoylamino)-4-methyl-6-chlorophenyl  $\beta$ -Naphthoate.**—The above-described  $\alpha$ -naphthoylamino-phenol was treated with  $\beta$ -naphthoyl chloride. A yield of 89% of diacyl derivative was obtained. Colorless needles separated from a mixture of chloroform and ligroin; m. p., 168–169°. A mixture of this substance and the di-

<sup>28</sup> This was obtained by the action of phosphorus pentachloride on  $\beta$ -naphthoic acid. The first attempt to prepare the acid was made by the Grignard synthesis, using  $\beta$ -naphthyl iodide, which was obtained by a modification of the directions of Schmidlin and Huber [*Ber.*, 43, 2829 (1910)]. It was found better to replace sulfuric by hydrochloric acid and to reduce the amount of water employed in diazotization. Attention should also be called to the necessity for precaution against frothing at the beginning of the vacuum distillation. A Grignard reagent was readily obtained from the iodide, but conversion into the acid, which was so satisfactory with the alpha compound, was not successful here. The acid was finally obtained by hydrolysis of  $\beta$ -naphthonitrile [Welkov, *Ber.*, 2, 407 (1869)] as described by Colver with Noyes [*THIS JOURNAL*, 43, 902 (1921)]; yield, 80%.



naphthoyl derivative specified above melted at 160–165°. <sup>29</sup> Analysis of this product showed that it is isomeric with the one described above.

*Anal.* Calcd. for  $C_{23}H_{20}O_3NCl$ : Cl, 7.62. Found: 8.12.

Hydrolysis of the product obtained by the action of  $\beta$ -naphthoyl chloride on  $\alpha$ -naphthoylamino-4-methyl-6-chlorophenol gave only the last-named substance and  $\beta$ -naphthoic acid in 84% yield. When the substance melting at 208° was hydrolyzed, the same products were recovered to the extent of 86%.

### $\beta$ -Naphthoyl and 5-Bromo- $\alpha$ -naphthoyl

**5-Bromo- $\alpha$ -naphthoyl Chloride.**—Twenty g. of the corresponding acid, <sup>80</sup> m. p., 242–244°, mixed with 5 molecular proportions of thionyl chloride, was refluxed on a water-bath until solution took place; the liquid was then cooled and filtered, and unchanged thionyl chloride distilled under reduced pressure. The residue, which solidified on cooling, gave an 80% yield of colorless plates when crystallized from ligroin; m. p., 84°.

*Anal.* Calcd. for  $C_{11}H_6OCIBr$ : Hal., 42.87. Found: 42.40.

**2-(5-Bromo- $\alpha$ -naphthoylamino)-4-methyl-6-chlorophenol.**—This compound was obtained by hydrolysis of the corresponding diacyl derivative which, in turn, was prepared by treatment of the aminohydrochloride with 2.5 molecular proportions of the required acid chloride; yield, 92%. Crystallization from acetic acid gave colorless needles; m. p., 206°. It showed phenolic properties.

*Anal.* Calcd. for  $C_{18}H_{13}O_2NClBr$ : Hal., 29.61. Found: 29.87.

**2-(5-Bromo- $\alpha$ -naphthoylamino)-4-methyl-6-chlorophenyl  $\beta$ -naphthoate.**—The  $\alpha$ -naphthoylamino-phenol upon treatment with  $\beta$ -naphthoyl chloride gave the diacyl derivative in yields of 90%. Purification from a mixture of chloroform and ligroin gave clusters of nearly colorless needles; m. p., 198–199°.

*Anal.* Calcd. for  $C_{29}H_{19}O_3NClBr$ : Hal., 21.20. Found: 21.46.

**2-( $\beta$ -Naphthoylamino)-4-methyl-6-chlorophenyl 5-bromo- $\alpha$ -naphthoate.**—This product was obtained in 93% yield by acylation of the  $\beta$ -naphthoylamino-phenol. Crystallization from a mixture of chloroform and ligroin gave nearly colorless prisms; m. p., 206°. A mixture of this substance and the diacyl derivative just described softened at 178° and melted at 192–196°.

*Anal.* Calcd. for  $C_{29}H_{19}O_3NClBr$ : Hal., 21.20. Found: 20.85.

Hydrolysis of the dinaphthoyl derivatives described above gave the same products, namely, 2-(5-bromo- $\alpha$ -naphthoylamino)-4-methyl-6-chlorophenol and  $\beta$ -naphthoic acid.

### *p*-Toluyyl and Phenylacetyl

**2-Phenylacetylamino-4-methyl-6-chlorophenol.**—This product was obtained in 70% yields by hydrolysis of the corresponding diacyl derivative which, in turn, was prepared by the action of phenylacetyl chloride <sup>31</sup> on the hydrochloride of the required aminophenol. It formed colorless needles from dil. alcohol; m. p., 119°.

<sup>29</sup> When the acylation solution (which contained a mixture of chloroform and pyridine) was refluxed for five minutes on the water-bath, a mixture of the two diacyl derivatives was produced. When pyridine only was used as solvent, heating gave the normal product alone.

<sup>30</sup> Prepared according to the directions of Eckstrand [*J. prakt. Chem.*, [2] 38, 739 (1888)], who recorded 246° as the melting point.

<sup>31</sup> This was prepared by the action of thionyl chloride on phenylacetic acid as described for other acid chlorides used in this work. It was purified by distillation under reduced pressure, and boiled at 110–111° (23 mm.). Anschütz and Berns [*Ber.*, 20, 1389 (1887)] recorded 102° at 17 mm. for a product made from phosphorus pentachloride.

*Anal.* Calcd. for  $C_{15}H_{14}O_2NCl$ : Cl, 12.88. Found: 13.03.

**2-(*p*-Toluylamino)-4-methyl-6-chlorophenol.**—Hydrolysis of the diacyl derivative obtained by the action of *p*-toluy chloride<sup>32</sup> on the aminohydrochloride mentioned above gave a 63% yield of product. Crystallization from alcohol gave colorless needles; m. p., 169°.

*Anal.* Calcd. for  $C_{15}H_{14}O_2NCl$ : Cl, 12.88. Found: 13.01.

**2-Phenylacetyl-amino-4-methyl-6-chlorophenyl *p*-Toluate.**—Acylation of the *p*-toluyaminophenol described above with phenylacetyl chloride gave a yield of 61% of diacyl derivative. Crystallization from alcohol formed fine needles melting at 170° and insoluble in aqueous alkali.

*Anal.* Calcd. for  $C_{23}H_{20}O_3NCl$ : Cl, 9.02. Found: 9.33.

**Action of *p*-Toluy Chloride on 2-Phenylacetyl-amino-4-methyl-6-chlorophenol.**—This reaction gave a 75% yield of a diacyl derivative which crystallized from alcohol in colorless needles, m. p., 170°, and identical with the product obtained by introduction of the radicals in the reverse order. Hydrolysis of this material gave only the *N*-phenylacetyl derivative and *p*-toluic acid.

### *o*-Nitrobenzoyl and *p*-Nitrobenzoyl

**2-(*o*-Nitrobenzoylamino)-4-methyl-6-chlorophenol.**—To obtain this compound the aminohydrochloride of the base was converted into the *O*-acyl-*N*-acyl derivative, and the latter hydrolyzed. Crystallization of this material from alcohol gave straw-colored needles; m. p., 167°; yield, 75%.

*Anal.* Calcd. for  $C_{14}H_{11}O_4N_2Cl$ : Cl, 11.58. Found: 11.73.

**2-(*p*-Nitrobenzoylamino)-4-methyl-6-chlorophenol.**—This was prepared in 81% yield by hydrolysis of the corresponding diacylated compound. Crystallization from alcohol gave lemon-colored needles, m. p. 206°.

*Anal.* Calcd. for  $C_{14}H_{11}O_4N_2Cl$ : Cl, 11.58. Found: 11.56.

**2-(*o*-Nitrobenzoylamino)-4-methyl-6-chlorophenyl *p*-Nitrobenzoate.**—The *N*-*p*-nitrobenzoylamino-phenol described above was treated with slightly more than the calculated amount of *o*-nitrobenzoyl chloride. The diacyl derivative was obtained in 90% yield. Clusters of colorless needles radiating from common centers were obtained by crystallization from alcohol; m. p., 229–230°. Treatment of the *N*-*o*-nitrobenzoylamino-phenol with *p*-nitrobenzoyl chloride gave the same product.

*Anal.* Calcd. for  $C_{21}H_{14}O_7N_3Cl$ : Cl, 7.79. Found: 7.81.

By hydrolysis of this material 90% of it was recovered as 2-(*o*-nitrobenzoylamino)-4-methyl-6-chlorophenol and *p*-nitrobenzoic acid, respectively.

### *o*-Nitrobenzoyl and *m*-Nitrobenzoyl

**2-(*m*-Nitrobenzoylamino)-4-methyl-6-chlorophenol.**—This was secured by hydrolysis of the corresponding diacyl derivative in 82% yield. Crystallization from ethyl acetate gave nearly colorless needles, m. p. 219°.

*Anal.* Calcd. for  $C_{14}H_{11}O_4N_2Cl$ : Cl, 11.58. Found: 11.38.

**2-(*o*-Nitrobenzoylamino)-4-methyl-6-chlorophenyl *m*-Nitrobenzoate.**—The *N*-*m*-nitrobenzoylamino-phenol just described was treated with *o*-nitrobenzoyl chloride and gave a 92% yield of material which, upon crystallization from acetic acid, formed colorless masses resembling cotton; m. p., 216–217°. It was insoluble in aqueous alkali.

<sup>32</sup> The product here used was a straw-colored liquid that boiled between 214° and 218°. Cahours [*Ann.*, **108**, 317 (1858)] recorded 214–216°, while Ador and Rilliet [*Ber.*, **12**, 2299 (1879)] found 224–226° at 720 mm.

*Anal.* Calcd. for  $C_{21}H_{14}O_7N_3Cl$ : Cl, 7.79. Found: 7.86.

Treatment of the 2-*o*-nitrobenzoylamino-phenol with *m*-nitrobenzoyl chloride gave the same product. Hydrolysis of this material gave only the *N*-*o*-nitrobenzoylamino-phenol and *m*-nitrobenzoic acid.

### *o*-Chlorobenzoyl and *p*-Chlorobenzoyl

**2-(*o*-Chlorobenzoylamino)-4-methyl-6-chlorophenol.**—Hydrolysis of the diacyl derivative obtained by the action of *o*-chlorobenzoyl chloride<sup>33</sup> on the required aminohydrochloride gave a phenolic compound that was purified by adding water to a boiling alcoholic solution of the material and cooling. Colorless needles separated; m. p., 138°.

*Anal.* Calcd. for  $C_{14}H_{11}O_2NCl_2$ : Cl, 23.98. Found: 23.86.

**2-(*p*-Chlorobenzoylamino)-4-methyl-6-chlorophenol.**—By repeating the above-described experiment with *p*-chlorobenzoyl chloride<sup>34</sup> a 64% yield of the required *N*-acyl derivative resulted. It formed colorless needles from alcohol; m. p., 187°.

*Anal.* Calcd. for  $C_{14}H_{11}O_2NCl_2$ : Cl, 23.98. Found: 23.94.

Treatment of this product with *o*-chlorobenzoyl chloride gave an 82% yield of diacylated compound which by crystallization from a mixture of chloroform and ligroin formed needles; m. p., 216–217°. Introduction of the chlorobenzoyl radicals in the reverse order produced the same substance.

*Anal.* Calcd. for  $C_{21}H_{14}O_3NCl_3$ : Cl, 24.51. Found: 24.50.

By hydrolysis of this material 84% of it was recovered in the form of the *N*-*o*-chlorobenzoylamino-phenol, m. p. 135–136°, and *p*-chlorobenzoic acid, respectively.

### *o*-Iodobenzoyl and *p*-Iodobenzoyl

**2-(*o*-Iodobenzoylamino)-4-methyl-6-chlorophenol.**—The required aminohydrochloride was treated with *o*-iodobenzoyl chloride,<sup>35</sup> and the resulting diacylated compound hydrolyzed. The phenolic product crystallized from alcohol in short, colorless needles; m. p., 147°.

*Anal.* Calcd. for  $C_{14}H_{11}O_2NClI$ : N, 3.61; Hal., 41.91. Found: N, 3.84; Hal., 40.70.<sup>36</sup>

**2-(*p*-Iodobenzoylamino)-4-methyl-6-chlorophenol.**—This compound was obtained by following the directions given above for its isomer.<sup>37</sup> A 74% yield of product that gave nearly colorless needles from alcohol was obtained; m. p., 202°.

*Anal.* Calcd. for  $C_{24}H_{11}O_2NClI$ : Hal., 41.91. Found: 40.58.

**Action of *o*-Iodobenzoyl Chloride on 2-(*p*-Iodobenzoylamino)-4-methyl-6-chlorophenol.**—This reaction gave a diacyl derivative in 80% yield, that crystallized from chloroform in colorless masses resembling cotton; m. p., 213°.

<sup>33</sup> This product was obtained by the method described by Raiford and Couture (Ref. 8 a, p. 2317) for the *para* isomer.

<sup>34</sup> Emmerling, *Ber.*, **8**, 880 (1875).

<sup>35</sup> *o*-Iodobenzoic acid was prepared in 92% yield by a modification of Wachter's method [*Ber.*, **26**, 1744 (1893)]. From this the acid chloride was obtained by treatment with thionyl chloride. The product crystallized in short, colorless needles that melted between 35° and 38°. Wachter reported light yellow crystals melting at 35–40°.

<sup>36</sup> It is well known that the Carius method may give low results with iodine compounds [Linnemann, *Ann.*, **160**, 206 (1871)].

<sup>37</sup> The *p*-iodobenzoyl chloride used in this work and prepared by the action of thionyl chloride on *p*-iodobenzoic acid, m. p. as found by Beran [*Ber.*, **18**, 137 (1885)], 65–66°. Hoffmann [*Ann.*, **264**, 167 (1891)] found 77–78°.

*Anal.* Calcd. for  $C_{21}H_{14}O_3NCl_2$ : Hal., 46.86. Found: 46.96.

The action of *p*-iodobenzoyl chloride on the *N*-*o*-iodobenzoyl-aminophenol gave a product that formed colorless needles from chloroform; m. p., 153–155°. Repeated crystallization did not alter this.

*Anal.* Calcd. for  $C_{21}H_{14}O_3NCl_2$ : Hal., 46.86. Found: 47.11.

Hydrolysis of these derivatives gave two products which were identified as the *N*-*o*-iodobenzoylaminophenol, melting at 147°, and *p*-iodobenzoic acid.

### Benzoyl and 3,5-Dinitrobenzoyl

**2-(3,5-Dinitrobenzoylamino)-4-methyl-6-chlorophenol.**—This compound was obtained by hydrolysis of the corresponding diacyl derivative, which was prepared by the action of 3,5-dinitrobenzoyl chloride<sup>38</sup> on the required aminohydrochloride; yield, 68%. Crystallization from acetic acid gave lemon-colored needles; m. p., 243–244°. This compound is much less readily soluble in aqueous alkali than is usual for similar substances, but analysis indicated a phenolic substance.

*Anal.* Calcd. for  $C_{14}H_{10}O_6N_3Cl$ : Cl, 10.08. Found: 10.03.

**Action of Benzoyl Chloride on 2-(3,5-Dinitrobenzoylamino)-4-methyl-6-chlorophenol.**—The diacyl derivative was obtained in 81% yield. Crystallization from acetic acid gave colorless needles; m. p., 241–242°.

*Anal.* Calcd. for  $C_{21}H_{14}O_7N_3Cl$ : Cl, 7.78. Found: 7.81.

The same product was obtained in 74% yield by the action of 3,5-dinitrobenzoyl chloride on 2-benzoylamino-4-methyl-6-chlorophenol. By hydrolysis, 89% of this material was recovered in the form of 2-benzoylamino-4-methyl-6-chlorophenol and 3,5-dinitrobenzoic acid. Nothing else could be isolated.

### Acetyl and Benzenesulfonyl

**2-Benzenesulfonylamino-4-methyl-6-chlorophenol.**—This substance was obtained by hydrolysis of the corresponding diacyl derivative; m. p., 124–125°. Contrary to previous experience, this was best carried out by boiling the material with a 10% aqueous solution of sodium hydroxide under a reflux condenser for six to eight hours. The solid precipitated by acid was crystallized from alcohol in colorless needles; m. p., 185–186°.

*Anal.* Calcd. for  $C_{13}H_{12}O_3NClS$ : S, 10.75. Found: 10.63.

**Action of Acetic Anhydride on 2-Benzenesulfonylamino-4-methyl-6-chlorophenol.**—This diacyl derivative was obtained in 96% yield, as colorless needles from alcohol; m. p., 142–143°. It is insoluble in aqueous alkali.

*Anal.* Calcd. for  $C_{15}H_{14}O_4NClS$ : S, 9.42. Found: 9.20.

Treatment of the 2-acetylamino-phenol with benzenesulfonyl chloride gave an oil that solidified on standing; yield, 86%. Purification from ligroin (b. p., 60–80°) gave colorless crystals; m. p., 95–96°. Analysis shows that this compound has the composition indicated above.

*Anal.* Calcd. for  $C_{15}H_{14}O_4NClS$ : S, 9.42. Found: 9.15.

Hydrolysis of the product melting at 95–96° gave an 85% yield of 2-acetylamino-4-methyl-6-chlorophenol, while similar treatment of that melting at 142–143° gave 2-benzenesulfonyl-amino-4-methyl-6-chlorophenol.

<sup>38</sup> Prepared by the action of three molecular proportions of thionyl chloride on 3,5-dinitrobenzoic acid, and obtained as long colorless crystals, from ligroin, that melted at 66–68°. Cohen and Armes, *J. Chem. Soc.*, 89, 1479; (1906).

### Benzoyl and Benzenesulfonyl

**Action of Benzoyl Chloride on 2-Benzenesulfonylamino-4-methyl-6-chlorophenol.**—The product was obtained in 92% yield, and crystallization from alcohol gave colorless prisms; m. p., 169–170°.

*Anal.* Calcd. for  $C_{20}H_{16}O_4NCIS$ : S, 7.97. Found: 8.00.

Treatment of 2-benzoylamino-4-methyl-6-chlorophenol with slightly more than the calculated amount of benzenesulfonyl chloride by the method described gave an oil that solidified on standing. Repeated crystallization from alcohol gave a nearly colorless product; m. p., 116–117°. The Schotten-Baumann method produced the same substance.

*Anal.* Calcd. for  $C_{20}H_{16}O_4NCIS$ : S, 7.97. Found: 8.15.

When hydrolyzed, the compound described above gave 2-benzoylamino-4-methyl-6-chlorophenol in 98% yield. The isomeric product gave 81% of 2-benzenesulfonylamino-4-methyl-6-chlorophenol.

### Summary and Conclusions

1. In each of the eleven series in which both of the acyl radicals were of the structure  $O = \overset{|}{C} - R$ , rearrangement occurred at some point in the cycle. This type of change may take place during acylation or hydrolysis, depending on the particular radicals present.

2. In eight of these series the pair of radicals in question gave identical mixed diacyl derivatives regardless of the order in which the radicals were introduced. Hydrolysis of these products showed that the most acidic radical was on nitrogen.

3. In three cases where either a mixture of derivatives was obtained upon acylation or a mixture of *N*-acylamino-phenols was obtained on hydrolysis, the results were not decisive.

4. In one case the less acidic radical was found on nitrogen after hydrolysis.

5. When one acyl radical was of the structure  $O = \overset{|}{C} - R$  and the other  $O = \overset{|}{S} = O$ , no rearrangement was observed at any point in the cycle. This will be studied further.

6. The relative acidity of the acyl radical is apparently an important, though not always decisive, factor in this rearrangement.

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