

5. In the case of carbonyl compounds a carbon with an open sextet may be formed by the addition of a positive ion to the oxygen. In this case also the presence of the open sextet induces rearrangement.

6. The application of these simple principles is already proving helpful in experimental studies of "abnormal" reactions of simple aliphatic compounds.

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ACYL DERIVATIVES OF ORTHO-AMINOPHENOL. I

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When diacyl derivatives of *o*-aminophenol were prepared by the usual methods, it was found in many cases that the order of introduction of the two different acyl groups has no influence upon the formation of the diacyl, identical products being isolated from the two acylations. The position of the acyl groups can be determined by removing the groups attached to the oxygen by saponification with dilute alkali, and determining from the physical constants of the remaining monoacylated product the group attached to the nitrogen. The identical diacyls mentioned above were found to saponify to yield identical products, as would be expected.

The formation of identical rather than isomeric products on reversing the order of acylation indicated that during acylation a rearrangement must have occurred in one of the two cases. The formation of isomeric diacyls and the production of the same saponification product indicate that a rearrangement must have occurred during saponification. Some evidence has indicated that certain acyl groups have more power than others to bring about this migration, weight and acidity of the groups being considered to have the predominating influence in their obtaining a position in the more basic amino group.

Previous work on this subject by Ransom,¹ Ransom and Nelson,² Nelson and Rothrock,³ and Raiford and Clark⁴ is discussed in the literature.

The work of Pollard and Nelson,⁵ using phenylacetyl chloride as one of the acylating agents in each diacyl throughout a series of experiments, indicated that relative acidity and weight are not the controlling factors in this type of rearrangement.

¹ Ransom, *Am. Chem. J.*, **23**, 1 (1900).

² Ransom and Nelson, *THIS JOURNAL*, **36**, 390 (1914).

³ Nelson and Rothrock, *ibid.*, **51**, 2761 (1929).

⁴ Raiford and Clark, *ibid.*, **48**, 483 (1926).

⁵ Pollard and Nelson, *ibid.*, **53**, 996 (1931). A more extensive bibliography is given in this article.

To determine whether similar results would be obtained by using the hydrocinnamyl group as a constant was the purpose of this investigation. Hydrocinnamyl chloride was used as one of the acylating agents in the preparation of all diacyl derivatives of *o*-aminophenol in these experiments. This selection afforded a rather heavy group and one which is appreciably acidic in nature to check against the acetyl, propionyl, valeryl, isovaleryl, phenylacetyl and benzoyl groups.

When *o*-hydrocinnamylaminophenol was acylated with acetyl chloride, a diacyl melting at 79.5–81° was produced, while the acylation of *o*-acetylaminophenol with hydrocinnamyl chloride gave a diacyl melting at 124.5–126°. Saponification of each of these diacyls produced only *o*-hydrocinnamylaminophenol, indicating that in the latter case migration of the hydrocinnamyl group from the oxygen to the nitrogen must have occurred. Similar results were obtained with diacyls containing, respectively, the valeryl, isovaleryl and benzoyl groups. The saponification of these isomers involved rearrangements in which the hydrocinnamyl group replaced the lighter and less acidic valeryl and isovaleryl and the lighter and more acidic benzoyl group.

o-Hydrocinnamylaminophenol acylated with propionyl chloride gave a diacyl melting at 113.5–115.5°, while the acylation of *o*-propionylaminophenol with hydrocinnamyl chloride gave a diacyl melting at 102.5–104.5°. A mixture of these two products melted at 110–115°, indicating that each might be an equilibrium mixture of the two possible diacyls. However, each product gave only *o*-hydrocinnamylaminophenol on saponification.

Acylation of *o*-hydrocinnamylaminophenol with phenylacetyl chloride gave a diacyl melting at 90–92°, while acylation of *o*-phenylacetylaminophenol with hydrocinnamyl chloride gave a diacyl melting at 81–83°. A mixture of these two products melted at 67–70°, showing the two to be different. Saponification of each of these diacyls gave approximately 60% *o*-hydrocinnamylaminophenol and 40% *o*-phenylacetylaminophenol, showing that a partial rearrangement occurred.

Experimental

o-Hydrocinnamylaminophenol was prepared by the method of Groenvik⁶ using *o*-aminophenol and the acid chloride. Its properties are summarized below.

Formula	M. p., °C.	Yield, %	Analysis, N, % Calcd.	Found
$\text{HOC}_6\text{H}_4\text{NHCOCH}_2\text{CH}_2\text{C}_6\text{H}_5$	131.5–132	70	5.81	5.65

The other monoacyls used, which have been described previously, were made by the same method.

o-Hydrocinnamylaminophenyl Acetate ($\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{CONHC}_6\text{H}_4\text{OCOCH}_3$).—To 5 g. of *o*-hydrocinnamylaminophenol an excess of acetyl chloride was added. After the addition of a drop of sulfuric acid, the mixture was stirred and heated on the water-bath

⁶ Groenvik, *Bull. soc. chim.*, [2] 25, 173 (1876).

for three hours. A brown oil formed which was washed well with hot water and upon cooling in an ice bath solidified. This brown solid was dissolved in hot 90% alcohol and filtered. Repeated crystallizations from dilute alcohol gave light tan crystals melting at 79.5–81°.

About 1 g. of this compound was saponified in the equivalent quantity of 10% potassium hydroxide. After complete solution resulted, the solution was filtered and acidified with dilute hydrochloric acid. A flesh-colored precipitate formed which was filtered, washed and crystallized from dilute alcohol. These crystals melted at 129.5–131° and when mixed with *o*-hydrocinnamylaminophenol (m. p. 131.5–132°) melted at 130–131.5°, showing them to be the same.

o-Acetylaminophenyl Hydrocinnamate ($\text{CH}_3\text{COHNC}_6\text{H}_5\text{OCOCH}_2\text{CH}_2\text{C}_6\text{H}_5$).—A slight excess of hydrocinnamyl chloride was added to 6 g. of *o*-acetylaminophenol. A drop of sulfuric acid was added, the mixture stirred and heated on the water-bath for two hours. A light brown oil formed which was washed well with hot water and cooled in an ice-bath. On standing the oil solidified. The solid was dissolved in hot alcohol and on cooling formed light pink flakes. These were recrystallized from dilute alcohol and then from toluene. These crystals melted at 124.5–126°.

TABLE I
DIACYL DERIVATIVES OF *o*-AMINOPHENOL

Name	Formula
1 <i>o</i> -Hydrocinnamylaminophenyl acetate	$\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{CONHC}_6\text{H}_5\text{OCOCH}_3$
2 <i>o</i> -Acetylaminophenyl hydrocinnamate	$\text{CH}_3\text{CONHC}_6\text{H}_5\text{OCOCH}_2\text{CH}_2\text{C}_6\text{H}_5$
3 <i>o</i> -Hydrocinnamylaminophenyl propionate	$\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{CONHC}_6\text{H}_5\text{OCOC}_2\text{H}_5$
4 <i>o</i> -Propionylaminophenyl hydrocinnamate	$\text{C}_2\text{H}_5\text{CONHC}_6\text{H}_5\text{OCOCH}_2\text{CH}_2\text{C}_6\text{H}_5$
5 <i>o</i> -Hydrocinnamylaminophenyl valerate	$\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{CONHC}_6\text{H}_5\text{OCOC}_4\text{H}_9$
6 <i>o</i> -Valerylaminophenyl hydrocinnamate	$\text{C}_4\text{H}_9\text{CONHC}_6\text{H}_5\text{OCOCH}_2\text{CH}_2\text{C}_6\text{H}_5$
7 <i>o</i> -Hydrocinnamylaminophenyl isovalerate	$\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{CONHC}_6\text{H}_5\text{OCOC}_4\text{H}_9$
8 <i>o</i> -Isovalerylaminophenyl hydrocinnamate	$\text{C}_4\text{H}_9\text{CONHC}_6\text{H}_5\text{OCOCH}_2\text{CH}_2\text{C}_6\text{H}_5$
9 <i>o</i> -Hydrocinnamylaminophenyl phenylacetate	$\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{CONHC}_6\text{H}_5\text{OCOCH}_2\text{C}_6\text{H}_5$
10 <i>o</i> -Phenylacetylaminophenyl hydrocinnamate	$\text{C}_6\text{H}_5\text{CH}_2\text{CONHC}_6\text{H}_5\text{OCOCH}_2\text{CH}_2\text{C}_6\text{H}_5$
11 <i>o</i> -Hydrocinnamylaminophenyl benzoate	$\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{CONHC}_6\text{H}_5\text{OCOC}_6\text{H}_5$
12 <i>o</i> -Benzoylaminophenyl hydrocinnamate	$\text{C}_6\text{H}_5\text{CONHC}_6\text{H}_5\text{OCOCH}_2\text{CH}_2\text{C}_6\text{H}_5$

	M. p., °C.	Yield, %	Analyses, Calcd.	N, % Found	Saponification product
1	79.5–81	51	4.97	5.25	$\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{CONHC}_6\text{H}_5\text{OH}$
2	124.5–126	67	4.97	5.07	$\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{CONHC}_6\text{H}_5\text{OH}$
3	113.5–115.5	55	4.69	4.58	$\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{CONHC}_6\text{H}_5\text{OH}$
4	102.5–104.5	84	4.69	4.70	$\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{CONHC}_6\text{H}_5\text{OH}$
5	74–75.5	85	4.32	4.18	$\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{CONHC}_6\text{H}_5\text{OH}$
6	72.5–74	52	4.32	4.18	$\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{CONHC}_6\text{H}_5\text{OH}$
7	92–93	84	4.32	4.50	$\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{CONHC}_6\text{H}_5\text{OH}$
8	73.5–74	52	4.32	4.25	$\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{CONHC}_6\text{H}_5\text{OH}$
9	90–92	30	3.90	3.90	60% $\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{CONHC}_6\text{H}_5\text{OH}$ 40% $\text{C}_6\text{H}_5\text{CH}_2\text{CONHC}_6\text{H}_5\text{OH}$
10	81–83	45	3.90	4.05	60% $\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{CONHC}_6\text{H}_5\text{OH}$ 40% $\text{C}_6\text{H}_5\text{CH}_2\text{CONHC}_6\text{H}_5\text{OH}$
11	116.5–118.5	55	4.06	4.05	$\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{CONHC}_6\text{H}_5\text{OH}$
12	122.5–124.5	44	4.06	4.20	$\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{CONHC}_6\text{H}_5\text{OH}$

This diacyl was saponified in approximately the same manner as the preceding one and yielded *o*-hydrocinnamylaminophenol. A rearrangement must have occurred during saponification.

All diacyl derivatives of *o*-aminophenol were made by the method described above using the monoacyl, the acid chloride and a drop of sulfuric acid, which is a modification of the method of Jacobs, Heidelberger and Rolf.⁷ The properties of all of these diacyls are summarized in Table I.

The melting points in the cases of two pairs of isomers listed above as 5, 6, 11 and 12 might indicate the possibility that in each case they were identical substances in an impure state, but the facts that each substance appeared to be homogeneous and the melting points of the mixtures were decidedly lower lead to the conclusion that they were isomers.

Mixed melting point of 5 and 6	52-54°
Mixed melting point of 11 and 12	90-93°

Summary

A study of the diacyl derivatives of *o*-aminophenol, when one of the acyl groups was always the hydrocinnamyl radical, has been made. The hydrocinnamyl group was checked against the acetyl, propionyl, valeryl, isovaleryl, phenylacetyl and benzoyl groups.

In five cases out of six, isomers were obtained depending on the order of introduction of the acyl groups.

In five cases out of six, complete rearrangement occurred during saponification and one case showed partial rearrangement. When complete rearrangement did occur the nitrogen atom was shown to be attached to the heavier and more acidic group in four cases and to the heavier and less acidic in one case.

In the case where partial rearrangement occurred during saponification, the saponification products showed 60% of the nitrogen to be attached to the heavier and less acidic group and 40% to be attached to the lighter and more acidic group.

New mono and diacyl derivatives of *o*-aminophenol have been made and studied.

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⁷ Jacobs, Heidelberger and Rolf, *THIS JOURNAL*, **41**, 458 (1919).