

ACYL DERIVATIVES OF ORTHO-AMINOPHENOL

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In the preparation of diacyl derivatives of o-aminophenol 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. In order to determine the position of the acyl groups the diacyl was saponified with dilute alkali, which removes the group attached to the oxygen. The resulting monoacylated product was identified by melting point determinations, showing which of the groups was attached to the nitrogen. The above mentioned identical diacyls were found to saponify to yield identical products, as would be expected.

The formation of such identical rather than isomeric products by reversing the order of acylation indicated that during acylation a rearrangement must have occurred in one of the two cases. That a rearrangement occurs during saponification is indicated by the fact that the same saponification product is obtained from isomeric diacyls. There has been some evidence that certain acyl groups have more power than others to bring about such a 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 Ransom¹, Ransom and Nelson², Nelson and Rothrock³, and Raiford and Clark⁴ is discussed in the literature. Pollard and Nelson⁵, using phenyl acetyl chloride as one of the acylating agents in each diacyl throughout a series of experiments, showed that weight and relative acidity are not the controlling factors in this type of rearrangement. Pollard, Sparks, and Moore⁶ using hydrocinnamyl chloride as one of the acylating agents in a series of experiments found that, 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 in four cases and to the heavier and less acidic in one case. The saponification products showed 60% of the nitrogen attached to the heavier and less acidic group and 40% to be attached to the lighter and more acidic group in the case where partial rearrangement occurred during saponification.

¹ Ransom: *Am. Chem. J.* 23, 1. 1900.

² Ransom and Nelson: *J. Am. Chem. Soc.* 36, 390. 1914.

³ Nelson and Rothrock: *Ibid.* 51, 2761. 1929.

⁴ Raiford and Clark: *Ibid.* 48, 483. 1926.

⁵ Pollard and Nelson: *J. Am. Chem. Soc.* 53, 966. 1931.

⁶ Pollard, Sparks, and Moore: *Ibid.* 54, 3283. 1932.

The purpose of this investigation was to determine the results when a chlorocarbonate was used as one of the acylating agents in the preparation of each of the diacyls. Methyl chlorocarbonate was chosen as this constant acylating agent.

When *o*-hydrocinnamylaminophenol was acylated with methyl chlorocarbonate a diacyl melting at 60.8-61.5° was produced, while the acylation of *o*-hydroxymethyl carbanilate with hydrocinnamyl chloride gave a diacyl melting at 61.-61.5°. A mixture of these two products melted at 60.5-61.5° indicating the two to be identical; hence a rearrangement occurred during acylation. Saponification of this diacyl produced *o*-hydrocinnamylaminophenol.

o-Isovalerylaminophenol acylated with methyl chlorocarbonate gave a diacyl melting at 68-69°, while the acylation of *o*-hydroxymethyl carbanilate gave a diacyl melting at 67.5-69°. A mixture of these two products melted at 68-69°. The two diacyls are identical and therefore a rearrangement occurred during acylation. Saponification of this diacyl yielded *o*-isovalerylaminophenol.

Experimental

The monoacyls used were prepared by the method of Groenvik⁷ using *o*-aminophenol and the acid chloride. The diacyls were prepared by the Schotten-Baumann reaction.

Action of Methyl Chlorocarbonate on o-Hydrocinnamylaminophenol. To 5 g. of *o*-hydrocinnamylaminophenol dissolved in an equivalent amount of dilute potassium hydroxide, a slight excess of methyl chlorocarbonate was added. The reaction mixture was shaken and allowed to stand for about half an hour. A brown oil formed which was washed well with hot water. On standing at room temperature the oil solidified. This solid was dissolved in hot 90% alcohol, containing norite, filtered and the filtrate cooled in an ice bath. White oily flakes formed. Water was added and the flakes filtered off. These were purified by recrystallizations from 90% alcohol. The crystals were dried in a desiccator and melted at 60.8-61.5°.

About 1 g. of this diacyl was saponified in hot dilute potassium hydroxide. After complete solution resulted, it was filtered and acidified with concentrated hydrochloric acid. A light tan crystalline precipitate formed which on recrystallization from dilute alcohol melted at 130.5-131°. Mixed with *o*-hydrocinnamylaminophenol (m.p. 131.5-132°) they melted at 129-131°. The saponification product was therefore *o*-hydrocinnamylaminophenol.

Action of Hydrocinnamyl Chloride on o-Hydroxy Methyl Carbanilate. To a filtered solution, formed by dissolving 5 g. of *o*-hydroxy methyl carbanilate in an equivalent amount of dilute potassium hydroxide, about 6 g. of hydrocinnamyl chloride was added. A brown oil formed and the mixture was allowed to stand for about two hours with frequent shaking. The oil was washed well with hot water and solidified on standing in an ice bath. The solid was taken up in hot 90%

⁷ Groenvik: Bull. soc. chim. [2] 25, 173. 1876.

alcohol, containing norite, the solution filtered and cooled. White oily flakes were obtained which were purified by recrystallizations from 90% alcohol. The purified product melted at 61-61.5° and a mixture of it and the diacyl formed by the introduction of the groups in the reverse order melted at 60.5-61.5°. Thus the two are identical and a rearrangement occurred during acylation.

About 1g. of this diacyl was saponified in the same manner, and o-hydrocinnamylaminophenol was formed, as would be expected.

TABLE I. Diacyl Derivatives of o-Aminophenol

Name		Formula		
1.	o-Hydrocinnamylaminophenyl methyl carbonate.....	$C_6H_5CH_2CH_2CONHC_6H_4OCOOCH_3$		
2.	o-Isovalerylaminophenyl methyl carbonate.....	$C_4H_9CONHC_6H_4OCOOCH_3$		

M. P. °C	Yield %	Analyses, Calcd.	N, % Found	Saponification Product
1. 60.5-61.5	80	4.68	4.85	$C_6H_5CH_2CH_2CONHC_6H_4OH$
2. 68. -69.	75	5.55	5.80	$C_4H_9CONHC_6H_4OH$

Diacyl 2 was prepared by a method similar to that described for diacyl 1. The names and formulae assigned to the diacyls are on the assumption that no rearrangement occurred during saponification.

Summary

A study of two diacyl derivatives of o-aminophenol has been made. Methyl chlorocarbonate was used as an acylating agent against the hydrocinnamyl and isovaleryl groups.

A rearrangement occurred during acylation in both cases, identical products being isolated when the order of the introduction of the groups was reversed.

The saponification products in both cases were not carbanilates.