[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF PURDUE UNIVERSITY]

ACYL DERIVATIVES OF ORTHO-AMINOPHENOL. V

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When diacyl derivatives of *o*-aminophenol are prepared by the usual methods, it is found in most 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 in the molecule can be determined by removing the group attached to oxygen by saponification with dilute alkali, and determining from the physical constants of the remaining mono-acylated product the group attached to the nitrogen. The identical diacyls mentioned above are 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 indicates that during acylation a rearrangement must have occurred in one of the two cases. It is found that certain acyl groups have more power than others to bring about this migration, weight and acidity of the group being considered to have the predominating influence in their obtaining a position in the more basic amino group in preference to the phenol group.

Previous work on this subject by Ransom,[1] Ransom and Nelson,[2] Nelson and others,[3] and Raiford and others[4] is discussed in the literature.

The work of Ransom and of Ransom and Nelson indicated that, in the cases observed, carbalkoxy (COOR) groups had the power to displace carbonyl (COR) groups from their position on the nitrogen atom during the introduction of the second acyl group. Nelson, Shock and Sowers[5] found, however, that the *n*-carbopropoxy group, *n*-C_3H_7OCO, was displaced from the nitrogen atom by the benzoyl group, while the *iso*carbopropoxy group, *iso*-C_3H_7OCO, was able to displace the benzoyl group from the nitrogen. This peculiar action was also investigated by the present authors and the results were confirmed. It was found in addition, however, that rearrangement was not complete and that both possible monoacyls were produced on saponification. The identical diacyls may then have been either identical equilibrium mixtures or the same pure compound, in which last case rearrangement must have occurred during saponification.

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

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

[3] Nelson and others, *ibid.*, **48**, 1677 (1926); (b) **48**, 1680 (1926); (c) **49**, 3129 (1927); (d) **50**, 919 (1928).

[4] Raiford and others, *ibid.*, **41**, 2068 (1919); (b) **44**, 1792 (1922); (c) **45**, 469 (1923); (d) **45**, 1728 (1923); (e) **46**, 430 (1924); (f) **46**, 2051 (1924); (g) **46**, 2246 (1924); (h) **46**, 2305 (1924); (i) **47**, 1111 (1925); (j) **47**, 1454 (1925); (k) **48**, 483 (1926).

[5] Nelson, Shock and Sowers, THIS JOURNAL, **49**, 3129 (1927).

This investigation was undertaken with the view of determining whether any other differences in the action of *iso*- and *n*-acyl groups could be found, and to study a number of other carbalkoxy-benzoyl diacyl derivatives of *o*-aminophenol.

When *o*-benzoylaminophenol was acylated with *n*-butylchlorocarbonate, the same diacyl was obtained as when *n*-butyl-*o*-hydroxycarbanilate was acylated with benzoyl chloride. Saponification yielded in both cases *n*-butyl-*o*-hydroxycarbanilate, proving that in the diacyl the *n*-carbobutoxy group must have been attached to the nitrogen. In the first acylation, therefore, the benzoyl group rearranged to the oxygen.

In the same way, when *o*-benzoylaminophenol was acylated with *iso*butylchlorocarbonate, the same diacyl was produced as when *iso*butyl-*o*-hydroxycarbanilate was acylated with benzoyl chloride. Here again saponification showed that the diacyl had the benzoyl group attached to the oxygen. In this case there is no difference in the action of the two pairs of isomeric carbalkoxy groups used against the benzoyl group.

Other structurally isomeric aliphatic acyl groups were next studied with the same purpose in mind. When *o*-benzoylaminophenol was acylated with *n*-valeryl anhydride, a diacyl, *o*-benzoylaminophenol *n*-valerate, was formed, while on treating *o*-*n*-valerylaminophenol with benzoyl chloride, an isomeric diacyl *o*-*n*-valerylaminophenyl benzoate, resulted. Saponification of each of these produced only *o*-benzoylaminophenol, indicating that in the latter case migration of the benzoyl group from the oxygen to the nitrogen must have occurred.

Similar results were obtained with the groups *iso*valeryl and benzoyl. Acylation of *o*-benzoylaminophenol with *iso*valeryl chloride produced a diacyl, *o*-benzoylaminophenyl *iso*valerate. Acylation of *o*-*iso*valerylaminophenol with benzoyl chloride produced a diacyl, *o*-*iso*valerylaminophenyl benzoate. Saponification of the first product yielded only *o*-benzoylaminophenol, while saponification of the latter yielded largely *o*-benzoylaminophenol and a small amount of *o*-*iso*valerylaminophenol. In this last case rearrangement is not quite complete during saponification. Obviously, however, the reaction is quite similar to that occurring in the case of the *n*-valeryl group.

When methyl *o*-hydroxycarbanilate was acylated with benzoyl chloride the same diacyl was produced as when *o*-benzoylaminophenol was acylated with methyl chlorocarbonate. Saponification of the diacyl yielded mainly *o*-benzoylaminophenol with a small amount of methyl *o*-hydroxycarbanilate.

The investigations up to this time on the benzoyl-carbalkoxy diacyl derivatives of *o*-aminophenol may be summarized in the following table.

The action of the carbomethoxy group may be explained as due to the difference in weight between it and the benzoyl group, but this does not

TABLE I

BENZOYL-CARBALKOXY DIACYL DERIVATIVES OF *o*-AMINOPHENOL

Group used against benzoyl	Diacyl derivatives	Saponification product	Observer
CH_3OCO	Identical	CH_3OCO on O	Authors
C_2H_5OCO	Identical	C_2H_5OCO on N	Ransom
n-C_3H_7OCO	Identical	Mixture	Authors, Nelson and others
iso-C_3H_7OCO	Identical	*iso*-C_3H_7OCO on N	Nelson and others
n-C_4H_9OCO	Identical	*n*-C_4H_9OCO on N	Authors
iso-C_4H_9OCO	Identical	*iso*-C_4H_9OCO on N	Authors
iso-$C_5H_{11}OCO$	Identical	*iso*-$C_5H_{11}OCO$ on N	Ransom and Nelson

Ransom, *Am. Chem. J.*, **23**, 1 (1900); Nelson, Shock and Sowers, THIS JOURNAL, **49**, 3129 (1927); Ransom and Nelson, *ibid.*, **36**, 390 (1914).

explain why the only slightly heavier carbethoxy group acts differently, nor would it explain the behavior of the *n*-carbopropoxy group. Certain unknown factors must influence these rearrangements.

Experimental

All monoacyls were prepared by the method of Groenvik,[6] using *o*-aminophenol and the acid chloride. Their properties are summarized in Table II.

TABLE II

MONOACYL DERIVATIVES

				Analysis, N, %	
Name	Formula	M. p., °C.	Yield, %	Calcd.	Found
o-*n*-Valerylaminophenol	$HOC_6H_4NHCOC_4H_9$	79	90	7.25	7.11
o-*Iso*valerylaminophenol	$HOC_6H_4NHCOC_4H_9$	100.5–102		7.25	7.13
Methyl *o*-hydroxycarbanilate	$HOC_6H_4NHCO_2CH_3$	122–123	75	8.38	8.20

The other monoacyls studied, which have been described previously, were prepared by the same method.

The diacyl derivatives of *o*-aminophenol were prepared by the Schotten-Baumann reaction and their properties are summarized in Table III.

TABLE III

PROPERTIES OF DIACYL DERIVATIVES

	Name	Saponification product
1	*o*-*n*-Carbobutoxyaminophenyl benzoate[a]	*n*-Butyl-*o*-hydroxycarbanilate
2	*o*-*Iso*carbobutoxyaminophenyl benzoate[a]	*Iso*butyl-*o*-hydroxycarbanilate
3	*o*-Benzoylaminophenylmethyl carbonate[a]	*o*-Benzoylaminophenol and some methyl *o*-hydroxycarbanilate
4	*o*-*n*-Valerylaminophenyl benzoate	*o*-Benzoylaminophenol
5	*o*-Benzoylaminophenyl *n*-valerate	*o*-Benzoylaminophenol
6	*o*-*Iso*valerylaminophenyl benzoate	*o*-Benzoylaminophenol and some *o*-*Iso*-valerylaminophenol
7	*o*-Benzoylaminophenyl *iso*valerate[b]	*o*-Benzoylaminophenol

[a] The same product was formed when the acyl groups were introduced in the reverse order. [b] Prepared by the method of Einhorn and Hollandt, *Ann.*, **301**, 101 (1898).

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

TABLE III (*Concluded*)

	Formula	M. p., °C.	Yield, %	Nitrogen, analyses, % Calcd.	Found
1	$C_4H_9CO_2HNC_6H_4OCOC_6H_5$	62.5	63	4.47	4.54
2	$C_4H_9CO_2HNC_6H_4OCOC_6H_5$	85.5–85.8	60	4.47	4.35
3	$C_6H_5COHNC_6H_4OCO_2CH_3$	128	78	5.17	5.07
4	$C_4H_9COHNC_6H_4OCOC_6H_5$	73–74	45	4.71	4.75
5	$C_6H_5COHNC_6H_4OCOC_4H_9$	103.5–104.5	36	4.71	4.73
6	$C_4H_9COHNC_6H_4OCOC_6H_5$	96–97.5	29	4.71	4.69
7	$C_6H_5COHNC_6H_4OCOC_4H_9$	113.5–117	35	4.71	4.57

Summary

1. A study has been made of the diacyl derivatives of *o*-aminophenol, using the benzoyl group against a series of carbalkoxy groups. It is found that the carbalkoxy group is able in most cases to displace the benzoyl group from the nitrogen. Where, however, there is a large difference in the weights of the two groups, as in the case of carbomethoxy (CH_3OCO) and the benzoyl (C_6H_5CO) groups, the benzoyl group is able to displace the lighter group completely, though the reverse takes place when the next heavier (C_2H_5OCO) group is used.
2. No evidence of differences in the action of *normal* and *iso*-acyl groups when used against the benzoyl group is observed in the case of the *n*- and *iso*carbobutoxy (C_4H_9OCO) groups and of the *n*- and *iso*valeryl (C_4H_9CO) groups.
3. New mono- and diacyl derivatives of *o*-aminophenol have been prepared and studied.

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THE EFFECT OF VARIOUS PREPARATIONS ON THE GROWTH OF BAKERS' AND BREWERS' YEASTS

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In a previous paper[1] the fact was emphasized that different strains of yeast, all of which are called by the name *Saccharomyces cerevisiae*, may react quite differently toward nutrilites.[2]

Since this article was written considerable progress has been made in this Laboratory in concentrating the active material from yeast and other sources, the purification of which was the main object of our research. Before carrying the purification further we were interested to know how important the substance in question might be; whether, for example, it functions for one strain of yeast only or whether it might not be important in the nutrition of several strains of yeast. A second reason for making

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[1] Williams, Wilson and Von der Ahe, THIS JOURNAL, **49**, 227 (1927).

[2] See Williams, *Science*, **67**, 607 (1928).