[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE WASHINGTON SQUARE COLLEGE OF NEW YORK UNIVERSITY]

The Synthesis of Phenolic Long Chain Fatty Acids

BY JOSEPH B. NIEDERL AND CASIMIRO LIOTTA

In continuation of our studies of the addition reaction of phenols to ethenoid and ethinoid type linkages and the intramolecular rearrangements of phenyl ethers, hydroxyphenyl substituted long chain fatty acids have been prepared by both methods. The case of *m*-cresol and oleic acid may be cited as a typical example. Reaction proceeded in a normal manner and the theoretical postulations by Niederl and co-workers[1] for the reaction mechanism involved can *a posteriori* be applied without further modifications and the experimental procedure may be given summarily as follows.

The Addition Reaction.—Equimolar mixtures of oleic acid and *m*-cresol were treated with a cationoid condensing agent (sulfuric and glacial acetic acid mixtures). According to Ssabanejew and others[2] sulfuric acid reacts with oleic acid to form the ι-hydroxystearic acid sulfate, which then interacts with the *m*-cresol to produce the intermediary ι-*m*-cresoxystearic acid, which on subsequent intramolecular rearrangement yields the isomeric ι-(2-hydroxy-4-methylphenyl)-stearic acid. The experimental procedure involved extraction with water, alkali and vacuum distillation. The final product, the above ι-(2-hydroxy-4-methyl-phenyl)-stearic acid, has a pleasant thymol-like odor and shows the expected fatty acid as well as phenolic characteristics and highly interesting physiological properties.

The Intramolecular Rearrangement.—By the addition of hydrobromic acid to oleic acid first the ϑ- or ι-bromostearic acid[3] was prepared from which by interaction with potassium *m*-cresolate the ϑ- or ι-*m*-cresoxystearic acid was obtained. This ether then was subjected to intramolecular rearrangement using a sulfuric–acetic acid mixture. The isomeric phenol thus produced was identical with the one cited above. The bromostearic acid therefore must be the ι-bromostearic acid, which is in agreement with the findings of Arnaud and Posternak.[4]

ι-*m*-Cresoxystearic Acid $\mathrm{CH_3(CH_2)_7\overset{\displaystyle OC_6H_4CH_3}{\overset{|}{C}}H(CH_2)_8COOH}$, liquid, b. p. 280° (23–24 mm.) uncorr.

Anal. Calcd. for $C_{25}H_{42}O_3$: C, 76.92; H, 10.76; neut. equiv., 390. Found: C, 77.70; H, 10.98; neut. equiv., 390.6.

ι-(2-Hydroxy-4-methylphenyl)-stearic Acid, $\mathrm{CH_3(CH_2)_7\overset{\displaystyle CH_3C_6H_3OH}{\overset{|}{C}}H(CH_2)_8COOH}$, solid, m. p. 37°, uncorr.

Anal. Calcd. for $C_{25}H_{42}O_3$: C, 76.92; H, 10.76; neut. equiv., 390. Found: C, 76.22, 76.70; H, 12.12, 10.90; neut. equiv., 396.

(1) Niederl and co-workers, THIS JOURNAL, **50**, 2230 (1928); **51**, 2426 (1929); **53**, 272, 806, 1928, 3390 (1931); **54**, 1063 (1932); **55**, 284 (1933); *Monatsh.*, **51**, 1028 (1929); **60**, 150 (1932); *Z. angew. Chem.*, **44**, 467 (1931).

(2) Ssabanejew, *Ber.*, **19**, 239 (Ref.) (1886); Shukow and Schestakow, *Chem. Centr.*, I, 825 (1903).

(3) Piotrowski, *Ber.*, **23**, 2532 (1890); Bayer and Co., German Patent 186,740 (1907).

(4) Arnaud and Posternak, *Compt. rend.*, **150**, 1526 (1910).

Inasmuch as such a product combines the highly desirable physical and chemical characteristics of a long chain fatty acid and a phenol in one, extensive studies in related systems (mono- and di-basic, acyclic as well as isocyclic unsaturated acids and phenolic (thio-phenolic)[5] compounds are in progress.

(5) B. Whitman, Research Report, New York University, 1933.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

A New Preparation of Ninhydrin

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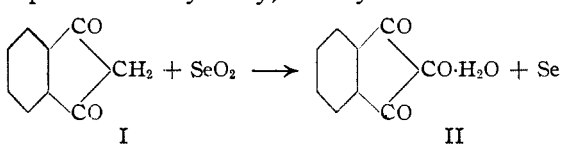
Ninhydrin, triketohydrindene hydrate, has been found to be an extremely valuable reagent for the detection of uncombined amino and carboxyl groups[2] in proteins, peptides and amino acids and in the diagnosis of pregnancy.[3] The only method of preparation, that by Ruhemann,[4] is laborious, expensive and requires starting materials not readily available.

In the present work it was found that diketohydrindene (I), prepared from diethyl phthalate and ethyl acetate according to the method mentioned by Wislicenus,[5] can be readily oxidized to ninhydrin (II) by means of selenious acid or selenium dioxide. The value of this selective oxidizing agent has been pointed out by Riley, Morley and Friend.[6]



I II

A thorough study of this oxidation reaction was made and the maximum yields obtainable were found to be 31–35%. Variations in the order of mixing the reagents, solvents, temperature and use of selenious acid instead of sublimed selenium dioxide have failed to increase the yield. The low yield is apparently due to a bimolecular product formed by the combination of two molecules of diketohydrindene or by the combination of one of the latter with one of triketohydrindene. Similar bimolecular products were formed by the action of hydrogen peroxide on 1,3-diketo-

(1) Junior Fellow, The Textile Foundation. Published by permission of The Textile Foundation, Washington, D. C.

(2) Ruhemann, *J. Chem. Soc.*, **97**, 2025 (1910); Harding and MacLean, *J. Biol. Chem.*, **20**, 217 (1915); Herzfeld, *Biochem. Z.*, **59**, 249 (1914).

(3) Warfield, *J. Am. Med. Assoc.*, **62**, 436 (1914).

(4) Ruhemann, *J. Chem. Soc.*, **97**, 1438 (1910). The present quotation on ninhydrin is $25.00 per gram.

(5) Wislicenus, *Ann.*, **246**, 347 (1888).

(6) Riley, Morley and Friend, *J. Chem. Soc.*, 1875 (1932).