Mo., for a research grant for the completion of this investigation.

Summary

Equimolar condensations of monohydroxyphenols with saturated aliphatic aldehydes were studied. It was found that polymers result in quantitative yields. Upon slow pyrolysis, these polymers yield the corresponding saturated primary alkylphenols. These types of condensations are being extended to unsaturated and aromatic aldehydes, reducing saccharides as well as to ketones, particularly cyclic ketones (cyclopentanone, cyclohexanone, alkyl cyclohexanones and camphor).

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[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE UPJOHN COMPANY]

Some Derivatives of Ortho-Hydroxyphenylmercuric Chloride

BY HANS P. ANDERSEN AND MERRILL C. HART

In earlier reports it has been shown that variations in structure have a limited influence on bacteriostatic properties of organic mercury compounds,[1] and that more complex structures were not as effective as mercury derivatives of hydrocarbons or phenols with limited substituents.[2] One very effective mercurial was found to be *o*-hydroxyphenylmercuric chloride, this compound also being bactericidal at some dilutions.[2] It seemed that possible derivatives of this compound could be prepared which would have similar properties.

Some imide derivatives of phenylmercuric nitrate have been described as being used in germicidal detergent or cosmetic compositions.[3]

In the present work some imide derivatives of *o*-hydroxyphenylmercuric chloride have been prepared and their bacteriological properties evaluated.[4] One has been found to be equally as good as the parent compound. It was found that, in general, imide derivatives were readily formed in alkaline solution, especially if the imide contained a carbonyl group. An attempt was made to prepare derivatives of pyrrole, auramine, carbazole and piperidine but only in the case of piperidine was a product obtained in the form of the hydrochloride. This was formed in the absence of alkali.

Although the simplest structures are most effective, it was thought that fatty acid derivatives might facilitate the *in vivo* activity by increasing diffusion into the surfaces in contact with the antiseptic. A few representative phenolmercuric fatty acid compounds have been prepared and described.

The table gives the results obtained together with melting points and analytical data.

TABLE I

Compound with $HOC_6H_4HgCl(o-)$	Yield, %	M. p., °C.	Mercury analyses, % Calcd.	Found	Inhibiting dilution to *Staph. aureus* in 5 min.
Succinimide	72.3	232–235	51.1	50.8	1-75,000[a,b]
Saccharine	53.7	242–243	42.5	42.1	1-10,000
Phthalimide	96.3	223–224	45.5	45.6	1-20,000
Piperidine	79.3	126	48.3[c]	47.8	1-30,000
Theobromine	51	145–165	40.8[d]	40.3	1-10,000
Barbituric acid	48	...	56.1	56.3	1-20,000
Acetic acid	...	150–151	56.8	56.7	1-40,000
Pelargonic acid	60.7	135	44.4	44.1	1-20,000
Oleic acid	64.3	95–96	34.8	34.98	1-20,000
Lauric acid	74	135.5-136.5	40.6	40.3	1-20,000
Myristic acid	72	135–136[e]	38.5	38.3	1-10,000
Palmitic acid	90	129-131	36.5	36.3	1-10,000
Stearic acid	70	135–137[e]	34.7	34.4	1-10,000

[a] This compound was bactericidal 1-1000. [b] Phenol control 1-80. [c] This is the mercury content of the hydrochloride. Calcd. for $C_{11}H_{15}OHgHCl$: Cl, 8.81. Found: Cl, 8.41. [d] Monohydrate. [e] Mixed melting points with pelargonic and lauric acid derivatives were depressed.

Experimental

***o*-Hydroxyphenylmercuric Succinimide.**—Three and three-tenths grams of succinimide in 18.7 cc. of water, was added to 10.95 g. of *o*-hydroxyphenylmercuric chloride in 25 cc. of warm alcohol. This was cooled as much as possible without forming a precipitate and then 18.7 cc. of 10% potassium hydroxide was added. After shaking and further cooling, 11 g. of crude product was obtained melting at 222°. This was recrystallized from 200 cc. of alcohol and 100 cc. of water to give a final yield of 72.3%. The melting point was 232–235°.

The other imide derivatives were made in the same manner using either water or alcohol, depending on which was the better solvent for carrying out the reaction.

***o*-Hydroxyphenylmercuric Piperidine Hydrochloride.**—Five cubic centimeters of piperidine was added to 16.4 g.

(1) Hart and Andersen, THIS JOURNAL, **56**, 2752 (1934).

(2) Hart and Andersen, *ibid.*, **57**, 1059 (1935). See also Phatak and Leake, *J. Pharmacol.*, **56**, 265 (1936).

(3) British Patent 432,689, July 31, 1935.

(4) We are indebted to Mr. E. A. Gibson, Bacteriological Laboratory, for these results.

of *o*-hydroxyphenylmercuric chloride in 25 cc. of alcohol. The product melted at 126°; yield 79.3%. The analytical data indicate that the hydrochloride is formed and that treatment with potassium hydroxide gives an *o*-hydroxyphenylmercuric hydroxide derivative. It is not stable to acetic acid, probably forming *o*-hydroxyphenylmercuric acetate.

***o*-Hydroxyphenylmercuric Hydroxide.**—Ten grams of *o*-hydroxyphenylmercuric chloride in 25 cc. of alcohol was treated with 17 cc. of 10% alcoholic potassium hydroxide, warming slightly and stirring vigorously. The product is insoluble.

Anal. Calcd. for $C_6H_6O_2Hg$: Hg, 64.5. Found: Hg, 64.7.

***o*-Hydroxyphenylmercuric Fatty Acid Compounds.**—The calculated quantity of *o*-hydroxyphenylmercuric hydroxide was suspended in warm alcohol and the fatty acid added and stirred with warming until solution resulted. On cooling the fatty acid derivative precipitated. It was recrystallized from alcohol and dissolved in dilute alcohol or alkaline solution for bacteriological study.

Summary

A number of imide derivatives of *o*-hydroxyphenylmercuric chloride have been prepared, one of which has bacteriostatic properties similar to the parent compound.

Some fatty acid compounds with *o*-hydroxyphenylmercuric hydroxide have been made which may promise to give enhanced *in vivo* activity.

KALAMAZOO, MICH. RECEIVED APRIL 21, 1937

[CONTRIBUTION FROM THE DEPARTMENTS OF BIOCHEMISTRY AND CHEMISTRY, UNIVERSITY OF NORTH CAROLINA]

The Identification of the Amino Acids: *p*-Toluenesulfonyl[1] Chloride as a Reagent

BY EVAN W. MCCHESNEY AND WM. KIRK SWANN, JR.

I. Introduction

Numerous reagents have been employed for the identification of the amino acids. Among these perhaps the most important group are those reagents which conjugate readily with the amino group, such as benzoyl chloride, β-naphthalenesulfonyl chloride, benzenesulfonyl chloride, *p*-nitrobenzoyl chloride, and phenyl isocyanate. With the passing of years, however, and the discovery of new amino acids, there have come to be gaps in our knowledge such that the derivatives of all of the known amino acids with any one of these reagents do not seem to have been described. Also, in some cases, the derivatives have been prepared, but it has not been possible to crystallize them. The result of this situation is that an investigator who has at hand a small amount of an unknown amino acid cannot rely safely on one derivative for the identification, since it may not crystallize, or it may not have been described. The object of this work has been to find, if possible, one derivative which would be satisfactory for all of the amino acids, and to describe it for those which are at present recognized as products of protein hydrolysis and are commercially available.

For this work two reagents not extensively used thus far in amino acid work were selected for study: *p*-toluenesulfonyl chloride and *p*-bromobenzenesulfonyl chloride. It was soon found that the derivatives obtained with the former crystallized much more readily; therefore it was selected to complete the study. The idea of using *p*-toluenesulfonyl chloride as a reagent for the amino acids is not a new one, Oseki[2] having prepared about a dozen of the compounds, and several other investigators having prepared one or more of them (see references to Table I). A considerable number of the amino acids have not been included in these studies, however, and in some cases there are serious discrepancies in the melting points recorded (see, for example, *d*-alanine, *d*-valine, and *l*-leucine in Table I). It therefore seemed worth while to try to repeat all of the work previously done and, if possible, to complete the list.

II. Materials.—The amino acids used in this work were the highest grade products of the Eastman Kodak Co., the Pfanstiehl Chemical Co., and Hoffman-La Roche, Inc., except those which are commonly prepared in the laboratory (glycine, *d,l*-alanine, *l*-tyrosine, *l*-cystine, and *d*-glutamic acid). The latter were prepared by the standard methods, crystallized from the appropriate solvents, and their purity was demonstrated by nitrogen analyses. The *p*-toluenesulfonyl chloride was an Eastman product, m. p. 67–69° (m. p. in the literature is 69°[3]).

III. Method.—The method used[4] is such a familiar one that it requires little comment. The amino acid, 0.01 equivalent as to combining power, is dissolved in 20 cc. of *N* sodium hydroxide, an ethereal solution of 2 g.

(1) Presented at the Chapel Hill meeting of the American Chemical Society, April 14, 1937.

(2) Oseki, *J. Tokyo Chem. Soc.*, **41**, 8 (1920).

(3) *Cf.* Beilstein, "Handbuch der organischen Chemie," 4th ed., Vol. XI, p. 103.

(4) Fischer and Bergell, *Ber.*, **35**, 3779 (1902).