METHOD FOR THE PRODUCTION OF HYDROXY ACIDS

By A. W. RALSTON and S. T. BAUER

Armour and Company, Chicago

IT is well known that the chemical and physical properties of fatty acids containing hydroxyl groups differ in a number of respects from ordinary saturated or unsaturated fatty acids. This difference brings about a number of uses for hydroxy acids specifically dependent upon the presence of the hydroxyl group or groups in the chain. As an example one may cite the many special uses for fatty acids obtained from castor oil to which fatty acids obtained from other animal and vegetable oils cannot be applied. This difference can be ascribed to the fact that *ricinoleic* acid, which is the characteristic fatty acid of castor oil, differs from oleic acid in the fact that it contains one hydroxy group.

In view of the above it is evident that the development of a commercial method for the production of hydroxy acids from unsaturated fatty acids is a subject of some importance. Such methods when developed make us independent of natural sources and in addition a synthetic method is subject to variations resulting in different types of products, which is not true when one must rely upon naturally occurring products. If a satisfactory synthetic method is developed which is capable of adding, say, 1, 2, 3, and so forth, hydroxyl groups to fatty acids, one has a gradation of properties attended by a specific adaptation to a number of uses. In view of the above the writers decided it would be of interest to attempt the development of a method capable of producing hydroxy acids from unsaturated fatty acids in commercial quantities and at a price capable of competing with natural occurring hydroxy acids.

For the study of hydroxylation the writers chose the hydroxylation of oleic acid to dihydroxystearic acid and this paper deals essentially with this phase of our work. This reaction was chosen because considerable prior work by other investigators has been done upon these compounds and products could be readily identified. The chief interest of the writers, however, was not so much in a detailed study of this one reaction but in the development of a method capable of producing hydroxylated acids from unsaturated fatty acids. Dihydroxystearic acid contains two asymmetric carbon atoms. Thus four optically active compounds are theoretically possible; two of these correspond to a cis and two to a trans-configuration.

Oleic acid as a rule has been considered as a *cis-octadecenoic* acid, but in view of recent work by Bertram (1) some question is raised as to the fact that oleic acid may have a trans configuration. Lewkowitsch (2) describes the following dihydroxy acids: Dihydroxystearic acid by oxidation of oleic acid with $KMnO_4$, melting point 132°. Dihydroxystearic acid by oxidation of elaidic acid with $KMnO_4$, melting point 98-99°. It is evident that a large number of other dihydroxy acids are theoretically possible according to the position of the double bond. For example, Le Sueur (3) has prepared 2,3-dihydroxystearic acid, melting point 126°, by the oxidation of 2,3-oleic acid with $KMnO_4$. A considerable number of other dihydroxystearic acids have been reported in the literature, of which the following may be mentioned:

Dihydroxystearic acid, melting point 66-68°, by action of concentrated sulfuric acid upon ricinoleic acid (4). Dihydroxystearic acid from petroselenic acid by oxidation with $KMnO_4$, melting point 122° (2). Natural dihydroxystearic acid, melting point 141-3°, has also been obtained by cooling castor oil. Nicolet and Poulter (5) reported interesting syntheses of dihydroxy acids from oleic and ealidic. Treatment of oleic acid with chlorine and sodium carbonate gave the chlorhydrin, which was an oil. Treatment of this chlorhydrin with sodium ethylate and then hydrochloric acid resulted in the formation of an epoxide, melting point 53.8°, which on further treatment with sulfuric acid resulted in dihydroxystearic acid, melting point 96°. When elaidic acid was so treated an epoxide, melting point 53.8°, was obtained which when treated with sulfuric acid resulted in a dihydroxystearic acid, melting point 133°.

Oleic acid is usually considered to contain the double bond in the 9,10 position. The acid as ordinarily obtained consists of a mixture of several olefinic acids containing one double bond. In the opinion of Shukoff and Schestakoff (6) oleic acid consists of a mixture of acids, the double bond being in 9,10, 3,4 or 4,5 positions. Since commercial oleic acid was used in these experiments it will be necessary to bear the work of these investigators in mind, and there is, therefore, some question as to whether all of our hydroxylation was at the 9,10 carbon atom because of the presence of acids containing double bonds in other than the 9,10 position.

Of the methods now generally recognized for the preparation of hydroxy acids the following are the best known:

1. Oxidation with potassium permanganate.

When alkaline potassium permanganate is used Lapworth and Mottram (7) recommend for the oxidation of oleic acid a temperature range between 0-10°, a concentration of oleic acid not exceeding 0.1 per cent, and a concentration of potassium permanganate not exceeding 1 per cent. By this method a dihydroxystearic acid, melting point 132°, was obtained when oleic acid was oxidized. Robinson and Robinson (8) recommend for this oxidation a temperature of 0°C. and the addition of 0.5 N $KMnO_4$ to an alkaline solution of the oleic acid. Since hydroxylation is the first step in the cleavage of the double bond care must be used that high temperatures are not employed. Nicolet (9) prepared a dihydroxystearic acid, melting point 131.5°, by permanganate oxidation of oleic acid, the excess oxidizing agent being removed by sodium sulfite and sulfuric acid.

2. Oxidation with sodium chlorate.

Medvedev and Alexejewa (10) recommend osmium tetroxide as a catalyst for this reaction. These investigators obtained a dihydroxy acid, melting point 132°, from oleic acid by this method.

3. Oxidation with hydrogen peroxide.

Hilditch (11) recommends oxidation in glacial acetic acid or acetone at about 60°, and obtained thereby a dihydroxystearic acid, melting point 132°, from oleic acid.

4. Halogenation followed by dehalogenation.

Albitski (12) (13) treated chlorinated oleic acid with an aqueous alkaline solution thereby obtaining dihydroxy acids. This method is of somewhat general application for the introduction of hydroxyl groups into a chain. Conditions must be carefully controlled or various side reactions resulting in decreased yields are encountered.

5. Addition of hypochlorous acid.

Hypochlorous acid adds directly to the double bond forming the chlorhydrin when treated with aqueous or alcoholic potassium hydroxide solution and results in the formation of dihydroxy acids. Essex and Ward (14) (15).

A study of the above methods will show that direct hydroxylation is only obtained where chemicals such as potassium permanganate or hydrogen peroxide are employed. Methods such as the addition of hypochlorous acid followed by treatment with alkaline solutions necessitate an isolation of the intermediate product and a further treatment. Such methods while quite adaptable to laboratory studies are not suitable to commercial production because of the expensive oxidizing agents employed. Methods such as halogenation followed by dehalogenation or addition of hypochlorous acid necessitate several steps. The writers, therefore, set out to develop a method whereby unsaturated fatty acids can be hydroxylated directly by the use of inexpensive chemicals available in large quantities.

Sweeney and Ralston (16) showed that when chlorine is passed into a solution of lime in the presence of a small amount of nickel nitrate oxygen is evolved in essentially quantitative amounts. The mechanism of this reaction was assumed to be the formation of sodium hypochlorite which oxidizes the nickel to nickel peroxide (Ni_2O_7). The peroxide is then decomposed with the loss of oxygen and is subsequently regenerated. Thus as long as the system remains alkaline oxygen is evolved at a rate depending upon the rate of addition of the chlorine. The catalyst can be recovered and used essentially indefinitely. It was thought that this reaction could be used for the hydroxylation of unsaturated fatty acids. Since sodium hydroxide can be substituted for calcium hydroxide for the formation of the peroxide this change is indicated because of the insolubility of most calcium soaps of fatty acids. It was expected that chlorination of the double bonds would not take precedent over the series of oxidation reactions. Preliminary runs showed the above speculations to be correct. Because the actual oxidizing agent is the peroxide, no intermediate chlorhydrin formation was encountered. The oleic acid was dissolved in a solution containing an excess of sodium hydroxide, a small amount of nickel nitrate solution was added and chlorine was bubbled in under various conditions. The resulting product proved to be dihydroxystearic acid and no tendency toward halohydrogenation or chlorination was evidenced. A detailed description of the method follows:

A solution was prepared containing 40 grams potassium permanganate, 5 grams of nickel nitrate, several crystals of manganous chloride in 1000 cc. of distilled water. Chlorine was bubbled in at the rate of 10 cc. per minute. Fifty grams of oleic acid was added simultaneously with the chlorine addition and over a period of four and one-half hours, after which time the solution was acidified with HCl and the acids recovered. After acidification the acids were obtained as a low melting solid mass. When recrystallized from acetone an acid was obtained, melting point 114-16°. This acid had a molecular weight of 314 (theoretical for dihydroxystearic acid—316). Acetyl value showed 9.71 per cent hydroxyl (theoretical —10.4 per cent). Mixed melting point with a dihydroxystearic acid (M.P. 123-7°) obtained by the oxidation of oleic acid by potassium permanganate showed no depression. It is therefore assumed that the product is essentially a 9,10-dihydroxystearic acid. The ethoxy derivative prepared by the method of Nicolet and Poulter (loc. cit.) had a melting point of 87°, which is in line with the theoretical.

Repeated runs gave essentially equivalent results. Other catalytic combinations, such as nickel nitrate with ferrous chloride, nickel chloride with zinc chloride, cobalt nitrate with manganous chloride, etc., were tried. Of these combinations the nickel nitrate, manganous chloride mixture was found to be the most effective.

The mechanism of the reaction is assumed to be that the nickel peroxide acts as an oxygen carrier, the oxygen adding on to the oleic acid at the double bond to form an epoxide in the oleic acid molecule. The epoxide immediately hydrates with water to give the dihydroxy compound under the conditions of the experiment.

It is evident that this reaction is capable of general application for the hydroxylation or oxidation of unsaturated acidic compounds in general. The low temperatures necessary and products obtained show that this oxidation somewhat parallels that obtained when oxidizing agents such as potassium permanganate are employed. It differs from other methods heretofore reported inasmuch as the oxidizing agent is continually regenerated. Further work is being continued upon the preparation of polyhydroxylated acids starting with acids other than oleic.

Bibliography

(1) Bertram, Chemische Weekbladt 33, 3 (1936).

(2) Lewkowitsch. Volume I.

(3) Le Sueur. J. Chem. Soc. 85, 1712 (1904).

(4) Grün. Ber. 39, 4400 (1906).

(5) Nicolet and Poulter. J. A. C. S. 52, 1186 (1930).

(6) Shukoff and Schestakoff. J. Rus. Phys. Chem. Soc. 40, 830 (1908).

(7) Lapworth and Mottram. J. Chem. Soc. 127, 1628 (1925).

(8) Robinson and Robinson. J. Chem. Soc. 127, 177 (1925).

(9) Nicolet. J. A. C. S. 44, 1139 (1922).

(10) Medvedev and Alexjewa. Papers Pure Applied Chem., Karpow Institute, Moscow (Russ.), 128-42 (1927).

(11) Hilditch. J. Chem. Soc. 1828 (1926).

(12) Albitski. J. Rus. Phys. Chem. Soc. 31, 76 (1899).

(13) Albitski. J. Rus. Phys. Chem. Soc. 34, 788 (1902).

(14) Essex and Ward. U. S. Patent 1,594,608.

(15) Essex and Ward. U. S. Patent 1,626,398.

(16) Sweeney and Ralston. Ind. Eng. Chem. 22, 716 (1930).