depend, under limited conditions, on the first power of the concentration of the catalyst and on the second power of the concentration of maleic acid. A theory of the reaction is given which is in accord with the present known facts of the transmutation of maleic acid to fumaric acid.

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OXIDATION OF FUMARIC AND OF MALEIC ACID TO TARTARIC ACID[1]

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The recent success of Messrs. Weiss and Downs[3] in making fumaric and maleic acids easily available directed our interest to the production of racemic and *meso*tartaric acids from these sources.

Of the methods reported in the literature, namely, bromination and subsequent hydrolysis,[4] oxidation with permanganate,[5] or oxidation by a mixture of potassium chlorate and osmium[6] tetra-oxide, the latter was chosen for intensive study, since preliminary experience with the others had shown the existence of serious limitations in their use. K. A. Hofmann, who first reported the osmium tetra-oxide method, states that he recovered 7 g. of primary sodium tartrate (monohydrate) and 4 g. of calcium racemate (tetrahydrate) as a result of the reaction of 10 g. of fumaric acid with 5 g. of sodium carbonate, 12 g. of sodium chlorate and 0.02 g. of osmium tetra-oxide in 100 cc. of water for six to ten hours at 40°. From the reaction of a similar mixture in which the fumaric acid was replaced by maleic acid, 16 g. of calcium mesotartrate (trihydrate) was recovered. The first result represents 60% of the tartaric acid theoretically possible, and the second, a 72% yield. In each instance, the sodium carbonate was sufficient in amount to convert the initial acid into the acid salt.

It seemed probable that the method could be improved since no extensive study had been reported by Hofmann and since the loss through side action should be a function of the hydrogen-ion concentration. This proved to be the case. We herewith report an improved method by which 97+% yield of the respective acids may be obtained under conditions which are practical for the average preparative laboratory.

[1] Presented by title at the Organic Division of the Convention of the American Chemical Society, April, 1924.

[2] The principal part of the experimental work of this paper was completed by Nicholas A. Milas in fulfilment of part of the requirements for the degree of Master of Science at the University of Chicago, 1923.

[3] Weiss and Downs, *J. Ind. Eng. Chem.*, **12,** 228 (1920).

[4] Lossen, *Ann.*, **300,** 24 (1898).

[5] Kekulé and Anschütz, *Ber.*, **13,** 2150 (1880).

[6] Hofmann, Ehrhart and Schneider, *Ber.*, **46,** 1667 (1914).

The Reaction.—The principal reduction products of chlorate in the reaction are chlorite and chloride, principally the latter. Only traces of free chlorine or hypochlorites could be distinguished by the test with metallic mercury.[7] Chlorite was identified by its ability to bleach indigo.

The oxidation product of fumaric acid is racemic acid and that of maleic acid is mesotartaric acid. If the method of Hofmann is used, there is also destructive oxidation of the initial acids as indicated by the evolution of carbon dioxide.

Empirical equations for the reaction are:

$$H_2C_4H_2O_4 + H_2O + OsO_4 = H_2C_4H_4O_6 + OsO_3$$
$$OsO_3 + KClO_3 = KClO_2 + OsO_4$$

or

$$3OsO_3 + KClO_3 = KCl + 3OsO_4$$

In the above reactions the catalyst is represented as being reduced to the trioxide form. This is purely hypothetical as the actual reduction product has not been identified.

Hofmann believes that an intermediate compound of osmium tetraoxide and potassium chlorate accomplishes the change. To this we do not subscribe. However, the discussion of this detail is postponed to another time.

Materials.—Commercial fumaric acid[8] was purified by recrystallization from hot water. For most of our work with maleic acid, the crude acid was transformed into the easily purified anhydride by the method described by Terry and Eichelberger.[9] After the conditions for success were understood, the commercial acid was transformed into the sodium acid salt which was purified by recrystallization[10] from hot water. The sodium acid maleate, which is a trihydrate, is entirely suitable for oxidation experiments when one equivalent of hydrochloric acid is added to its solution. The purity of the salt may be tested by titration of a weighed sample.

Sodium chlorate or carbonate, potassium chlorate or carbonate of so-called C. P. grade were used. Previous to tests of the reaction mixtures for the formation of chloride, they were carefully freed from this substance.

The Catalyst.—The catalyst, osmium tetra-oxide, must be handled with special care, since it is volatile and extremely destructive of sensitive body tissues such as those of the lungs or the eyes. Before a tube of the acid is opened, it should be chilled in an ice-and-salt bath. When opened it is quickly dropped into a volumetric flask in which the solution is then made up. The operator should wear gas-tight goggles during the operation or at any time when he is exposed even to dilute vapors of the oxide, as it is reported that the lens of the eye becomes clouded with a precipitate of the metal as a result of continuous slight exposures. If the tubes are opened without the precautions stated above, temporary blindness is likely to occur. Rubber or cork stoppers should not be used to close the container. If the original tube is weighed at the start and the pieces of the tube are collected and weighed afterward, an approximate estimate of the contents may be obtained. This is desirable since the tubes we have used have been found to vary from 0.9 to 0.5 g. in weight of contents.

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[7] Both for this test and the following see Treadwell and Hall "Analytical Chemistry," 1921.

[8] From the General Chemical Company.

[9] Terry and Eichelberger, THIS JOURNAL, **47**, 1067 (1925).

[10] For solubility data, see Weiss and Downs, *ibid.*, **45**, 2345 (1923).

Reactions were carried out in 250cc. flasks, attached by cork stoppers to condenser tubes about 60 cm. long and open to the air. Since the partial pressure of osmium tetra-oxide in the vapor of the solution is extremely small, the loss from volatilization was less than 0.5% (as shown by test). Under conditions finally adopted, it is feasible to use a closed container such as a stout bottle with well-ground stopper so that even the above tiny loss may be avoided.

The catalyst may be recovered by cooling the mixture and extracting it with a suitable oil. We used benzene, and three extractions proved sufficient to reduce the concentration of the catalyst to less than 1% of the initial value. The benzene solution was treated with concd. sodium hydroxide solution which acquired the osmium tetraoxide, presumably in the form of a salt.[11] The sodium hydroxide solution was made neutral in a closed container. The catalyst can be precipitated from the solution by adding a small quantity of sodium hydroxide and formaldehyde. A black precipitate, probably osmium trioxide, is collected on a filter and dissolved in potassium chlorate solution. The precipitation of the catalyst as trioxide can be omitted if the salt formed from neutralization of the sodium hydroxide is not objectionable.

Test for Completeness of Reaction.—In the exploration of the method, it was of importance to be able to test for the completeness of the reaction. This was done as follows: a small lot was withdrawn from the reaction mixture; the catalyst was extracted from it by shaking the solution with benzene; then 5 cc. of the water layer was made neutral (to litmus) and to it was added 5 g. of sodium bromide and the whole made up to 50 cc.; one-half cc. of dilute(saturated solution diluted one to three) bromine water was added. When the color remained for less than five minutes, the reaction for which the test was made was incomplete. Phenolphthalein should not be used as indicator since bromine gives with it a yellow precipitate (tetrabromo-phenolphthalein), which obscures the test.

The underlying principle of the test is that salts of both initial and final acid are attacked by hypobromous acid, but only the neutral sodium fumarate or sodium maleate is attacked by bromine.[9] The large excess of sodium bromide suppresses the hydrolysis of bromine. The tiny quantity of the latter used insures that only inconsiderable traces of fumarate or maleate remain. Similar tests with equivalent mixtures of *meso*tartrate and racemate keep their color more than an hour.

Since the osmium tetra-oxide is handled in small lots, it is best not to attempt a precise analysis to determine the correct amount to use, etc., but to insure that a given reaction is finished by the use of the above test.

To test for the completeness of removal of catalyst from a given solution, the thiocarbamide test of Chugaev[12] may be used. A small excess of thiocarbamide and a few drops of 6 *N* hydrochloric acid are added to the sample to be tested and the mixture is warmed. A red color indicates the presence of osmium tetra-oxide. The absence of color indicates that not more than one part of oxide is present in 100,000.

[11] Chugaev, *Compt. rend.*, **167**, 162 (1918).

[12] Chugaev, *ibid.*. **167**, 235 (1918).

Determination of Yield.—Racemic acid was determined as follows. The solution, freed from catalyst, was made neutral with potassium hydroxide. Then acetic acid was added in amount slightly in excess of that needed to make the potassium acid tartrate. The crystals were not separated from the solution until after some hours' (overnight) standing in an ice-bath. They were then collected, washed with alcohol and titrated with barium hydroxide, using phenolphthalein as indicator. The baryta was standardized with pure fumaric acid or with hydrochloric acid which in turn had been analyzed by the silver chloride method.

*Meso*tartaric acid was determined from the weight of calcium salt, precipitated from neutral solution. Precipitate and solution were permitted to remain in contact overnight to insure complete separation. The composition of the salt was checked by ignition of a weighed sample, and titration of the residue in the manner customary for the analysis of calcium salts of organic acids.

Representative Experiments.—Table IA gives the results of representative experiments with fumaric acid, and Table IB the same data for maleic acid. The column headings are self-explanatory except that quantities are given in millimoles unless otherwise designated. The osmium tetraoxide solution contained 0.009 g. per cc. Whether X signifies sodium or potassium is indicated by the symbol in brackets at the right of the numerals.

TABLE I

REPRESENTATIVE EXPERIMENTS

A. FUMARIC ACID

Expt.	Temp. °C.	X_2CO_3	Acid	$XClO_3$	H_2O Cc.	OsO_4 soln. Cc.	Time Hours	Yield %
1	50	39 (Na)	43	56.5 (Na)	75	1	12	39
2	40	40 (Na)	86	113 (Na)	100	2	12	90
3	45–50	39 (Na)	86	113 (K)	150	2	14	91
4	50	40 (K)	86	113 (Na)	150	2	10	91
5	50	9.8 (Na)	43	56.5 (Na)	75	1	12	95
6	50	0.0	43	56.5 (Na)	75	1	12	95.5
7	50	0.0	86	113 (K)	150	10	5	99.5

B. MALEIC ACID

Expt.	Temp. °C.	X_2CO_3	Acid	$XClO_3$	H_2O Cc.	OsO_4 soln. Cc.	Time Hours	Yield %
1	40	40 (Na)	86	113 (Na)	100	2	10	74
2	50	0.0	86	113 (Na)	140	10	7	98
3	50	0.0	86	113 (Na)	140	10	9	98

When the neutral salt of fumaric acid is used, Expt. 1, the yield is 39%. When the acid salt is used, Expts. 2–4, the yield is 90–91%, while with the free acid, Expts. 6 and 7, as high as 99.5% is secured. In the case of maleic acid, the neutral salt was not experimented with. The acid salt netted a 74% yield, Expt. 1, and the free acid 98%, Expts. 2 and 3.

It thus developed that the sodium carbonate recommended by Hofmann did harm, and that the most favorable conditions were obtained by using the free acids themselves. Since the catalyst could be recovered, there was no reason for using low concentrations of the latter. Accordingly, in the later experiments, 10 cc. of solution, or about 0.1 g. was used in each experiment.

The concentrations of fumaric and maleic acid were as great as were desirable for subsequent separation of the products, so that no attempt was made to increase them. The use of higher temperatures entails a new study of optimum hydrogen-ion concentration, etc. If the above mixtures are used at 80° only an 80% yield will be secured. Doubtless, a suitable increase in hydrogen-ion concentration will improve the yield. It is to be anticipated that at high temperatures the tartaric acids themselves will be oxidized. Since the time of operation was within convenient limits, no further effort was made to use temperatures higher than 50°.

If the quantity of potassium chlorate is reduced to 5 g. instead of 13.6 (113 millimoles), the time for the completion of the reaction is not appreciably altered. However, a slight evolution of carbon dioxide will be observed, and the yield will be found to be about 92%. Apparently, it is critical that the catalyst be reoxidized at great speed. A full discussion of this important fact will be given in a later paper together with evidence as to the detail of the reaction. For the present, our purpose is to describe the experimental conditions necessary for an efficient preparation of the tartaric acids.

Presence of Isomeric Acids in the Product.—The possibility of the presence of racemic acid in the *meso* acid, and of the *meso* acid in the racemic acid was explored by examination under the microscope of the crystals of the calcium salts of the different products after the method of Holleman.[13] The presence of tiny quantities of isomeric acid was recognized in each case, but it was estimated that the contamination amounted to less than 1%. This conclusion was confirmed by precipitation methods. Thus the solution of the *meso* acid gave no precipitate on addition of a saturated solution of calcium sulfate. The filtrate from the precipitation of potassium acid racemate was treated with calcium chloride and neutralized, and the precipitated calcium tartrate collected. The weight of salt corresponded to less than 1% of the total racemate.

Use of the Reactions in Preparative Processes.—In making preparations of tartrates by the reactions in question, the proportions of reagents to be used are those of Expt. 7, Table IA, and Expt. 3, Table IB, namely, 13.6 g. of potassium chlorate or 11.9 of sodium chlorate for every 10 g. of either fumaric or maleic acid or 16.5 g. of sodium acid maleate. When the latter is used, an equivalent of hydrochloric acid is added. One-

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[13] Holleman, *Rec. trav. chim.*, **17**, 69 (1898).

tenth g. of catalyst is conveniently employed, but when time is no object, smaller quantities can be used. The final volume of the solution is 150 cc. per 10 g. of initial acid.

Preparation of Potassium Acid Racemate.—The reaction mixture is prepared as described above. If sodium chlorate has been used, an equivalent of potassium chloride should be added to the solution to overcome the increase in solubility of the potassium acid racemate owing to the presence of sodium ion in solution. Similarly, sodium hydroxide may be used to make the acid salt instead of potassium hydroxide when an excess of potassium chloride is added to complete the precipitation of the potassium acid racemate.

Preparation of Racemic Acid.—Although the calcium salt is well adapted for the determination of yield, it is not desirable to use it as an intermediate in the preparation of the free acid, since an appreciable quantity of calcium sulfate is precipitated with the latter. The barium salt (of racemic acid) is precipitated from the neutral solution, and is collected and treated with an equivalent of sulfuric acid. The mixture is digested on the water-bath for approximately an hour, or until the liquid contains only a trace of sulfate. Precipitate and solution are separated in the usual way, and the latter is evaporated on the water-bath until crystals form. It is then cooled, and the evaporation is continued at ordinary temperatures.[14] The product is the monohydrate. The anhydrous acid can be prepared[15] by drying the monohydrate at 100°.

Preparation of the Meso Acid.—The preparation of the *meso*tartaric acid is attended by the usual difficulties in preparing a substance that is extremely soluble in water. The initial stages of the preparation are carried out in the same way as for racemic acid to the stage of the evaporation of the filtrate from the separation of barium sulfate. As the filtrate becomes viscous, it is transferred to a weighed dish and the evaporation is carried on until the weight of solution is about one and one-half times the weight of acid expected. The liquid is then put into an ice-bath and seeded with crystals of the acid. In the course of an hour, coarse crystals of monohydrate will have separated from solution. The evaporation is then completed at ordinary temperatures. If the evaporation is carried past the first stage described above, a gummy liquid results which very slowly changes to a compact, crystalline mass. The anhydrous acid[16] is prepared by drying the hydrate at 100°.

The *meso* acid may be prepared from the calcium salt by the same method as for the barium salt, except that a final removal of calcium sulfate is

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[14] Scacchi [*Atti Accad. scienez fische matemat.* (*Napoli*), **4**, No. 4 (1869)] states that crystals separating above 73° are the anhydrous acid. (Beilstein, Vol. III, p. 523.)

[15] Berzelius, *Ann. Physik,* 19, 321.

[16] Dessaignes, *Ann. Spl.,* **2**, 245.

brought about by adding five volumes of alcohol to the concentrated water solution of the acid. There should be at least 1 cc. of the mixture for every 0.3 g. of acid expected in order to keep the latter in solution. After the calcium sulfate precipitate has been removed, the solution is diluted greatly and the alcohol distilled from it. The concentration of the residue and preparation of crystals are continued as in the barium salt method.

Theory of the Addition of the Hydroxyl Groups.—The addition of hydroxyl groups as accomplished in the reaction described above takes place in the manner called "cis addition" as would be anticipated by the application of Wislicenus' postulate or the Le Bel and van't Hoff hypothesis. This result may be correlated with our present knowledge of halogen addition at the double bond between carbon atoms, a reaction which commonly occurs in the manner called "trans addition." This study has been presented elsewhere[9] and the reader is referred to the article in question for the complete argument.

Summary

The following experimental results are reported.

1. The A. K. Hofmann method for oxidation of maleic acid to *meso*-tartaric acid, and fumaric acid to racemic acid by action of potassium or sodium chlorate and osmium tetra-oxide has been greatly improved by treating the free acids themselves instead of the acid salts. Details for the efficient operation of the process are given.

2. A test for the completeness of the oxidation of fumaric and maleic acids is given. This constitutes an additional essential improvement, since it is undesirable to handle large lots of osmium tetra-oxide or to carry out precise analyses on small lots, so that some uncertainty exists as to the time necessary for complete reaction.

Inasmuch as the racemic and *meso*tartaric acids formed contain less than 1% one of the other, and since the yields are better than 97% of an equivalent to the quantity of initial acid taken, these methods of preparation are recommended.

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