

## ✂ Oxidation of Unsaturated and Hydroxy Fatty Acids by Ruthenium Tetroxide and Ruthenium Oxyanions

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### ABSTRACT

The reactions of ruthenium VIII tetroxide ( $\text{RuO}_4$ ) and the ruthenium VII and VI oxyanions, perruthenate ( $\text{RuO}_4^-$ ) and ruthenate ( $\text{RuO}_4^{=}$ ) with hydroxy substituted and unsaturated fatty acids have been studied. At a 1:1 molar ratio, ruthenium tetroxide ( $\text{RuO}_4$ ) and both oxyanions ( $\text{RuO}_4^-$  and  $\text{RuO}_4^{=}$ ) oxidized 12-hydroxystearic acid to 12-ketostearic acid. With 9,10-dihydroxystearic acid, the type of oxidation products obtained depended on the amount of ruthenium oxidant used. At high ratios of oxidant to substrate, cleavage to pelargonic and azelaic acids occurred whereas at lower ratios, partial oxidation to diketo and acyloin derivatives predominated. The oxidation of oleic acid with excess ruthenium tetroxide ( $\text{RuO}_4$ ) or perruthenate anion ( $\text{RuO}_4^-$ ) gave the cleavage products pelargonic and azelaic acid through the intermediate formation of dihydroxy and diketo intermediates. Ruthenate anion ( $\text{RuO}_4^{=}$ ) did not react with the double bond of oleic acid.

### INTRODUCTION

Ruthenium tetroxide ( $\text{RuO}_4$ ) is recognized as one of the more potent oxidizing agents of organic substrates (1-6). In practice,  $\text{RuO}_4$  is conveniently generated from a catalytic amount of ruthenium dioxide and a large excess of an oxygen donor such as sodium meta-periodate or sodium hypochlorite (5); these oxidants also regenerate  $\text{RuO}_4$  from

any  $\text{RuO}_2$  product formed during the oxidation of the organic substrate. The latter reoxidation procedure with  $\text{RuO}_2$  has been successfully used for the oxidation of cyclobutanols to cyclobutanones (1), substituted benzene compounds to alicyclic carboxylic acids (1), alkynes to  $\alpha$ -diketones or carboxylic acids (3), cycloalkanes to cycloalkanones or carboxylic acids (5), and cycloalkenes to aldehydes (7). In a previous study, we reported a procedure for the oxidative cleavage of monounsaturated fatty acids using ruthenium dioxide and sodium hypochlorite (8,9). The use of sodium hypochlorite as the cooxidant required that the reaction be done under basic conditions to prevent the formation of chlorine-containing compounds. However, ruthenium tetroxide is reported to be stable only below pH 7 (10). Under alkaline conditions (pH 7-12), ruthenium tetroxide is reduced to perruthenate anion ( $\text{RuO}_4^-$ ) and at pH greater than 12, the perruthenate anion is further reduced to ruthenate anion ( $\text{RuO}_4^{=}$ ) (10). When catalytic amounts of ruthenium dioxide together with large amounts of sodium hypochlorite are used for the oxidation of unsaturated fatty acids under alkaline conditions, it is unclear which ruthenium species are formed and which ones are oxidizing the unsaturated fatty acid. To better understand the reaction pathway of the oxidation and to identify the

true ruthenium oxidant in this reaction, this paper describes the oxidative behavior of the ruthenium species when reacted with unsaturated fatty acids, hydroxy fatty acids and hydroxy unsaturated fatty acids, respectively.

## EXPERIMENTAL PROCEDURES

### Materials

Oleic acid (98%) and ricinoleic acid (98%) were obtained from Applied Science Labs (State College, PA). 12-Hydroxystearic acid was obtained by catalytic hydrogenation of ricinoleic acid. *erythro*-9,10-Dihydroxystearic acid was obtained by  $\text{KMnO}_4$  oxidation of oleic acid (8).

Sodium salts of fatty acids were prepared by reacting the fatty acid with an equivalent of sodium hydroxide in 90~95% aq ethanol. The soaps were recrystallized from ethanol. Methyl esters of fatty acids were prepared using  $\text{BF}_3$ /methanol reagent. Ruthenium dioxide ( $\text{RuO}_2 \cdot x\text{H}_2\text{O}$ , 53% metal) was purchased from Engelhardt Ind., (Newark, NJ) and potassium perruthenate ( $\text{KRuO}_4$ ) was purchased from Alfa Products (Danvers, MA).

Gas liquid chromatography (GLC) was conducted with a Hewlett Packard Model 7620 chromatograph equipped with dual flame ionization detectors. Separations were obtained on 8 ft  $\times$  1/8 in. silanized stainless steel columns packed with 7.5% EGA + 2%  $\text{H}_3\text{PO}_4$  on 90-100 mesh Anakron ABS or 3% SP-2100 DOH on 100/120 Supelcoport. Quantitation of peak areas were obtained with a Consolidated Scientific Industries Supergrator-2-integrator and all have been expressed as area % using methyl palmitate as an internal standard.

*Preparation of ruthenium tetroxide ( $\text{RuO}_4$ ) solution.* An excess of sodium periodate (4 g) and 25 mL of  $\text{H}_2\text{O}$  were placed into a 200-mL round-bottom flask equipped with a magnetic stirring bar and condenser. Ruthenium dioxide ( $\text{RuO}_2 \cdot x\text{H}_2\text{O}$ , 1 g) and 50 mL of carbon tetrachloride were added to the flask. The reaction was stirred 1 hr at room temperature and the carbon tetrachloride layer was separated from the aq layer. The water layer was extracted with 20 mL of carbon tetrachloride and the combined carbon tetrachloride solutions were stored over aq periodate solution in the refrigerator. The ultraviolet (UV) spectrum of this  $\text{RuO}_4$  solution agreed with the published spectrum and the concentrations were determined using known extinction coefficients for the maxima at 385 nm and 310 nm (11).

*Preparation of sodium ruthenate.* A solution of sodium ruthenate (50 mL, 0.037 M) was prepared by stirring equal volumes of 1.0 M aq sodium hydroxide solution with a solution of ruthenium tetroxide in carbon tetrachloride for 2 hr at ambient temperature. The 2 layers were separated and the aq layer was extracted with 50 mL of carbon tetrachloride to remove unreduced ruthenium tetroxide. The aq layer was allowed to stand at room temperature for 2 days. During this time, ruthenium tetroxide is first reduced to perruthenate ion ( $\text{RuO}_4^-$ ) and then to ruthenate ion ( $\text{RuO}_4^{=}$ ).

The UV-visible spectrum of this  $\text{RuO}_4^{=}$  solution was identical to the published spectrum and the concentration of  $\text{RuO}_4^{=}$  was determined using absorption maxima at 465 nm and 385 nm (11).

*Preparation of potassium perruthenate solution.* Because of the difficulty of stabilizing perruthenate solutions under basic conditions, we purchased potassium perruthenate from Alfa Chemicals (Danvers, MA). The UV-visible spectrum in an aq alkaline solution was identical to the published spectrum and the concentrations were determined using absorption maxima at 385 and 310 nm (11).

## Procedures

*Oxidation of methyl 12-hydroxystearate by ruthenium tetroxide.* Methyl 12-hydroxystearate (0.314 g, 1.0 mmol) and 30 mL of carbon tetrachloride were placed into a 250-mL 3-necked round-bottom flask equipped with thermometer, addition funnel, condenser and magnetic stirrer. All other experiments were run using the same apparatus. Distilled water (30 mL) was added to the homogeneous solution, then 27.0 mL (0.037 M, 1.0 mmol) of ruthenium tetroxide in carbon tetrachloride was added by drops to the flask over a 15-min period at room temperature. After the reaction mixture was stirred for 2 hr, isopropanol was added to destroy excess  $\text{RuO}_4$ , and the 2 layers were separated. The aq layer, after 1.0 M aq sodium hydroxide solution was added to pH above 12, was filtered through Celite to remove suspended  $\text{RuO}_2$ . The filtrate was acidified with conc HCl to pH 2 and extracted with ether ( $3 \times 50$  mL). The carbon tetrachloride layer was filtered through Celite. Both organic layers were washed with  $\text{H}_2\text{O}$ , dried over  $\text{MgSO}_4$ , the 2 organic layers were combined, and the solvent was removed in vacuo to give 0.342 g of product. The oxidation product, after esterification with  $\text{BF}_3/\text{CH}_3\text{OH}$ , was analyzed by GLC and thin layer chromatography (TLC), then identified by comparison with a standard.

*Oxidation of sodium 12-hydroxystearate by potassium perruthenate.* Sodium 12-hydroxystearate (0.2415 g, 0.75 mmol) was dissolved in 50 mL of distilled water. To this stirred solution was added 50 mL of 0.015 M  $\text{KRuO}_4$  solution (0.75 mmol) over a 15-min period at room temperature. After 2 hr, isopropanol was added to the flask until the starch-iodide test was negative, then 1.0 M aq NaOH solution was added to pH above 12. The mixture was then filtered through Celite to remove suspended solid  $\text{RuO}_2$ . The clear filtrate was acidified with conc HCl to pH 2 and extracted with ether ( $3 \times 50$  mL). The combined ether extracts were washed with  $\text{H}_2\text{O}$ , dried over  $\text{MgSO}_4$ , and the solvent was removed in vacuo to give 0.24 g of product. The oxidation product, after esterifying with  $\text{BF}_3/\text{CH}_3\text{OH}$ , was analyzed by GLC and TLC, then identified by comparison with a standard.

*Oxidation of sodium 12-hydroxystearate by sodium ruthenate.* Sodium 12-hydroxystearate (0.2415 g, 0.75 mmol) was dissolved in 50 mL of 1.0 M NaOH aq solution. To this homogeneous solution was added 15.86 mL of 0.0473 M  $\text{Na}_2\text{RuO}_4$  solution (0.75 mmol) by drops over a 15-min period at room temperature. After the mixture was stirred for 2 hr at room temperature, isopropanol was added until the starch-iodide test was negative. The mixture was then filtered through Celite to remove suspended solid  $\text{RuO}_2$ . Isolation and identification of oxidation products were made by the previously described procedure. A series of similar oxidation reactions were also done with the 3 ruthenium oxidants using 9,10-dihydroxystearic acid, oleic acid and ricinoleic acid, as well as their methyl esters as the substrates. Product distribution was studied by varying the molar ratios of oxidant to substrate.

## RESULTS AND DISCUSSION

As noted previously, aq solutions of ruthenium tetroxide ( $\text{RuO}_4$ ) are unstable at pH  $>7$  (10). When alkaline sodium hypochlorite is used to generate  $\text{RuO}_4$ , the latter rapidly disproportionates to a mixture of ruthenium oxyanions. On the other hand, chlorocarbon solutions of  $\text{RuO}_4$  are reported as being stable for long periods of time at 5 C (12). In the present study, therefore, we carried out the oxidation of the organic substrate with carbon tetrachloride solutions of  $\text{RuO}_4$ . To facilitate the removal of the ruthenium dioxide ( $\text{RuO}_2$ ) formed by reduction, it was necessary



yielded, in addition to the expected products **7a** and **11**, large amounts of heptanoic acid, **12** (Equation IV). The formation of **12** could result from cleavage of the C<sub>11</sub>-C<sub>12</sub> bond of **10a** or by subsequent oxidation of ketoacid **11** by the perruthenate anion. When RuO<sub>4</sub> was used to oxidize the methyl ester **9b** in organic solvent, a similar product mixture was obtained with the exception that, under these so-called neutral conditions, ~20% of the ketoacid **11** decarboxylated to 2-octanone.

Surprisingly, when ruthenate anion, RuO<sub>4</sub><sup>=</sup>, was allowed to react with acid **9a** at a 1:1 stoichiometry, minor amounts (~25%) of the cleavage acids **11**, **7a** and **12** were also formed in addition to the expected ketoacid **10a**. At higher molar ratios of oxidant to substrate, more of the cleavage products **11** and **7a** predominate (>80% yield). The acids **7a** and **11** seemed to form after the formation of 12-ketoleic acid **10a**; therefore, the ruthenate anion may attack the enolate anion of acid **10a** with subsequent cleavage of the C<sub>11,12</sub> and C<sub>9,10</sub> bonds. This result was unexpected because RuO<sub>4</sub><sup>=</sup> did not attack isolated double bonds and smoothly converted 12-hydroxystearate to 12-ketostearate.

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