Oxidation of Unsaturated Fatty Acids with Ruthenium and Osmium Tetroxide[1]

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ABSTRACT AND SUMMARY

The oxidation of the alkali metal salts of oleic and undecylenic acid with ruthenium and osmium tetroxides is reported. The oxidants are used in catalytic amounts in conjunction with an excess of the inexpensive cooxidant sodium hypochlorite. Ruthenium tetroxide cleaves the carbon-carbon double bond of potassium oleate, to give pelargonic and azelaic acids quantitatively, while sodium undecylenate gives sebacic acid. With osmium tetroxide, hydroxylation of the double bond of potassium oleate gives a 95% yield of *erythro*-9,10-dihydroxystearic acid. The osmium tetroxide oxidation of sodium undecylenate results in the formation of 10,11-dihydroxyundecanoic acid and the cleavage product sebacic acid in varying yields.

INTRODUCTION

The oxidation of organic compounds with a carbon tetrachloride solution of ruthenium tetroxide (RuO_4) was first introduced by Djerassi and Engle (1), but only recently have the advantages of this powerful oxidizing agent been recognized (2-7). The use of stoichiometric amounts of ruthenium tetroxide is not necessary because of the reversible interconversion between ruthenium dioxide and ruthenium tetroxide. This interconversion is conveniently carried out by using a catalytic amount of ruthenium dioxide (RuO_2) in conjunction with an oxygen donor, such as sodium metaperiodate or sodium hypochlorite. Both of these oxidants regenerate RuO_4 from the RuO_2 produced during the oxidation of the organic substrate. This reoxidation procedure has been successfully employed for the oxidation of cyclobutanols to cyclobutanones (2), of substituted benzene compounds to alicyclic carboxylic acids (4), and of alkynes to α-diketones (4). The products of alkene oxidation with RuO_4 are reported to be similar to those obtained from ozonolysis. For example, Rylander and Berkowitz (8) reported that RuO_4 oxidation of cyclohexene and 1-octene produced adipaldehyde and heptaldehyde, respectively. In a later study, Wolfe et al. (9) obtained adipic acid in good yield when cyclohexene was oxidized by the RuO_2–sodium hypochlorite reoxidation procedure. We found (10) that this procedure gave good yields of cleavage products from acyclic alkenes only when the oxidations were carried out with added sodium hydroxide and a phase transfer catalyst. In the absence of the added base, chlorinated byproducts were the major reaction products. Whereas ruthenium tetroxide cleaves olefinic bonds, osmium tetroxide (OsO_4) hydroxylates alkenes to vicinal diols (11). A number of reoxidation procedures using catalytic amounts of osmium tetroxide in conjunction with a cooxidant such as metal chlorates and hydrogen peroxide have been developed. However, these procedures frequently result in over oxidation to yield cleavage products (12). Osmium tetroxide and sodium hypochlorite have been used together to a limited extent to hydroxylate olefins (13); however, chlorination accompanied hydroxylation. Neither the RuO_4 nor the OsO_4-sodium hypochlorite reoxidation procedure has been used to oxidize fatty acids. This paper describes our application of the above reactions to the oxidation of monounsaturated fatty acids.

EXPERIMENTAL PROCEDURES

Materials

Oleic acid (98%) and undecylenic acid (97%) were obtained from Applied Science Labs (State College, PA). Ruthenium dioxide ($RuO_2 \cdot H_2O_n$, 53% metal) was purchased from Engelhardt Ind., (Newark, NJ) and osmium tetroxide[2] (99%) was obtained from Eastman Chemical Co. (Rochester, NY). Potassium and sodium salts of the fatty acids were prepared by reacting the fatty acid with an equivalent of alkali metal hydroxide in absolute ethanol. The soaps were recrystallized from ethanol. Sodium hypochlorite solution (Clorox, 5.75% by weight, iodometry) was purchased at a local supermarket. All other reagents were purchased from commercial chemical supply houses and were used as received.

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 x 1/8 in. silanized stainless steel columns packed with 7.5% EGA + 2% H_3PO_4 supported on 90-100 mesh Anakrom ABS. Methyl esters were prepared by reacting the free carboxylic acid with an ether solution (∿3%) of diazomethane.

Procedures

Cleavage of potassium oleate with RuO_4-NaOCl: A solution of potassium oleate (16.0 g, 50 mmole) in water (200 ml) was placed into a 1-liter Morton flask equipped with a mechanical stirrer, addition funnel, and condenser. To this solution was added solid RuO_2 [0.378 g (51%), 1.45 mmole]. The stirred reaction mixture was cooled to 20 C, and then sodium hypochlorite solution (376 ml of 5.75% soln., 290 mmole) containing dissolved NaOH (10.6 g, 265 mmole) was added dropwise over a 20-min period at 20-25 C. The mixture was stirred for an additional 40 min after which the starch-iodide test for hypochlorite ion was negative. The mixture was then filtered through Celite to remove suspended solid RuO_2. The clear filtrate was acidified with conc. HCl to pH 2 and extracted with ether (3 x 100 ml). The combined ether extracts were washed with H_2O, dried over $MgSO_4$, and the solvent removed in vacuo to give the crude oxidation product (19.7 g). The latter product was triturated with petroleum ether (bp 30-60 C), and the insoluble azelaic acid collected by filtration (8.8 g, 94% yield, mp = 98-100 C). The filtrate was then stripped of solvent in vacuo to yield the crude pelargonic acid (8.6 g). Gas liquid chromatography (GLC) of the methyl ester indicated it was mainly methyl pelargonate (94%) containing ∿5% methyl azelate and a trace of methyl stearate (<1%).

The oxidation of sodium undecylenate was conducted in a similar manner. The crude sebacic acid was isolated after

[1]Presented at the AOCS Meeting, New Orleans, April 1976.

[2]Proper precautionary measures should be exercised when handling osmium and ruthenium tetroxide in view of their poisonous nature and strong oxidizing properties.

extraction of the acidified reaction mixture with ether and removal of solvent (9.6 g, 95% yield, mp = 129-133 C).

Hydroxylation of potassium oleate with OsO_4-NaOCl: Into a l-liter round bottom flask was placed a solution of potassium oleate (8.0 g, 25 mmole) in water (100 ml). To this solution was added a solution of OsO_4 in water (20 ml, 1% by weight, 0.725 mmole) which turned the reaction mixture a violet color. The stirred mixture was then cooled to 15 C and sodium hypochlorite solution (65 ml, 5.75%, 50 mmole) containing added NaOH (2 g, 50 mmole) was added dropwise over a period of 1 hr at 15-20 C. The stirring was continued until the starch iodide test for hypochlorite ion was negative (∿45 min) at which time the mixture was acidified with conc. HCl to pH 2. The crude dihydroxystearic acid was filtered, washed with H_2O, and dried in a vacuum oven (8.2 g). Recrystallization from ethanol gave pure *erythro*-9,10-dihydroxystearic acid as white platelets (7.3 g, 92% yield) with mp 128-129 C, lit. mp 131 C (14).

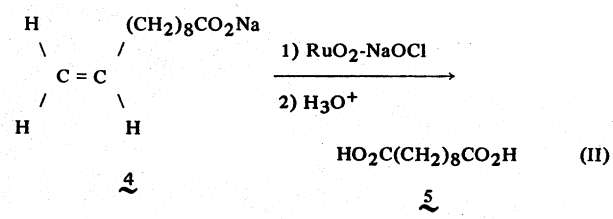
RESULTS AND DISCUSSION

In a previous paper we reported the phase transfer catalyzed ruthenium tetroxide (RuO_4) oxidation of alkenes to carboxylic acids, using the RuO_2-sodium hypochlorite reoxidation procedure (10). Extension of the above two-phase reaction to unsaturated fatty esters proved impractical, since soap formation seriously complicated the reaction procedure. Use of a two-phase system is indicated only when the substrate to be oxidized has a very low solubility in water and the oxidizing agent is more soluble in the aqueous medium. Alkali metal salts of unsaturated fatty acids, however, have a significant solubility in water and can therefore be oxidized conveniently in an aqueous (single phase) medium with the RuO_2-sodium hypochlorite reoxidation procedure (equation I). Initially, potassium oleate, 1, was used rather than the sodium salt, since the former has greater water solubility.

$$\underset{\underset{1}{\sim}}{CH_3(CH_2)_7CH=CH(CH_2)_7CO_2K} \xrightarrow[2)\ H_3O^+]{1)\ RuO_2\text{-}NaOCl} \underset{\underset{2}{\sim}}{CH_3(CH_2)_7CO_2H} + \underset{\underset{3}{\sim}}{HO_2C(CH_2)_7CO_2H} \qquad (I)$$

Ruthenium dioxide, a black granular solid, is insoluble in aqueous solutions of potassium oleate (1). However, upon addition of sodium hypochlorite solution to the suspension, the RuO_2 is immediately oxidized to ruthenium tetroxide (RuO_4) yielding a yellow solution. After a few minutes the reaction mixture turns black-brown in color accompanied by an exotherm. This indicates that oxidation of potassium oleate, 1, has occurred, and that the RuO_4 has been reduced to its lower oxidation state. During the progress of the oxidation of potassium oleate, the addition of sodium hypochlorite was continued and the color of the reaction mixture was maintained at yellow-brown until all of the required NaOCl solution had been added at 20-25 C. The reaction was stopped when the starch-iodide test for sodium hypochlorite was negative. After removal of the precipitated RuO_2 and acidification of the reaction mixture, pelargonic acid 2 and azelaic acid 3 were isolated in nearly quantitative yields. The stoichiometry of this reaction requires 4 moles of NaOCl per mole of potassium oleate, 1. To ensure complete cleavage of 1, a 50% molar excess of sodium hypochlorite was used. The molar ratio of oleate to RuO_2 used in the above experiment was 35:1. This ratio was chosen from results obtained in our study on the oxidation of alkenes (10). In the present work, however, it was found that this ratio could be increased to 100:1, with no decrease in the yield of cleavage products, 2 and 3. The latter experiments, however, required longer reaction times for the complete oxidation of 1. As previously noted (10,15), it was necessary to keep the reaction mixture above pH 10 by adding excess NaOH to the NaOCl solution. More importantly, NaOCl alone or in the presence of added base cannot be used as oxidant, since in the absence of RuO_2 no oxidation of potassium oleate was obtained. An important advantage of this procedure is that the RuO_2 can be recovered and reused for subsequent oxidations. For example, the precipitated RuO_2 was removed at the end of the reaction by filtration through Celite. The finely dispersed black RuO_2 was easily extracted with NaOCl solution from the filter aid. With this procedure only minor losses of RuO_2 were incurred. Subsequent reuse of the recovered RuO_2 gave yields similar to those obtained when fresh RuO_2 was used. Furthermore, it was not necessary to use the potassium salt of oleic acid, since sodium oleate, either preformed or formed in situ, was readily oxidized to pelargonic and azelaic acids. The only difference in these experiments was that initially the sodium salt was not in complete solution.

We also studied the RuO_4 oxidation of sodium undecylenate, 4, using the RuO_2-sodium hypochlorite reoxidation procedure, equation II. The product isolated in >95% yield after workup was sebacic acid, 5. Presumably, formic acid was a coproduct, but it was not isolated from the reaction mixture. The sodium salt 4 was used in this instance, since its water solubility is sufficiently greater. The molar ratio of reactants was the same as that used with potassium oleate, 1, and no attempt was made to maximize the molar ratio of sodium undecylenate to RuO_2.



The hydroxylation of unsaturated fatty acid salts by oxidants in conjunction with a reoxidant, such as potassium permanganate with sodium periodate and osmium tetroxide and sodium chlorate, are well known reactions (12,16). The systems studied to date, however, suffer from several disadvantages including overoxidation of the diol to cleavage products, the necessity to control pH during the course of the reaction, the tedious removal of reduced oxidants, and the use of stoichiometric amounts of expensive cooxidants. Although the reoxidation system osmium tetroxide and sodium hypochlorite has been used to hydroxylate water soluble olefins (13), such as allyl alcohol, this pair of reagents has not been studied with fatty acid soaps. We have now extended the use of this reoxidation procedure to the hydroxylation of potassium oleate 1 to dihydroxystearic acid 6, equation III.

$$\underset{\underset{1}{\sim}}{CH_3(CH_2)_7CH=CH(CH_2)_7CO_2K} \xrightarrow[2)\ H_3O^+]{1)\ OsO_4,NaOCl} \underset{\underset{6}{\sim}}{CH_3(CH_2)_7\underset{\underset{OH}{|}}{CH}-\underset{\underset{OH}{|}}{CH}(CH_2)_7CO_2H} \qquad (III)$$

The addition of OsO_4 (1% in H_2O) to an aqueous solution

of potassium oleate, 1 resulted in the immediate appearance of a violet color, characteristic of a reduced state of osmium. Addition of basic sodium hypochlorite solution to the reaction resulted in the immediate discharge of the violet color, yielding a pink solution. The addition of sodium hypochlorite solution was made over a period of 1 hr, and during this time the reaction temperature was maintained at 15-20 C. At the end of this time any excess NaOCl and OsO_4 were reduced by the addition of sodium bisulfite solution, and the reaction mixture was acidified. The precipitated 9,10-dihydroxystearic acid, 6, was then isolated in 95% yield. The product was determined to be the *erythro* isomer (14). This stereochemical result is consistent with the generally accepted mechanism of hydroxylation by OsO_4 (11). As found with the RuO_2-NaOCl reoxidation procedure, the presence of excess sodium hydroxide was required in order to obtain good yields of dihydroxystearic acid. The hydroxylation reaction could be conducted as well by starting with the sodium salt of oleic acid. No oxidation was observed in the absence of the OsO_4. Extension of this hydroxylation procedure to sodium undecylenate, equation IV, gave less satisfactory results. Repeatedly, overoxidation of the desired diol, 7, to sebacic acid occurred.

$$\underset{\mathbf{2}}{CH_2 = CH(CH_2)_8CO_2Na} \xrightarrow[2)\ H_3O^+]{1)\ OsO_4, NaOCl} \underset{\mathbf{7}}{\begin{matrix} CH_2 & - & CH(CH_2)_8CO_2H \\ | & & | \\ OH & & OH \end{matrix}} + \mathbf{5} \qquad \text{(IV)}$$

We did not find conditions for completely eliminating overoxidation. Our best yields of the desired 10,11=dihydroxyundecanoic acid, 7, were in the range of 50-60%. The rapid overoxidation of 7 to 5 by oxidants has also been noted in other studies (16).