

THE OXIDATION OF CYCLOBUTANOLS AND AROMATIC
RINGS WITH RUTHENIUM TETROXIDE

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The oxidation of organic compounds with ruthenium tetroxide was first reported by Djerassi,¹ who oxidized sulfides to sulfoxides and sulfones, phenanthrene to phenanthraquinone, and found that ether, benzene, and pyridine are oxidized, whereas carbon tetrachloride, chloroform, alkanes, water, ketones, and esters are relatively inert. Rylander² noted the oxidation of secondary alcohols to ketones, primary alcohols to aldehydes and carboxylic acids, ethers to esters, amides to imides, alkenes to aldehydes, aldehydes to acids, and alkylbenzenes, 1-nitronaphthalene, azo compounds, acetylenes, and amines to unidentified products. A useful procedure introduced³ in the oxidation of pyrene to the 4,5- and 1,6-quinones consists in using sodium periodate to reoxidize to the tetroxide ruthenium dioxide formed by the tetroxide-substrate reaction. This procedure was also used by Nakato⁴ who obtained equally good yields in the oxidation of steroidal alcohols using 100%, 10%, or 1 mole % ruthenium tetroxide in the presence of sodium periodate. The strong adsorption of aldehydes and acids on the RuO₂ precipitate reduces yields of these products, and this, together with economy, seems to favor the periodate reoxidation procedure. Although ruthenium tetroxide and ozone usually give similar products in the oxidation of alkenes, only the former is useful in the oxidation of 3-alkylidenegris-2'-enes to gris-3-ones.⁵

We have examined what are probably the most useful applications of the reagent, the oxidation of cyclobutanols to cyclobutanones, and benzene rings to carboxylic acid groups. Neither reaction has been previously reported. Both should be useful in synthesis, and the oxidation of aromatic rings can be an extremely convenient and versatile tool in structural and stereochemical studies.

Our first interest in RuO₄ was concerned with establishing the stereochemistry of a 3-phenylcyclobutanecarboxylic acid sample, which was presumably the cis isomer.** Beard and Burger⁶

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had previously treated the compound with ozone in a fruitless attempt to oxidize the aromatic ring. Our oxidation with RuO_4 gave cis-1,3-cyclobutanedicarboxylic acid, which was identified as the dimethyl ester. Similarly, authentic cis-2-phenylcyclobutanecarboxylic acid was oxidized to cis-1,2-cyclobutanedicarboxylic acid, with retention of configuration.

Although the RuO_4 oxidations of secondary alcohols to ketones have previously been reported,^{2,4} oxidations of cyclobutanol to cyclobutanone have not. Normally such oxidations at a 4-membered ring proceed in yields of 30-40%. Using the NaIO_4 reoxidation procedure and catalytic amounts of RuO_4 , we have oxidized ethyl 3-hydroxycyclobutanecarboxylate to ethyl 3-ketocyclobutanecarboxylate in 78% yield.

The ability of RuO_4 to oxidize aromatic rings was further examined on a preparative scale (using NaIO_4) by the oxidation of p-tert.-butylphenol to pivalic acid, and by the oxidation of phenylcyclohexane to cyclohexanecarboxylic acid. In other experiments primary alcohols have been oxidized to aldehydes in poor to good yields.

Ruthenium tetroxide is conveniently prepared as a CCl_4 solution by stirring either RuCl_3 or RuO_2 with a slight excess of aqueous NaIO_4 and CCl_4 overnight at room temperature. 3-Phenylcyclobutanecarboxylic acid (1 drop) was oxidized with 0.06g. of RuO_4 in 10 ml. of CCl_4 . The precipitated RuO_2 was removed by filtration and washed with methanol. Solvent was removed from the combined organic phases by reduced-pressure distillation, and the residue was dissolved in methanol. One drop of 2N HCl was added and the solution was heated on a steam bath for 2 hours. Removal of the bulk of the methanol followed by analysis on a gas chromatograph--mass spectrometer combination showed the presence of cis-dimethyl cyclobutane-1,3-dicarboxylate with no trace of the trans isomer [retention times and mass spectrum were compared with those of authentic cis and trans ester samples]. The isomeric acid cis-2-phenylcyclobutanecarboxylic acid was oxidized to cis-dimethyl cyclobutane-1,2-dicarboxylate and identified by the same procedures.

Phenylcyclohexane (4.0 g., 0.025 mole) was oxidized in 20 ml. of CCl_4 by addition to a mixture of 32.1 g. (0.15 mole) of NaIO_4 in 250 ml. of water and ca. 3 mg. of RuO_4 in CCl_4 . The mixture was vigorously stirred for 10 days at about 60°, until the yellow color of RuO_4 persisted. Separation of the layers, extraction of the aqueous layer with chloroform, drying with MgSO_4 , and evaporation of the solvent gave 0.60 g. (25%) of crude cyclohexanecarboxylic acid, which was

identified by the infrared spectrum. Similarly, 3.75 g. (0.025 mole) of p-tert-butylphenol was oxidized for several days at room temperature to 0.3 g. (12%) of pivalic acid.

Ethyl 3-hydroxycyclobutanecarboxylate (7.2 g., 0.050 mole) in 25 ml. of CCl_4 , 21.4 g (0.10 mole) of NaIO_4 in 150 ml. of water, and 0.03 g. (0.0002 mole) of RuO_4 in CCl_4 were vigorously stirred overnight. The above work-up procedure and distillation yielded 5.5 g. (78%) of ethyl 3-ketocyclobutanecarboxylate, b.p. 86-90° (0.55 mm.). Other oxidations of alcohols have been carried out similarly, except that 0.1-0.2 mole% of RuO_2 replaced the RuO_4 . Products were identified by g.c. retention times and by infrared spectra. The reactions were: cyclohexanol to cyclohexanone (79%), 1-heptanol to heptaldehyde (14%), benzyl alcohol to benzaldehyde (72%), and 2-phenyl-1-propanol to hydratropaldehyde (48%).

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