学位論文の要旨		
Abstract of Thesis		
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学位論文題目 Title of Thesis (学位論文題目が英語の場合は和訳を付記)

Study on the Reaction of Ozone with Alkenes and Other Organic Molecules (オゾンとアルケンおよびその他の有機分子との反応に関する研究)

## 学位論文の要旨 Abstract of Thesis

Throughout this project, the ozonation of various organic compounds under different conditions has been investigated. The study is divided into two main parts. The first part is concerned with the synthetic study of ozonides via the reaction of ozone with various alkenes under dry conditions. The second part is concerned with the ozone oxidation of the benzylic methylene position.

In the first part, the synthetic study of ozonides, the synthesis of ozonides via the reaction of alkenes and ozone under dry conditions was investigated. After several attempts, it was found that the influx of a pre-dried ozone stream into a dichloromethane solution of the olefinic substrates in the presence of molecular sieve 4Å afforded the corresponding ozonides in good to high yields. The reaction in the absence of a molecular sieve gave either poor or messy results. The synthesis of ozonides under dry conditions was efficient with most of the simple ozonides. The structure of ozonide **76** was investigated and was unambiguously confirmed by XRD analysis.

In addition, the synthetic study of ozonide mediated by molecular sieve under solvent-free conditions was examined. In this study, the alkene substrates were loaded over a roughly ground molecular sieve and exposed to an ozone stream at a low temperature (-78 °C) to give the corresponding ozonides in reasonable yields. The experimental results suggested that the molecular sieve is expected to work as a solid supporter which enhances the affinity of the carbonyl and oxy-carbonyl intermediates to undergo [3+2] cycloaddition over the molecular sieve surface affording the desired ozonides in addition to the typical drying role of the molecular sieve that removes any residual water molecules during the ozonation reaction. The ozonation under the solvent-free protocol is effective, particularly for the multi-substituted alkenes that did not give ozonide derivatives in solutions.

The synthesized ozonides were found to be stable enough to be purified by silica gel column chromatography at room temperature and could be stored at the same temperature for several weeks and stored in the freezer for several months. All the synthesized ozonides and their alkenes' substrates were confirmed through various spectroscopic methods.

The cytotoxicity of some of the stable synthesized ozonides was investigated against HeLa carcinoma cells, and ozonide 74 showed a modest cytotoxicity ( $IC_{50} = 9.81 \ \mu g/ml$ ), compared to adriamycin ( $IC_{50} = 0.47 \ \mu g/ml$ )

reference, against HeLa carcinoma cell lines. Based on the reported biological significance of the peroxides, ozonides are expected to have other pharmacological activities, e.g. anti-malarial.

In the second part, the unexpected oxidation reaction of the benzyl  $CH_2$  position, by ozone stream, to give the corresponding carbonyl products was investigated. In this study, the oxidation of the alkylarenes gave the corresponding ketones in modest to good yields according to the alkylarene structure. On the other hand, the oxidation of the benzylethers to the corresponding esters was examined and the esters have been afforded in reasonable yields. The oxidation of acetal gave the corresponding carbonate in modest yield. The oxidation of alcohols to the acids usually gives unidentified or messy products. The oxidation products were found to be affected by the structure of the substrates. Although the oxidation of organic compounds by ozone is sensitive to the present functional groups, e.g. multiple bonds, the oxidation of other compounds under the metal-free and mild conditions could be accomplished in good yields. Furthermore, the oxidation of benzylethers may represent an alternative benzyl deprotection method since the benzoate can be readily hydrolyzed to alcohols.