Green Chemistry: Phase-Transfer Catalyzed Oxidation of Cholesterol and Related Compounds with Sodium Hypochlorite

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Abstract

Phase transfer catalyzed oxidations of cholesterol and related compounds with sodium hypochlorite in ethyl acetate resulted in good to excellent yields of oxidized products. These reactions are mild, efficient, and safe. The experimental procedures and workups are very convenient. A representative sample of our oxidation results using primary, secondary, and benzylic alcohols as well as some of our recent results on selective oxidation of alcohols using this system will be presented.

Introduction

Oxidation is an important type of reaction in organic synthesis and as such is used in most research laboratories. Commonly used oxidants include nitric acid, which is dangerous and very corrosive, and salts of manganese or chromium, which are highly toxic, mutagenic, cancer suspecting agents, environmentally harmful, and often messy.[1]

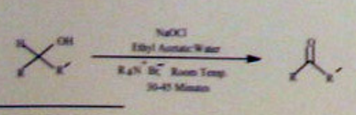
In this paper, we report a safer sodium hypochlorite procedure for the oxidation of alcohols. In addition, our experimental procedures and work-ups are easy, the yields of oxidation products are good to excellent, and the reaction time is short. Thus, our method is even more attractive than the previously described methods for oxidation of alcohols.[1-2] It is hoped that this method will have an immediate application in the way oxidation chemistry reactions, in particular, the oxidation of alcohols are performed.

DISADVANTAGES TO USING CONVENTIONAL OXIDIZING AGENTS

- **Pyridium Chlorochromate (PCC)**
  - Cancer suspect agent
  - Possible mutagent
  - Environmentally harmful
- **Jones Reagent (CrO_3 in aqueous acetone)**
  - Highly toxic, mutagent
  - Cancer suspect agent
  - Environmentally harmful
- **Pyridium Dichromate (PDC)**
  - Cancer suspect agent,
  - Mutagent,
  - Skin irritant
  - Environmentally harmful
- **Collins Reagent (Chromium trioxide-pyridine, $C_6H_6N.CrO_3$)**
  - Cancer suspect agent
  - Mutagent, irritant
  - Environmentally harmful
- **Nitric acid (HNO_3)**
  - Dangerous
  - Very Corrosive

General Reaction

Oxidation of Alcohols *via* NaOCl:



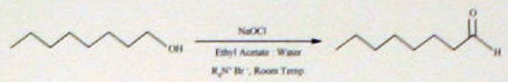
R=Alkyl Group, R'=H
R=R'=Alkyl Groups
R=Aryl Group, R'=H
R=R'=Aryl Groups

ADVANTAGES TO USING NaOCl AS AN OXIDIZING AGENT

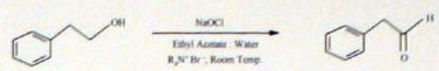
- **Environmentally safe**
- **Inexpensive oxidant**
- **Available in grocery stores as household bleach**
- **Easy experimental procedure**

Results

PHASE TRANSFER CATALYZED OXIDATION OF PRIMARY ALCOHOLS WITH NaOCl

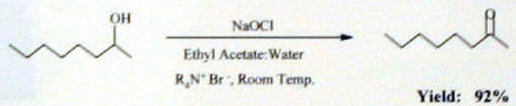


Yield: 86%

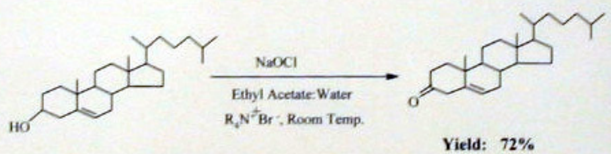


Yield: 73%

PHASE TRANSFER CATALYZED OXIDATION OF SECONDARY ALCOHOLS WITH NaOCl

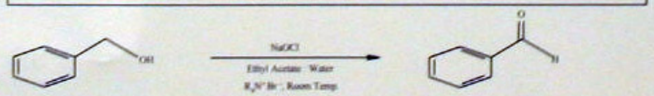


Yield: 92%

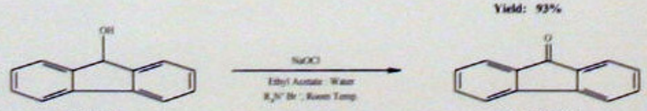


Yield: 72%

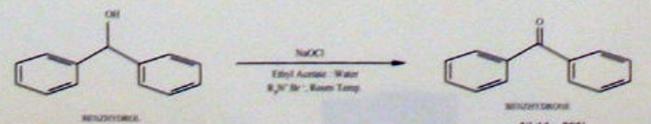
PHASE TRANSFER CATALYZED OXIDATION OF BENZYLIC ALCOHOLS WITH NaOCl



Yield: 93%



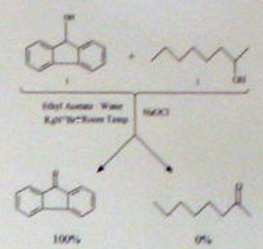
Yield: 92%



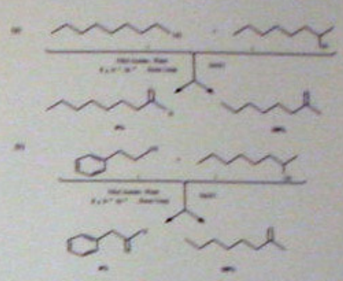
Yield: 80%

Results (Cont.)

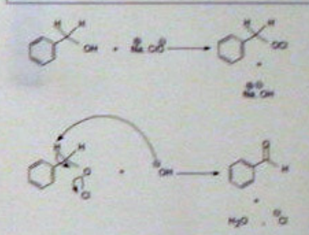
1:1 Competitive Oxidation Reactions: Benzylic vs. Secondary



1:1 Competitive Oxidation Reactions: Primary vs Secondary



MECHANISM OF PHASE TRANSFER CATALYZED OXIDATION OF ALCOHOLS WITH NaOCl



Conclusion

- Phase-transfer catalyzed oxidation of primary, secondary, and benzylic alcohols with sodium hypochlorite gave good to excellent yields of the desired oxidized products.
- Experimental procedure is convenient, and environmentally safe.
- Oxidation is selective:

  Benzylic alcohols > 2° Alcohols > 1° Alcohols

- The capability of sodium hypochlorite as an oxidant in the oxidation of other classes of organic functional groups are currently under investigation.

References

1. Collins, J. C.; Hes, W.W.; Franck, F. J. *Tetrahedron Lett.* **1968,** 3363.; Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975,** 2647.; Corey, E. J.; Schmidt, G. *Tetraderon Lett.* **1979,** 399.; Cheng, Y. S.; Liu, W. L.; Chen, S. *Synthesis*, **1980**
2. Stevens, R.V.; Chapman, K.T.; Stubbs, C. A.; Tam, W.W.; Albizatie, K. F. *Tetrahedron Lett.* **1982,** *23,* 4647.