

Selective and Efficient Oxidation of Aldehydes to Their Corresponding Carboxylic Acids Using H₂O₂/HCl in the Presence of Hydroxylamine Hydrochloride

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A wide variety of aldehydes were efficiently converted to their corresponding carboxylic acids in high yields using H₂O₂/HCl in the presence of hydroxylamine hydrochloride. In addition, selective oxidation of aldehydes in the presence of other functional groups such as hydroxyl group, carbon-carbon double bond and other heteroatoms can be considered a noteworthy advantage of this method.

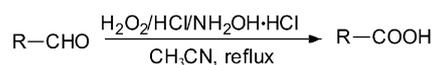
Keywords hydrogen peroxide, oxidation, aldehyde, carboxylic acid, hydroxylamine hydrochloride

Introduction

Development of clean and environmentally acceptable oxidative methodologies is extensively important for organic synthesis both from environmental and economic points of view.^{1–4} Over the past few years, the importance of hydrogen peroxide and its derivatives as oxidizing agents has grown considerably. In contrast to other oxidizing agents, hydrogen peroxide is the most attractive one from an environmental viewpoint. It is an ideal waste-avoiding oxidant, since water is the only theoretical by-product, and is very attractive as an oxidant for liquid-phase reactions, because of its solubility in water and many organic solvents.⁵ Aldehydes are important intermediates in synthetic organic chemistry as well as a significant pollutant in the human environment.^{6–8} The oxidation of aldehydes to the corresponding carboxylic acids is an important synthetic transformation and a variety of conventional oxidants, notably Mn and Cr based ones,^{9–11} which produce abundant amounts of undesirable wastes are reported in the literature to accomplish this transformation. Therefore, in the recent years various improved methodologies using hydrogen peroxide as an oxidant under severe basic conditions¹² or in combination with other reagents such as formic acid, MTO, and other transition metals have been reported in the literature.^{13–18} However, these methods are associated with the drawbacks such as using of toxic and heavy metals, high cost, and lower yields of the desired products.

Herein, we describe the successful use of the H₂O₂/HCl system in the presence of hydroxylamine hydrochloride as a method to oxidize aromatic and aliphatic aldehydes efficiently to their corresponding carboxylic acids in refluxing acetonitrile (Scheme 1).

Scheme 1



Results and discussion

To evaluate the solvent effect, the oxidation of 4-methylbenzaldehyde was carried out under similar reaction conditions using various organic solvents such as toluene, dichloromethane, methanol, and acetonitrile (Table 1). Among the various solvents studied acetonitrile was found to be the best solvent for this transformation.

Table 1 The solvent effect on the oxidation of *p*-tolualdehyde

| $4\text{-MeC}_6\text{H}_4\text{CHO} \xrightarrow[\text{Solvent, reflux}]{\text{H}_2\text{O}_2/\text{HCl}/\text{NH}_2\text{OH}\cdot\text{HCl}} 4\text{-MeC}_6\text{H}_4\text{COOH}$ | | | |
|--|---------------------------------|--------|-----------------------|
| Entry | Solvent ^a | Time/h | Yield ^b /% |
| 1 | CH ₃ CN | 2 | 92 |
| 2 | CH ₂ Cl ₂ | 2 | 40 |
| 3 | PhCH ₃ | 2 | 40 |
| 4 | MeOH | 2 | 60 |

^a V(Aldehyde) : V(H₂O₂) : V(HCl) : V(NH₂OH·HCl) = 1 : 5 : 3 : 2.5. ^b Isolated yields.

It was also observed that the addition of hydrogen peroxide in one portion gave a poor yield of the desired product while its dropwise addition gave the maximum yield of the product in a shorter reaction time.

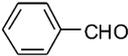
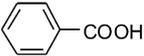
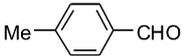
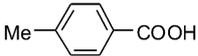
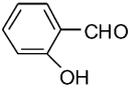
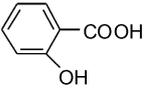
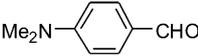
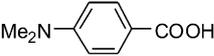
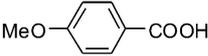
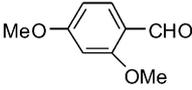
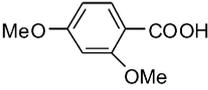
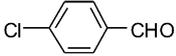
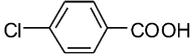
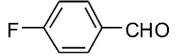
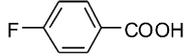
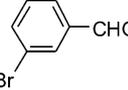
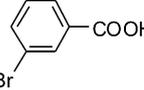
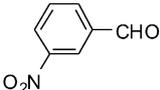
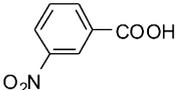
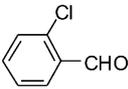
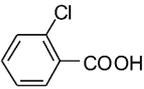
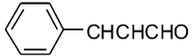
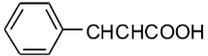
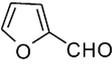
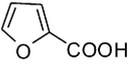
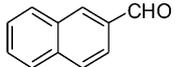
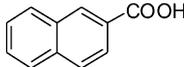
It was noted that in the absence of hydroxylamine hydrochloride, no carboxylic acid could be formed from aldehydes. A volume ratio of 1 : 5 : 3 : 2.5 for alde-

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hyde/H₂O₂/HCl/NH₂OH·HCl was found to be optimum for the oxidation of aldehydes and the results are presented in Table 2. As shown, both aldehydes bearing electron-donating (Entries 2—6) and electron-withdrawing (Entries 7—11) substituents afforded desired benzoic acids in good to excellent yields.

All the aldehydes were selectively and smoothly converted to the corresponding acids in good to excellent yields without any evidence for the formation of chlorinated and other products. The presence of other functional groups such as hydroxyl group, carbon-carbon double bond and other heteroatoms (Table 2 Entries

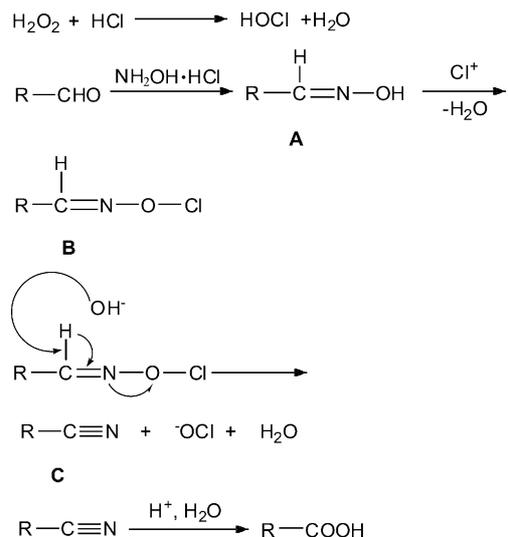
Table 2 Oxidation of aldehydes to their corresponding carboxylic acids using H₂O₂/HCl in the presence of NH₂OH·HCl

| Entry | Substrate | Product ^a | Yield ^b /% | t/h | m.p. ¹⁹ |
|-------|---|---|-----------------------|------|--------------------|
| 1 |  |  | 95 | 1.00 | 120 |
| 2 |  |  | 92 | 2.00 | 176 |
| 3 |  |  | 92 | 1.20 | 158 |
| 4 |  |  | 80 | 2.20 | 241 |
| 5 |  |  | 93 | 1.20 | 182 |
| 6 |  |  | 97 | 1.50 | 105—107 |
| 7 |  |  | 96 | 3.00 | 242 |
| 8 |  |  | 98 | 1.25 | 181 |
| 9 |  |  | 95 | 1.25 | 152 |
| 10 |  |  | 90 | 1.00 | 140 |
| 11 |  |  | 85 | 1.25 | 141 |
| 12 |  |  | 80 | 2.00 | 130 |
| 13 |  |  | 85 | 2.00 | 126—129 |
| 14 |  |  | 95 | 3.00 | 183 |
| 15 | CH ₃ (CH ₂) ₈ CHO | CH ₃ (CH ₂) ₈ COOH | 95 | 3.50 | 31 |
| 16 | CH ₃ CH ₂ CHO | CH ₃ CH ₂ COOH | 92 | 2.00 | Oil |

^aThe products were characterized by comparison of their spectroscopic and physical data with those reported in literature. ^bYields refer to pure isolated products.

3, 4; 12, 13) was found to be inert and aldehydes were selectively converted into acids without affecting these groups. The proposed mechanism for the oxidation of aldehydes to their corresponding carboxylic acids is shown in Scheme 2. The first step involves the formation of aldoxime **A** followed by its reaction with chlorine ion to generate intermediate **B** that subsequently undergoes elimination thermally to produce the nitrile **C** with the liberation of HOCl. Hydrolysis of nitrile leads to the formation of the corresponding carboxylic acid.

Scheme 2 Proposed mechanism for the oxidation of aldehydes



Conclusion

In conclusion, in this study a new and efficient procedure for the oxidation of aromatic and aliphatic aldehydes to their corresponding carboxylic acids is described. The method offers several advantages including excellent yields of the products, safe handling and experimental simplicity, which make it a useful and attractive process for this transformation.

Experimental

General remarks

The aldehydes were purchased from Merck chemical company and used without further purification. All of the products were characterized by comparison of their spectral and physical data with those of authentic samples. Yields refer to isolated products.

General procedure for oxidation of aldehydes to the corresponding carboxylic acids with H₂O₂/HCl in the presence of hydroxylamine hydrochloride

The appropriate aldehyde (1 mmol), hydroxylamine hydrochloride (0.175 g, 2.5 mmol), 30% H₂O₂ (5 mmol), 37% HCl (3 mmol) and acetonitrile (5 mL) in a 50 mL round-bottomed flask equipped with a condenser were

mixed sufficiently. The reaction mixture was refluxed at 80 °C for the time specified in Table 2. The progress of the reaction was monitored by TLC. At the end of the reaction, the excess hydrogen peroxide was deactivated by the addition of saturated aqueous Na₂S₂O₃ (30 mL). The organic layer was extracted with ethyl acetate (3 × 15 mL). After drying the solution and evaporation of ethyl acetate, the residue was purified on a silica gel column using *n*-hexane/ethyl acetate (80 : 20) as eluent. Evaporation of the solvent gave the pure product (Table 2).

Acknowledgements

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References

- Punniyamurthy, T.; Velusamy, S.; Iqbal, J. *Chem. Rev.* **2005**, *105*, 2329.
- Sheldon, R. A.; Kochi, J. K. *Metal Catalyzed Oxidations of Organic Compounds*, Academic Press, New York, **1981**.
- Simandi, L. I. *Catalytic Activation of Dioxygen by Metal Complexes*, Kluwer Academic Publishers, Netherlands, **1992**.
- Clark, J.; Macquarrie, D. *Handbook of Green Chemistry and Technology*, Blackwell, M. A., **2002**.
- Grigoropoulou, G.; Clark, J. H.; Elings, J. A. *Green Chem.* **2003**, *5*, 1.
- Sheldon, R. A.; Kochi, J. K. *Metal-Catalyzed Oxidations of Organic Compounds*, Academic Press, New York, **1981**.
- Maslov, S. A.; Blumberg, E. A. *Russ. Chem. Rev.* **1976**, *45*, 303.
- Harrison, R. M. In *Indoor Air Pollution and Health*, Vol. 10, Royal Society of Chemistry, Cambridge, **1996**, p. 101.
- Hudlicky, M. *Oxidations in Organic Chemistry*, American Chemical Society, Washington, D. C., **1990**, p. 174.
- Hainess, A. H. *Methods for the Oxidation of Organic Compounds*, Academic Press, New York, **1988**, pp. 221, 423.
- Ogliaruso, M. A.; Volfe, J. F. In *Synthesis of Carboxylic Acids Esters and Their Derivatives*, Eds: Patai, S.; Rappoport, Z., Wiley, Chichester, **1991**, p. 357.
- Birkinshaw, J. H.; Raistrick, H.; Ross, D. J.; Stickings, C. E. *J. Biochem. (London)* **1952**, *5*, 610.
- Delcanale, E.; Montanari, F. *J. Org. Chem.* **1986**, *51*, 567.
- Choi, J. K.; Chang, Y. K.; Hong, S. Y. *Tetrahedron Lett.* **1988**, *29*, 1667.
- Dodd, R. H.; Le Hyaric, M. *Synthesis* **1993**, 295.
- Heaney, H.; Newbold, A. J. *Tetrahedron Lett.* **2001**, *42*, 6607.
- Sato, K.; Hyodo, M.; Takagi, J.; Aoki, M.; Noyori, R. *Tetrahedron Lett.* **2000**, *41*, 1439.
- Heaney, H. *Top Curr. Chem.* **1993**, *164*, 1.
- (a) Vogel, A. I. *Vogel's Textbook of Practical Organic Chemistry*, 5th ed., John Wiley and Sons, New York, **1989**.
(b) Buckingham, J.; MacDonald, F. *Dictionary of Organic Compounds*, 6th ed., Chapman and Hall, London, **1996**.

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