

Carboxylic Acids from Primary Alcohols and Aldehydes by a Pyridinium Chlorochromate Catalyzed Oxidation

Mo Hunsen*

Department of Chemistry, Kenyon College, Gambier, OH 43022, USA
Fax +1(740)4275731; E-mail: hunsenm@kenyon.edu.

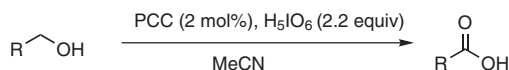
Received 8 February 2005; revised 4 April 2005

Abstract: A facile and quantitative preparation of carboxylic acids by a pyridinium chlorochromate (PCC) catalyzed (2 mol%) oxidation of primary alcohols and aldehydes using 2.2 equivalents and 1.1 equivalents of H_5IO_6 , respectively, in acetonitrile is described here.

Key words: alcohols, aldehydes, oxidation, carboxylic acids, catalysis, pyridinium chlorochromate (PCC), periodic acid

One the most fundamental reactions in synthetic organic chemistry, oxidation, has been the subject of extensive studies.¹ Current methods for direct conversion of primary alcohols to carboxylic acids include $\text{RuCl}_3/\text{NaIO}_4$,² $\text{CrO}_3/\text{H}_2\text{SO}_4$,³ $\text{TEMPO}/\text{NaClO}$,⁴ $\text{Na}_2\text{WO}_4/\text{H}_2\text{O}_2$,⁵ and $\text{TEMPO}/\text{NaClO}_2$ in solution⁶ and solid⁷ phase. Alternatively, Swern oxidation⁸ followed by NaClO_2 ⁹ or $[\text{CH}_3(n\text{-C}_8\text{H}_{17})_3\text{N}]\text{HSO}_4\text{-H}_2\text{O}_2$ ¹⁰ oxidation of the aldehyde could deliver the carboxylic acid. Recently oxidation of (homo-)allylic and (homo-)propargylic alcohols to ketones and carboxylic acids was achieved using $\text{Na}_2\text{Cr}_2\text{O}_7/\text{NaIO}_4$.¹¹ A CrO_3 -catalyzed^{12a} periodic acid oxidation of primary alcohols to carboxylic acids that works very well for electron-poor benzylic alcohols is also reported. However, the CrO_3 -catalyzed oxidation gives complex mixtures when it comes to electron-rich benzylic and homobenzylic alcohols. It also gives lower yields for benzylic alcohols and fails for allylic and propargylic alcohols. In light of the importance of oxidation reaction in the industry, there is still a need for new environmentally friendly methods for direct oxidation of primary alcohols to carboxylic acids especially in the presence of other functional groups.

PCC is one of the reagents of choice for oxidation of primary alcohols to aldehydes and secondary alcohols to ketones.^{13,14} Unlike CrO_3 , PCC has a long shelf life and better solubility in organic solvents. One of the major problems in oxidation reactions using chromium is its carcinogenicity. Recently,¹⁵ we have shown that PCC can be used catalytically to prepare aldehydes and ketones from primary and secondary alcohols, respectively, using periodic acid as the terminal oxidant. This is an environmentally compatible oxidation since periodic acid is a recyclable oxidant and less waste is generated. We hy-



Scheme 1

pothesized that the PCC/periodic acid combination may form chlorochromatoperiodate¹⁶ that is possibly capable of oxidations beyond what is possible by the individual reagents.

To further study the scope and limitations of this PCC-catalyzed oxidation, we have investigated the preparation of carboxylic acids directly from primary alcohols and aldehydes and the results are reported here. Using only a catalytic (2 mol%) amount of pyridinium chlorochromate with 2.2 equivalents and 1.1 equivalents of H_5IO_6 , for alcohols and aldehydes respectively, a clean and quantitative conversion of primary alcohols and aldehydes to carboxylic acids is achieved (Schemes 1 and 2).

As shown in Table 1 various primary alcohols were oxidized with PCC/ H_5IO_6 to give the corresponding acids in quantitative yields. Benzylic (entries 1, 4–7 and 10), aliphatic (entries 2 and 12) as well as homobenzylic (entries 3, 8, 9, and 11) alcohols oxidized smoothly in a short amount of time. Electron-poor (entries 5 and 6) as well as electron-rich (entry 4 and 7) benzyl alcohols were oxidized without any problem. The electron-rich homobenzylic alcohols (entries 3, 8, and 9) were also oxidized effortlessly. It is worth mentioning that unlike the CrO_3 catalyzed^{12a} oxidation, the PCC-catalyzed oxidation works very well for benzylic alcohols as well as for electron-rich benzylic and homobenzylic alcohols. In addition, the naphthalene ring (entries 10 and 11) did not get oxidized under the above-mentioned reaction conditions in contrast to the $\text{CrO}_3/\text{H}_5\text{IO}_6$ ^{12b} oxidation. The aliphatic diol (entry 12) cleanly oxidized to the α,ω -dicarboxylic acid without the formation of the lactone. It is also noteworthy that in a control experiment where the reaction was repeated under the same condition but in the absence of PCC, no oxidation of benzyl alcohol to benzoic acid was observed. Our attempt to oxidize an allylic alcohol (cinnamyl alcohol) was not successful as it gave a complex mixture.

In most of the cases no green coloration was observed as the reaction progresses and no addition of water was required in contrast to the $\text{CrO}_3/\text{H}_5\text{IO}_6$ ^{12a} oxidation. The pyridinium ion would help solubilize the oxidant. We hypothesize that the mechanism may involve hydration of

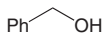

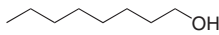
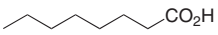
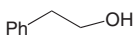
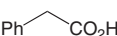
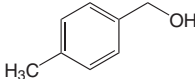
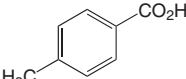
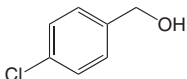
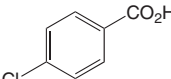
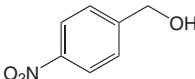
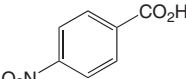
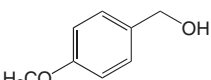
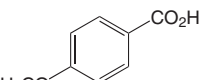
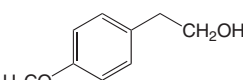
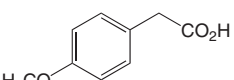
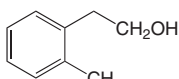
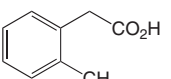
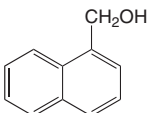
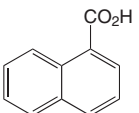
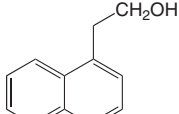
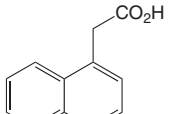
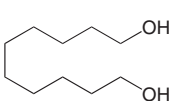
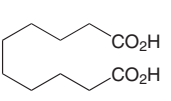
the aldehydes that would form under the reaction condition with H_2O (that forms when H_5IO_6 is converted to HIO_3 and H_2O) to generate the carboxylic acids.

Next, we investigated the oxidation of aldehydes to carboxylic acids (Scheme 2). The oxidation of aldehydes was completed in a shorter time and the clean carboxylic acids were obtained quantitatively. The only difference from the procedure given below for the oxidation of primary alcohols was that the reaction time was 90 minutes and the amount of periodic acid, which was 1.1 equivalents. As shown in Table 2, aliphatic (entries 1, 2, and 10) as well as propargylic (entry 11), and vinyl (entry 12) aldehydes

all oxidized cleanly. Benzaldehyde (entry 3) as well as electron-rich (entry 4 and 7), and electron-poor (entries 5, 6, 8, and 9) benzaldehydes also oxidized effortlessly to deliver the carboxylic acids quantitatively.

We have also studied this oxidation reaction using water as a solvent. Using 2 mol% PCC and a phase transfer catalyst (tetrabutylammonium iodide) in water we have quantitatively oxidized benzyl alcohol and benzaldehyde to benzoic acid (data not shown) with 2.3 equivalents and 1.2 equivalents of periodic acid, respectively. Although the reaction was much slower (48 h), the work up was much easier involving just filtering the water insoluble

Table 1 Oxidation of Primary Alcohols to Carboxylic Acids with PCC/ H_5IO_6 ^a

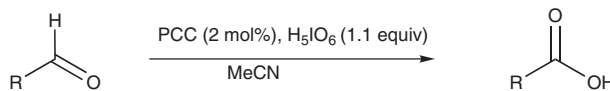
Entry	Substrate	Product	Yield ^b (%)
1			96
2			99
3			99
4			98
5			98
6			99
7			97
8			99
9			98
10			96
11			97
12			98

^a The reactions were conducted in MeCN using H_5IO_6 (2.2 equiv) and PCC (2 mol%). The products were characterized by comparing their NMR spectra with those reported by Aldrich and with authentic samples.

^b NMR spectra of the products showed only the desired products and no unreacted starting material was observed.

carboxylic acid and washing the product with saturated aqueous NaHSO_3 solution and water. Using water as a solvent is a greener process as no organic solvent was used during the reaction and work up. Further investigation on catalytic oxidations in the aqueous phase is in progress and will be reported in due course.

In conclusion, we have shown for the first time that pyridinium chlorochromate efficiently catalyzes the oxidation of primary alcohols directly to carboxylic acids using periodic acid as the co-oxidant. This procedure affords the acids in quantitative yields in a short amount of time. We have also shown that aldehydes can be quantitatively oxidized in a shorter amount of time using only 1.1 equivalents of periodic acid and a catalytic amount of PCC.



Scheme 2

Synthesis of Benzoic acid (Table 1, Entry 1); Typical Procedure

To MeCN (40 mL) was added H_5IO_6 (2.50 g, 11 mmol) and the mixture was stirred vigorously at r.t. for 15 min. Benzyl alcohol (0.54 g, 5 mmol) was then added (in ice-water bath) followed by addition of PCC (22 mg, 2 mol%) in MeCN (2×5 mL) and the reaction mixture was stirred for 3 h. The reaction mixture was then diluted with EtOAc (100 mL) and washed with brine–water (1:1), sat. aq NaHSO_3 solution, and brine, respectively, dried over anhyd Na_2SO_4 and concentrated to give the clean carboxylic acid (0.59 g, 96% yield).

Table 2 Oxidation of Aldehydes to Carboxylic Acids with PCC/ H_5IO_6 ^a

Entry	Substrate	Product	Yield ^b (%)
1			97
2			95
3			98
4			99
5			95 ^c
6			95
7			97
8			96
9			99
10			97
11			96 ^d
12			43 ^e

^a The reactions were conducted in MeCN using H_5IO_6 (1.1 equiv) and PCC (2 mol%) for 1.5 h. The products were characterized by comparing their NMR spectra with those reported by Aldrich and with authentic samples.

^b NMR spectra of the products showed only the desired products unless otherwise noted.

^c Three percent starting material was left unreacted.

^d Two percent starting material was left unreacted.

^e Some of the product is lost during workup due to its water solubility.

Acknowledgment

MH thanks Kenyon College for the generous start up fund.

References

- (1) (a) Hudlicky, M. *Oxidations in Organic Chemistry*, ACS Monograph 186; American Chemical Society: Washington DC, **1990**. (b) Sheldon, R. A.; Kochi, J. K. *Metal-Catalyzed Oxidations of Organic Compounds*; Academic Press: New York, **1981**.
- (2) Carlsen, P. H. J.; Katsuki, T.; Martin, V. S.; Sharpless, K. B. *J. Org. Chem.* **1981**, *46*, 3936.
- (3) (a) Bowden, K.; Heilbron, I. M.; Jones, E. R. H.; Weedon, B. C. L. *J. Chem. Soc.* **1946**, 39. (b) Bowers, A.; Halsall, T. G.; Jones, E. R. H.; Lemin, A. J. *J. Chem. Soc.* **1953**, 2548. (c) Millar, J. G.; Oehlschlager, A. C.; Wong, J. W. *J. Org. Chem.* **1983**, *48*, 4404.
- (4) (a) de Nooy, A. E. J.; Besemer, A. C.; Bekkum, H. V. *Synthesis* **1996**, 1153. (b) Bobbitt, J. M.; Flores, M. C. L. *Heterocycles* **1988**, *27*, 509. (c) Anelli, P. L.; Biffi, C.; Montanari, F.; Quici, S. *J. Org. Chem.* **1987**, *52*, 2559. (d) Miyazawa, T.; Endo, T.; Shiihashi, S.; Okawara, M. *J. Org. Chem.* **1985**, *50*, 1332. (e) Rychnovsky, S. D.; Vaidyanathan, R. *J. Org. Chem.* **1999**, *64*, 310.
- (5) Sato, K.; Aoki, M.; Takagi, J.; Noyori, R. *J. Am. Chem. Soc.* **1997**, *119*, 12386.
- (6) Zhao, M.; Li, J.; Mano, E.; Song, Z.; Tschaen, D. M.; Grabowski, E. J. J.; Reider, P. J. *J. Org. Chem.* **1999**, *64*, 2564.
- (7) Yasuda, K.; Ley, S. V. *J. Chem. Soc., Perkin Trans. 1* **2002**, 1024.
- (8) (a) Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480. (b) Mancuso, A. J.; Brownfan, D. S.; Swern, D. *J. Org. Chem.* **1979**, *44*, 4148. (c) Ireland, R.; Norbeck, D. *J. Org. Chem.* **1985**, *50*, 2198.
- (9) (a) Lindgren, B. O.; Nilsson, T. *Acta Chem. Scand.* **1973**, *27*, 888. (b) Dalcanale, E.; Montanari, F. *J. Org. Chem.* **1986**, *51*, 567.
- (10) Sato, K.; Hyodo, M.; Tagaki, J.; Aoki, M.; Noyori, R. *Tetrahedron Lett.* **2000**, *41*, 1439.
- (11) For oxidation of (homo-)allylic and (homo-)propargylic alcohols to ketones and carboxylic acids see: de Vondervoort, L. S.; Bouttemy, S.; Padrón, J. M.; Bras, J. L.; Muzart, J.; Alsters, P. L. *Synlett* **2002**, 243.
- (12) (a) Zhao, M.; Li, J.; Song, Z.; Desmond, R.; Tschaen, D. M.; Grabowski, E. J. J.; Reider, P. J. *Tetrahedron Lett.* **1998**, *39*, 5323. (b) Yamazaki, S. *Tetrahedron Lett.* **2001**, *42*, 3355.
- (13) (a) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647. (b) Piancatelli, G.; Scettri, A.; D'Auria, M. *Synthesis* **1982**, 245. (c) Eyned Vanden, J. J.; Mayence, A.; Maquestiau, A. *Tetrahedron* **1992**, *48*, 463. (d) Cainelli, G.; Cardillo, G. *Chromium Oxidations in Organic Chemistry*; Springer Verlag: New York, **1984**.
- (14) For a review on chromium-catalyzed oxidations in organic synthesis, see: Muzart, J. *Chem. Rev.* **1992**, *92*, 113.
- (15) Hunsen, M. *Tetrahedron Lett.* **2005**, *46*, 1651.
- (16) For complexation of chromate and periodate, see: Okumura, A.; Kitani, M.; Murata, M. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 1522.