

# Pyridinium chlorochromate catalyzed oxidation of alcohols to aldehydes and ketones with periodic acid

Mo Hunsen\*

Department of Chemistry, Kenyon College, Tomsich Hall, Gambier, OH 43022, USA

Received 10 October 2004; revised 12 January 2005; accepted 17 January 2005

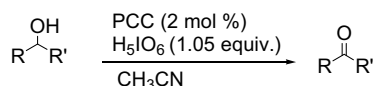
Available online 1 February 2005

**Abstract**—A facile pyridinium chlorochromate (PCC) catalyzed (2 mol%) oxidation of alcohols to ketones and aldehydes using 1.05 equiv of  $H_5IO_6$  in acetonitrile is described here.

© 2005 Elsevier Ltd. All rights reserved.

Oxidation, one the most fundamental reactions in synthetic organic chemistry, has been the subject of numerous studies.<sup>1,2</sup> One of the reagents of choice for oxidation of primary alcohols to aldehydes and secondary alcohols to ketones is pyridinium chlorochromate (PCC).<sup>3</sup> Other methods include the Swern and co-workers<sup>4</sup> and Dess–Martin<sup>5</sup> oxidations. Although PCC oxidations are routinely performed in organic transformations the requirement of at least a stoichiometric amount of PCC to complete the oxidation is a disadvantage due to the high toxicity of chromium reagents (cancer suspect agents). Therefore, new methods for oxidation of alcohols to the corresponding carbonyl compounds and that generate less chromium waste are still needed.

We report herein a facile and efficient oxidation of primary and secondary alcohols to aldehydes and ketones. Using only 2 mol% of pyridinium chlorochromate (PCC) and 1.05 equiv of the co-oxidant,  $H_5IO_6$ , in acetonitrile we have oxidized 1° and 2° alcohols to the corresponding carbonyl compounds (Scheme 1).



Scheme 1.

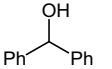
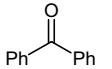
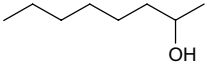
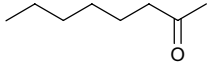
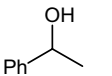
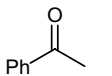
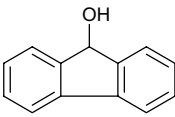
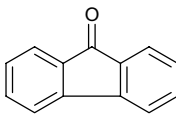
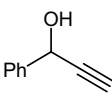
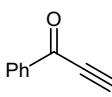
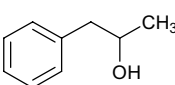
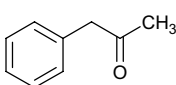
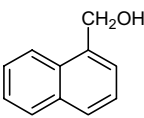
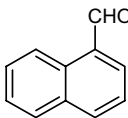
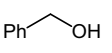
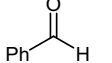
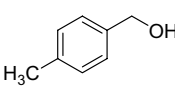
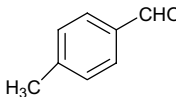
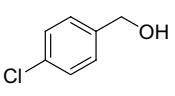
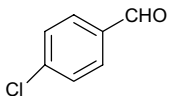
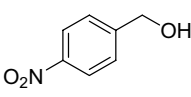
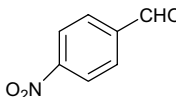
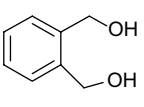
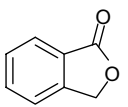
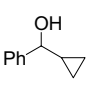
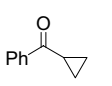
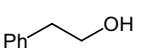
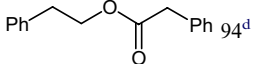
**Keywords:** Oxidation; Alcohols; Catalysis; Pyridinium chlorochromate (PCC); Periodic acid; Aldehydes; Ketones.

\*Tel.: +1 740 427 5091; fax: +1 740 427 5731; e-mail: [hunsenm@kenyon.edu](mailto:hunsenm@kenyon.edu)

Various alcohols were oxidized with PCC/ $H_5IO_6$  to give the corresponding carbonyl compounds mostly in quantitative yields and the results are shown in Table 1. Most of the crude products were quite pure based on their  $^1H$  and  $^{13}C$  NMR spectra. Benzylic 2° alcohols (entries 1, 3–5) oxidize smoothly to give the ketones in a short amount of time. The aliphatic (entry 2) and homobenzylic (entry 6) 2° alcohols also oxidized cleanly to the corresponding ketones with out any problems. It is worth noting that the alkyne (entry 5) and cyclopropyl group (entry 13) were not affected in this oxidation protocol. An attempt to oxidize an allylic alcohol<sup>6</sup> (cinnamyl alcohol) resulted in the formation of a mixture of products (data not shown). Oxidation of 1-naphthalenemethanol (entry 7) gave the aldehyde without oxidation of the naphthalene ring unlike the  $CrO_3/H_5IO_6$  oxidation.<sup>7</sup> Benzyl alcohol (entry 8) as well as its electron poor derivatives (entries 10 and 11) and electron-rich derivative (entry 9) all oxidized effortlessly to give corresponding aldehydes in a very good to excellent yields. An attempt to oxidize a benzylic diol (entry 12) gave the lactone quantitatively and not a dialdehyde. Similarly our attempt to oxidize a non-benzylic primary alcohol, phenethyl alcohol (entry 14) delivered the ester cleanly and not the aldehyde, while oxidation of 1-octanol gave a complex mixture.

We hypothesize that a covalently attached chloride ion may facilitate the regeneration of the catalyst. No addition of water was required in contrast to the  $CrO_3/H_5IO_6$  oxidation. We further hypothesize that the PCC/periodic acid combination may form chlorochromatoperiodate (CCP), possibly a more powerful oxidizing agent than the chlorochromate (Scheme 2) and Cr

**Table 1.** Oxidation of alcohols to aldehydes and ketones with PCC/ $\text{H}_5\text{IO}_6^{\text{a}}$ 

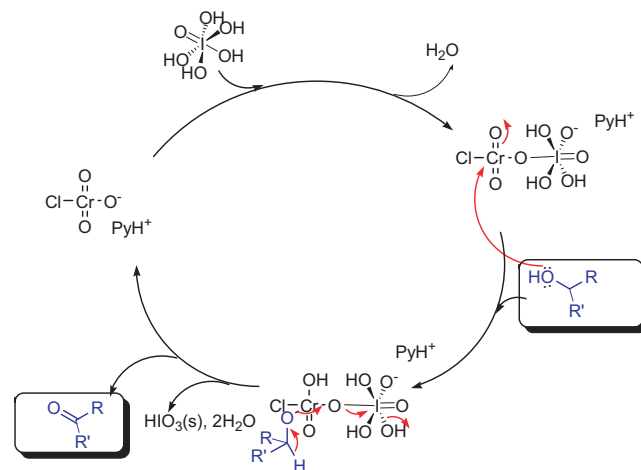
| Entry | Substrate   | Product   | Yield (%) <sup>b</sup> |
|-------|---|---|------------------------|
| 1     |    |    | 97                     |
| 2     |    |    | 93                     |
| 3     |    |    | 97                     |
| 4     |    |    | 98                     |
| 5     |    |    | 89                     |
| 6     |    |    | 98                     |
| 7     |   |   | 98                     |
| 8     |  |  | 72                     |
| 9     |  |  | 96                     |
| 10    |  |  | 89                     |
| 11    |  |  | 71                     |
| 12    |  |  | 99 <sup>c</sup>        |
| 13    |  |  | 96                     |
| 14    |  |  | 94 <sup>d</sup>        |

<sup>a</sup> The reactions were conducted in acetonitrile using 1.05 equiv of  $\text{H}_5\text{IO}_6$  and 2 mol% PCC at 0 °C to rt for 2 h. The products were characterized by comparing their NMR spectra with those reported by Aldrich and with authentic samples.

<sup>b</sup> Isolated yield.

<sup>c</sup> This entry gave the lactone.

<sup>d</sup> This entry gave the ester.

**Scheme 2.**

may retain its +6 oxidation state throughout the reaction until all the periodic acid is consumed.<sup>8</sup> Further investigation on the scope and limitations of the PCC/ $\text{H}_5\text{IO}_6$  reagent is in progress.

The synthesis of benzophenone is representative. To 40 mL of acetonitrile was added 1.19 g (5.15 mmol) of  $\text{H}_5\text{IO}_6$  and stirred vigorously at rt for 15 min. Benzhydrol (0.92 g, 5 mmol) was then added (in ice-bath) followed by addition of 20 mg (1.86 mol%) PCC in 10 mL acetonitrile (in two portions) and the reaction mixture was stirred for 2 h. The reaction mixture was then diluted with 100 mL ethyl acetate and washed with 1:1 brine:water, saturated aq  $\text{Na}_2\text{SO}_3$  solution, and brine, respectively, dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated to give the ketone. The crude product was purified by silica gel flash chromatography (hexanes:ethyl acetate, 8:1) to yield 0.88 g (97%). Most of the crude products were very clean and could be used directly for further applications.

In summary, pyridinium chlorochromate was found to be a facile and efficient catalyst for the oxidation of alcohols to aldehydes and ketones using periodic acid as a cooxidant. This procedure gives the carbonyl compounds in high yields in a short amount of time.

### Acknowledgements

M.H. thanks Kenyon College for the generous start up fund.

### References and notes

- (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: New York 1981.
- For a review on chromium-catalyzed oxidations in organic synthesis, see: Muzart, J. *Chem. Rev.* **1992**, *92*, 113–140.

3. (a) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647; (b) Piancatelli, G.; Scettri, A.; D'Auria, M. *Synthesis* **1982**, 245; (c) Eyned, J. J. Vanden; Mayence, A.; Maquestiau, A. *Tetrahedron* **1992**, *48*, 463; (d) Cainelli, G.; Cardillo, G. *Chromium Oxidations in Organic Chemistry*; Springer: New York, 1984.
4. (a) Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480–2482; (b) Mancuso, A. J.; Brownfan, D. S.; Swern, D. *J. Org. Chem.* **1979**, *44*, 4148–4150; (c) Ireland, R.; Norbeck, D. *J. Org. Chem.* **1985**, *50*, 2198–2200.
5. Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155–4156.
6. (a) Allylic alcohols also gave a mixture of products in a  $[\text{Cr}(\text{acac})_3]/\text{H}_3\text{IO}_6$  oxidation, see: Xu, L.; Trudell, M. L. *Tetrahedron Lett.* **2003**, *44*, 2553–2555; (b) For a recent article on oxidation of (homo-)allylic and (homo-)propargylic alcohols using  $\text{Na}_2\text{Cr}_2\text{O}_7/\text{NaIO}_4/\text{HNO}_3$  or  $\text{H}_2\text{SO}_4$ , see: Vondervoort, L. S. de; Bouttemy, S.; Padrón, J. M.; Bras, J. L.; Muzart, J.; Alsters, P. L. *Synlett* **2002**, 243–246.
7. Zhao, M.; Li, J.; Song, Z.; Desmond, R.; Tschäen, D. M.; Grabowski, E. J. J.; Reider, P. J. *Tetrahedron Lett.* **1998**, *39*, 5323–5326.
8. For complexation of chromate and periodate, see: Okumura, A.; Kitani, M.; Murata, M. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 1522–1530.