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LETTERS

A mild and efficient oxidation of alcohols to aldehydes and ketones with periodic acid catalyzed by chromium(III) acetylacetonate

Liang Xu[b] and Mark L. Trudell[a,*]

[a]*Department of Chemistry, University of New Orleans, New Orleans, LA 70148, USA*
[b]*St Charles Pharmaceuticals, Inc., PO Box 850185, New Orleans, LA 70185, USA*

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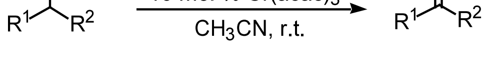
Abstract—Chromium(III) acetylacetonate was found to be an efficient catalyst (10 mol%) for the oxidation of alcohols to aldehydes and ketones with periodic acid (1.5 equiv.) in acetonitrile at room temperature.

The oxidation of alcohols to the corresponding aldehyde or ketone is one of the most important functional group transformations in organic synthesis. Despite the availability of many reagents for this transformation,[1] there still exists a need for mild and efficient methods. Chromium-based reagents play a vital role in organic chemistry as oxidants for alcohols but such transformations are most frequently accomplished by using highly toxic Cr(VI)-based reagents. These transformations typically employ a minimum of a stoichiometric amount of chromium reagent and in some systems require large excesses to obtain complete conversion.[2] Chromium-catalyzed oxidations are therefore of particular interest due to concerns of functional group selectivity and environmental factors.[3]

Chromium(III) acetylacetonate [Cr(acac)$_3$] was first reported to be an active catalyst for oxidation of secondary alcohols to ketones using *t*-BuOOH as co-oxidant. However, high reaction temperatures and long reaction times were required affording only low yields of the corresponding ketones.[4] Herein, we report a mild and efficient oxidation of alcohols to the corresponding aldehydes and ketones with periodic acid catalyzed by Cr(acac)$_3$ in acetonitrile at room temperature (Scheme 1).



Scheme 1.

The results for the oxidation of a variety of alcohols are summarized in Table 1. Benzyl alcohols with either electron donating groups (entries 1–3) or electron withdrawing groups (entry 4) were oxidized smoothly to the corresponding aldehydes in high yields with 1.5 equiv. of periodic acid (H_5IO_6) catalyzed by 10 mol% of Cr(acac)$_3$. As expected, secondary alcohols were oxidized more quickly than primary alcohols. Most oxidations of secondary alcohols were completed within one hour and gave the corresponding ketones cleanly.

The Cr(acac)$_3$/H_5IO_6 oxidation system was tolerant of a variety of other functional groups. The 2-naphthalenemethanol was oxidized to 2-naphthaldehyde in 91% yield (entry 5). Under these conditions the naphthyl ring was not affected even when the reaction mixture was stirred at room temperature for 18 h in the presence of two or more equivalents of periodic acid. This is in contrast to CrO$_3$-catalyzed oxidations in which the aromatic ring has been reported to be easily oxidized to a quinone.[5] In addition, the carbon–carbon triple bond of 1-phenylpropargyl alcohol (entry 9) and the cyclopropyl ring of α-cyclopropyl-benzylalcohol (entry 11) were compatible with the Cr(acac)$_3$/H_5IO_6 system. One limitation of this system appears to be the oxidation of allylic alcohols which gave complex mixtures of by-products. The oxidation of cinnamyl alcohol (entry 12)

Keywords: oxidation; alcohols; periodic acid; chromium(III) acetylacetonate.

* Corresponding author. Tel.: +1-504 280-7337; fax: +1-504-280-6860; e-mail: mtrudell@uno.edu

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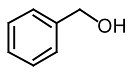
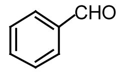
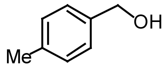
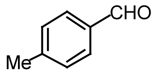
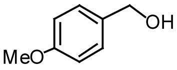
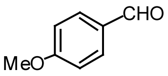
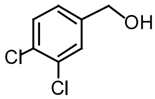
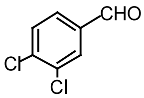
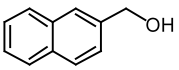
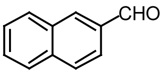
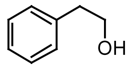
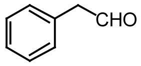
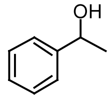
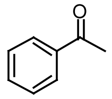
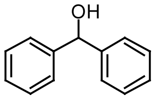
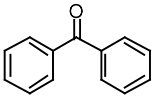
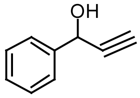
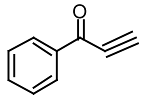
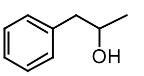
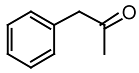
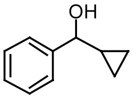
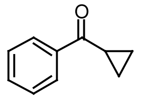
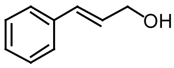
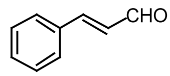
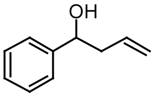
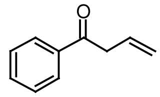
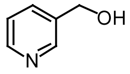
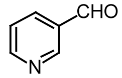
Table 1. Oxidation of alcohols with $Cr(acac)_3/H_5IO_6^a$

Entry	Substrate	H_5IO_6 (equiv.)	$Cr(acac)_3$ (mol%)	Time (h)	Product	Yield[b]
1		1.5	10	3		93
2		1.5	10	4		92
3		1.5	5	1		90
4		1.5	10	4		92
5		2.0	10	18		91
6		1.5	10	5		89
7		1.5	10	1		96
8		1.5	10	2		96
9		1.5	10	1		94
10		1.5	10	1		94
11		1.5	10	1		94
12		1.5	10	1		20
13		1.5	10	1		88[c]
14		3.0	10	6		82

[a] Reactions in CH_3CN at room temperature. [b] Isolated yields.
[c] The solution of $Cr(acac)_3/H_5IO_6$ in CH_3CN was stirred for 15 min prior to addition of the alcohol.

with $Cr(acac)_3/H_5IO_6$ afforded cinnamaldehyde in 20% yield after chromatography. However, the oxidation of homoallylic alcohol, 4-phenyl-1-buten-4-ol afforded the corresponding ketone (entry 13) in 88% yield. In this example a higher yield was obtained if the $Cr(acac)_3/H_5IO_6$ solution was stirred for 15 min prior to addition of the alcohol. It is also noteworthy that none of the corresponding enone that would result from isomerization of the terminal carbon–carbon double bond was observed. Finally, the 3-pyridylcarbinol was oxidized to nicotinaldehyde (entry 14) in 82% yield. The basic nitrogen atom of the pyridine ring did not adversely affect the catalytic activity of the Cr(acac)$_3$/H_5IO_6 system.

As part of an effort to explore the scope of substrate alcohols that could be oxidized with this system several functional groups were identified to be not compatible with the Cr(acac)$_3$/H_5IO_6 system. Alcohols that contained a sulfide or sulfoxide group suffered from competitive oxidation at sulfur to give mixtures of sulfoxides and sulfones.[10] In addition, alcohols that contained silyl ethers (OTMS and OTBS), *N*-*t*-butoxycarbonyl (N-Boc) and phenolic groups gave poor yields or intractable product mixtures.

Based on preliminary studies, Cr(acac)$_3$ appears to be the reagent of choice for this catalytic process. Other Cr(III) substrates, including chromium(III) chloride hexahydrate, chromium(III) acetate hydroxide and chromium(III) oxide, were inferior as catalysts at the same loading concentrations. Although the mechanism of this oxidation is not fully understood at this time, the actual oxidant is probably a Cr(IV), Cr(V) or Cr(VI) species, since neither Cr(acac)$_3$ nor H_5IO_6 independently oxidized benzyl alcohol to benzaldehyde within the typical reaction times. Also the initial addition of Cr(acac)$_3$ to a solution of periodic acid in acetonitrile immediately afforded a precipitate. The precipitate is believed to be formed by the reduction of H_5IO_6 upon oxidation of the Cr(III) complex to a higher oxidation-state chromium species.[6–9] Moreover, the reaction mixtures gradually turned green over time indicating that some of the Cr(III) species failed to turn over to other higher oxidation states. Further studies to elucidate the mechanism are under investigation and will be reported in due course.

Representative experimental procedure: Periodic acid (1.7 g, 7.5 mmol) and Cr(acac)$_3$ (175 mg, 0.50 mmol, purchased from Aldrich Chemical Co. Milwaukee, WI) were added to acetonitrile (30 mL) and stirred at room temperature. *sec*-Phenethyl alcohol (610 mg, 5.0 mmol) was then added and stirring was continued at room temperature for 1 h. The reaction mixture was diluted with ethyl acetate (150 mL), washed, respectively, with water, saturated aqueous Na_2SO_3 solution, brine, and then dried over $MgSO_4$. After removal of the solvent, the residue was purified by silica gel flash chromatography (SiO_2, EtOAc:hexanes, 1:8) to afford acetophenone (580 mg, 96%).

In summary, the Cr(acac)$_3$ was found to be an efficient catalyst for the oxidation of alcohols to aldehydes and ketones by using periodic acid as a co-oxidant. This new procedure is very simple and cleanly affords the desired carbonyl compounds in high yields.

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