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PYRIDINIUM CHLOROCHROMATE. AN EFFICIENT REAGENT FOR OXIDATION OF PRIMARY AND SECONDARY ALCOHOLS TO CARBONYL COMPOUNDS

E. J. Corey and J. William Suggs

Department of Chemistry, Harvard University, Cambridge, Massachusetts 02138, USA

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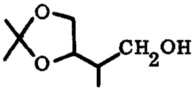
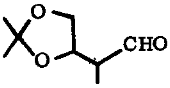
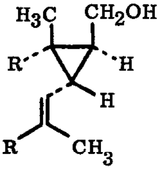
Pyridinium chlorochromate, $C_5H_5NHCrO_3Cl$, a readily available, stable reagent, oxidizes a wide variety of alcohols to carbonyl compounds with high efficiency. It is easily and safely prepared by the addition of pyridine to a solution of chromium trioxide in 6 M HCl followed by filtration to obtain the yellow-orange, air-stable solid. Yields of aldehydes and ketones obtained with 1.5 molar equivalents are typically equal to or greater than those obtained with the Collins reagent[1] (using the customary five- or six-fold excess). On the basis of the results obtained thus far this reagent obviously qualifies as an important addition to the present methodology,[2-7] particularly for moderate to large scale oxidations.

In a typical small scale experiment pyridinium chlorochromate (1.5 mmol) was suspended in methylene chloride (ca. 2 ml), and the alcohol (1 mmol in 0.5 to 1.5 ml of CH_2Cl_2) was rapidly added at room temperature. The solution became briefly homogeneous before depositing the black insoluble reduced reagent. After 1-2 hours the oxidation, followed by either thin layer chromatography or vapor phase chromatography, was complete. The black reaction mixture was diluted with 5 volumes of anhydrous ether, the solvent was decanted, and the black solid was washed twice with ether (causing it to become granular). Product was isolated simply by filtration of the organic extracts through Florisil and evaporation of the solvent at reduced pressure. Use of more polar reaction solvents such as acetonitrile or acetone (in which the reagent is soluble) leads to inconveniently long reaction times. The results of representative experiments are summarized in the table.

The slightly acidic character of the reagent can be modified by buffering the reaction mixture with powdered sodium acetate. By this expedient even such acid-labile groups as tetrahydropyranyl ethers survive. The mildly acidic character of pyridinium chlorochromate has been used to advantage in essentially a one-flask synthesis of pulegone (III) from citronellol (I), as outlined below (72% overall yield).[8] The β,γ-unsaturated ketone II, which was the end product of oxidation, furnished pulegone after exposure to base.

Table[a]

Alcohol	Product[b]	% Yield
1-Decanol	Decanal	92
1,6-Hexanediol	Hexanedial	68
Benzhydrol	Benzophenone	100
4-*t*-Butylcyclohexanol	4-*t*-Butylcyclohexanone	97
Oct-2-yn-1-ol	Oct-2-ynal	84
1-Heptanol[d]	Heptanal	78
		85
 R = $(CH_3)_2C{=}CHCH_2CH_2C(CH_3){=}CHCH_2CH_2$- (Presqualene alcohol)	Presqualene aldehyde	78
Citronellol[e]	Citronellal	82
$HOCH_2CH\overset{cis}{=}CHCH_2OTHP$[e]	$CHOCH\overset{tr}{=}CHCH_2OTHP$	81

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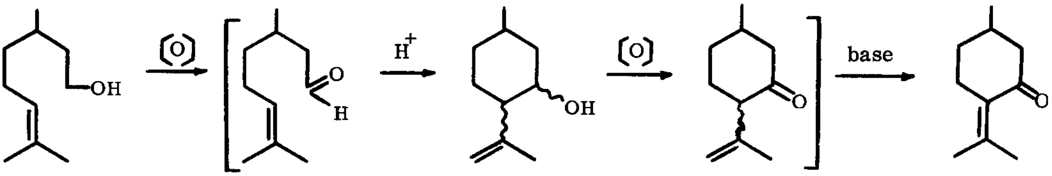
[a] Unless otherwise indicated, oxidation was performed at 25° with 1-2 mmol of alcohol.

[b] Products were characterized by comparison with authentic material (nmr and ir spectra, and thin layer or vapor phase chromatography).

[c] All yields refer to isolated product. [d] Performed with 0.1 mol of alcohol.

[e] Sodium acetate was added to buffer the reaction mixture; 2 equiv. of pyridinium chlorochromate was used.



I II III

The following procedure was used for the preparation of the reagent.

Pyridinium Chlorochromate.[9] To 184 ml of 6 M HCl (1.1 mol) was added 100 g (1 mol) of CrO_3 rapidly with stirring. After 5 min. the homogeneous solution was cooled to 0° and 79.1 g (1 mol) of pyridine was carefully added over 10 min. Recooling to 0° gave a yellow-orange solid which was collected on a sintered glass funnel and dried for 1 hr in vacuo (yield 180.8 g, 84%). The solid is not appreciably hygroscopic and can be stored for extended periods at room temperature without change. Anal.[10] Calcd. for $C_5H_6NO_3ClCr$: C, 27.83; H, 2.81; N, 6.50; Cl, 16.45; Cr, 24.13. Found: C, 27.95; H, 2.83; N, 6.31; Cl, 16.65; Cr, 24.15.

Heptanal was prepared on a 0.1 mole scale so as to facilitate a comparison with the use of Collins reagent as described for the same case on a 0.05 mole scale in Organic Syntheses.[11] Our procedure can be seen as clearly more economical and convenient than the Collins method (which uses 6 times as much solvent and 4 times as much oxidizing agent).

Heptanal. In a 500-ml round-bottomed flask fitted with a reflux condenser was suspended 32.3 g (150 mmol) of pyridinium chlorochromate in 200 ml of anhydrous CH_2Cl_2. 1-Heptanol (11.6 g, 100 mmol) in 20 ml of CH_2Cl_2 was added in one portion to the magnetically stirred solution. After 1.5 hr 200 ml of dry ether was added and the supernatant decanted from the black gum. The insoluble residue was washed thoroughly 3 times with 50-ml portions of anhydrous ether whereupon it became a black granular solid. The combined organic solution was passed through a short pad of Florisil, and the solvent was removed by distillation. Distillation of the residual oil through a short Vigreux column gave 8.87 g (78%) of heptanal, bp_{30} 59-61°; ir and nmr spectra identical with authentic material.

A final example is given to illustrate the procedure used with the acetate-buffered reagent.[12]

Citronellal. Pyridinium chlorochromate (1.23 g, 5.7 mmol) and sodium acetate (0.093 g, 1.14 mmol) were suspended in 5 ml of anhydrous CH_2Cl_2, and citronellol (0.59 g, 3.8 mmol) in 5 ml of CH_2Cl_2 was added in one portion to the magnetically stirred solution. After 2 hr the reaction was worked up as described above to yield 0.523 g of crude citronellal. Column chromatography on silica gel gave 0.479 g (82%) of citronellal, pure by vpc and tlc analysis; ir and nmr spectra identical with authentic material.

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12. This work was assisted financially by a grant from the National Science Foundation.