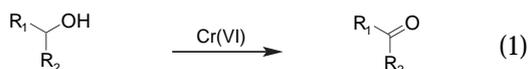


A Facile Oxidation of Alcohols Using Pyridinium Chlorochromate/Silica Gel[†]

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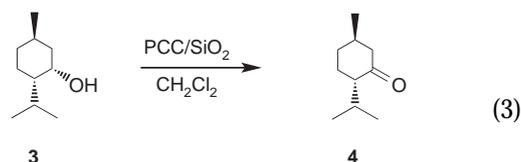
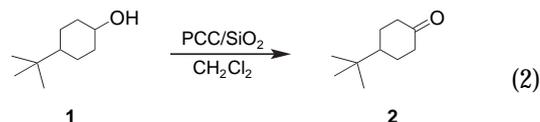
Oxochromium(VI) reagents are the most widely used oxidants in organic synthesis for the conversion of alcohols to carbonyl compounds (1) (eq 1).



Pyridinium chlorochromate (PCC), introduced by Corey and Suggs in 1976 (2), has surpassed the Jones reagent (chromic acid) (3) and the Collins reagent (4) (chromium trioxide/pyridine complex) in frequency of usage in contemporary organic synthesis. When compared with the Jones reagent, PCC is milder and less acidic and promotes fewer side reactions that are due to overoxidation. In contrast with the Collins reagent, PCC is easier and safer to prepare, shelf-stable, and more efficient, since up to a sixfold excess of Collins reagent may be required to effect a complete reaction. Both the PCC and Collins oxidations are characterized by the formation of tarry reduced chromium by-products, which will entrain the desired products and in most cases will complicate an otherwise simple and straightforward purification procedure. The employment of adsorbents in oxochromium(VI)-mediated oxidations of alcohols has led to an improvement in the yields and versatility of these processes in which the removal of the reduced chromium tars is promoted. PCC has been used in conjunction with Celite, molecular sieves, alumina, or silica gel (5–8) to facilitate removal of polymeric reduced chromium by-products or to provide anhydrous conditions that would otherwise lead to unwanted side reactions and decreased yields. In addition, acid-sensitive protecting groups such as tetrahydropyranyl and *tert*-butyldimethylsilyl ethers remain intact and thus respectable yields of protected products are realized, which lends great value during the course of a complex multistep synthesis. Since our first report of the PCC/silica gel reagent system (9), with and without promotion by ultrasound, the method has been used in several synthetic efforts (10–12).

Adapting of the standard PCC protocol for an experiment in the introductory organic chemistry course or advanced organic chemistry laboratory course required streamlining the process so that the experiment may be accomplished in a 3- or 4-hour period. We found that the silica gel modification conveniently facilitated the process so that an undergraduate student could complete the entire procedure in 3 hours. In performing the exercises students work with the standard equipment found in a typical organic chemistry teaching laboratory. The model procedures included with this com-

munication are the oxidation of *cis,trans*-4-*tert*-butylcyclohexanol (1) to 4-*tert*-butylcyclohexanone (2) (eq 2) and *d,l*-menthol (3) to *d,l*-menthone (4) (eq 3).



Inasmuch as there are health and environmental concerns associated with the use of oxochromium(VI) reagents (13–17), several well-documented methods address the disposal of excess reagents and their by-products (18). During the PCC/silica gel-promoted oxidation the reduced chromium by-products are adsorbed on the silica gel, forming a microgranular solid that is easily removed by the subsequent filtration. The celite/silica gel residues are then deposited in the solid waste containers for disposal.¹ While the conversion of *cis,trans*-4-*tert*-butylcyclohexanol to the corresponding ketone gives superior results in terms of an undergraduate protocol, other secondary and primary alcohols (9) will serve as useful substrates in demonstrating the oxidation reaction. In cases involving the oxidation of primary alcohols to aldehydes by oxochromium(VI), yields are often compromised owing to side reactions resulting in the formation of carboxylic acids. When overoxidation of a product aldehyde to a carboxylic acid poses a constant problem during a chromium(VI)-mediated oxidation, the usual alternative is the Swern oxidation (19), which utilizes dimethylsulfoxide/oxalyl chloride. While overoxidation is avoided using Swern conditions, the annoying odor of by-products and troublesome removal of DMSO may make the purification of products lengthy. The anhydrous conditions maintained by a PCC/silica gel oxidation serve to minimize the formation of carboxylic acids as products of the side reaction involving aldehyde hydrate oxidation. Many other oxochromium(VI) amine oxidants have been developed (20) in an effort to simplify the workup and purification of the products, improve selectivity or minimize deleterious side reactions; however, the versatility, cost, and availability of PCC have expanded the visibility of this reagent from complex synthesis to organic chemistry textbooks.

[†] This paper is dedicated to the memory of Professor William G. Dauben, University of California, Berkeley.

Experimental Procedure

Preparation of 4-*tert*-Butylcyclohexanone (2)

A mixture of commercial-grade pyridinium chlorochromate² (2.76 g, 12.8 mmol) and silica gel (2.77 g, 70–230 mesh, E. Merck) was ground to a fine powder using a mortar and pestle.³ The light orange mixture was added to a round-bottom flask (250 mL) and 30 mL of methylene chloride was added. While swirling the orange suspension, 1.0 g (6.4 mmol) of *cis,trans*-4-*tert*-butylcyclohexanol was added in one portion and swirling was continued. The solution darkened (5 min) and within 15 min thin-layer chromatographic (TLC) analysis⁴ indicated a complete reaction. The reaction mixture was diluted with diethyl ether (50 mL) and filtered under aspirator vacuum using a Buchner funnel (63 mm) layered with Celite (1 cm) and silica gel (2.5–3 cm). The filtrate was concentrated under vacuum and the resulting oil was diluted with ether (20 mL), washed with water (2 × 25 mL), and finally washed with saturated aqueous sodium chloride (25 mL). The organic layer was then dried over anhydrous sodium sulfate (2 g) and the drying agent was removed by suction filtration. Concentration of the ether solution under vacuum afforded 4-*tert*-butylcyclohexanone as a yellow oil, which crystallized on standing. Yield: 0.97 g (98%); R_f .25 (hexanes/ethylacetate, 4:1); mp: 46–48 °C (lit. value [21]: 47–50 °C). IR (neat) 2950, 1720, 1360 cm^{-1} ; NMR (CDCl_3 , 300 MHz) δ 0.9 (s, 9H), 1.21 (m, 3H), 2.1 (m, 2H), 2.27 (m, 4H).

Preparation of *d,l*-Menthone (4)

Pyridinium chlorochromate (4.85 g, 22.5 mmol) was ground with silica gel (4.85 g, 70–230 mesh, E. Merck) and placed in a round-bottom flask containing methylene chloride (50 mL). To the resulting orange suspension was added a solution of *d,l*-menthol (3) (2.34 g, 15 mmol) in methylene chloride (10 mL) while stirring at room temperature. After 90 min the resulting dark-brown suspension was diluted with diethyl ether (120 mL) and filtered at reduced pressure through a Buchner funnel layered with Celite (1 cm) and silica gel (2.5–3 cm, 70–230 mesh). The filtrate was concentrated and distilled to give *d,l*-menthone (4). Yield: 2.23 g (97%); R_f .65 (hexanes/ether, 1:1); bp 101–104 °C (5 torr) (lit. value [22]: 98–100 °C [18 torr]). IR (neat) 2950, 1710, 1450, 1200 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 0.85 (d, 3H), 0.9 (d, 3H), 1.0 (d, 3H), 1.35 (m, 2H), 1.9 (m, 2H), 2.05 (m, 3H), 2.15 (m, 1H), 2.35 (dd, 1H).

Notes

1. The reduced chromium residues were suspended in water and the pH was adjusted to 2 with concentrated sulfuric acid. A 50% excess of aqueous sodium bisulfite was added gradually with stirring at room temperature, whereupon a color change to green indicated complete conversion to reduced chromium. These solutions were secured for disposal.

2. Available from the Aldrich Chemical Co.

3. The grinding operation should be conducted in a hood owing to generation of fine dust. Latex or PVC gloves should be worn during the grinding process.

4. The thin-layer chromatographic analyses utilized scored glass-backed E. Merck Kieselgel 60 F_{254} plates (70 × 10 mm). The developed chromatograms were visualized using anisaldehyde/acetic acid/ethanol stain, 2,4-dinitrophenylhydrazine/ethanol stain, or ultraviolet lamp. Visualization by staining was determined by evaporating the solvent from the TLC plate followed by rapidly dipping the plate into the stain and then heating the plate using a heat gun or hot-plate.

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