## **Preliminary communication**

# Pyridinium dichromate-acetic anhydride: a new and highly efficient reagent for the oxidation of alcohols

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Among the reagents for the oxidation of alcohols to the corresponding carbonyl compounds, those derived from chromium(VI)-based oxidants such as pyridinium dichromate<sup>1</sup> (PDC) and pyridinium chlorochromate<sup>2</sup> (PCC) are particularly valuable.

Stensiö and Wachtmeister<sup>3</sup> observed that oxidation with the chromium(VI) oxidepyridine complex was fast when performed in acetic acid. Some years ago, we discovered the activation exerted by acetic anhydride upon oxidations in dichloromethane involving the Collins reagent<sup>4</sup>,  $(C_5H_5N)_2CrO_3$ . From this observation, the chromium(VI) oxidepyridine-acetic anhydride (1:2:1) reagent was developed<sup>5</sup>. Efficient and rapid oxidation of partially protected carbohydrates was achieved in excellent yields, in spite of the electron-deficient nature of the carbon backbone which renders these compounds rather unreactive towards oxidation. The utility of this reagent for the oxidation of selectively protected nucleosides has been demonstrated<sup>6,7</sup>. Generally, 3–4 molar equivalents of oxidant to substrate are required with the chromium(VI) oxide-pyridine-acetic anhydride reagent. It was thought that an acylated chromic ester could be the reactive intermediate, and indirect approaches for generating this species have been examined because it would be too reactive to isolate.

We now report that pyridinium dichromate-acetic anhydride (PDCA) is a particularly promising reagent. Smooth and efficient oxidation of secondary alcohols in dichloromethane was achieved, to give high yields of products, using typically 0.6 molar equivalent of pyridinium dichromate and 3.0 molar equivalents of acetic anhydride. Even the unreactive hydroxyl group of 1,2:5,6-di-O-isopropylidene- $\alpha$ -D-glucofuranose was oxidised efficiently (96% yield). For the oxidation of primary alcohols to aldehydes, typically 0.7 molar equivalent of pyridinium dichromate and 3.0 molar equivalents of acetic anhydride were used. The slight excess of oxidant (as compared to that for secondary alcohols) was used in order to ensure a fast reaction and thus minimise the formation of an ester derived from two substrate molecules. Further oxidation of the resulting aldehyde to carboxylic acid was retarded by N,N-dimethylformamide. Thus, for the oxidation of primary alcohols, dichloromethane-N,N-dimethylformamide (4:1) is used as solvent. This solvent system is also effective for substrates not readily soluble in dichloromethane alone, e.g., nucleoside deriva-



## TABLE I<sup>a</sup>

<sup>a</sup> Oxidations were performed at 40° (0.5-2 h) with 1.0 mmol of alcohol. <sup>b</sup> All yields refer to isolated product. <sup>c</sup> Products were characterised by comparison of n.m.r. and i.r. spectra and optical rotation with literature data.

tives. Oxidation of primary alcohols to carboxylic acids is readily achieved by increasing the amount of oxidant.

In contrast to some other systems examined, no competitive acetylation of substrates was observed with the PDCA reagent. In spite of its reactivity, PDCA appears to be a mild and neutral oxidant. In a forced experiment, methyl 4,6-O-benzylidene-2-O-tosyl- $\alpha$ -Dglucopyranoside was oxidised in refluxing dichloromethane for 16 h without any noticeable amount of decomposition or cleavage of the acid-sensitive benzylidene acetal being observed.

In a typical small-scale oxidation, a solution of the alcohol (1 mmol) in the minimum amount of dichloromethane [or dichloromethane–N,N-dimethylformamide (4:1)] was added to a stirred, freshly prepared mixture of pyridinium dichromate (0.6 or 0.7 mmol) and acetic anhydride (3 mmol) in dichloromethane (3 mL) [or dichloromethane– N,N-dimethylformamide (4:1, 3 mL)]. The mixture was boiled under reflux for 0.5-2 h, and then added to the top of a short column of silica gel in ethyl acetate, with a layer of ethyl acetate on top of the gel in which the chromium compounds were precipitated before elution. The product was thoroughly eluted with ethyl acetate in one fraction. (In the oxidation of primary alcohols, a faster moving minor component, an ester formed from two substrate molecules, was removed in a separate fraction.) The colorless eluate was concentrated to near dryness, and toluene was distilled several times from the residue in order to remove any acetic acid or pyridine. The yields of products are given in Table I.

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