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Selective oxidation of organic compounds using pyridinium-1-sulfonate fluorochromate, $C_5H_5NSO_3H$ [CrO_3F] (*PSFC*)

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Abstract Efficient selective oxidation of primary, secondary, and benzylic alcohols to the corresponding carbonyl compounds by a new chromium oxidizing reagent, pyridinium-1-sulfonate fluorochromate, $C_5H_5NSO_3H$ [CrO_3F] (*PSFC*) is reported. Various cholesterol derivatives were easily converted to related oxocholesterol from allylic oxidation at lower temperature in comparison to other general oxidants. This oxidation procedure is simple and affords good yields.

Keywords Oxidation; Oxidizing reagent; Pyridinium-1-sulfonate fluorochromate; Carbonyl compounds.

Introduction

Oxidation of alcohols to the corresponding aldehydes and ketones is a fundamental reaction that is encountered at all levels of organic synthesis [1–4]. The classical oxidants for this transformation are compounds of hexavalent chromium. However, the most important problem in related oxidation is that overoxidation can occur during the reaction. In an attempt to avoid this difficulty the trend has been to develop the use of complexes and supported reagents. Some of the typical examples are the *Collins* reagent [5], the chromium trioxide-3,5-dimethylpyrazole complex [6], pyridinium chlorochromate [7], pyridinium dichromate [8], 2,2′-bipyridinium chlorochromate [9], and pyridinium fluorochromate [10].

In continuation of our research program dealing with mild oxidation [11], we now report here a mild, reasonable, and chemoselective oxidizing agent for the oxidation of alcohols and bioorganic substrates.

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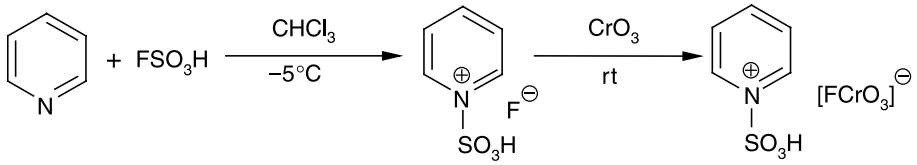
Results and discussion

The synthesis of the reagent *PSFC* is shown in Scheme 1. In the first step, pyridinium sulfonate fluoride can be readily prepared by the reaction of pyridine with fluorosulfonic acid in chloroform. Consequently, *PSFC* is synthesized through the reaction of CrO_3 with aqueous pyridinium-1-sulfonate fluoride. *PSFC* is soluble in dichloromethane, acetonitril, chloroform, and acetone. Its melting point is 79°C. The *pH* value of a 0.01 *M* aqueous solution of *PSFC* is 4.8. Noteworthy, the *pH* of 0.01 *M* solutions of pyridinium fluorochromate, pyridinium chlorochromate, quinolinium fluorochromate, and pyridinium-1-sulfonate chlorochromate, *PSCC* [11], were found to be 2.45, 1.75, 3.35, and 4.2. Accordingly, *PSFC* has a far less acidic character compared to its analogous reagents. Substrate/oxidant molar ratios of 1:1.1 to 1:1.5 for entries 1–15 as well as 1:5 for entries 16, 17 were employed.

In order to evaluate scope and limitations of this reagent as an oxidant, it was applied to several ver-



Scheme 1

Table 1 Oxidation of organic substrates with *PSFC*

Entry	Substrates	Time/min	Products	Yield/%
1	Ethyl alcohol	10	Acetaldehyde	84
2	*p*-Chlorobenzyl alcohol	10	*p*-Chlorobenzaldehyde	72
3	*p*-Methoxybenzyl alcohol	4	*p*-Methoxybenzaldehyde	98
4	Benzyl alcohol	7	Benzaldehyde	93
5	Furfuryl alcohol	11	Furfural	81
6	1-Pentanol	12	1-Pentanal	80
7	Methanol	12	Formaldehyde	82
8	2-Methyl-1-propanol	13	2-Methylpropanal	85
9	Cyclohexanol	13	Cyclohexanone	86
10	1-Butanol	14	1-Butanal	84
11	Ethylene glycol	13	Glyoxal	75
12	Allyl alcohol	9	Acrolein	95
13	Anthracene	10	9,10-Dihydro-9,10-anthracenedione (anthraquinone)	75
14	Phenanthrene	40	9,10-Phenanthrenedione (9,10-phenanthrenequinone)	81
15	Anthralin (1,8-dihyroxy-9-anthrone)	55	1,8-Dihydroxy-9,10-anthracenedione	88
16	Cholesteryl benzoate	120	3-Benzoyloxy-7-oxocholesterol	81
17	Cholesteryl acetate	120	3-Acetoxy-7-oxocholesterol	85

satile substrates. *PSFC* readily oxidizes primary, secondary, allylic, and benzylic alcohols to their corresponding carbonyls. Also, anthralin (1,8-dihydroxy-9-anthrone), cholesteryl benzoate, cholesteryl acetate, and phenanthrene were oxidized to 1,8-dihydroxy-9,10-antracenedione, 3-benzoyloxy-7-oxocholesterol, 3-acetoxy-7-oxocholesterol, and 9,10-phenanthrenedione (9,10-phenanthrenequinone) by *PSFC* (Table 1). Particularly, anthralin derivatives are applied in the treatment of psoriasis and other chronic skin conditions because of its antiseptic, irritant, and keratolytic properties (entry 15) [12]. In yet another example, 7-oxosteroids are known as inhibitors of mammalian sterol biosynthesis (entries 16 and 17) [13, 14].

Oxidation of the above substrates with *PSFC* is similar to the *PSCC* reagent, mechanistically and chemoselectively (Table 1). The fluorine atom in *PSFC* stabilizes the proposed intermediate halochromate anion. Hence, the reaction time of oxidations with *PSFC* is much shorter than for *PSCC* oxidant for similar substrates and in even better yields. In addition, a very facile allylic oxidation of cholesterol derivatives suggests that *PSFC* is also a capable oxidant for this purpose (entries 16 and 17, Table 1).

For the brown residue remaining after the oxidation reaction the magnetic susceptibility was measured to amount 2.88 BM at room temperature. Thus, the oxidation level of the metal is 3.8–4.1. This corroborates that the isolated solid product is $C_5H_5NSO_3H$ [CrO_2F].

In general, higher yields of the desired carbonyl compounds from alcohols and oxocholesterol derivatives from allylic oxidation are obtained at lower temperature and with shorter reaction times in comparison to other general oxidants. In conclusion we demonstrated a convenient and mild method for the oxidation of organic substrates in high yield by using *PSFC*.

Experimental

^{1}H and ^{13}C NMR spectra were recorded using a JEOL JNM-EX90A spectrometer. Chemical shifts (δ) are given in ppm relative to *TMS*. The IR spectra were obtained using a Nicolet FT-IR Magna 550 spectrograph. Melting point was

measured in open capillary tubes with an Electrothermal-9200 melting point apparatus.

Preparation of pyridinium-1-sulfonate fluorochromate, $C_5H_5NSO_3H$ [CrO_3F] (PSFC)

Fluorosulfonic acid (5.43 g) was added drop-wise to a stirred solution of 2.5 g pyridine in 40 cm^3 $CHCl_3$ at 0–5°C (very exothermic reaction). The reaction mixture was stirred at the same temperature for 20 min. Pyridinium-1-sulfonate fluoride was formed as a white solid and separated. This solid (3.8 g) was dissolved in 5 cm^3 H_2O and 2 g CrO_3 were added and the mixture was stirred for 30 min at room temperature whereby an orange-red solution was obtained. The reaction mixture was then cooled in an ice bath and filtered, yield 92%. Mp 79°C; ^{1}H NMR (90 MHz, CH_3CN): $\delta = 8.1$ (m, 2H, *m*-CH), 8.6 (m, 1H, *p*-CH), 8.9 (m, 2H, *o*-CH) ppm; ^{13}C NMR (90 MHz, CH_3CN): $\delta = 131.1$ (2C, *m*-CH), 149.1 (1C, *p*-CH), 183.2 (2C, *o*-CH) ppm; IR (KBr): $\bar{\nu} = 948$ (s, Cr–O), 918 (s, Cr–O), 627 (m, Cr–F), 1150–1250 (s, SO_3) 1450–1650 (originating from the pyridinium sulfonate cation) cm^{-1}; UV(CH_3CN): $\lambda = 329$–430 (Cr–F), 255, 288 (originating from the pyridinium sulfonate cation) nm. Elemental analysis: found: Cr 17.96, F 6.97, C 21.54, N 5.09, H 1.91%, calcd.: Cr 17.65, F 6.81, C 21.50, N 5.01, H 2.15%.

Preparing this reagent with pyridinium-1-sulfonate chloride in the presence of tetramethylammounium fluoride and CrO_3 in dry CH_3CN has the same result but is inferior.

General procedure for the application of PSFC as an oxidizing agent

To a stirred solution of >5 mmol *PSFC* in 10 cm^3 dry CH_3CN, a solution of 5 mmol substrate in 10 cm^3 CH_3CN was added in one portion. Stirring was continued for 30 min to give a yellow solution. The progress of the reaction was monitored by thin layer chromatography (ethyl acetate:*n*-hexane = 2:8). After completion of the reaction, 50 cm^3 dry diethyl ether were added thoroughly shaken. The organic layer was decanted and the residue was washed with 3×20 cm^3 dry diethyl ether. The combined organic layers were passed through a short pad of celite to trap the reduced chromium. The product of oxidation was also washed thoroughly with 3×10 cm^3 diethyl ether. The solvent is removed in a rotavapor under reduced pressure. The known products proved to be identical with the original common compounds by means of spectroscopic measurements.

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