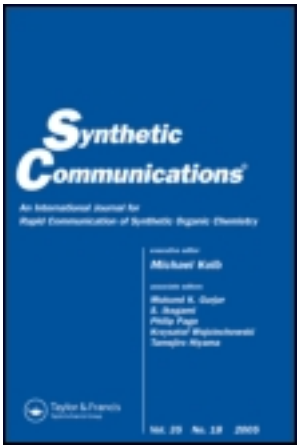

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Synthesis and Application of 2,6-Dicarboxy Pyridinium Fluorochromate as a New Solid-Phase Oxidant

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Synthesis and Application of 2,6-Dicarboxy Pyridinium Fluorochromate as a New Solid-Phase Oxidant

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Abstract: 2,6-Dicarboxypyridinium fluorochromate (2,6-DCPFC) was prepared and used for oxidation of alcohols, phenols, and hydroquinones under solvent-free conditions. This new compound is more efficient and has certain advantages over similar oxidizing agents in terms of the amount of oxidant, lack of solvent, short reaction times, and high yields.

Keywords: Alcohols, 2,6-dicarboxypyridinium fluorochromate, hydroquinones, oxidation, phenols, solvent-free

Organic reactions were found to occur efficiently in the solid state. There is an increasing interest in the use of environmentally benign reagents and conditions[1,2] and particularly solvent-free procedures.[3] Avoiding organic solvents during the reactions in organic synthesis leads to a clean, efficient, and economical technology. In solid-state reactions, workup is considerably simplified, cost is reduced, increased amounts of reactants can be used in the same equipment, and reactivities and sometimes selectivities are enhanced without dilution.[4] Organic solid-state reactions are usually carried out by keeping a mixture of finely powdered reactant and reagent at room temperature. In some cases, these reactions are accelerated by heating, shaking, irradiation with ultrasound or microwave, and grinding of the reaction mixture using a mortar and pestle.[5]

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The oxidation of organic substrates is important in modern organic synthesis. The oxidation of primary and secondary alcohols to the corresponding aldehydes and ketones is a fundamental area that is encountered at all levels of organic synthesis. Therefore, the search for oxidizing agents is of interest to synthetic organic chemists.[6] Numerous reagents and methods have been developed to carry out this important reaction. In particular, there is continued interest in the development of new chromium(VI) reagents for the effective oxidation of alcohols under mild conditions. Of the large number of mild chromium-based oxidizing agents available, many prove impractical when the reactions are performed on a large (mol) scale,[7] although in recent years significant improvements have been achieved by the use of new oxidizing agents, such as pyridinium chlorochromate,[8] pyridinium dichromate,[9] 2,2′-bipyridinium chlorochromate,[10] pyridinium fluorochromate,[11] buthylaminium fluorochromate,[12] quinolinium fluorochromate,[13] piperidinium chlorochromate,[14] tetramethylammonium fluorochromate,[15] and 2,6-dicarboxypyridinium chlorochromate.[16]

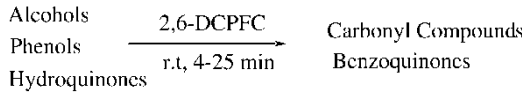
In general, most of the reactions described in the literature are carried out in aliphatic or aromatic hydrocarbons, chlorinated hydrocarbons, diethyl ether, THF, ethyl acetate, acetone, and acetonitrile.

Recently, we have noticed that 2,6-dicarboxypyridinium moiety in chromium(VI) reagents is very important in the oxidation of organic substrates.[16] So, as a part of our program related to developing new oxidation methods, we report here a new, simple, and general procedure that can be used for the oxidative transformation of primary and secondary alcohols, phenols, and hydroquinones into the corresponding carbonyl compounds under solvent-free conditions.

2,6-Dicarboxy pyridinium fluorochromate (2,6-DCPFC) is easily prepared by the reaction of pyridine-2,6-dicarboxylic acid with chromium trioxide in HF. The chromium content of the reagent was determined by atomic absorption. Also, elemental analysis (C, H, N) were performed and the experimental and calculated results are in very good agreement. This reagent is soluble in polar solvents such as acetonitrile and acetone; slightly soluble in THF, chloroform, and dichloromethane; and insoluble in benzene, *n*-hexane, and carbon tetrachloride.

A wide variety of alcohols such as benzylic, allylic, aliphatic, phenols, and hydroquinones have been converted to their corresponding carbonyl compounds using this reagent, in solid phase at room temperature (Scheme 1).

In this method, the oxidant was carefully added to the substrate and the mixture in a mortar was ground at room temperature until TLC analysis

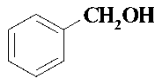
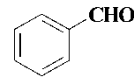
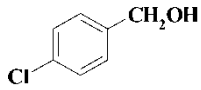
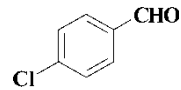
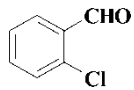
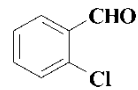
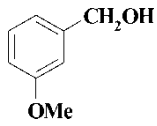
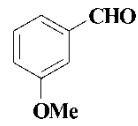
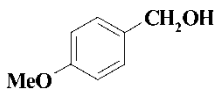
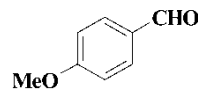
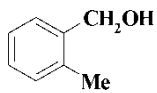
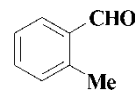


Scheme 1.

indicated a completed reaction. The oxidations were completed within 4–25 min. The residue was then washed with a minimum amount of solvent such as dichloromethane or diethyl ether. Distillation of the solvent gave a product that is of acceptable purity for most purposes. During the reactions, the color of the oxidant changed from orange to violet, providing visual means for ascertaining the progress of reaction. The results, which are shown in Table 1, indicate that the method is generally applicable to a range of alcohols, phenols, and hydroquinones and gives the corresponding oxidized compounds in excellent yields. Although most of the reactions were carried out on a 1–5 mmol scale, to show the applicability of this method in large scale, we have examined the oxidation of benzyl alcohol in 30-mmol scale and obtained the same result.

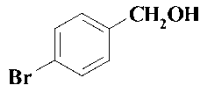
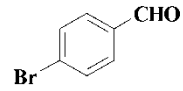
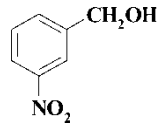
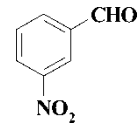
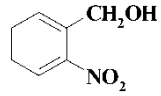
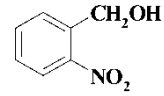
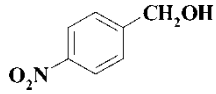
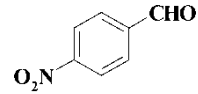
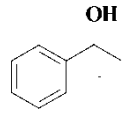
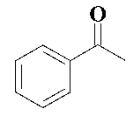
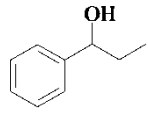
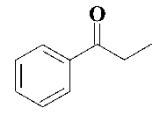
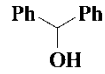
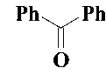
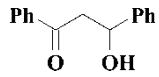
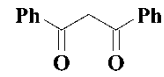
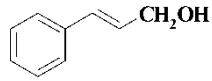
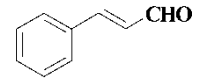
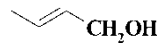
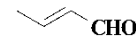
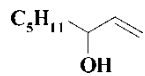
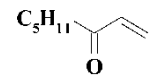
As shown in Table 1, in the case of secondary alcohols, the oxidation requires longer reaction times (entries 11–14). Under the same reaction conditions, primary and secondary allylic alcohols are oxidized to their α, β-unsaturated carbonyl compounds without the cleavage of carbon–carbon double bonds (entries 15–17). Furthermore, hydroquinones (entries 18–19) and

Table 1. Oxidation of alcohols, phenols, and hydroquinones using 2,6-DCPFC under solvent-free conditions at room temperature[a]

Entry	Substrate	Product	Time (min)	Yield[b] (%)
1			4	92
2			6	90
3			6	90
4			6	91
5			5	90
6			5	90

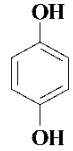
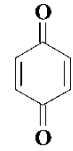
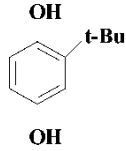
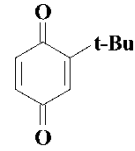
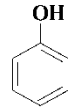
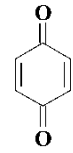
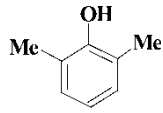
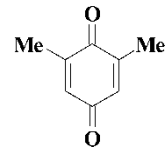
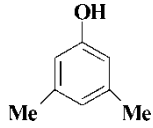
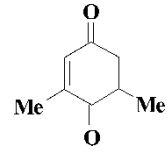
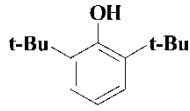
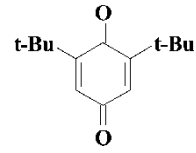
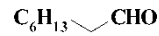
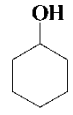
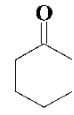
(continued)

Table 1. Continued

Entry	Substrate	Product	Time (min)	Yield[b] (%)
7			7	89
8			7	87
9			10	88
10			10	95
11			10	92
12			10	90
13			13	98
14			25[c]	90
15			15	89
16			15	87
17			10	88

(continued)

Table 1. Continued

Entry	Substrate	Product	Time (min)	Yield[b] (%)
18			4	95
19			7	93
20			4	94
21			5	89
22			10	86
23			8	90
24			15	85
25			20	89
26	**Borneol**	**Camphor**	18	85

[a]Products were confirmed by comparison with authentic samples (IR, ^{1}H NMR, GC).
[b]Yield of isolated pure carbonyl compound.
[c]This reaction was carried out with 2,6-DCPFC/alcohol: (3/1) molar ratio.

phenols (entries 20–23) are oxidized to give excellent yields of the corresponding benzoquinones. Another noteworthy advantage of this reagent is the exclusive oxidation of aliphatic alcohols (entries 24–26).

It is interesting to mention that in the oxidation of alcohols, the overoxidation of products to the corresponding carboxylic acids was not observed at all.

To compare the reactivity of this reagent with and without solvent, the oxidation of benzyl alcohol and hydroquinone as a model substrate was carried out in solvents such as CH_2Cl_2, $CHCl_3$, hexane, THF, and acetonitrile. In most cases, the reaction proceeded slowly and was not completed except in acetonitrile, which gave nearly same reactivity as in solid-phase conditions.

It has also been found that this reagent has certain advantages over similar oxidizing agents in terms of amounts of oxidant, short reaction times required, higher product yields, and especially milder conditions (Table 2).

In conclusion, we have developed an efficient, solvent-free method for the oxidation of alcohols, phenols, and hydroquinones that possesses significant advantages over the existing methods such as simple procedure, easy reaction workup, efficiency, high yields, and lack of solvent.[11,17] These advantages make this reagent a useful addition to the category of reagents used for the oxidation of organic substrates.

Table 2. Oxidation of alcohols by 2,6-DCPFC in comparison with other oxidants

Substrate	Reagent	Ratio of oxidant–substrate	Time	Conditions	Yield (%)	Ref.
$PhCH_2OH$	2,6-	1:1	4 min	Solvent-free, rt	92	—
Cyclohexanol	DCPFC[a]	1:1	20 min		89	
$PhCH_2OH$	4-APCC[b]	1.5:1	2 h	Support on	97	[18]
Cyclohexanol		1.5:1	6 h	silicagel	85	
$PhCH_2OH$	QFC[c]	1.5:1	2 h	Support on	91	[13]
Cyclohexanol		1.5:1	6 h	alumina	72	
$PhCH_2OH$	MnO_2	12.2:1	48 h	Solvent-free, rt	77	[19]
Cyclohexanol		12.2:1	72 h		67	
$PhCH_2OH$	PFC[d]	1:1	45 min	CH_2Cl_2, rt	90	[11]
Cyclohexanol		1:1	210 min		89	
$PhCH_2OH$	IQFC[e]	1:1	60 min	CH_2Cl_2, rt	91	[17]
Cyclohexanol		1:1	240 min		90	
$PhCH_2OH$	PCC[f]	7.5:5	1 h	Support on	82	[20]
Cyclohexanol		Not reported	—	alumina	—	

[a]2,6-Dicarboxy pyridinium fluorochromate.
[b]4-Aminopyridinium chlorochromate.
[c]Quinolinium fluorochromate.
[d]Pyridinium fluorochromate.
[e]Isoquinolinium fluorochromate.
[f]Pyridinium chlorochromate.

EXPERIMENTAL

Preparation of 2,6-Dicarboxypyridinium Fluorochromate (2,6-DCPFC)

To a solution of 2 g (0.02 mol) CrO_3 in 1.0 ml of water in a polyethylene beaker, 1.5 ml (0.03 mol) 40% of hydrofluoric acid was added with stirring. An orange-red solution was obtained. The reaction mixture was then cooled in an ice bath ($-5^{\circ}C$) and 3.342 g (0.02 mol) of pyridine-2,6-dicarboxylic acid was added portionwise, with stirring. When an orange crystalline compound separated out, this was filtered under vacuum, using a polyethylene funnel, washed with petroleum ether (3×10 ml), rapidly dried in a vacuum desicator, and finally stored in a polyethylene bag. The yield of 2,6-DCPFC was found to be 5.28 g (92%). Analysis: $C_7H_6NO_4[CrO_3F]$ calculated: Cr, 18.11%; C, 29.28%; N, 4.88%; H, 2.10%. Found: Cr, 18.09%; C, 29.25%; N, 4.86%; H, 2.03%.

General Procedure for the Conversion of Alcohols, Phenols, and Hydroquinones to the Corresponding Carbonyl Compounds

A mixture of substrate (1 mmol) and oxidizing agent (1 mmol, 0.287 g) in a mortar was ground for the time specified in Table 1. When TLC showed complete disappearance of substrate (alcohol, phenol, or hydroquinone), the residue was then washed with a minimum amount of solvent such as dichloromethane or diethyl ether. Distillation of the solvent gave a product that is of acceptable purity for most purposes. If necessary, products were purified by column chromatography (eluent: hexane–EtOAc). The products were identified by IR, ^{1}H NMR, and GC.

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