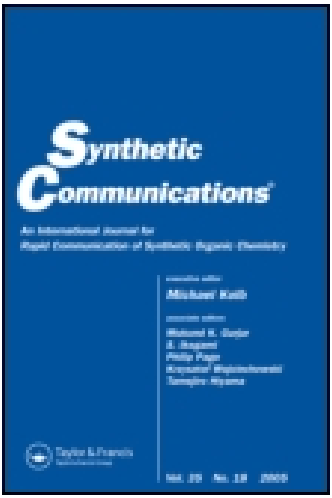

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OXIDATIVE DEPROTECTION OF OXIMES USING PYRIDINIUM FLUOROCHROMATE AND HYDROGEN PEROXIDE

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ABSTRACT

A simple convenient procedure of oxidative deoximation has been developed using pyridinium fluorochromate (PFC), in combination with 30% hydrogen peroxide. The method has been found to be effective for a wide range of aliphatic and aromatic oximes, and may be used for selective cleavage of aldoximes in the presence of ketoximes.

Deprotection of oximes has evoked considerable interest in recent years[1–23] because the functional group transformations involving aldehydes and ketones play an important role in many organic syntheses. Apart from their usefulness as protecting groups of aldehydes and ketones,[24] oximes synthesized from noncarbonyl sources[25–27] may be utilized as precursors of carbonyl compounds. A plethora of oxidative deoximation procedures[1–20] are enumerated in the literature. It is significant that some of the methods are specific for the cleavage of ketoximes[11,16,21] and cannot be used for

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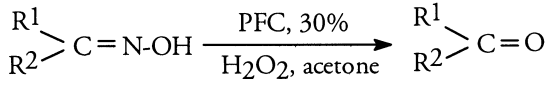
the regeneration of aldehydes from aldoximes. Therefore, efforts have been focused on developing newer efficient general protocols of deoximation involving cheap readily available reagents. In view of the reported formation of strongly oxidizing diperoxo oxochromium (VI) species $[Cr^{VI}O(O_2)_2OH]^{-5}$ on treatment of potassium dichromate with hydrogen peroxide in neutral or slightly acidic conditions, we became interested to examine the scope of the versatile oxochromium (VI) reagent, pyridinium fluorochromate (PFC) in combination with 30% hydrogen peroxide as a reagent for oxidative deoximation in general. Herein we describe a simple method of regeneration of carbonyl compounds with this reagent from a wide range of aldoximes and ketoximes with varying structural and steric parameters. The results of some representative transformations are presented in Table 1.

Regeneration of carbonyl compounds from aldoximes and aliphatic ketoximes (entries 1–7) was very fast. However, some overoxidation to the corresponding carboxylic acids (10–30%) was observed for aldoximes, particularly for those with electron-releasing ortho-/para-substituents (entries 1–6). However, overoxidation was considerably minimized by slow addition of 30% hydrogen peroxide to a mixture of oxime and pyridinium fluorochromate at $-10^{\circ}C$. Aromatic ketoximes and conjugated oximes displayed lower levels of reactivity and required longer reaction time. The optimized reaction conditions for the cleavage of 1 mmol of oxime were determined to be 2 mmol of pyridinium fluorochromate and 0.5 mL of 30% hydrogen peroxide. However, application of the optimized reaction conditions to sterically hindered oximes (e.g., camphor oxime, 1-tetralone oxime) led to slow deprotection. Addition of an extra amount of the reagent (4 mol equivalent of pyridinium fluorochromate, 1 mL 30% hydrogen peroxide) improved the yield and considerably shortened the reaction time (entries 19, 20). Conjugated or unconjugated carbon-carbon double bonds (entries 6, 10, 11), ester (entry 21), and methylenedioxy functions (entry 5) were not affected during the cleavage process.



The deactivating effect of electron-withdrawing group (entry 9) and steric congestion factor (entries 19, 20) were demonstrated clearly. The remarkable reactivity differential of aldoximes and ketoximes is potentially useful for chemoselective deprotection in a situation where both the functions exist. In a model experiment, exposure of an equimolar mixture of *syn*-benzaldehyde oxime and benzophenone oxime to the reagent (2 mol equivalent

Table 1. Oxidation of Oximes with Pyridinium Fluorochromale and 30% Hydrogen Peroxide

Entry	Substrate	Reaction time	Yield[a] of carbonyl compound (%)
1.	*syn*-Benzaldehyde oxime	20 min	74 (83[b])
2.	2-Methoxybenzaldehyde oxime	10 min	64 (86[b])
3.	2,4-Dimethoxybenzaldehyde oxime	10 min	54 (89[b])
4.	4-Dimethylaminobenzaldehyde oxime	10 min	68 (90[b])
5.	3,4-Methylenedioxybenzaldehyde oxime	15 min	70 (80[b])
6.	Citral oxime	15 min	78 (95[b])
7.	Isobutyl methyl ketone oxime	20 min	98
8.	*t*-butyl methyl ketone oxime	1.5 h	97
9.	4-Nitrobenzaldehyde oxime	5 h	89
10.	Cinnamaldehyde oxime	3 h	88
11.	Mesityl oxide oxime	4 h	92
12.	Acetophenone oxime	4 h	92
13.	2-Chloroacetophenone oxime	6 h	94
14.	Benzophenone oxime	5 h	98
15.	Anthrone oxime	6.5 h	96
16.	(a) *Z*-Benzil monoxime	6 h	90
	(b) *E*-Benzil monoxime	4 h	92
17.	Cyclohexanone oxime	3 h	98
18.	Cyclopentanone oxime	2.5 h	96
19.	1-Tetralone oxime	24 h (18 h[c])	78 (92[c])
20.	Camphor oxime	30 h (20 h[c])	88 (96[c])
21.	4-Carbethoxy-3-methyl-2-cyclo-hexen-1-one oxime (Hagemann's ester oxime)	8 h	86

[a]Yields refer to chromatographically isolated pure products; the products were fully characterized by their physical properties (m.p./b.p.), spectral characteristics (IR, ^{1}H NMR), and comparison with authentic samples;
[b]Values in parentheses indicate yields when the reaction was carried out at -10°C;
[c]Typical reaction conditions: To a well-stirred solution of camphor oxime (1.19 mmol) in acetone (10 mL) was added pyridinium fluorochromate (4.8 mmol) in three portions; 30% hydrogen peroxide (1.2 mL) was then added dropwise, maintaining the room temperature, and the reaction mixture was stirred for 20 h at room temperature.

pyridinium fluorochromate, 0.5 mL 30% hydrogen peroxide) at -10° for 20 min led to the isolation of benzaldehyde and unreacted benzophenone oxime only. The slower deoximation of Z-benzil monoxime, in comparison with the *E*-oxime, may be attributed to the engagement of oxime hydroxy

group in hydrogen bonding with suitably disposed *syn*-benzoyl group in the former, thereby preventing the formation of chromate ester intermediate. The necessity of a free hydroxy group for successful deoximation was further confirmed by the complete failure of acetophenone O-methyl oxime to react.

In summary, a simple method of deoximation based on pyridinium fluorochromate and 30% hydrogen peroxide has been developed. This protocol is found to be effective for a wide variety of aliphatic, aromatic, and cyclic oximes and may be used for selective deoximation of aldoximes in the presence of ketoximes by proper choice of reaction conditions.

EXPERIMENTAL

Representative Procedure for the Deoximation with Pyridinium Fluorochromate and 30% Hydrogen Peroxide

To a well-stirred solution of pyridinium fluorochromate (5.97 g, 30 mmol) and benzophenone oxime (2.95 g, 15 mmol) in acetone (30 mL), a 30% hydrogen peroxide solution (7.5 mL) was added dropwise maintaining the temperature to $0^\circ - 10^\circ$C. The reaction was stirred for 5 h (TLC-monitored) and then acetone was slowly removed under reduced pressure. The residue was extracted with ether (3×25 mL) after addition of water (10 mL). The combined ethereal extract was washed successively with 5% sodium sulphite solution (10 mL), 1 N HCl, and water (15 mL). The washed and dried (Na_2SO_4) extract gave crude product after removal of solvent. Chromatography over silica gel (60–120 mesh, 20 g) afforded benzophenone (2.67 g, 98%).

Deprotection of Aldoximes with Pyridinium Fluorochromate and 30% Hydrogen Peroxide Under Controlled Condition

To a well-stirred mixture of *syn*-benzaldehyde oxime (0.48 g, 4 mmol) and pyridinium fluorochromate (1.6 g, 8 mmol) in acetone (20 mL) in a two-neck flask, was added 30% hydrogen peroxide solution (2 mL) dropwise over a period of 10 min, maintaining the temperature at -10°C. After the addition was complete, the mixture was stirred at -10°C for another 10 min. Removal of acetone in vacuo, usual work-up, and chromatographic purification gave benzaldehyde (0.35 g, 83%).

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