Quinolinium fluorochromate: an efficient and selective reagent for the deprotection of semicarbazones under non-aqueous conditions

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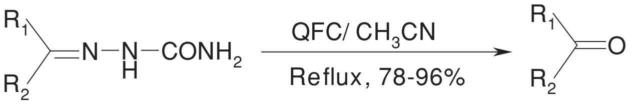
A variety of semicarbazones are transformed to their carbonyl compounds with quinolinium fluorochromate (QFC) in high yields under mild and non-aqueous conditions. Selective deprotection of semicarbazones and oximes in the presence of *p*-nitrophenylhydrazones or 2,4-dinitrophenylhydrazones is noteworthy advantage of this reagent.

Keywords: quinolinium fluorochromate, semicarbazones, oxime, deprotection

Functional group manipulations are of paramount importance to synthetic organic chemists and hence the development of novel transformations still remains of great interest. The conversion of semicarbazones to their carbonyl analogues has received considerable attention. Semicarbazones are preferred over oximes and hydrazones for isolation and purification of carbonyl compounds.[1] Semicarbazones not only are used for the characterisation and purification of carbonyl compounds but also play an important role in the protection of carbonyl compounds, as they are highly crystalline and stable compounds.[2]

Regeneration of the parent carbonyl compounds from semicarbazones is a necessary and important step in the above mentioned applications of semicarbazones. In recent years, many efforts have been made to develop efficient and mild methods for the oxidative cleavage of semicarbazones. Several deprotection methods have some advantages over the classical hydrolysis method.[3-19]

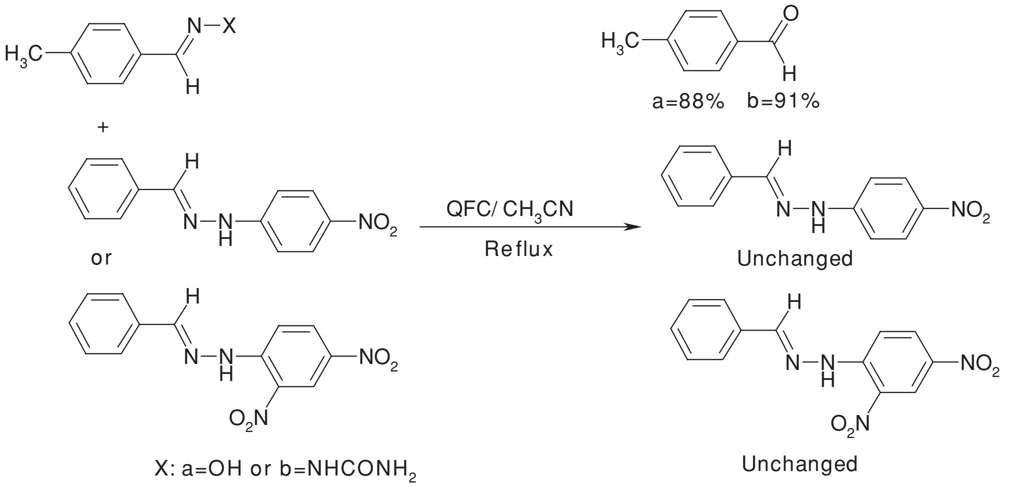
Although some of the reported methods are carried out under mild conditions, most of those for the regeneration of carbonyl compounds from semicarbazones require strong acid media,[20] strong oxidising agents,[21] rare reagents,[22] poor yields,[23] long reaction times[24] and or sometimes tedious workup procedures.[25] Therefore, it was useful to find a good method, and a readily available and safer reagent for the regeneration of carbonyl compounds.



Scheme 1

Recently, we have reported several chromium(VI) based oxidants for oxidative transformations under nonaqueous and or solvent-free conditions.[26] As part of our ongoing programs and interest in the introduction of new application of quinolinium fluorochromate, QFC, we became interested in developing a convenient method for conversion of semicarbazones to the corresponding carbonyl compounds. We now report QFC as an efficient reagent for the deprotection of semicarbazones (Scheme 1). QFC is readily prepared and requires no special handling. Several solvents including acetonitrile, dichloromethane, chloroform, diethylether, tetrahydrofuran and dioxane were investigated during the course of this study; the best results were achieved using acetonitrile. As shown in Table 1, when a variety of semicarbazones were reacted with QFC in refluxing acetonitrile, the corresponding carbonyl analogues were obtained in good to excellent yields.

The reaction seems quite general. The semicarbazones of not only aromatic ketones and aldehydes but also aliphatic and cyclic ketones and aldehydes react with QFC smoothly to give the corresponding carbonyl compounds. When we treated α,β-unsaturated semicarbazone derivatives and *o*-hydroxy-



Scheme 1

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Table 1 Deprotection of semicarbazones to carbonyl compounds

Entry	Substrate	Time/h	Product [a]	Yield [b]
1	$C_6H_5CH=NNHCONH_2$	2	C_6H_5CHO	92
2	p-$NO_2C_6H_4CH=NNHCONH_2$	4	p-$NO_2C_6H_4CHO$	86
3	o-$HOC_6H_4CH=NNHCONH_2$	4	o-HOC_6H_4CHO	92
4	$CH_3CH=CHCH=NNHCONH_2$	1.5	$CH_3CH=CHCHO$	94
5	$C_6\ H_5C(CH_2CH_3)=NNHCONH_2$	3.5	$C_6H_5CO(CH_2\ CH_3)$	78
6	m-$CH_3OC_6H_4CH=NNHCONH_2$	3	m-$CH_3OC_6H_4CHO$	93
7	$(C_6H_5)_2C=NNHCONH_2$	5	$(C_6H_5)_2CO$	83
8	m-$NO_2C_6H_4CH=NNHCONH_2$	3	m-$NO_2C_6H_4CHO$	82
9	p-$BrC_6H_4CH=NNHCONH_2$	2.5	p-BrC_6H_4CHO	94
10	p-$CH_3OC_6H_4CH=NNHCONH_2$	2.5	p-$CH_3OC_6H_4CHO$	94
11	p-$CH_3C_6H_4CH=NNHCONH_2$	2	p-$CH_3C_6H_4CHO$	91
12	$C_6H_5CH=CHCH=NNHCONH_2$	1.5	$C_6H_5CH=CHCHO$	96
13	$C_6H_5C(CH_3)=NNHCONH_2$	3.5	$C_6H_5CO(CH_3)$	83
14	Cyclohexanone semicarbazone	3	Cyclohexanone	90
15	Furfuryl semicarbazone	2.5	Furfural	91
16	(+) Camphor semicarbazone	3	(+) Camphor	88

[a] Products were confirmed by comparison with authentic samples (IR,^{1}H NMR,TLC).

[b] Yield of isolated pure carbonyl compound.

benzaldehyde semicarbazone, only the C=N bond was selectively oxidised to the corresponding carbonyl compounds, and the reagent was ineffective in oxidising hydroxyl group and carbon–carbon double bond (Table 1, entries 3, 4 and 12).

A noteworthy advantage of the reagent is the exclusive oxidation of semicarbazones and oximes irrespective of the presence of 4-nitrophenylhydrazones or 2,4-dinitrophenyl-hydrazones. When mixtures of 4-methylbenzaldehyde semicarbazone or 4-methylbenzaldehyde oxime and benzaldehyde 4-nitrophenylhydrazone or benzaldehyde 2,4-dinitrophenylhydrazone were treated with QFC, only the semicarbazone or oxime were selectively oxidised to the corresponding carbonyl compound and 4-nitrophenylhydrazone or 2,4-dinitrophenylhydrazone remained unchanged (Scheme 2). Such a selectivity has not been reported with other reagents.[19,22,24] This is a noteworthy feature of the above protocol and represents a useful practical achievement in such deprotection.

This work demonstrates a new, useful, mild and selective method for deprotection of semicarbazones. The advantages include high yields, short reaction times, easily prepared, inexpensive and crystalline solid reagent and simple workup procedure.

Experimental

IR spectra were determined on a SP–1100, P-UV–Com instrument. ^{1}HNMR spectra were recorded with a EM 360 A (60 MHz) spectrometer. Solvent was freshly distilled. Semicarbazones were prepared according to the described procedure.[27] QFC was prepared according to the literature.[28]

General procedure for the deprotection of semicarbazones to carbonyl compound

To a stirred solution of semicarbazones (1mmol) in acetonitrile were added solid QFC (3mmol) portions in 2–5 minutes. The reaction mixture was refluxed for 1.5–5 h. The progress of the reaction was monitored by TLC (eluent: hexane/ethyl acetate 8:2). After the reaction was completed the mixture was filtered, then the solid material was washed with acetonitrile several times. The combined organic phase was removed in vacuum to afford the crude product, which was purified by column chromatography on silica gel eluted with hexane/ethyl acetate (8:2). Pure compounds were obtained in 78–96% yields (Table 1).

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