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2,6-Dicarboxypyridinium Chlorochromate. An Efficient and Selective Reagent for the Mild Deprotection of Acetals, Thioacetals, and 1,1-Diacetates to Carbonyl Compounds

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Summary. 2,6-Dicarboxypyridinium chlorochromate (2,6-*DCPCC*) was found to be an efficient reagent for the conversion of acetals, thioacetals, and 1,1-diacetates to their corresponding carbonyl compounds under neutral and anhydrous conditions in good to excellent yields. Selective deprotection of acetals or 1,1-diacetates in the presence of thioacetals at room temperature is also observed with this reagent.

Keywords. 2,6-*DCPCC*; Deprotection; Acetals; Thioacetals; 1,1-Diacetates.

Introduction

The protection of carbonyl compounds as their acetals and ketals has found wide application in multistep syntheses [1]. In recent years, several reagents have been used for the conversion of acetals and ketals into carbonyl compounds such as phosphorous triiodide [2a], titanium(IV) chloride [2b], bismuth nitrate [2c], cerium(III) chloride [2d], oxone [2e], and decaborane [2f]. However, some of the reported methods suffer from one or more disadvantages, such as long reaction times, low yields, and tedious work-ups.

Being stable under both acidic and basic conditions, the dithioacetal group is suitable as a protecting group of carbonyl compounds [1a, 1b]. In addition to carbonyl protection, they behave as masked acyl anions [3] in carbon–carbon bond forming reactions. A number of methods for dethioacetalization, such as clay supported ammonium nitrate (clayan) [4a], zirconium sulfonyl phosphonate [4b],

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hv/pyrylium/O_2 [4c], isoamyl nitrite [4d], diacetoxyiodobenzene [4e], $(CF_3CO_2)_2IPh$ [4f], tetrabutyl ammonium tribromide [4g], and $FeCl_3$ [4h] have been described. However, some major disadvantages are low chemoselectivity, stoichiometric use of expensive reagents, the presence of a strong *Lewis* acid, and necessity for an aqueous solvent.

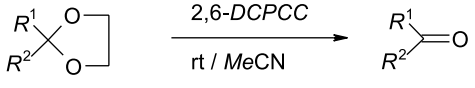
The formation of diacetyl acetals constitutes one of the simplest methods to derivatize the aldehyde moiety [1a]. These compounds are stable to oxidants [5], easily prepared [6], and they are starting materials for *Diels-Alder* reactions [7]. A number of methods have been documented for the conversion of 1,1-diacetates to corresponding aldehydes. The following methods have been used: alcoholic sulfuric [8a] or hydrochloric acid [8b], sodium hydroxide or potassium carbonate in aqueous *THF* [5], boron triiodide *N*,*N*-diethylaniline complex [8c], ceric ammonium nitrate coated on silicagel in dichloromethane [8d], neutral alumina under microwave irradiation [8e], potassium phenoxides [8f], montmorillonite K10 [8g] and KSF [8h] under microwave irradiation, montmorillonite K10 and KSF in refluxing dichloromethane [8i], expensive graphite [8j], scandium triflate [8k], bismuth(III) chloride [8l], envirocoat EPZG under microwave irradiation [8m], CBr_4 in refluxing acetonitrile [8n], and zirconium sulfophenyl phosphonate [8o].

Recently, we have introduced 2,6-dicarboxypyridinium chlorochromate (2,6-*DCPCC*) as an efficient reagent for oxidation of alcohols, trimethylsilyl ethers, *THP* ethers, and oximes to the corresponding carbonyl compounds under non-aqueous conditions [9]. We now report a new and convenient method for the deprotection of acetals, thioacetals, and 1,1-diacetates to carbonyl compounds in high yields.

Results and Discussion

A series of acetals and ketals dissolved in acetonitrile were deprotected with 2,6-*DCPCC* (Scheme 1) [10]. The results shown in Table 1 indicate that the reaction was successful for a variety of acetals of aromatic aldehydes (entries 1a–5a) and ketals of aromatic (entries 6a–9a) and aliphatic ketones (entries 10a–11a). It is noteworthy that, unlike other methods, the major drawback of over-oxidation of the aldehydes to their carboxylic acids was not observed.

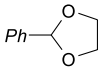
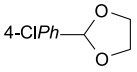
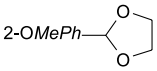
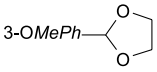
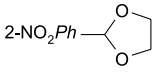
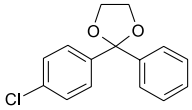
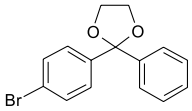
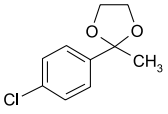
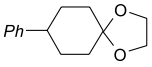
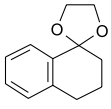
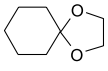
Some representative thio derivatives of aldehydes and ketones were readily deprotected into their parent carbonyl compounds in good yields in acetonitrile (Scheme 2) [11]. Although acetals underwent deprotection at room temperature in less than 30 min, the deprotection of thioacetals was relatively slow and proceeded in refluxing acetonitrile only. The reaction is general for propanediyl *S*,*S*-acetals of aliphatic, araliphatic, and aromatic carbonyl compounds (Table 2).



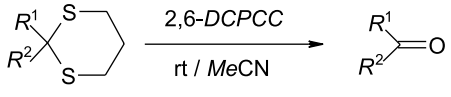
R^1, R^2 = alkyl, aryl, or H

Scheme 1

Table 1. Deprotection of acetals with 2,6-*DCPCC*[a]

Entry	Substrate	Time/min	Yield/%[b]
1a		12	93
2a		15	93
3a		16	94
4a		15	94
5a		16	95
6a		15	95
7a		14	94
8a		25	92
9a		16	90
10a		15	89
11a		28	88

[a] Reactions are performed at room temperature using 1:1 molar ratio of substrates to reagent; [b] yields refer to isolated products

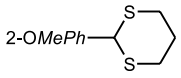
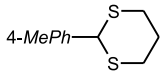
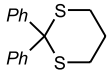
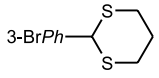
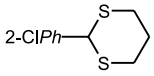
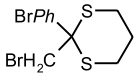
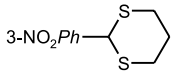
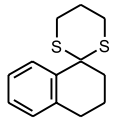


R^1, R^2 = alkyl, aryl, or H

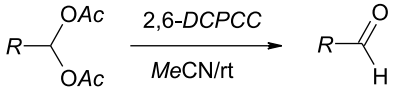
Scheme 2

1,1-Diacetates dissolved in acetonitrile were deprotected using 2,6-*DCPCC* to give the corresponding aldehydes at room temperature (Scheme 3). The results shown in Table 3 indicate that the reaction is successful for a variety of

Table 2. Deprotection of thioacetals with 2,6-*DCPCC*[a]

Entry	Substrate	Time/min	Yield/%[b]
1b		30	95
2b		45	95
3b		88	93
4b		115	90
5b		128	88
6b		120	87
7b		120	60
8b		100	70

[a] Reactions are performed at reflux temperature using 1:2.5 molar ratio of substrates to reagent; [b] yields refer to isolated products



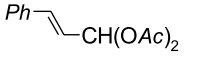
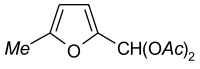
Scheme 3

1,1-diacetates of aromatic (entries 1c–15c) and aliphatic aldehydes (entries 16c–18c). It should be noted that the phenolic acetate function (entry 15c) remains unaffected under these reaction conditions.

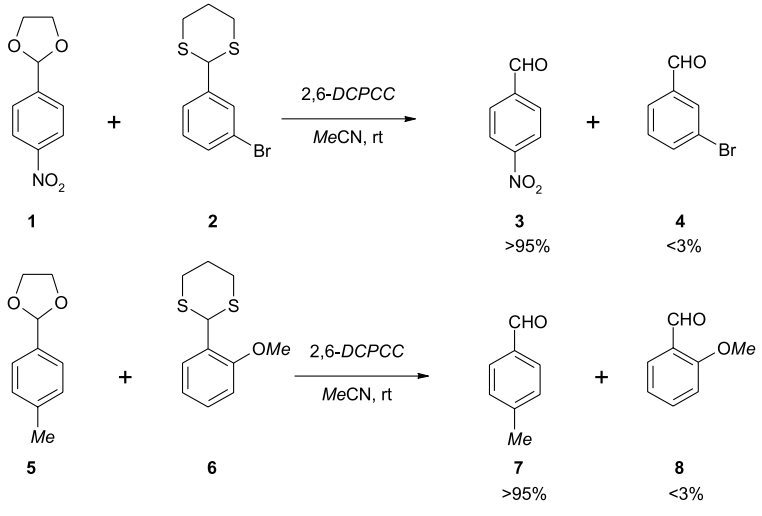
It is interesting to mention that 2,6-*DCPCC* can selectively cleave acetals or 1,1-diacetates in the presence of thioacetals at room temperature. When mixtures of equimolar amounts of acetals **1** or **5** in the presence of thioacetals **2** or **6** were treated with 2,6-*DCPCC*, only the acetals were deprotected and the thioacetals remained unchanged (Scheme 4). Similarly when a mixture of equimolar amounts of 1,1-diacetate **9** in the presence of thioacetal **6** was treated with 2,6-*DCPCC*, only the 1,1-diacetate was deprotected and thioacetal remained unchanged (Scheme 5).

In conclusion, we have shown that 2,6-*DCPCC* is an efficient, rapid, mild, and inexpensive reagent for conversion of aliphatic and aromatic acetals, ketals, and 1,1-diacetates to their corresponding carbonyl compounds. Deprotection of

Table 3. Deprotection of 1,1-diacetates with 2,6-DCPCC in *Me*CN[a]

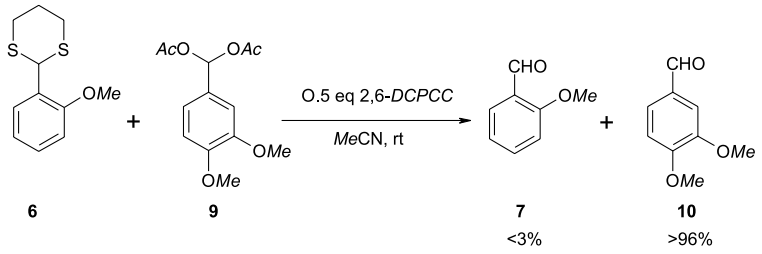
Entry	Substrate	Time/min	Yield/%[b]
1c	*Ph*–CH(O*Ac*)$_2$	12	96
2c	4-*MePh*–CH(O*Ac*)$_2$	8	96
3c	2-O*MePh*–CH(O*Ac*)$_2$	7	93
4c	2,5-di-O*MePh*–CH(O*Ac*)$_2$	5	96
5c	3,4-di-O*MePh*–CH(O*Ac*)$_2$	5	96
6c	4-O*BzPh*–CH(O*Ac*)$_2$	8	93
7c	1-Naphthyl–CH(O*Ac*)$_2$	14	90
8c		11	90
9c	4-Cl*Ph*–CH(O*Ac*)$_2$	23	90
10c	2-Cl*Ph*–CH(O*Ac*)$_2$	30	88
11c	4-Br*Ph*–CH(O*Ac*)$_2$	22	88
12c	4-*PhPh*–CH(O*Ac*)$_2$	30	70
13c		10	84
14c	4-(*Ac*O)$_2$CH–*Ph*–CH(O*Ac*)$_2$	20	94
15c	4-*Ac*O*Ph*–CH(O*Ac*)$_2$	15	95
16c	*n*-Hexyl–CH(O*Ac*)$_2$	15	96
17c	*Et*$_2$HC–CH(O*Ac*)$_2$	15	96
18c	*n-Pr*–CH(O*Ac*)$_2$	15	95

[a] Reactions are performed at room temperature using 1:0.5 molar ratio of substrates to reagent; [b] yields refer to isolated products



Scheme 4

thioacetals with 2,6-*DCPCC* requires a higher molar ratio of the oxidant, much longer reaction times, and higher temperature. This reagent deprotects acetals and 1,1-diacetates quantitatively irrespective of the presence of thioacetals.



6 9 7 <3% 10 >96%

Scheme 5

Experimental

Infrared spectra were recorded on Pye-unicam SP 1100 spectrometer. ^{1}H NMR spectra were obtained at 250 MHz using a Bruker spectrometer in $CDCl_3$ as the solvent and tetramethyl silane (*TMS*) as internal reference. Melting points were measured with Electro thermal 9100. Purification was achieved by distillation or silica gel column chromatography (mesh 27–30). Acetals [10], thioacetals [11], and 1,1-diacetates [5] were prepared according to literature.

General Procedure for the Deprotection of Acetals with 2,6-DCPCC

In a round-bottomed flask, a solution of 1 mmol of acetal in 10 cm^3 of *Me*CN was treated with 1 mmol of 2,6-*DCPCC* and the mixture was stirred at room temperature. The progress of the reaction was monitored by GC or TLC. The reaction mixture was filtered and the solid material was washed with 20 cm^3 of *n*-hexane. The filtrate was washed with 3×10 cm^3 of water. Purification of the crude product on a silica gel plate or silica gel column (eluent: *n*-hexane/*Et*O*Ac*) afforded the pure carbonyl compound. All products (Table 1) were characterized by their melting points, IR, ^{1}H NMR spectroscopic data, and also by comparison with authentic samples.

General Procedure for the Deprotection of Thioacetals with 2,6-DCPCC

In a round-bottomed flask, a solution of 1 mmol of thioacetal was treated with 2.5 mmol of 2,6-*DCPCC* and the mixture was stirred under reflux in acetonitrile. The progress of the reaction was monitored by GC or TLC. The reaction mixture was filtered and the solid material was washed with 20 cm^3 of *n*-hexane. The filtrate was washed with 3×10 cm^3 of water. Purification of the crude product on a silica gel plate or silica gel column (eluent: *n*-hexane/CH_2Cl_2) afforded the pure carbonyl compound. All products (Table 2) were characterized by their melting points, IR, ^{1}H NMR spectroscopic data, and also by comparison with authentic samples.

General Procedure for Deprotection of 1,1-Diacetates with 2,6-DCPCC

In a round-bottomed flask, a solution of 1 mmol of 1,1-diacetate [5] in 10 cm^3 of *Me*CN was treated with 0.5 mmol of 2,6-*DCPCC* and the mixture was stirred at room temperature. The progress of the reaction was monitored by GC or TLC. The reaction mixture was filtered and the solid material was washed with 20 cm^3 of *n*-hexane. Purification of the crude product on a silica gel column (eluent: *n*-hexane/ether (3/1)) afforded the pure carbonyl compound. All products (Table 3) were characterized by their melting points, IR, ^{1}H NMR spectroscopic data, and also by comparison with authentic samples.

Acknowledgement

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