2,3-Dichloro-5,6-dicyano-*p*-benzoquinone as a Mild and Efficient Catalyst for the Deprotection of Acetals

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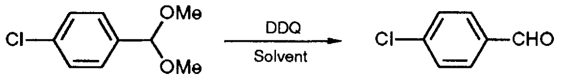
In the presence of a catalytic amount of 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ), acetals are readily hydrolysed to the corresponding aldehydes or ketones in aqueous acetonitrile under neutral conditions.

Conversion of acetals into aldehydes or ketones is one of the most important reactions in organic synthesis. This is normally accomplished by acid-catalysed hydrolysis. For the hydrolysis of dimethyl acetals, many protic acid catalysts such as hydrochloric acid,[1] acetic acid,[2] oxalic acid,[3] tartaric acid,[4] Dowex-50 (H^+) resin[5] and *N*-hydroxybenzenesulfonamide[6] have already been proposed. Barton *et al.* have devised the oxidative cleavage of ketone ethylene acetals to ketones by trityl tetrafluoroborate.[7]

Recently, we reported that DDQ was an efficient catalyst for the tetrahydropyranylation of alcohols.[8] Oikawa *et al.* reported that a *p*-methoxybenzyl or 3,4-dimethoxybenzyl protecting group of alcohols was removed by stoichiometric amounts of DDQ.[9] Reactions using DDQ have advantages over the conventional methods using acidic catalysts, in the mildness of the reaction conditions because DDQ is a neutral molecule. In this paper, we report a simple and efficient method for the transformation of acetals into the corresponding aldehydes or ketones by use of a catalytic amount of DDQ.

First, the hydrolysis of *p*-chlorobenzaldehyde dimethyl acetal in several solvents was examined. As shown in Table 1, the best result was obtained using $MeCN–H_2O$ (9 : 1). The reaction in other solvents such as $CH_2Cl_2–H_2O$, benzene–H_2O, or tetrahydrofuran–H_2O proceeded more slowly. This reaction is only achieved in the presence of water. When water was not added, only a trace amount of the desired product was obtained (entry 5). The results of the hydrolysis of benzophenone dimethyl acetal using DDQ are shown in Table 2.

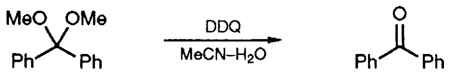
Table 1 Hydrolysis of *p*-chlorobenzaldehyde dimethyl acetal by DDQ in various solvents[a]



Entry	Solvent	*t*/h	Yield (%)[b]
1	$MeCN–H_2O$ (9 : 1)	1	92
2	$CH_2Cl_2–H_2O$ (9 : 1)	6	88
3	Benzene–H_2O (9 : 1)	6	25
4	THF–H_2O (9 : 1)	6	83
5	MeCN	1	4

[a] DDQ (0.1 mmol), recrystallized from benzene–hexane, was added to a solution of *p*-chlorobenzaldehyde dimethyl acetal (1.0 mmol) in solvent (7.0 ml) at room temp. [b] Isolated yields.

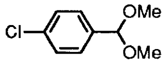
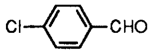
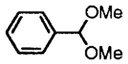
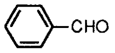
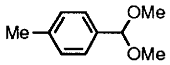
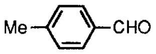
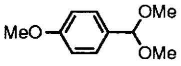
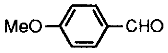
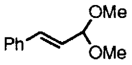
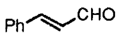
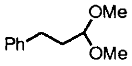
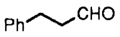
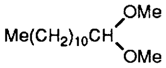
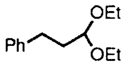
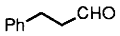
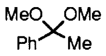
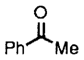
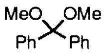
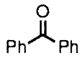
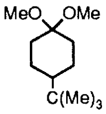
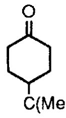
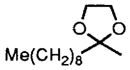
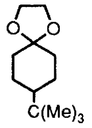
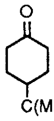
Table 2 Hydrolysis of benzophenone dimethyl acetal by DDQ[a]



	DDQ			
Entry	Supplier	Recrystallization	*t*/h	Yield (%)[b]
1	Waco	Once	1	100
2	Waco	Three times	1	99
3[c]	Waco	Three times	1	99
4	Merck	Once	1	99
5	Merck	Three times	1	100
6	Aldrich	Once	1	98
7	Aldrich	Three times	1	100
8[d]			1	0[e]

[a] DDQ, recrystallized from benzene–hexane, (0.1 mmol) was added to a solution of acetal (1.0 mmol) in $MeCN–H_2O$ (9 : 1) (7.0 ml) at room temp. [b] Isolated yields. [c] Reaction was carried out under N_2. [d] DDQ was not added. [e] Starting material (100%) was recovered.

Table 3 Hydrolysis of various acetals by DDQ[a]

Entry	Acetal	*t*/h	Product	Yield (%)[b]
1		1		92
2		1		75[c]
3		1		82
4		1		91
5		1		100
6		7		96
7	 $Me(CH_2)_{10}CH(OMe)_2$	2	$Me(CH_2)_{10}CHO$	81
8		5		94
9		1		90
10		1		100
11		1		92
12		3	$Me(CH_2)_8C(O)Me$	95
13		3		68[d, e]

[a] DDQ (0.1 mmol) was added to a solution of the acetal (1.0 mol) in $MeCN–H_2O$ (9 : 1) (7.0 ml) at room temp. [b] Isolated yields. [c] Yield is low because of high volatility of benzaldehyde. [d] DDQ (0.2 mmol) was used. [e] The starting material (23%) was recovered.

Next, the deprotection of various acetals catalysed by DDQ was examined and the results are summarized in Table 3. In every case, the reaction proceeds smoothly at room temperature in aqueous acetonitrile to give the corresponding aldehydes or ketones in good yields. Hydrolysis of benzyl or allylic derivatives (entries 1–5) is faster than that of aliphatic ones (entries 6–8). This method can also be effective for ketone ethylene acetals as well as ketone dimethyl acetals.

A typical procedure is as follows: DDQ (0.1 mmol) was added to a solution of *p*-chlorobenzaldehyde dimethyl acetal (1.0 mmol) in MeCN–H_2O (9 : 1) (7.0 ml). After stirring for 1 h at room temperature, the solvent was evaporated and the residue was chromatographed (benzene) on silica gel to give *p*-chlorobenzaldehyde in 92% yield.

In summary, this method constitutes a new procedure for deprotection of acetals with the considerable advantage of being under neutral conditions. Further investigations on mechanism of the present reaction are in progress.

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