DDQ as a Versatile Reagent for Oxidative Cleavage of Tosylhydrazones and Oximes

S. Chandrasekhar,* Ch. Raji Reddy, and M. Venkat Reddy
Indian Institute of Chemical Technology, Hyderabad 500007, India

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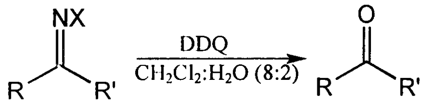
2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) was found to be a very efficient oxidative reagent for the selective cleavage of tosylhydrazones and oximes of carbonyl compounds for the first time.

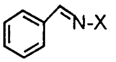
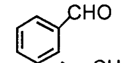
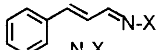
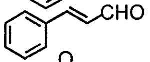
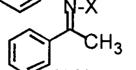
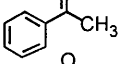
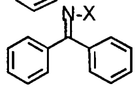
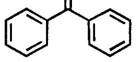
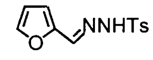
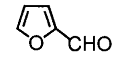
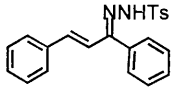
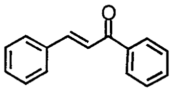
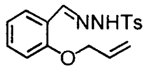
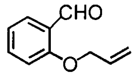
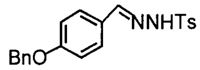
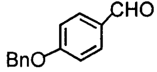
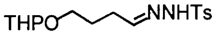
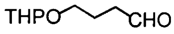
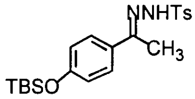
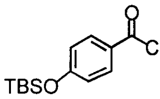
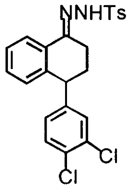
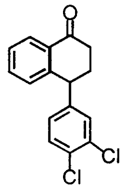
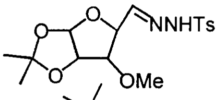
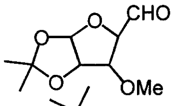
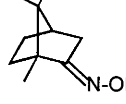
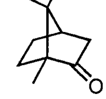
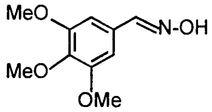
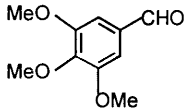
The title reagent namely DDQ has played an important role as a reagent of choice in dehydrogenative aromatisation[1] and in deprotection of MPM ethers.[2] This reagent is also found to be an efficient catalyst in tetrahydropyranylation of alcohols[3] and dethioacetalisation of aldehydes.[4] Our own interest in DDQ has culminated in developing a new methodology for selective deprotection of allyl ethers of primary alcohols[5] and also a new catalytic cycle of DDQ to DDHQ to DDQ is reported for deprotection of -OMPM ethers.[6] While working on deprotection of allyl ether of salicylaldehyde tosylhydrazone, we have observed a clean cleavage of tosylhydrazone instead of expected allyl ether cleavage in 95% yield (entry 7, Table 1). A careful literature survey has revealed that DDQ has previously never been utilised for this important transformation. Interestingly few oxidation reagents viz. Oxone,®[7] *tert*-butyl hydroperoxide,[8] clay-supported ferric nitrite,[9] *o*-iodoxy benzoic acid (IBX),[10] PCC-H_2O_2,[11] trimethylammonium chlorochromate,[12] CrO_3-chlorotrimethylsilane[13] performed this transformation to some extent. Few acidic[14] and basic reagents[15] also are used for the regeneration of carbonyl compounds from tosylhydrazones. Almost all the above reagents cleaved oximes as well. Our experience has revealed that DDQ also has effectively cleaved tosylhydrazones and oximes to carbonyl compounds (Equation 1) in excellent yields (vide supra).[16]



Equation 1

X= -NHTs, -OH
R= alkyl, aryl R'= H, alkyl, aryl

Table 1 Oxidative cleavage of tosylhydrazones and oximes with DDQ

entry	substrate	time/h	product	yield/%[a]
1		2		85
2		2		90
3		2.5		85
4		3.5		87
	(X= -NHTs or -OH)			
5		2		80
6		2.5		85
7		2		95
8		2		90
9		2		78
10		2.5		85
11		3.5		80
12		2.5		85
13		3.5		88
14		2.5		89

[a] Yields calculated after column chromatography of the products.

The results pertaining to selective cleavage of tosylhydrazones and oximes are reported herein (Table 1). The substrates studied include both aldehyde and keto derivatives. The over oxidation prone benzaldehyde tosylhydrazone and oxime allowed for a clean recovery of benzaldehyde without any traces of benzoic acid formation (entry 1). Similarly cinnamaldehyde derivative (entry 2) is subjected to cleavage conditions with good success. Other aldehyde hydrazones include furfural (entry 5), 2-*O*-allyl salicylaldehyde (entry 7) and *p*-benzyloxybenzaldehyde (entry 8). Keto derivatives namely, acetophenone hydrazone as well as oxime (entry 4), benzylideneacetophenone-hydrazone (entry 6), *p*-*O*-*tert*-butyldimethylsilylacetophenone (entry 10) were decently behaved with over 80% yields. More complex 4-(3,4-dichlorophenyl) tetrahydronaphthalone tosylhydrazone (entry 11) and sugar hydrazone (entry 12) were also subjected to present cleavage conditions to recover the parent carbonyl compounds in 80% and 85% yields respectively. The oximes studied include camphor oxime (entry 13) and trimethoxybenzaldehyde oxime (entry 14). It has been observed during the oxidative deprotection studies that the sensitive protective groups such as *O*-allyl ether (entry 7), benzyl ether (entry 8), -OTHP ether (entry 9), *O*-silyl ether (entry 10) and acetonide (entry 12) were stable.

In conclusion, DDQ is demonstrated as a versatile oxidative reagent for selective deprotection of tosylhydrazones and oximes of carbonyl compounds in high yields.[17] The key feature of the present study is that sensitive over oxidation prone substrates also being well responding to present protocol.

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16 General Procedure: To a solution of tosylhydrazone or oxime (3 mmoles) in CH_2Cl_2-H_2O (8:2, 10 mL) was added DDQ (5 mmoles) and stirred for given time (Table 1) at room temperature. The reaction mixture was extracted with CH_2Cl_2, washed with 10% $NaHCO_3$ solution followed by water and brine. The organic layer was dried (Na_2SO_4) and evaporated *in vacuo* to afford the crude product which was purified by column chromatography on silica gel.

17 All the products were characterized by ^1H NMR, HRMS and IR comparison with authentic samples in case of commercially available carbonyl compounds.

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