

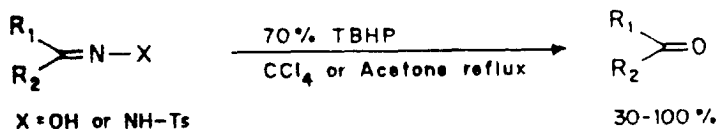
Facile Regeneration of Carbonyl Compounds from Oximes and Tosylhydrazones with TBHP

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Abstract : 70% *tert*-Butyl hydroperoxide (TBHP) has been found to be an efficient and selective reagent for the mild oxidative cleavage of the C=N of oximes and tosylhydrazones to yield their corresponding carbonyl compounds © 1997, Elsevier Science Ltd. All rights reserved.

There has been considerable interest in the development of mild techniques for the conversion of oximes and tosylhydrazones into their corresponding carbonyl compounds.¹ This is because such derivatives of carbonyl compounds serve as efficient protecting groups for aldehydes and ketones in organic synthesis.² Most of the known methods of regenerating carbonyl compounds from their nitrogen derivatives require strongly acidic³, oxidative⁴ or reductive⁵ reactions. Recently, clay-supported ferric nitrite⁶, dimethyl dioxirane⁷ and TS-1 - H₂O₂ combination⁸ have been reported to cleave the C=N of oximes and tosylhydrazones. However, many of the conventional procedures for regeneration of carbonyl function from such nitrogen derivatives have several limitations i.e. toxicity of reagent e.g. (PhSeO)₂O⁹, pyrophoric nature of Na₂O₂ and the use of expensive transition metals. Clearly, it is desirable that a method which involves relatively mild reaction conditions (no transition metals) and which leads to high recoveries of a wide range of aldehydes and ketones should be available. We now report an efficient and neutral method for the effective cleavage of C=N of oximes and tosylhydrazones with 70% TBHP (Scheme 1).



Scheme-1

Table 1 : Oxidative cleavage of oximes with 70% TBHP in refluxing CCl₄

Entry	Substrate	TBHP (moles)	t/h	Product ^a	Yield ^b (%)
1	Acetophenone oxime	2	8	Acetophenone	80
2	4-Nitroacetophenone oxime	2	18	4-Nitroacetophenone	70.3
3	4-Methoxybenzaloxime	2	18	4-Methoxybenzaldehyde	30 ^c
4	4-Chlorobenzaloxime	2	18	4-Chlorobenzaldehyde	40 ^c
5	Benzophenone oxime	1.1	4	Benzophenone	98
6	4-Chlorobenzophenone oxime	1.1	4	4-Chlorobenzophenone	98
7	4-Methoxybenzophenone oxime	1.1	4	4-Methoxybenzophenone	100
8	1-Tetralone oxime	2	18	1-Tetralone	68.4
9	2-Heptanone oxime	2	18	2-Heptanone	80
10	Camphor oxime	2	18	Camphor	78
11	β -Ionone oxime	2	18	β -Ionone	62
12	Cinnamaloxime	2	18	Cinnamaldehyde	35 ^c

a : Characterized by IR, ¹H & ¹³C NMR and MS. **b** : Isolated after chromatographic purification. **c** : The rest is essentially the over oxidized product (acid).

Oximes or tosylhydrazones when refluxed in CCl₄ or acetone respectively with TBHP give the corresponding carbonyl compounds in excellent yields. In a typical reaction procedure, a mixture of benzophenone oxime (0.01 mol) and 70% TBHP (0.011 mol) in carbon tetrachloride (20 ml) was refluxed for 4 h. After the reaction was complete (TLC), solvent was distilled off and the product purified by flash chromatography to afford benzophenone in virtually 100% yield and purity.

Table 1 summarizes the results of various oximes which underwent oxidative cleavage to form carbonyl compounds with 70% TBHP in refluxing CCl₄. The rate of oxidative cleavage of benzophenone oximes was fast, requiring only 1.1 mole of TBHP and 4 h. Even the sterically hindered camphor oxime was successfully converted to camphor in good yield. Interestingly, the unsaturated oximes underwent deoxygenation without affecting the C=C bond. However, the yields of the aldoximes were low presumably due to the over oxidation of the regenerated aldehydes to acids.

Table 2 shows the oxidative cleavage of tosylhydrazones with 70% TBHP to give the corresponding carbonyl compounds in excellent yields, particularly for aromatic tosylhydrazones. However, the present method fails to oxidatively cleave both aliphatic and heteroaryl tosylhydrazones. Table 3 presents the effect of various solvents for the oxidative cleavage of 4-chlorobenzophenone oxime with 2 moles of 70% TBHP. While CCl₄ was found to be an excellent

Table 2 : Oxidative cleavage of tosylhydrazones with 70% TBHP in refluxing acetone

Entry	Substrate	TBHP (moles)	t/h	Product ^a	Yield ^b (%)
1	Acetophenone tosylhydrazone	2	10	Acetophenone	80
2	4-Nitroacetophenone tosylhydrazone	2	10	4-Nitroacetophenone	85
3	4-Methylacetophenone tosylhydrazone	2	10	4-Methylacetophenone	100
4	Benzophenone tosylhydrazone	2	8	Benzophenone	68
5	4-Chlorobenzophenone tosylhydrazone	2	8	4-Chlorobenzophenone	50
6	1-Tetralone tosylhydrazone	2	8	1-Tetralone	100
7	Cyclohexanone tosylhydrazone	3	18	Cyclohexanone	0
8	2-Heptanone tosylhydrazone	2	18	2-Heptanone	0
9	Pyridine-2-carboxaldehyde tosylhydrazone	2	18	Pyridine-2-carboxaldehyde	0

a : Characterized thoroughly by IR, ¹H and ¹³C NMR and MS; b : Yield refers to isolated, purified product. solvent for the oxidative cleavage of oximes, the rate of the same reaction was found to be very slow with 30% H₂O₂ used as the oxidant. Mechanistically, the reaction appears to be initiated via electrophilic oxidation of C=N of oximes and tosylhydrazones with TBHP (pK_a = 12.8 and active oxygen = 17.8%)¹⁰ to oxaziridines which may be converted¹¹ immediately into the carbonyl compounds by fragmentation.

Table 3 : The effect of solvent on the oxidative cleavage of 4-chlorobenzophenone oxime with hydroperoxides

Entry	Solvent	Oxidant (2 moles)	t/h	Temp.	Yield ^a of 4-Chlorobenzophenone (%)
1	Carbon tetrachloride	70% TBHP	57	25°C	66
2	Carbon tetrachloride	70% TBHP	2	reflux	100
3	Acetone	70% TBHP	16	reflux	100
4	Methanol	70% TBHP	45	reflux	72
5	Carbon tetrachloride	30% H ₂ O ₂	24	reflux	80
6	Methanol	30% H ₂ O ₂	35	reflux	27

a : Yields are for isolated, purified product.

In conclusion, we hope that the present deprotection methodology of oximes and tosylhydrazones finds wide application in organic synthesis because of its simplicity and use of a readily available oxidant (70% TBHP) under neutral conditions.

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