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One-Step Conversion of Oximes to *Gem*-Chloro-Nitro Derivatives

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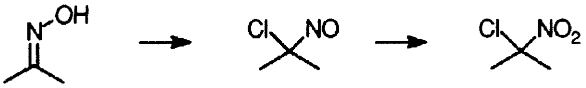
Abstract: a new method for one-pot conversion of oximes to *gem*-chloro-nitro compounds using Oxone and sodium chloride is described.

Keywords: oximes; oxidation; nitro compounds; diastereoselection.

Gem-chloro-nitro compounds are versatile intermediates in organic synthesis for the preparation of molecules containing nitro groups. The preparation of these compounds is usually achieved, with good results, by chlorination-oxidation of oximes.[1] The oxime is initially transformed by chlorination into the *gem*-chloro-nitroso derivative, which is then oxidized to the desired *gem*-chloro-nitro compound.



The first step of the transformation is achieved by the use of elemental chlorine[2] aqueous hypochlorous acid,[2] *t*-butyl hypochlorite.[3] The resulting chloro-nitroso compound is further oxidized with nitric,[4] trifluoroperoxyacetic[5] or *m*-chloroperbenzoic acids,[6] ozone,[7] aqueous sodium[2] or *n*butylammonium hypochlorite.[3] The one-pot conversion can be obtained using N,N,N,-trihalo-1,3,5-triazines[8] or chloroperoxidase in the presence of H_2O_2 and KCl.[9]

The methods reported have some limitations such as: use of strong and non-selective oxidizing agents, toxic and expensive reagents, low yields and long reaction times.

We wish to report that commercial potassium hydrogen monopersulfate (Oxone®) in the presence of NaCl can be used for selective conversion of oximes into *gem*-chloro-nitro derivatives under mild conditions in a one-pot procedure. When oximes are treated with Oxone® and NaCl supported on wet basic alumina[10] in chloroform at 45 °C, *gem*-chloro-nitro compounds are produced in good yields (Table).

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Table. Chlorination-oxidation of oximes

Entry	Product	Time (h)	Yield (%)[a]
1	1-chloro-1-nitro-cyclohexane	4	79
2	5-chloro-5-nitro-nonane	2	84
3	1-chloro-1-nitro-4-*t*butyl-cyclohexane	4	80
4	1-chloro-1-nitro-cycloctane	1	83
5	2-chloro-2-nitro-adamantane	1	74
6	1β-chloro-1-nitro-*trans*-decaline	2	77
7	(1R,3R,5S)-3-chloro-3-nitro-menthane	7	66
8	3α-acetoxy-17β-chloro-17-nitro-androstane	1	73

[a] Yields in pure isolated products, characterized by IR, GC-MS, ^{1}H NMR and ^{13}C NMR.

The process is carried out by the species produced as a result of the Oxone®-oxidation of the chloride anion.[11] It is important to note that only in the case of chlorination-oxidation of a phenyl-methyl-oxime does the reaction occurs with the formation of the parent ketone and 1-chloro-1-phenyl-ethene (8:1), being unprecedented. The reaction is diasteroselective (entries 6, 7, 8) as shown by GC-MS and comparison of NMR data with those reported in the literature,[12] giving the diasteroisomer in which the nitro group occupies an axial position.

The procedure described is equally effective or better than any procedure yet reported and is also effective for the transformation of sterically hindered substrates.

Typical procedure. Oxone® was added to a well stirred suspension of NaCl (3 mmol) and wet basic alumina (6 g) in chloroform (15 mL) and the mixture heated at 45 °C for 5 min. A solution of oxime (0.6 mmol) in chloroform (1.5 mL) was the added and the reaction mixture stirred until the deep blue color disappeared (1-7 h, see Table). The mixture was filtered under vacuum and the solution evaporated under reduced pressure. The crude material was purified by chromatography on Al_2O_3 (III) (eluent petroleum ether) affording the desired *gem*-chloro-nitro compound.

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