

A VERSATILE METHOD FOR THE CONVERSION OF OXIMES TO NITROALKANES

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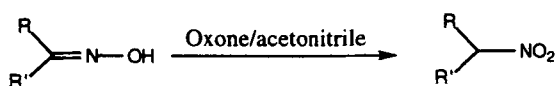
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Abstract: A convenient oxidation of oximes to nitroalkanes has been developed using oxone® in acetonitrile.

Nitroalkanes represent a versatile raw materials in the preparation of pharmaceutical active ingredients. The importance of nitroalkane chemistry in general organic synthesis has already received wide recognition¹. They have been prepared traditionally from alkyl halides², primary amines³, oximes⁴ and nitroso compounds⁵. Direct nitration of alkanes was also reported using stable nitronium salts as nitrating agent⁶. Previous methods reported in the literature have been rather unsatisfactory. Bamberger has for example, reported the oxidation of benzaldehyde oxime to phenylnitromethane, but the yield was very low and a complex mixture of products was obtained⁷. Iffland described a tedious three step procedure for the oxidation of oximes into nitro compounds⁸.

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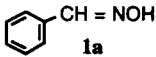
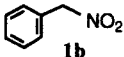
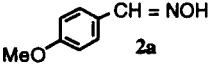
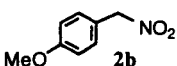

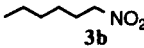
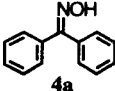
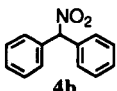
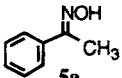

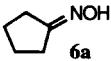

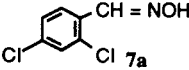
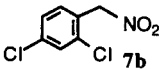
A very general protocol in order to accomplish the preparation of nitroalkanes implies the oxidation of nitrogen containing derivatives. The oxidation of nitrogen derivatives although less explored seems to offer a well grounded alternative to the above cited methods. Since oximes are readily obtained from the corresponding carbonyl compounds, these can be regarded as a ideal substrates for the direct preparation of a variety of nitroalkanes. Oximes are currently oxidized to their corresponding nitroalkanes employing sodium perborate in glacial acetic acid⁹, peroxytrifluoroacetic acid^{4a} or urea-hydrogen peroxide complex in acetonitrile^{4b} and Benz-Mo in acetonitrile^{4c}. However, there still exists a need for the development of new, mild methods for this transformation.



It has been found that under the proper conditions oxone® is a remarkably efficient and mild reagent for the oxidation of oximes to nitroalkanes. Potassium monopersulfate triple salt (2KHSO₅, KHSO₄, K₂SO₄) is an inexpensive and powerful oxidant used for a variety of oxidations e.g. aromatic amines¹⁰, boronic acids and esters¹¹ and secondary amines¹². In this connection, we have recently carried out a facile oxidation of nitriles to amides¹³.

In continuation of our studies on environmentally benign oxidations¹⁴, we report here the one-step oxidation of oximes to the corresponding nitro compounds under mild conditions. As illustrated in the Table-1, oximes when treated with oxone® in acetonitrile at 45°C give the parent nitro compounds with some of the corresponding carbonyl compounds as by products. The yield of nitro compound is dependent on the reaction conditions. For e.g. benzophenone

Table-1 : Oxidation of oximes with oxone in acetonitrile at 45°C

Oximes	Reaction time (h)	Nitro alkanes ^a	Yield ^b (%)	m.p. ^o C/b.p. ^o C/Torr Found	Reported
 1a	4.0	 1b	72	110/15	97/4 ^{4a}
 2a	4.5	 2b	75 ¹⁵	-	-
 3a	6.0	 3b	70	80/15	91/24 ¹⁵
 4a	8.0	 4b	60	88-90	90-91 ¹⁶
 5a	7.5	 5b	57	124/1.5	61/0.45 ¹⁷
 6a	10.0	 6b	52	81/5	90/40 ^{4a}
 7a	5.0	 7b	73 ¹⁵	-	-

a) All the products were analytically pure and their structures fully supported by spectroscopic data. b) Isolated yields.

oxime was unreacted along with some benzophenone after 3 h at room temperature. At 45°C, a 60% yield of nitrodiphenylmethane was obtained. The role of acetonitrile as solvent for the oxidation of oximes to nitro alkanes is very crucial one. It seems reasonable to assume that it functions as a base which catalyzes the prototropic transformation of the aci-nitroalkane to its stable tautomer.

In summary, the present method is a convenient, safe and general procedure for the preparation of primary and secondary nitro compounds. The method is also applicable to sterically hindered oximes where the use of peroxytrifluoroacetic acid generally fails.

General Procedure : A freshly prepared solution of oxone (11.7 g, 19.0 mmol) in 23 ml of water and aqueous acetone solution (20 ml) was added simultaneously to a vigorously stirred mixture of oxime (0.52 g, 3.8 mmol), acetonitrile (5 ml) and aq. phosphate buffer (pH 7.5, 0.05M) in water (20 ml) was stirred at 45°C for the specified time (Table). The reaction was monitored by TLC. After completion of the reaction, the reaction mixture was cooled to room temperature, the product was extracted into ether (2x25 ml), washed with saturated brine, dried (Na₂SO₄) and the solvent removed *in vacuo* to afford the crude product which was purified through a silica gel column eluted with chloroform-pentane (1:4).

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15. Some characterization data for new compounds : **2b** : oil, ^1H NMR (CDCl_3) : δ 3.95 (s, 3H), 5.45 (s, 2H), 6.78 (d, 2H, $J = 9.0$ Hz), 7.08 (d, 2H, $J = 9.0$ Hz). IR (Neat) ν 1550 and 1355 cm^{-1} (NO_2). **7b** : oil, ^1H NMR (CDCl_3) : δ 5.52 (s, 2H), 6.85 (d, 2H, $J = 9.0$ Hz), 7.42 (s, 1H). Compound **3b** b.p. is compared with authentic sample obtained from Aldrich Chemical Co.
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