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Effective 'non-aqueous hydrolysis' of oximes with iodic acid in dichloromethane under mild, heterogeneous conditions

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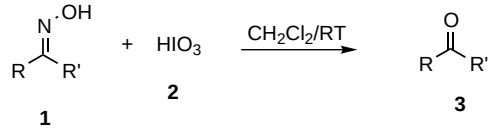
Abstract—Ketoximes and aromatic aldoximes are converted to the corresponding carbonyl compounds in excellent yields (67–97%), upon treatment with a suspension of iodic acid in dry CH_2Cl_2 at room temperature.

The hydrolysis of oximes to the corresponding carbonyl compounds has been of considerable interest in recent years for at least two reasons.[1] Firstly, oxime derivatives are often used to purify, characterise and protect aldehydes and ketones,[2] so the regeneration of the parent carbonyl compounds is important. Secondly, oximes may be accessed by routes not involving the carbonyl function such as the Barton reaction and the reduction of nitro compounds,[3] and so subsequent hydrolysis would define a route to the parent carbonyl compounds. A variety of methods is presently available for the hydrolytic deblocking of oximes, mostly involving either aqueous acid or oxidative cleavage; importantly, it seems necessary to prevent the reversal of the hydrolysis by either protonation or oxidation of the derived hydroxylamine.

In the course of our studies on the Beckmann reaction[4] we discovered that a variety of oximes (**1**) are effectively hydrolysed by a suspension of iodic acid (**2**) in dry dichloromethane at room temperature (Scheme 1). The corresponding carbonyl derivatives (**3**) were isolated in excellent yields after a simple work-up (Table 1).†

Interestingly, the addition of molecular sieves to the reaction medium did not prevent the effective hydrolysis, indicating that water is not involved. Also, a minimum of three equiv. of iodic acid (**2**) were found to be



1 **2** **3**

Scheme 1.

Table 1. The effective hydrolysis of the oximes **1** (Scheme 1) to the carbonyl compounds **3** with iodic acid (**2**): reaction time and yields of **3**[a]

1	R	R′	Time (h)	**3**	Yield (%)
a	Ph	Ph	6	**a**	92
b	Me	Ph	18	**b**	97
c	Me	*p*-Tolyl	11	**c**	67[b]
d	α-Tetralone oxime		20	**d**	90
e	-$(CH_2)_5$-		23	**e**	72[c]
f	1-Naphthaldehyde oxime		13	**f**	91
g	H	*p*-Anisyl	21	**g**	94
h	Veratraldehyde oxime		24	**h**	83

[a] The final products in the case of entries **d**, **f** and **h** are also the corresponding carbonyl compounds; the oximes **1** were prepared by standard methods and identified by their IR spectra and mp's; **3** were identified spectrally (IR, 300 MHz ^{1}H NMR and GC–MS: the yields shown have been adjusted for the GC purity, and M^+ was always observed).

[b] A by-product, that is most likely 3-iodo-4-methylphenyl methyl ketone[7] based on the spectral and GC–MS data (M^+ 260), was observed in 22% yield.

[c] GC analysis indicated the formation of high molecular weight products also (~20%, as yet unidentified).

Keywords: hydrolysis; iodic acid; non-aqueous; oximes.

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† Typical procedures: A solution of the oxime (1 mmol) in dry CH_2Cl_2 (5 ml) was treated with **2** (3 mmol) and the resulting suspension stirred at room temperature (with or without 4 Å molecular sieves), the reaction being monitored by TLC (SiO_2; eluent: EtOAc/hexane). Upon completion the reaction mixture was diluted with CH_2Cl_2, washed with water and decolourised with activated charcoal at 45°C; filtration to remove the charcoal, followed by drying (Na_2SO_4) and distillation of the solvent furnished the carbonyl compounds **3**.

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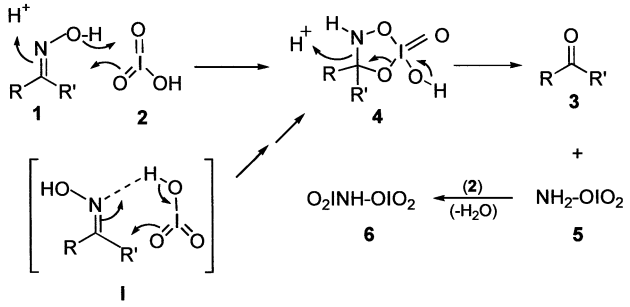
required for the reaction to be complete; and further amounts of **2** speeded up the reaction. These observations indicate the formal mechanism shown in Scheme 2, which essentially involves the formation of the cyclic iodate species **4** and its subsequent decomposition. The formation of **4** effectively involves the addition of the oxime hydroxyl group in **1** across an I=O unit in **2** and of an hydroxyl group of the iodate moiety across the oxime C=N unit: the simpler, concerted process is shown although the above additions may be stepwise. (Another alternative involves the hetero-ene process represented in **I**, followed by cyclisation to **4**.) The cyclic iodate **4** decomposes to the carbonyl compound **3** and *O*-iodylhydroxylamine (**5**).

Further condensation of the putative **5** with **2** to the bis-iodylhydroxylamine **6** would render the overall reaction irreversible (by analogy to the greater stability of *N*-acylhydroxylamines relative to the *O*-acylhydroxylamines;[5] an *O*- to *N*-iodyl transfer in **5** would also be effective but may be slow). Although the final fate of the putative **6** is unclear, the appearance of a brownish-red colouration towards the end of the reaction requires mention: this possibly indicates the presence of products bearing nitrogen in its higher oxidation states, derived by the effective oxidation of hydroxylamine. (Although redox potential data indicate that hydroxylamines are stable to oxidation in aqueous acid,[6] this may not apply to the non-aqueous heterogeneous conditions employed in the present case.)

In fact, in the case of the methyl tolyl ketone **3c**, a side-product that is most likely 3-iodo-4-methylphenyl methyl ketone was observed in 22% yield by GC–MS; this tentative assignment follows from the known[7] electrophilic iodination of **3c**. This indicates an aromatic electrophilic substitution, possibly with elemental iodine formed by the effective reduction of iodic acid by hydroxylamine. (A combination of iodine and iodic acid is known to effect the iodination of the aromatic nucleus.[8]) Also, the formation and subsequent decomposition of the cyclic adduct **4** may well be catalysed by **2** (as indicated); and the relative insolubility of **2** suggests the reaction occurs either at the solid surface or via a minuscule form in solution. All these may explain the observation that an excess of **2** is required for the reaction to be complete in reasonable time.



Scheme 2.

Iodic acid (**2**) is a rather mild inorganic acid (pK_a 0.80) of moderate oxidising power in aqueous acid,[9] and of low toxicity to humans as it has been used in medicine.[10] It has apparently found only limited use in organic synthesis so far.[11] Remarkably, the present method does not involve water although it is effectively a hydrolysis, and so would be suitable for substrates that might be sensitive to aqueous acid. The other advantages are the ready availability of iodic acid, its low toxicity, the ambient temperatures employed and the exceedingly simple work-up.

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