

Communication

Efficient Preparation of Aldoximes from Arylaldehydes, Ethylenediamine and Oxone[®] in Water

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Abstract: The one-pot reaction of aromatic aldehydes, ethylenediamine and Oxone[®] (2KHSO₅·KHSO₄·K₂SO₄) in pure water was found to unexpectedly afford aldoximes in excellent yields.

Keywords: Aldoximes, aryl aldehydes, ethylenediamine, Oxone[®], water

Introduction

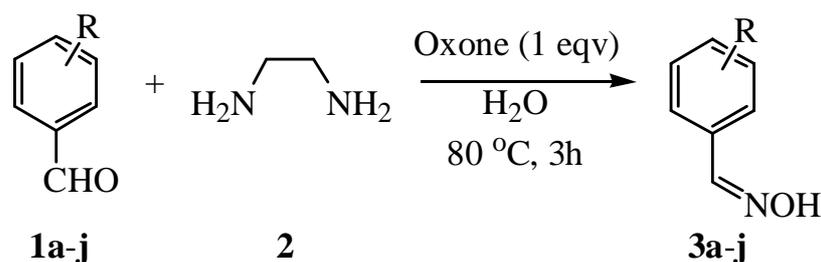
Oximation has attracted intensive attention for several decades as an efficient method for characterization and purification of carbonyl compounds. Due to the nucleophilic character of oximes, they have been widely used for the preparation of a variety of nitrogen-containing compounds such as amides [1], hydroximinoyl chlorides [2], nitrones [3] and nitriles [4]. Oximes were usually prepared by the reaction of carbonyl compounds and hydroxylamine hydrochloride with adjustment of pH using a basic aqueous medium. Recently, some new techniques such as microwave irradiation [5] and solvent-free heating [6] were applied to this reaction. Oxidation of amines or hydroxylamines was another usual method for the synthesis of oximes [7].

On the other hand, the use of water as a reaction medium has attracted notable interest and offers a clean, economical and environmentally-safe protocol for many reactions [8]. In fact, more and more reactions have been reported to proceed smoothly and efficiently in water. In continuation of our interest in organic reactions in water [9], herein we report the unexpected formation of aldoximes from the one-pot reaction of aromatic aldehydes and ethylenediamine with Oxone[®] in water.

Results and Discussion

Fujioka's, Konwar's and Sayama's groups have reported the reactions of aldehydes and ethylenediamine with oxidation by N-bromo(chloro)succinimide (NXS) [10], I₂/KI/K₂CO₃/H₂O system [11] or pyridinium hydrobromide perbromide (PHPB) [12]. These reactions afforded dihydroimidazole-type products. Oxone[®] has been widely used in organic reactions in recent years as an efficient and clean oxidant [13]. When we employed Oxone[®] as the oxidant for the reactions of aromatic aldehydes **1a-j** and ethylenediamine (**2**) in pure water, to our surprise, no dihydroimidazoles were observed, and instead, aldoximes **3a-j** were produced in excellent yields (Scheme 1).

Scheme 1.



The procedure involves addition of ethylenediamine to an aqueous mixture of aldehyde and Oxone[®] in water, followed by vigorous stirring in an oil bath to afford the aldoximes. The reaction was affected prominently by the quantity of Oxone[®] employed and the optimum amount of this reagent was found to be one equivalent. If 1.5 equivalents or more of Oxone[®] were used, the aromatic aldehydes could be partially oxidized to the corresponding benzoic acids. If 0.5 equivalents or less of Oxone[®] were used, the conversions were relatively low. The ethylenediamine was used in slight excess. The reaction yields for the one-pot synthesis of aldoximes with the optimum molar ratio of **1**, **2** and Oxone[®] as 1:1.1:1 are listed in Table 1, along with the melting points of the products.

Table 1. One-pot synthesis of aldoximes from aldehydes, **2** and Oxone[®].

Entry	R	Product	Yield / % ^a	Mp (lit) / °C
1	H	3a	92	30-32 (33-35 [5])
2	4-CH ₃	3b	93	73-74 (76-78 [14])
3	4-CH ₃ O	3c	92	47-49 (48-49 [15])
4	3,4-CH ₃	3d	90	67-68 (69 [16])
5	4-Cl	3e	93	110-111 (107-109 [14])
6	2-Cl	3f	91	74-75 (74-75 [17])
7	3,4-Cl	3g	95	120-121
8	4-NO ₂	3h	88	131-132 (132-133 [17])
9	3-NO ₂	3i	86	123-124 (121-122 [17])
10	4-CN	3j	88	180-181 (174-176 [18])

^a Isolated yields based on aldehydes.

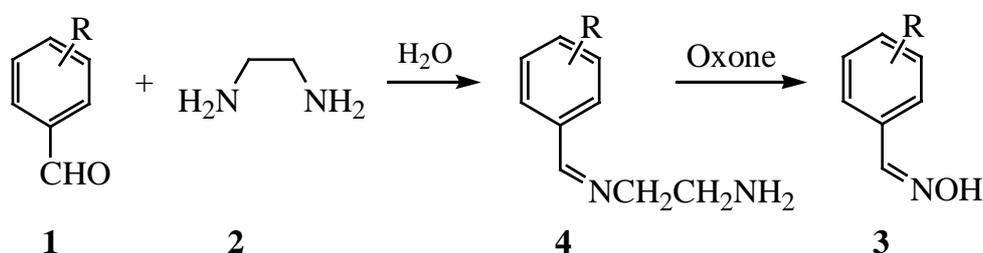
From Table 1 it can be seen that all of the reactions of aldehydes **1a-j** with **2** and Oxone[®] gave very good yields of aldoximes **3a-j**. All of the products except for **3g** were known compounds and their structures were confirmed by comparison of their melting points, ¹H- and ¹³C-NMR and IR spectra with reported data [5, 14-18].

The use of other amines replacing ethylenediamine was studied under the same conditions. Diamines such as 1,3-diaminopropane and 1,3-diaminohexane and aliphatic amines such as methylamine and butylamine afforded very low yields of the aldoximes, while *p*-tolylamine and hydrazine gave no aldoximes. These results demonstrated the advantage and special activity of ethylenediamine for the formation of aldoximes.

Other oxidants such as FeCl₃, (NH₄)₂Ce(NO₃)₆, KMnO₄, PhI(OAc)₂ and K₂S₂O₈ instead of Oxone[®] have also been examined. None of these oxidants gave any aldoxime products, but rather generated the corresponding benzoic acids, thus clearly exhibiting the effectiveness of Oxone[®] for producing aldoximes from aldehydes and ethylenediamine. Aliphatic aldehydes have also been used for these reactions, but unfortunately, they did not react with ethylenediamine and Oxone[®] to afford aldoximes.

Additional control experiments were conducted to gain insight into the reaction mechanism. If the aqueous solution of **2** and Oxone[®] was stirred at 80 °C for 3 h, and then an aldehyde was added and the resulting mixture stirred for another 3 h, no aldoxime was obtained. When Oxone[®] was added after the aqueous solution of an aldehyde and **2** was stirred at 80 °C for 3 h, the desired aldoxime was successfully prepared in high yield. Consequently, the reaction mechanism is believed to proceed via the imine intermediate **4**, which was then oxidized by Oxone[®] to form the aldoxime product **3**. Indeed, the reaction of the imine preformed from an aldehyde and **2** with Oxone[®] for 3 h at 80 °C (Scheme 2) gave yields comparable to those obtained with the three-component one-pot process. Thus, for example, the oxidation of the imine **4a** prepared from **1a** and **2** with Oxone[®] for 3 h at 80 °C afforded **3a** in 89% yield, close to the 92% yield observed for the one-pot procedure (Table 1, entry 1). In contrast, the Oxone[®] oxidation of the imines formed from **1a** and 1,3-diaminopropane, 1,3-diaminohexane, methylamine or butylamine gave only small amounts of **3a**, in contrast with the three-component one-pot process. These results again demonstrated the unique property of ethylenediamine for the generation of aldoximes.

Scheme 2.



Conclusions

In summary, we have discovered a novel reaction of aromatic aldehydes, ethylenediamine and Oxone[®] in pure water that provides a new route for the preparation of the corresponding aldoximes. Using this protocol, aldoximes were obtained with excellent yields.

Experimental

General

¹H-NMR and ¹³C-NMR spectra were recorded at 300 MHz and 75 MHz respectively on a Bruker Avance-300 spectrometer using CDCl₃ as solvent. Chemical shifts (δ) are given in ppm relative to TMS as an internal standard and coupling constants (*J*) in Hz. IR spectra were taken on a Bruker Vector-22 spectrometer in KBr pellets and are reported in cm⁻¹. Melting points were determined on a XT-4 apparatus and are uncorrected.

General procedure for aldoxime synthesis

Typically, to an aqueous mixture of aldehyde **1a-j** (0.5 mmol) and Oxone[®] (307.4 mg, 0.5 mmol) in water (2 mL) was added **2** (40 μL, 0.55 mmol), then the reaction mixture was stirred vigorously in an oil bath preset at 80 °C for 3 h (monitored by TLC). After the reaction mixture had cooled, the precipitated-out solid was filtered and washed with water (10 × 2 mL) to give the crude product, except for **3a** and **3c**. Because of the lower m.p. of **3a** and **3c**, the crude product failed to precipitate out from the reaction mixtures, and required extraction with ethyl acetate (15 mL × 2). The extract was dried over anhydrous sodium sulfate and then filtered. The filtrate was evaporated under vacuum to afford the crude product. All of the crude products were purified by column chromatography over silica gel with petroleum ether/ethyl acetate as the eluent to give pure aldoximes **3a-j**. All products **3a-j**, except for the previously unknown compound *3,4-Dichloro-benzaldehyde oxime* (**3g**) have been reported previously and their identities have been confirmed by their ¹H-NMR, ¹³C-NMR, IR spectra and melting point. The spectral data of **3g** were as follows: IR (KBr) ν 3311, 1632, 1556, 1480, 1460, 1377, 1325, 1269, 1215, 1135, 1032, 993, 966, 947, 915, 883, 872, 816, 776, 697, 675, 576, 551; ¹H-NMR (CDCl₃) δ 7.40 (dd, *J* = 8.2, 1.5 Hz, 1H, ArH), 7.46 (d, *J* = 8.2 Hz, 1H, ArH), 7.68 (d, *J* = 1.5 Hz, 1H, ArH), 7.68 (s, 1H, CH), 8.06 (s, 1H, OH); ¹³C-NMR (CDCl₃) 148.5, 134.2, 133.4, 132.1, 131.0, 128.8, 126.2

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Sample Availability: Samples of the compounds **3a-j** are available from the authors.