



REGULAR ARTICLE

The local and natural sources in synthetic methods: the practical synthesis of aryl oximes from aryl aldehydes under catalyst-free conditions in mineral water

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Abstract. The synthesis of oximes from aryl aldehydes was prepared using hydroxylamine hydrochloride. The obtained oxime compounds were synthesized at maximum efficiency in mineral water at room temperature. The developed method is economical, practical and environmentally friendly. All of the aldehydes were converted the oxime a method using local sources and useful for industrial applications is introduced in the literature.

Keywords. Mineral water; Aryl oxime; Local sources; Aryl aldehyde; Green Synthesis.

1. Introduction

Chemical industry materials have greatly improved the quality of our life. However, it is very important to produce these products in an environmentally compatible and economically acceptable way. Therefore, today green chemistry has turned into a scientific industrial application field. Scientists working on synthetic chemistry are working to develop more environmentally friendly methods and better chemical steps to synthesize the target product, both academically and industrially. One of the basic principles of green chemistry is to use safer, cleaner and environmentally friendly solvents.^{1–5}

The choice of a certain solvent in a synthetic reaction has environmental and economic consequences. Therefore, the development and improvement of various solvents compatible with nature are important for green chemistry. The water is reported as an environmentally friendly solvent for synthetic reaction transformations.^{6–9}

Like water, mineral water can be of interest to the scientific community because of its easy availability and environmental friendliness and can be used as a solvent in many organic synthesis reactions. In fact,

the effect and popularity of mineral water are due to the natural minerals in it.

Ariloxime production is also among the important reactions in organic chemistry. Oxime derivatives are an important synthetic main product and intermediate product in multi-step organic synthesis, and their use as pharmacology, catalyst, agriculture and bioactive reagent are among the developing application areas of oximes.^{1,10–13}

In addition, oxime compounds can be converted to amines¹⁴ by reduction reactions, nitriles^{15,16} by oxidation reactions, and amides¹⁷ by Beckmann rearrangement. In addition, oximes can serve as ligands in the formation of different metal complexes. Moreover, since the selectivity of such reactions is low, many by-products are likely to be formed. C-N bonds are formed in the production of oximes and the selectivity of these reactions is high. Such reactions are usually carried out in the presence of catalysts (acid, base, heterogeneous catalyst).^{18–20}

However, the method to be developed in the synthesis of oximes should have some advantages: (i) catalyst-free conditions (ii) sustainable and one-pot reaction (iii) high efficiency (iv) an environmentally friendly solvent.^{20,21}

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A series of aryl aldehydes have been transformed into various aryl oximes as a result of the addition-elimination reaction with hydroxylamine hydrochloride. Reactions were carried out without catalyst and at room temperature. Moreover, mineral water is used as a solvent. The reason why mineral water is preferred instead of pure water is the salts in mineral water. The presence of carbonate and sulphate structures enabled the reactions to take place in a shorter time and with higher yields. In addition, aryl oximes were synthesized under more economical conditions using local sources. The developed method is an industry-applicable method due to its economical and environmentally friendly features.

2. Experimental

2.1 Materials

The aryl aldehyde compounds, and $\text{NH}_2\text{OH}\cdot\text{HCl}$ used in the study were obtained from Sigma-Aldrich.

2.2 Characterization methods

The NMR spectra were recorded on an AVANCE III 400 MHz spectrometer.

2.3 General procedure for the synthesis of oxime compounds

Into a reaction vessel at room temperature were placed the aryl aldehyde derivatives (0.25 mmol), and $\text{NH}_2\text{OH}\cdot\text{HCl}$ (0.3 mmol). 2.0 mL of mineral water/methanol (h/h=1/1) solvent mixture was added to the reaction vessel. The progress of the reaction was monitored by TLC analysis. After the reaction is complete, the reaction mixture was work-up with an ethylacetate-water mixture. After the organic phase was separated, drying was carried out with Na_2SO_4 . After filtration, the solvent was removed by the evaporator. The products were provided by flash column chromatography. The products were determined by $^1\text{H-NMR}$ and $^{13}\text{C NMR}$ analysis.

3. Results and Discussion

4-nitro benzaldehyde was used for the optimization of the method. Our primary goal in the trials was to create under catalyst-free conditions in mineral water. Firstly, toluene was used as an apolar solvent.

However, the oxime was obtained with a 30% yield in 60 min (Table 1, entry 1). Then, an increase in product yield was observed when methanol was used as a polar solvent (Table 1, entry 2). By using water together with methanol, the same yields were achieved in a shorter time (Table 1, entries 3, 4). However, something was still missing. Either the catalyst or a salt structure such as NaHCO_3 , which is often used in the literature, would be used. But we preferred to use mineral water. By using mineral water instead of pure water, a 4-nitrobenzaldehyde oxime compound was obtained in 10 min and with 99% yield. With the thought that the pH of the environment would also be important, pH was measured and the synthesis of aryl oxime derivatives was carried out under acidic conditions (Table 1, entry 5).

The final procedure was created: 0.25 mmol of the 4-nitrobenzaldehyde, and 0.30 mmol $\text{NH}_2\text{OH}\cdot\text{HCl}$ gave an adequate performance for the conversion of 4-nitrobenzaldehyde into 4-nitrobenzaldehyde oxime with 2.0 mL of mineral water/methanol (v/v=1/1) (Table 1, entry 5).

Table 2 summarizes the results obtained in the synthesis of aryl oximes in the presence of mineral water. In the series of aryl aldehyde compounds tested, they were all converted to the respective oxime derivatives with the quantitative yields in 10 min at room temperature. Although there were small changes in reaction time and yields according to the functional groups attached to the aromatic ring, products with high yields were generally obtained in a short time. Especially the presence of electron donor and electron-withdrawing groups in the para position of the aromatic ring summarizes the state of the reaction better. For example, 4-nitrobenzaldehyde was converted to 4-nitrobenzaldehyde oxime with 95% yield within 10 min (Table 2, entry 1). 4-hydroxybenzaldehyde was converted to 4-hydroxybenzaldehyde oxime with 80% yield within 10 min (Table 2, entry 7). The electron donor functional groups usually cause a decrease in reaction efficiency but affect this situation in the position where the functional group is attached.

The presence of an electronegative atom or group of atoms attached to the ortho position enables the reaction to take place faster and with higher efficiency. For example, 2-hydroxy-1-naphthaldehyde was converted to 2-hydroxy-1-naphthaldehyde oxime with 83% yield within 5 min (Table 2, entry 8). Because these atom or atom groups increase the electropositivity of the carbonyl group by making hydrogen bonding with the aldehyde group (Scheme 1).

NH_2OH , used as the amine source in the reaction, is stabilized with hydrochloric acid (HCl). The amine

Table 1. Optimization of the reaction conditions^a

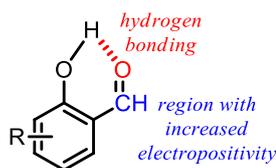
Entry	Solvent 1	Solvent 2	Temp. (°C)	Time (min)	Yield ^b (%)	pH
1	Toluene	-	rt	60	30	-
2	Methanol	-	rt	60	50	-
3	Methanol	Water	rt	10	48	2.5
4	Methanol	Water	rt	60	60	2.5
5 ^c	Methanol	Mineral water	rt	10	99	2.5

^aReaction Conditions: 0.25 mmol of 4-nitrobenzaldehyde, 0.30 mmol NH₂OH.HCl, ^bThe yield was determined by the analysis of the ¹H NMR spectra, ^cMethanol/mineral water (1/1 v/v).

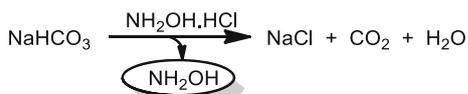
Table 2. The reaction of aldehydes with hydroxylamine hydrochloride^a

Entry	R	Time, min	Isolated yield ^b , %	Lit.
1	4-NO ₂ C ₆ H ₄	10	95	22
2	4-ClC ₆ H ₄	10	95	22
3	4-BrC ₆ H ₄	10	95	23
4	4-IC ₆ H ₄	10	90	24
5	2-OH, 5-NO ₂ C ₆ H ₃	7	88	24
6	2-OH, 4-MeC ₆ H ₃	10	87	24
7	4-OHC ₆ H ₄	10	80	25
8	2-OH, 1-naphthyl	5	83	26
9	2,5-(MeO) ₂ C ₆ H ₃	7	95	27
10	3,4,5-(MeO) ₃ C ₆ H ₂	10	95	28
11	3,4-Cl ₂ C ₆ H ₃	10	95	29

^aUnless otherwise stated, 0.25 mmol of substrate, 0.30 mmol NH₂OH.HCl, 2 mL of mineral water/methanol (v/v=1/1), at room temperature, ^bAll products are known compounds and exhibit satisfactory spectroscopic data.

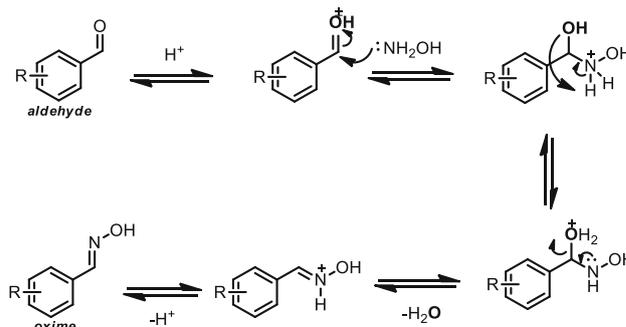
**Scheme 1.** The hydrogen bonding that increases electropositivity.

source is activated by mineral water (containing carbonate, sulphate, etc., salts) added to the reaction medium. The resulting hydroxy amine compound reacts with the aldehyde derivatives to obtain the oxime

**Scheme 2.** The neutralization reaction of NaHCO₃.

derivatives. Moreover, water and carbon dioxide formation is observed in the environment (Scheme 2).

As a result, it was observed that the reactions were completed in a shorter time in the presence of mineral water. The proposed mechanism is given below (Scheme 3).

**Scheme 3.** Proposed mechanism.

4. Conclusions

As a result, in the presence of mineral water and at room temperature, oxime compounds were obtained in high yields and within about 10 min as a result of the addition-elimination reaction of aldehyde compounds with the hydroxylamine hydrochloride compound. It is of great industrial importance because the method is practical, economical and eco-friendly. The method has many strengths: (i) free from unnecessary chemicals, (ii) energy savings, and (iii) use of both local and natural resources.

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Declaration

Conflict of interest The authors declare no conflict of interest

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