



# SYNTHESIS OF OXIMES IN AQUEOUS MEDIUM USING HYAMINE<sup>®</sup> AS AN ECOFRIENDLY CATALYST AT AMBIENT TEMPERATURE

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## ABSTRACT

An environmentally benign, highly efficient method for the conversion of aldehydes to aldoximes using a Hyamine<sup>®</sup> as a catalyst in water, at ambient temperature is presented. The major advantages of the method are high yields, short reaction time, ease of operation and use of aqueous medium.

**Keywords :** Oximes, Aldehydes, Hyamine<sup>®</sup>, Ecofriendly, Ambient temperature, Water.

## INTRODUCTION

Use of solvent for the processes in chemical industry defines a major part of the environmental performance and also has impact on cost, safety and health issues. The idea of “green” solvents expresses the goal to minimize adverse environmental impact resulting from the use of solvents. Despite the use of hazardous organic solvents, much of the efforts have been made to develop green methodologies with supercritical solvents,<sup>1</sup> ionic liquids,<sup>2</sup> etc. However, use of these solvents generally ploughed with high pressure conditions, use of expensive reagents and lengthy workouts. In tune with the search for green solvents, the use of water as a reaction medium has attracted notable interest and offers a clean, economical and environmentally safe protocol for many reactions.<sup>3</sup> The significant enhancement to the rate of the reaction in water has been attributed to hydrophobic packing,<sup>4</sup> solvent polarity,<sup>5</sup> hydration,<sup>6</sup> and hydrogen bonding.<sup>7</sup>

Transformation of carbonyl functionalities into oximes 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<sup>8</sup>, hydroximinoyl chlorides<sup>9</sup>, nitrones<sup>10</sup> and nitriles<sup>11</sup>. 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 ultrasound irradiation<sup>12a</sup>, microwave irradiation<sup>12b</sup> and solvent free heating<sup>13</sup> were applied to this reaction. Oxidation of amines or hydroxylamines was another usual method for the synthesis of oximes<sup>14</sup>.

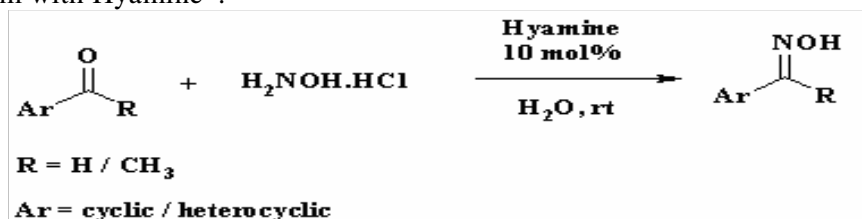
Oximes are generally prepared by using either acidic or basic catalysts. Conventionally, they are prepared by refluxing an alcoholic solution of a carbonyl compound with hydroxylamine hydrochloride and pyridine<sup>15</sup>. Other alternative procedures have also been reported over the past few years, using ionic liquids,<sup>16</sup> polyoxometalates,<sup>17</sup> oxone<sup>®</sup>,<sup>18</sup> Alumina sulfuric acid,<sup>19</sup> formic acid,<sup>20</sup> pyridine/chloroform,<sup>21</sup> sulfuric acids,<sup>22</sup> basic Al<sub>2</sub>O<sub>3</sub>,<sup>23</sup> TiO<sub>2</sub>/SO<sub>4</sub><sup>2-</sup> a solid superacid.<sup>24</sup> Oximes have also been synthesized from nitriles,<sup>25</sup> phosphonium compounds<sup>26</sup> and *via* microwave irradiation (MWI) of ketones, NH<sub>2</sub>OH·HCl and NaOAc in EtOH<sup>27</sup>. However, these methods are plagued by disadvantages such as low yields, long reaction time, effluent pollution, etc. Hence, an environmentally benign method with respect to cost efficiency, solvent suitability, hazardous reagents as well as acceptable reaction conditions for synthesis of oximes is highly warranted.

An intriguing line in the development of ecofriendly methodologies is being fuelled by basic paradigm shift from use of traditional catalysts to ecofriendly catalysts since they fulfill the principles of green chemistry. Hyamine<sup>®</sup> (Hyamine<sup>®</sup> 1622 *viz.*, Benzethonium chloride is a registered trademark of Lonza

Inc.) as a surfactant can receive considerable attention as a versatile catalyst because of its high catalytic activity, stability, ease of handling, easy preparation method and low toxicity.

## RESULTS AND DISCUSSION

In continuation of research devoted to the development of green chemistry by performing reactions under uncatalyzed conditions, solvent-free conditions, by using water as reactions medium, we report herein an ecofriendly conversion of carbonyls to oximes using Hyamine<sup>®</sup> as a catalyst in aqueous medium at ambient temperature. (Scheme 1). To the best of our knowledge this is a first report in aqueous medium with Hyamine<sup>®</sup>.



Scheme-1

An attempt was made to synthesize the simple aldoxime, 4-methoxybenzaloxime, using equimolar mixture of anisaldehyde and hydroxylamine hydrochloride and Hyamine<sup>®</sup> (10 mol %), the product was obtained in almost quantitative yield within 60 minutes at room temperature in aqueous medium (Table 1, entry 1). However, catalyzing ability of a Hyamine<sup>®</sup> in oxime synthesis undergoes a real test when it comes to reaction between aldehydes having both electron donating as well as electron withdrawing substituents and hydroxylamine hydrochloride. Gratifyingly, a series of aldoximes were synthesized using different aldehydes and hydroxylamine hydrochloride and results are summarized in Table 1. It is evident that electron rich and electron deficient aldehydes as well as heterocyclic systems such as thiophene-2-carboxaldehyde, furan-4-carboxaldehyde reacted smoothly with hydroxylamine hydrochloride to produce high yields of corresponding oximes. Interestingly, ketones like acetophenones did not react with hydroxylamine hydrochloride using above mentioned conditions thus demonstrating the chemoselectivity of Hyamine<sup>®</sup> towards aldehydes versus ketones. All the products were characterized by comparison of their physical constant and spectral analysis with those of literature.

In conclusion, in this report we have described synthesis of oximes using Hyamine<sup>®</sup> as a catalyst in aqueous medium at ambient temperature. The described procedure works well for a variety of aldehydes. The simplicity of the experimental procedure, chemoselectivity over ketones and the environmental compatibility of the catalyst render this as an experimentally easy and attractive method for the conversion of aldehydes to oximes.

## EXPERIMENTAL

### General procedure for conversion of aldehydes to oximes

A mixture of an aldehyde (2.5 mmol), hydroxylamine hydrochloride (3 mmol) in water (5 mL) and Hyamine<sup>®</sup> (10 mol %) was stirred and the progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was filtered to obtain the desired oxime. These products were characterized by physical constants and usual spectral techniques.

### Spectroscopic data

<sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra were recorded at 300 MHz and 75 MHz respectively on a Bruker Avance-300 spectrometer using CDCl<sub>3</sub> as solvent. Chemical shifts (δ) are given in ppm relative to TMS as an internal standard and coupling constants (*J*) in Hz.

**N-(4-Methoxy-benzyl)-hydroxylamine (Table 1, entry 1):** <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 3.84 (3H, s, OCH<sub>3</sub>) 6.92 (2H, d, *J* = 6.9 Hz, ArH), 7.53 (2H, d, *J* = 6.9 Hz, ArH), 8.13 (1H, s, CH), 8.90 (1H, brs, OH) <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): 55.34, 114.26, 124.56, 128.54, 149.93 and 161.07.

**N-(4-Methyl-benzyl)-hydroxylamine (Table 1, entry 3):**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.38 (3H, s,  $\text{CH}_3$ ) 7.21 (2H, d,  $J = 7.8$  Hz, ArH), 7.49 (2H, d,  $J = 7.8$  Hz, ArH), 8.14 (1H, s, CH)  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ): 21.43, 126.98, 129.17, 129.49, 140.28 and 150.34.

**N-Benzyl-hydroxylamine (Table 1, entry 5):**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.40-7.46 (3H, m, ArH), 7.57-7.62 (2H, m, ArH), 8.2 (1H, s, CH), 9.19 (1H, brs, OH)  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ): 127.08, 128.82, 130.12, 131.89 and 150.42.

**N-(4-Chloro-benzyl)-hydroxylamine (Table 1, entry 7):**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.37 (2H, d,  $J = 8.4$  Hz, ArH), 7.53 (2H, d,  $J = 8.4$  Hz, ArH), 8.11 (1H, s, CH)  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ): 128.18, 129.03, 130.50, 135.94 and 149.35.

**N-(3-Nitro-benzyl)-hydroxylamine (Table 1, entry 8):**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.59 (1H, t,  $J = 8.1$  Hz, ArH), 7.84 (1H, s, CH), 7.92 (1H, d,  $J = 7.8$  Hz, ArH), 8.22-8.26 (2H, m, ArH), 8.44 (1H, brs, OH)

**N-(4-Isopropyl-benzyl)-hydroxylamine (Table 1, entry 10):**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.27 (6H, d,  $J = 6.9$  Hz, 2 x  $\text{CH}_3$ ), 2.86-3.00 (1H, m, CH) 7.26 (2H, d,  $J = 8.1$  Hz, ArH), 7.52 (2H, d,  $J = 8.1$  Hz, ArH), 8.14 (1H, s, CH), 8.18 (1H, brs, OH)

**N-(3,4-Dimethoxy-benzyl)-hydroxylamine (Table 1, entry 14):**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  3.91 (6H, s, 2 x  $\text{OCH}_3$ ) 6.87 (2H, d,  $J = 8.1$  Hz, ArH), 7.04 (2H, d,  $J = 8.1$  Hz, ArH), 7.23 (1H, s, ArH), 8.09 (1H, s, CH), 8.30 (1H, brs, OH)  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ): 55.87, 55.92, 107.99, 110.75, 121.67, 124.84, 149.30, 150.20 and 150.80.

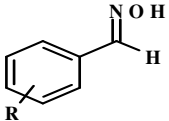
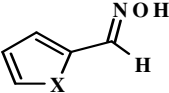
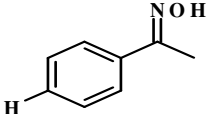
**N-Thiophen-2-ylmethyl-hydroxylamine (Table 1, entry 15):**  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.12 (1H, t,  $J = 5.1$  Hz, ArH), 7.43 (1H, d,  $J = 3.6$  Hz, ArH), 7.59 (1H, d,  $J = 5.1$  Hz, ArH), 7.76 (1H, s, CH), 9.70 (1H, brs, OH)  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ): 126.27, 130.89, 131.76, 131.95 and 141.18.

## REFERENCES

1. (a) N. Celebi, N. Yildiz, A. S. Demir and A. Calimli, *J. Supercritical Fluids*, **41**, 386 (2007); (b) V. Pauchon, Z. Cisse, M. Chavret and J. Jose, *J. Supercritical Fluids*, **32**, 115 (2004).
2. V. I. Parvulescu and C. Hardacre, *Chem. Rev.*, **107**, 2615 (2007).
3. C. J. Li, *Chem. Rev.*, **105**, 3095 (2005).
4. D. C. Rideout and R. L. Breslow, *J. Am. Chem. Soc.*, **102**, 7816 (1980).
5. C. Reichardt, Verlag Chemie: Weinheim, 1 (1979).
6. (a) T. Rispens, J. B. F. N. Engberts, *J. Org. Chem.* **67**, 7369 (2002); (b) W. Blokzijl, J. B. F. N. Engberts and M. J. J. Blandamer, *Am. Chem. Soc.*, **112**, 1197 (1990); (c) W. Blokzijl, J. B. F. N. Engberts, *J. Am. Chem. Soc.*, **113**, 5440 (1991); (d) W. Blokzijl, J. B. F. N. Engberts, *Angew. Chem. Int. Ed. Engl.*, **32**, 1545 (1993).
7. Blake, J. F. and Jorgensen, W. L. *J. Am. Chem. Soc.*, **113**, 7430 (1991).
8. S. Park, Y. Choi, H. Han, S. H. Yang and S. Chang, *Chem. Commun.*, 1936 (2003).
9. (a) Y. H. Chiang, *J. Org. Chem.*, **36**, 2146 (1971); (b) K. C. Liu, B. R. Shelton and R. K. How, *J. Org. Chem.*, **45**, 3916 (1980).
10. (a) E. F. Schoenewaldt, R. B. Kinnel and P. Davis, *J. Org. Chem.*, **33**, 4270 (1968); (b) P. A. S. Smith and J. E. Robertson, *J. Am. Chem. Soc.*, **84**, 1197 (1962); (c) E. Buehler, *J. Org. Chem.*, **32**, 261 (1967).
11. a) M. H. Sarvari, *Synthesis*, 787 (2005); (b) G. Sosnovsky, J. A. Krogh, *Synthesis*, 703 (1978).
12. (a) J.-T. Li, X.-L. Li and T.-S. Li, *Chinese J. Org. Chem.*, **26(11)**, 1594 (2006) and references cited there in.; (b) A. R. Hajipour, S. E. Mallakpour and G. Imanzadeh, *J. Chem. Res. (S)*, 228 (1999).
13. (a) H. Sharghi and M. Hosseini, *Synthesis*, 1057 (2002); (b) H. Sharghi, and H. M. Sarvari, *Synlett*, 99 (2001).
14. (a) K. C. Nicolaou, C. J. N. Mathison and T. Montagnon, *J. Am. Chem. Soc.*, **126**, 5192 (2004); (b) K. C. Nicolaou, C. J. N. Mathison, T. Montagnon, *Angew. Chem. Int. Ed. Engl.*, **115**, 4211 (2003); (c) R. Joseph, T. Ravindranathan and A. Sudalai, *Tetrahedron Lett.*, **36**, 1903 (1995); (d) Y. M. A. Yamada, H. Tabata, H. Takahashi and S. Ikegami, *Synlett*, 2031 (2002).
15. T. W. Greene and P. G. M. Wuts, *Protective Groups in Organic Synthesis*, 2nd edn., John Wiley & Sons, Inc., New York, 214 (1991).

16. A. R. Hajipour, F. Rafiee and A. E. Ruoho, *J. Iran. Chem. Soc.*, **7(1)**, 114 (2010).
17. R. Fazaeli, S. Tangestaninejad and H. Aliyan, *Catal. Commun.*, **8(2)**, 205 (2007)
18. J.-J. Xia and G.-W. Wang, *Molecules*, **12**, 231 (2007)
19. M. Hosseini-Sarvari and H. Sharghi, *J. Chem. Res.*, **2006(3)**, 205 (2006)
20. G. A. Olah and T. Keumi, *Synthesis*, 12 (1979).
21. G. Sosnovsky, J. A. Krogh and S. G. Umhoefer, *Synthesis*, 722 (1979).
22. K. Weissermer and H. J. Arpe, *Industrial Organic Chemistry*, 222 (1978).
23. G. L. Kad, M. Bhandari, J. Kaur, R. Rathee and J. Singh, *Green Chem.*, **3**, 275 (2001)
24. J.-J. Guo, T.-S. Jin, S.-L. Zhang and T. -S. Li, *Green Chem.*, **3**, 193 (2001).
25. M. Kizil and J. A. Murphy, *Tetrahedron*, **53**, 16847 (1997).
26. F. Palacios, D. Aparicio, J. M. De Los Santos and E. Rodriguez, *Tetrahedron*, **54**, 599 (1998).
27. A. K. Mitra , A. De and N. Karchaudhuri, *J. Indian Chem. Soc.*, **76**, 218 (1999).

Table-1: Convesion of aldehydes into aldoximes

Entry	Product	Time (min)	Yield (%)
			
1	R = 4-OMe	60	95
2	R =3-Cl	50	88
3	R = 4-Me	40	90
4	R = 2-NO <sub>2</sub>	55	91
5	R = H	40	98
6	R = 4-CN	80	85
7	R = 4-Cl	45	90
8	R =3-NO <sub>2</sub>	70	88
9	R = 4-NO <sub>2</sub>	85	85
10	R = 4- <sup>t</sup> Pr	60	91
11	R = 4-N(Me) <sub>2</sub>	90	85
12	R = 4-OH	50	89
13	R = 2-OH	55	93
14	R = 3-OMe, 4-OMe	45	94
			
15	X = S	40	95
16	X = O	45	93
			
17	R = H	12 <sup>C</sup>	NR
18	R = 4- Cl	12 <sup>C</sup>	NR

<sup>a</sup> All products were proved by spectroscopic data.

<sup>b</sup> Yields refer to pure, isolated products.

<sup>c</sup> Time in hours

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