

## Research Article

# Rapid regeneration of Carbonyl compounds from Oximes Under Mild Lewis acid conditions using NaI/ BF<sub>3</sub>.Et<sub>2</sub>O

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## ABSTRACT

A simple and efficient protocol for the regeneration of carbonyl compounds was demonstrated under mild Lewis acid conditions using NaI/ BF<sub>3</sub>.Et<sub>2</sub>O. Varieties of oximes were synthesized (**1-19**) and converted to their corresponding carbonyls with excellent yields, selectivity, and highly reduced reaction times with minimized side products. A systematic study of the conditions of experimentation was resulted to propose a possible mechanism of the progress of the reaction.

**Keywords:** Oximes, Sodium iodide/ Borontrifluoride-etherate, Carbonyl compounds.

## INTRODUCTION

Oximes of carbonyl compounds are important, because they are frequently used to protect carbonyl compounds in the course of total synthesis and assumed added importance after the discovery of Barton reaction<sup>1</sup> in which the oximes are produced at non-activated hydrocarbon sites. The generation of carbonyl compounds from oximes represents a potential route for the synthesis of ketones and aldehydes<sup>2</sup>. Therefore, there has been a continuous interest in the development of methods for the efficient regeneration of carbonyls from their parent nitrogen derivatives and an efficient catalytic cleavage would therefore be considerable benefit.

A variety of methods have been developed for the conversion of oximes into their corresponding carbonyl compounds. In which, mostly consists of oxidative<sup>3</sup>, reductive<sup>4</sup>, acid catalyzed<sup>5</sup>, that requires strong acids and co-solvent in relation to the stability of oximes. Recent reports also identified methods including clay supported<sup>6</sup> and microwave assisted<sup>7</sup>. Although literature enumerates plethora of methods which involve reagents

that are often hazardous or very toxic, expensive or not readily available<sup>8</sup>.

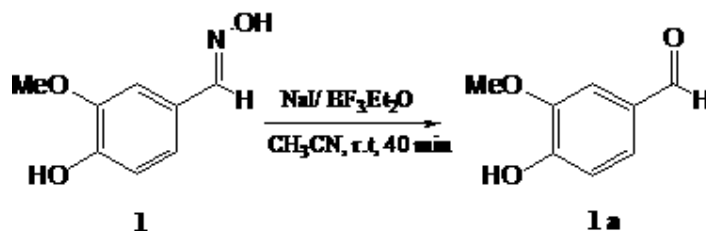
Careful scrutiny of the methods reveals that most of these methods represent a different balance of yields, reflux temperatures, longer reaction times, toxicity, expense, selectivity and convenience. Consequently, there is a scope for further development of milder reaction conditions and with better yields. Herein, we studied the importance of BF<sub>3</sub>.Et<sub>2</sub>O in combination with NaI for the rapid conversion of oximes into their corresponding carbonyl compounds with excellent yields, selectivity and short reaction times.

## RESULTS AND DISCUSSION

In the course of our studies on the development of Lewis acid catalyzed organic transformation<sup>9</sup>, we wish to report in this communication a new catalyst for the direct conversion of oximes into aldehydes and ketones under mild Lewis acid conditions using borontrifluoride-etherate and sodium iodide. The versatility of the combination of borontrifluoride etherate/halide ion has been well exemplified in organic chemistry in which, most methods focused on mild and

regioselective cleavage of ether<sup>10</sup> conversion of benzylic, allylic and tertiary alcohols to halides<sup>11</sup>, degeneration of sulfoxides to sulfides<sup>12</sup>, a non aqueous conversion of acetals and ketals to the carbonyl compounds<sup>13</sup>, and selective cleavage of benzyl ethers<sup>14</sup> were well studied in the literature and no one has studied the importance of this reagent towards the above mentioned purpose. Recent reports also studied the utility of this reagent for the efficient selective reduction of aromatic azides to amines<sup>15</sup>.

An easy release of the  $\text{BF}_3$  component from this complex and it's further coordinating with either oxygen atom or other heteroatom bringing about specific transformations has also been well specified in organic reactions<sup>12</sup>. We have developed a convenient method for the deoxygenation of aldoximes and ketoximes to their corresponding carbonyl compounds using  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  together with  $\text{NaI}$ . The utility of this reagent for the regeneration of carbonyls were well studied and a variety of oximes were synthesized in terms to study the selectivity as well as to monitor the reaction yields.



**Scheme. 1: Deoxygenation of Oximes into Carbonyl compounds**

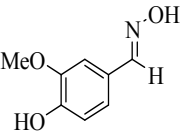
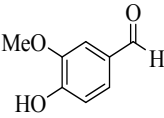
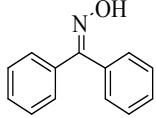
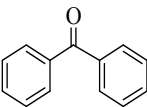
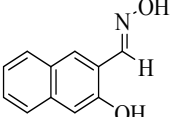
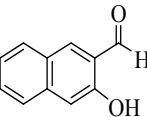
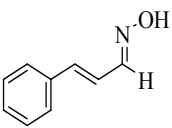
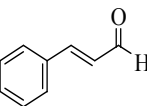
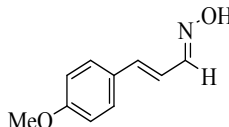
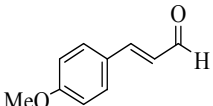
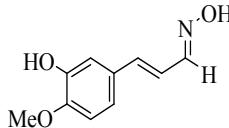
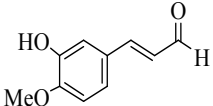
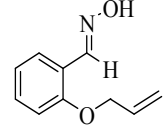
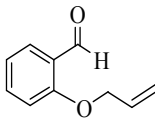
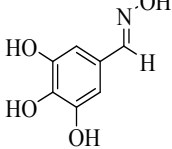
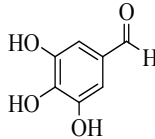
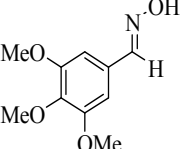
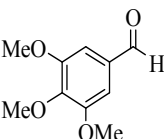
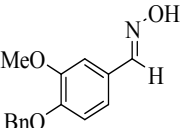
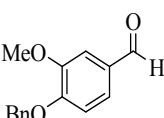
In the first step of the analysis, 3-methoxy-4-hydroxy benzaldehyde oxime **1** was treated with  $\text{NaI}/\text{BF}_3 \cdot \text{Et}_2\text{O}$  in acetonitrile for 30 min. at ambient temperature. A complete conversion (monitored by TLC) resulted in the formation of 3-methoxy-4-hydroxy benzaldehyde **1a** with 90% yield (isolated yields) and there was no evidence of the formation of side product. Similarly, varieties of oximes (**2a-19a**) were prepared using standard oximation method by the reaction of carbonyl compounds with hydroxylamine hydrochloride. Resulted oximes were examined with the treatment of reagent and were converted into the respective carbonyl compounds in 50-92% yields.

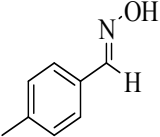
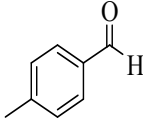
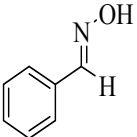
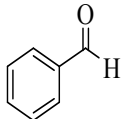
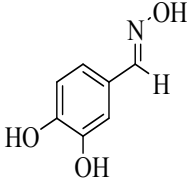
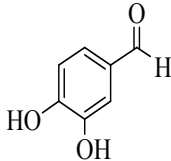
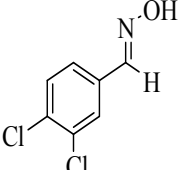
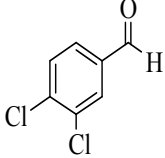
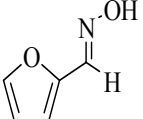
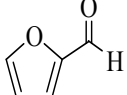
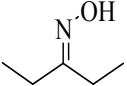
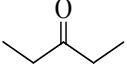
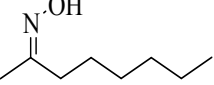
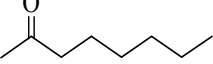
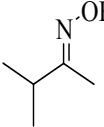
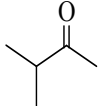
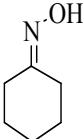
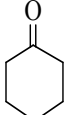
A close monitoring the reaction conditions and the products reveals that electron donating groups on the phenyl ring resulting in slight lowering the yields and this is due to decrease the electrophilic character of the carbonyl carbon. Rate of conversion of aldoximes is faster compare to that of ketoximes. This is due to the low reactivity of ketoximes over aldoximes. Increase in the electrophilic

character might improve the formation of complex with  $-\text{OBF}_3$  further resulting in improves the reaction yields.

In terms to study the selectivity, we used a wide variety of oximes in which substrate **6** an  $\alpha, \beta$ -unsaturated aldehyde was treated with the reagent resulting in the formation of **6a** in high yield. In the similar fashion substrate **7** undergo treatment with reagent resulting in the formation of **7a** with moderate yield and excellent selectivity. It indicates that oximes can be selectively deprotected in the presence of other functional groups such as  $-\text{OMe}$ ,  $\text{O-allyl}$ ,  $\text{OBn}$ . In all these cases  $-\text{OBF}_3^-$ , act as an excellent leaving group and iodide ion as best nucleophile resulting in the conversion of oximes into carbonyl compounds. The experimental optimization of reaction and their yields were summarized in **Table-1**. In all the cases the reaction proceeds in high yields at room temperature within the short reaction times (0.4-2 h).

**Table 1: Deoximization of oximes into carbonyl compounds using NaI/BF<sub>3</sub>.Et<sub>2</sub>O**

Entry	Substrate	Product <sup>a</sup> (1a-12a)	Time (min)	Yield <sup>b</sup> (%)
1			40	90
2			60	72
3			45	90
4			55	80
5			80	72
6			60	85
7			55	84
8			50	87
9			60	50
10			120	84

Entry	Substrate	Product <sup>a</sup> (1a-12a)	Time (min)	Yield <sup>b</sup> (%)
11			55	78
12			45	86
13			45	90
14			45	92
15			55	84
16			90	75
17			80	70
18			45	87
19			60	70

<sup>a</sup>All the compounds were characterized by using IR, NMR, Mass and comparing the authentic samples. <sup>b</sup> Isolated yields

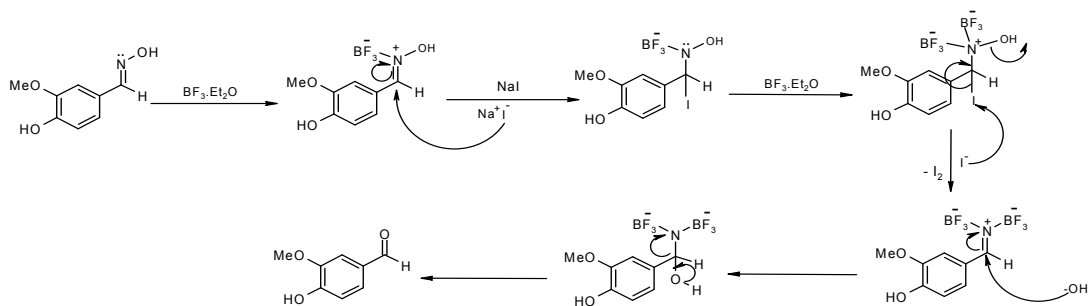
In view of the above-observed selectivity, mildness, less reaction times, it is believed that the scope and generality of the reaction has considerably improved with respect to deprotection of various oximes.

A systematic study of the conditions of experimentation was studied and a proposed mechanism, which determines the progress of the reaction, was depicted in **Scheme-2**. Borontrifluoride-etherate catalysis in coordination with hetero atom increases the electrophilic character and further  $I^-$  act as best nucleophile to activate this complex to further release iodine resulting in the formation of corresponding aldehydes and ketones in excellent yields.

To show the efficiency and applicability of the reagent we studied the importance of sodium iodide in the reaction. Compound **1** was treated with  $BF_3 \cdot Et_2O$  in the absence of sodium iodide, we did not see the formation of any product even after 10 h, where as, the addition sodium iodide considerably progress the reaction towards product **1a** and observed the release of free  $I_2$  which is confirmed by

iodine liberation test also supported by acidic pH of the reaction. These observations clearly indicate the role and significance of sodium iodide in the rapid conversion of oximes into their corresponding carbonyl compounds. Only the combination of the reagent clearly demonstrated the formation complex and further resulted in the conversion of product under short reaction times. Several oximes were prepared by reported literature and further treatment with reagents yielded corresponding carbonyls in excellent yields and selectivity (**Table-1**).

In conclusion, a simple and efficient protocol for the regeneration of carbonyl compounds using  $NaI/BF_3 \cdot Et_2O$  has been demonstrated. The advantage of this new method is mild reaction conditions, highly reduced reaction times, and minimization of side products, simple experimental procedure<sup>16</sup> and excellent yields. These advantages are very useful in complex multiple synthesis. The present method consulate a useful alternative to the available procedures.



**Scheme. 2: Proposed mechanism for the regeneration of carbonyl compounds from oximes using  $NaI/BF_3 \cdot Et_2O$**

#### Spectral data for selected compounds

3-methoxy-4-hydroxy benzaldoxime (**1**): IR (KBr):  $\nu_{max}$  3451 (-OH), 2941, 1642, 1598, 1156, 948, 970  $cm^{-1}$ ,  $^1H$  NMR ( $CDCl_3$ , 200 MHz):  $\delta$  8.0 (1H, s, -CH=N), 7.20 (1H, dd,  $J = 8.0, 2.0$  Hz, H-6), 6.95 (1H, d,  $J = 2.0$  Hz, H-2), 6.89 (1H, d,  $J = 8.0$  Hz, H-5), 5.70 (1H, s, Ar-OH), 3.95 (3H, s, Ar-OMe), EIMS: 168 ( $M^+ + H$ ).

3-methoxy-4-hydroxy benzaldehyde (**1a**): IR (KBr):  $\nu_{max}$  3480 (Ar-OH), 2941, 1718, 1606, 1150  $cm^{-1}$ ,  $^1H$  NMR ( $CDCl_3$ , 200 MHz):  $\delta$  9.81 (1H, s, -CH=O), 7.42 (1H, dd,  $J = 7.9, 2.0$  Hz, H-6), 7.39 (1H, d,  $J = 2.0$  Hz, H-2), 7.05 (1H, d,  $J = 7.9$  Hz, H-5), 6.39 (1H, s, Ar-OH), 3.98 (3H, s, Ar-OMe), EIMS: 153 ( $M^+ + H$ ).

3-hydroxy-4-methoxy cinnamaldoxime (**6**): IR (KBr):  $\nu_{max}$  3462, 2984, 1587, 1156, 992  $cm^{-1}$ ,  $^1H$  NMR ( $CDCl_3$ , 200 MHz):  $\delta$  8.25 (1H, s, -

CHO) 7.25 (1H, d,  $J = 16.0$  Hz, -CH=CH), 6.98 (1H, dd,  $J = 8.0, 1.5$  Hz, H-6), 6.80 (1H, d,  $J = 1.5$  Hz, H-2), 6.75 (1H, d,  $J = 8.0$  Hz, H-5), 6.28 (1H, d,  $J = 16.0$  Hz, -CH=CH), 5.60 (1H, s, -OH, Ar-OH), 3.82 (3H, s, Ar-OMe), EIMS: 194 ( $M^+ + H$ ).

3-hydroxy-4-methoxy cinnamaldehyde (**6a**): IR (KBr):  $\nu_{max}$  3462, 2984, 1587, 1156  $cm^{-1}$ ,  $^1H$  NMR ( $CDCl_3$ , 200 MHz):  $\delta$  10.05 (1H, s, -CHO) 7.55 (1H, d,  $J = 16.0$  Hz, -CH=CH), 7.18 (1H, dd,  $J = 8.0, 2.0$  Hz, H-6), 7.08 (1H, d,  $J = 2.0$  Hz, H-2), 6.98 (1H, d,  $J = 8.0$  Hz, H-5), 6.40 (1H, d,  $J = 16.0$  Hz, -CH=CH), 5.90 (1H, s, -OH, Ar-OH), 3.89 (3H, s, Ar-OMe), EIMS: 179 ( $M^+ + H$ ).

2-O-allyl benzaldoxime (**7**): IR (KBr):  $\nu_{max}$  3425, 2895, 1597, 1065, 988  $cm^{-1}$ ,  $^1H$  NMR ( $CDCl_3$ , 200 MHz):  $\delta$  8.10 (1H, s, -CH=N-OH), 7.14-7.35 (4H, m, Ar-H), 5.72-5.74 (1H, m, -

CH=CH<sub>2</sub>), 5.23-5.35 (2H, m, -CH=CH<sub>2</sub>), 4.49 (2H, t, *J* = 12.5, 6.0 Hz, -OCH<sub>2</sub>), EIMS: 178 (M<sup>+</sup>+H).

2-O-allyl benzaldehyde (**7a**): IR (KBr):  $\nu_{\max}$  2895, 1728, 1597, 1065 cm<sup>-1</sup>, <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz):  $\delta$  10.02 (1H, s, -CH=O), 7.45 (1H, dd, *J* = 8.0, 2.0 Hz, H-6), 7.23-7.25 (1H, m, H-4), 6.75-6.80 (1H, m, H-5), 6.65 (1H, dd, *J* = 7.8, 2.0 Hz, H-3), 5.75-5.80 (1H, m, -CH=CH<sub>2</sub>), 5.28-5.42 (2H, m, -CH=CH<sub>2</sub>), 4.65 (2H, t, *J* = 12.0, 6.0 Hz, -OCH<sub>2</sub>), EIMS: 163 (M<sup>+</sup>+H).

3-methoxy-4-O-benzyl benzaldoxime (**10**): IR (KBr):  $\nu_{\max}$  3451(-OH), 2941, 1642, 1598, 1156 cm<sup>-1</sup>, <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz)  $\delta$  8.0 (1H, s, -CH=N), 7.40-7.30 (5H, m, -Ph), 7.20 (1H, dd, *J* = 7.9, 2.0 Hz, H-6), 6.95 (1H, d, *J* = 2.0 Hz, H-2), 6.89 (1H, d, *J* = 7.9 Hz, H-5), 5.70 (1H, s, Ar-OH), 5.18 (2H, s, CH<sub>2</sub>-Ph) 3.95 (3H, s, Ar-OMe), EIMS: 258 (M<sup>+</sup>+H).

3,4-di chloro benzaldoxime (**14**): IR (KBr):  $\nu_{\max}$  3480, 2941, 1642, 1606, 968 cm<sup>-1</sup>, <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz):  $\delta$  8.20 (1H, s, -CH=N-OH), 7.60 (1H, d, *J* = 2.0 Hz, H-2), 7.42 (1H, dd, *J* = 8.0, 2.0 Hz, H-6), 7.35 (1H, d, *J* = 8.0 Hz, H-5), EIMS: 191 (M<sup>+</sup>+H).

3,4-di chloro benzaldehyde (**14a**): IR (KBr):  $\nu_{\max}$  2982, 1648, 1730, 1606 cm<sup>-1</sup>, <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz):  $\delta$  10.10 (1H, s, -CH=O), 7.70 (1H, d, *J* = 2.0 Hz H-2), 7.68 (1H, dd, *J* = 8.0, 2.0 Hz, H-6), 7.30 (1H, d, *J* = 8.0 Hz, 2 Hz, H-5), EIMS: 176 (M<sup>+</sup>+H).

2-Octanonoxime (**17**): IR (KBr):  $\nu_{\max}$  3415, 2992, 1325, 978 cm<sup>-1</sup>, <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz):  $\delta$  8.90 (1H, s, -C=N-OH), 2.20 (2H, t, *J* = 14.0, 8.1 Hz, H-3), 1.86 (3H, s, -CH<sub>3</sub>, H-1), 1.20-1.60 (8H, m, 4 x -CH<sub>2</sub>, H-4, 5, 6, 7), 0.89 (3H, t, *J* = 12.0, 6.6 Hz, H-8), EIMS: 144 (M<sup>+</sup>+H).

2-Octanone (**17a**): IR (KBr):  $\nu_{\max}$  3425, 2994, 1715, 1298, 865 cm<sup>-1</sup>, <sup>1</sup>H NMR (CDCl<sub>3</sub>, 200 MHz):  $\delta$  2.10 (2H, t, *J* = 14.0, 8.1 Hz, H-3), 2.02 (3H, s, -CH<sub>3</sub>, H-1), 1.08-1.15 (8H, m, 4 x -CH<sub>2</sub>, H-4,5,6,7), 0.79 (3H, t, *J* = 12.0, 6.6 Hz, H-8), EIMS: 128 (M<sup>+</sup>+H).

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16. Experimental Procedure: To a stirred solution of oxime (3 mmol) and NaI (6 mmol) in 15 ml acetonitrile was added BF<sub>3</sub>.Et<sub>2</sub>O (6 mmol) in acetonitrile slowly and the resulting mixture was stirred at room temperature under Ar for the specified time as indicated in Table-1. After the disappearance of the starting material as indicated by TLC, the reaction mixture was quenched with ice cold water (20 ml), and added aqueous solution of 15% of sodium thiosulphate (15 mL) and extract with ether (2 x 25 ml). The combined organic layers were washed with bicarbonate (10 mL) and brine (10 mL) dried over anhydrous sodium sulphate. The solvent was evaporated and the residue was purified by column chromatography to obtained pure compound with excellent yield and purity.