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Cupper supported silica promoted one-pot synthesis of aromatic oxime derivatives

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ABSTRACT

*A simple and efficient approach towards one step synthesis of high-yielding conversion of aromatic oximes**(3a-t)**has been developed by condensation of aromatic aldehydes, hydroxylamine hydrochloride and Cu-Sio$_2$ in aqueous ethanol.*

Key Words: Aromatic aldehydes, Hydroxylamine hydrochloride, Cu support SiO_2, Aqueous ethanol.

INTRODUCTION

The oximes are most useful derivatives of aldehydes and ketones, both for the purposes of characterization and also as the key intermediates in the important Beckmann rearrangement [1-3]. They are also used as precursors in the synthesis of variety of organic compounds α-phenyl-*N*-substituted nitrones and *O*-alkyl benzaldoximes [4] and also in the preparation of 1,3-dipolar reagents [5].Although several methods for their synthesis [1,2,6-8] have been reported in the literature most are associated with long reaction times, tedious reaction conditions and low yields.

A typical experiment would involve heating a mixture of the carbonyl compound and hydroxylamine hydrochloride in water or ethanol, along with a base such as pyridine or sodium acetate [1].Few other procedures also have been reported under solvent free conditions using molecular sieves [6]. Hence there is a need for an efficient mild and environmentally friendly procedure for the synthesis of oximes.

In recent years, the use of heterogeneous catalysts has received considerable interest in various disciplines including organic synthesis. They are advantageous over their homogeneous counterparts due to the prime advantage that in most of the cases the catalyst Ni supported Silicahave been used as efficient heterogeneous catalysts for many organic transformations because of their low cost, ease of preparationand ease of handling [9-10].

MATERIALS AND METHODS

Experimental Section

All reagents and solvents were purchased and used without further purification. Melting points were determined on a Fisher–Johns melting point apparatus were uncorrected. Crude products were purified by column chromatography on silica gel of 60–120 mesh. The NMR spectra were recorded on a varian 300 MHz spectrometer for ^{1}H NMR. The chemical shifts were reported as ppm down field using TMS as an internal standard. LCMS Mass spectra were recorded on a MASPEC low resolution mass spectrometer operating at 70 eV.

RESULTS AND DISCUSSION

For the development of useful synthetic methodologies we have observed that substituted aromatic aldehydes are conveniently converted into their oximes by treatment with hydroxylamine hydrochloridein the presence of Cu supported silica in aqueous ethanol at room temperature (Scheme 1), to afforded excellent yields.

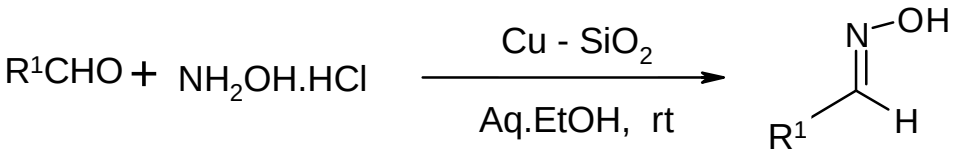
A series of oximes were prepared from several aromatic aldehydes, hydroxylamine hydrochloridewith Cu supported silica (Table-1)by following the above method. No additional catalyst was required and the conversion was completed within 2-3h. The products were obtained in good yields without any side products. The structures of the products were established by melting point comparison and spectral (^{1}H-NMR &LCMS) data. The Cu supported silica has been applied here as an efficient green reaction medium for the preparation of oximes. It is an inexpensive, low toxicity,and eco-friendlyreaction.Their applications as a reaction medium in organic synthesis havenot yet been fully explored.

***General procedure for the synthesis of oximes*:**

To a stirred suspension of substituted aromatic aldehydes **1** (1 mmol), hydroxylamine hydrochloride (1.5 mmol) **2** and Cu supported silica (2 mmol) was added in aqueous ethanol and the mixture was stirred at room temperature for 2-3h (TLC showed the completion of reaction). The reaction mixture was poured into crushed ice and filtered, washed with water. The filtrate was extracted with ethyl acetate. Finally, the pure compound (**3a-t)**was afforded by the column chromatography. The physical data (mp, Anal, NMR& LCMS) of the compound are present below.

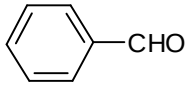
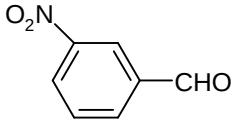
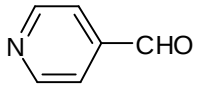
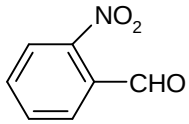
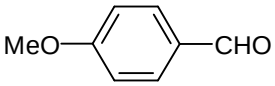
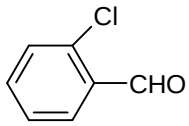
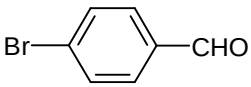
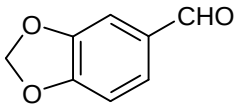
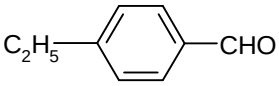
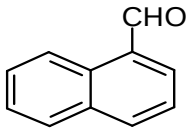
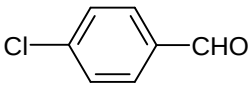
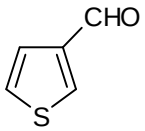
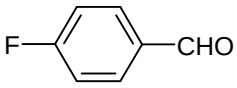
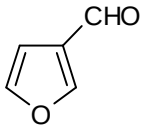
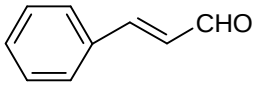
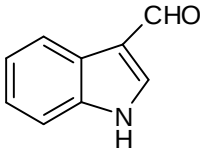
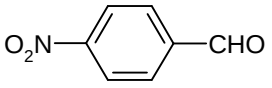
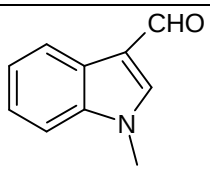
BenzaldehydeOxime (3a).Pale yellow solid; Yield 90%; m.p. 30-32 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.85 (S, 1H, OH), 8.15 (s, 1H, CH), 7.70-7.58 (m, 2H, ArH),7.50-7.42 (m, 3H, ArH); LCMS (*m*/*z*) 122 (M+1H). Anal. Calcd. for C_7H_7NO: C, 69.41, H, 5.82, N, 11.56; Found: C, 69.58, H, 5.68, N, 11.63.

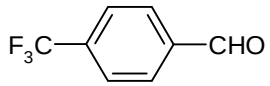
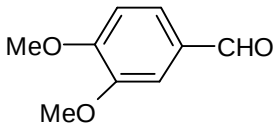
(Scheme 1)



1 **2** **3 a-t**

(Table 1)

Entry	R^1	Entry	R^1
3a		**3k**	
3b		**3l**	
3c		**3m**	
3d		**3n**	
3e		**3o**	
3f		**3p**	
3g		**3q**	
3h		**3r**	
3i		**3s**	

3j		**3t**	

Pyridine-4-aldehyde Oxime (3b). Yellow solid; 89%; m.p. 129-131 ^{o}C; ^{1}H NMR (300 MHz, DMSO-d_6)δ 10.25 (s, 1H, OH), 8.30 (s, 1H, CH), 8.50-8.39 (d, 2H, *J* = 9.0Hz, ArH), 7.82-7.68 (d, 2H, *J* = 9.0Hz, ArH); LCMS (m/z): 122 $[M]^{+}$. Anal. Calcd for $C_6H_6N_2O$: C, 59.01; H, 4.91; N, 22.95. Found: C, 58.83; H, 4.95; N, 22.99.

p-Methoxybenzaldehyde Oxime (3c).Pale orange solid; Yield 92%; m.p. 65-67^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$): *δ*9.90 (s, 1H, OH), 8.20 (s, 1H, CH), 7.60 (d, 8.6 Hz, 2H, ArH), 7.10 (d, *J* = 8.6 Hz, 2H, ArH), 3.80 (s, 3H, OCH_3); LCMS (*m*/*z*)152 (M+1H).Anal. Calcd. for $C_8H_9NO_2$: C, 63.57, H, 6.00, N, 9.27; Found: C, 63.65, H, 5.81, N, 9.33.

p-Bromobenzaldehyde Oxime (3d). White solid; Yield 95%; m.p. 102-104^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$): *δ*9.95 (s, 1H, OH), 8.23 (s, 1H, CH), 7.62 (d, *J* = 8.6 Hz, 2H, ArH), 7.48 (d, *J* = 8.6 Hz, 2H, ArH); LCMS (*m*/*z*)202 (M+2H).Anal. Calcd. for C_7H_6 BrNO: C, 42.03, H, 3.02, N, 7.00; Found: C, 41.89, H, 3.11, N, 7.11.

p-Ethylbenzaldehyde Oxime (3e). Yellow solid; Yield 88%; m.p. 125-127^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$): *δ*9.84 (S, 1H, OH), 8.10 (s, 1H, CH), 7.70-7.58 (m, 2H, ArH), 7.40-7.35 (m, 3H, ArH), 2.80 (q, 2H, CH_2), 1.30 (t, 3H, $CH_3$0; LCMS (*m*/*z*)136 (M+1H).Anal. Calcd. for C_8H_9NO: C, 71.09, H, 6.69, N, 10.42; Found: C, 71.07, H, 6.61, N, 10.43

p-Chlorobenzaldehyde Oxime (3f). Pale yellow solid; Yield 92%; m.p. 108-110^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$): *δ*9.90 (s, 1H, OH), 8.18 (s, 1H, CH), 7.58 (d, *J* = 8.6 Hz, 2H, ArH), 7.40 (d, *J* = 8.6 Hz, 2H, ArH); LCMS (*m*/*z*)156 (M+1H).Anal. Calcd. for C_7H_6ClNO: C, 54.01, H, 3.84, N, 9.00; Found: C, 54.16, H, 3.93, N, 8.89.

p-Fluorobenzaldehyde Oxime (3g). Pale yellow solid; Yield 90%; m.p. 142-144^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$): *δ*9.90 (s, 1H, OH), 8.20 (s, 1H, CH), 7.72-7.58 (m, 2H, ArH), 7.48-7.38 (m, 2H, ArH); LCMS (*m*/*z*)140 (M+1H).Anal. Calcd. for C_7H_6 FNO: C, 60.39, H, 4.36, N, 10.10; Found: C, 60.49, H, 4.46, N, 9.91.

Cinnamaldehyde Oxime (3h). Pale orange solid; Yield 90%; m.p. 138-140^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$): *δ*10.35 (s, 1H, OH), 8.02-7.96 (m, 1H, CH), 7.62-7.48 (m, 5H, ArH) 6.90-6.85 (m, 2H, CH); LCMS (*m*/*z*)148 (M+1H).Anal. Calcd. for C_9H_9NO: C, 73.41, H, 6.16, N, 9.50; Found: C, 73.28, H, 6.29, N, 9.38.

p-Nitrobenzaldehyde Oxime (3i). Pale orange solid; Yield 93%; m.p. 129-131^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$): *δ*9.96 (s, 1H, OH), 8.15 (s, 1H, CH), 8.37 (d, *J* = 8.8 Hz, 2H, ArH), 7.92 (d, *J* = 8.8 Hz, 2H, ArH); LCMS (*m*/*z*)167 (M+1H).Anal. Calcd. for $C_7H_6N_2O_3$: C, 50.60, H, 3.65, N, 16.85; Found: C, 50.73, H, 3.51, N, 16.97.

p-(Trifluoromethyl)benzaldehyde Oxime (3j). White solid; Yield 91%; m.p. 206-208^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$): δ9.90 (s, 1H, OH), 8.25 (s, 1H, CH), 7.80 (d, *J* = 8.4 Hz, 2H, ArH), 7.58 (d, *J* = 8.4 Hz, 2H, ArH); LCMS (*m*/*z*)190 (M+1H).Anal. Calcd. for $C_8H_6F_3NO$: C, 50.80, H, 3.21, N, 7.40; Found: C, 5.67, H, 3.28, N, 7.58.

m-Nitrobenzaldehyde Oxime (3k). Light brown solid; Yield 96%; m.p. 124-125^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$): δ9.94 (s, 1H, OH), 8.20 (s, 1H, CH), 8.30-8.26 (m, 2H, ArH), 7.95 (d, *J* = 8.1 Hz, H, ArH), 7.68 (d, *J* = 8.1 Hz, 1H, ArH); LCMS (*m*/*z*)167 (M+1H).Anal. Calcd. for $C_7H_6N_2O_3$: C, 50.60, H, 3.65, N, 16.85; Found: C, 50.73, H, 3.51, N, 16.97.

o-Nitrobenzaldehyde Oxime (3l). Brown solid; Yield 96%; m.p. 112-113^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$): δ9.95 (s, 1H, OH), 8.35 (s, 1H, CH), 7.92 (d, *J* = 8.2 Hz, 1H, ArH), 7.95 (d, *J* = 7.7 Hz, 1H, ArH), 7.68 (t, *J* = 7.7 Hz, 1H, ArH), 7.60 (t, *J* = 8.2 Hz, 1H, ArH); LCMS (*m*/*z*)167 (M+1H).Anal. Calcd. for $C_7H_6N_2O_3$: C, 50.60, H, 3.65, N, 16.85; Found: C, 50.73, H, 3.51, N, 16.97.

o-Chlorobenzaldehyde Oxime (3m). Pale orange solid; Yield 94%; m.p. 74-75^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$): δ9.95 (s, 1H, OH), 8.20 (s, 1H, CH), 7.90-7.78 (m, 1H, ArH), 7.65-7.52 (m, 1H, ArH), 7.46-7.30 (m, 2H, ArH); LCMS (*m*/*z*)156 (M+1H).Anal. Calcd. for C_7H_6ClNO: C, 54.01, H, 3.84, N, 9.00; Found: C, 54.16, H, 3.93, N, 8.89.

Benzo[1,3]dioxole-5-carboxaldehyde Oxime (3n). White solid; Yield 89%; m.p. 130-132^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$): δ9.92 (s, 1H, OH), 8.10 (s, 1H, CH), 7.60 (s, 1H, ArH), 7.44 (d, *J* = 7.4 Hz, 1H, ArH), 7.12 (d, *J* = 7.4 Hz, 1H, ArH), 6.05 (s, 2H, CH_2); LCMS (*m*/*z*)166 (M+1H).Anal. Calcd. for $C_8H_7NO_3$: C, 58.20, H, 4.26, N, 8.50; Found: C, 58.34, H,4.33, N, 8.69.

Naphthalene-1-carboxaldehyde Oxime (3o). White solid; Yield 93%; m.p. 105-106^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$): δ9.90 (s, 1H, OH), 8.40 (s, 1H, CH), 8.28 (d, J = 8.3 Hz, 1H, ArH), 7.98-7.89 (m, 2H, ArH), 7.80 (d, *J* = 7.2 Hz, 1H, ArH), 7.65-7.48 (m, 3H, ArH); LCMS (*m*/*z*)172 (M+1H).Anal. Calcd. for $C_{11}H_9NO$: C, 77.20, H, 5.32, N, 8.50; Found: C, 77.29, H,5.19, N, 8.62.

3-Thiophenecarboxaldehyde Oxime (3p). Light brown solid; Yield 95%; m.p. 89-90^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$): δ10.25 (s, 1H, OH), 8.48 (s, 1H, CH), 7.85-7.10 (m, 3H, ArH); LCMS (*m*/*z*)128 (M+1H).Anal. Calcd. for C_5H_5NOS: C, 47.25, H, 3.96, N, 11.02; Found: C, 47.15, H, 4.15, N, 11.19.

3-Furancarboxaldehyde Oxime (3q). Brown solid; Yield 90%; m.p. 112-114^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$): δ10.35 (s, 1H, OH), 8.35 (s, 1H, CH), 7.90-7.10 (m, 3H, ArH); LCMS (*m*/*z*)112 (M+1H).Anal. Calcd. for $C_5H_5NO_2$: C, 54.06, H, 4.55, N, 12.65; Found: C, 53.92, H,4.68, N, 12.75.

1-H-Indole-3-carboxaldehyde Oxime (3r). White solid; Yield 93%; m.p. 136-138^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$): δ11.06 (s, 1H, NH), 10.15 (s, 1H, OH), 8.35 (s, 1H, CH), 8.10 (d, *J* = 7.8Hz, 1H, ArH), 7.95 (s, 1H, ArH), 7.69 (d, *J* = 7.6 Hz, 1H, ArH), 7.52-7.24 (m, 2H); LCMS (*m*/*z*)161 (M+1H).Anal. Calcd. for $C_9H_8N_2O$: C, 67.50, H, 5.06, N, 17.47; Found: C, 67.61, H,4.89, N, 17.61.

1-Methylindole-3-carboxaldehyde Oxime (3s). White solid; Yield 94%; m.p. 129-131^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$): δ10.35 (s, 1H, OH), 8.35 (s, 1H, CH), 8.18 (s, 1H, ArH), 7.81-7.35 (m, 4H, ArH), 3.85 (s, 3H, CH_3); LCMS (*m*/*z*)175 (M+1H).Anal. Calcd. for $C_{10}H_{10}N_2O$: C, 68.95, H, 5.80, N, 16.10; Found: C, 69.12, H,5.92, N, 15.89.

3,4-DiMethoxybenzaldehyde Oxime (3t). White solid; Yield 93%; m.p. 95-96^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$): δ9.90 (s, 1H, OH), 8.10 (s, 1H, CH), 7.58(d, J = 8.0Hz, 1H, ArH), 7.38, (d, J = 8.0 Hz, 1H, ArH), 6.9 (d, J = 8.0 Hz, 1H, ArH), 3.90 (m, 6H, $2CH_3$); LCMS (*m*/*z*)182 (M+1H).Anal. Calcd. for $C_9H_{11}NO_3$: C, 59.68, H, 6.15, N, 7.75; Found: C, 59.78, H,6.24, N, 7.84.

CONCLUSION

In conclusion, we have developed a simple and efficient method for the synthesis of oximes**3a-t** from substituted aromatic aldehydes **1**by treatment with $NH_2OH.HCl$**2**usingCu supported silica at room temperature. The mildness and eco-friendly nature of the synthesis conversion and excellent yields are notable advantages of this method.

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