

AMINO ACID CATALYZED GREEN SYNTHESIS OF 5-ARYLFURAN-2-CARBALDEHYDE OXIMES

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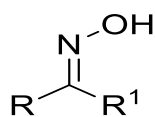
Abstract.

Oximes are nitrogen-containing organic compounds and prepared by the condensation reaction of carbonyl compounds with hydroxylamine hydrochloride in the presence of base. Sometimes acid or base sensitive functional group present in aldehyde and ketone, so these classical methods are not suitable for these aldehydes and ketones. So the several improvements have been made for the synthesis of oxime. Several catalysts can be used for the synthesis of oximes. We used various amino acids for the synthesis of 5-Arylfuran-2-carbaldehyde oximes. These were found to be excellent catalysts for the synthesis of oximes.

Keywords; Oxime, amino acid, 5-Arylfuran-2-carbaldehyde etc.

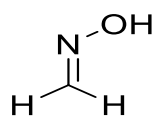
Introduction:

Oximes are nitrogen-containing organic compounds [1]. Basically, oximes belongs to the imines family [2], easily available [3] and well known organic compounds [3, 4]. Oximes are highly crystalline compounds. They are used for the protection of carbonyl compounds, but also for the purification of carbonyl compounds [2, 5].



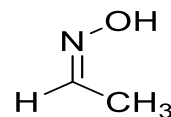
[1]

R¹: H, CH₃



[2]

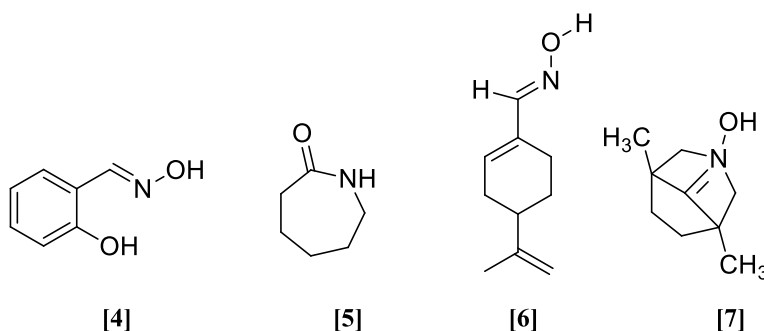
R: H, alkyl, aryl



[3]

Oximes were usually prepared by the condensation reaction of carbonyl compounds with NH₂OH.HCl (hydroxylamine hydrochloride) in the presence of base [6]. Oximation is an important reaction in organic chemistry because oximes not only protect the ketonic and

aldehydic functions but also used for the identification and purification of aldehydes and ketones [5, 7]. Oximes also have different types of applications in different fields. Oximes have many important applications in the field of agriculture. They are used as fungicides and herbicides [8]. In the coordination chemistry oximes act as versatile ligands. In hydrometallurgy, salicylaldoxime (4) is used as a chelator and extractant for the extraction of several substances [9]. In industry, oximes acts as an intermediate for the synthesis of caprolactam (5) [10]. Perillartine, (6) which is also known as perilla sugar is used as artificial sweetener. It is the oxime of perillaldehyde. It is 2000 times as sweet as sucrose. Mainly in Japan it is used as artificial sweetener. Some oximes are used as commercial fragrances i.e. buccoxime (7) and 5-methyl-3-heptanone oxime [11]. Some oxime used as nerve agent's antidotes. These antidotes are methoxime, pralidoxime. Some oxime exhibit antimicrobial, analgesic, local anesthetic and antifungal activities [12].



Currently, several methods for the synthesis of oximes are described in the literature such as the use of formic acid HCOOH [13], pyridine chloroform[14], CaO [15], ethanol-pyridine [16], ZnO [17], sodium hydroxide NaOH [18-21], sodium sulphate Na₂SO₄ under ultrasound irradiation [13], ethylenediamine and oxone [22], hyamine [23], Bi₂O₃[24], Cu-SiO₂[25], DOWEX(R)50WX4 [26], Na₂CaP₂O₇[27], Fe₃O₄ [28], K₂CO₃ [29], animal bone meal [30], chemically treated eggshell wastes as a heterogeneous catalyst [31], Cu-SiO₂[25], phase transfer catalysts PTC [18], wet basic Al₂O₃ in the presence of microwave irradiation [32], heterogeneous polyoxometalates [33, 34], basic ionic liquid 1-butyl-3-methylimidazolium hydroxide [35], NH₂OH.HCl in the presence of K₂CO₃ [29], NH₃ with an oxidant catalyst system [36-41], Dowex 50WX4 [26], SiO₂ with NH₂OH in the presence of microwave [42], CaO in the absence of solvent [15], ethylenediamine with oxone [22], Na₂SO₄ over ultrasound irradiation [13],

TiO₂/SO₄²⁻ solid super acid [43], clay based titanium silicalite-1 [44], titanyl acetylacetonate with NH₂OH [45], host (dealuminated zeolite Y)-guest (12-molybdo-phosphoric acid) nanocomposite [46], Bi₂O₃ with NH₂HCl [24] and organo-SOMO catalysts [47]. We prepared oximes in our laboratory by refluxing 5-Arylfuran-2-carbaldehydes with hydroxylamine hydrochloride by using piperidine as a catalyst [48]. But all these methods have number of limitations. They generate large amount of toxic wastes, the reagents used are very expensive. Therefore, it is necessary to develop new methods for the synthesis of oximes which require mild and environment friendly conditions in order to reduce the adverse effects on human beings. This can be done by minimizing or eliminating the use of toxic catalyst and generation of hazardous by-products or wastes. So herein we wish to report the facile synthesis of 5-Arylfuran-2-Carbaldehyde oximes in ethanol as solvent in the presence of various amino acids as catalysts.

Experimental:

Reagents and chemicals:

All the chemicals and reagents used in the present study were of analytical grade and purchased from Merck or Aldrich. The chemicals were used without further purification; if required, standard methods were used for their purification.

Instrumentation:

The melting points of the synthesized compounds were determined on Gallenkemp melting point apparatus and are uncorrected. FTIR spectra were recorded in the spectral range 4000-400 cm⁻¹ on Bruker Tensor 27 using standard methods. The ¹H NMR and ¹³C-NMR spectra were taken on Bruker DPX instrument at 400 MHz. High resolution mass spectra were recorded on Finnigan MAT 312.

Synthesis of Oximes: General Method A

Equimolar quantities of 5-Arylfuran-2-carbaldehyde (1-3) (0.01 mole) and hydroxylamine hydrochloride (0.01 mole) were taken into a round bottom flask of 50ml. Add 0.01mmol of catalyst into the reaction mixture. Different amino acid i.e. glutamic acid, tryptophan, glycine, leucine, methionine, phenyl alanine, proline, valine, arginine were used as catalysts. Reaction

mixture was refluxed for 4 hours in the presence of ethanol (EtOH) solvent. After completion of time, desired product was obtained in form of precipitates, filtered and recrystallizes it from ethanol.

By following General method "A" these oximes were prepared by using different amino acids as a catalyst.

Synthesis of 5-(2-nitrophenyl) furan-2-carbaldehyde oxime (1)[48]:

M.P:194°C, **FTIR (KBr)** (ν , cm^{-1}): 1639.02 (C=N oxime) 1532.80 and 1350.86 (Asym and sym -NO₂), **¹H NMR** (CDCl₃, 300MHz), δ ppm(*J*, Hz): 7.992-7.267 (4H, m, **arom.**), 7.096 (1H, d, *J* = 3.9, H-3), 6.910 (1H, d, *J* = 3.9, H-4) **¹³C NMR** (CDCl₃, 75 MHz) δ ppm: 151.03, 150.28, 150.25, 147.17, 132.82, 130.27, 129.58, 124.25, 122.20, 119.50, 112.40 (Ar-C) Anal.Calcd.for C₁₁H₈N₂O₄: C 56.89; H 3.44; N 12.06, Found C 56.75; H 3.40; N 11.86 %,

Synthesis of 5-(2-methyl-5-nitrophenyl) furan-2-carbaldehyde oxime (2)[48]:

M.P: 178°C **FTIR (KBr)** (ν , cm^{-1}): 2361.34 (Aromatic ring), 1643.67 (C=N oxime), 1523.78 and 1360.65 (Asym and sym -NO₂), **¹H NMR** (CDCl₃, 300MHz), δ ppm(*J*, Hz): 87.852-7.425 (3H, m, **arom.**), 7.235 (1H, d, *J* = 2.3, **H-3**), 6.980 (1H, d, *J* = 2.3, **H-4**), 2.428 (3H, s, **CH₃**). **¹³C NMR** (CDCl₃, 75 MHz) δ ppm:154.39, 151.23, 133.98, 132.65, 131.06, 130.98, 129.76, 127.54, 122.83, 118.96, 110.67 (Ar-C), 15.67 (CH₃) **Anal.Calcd.** for C₁₂H₁₀N₂O₄: C 58.53; H 4.06; N 11.38, **Found** C 58.42; H 3.92; N 11.09 %,

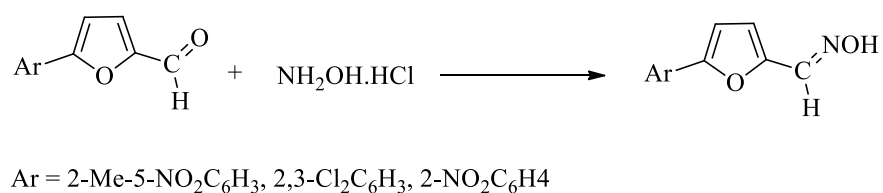
Synthesis of 5-(2,3-dichlorophenyl) furan-2-carbaldehyde oxime (3)[48]:

M.P: 210-212°C**FTIR (KBr)** (ν , cm^{-1}): 2360.98 (Aromatic ring), 1640.89 (C=N oxime), 1091.29 (C-Cl). **¹H NMR** (CDCl₃, 300MHz), δ ppm (*J*, Hz): 7.930-7.420 (3H, m, **arom.**), 7.378 (1H, d, *J* = 2.9, **H-3**), 6.993 (1H, d, *J* = 2.9, **H-4**). **¹³C NMR** (CDCl₃, 75 MHz) δ ppm:155.43, 151.89, 133.90, 132.73, 131.56, 130.90, 128.79, 127.65, 121.80, 119.60, 110.65 (Ar-C)**Anal.Calcd.** for C₁₁H₇Cl₂NO₂: C 51.76; H 2.74; N 5.49 **Found** C 51.49; H 2.85; N 5.68 %.

Results and discussion

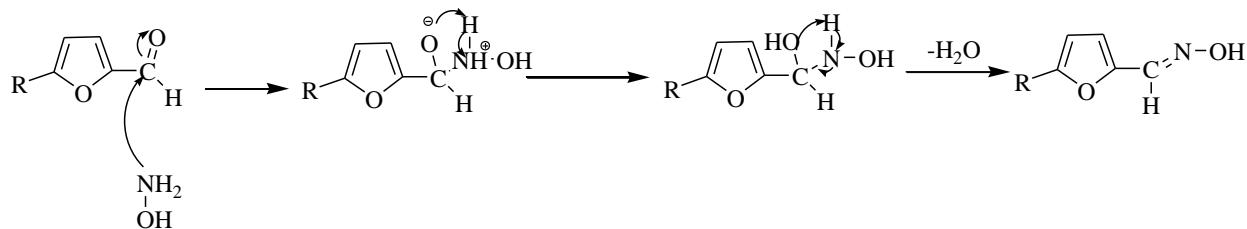
During the work various 5-arylfuran-2-carbaldehyde oximes were prepared by the reaction of 5-arylfuran-2-carbaldehydes with hydroxylamine hydrochloride in the presence of different amino acids as catalysts.

Synthesis of 5-arylfuran-2-carbaldehyde oximes:



Scheme:1

General Mechanism:

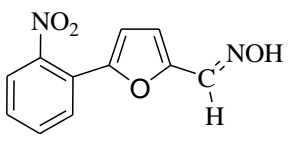
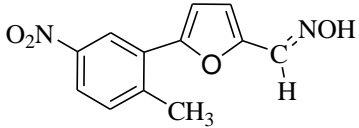
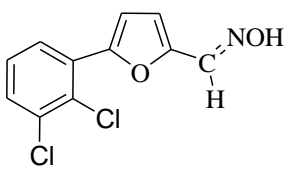


Scheme:2

Keeping in view the efficacy of amino acid catalysts for the synthesis of 2,4,5-triaryl-1*H*-imidazoles [49] with encouraging results, various amino acid were used for the synthesis of 5-Arylfuran-2-carbaldehydes. Once again, excellent yields were obtained (**Scheme-I**, Table-1) under solvent less condition (green procedure) by just heating a mixture of aromatic aldehyde and hydroxylamine hydrochloride with the amino acid catalyst for a few minutes on a water bath to give the product in excellent yields. One of the major advantages of using amino acids as catalysts is in the isolation and purification of the desired product. The amino acids are usually soluble in water and are eliminated during work-up and purification.

A plausible mechanistic explanation for the amino acid catalyzed synthesis of 5-Arylfuran-2-carbaldehyde oximes has been depicted in **Scheme-2**. For the present work, only a few representative aromatic aldehydes were used to check the feasibility of amino acid catalysis in these reactions. The yields in all three cases were comparable.

Table 1: Amino acid catalyzed synthesis of of 5-Arylfuran-2-carbaldehyde oxime:

Structure of Product	Catalyst	%Yield
	Glutamic acid	97
	Tryptophan	92
	Glycine	85
	Leucine	90
	Methionine	88
	Phenyl alanine	82
	Proline	88
	Valine	70
	Arginine	76
		Glutamic acid
Tryptophan		90
Glycine		80
Leucine		94
Methionine		80
Phenyl alanine		84
Proline		90
Valine		85
Arginine		88
		Glutamic acid
	Tryptophan	90
	Glycine	90
	Leucine	92
	Methionine	88
	Phenyl alanine	90
	Proline	90
	Valine	86
	Arginine	90

In conclusion, an efficient and another green method for the synthesis of 5-Arylfura-2-carbaldehydes, mediated by amino acids is presented. Seven representative amino acids have been used but the list is not exhaustive

Acknowledgments

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Conflict of Interest

There is no conflict of interest

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