

A quick one-pot synthesis of thermodynamically stable stereoselective aldoximes in the presence of dry citric acid under microwave irradiation

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Abstract

Aldoximes play an important role in organic chemistry, particularly in the purification and isolation of parent aldehydes. Moreover, many aldoximes have pharmacological and agricultural applications. Regarding stereoselective aldoximes, the *E*-isomer is typically more biologically active and possesses greater fungicidal and insecticidal properties. In the present study, the synthesis of *E*-aldoximes with high yields is reported.

Keywords: Aldoximes, stereoselectivity, biologically active

Introduction

Aldoximes have notable pharmacological and agricultural applications [1]. The *E*-isomer is found to be more biologically active, possessing superior fungicidal and insecticidal properties [2]. In this study, aldoximes of various substituted aldehydes were prepared in the presence of hydroxylamine hydrochloride and citric acid under microwave irradiation in dry media conditions. Substituted aldehydes with various electron-donating and electron-withdrawing groups yielded *E*- and *Z*-isomers in varying proportions [3]. Using citric acid as a catalyst, a higher yield of the stereoselective *E*-isomer was obtained for aldehydes with electron-donating substituents compared to those with electron-withdrawing substituents. The *E*-isomer, being thermodynamically more stable, was isolated in greater yields when both the microwave irradiation time and the quantity of the citric acid catalyst were increased.

Experimental In a typical procedure, a substituted aldehyde (1 mmol) and hydroxylamine hydrochloride (1.2 mmol) were mixed with either 0.5 g or 1.0 g of citric acid (acting as a catalyst) in an Erlenmeyer flask. The mixture was irradiated at 400 W in a domestic microwave oven (Kenstar OM-9925E, 800 W, operating at 2450 MHz), and the reaction progress was monitored by TLC until completion. The flask was then removed and cooled, and dichloromethane (50 mL) was added [4]. The catalyst was filtered off, and the resultant solution was dried over anhydrous aluminum chloride and evaporated. The crude residue was purified by column chromatography to afford the desired *E*-oxime.

Results and Discussion

Oximes are commonly synthesized by condensing carbonyl compounds with hydroxylamine hydrochloride in an acidic medium, although many other methods exist. However, this traditional method usually yields a mixture of *Z*- and *E*-stereoisomeric oximes.

The yields of the *E*-stereoisomeric aldoximes obtained using different amounts of catalyst and radiation times were compared. A higher yield of the stereoselective *E*-isomer was obtained for aldehydes with electron-donating substituents, such as 4-hydroxybenzaldehyde (taken as a reference compound), compared to benzaldehyde or those

with electron-withdrawing groups. Furthermore, when the microwave irradiation time was doubled to 2 minutes, a significant increase in the yield of the *E*-stereoisomer was observed.

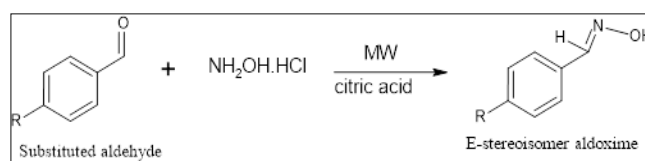


Table 1: Optimization of Microwave Power and Irradiation Time for Maximum Yield

Reactant	Microwave power (W)	Time (min.)	Yield %
4-Hydroxybenzaldehyde	80	1	55
		2	62
	160	1	60
		2	68
	240	1	64
		2	71
	320	1	71
		2	92
	400	1	60
		2	85
	480	1	67
		2	70
	560	1	65
		2	69

Table 2: Synthesis of *E*-aldoximes under MW using citric acid

Aldehyde	Citric Acid amount	Radiation time	Yield of <i>E</i> -isomer (%)
Benzaldehyde	0.5 g	1 min	60
	1.0 gm	2 min.	85
4-Hydroxybenzaldehyde	0.5 g	1 min	71
	1 g	2 min	92
Cinnamaldehyde	0.5 g	1 min	68
	1.0 gm	2 min.	90
3-Nitrobenzaldehyde	0.5 g	1 min	61
	1.0 gm	2 min.	78
4-Chlorobenzaldehyde	0.5 g	1 min	69
	1.0 gm	2 min.	91

The result obtained were confirmed by spectroscopic data and melting point of respective isomer of given aldoximes.

Applications of E-aldoximes

Purification and isolation of carbonyls

Oximes provide an efficient method for isolating and purifying aldehydes and ketones, particularly volatile or impure carbonyl compounds. Conversion into crystalline oximes allows easy separation and purification by recrystallisation. The original carbonyl can then be regenerated by mild hydrolysis ^[5, 6].

Characterisation of carbonyls

Oxime formation is a reliable method for identifying aldehydes and ketones. The crystalline oxime can be identified by its characteristic melting point. IR spectroscopy further confirms the conversion of the C=O group into C=N–OH through the disappearance of the carbonyl band and appearance of characteristic C=N and O–H bands ^[7].

Oxime applications in pharmacology

Oximes have an important role in pharmacology as they act as biologically active compounds and drug intermediates. Pralidoxime and obidoxime are used as antidotes for organophosphate poisoning by reactivating inhibited acetylcholinesterase. Oxime groups are also present in drugs such as cefuroxime and other therapeutic agents ^[8].

Conversion of oximes into useful compounds

Oximes are valuable synthetic intermediates. Ketoximes undergo the Beckmann rearrangement to form amides, notably cyclohexanone oxime to ϵ -caprolactam for Nylon-6 production. Oximes can also be reduced to primary amines, while aldoximes can be dehydrated to nitriles. Thus, efficient green synthesis of oximes provides useful routes to important chemical products ^[9, 10].

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