

Synthesis and Characterization of N-Methyl and N-Benzyl Cinnamohydroxamic Acids

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N-methyl and N-benzyl cinnamohydroxamic acid was prepared by coupling reaction between N-methyl hydroxylamine and N-benzyl hydroxylamine with cinnamoyl chloride. The compounds were structurally characterized with ¹H NMR, IR and elemental analysis.

Keywords: Synthesis, Cinnamohydroxamic acid, Hydroxylamine.

INTRODUCTION

Hydroxamic acids are prepared commonly from esters or acid chlorides or carboxylic acids. Hydroxamic acids can also be synthesized from aldehydes *via* Angeli-Rimini reaction, a well-known hydroxamic acid reaction is Lossen rearrangement [1]. In this paper, N-methyl and N-benzyl cinnamohydroxamic acids are synthesized by the acylation of acid chloride or acid anhydride.

Cinnamohydroxamic acid and their derivatives are weak acid than the carboxylic acids. Hydroxamic acids formed N-acid or O-acids by the deprotonation of nitrogen or oxygen [2]. Solubility is one of the most important physico-chemical parameters which plays an important role in drug manufacturing process on the basis of solubility of cinnamohydroxamic acids (solute) in liquid solvent [3]. They are often used as pharmacological [4-14] and drug discovery process [15-22].

EXPERIMENTAL

Cinnamoyl hydroxylamine was procured from Sigma Aldrich. All the compounds were precoured from Merck and of AR grade. Melting points were determined on a melting point apparatus and also determined by Thiele's tube using liquid paraffin by open capillary method. ¹H NMR spectrum of the compounds were carried out using Bruker Advance 400 MHz spectrometer at SAIF Panjab University, Chandigarh, India. The solvent used was CDCl₃ and DMSO. IR spectra were recorded on a FTIR 390/2014/0514/290514, Department of Chemistry, Gujarat University, Ahmedabad, India. The spectrum was recorded using the KBr Pellets.

Synthesis of N-methyl cinnamohydroxamic acid (1a):

N-Methyl hydroxylamine (0.1 mol) was coupled with an ethereal solution (50 mL) of cinnamoyl chloride (0.1 mol) in the presence of saturated aqueous solution of sodium carbonate (0.1 mol) on the magnetic stirrer with external cooling, keep 0-5 °C temperature constant reaction, and recrystallize with methanol [23] (Fig. 1). Colorless shiny crystal N-methyl cinnamohydroxamic acid was obtained.

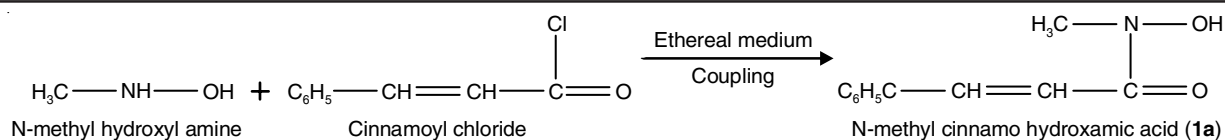
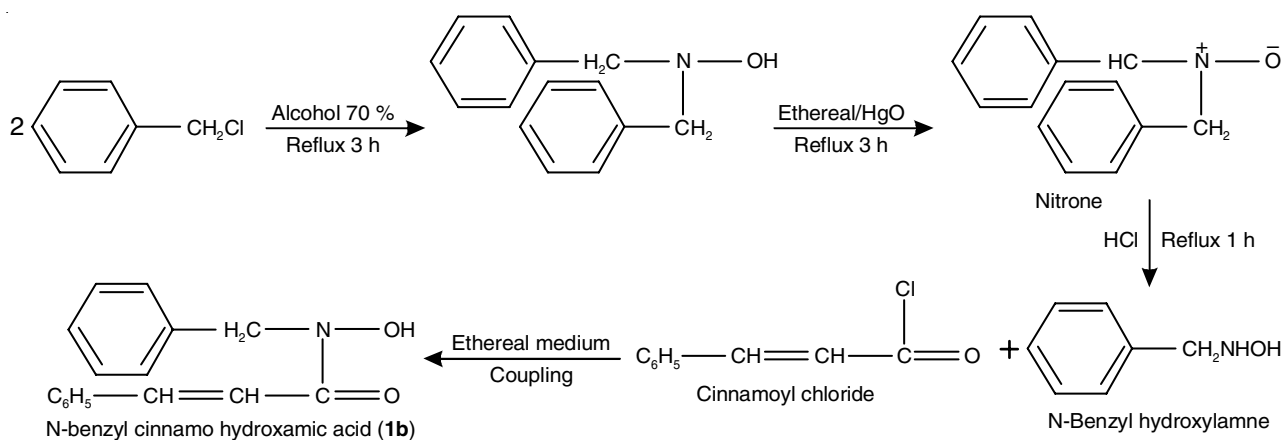
Synthesis of N-benzyl cinnamohydroxamic acid (1b):

N-benzyl hydroxylamine (0.1 mol) was coupled with ethereal solution (50 mL) of cinnamoyl chloride (0.1 mol) in the presence of saturated aqueous solution of sodium carbonate (0.1 mol) on the magnetic stirrer. Keep the temperature below than 5 °C during the reaction and recrystallize with chloroform and petroleum ether white shining N-benzyl cinnamohydroxamic acid (1b) was obtained [23] (Fig. 2).

RESULTS AND DISCUSSION

The physico-chemical and elemental analysis of N-methyl (1a) and N-benzyl cinnamohydroxamic acid (1b) has been reported in Table-1.

¹H NMR: The proton magnetic spectra of N-methyl and N-benzyl cinnamohydroxamic acid are investigated and result is given in Table-2. The chemical shift due to protons attached to nitrogen atom in N-methyl cinnamohydroxamic acid, is observed at 2.51 δ and chemical shift due to proton attached to -CH₂ in N-benzyl cinnamohydroxamic acid. The sharp singlet observed in the spectra of N-methyl and N-benzyl cinnamohydroxamic acids due to six magnetically equivalent

Fig. 1. Synthesis of N-methyl cinnamo hydroxamic acid (**1a**)Fig. 2. Synthesis of N-benzyl cinnamo hydroxamic acid (**1b**)TABLE-1
PHYSICO-CHEMICAL DATA OF COMPOUNDS **1a** AND **1b**

Compound	Structure	m.f.	m.w.	m.p. (°C)	Yield (%)	Elemental analysis (%):		
						Calcd.	(Found)	
						C	H	N
1a		$\text{C}_{10}\text{H}_{11}\text{NO}_2$	177.20	160	75	67.78 (67.098)	6.21 (4.985)	7.90 (3.909)
1b		$\text{C}_{16}\text{H}_{15}\text{NO}_2$	253.30	84	80	75.86 (72.026)	5.96 (5.483)	5.52 (4.672)

TABLE-2

¹H NMR SIGNALS OF SYNTHESIZED N-METHYL CINNAMO HYDROXAMIC ACID (**1a**) AND N-BENZYL CINNAMO-HYDROXAMIC ACID (**1b**): DI METHYL SULPHOXIDE

Cinnamon hydroxamic acid	Signal (cps)	Chemical shift (τ)	Multiplicity	Assigned group
1a	339	3.39	Singlet	CH ₃ -N-
	—	—	—	O-H
	665	6.65	Doublet	=CH
	768	7.68	Singlet	CH=
1b	741	7.41	Doublet	
	735	7.35	Triplet	
	251	2.51	Singlet	-CH ₂
	—	—	—	O-H
	643	6.43	Doublet	=CH
	757	7.57	Singlet	CH=
	734	7.34	Doublet	

proton present in benzene ring. The ring current effect due to π electrons causes deshielding of aromatic protons which result the chemical shift at high value. The doublet N-methyl (6.43-7.35 δ) and N-benzyl (6.65-7.41 δ) observed, compounds are due to chemically distinct protons. The splitting is due to spin-spin coupling, splitting takes place when the non-equivalent proton is present.

In the IR spectra of N-methyl and N-benzyl cinnamo-hydroxamic acids, four regions of strong absorption were observed. The band due to O-H stretching occur between 3092-3026 cm^{-1} as a broad peak ranging from strong intensity to medium intensity. The absorption bands due to (OH) stretching vibration when free are observed around 3830 cm^{-1} but in case of hydrogen reported the shift in the wavelength of this band is towards lower frequency. Absorption near 1820-1698 cm^{-1} in N-methyl and N-benzyl cinnamohydroxamic acid examined here the characteristic C=O stretching vibration is assigned in the region 1740-1620 cm^{-1} . The position of carbonyl stretching frequency is much more influenced by molecular structure and shifted to 1000 cm^{-1} frequency due to strong intramolecular bonding. The appearance of spectra range between 1493-1447 cm^{-1} is assigned to C-N stretching vibration, while the position

of N-O stretching bands has been assigned in 1098-1072 cm^{-1} region.

IR of N-methyl cinnamohydroxamic acid (1a): (3092) O-H stretching, (1698) C-H stretching, (1620) C=O stretching, (1574) C=C stretching, (1447) C-N stretching, (1402) C-H stretching, (1329) C-H bending, (1281) C-N stretching (unsymmetrically), (1069) N-H bending (out-of-plane), (977) N-O stretching, (860) C-C-C stretching, (766) C-H rocking, (738) C-H rocking, (682) C-H twisting.

IR of N-benzyl cinnamohydroxamic acid (1b): (3026) O-H stretching, (2826) C-H stretching, (1685) C=O stretching, (1576) C=C stretching, (1418) C-H stretching, (1312) C-H bending, (1283) C-N stretching, (1220) C-N stretching (unsymmetrically), (1098) N-H bending (out-of-plane), (1072) N-O stretching, (877) C-C-C stretching, (847) C-H rocking, (766) C-H rocking, (704) C-H twisting, (587) C-H twisting, (540) C-C=, (482) C-N-C.

Conclusion

N-Methyl and N-benzyl cinnamohydroxamic acids have synthesized by the acylation of acid chlorides or acid anhydride chemicals in a good yield (75-80 %). The ^1H NMR and IR studies confirmed the structure of synthesized N-methyl and N-benzylcinnamohydroxamic acid.

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