

Study the Vital Activity of Some the Prepared Cinnamaldehyde Derivatives

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ABSTRACT

Five compounds were synthesized, which are derivatives of cinnamaldehyde, including P-ethoxy cinnamaldehyde, referred to as compound (a). From it, compounds (b, c, d, and e) were obtained by combining it with a group of compounds and using specific solvents suitable for each preparation. They were also characterized using IR, H1NMR and C13NMR with CDCl₃. To demonstrate their biological efficacy, we will study their effects on various types of bacteria as well as cancer cell lines and fungal of type *Penicillium*.

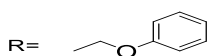
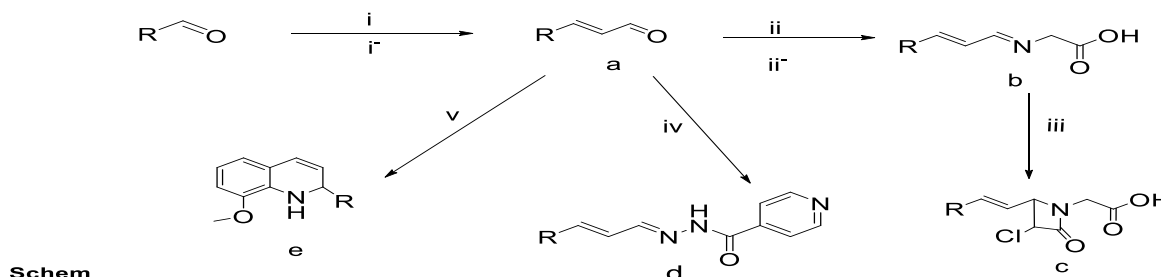
Keywords: Cinnamaldehyde, 1,2-dihydroquinoline.

1. INTRODUCTION

The world is still searching for the development of organic inhibitors that reduce corrosion and are effective for industrial use. These natural inhibitors are always available and relatively low-cost, and most importantly, they are environmentally friendly, such as essential oils including cinnamon oil or cinnamaldehyde[1].

CA is an organic compound primarily used in the chemical and fragrance industries. It is one of the aromatic aldehydes, and chemically, the structure of cinnamaldehyde consists of an aldehyde group (-CHO) attached to two carbon atoms with a double bond (C=C) and a benzene ring (C₆H₆)[2]. Cinnamaldehyde is found in plants such as cinnamon, in the production of pesticides, and in the medical field as an antifungal[3] and antibacterial [4]. Cinnamaldehyde is considered a highly reactive compound that can be used in chemical reactions to produce compounds such as p-ethoxy cinnamaldehyde [5]. Some studies suggest that cinnamon may have the ability to prevent type 2 diabetes[6], and it has a blood pressure-lowering effect and regulates blood fat levels, as well as arthritis. It has antioxidant effects, in addition to anti-cancer[7, 8] and anti-inflammatory properties. It constitutes about 65% of the cinnamon extract. Studies have shown that (CA) can enhance levels of reactive oxygen species (ROS) within cells by inducing dysfunction in energy-producing mitochondria[7].

The synthesized Schiff base is a chemical compound formed by the reaction of an amino acid with cinnamaldehyde. It is characterized by the presence of an imine group (C=N) in its structure[9], which has significant biological properties, including corrosion protection[1]. This is due to its high electron density from aromatic groups and the presence of heteroatoms like nitrogen. Additionally, it can interact with proteins or other molecules, and it has antifungal and antibacterial properties, as well as the potential for use in the development of pharmaceutical compounds[2].



i/ CH₃CHO, CH₃CH₂OCOCH₃

i'/ NaOH, H₂O, reflux, 2h

ii/ NH₂CH₂COOH, CH₃CH₂OH, H⁺

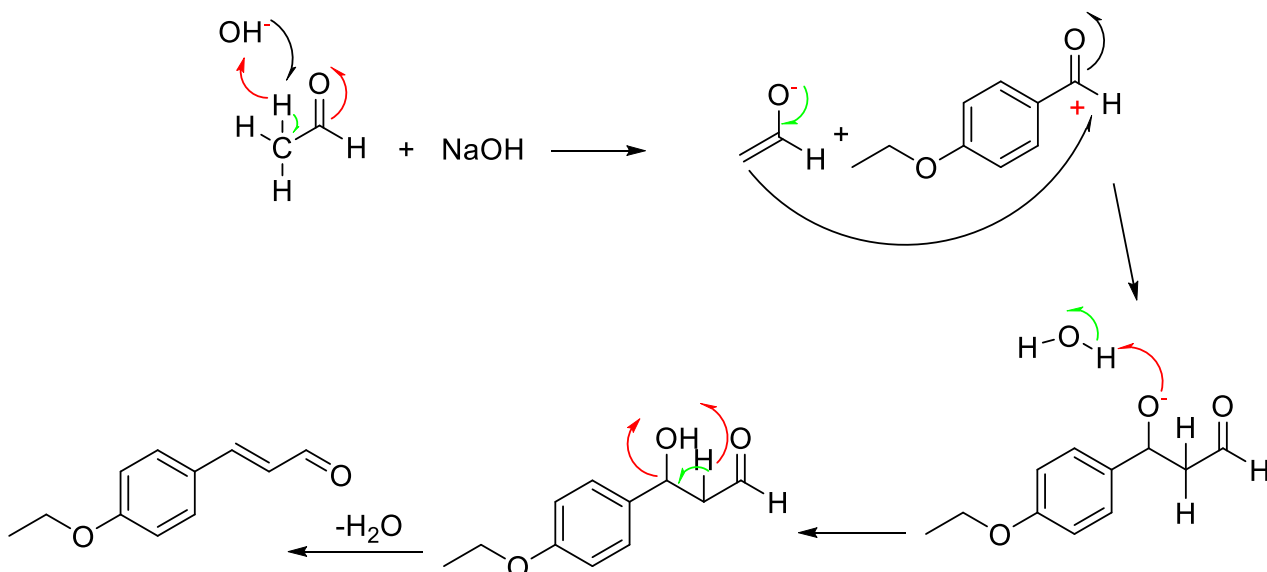
ii'/ CH₃CH₂OCH₂CH₃, 24h, reflux

iii/ ClCOCH₂Cl, 18h, (Et)₃N

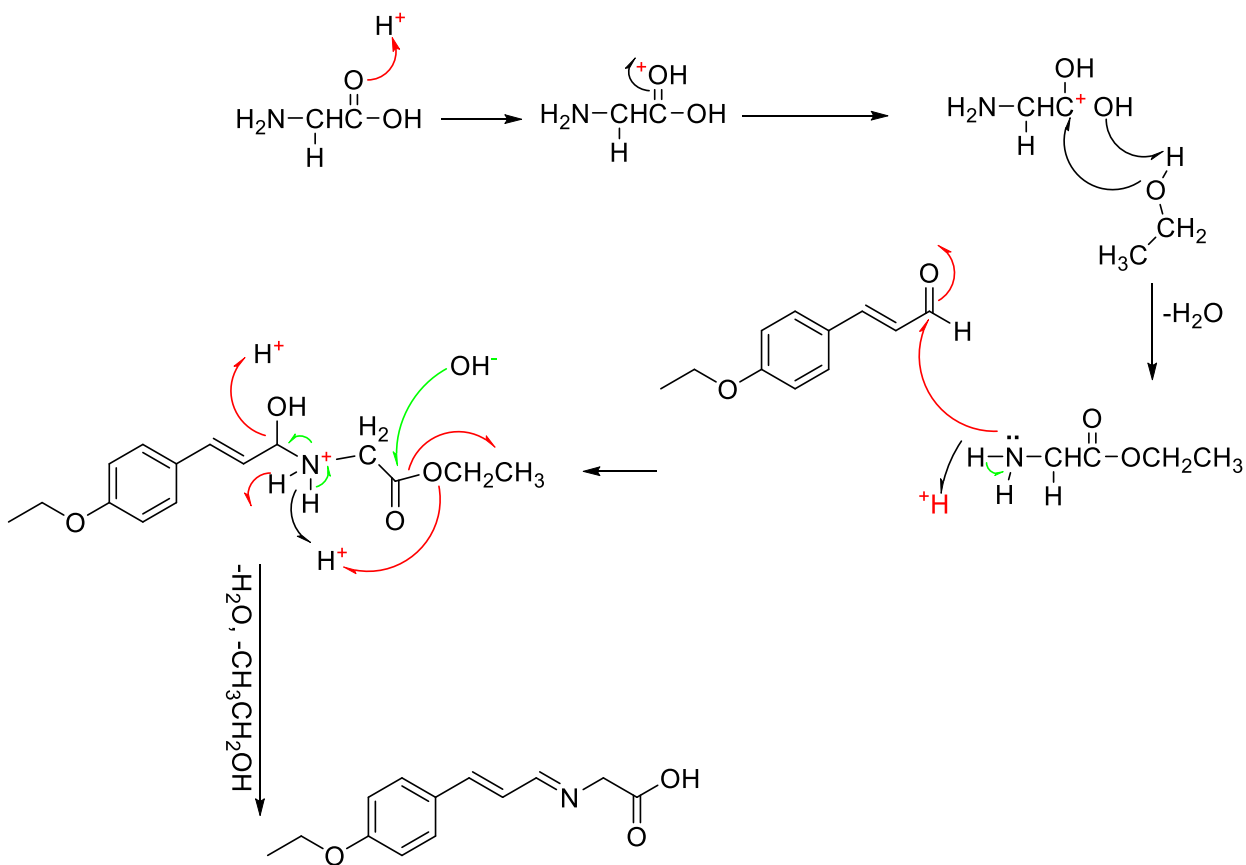
iv/Isoniazid, CH₃CN, reflux, 2h, -H₂O, 60°C

v/ 2-Methoxyaniline, CH₂SO₄, -H₂O, PhNO₂, 130°C

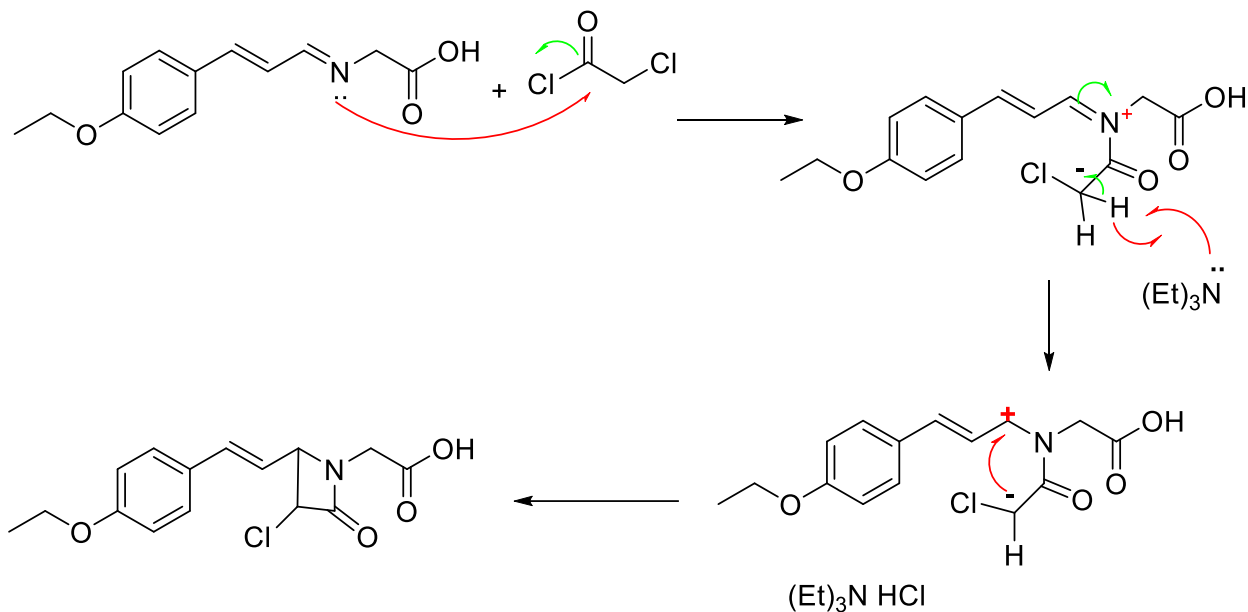
Mechanism of reaction (a)



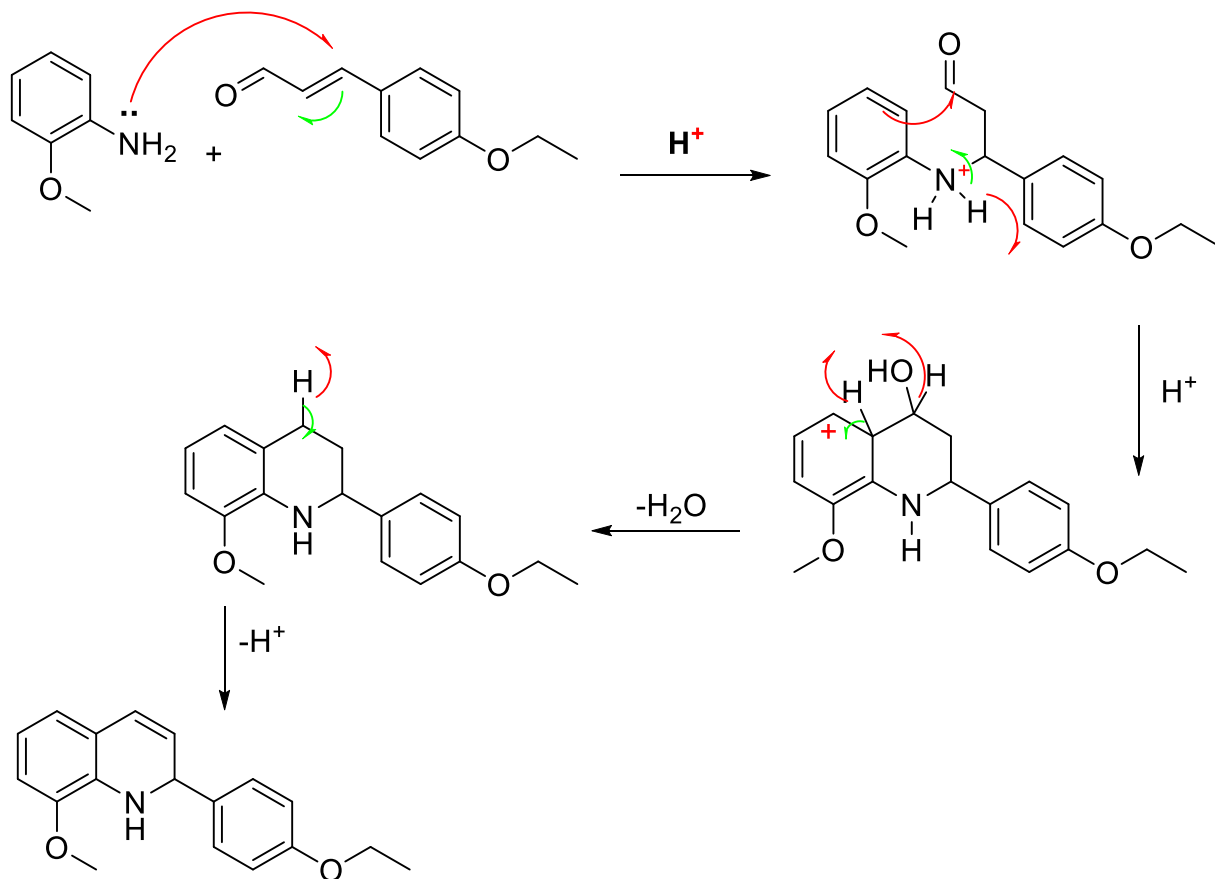
Mechanism of reaction (b)



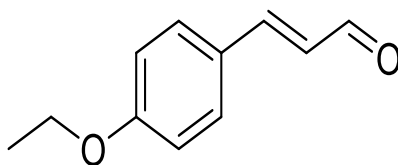
Mechanism of reaction (c)



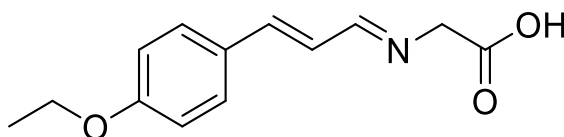
Mechanism of reaction (e) (Skraup synthesis)



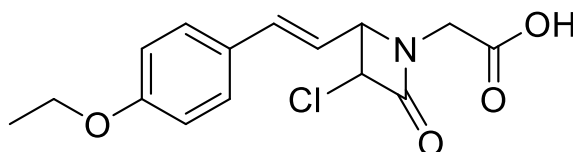
Experimental

3-(4-ethoxyphenyl) acryl aldehyde (a)

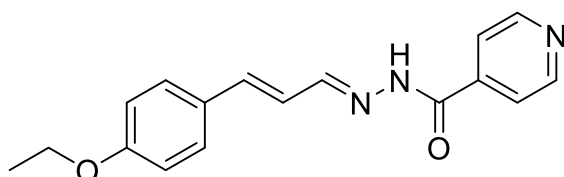
After adding a NaOH solution, a 40% CH₃CHO solution, and P-Et-C₆H₅CHO (M.p=20.7°C) to the reaction flask, it was heated to boiling (3h). The molar feeding ratio is P-Et-O-C₆H₅CHO, NaOH, CH₃CHO is 1:1:1. After allowing it to reach room temperature, we extract the ethyl acetate, mix the organic layer, wash with brine, dry with anhydrous magnesium sulfate, filter, and reduce the pressure to recover the ethyl acetate solvent and obtain the crude products (yield= 80%)

2 - 3-(4-ethoxyphenyl) allylidene) amino) acetic acid (b)

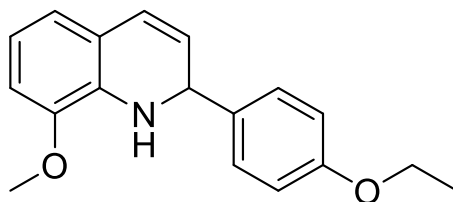
6.7 mmol of amino acid 0.5 g of glycine and are taken in 30mL CH₃CH₂OH and heated under stirring condition at 50 °C for 2 h to get a clear solution. To this solution 1.25-fold trans-cinnamaldehyde (1.4 g) is added drop wise and refluxed for 24 h in (H⁺). After concentrating the solution, 15:20 mL CH₃CH₂OCH₂CH₃ is added which precipitates out the desired cinnamaldehyde - amino acid conjugated Schiff base. The precipitate is washed with diethyl ether for several times and dried under vacuum (yield =75 %).

3- 2-(3-chloro-2-(4-ethoxystyryl)-4-oxoazetid-1-yl) acetic acid (c)

0. 2 mol (4.65g) of compound (b) are added to 0. 2 mole (4.65g) of chloroacetyl chloride in a 40 ml round-bottom flask with 0. 2 mole (4.65g) of triethylamine in benzene, then boiled for 15 h. The triethylamine hydrochloride is removed, and the benzene is distilled to obtain compound C, which can be recrystallized again using ethanol [Yield 80%].

3-(4-ethoxyphenyl) allylidene)isonicotinohydrazide (d)

by directly mixing an equimolar ratio (1:1) of either isoniazid with 4-Ethoxy cinnamaldehyde in 25mL of hot acetonitrile and heated under reflux at 65 °C for 3 h and partial water withdrawal (-H₂O). Yield 65%.

2-(4-ethoxyphenyl)-8-methoxy-1,2-dihydroquinoline (e)

1.5 moles of 4-ethoxy cinnamaldehyde are taken with 1 mole of 2-methoxyaniline at a temperature of 140 degrees Celsius, and by acidifying with concentrated sulfuric acid and nitrobenzene, we obtain compound. Yield 70 %.

Table (1)/ Detailed data for the compounds synthesized from a-b

Compd	C.F	Mw	M.p °C	Yield	%Analysis /calcd (manual)				
					C	H	N	O	Cl
A	C ₁₁ H ₁₂ O ₂	176	38.17	80%	74.98/75	6.86/6.8	-	18.16/18.2	-
B	C ₁₃ H ₁₅ NO ₃	233	200	75%	66.94/67	6.48/6.4	6.00/6	20.58/20.6	-
C	C ₁₅ H ₁₆ ClNO ₄	309.5	346.16	80%	58.17/58	5.21/5.1	4.52/4.5	20.60/20.7	11.44/11.5
D	C ₁₇ H ₁₇ N ₃ O ₂	295	198-201	65%	69.14/96	5.80/5.8	14.23/14	10.83/10.8	-
D	C ₁₈ H ₁₉ NO ₂	281	274.04	70%	76.84/77	6.81/6.8	4.98/5	11.37/11.4	-

2. RESULTS AND DISCUSSION

After measuring the melting point of the first synthesized compound, it was found to be 38.17°C, while the compound we started with, p-ethoxy benzaldehyde, had a melting point of 20.71°C. This indicates that the formed compound has an increased number of carbon atoms as well as other components.

a/ IR/ [C=O 1685 cm⁻¹, C=C 1650cm⁻¹, CHO 2850-2750cm⁻¹, Ph 900-800, CH 3068 SP₂, CH 2971SP₃]. H¹NMR/ CH₃(3H, T,1.34), CH₂(2H, q,4.05), =CH (1H, d,6.63), =CH-Ph (1H, d,7.7), CHO (1H, S, 9.68), Ph (1H, d,7.01), Ph (1H, d,7.68), C¹³NMR (CH₃ 14.8, CH₂ 64.6, AR 158.6 114.3 129.8, C=C 152.6 128.9, C=O 193.5).

b/ IR/ [C=O 1710cm⁻¹, OH 3200-3100cm⁻¹, C=N 1590-1580 cm⁻¹, C=C 1625cm⁻¹, C-O 1200cm⁻¹], H¹NMR/=CH(1H,d,6.85)/ Ph-CH=(1H,d,7.22)/COOH(1H,S,12.22)/ Ph(1H, d,7.01)/ Ph(1H, d,7.68)/ CH=N(1H,d, 8.27)/ CH₂(1H, S,2.3), C¹³NMR(C=C 133.3 119.9, C=N 162.8, N-C 61.5, C=O 171.3).

c/ IR/[C-N 1250-1150cm⁻¹, C=O 1725-1700cm⁻¹, COOH 3300-2500cm⁻¹, C-Cl 800-600cm⁻¹], H¹NMR Ph(1H, d,7.01)/ Ph(1H, d,7.62)/ Ph-CH=(1H,d,6.56)/ =CH(1H, d,6.19)/ CH-N(1H,d,4.19)/CH₂(1H, S,4.14)/ CHCl (1H,d,4.83) / COOH(1H,S,13.03), C¹³NMR (Ar-C 128, C=C 134.4 128.8, C-N 57, C-Cl 60, C=O 166.8, N-C 52.5, C=O 173.1).

d/ IR/ [C=N 1500cm⁻¹, N-H 3250 cm⁻¹,C=O 1650 cm⁻¹, =C-H 1400-1600 cm⁻¹], H¹NMR/ Ph(1H, d,7.01)/ Ph(1H, d,7.68)/ PhCH=(1H,d,7.22)/=CH(1H, d,6.85)/ CH=N(1H,d,7.94)/NHCO(1H,S,10.87)/Ar(1H, d,7.82)Ar(1H,d, 8.78), C¹³NMR(C=C 134.1 126.3, C=N 137.2, C=O 163.2, Cycle Pir 140.8, 121.7, 149.7).

e/ IR/ [C-H SP₃ 3000-2800cm⁻¹, C-H SP₂ 3100-3000cm⁻¹, Ar-C-O 1300-1100cm⁻¹, C=C 1600-1400cm⁻¹, C-N 1650-1600cm⁻¹], H¹NMR/ CH₃ (3H,T,1.34)/ CH₂ (2H, q, 4.05)/CH₃O(3H,S,3.86)/NH(1H,S,7.83)/CH-Ph(1H,d,4.59)/=CH(1H,d,7.16)/ =CH(1H,d,6.85), C¹³NMR cycle Quoin(2C 63.2, 3C129.5, 3C124.7, 5C 121.7, 6C 118, 7C 112.6, 8C 147, 9C 141.1, 10C122.9, C-O 55.8).

Microbiological Analysis Results.

Table (2)/ The antibacterial and antifungal activity targeted for the synthesized compounds

Compound	E. coli	S-aureus	P-digitatum
A	/	/	+++
B	-	-	-
C	++	+	/
D	+++	+++	/
E	++	++	/

The synthesized compounds were tested against two types of bacteria, Escherichia coli and Staphylococcus aureus, and it was found that they yielded good positive results compared to ampicillin, penicillin, and tetracycline, to which the bacteria have become more resistant, especially Escherichia coli

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