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Research Article

SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL ACTIVITY OF SOME HETERO BENZOCAINE DERVIVATIVES

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ABSTRACT

The present study deals with condensation of urea, thiourea, semicarbazide and thiosemicarbazide with Ethyl-4[(chloroacetyl) amino] benzoate under microwave irradiation in the presence of ethanol to afford two oxazole and thiazole derivatives. The synthesized compounds were characterized by spectral data such as IR, NMR; Mass. Compounds were screened for antimicrobial activity against strains of gram positive, and gram negative and fungal strains. All compounds showed good antibacterial and antifungal activity.

Keywords: Benzocaine, Oxazole, Thiazole, Antimicrobial, Urea, Thiourea, Semicarbazide, Thiosemicarbazide.

INTRODUCTION

Various heterocyclic compounds possess wide range of biological and pharmacological activities. Much attention has been paid during the last few decades to oxazole and thiazole moieties associated with a broad spectrum of activity such as antibacterial, antifungal, Pesticidal, insecticidal, anti-inflammatory, antitumor1, 3, 5, 9 etc., the demand for a new class of antimicrobial agents is substantially high in the last decade due to increased resistance towards various available antibiotics. An attempt has been made to synthesize two series of new oxazole and thiazole derivatives using microwave irradiation2, 7. Our present study deals with condensation of urea, thiourea, semicarbazide and thiosemicarbazide with Ethyl-4[(chloroacetyl)amino]benzoate under microwave irradiation in the presence of ethanol to afford corresponding two oxazole and thiazole derivatives such as Ethyl-4-[(2-amino-1,3-oxazole-4-yl)amino]benzoate, Ethyl-4-[(2- hydrazine-1,3-thiazol-4-ylamino]benzoate,Ethyl-4-[(2-amino-1,3-thiazol-4-ylamino]benzoate, Ethyl-4-[(2-hydrazino-1,3-thiazol-4-ylamino]benzoate. The synthesized compounds were characterized by spectral data such as IR, NMR, and mass spectrum data. The synthesized compounds were screened for antimicrobial activity against strains of gram positive (Staphylococcus aureus, Bacillus cereus), gram negative (Pseudomonus aeruginosa, E.coli) and fungal strains (Asperigillus niger, Aspergillus fumigates.). All compounds showed good antibacterial and antifungal activity.

MATERIALS AND METHOD

Melting point of the synthesized compounds were determined in open capillary tubes and were found uncorrected. IR spectra were recorded on ABB BUMEM FTIR Spectrophotometer with KBr pellets. H^1 NMR Spectra was recorded on Burker AV 400MHz and Mass Spectra were recorded on GCMS QD 5000 Shimadzu. The test compounds were synthesised by the following procedure.

Synthesis of ethyl-4-[(chloroacetyl) amino] benzoate

Ethyl 4 amino benzoate (0.1mole) in 120ml of ethanol was shaken in a magnetic stirrer for 1 ½ hours. Chloroacetyl chloride (0.1mole) was added in drops to the above mixture. The mixture was then allowed to be stirred for 1 hour. The stirred mixture was then refluxed for 2 hours. The mixture was then poured into ice cold water. The mass obtained was filtered and recrystallized with ethanol.

Scheme I

Synthesis of Compound I: Ethyl-4-[(2 amino-1, 3-oxazole-4-yl) amino] benzoate

Ethyl-4-[(chloroacetyl) amino] benzoate (0.01mole) and Urea (0.01mole) were dissolved in ethanol; the mixture was irradiated in microwave oven at a low power for 15 minutes. The solid mass was recrystallized using ethanol to afford 70% yield. Rf = 0.8, Melting Point 220-224ºC.

IR (KBr max cm^{-1}): 3488(NH Str), 1713(C=N), 1360 (C-O), 2835(C-H Aro str)

NMR: δ4 (NH), δ7.9 (CH) (oxazole), δ2.78 (CH_3), δ7.2-6.8 (Ar H)

MASS: $C_{12}H_{14}N_3O_3$, m/z: 248.10

Scheme II

Synthesis of Compound II: Ethyl-4-[(2-amino-1, 3-thiazol-4-yl) amino] benzoate

Ethyl-4-[(chloroacetyl) amino] benzoate (0.01mole) and Thiourea (0.01mole) were dissolved in ethanol; the mixture was irradiated in microwave oven at a low power for 10 minutes. The solid mass was recrystallized using ethanol to afford 80% yield. Rf = 0.8, Melting Point 198-202ºC.

IR (KBr max cm^{-1}): 3273(NH Str), 1619(C=N), 1473 (C-O), 2865(C-H Aro str), 730(C-S)

NMR: δ4 (NH), δ7.9 (CH) (oxazole), δ2.78 (CH_3), δ9.2 (NH_2) Thiourea

MASS: $C_{12}H_{14}N_3O_3$, m/z: 248.10

Scheme III

Synthesis of Compound III: Ethyl-4-[(2-hydrazinyl-1, 3-thiazol-4-yl) amino] benzoate

Ethyl-4-[(chloroacetyl) amino] benzoate (0.01mole) and thiosemicarbazide (0.01mole) were dissolved in ethanol; the mixture was irradiated in microwave oven at a low power for 12 minutes. The solid mass was recrystallized using ethanol to afford 72% yield. Rf = 0.8, Melting Point 217-220ºC.

IR (KBr max cm^{-1}): 3495(NH Str), 1643(C=N), 1367 (C-O), 2997(C-H Aro str), 730 (C-S)

NMR: δ8.04 (NH), δ7.53 (CH) (thiazole), δ2.78 (CH_3)

MASS: $C_{12}H_{13}N_4O_2S$, m/z: 279.0

Scheme IV

Synthesis of Compound IV: Ethyl-4-[(2-hydrazinyl-1, 3 -oxazol-4-yl) amino] benzoate

Ethyl-4-[(Chloroacetyl) amino] benzoate (0.01mole) and Semicarbazide (0.01mole) were dissolved in ethanol; the mixture was irradiated in microwave oven at a low power for 18 minutes. The solid mass was recrystallized using ethanol to afford 70% yield. Rf = 0.8, Melting Point 140-142ºC.

IR (KBr max cm^{-1}): 3431(NH Str), 1685(C=N), 1363 (C-O), 2995(C-H Aro str)

NMR: δ8.2 (NH), δ7.53 (CH) (oxazole), δ2.78 (CH_3)

MASS: $C_{12}H_{15}N_4O_3$, m/z: 263.7

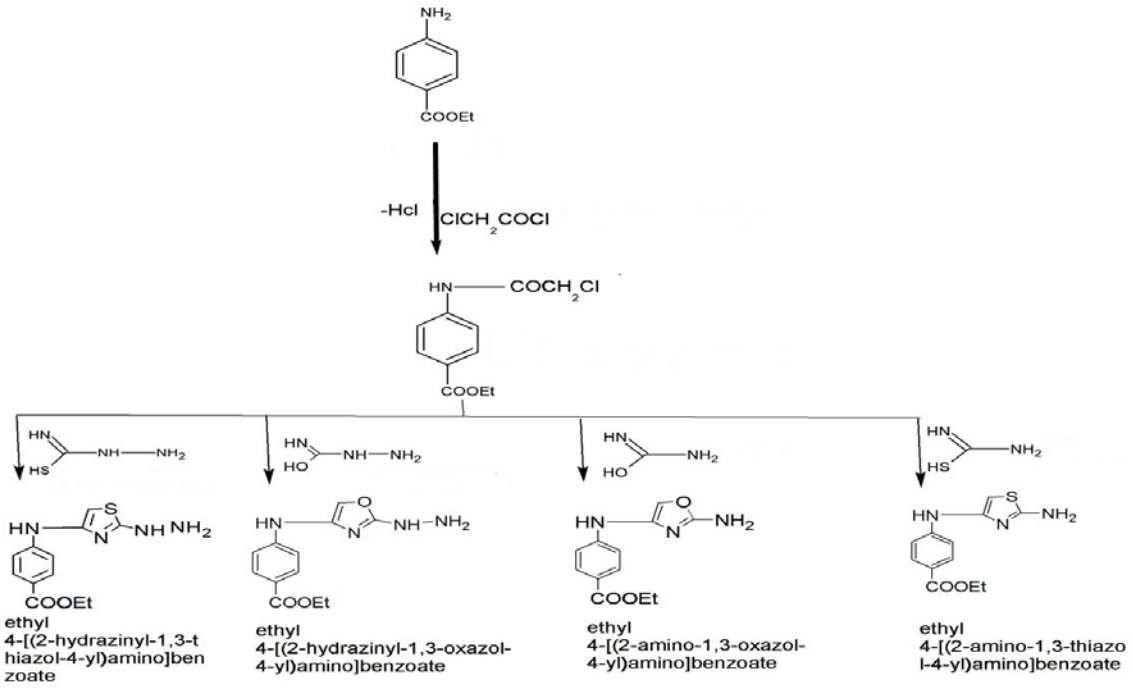

Fig. 1: Synthesis of Benzocaine Derivatives

Antimicrobial Activity

The synthesized compounds were subjected to antimicrobial activity. Antimicrobial activities were observed for all compounds using strains of gram positive such as (Staphylococcus aureus, Bacillus cereus), gram negative (Pseudomonus aeruginosa, E.coli) and fungal strains (Asperigillus niger, Aspergillus fumigates.)

The antimicrobial activities of the synthesized compounds were studied by disc diffusion method. Bacterial inoculums were spread on Nutrient agar. After the inoculums dried 6 mm diameter wells were made in the agar plate with a sterile cork borer. The synthesized compounds were dissolved in DMF at concentrations of 10 µg , 20 µg, 30 µg per ml. Ciprofloxacin 50 µg/ml was used as standard for the antibacterial activity and Ketoconazole was used as standard for the antifungal activity. The Petri plates were incubated at 37ºC for 24 hours. The Zone of inhibition was measured in mm to estimate the potency of the test compounds.

Organisms	Staphylococcus aureus (µg/ml)				Bacillus cereus (µg/ml)				Escherichia Coli (µg/ml)				Pseudomonas aeruginosa (µg/ml)				Aspergillus niger (µg/ml)				Aspergillus fumigates (µg/ml)			
Compound	*Std*	*10*	*20*	*30*	*Std*	*10*	*20*	*30*	*Std*	*10*	*20*	*30*	*Std*	*10*	*20*	*30*	*Std*	*10*	*20*	*30*	*Std*	*10*	*20*	*30*
A	38	15	23	26	39	16	20	26	40	19	25	29	40	16	26	29	40	15	18	25	39	17	24	28
B	38	14	21	24	39	15	22	25	40	18	23	28	40	16	25	27	40	15	19	27	39	19	23	27
C	38	16	19	25	38	17	21	24	39	14	19	24	40	19	24	28	39	16	20	24	38	15	22	25
D	38	15	22	28	39	19	24	28	40	16	22	26	40	16	25	29	39	17	22	29	39	19	25	29

Fig. 2: Zone of Inhibition by Disc Diffusion method in mm

RESULTS AND DISCUSSION

The synthesized compounds were characterized through IR, H^1 NMR and mass spectra. All synthesised compounds in the present study showed expected characteristic absorption bands for phenolic OH, NH, C=N, C-O, C-H, C-S. The investigation of antimicrobial screening data revealed that all the tested compounds shown good antimicrobial activity.

CONCLUSION

The synthesized compounds were subjected to antimicrobial activity. Concentrations of 10µg, 20µg, 30µg per ml were screened for antimicrobial activity. Among the synthesized compounds 30 µg/ml concentration of all synthesised compounds showed good antimicrobial activity against gram positive such as (Staphylococcus aureus, Bacillus cereus), gram negative (Pseudomonus aeruginosa, E.coli) and fungal strains (Asperigillus niger, Aspergillus fumigates and comparatively potent than standard.

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