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Synthesis, Characterization and Antimicrobial Activity of Some Oxazole and Thiazole Derivatives

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ABSTRACT

Present study deals in the reaction of anilines with chloroacetyl chloride to produce an intermediate, which undergoes condensation with urea and thiourea under microwave irradiation in the presence of ethanol to produce oxazole and thiazole derivatives. The synthesized compounds were characterized by spectral data such as IR, NMR and Mass. Compounds were screened for antimicrobial activity against strains of gram positive, and gram negative. All compounds showed moderate antibacterial activity.

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INTRODUCTION

Heterocyclic compounds have attracted attention in recent time due to its increasing importance in the field of pharmaceuticals and industries. Substitutions in oxazole and thiazole derivatives has provided marked biological activities like antibacterial, antifungal, anti-inflammatory[1,2,3]. These compounds have many established literature as potent anti-bacterial and anti-fungal agents. In focus of above observations and the demand for a new class of antimicrobial agents is substantially high in the last decade due to increased resistance towards various available antibiotics[2,4]. An attempt has been made to synthesize two series of new oxazole and thiazole derivatives using microwave irradiation, with the hope to get better antibacterial agents.

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*). All compounds showed good to moderate antibacterial activity.

MATERIALS AND METHODS

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

Synthesis of 2-Chloro-N-phenylacetamide derivatives (3a-3d)

Aniline derivatives (0.1 mole) in 120 ml of ethanol were shaken in a magnetic stirrer for 2-3 hours. Chloroacetyl chloride (0.1 mole) was added drop by drop to the above mixture. The mixture was then stirred for 1-2 hours. DMF was used as a solvent with K_2CrO_3 as a base. The stirred mixture was then refluxed for 2-2.5 hours and poured into ice cold water. The mass obtained was filtered and recrystallized from ethanol[4].

Synthesis of N^4-phenyloxazole-2,4-diamine (4a)

2-Chloro- N- phenylacetamide (0.01 mole) and Urea (0.01 mole) 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 produce 60 % yield. Rf = 0.8, Melting Point 210-214ºC.

IR (KBr max cm^{-1}): 3498 (NH Str), 1722 (C=N), 1372 (C-O), 2844 (C-H Str)

NMR: δ4 (NH), δ6.98 (NH_2), δ7.8 (CH) (Oxazole), δ7.1-6.7 (Ar-H)

MASS: m/z: 175.01

Synthesis of N^4-(4-fluorophenyl) oxazole-2, 4-diamine (4b)

2-Chloro- N-(4-fluorophenyl) acetamide (0.01 mole) and Urea (0.01 mole) 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 produce 40 % yield. Rf = 0.6, Melting Point 230-234ºC

IR (KBr max cm^{-1}): 3497 (NH Str), 1723 (C=N), 1376 (C-O), 2854 (C-H Str)

NMR: δ4.2 (NH), δ6.98 (NH_2), δ7.9 (CH) (Oxazole), δ7.2-6.8 (Ar-H)

MASS: m/z: 193.02

Synthesis of N^4-(4-chlorophenyl) oxazole-2,4-diamine (4c)

2-Chloro- N-(4-chlorophenyl) acetamide (0.01mole) and Urea (0.01 mole) were dissolved in ethanol; the mixture was irradiated in microwave oven at a low power for 20 minutes. The solid mass was recrystallized using ethanol to produce 45 % yield. Rf = 0.5, Melting Point 240-244ºC.

IR (KBr max cm^{-1}): 3499 (NH Str), 1721 (C=N), 1360 (C-O), 2845 (C-H Str)

NMR: δ4.1 (NH), δ6.98 (NH_2), δ7.9 (CH) (Oxazole), δ7.2-6.8 (Ar-H)

MASS: m/z: 209.05

Synthesis of N^4-(p-tolyl) oxazole-2,4-diamine (4d)

2-Chloro- N-(4-tolyl) acetamide (0.01 mole) and Urea (0.01 mole) were dissolved in ethanol; the mixture was irradiated in microwave oven at a low power for 19 minutes. The solid mass was recrystallized using ethanol to produce 50 % yield. Rf = 0.7, Melting Point 225-229ºC.

IR (KBr max cm^{-1}): 3496 (NH Str), 1722 (C=N), 1378 (C-O), 2834 (C-H Str)

NMR: δ4 (NH), δ6.98 (NH_2), δ7.8 (CH) (Oxazole), δ7.1-6.7 (Ar-H), δ2.33 ($C-CH_3$)

MASS: m/z; 189.06

Synthesis of N^4-phenylthiazole-2,4-diamine (5a)

2-Chloro- N- phenyl acetamide (0.01 mole) and Thiourea (0.01 mole) 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 200-204ºC.

IR (KBr max cm-1): 3296 (NH Str), 1622 (C=N), 758 (C-S), 2864 (C-H Str)

NMR: δ4 (NH), δ6.98 (NH_2), δ8.58 (CH),

MASS: m/z; 189.06

Synthesis of N^4-(4-fluoro)phenylthiazole-2,4-diamine (5b)

2-Chloro- N-(4-fluorophenyl) acetamide (0.01 mole) and Thiourea (0.01 mole) 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 70 % yield. Rf = 0.7, Melting Point 210-214ºC.

IR (KBr max cm-1): 3298 (NH Str), 1624 (C=N), 759 (C-S), 2862 (C-H Str)

NMR: δ4 (NH), δ6.97 (NH2), δ8.56 (CH),

MASS: m/z; 209.01

Synthesis of N^4-(4-chloro) phenylthiazole-2, 4-diamine (5c)

2-Chloro- N-(4-chlorophenyl) acetamide (0.01 mole) and Thiourea (0.01 mole) 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 60 % yield. Rf = 0.9, Melting Point 230-233ºC.

IR (KBr max cm-1): 3297 (NH Str), 1629 (C=N), 758 (C-S), 2860 (C-H Str)

NMR: δ4 (NH), δ6.97 (NH2), δ8.59 (CH),

MASS: m/z; 225.01

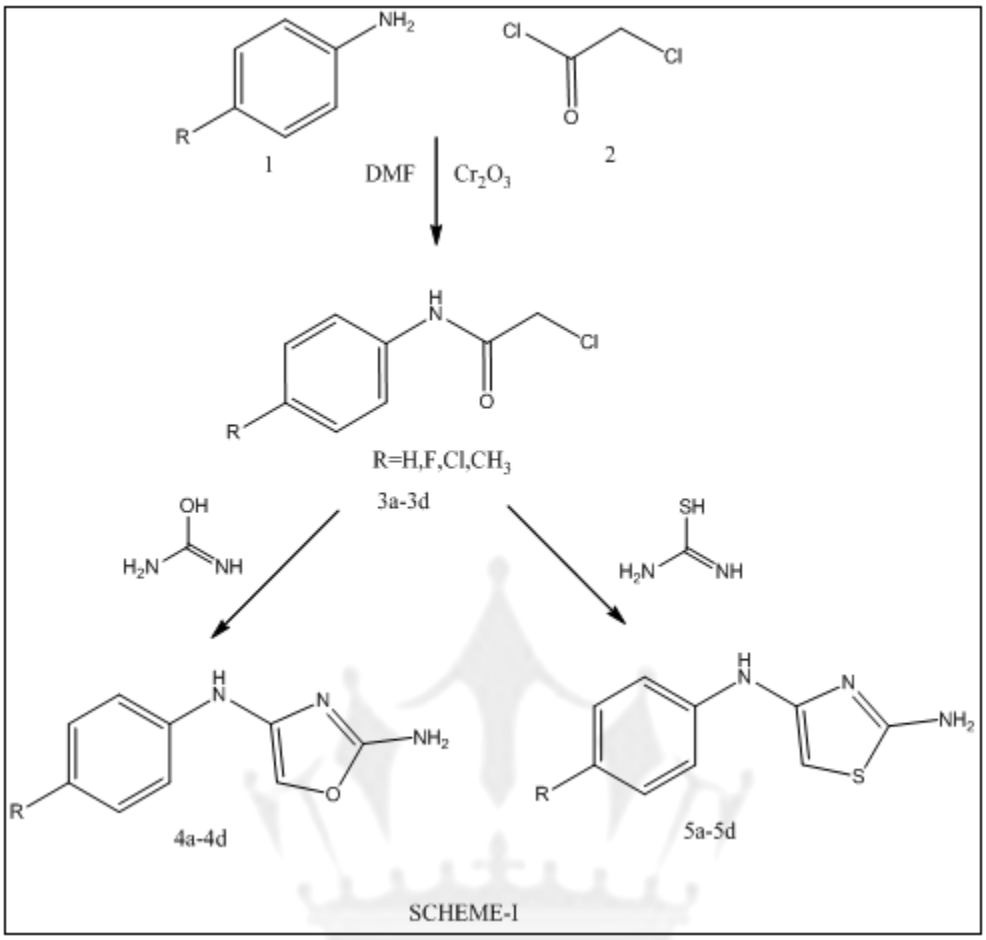
Synthesis of N^4-(p-tolyl) thiazole-2,4-diamine (5d)

2-Chloro- N-(4-tolyl) acetamide (0.01 mole) and Thiourea (0.01 mole) 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 65 % yield. Rf = 0.6, Melting Point 205-209ºC.

IR (KBr max cm-1): 3291 (NH Str), 1620 (C=N), 753 (C-S), 2869 (C-H Str), 2.79 (CH_3)

NMR: δ4 (NH), δ6.97 (NH2), δ8.59 (CH), δ2.44 (C-CH_3)

MASS: m/z; 205.05



SCHEME-1

Antimicrobial Activity

The synthesized compounds were exposed 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*). 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, per ml. Ciprofloxacin 50 µg/ml was used as standard for the antibacterial 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[6]. Results are shown in Table-I**.**

TABLE I. Zone of Inhibition by Disc Diffusion method in mm

Sl. No.	Compounds	Concentration (µgm/ml)	Zone of Inhibition(mm) *S. aureus, B.cereus, E. coli, P. aeruginosa*			
1	4a	10	14	12	26	18
		20	19	15	30	21
2	4b	10	16	18	30	23
		20	22	25	35	25
3	4c	10	18	19	31	26
		20	23	26	33	30
4	4d	10	15	14	28	15
		20	17	18	30	19
5	5a	10	15	13	23	24
		20	21	19	26	27
6	5b	10	18	16	25	26
		20	23	20	31	29
7	5c	10	19	21	28	13
		20	24	30	34	17
8	5d	10	16	23	30	23
		20	25	33	36	29
9	Std.	50	37	39	42	41

RESULTS AND DISCUSSION

All the synthesized compounds were characterized by spectral data such as IR, NMR, and mass spectrum data. They showed expected characteristic absorption bands for various groups like C=N, C-S, C-O, C-CH_3 etc. The synthesized compounds were screened for antimicrobial activity against strains of gram positive and gram negative. All compounds showed good to moderate antibacterial activity.

CONCLUSION

A set of eight compounds were synthesized, characterized and subjected to antimicrobial activities against Ciprofloxacin. Concentration at 20 μg/ml showed better activities against gram positive and gram negative bacterial strains. Among all the compounds, 4b, 4c, 5b, 5c showed better activities, this may be because of presence of electron withdrawing functional groups like Chlorine (Cl) and Fluorine (F). All the synthesized compounds can be compared with that of the standard.

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