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SYNTHESIS AND ANTIBACTERIAL ACTIVITY OF SOME NEW SUBSTITUTED AZETIDINE DERIVATIVES

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ABSTRACT

Four-membered nitrogen heterocycles such as β-lactams and azetidines are useful substrates in organic chemistry for the design and preparation of biologically active compounds. New series of 4(3-Chloro-(Substituted-Phenyl)-4-oxoazetidine1-yl)1-phenylthiosemicaebazide derivative were synthesized by the reaction of Schiff base with 2-Chloro acetyl chloride. Synthesized compounds were evaluated for their Anti- bacterial activity against Gram positive bacteria (Bacillus Subtilis) and gram negative bacteria (Klebsiella pneumonia). In this synthesis 6 derivatives are used named as NM_1, NM_2, NM_3, NM_4, NM_5 and NM_6.Synthesized compounds show significant activity against bacteria strains on agar plate. Their structures were established on the basis of elemental analysis, IR and NMR spectral data. The different substituted azetidine derivatives were synthesized followed by cyclization reaction. The newly synthesized azetidine derivatives were evaluated for their antimicrobial activity. The synthesized compounds NM_1 showed effective antimicrobial activity. This clearly indicates that new azetidine derivatives can be effectively synthesized by method mentioned in this study.

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INTRODUCTION:

Azetidine is the four membered heterocyclic compound which contain one Nitrogen atom in their ring. β-lactams and azetidines have caught the attention of organic chemists and medical researchers. The azetidines are four-membered nitrogen heterocycles of great interest for fundamental research and useful for practical applications[1].

Scheme: Synthesis of proposed derivatives.

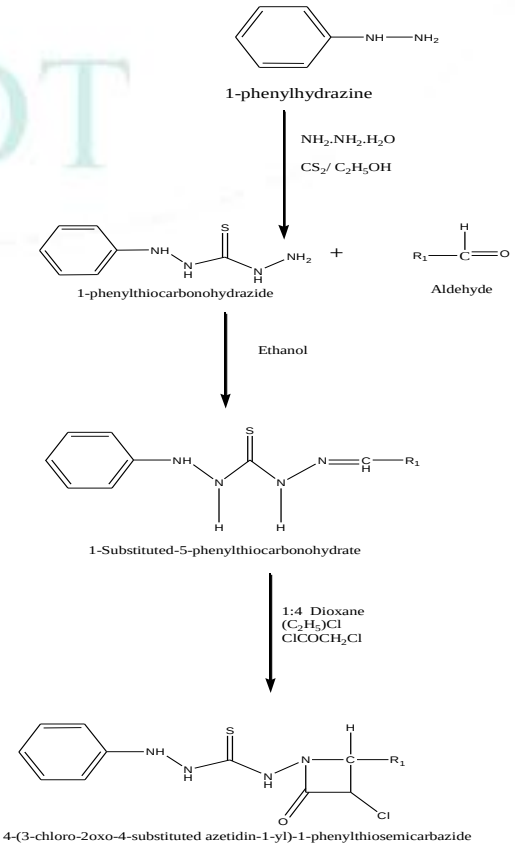
Substituted aldehyde: NM_1= Benzaldehyde, NM2= P-Chloro benzaldehyde, NM_3= 3-Nitrobenzaldehyde, NM_4= Diamino benzaldehyde, NM_5= 4-Bromo benzaldehyde and NM_6= 2-Chlorobenzaldehyde.

MATERIALS AND METHOD:

Synthesis of 1-Phenylthiocarbonohydrazide

Phenyl hydrazine (0.1mole) was dissolved in ethanol (95% 50ml) and ammonia solution 20ml. The CS_2 20ml was added slowly within 15 minute with shaking and solution is allowed to stand for 1hr.

Experimental:



Synthesis of 1-Substituted-5-phenylthiocarbohydrate

Aldehyde (0.01Mole) was added in the solid which obtained by compound A. Ethanol (30-35ml) was added into it. The solution mixture was refluxed for 3hr. The mixture was cooled at the room temperature and allowed to stand it for the 5hrs. The solid product was thus obtained and washed with ice cold water. Then recrystalized by ethanol[2-4].

Synthesis of 4-(3-chloro-2oxo-4-Substitutedazetidine-1-yl)-1-phenylthiosemicarbazide

A solid which is obtained by compound B (0.1mole) is added in the chloroacetyl chloride (0.1mole) in the presence of Et_2N was dissolved in acetone at room temperature and allow to reaction. The reaction mixture was first continuously stirred on a magnetic stirrer for about 2-3hr in the ice bath. Then kept it over night and make it in a powder form in the presence of Ethanol and filter it.

Analytical data of synthesized compound:

NM_1: IR(cm^{-1}): 771(C─Cl), 3034,2936(CH stretching aromatic), 1552(C═C aromatic), 1056(C─N stretching), 1645(C═O ketone), 3420(N─H bending), 3089(CH aromatic ring)

NMR: H^1NMR ($CDCl_3$), δ 6.91-8.21(m,6H, Ar-H), 4.27(s;1H;CH), 7.88(s; NH amide)

NM_2: IR(cm^{-1}): 1554(C═C aromatic), 774(C─Cl), 1059(C─N stretching), 3028, (CH stretching aromatic), 1647(C═O ketone), 3424(N─H bending), 3085(CH aromatic ring)

NMR: H^1NMR ($CDCl_3$), δ 4.23(s;1H;CH), 7.85(s; NH amide) 6.94-8.20(m,6H, Ar-H),

NM_3: IR(cm^{-1}): 3030,2932(CH stretching aromatic), 1550(C═C aromatic), 775(C─Cl), 1058(C─N stretching), 1640(C═O ketone), 3425(N─H bending), 3084(CH aromatic ring)

NMR: H^1NMR ($CDCl_3$), δ 6.90(m,6H, Ar-H), 4.24(s;1H;CH), 7.84(s; NH amide), 1410(NO_2)

NM_4: IR(cm^{-1}): 3431(N─H bending), 3038, (CH stretching aromatic), 1556(C═C aromatic), 773(C─Cl), 1060(C─N stretching), 1652(C═O ketone), 3090(CH aromatic ring)

NMR: H^1NMR ($CDCl_3$), δ 4.26 (s;1H;CH) 8.26(m,6H, Ar-H), 7.83(s; NH amide)

NM_5: IR(cm^{-1}): 1046(C─N stretching), 3041,2942(CH stretching aromatic), 1558(C═C aromatic), 772(C─Cl), 1649(C═O ketone), 3426(N─H bending), 3094(CH aromatic ring)

NMR: H^1NMR ($CDCl_3$), δ 6.97-7.27(m,6H, Ar-H), 4.22(s;1H;CH), 7.82(s; NH amide)

NM_6: IR(cm^{-1}): 1560(C═C aromatic), 779(C─Cl), 1072(C─N stretching), 1654(C═O ketone), 3416(N─H bending), 3096(CH aromatic ring), 3042 (CH stretching aromatic)

NMR: H^1NMR ($CDCl_3$), δ 7.78(s; NH amide) ,4.37(s;1H;CH), 6.82-8.31(m,6H, Ar-H),

Antibacterial evaluation:

Cup- Plate Method: It is one of the official method in IP where the test sample diffuse from the cup through an agar layer in Petri dish or plate to such an extent that growth of added microorganism is restricted entirely to circular area.

RESULT AND DISCUSSION:

Table 1: Zone of Inhibition

S. No.	Solutions	(+)ve bacteria (*Bacillus Subtilis*)	(-)ve Bacteria (*Klebsiella pneumonia*)
1	Test Solution (100µg/ml)		
	NM_1	18mm	26mm
	NM_2	16mm	24mm
	NM_3	15mm	19mm
	NM_4	14mm	18mm
	NM_5	16mm	11mm
	NM_6	12mm	14mm
2	Standard (AmoxicillinTrihydrate) (50µg/ml)	16mm	24mm

CONCLUSION:

This research work was oriented towards the finding of newer Azetidine derivative with antimicrobial activity. The different substituted azetidine derivatives were synthesized followed by cyclization reaction. The newly synthesized azetidine derivatives were evaluated for their antimicrobial activity. The synthesized compounds NM_1 showed effective antimicrobial activity. This clearly indicates that new azetidine derivatives can be effectively synthesized by method mentioned in this study. These synthesized compounds exhhibit significant antimicrobial activity.

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