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Schiff's bases of piperidone derivative as microbial growth inhibitors

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Abstract

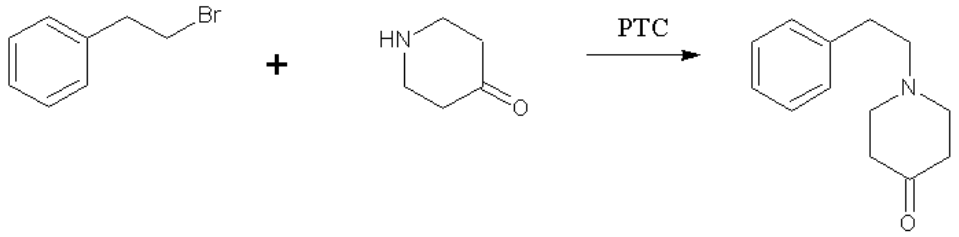
Piperidones are a class of chemical compounds sharing the piperidone skeleton. A classic named reaction for the synthesis of piperidones is the Petrenko-Kritschenko Piperidone synthesis which involves combining a alkyl-1, 3-acetonedicarboxylate with benzaldehyde and an amine. This multicomponent reaction reaction related to the Hantzsch pyridine synthesis.Some 4-piperidones give very good antimicrobial activity. So, here are some substituents of 4-piperidone to check whether I t give same activity or not.

Introduction

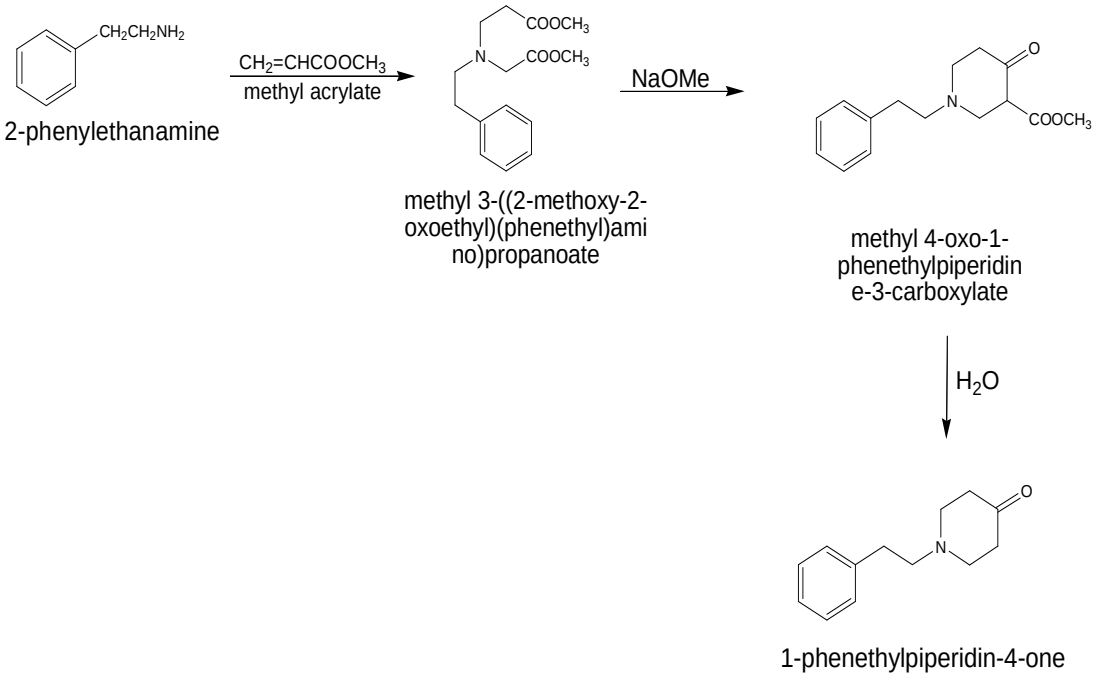
4-Piperidinone is a derivative of piperidine with the molecular formula C_5H_9NO. 4-Piperidone is used as an intermediate in the manufacture of chemicals and pharmaceutical drugs (e.g., fentanyl)[1]. Its proven applications in Wittig Reaction with Phosphorous Ylides, Organic Photoreceptor Synthesis, Removal of Sulphur Compounds from Gases, Pethidine Synthesis, Pharmaceutical Synthesis, Synthesis of Spiro Heterocycles & Fused ring Systems[2].

N-Phenethyl-4-piperidone*Preparation*

N-Phenethyl-4-piperidone can be prepared via a simple S_N2 substitution by reacting phenethyl bromide with 4-piperidinone in the presence of a phase transfer catalyst (PTC)[3].



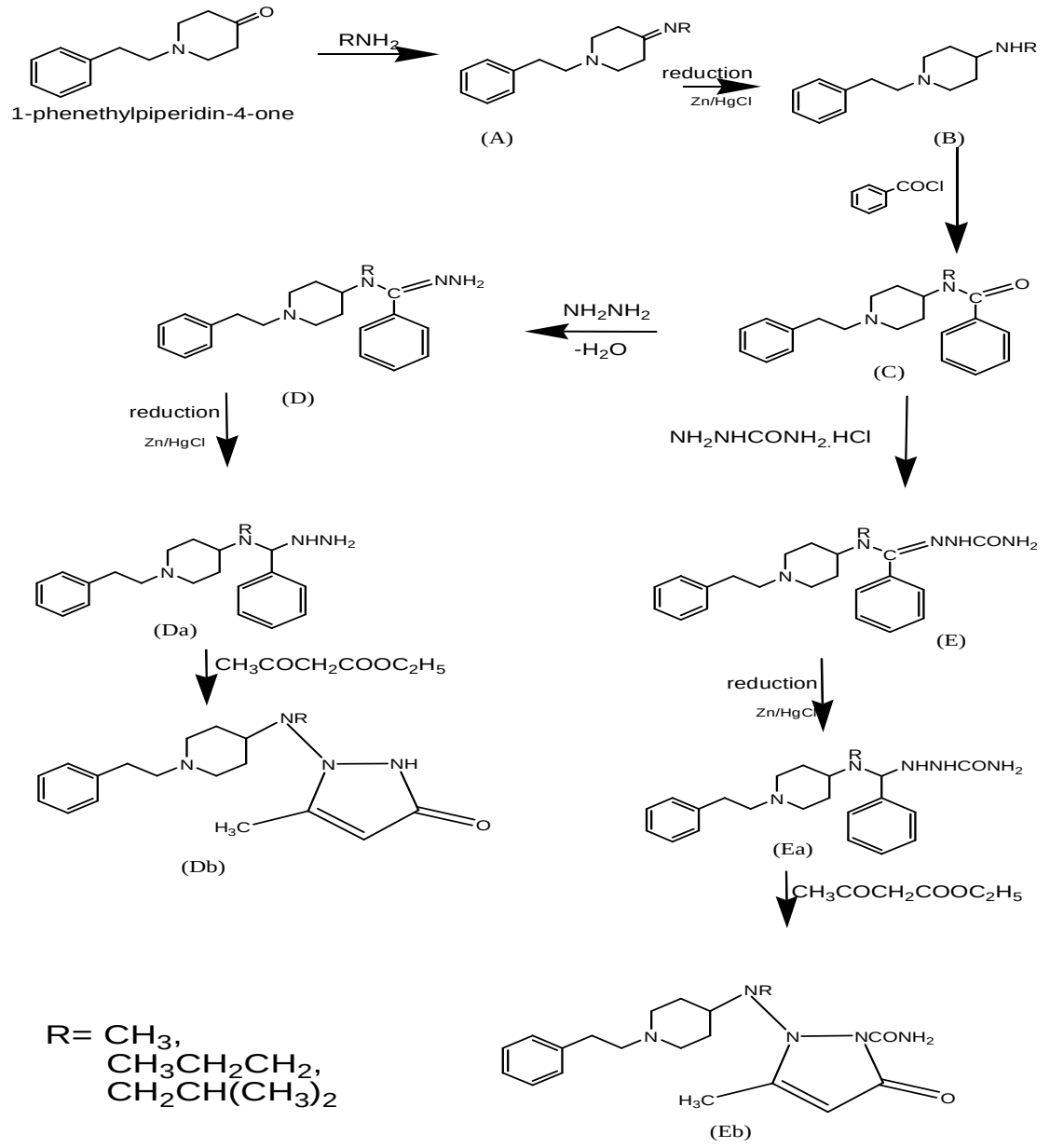
Scheme of preparation of Phenyl ethyl 4-piperidone



Procedure for reactions with different amines

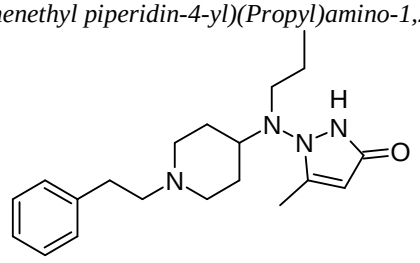
Phenyl ethyl 4-piperidone reacts with different amines [propylamine (I), isobutyl amine (II), methylamine (III)] respectively in presence of toluene as a solvent and water is removed and Schiff base is formed. Then this Schiff base undergoes reduction in presence of Zn-Hg /HCl and reduced product of Schiff base is obtained. Then it is reacted with benzoyl chloride and form benzoylated product, after benzoylation it reacts with two different azides: Hydrazide hydrate and semicarbazide .HCl and forms again Schiff base for both azides which further undergoes for clemensen reduction by reacting with ZnHg/HCl.the reduction product of both azides reacts with ethyl acetoacetate and undergoes cyclization and formed cyclized product[4,5].

General scheme for different synthesized products

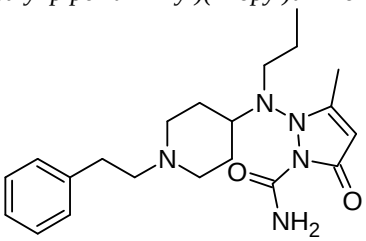


Synthesized Compounds

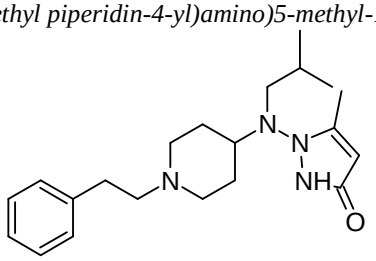
(IDb) 5-methyl-1-((1-Phenethyl piperidin-4-yl)(Propyl)amino-1,2,dihydropyrazol-3-one



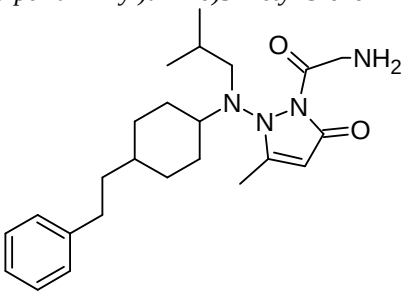
(IEb) 5-methyl-3-oxo-1-((1-Phenethyl piperidin-4-yl)(Propyl)amino-1H-pyrazole-2(3H)-carboxamide



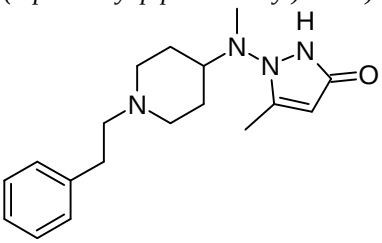
(IIDb) 1(isobutyl (1-phenethyl piperidin-4-yl)amino)5-methyl-1,2-dihydropyrazol-3-one



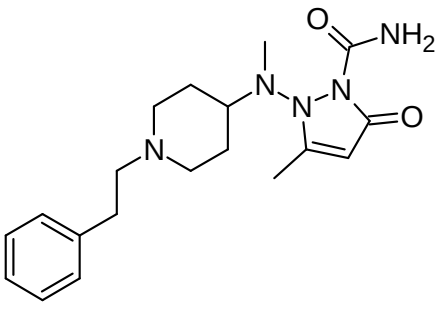
(IIEb) 1-(isobutyl(1-phenethylpiperidin-4-yl)amino)5-metyl-3-oxo-1H-pyrazol-2- (3H)carboxamide



(IIIDb) 5-methyl-1-(methyl(1-phenethyl piperidin -4-yl)amino)-1,2-dihydropyrazol-3-one



(IIIEb) 5-methyl-1-(methyl(1-phenethyl piperidin-4-yl)amino)-3-oxo-1H-pyrazol-2(3H)-carboxamide



Physicochemical Parameters of Synthesis Compound

Compound	Mol.formula	Mol.wt (g/mol)	Polarity	R_f[a]	Composition C,H,N(%) (cacltd.)	Composition C, H, N (%) (Found)
PhenEthyl 4Piperidone	$C_{13}H_{17}NO$	203.28	Polar	0.55	C,76.81;H,8.43; N,6.89; O, 7.87	C,76.82;H,8.52; N,6.79; O, 6.67
IDb	$C_{20}H_{30}N_4O$	342.48	Semipolar	0.58	C,70.14;H,8.83; N,16.36;O,4.67	C,70.24;H,7.43; N,16.36;O,4.67
IEb	$C_{21}H_{31}N_5O_2$	385.55	Semipolar	0.62	C,65.43;H,8.11; N,18.17;O,8.30	C,58.43;H,8.01; N,18.27;O,8.60
IIDb	$C_{21}H_{32}N_4O$	356.50	Semipolar	0.64	C,70.75;H,9.05; N,15.72;O,4.49	C,71.65;H,8.05; N,15.72;O,4.49
IIEb	$C_{22}H_{33}N_5O_2$	399.53	Semipolar	0.56	C,66.14;H,8.33; N,17.53;O,8.01	C,67.14;H,8.43; N,16.63;O,7.05
IIIDb	$C_{18}H_{26}N_4O$	314.43	Semipolar	0.5	C,68.76;H,8.33; N,17.82;O,5.09	C,67.76;H,7.33; N,17.82;O,5.09
IIIEb	$C_{19}H_{27}N_5O_2$	351.52	Semipolar	0.56	C,63.84;H,7.61; N,19.59;O,8.95	C,64.84;H,7.51; N,18.59;O,8.90

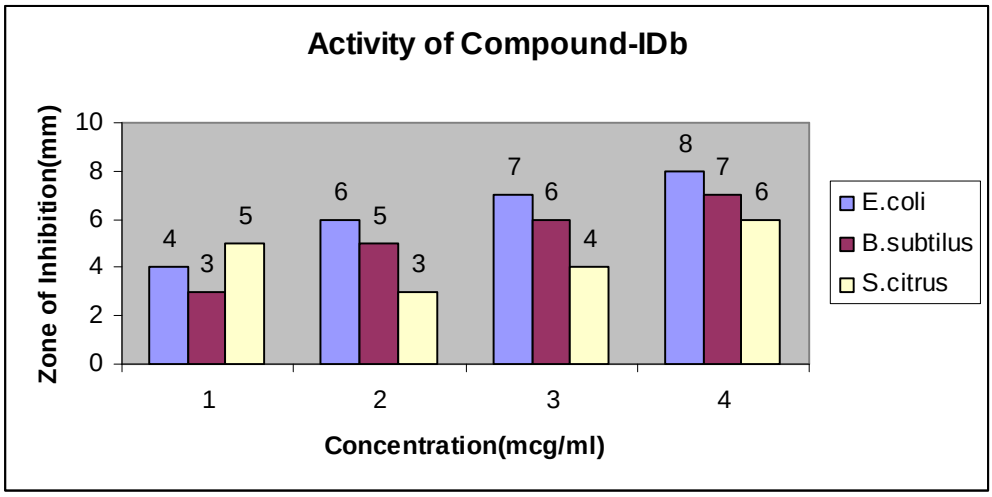
a-Ethyl acetate: Hexane (7:3)

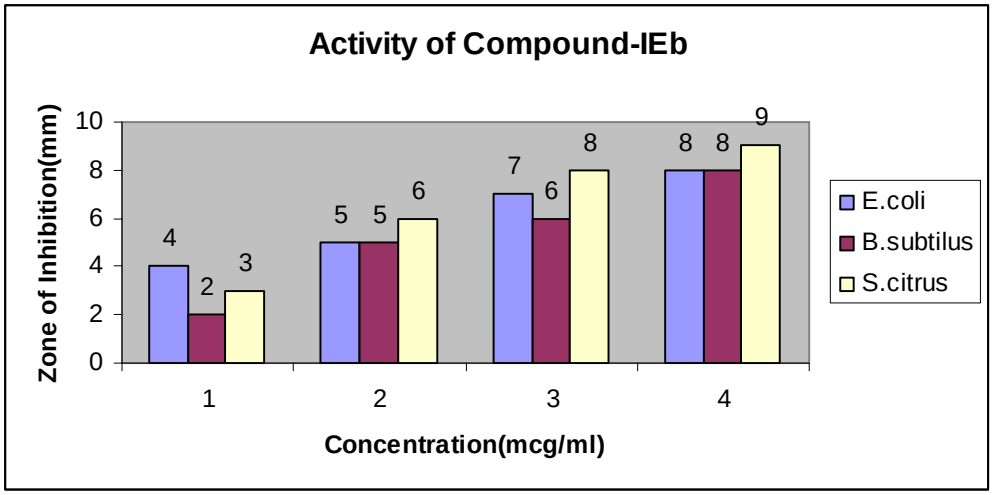
Antibacterial activity

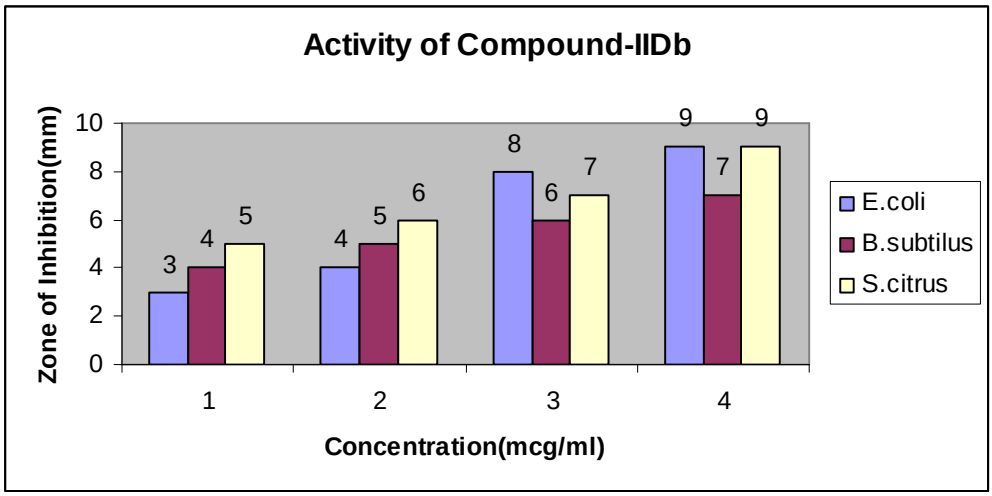
COMPOUNDS	CONC.(µg/ml)	ZONE OF INHIBITION(mm)		
		E.coli	*B.subtilis*	*S.citrus*
(IDb)	100	4 ±0.2	3 ±0.5	4 ±0.4
	250	6± 0.5	5± 0.2	3 0.2
	500	7 ±0.3	6 ±0.2	5± 0.5
	750	8 ±0.4	7 ±0.3	6± 0.1
(IEb)	100	4± 0.1	2± 0.3	3± 0.6
	250	5 ±0.4	5± 0.1	6 ±0.3
	500	7 ±0.2	6± 0.1	8± 0.3
	750	8± 0.4	8± 0.1	9 ±0.5
(IIDb)	100	3 ±0.2	4±0.1	5 ±0.3
	250	4±0.5	5± 0.4	6± 0.2
	500	8±0.1	6±0.1	7±0.6
	750	9±0.5	7±0.4	9±0.3
	100	4± 0.1	2± 0.3	3± 0.6

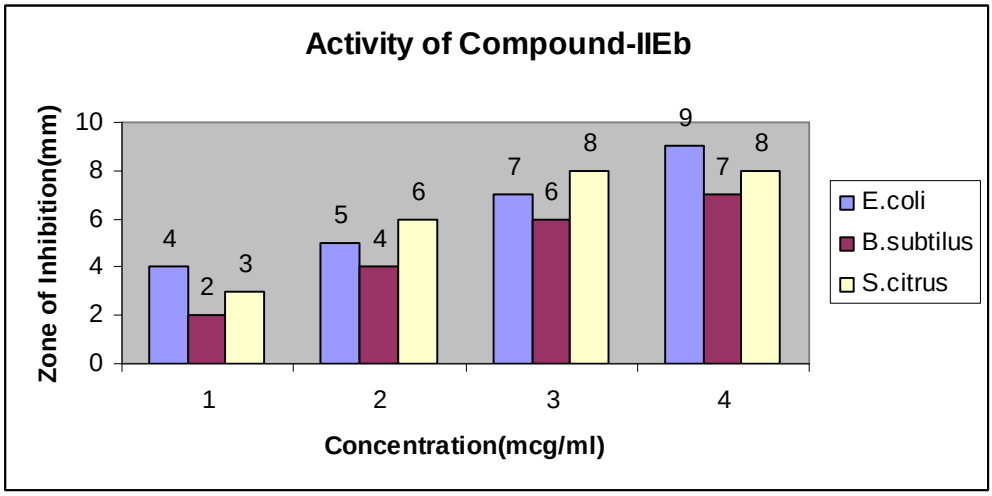
(IIEb)	250	5±0.5	4± 0.4	6± 0.2
	500	7 ±0.2	6± 0.1	8± 0.3
	750	9±0.5	7±0.4	8±0.3
(IIIDb)	100	3 ±0.2	4±0.1	5 ±0.3
	250	5±0.5	6± 0.4	7± 0.2
	500	7±0.1	6±0.1	7±0.6
	750	9±0.2	7±0.5	8±0.6
(IIIEb)	100	5 ±0.5	6±0.2	5 ±0.3
	250	6±0.5	7± 0.4	6± 0.2
	500	8±0.1	7±0.1	8±0.6
	750	9±0.5	8±0.4	9±0.3
Streptomycin	100	10±0.1	10±0.4	11±0.2
	250	12±0.5	11±0.6	11±0.2
	500	14±0.4	14±0.1	12±0.5
	750	14±0.1	16±0.2	14±0.3
Ampicillin	100	9±0.3	8±0.1	7±0.2
	250	11±0.2	10±0.3	11±o.6
	500	12±0.7	12±0.5	12±0.4
	750	14±0.5	13±0.6	14±0.3

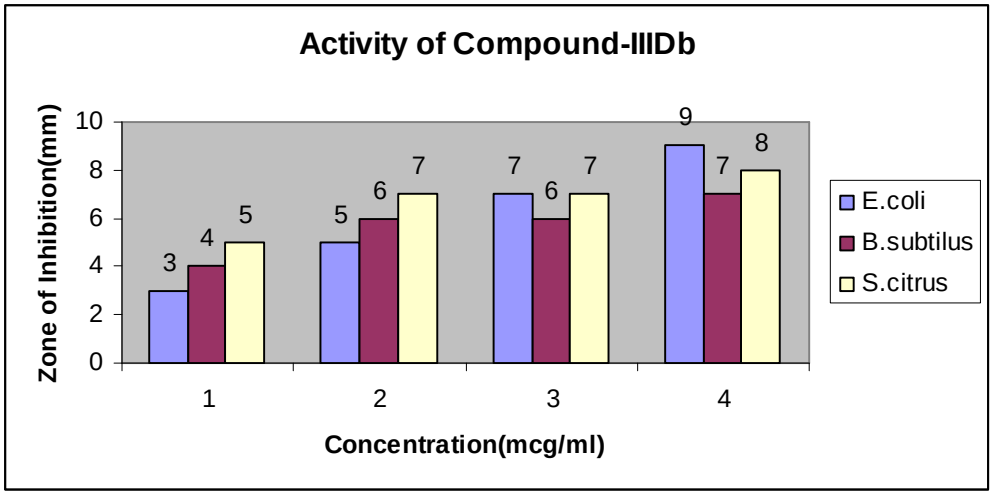
Histogram for Antimicrobial study of synthesized compounds

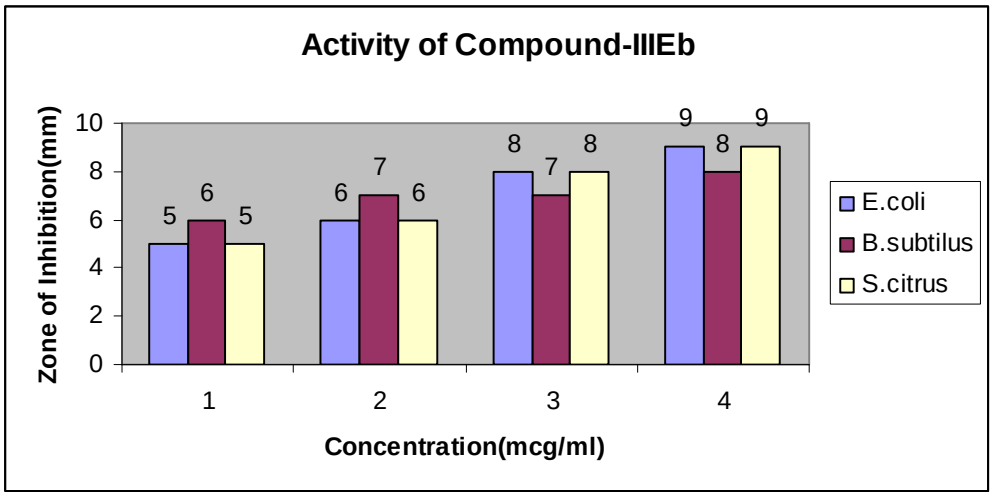


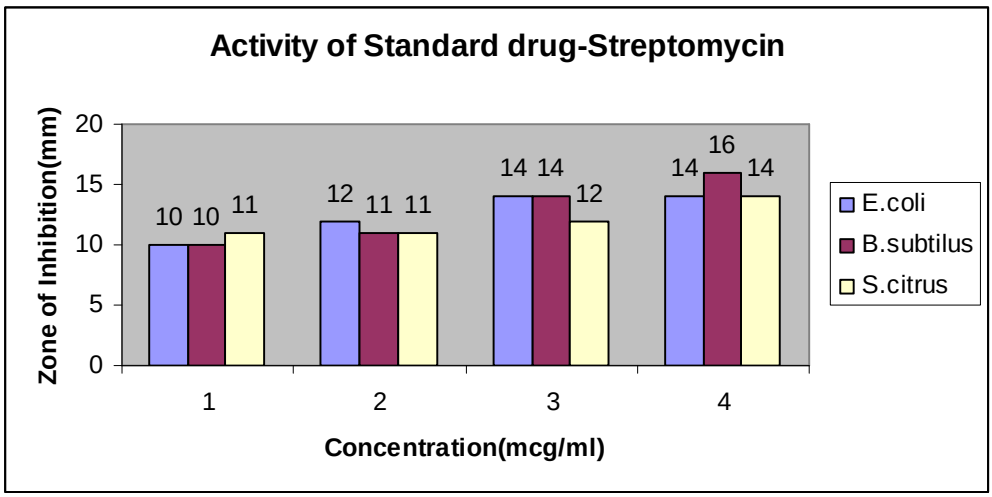

Activity of Compound-IEb
Zone of Inhibition(mm)
0
2
4
6
8
10
4
2
3
5
5
6
7
6
8
8
8
9
1
2
3
4
Concentration(mcg/ml)
E.coli
B.subtilus
S.citrus

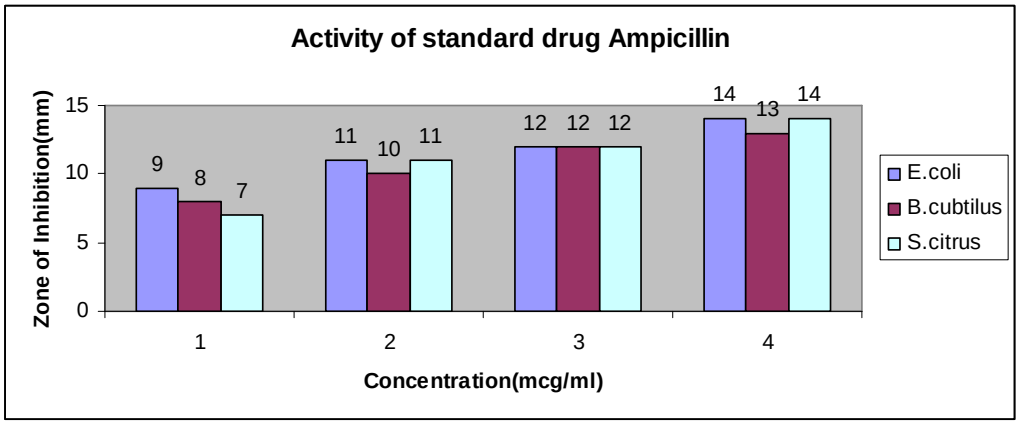

Activity of Compound-IIDb
Zone of Inhibition(mm)
0
2
4
6
8
10
3
4
5
4
5
6
8
6
7
9
7
9
1
2
3
4
Concentration(mcg/ml)
E.coli
B.subtilus
S.citrus


Activity of Compound-IIEb
Zone of Inhibition(mm)
0
2
4
6
8
10
4
2
3
5
4
6
7
6
8
9
7
8
1
2
3
4
Concentration(mcg/ml)
E.coli
B.subtilus
S.citrus


Activity of Compound-IIIDb
Zone of Inhibition(mm)
Concentration(mcg/ml)
E.coli
B.subtilus
S.citrus
3 4 5
5 6 7
7 6 7
9 7 8


Activity of Compound-IIIEb
Zone of Inhibition(mm)
Concentration(mcg/ml)
E.coli
B.subtilus
S.citrus
5 6 5
6 7 6
8 7 8
9 8 9

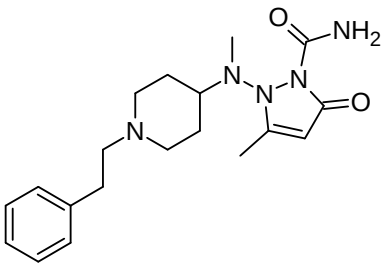

Activity of Standard drug-Streptomycin
Zone of Inhibition(mm)
Concentration(mcg/ml)
E.coli
B.subtilus
S.citrus
10 10 11
12 11 11
14 14 12
14 16 14



Conclusion

All the newly synthesized compounds IDb, IEb, IIDb, IIEb, IIIDb, IIIEb were screened for antimicrobial activity. The test solutions of synthesized compounds of 100µg/ml, 250µg/ml, 500 µg/ml and 750 µg/ml were prepared in a methanol. Streptomycin was used as standard reference drug and methanol as a control.

Among the all synthesized compounds, compound IIIEb gives a better antimicrobial activity against gram positive (*S.citrus* and *B.subtilis*) and gram negative (*E.coli*) bacteria than other synthesized compounds.



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