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Journal of Chemical and Pharmaceutical Research

J. Chem. Pharm. Res., 2010, 2(2): 50-56

ISSN No: 0975-7384

Antimicrobial and antifungal screening of indanone acetic acid derivatives

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Abstract

Indanone acetic acid is a non-heterocyclic fused ring of benzene with cyclopentananone moiety with acetic acid side chain in 1-position. This specific moiety has been synthesised and condensed with various substituents like PABA, piperidine, morpholine, benzimidazole, piperazine, pyrazolone and hydrazine to get the desired product for animicrobial screening by zone of inhibition study and MIC values with respect to some gram positive and gram negative microbes and fungal strains with reference standard antibiotics. The satisfactory result has been found in the antimicrobial and antifungal screening.

Key words: indanone acetic acid, antimicrobial, antifungal activity.

Introduction

Naturally occurring 1-indanone derivatives form a rre class of natural products geerally called pterosins. Some of this pterosins possess antimicrobial activity and some are moderately toxic for HeLa cells.sticher and co workers, during therir search for naturally occurring bioactive compounds isolated indanone as yellow oil from the cells of the cultured cynobacterium nostoc commune and was shown toexibit antibacterial activity.

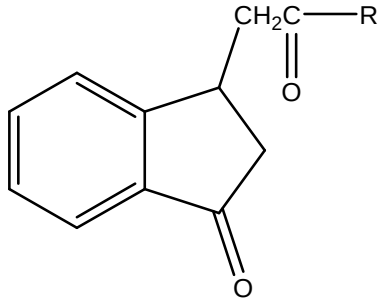
An antimicrobial is a substance that kills or inhibits the growth of microorganisms such as bacteria, fungi, or protozoans, as well as destroying viruses.Antimicrobial were evaluated for their in vitro antimicrobial againstGram positive bacteria and gram negative bacteria.Gram positive bacteria like Bacillus subtiils, Staphylococcus aureus, Pneumococci. Gram negative

bacteria like E.coli, psuedomonas, enterobacteria, klebsiella. Antimicrobials drugs are designed to kill or prevent the growth of micro organism (Bacteria, fungi and virus). Bacteria, fungi and viruses are responsible for almost all commonly infectious diseases1.
An antifungal drug is medication used to treat fungal infections such as athlete's foot, ringworm, candidiasis (thrush), serious systemic infections such as cryptococcal meningitis, and others. The fungal infections are superficial and systemic.The causing infections of the hair, mucous memberanes,nails or skin include candida and dermatophyte fungi.drugs are active against fungi like Candida albicans, Aspergilus niger, etc.

Materials and methods

Experimental section

Procedure:



Molecular Design

Synthesis of diethyl 3,5-diacetyl-4-phenyl haptandioate

Take 1mole (30 ml) benzaldehyde and 2 mole (78 ml) ethylacetoacetate in a 500 ml beaker. Add diethylamine (10 ml) into the mixture and heat the mixture on water bath for 30-40 mins. with stirring. After heating we get yellow color product. Add rectified spirit and water so diethyl 3,5-diacetyl-4-phenyl haptandioate totally ppts out.

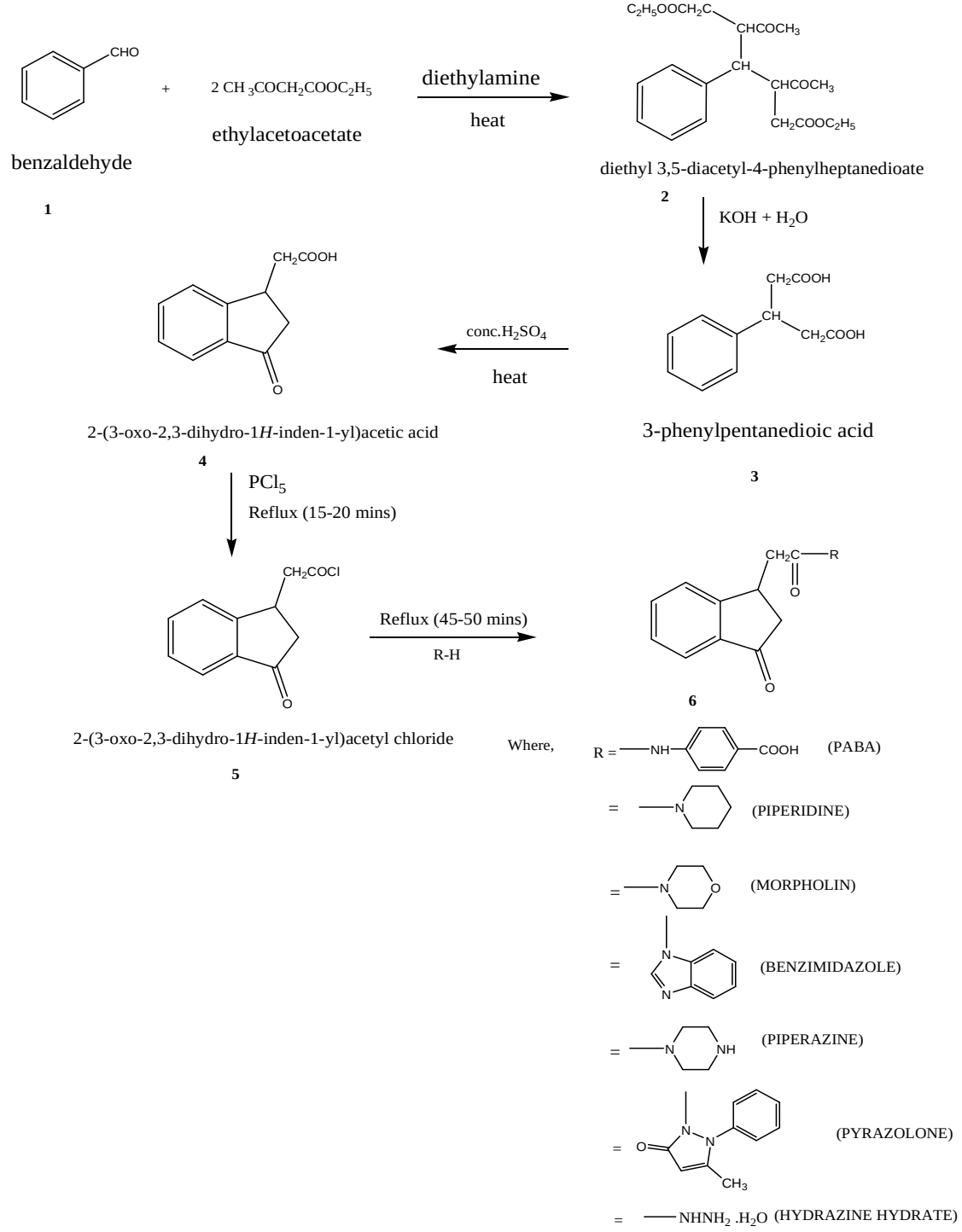
Synthesis of 3-phenyl pantandioic acid

50g of KOH dissolved in 50ml water in 500ml beaker.add 50g of diethyl 3,5-diacetyl-4-phenyl haptandioate and dissolved it and heat the mixture on water bath for 30-40 mins.after heating add conc. HCl slowely in cold condition till solution becomes acidic.after that add water into the mixture for remove the inorganic substances.now, dispersed oily part into the solution during heating then add charcoal and filter through the vaccum filtration. Filterate cool overnight in freeze.after we get white color 3-phenyl pantandioic acid.

Synthesis of 2-(3-oxo-2,3-dihydro-4-inden-1-yl)acetic acid

30g of 3-phenyl pantandioic acid dissolved in 90ml conc. H2SO4 in beaker.heat the mixture on waterbath for 30 mins.after completion of heating add this solution into the crushed ice.so, we get 2-(3-oxo-2,3-dihydro-4-inden-1-yl)acetic acid.

SCHEME OF SYNTHESIS



6a) Synthesis of 4-[(3-oxo-2,3-dihydro-1H –inden-1-yl)acetyl]amino benzoic acid

Take 1mole (4g) of 2-(3-oxo-2,3-dihydro-4-inden-1-yl)acetic acid dissolved in solvent methanol in round bottom flask (Rbf).add 1mole (4.40g) of PCl5 and reflux it for 15-20 mins.after that add p-amino benzoic acid (PABA) dropwise which is dissolved in methanol.reflux for 50-60

mins.then add this solution into crushed ice. so, we get crude 4-[(3-oxo-2,3-dihydro-1H –inden-1-yl)acetyl]amino benzoic acid. Recrystallised from methanol and water.

6b) Synthesis of 3-(2-oxo-2-piperidine-1-yl ethyl) indan-1-one

Take 1mole (4g) of 2-(3-oxo-2,3-dihydro-4-inden-1-yl)acetic acid dissolved in solvent methanol in round bottom flask (Rbf).add 1mole (4.40g) of PCl5 and reflux it for 15-20 mins.after that add piperidine dropwise and reflux for 50-60 mins.then add this solution into crushed ice. so, we get crude 3(2-oxo-2-piperidine-1-yl ethyl) indan-1-one. Recrystallised from methanol and water.

6c) Synthesis of 3-(2-morpholin-1-yl-2-oxo ethyl)indan-1-one

Take 1mole (4g) of 2-(3-oxo-2,3-dihydro-4-inden-1-yl)acetic acid dissolved in solvent methanol in round bottom flask (Rbf).add 1mole (4.40g) of PCl5 and reflux it for 15-20 mins.after that add morpholin dropwise and reflux for 50-60 mins.then add this solution into crushed ice. so, we get crude 3-(2-morpholin-1-yl-2-oxo ethyl)indan-1-one. Recrystallised from methanol and water.

6d) Synthesis of 3-[2-(1H benzimidazole-1-yl)-2-oxoethyl]inden-1-one

Take 1mole (4g) of 2-(3-oxo-2,3-dihydro-4-inden-1-yl)acetic acid dissolved in solvent methanol in round bottom flask (Rbf).add 1mole (4.40g) of PCl5 and reflux it for 15-20 mins.after that add benzimidazole dropwise which is dissolved in methanol.reflux for 50-60 mins.then add this solution into crushed ice. so, we get crude 3-[2-(1H benzimidazole-1-yl)-2-oxoethyl]inden-1-one. Recrystallised from methanol and water.

6e) Synthesis of 3-(2-oxo-2-piperazine-1-yl ethyl)indan-1-one

Take 1mole (4g) of 2-(3-oxo-2,3-dihydro-4-inden-1-yl)acetic acid dissolved in solvent methanol in round bottom flask (Rbf).add 1mole (4.40g) of PCl5 and reflux it for 15-20 mins.after that add piperazine dropwise and reflux for 50-60 mins.then add this solution into crushed ice. so, we get crude 3-(2-oxo-2-piperazine-1-yl ethyl)indan-1-one. Recrystallised from methanol and water.

6f) Synthesis of 5-methyl-2[(3-oxo-2,3-dihydro-1H-inden-1-yl)acetyl]-1-phenyl-1,2-dihydro-3H-pyrazole-3-one

Take 1mole (4g) of 2-(3-oxo-2,3-dihydro-4-inden-1-yl)acetic acid dissolved in solvent methanol in round bottom flask (Rbf).add 1mole (5ml) of SOCl2 and reflux it for 15-20 mins.after that add pyrazolone and reflux for 50-60 mins.then add this solution into crushed ice. so, we get crude 5-methyl-2[(3-oxo-2,3-dihydro-1H-inden-1-yl)acetyl]-1-phenyl-1,2-dihydro-3H-pyrazole-3-one. Recrystallised from methanol and water.

6g) Synthesis of 2-(3-oxo-2,3-dihydro-1H-inden-1-yl)acetohydrazine

Take 1mole (4g) of 2-(3-oxo-2,3-dihydro-4-inden-1-yl)acetic acid dissolved in solvent methanol in round bottom flask (Rbf).add 1mole (4.40g) of PCl5 and reflux it for 15-20 mins.after that add hydrazine hydrate dropwise and reflux for 50-60 mins.then add this solution into crushed ice. so, we get crude 2-(3-oxo-2,3-dihydro-1H-inden-1-yl)acetohydrazine. Recrystallised from ethanol and water.

Table: 1 Physico Chemical Parameters of Synthesized Compounds

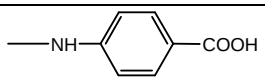
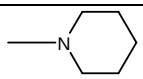
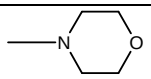
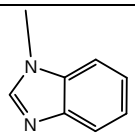
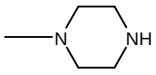
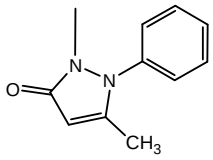
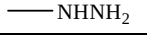
Compounds	Mol.formula	Mol.wt	R	Melting point (0C)	%Yield (%)
2	$C_{21}H_{28}O_6$	376	-	125	94
3	$C_{11}H_{12}O_4$	208	-		78
4	$C_{11}H_{10}O_3$	190	-	128	66
6a	$C_{18}H_{15}NO_4$	309		82	64
6b	$C_{16}H_{19}NO_2$	257		72	58
6c	$C_{15}H_{17}NO_3$	259		54	61
6d	$C_{18}H_{14}N_2O_2$	290		46	63
6e	$C_{15}H_{18}N_2O_2$	258		50	63
6f	$C_{21}H_{18}N_2O_3$	346		88	58
6g	$C_{11}H_{13}N_2O_2$	206		134	62

Table: 2 Spectral Data of Synthesized Compounds

Compounds	Spectral Data
6a	OH (3560), C=O (1710), C-H (2952); 310 (M+1)
6b	C=O (1700), C-N (1174, 1282), C-H (3O26); 258.9 (M+2)
6c	C=O (1700), C-O (1205), C-N (1280), C-H (2952); 259 (M.ion)
6d	C=O (1715), C-H (3023), C=N (1560,1610), C-N (1172); 289(M.ion)
6e	C=O (1700), C-H (2952); 259 (M+1)
6f	C=O (1714), C=C (1650), CH3 (2885); 349 (M+3)
6g	C=O (1720, N-H (1290), NH2 (1259), C-H (2944); 203(M.ion)

Table: 3

Compounds	CONC.(µg/ml)	Zone of inhibition (mm)		
		S.aureus	**E.coli**	**B.subtilis**
6a	700	8	9	10
	800	10	11	10
	900	10	12	12
	1000	12	14	15
6b	700	9	10	10
	800	10	14	12
	900	12	14	14
	1000	15	16	14
6c	700	10	10	7
	800	12	12	10
	900	13	14	12
	1000	16	15	13
6d	700	7	6	8
	800	10	9	10
	900	13	12	12
	1000	14	13	12
6e	700	12	12	10
	800	15	13	12
	900	15	15	14
	1000	17	15	17
6f	700	8	7	10
	800	10	10	12
	900	10	14	14
	1000	14	16	16
6g	700	10	10	12
	800	12	12	12
	900	14	12	13
	1000	16	15	15

Results

From IR, Mass and NMR spectra data synthesized compounds are confirmed in structural network and they give antimicrobial activity against gram positive and gram negative bacteria and fungal strains.

Conclusion

Among the all synthesized compounds compound 5e gives a better antimicrobial activity against gram positive and gram negative bacteria than other synthesized compounds.

Acknowledgements

The authors wish to thank Shri Sarvajanik Pharmacy College, Hemchandracharya North Gujarat University, Mehsana, Gujarat, India for providing facility to carry out the research work.

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