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Synthesis, Characterization and Evaluation of Antimicrobial Activity of Various Mannich Bases of Isoindoledione Derivatives

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Abstract: ***Isoindoledione possess a structural feature–CO-N(R)-CO- , an imide ring which help them to be biologically active and pharmaceutically useful. Isoindoledione have received attention due to their antibacterial, antifungal, analgesic, antitumor, anxiolytic and anti HIV-1 activities. When Isoindoledione is subjected to Mannich condensation, it yields Mannich bases which may display more biological activities. The increasing popularity of the Mannich reaction has been fueled by the ubiquitous nature of nitrogen containing compounds in drugs and natural products. The aim of the present study is to synthesis Mannich bases of Isoindoledione by Mannich condensation reaction. Isoindoledione reacts with various substituted aromatic aldehydes and substituted amines in presence of mineral acid to give various Mannich bases of Isoindoledione. The synthesized compounds will be characterized by elemental analysis, TLC and structure will confirmed by IR analysis and NMR analysis. Antimicrobial screening of the compounds will be carried out using Serial dilution method.***

Keywords: Isoindoledione, Phthalimide, Mannich base, N-Mannich base, antimicrobial activity, parallel synthesizer, MIC

1. Introduction

An Antimicrobial agent is any substance of natural, semi synthetic or synthetic origin that kills or inhibits the growth of microorganisms. It includes all agents that act against all types of microorganisms – bacteria (antibacterial), viruses (antiviral), fungi (antifungal) and protozoa (antiprotozoal).

In contrast an antibiotic is substance produced by microorganisms that at a low concentration inhibits or kills another microorganism. Thus, antibiotics do not include antimicrobial substances that are synthetic (sulfonamides and quinolones), or semi synthetic (methicillin and amoxicillin), or those which come from plants (quercetin and alkaloids) or animals (lysozyme).

So all antibiotics are antimicrobials, but not all antimicrobials are antibiotics. The term "antibacterial", being the largest and most widely known and studied class of antimicrobials, is often used interchangeably with the term "antimicrobials"Antimicrobial agents may act as either bacteriostatic or bactericidal. In case of antifungal agents, the term used is fungi static. Bacteriostatic drugs arrest the growth and replication of the bacteria and thus limit the spread of the infection. A bacteriostatic agent often is adequate in uncomplicated infections because the host defenses usually help eradicate themicroorgansims[1].Examples of bacteriostatic agents are chloramphenicol, tetracyclines, sulfonamides, trimethoprim, clindamycin, nitrofurantion etc.

Bactericidal drugs kills or irreversibly damage the multiplying bacteria, so that the total number of viable organisms decreases[2].Examples includes beta lactam antibiotics, cotrimoxazole, aminoglycosides, vancomycin, isoniazid, rifampcin etc.

A given agent may show the bactericidal actions under some conditions but bacteriostatic under other, depending on the concentration and the target bacteria.

Isoindoledione, commonly known as Phthalimide is a cyclic imide with two carbonyl groups. Various derivatives could be synthesized for this compound by addition or condensation on carbonyl group, or substitution on N-H group or aromatic ring. Isoindoledione derivatives are reported to have various pharmacological activities like antimicrobial[3,4], antihypertensive[5,6], antiviral[7], antitumer[8], antiiflametory[9,10], HIV-I Integrase inhibitor[11], analgesic[12], anxiolytic[13] etc. and also act as ligand to form bioactive metal complexes[14].

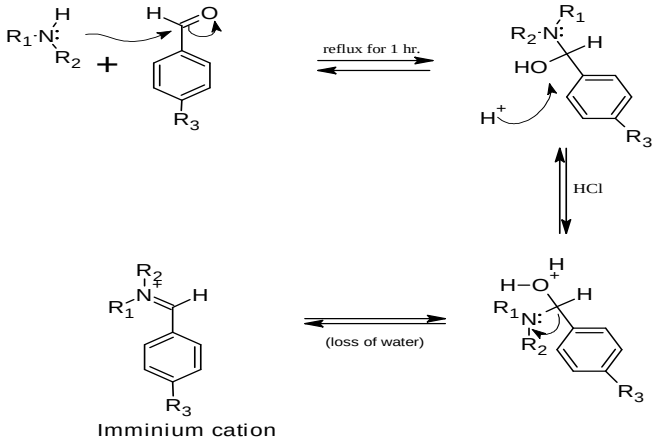
The method followed to synthesize the Isoindoledione derivatives is Mannich reaction. The reaction name is on the honor of Carl Mannich, founder of this mechanism. The first part of this mechanism is generation of iminium ion intermediate by nucleophilic addition reaction. The primary or secondary amine or ammonia attacks to carbonyl carbon of an aldehydes to give the addition product. And the second part is attack of iminium ion on a molecule containing active hydrogen, to give the substitution product. So for this reaction we require an amine, a non-enolizable aldehyde and a compound containing active hydrogen. If the active hydrogen is attached to nitrogen of the compound then the product is called N-mannich base as immine group get attach to this hydrogen only. Initialy most commonly only formaldehyde was being used as non-enolizable aldehyde. But later various substituted benzaldehyde or other aromatic aldehyde also found to be suitable for the reaction[15-19]. In the present study we used various various cyclic secondary amine, substituted benzaldehyde and Phthalimide as a compound with active hydrogen. So it gives the formation of N- Mannich base. In the synthesis of N-Mannich base, two nitrogen containing compounds are added into the reaction

mixture. The question is which of them will go for generation of iminium ion and which contains active hydrogen. The compound which has free lone pair on nitrogen will undergo for the generation of iminium ion. Those compound which lone pair on nitrogen are not free that is either participate in resonance (e.g. imidazole, benzimidazole, indole etc.) or next to carbonyl group to show keto-enol tautomerism (e.g. phthalimide, succinamide etc.) cannot go for generation of iminium ion. So these compounds are generally used for the synthesis of N-Mannich bases[20-27].

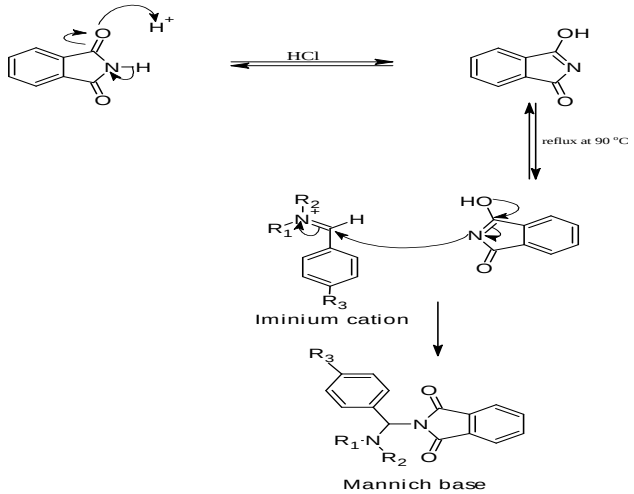
2. Mechanism of Synthesis

Mechanism is based on synthesis of N-Mannich base. This is single step mechanism, in which first part is generation of intermediate i.e. Iminium ion, which reacts with the compound containing active hydrogen to give Mannich base. So it is single pot two part mechanism, which is catalyzed by an acid.

Generation of iminium ion-



Synthesis of Mannich base-



3. Scheme of Synthesis

Table 1: Scheme of synthesis

Compound with active hydrogen	Non-enolisable aldehyde	Secondary amines
Phthalimide	Benzaldehyde	Thiomorpholine
		thiazolidine
		Piperazine
		Morpholine
		Pyrolidine
		piperidine
	p-chlorobenzaldehyde	Thiomorpholine
		thiazolidine
		Piperazine
		Morpholine
		Pyrolidine
		piperidine
	p-hydroxybenzaldehyde	Thiomorpholine
		thiazolidine
		Piperazine
		Morpholine
		Pyrolidine
		piperidine
	p-methoxybenzaldehyde	Thiomorpholine
		thiazolidine
		Piperazine
		Morpholine
		Pyrolidine
		piperidine

4. Synthetic Procedure

In 50 ml of ethanol Non-enolisable aldehyde (0.03mol) and secondary amine (0.03mol) were mixed. 5 drops of HCl was also added as catalyst then compound with active hydrogen phthalimide (0.03mol) was added and heated at 65°C for next 5 hours with continuous stirring by magnetic stirrer set at 90 rpm, on parallel synthesizer. Reaction was monitored on TLC. After the completion of reaction, mixture was cooled on ice bath. The solid product formed was filtered and washed with distilled water. It was dried at 60°C and recrystallized by ethanol.

5. Experimental

The melting point was determined by Lab India Visual Melting point Apparatus and uncorrected. The IR spectra of the synthesized compounds were recorded on Bruker ATR spectrophotometer. The ^{1}H NMR were recorded in $CDCl_3$ using Bruker NMR spectrometer and chemical shifts are reported as parts per million (ppm) using tetramethylsilane (TMS) as internal standard. All the compounds were synthesized by Rodleys Tech Parallel Synthesizer. Reactions were monitored using thin layer chromatography (TLC).The visualization was done using iodine vapour.

Table

2: Physical Data of synthesized compounds

Compound	**Molecular Formula**	**Molecular Weight**	**M.P(°C)**	**Yield (%)**
C1(2-[phenyl(thiomorpholin-4-yl)methyl]-1*H*-isoindole-1,3(2*H*)-dione)	$C_{19}H_{18}N_2O_2S$	338	238-241	63.10
C2(2-[phenyl(1,3-thiazolidin-3-yl)methyl]-1*H*-isoindole-1,3(2*H*)-dione)	$C_{18}H_{16}N_2O_2S$	324	247-249	57.40
C3(bis-2-[phenyl(piperazin-1-yl)methyl]-1*H*-isoindole-1,3(2*H*)-dione)	$C_{34}H_{28}N_4O_4$	556	226-228	64.30
C4(2-[morpholin-4-yl(phenyl)methyl]-1H-isoindole-1,3(2H)-dione)	$C_{19}H_{18}N_2O_3$	322	239-241	58

C5(2-[phenyl(pyrrolidin-1-yl)methyl]-1H-isoindole-1,3(2H)-dione)	$C_{19}H_{18}N_2O_2$	306	243-244	54.20
C6(2-[phenyl(piperidin-1-yl)methyl]-1H-isoindole-1,3(2H)-dione)	$C_{20}H_{20}N_2O_2$	320	234-237	58.80
C7(2-[(4-chlorophenyl) (thiomorpholin-4-yl)methyl]-1H-isoindole-1,3(2H)-dione)	$C_{19}H_{17}ClN_2O_2S$	372	183-184	62.10
C8(2-[(4-chlorophenyl)(1,3-thiazolidin-3-yl)methyl]-1H-isoindole-1,3(2H)-dione)	$C_{18}H_{15}ClN_2O_2S$	358	186-189	54.30
C9(bis-2-[(4-chlorophenyl) (piperazin-1-yl)methyl]-1H-isoindole-1,3(2H)-dione)	$C_{34}H_{26}Cl_2N_4O_4$	625	232-234	56.50
C10(2-[(4-chlorophenyl) (morpholin-4-yl)methyl]-1H-isoindole-1,3(2H)-dione)	$C_{19}H_{17}ClN_2O_3$	356	196-198	56.20
C11(2-[(4-chlorophenyl) (pyrrolidin-1-yl)methyl]-1H-isoindole-1,3(2H)-dione)	$C_{19}H_{17}ClN_2O_2$	340	249-251	53.90
C12(2-[(4-chlorophenyl) (piperidin-1-yl)methyl]-1H-isoindole-1,3(2H)-dione)	$C_{20}H_{19}ClN_2O_2$	354	184-186	73.20
C13(2-[(4-hydroxyphenyl) (thiomorpholin-4-yl)methyl]-1*H*-isoindole-1,3(2*H*)-dione)	$C_{19}H_{18}N_2O_3S$	354.42	242-246	62.30
C14(2-[(4-hydroxyphenyl)(1,3-thiazolidin-3-yl)methyl]-1*H*-isoindole-1,3(2*H*)-dione)	$C_{18}H_{16}N_2O_3S$	340.39	186-189	62.70
C15(bis-2-[(4-hydroxyphenyl) (piperazin-1-yl)methyl]-1*H*-isoindole-1,3(2*H*)-dione)	$C_{34}H_{28}N_4O_6$	588.60	234-237	59.10
C16(2-[(4-hydroxyphenyl) (morpholin-4-yl)methyl]-1*H*-isoindole-1,3(2*H*)-dione)	$C_{19}H_{18}N_2O_4$	338.85	212-215	54.60
C17(2-[(4-hydroxyphenyl) (pyrrolidin-1-yl)methyl]-1*H*-isoindole-1,3(2*H*)-dione)	$C_{19}H_{18}N_2O_3$	322.25	243-245	64.30
C18(2-[(4-hydroxyphenyl) (piperidin-1-yl)methyl]-1*H*-isoindole-1,3(2*H*)-dione)	$C_{20}H_{20}N_2O_3$	336.38	239-241	57.60
C19(2-[(4-methoxyphenyl) (thiomorpholin-4-yl)methyl]-1*H*-isoindole-1,3(2*H*)-dione)	$C_{20}H_{20}N_2O_3S$	368.44	173-174	49.60
C20(2-[(4-methoxyphenyl)(1,3-thiazolidin-3-yl)methyl]-1*H*-isoindole-1,3(2*H*)-dione**)**	$C_{19}H_{18}N_2O_3S$	354.42	169-170	53.40
C21(bis2-[(4-methoxyphenyl) (piperazin-1-yl)methyl]-1*H*-isoindole-1,3(2*H*)-dione)	$C_{39}H_{32}N_4O_6$	616.66	218-221	53.70
C22(2-[(4-methoxyphenyl) (morpholin-4-yl)methyl]-1*H*-isoindole-1,3(2*H*)-dione)	$C_{20}H_{20}N_2O_4$	352.38	227-230	59.20
C23(2-[(4-methoxyphenyl) (pyrrolidin-1-yl)methyl]-1*H*-isoindole-1,3(2*H*)-dione)	$C_{20}H_{20}N_2O_3$	336.38	243-245	53.80
C24(2-[(4-methoxyphenyl) (piperidin-1-yl)methyl]-1*H*-isoindole-1,3(2*H*)-dione)	$C_{21}H_{22}N_2O_3$	350.41	182-185	54.90

Table 3: Analytical Data of the synthesized compounds

Compounds	R_f *value*	*ATR*	*NMR(CDCl3)* δ
C1	0.69	185cm^{-1}(Ar-C-Hstr), 2931cm^{-1} (aliphatic C –H str), 1719cm^{-1} (C=Ostr), 1602cm^{-1}{Ar-C=N str), 1520 cm^{-1}(Ar-C=C str), 1306 cm^{-1} (C-N str), 646cm^{-1}(C-S-C str)	7.30-7.81 (m, 9H, Ar-H),6.50 (s,1H,CH), 3.87(4H,S-CH_2), 2.36(4H,N-CH_2)
C2	0.74	3188 cm^{-1}(Ar-C-Hstr), 2932 cm^{-1} (aliphatic C –H str), 1718 cm^{-1} (C=O str), 1600cm^{-1}(Ar-C=N str), 1523cm^{-1}(Ar-C=C str), 1305 cm^{-1} (C-N str),642 cm^{-1}(C-S-C str)	7.39-7.55(m,9H,Ar-H),6.50(s,1H,CH), 1.69-1.80(6H,aliphatic CH_2)
C3	0.54	1717 cm^{-1}(C=O str),1602cm^{-1}{Ar-C=N str), 1522 cm^{-1}(Ar-C=C str), 1307 cm^{-1}(C-N str)	7.22-7.89 (m, 18H, Ar-H),6.52 (s,2H,CH), 2.52 (8H,aliphaticCH_2)
C4	0.63	3192 cm^{-1}(Ar-C-Hstr),2927 cm^{-1} (aliphatic C –H str), 1714 cm^{-1} (C=O str),1600cm^{-1}{Ar-C=N str), 1522 cm^{-1}(Ar-C=C str), 1305 cm^{-1} (C-N str),1050cm^{-1}(C-O-C str)	7.60-7.71 (m, 9H, Ar-H),6.49 (s,1H,CH), 3.79 (4H,O-CH_2), 2.40(4H,N-CH_2)
C5	0.49	3196 cm^{-1}(Ar-C-Hstr),2924 cm^{-1} (aliphatic C –H str), 1718 cm^{-1} (C=O str),1602cm^{-1}{Ar-C=N str), 1520 cm^{-1}(Ar-C=C str), 1306 cm^{-1} (C-N str)	7.21-7.89 (m, 9H, Ar-H),6.30 (s,1H,CH), 1.98(4H,N-CH_2), 1.59(4H,aliphatic CH_2)
C6	0.77	2928 cm^{-1}(aliphatic C –H str), 1720 cm^{-1}(C=O str),1521 cm^{-1} (Ar-C=C str), 1307 cm^{-1}(C-N str)	7.21-7.89 (m, 9H, Ar-H),6.31 (s,1H,CH), 1.98(4H,N-CH_2), 1.59(6H,aliphatic CH_2)
C7	0.57	3063 cm^{-1}(aliphatic C –H str), 1716 cm^{-1}(C=O str), 1516 cm^{-1} (Ar-C=C str), 1305 cm^{-1}(C-N str), 712cm^{-1} (C-Cl str), 646cm^{-1} (C-S-C str)	7.30-7.81(m,8H,Ar-H), 6.50 (s,1H,CH), 3.86(4H,S-CH_2),2.29(4H,N-CH_2)
C8	0.61	3193 cm^{-1}(Ar-C-Hstr),3062 cm^{-1} (aliphatic C –H str), 1714 cm^{-1} (C=O str), 1520 cm^{-1}(Ar-C=C str), 1306 cm^{-1}(C-N str), 713cm^{-1} (C-Cl str), 646cm^{-1} (C-S-C str)	7.39-7.56(m,8H,Ar-H),6.50(s,1H,CH), 1.72-1.90(6H, aliphatic CH_2)
C9	0.75	3193 cm^{-1}(Ar-C-Hstr), 1718 cm^{-1} (C=O str), 1511 cm^{-1}(Ar-C=C str), 1303 cm^{-1}(C-N str),712cm^{-1}(C-Clstr)	7.22-7.89(m,16H,Ar-H),6.52(s,2H,CH), 2.59(8H,aliphaticCH_2)
C10	0.84	3193 cm^{-1}(Ar-C-Hstr),3061 cm^{-1}(aliphatic C –H str), 1716 cm^{-1}(C=O str), 1516 cm^{-1}(Ar-C=C str), 1305 cm^{-1}(C-N str), 1049 cm^{-1} (C-O-C str), 712cm^{-1}(C-Clstr)	7.39-7.71(m, 8H, Ar-H), 6.49 (s,1H,CH), 3.89(d,4H,O-CH_2), 2.38(d,4H,N-CH_2)
C11	0.67	3226 cm^{-1}(Ar-C-Hstr), 1666 cm^{-1}(C=O str), 1502 cm^{-1}(Ar-C=C str),1395 cm^{-1}(C-N str), 712cm^{-1} (C-Clstr)	7.21-7.89(m,8H,Ar-H), 6.30(s,1H,CH),1.98(d,4H,N-CH_2),1.59 (d,4H,aliphatic-CH_2)
C12	0.57	3194 cm^{-1}(Ar-C-Hstr),3063cm^{-1} (aliphatic C –H str), 1716 cm^{-1} (C=O str), 1455 cm^{-1}(Ar-C=C str), 1305 cm^{-1}(C-N str), 712cm^{-1} (C-Clstr)	7.21-7.89 (m,8H,Ar-H), 6.30 (s,1H,CH), 1.98(4H,N-CH_2), 1.59(6H,aliphatic-CH_2)
C13	0.83	3338cm^{-1}(O-H str), 2971 cm^{-1} (aliphatic C –H str), 1719 cm^{-1} (C=Ostr), 1464cm^{-1}(Ar-C=C str), 1304 cm^{-1}(C-N str), 646 cm^{-1}(C-S-C str)	8.90(s,1H,OH),7.30-7.81(m,8H,Ar-H), 6.50(s,1H,CH), 3.80(4H,S-CH_2), 2.31(4H,N-CH_2)
C14	0.72	3339 cm^{-1}(O-H str), 2970 cm^{-1}(aliphatic C –H str), 1720cm^{-1} (C=O str), 1306 cm^{-1}(C-N str), 646 cm^{-1}(C-S-C str)	8.47(s,1H,OH), 7.39-7.56 (m, 8H, Ar-H),6.50 (s,1H,CH),1.86-1.92(6H, aliphatic CH_2)
C15	0.61	3341cm^{-1}(OH str), 2971 cm^{-1} (aliphatic C –H str), 1685cm^{-1} (C=O str), 1466cm^{-1}(Ar-C=C str), 1388 cm^{-1}(C-N str)	7.22-7.89(m,16H,Ar-H),6.52(s,2H,CH), 4.20(s,2H,OH),2.59(8H,aliphaticCH_2).
C16	0.54	3201 cm^{-1}(OH str), 2971 cm^{-1} (aliphatic C –H str), 1719 cm^{-1}	7.39-7.71 (m, 8H, Ar-H),6.79(s,1H,OH),

		(C=O str), 1305 cm^{-1}(C-N str)	6.49(s,1H,CH),3.89(4H,O-CH_2), 2.36(4H,N-CH_2)
C17	0.60	3342 cm^{-1}(OH str), 2971 cm^{-1} (aliphatic C –H str), 1720cm^{-1} (C=O str), 1306 cm^{-1}(C-N str)	8.94(s,1H,OH),7.21-7.89 (m, 8H, Ar-H), 6.30(s,1H,CH),1.98(4H,N-CH_2), 1.59 (4H, aliphatic-CH_2)
C18	0.83	3343 cm^{-1}(OH str), 2970 cm^{-1} (aliphatic C –H str), 1720cm^{-1} (C=O str), 1305 cm^{-1}(C-N str)	8.50(s,1H,OH),7.21-7.89 (m, 8H, Ar-H) 6.30(s,1H,CH), 1.98(4H,N-CH_2),1.59 (6H, aliphatic-CH_2)
C19	0.73	3195 cm^{-1}(Ar-C-Hstr), 3065 cm^{-1}(aliphatic C–H str), 1745 cm^{-1}(C=O str), 1510 cm^{-1}(Ar-C=C str), 1307 cm^{-1}(C-N str), 1217cm^{-1} (C-O-C str), 644cm^{-1} (C-S-C str).	7.30-7.81(m,8H,Ar-H), 6.49(s,1H,CH), 4.20(3H,O-CH_3),3.71(4H,S-CH_2), 2.25(4H,N-CH_2)
C20	0.81	3191 cm^{-1}(Ar-C-Hstr),3064 cm^{-1} (aliphatic C –H str), 1747 cm^{-1} (C=O str), 1514 cm^{-1}(Ar-C=C str), 1306 cm^{-1}(C-N str), 1261cm^{-1} (C-O-C str) 644cm^{-1} (C-S-C str)	7.39-7.56(m,8H,Ar-H),6.49(s,1H,CH), 4.20(3H,O-CH_3),1.69-1.82(6H,aliphatic CH_2)
C21	0.84	3224 cm^{-1}(Ar-C-Hstr), 2999 cm^{-1}(aliphatic C –H str), 1664cm^{-1}(C=O str), 1505 cm^{-1}(Ar-C=C str),1259cm^{-1} (C-O-C str)	7.22-7.89(m, 16H, Ar-H), 6.52(s,2H,CH), 4.20(6H,O-CH_3),2.59(8H,aliphaticCH_2).
C22	0.71	3195 cm^{-1}(Ar-C-Hstr), 3083 cm^{-1}(aliphatic C –H str), 1744 cm^{-1}(C=O str), 1511 cm^{-1}(Ar-C=C str), 1305 cm^{-1}(C-N str), 1217cm^{-1} (C-O-C str)	7.39-7.71(m,8H,Ar-H), 6.49(s,1H,CH),4.20(3H,O-CH_3),3.89(4H,O-CH_2),2.38(4H,N-CH_2)
C23	0.65	3192cm^{-1}(Ar-C-Hstr), 3063 cm^{-1}(aliphatic C –H str),1745 cm^{-1}(C=O str), 1515 cm^{-1}(Ar-C=C str), 1306cm^{-1}(C-N str), 1170cm^{-1}(C-O-C str)	7.21-7.89(m,8H,Ar-H), 6.30(s,1H,CH),4.20(3H,O-CH_3),1.98(4H,N-CH_2),1.59(4H,aliphatic CH_2)
C24	0.82	3194 cm^{-1}(Ar-C-Hstr), 3063 cm^{-1}(aliphatic C –H str), 1745 cm^{-1}(C=O str), 1511 cm^{-1}(Ar-C=C str), 1306 cm^{-1}(C-N str), 1216cm^{-1} (C-O-C str)	7.21-7.89(m,8H,Ar-H), 6.30(s,1H,CH), 4.20(3H,O-CH_3), 1.98(4H,N-CH_2), 1.59(6H,aliphatic CH_2)

6. Antimicrobial Activity

All the synthesized compounds have been screened for anti-bacterial against two Gram positive Bacteria-B.subtilius and S.aureus and two Gram negative bacteria- E.coli and P.aerogunisona and for antifungal activity against Aspergillus niger using Serial Dilution Method.

Ciprofloxacin was used as reference standard for antibacterial activity. Ketoconazole was used as reference standard for antifungal activity.

Serial Dilution method is used to determine Minimum Inhibitory Concentration (MIC) of antimicrobial agent to inhibit the microorganisms. This can be achieved by dilution of agents in either agar or broth medium. In the present study, Broth dilution method was used to determine MIC. Nutrient Broth medium was used for antibacterial activity and Sabouraud medium for antifungal activity. All the synthesized compounds were diluted into 2,4,8, 16,32µg/ml and DMSO was used as control.

Table 4: MIC of the synthesized compounds

	MIC (conc. In µg/ml)				
Compounds	*B. Subtilius*	*S.aureus*	*E.coli*	*P. aerogunisona*	*A.niger*
c1	8	8	8	4	4
c2	8	8	4	4	4
c3	32	32	16	32	16
c4	16	16	8	8	16
c5	16	8	8	8	8
c6	32	16	16	16	16
c7	8	8	4	4	4
c8	8	4	4	4	4
c9	32	32	16	16	16
c10	32	16	16	16	8
c11	16	8	8	8	8
c12	16	16	16	8	16
c13	8	4	8	4	4
c14	8	4	4	4	4
c15	32	32	32	16	16
c16	32	16	16	16	16
c17	16	8	8	4	8
c18	32	16	8	16	8
c19	8	4	4	4	4
c20	8	4	4	4	4
c21	32	32	32	32	16
c22	16	16	16	16	8
c23	16	8	8	8	8
c24	8	16	8	16	16
Standard	0.2	0.4	0.4	0.2	0.64

7. Result and Discussion

From the above Results, it is found that compounds c1, c2, c7, c8, c13, c14, c19 & c20 are comparatively more active than all other compounds, for all i.e. fungus, Gram-Positive and Gram-Negative bacteria. The Phthalimide derivatives are found to be more active for Gram-Negative bacteria compare to gram-Positive. For the anti-fungal activity these compounds are found to be more active than anti-bacterial activity.

8. Conclusion and Future Scope

Various Isoindoledione derivatives are synthesized by Mannich Reaction and evaluated for their antimicrobial activity. The screening of synthesized compounds for antimicrobial activity showed that these compounds have appreciable antimicrobial activity. The results provide insights that will aid the optimization of the Isoindoledione derivatives for the better activity and may prove helpful for further lead optimization, virtual screening, molecular docking and molecular dynamics studies.

9. Acknowledgement

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