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SYNTHESIS, ANTIBACTERIAL AND ANTIFUNGAL ACTIVITY OF 2-{1'-ARYL-1'-[4''-(3'''- CHLOROPHENYL) PIPERAZIN-YL]-METHYL}-CYCLOHEXANONE HYDROCHLORIDE

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ABSTRACT

2-{1'-Aryl-1'-[4''-(3'''-chlorophenyl) piperazin-yl]-methyl}-cyclohexanone hydrochloride (4a-4l) have been synthesized. The products have been assayed for their antibacterial and antifungal activity against Gram+ve, Gram-ve bacteria and fungi. All the products were assigned with IR, ^{1}HNMR, Mass Spectra, TLC, and elemental analysis. Some of the products showed moderate activity, compare with known standard drugs.

KEYWORDS: 2-{1'-Aryl-1'-[4''-(3'''-chlorophenyl) piperazin-yl]-methyl}-cyclohexanone drugs.

INTRODUCTION

Piperazine derivatives showed a vital role largely due to the wide ranging of therapeutic activities. Taking into consideration diverse biodynamic activities such as analagesic[1], antibacterial[2], antidiabetic[3], antifungal[4], antiulcer[5,6], antihistaminic[7], anthlminitic[8], anti-inflammatory[9], antimicrobial[10]etc.

The Mannich bases (4a-4l) have been synthesized by the condensation of 4-(3'-chlorophenyl) piperazine hydrochloride, cyclohexanone with aromatic aldehyde in the presence of hydrochloric acid. All the products (4a-4l) were assigned with IR, ^{1}HNMR, Mass Spectra, TLC and Elemental analysis. The physical data recorded in Table no: I. antibacterial and anti-fungal activity recorded in Table no: II and comparable antibacterial and anti-fungal activity

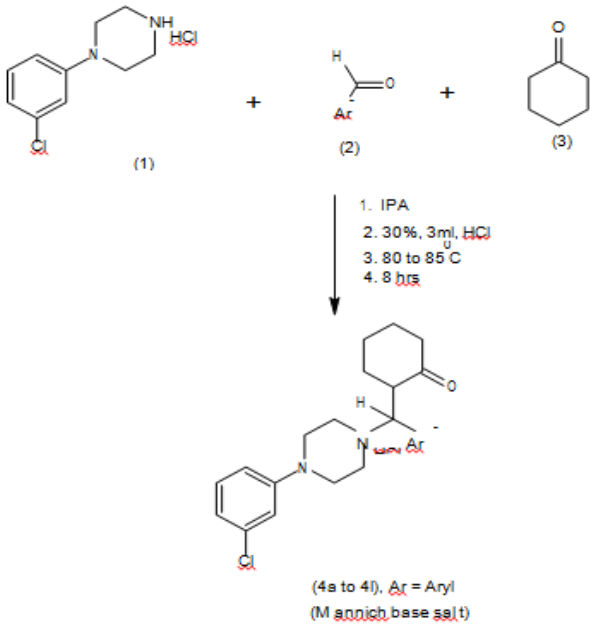
compared with known standard drugs represented in Table no: III.

ANTIBACTERIAL AND ANTIFUNGAL ACTIVITY

All the products (4a-4l) were tested by Cup-plate method[11] against the Gram positive Bacteria Bacillus megaterium; S.aureus, Gram negative bacteria Escherichia coli, S.Taphimarium and for antifungal activity against Aspergillus niger, Anrobacter awamori at a concentration of 50µg/ml, using DMF as a solvent. After 24hrs of incubation at 37°C, the zone of inhibition were measured in mm. The activity was compared with known standard drugs viz. Ampicillin, Chloramphenicol, Norfloxacin, Fluconazole at the same concentration (50µg/ml) which is represented in Table no II.

All the synthesized compounds (4a-4l) showed moderate to good and remarkable activities with known standard drugs at same concentration which is represented in Table no III.

REACTION SCHEME



EXPERIMENTAL SECTION

All the melting points were measured in open glass capillary method and are uncorrected. IR absorption Spectra (in cm^{-1}) were recorded on a SHIMADZU IR-435 spectrophotometer using KBr pellet method, ^{1}HNMR spectra on BRUKER (300mHz) spectrometer using $CDCl_3$ as internal standard (chemical shift in δppm) and Mass spectra on a Jeol-JMSD 300 Mass spectrometer at 70ev. The compounds were routinely checked by TLC method using silica

gel G.

Synthesis of 2-{1'-(4''''-Methoxyphenyl-1'-[4''-(3'''-chlorophenyl) piperazin-yl]-methyl}- cyclohexanone hydrochloriode (4e)

A compounds of 4-(3''-chlorophenyl) piperazine hydrochloride (2.33gm, 0.01m); cyclohexanone (0.98ml, 0.01m); 4-methoxy benzaldehyde (1.36ml, 0.01m); and hydrochloric acid (30%, 3.0ml) were charged in Isopropyl alcohol (10.0ml) solvent. The reaction mixture was refluxed 80-85°C for 8hrs. After the completion of reaction Isopropyl alcohol was distilled out(6.0ml to 7.0ml) and Acetone was charged (10.0ml). Reaction mixture was refluxed for two hrs and cooled to 30-35°C. The reaction mass was filtered and washed with Acetone (5.0ml) and dried. % Yield: 76.00%; M.P.: 203°C (Required: C: 69.82;H:7.03;N:6.79, $C_{24}H_{29}O_2N_2Cl$; Found: C: 69.70;H:7.02;N:6.70%). IR(KBr)(cm^{-1}): 2900 (C-H Str. Asym);2835(C-H Str.

Sym);1421(C-H Str. Def); 3370(C-H Str., aromatic);1149(C-H Str., i.p.def);750(C-H Str., OO.P def); 1303(C-N Str.), 1716 (C=0 str.)); ^{1}HNMR (δ ppm):2.83-2.87 (8H, d,d-CH_2); 3.20-3.41(8H,d,-CH_2); 3.77(3H,S,-OCH_3); 6.71-7.37(4H,m,Ar-H);m/z: 86,97,110,131,177,199,265,310,387,413.

Similarly other Mannich base salts(4a-4l) have been synthesized. The physical data of compounds represented in Table-I and antibacterial and anti-fungal activity of compounds (4a-4l) have been represented in Table-II and comparable antibacterial and anti-fungal activity represented in Table-III.

Table-I: The physical data of compounds (4a-4l).

Compounds	Ar	Molecular formula	M.P. °C	% Yield	%Nitrogen	
					Calculated	Found
4a	C_6H_5-	$C_{23}H_{27}ON_2Cl$	163	88.00	7.32	7.28
4b	2-Cl-C_6H_4-	C23H26ON2Cl2	188	75.22	6.73	6.69
4c	4-Cl-C_6H_4-	C23H26ON2Cl2	189	73.01	6.73	6.65
4d	4-F-C_6H_4-	$C_{23}H_{26}ON_2ClF$	167	70.50	6.99	6.72
4e	4-OCH_3-C_6H_4-	C24H29O2N2Cl	203	76.00	6.79	6.70
4f	2,5-$(OCH_3)_2$-C_6H_3-	C25H31O3N2Cl	189	71.15	6.33	6.31
4g	3,4-$(OCH_3)_2$-C_6H_3-	C25H31O3N2Cl	147	72.30	6.33	6.25
4h	3,4,5-$(OCH_3)_3$-C_6H_2-	C26H33O4N2Cl	183	78.25	5.93	5.88
4i	2-OH-C_6H_4-	C23H27O2N2Cl	194	71.60	7.03	7.01
4j	2-NO_2-C_6H_4-	C23H26O3N3Cl	203	81.00	9.82	9.80
4k	3-NO_2-C_6H_4-	C23H26O3N3Cl	211	85.15	9.82	9.79
4l	4-NO_2-C_6H_4-	C23H26O3N3Cl	224	87.20	9.82	9.75

Table-II

Compounds	Ar.	Antibacterial activity				Antifungal activity	
		Gram +ve bacteria		Gram –ve bacteria			
		B.mega	***S.aureus***	***E.coli***	***S.Taphimarium***	***A. niger***	***A. awamori***
4a	C_6H_5-	12	14	15	14	17	16
4b	2-Cl-C_6H_4-	17	19	20	19	20	19
4c	4-Cl-C_6H_4-	19	17	21	20	21	19
4d	4-F-C_6H_4-	18	20	21	22	24	17
4e	4-OCH_3-C_6H_4-	13	15	19	16	19	20
4f	2,5-$(OCH_3)_2$-C_6H_3-	17	19	15	20	18	21
4g	3,4-$(OCH_3)_2$-C_6H_3-	16	18	20	21	19	17
4h	3,4,5-$(OCH_3)_3$-C_6H_2-	15	17	18	19	19	16
4i	2-OH-C_6H_4-	18	16	17	18	22	17
4j	2-NO_2-C_6H_4-	20	21	19	18	23	21
4k	3-NO_2-C_6H_4-	21	16	17	19	22	20
4l	4-NO_2-C_6H_4-	19	18	18	21	23	18
Note: Zone of inhibition in mm							

Table-III Comparable antibacterial and anti-fungal activity with known standard drugs.

Compounds	Maximum antibacterial and anti-fungal activity					
	B.mega	***S.aureus***	***E.coli***	***S.Taphimariu m***	***A. niger***	***A. awamori***
(4a-4l) (50µg/ml)	4c,4j,4k,4l	4b,4d,4j	4b,4c,4d,4e, 4g,4j	4b,4c,4d,4f,4g ,4h,4k,4l	4b,4c,4d,4 e,4g,4h,4i, 4j,4k,4l	4b,4c,4e,4f4j,4k
Ampicillin 50µg/ml	22	21	20	21	-	-
Chloramphe nicol 50µg/ml	21	22	23	20	-	-
Norfloxacin 50µg/ml	23	20	22	21	-	-
Fluconazole 50µg/ml	-	-	-	-	21	21

CONCLUSION

The compounds 2-{1'-Aryl-1'[4''-(3'''-chlorophenyl) piperazin-yl)]-methyl}-cyclohexanone hydrochloride (4a-4l) have been synthesized. Some of the compounds showed good remarkable antibacterial and antifungal activity with compared with known standard drugs e.g: Ampicillin, Chloramphenicol, Norfloxacin and Fluconazole.

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