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SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF 2-{1'-ARYL-1'-[4''-(2'''-HYDROXY ETHOXY ETHYL) PIPERAZIN-YL]-METHYL}-CYCLOHEXANONE HYDROCHLORIDE

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ABSTRACT:

2-{1'-Aryl-1'-[4''-(2''-hydroxyethoxy ethyl)piperazin-yl]-methyl}-cyclohexanone hydrochloride (4a-4l) have been synthesized. The products have been assayed for their antimicrobial 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.

KEYWORD: Gram+ve, Gram-ve bacteria and fungi.

INTRODUCTION

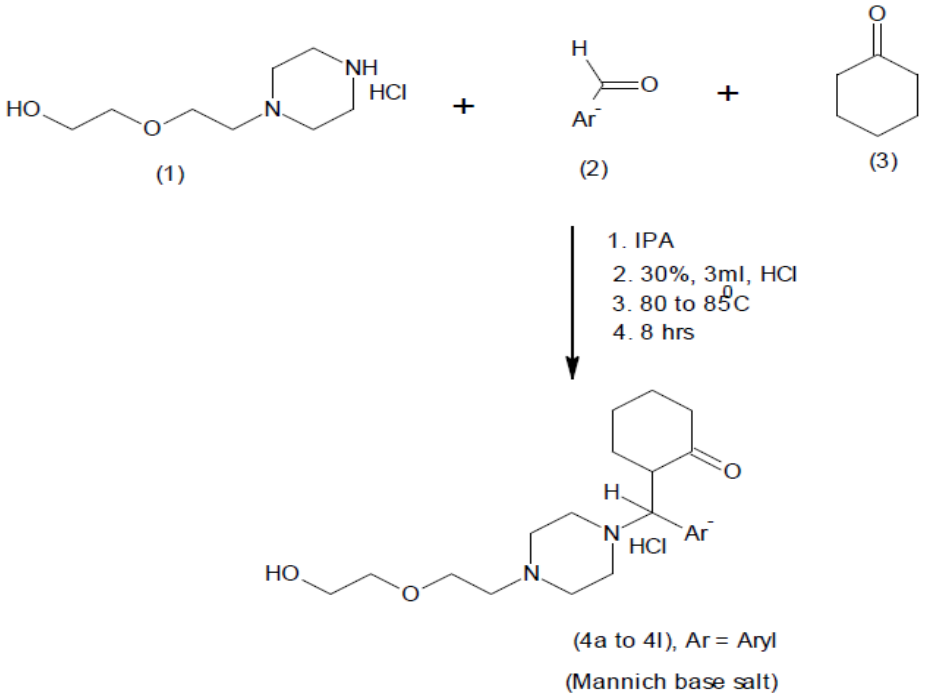
Piperazine derivatives showed a vital role largely due to the wide ranging biological activities. Taking into consideration diverse biodynamic activities such as analagesic[1], antibacterial[2], antidiabetic[3], antifungal[4], antiulcer[5,6], antihistaminic[7], anthlminitic[8], anti-inflammatory[9], antimicrobial[10] etc. In this fact to interesting biological activities, it appeared to interest to synthesized some new Mannich bases (4a-4l) have been synthesized by the condensation of 4-(2'-hydroxyethoxy ethyl) 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. Antimicrobial activity recorded in Table no: II and comparable antimicrobial compared with known standard drugs represented in Table no: III.

ANTIMICROBIAL ACTIVITY

All the products (4a-4l) were tested for their antimicrobial activity 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''-(2'''-Hydroxyethoxy ethyl) piperazin-yl]- methyl}-cyclohexanone hydrochloriode (4e)

A compound of 4-(2''-Hydroxyethoxy ethyl) piperazine hydrochloride (2.05gm, 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 8hours. After the completion of reaction Isopropyl alcohol was distilled (6.0ml to 7.0ml) and Acetone was charged (10.0ml). Reaction mixture was refluxed for two hours and cooled to 30- 35°C. The reaction mass was filtered and washed with Acetone (5.0ml) and dried. % Yield: 82.15%; M.P.: 185°C (Required: C:61.90; H:8.21; N:6.57, $C_{22}H_{35}O_4N_2Cl$; Found: C: 61.70;H:8.11;N:6.42%). IR(KBr)(cm^{-1}): 2943 (C-H Str. Asym); 2831(C-H Str. Sym); 1421(C-H Str. Def); 1701 (C=O Str), 3373(C-H Str., aromatic);1148(C-H Str., i.p.deft);766(C-H Str., o.o.p def); 1307(C-N Str.); 1HNMR (δ ppm):2.64-6.82 (8H, d,d-CH_2);3.18-3.50 (8H,d,-CH_2);3.87(3H, S.-OCH_3);6.85-7.06(4H,m, Ar-H); m/z: 85,96,108,115,130,176,194,233,288,330,390, 427.

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

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

Compound	Ar	Molecular formula	M.P. °C	% Yield	%Nitrogen	
					Calculated	Found
4a	C_6H_5-	C21H32O3N2Cl	163	79.80	7.08	7.01
4b	2-ClC_6H_4-	C21H31O3N2Cl2	178	72.00	6.50	6.26
4c	4-ClC_6H_4-	C21H31O3N2Cl2	202	71.50	6.50	6.31
4d	4-FC_6H_4-	C21H31O3N2F	210	78.69	6.77	6.52
4e	4-OCH_3 C_6H_4-	C22H35O4N2Cl	185	82.15	6.57	6.42
4f	2,5-(OCH_3) C_6H_3-	C23H37O5N2Cl	229	79.03	6.13	6.09
4g	3,4-(OCH_3) C_6H_3-	C23H37O5N2Cl	285	80.00	6.13	6.02
4h	3,4,5-(OCH_3) C_6H_2-	C24H39O5N2Cl	221	83.83	5.95	5.84
4i	2-OH-C_6H_4-	C21H31O4N2Cl	132	85.07	6.80	6.71
4j	2-$NO_2C_6H_4$-	C21H31O5N3Cl	199	90.11	9.53	9.47
4k	3-$NO_2C_6H_4$-	C21H31O5N3Cl	209	91.45	9.53	9.43
4l	4-$NO_2C_6H_4$-	C21H31O5N3Cl	239	93.34	9.53	9.40

Table-II.

Compound	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-	18	20	20	17	17	18
4b	2-ClC_6H_4-	15	17	23	21	20	20
4c	4-ClC_6H_4-	19	22	21	22	20	17
4d	4-FC_6H_4-	15	27	15	17	16	16
4e	4-OCH_3 C_6H_4-	17	19	17	20	19	19
4f	2,5-(OCH_3) C_6H_3-	17	18	14	18	18	15
4g	3,4-($OCH_{3)}$ C_6H_3-	19	20	17	20	20	18
4h	3,4,5-($OCH_{3)}$ C_6H_2-	18	19	20	21	22	20
4i	2-OH-C_6H_4-	13	14	12	15	13	15
4j	2-$NO_2C_6H_4$-	12	15	11	17	12	16
4k	3-$NO_2C_6H_4$-	14	17	13	13	15	14
4l	4-$NO_2C_6H_4$-	16	20	22	19	19	18
Note: Zone of inhibition in mm							

Table III: Comparable antimicrobial activity with known standard drugs.

Compound	Maximum antimicrobial activity					
	B.mega	***S.aureus***	***E.coli***	***S.Taphimarium***	***A. niger***	***A. awamori***
(4a-4l) (50µg/ml)	4c,4g	4a,4c,4d, 4g,4l	4a,4b,4c,4h, 4l	4b,4c,4e,4g,4h	4b,4c,4e,4g,4h,4l	4b,4e,4h
Ampicillin 50µg/ml	22	21	20	21	-	-
Chloramphenicol 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''-(2'''-Hydroxy ethoxy ethyl) piperazin-yl)]-methyl}-cyclohexanone hydrochloride (4a-4l) have been synthesized. Some of the compounds 4b,4c,4e,4g,4h,4l showed good remarkable antibacterial and antifungal activity with compared with known standard drugs e.g: Ampicillin, Chloramphenicol, Norfloxacin and Fluconazole.

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