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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, 1HNMR, Mass Spectra, TLC, and elemental analysis. Some of the products showed moderate activity, compare with known standard drugs.

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

INTRODUCTION

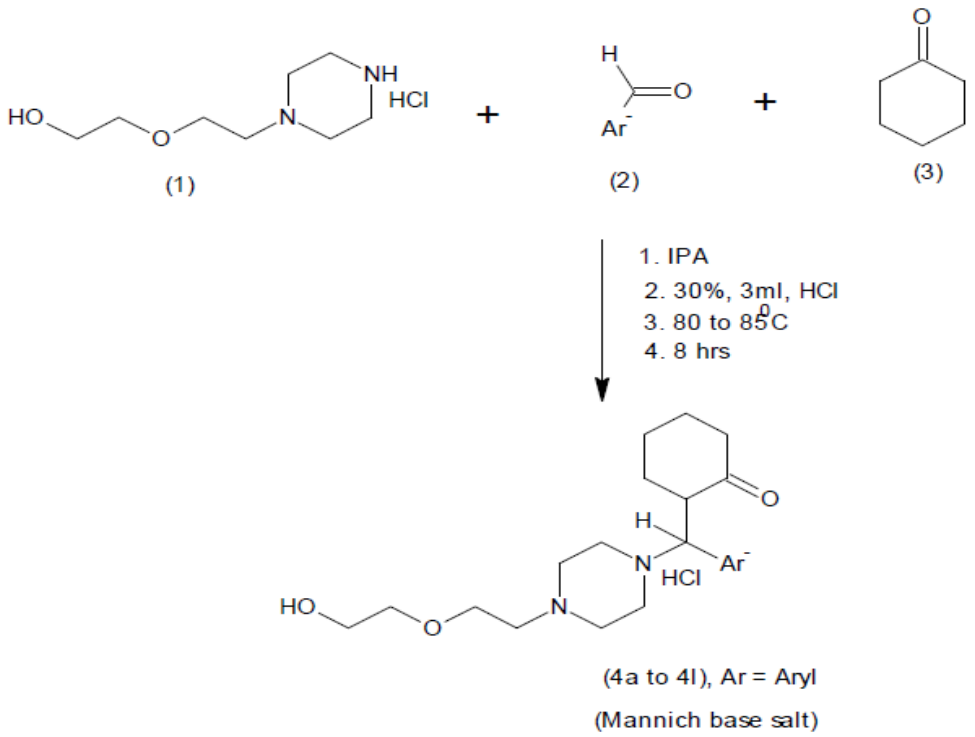
Piperazine derivatives showed a vital role largely due to the wide ranging biological activities. Taking into consideration diverse biodynamic activities such as analagesic1, antibacterial2, antidiabetic3, antifungal4, antialcer5, 6, antihistaminic7, anthlminitic8, antiinflammatory9, antimicrobial10etc. 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, 1HNMR, 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 method11 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, 1HNMR spectra on BRUKER (300mHz) spectrometer using CDCl3 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-CH2);3.18-3.50 (8H,d,-CH2);3.87(3H, S.-OCH3);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	C6H5-	$C_{21}H_{32}O_3N_2Cl$	163	79.80	7.08	7.01
4b	2-ClC6H4-	$C_{21}H_{31}O_3N_2C_{l2}$	178	72.00	6.50	6.26
4c	4-ClC6H4-	$C_{21}H_{31}O_3N_2C_{l2}$	202	71.50	6.50	6.31
4d	4-FC6H4-	$C_{21}H_{31}O_3N_2F$	210	78.69	6.77	6.52
4e	4-OCH3 C6H4-	$C_{22}H_{35}O_4N_2Cl$	185	82.15	6.57	6.42
4f	2,5-(OCH3) C6H3-	$C_{23}H_{37}O_5N_2Cl$	229	79.03	6.13	6.09
4g	3,4-(OCH3) C6H3-	$C_{23}H_{37}O_5N_2Cl$	285	80.00	6.13	6.02
4h	3,4,5-(OCH3) C6H2-	$C_{24}H_{39}O_5N_2Cl$	221	83.83	5.95	5.84
4i	2-OH-C6H4-	$C_{21}H_{31}O_4N_2Cl$	132	85.07	6.80	6.71
4j	2-NO2C6H4-	$C_{21}H_{31}O_5N_3Cl$	199	90.11	9.53	9.47
4k	3-NO2C6H4-	$C_{21}H_{31}O_5N_3Cl$	209	91.45	9.53	9.43
4l	4-NO2C6H4-	$C_{21}H_{31}O_5N_3Cl$	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	-	-
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''-(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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