MULTIDISCIPLINARY RESEARCH

Prof. Rajani Shikhare

MULTIDISCIPLINARY RESEARCH - Prof. Rajani Shikhare

Publisher	:	Anand Prakashan, Jaisingpura, Aurangabad.(M.S) Cell : 9970148704 Email: anandprakashan7@gmail.com
©	:	Author
Typeset At	:	Anand Computer Aurangabad.
Edition	:	December 2020
ISBN No	:	978-93-90004-07-2
Cover Design	:	Aura Design Mumbai.
Printed At	:	Om Offset Aurangabad.
Main Distributor	:	Anand Book Depot Jaisingpura, Aurangabad - 431004
Price	:	₹ 120 /-

18

Synthesis and Antimicrobial Screening of Novel Pyrazole Substituted Benzothiazepines

Bhagat S. S.[1], Rupnar B. D.[2] and Shirsat A. J.[3]

Department of Chemistry
R. B. Attal Arts, Science and Commerce
College, Georai. Dist Beed

Abstract:

The title compounds 1, 5-benzothiazepines benzothiazepine wereprepared by the reaction of Chalcones with amino thiophenol by cyclization under reflux condition. The synthesized compounds were characterized by Spectral analysis like IR, ^{1}HNMR and Mass Spectra.

Keywords: benzothiazepine, pyrazole

Introduction:

The [1, 5]-benzothiazepine framework is particularlyflexible and sorts in a countless number of famous drugs. Presently [1, 5]-benzothiazepin-2-ones are useful for coronary vasodilators, as calcium antagonists and as antidepressants. Atta-ur-Rahman and co-workers testified a series of 2, 4-diaryl-2, 3, 4, 5-tetrahydro- and 2, 4-diaryl-2, 3-dihydro-1, 5-benzothiazepines produced from chalcones. Several compounds showed important cholinesterase inhibiting activities. Amongst dihydro-1, 5-benzothiazepines revealednoteworthy radical-scavenging activities; and tetrahydro-1, 5-benzothiazepines were established to be inhibitors of AChE and BChE. Few compounds inhibited urease and inhibitors of α-glucosidase[1].

Subbanwad and co-workers studied benzothiazepines prepared from chalcones. The compounds were screened for antimicrobial activity. Good antimicrobial activity was shown by compounds having a chloro or methyl on the aromatic ring[2].

1,5-Benzothiazepines are a kind of compounds which have important biological activities [3,4]. Chakraborti A. K. and co-workers studied a new and efficient heterogeneous catalyst for thia-Michael addition to chalcones i.e. α,β-unsaturated carbonyl compounds under solvent-free conditions. The methodology is useful as it finds application for one-pot synthesis of 2, 3-dihydro-1, 5-benzothiazepines[5]. Here, I would like to report the newly synthesized benzothiazepine derivatives.

Experimental :

General procedure for the synthesis of 4-chloro-2-((E)-2-(3-(2, 4-difluorophenyl)-1-(4-fluorophenyl)-1*H*-pyrazol-4-yl)-2, 3-dihydrobenzo[b] [1, 4] thiazepin-4-yl) phenol (2c):

Compound **1c** (0.01 mol) and 2-aminothiophenol (0.01 mol) were taken in 100ml RBF with 15 ml ethanol. The contents were heated under reflux for 4 hr. Then to the reaction mixture, 2ml glacial acetic acid was added and heating was continued for further 4 hr. After completion of heating, the contents were cooled to room temperature and poured on to crushed ice. The solid thus obtained was separated by filtration. The resulting product was crystallized from ethanol.The compounds **2(a-h)**were prepared by following the general procedure. Physical data are recorded in **Table 1**. Their structures have been confirmed by IR, ^{1}HNMR and Mass spectra

IR (2c) (cm^{-1}): 980(C-Cl), 1210 (C-O), 1512 (Ar C=C), 1585(C=N), 3418(Ar-OH).

^{1}H NMR (2c) ($CDCl_3$)δ ppm: 3.0424-3.1038 (dd, 1H,-CH_2-,*J* =11.94 Hz & 12.7 Hz), 3.5301-3.5728 (dd, 1H,-CH_2-,*J* =5.0 Hz & 8.46 Hz),5.4252-5.4641(t,1H,-CH-,*J*=4.9Hz & 6.74 Hz),6.9641-6.9863(d, 1H, Ar-H,*J*=8.82 Hz), 7.1600-7.1881 (d, 1H, Ar-H, *J* =3.62 Hz),7.2105-7.3520(m, 4H, Ar-H), 7.4251-7.4642 (m, 2H, Ar-H), 7.5188-7.5971(m,2H,Ar-H),7.7112-7.7215(m, 3H, Ar-H),7.9580(s, 1H, Ar-H),8.2231 (s, 1H, Pyrazole-H),14.3448 (s, 1H, Ar-OH).

ES-MS (2c) (m/z): 561.1(M+1), 563.1(M+3).

Scheme1 :

Scheme1- Synthesis of various substituted 2-((*E*)-2-(3-(2, 4-difluorophenyl)-1-(4-fluorophenyl)-1*H*-pyrazol-4-yl)-2,3-dihydrobenzo[*b*][1,4]thiazepin-4-yl)phenol

Table 1: Physical data of compounds (2a-h)

Comp.	R_1	R_2	R_3	M.P. (^{0}C)	Yield (%)
2a	H	H	H	70-72	69
2b	H	H	CH_3	80-82	82
2c	H	H	Cl	240-242	57
2d	Cl	H	Cl	208-210	74
2e	H	H	F	95-97	67
2f	H	CH_3	Cl	224-226	78
2g	H	H	Br	220-222	72
2h	CH_3	H	CH_3	90-92	80

Results and Discussion :

Antimicrobial activity: Compounds **2(a-h)** were screened for their in vitro antimicrobial activity against *Escherichia coli (ATCC 25922), Pseudomonas aeruginosa (ATCC 27853), Staphylococcus aureus (ATCC 25923)* using Ciprofloxacin as a reference standard drug by paper disc diffusion method. Antifungal activity was evaluatedagainst *Candida sp.* using Fluconazole as standard drug. All the tests were evaluated at 100 μg/ml concentration. The culture media was Muller Hinton agar. The zone of inhibition was measured in mm after 24 hr of incubation at 37^{0}C. Microbial data for corresponding compounds is summarized in **Table 2.**

Table 2: Disc Diffusion Method

Sr. No.	Compound No.	Inhibition Zone Diameter (mm)					
		Candida sp.	*S. aureus*	*S.albus*	*Klebsiella pnuemoniae*	*E. coli*	*Pseudomonas sp.*
1.	2a	5	-	7	-	6	-
2.	2b	-	10	-	-	8	-
3.	2c	7	10	-	-	12	-
4.	2d	-	-	-	13	8	-
5.	2e	-	10	9	11	11	-
6.	2f	-	9	8	13	11	-
7.	2g	11	14	-	14	10	-
8.	2h	12	13	-	14	10	-
9.	Control	8	3	3	6	8	10
9.	Ciprofloxacin	---	20	22	22	21	23
10.	Fluconazole	23	---	---	---	---	---

Conclusion :

The novel synthesized compounds were tested against Gram positive and Gram negative bacterialstrains. As well as they were tested against Candida species. From the results it is concluded that, compounds 2g-2h exhibited moderate anti-microbial activity. The other compounds have shown goodactivity compared to standard drug.

Acknowledgements :

The authors are thankful to Principal Prof. R.V. Shikhare for providing laboratory facilities. The authors are grateful to Director, SAIF/CIL, Panjab University, Chandigarh for providing spectral data. The authors are thankful to Uday Khedkar, Director, BAC-TEST Laboratory, Nashik for antimicrobial analysis.

References:

1. Ansari, F. L.; Umbreen, S.; Hussain, L.; Makhmoor, T.; Nawaz, S. A.; Lodhi, M. A.; Khan, S.N.; Shaheen, F.; Choudhary, M. I.; Atta-ur-Rahman. *Chemistry & Biodiver.* **2005**, *2(4),* 487.
2. Subbanwad, G. R.; Baseer, M. A.; Vibhute, Y. B. *Ind. J. Pharm. Sci.* **2002**, *64(3),* 264.
3. Jin, S.; Wang, H. Z.; Huang, B. H.; Chun, J.; Mi, B. Y. *Chinese J. Synth. Chem.* **1997**, supplement: 564.
4. Lan, R. X .; Jin, S.; Li, Z. M. *Chinese Chem. Lett.* **1992***,* 3*,* 179–180.
5. Sharma, G.; Kumar, R. J.; Chakraborti, A. K. *Tetrahedron Lett.***2008**, *49(27),* 4272.