International Journal of Universal Print
ISSN: 2454-7263 ID: ACTRA 2018 066 Published Mar. 2018
Volume No. 04, Issue No.07, Copyright © Universal Print
Web: www.universalprint.org , Email: ijup@universalprint.org
Title Key: SYNTHESIS, CHARACTERIZATION AND ANTIMICROBAL …

SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL ANALYSIS OF VARIOUS SUBSTITUTED 2-(5-(3-(5-BROMOTHIOPHEN-2-YL)-1-PHENYL-1*H*-PYRAZOL-4-YL)-1*H*-PYRAZOL-3-YL) PHENOLS

Sunil S. Bhagat[a*], Amol J. Shirsat[a], Balaji D. Rupnar[a], Charansingh H. Gill[b]
[a]*Department of Chemistry, R. B. Attal Arts, Science and Commerce College, Georai, Dist- Beed-431127, Maharashtra, India*
[b]*Department of Chemistry, Dr. Babasaheb Ambedkar Marathwada University, Aurangabad-431004, Maharashtra, India*
E-mail-sunilbhagat2010@gmail.com

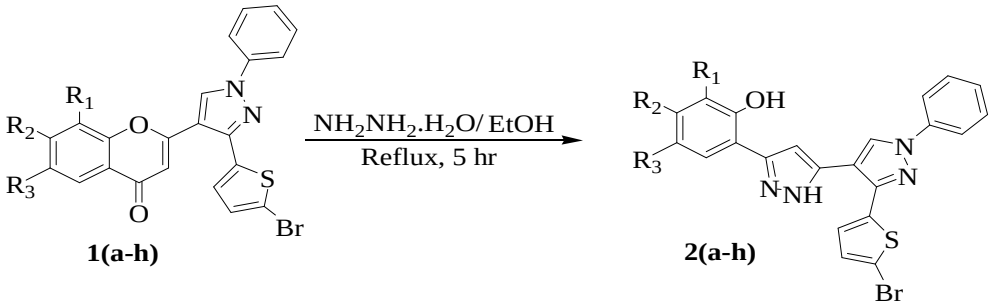
Abstract: The title compounds various substituted2-(5-(3-(5-bromothiophen-2-yl)-1-phenyl-1*H*-pyrazol-4-yl)-1*H*-pyrazol-3-yl) phenols **2(a-h)** have been synthesized from chromones **1(a-h)** by refluxing with potassium hydroxide. The structures of all newly synthesized compounds have been confirmed by IR, ^{1}H NMR and Mass spectral data. The synthesized compounds have been screened for their antimicrobial activity. Some of the compounds show moderate antimicrobial activity as compared to the reference drugs Ciprofloxacin and Fluconazole.
Keywords: Chromones, Antimicrobial activity

Introduction

Pyrazole is characterized by a 5-membered heterocyclic ring structure made up of three carbon atoms and two nitrogen atoms in adjacent positions.1-pyrazolyl-alanine,the first natural pyrazole, was obtained from watermelon seeds in 1959.It has pharmacological effects on humans, they are rare in nature. They have application in pharmaceutical industry and agrochemicals as active pharmaceuticals and herbicides. The current achievement of pyrazole COX-2 inhibitor has more emphasized the prominence of these heterocyclic rings in medicinal chemistry. A logical examination of this class of heterocyclic lead has shown that pyrazole containing pharmacoactive agents play vital role in medicinal chemistry**.** The occurrence of pyrazole nuclei in naturally active molecules has encouraged the need for well-designed and effective methods to make these heterocyclic lead [1].

Nitrogen-linked heterocyclic compounds gained substantial consideration in modern times because of their pesticidal and medicinal significance [2-4]. Pyrazole derivatives are important in pesticide industry and extensively used because of their antiviral[5], antitumor[6], anti-inflammatory[7], antibacterial[8], herbicidal[9], insecticidal[10], fungicidal activities[11], Angiotensin-I-converting enzymes inhibitory[12], molluscidal [13],and ulcerogenic activity[14].

International Journal of Universal Print
ISSN: 2454-7263 ID: ACTRA 2018 066 Published Mar. 2018
Volume No. 04, Issue No.07, Copyright © Universal Print
Web: www.universalprint.org , Email: ijup@universalprint.org
Title Key: SYNTHESIS, CHARACTERIZATION AND ANTIMICROBAL …



1(a-h) **2(a-h)**

Scheme 1

Experimental Section

General Procedure for the synthesis of2-(5-(3-(5-bromothiophen-2-yl)-1-phenyl-1*H*-pyrazol-4-yl)-1*H*-pyrazol-3-yl)-4-methylphenol (2b): Compound **1b** (0.003 mol) was taken in 100 ml RBF with 15 ml ethanol. To this reaction mixture 1 ml hydrazine hydrate and 0.5 gm KOH were added and the contents were heated under reflux for five hour. After completion of reaction (monitored by TLC), the contents were cooled to room temperature and poured over crushed ice and acidified with HCl. The solid thus obtained was separated by filtration and crystallized from ethanol. The compounds **2 (a-h)** were prepared by following the above procedure. The physical data of the compounds **2 (a-h)** were recorded in **Table 1**. Their structures have been confirmed by ^{1}HNMR, Mass and IR spectra.

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

Comp.	R_1	R_2	R_3	M.P. (^{o}C)	Yield (%)
2a	H	H	H	168-170	78
2b	H	H	CH_3	184-186	65
2c	H	H	Cl	136-138	78
2d	Cl	H	Cl	248-250	71
20	H	H	F	168-170	68
20	H	CH_3	Cl	238-240	72
20	H	H	Br	230-232	66
20	CH_3	H	CH_3	208-210	70

Selected spectral data of some representative compounds 2-(5-(3-(5-bromothiophen-2-yl)-1-phenyl-1*H*-pyrazol-4-yl)-4,5-dihydro-1*H*-pyrazol-3-yl)-4-chloro-5-methylphenol (2b):IR (cm^{-1}):1054(Ar-Br), 1264(C-O),1534(C=N),1650(Ar C=C), 2835(Ar-CH_3),3263(N-H),3438(O-H).**^{1}H NMR**(DMSO)δ ppm: 2.300 (s, 3H, CH_3), 6.8251(s,1H,Ar-

International Journal of Universal Print
ISSN: 2454-7263 ID: ACTRA 2018 066 Published Mar. 2018
Volume No. 04, Issue No.07, Copyright © Universal Print
Web: www.universalprint.org , Email: ijup@universalprint.org
Title Key: SYNTHESIS, CHARACTERIZATION AND ANTIMICROBAL …

H)H), 6.8510 (s, 1H, Ar-H), 6.9621-6.9819(m, 1H, Ar-H), 7.0534-7.1103 (m, 1H, Ar-H), 7.3255-7.4335(m, 4H, Ar-H),7.4952-7.5143(d, 1H, Ar-H,*J*=7.64 Hz) ,7.5143-7.5333(d, 1H, Ar-H, *J*=7.6 Hz),7.8733-7.8442(dd, 1H, Ar-H, *J*= 4.48 & 4.12 Hz), 7.9745(s,1H, Ar-H), 8.6148(s, 1H,Pyrazole-H),10.7410 (s, 1H,N-H),13.3261 (s, 1H, Ar-OH).**ES-MS** (m/z): 475(M-1), 477(M+2).

Results and Discussion

The pyrazole derivatives were synthesized successfully in moderate to good yields. The newly synthesized compounds were identified on the basis of melting point range, IR, ^{1}H NMR, Mass spectral analysis. All the newly synthesized derivatives were screened for antimicrobial activity using disc diffusion method.

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), Staphylococcus albus, Klebsiella pnuemoniae* using Ciprofloxacin as a reference standard drug by paper disc diffusion method. Antifungal activity was evaluated against *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^{o}C. DMSO is used as control.

Microbial data for corresponding compounds is summarized in **Table 2.**

Table 2 In-*vitro* antimicrobial activity of various substituted 2-(5-(3-(5-bromothiophen-2-yl)-1-phenyl-1*H*-pyrazol-4-yl)-1*H*-pyrazol-3-yl) phenols **2(a-h)**.

Sr. No.	Compound No.	**Inhibition Zone Diameter (mm)**					
		Candida sp.	*S. aureus*	*S.albus*	*Klebsiella pnuemoniae*	*E. coli*	*Pseudo monas sp.*
1.	2a	3.9	3.9	-	-	-	5
2.	2b	4	8	6	-	8	3
3.	2c	7	9	12	10.8	9	-
4.	2d	6	4	7	10.2	5	4
5.	2e	9	-	10	1.9	13	12
6.	2f	7	-	7	2	11	10
7.	2g	8	-	9	5	6	8
8.	2h	4	-	6	5	5	7
9.	Control	8	3	3	4	6	10
10.	Ciprofloxacin	---	20	22	22	21	23
11.	Fluconazole	23	---	---	---	---	---

International Journal of Universal Print
ISSN: 2454-7263 ID: ACTRA 2018 066 Published Mar. 2018
Volume No. 04, Issue No.07, Copyright © Universal Print
Web: www.universalprint.org , Email: ijup@universalprint.org
Title Key: SYNTHESIS, CHARACTERIZATION AND ANTIMICROBAL …

Acknowledgements
The authors are thankful to The Head, Department of Chemistry, Dr. Babasaheb Ambedkar Marathwada University, Aurangabad for providing laboratory facilities and Uday Khedkar, Director, BAC-TEST Laboratory, Nashik for antimicrobial analysis. One of the authors (**SSB**) is thankful to Principal Dr. R. V. Shikhare for constant encouragement.

References

[1] Eicher, T.; Hauptmann, S.The Chemistry of Heterocycles: Structure, Reactions, Syntheses, and Applications, Edition IInd, 2003, Wiley-VCH, ISBN 3527307206.
[2] Liu, X.H.; Chen, P.Q.; Wang, B.L.; Li, Y.H.; Wang, S.H.; Li, Z.M. Bioorg. Med. Chem. Lett.(2007), 17, 3784.
[3] Liu, X.H.; Zhang, C.Y.; Guo, W.C.; Li, Y.H.; Chen, P.Q.; Wang, T; Dong, W.L.; Sun, H.W.; Li, Z.M. J.Enzym.Inhib.Med. Chem. (2009), 73, 320.
[4] Liu, X.H.; Shi, Y.X.; Ma, Y.; Zhang, C.Y.; Dong, W.L.; Li, P.; Wang, B.L.; Li, B.J.; Li, Z.M. Eur. J. Med. Chem. (2009), 44, 2782.
[5] (a) Sayed, H.H.; Ali, M.A. Phosphorus Sulfur Silicon Relat Elem. (2008), 183, 156;(b) Rashad, A. E.; Hegab, M. I.; Abdel-Megeid, R. E.; Micky, J. A.; Abdel-Megeid, F. M. E. Bioorg. Med.Chem. (2008), 16, 7102 ;(c) Park, H.J.; Lee, K.;Park, S.J.;Ahn, B.; Lee, J.C.; Cho, H.; Lee, K.I. Bioorg Med Chem Lett.(2005), 15, 3307 ;(d).Peng-Cheng, L.; Zhu, H.; Li, H.; Sun, J.; Zhou, Y.Bioorg.Med.Chem. (2010), 18, 4606 ;(e) Barnes, B. J.; Izydore, R. A.; Hall, I. H. Anticancer Res., (2001), 21(4A), 2313; (f) Baraldi, P. G.; Balboni, G.; Pavani, M. G.; Spalluto, G.; Tabrizi, M. A.; Clercq, E. D. J. Med. Chem.(2001), 44(16), 2536.
[6] Baraldi, P. G.; Pavani, M. G.; Nunez, M. C.; Brigidi, P.; Vitali, B.; Gambari, R., Bioorg. Med. Chem., (2002), 10(2), 449.
[7] Burguete, A.; Pontiki, E.; Hadjipavlou-Litina, D.; Villar ,R.; Vicente, E.; Solano,B.;Ancizu, S.; Perez-Silanes, S.;Aldana, I.; Monge, A. Bioorg Med Chem Lett.(2007), 17, 6439.
[8] (a)Farghaly, A.A.; Vanelle, P.; El-Kashef, H.S. Heterocycl Comm. (2005), 11,255 ;(b) Sridhar, R.; Perumal ,P. J.; Etti, S.; Shanmugam, G.; Ponnuswamy, M. N.; Prabavathy, V. R.; Mathivanan, N.Bioorg. Med. Chem. Lett. (2004), 14, 6035.
[9] He, F.Q.; Liu, X.H.; Wang, B.L.; Li, Z.M. Heteroatom Chem. (2008), 19, 21.
[10] Jiang, L.; Wang, L.Z.; Wang, L.Y.; Xie, X.Y. HechengHuaxue.(2007), 15, 576.
[11] Yang, X.D.; Yu, Y.Y. Struct Chem (.2008), 19, 693.[12] Bonesi, M.; Loizzo, M. R.; Statti, G. A.; Michel, S.; Tillequin, F.; Menichini. Bioorg. Med. Chem. Lett.(2010), 20, 1990.
[13] Nawwar, G. A.; Swellem, R. H.; Ibrahim, A. M. Arch. Pharm., (1994), 17(2), 66.
[14] Ochi, T.; Sugiyama, A. Y.; Ohkubo, Y.; Sakane, K.; Tanaka, H. J. Pharmacol.(2001), 85(2), 175.