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Organic Chemistry

Elixir Org. Chem. 146 (2020) 54755-54757

ISSN: 2229-712X

Synthesis and Biological Evaluation of Novel Fused Heterocyclic Derivatives

C. Patil, S.Gulati and H.Patel

Department of Chemistry, Rabindranath Tagore University, Bhopal(M.P.), India

ARTICLE INFO

Article history:

Received: 20 July 2020;

Received in revised form:

25 August 2020;

Accepted: 5 September 2020;

Keywords

3-Methyl-1-phenyl- 1H-pyrazol -5-amine,

3-(5-Arylfuran-2-yl)-1-arylprop-2-en-1-one,

Antimicrobial Activity and Spectral studies

ABSTRACT

The reaction of 3-Methyl-1-phenyl- 1H-pyrazol -5-amine(1) with 3-(5-Arylfuran-2-yl)-1-arylprop-2-en-1-one(2a-l), formed a novel heterocyclic compounds, 6-(5-Arylfuran-2-yl)-3-methyl-1-phenyl-4-(4-substituedphenyl)-1H-pyrazolo[3,4-b]pyridine 3(a-l). The structures of all the compounds series (3a-l) were characterized analytically. The compounds were also monitored for anti microbial activity.

Introduction

In recent years number of research work were carried out on pyrazole moiety containing heterocyclic compounds because of their various biological activities such as anti-inflammatory, antimicrobial, analgesic, antifungal, antitumor and anxiolytic activities[1-6].Pyridines were reported with their anticancer, antiparasitic, antibacterial, antifungal agents and antifolate activity[8-12]. Hence, pyrazole and pyridine containing compounds into one molecule may have good medicinal property. Thus it was thought to explore this type of fuse molecules. The present communication deals with the synthetic approach shown in scheme-1.

Experimental

3-Methyl-1-phenyl- 1H-pyrazol -5-amine(1) with 3-(5-Aryl furan-2-yl)-1-arylprop-2-en-1-one2(a-l) were synthesis by reported method[13-14].All other reagents were used laboratory grade.

The IR spectra of all compounds were taken in KBr pellets on a Nicolet 400D spectrometer. Proton NMR spectra were recorded on a Bruker (400 MHz) spectrometer. Deuterated DMSO was used as a solvent. LC-MS of selected samples taken on LC-MSD-Trap-SL_01046. All the compounds were checked for their purity by TLC. The characterization data of all these compounds are given in Table.1.

The antibacterial activities of the series of compounds (3a-l) were studied against gram +Ve and –Ve bacteria shown in Table-2. The activity was measured at a conc, 50µg/ml by agar-cup plate method[15]. The %age inhibition of growth of bacteria by the compounds is shown in Table-2.

The antifungal activity of both the series of compounds (3a-l) were measured at 1000ppm concentration in vitro plant pathogen shown in Table-3 have been selected for study[16].

Synthesis of 6-(5-Arylfuran-2-yl)-3-methyl-1-phenyl -4-(4-substituedphenyl)-1H-pyrazolo[3,4-b] pyridine 3(a-l)

6-(5-Arylfuran-2-yl)-3-methyl-1-phenyl-4-(4-substituted phenyl) -1H-pyrazolo[3,4-b]pyridine 3(a-l) were prepared by conduction of 3-Methyl-1-phenyl-1H-pyrazol-5-amine (1) and 3-(5-arylfuran-2-yl)-1-arylprop-2-en-1-one2(a-l) in Ethanol at 90 °C with good yield. The reaction exists through a sequence of Michael addition, cyclization, dehydration and aromatization reactions. The solid product which precipitated was collected by filtration, washed with solid product with water, dried and crystallized from Ethyl alcohol. The details are given in Table-1.

Table 1. Physical and Analytical Data of the Compounds Synthesized (3a-l).

Comp. No.	Molecular Formula	M.P.* ˚C	Elemental Analysis		
			C%	H%	N%
			Calcd. (Found)	Calcd. (Found)	Calcd. (Found)
3a	$C_{29}H_{21}N_3O$ (427)	178 -179	81.48 (81.4)	4.95 (4.9)	9.83 (9.8)
3b	$C_{29}H_{20}N_3OCl$ (462)	166 -167	75.40 (75.3)	4.36 (4.3)	9.10 (9.0)
3c	$C_{29}H_{20}N_4O_3$ (472)	182 -183	73.72 (73.7)	4.27 (4.2)	11.86 (11.8)
3d	$C_{29}H_{20}N_3OBr$ (505)	169 -171	68.78 (68.7)	3.98 (3.9)	8.30 (8.2)
3e	$C_{29}H_{20}N_3OBr$ (505)	187 -188	68.78 (68.7)	3.98 (3.9)	8.30 (8.2)
3f	$C_{29}H_{19}N_3OClBr$ (541)	175 -176	64.40 (64.3)	3.54 (3.5)	7.77 (7.7)
3g	$C_{29}H_{19}N_4O_3Br$ (551)	186 -187	63.17 (63.1)	3.47 (3.4)	10.16 (10.1)
3h	$C_{29}H_{19}N_3OBr_2$ (585)	172 -173	59.51 (59.5)	3.27 (3.2)	7.18 (7.1)
3i	$C_{29}H_{20}N_4O_3$ (472)	166 -168	73.72 (73.7)	4.27 (4.2)	11.86 (11.8)
3j	$C_{29}H_{19}N_4O_3Cl$ (506.5)	183 -184	68.71 (68.7)	3.78 (3.7)	11.05 (11.0)
3k	$C_{29}H_{19}N_5O_5$ (517)	170 -172	67.31 (67.3)	3.70 (3.6)	13.53 (13.5)
3l	$C_{29}H_{19}N_4O_3Br$ (550)	179 -181	63.17 (63.1)	3.47 (3.4)	10.16 (10.1)

* *Uncorrected* LC-MS data for 3b:462, 3h: 584

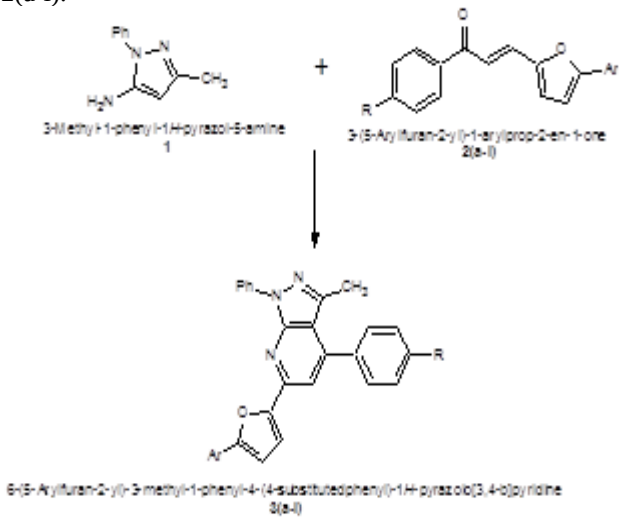
Tele: +919879841977

E-mail addresses: chetanpatilg302@gmail.com

Compds	a	b	c	d	e	f	g	h	i	j	k	l
R	H	H	H	H	Br	Br	Br	Br	NO_2	NO_2	NO_2	NO_2
Ar	Ph	4-ClPh	4- NO_2Ph	4- BrPh	Ph	4-ClPh	4- NO_2Ph	4- BrPh	Ph	4-ClPh	4- NO_2Ph	4- BrPh

Results and discussions

The 6-(5-Arylfuran-2-yl)-3-methyl-1-phenyl-4-(4-substitutedphenyl)-1*H*-pyrazolo[3,4-b]pyridine **3(a-l)** was synthesized by reaction of 3-Methyl-1-phenyl-1H-pyrazol-5-amine (1) with 3-(5-Arylfuran-2-yl)-1-arylprop-2-en-1-one 2(a-l).



The structures of **(3a-l)** were confirmed by elemental analysis and IR spectra showing an absorption bands at 3030-3080 cm^{-1}(C-H of Ar),1120cm^{-1}(C-N),1080(-Cl), 1555,1375 (-NO_2), 2960,1370 cm^{-1}(-CH_3), 690 cm^{-1} (C-Br), 750-800 cm^{-1} (C=N), 1180-1200 cm^{-1} (C-O).

(3a) 6-(5-Phenylfuran-2-yl)-3-methyl-1-phenyl-4-(phenyl)-1H-pyrazolo [3,4-b]pyridine : ^{1}H NMR (400MHz, DMSO-d_6 ,δ / *ppm*) 2.55(s, 3H, CH_3), 8.26(m, 1H, Ar-H of pyridine ring), 7.08, 7.2 (s, 2H,furan ring), 7.38-8.09 (m,15H,Ar-H).

(3b) 6-(5-(4-Chlorophenyl)furan-2-yl)-3-methyl-1-phenyl-4-(phenyl)-1*H*-pyrazolo [3,4-b]pyridine ^{1}H NMR (400MHz,DMSO-d_6 ,δ / *ppm*) 2.55(s,3H, CH_3), 8.26(m,1H, Ar-H of pyridine ring), 7.12, 7.18 (s, 2H, furan ring), 7.30-8.10 (m, 14H, Ar-H).

(3c) 6-(5-(4-Nitrophenyl)furan-2-yl)-3-methyl-1-phenyl-4-(phenyl)-1*H*-pyrazolo [3,4-b]pyridine :- ^{1}H NMR (400MHz,DMSO-d_6 ,δ / *ppm*) 2.55(s,3H, CH_3), 8.18(m,1H, Ar-H of pyridine ring), 7.08, 7.18 (s, 2H,furan ring), 7.20-8.10(m,14H, Ar-H).

(3d) 6-(5-(4-Bromophenyl)furan-2-yl)-3-methyl-1-phenyl-4-(phenyl)-1*H*-pyrazolo [3,4-b]pyridine:- ^{1}H NMR (400MHz,DMSO-d_6 ,δ / *ppm*) 2.55(s, 3H, CH_3), 8.20(m,1H, Ar-H of pyridine ring), 7.08, 7.18 (s, 2H,furan ring), 7.20-8.08(m,14H, Ar-H).

(3e) 6-(5-Phenylfuran-2-yl)-3-methyl-1-phenyl-4-(4-bromophenyl)-1*H*-pyrazolo [3,4-b]pyridine:- ^{1}H NMR (400MHz,DMSO-d_6 ,δ / *ppm*) 2.55(s, 3H, CH_3), 8.20(m,1H, Ar-H of pyridine ring), 6.90, 7.03 (s, 2H,furan ring), 7.18-8.08(m,14H, Ar-H).

(3f) 6-(5-(4-Chlorophenyl)furan-2-yl)-3-methyl-1-phenyl-4-(4-bromophenyl)-1*H*-pyrazolo [3,4-b]pyridine:- ^{1}H NMR (400MHz,DMSO-d_6 ,δ / *ppm*) 2.55(s, 3H, CH_3). 8.36(m,1H, Ar-H of pyridine ring), 6.95, 7.09 (s, 2H,furan ring), 7.18-8.08(m,14H, Ar-H)

(3g) 6-(5-(4-Nitrophenyl)furan-2-yl)-3-methyl-1-phenyl-4-(4-bromophenyl)-1*H*-pyrazolo [3,4-b]pyridine:- ^{1}H NMR (400MHz,DMSO-d_6 ,δ / *ppm*) 2.55(s, 3H, CH_3). 8.18(m,1H, Ar-H of pyridine ring), 6.95, 7.09 (s, 2H,furan ring), 7.10-8.08(m,14H, Ar-H)

(3h) 6-(5-(4-Bromophenyl)furan-2-yl)-3-methyl-1-phenyl-4-(4-bromophenyl)-1*H*-pyrazolo [3,4-b]pyridine:- ^{1}H NMR (400MHz,DMSO-d_6 ,δ / *ppm*) 2.55(s, 3H, CH_3). 8.38(m,1H, Ar-H of pyridine ring), 6.95, 7.09 (s, 2H,furan ring), 7.10-8.18(m,14H, Ar-H)

(3i) 6-(5-Phenylfuran-2-yl)-3-methyl-1-phenyl-4-(4-nitrophenyl)-1*H*-pyrazolo [3,4-b]pyridine:- ^{1}H NMR (400MHz,DMSO-d_6 ,δ / *ppm*) 2.55(s, 3H, CH_3), 8.18(m,1H, Ar-H of pyridine ring), 6.95, 7.04 (s, 2H,furan ring), 7.38-8.18(m,14H, Ar-H).

(3j) 6-(5-(4-Chlorophenyl)furan-2-yl)-3-methyl-1-phenyl-4-(4-nitrophenyl)-1*H*-pyrazolo [3,4-b]pyridine:- ^{1}H NMR (400MHz,DMSO-d_6 ,δ / *ppm*) 2.55(s, 3H, CH_3), 8.18(m,1H, Ar-H of pyridine ring), 6.95, 6.98 (s, 2H,furan ring), 7.05-8.08(m,14H, Ar-H).

(3k) 6-(5-(4-Nitrophenyl)furan-2-yl)-3-methyl-1-phenyl-4-(4-nitrophenyl)-1*H*-pyrazolo [3,4-b]pyridine:- ^{1}H NMR (400MHz,DMSO-d_6 ,δ / *ppm*) 2.55(s, 3H, CH_3), 8.23(m,1H, Ar-H of pyridine ring), 6.90, 6.95 (s, 2H,furan ring), 7.05-8.08(m,14H, Ar-H).

(3l) 6-(5-(4-Bromophenyl)furan-2-yl)-3-methyl-1-phenyl-4-(4-nitrophenyl)-1*H*-pyrazolo [3,4-b]pyridine:- ^{1}H NMR (400MHz,DMSO-d_6 ,δ / *ppm*) 2.55(s, 3H, CH_3), 8.18(m,1H, Ar-H of pyridine ring), 6.90, 6.95 (s, 2H,furan ring), 7.05-8.10(m,14H, Ar-H).

The C, H, N analysis data of all compounds are presented in Table-1.

All the elemental and spectral features suggest that the data are consistent with the predicted structure shown in Scheme-1. The LC-MS of selected compounds shows the peak of M^+ ion which is consistent of their molecular weight. All these facts confirm the structures 3(a-l).

Table 2. Antibacterial Activity of Compounds (3a-l)

Comp. No.	Zone of Inhibition(mm)			
	Gram +ve		Gram -ve	
	Bacillus subtilis	Staphylo Coccus aureus	Kllebsiella promioe	E.coli
3a	50	46	59	58
3b	51	48	60	59
3c	53	48	62	60
3d	50	47	59	59
3e	53	50	64	62
3f	59	53	67	68
3g	57	52	65	67
3h	54	51	65	66
3i	55	51	64	63
3j	66	53	72	70
3k	62	52	68	70
3l	58	51	67	69
Tetracycline	79	55	87	72

Table 3. Antifungal Activity of Compounds (3a-l)

Zone of Inhibition at 1000 ppm (%)				
Comp. No.	**Botryo-diplodia Theobr-omae**	**Nigrospora sp.**	**Penicillium expansum**	**Rhizopus nigricuns**
3a	58	66	57	55
3b	60	70	66	59
3c	61	69	65	61
3d	59	68	64	57
3e	62	68	64	62
3f	67	71	69	66
3g	67	70	68	65
3h	63	66	68	64
3i	64	69	66	63
3j	75	74	73	68
3k	68	72	72	66
3l	66	70	72	67

The examination of antibacterial activity data reveals that all compounds toxic against microbes and the compounds **3h** and **3i** found more active against the gram-positive and gram-negative bacteria. The results show that the compounds are good toxic for microbes.

References

[1] J.Jiao, A.Wang, M. Chen, M. Wang and C. Yang, "Novel 5-chloro-pyrazole derivatives containing a phenylhydrazone moiety as potent antifungal agents: synthesis, crystal structure, biological evaluation and a 3D-QSAR study", New J. Chem.,vol.43,pp. 6350-6360, 2019.

[2] A. L. Iglesias, V. Miranda-Soto, D. A. Pompa-Monroy, J. G. Martínez-Ortiz, G. C. Díaz-Trujillo and l. J. Villarreal-Gómez, "Biological Activity of New Schiff Base Compounds Derived from Substituted 3-Aminopyrazoles, the Role of Pyrazole on Bioactivity", Indian J PharmSci., vol.81(2) pp.333-343,2019.

[3] G. S. Hassan, D. E. Abdel Rahman, E. A. Abdel majeed, R.H. Refaey, S.M.Alaraby andY.M. Nissan, "New Pyrazole Derivatives: Synthesis, Anti-Inflammatory Activity, Cycloxy genase Inhibition Assay and Evaluation of mPGES", Eur J Med Chem.,vol.1(171),pp.332-342,2019.

[4] Y.S. Hassan,"Synthesis, Antibacterial and Antifungal Activity of Some New Pyrazoline and Pyrazole Derivatives", Molecules, 18,pp.2683-2711,2013.

[5] A.A.Bekhit, H.M. Ashour, Y.S.Abdel Ghany, A.D. Bekhit and A.Baraka,"Synthesis and biological evaluation of some thiazolyl and thiadiazolyl derivatives of 1H-pyrazole as anti-inflammatory antimicrobial agents". Eur J Med Chem,vol.43, pp.456-463,2008.

[6] N.E.A.El-Gamel and T.A.Farghaly, "Design and synthesis of novel complexes containing N-phenyl-1H-pyrazole moiety: Ni complex as potential antifungal and anti proliferative compound". SpectrochimActa A: Mol Biomol Spectrosc, vol. 115, pp.469-475,2013.

[7] P. J. Shah, H.S. Patel and B.P. Patel, "Synthesis, characterization and antimicrobial activity of novel sulpha piperazine containing arylazopyrazoles", Journal of Saudi Chemical Society,vol.17, pp.307-313,2013.

[8] A.M. Al-Majid, M. Shahidul and A. F. M. MotiurRahman, "Synthesis of Pyridine-Dicarboxamide-Cyclohexanone Derivatives: Anticancer and α-Glucosidase Inhibitory Activities and In Silico Study", Molecules,vol.24, pp.1332 - 1337,2019.

[9] N. A. A. Elkanzi, R. B. Bakr and A. A. Ghoneim, "Design, Synthesis, Molecular Modeling Study, and Antimicrobial Activity of Some Novel Pyrano[2,3-b]pyridine and Pyrrolo [2,3-b] pyrano[2.3-d]pyridine Derivatives", J. Heterocyclic Chem., vol.56,pp.406– 416,2019.

[10] P. Bagdi and S. Santra, "Synthesis of imidazo[1,2-a]pyridines: a decade update", Chem. Commun., vol.51,pp.1555-1575,2015.

[11] S. Kataev and B. Syropyatov, "Synthesis and Antiaggregant Activity of 3-(2-Aryl-2-oxoethyl)-3-methoxy-2-oxo-2,3–di hydroimidazo[1,2-a]pyridine Hydrochlorides", Pharmaceutical Chemistry Journal,vol.38,pp.181–182,2004.

[12] G. Puerstinger and J. Paeshuyse, "Antiviral 2,5-disubstituted imidazo[4,5-c]pyridines: From anti-pestivirus to anti-hepatitis C virus activity", Bioorg. Med. Chem. Lett.,vol.17(2), pp. 390-393,2007.

[13] M. Zarghani and B. Akhlaghinia, "Sulfonated nanohydroxy apatite functionalized with 2-aminoethyl dihydrogen phosphate (HAP@AEPH2-SO3H) as a new recyclable and eco-friendly catalyst for rapid one-pot synthesis of 4,4′-(aryl methylene) bis(3-methyl-1H-pyrazol-5-ol)s", RSC Adv.,vol.5, pp. 87769 -87780,2015.

[14] N. Mameda, S.Peraka, S.Kodumuri and N. Nama, "Synthesis of α,β-unsaturated ketones from alkynes and aldehydes over Hβ zeolite under solvent-free conditions ", RSC Adv.,vol.6, pp.58137-58141,2016.

[15] A.L. Barry, The Antimicrobial Susceptibility Test:Principal and Practices,4th ed., edited by Illuslea and Feger, Philadelphia,pp.180-182,1976.

[16] E.I. Nweze, P.K. Mukherjee and M.A.Ohannoum,"Agar-based disk diffusion assay for susceptibility testing of dermatophytes", J.Clin. Microbiology,vol.48(10),pp.3750-3752,2010.