ISSN: 0974 - 7516 Volume 11 Issue 2

Organic CHEMISTRY

An Indian Journal

Full Paper

OCAIJ, 11(2), 2015 [077-081]

Preparation, characterization and antimicrobial studies of novel imidazole combined molecule

Purvesh J.Shah

Department of Chemistry, K.K.Shah Jarodawala Maninagar Science College, Maninagar, Ahmedabad-380008, Gujarat (INDIA)

E-mail: purvesh23184@gmail.com

ABSTRACT

The condensation reaction of 4-benzylidene-2-m-tolyloxazol-5(4H)-one (2) with 2-amino substituted benzothiazole 3(A-F) was yielded a series of 4-benzylidene-1-(substitued-2-benzothiazolyl)-2-(4-methoxyphenyl)-1H-imidazol-5(4H)-one 4(A-F). The 4-benzylidene-2-m-tolyloxazol-5(4H)-one (2) has been prepared from cyclo condensation reaction of hippuric acid (1) and m-methyl benzaldehyde. The novel prepared compounds were characterized by IR, ^{1}H-NMR, ^{13}C-NMR and Mass spectral data. All the prepared compounds were screened for their antibacterial and antifungal activities.

KEYWORDS

2-amino benzthiazole;
Imidazole;
Antibacterial and Antifungal activities.

INTRODUCTION

The chemistry of heterocyclic compounds has been an interesting field for study. Majority of the drugs being introduced in pharmacopeias every year are heterocyclic compounds. Heterocyclic compounds represent an important class of drugs[1,2]. The synthesis of novel imidazoles analogs and investigation of their chemical and pharmacological behavior have gained more importance in recent decades for medicinal reasons[3]. Imidazole derivatives including saturated imidazoles are important heterocycles due to their antibacterial, antitubercular, antifungal, anti HIV, anti inflammatory, analgesic, anticancer and anticonvulsant activities[4-7]. They have also been utilized as a versatile template for the synthesis of compounds with potential enzyme inhibition activities[8]. Benzothiazole is one of the most essential heterocycle that has received awesome response owing to its diversified molecular design and remarkable optical, liquid and electronic properties[9]. Benzothiazole shows various biological activities such as antimicrobial[10-12], anticancer[13], anthelmintic[14], anti-diabetic[15] activities. Hence, it was thought of interest to merge both of thiazole and imidazole moieties which may enhance the drug activity of compounds to some extent or they may be possess some of the above mentioned biological activities. From this point of view, the objective of the present work is to prepare new derivatives of Imidazole- benzothiazole containing moiety. Hence the current communication contains the study on novel 4-benzylidene-1-(substitued-2-benzothiazolyl)-2-(m-tolyl)-1H-imidazol-5(4H)-one 4(A-F).

EXPERIMENTAL

The IR spectra were recorded in KBr pellets on

a Nicolet 400D spectrometer and ^{1}H NMR and ^{13}C NMR spectra were recorded in DMSO with TMS as internal standard on a Bruker spectrometer at 400 MHz and 100 MHz, respectively. LC-MS of selected samples taken on LC-MSD-Trap-SL_01046. Melting points were determined in open capillary tubes and were uncorrected.

Preparation of 4-benzylidene-2-m-tolyloxazol-5(4H)-one (2)

The mixture of hippuric acid (1) (0.1mole), m-methyl benzaldehyde (0.1mole), anhydrous sodium acetate (0.1mole) and acetic anhydride (0.2mole) warm on water bath with occasional stirring until solution is form. Boil the resulting solution for 2 hrs, cool to 0-5°C. Stir the yellowish brown solid product with water. The solid separated was collected by filtration, washed with ether, dried and recrystallized from ethyl acetate The yield of the product was 72 % and the product melts at 167-169°C. For $C_{17}H_{13}NO_2$(263) Calcd.:%C, 77.55;%H,4.98;%N,5.32, Found: % C, 77.5;% H,4.9;%N,5.3. IR (KBr);(cm^{-1}):3080(AromaticC-H stretch), 2848 (CH_3),760(Aromatic C-H bending),1620-1580 (Aromatic C-C stretch), 1790 (C=O lacton),1650(C=N),1260(C-N). ^{1}H NMR: 8.08 – 7.12(m,9H, Ar-H),7.98 (s,1H, C=CH), 2.32(s,3H, CH_3).^{13}C N-MR:21.4(CH_3), 131.9, 112.7 (C=C), 114.6-163.3(Ar-12C), 161.3 (C=N),166.4 (CO).

Preparation of 2-amino-4-substitued benzothiazoles 3(A-F)

The solution of substituted aniline (0.2 mole) and potassium thiocyanate (0.8 mole) in glacial acetic acid was added drop wise to 20% bromine glacial acetic acid (0.2 mole) with stirring, while the temperature was kept below 35°C. After all the bromine solution had been added. The mixture was stirred for 9-11 hrs, then filtered and the residue washed with water. The combined filtrate and washings were neutralized with ammonium hydroxide. The precipitate was collected on a filter and dried. The yields, melting points and other characterization data of these compounds are given in TABLE 1.

Preparation of 4-benzylidene-1-(substitued-2-benzo thiazolyl)-2-(m-tolyl)-1H-imidazol-5(4H)-one 4(A-F)

A mixture 4-benzylidene-2-m-tolyloxazol-5(4H)-one (2) (0.01mole) and 2-amino-4-substituted benzothiazoles 3(A-F) (0.01mole) was refluxed in presence of pyridine for 6-8 hours. Excess of pyridine was distilled off and resulting mass was poured on to crushed ice and neutralized with acid, filtered and crystallized from ethanol. The yields, melting

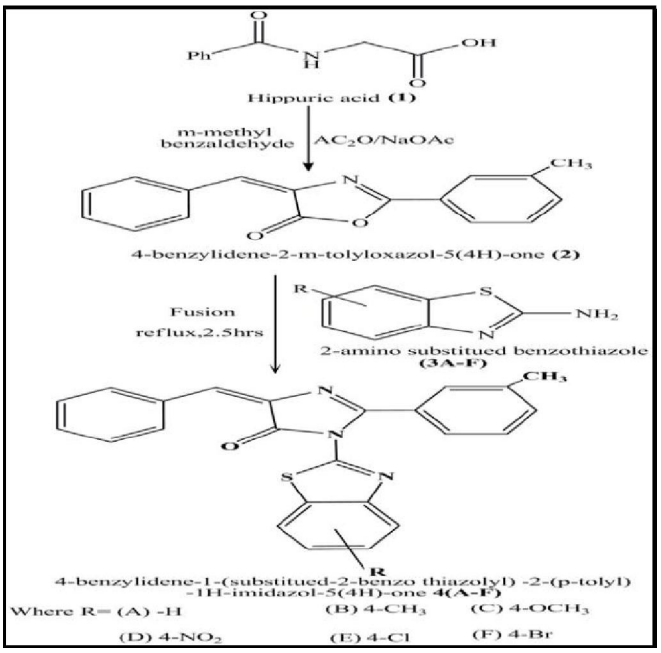

Figure 1

TABLE 1 : Analytical data and elemental analysis of compounds 3(A-F)

Compd.	LC-MS Data	M.P.* ^{0}C	Elemental Analysis			
			%C	%H	%N	%S
			Calcd. (Found)	Calcd. (Found)	Calcd. (Found)	Calcd. (Found)
3A	167	156-158	55.97 (55.9)	4.03 (4.0)	18.65 (18.6)	21.35 (21.3)
3B	179	160-162	58.51 (58.5)	4.91 (4.8)	17.06 (17.0)	19.52 (19.5)
3C	194	150-151	53.31 (53.2)	4.47 (4.4)	15.54 (15.5)	17.79 (17.7)
3D	215	152-154	43.07 (43.0)	2.58 (2.5)	21.53 (21.5)	16.43 (16.4)
3E	202	149-150	45.53 (45.5)	2.73 (2.7)	15.17 (15.1)	17.37 (17.3)
3F	241	157-159	36.70 (36.6)	2.20 (2.1)	12.23 (12.2)	14.00 (13.9)

*** Uncorrected**

TABLE 2 : Analytical data and elemental analysis of compounds 4(A-F)

Compd.	LC- MS Data	M.P. ^{0}C	Elemental Analysis			
			%C	% H	%N	%S
			Calcd. (Found	Calcd. (Found	Calcd. (Found	Calcd. (Found
4A	429	184-186	70.05 (70.0)	4.16 (4.1)	10.21 (10.1)	7.79 (7.7)
4B	435	190-191	70.57 (70.5)	4.50 (4.4)	9.88 (9.8)	7.54 (7.5)
4C	464	189-191	68.01 (68.0)	4.34 (4.3)	9.52 (9.5)	7.26 (7.2)
4D	472	192-193	63.15 (63.1)	3.53 (3.5)	12.27 (12.2)	7.02 (7.0)
4E	467	191-192	64.64 (64.6)	3.62 (3.6)	9.42 (9.4)	7.19 (7.1)
4F	494	197-199	58.78 (58.7)	3.29 (3.2)	8.57 (8.5)	6.54 (6.5)

*** Uncorrected**

points and other characterization data of these compounds are given in TABLE 2.

BIOLOGICAL SCREENING

Antibacterial activities

The antibacterial activities of all the compounds were studied against gram-positive bacteria (*Staphylococcus aureus and Bacillus subtilis*) and gram-negative bacteria (*E.coli, and klebsiella promioe*) at a concentration of 50µg/ML by agar cup plate method. A methanol system was used as control in this method. Similar conditions using tetracycline as a control was used standard for comparison. The area of inhibition of zone measured in mm. Compounds 3C, 3E, 4C and 4E were found more toxic for microbes. Other compounds found to be less or moderate active than tetracycline TABLE 3.

Antifungal activities

The fungicidal activity of all the compounds was studied at 1000 ppm concentration in vitro. Plant pathogenic organisms used were *Nigrospora Sp, Aspergillus niger, Botrydepladia thiobromine, and Rhizopus nigricum, Fusarium oxyporium*. The antifungal activity of all the compounds 3(A-F) and 4(A-F) were measured on each of these plant pathogenic strains on a potato dextrose agar (PDA) medium. Such a PDA medium contained potato 200g, dextrose 20g, agar 20g and water 1cc. Five days old cultures were employed. The compounds to be tested were suspended (1000ppm) in a PDA medium and autoclaved at 120^o C for 15 min. at 15atm. pressure. These media were poured into sterile petri plates and the organisms were inoculated after cooling the Petri plates. The percentage inhibition for fungi was calculated after five days using the formula given below:

Percentage of inhibition = 100(X-Y) / X

Where, X = Area of colony in control plate; Y = Area of colony in test plate.

The fungicidal activity displayed by various compounds 3(A-F) and 4(A-F) are shown in TABLE 4.

TABLE 3 : Antibacterial activities of compounds

Compounds	Zone of inhibition (mm)			
	Gram +Ve		Gram -Ve	
	Staphylococcus aureus	*Bacillus subtilis*	*E.coli*	*Klebsiella promioe*
3A	43	70	64	76
3B	45	71	63	74
3C	47	74	68	79
3D	49	72	67	78
3E	46	68	66	73
3F	45	69	64	75
4A	44	72	65	77
4B	46	73	67	76
4C	51	76	70	80
4D	52	75	72	81
4E	46	71	68	75
4F	46	73	69	74
Tetracycline	55	79	74	84

TABLE 4 : Antifungal activity of compounds

	Zone of Inhibition at 1000 ppm (%)				
Compounds	*Nigrospora Sp.*	*Aspergillus Niger*	*Botrydepladia Thiobromine*	*Rhizopus Nigricum*	*Fusarium oxyporium*
3A	61	59	63	54	62
3B	53	48	60	62	55
3C	68	66	72	70	69
3D	61	62	63	59	54
3E	63	62	64	74	66
3F	57	56	62	63	64
4A	61	60	65	59	54
4B	60	58	57	60	49
4C	71	66	75	63	60
4D	56	62	67	60	55
4E	62	65	69	63	61
4F	57	62	63	56	56

RESULTS AND DISCUSSION

In present communication the condensation reaction between hippuric acid (1) with m-methyl benzaldehyde gives 4-benzylidene-2-m-tolyloxazol-5(4H)-one (2). The structures of (2) were confirmed by elemental analysis and IR spectra showing an absorption band at 3080(Aromatic C-H stretch), 2848(CH_3), 760 (Aromatic C-H bending),1620-1580(Aromatic C-C stretch), 1790 (C=O lacton),1650 (C=N),1260(C-N); ^{1}H NMR: 8.08–7.12 (m, 9H, Ar-H), 7.98 (s,1H, C=CH), 2.32(s,3H, CH_3). ^{13}C N-MR: 166.4 (CO),163.3-114.6 (Ar-12C),161.3(C=N),131.9, 112.7 (C=C), 21.4 (CH_3). For $C_{17}H_{13}NO_2$(263) Calcd.: %C,77.55;% H,4.98; %N, 5.32, Found: % C, 77.5; %H, 4.9;%N, 5.3.

IR spectra of 3(A-F) are almost resemble those of the corresponding 4(A-F) only discernable variation observed that the bend at 3475cm^{-1}(NH_2) is absent and the new bands at 3080 (Aromatic C-H stretch), 2848(CH_3),760(Aromatic C-H bending), 1620-1580(Aromatic C-Cstretch),1790(C=O lacton), 1650 (C=N), 1260(C-N) are observed in

all the spectra of 4(A-F), which might be responsible for formation of imidazole ring systems.

^{1}H NMR: 7.63-7.09 (9H, s, Ar-H),7.45(1H, s, CH=C),2.35-2.32 (3H, s, CH_3).4A: 8.25-7.59(4H, m, Ar-H), 4B: 7.932-7.35 (3H, m, Ar-H), 2.42 (3H, s,-CH_3), 4C: 7.57-7.03 (3H, m, Ar-H), 1.32(s, 3H, CH_3), 4D: 8.67 -8.06(m,3H, Ar-H),4E:8.18-7.57 (m,3H, Ar-H), 4F: 8.76-7.69(m,3H, Ar-H); ^{13}C NMR: 139.7,135.4,130.2, 129.3,129.3,128.9, 128.9, 128.9, 128.8,128.7,128.5,128.3(Ar-C), 130.6, 114.7 (C=C), 170.4(C=O imidazole ring),158.1 (C=N), 160.3 (C=N benzothiazole ring), 21.4(CH_3), 4A:139.7,135.5, 125.4,124.8,122.2,118.6(Ar-C), 4B:147.3, 131.4, 126.8, 126.2, 124.7, 119.2 (Ar-C), 16.5 (CH_3),4C: 150.3,142.6, 132.3,122.1, 114.4,105.5 (Ar-C), 56.1 (OCH_3), 4D: 145.2, 142.2,128.3, 125.9, 125.5, 122.7(Ar-C), 4E:149.4, 132.6,126.1,122.2, 121.8,120.3 (Ar-C), 4F: 151.7, 128.8, 128.5, 126.8, 121.2, 116.7(Ar-C). The C, H, N, S analysis data of all compounds are presented in TABLE 2.

The examination of elemental analytical data reveals that the elemental contents are consistence with the predicted structure shown in Scheme-1. The IR data also direct for assignment of the predicted structure. The final structure of all compounds are confirmed by LC-MS. LC-MS data of all compounds are presented in TABLES 1 and 2.

CONCLUSION

In conclusion, novel 4-benzylidene-1-(substitued-2-benzo thiazolyl)-2-(m-tolyl)-1H-imidazol-5(4H)-ones has been synthesized by an extremely efficient process. All the novel synthesized compounds show moderate to excellent antibacterial and antifungal activities.

REFERENCES

[1] N.B.Patel, F.M.Shaikh; Indian Journal Of Chemistry Section B-Organic Chemistry Including Medicinal Chemistry., **49(7)**, 929 **(2010)**.

[2] P.J.Shah; Current Trends in Biotechnology and Chemical Research, **2(1)**, 45 **(2012)**.

[3] P.Raghavendra, G.Veena, G.A.Kumar, E.R.Kumar, N.Sangeetha, B.Sirivennela, S.Smarani, H.P.Kumar, R.Suthakaran; International Journal of Chemical and Analytical Science., **2(6)**, 62 **(2011)**.

[4] K.Shalini, P.K.Sharma, N.Kumar; Chem.Sin., **1**, 36 **(2010)**.

[5] A.Husain, S.Drabu, N.Kumar; Acta Pol Pharm-Drug Res., **66**, 243 **(2009)**.

[6] J.K.Neves, S.P.Botelho, C.M.De Melo, V.R.Pereira, M.C.De Lima, I.R.Pitta; Parasitol Res., **107**, 531 **(2010)**.

[7] V.Sharma, M.S.Khan; Eur.J.Med.Chem., **36**, 651 **(2001)**.

[8] M.V.Patel, R.Bell, S.Majest, R.Henry, T.Kolasa; J.Org.Chem., **69**, 7058 **(2004)**.

[9] S.Ha, T.Koh, S.Ong, T.Lee, Y.Sivasothy; Molbank., M609, 1 **(2009)**.

[10] R.M.Kumbhare, V.N.Ingle; Ind.J.Chem., **48B** ,996 **(2009)**.

[11] B.Rajeeva, N.Srinivasulu, S.Shantakumar; E-Journal of Chemistry., **6(3)**, 775 **(2009)**.

[12] M.Maharan, S.William, F.Ramzy, A.Sembel; Molecules., **12**, 622 **(2007)**.

[13] H.L.K.Stanton, R.Gambari, H.C.Chung, C.O.T.Johny, C.Filly, S.C.C.Albert; Bioorg.Med.Chem., **16**, 3626 **(2008)**.

[14] M.Sreenivasa, E.Jaychand, B.Shivakumar, K.Jayrajkumar, J.Vijaykumar; Arch Pharm Sci. and Res., **1(2)**, 150 **(2009)**.

[15] S.Pattan, C.Suresh, V.Pujar, V.Reddy, V.Rasal, B.Koti; Ind.J.Chem., **44B**, 2404 **(2005)**.