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Synthesis and Antimicrobial Evaluation of Novel 1-Benzoyl Pyrazole Derivatives

Rajiv A. Shah[1] and Dipti K. Dodiya[2]*

1 Department of Chemistry, Sheth L.H. Science College, Mansa-382 845, Gujarat, India

2 Department of Chemistry, Government Science College, Gandhinagar-382 016, Gujarat, India

ABSTRACT:

Novel 1-benzoyl-5-(aryl)-{3-[4-(2-phenyl-4-benzylidene-5-oxo-imidazol-1-yl)]phenyl}-4,5-dihydropyrazols were synthesized by the reaction of 4-benzylidene-1-{4-[3-(aryl)prop-2-enoyl]phenyl}-2-phenyl-imidazol-5-one with hydrazine hydrate followed by reaction with benzoyl chloride in presence of pyridine. All the newly synthesized pyrazoles were characterized by different spectroscopic techniques and elemental analyses. All the compounds were evaluated for their antibacterial activity against S. aureus, E.coli and for their antifungal activity against C. albicans.

KEYWORDS: Pyrazoles, Antibacterial activity, Antifungal activity

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For Correspondence:

Dr. D. K. Dodiya

Asst. Professor,

Govt. Science College,

Gandhinagar.

(www.jpsbr.org)

INTRODUCTION:

Pyrazole and its derivatives have received considerable attraction of researchers due to their broad spectrum of biological activities and they represent one of the most active classes of heterocyclic compounds [1]. Many literature reports were found reporting their wide spectrum of biological activities such as antitumor, antibacterial, antifungal, antiviral, antiparasitic, antitubercular, insecticidal, anti-inflammatory, antidiabetic and analgesic compounds [2–12]. Furthermore, they are also useful as synthons and intermediates [13-15].

Number of research articles were found reporting design and synthesis of pyrazoles containing different aryl groups as substituents [16-22]. In view of these observations and as a continuation of our efforts in synthesizing bioactive heterocycles [23-25], it was thought worthwhile to synthesize a series of novel 1-benzoyl pyrazole derivatives and evaluate them for their antibacterial and antifungal activity.

MATERIALS AND METHODS

Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded on SHIMADZU-FT-IR-8400 [Fourier transform–infrared (FT-IR)]. The IR spectra were taken using KBr pellets. 1H NMR were recorded on Bruker AMX spectrometer. Elemental analysis was carried out using Heraus CHN rapid analyzer. All the chemicals were commercial products and were used without further purification.

General Procedure for the Synthesis of 5-(Aryl)-{3-[4-(2-phenyl-4-benzylidene-5-oxo-imidazol-1-yl)]phenyl}-4,5-dihydro pyrazoles (2a-g):

A mixture of 4-benzylidene-1-{4-[3-(aryl)prop-2-enoyl]phenyl}-2-phenyl-imidazol-5-one **(1a-g)** (0.01 M) and 99% hydrazine hydrate (0.015 M) in ethanol (50 mL) was refluxed gently and the progress of the reaction was monitored by TLC. Upon completion of the reaction, the mixture was concentrated and allowed to cool. The resulting solid was filtered, washed with ethanol and recrystallised from ethanol.

General Procedure for the Synthesis of 1-benzoyl-5-(aryl)-{3-[4-(2-phenyl-4-benzylidene-5-oxo-imidazol-1-yl)]phenyl}-4,5-dihydropyrazols (3a-g):

A mixture of 5-(Aryl)-{3-[4-(2-phenyl-4-benzylidene-5-oxo-imidazol-1-yl)]phenyl}-4,5-dihydro pyrazoles **(2a-g)** (0.01 M) and benzoyl chloride (0.01 M) in dry pyridine (25 mL) was stirred at room temperature and the progress of the reaction was monitored by TLC. Upon completion of the reaction, the reaction mixture treated with cold dilute HCl (2 N). The resulting solid was filtered and washed successively with water, cold NaOH (2%) and water, and recrystallised from glacial acetic acid.

1-benzoyl-5-(4-chlorophenyl)-{3-[4-(2-phenyl-4-benzylidene-5-oxo-imidazol-1-yl)]phenyl}-4,5-dihydropyrazole 3a: Yield 66%. mp 218-220 °C. ^{1}H NMR, δ 1.08 (d, 2H, CH_2), 2.32 (t, 1H, CH), 5.72 (s, 1H, CH=), 6.82-7.79 (m, 23H, Ar-H). MS: m/z 607. Anal. Calcd. for $C_{38}H_{27}ClN_4O_2$: C, 75.18; H, 4.48; N, 9.23; Found: C, 75.16; H, 4.45; N, 9.21.

1-benzoyl-5-(2-chlorophenyl)-{3-[4-(2-phenyl-4-benzylidene-5-oxo-imidazol-1-yl)]phenyl}-4,5-dihydropyrazole 3b: Yield 54%. mp 214-216 °C. ^{1}H NMR, δ 1.15 (d, 2H, CH_2), 2.36 (t, 1H, CH), 5.74 (s, 1H, CH=), 6.93-7.83 (m, 23H, Ar-H). MS: m/z 607. Anal. Calcd. for $C_{38}H_{27}ClN_4O_2$: C, 75.18; H, 4.48; N, 9.23; Found: C, 75.15; H, 4.46; N, 9.20.

1-benzoyl-5-(2-nitrophenyl)-{3-[4-(2-phenyl-4-benzylidene-5-oxo-imidazol-1-yl)]phenyl}-4,5-dihydropyrazole 3c: Yield 62%. mp 227-229 °C. ^{1}H NMR, δ 1.18 (d, 2H, CH_2), 2.41 (t, 1H, CH), 5.64 (s, 1H, CH=), 6.85-7.86 (m, 23H, Ar-H). MS: m/z 617. Anal. Calcd. for $C_{38}H_{27}N_5O_4$: C, 73.89; H, 4.41; N, 11.34; Found: C, 73.86; H, 4.39; N, 11.32.

1-benzoyl-5-(2-hydroxyphenyl)-{3-[4-(2-phenyl-4-benzylidene-5-oxo-imidazol-1-yl)]phenyl}-4,5-dihydropyrazole 3d: Yield 65%. mp 192-194 °C. ^{1}H NMR, δ 1.11 (d, 2H, CH_2), 2.57 (t, 1H, CH), 8.82 (s, 1H, OH), 5.81 (s, 1H, CH=), 6.91-7.93 (m, 23H, Ar-H). MS: m/z 588. Anal. Calcd. for $C_{38}H_{28}N_4O_3$: C, 77.53; H, 4.79; N, 9.52; Found: C, 77.51; H, 4.77; N, 9.49.

1-benzoyl-5-(4-hydroxyphenyl)-{3-[4-(2-phenyl-4-benzylidene-5-oxo-imidazol-1-yl)]phenyl}-4,5-dihydropyrazole 3e: Yield 68%. mp 212-214 °C. ^{1}H NMR, δ 1.19 (d, 2H, CH_2), 2.38 (t, 1H, CH), 8.77 (s, 1H, OH), 5.72 (s, 1H, CH=), 6.85-7.87 (m, 23H, Ar-H). MS: m/z 588. Anal. Calcd. for $C_{38}H_{28}N_4O_3$: C, 77.53; H, 4.79; N, 9.52; Found: C, 77.50; H, 4.78; N, 9.50.

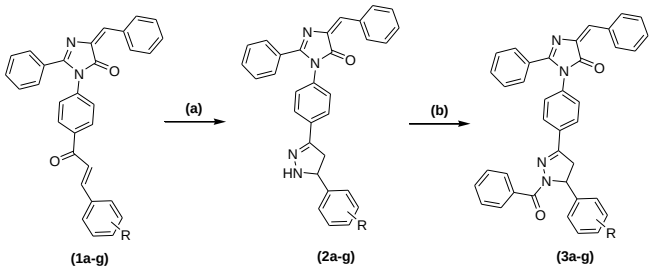
1-benzoyl-5-(4-dimethylamino-phenyl)-{3-[4-(2-phenyl-4-benzylidene-5-oxo-imidazol-1-yl)]phenyl}-4,5-dihydropyrazole 3f: Yield 73%. mp 194-196 °C. ^{1}H NMR, δ 1.21 (d, 2H, CH_2), 2.43 (t, 1H, CH), 2.78 (s, 6H, NCH_3), 5.79 (s, 1H, CH=), 6.82-7.90 (m, 23H, Ar-H). MS: m/z 615. Anal. Calcd. for $C_{40}H_{33}N_5O_2$: C, 78.03; H, 5.40; N, 11.37; Found: C, 78.01; H, 5.37; N, 11.35.

1-benzoyl-5-(4-methoxyphenyl)-{3-[4-(2-phenyl-4-benzylidene-5-oxo-imidazol-1-yl)]phenyl}-4,5-dihydropyrazole 3g: Yield 55%. mp 242-244 °C. ^{1}H NMR, δ 1.09 (d, 2H, CH_2), 2.54 (t, 1H, CH), 3.92 (s, 3H, OCH_3), 5.81 (s, 1H, CH=), 6.89-7.81 (m, 23H, Ar-H). MS: m/z 602. Anal. Calcd. for $C_{39}H_{30}N_4O_3$: C, 77.72; H, 5.02; N, 9.30; Found: C, 77.70; H, 5.00; N, 9.27.

RESULTS AND DISCUSSION

Chemistry

Mixture of 4-benzylidene-1-{4-[3-(aryl)prop-2-enoyl]phenyl}-2-phenyl-imidazol-5-one **(1a-g)** and hydrazine hydrate in ethanol was refluxed to get the starting 5-(Aryl)-{3-[4-(2-phenyl-4-benzylidene-5-oxo-imidazol-1-yl)]phenyl}-4,5-dihydro pyrazoles **(2a-g)**, which were then reacted with benzoyl chloride in presence of dry pyridine to furnish the title compounds 1-benzoyl-5-(aryl)-{3-[4-(2-phenyl-4-benzylidene-5-oxo-imidazol-1-yl)]phenyl}-4,5-dihydropyrazols **(3a-g) (Scheme 1)**.



(a) NH_2NH_2, ethanol; (b) Benzoyl chloride, dry pyridine, stirring, RT

3a R= 4-Cl 3e R= 4- OH
3b R= 2-Cl 3f R= 4-$(NCH_3)_2$
3c R= 2- NO_2 3g R= 4-OCH_3
3d R= 2-OH

Scheme 1. Synthesis of 1-benzoyl pyrazoles (3a-g)

All the newly synthesized 1-benzoyl pyrazole compounds **(3a-g)** were characterized by different spectroscopic techniques and elemental analyses. The purity of the compounds was controlled by TLC. The spectral data of all the newly synthesized compounds were in full agreement with the proposed structures.

Biological screening

The compounds **(3a-g)** were evaluated for their antibacterial activity against Escherichia coli, Staphylococcus aureus and antifungal activity against Candida albicans using the cup-plate method. After 24 h of incubation at 37 °C, the zones of inhibition were measured in mm. The activities were compared with those of some known drugs, viz. Penicillin, Kanamycin and Amphotericin B. The results are summarized in **Table 1**.

CONCLUSION

The newly synthesized 1-benzoyl pyrazoles exhibited moderate to good antimicrobial activity, which makes them suitable as leads for further structural modification in order to develop new classes of antimicrobial compounds.

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REFERENCES

[1] Yerragunta V, Suman D, Swamy K, Anusha V, Patil P and Naresh M. Pyrazole and Its Biological Activity, PharmaTutor, 2014; 2(1):40-48.

[2] Song H, Liu Y, Xiong L, Li Y, Yang N and Wang Q. Design, Synthesis and Insecticidal Activity of Novel Pyrazole Derivatives Containing α-hydroxymethyl-N-Benzylcarboxamide, α-Chloromethyl-N-Benzyl Carboxamide, and 4,5-Dihydrooxazole moieties, J. Agric. Food Chem., 2012; 60:1470–1479.

[3] Sharshira EM, Hamada NMM. Synthesis and Antimicrobial Evaluation of Some Pyrazole Derivatives. Molecules, 2012; 17:4962–4971.

[4] Nayak N, Ramprasad J and Dalimba U. New INH–pyrazole analogs: Design, synthesis and evaluation of antitubercular and antibacterial activity. Bioorg Med Chem Lett., 2015; 25(23):5540–5545.

[5] Khaled RA, Abdellatifa AM and Knausc EE. Synthesis of new 1-(4-methane(amino)sulfonylphenyl)-5-(4-substituted-aminomethylphenyl)-3-trifluoromethyl-1H-pyrazoles: A search for novel nitric oxide donor anti-inflammatory agents. Bioorg Med Chem Lett., 2014; 24(21):5015–5021.

[6] Rashad AE, Shamroukh AH, Hegab MI and Awad HM. Synthesis of Some Biologically Active Pyrazoles and C-Nucleosides. Acta Chim. Slov., 2005; 52:429–434.

[7] Rashad AE, Hegab M, Abdel-Megeid RE, Micky JA and Abdel-Megeid FME. Synthesis and Antiviral Evaluation of Some New Pyrazole and Fused Pyrazolo Pyrimidine Derivatives. Bioorg. Med. Chem., 2008; 16:7102–7106.

[8] Bhat BA, Dhar KL, Saxena AK, Shanmugavel M and Qazi GN. Synthesis and Biological Evaluation of Chalcones and Their Derived Pyrazoles as Potential Cytotoxic Agents. Bioorg. Med. Chem. Lett., 2005; 15:3177–3180.

[9] Horrocks P, Pickard MR, Parekh HH, Patel SP and Pathak RB. Synthesis and Biological Evaluation of 3-(4-Chlorophenyl)-4-Substituted Pyrazole Derivatives. Org. Biomol. Chem., 2013; 11:4891–4898.

[10] Holla BS, Akberali PM and Shivanada MK. Studies on Arylfuran Derivative: Part X. Synthesis and Antibacterial Properties of Arylfuryl-Δ2-Pyrazolines. Farmaco, 2000; 55:256–263.

[11] Maggio B, Daidone G, Raffa D, Plescia S, Mantione L, Cutuli VMC, Mangano NG and Caruso A. Synthesis and Pharmacological Study of ethyl 1-methyl-5-(substituted-3,4-dihydro-4-oxoquinazolin-3-yl)-1H-pyrazole-4-acetates. Eur. J. Med. Chem., 2001; 36: 737–742.

[12] Kalirajan R, Palanivelu M, Rajamanickam V, Vinothapooshan G and Andarajagopal K. Synthesis and Biological Evaluation of Some Heterocyclic Derivatives of Chalcones. Int. J. Chem. Sci., 2007; 5:73–80.

[13] MallikarjunaRao R, Sreeramulu J, Ravindranath LK, NagarajaReddy G, Hanumanthurayudu K, Nageswara Reddy G, Jayaraju A, Madhusudhan P. Synthesis and biological screening of some Pyridine and Pyrrole Derivatives of Pyrazolo [3,4-c] pyrazoles. J. Chem. Pharm. Res., 2012; 4:272–278.

[14] Mohareb RM, El-Sayed NNE and Abdelaziz MA. Uses of Cyanoacetylhydrazine in Heterocyclic Synthesis: Novel Synthesis of Pyrazole Derivatives with Anti-tumor Activities. Molecules, 2012; 17:8449–8463.

[15] Kumar KA and Jayaroopa P. Pyrazoles: Synthetic Strategies and Their Pharmaceutical Applications-An Overview. Int. J. PharmTech Res., 2013; 5, 1473–1486.

[16] El-Emary, T.I. Synthesis of Newly Substituted Pyrazoles and Substituted Pyrazolo [3,4-b] pyridines Based on 5-Amino-3-methyl-1-phenyl pyrazole. J. Chin. Chem. Soc., 2007; 54:507–518.

[17] Hamada NM. Synthesis and Spectral Studies of Some Novel Pyrazole Derivatives from Chalcones Precursors. Heterocycl. Commun., 2009; 15:327–334.

[18] Hu H, Ge C, Ding L and Zhang A. Synthesis of Novel 1-[(2,6-Dichloro-4-trifluoro-methyl)phenyl]-3-aryl-1H-pyrazole-4-carbaldehydes. Molecules, 2010; 15:7472–7481.

[19] Sharshira EM and Hamada NMM. Synthesis and in Vitro Antimicrobial Activity of Some Pyrazolyl-1-carboxamide Derivatives. Molecules, 2011; 16:7736–7745.

[20] Ghorab MM, Ragab FA, Heiba HI and Agha HM. Synthesis of Some Novel Sulfonamides Containing Biologically Active Alkanoic Acid, Acetamide, Thiazole, and Pyrrole Moieties of Expected Antitumor and Radiosensitizing Activities. J. Basic Appl. Chem., 2011; 1:8–14.

[21] Fadda AA, Abdel-Latif E and El-Mekawy RE. Synthesis of Some New Aryl Azo Thiophene and Arylazopyrazole Derivatives as Antitumor Agents. Pharmacol. Pharm., 2012; 3:148–157.

[22] Ghorab MM, El-Gazzar MG, Alsaid MS. Synthesis, Characterization and Anti-Breast Cancer Activity of New 4-Aminoantipyrine-Based Heterocycles. Int. J. Mol. Sci. 2014; 15:7539–7553.

[23] Trivedi AR, Dodiya DK, Surani J, Jarsania S, Mathukia H, Ravat N and Shah VH. Facile one pot synthesis and antimycobacterial evaluation of pyrazolo[3,4-d]pyrimidines. Arch. Pharm., 2008; 341(7):435-439.

[24] Trivedi AR, Dodiya DK, Dholariya BH, Kataria VB, Bhuva VR and Shah VH. Synthesis and biological evaluation of some novel N-aryl-1,4-dihydropyridines as potential antitubercular agents. Bioorg Med Chem Lett., 2011; 21(18): 5181-5183.

[25] Shah RA, Patel PS, Trivedi DK and Vyas PJ. Synthesis and characterization of 4-{4-(2-phenyl-4-benzylidene-5-oxo-imidazol-1-yl) phenyl}-6-(substituted phenyl)-1,2,5,6-tetrahydropyrimidin-2-thione derivatives and study of their antimicrobial activities. Ultra Chemistry, 2010; 6(1):15-18.

Table-1. **Antimicrobial Evaluation of 1-benzoyl pyrazoles (3a-g)**

Compound	Antibacterial Activity		Antifungal Activity
	E. coli	S. aureus	C. albicans
3a	17	-	17
3b	15	18	15
3c	12	11	17
3d	18	14	-
3e	14	14	19
3f	15	15	17
3g	16	16	11
Penicillin	18	20	-
Kanamycin	19	24	-
Amphotericin B	-	-	21