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RESEARCH ARTICLE

Synthesis and Antimicrobial Evaluation of 1-Acetylpyrazole Derivatives

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ABSTRACT

A series of novel 1-acetyl-5-(aryl)-{3-[4-(2-phenyl-4-p-methoxybenzylidene-5-oxo-imidazol-1-yl)]phenyl}-4,5-dihydropyrazoles was synthesized by the reaction of 4-(4-methoxybenzylidene)-1-{4-[3-(aryl)prop-2-enoyl]phenyl}-2-phenyl-imidazol-5-ones with hydrazine hydrate followed by reaction with acetic acid. All the newly synthesized 1-acetyl pyrazoles were characterized by different spectroscopic techniques and elemental analyses. All the compounds were evaluated for their antibacterial and antifungal activity.

KEYWORDS

Chalcone, Hydrazine Hydrate, 1-Acetyl Pyrazole, Antibacterial Activity, Antifungal Activity

INTRODUCTION

Pyrazole and its derivatives possess a broad spectrum of biological activities and represent one of the most active classes of heterocyclic compounds[1]. Literature survey revealed many reports mentioning their wide spectrum of biological activities such as antitumor, antibacterial, antifungal, antiviral, antiparasitic, antitubercular, insecticidal, anti-inflammatory, antidiabetic and analgesic activities[2–12]. Furthermore, they are also useful as synthons and intermediates[13-17].

In view of these observations and as a continuation of our efforts in synthesizing bioactive heterocycles[18-20], it was thought worthwhile to synthesize a series of novel 1-acetyl pyrazole derivatives and evaluate them for their antibacterial and antifungal activity.

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MATERIAL 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. ^{1}H 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-p-methoxy-benzylidene-5-oxo-imidazol-1-yl)]phenyl}-4,5-dihydropyrazoles (2a-g)

A mixture of 4-(4-methoxybenzylidene)-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 for 3-4 hours. 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-acetyl-5-(aryl)-{3-[4-(2-phenyl-4-p-methoxy-benzylidene-5-oxo-imidazol-1-yl)]phenyl}-4,5-dihydropyrazoles (3a-g):

A mixture of 5-(Aryl)-{3-[4-(2-phenyl-4-p-methoxybenzylidene-5-oxo-imidazol-1-yl)] phenyl}-4,5-dihydro pyrazole **(2a-g)** (0.01M) and acetic acid (10 ml) was refluxed for 3-5 hours.

The progress of the reaction was monitored by TLC. Upon completion of the reaction, the solution was concentrated, cooled; the resulting solid was filtered, washed with water and recrystallised from ethanol.

1-acetyl-5-(phenyl)-{3-[4-(2-phenyl-4-p-methoxybenzylidene-5-oxo-imidazol-1-yl)] phenyl}-4,5-dihydropyrazole 3a: Yield 64%. mp 186-188 °C. ^{1}H NMR, δ 1.16 (d, 2H, CH_2), 1.81 (s, 3H, $COCH_3$), 2.54 (t, 1H, CH), 3.45 (s, 3H, OCH_3), 5.61 (s, 1H, CH=), 6.75-7.66 (m, 18H, Ar-H). MS: m/z 540. Anal. Calcd. for $C_{34}H_{28}N_4O_3$: C, 75.54; H, 5.22; N, 10.36; Found: C, 75.51; H, 5.19; N, 10.33.

1-acetyl-5-(2-chlorophenyl)-{3-[4-(2-phenyl-4-p-methoxybenzylidene-5-oxo-imidazol-1-yl)] phenyl}-4,5-dihydropyrazole 3b: Yield 68%. mp 208-210 °C. ^{1}H NMR, δ 1.13 (d, 2H, CH_2), 1.90 (s, 3H, $COCH_3$), 2.51 (t, 1H, CH), 3.48 (s, 3H, OCH_3), 5.65 (s, 1H, CH=), 6.80-7.52 (m, 17H, Ar-H). MS: m/z 575. Anal. Calcd. for $C_{34}H_{27}ClN_4O_3$: C, 71.01; H, 4.73; N, 9.74; Found: C, 71.00; H, 4.70; N, 9.70.

1-acetyl-5-(4-chlorophenyl)-{3-[4-(2-phenyl-4-p-methoxybenzylidene-5-oxo-imidazol-1-yl)] phenyl}-4,5-dihydropyrazole 3c: Yield 65%. mp 202-204 °C. ^{1}H NMR, δ 1.21 (d, 2H, CH_2), 1.85 (s, 3H, $COCH_3$), 2.48 (t, 1H, CH), 3.51 (s, 3H, OCH_3), 5.68 (s, 1H, CH=), 6.72-7.62 (m, 17H, Ar-H). MS: m/z 575. Anal. Calcd. for $C_{34}H_{27}ClN_4O_3$: C, 71.01; H, 4.73; N, 9.74; Found: C, 71.04; H, 4.72; N, 9.71.

1-acetyl-5-(2-hydroxyphenyl)-{3-[4-(2-phenyl-4-p-methoxybenzylidene-5-oxo-imidazol-1-yl)] phenyl}-4,5-dihydropyrazole 3d: Yield 62%. mp 174-176 °C. ^{1}H NMR, δ 1.21 (d, 2H, CH_2), 1.89 (s, 3H, $COCH_3$), 2.62 (t, 1H, CH), 3.52 (s, 3H, OCH_3), 4.57 (s, 1H, OH), 5.70 (s, 1H, CH=), 6.65-7.65 (m, 17H, Ar-H). MS: m/z 556. Anal. Calcd. for $C_{34}H_{28}N_4O_4$: C, 73.37; H, 5.07; N, 10.07; Found: C, 73.33; H, 5.05; N, 10.04.

1-acetyl-5-(4-hydroxyphenyl)-{3-[4-(2-phenyl-4-p-methoxybenzylidene-5-oxo-imidazol-1-yl)] phenyl}-4,5-dihydropyrazole 3e: Yield 66%. mp 240-242 °C. ^{1}H NMR, δ 1.23 (d, 2H, CH_2), 1.85 (s, 3H, $COCH_3$), 2.45 (t, 1H, CH), 3.52 (s, 3H, OCH_3), 4.51 (s, 1H, OH), 5.67 (s, 1H, CH=), 6.74-7.54 (m, 17H, Ar-H). MS: m/z 556. Anal. Calcd. for $C_{34}H_{28}N_4O_4$: C, 73.37; H, 5.07; N, 10.07; Found: C, 73.34; H, 5.04; N, 10.04.

1-acetyl-5-(3-nitrophenyl)-{3-[4-(2-phenyl-4-p-methoxybenzylidene-5-oxo-imidazol-1-yl)] phenyl}-4,5-dihydropyrazole 3f: Yield 59%. mp 196-198 °C. ^{1}H NMR, δ 1.15 (d, 2H, CH_2), 1.93 (s, 3H, $COCH_3$), 2.47 (t, 1H, CH), 3.46 (s, 3H, OCH_3), 5.61 (s, 1H, CH=), 6.69-7.51 (m, 17H, Ar-H). MS: m/z 585. Anal. Calcd. for $C_{34}H_{27}N_5O_5$: C, 69.73; H, 4.65; N, 11.96; Found: C, 69.71; H, 4.61; N, 11.92.

1-acetyl-5-(4-dimethylamino-phenyl)-{3-[4-(2-phenyl-4-p-methoxybenzylidene-5-oxo-imidazol-1-yl)]phenyl}-4,5-dihydropyrazole 3g: Yield 71%. mp 252-254 °C. ^{1}H NMR, δ 1.23 (d, 2H, CH_2), 1.85 (s, 3H, $COCH_3$), 2.42 (t, 1H, CH), 2.93 (s, 6H, NCH_3), 3.56 (s, 3H, OCH_3), 5.70 (s, 1H, CH=), 6.73-7.53 (m, 17H, Ar-H). MS: m/z 583. Anal. Calcd. for $C_{36}H_{33}N_5O_3$: C, 74.08; H, 5.70; N, 12.00; Found: C, 74.04; H, 5.68; N, 11.97.

RESULTS AND DISCUSSION

Chemistry

The synthesis of 5-(Aryl)-{3-[4-(2-phenyl-4-p-methoxybenzylidene-5-oxo-imidazol-1-yl)] phenyl}-4,5-dihydro pyrazoles **(2a-g)** was accomplished by refluxing 4-(4-methoxybenzylidene)-1-{4-[3-(aryl)prop-2-enoyl]phenyl}-2-phenyl-imidazol-5-one **(1a-g)** and hydrazine hydrate using ethanol as solvent, which were then reacted with glacial acetic acid to furnish the title compounds 1-acetyl-5-(aryl)-{3-[4-(2-phenyl-4-p-methoxybenzylidene-5-oxo-

imidazol-1-yl)]phenyl}-4,5-dihydropyrazoles **(3a - g) (Scheme 1)**.

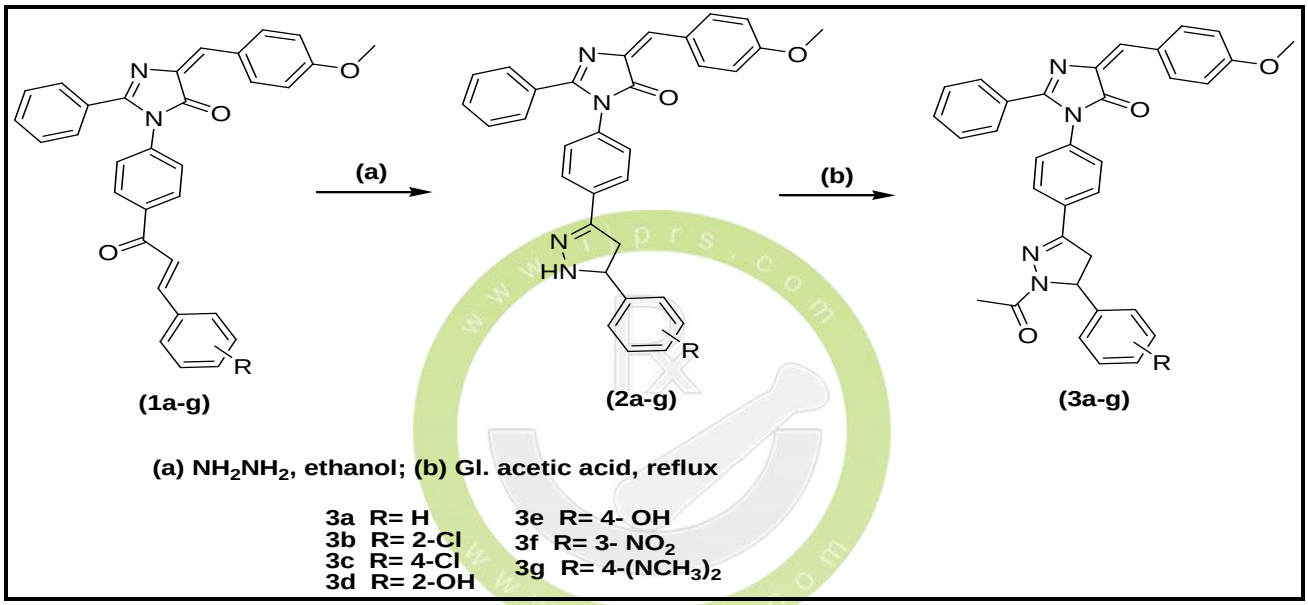
All the newly synthesized 1-acetyl pyrazoles were characterized by different spectroscopic techniques and elemental analyses.

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.



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

Table 1: Antimicrobial Evaluation of 1-acetyl pyrazoles (3a-g)

Compound	Antibacterial Activity		Antifungal Activity
	E. coli	S. aureus	C. albicans
3a	16	17	17
3b	18	19	16
3c	16	16	15
3d	13	14	20
3e	15	18	17
3f	16	13	13
3g	16	15	16
Penicillin	18	20	-
Kanamycin	19	24	-
Amphotericin B	-	-	21

CONCLUSION

To summarize, a series of novel 1-acetyl pyrazoles was synthesized. The newly synthesized heterocycles exhibited moderate to promising antimicrobial activity against standard strains. These results make them interesting lead molecules for further synthesis of related heterocycles and their biological evaluation.

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