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Synthesis and Characterization of Substituted Benzimidazole derivatives

Abstract:

Benzimidazole is one of the heterocyclic compounds with very important biological activities. In this view, it was proposed to synthesize some novel Benzimidazole derivatives from Schiff bases. Here the synthesis of O-phenylene diamine(0.25mol) and compounds(0.25mol)were heated on water bath at 100° C for 12hrs reflux in chloroform and mixture just alkaline with10% NaOH solution and separated the crude benzimidazole derivatives. Their structures were confirmed by IR, 1HNMR and 13CNMR.

Keywords: Benzimidazole, Phenylene diamine, Schiff base, sulphonamides derivatives.

Introduction:

Medicines and heterocycles are both interrelated because humans are totally dependent on the drugs derived from heterocyclic rings. Nitrogen heterocycles are of special interest as they constitute an important class of natural and non-natural products, many of which exhibit useful biological activities. Pyrroles and their derivatives exhibit different important biological activities like antibacterial, antioxidant, cytotoxic, insecticidal, anti-inflammatory, anticoagulant, antiallergic, antiarhythmic, hypotensive and anticonvulsant [1-7] etc. Pyrazoles and their derivatives exhibit a broad spectrum of biological activities such as antimicrobial [8], antiinflammatory [9] and antitumor [10] activities, antibacterial [11], antifungal [12], antiviral [13], antitubercular [14], antioxidant [15], antiandrogenic [16] etc. On the other hand, sulfonamides and their different derivatives are extensively used in medicine due to their pharmacological properties such as antibacterial activity [17, 18]. The newly synthesized compounds were evaluated as antimicrobial agents against gram positive and gram negative bacteria and fungi.

Benzimidazole is a heterocyclic compound consisting of benzene ring fused with imidazole ring. The chemistry and pharmacology of benzimidazoles have been of great interest to medicinal chemistry [26] because its derivatives possessed various biological activates [27] such as anticancer [28-30], antihypertensive [31], antimicrobial [32-34], Moreover benzimidazoles [35] are important intermediates in organic reaction.

Experimental:

Synthesis of 1-N-phenyl-3-phenyl-4-formyl pyrazole (PFP): (1E)-1-(phenyl)-ethanone-(phenyl)-hydrazone (0.01 mol) was added in mixture of VilsmeirHaack reagent and refluxed for 5 hrs. Thereaction mixture was poured into ice followed by neutralization using sodium bicarbonate. Crude product was isolated and crystallized from ethanol. Yield was about 82%.

Synthesis of sulfonamide derivatives of Arylidine–[1-N-phenyl-3-phenyl-pyrazole]

1-N-phenyl-3-phenyl-4-formyl pyrazole (PFP)

(0.01 mol) and various aromatic amine sulfonamides (0.01 mol) in 50ml acetic acid was refluxed for about 10-12 hrs. on oil bath with TLC monitoring. The reaction mixture was cooled and it was poured in to ice water and extracted with ethyl acetate and water. The solvent was evaporated to give the solid product. It was crystallized from ethyl acetate-hexane using decolorizing charcoal to give various anils having good yields.

Synthesis of 5-[1-N-phenyl-3-phenyl-pyrazole]-2-oxo-1-N-(phenyl-sulfonamide)-3,5dihydro-1H-pyrrole-4-carboxylic acid

Maleic anhydride (0.1mol) and imine (0.1mol) were heated at reflux in chloroform (30ml) for about 5 hours with TLC monitoring. After the mixture was allowed to stand for 2 days, the solid was filtered. The product thus forme dwas recrystallized from ethanol to give pure 5-[1-Nphenyl-3-phenyl-pyrazole]-2-oxo-1-N-aryl-3,5-dihydro-1Hpyrrole-4-carboxylic acid in yield. The analytical and spectral data of the compounds are described

Synthesis of 5-[1-N-phenyl-3-phenyl-pyrazole]-2-oxo-1-N-(phenyl-sulfonamide)-3,5dihydro-1H-pyrrole-4-(2'-benzimidazole)

O-phenylenediamine (0.25mole) and compounds (0.25mole) were heated on water bath at 100° C for 2hrs in chloroform (30ml) as a solvent. After the mixture was allowed to cool and 10 % NaOH solution was added slowly with constant stirring, until the mixture was just alkaline to litmus. Filter off the crude benzimidazole derivatives at the pump. Washed with cold water, The product thus formed was recrystallized from ethanol to give pure 5-[1-N-phenyl-3-phenylpyrazole]-2-oxo-1-N-aryl-3,5-dihydro-1Hpyrrole-4-(2'-benzimidazole) in yield.

SCHEME:1

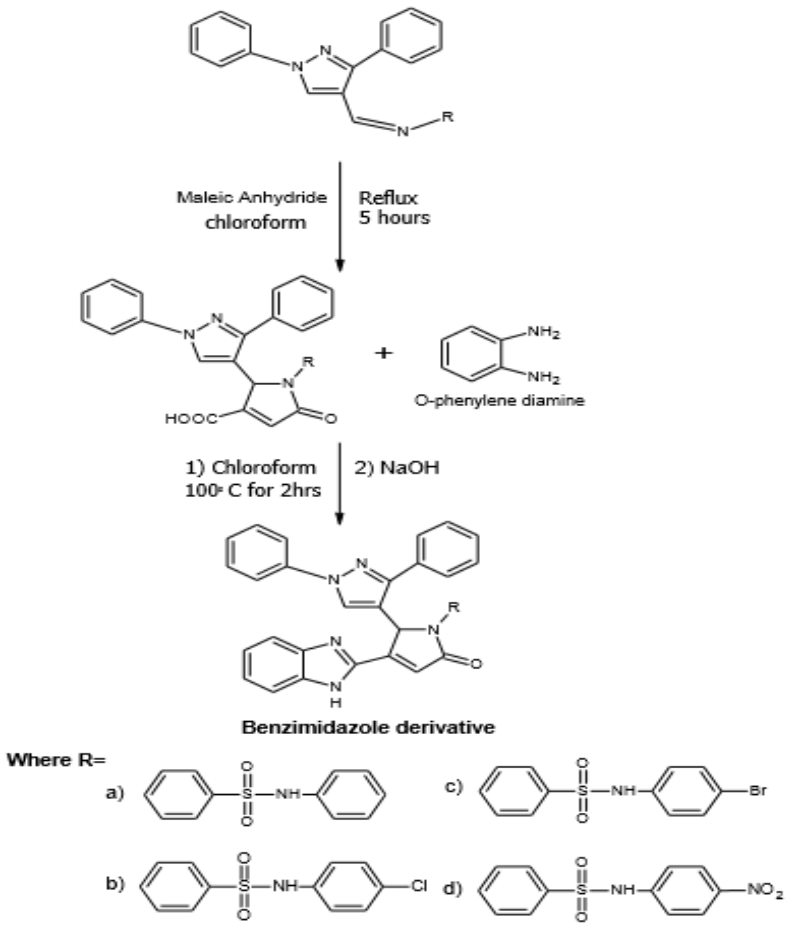

Table 1: Physical constant of 5-[1-N-phenyl-3-phenyl-pyrazole]-2-oxo-1-N-(phenylsulfonamide)-3, 5-dihydro-1H-pyrrole-4-(2'-benzimidazole).

Compd.	R	Mol. Formula (Mol. Wt)	M.P. °C	Yield %	% of C,H,N & S Calcd. / Found			
					C	H	N	S
A	$C_{12}H_{12}N_2O_2S$	$C_{38}H_{28}N_6O_3S$	213°C	67%	70.4 /70.2	4.3 /4.1	12.9 /12.7	4.9 /4.8
B	$C_{12}H_{11}N_2O_2SCl$-	$C_{38}H_{27}N_6O_3SCl$	205 °C	65%	66.8 / 66.8	4.0 / 3.8	12.3 / 12.0	4.7 / 4.6
C	$C_{12}H_{11}N_2O_2SBr$-	$C_{38}H_{27}N_6O_3SBr$	196 °C	60%	62.7 / 2.5	3.7 / 3.6	11.5 / 11.4	4.4 / 4.2
D	$C_{12}H_{11}N_3O_4S$	$C_{38}H_{27}N_7O_5S$	212 °C	63%	65.8 / 65.7	3.9 / 3.8	12.1 / 12.0	4.6 /4.5

5-[1-N-phenyl-3-phenyl-pyrazole]-2-oxo-1-N-(phenyl-sulfonamide)-3,5-dihydro-1Hpyrrole-4-(2'-benzimidazole): IR (cm-1): 3054(Ar-C-H str.), 1670 (C=O str. of COOH),1717 (C=O of pyrrole-2-one), 32503330 (-NH of –SO2NH), 1040 (N-N str.), 3250 N-H of benzimidazole NMR(δ,ppm): 6.15-8.13 (m, aromatic H of pyrazole), 4.7 (s,H of C5H), 5.15(s, H of C3H).

5-[1-N-phenyl-3-phenyl-pyrazole]-2-oxo-1-N-(4'-chloro-N-phenyl-sulfonamide)-3,5-dihydro1H-pyrrole-4-(2'-benzimidazole): IR (Cm-1): 3030(Ar-C-H str.), 1670 (C=O str. of COOH),1717 (C=O of pyrrole-2-one), 32503330 (-NH of –SO2NH), 1045 (N-N str.), 3377 N-H of benzimidazole NMR(δ,ppm): 6.13-8.13 (m, aromatic H of pyrazole), 4.7 (s,H of C5H), 5.15(s, H of C3H).

5-[1-N-phenyl-3-phenyl-pyrazole]-2-oxo-1-N-(4'-bromo-N-phenyl-sulfonamide)-3,5-dihydro1H-pyrrole-4-(2'-benzimidazole): IR (Cm-1): 3030(Ar-C-H str.), 1670 (C=O str. of COOH),1717 (C=O of pyrrole-2-one), 32503330 (-NH of –SO2NH), 1040 (N-N str.), 3377 N-H of benzimidazole NMR(δ,ppm): 6.13-8.13 (m, aromatic H of pyrazole), 4.7 (s,H of C5H), 5.15(s, H of C3H).

5-[1-N-phenyl-3-phenyl-pyrazole]-2-oxo-1-N-(4'-nitro-N-phenyl-sulfonamide)-3,5-dihydro1H-pyrrole-4-(2'-benzimidazole): IR (Cm-1): 3030(Ar-C-H str.), 1670 (C=O str. of COOH),1717 (C=O of pyrrole-2-one), 32503330 (-NH of –SO2NH), 1040 (N-N str.), 3377 N-H of benzimidazole NMR(δ,ppm): 6.13-8.15 (m, aromatic H of pyrazole), 4.7 (s,H of C5H), 5.15(s, H of C3H).

Result and Discussion: Structures of all synthesized compounds were confirmed by analytical and spectral data. The C, H, N and Scontents of the prepared compounds were consistent with their predicted structures as shown in Scheme-I. The infrared spectra show the band in the region 1680-1710cm-1 for carbonyl (>C=O) group, which is the characteristic band for the cyclic 2H-pyrrole-2-one ring and 1040Cm-1(N-N str.), 3250& 3377Cm-1 N-H of benzimidazole. The proton magnetic resonance spectra of the prepared compounds show singlet at 5.15 δ for C-H proton at position-5 in the 2Hpyrrole-2-one ring and 8.13δ for benzimidazole derivative. All other signals are at their respective positions in the NMR (PMR) spectrum.

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