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Research Article

SYNTHESIS OF NEWER HETEROCYCLIC MOLECULES USING COMBINATION OF BENZIMIDAZOLE AND PYRAZOLE

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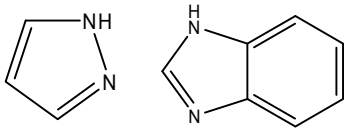
ABSTRACT
Benzimidazole and pyrazole are heterocyclic compound that play crucial roles in the function of a number of biologically important molecules. Benzimidazole and pyrazole derivatives have shown different therapeutic properties such as antiulcer, antihelminthic, antihypertensive, anticoagulant, antiallergic, analgesic, anti-inflammatory, antimicrobial, antiviral, antiparasitic, antioxidant etc. As per the literature the by simple nucleophillic reaction we formed the 1-(1H-benzoimidazol-1-yl)-2-chloroethanone. Then addition reaction with hydrazine to give 2-(1H-benzo[d]imidazol-1-yl) acetohydrazide. After that we use ethylacetoacatate to give 1-(2-(1H-benzo[d]imidazol-1-yl) acetyl)-3-methyl-1H-pyrazol-5(4H)-one by cyclisation. Followed by addition of different aldehyde to give newer heterocyclic derivatives. These all newer compounds were characterized by IR, MASS and NMR spectroscopy.
Key words: Benzimidazole, Pyrazole, IR, MASS, NMR

INTRODUCTION

Health, "the state of complete physical, mental and social well being and not just absence of discomfort or disease" is one of the basic human necessities and has been a constant worry. The sincere attempt by man to control or cure diseases has led to the search of newer drugs or suitable derivatives of the existing drugs.

Heterocyclic compounds having five or six membered ring with at least one hetero atom as the ring member, that are relatively stable and exhibit aromatic character.[1]



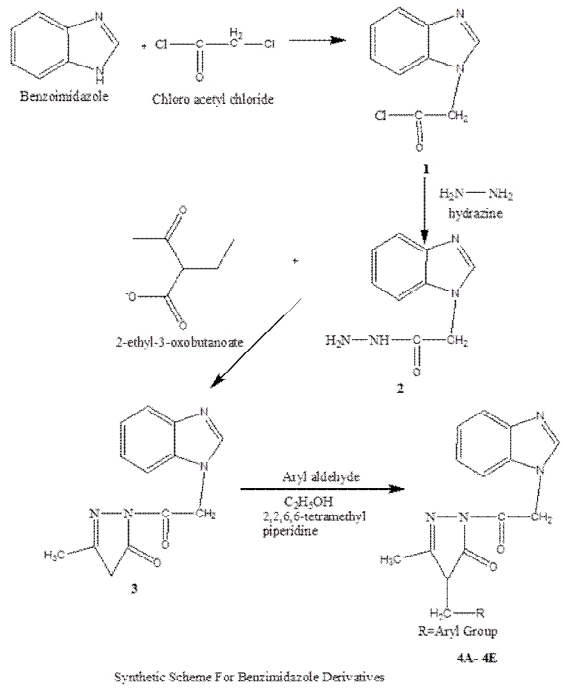
Pyrazole Benzimidazole

Benzimidazole and pyrazole are heterocyclic compound that play crucial roles in the function of a number of biologically important molecules. Benzimidazole and pyrazole derivatives have shown different therapeutic properties such as antiulcer, antihelminthic, antihypertensive, anticoagulant, antiallergic, analgesic, anti-inflammatory, antimicrobial, antiviral, antiparasitic, antioxidant etc. It is also reported that, the heterocycles nucleus is an essential part of many antineoplastic derivatives.[2,3,4,5,6,7]

Benzimidazole and pyrazole act by intercalation or block cell growth by inhibit the enzymes directly responsible for the formation of nucleic acids. For example, the topoisomerases, a group of enzymes that are responsible for the super coiling, cleavage and rejoining of DNA, are inhibited by a number of such heterocyclic rings containing compounds. This inhibition is believed to prevent DNA transcription.[8]

EXPERIMENTAL

Synthetic scheme[9,10]



Synthetic Scheme For Benzimidazole Derivatives

Methods of Preparation

Preparation of 1-(1H-benzoimidazol-1-yl)-2-chloroethanone [1]

1mole of benzimidazole, 1mole chloroacetylchloride, acetone and ferrous chloride were mixed in round bottom flask. The reaction mixture was refluxed for 3 hrs. The reaction mixture was cooled on ice bath. The precipitates were filtered and washed with cold water. The product was recrystallised from ethanol. % yield is 75.66% and melting point of compound is 104-107˚C.

Preparation of 2-(1H-benzo[d]imidazol-1-yl) acetohydrazide [2]

In a solution of 1 mol of 1-(1H-benzoimidazol-1-yl)-2-chloroethanone and ethanol add 1 mol hydrazine hydrate

were mixed in round bottom flask. The reaction mixture was refluxed for 5 hrs. The excess ethanol was removed under vacuum and reaction mixture was allowed to cooled on icebath. And dilute it with ice cold water. The precipitates were filtered and washed with ice cold water. The product was recrystallised from ethanol. % yield is 54% and melting point of compound is 129-132˚C.

Preparation of 1-(2-(1H-benzo[d]imidazol-1-yl) acetyl)-3-methyl-1H-pyrazol-5(4H)-one [3]

A mixture of 1 mol 2-(1H-benzo[d]imidazol-1-yl) aceto hydrazide and 1 mol ethyl acetoacetate were heated on water bath for 3 hrs. The reaction mixture was allowed to cooled on icebath. The precipitates were filtered and washed with ether. The product was recrystallised from ethanol. % yield is 65% and melting point of compound is 178-184˚C.

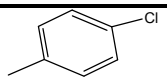
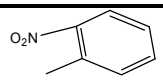
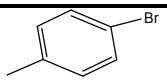
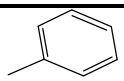
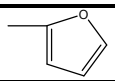
Preparation of compound 4A-4E

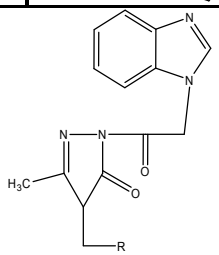
An equimolar quantity of 1-(2-(1H-benzo[d]imidazol-1-yl) acetyl)-3-methyl-1H-pyrazol-5(4H)-one and aryl aldehyde mixed. Add 2 ml ethanol followed by 1-2 drops of 2, 2, 6, 6-tetramethyl piperidine. Reflux it for 2 hrs at 90˚C. Cool the reaction mixture, after cooling, the solid mass was scraped out from the flask and placed in to flask containing 95% ethanol (20 ml) and filter it. Recrystallize it with ethanol.

RESULT AND DISCUSSION

Spectral characterization

The melting point of the synthesized compounds were determined in open capillary using VEEGO MELTING POINT APPARATUS model VMP-D and recorded in Celsius without correction. The Infrared spectra for the synthesized compounds were recorded using SHIMADZU-FTIR 8400S spectrometer using KBr as a back ground. Also using JASCO-FTIR 5300 and BUCK SCIENTIFIC INC. M500. NMR spectra of the synthesized compounds were taken using BRUKER ADVANCE-II 400 MHZ, VARIAN MERCURY YH-3OO MHZ, BRUKER ADVANCE-II 400MHZ and GEMINI-200MHZ "ciba" spectrometer using tetramethyl silane as an internal standard. Mass spectra of the synthesized compounds were taken using 2010EV LCMS SHIMADZU, SHIMADZU GL-MS.

Comp. No.	-R
4A	
4B	
4C	
4D	
4E	



Comp. No.	% Yield	M.P	Mol. Wt.	Mass (m/e)	IR(cm^{-1})	^{1}HNMR(δ ppm)
4A	53.67	165-169˚C	391	413.2 (M+Na)	1520 cm^{-1} (-C=C-) 3016&2937 cm^{-1} (-Ar) 815&864 cm^{-1} (p- substitution) 1599 cm^{-1} (-C=N-) 1520 cm^{-1} ($-CH_2$) 1715 cm^{-1} (-C=O) 1599 cm^{-1} (-CONH) 748&712 cm^{-1} (-Cl)	7.0-8.10 (m, 8H, Ar-H) 8.2 (s, 1H, imidazole) 4.0 (d, 2H, -CH2) 2.4 (s, 1H, methine, diazole) 3.0, 2.9 (s, 2H, -CH2 diazole)
4B	55.28	185-187˚C	391	391.9 (M+1)	3289&2919 cm^{-1} (-Ar) 821 cm^{-1} (o- substitution) 1320 cm^{-1} ($-CH_3$) 1703 cm^{-1} (-C=O) 1660 cm^{-1} (-CONH) 1551 cm^{-1} ($-NO_2$)	7.0-7.99 (m, 8H, Ar-H) 8.00 (s, 1H, imidazole) 4.6 (d, 2H, -CH2) 2.6 (s, 1H, methine, diazole) 3.2, 3.1 (s, 2H, -CH2 diazole) 1.2 (s, 3H, -CH3 diazole)
4C	58.25	180-186˚C	424	424.9 (M+1)	1516 cm^{-1} (-C=C-) 2914 cm^{-1} (-Ar) 808&875 cm^{-1} (p- substitution) 1599 cm^{-1} (-C=N-) 1456 cm^{-1} ($-CH_2$) 1711 cm^{-1} (-C=O) 679 cm^{-1} (-Br)	7.0-8.00 (m, 8H, Ar-H) 8.2 (s, 1H, imidazole) 4.9 (d, 2H, -CH2) 2.6 (s, 1H, methine, diazole) 3.0, 3.3 (s, 2H, -CH2 diazole) 1.1 (s, 3H, -CH3 diazole)
4D	51.25	150-153˚C	346	343.1 (M-3)	1600-1400 cm^{-1} (-C=C-) 2923&2846 cm^{-1} (-Ar) 1690-1640 cm^{-1} (-C=N-) 1460 cm^{-1} ($-CH_2$) 1727 cm^{-1} (-C=O)	7.1-8.00 (m, 8H, Ar-H) 8.02 (s, 1H, imidazole) 3.4 (d, 2H, -CH2) 2.09 (s, 1H, methine, diazole) 2.9, 2.6 (s, 2H, -CH2 diazole) 1.24 (s, 3H, -CH3 diazole)
4E	56.66	127-133˚C	337	336 (M-1)	1496 cm^{-1} (-C=C-) 3095&2925cm^{-1} (-Ar) 1672 cm^{-1} (-C=N-) 1496 cm^{-1} ($-CH_2$) 1672 cm^{-1} (-C=O) 1156&1016 cm^{-1} (-C-O-C-)	-

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