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SYNTHESIS AND ANTI OXIDANT ACTIVITY OF 1-BENZYL-2-(1H-INDOL-2YL)-1H-BENZO IMIDAZOLE

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ABSTRACT

Benzimidazoles are important class of heterocyclic compounds possessing interesting biological and Pharmacological properties as anti-inflammatory, anti-cancer, anti-bacterial, anti-viral, antipyretic, antiarrhythmic, tranquilizing, muscle relaxing, anticonvulsant, anti-diabetic and anti-fungal agents. It is a prototypical pharmaceutical lead structure in modern medicinal chemistry. It is an organic compound, it is an aromatic heterocyclic classified as a bicyclic compund. It is a highly polar compound. It is amphoteric in nature. I.e. it can function as both an acid and as a base.

KEYWORDS: benzimidazole, benzaldehyde, spectral analysis, anti oxidant.

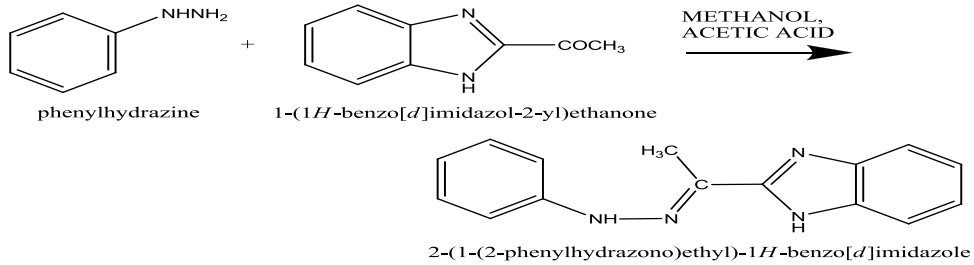
INTRODUCTION

Benzmidazole is the chemical species of heterocyclic ring compound with two nitrogen atoms are replacing carbon-hydrogen units in the 1 and 3rd position of cyclo pentane ring structure, classified as a bicyclic compund and having non-adjacent nitrogen atoms. Many anthelmintic drugs (albendazole, mebendazole, triclabendazole etc.,) belong to the benzimidazole class of compounds. The benzimidazole opiod family includes a number of strong agents eg. Etonitazene. Several dyes are derived from benzimidazole. It is involved in the synthesis of the antiandrogen Galeterone.

MATERIALS AND METHODS

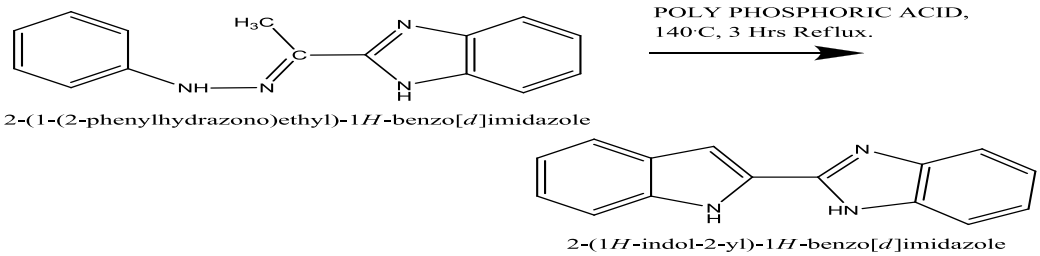
Scheme of the work

Step: 1 Synthesis of 2-(1-(2-Phenylhydrazono) ETHYL)-1H-Benzo Imidazole.



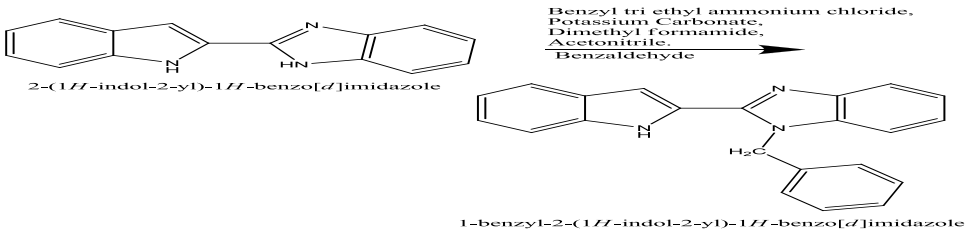
- A mixture of benzoimidazol ethanone 3.2gms and phenyl hydrazine (0.1mole), 50 ml of acetic acid and methanol (25ml) was reflexed for 3 hours.
- .At the end of this period the mixture was cooled and poured into ice cold water.
- The seperated solid was filtered, washed with water and dried to get crude product which on recrystallized from hot methanol gives pure 2-[1-(2-phenyl hydrazono)ethyl]1H benzoimidazole (compound-1).

Step. 2: Synthesis of 2-(1H-INDOL-2YL)-1H BENZO IMIDAZOLE.



- A mixture of polyphosphoric acid (PPA) 25 ml and 2-[1-(2-phenyl hydrazono)ethyl]1H benzoimidazole (compound-1) 0.1 mole in a 100ml round bottomed flask was heated with occasional stirring at 80˚C for 4 hours.
- At the end of this period, the mixture was cooled and poured into ice cold water.
- The seperated solid was filtered.
- The filtered solid was treated with a few drops of ammonia solution.
- The resulting solid was filtered and dried to obtain 2-(1H indol-2yl)1-H benzoimidazole (compound-2).
- The crude product obtained above was recrystalized from methanol-DMF solution to obtain pure compound-2.

Step. 3: Synthesis of N-(2-(1H-INDOL-2YL)1H BENZOIMIDAZOLE-1-YL) Benzamide.



• A mixture of compound-2 (0.1 mole), Pottasium carbonate (0.1 mole) benzyl triethyl ammonium chloride (TEBAC) 10mg, acetonitrile 20ml and benzaldehyde (0.1 mole) in a round bottomed flask was heated with occasional stirring for 5 hours.

• At the end of this period the mixture was poured into ice cold water.

• The separated solid was filtered and dried to obtain 2-(1H-indol-2yl)-1-aryl-1H-benzoimidazole (compound-3), which are recrystalized from hot methanol to obtain compound-3.

Physical characterization

✓ Molecular formula : $C_{22}H_{17}N_3$

✓ Molecular weight (gm) : 323.14g/mol

✓ Soluble in Methanol, Ethanol, Chloroform and DMSO.

✓ Melting point : 105ºC

✓ Melting points were determined using Veego Digital melting point apparatus.

✓ The purity of synthesis compound was monitored on TLC.

✓ Absorbent used : Precoated Silica gel- G plate

✓ Mobile Phase : Acetic acid : n-butanol : Water (7:3:1)

✓ R_f value: 0.80.

Biological screening

***In-Vitro* Anti-Oxidant Activity:** Free radicals are reactive atom or group of atoms that has one or more unpaired electrons, especially one that is produced in the body by natural biological processes or introduced from outside (as in tobacco smoke, toxins or pollutants) and that can damage cells proteins and DNA by altering their chemical structure. Free radicals are generally considered as a fragment of molecules and which are extremely reactive and short valid. They are produced continuously in cells either as accidental by products of metabolism or deliberately during phagocytosis. Free radicals can be formed in three ways.

- By the haemolytic cleavage of a covalent bond of a normal molecule, with each fragment retaining one of the paired electrons.
- By the addition of a single from a normal molecule.
- By the addition of a single electron to a normal molecule.

The later, electron transfer, is a far more common process in biological systems, than the other two. The most important free radicals in biological system are radical derivative of oxygen.

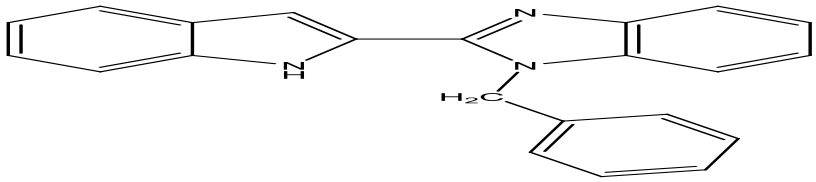
Nitric oxide radical-Scavenging Activity

Reagents

- Sodium nitroprusside
- Standard phosphate buffer solution
- Griess Reagent (mixing the equal volume of 1% sulphanilamide in 2% phosphoric acid & 0.1% naphthyl ethylene diamine dihydrochloride in water).

Standard: Ascorbic acid

Spectral analysis



IUPAC Name

1-benzyl-2-(1*H*-indol-2-yl)-1*H*-benzo[*d*]imidazole

RESULTS AND DISCUSSION

^{1}HNMR Interpretation

^{1}HNMR Spectral data Absorption position (in PPM)	
7.32 - 7.61	m, 6H, CH
6.20 – 6.36	d, 6H, CH
5.24	s, 2H, CH_2
4.61	d, 2H, NH

Synthesis: The present study report the synthesis of benzimidazole derivatives nucleophillic substitution of phenylhydrazine with 1-(H-benzoimidazole-2yl) ethanone was carried out stepwise at different temperature. The first step involves substitution of 1-(H-

benzoimidazole-2yl) ethanone and the next by polyphosphoric acid. The final benzimidazole derivative in the synthesized compound 3 was replaced by benzaldehyde. Since the report regarding this compound suggest a benzimidazole posses a good bioactive moiety.

Physical Characterization: Melting points of the synthesized compound was taken in open capillary tubes and was uncorrected and were found to be in the range 100-120˚C.

TLC was performed using precoated silica gel plates of 0.25mm thickness. Eluents used were Acetic acid: n-butanol: Water (7:3:1) spots were visualized in U.V. light.

At room temperature solubility of newly synthesized compounds were determined by various organic solvents and it was found that all compounds were freely soluble in Methanol, Ethanol, DMSO and DMF.

***IN-Vitro* Anti-Oxidant Activity**

In the assay, 2ml of sodiumnitroprusside (10mM) in 0.5ml phosphate –buffered saline (PBS) was mixed with 0.5ml of different concentration of sample ranging from (50-250µg/ml) prepared in methanol and incubated at 25ºC for 150min. A control without the test compound, but with an equivalent amount of methanol, was taken. After 30 min, 1.5ml of incubated solution was removed and diluted with 1.5ml of Griess reagent. Absorbance of chromosphore formed during diazotization of the nitrite with sulphanilamide and subsequent coupling with NEDD was measured at 546nm and the percentage scavenging activity measured with reference to the standard.

$$\% \text{ inhibition} = \frac{\text{Abs.control-Abs.of test}}{\text{Abs. control}} \times 100$$

Compounds	50µg/ml	100µg/ml	150µg/ml	200µg/ml	250µg/ml
S_1	59	63	70	81	86
STD	64	69	77	85	92

CONCLUSION

In the present study certain benzimidazole derivatives were synthesized and characterized by^{1}HNMR. The synthesized compound show characteristic absorption peaks –in ^{1}HNMR spectra. Expected molecules in (m+) fragments were observed for the entire compounds in mass spectra. The synthesized compound was subjected to biological evaluation. The

compound were evaluated for anti-oxidant studies revealed that the substitution of different aromatic amines to parent benzimidazole nucleus show the moderate activity.

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