Research Article

Design, Synthesis and Evaluation of Novel Triphenyl Imidazole Derivatives Through *In silico* Studies

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ABSTRACT

This study focuses on the design, synthesis and insilico analysis of novel Triphenyl imidazole derivatives. Debus– Radiziszewski imidazole synthesis is a simple and highly efficient method for synthesis of 2, 4, 5 - triphenyl imidazoles derivatives. Microwave assisted synthesis has emerged as a new lead in organic synthesis which makes the synthetic chemistry easy and effective. The structural integrity of the synthesized compounds was confirmed via comprehensive spectroscopic techniques, including Infrared Spectroscopy (IR). Molecular docking is studied to predict the binding affinity of ligands to receptor proteins. These findings not only validate the successful synthesis of the Triphenyl imidazole derivatives but also highlight their potential for further drug development.

Keywords: 2, 4, 5-Triphenyl imidazole, benzaldehydes, Taurine dehydrogenase inhibitor, Triphenyl imidazole derivatives.

INTRODUCTION

Drug discovery is a process which aims at identifying a compound therapeutically useful in curing and treating disease. This process involves the identification of candidates, synthesis, characterization, validation, optimization, and screening for therapeutic efficacy. Once a compound has shown its significance in these investigations, it will initiate the process of drug development earlier to clinical trials.

2, 4, 5 -TRIPHENYL IMIDAZOLE derivatives are an important class of heterocyclic compounds. Imidazoles is an important skeleton, which is playing a role in the preparation of substances with different biological activities. Imidazoles are known to possess antimicrobial, antifungal, antibacterial, bacteriostatic, antitumor, anti-HIV, antitubercular, etc.

2, 4, 5-Triphenyl imidazole is formed by the fusion of, benzil and benzaldehyde. Molecular weight of the 2, 4, 5, - Triphenyl imidazole is 296.37g/mol, with a molecular formula of $C_{21}H_{16}N_2$, and it is a Yellowish white crystalline powder, at standard conditions. Chemically, it is a high melting solid, purified by recrystallization, and has a melting point 274-278°C and occur as solid with 97 % purity. The compounds were synthesized under microwave irradiation method. This method of synthesis was affording the remarkable advantage such as inexpensive, simple procedure, much faster (1-3mins) reaction and high yield of products[1, 2].

MATERIALS AND METHODS

The common procedure for their synthesis Debus-Radiziszewski imidazole synthesis, in this method condensation occurs between benzyl, ammonia and aldehydes like benzaldehyde, p- bromobenzaldehyde, p-hydroxybenzaldehyde, p-chlorobenzaldehyde, p-nitrobenzaldehyde, p- methoxybenzaldehyde, p-dimethylaminobenzaldehyde, p-tolualdehyde. Therefore, the condensation of Benzil with various benzaldehydes results in formation of various 2, 4, 5-triphenyl imidazole derivatives[1, 7].

5g benzil, 5g different aldehydes and to this 2ml ammonia is added and stirred well and is placed in microwave oven. Place it for 2 mins. Then it is cooled, filtered and dried. It is recrystallized using ethanol as solvent, the given fig 1 is showing the schematic representation of the synthesis.

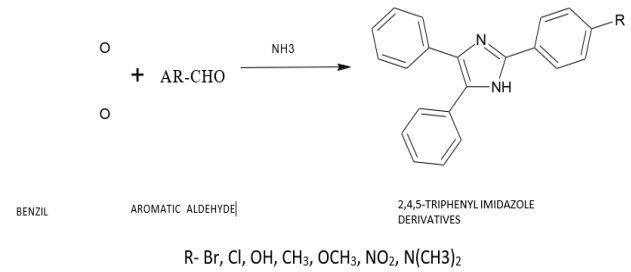


Figure 1: General scheme for the method of synthesis

Thin layer chromatography was conducted with synthesized product. The TLC plate is prepared by spreading with silica and is dried in oven at 110°C for 30mins. Then the solvent system is prepared, chloroform: ethanol in ratio 9:1. Sample and reagents are spotted 1cm away from the bottom of the plate. Total 8 plates were prepared for each product. The plate is dipped in the solvent taken in a beaker in a manner that the spots will not dip completely and allow the solvent to rise 2/3rd of plate height for better and effective result. Melting point was determined by open tube capillary method[3].

FTIR Sample is prepared by taking small amount of sample and triturating well. Ensure that the FTIR instrument is properly calibrated, typically using a polystyrene standard

or other suitable calibration material. Maintain appropriate temperature and humidity levels, as moisture can affect the readings. Take a pinch of sample place it in the FTIR sample holder, make sure it is properly aligned in the optical path of the instrument. Start the FTIR analysis. The instrument will pass infrared light through the sample. The sample will absorb specific wavelengths of infrared light corresponding to its molecular vibrations[4]. The resulting spectrum will display the absorbance or transmittance against the frequency (wavenumber) in cm^{-1}.

Molinspiration:

Using MOLINSPIRATION software physico-chemical properties was determined.

Table 1: Physical and spectral characterization of the synthesized compounds

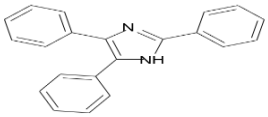
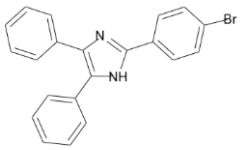
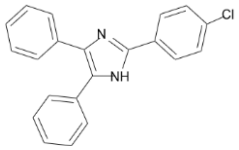
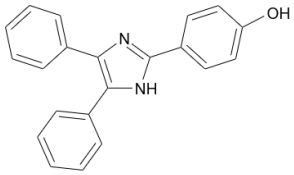
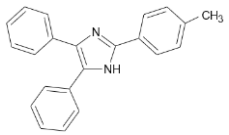
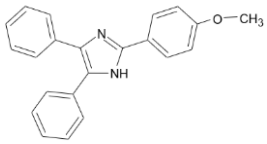
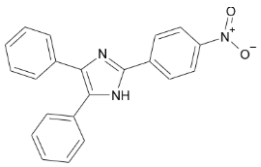
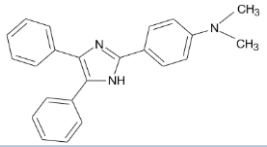
Sl No.	Compound	Molecular formula	Melting point	Color	IR spectrum (cm^{-1})
1.	Tb1 	$C_{21}H_{16}N_2$	264°C	Pale yellow	C=N (1640cm^{-1}), C-C (1200cm^{-1}), C=C (1450cm^{-1}), N-H (1600cm^{-1}), C-N (1100cm^{-1})
2.	Tb2 	$C_{21}H_{15}N_2Br$	150°C	Yellowish white	C=N (1640cm^{-1}) C-C (1200cm^{-1}) C=C (1450cm^{-1}) N-H (1600cm^{-1}) C-N (1100cm^{-1}) C-Br (650cm^{-1})
3.	Tb3 	$C_{21}H_{15}N_2cl$	210°C	Yellow	C=N (1640cm^{-1}), C-C (1200cm^{-1}), C=C (1450cm^{-1}), N-H (1600cm^{-1}), C-N(1100cm^{-1}), C-Cl (750cm^{-1})
4.	Tb4 	$C_{21}H_{15}N_2O$	110°C	Yellowish white	C=N 1640cm^{-1}), C-C (1200cm^{-1}), C=C 1450cm^{-1}), N-H 1600cm^{-1}), C-N (1100cm^{-1}), O-H(3100cm^{-1}), C-O (1048cm^{-1})
5.	Tb5 	$C_{22}H_{18}N_2$	84°C	Dark yellow	C=N (1640cm^{-1}), C-C (1150cm^{-1}), C=C (1450cm^{-1}), N-H (1600cm^{-1}), C-N (1100cm^{-1})
6.	Tb6 	$C_{22}H_{18}N_2O$	92°C	Yellow	C=N 1640cm^{-1}), C-C (1200cm^{-1}), C=C 1450cm^{-1}), N-H 1600cm^{-1}), C-N (1100cm^{-1}), C-O (1045cm^{-1})
7.	Tb7 	$C_{21}H_{15}N_3O_2$	198°C	Yellowish white	C=N 1640cm^{-1}), C-C (1200cm^{-1}), C=C 1450cm^{-1}), N-H 1600cm^{-1}), C-N(1100cm^{-1}), N-O (1350cm^{-1})
8.	Tb8 	$C_{23}H_{21}N_3$	90°C	Pale yellow	C=N (1640cm^{-1}), C-C (1200cm^{-1}), C=C 1450cm^{-1}), N-H (1600cm^{-1}), C-N (1100cm^{-1})

Table 2: PASS prediction results for the synthesized compounds against various enzymes

Sl No.	Compound	Taurine dehydrogenase inhibitor		Glycosylphoshatidyl inositol phospholipase D inhibitor		Centromere associated protein inhibitor	
		pa	pi	pa	pi	pa	pi
1.	Tb 1	0.817	0.010	0.833	0.008	0.750	0.005
2.	Tb 2	-	-	-	-	0.869	0.003
3.	Tb 3	0.817	0.010	0.871	0.004	0.771	0.005
4.	Tb 4	0.792	0.014	0.721	0.30	-	-
5.	Tb 5	0.776	0.017	-	-	0.753	0.005
6.	Tb 6	0.773	0.017	-	-	-	-
7.	Tb 7	0.703	0.031	-	-	-	-
8.	Tb 8	0.894	0.004	0.768	0.019	-	-

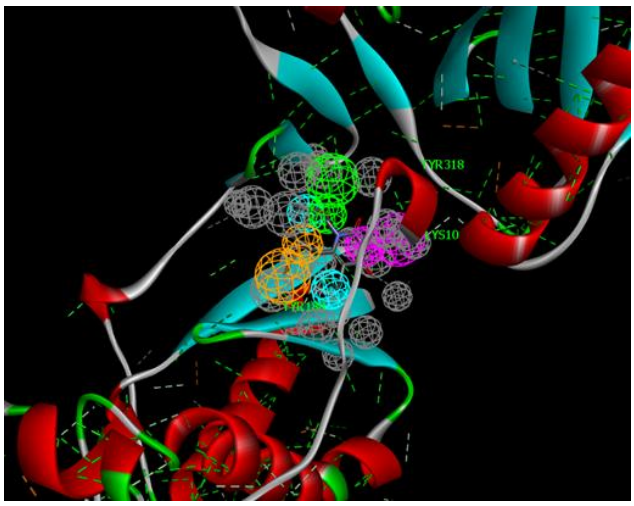


Figure 2: Docking interaction of Tb5 against Taurine dehydrogenase

PASS prediction:

The structure of a molecule may be drawn using Chemsketch. The structure of the molecule may be saved Chemsketch document then converted into Smiles format and utilized to predict the biological spectrum using the PASS online version. The result was presented as Pa (probability for active compound) and Pi (probability for inactive compound). Here, Pa > Pi is considered on the scale of 0.000–1.000, and in general, Pa + Pi ≠ 1. The PASS prediction results were interpreted and used in a flexible manner. When Pa > 0.7, the chance to find the activity experimentally is high; if 0.5 < Pa < 0.7, the chance to find the activity experimentally is less, but the compound is probably not so similar to known pharmaceutical agents[5].

Molecular docking:

PYREX software is used for molecular docking. Pass prediction is conducted and this process often involves screening various compounds against different receptors, then analyzing which receptor interactions lead to the most potent biological effects and selecting the one with the highest activity which is taurine dehydrogenase inhibitor is identified. Obtain the 3D structure of the protein (receptor) from a structural database like PDB (Protein Data Bank). Also, the 3D structure of ligand is taken from CHEMSKETCH SOFTWARE. Specify the location of binding pocket. Amino acids of both A and B chain was selected. Input the prepared protein and ligand structures along with the selected docking parameters. Analyze the docking score and determined the affinity of binding[6].

Table 3: Binding affinity of the synthesized compounds against Taurine dehydrogenase

Sl No.	Compound	Binding affinity
1.	Tb 1	-7.1
2.	Tb 2	-7.6
3.	Tb 3	-7.0
4.	Tb 4	-7.5
5.	Tb 5	-9.7
6.	Tb 6	-9.4
7.	Tb 7	-8.0
8.	Tb 8	-7.5

RESULT AND DISCUSSION

Various derivatives of 2, 4, 5 - Triphenyl imidazole were synthesized by microwave assisted method. It's structure and properties were determined using various software such as Chemsketch, Molinspiration, PASS prediction and docking using PYREX. Purity of synthesized compounds were identified by TLC. The melting point was determined by open tube capillary method and the physico-chemical properties were calculated using Molinspiration. The physical properties and the results of IR spectroscopy are given in the Table 1.

PASS prediction:

After conducting the PASS prediction, it is observed that in most of the synthesized compounds the value of pa is greater than 0.7 in taurine dehydrogenase inhibitor. The result of pass prediction is given in the Table 2 and Fig. 2 shows the interactions:

Molecular docking:

In docking studies, the selected protein is taurine dehydrogenase inhibitor (1gqw) obtained from protein data bank. The binding affinity of the compounds is mentioned in Table. 3. The compounds Tb5 and Tb6 shows greater binding affinity towards taurine dehydrogenase inhibitor.

FUTURE ASPECTS

Triphenyl imidazole can be considered as a privileged structure. Due to the emergence as an important chemical moiety, demonstrating a wide range of physicochemical and biological activities, Triphenyl imidazole has become an important subject of extensive research. It possesses unique physicochemical properties that provide a huge possibility of a large number of targeted modifications. The scientific world has witnessed several researches utilizing Triphenyl imidazole possess antifungal, antimicrobial, anti-cancer and enzyme inhibition. Therefore, immense effort has been taken in the development of newer synthetic strategies as well as novel methodologies to modify the Triphenyl imidazole framework with proper functional groups. These lead to develop future potent therapeutic agents with limited side effects which used for removing pollutants, such as heavy metals or organic toxins, from the environment. This could contribute to environmental remediation efforts. The future of Triphenyl imidazole looks promising, especially if its potential in diverse fields can be fully realized through continued research and innovation.

CONCLUSION

In conclusion, among the seven synthesized derivatives of 2,4,5-Triphenyl imidazole, certain modifications have enhanced biological activity, with Tb5 (bearing a methyl group, CH_3) demonstrating the most promising results. Molecular docking studies indicate that Tb5 exhibits a stronger binding affinity for the selected receptor, suggesting its potential as a lead compound for further optimization. These findings highlight the significance of structural modifications in improving bioactivity and provide a foundation for future drug development efforts.

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