A Facile And Efficient Novel Synthesis Of 2-iodo-imidazo [2,1] thiazole Derivatives By Using Bleaching Earth Clay pH-12.5 / PEG-400 As An Environment-Benign Catalyst And Its Anti-Microbial Activity.

Prashant P. Mogle[1,2], Sunil V Gaikwad[3], Santosh Pohare[5], Madhav Hebade[6], Milind Gaikwad[4], Bhaskar S. Dawane[1]*

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Abstract

Here in we reported the green and novel protocol for the synthesis of 2-iodo-imidazothiazole derivatives from substituted phenacyl bromides and substituted 2-amino-4-aryl thiazoles using BEC (pH 12.5, 10% by weight) as a recyclable heterogeneous catalyst in environmentally sustainable reaction medium PEG-400. The anti-microbial activity was evaluated by using a disc diffusion assay with Staphylococci Aureus (MTCC-96), Escherichia coli, (MTCC-1588), and Candida albicans (MTCC-3018). According to the antimicrobial results the compounds 3**b**, **3c**, **3e**, **3f**, and **3k** had good antimicrobial activity. This result helps us for the identification of lead compounds with a 50% inhibitory concentration (IC50) of 18 to 28 mm Consequently, the molecular docking with PDB:2Q85 Crystal Structure of *E. Coli* and PDB:3u2d *S. aureus* GyrB ATPase shows all the molecules are well packed in the active sites of the selected protein. The derivatives were characterized using spectroscopic methods, Molecular docking and screened for antimicrobial strains. The current method has several advantages, including catalyst recyclability, superior product yield, a quicker reaction time, and the absence of hazardous reagents.

Keywords: 2-iodo-imidazothiazole, 2-amino-4-aryl thiazoles, Bleaching earth clay, and PEG-400.

[1]School of Chemical Science, Swami Ramanand Teerth Marathwada University, Nanded- 431606, India
[2]Sonopant Dandekar Arts, V.S Apte Commerce, and M.H. Mehta Science College, Palghar-401404, India
[3]Department of Organic Chemistry, Faculty of Natural Sciences, Comenius University in Bratislava, Ilkovicova 6, 842 15 Bratislava, Slovakia,
[4]VPMK's Arts, Commerce and Science College, Kinhavali, Thane-421403, India
[5]Badrinarayan Barwale Arts, Commerce and Science College, Jalna-431213, India
[6]Dr. D. Y. Patil Arts, Commerce and Science College, Affiliated to Savitribai Phule Pune University, Pune, 411018

***Corresponding Author: -** Bhaskar S. Dawane
*School of Chemical Science, Swami Ramanand Teerth Marathwada University, Nanded- 431606, India

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1. INTRODUCTION

Fused heterobicyclic systems containing bridgehead nitrogen and sulphur atoms have recently gained immense significance in medicinal chemistry and health because of their intriguing chemical, biological, and pharmacological properties. In that, imidazothiazole derivatives are particularly appealing due to the bis heterocyclic moieties i.e., imidazole and thiazole fused together and exhibit a broad range of biological activity and pharmacological diversity[1]. Imidazothiazole analogue shows pledge as antimicrobial[2,3], anti-tuberculosis[4,5] , antibacterial[6], anti-inflammatory[7,] and anticancer activities[8,9]. Imidazothiazole ring is present as a key structural motif in several drug molecules like Levamisole[10], pifithrin-β[11], and anxiolytic agent[12]. As a result of the renowned chemical and biological significance of the imidazothiazole ring, the organic community has been drawn to develop an ideal method for the synthesis of imidazothiazole and its derivatives.

Therefore, extensive research has been conducted to develop synthetic methods for forming the imidazothiazole ring. In the acetic acid, formalin, and amines, the α-Bromo-4-(methyl sulfonyl) acetophenone was added and stirred at 50 ^oC[13], by reacting 4-phenylthiazol-2-amine, aromatic aldehyde, and isocyanide in ethanol at 50 ^oC[14], oxidative cyclization of 2-amino benzothiazole and ketone via $FeCl_3/ZnCl_2$ catalysed[15], one-pot Pd-catalysed bi-cyclization of tert-butyl isonitrile with thioamides, the reaction of amines and imidazo [2,1-b] thiazole-5-carboxylic acid[16], and two-step reaction between 1H-benzo[d]imidazole-2-thiol & ethyl-4-chloro-oxo butanoate along with cyclization in presence of sulphuric acid[17].

The disclosed methods have some drawbacks like using hazardous chemicals, toxic or metal catalysts, reactions requiring longer time, higher temperature, and low product. In spite of the limitations of the reported methods, there is still an immense chance to design and develop new catalysts for the synthesis of imidazothiazole that are environmentally friendly.

Sustainable chemistry is a buzzword that refers to efficient, safe, and effective chemical methods for synthesizing bioactive molecules. Bleaching earth clay (pH 12.5) has emerged as a consistent heterogeneous catalyst that domiciles several green chemistry concerns such as being easily separable, eco-friendly, economical, and non-toxic[18]. BEC have been used as catalysts in various base-catalyzed chemical conversions due to their green properties and potential to improve rate and selectivity[19,20]. The clay's tiny grain size results in a large surface area as compared to other solid-supported catalysts. Another feature of sustainable chemistry is the replacement of green solvents such as polyethylene glycol-400 (PEG-400) for hazardous solvents[21]. PEG-400 has been developed as alternative green reaction media with unique properties such as thermic stability, economic viability, non-volatility, immiscibility with a variety of organic solvents, and recyclability[22,23].

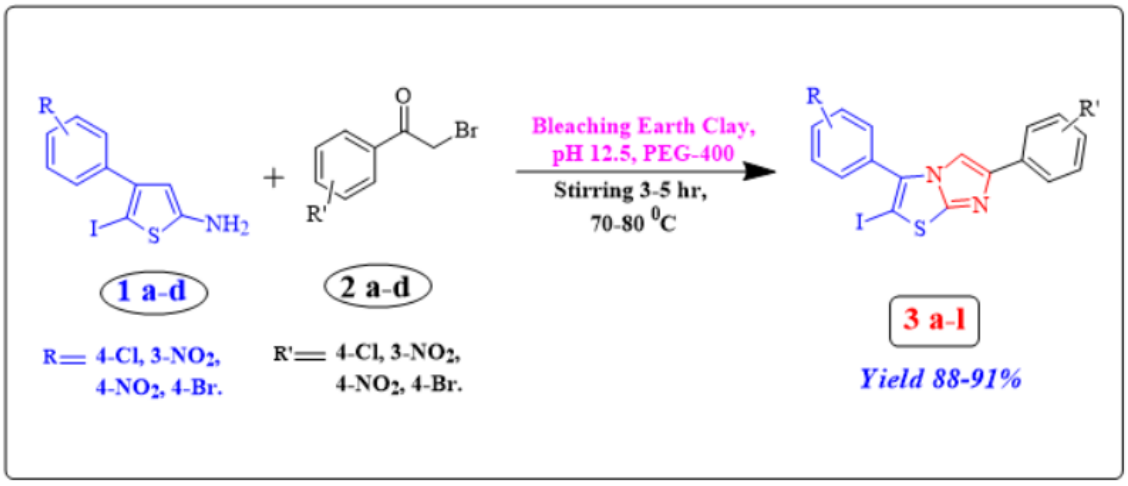
Multi-drug-resistant microbes and drug-resistant fungi are being reported globally several years after their appearance, hiring to the complexity of anti-microbial therapies[24,25]. The design and investigation of new compounds in order to prevent antimicrobial resistance and develop effective treatments. Halogenated aromatic compounds are a significant class of building blocks used in the synthesis of heterocycles and as therapeutic ingredients[26,27]. Here, we report a simple and dynamic methodology for synthesizing 2-iodo-imidazo [2,1] thiazole derivatives[28] from 5-iodo-2-amino thiazole and substituted phenacyl bromide. The molecular structure of the derivatives was confirmed by spectral data. They were explored for their anti-microbial activities and molecular docking application.

We are in continuous research on to finding out the potential multi-drug-resistant microbes[29, 30, 31]. here in we have prepared novel 2-iodo-imidazo [2,1] thiazole derivatives with greener method[32].

1.2 Results and Discussion

1.2.1 Chemistry

As part of our ongoing interest in improving the practicability and eco-friendliness of bioactive compound synthesis, we present here a simple, eco-friendly method. A mixture of iodinated substituted thiazole (0.001 mol) (**1 a-d**) was taken in green solvent PEG-400 and stirred for about 1 hour at 50-60 ^oC using Bleaching earth Clay (pH 12.5 10wt %). Subsequently in reaction mixtures slowly add substituted phenacyl bromide (0.001 mol) (**2 a-d**) and continue the stirring for 4 hours with a rising temperature of 70-80 ^oC. **(Scheme 1.1)** After complete conversion as indicated by TLC, the catalyst was filtered out by simple filtration and the mother liquor was poured onto ice-cold water, the solid separated out, neutralized, and filtered out the product. The resultant product was dried and recrystallized from methanol.



Scheme 1.1 Synthetic pathway of 2-iodo-imidazo [2,1] thiazole derivatives.

All the compounds were thoroughly characterized by the spectral analysis technique. The IR spectra for compound (**3b)** show the signal at 2900-3000 cm^{-1} characteristics for the Ar-CH, the band appears at 650-700 cm^{-1} for C-I stretching. In 1H NMR spectra for all nine protons at δ 7.32 – 8.55 ppm are appearing in the aromatic region in the form of multiplet. Moreover, the mass spectrum of compound (**3b**) indicates the molecular ion peak [M+H] at 472.3 confirming the formation of the imidazothiazole nucleus.

The reaction parameters were optimized by the classic reaction of 4-chlorophenyl-iodothiazol-2-amine and 4-chloro phenacyl bromide. Initially, we considered solvent parameters and studied reactions in different solvents like water, methanol, ethanol, DMSO, and PEG-400. It was observed that the imidazothiazole formation in PEG-400 solvent proceeds with excellent yield (**Table 1.1, entry 6**). Whereas reactions in methanol, ethanol, and DMSO solvent afforded a low yield of the product (**Table 1.1, entries 2–4**). No product formation was observed when water was used as a solvent (**Table 1.1, entry 1**). 4-chlorophenyl-iodothiazol-2-amine in optimized reaction condition 10 wt.% BEC (pH 12.5) catalyst and solvent play a key role in the activity and performance of the catalyst. We were able to further evaluate catalyst loading after seeing promising results with PEG-400 as a solvent over a 10 wt.% BEC pH 12.5 catalyst. It reveals that a catalyst loading of 10% BEC pH 12.5 is sufficient for the desired conversion. While 20 wt.% BEC pH 12.5 loading did not result in a significant increase in product yield. This result inspires us to investigate the methodology scope for the synthesis of imidazothiazole using PEG-400 as a solvent.

Table 1.1: Screening of reaction condition with respect to solvent and catalyst loading 3a**a**

Entry	Solvent	Catalyst	Yield **b** (%) b
1	Water	BEC (5 wt.%)	0
2	Methanol	BEC (5 wt.%)	50
3	Ethanol	BEC (5 wt.%)	52
4	DMSO	BEC (5 wt.%)	60
5	PEG-400	BEC (5 wt.%)	80
6	PEG-400	BEC (10 wt.%)	91
7	PEG-400	BEC (20 wt.%)	80

a Reaction conditions: Phenacyl bromide (0.001 mole), 5-iodo-2-amino thiazole (0.001 mmol), 10 wt.% BEC (pH 12.5) in 10 ml PEG-400, at 70-80 ºC for 30 min. b Isolated yields after crystallisation.

The result signified that 10 wt.% BEC (pH 12.5) was found to be sufficient to produce a yield of the product of up to 91% with the successful completion of the reaction. The used catalyst can be recycled and reused without further purification for the next reaction. The catalytic activity of the catalyst was evaluated using the BEC for 5-6 runs, and it was

noticed that the catalyst had good catalytic power for up to five runs with minimal loss of activity.

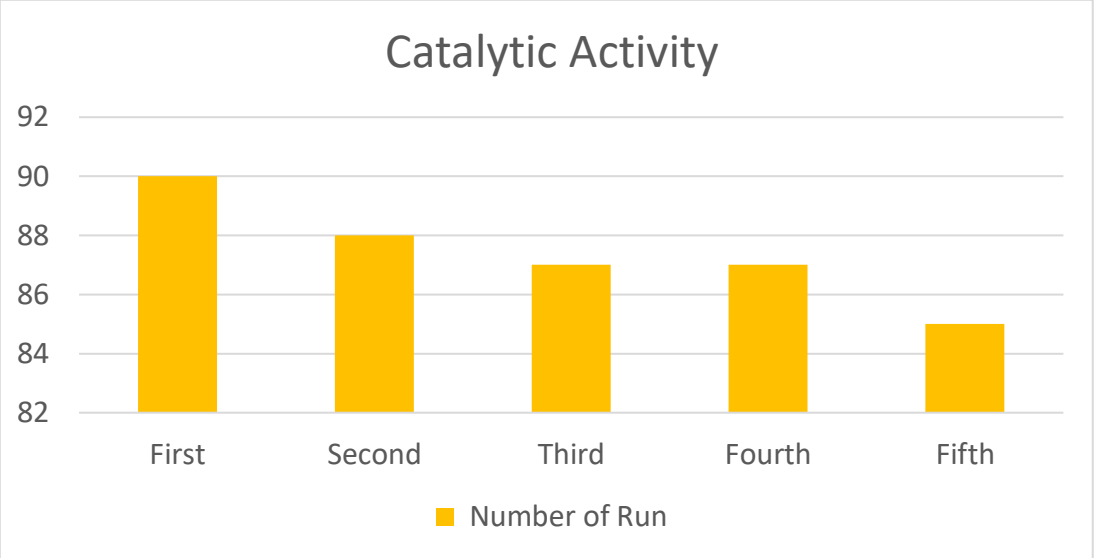
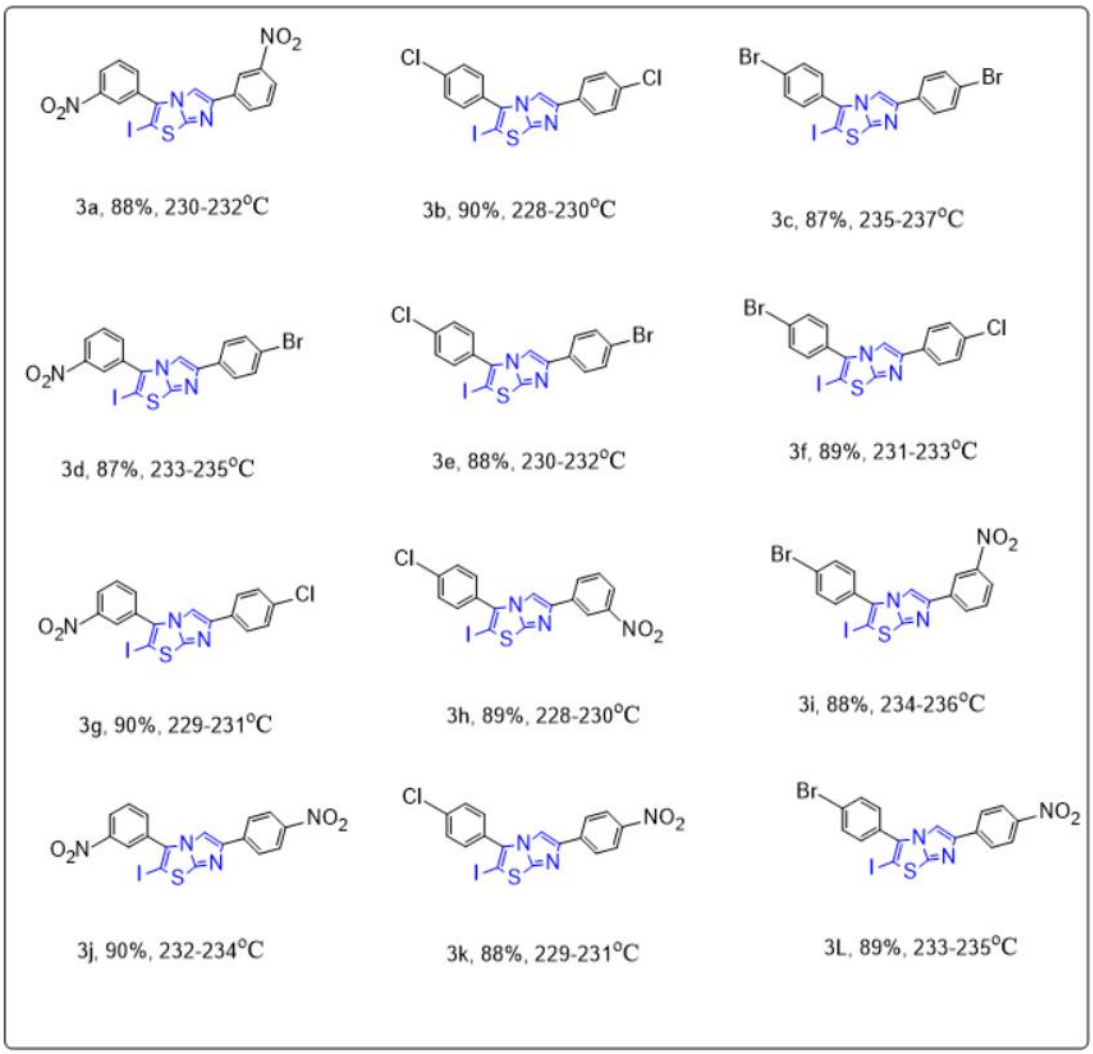
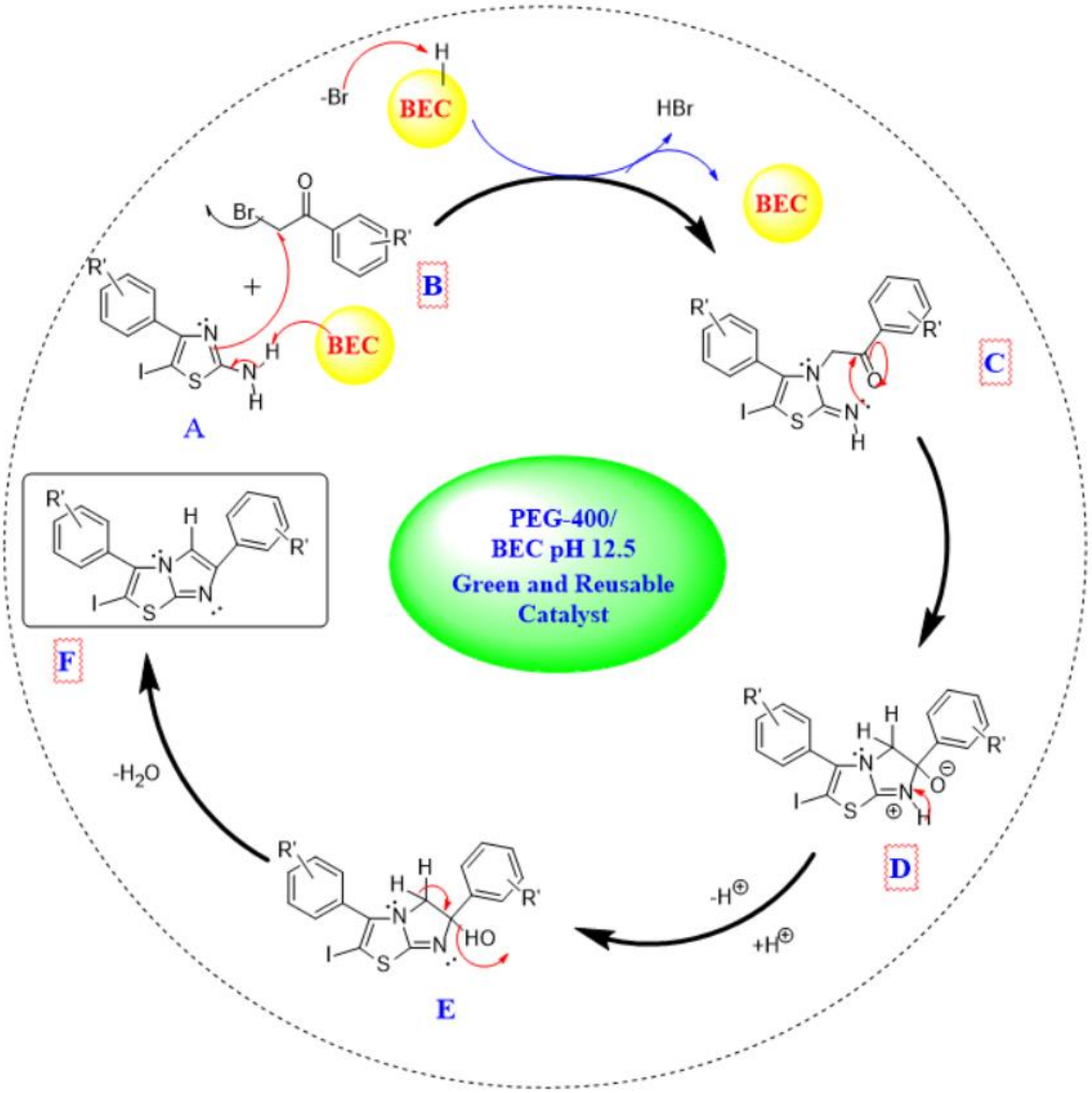


Table 1.2 Physico-chemical data of synthesized derivative (3a-l)



Yield in %. M.P. ^{0}C.

The plausible pathway for the expected reaction is shown in **Scheme 1.1**. The reaction begins with the abstraction of the proton from substituted iodothiazol-2-amine (**A**) in the presence of BEC (pH 12.5) and then reacts with substituted phenacyl bromide (**B**), to form intermediate steps **C**, **D**, **E**, and finally, cyclization with dehydration occur to offer desired product 2-iodo-imidazo [2,1] thiazole derivatives. (**F**)



Scheme 1.2. A plausible mechanistic way for the synthesis of 2-iodo-imidazo [2,1] thiazole derivatives. (**3a-l**)

1.2.2 Biology:

Antimicrobial activity.

The newly synthesized compounds (**3a-l**) were evaluated for their antimicrobial activity against two bacteria strains viz. Staphylococci Aureus, Escherichia coli, and one fungal strain Candida albicans using disc diffusion assay, and the results are abbreviated graphically in (**Fig. 1.3**) which clearly indicates the differential acuteness of bacteria strains & fungal strains to the used test samples.

According to the results, the compounds **3b**, **3c**, **3e**, **3f**, and **3k** had good antimicrobial activity against microbial strains Staphylococci Aureus, Escherichia coli, and Candida albicans. All of the remaining derivatives demonstrated good to moderate activity against the same fungal strains.

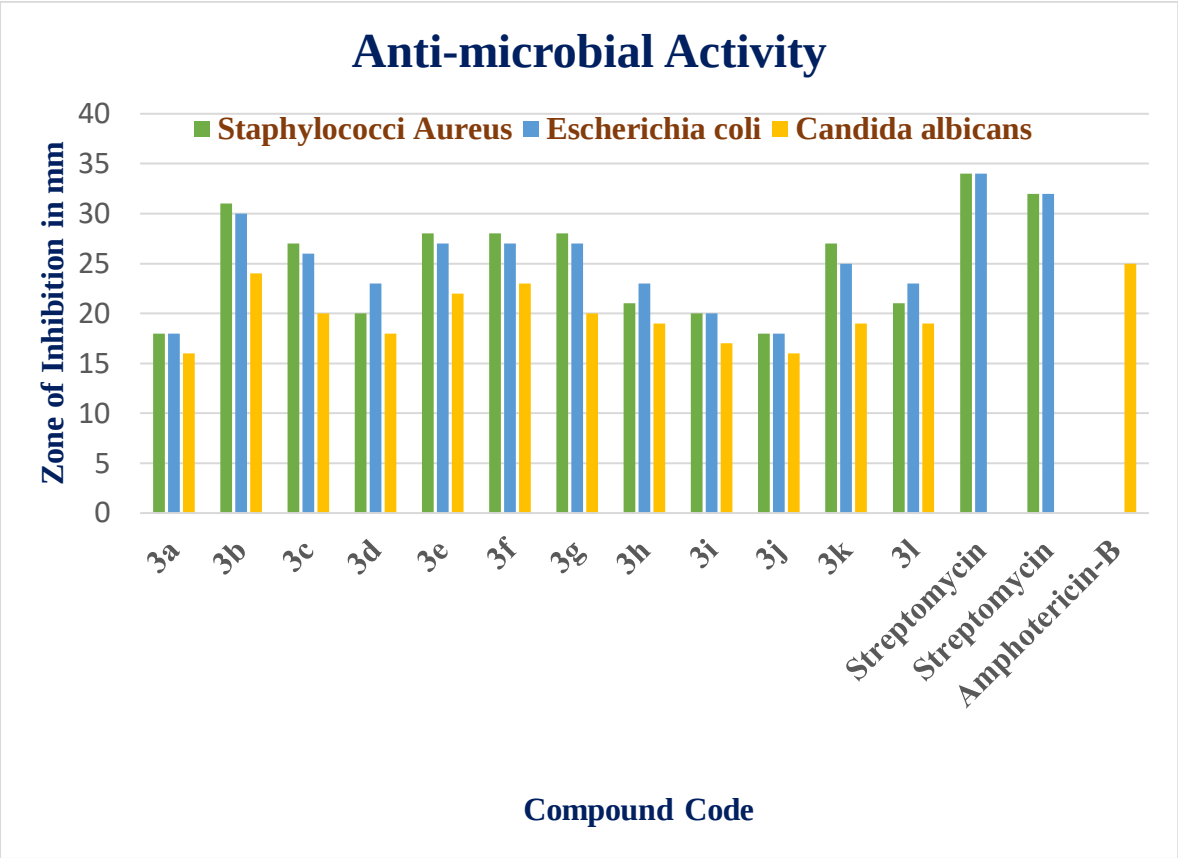


Fig.1.3 Antimicrobial evaluation of 2-iodo-imidazo [2,1] thiazole derivatives (**3a-l**)

Molecular Docking:

In molecular docking approach such as Insilco docking modus operandi is a significant machine to find out the cellular target for different inhibitors. Exceptionally, such a tools scientist can be used in the absence of advance laboratory to carried out enzymatic in vivo and in vitro examination. Herein, we have performed the Insilco study with our synthesized **3a-3l** imidazole pyrazole derivatives for the antifungal activity. This study gives rise to a clear idea about the synthesized molecule's potency with their ligand−protein interactions.

The docking analysis was carried out by Auto dock software [1, 2] and the 2D results are visualized with discovery studio visualizer[33]. Based on the invitro antimicrobial activity results with Staphylococci Aureus (MTCC-96), Escherichia coli, (MTCC-1588) and Candida albicans (MTCC-3018) of synthesized compounds, herein we have done the molecular docking against the 2Q85 Crystal Structure of E. Coli Mur B bound to a Naphthyl Tetronic Acid inhibitor and we have performed the in-silicon docking calculation with this selected protein and found that all the ligands show a very good binding affinity with the active site of the protein and are well fitted in the active site of the enzyme. The docking results indicates the all the synthesized molecules are well fitted in the cavity of the 2Q85 protein. The compound **3A** (**Figure 1.4**) indicate excellent bonding interaction with the selected protein and molecules were fitted in the binding pocket of the pdb:2Q85 protein with -9.0 kcal/mol. The **figure 1.4, A** shows the 2D view of the **3A** in the active sites of the pdb:2Q85 protein possessing the desire hydrogen as well van der Waals bond and H- bonds of interaction with the amino acid residues. The molecules 3A show the hydrogen bond with the SER:229, GLN:288 and LYS:262 amino acid. The ligand 3A interact with SER:229 with the C=O-----H (2.8Å) and GLN:288 shows the interaction with H----N-H (2.4 Å) bond distance 3A molecule and LYS:262 residue shows the H-bond with CO……. group having (2.9Å) H-bond distance (**Figure 1.4**). While, the molecule 3A also display the van der Waals interaction with LEU:290, GLY228, VAL:291, ARG:214, TYR:190, TYR:254, ARG:214, amino acids as well as Pi-alkyl LEU:218, ALA:264 amino acids residues.

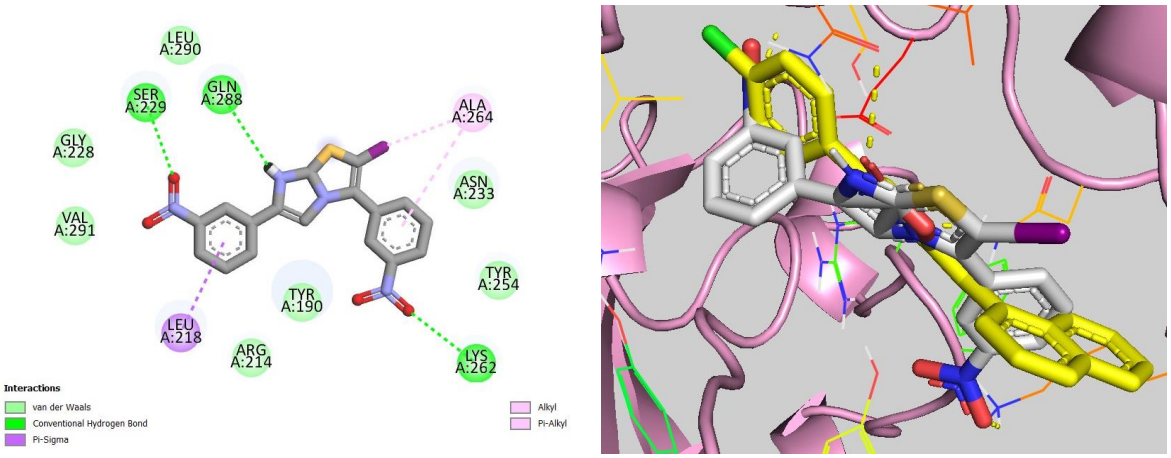


Figure **1.4** A) 2D view shows the binding interaction of the 3A ligand in the active sites of PDB:2Q85 protein B) The Cartoon models indicates the

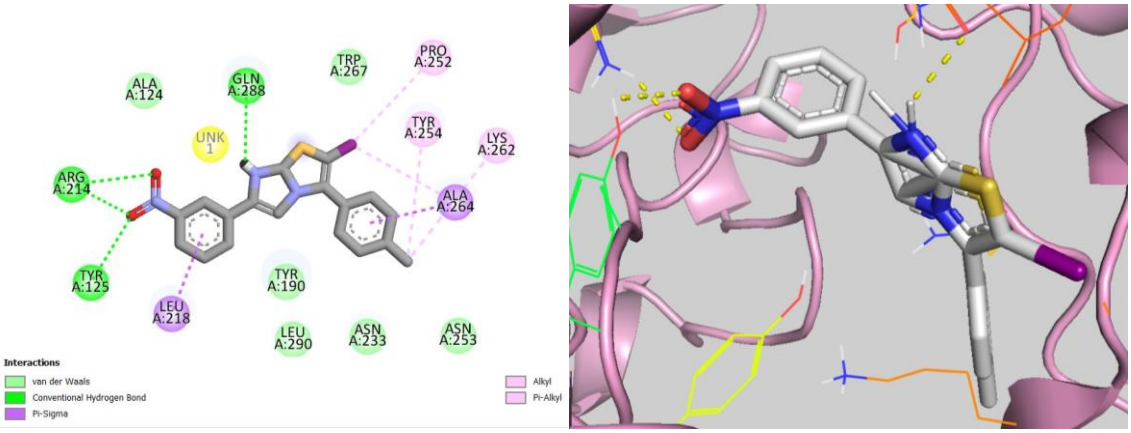


Figure **1.5**. A) 2D view shows binding interaction of the 3H ligand in the active sites of PDB:2Q85 protein B) The Cartoon models indicates the

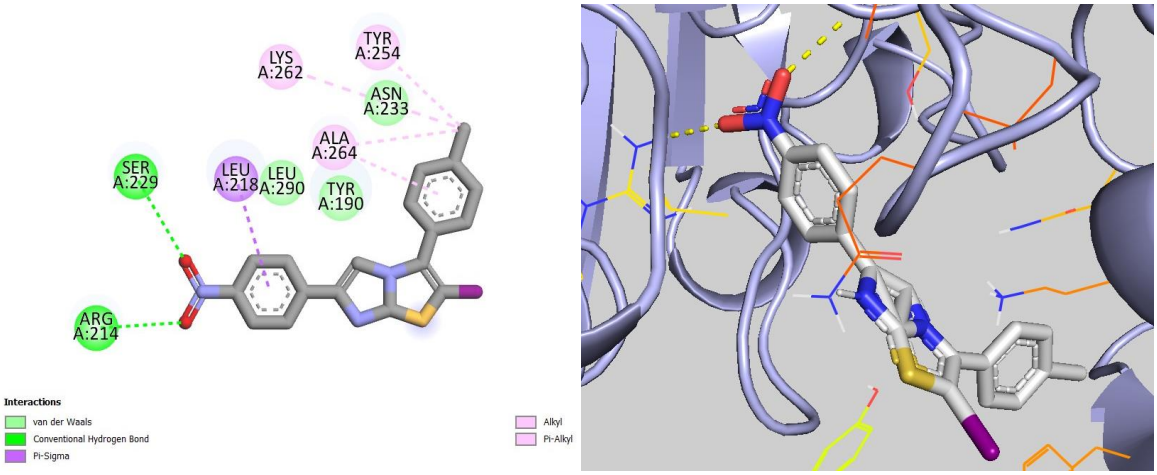


Figure **1.6**. A) 2D view of shows the binding interaction of the 3K ligand in the active sites of PDB: 2Q85 protein B) The Cartoon models indicates the ligand

Similarly, the figure **1.5** and figure **1.6**, the molecules 3H and 3K are docked in the cavity of active sites of protein PDB:2Q85, and shows the very good H-bonding and feasible Pi-alkyl and Van-der walls force of interaction with essential amino acids residues. This docking results are evidence for the biological the results, this indicate the molecules could be the prominent drug candidates for the further bio steric research.

1.3 Material and Method

1.3.1 Chemistry

All the melting points were uncorrected and regulated in an open capillary tube. The chemicals and solvents used were of laboratory grade and were purified. Completion of the reaction was monitored by thin layer chromatography on precoated aluminium silica sheets (Merck, Germany) using UV-chamber for detection. BEC (pH 12.5) was gifted from Supreme Silicone Pune Pvt. Limited. IR spectra were recorded in KBr pellets on an FTIR Shimadzu spectrophotometer. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded in (DMSO)-d6 with an Avance spectrometer (Bruker, Germany) at a 300-MHz frequency using TMS as an internal standard; chemical shifts were expressed in parts per million. Multiplicities are proclaimed as follows: s (singlet), d (doublet), t (triplet), and m (multiplet). Mass spectra were recorded on an EI-Shimadzu QP 2010 PLUS GC-MS system (Shimadzu, Japan). Elemental analysis was performed on a Carlo Erba 106 Perkin-Elmer model 240 analyzer (Perkin-Elmer, USA).

1.3.2. General procedure for the synthesis of 2-iodo-imidazo[2,1-b] thiazole (3a-l)

In a 100 ml round-bottomed flask (RBF) an equimolar quantity of iodinated substituted thiazole (0.001 mol) (**1 a-d**) was taken in green solvent PEG-400 and stirred for about 1 hour at 70-80 ºC using Bleaching earth Clay (pH 12.5 10wt %). Subsequently to this reaction mixture add an equimolar quantity of substituted phenacyl bromide (0.001 mol) (**2 a-d**) and again stirred for 4 hours with continuous heating at 70-80ºC. After complete conversion as indicated by TLC, the catalyst was filtered out by simple filtration and the mother liquor was poured onto ice-cold water, the solid separated out, neutralized, and filtered out the product. The resultant product was dried and recrystallized from methanol.

1.3.2.1. 2-iodo-3,6-bis (3-nitrophenyl) imidazo [2,1-b] thiazole (**3a**)

M.P. 230-232 ºC, Yield, 88%; IR (KBr, cm^{-1}): 2900-3120 (Ar-H), 650-700 (C-I stretching); ^{1}H NMR (400 MHz, DMSO-d_6, TMS, δ, ppm): 7.32 – 8.65 (m, 9H, Ar–H); ^{13}C NMR (100 MHz, DMSO-d_6, TMS, δ, ppm): 157.66, 149.69, 140.45, 135.23, 131.71, 131.25, 128.79, 121.46, 115.59, 106.54; EIMS: 492.2 [M+]; Calculated (found) for $C_{17}H_9IN_4O_4S$: 493.2.

1.3.2.2. 3,6-bis(4-chlorophenyl)-2-iodoimidazo[2,1-b] thiazole **(3b)**

M.P. 228-230 ºC, Yield, 90%; IR (KBr, cm^{-1}): 2900-3000 (Ar-H), 650-700 (C-I stretching); ^{1}H NMR (400 MHz, DMSO-d_6, TMS, δ, ppm): 7.32 – 8.55 (m, 9H, Ar–H); ^{13}C NMR (100 MHz, DMSO-d_6, TMS, δ, ppm): 155.69, 149.70, 140.45, 135.23, 131.16, 129.36, 128.73, 115.61, 106.75; EIMS: 472.3 [M+]; Calculated (found) for $C_{17}H_9Cl_2IN_2S$: 471.14.

1.3.2.3. 3,6-bis(4-bromophenyl)-2-iodoimidazo[2,1-b] thiazole **(3c)**

M.P. 235-237 ºC, Yield, 87%; IR (KBr, cm^{-1}): 2921-3088 (Ar-H), 650-700 (C-I stretching); ^{1}H NMR (400 MHz, DMSO-d_6, TMS, δ, ppm): 7.30 – 7.86 (m, 9H, Ar–H); ^{13}C NMR (100 MHz, DMSO-d_6, TMS, δ, ppm): 155.69, 149.70, 140.45, 135.23, 131.16, 129.36, 128.73, 115.61, 106.75; EIMS: 561.1 [M+]; Calculated (found) for $C_{17}H_9Br_2IN_2S$: 560.04.

1.3.2.4.*6-(4-bromophenyl)-2-iodo-3-(3 nitrophenyl) imidazo[2,1-b] thiazole* **(3d)**

M.P. 233-235 ºC, Yield, 87%; IR (KBr, cm^{-1}): 2900-3120 (Ar-H), 650-700 (C-I stretching); ^{1}H-NMR (400 MHz, DMSO-d_6, TMS, δ, ppm): 7.32 – 8.65 (m, 9H, Ar–H); ^{13}C-NMR (100 MHz, DMSO-d_6, TMS, δ, ppm): 157.66, 149.69, 140.45, 135.23, 131.71, 131.25, 128.79, 121.46, 115.59, 106.54; EIMS: 527.0 [M+]; Calculated (found) for $C_{17}H_9BrIN_3O_2S$: 526.15

1.3.2.5. *6-(4-bromophenyl)-3-(4-chlorophenyl)-2-iodoimidazo[2,1-b] thiazole* **(3e)**

M.P. 230-232 ºC, Yield, 88%; IR (KBr, cm^{-1}): 2900-3120 (Ar-H), 650-700 (C-I stretching); ^{1}H NMR (400 MHz, DMSO-d_6, TMS, δ, ppm): 7.32 – 8.65 (m, 9H, Ar–H); ^{13}C NMR (100 MHz, DMSO-d_6, TMS, δ, ppm): 157.66, 149.69, 140.45, 135.23, 131.71, 131.25, 128.79, 121.46, 115.59, 106.54; EIMS: 560.1 [M+]; Calculated (found) for $C_{17}H_9BrClIN_2S$: 515.59

1.3.2.6. *3-(4-bromophenyl)-6-(4-chlorophenyl)-2-iodoimidazo[2,1-b] thiazole* **(3f)**

M.P. 231-233 ºC, Yield, 89%; IR (KBr, cm-1): 2900-3120 (Ar-H), 650-700 (C-I stretching); ^{1}H NMR (400 MHz, DMSO-d_6, TMS, δ, ppm): 7.32 – 8.65 (m, 9H, Ar–H); ^{13}C NMR (100 MHz, DMSO-d_6, TMS, δ, ppm): 157.66, 149.69, 140.45, 135.23, 131.71, 131.25, 128.79, 121.46, 115.59, 106.54; EIMS: 560.1 [M+]; Calculated (found) for $C_{17}H_9BrClIN_2S$: 515.59

1.3.2.7. *6-(4-chlorophenyl)-2-iodo-3-(3 nitrophenyl) imidazo[2,1-b] thiazole* **(3g)**

M.P. 229-231 ˚C, Yield, 90%; IR (KBr, cm^{-1}): 2900-3120 (Ar-H), 650-700 (C-I stretching); ^{1}H NMR (400 MHz, DMSO-*d6*, TMS, δ, ppm): 7.32 – 8.65 (m, 9H, Ar–H); ^{13}C NMR (100 MHz, DMSO-d_6, TMS, δ, ppm): 157.66, 149.69, 140.45, 135.23, 131.71, 131.25, 128.79, 121.46, 115.59, 106.54; EIMS: 482.1 [M+]; Calculated (found) for $C_{17}H_9ClIN_3O_2S$: 481.69

1.3.2.8. *3-(4-chlorophenyl)-2-iodo-6-(3-nitrophenyl) imidazo[2,1-b] thiazole* **(3h)**

M.P. 228–230 ºC, Yield, 89%; IR (KBr, cm^{-1}): 2900-3120 (Ar-H), 650-700 (C-I stretching); ^{1}H NMR (400 MHz, DMSO-d_6, TMS, δ, ppm): 7.32 – 8.65 (m, 9H, Ar–H); ^{13}C NMR (100 MHz, DMSO-

d6, TMS, δ, ppm): 157.66, 149.69, 140.45, 135.23, 131.71, 131.25, 128.79, 121.46, 115.59, 106.54; EIMS: 482.1 [M+]; Calculated (found) for $C_{17}H_9ClIN_3O_2S$: 481.69

1.3.2.9. *3-(4-bromophenyl)-2-iodo-6-(3-nitrophenyl) imidazo[2,1-b] thiazole* **(3i)**

M.P. 234-236 ºC, Yield, 88%; IR (KBr, cm^{-1}): 2900-3120 (Ar-H), 650-700 (C-I stretching); ^1H NMR (400 MHz, DMSO-d_6, TMS, δ, ppm): 7.32 – 8.65 (m, 9H, Ar–H); ^{13}C NMR (100 MHz, DMSO-d_6, TMS, δ, ppm): 157.66, 149.69, 140.45, 135.23, 131.71, 131.25, 128.79, 121.46, 115.59, 106.54; EIMS: 527.0 [M+]; Calculated (found) for $C_{17}H_9BrIN_3O_2S$: 526.15

1.3.2.10. 2-iodo-3,6-bis (4-nitrophenyl) imidazo [2,1-b] thiazole (**3j**)

M.P. 232-234 ºC, Yield, 90%; IR (KBr, cm^{-1}): 2900-3120 (Ar-H), 650-700 (C-I stretching); ^1H NMR (400 MHz, DMSO-d_6, TMS, δ, ppm): 7.32 – 8.65 (m, 9H, Ar–H); ^{13}C NMR (100 MHz, DMSO-d_6, TMS, δ, ppm): 157.66, 149.69, 140.45, 135.23, 131.71, 131.25, 128.79, 121.46, 115.59, 106.54; EIMS: 491.1 [M+]; Calculated (found) for $C_{17}H_9IN_4O_4S$: 492.25

1.3.2.11. 3-(4-chlorophenyl)-2-iodo-6-(4-nitrophenyl) imidazo[2,1-b] thiazole (**3k**)

M.P. 229-231 ºC, Yield, 88%; IR (KBr, cm^{-1}): 2900-3120 (Ar-H), 650-700 (C-I stretching); ^1H NMR (400 MHz, DMSO-*d6*, TMS, δ, ppm): 7.32 – 8.65 (m, 9H, Ar–H); ^{13}C NMR (100 MHz, DMSO-d_6, TMS, δ, ppm): 157.66, 149.69, 140.45, 135.23, 131.71, 131.25, 128.79, 121.46, 115.59, 106.54; EIMS: 482.1 [M+]; Calculated (found) for $C_{17}H_9ClIN_3O_2S$: 481.69

1.3.2.12. 3-(4-bromophenyl)-2-iodo-6-(4-nitrophenyl) imidazo[2,1-b] thiazole (**3l**)

M.P. 233-235 ºC, Yield, 89%; IR (KBr, cm^{-1}): 2900-3120 (Ar-H), 650-700 (C-I stretching); ^1H NMR (400 MHz, DMSO-*d6*, TMS, δ, ppm): 7.32 – 8.65 (m, 9H, Ar–H); ^{13}C NMR (100 MHz, DMSO-d_6, TMS, δ, ppm): 157.66, 149.69, 140.45, 135.23, 131.71, 131.25, 128.79, 121.46, 115.59, 106.54; EIMS: 527.0 [M+]; Calculated (found) for $C_{17}H_9BrIN_3O_2S$: 526.15

2. CONCLUSION

In conclusion, we have developed a slight, effectual, and environmentally benign synthetic method for 2-iodo-imidazothizole derivatives from substituted phenacyl bromides and substituted 2-amino-4-aryl thiazoles using BEC (pH 12.5, 10% by weight) as a recyclable heterogeneous catalyst in environmentally sustainable reaction medium PEG-400. The key feature of the protocol involves catalyst recyclability, superior product yield, a quicker reaction time, and the absence of hazardous reagents. The 2-iodo-imidazothizole derivatives were screened for antimicrobial activities, among them the compounds **3b**, **3c**, **3e**, **3f**, and **3k** had good antimicrobial activity against microbial strains Staphylococci Aureus, Escherichia coli, and Candida albicans.

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Spectra of some selected compounds

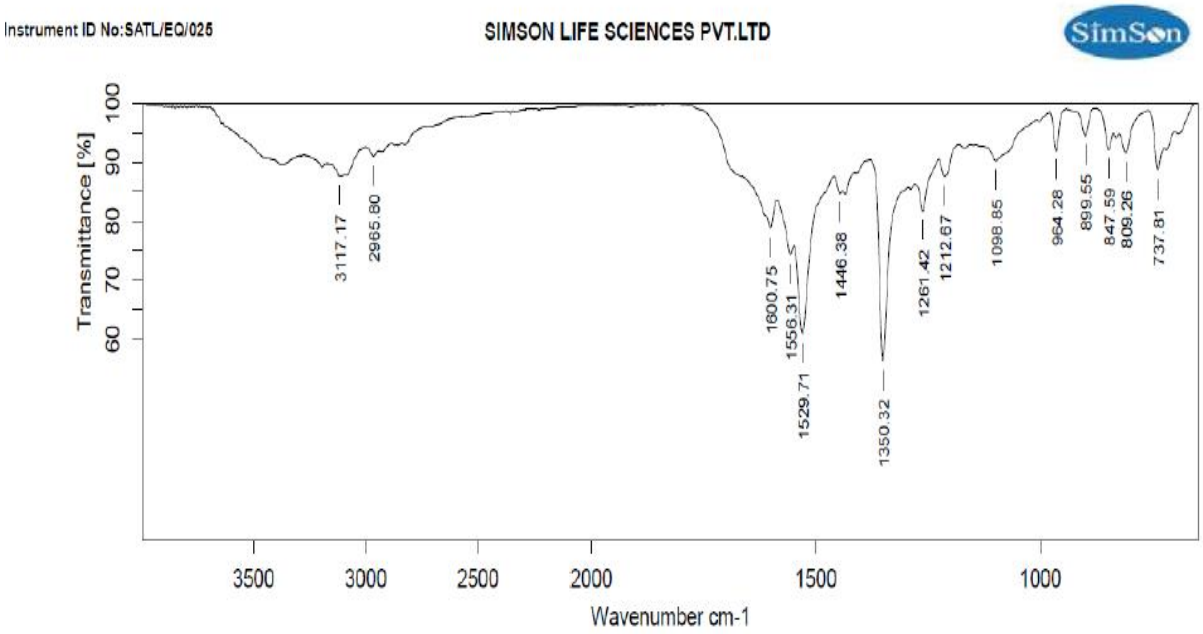

Fig. 1.7 IR of compound 3a

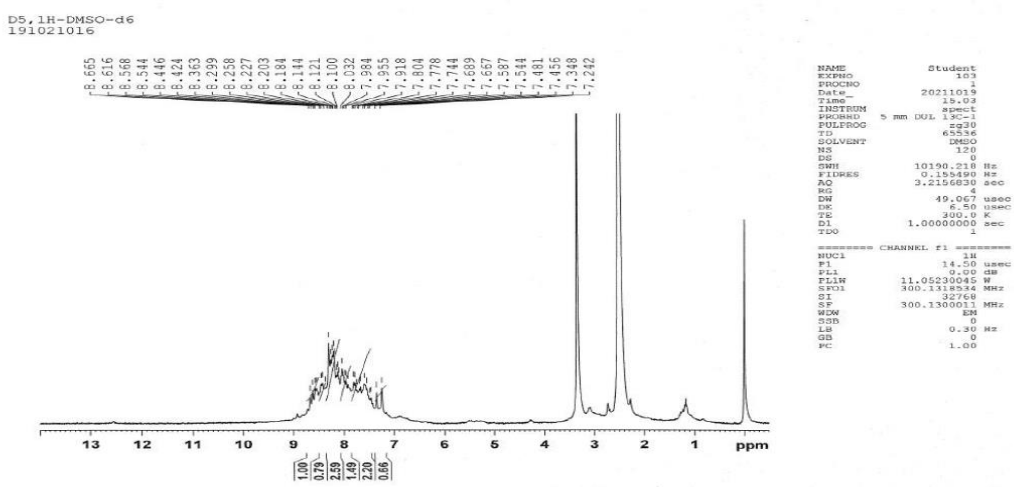

Fig. 1.8 ^{1}H-NMR of compound 3a

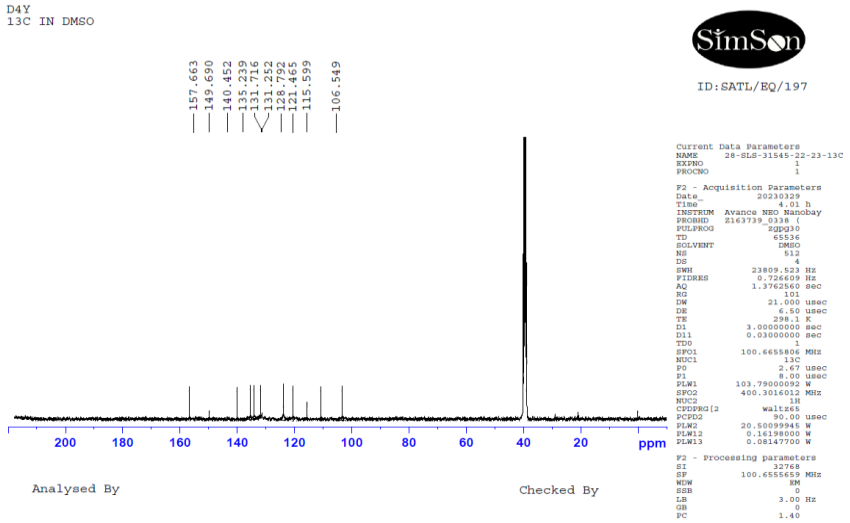

Fig. 1.9 ^{13}C-NMR of compound 3a

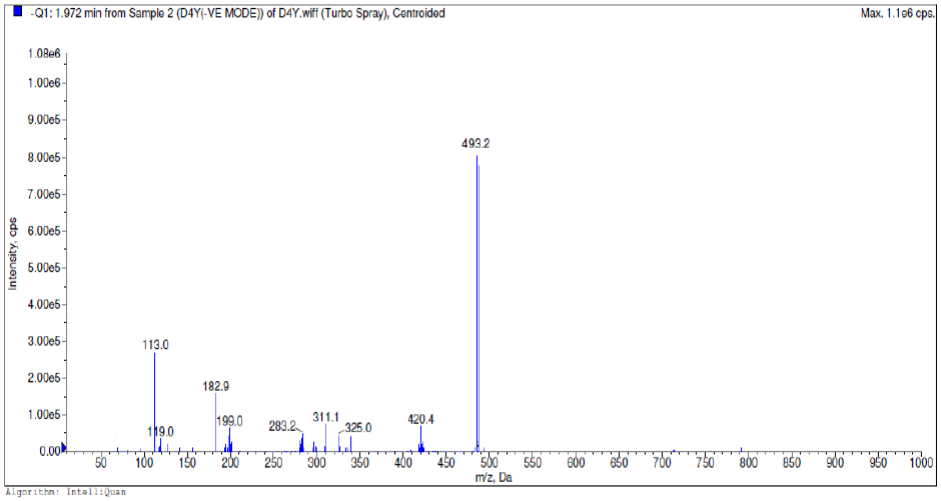

Fig. 1.10 Mass of compound 3a

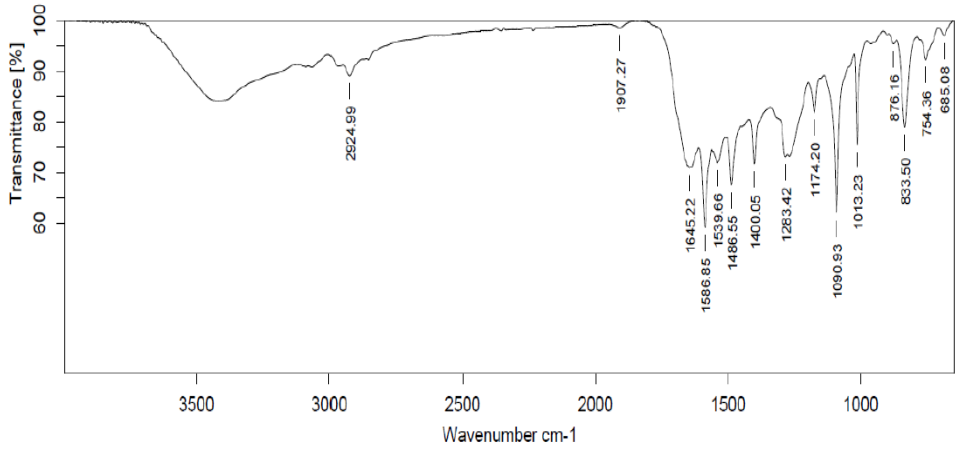

Fig. 1.11 IR of compound 3b

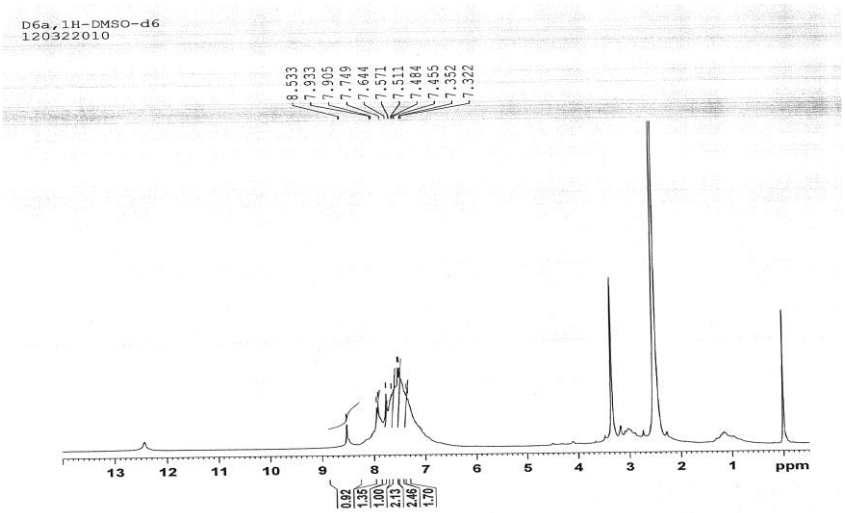

Fig. 1.12 ^{1}H-NMR of compound 3b

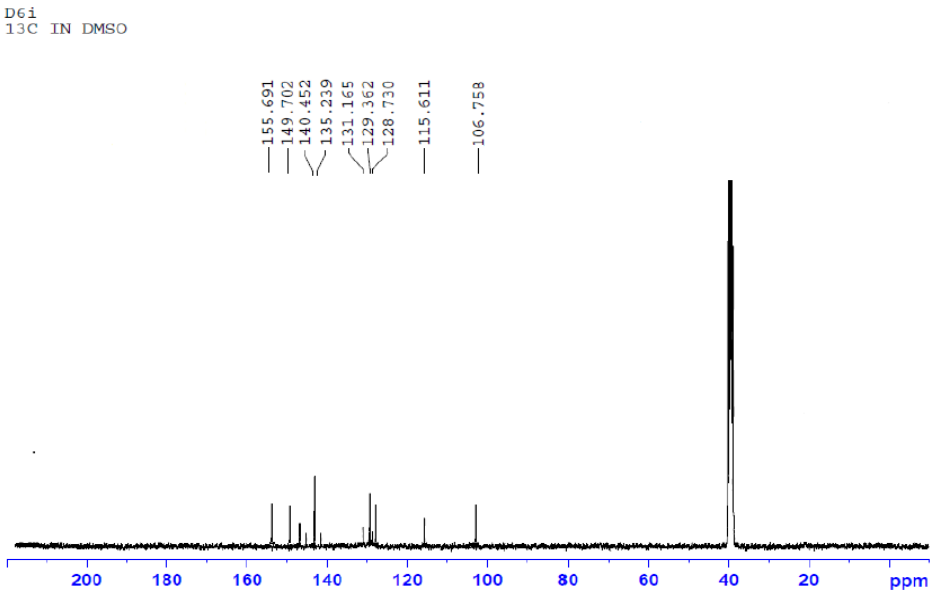

Fig. 1.13 ^{13}C-NMR of compound 3b

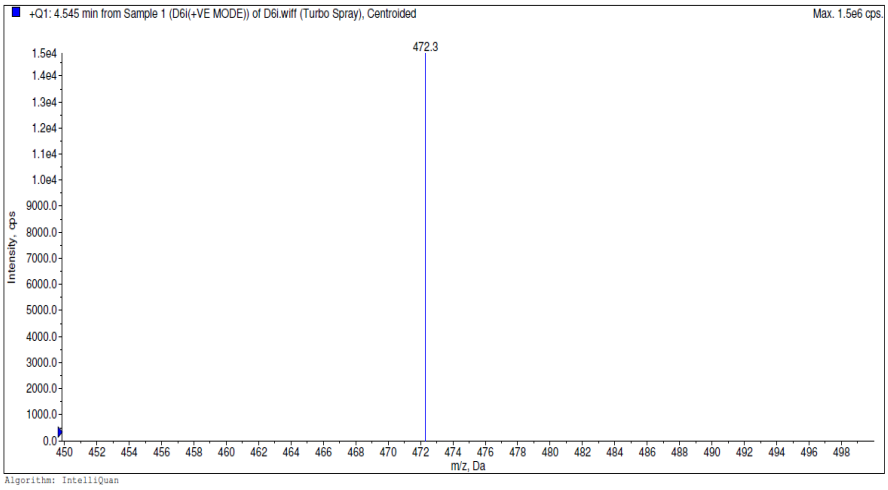

Fig. 1.14 Mass of compound 3b

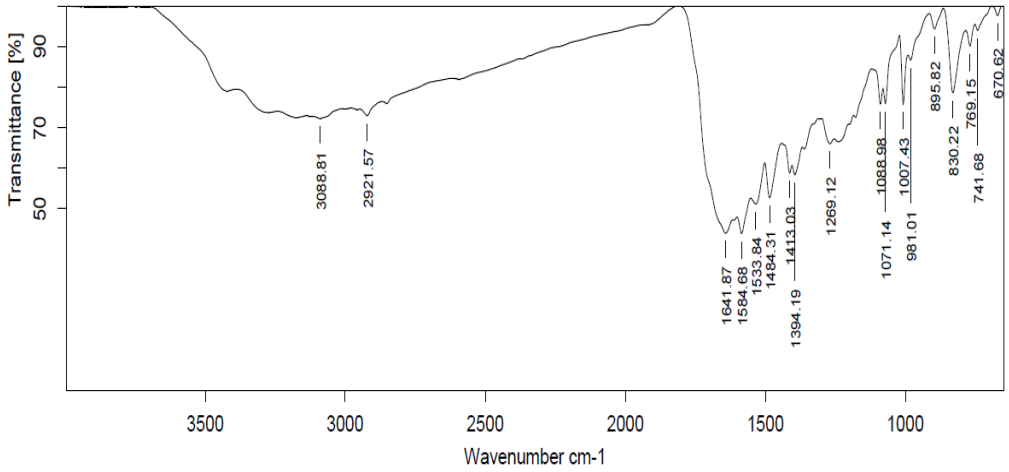

Fig. 1.15 IR of compound 3c

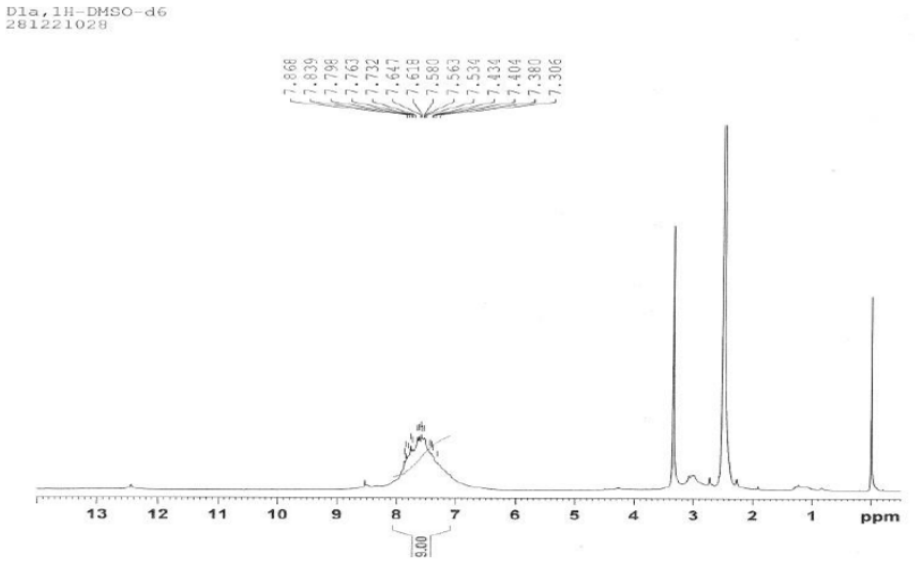

Fig. 1.16 ^{1}H-NMR of compound 3c

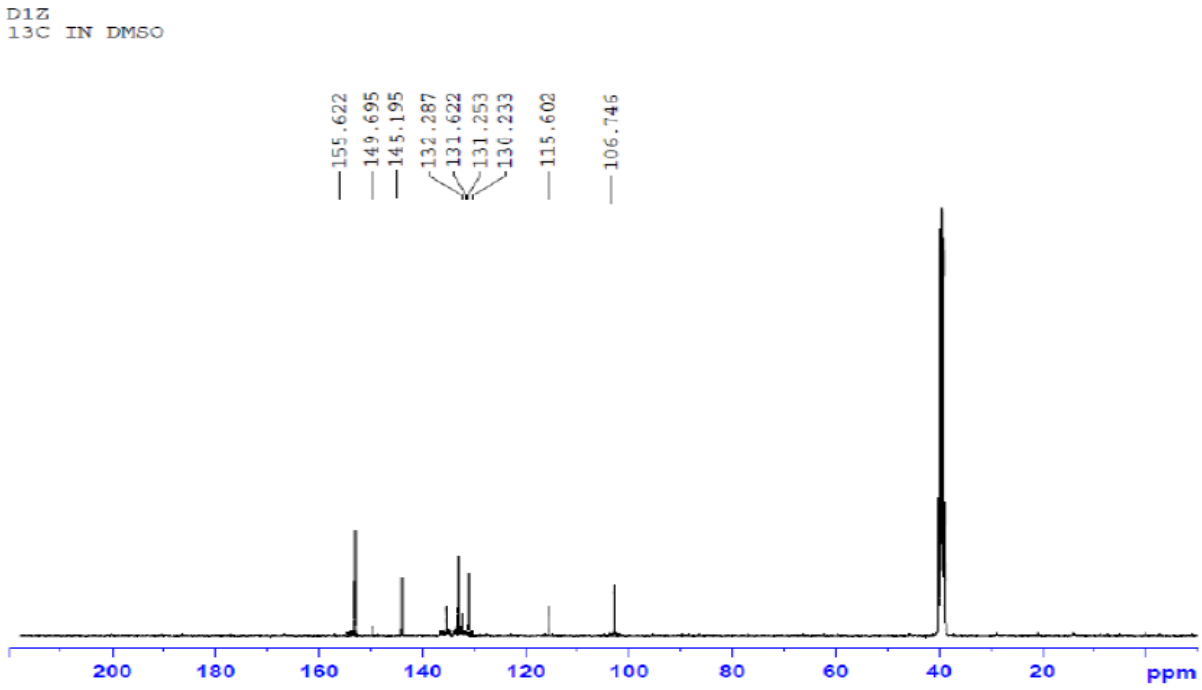

Fig. 1.17 ^{13}C-NMR of compound 3c

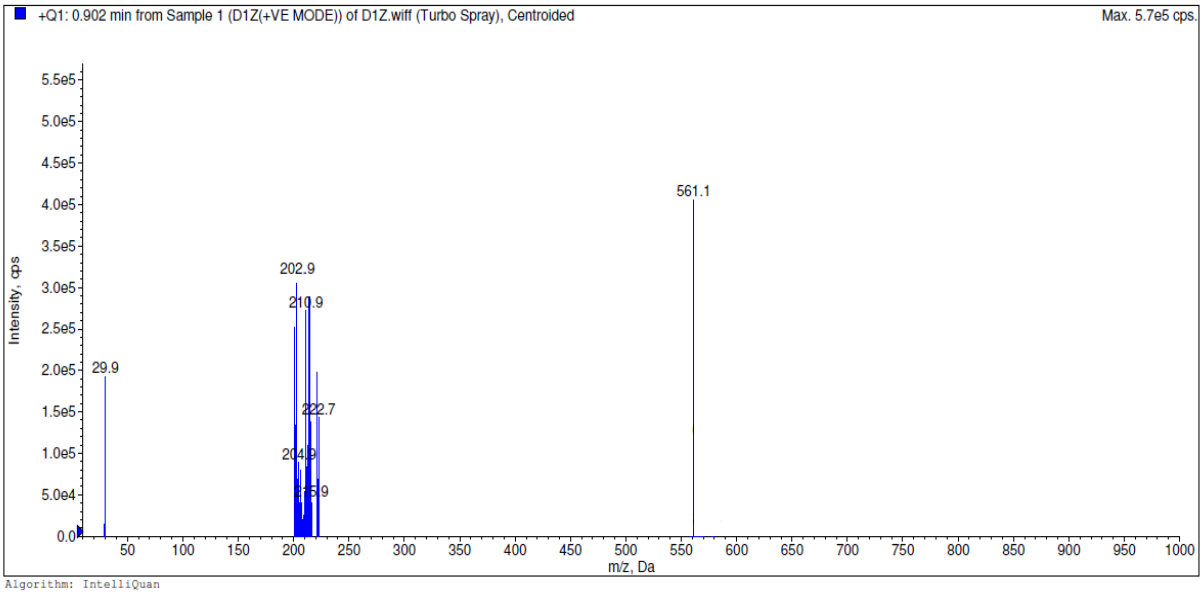

Fig. 1.18 Mass of compound 3c

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