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Microwave Assisted Synthesis of Flouro Chloro Benzimidazolo Substituted Thiazolidinone Derivatives for Antimicrobial Activities

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ABSRACT

Flouro chloro benzimidazolo substituted thiazolidinone derivatives synthesized by reacting 3-chloro, 4-flouro Ortho phenylenediamine with Para amino benzoic acid and followed by different aromatic aldehyde and thioglycolic acid in presence of aluminium chloride. The compound shows absorption bands ranging from 3433- 3320 cm^{-1} for N-H, 3149-3034 cm^{-1} for C-H aromatic stretching and 1521-1342 cm^{-1} for NO_2 functional group. In ^{1}HNMR the presence of methylene proton and methyl protons between δ 2.49 ppm and δ 3.31 ppm respectively was observed respectively. For aromatic protons multiplets were observed between δ 6.8-7.25 ppm and N-H δ 6.8ppm. A series of 7 derivatives were prepared and 7 were tested for Antibacterial activity on Gram (+ve) and Gram (-ve) bacteria. Derivatives were confirmed by TLC, Melting point, IR, NMR and Mass spectrometry. In Antibacterial activity SP203, SP206, SP207 have shown better activity against Gram negative bacteria *E coli*, and SP201 and SP207 have shown good activity against Gram positive bacteria *S. aureus*.

KEYWORDS: Benzimidazole, Thiazolidinone, Thioglycolic acid, Aromatic Aldehyde, Antibacterial activity.

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INTRODUCTION

In recent years the heterocyclic compounds are very much used as antimicrobial agents. Benzimidazole an important class of nitrogen containing heterocyclic while thiazolidinone are heterocyclic compound containing sulfur and nitrogen in a five member ring with variety of biological activities. Different derivatives of benzimidazole are found to possess different activities. Benzimidazole derivatives are known to possess antimicrobial[1], antifungal[2], antitubercular[3], anticancer[4], antitumour[5], antihepatitis-c-virus[6], antiallergic[7], anti-Hiv[8], analgesic[9], antipsychotic[10], antidepresant[11], antianxiety[12], antiviral[13], antihypertensive[14], antiulcer[15], antiinflammatory[16], topoisomerase inhibitor[17], thromboxaneA_2 receptor antagonist[18] and $5HT_3$ antagonist[19]. Benzimidazole ring contains benzene ring fused with imidazole ring. Different substitutions on Benzimidazolo-thiazolidinone moiety on different positions are found to possess different activities.

MATERIAL AND METHOD

Chemical used like sodium bicarbonate, aromatic aldehyde, 3-chloro, 4- flouro aniline and sulphuric acid were purchased from Sd fine chemical Mumbai. Microwave method is used for carrying out chemical transformations which are pollution free and eco-friendly. Commercial microwave oven is used as a convenient source of heat in the laboratory. The microwave assisted organic reactions occur more rapidly, safely and with higher chemical yields, render the microwave method superior to conventional method. Microwave heating is able to heat the target compounds without heating entire furnace or oil bath, which saves time and energy. As a result of this it became an established tool for the high speed synthesis of novel chemical entities. 2-substituted 3-(4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2yl)phenyl)thiazolidin-4-one are synthesized using three steps: Synthesis of 4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl) benzenamine, synthesis of 2-substituted schiffs base and finally synthesis of 2-substituted 3-(4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2 yl)phenyl) thiazolidin-4-one. Melting points were determined by an open capillary method and are uncorrected. The completion of the reaction and purity of the compounds were checked by thin layer chromatography. IR spectra were recorded on Jasco V410 FT-IR spectrometer by diffuse reflectance technique using KBr pressed pellet technique. ^{1}HNMR spectra were recorded on Bruker Ultraspec AMX400 MHz spectrometer and VRO-300 MHz spectrometer.

SYNTHESIS OF FLOURO-CHLORO BENZIMIDAZOLO SUBSTITUTED THIAZOLIDIN ONE DERIVATIVES BY CONVENTIONAL METHOD

Synthesis of 4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl) benzenamine:[20]

A mixture of 3-chloro, 4-fluoro Ortho phenylenediamine (0.1mol) and Para amino benzoic acid (0.1mol) was heated on a water bath for 6 h with solvent ethanol. It was cooled and 10% sodium hydroxide solution was added slowly with constant stirring until just alkaline. The crude product (SP) was filtered, washed with ice cold water, decolorized and washed with water repeatedly and dried. The product was then recrystallized from ethanol in hydrochloric acid. Melting point was 180^{o}C.

Synthesis of 3-(4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl)phenyl)-2-(2-hydroxyphenyl) thiazolidin-4-one (SP201)

To the compound 4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl) benzenamine (SP) (0.07mol) in 50 ml of ethanol containing few drops of glacial acetic acid, salicylaldehyde (0.07 mol) was added and the mixture was refluxed for 9 h. It was then cooled, poured into crushed ice, filtered, washed, dried and recrystallized from ethanol to yield 2-((4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl)phenylimino)methyl) phenol (SP2). To the product SP2 (0.1mol), thioglycolic acid (0.1mol) was added in presence of anhydrous aluminium chloride (100mg) and refluxed at 120^{o}C for 18 h. The reaction mixture was then cooled, triturated with an excess of 10% sodium bicarbonate solution, filtered, washed with water, dried and recrystallized from ethanol to afford the title compound (SP201). Molecular formula- $C_{22}H_{15}N_3O_2SClF$, molecular weigh- 439.45, Yield- 59%, Colour- Brown solid, **IR (cm^{-1}, KBr):** -N-H (Stretching) 3482.31, O-H (Stretching) 3299.62, =C-H (Stretching) 3067.23, C=O 1724.054, C-N 1574.54, C=C 1401.035, F 1286.26, C-S 754.97, Cl 542.87. **^{1}HNMR, ppm (DMSO):** 1H Ar C-H 7.21, 1H Ar N-H 6.82, 1H O-H 5.12, 3H CH_3 3.12, 2H CH_2 2.54.

Synthesis of 3-(4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl)phenyl)-2-(furan-3-yl) thiazolid in-4-one (SP202)

To the compound 4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl) benzenamine (SP) (0.07mol) in 50 ml of ethanol containing few drops of glacial acetic acid, furfuraldehyde (0.07) was added and the mixture was refluxed for 9 h. It was then cooled, poured into crushed ice, filtered, washed, dried and recrystallized from ethanol to yield (E)-4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl)-N-((furan-2-yl)methylene) benzenamine (SP2). To the product SP2 (0.1mol), thioglycolic acid (0.1mol) was added in presence of anhydrous aluminium chloride (100mg) and refluxed at 120^{o}C for 19 h. The reaction mixture was then cooled, triturated with an excess of 10% sodium bicarbonate solution, filtered,

washed with water, dried and recrystallized from ethanol to afford the title compound (SP202). Molecular formula- $C_{20}H_{13}N_3O_2SClF$, molecular weigh- 413.46, Yield- 62% , Colour- Grey solid, **IR (cm^{-1}, KBr):** -N-H (Stretching) 3263.97, =C-H (Stretching) 3057.32, C=O 1448.28, C-N 1397.18, C=C 992.191(O-Furan ring bending), F 834.22, C-S 698.12, Cl 543.82. **^{1}HNMR, ppm (DMSO):** 1H Ar N-H 7.91, 2H Ar C-H 7.22, 3H CH_3 3.54, 2H CH_2 2.50.

Synthesis of 3-(4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl)phenyl)-2-(4-methoxyphenyl) thiazolidin-4-one (SP203)

To the compound 4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl) benzenamine (SP) (0.07mol) in 50 ml of ethanol containing few drops of glacial acetic acid, anisaldehyde (0.07) was added and the mixture was refluxed for 9 h. It was then cooled, poured into crushed ice, filtered, washed, dried and recrystallized from ethanol to yield (E)-N-(4-methoxybenzylidene)-4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl)benzenamine (SP2). To the product SP2 (0.1mol) thioglycolic acid (0.1mol) was added in presence of anhydrous aluminium chloride (100mg) and refluxed at 120^{o}C for 16 h . The reaction mixture was then cooled, triturated with an excess of 10% sodium bicarbonate solution, filtered, washed with water, dried and recrystallized from ethanol to afford the title compound (SP203). Molecular formula- $C_{23}H_{17}N_3O_2SClF$, molecular weigh- 452.45, Yield- 70%, Colour- White solid, **IR (cm^{-1}, KBr):** -N-H (Stretching) 3272.63, =C-H (Stretching) 3052.26, C=O 1663.32, C-N1616.063, C=C 1447.314, C-O-C 1100.15, F 993.16, C-S 698.17, Cl 541.88, **^{1}HNMR, ppm (DMSO):** 1H Ar C-H 7.22, 1H Ar N-H 6.82, 3H CH_3 3.32, 2H CH_2 2.54.

Synthesis of 3-(4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl)phenyl)-2-styrylthiazolidin-4-one (SP204)

To the compound 4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl) benzenamine (SP) (0.07mol) in 50 ml of ethanol containing few drops of glacial acetic acid, benzaldehyde (0.07 mol) was added and the mixture was refluxed for 9 h. It was then cooled, poured into crushed ice, filtered, washed, dried and recrystallized from ethanol to yield E)-N-benzylidene-4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl) benzenamine (SP2). To the product SP2 (0.1mol), thioglycolic acid (0.1mol) was added in presence of anhydrous aluminium chloride (100mg) and refluxed at 120^{o}C for 17 h. The reaction mixture was then cooled, triturated with an excess of 10% sodium bicarbonate solution, filtered, washed with water, dried and recrystallized from ethanol to afford the title compound (SP204). Molecular formula-

$C_{24}H_{17}N_3OSClF$, molecular weigh- 449.46, Yield- 83%, Colour- yellow solid, **IR (cm^{-1}, KBr):** -N-H (Stretching) 3447.16, =C-H (Stretching) 3052.10, C=O 1734.39, C-N 1578.46, C=C 1400.15, F 1282.45, C-S 762.74, Cl 5390.04. **^{1}HNMR, ppm (DMSO):** 1H Ar C-H 7.22, 1H Ar N-H 6.83, 1H =C-H 5.33, 3H CH_3 3.23, 2H CH_2 2.52.

Synthesis of 3-(4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl)phenyl)-2-phenylthiazolidin-4-one (SP205)

To the compound 4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl) benzenamine (SP) (0.07mol) in 50 ml of ethanol containing few drops of glacial acetic acid, Cinnamaldehyde (0.07 mol) was added and the mixture was refluxed for 9 hours. It was then cooled, poured into crushed ice, filtered, washed, dried and recrystallized from ethanol to yield (15E)-4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl)-N-((E)-3-phenylallylidene)benzenamine ((SP2). To the product SP2 (0.1mol), thioglycolic acid (0.1mol) was added in presence of anhydrous aluminium chloride (100mg) and refluxed at 120^{o}C for 14 h. The reaction mixture was then cooled, triturated with an excess of 10% sodium bicarbonate solution, filtered, washed with water, dried and recrystallized from ethanol to afford the title compound (SP205). Molecular formula- $C_{22}H_{15}N_3OSClF$, molecular weigh- 423.47, Yield- 62%, Colour- Brown solid, **IR (cm^{-1}, KBr):** -N-H (Stretching) 3493.45, =C-H (Stretching) 3082.23, C=O 1729.84, C-N 1636.33, C=C 1496.42, F 1269.92, C-S 700.031, Cl 687.71. **^{1}HNMR, ppm (DMSO):** 1H Ar C-H 7.28, 1H Ar N-H 6.33, 1H =C-H 5.30, 3H CH_3 3.73, 2H CH_2 2.53.

Synthesis of 3-(4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl)phenyl)-2-(2-nitrophenyl) thiazolidin-4-one (SP206)

To the compound 4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl) benzenamine (SP) (0.07mol) in 50 ml of ethanol containing few drops of glacial acetic acid, 2-nitro benzaldehyde (0.07 mol) was added and the mixture was refluxed for 9 h. It was then cooled, poured into crushed ice, filtered, washed, dried and recrystallized from ethanol to yield (E)-N-(2-nitrobenzylidene)-4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl)benzenamine (SP2). To the product SP2 (0.1mol) thioglycolic acid (0.1mol) was added in presence of anhydrous aluminium chloride (100mg) and refluxed at 120^{o}C for 17 h. The reaction mixture was then cooled, triturated with an excess of 10% sodium bicarbonate solution, filtered, washed with water, dried and recrystallized from ethanol to afford the title compound (SP206). Molecular formula- $C_{22}H_{14}N_4O_3SClF$, molecular weigh- 467.46, Yield- 71%, Colour- Brown

solid, **IR (cm^{-1}, KBr):** -N-H (Stretching) 3485.71, =C-H (Stretching) 3057.45, C=O 1730.84, C-N 1582.32, NO_2 1523.40, C=C 1455.03, F 1256.42, C-S 701.22, Cl 688.71. **^{1}HNMR, ppm (DMSO):** 1H Ar C-H 7.02, 1H Ar N-H 6.89, 1H =C-H 5.30, 3H CH_3 3.33, 2H CH_2 2.02.

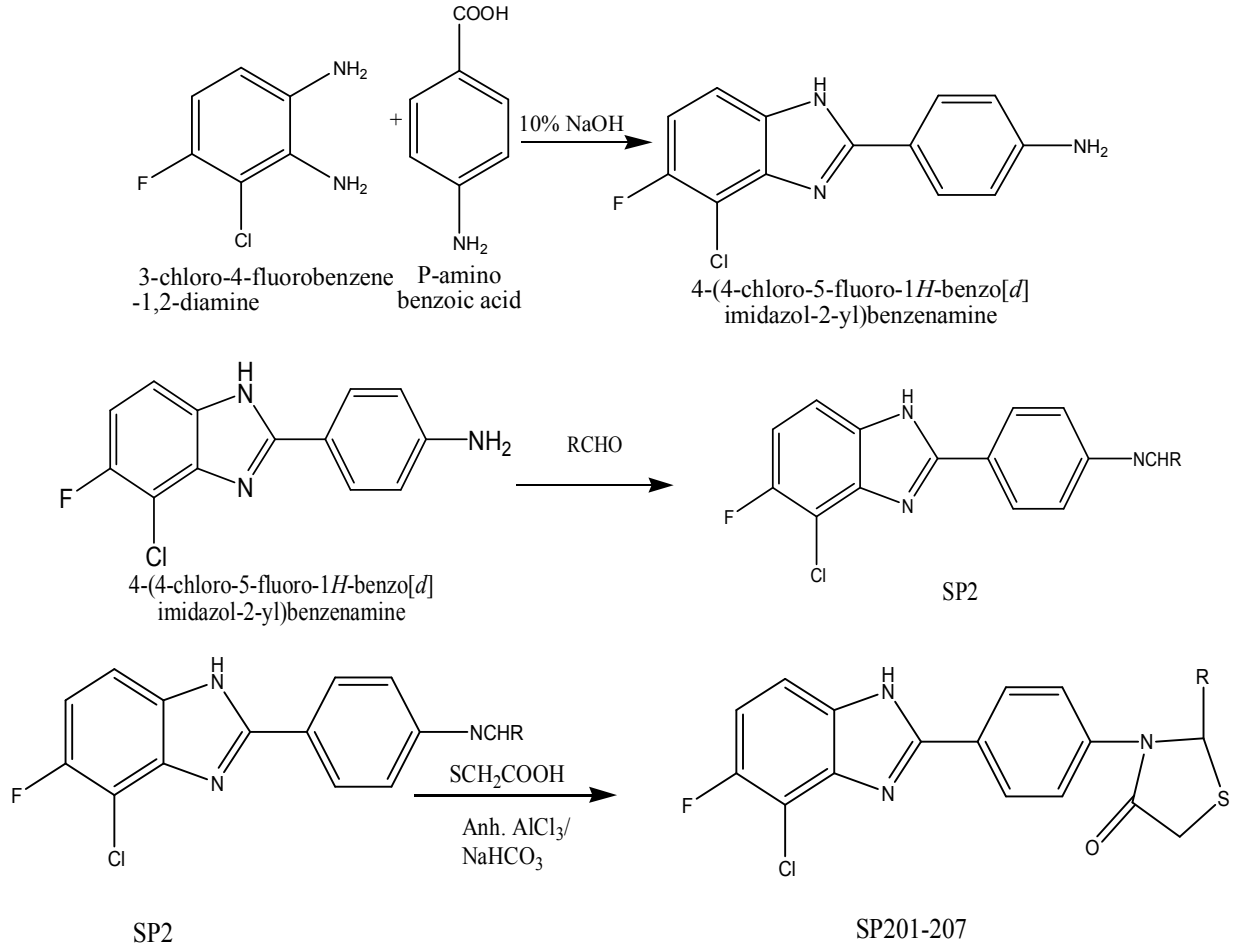
Synthesis of 3-(4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl)phenyl)-2-(3,4-dimethoxyphen yl) thiazolidin-4-one (SP207)

To the compound 4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl) benzenamine (SP) (0.07mol) in 50 ml of ethanol containing few drops of glacial acetic acid, 3,4-dimethoxy benzaldehyde (0.07 mol) was added and the mixture was refluxed for 9 h. It was then cooled, poured into crushed ice, filtered, washed, dried and recrystallized from ethanol to yield (E)-N-(3,4-dimethoxybenzylidene)-4-(4-chloro-5-fluoro-1H-benzo[d]imidazol -2-yl)benzenamine (SP2). To the product SP2 (0.1mol), thioglycolic acid (0.1mol) was added in presence of anhydrous aluminium chloride (100mg) and refluxed at 120^{o}C for 18 h. The reaction mixture was then cooled, triturated with an excess of 10% sodium bicarbonate solution, filtered, washed with water, dried and recrystallized from ethanol to afford the title compound (SP207). Molecular formula- $C_{24}H_{19}N_3O_3SClF$, molecular weigh- 483.45, Yield- 82%, Colour- Yellow solid, **IR (cm^{-1}, KBr):** -N-H (Stretching) 3489.51, =C-H (Stretching) 3047.55, C=O 1609.34, C=C 1453.14, C-N 1406.83, C-O-C 1254.43, F 1203.42, C-S 697.32, Cl 504.21. **^{1}HNMR, ppm (DMSO):** 1H Ar C-H 7.02, 1H Ar N-H 6.43, 1H =C-H 5.43, 3H CH_3 3.43, 2H CH_2 2.42.

SYNTHESIS OF FLOURO-CHLORO BENZIMIDAZOLO SUBSTITUTED THIAZOLIDIN ONE DERIVATIVES BY MICROWAVE ASSISTED METHOD

Synthesis of 4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl) benzenamine[20]

A mixture of 3-chloro, 4-fluoro Ortho phenylenediamine (0.1mol) and Para amino benzoic acid (0.1mol) was irradiated in a microwave at 320 W for 7 min with solvent ethanol. It was cooled and 10% sodium hydroxide solution was added slowly with constant stirring until just alkaline. The crude product (SP) was filtered, washed with ice cold water, decolorized and washed with water repeatedly and dried. The product was then recrystallized from ethanol in hydrochloric acid. Melting point was 180^{o}C.



R= SP201-C_6H_4-OH, SP202-C_6H_4-O, SP203-C_6H_4-OCH_3, SP204-C_6H_5, SP205 -C_6H_4-CH=CH-, SP206-C_6H_4-NO_2, SP207-C_6H_4-$(OCH_3)_2$.

Figure1: Scheme of general synthesis.

Synthesis of 3-(4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl)phenyl)-2-(2-hydroxyphenyl) thiazolidin-4-one (SP201)

To the compound 4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl) benzenamine (SP) (0.07mol) in 50 ml of ethanol containing few drops of glacial acetic acid, salicylaldehyde (0.07 mol) was added and the mixture was irradiated in a microwave at 320 W for 15 min. It was then cooled, poured into crushed ice, filtered, washed, dried and recrystallized from ethanol to yield 2-((4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl)phenylimino)methyl) phenol (SP2). To the product SP2 (0.1mol), thioglycolic acid (0.1mol) was added in presence of anhydrous aluminium chloride (100mg) and irradiated in a microwave at 320 W for 22 min. The reaction mixture was then cooled, triturated with

an excess of 10% sodium bicarbonate solution, filtered, washed with water, dried and recrystallized from ethanol to afford the title compound (SP201). Molecular formula- $C_{22}H_{15}N_3O_2SClF$, molecular weigh- 439.45, Yield- 91%, Colour- Brown solid, **IR (cm^{-1}, KBr):** -N-H (Stretching) 3482.31, O-H (Stretching) 3299.62, =C-H (Stretching) 3067.23, C=O 1724.054, C-N 1574.54, C=C 1401.035, F 1286.26, C-S 754.97, Cl 542.87. **^{1}HNMR, ppm (DMSO):** 1H Ar C-H 7.21, 1H Ar N-H 6.82, 1H O-H 5.12, 3H CH_3 3.12, 2H CH_2 2.54.

Synthesis of 3-(4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl)phenyl)-2-(furan-3-yl) thiazolid in-4-one (SP202)

To the compound 4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl) benzenamine (SP) (0.07mol) in 50 ml of ethanol containing few drops of glacial acetic acid, furfuraldehyde (0.07) was added and the mixture was irradiated in a microwave at 320 W for 15 min. It was then cooled, poured into crushed ice, filtered, washed, dried and recrystallized from ethanol to yield (E)-4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl)-N-((furan-2-yl)methylene) benzenamine (SP2). To the product SP2 (0.1mol), thioglycolic acid (0.1mol) was added in presence of anhydrous aluminium chloride (100mg) and irradiated in a microwave at 320 W for 27 min. The reaction mixture was then cooled, triturated with an excess of 10% sodium bicarbonate solution, filtered, washed with water, dried and recrystallized from ethanol to afford the title compound (SP202). Molecular formula- $C_{20}H_{13}N_3O_2SClF$, molecular weigh- 413.46, Yield- 86% , Colour- Grey solid, **IR (cm^{-1}, KBr):** -N-H (Stretching) 3263.97, =C-H (Stretching) 3057.32, C=O 1448.28, C-N 1397.18, C=C 992.191(O-Furan ring bending), F 834.22, C-S 698.12, Cl 543.82. **^{1}HNMR, ppm (DMSO):** 1H Ar N-H 7.91, 2H Ar C-H 7.22, 3H CH_3 3.54, 2H CH_2 2.50.

Synthesis of 3-(4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl)phenyl)-2-(4-methoxyphenyl) thiazolidin-4-one (SP203)

To the compound 4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl) benzenamine (SP) (0.07mol) in 50 ml of ethanol containing few drops of glacial acetic acid, anisaldehyde (0.07) was added and the mixture was irradiated in a microwave at 320 W for 15 min. It was then cooled, poured into crushed ice, filtered, washed, dried and recrystallized from ethanol to yield (E)-N-(4-methoxybenzylidene)-4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl)benzenamine (SP2). To the product SP2 (0.1mol) thioglycolic acid (0.1mol) was added in presence of anhydrous aluminium chloride (100mg) and

irradiated in a microwave at 320 W for 28 min. The reaction mixture was then cooled, triturated with an excess of 10% sodium bicarbonate solution, filtered, washed with water, dried and recrystallized from ethanol to afford the title compound (SP203). Molecular formula- $C_{23}H_{17}N_3O_2SClF$, molecular weigh- 452.45, Yield- 88%, Colour- White solid, **IR (cm^{-1}, KBr):** -N-H (Stretching) 3272.63, =C-H (Stretching) 3052.26, C=O 1663.32, C-N1616.063, C=C 1447.314, C-O-C 1100.15, F 993.16, C-S 698.17, Cl 541.88, **^{1}HNMR, ppm (DMSO):** 1H Ar C-H 7.22, 1H Ar N-H 6.82, 3H CH_3 3.32, 2H CH_2 2.54.

Synthesis of 3-(4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl)phenyl)-2-styrylthiazolidin-4-one (SP204)

To the compound 4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl) benzenamine (SP) (0.07mol) in 50 ml of ethanol containing few drops of glacial acetic acid, benzaldehyde (0.07 mol) was added and the mixture was irradiated in a microwave at 320 W for 15 min. It was then cooled, poured into crushed ice, filtered, washed, dried and recrystallized from ethanol to yield E)-N-benzylidene-4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl) benzenamine (SP2). To the product SP2 (0.1mol), thioglycolic acid (0.1mol) was added in presence of anhydrous aluminium chloride (100mg) and irradiated in a microwave at 320 W for 32 min. The reaction mixture was then cooled, triturated with an excess of 10% sodium bicarbonate solution, filtered, washed with water, dried and recrystallized from ethanol to afford the title compound (SP204). Molecular formula- $C_{24}H_{17}N_3OSClF$, molecular weigh- 449.46, Yield- 92%, Colour- yellow solid, **IR (cm^{-1}, KBr):** -N-H (Stretching) 3447.16, =C-H (Stretching) 3052.10, C=O 1734.39, C-N 1578.46, C=C 1400.15, F 1282.45, C-S 762.74, Cl 5390.04. **^{1}HNMR, ppm (DMSO):** 1H Ar C-H 7.22, 1H Ar N-H 6.83, 1H =C-H 5.33, 3H CH_3 3.23, 2H CH_2 2.52.

Synthesis of 3-(4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl)phenyl)-2-phenylthiazolidin-4-one (SP205)

To the compound 4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl) benzenamine (SP) (0.07mol) in 50 ml of ethanol containing few drops of glacial acetic acid, Cinnamaldehyde (0.07 mol) was added and the mixture was irradiated in a microwave at 320 W for 15 min. It was then cooled, poured into crushed ice, filtered, washed, dried and recrystallized from ethanol to yield (15E)-4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl)-N-((E)-3-phenylallylidene)benzenamine ((SP2). To the product SP2 (0.1mol), thioglycolic acid (0.1mol) was added in presence of anhydrous aluminium chloride (100mg)

and irradiated in a microwave at 320 W for 35 min. The reaction mixture was then cooled, triturated with an excess of 10% sodium bicarbonate solution, filtered, washed with water, dried and recrystallized from ethanol to afford the title compound (SP205). Molecular formula- $C_{22}H_{15}N_3OSClF$, molecular weigh- 423.47, Yield- 76%, Colour- Brown solid, **IR (cm^{-1}, KBr):** -N-H (Stretching) 3493.45, =C-H (Stretching) 3082.23, C=O 1729.84, C-N 1636.33, C=C 1496.42, F 1269.92, C-S 700.031, Cl 687.71. **^{1}HNMR, ppm (DMSO):** 1H Ar C-H 7.28, 1H Ar N-H 6.33, 1H =C-H 5.30, 3H CH_3 3.73, 2H CH_2 2.53.

Synthesis of 3-(4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl)phenyl)-2-(2-nitrophenyl) thiazolidin-4-one (SP206)

To the compound 4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl) benzenamine (SP) (0.07mol) in 50 ml of ethanol containing few drops of glacial acetic acid, 2-nitro benzaldehyde (0.07 mol) was added and the mixture was irradiated in a microwave at 320 W for 15 min. It was then cooled, poured into crushed ice, filtered, washed, dried and recrystallized from ethanol to yield (E)-N-(2-nitrobenzylidene)-4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl)benzenamine (SP2). To the product SP2 (0.1mol) thioglycolic acid (0.1mol) was added in presence of anhydrous aluminium chloride (100mg) and irradiated in a microwave at 320 W for 30 min. The reaction mixture was then cooled, triturated with an excess of 10% sodium bicarbonate solution, filtered, washed with water, dried and recrystallized from ethanol to afford the title compound (SP206). Molecular formula- $C_{22}H_{14}N_4O_3SClF$, molecular weigh- 467.46, Yield- 79%, Colour- Brown solid, **IR (cm^{-1}, KBr):** -N-H (Stretching) 3485.71, =C-H (Stretching) 3057.45, C=O 1730.84, C-N 1582.32, NO_2 1523.40, C=C 1455.03, F 1256.42, C-S 701.22, Cl 688.71. **^{1}HNMR, ppm (DMSO):** 1H Ar C-H 7.02, 1H Ar N-H 6.89, 1H =C-H 5.30, 3H CH_3 3.33, 2H CH_2 2.02.

Synthesis of 3-(4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl)phenyl)-2-(3,4-dimethoxyphen yl) thiazolidin-4-one (SP207)

To the compound 4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl) benzenamine (SP) (0.07mol) in 50 ml of ethanol containing few drops of glacial acetic acid, 3,4-dimethoxy benzaldehyde (0.07 mol) was added and the mixture was irradiated in a microwave at 320 W for 15 min. It was then cooled, poured into crushed ice, filtered, washed, dried and recrystallized from ethanol to yield (E)-N-(3,4-dimethoxybenzylidene)-4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl)benzenamine(SP2). To the

product SP2 (0.1mol), thioglycolic acid (0.1mol) was added in presence of anhydrous aluminium chloride (100mg) and irradiated in a microwave at 320 W for 25 min. The reaction mixture was then cooled, triturated with an excess of 10% sodium bicarbonate solution, filtered, washed with water, dried and recrystallized from ethanol to afford the title compound (SP207). Molecular formula- $C_{24}H_{19}N_3O_3SClF$, molecular weigh- 483.45, Yield- 87%, Colour- Yellow solid, **IR (cm^{-1}, KBr):** -N-H (Stretching) 3489.51, =C-H (Stretching) 3047.55, C=O 1609.34, C=C 1453.14, C-N 1406.83, C-O-C 1254.43, F 1203.42, C-S 697.32, Cl 504.21. **^{1}HNMR, ppm (DMSO):** 1H Ar C-H 7.02, 1H Ar N-H 6.43, 1H =C-H 5.43, 3H CH_3 3.43, 2H CH_2 2.42.

Table 1: Comparision between conventional and microwave irradiation synthesis (time required and % yield)

Code	R	Conventional synthesis		Microwave synthesis	
		Yield (%)	Time (h)	Yield (%)	Time (min)
SP201	$-C_6H_4-OH$	59%	18	91%	22
SP202	$-C_6H_4-O$	62%	19	86%	27
SP203	$-C_6H_4-OCH_3$	70%	16	88%	28
SP204	$-C_6H_5$	83%	17	92%	32
SP205	$-C_6H_4-CH=CH-$	62%	14	76%	35
SP206	$-C_6H_4-NO_2$	71%	17	79%	30
SP207	$-C_6H_4-(OCH_3)_2$	82%	18	87%	25

EVALUATION OF ANTIMICROBIAL ACTIVITY

The Petri dishes were washed thoroughly and sterilized in hot air oven at 170° C for one hour. 30 ml of sterile nutrient agar medium for bacteria was poured into sterile Petri dishes and allowed to solidify. The Petri dishes were incubated at 37° C for 24 hours to check for sterility. The medium was seeded with the organism by spread plate method using sterile cotton swabs and then placed the disc of Whatmann filter paper, pre-saturated with different dilution of SP201, SP202, SP203, SP204, SP205, SP206, SP207 and amoxicillin at a concentration 100 µg/ml was taken as standard reference. Petri dishes were incubated at 37° C for 48 hours and zone of inhibitions were observed and measured in mm.

Table2: Antimicrobial activity of derivatives.

Derivatives Code	Dose (µg/ml)	Zone of inhibition (mm)	
		S. aureus (Gram+ve)	E. coli (Gram-ve)
SP201	100	13mm	10mm
SP202		-	11mm
SP203		-	**12mm**
SP204		-	8mm
SP205		10mm	10mm
SP206		10mm	**12mm**
SP207		13mm	**12mm**
STANDARD DRUG (AMOXICILLIN)		**27mm**	**13mm**

RESULT AND DISCUSSION

We have synthesized a series of seven derivatives of 2-substituted 3-(4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2 yl)phenyl) thiazolidin-4-one by reacting with 3-chloro-4-fluoro ortho phenylene diamine with para amino benzoic acid as depicted in scheme. The intermediate compound i.e SP2a was prepared by substituting different aromatic aldehydes with amine of 4-(4-chloro-5-fluoro-1H-benzo[d]imidazol-2-yl)benzenamine and thioglycolic acid by using conventional and microwave method according to the literature. The compound 2-substituted 3-(4-(4-chloro-5-fluoro-1h-benzo[d]imidazol-2yl)phenyl) thiazolidin-4-one was confirmed by FT-IR, ^{1}HNMR, Mass spectroscopy, melting point and TLC. The compound shows absorption bands ranging from 3433-3320 cm^{-1} for N-H, 3149-3034 cm^{-1} for C-H aromatic stretching and 1521-1342 cm^{-1} for NO_2 functional group.In ^{1}HNMR the presence of methylene proton and methyl protons between δ 2.49 ppm and δ 3.31 ppm respectively was observed respectively. For aromatic protons multiplets were observed between δ 6.8-7.25 ppm and N-H δ 6.8ppm.So all these confirmation authenticates for all synthesized compounds.The synthesized compounds were evaluated for antimicrobial activity by disc diffusion method. The antibacterial activity as calculated by zones of inhibition against *S. aureus* and *E coli*. A series of 7 derivatives were prepared and 7 were tested for antimicrobial activity on Gram (+ve) and Gram (-ve) bacteria. In antimicrobial activity SP203, SP206, SP207 show significant activity against *E coli*, and SP201 and SP207 show good activity against *S. aureus* compared with amoxicillin at 100 ug/ml.

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