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Synthesis of 3-(4-(imidazo [4,5-b]pyridine-2-yl)phenylamino)-2 arylthiazolidin-4-ones and 1-(4-(3H-imidazo[4,5-b]pyridine2-yl)pheylamino)-3-chloro-4-arylazetidin-2-ones.

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ABSTRACT

2, 3-Diaminopyrindine **(1)** reacts with 4—bromobenzaldehyde **(2)** and gives 2-(4-bromophenyl)-3H-imidazo[4,5-b]pridine **(3)**. The bromo group is substituted by hydrazine hydrate to produce compound **(4).** Then it is condensedwith different aldehydes and the product obtained is reacted thioglycolic acid and chloroacetyl chloride to offer 3-(4-(3H-imidazo[4,5-b]pyridine-2-yl)phenylamino)-2-arylthiazolidin-4-onesm **(6a-i)** and 1-(4(3H-imidazo[4,5-b]pyridine-2-yl) phenylamino)-3-chloro-4-arylazetidin-2-ones (**7a-i)** respectively.

Keywords: synthesis, pyridine, hydrazine, thioglycolic acid

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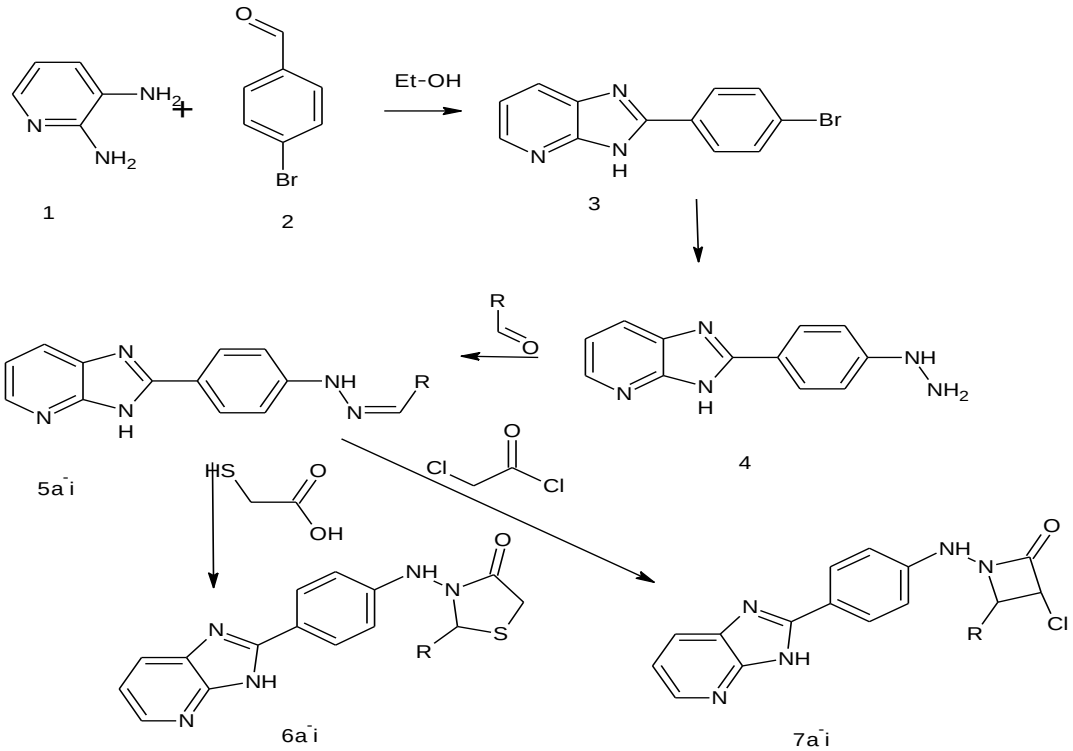
INTRODUCTION

2, 3 diaminopyridine and imidazo [4,5-b]pyridines have been proved to be useful precursors for the synthesis of a variety of medicinal agents. The heterocycles derived from these intermediates have recently been evaluated as antagonists of various biological receptors, including angiotensis-II,[1] platelet activating factor (PAF)[2] metabotropic glutamate subtype V[3]. substituted Imidazo [4,5-b]pyridines have also been tested for their potential as anticancer,[4] inotropic,[5] and Selective antihistamine (H1) agents.[6] Imidazo [4,5-b]pyridines derivatives were also reported as Aurora kinases,[7] cyclic PDF inhibitors.[8] Hence, the synthesis of Imidazo [4,5-b]pyridines derivatives is currently of great interest. Various methods [9-16] reported for the synthesis of Imidazo [4,5-b]pyridines were based on cyclocondensation of 2,3 pyridinediamine with Carboxylic acid derivates or on condensation with aldehydes. Hence, it is imperative to develop a convenient, efficient, and user friendly method for the synthesis of 2-substituted-1H-Imidazo [4,5-b]pyridine.

Nowadays, the organic reactions in aqueous media and EtOH have attracted much attention in Synthetic organic chemistry as water is the most abundant, cheapest, and environmental-friendly Solvent. It also exhibits a unique reactivity and selectivity different from conventional organic solvents. A very diverse range of biological activities are associated with 4-thiazolidinones and 2-Azetidinones. Keeping the conjecture in mind, numerous compounds having moiety are Prepared.[17-20]

Scheme :



R=phenyl, 3-chlorophenyl, 4-chlorophenyl, 2- chlorophenyl, 4-methoxyphenyl,3-Methoxyphenyl, 2-methoxyphenyl, 4-nitrophenyl, 2- nitrophenyl

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EXPERIMENTAL

The IR spectra recorded on brucher-IFS-66 FTIR instrument. 500 Mhz NMR spectra were recorded using tetramethyl silane as an instrument standard in DMSO-d_6. Chemical shifts are expressed in ppm and mass spectrum on a Hewelett Packard mass spectrometer operating at 70ev. The purity of the compounds was checked by TLC and spots were visualized in iodine vapour.

2-(4-bromophenyl)-3H-Imidazo [4,5-b]pyridine(3)

2,3-Diaminopyridine (0.001 m mole) and 4-bromobenzaldehyde (0.001 m mole) in Ethanol containing a few drops of pyridine are refluxed for 5-6 hours. It was then cooled, concentrated and poured into crushed ice and filtered. The solid thus obtained was purified by recrystallization from ethanol.

IR (K Br): 3522.02 cm^{-1} (NH), 3074.53 cm^{-1} (C-H aromatic), 1583.56cm^{-1} (C=N), 1199.72 cm^{-1} (C-N).
^{1} H NMR in DMSO-d_6: 7.75(dd, 4H),8.01 (dd, 1H) 8.80 (d,1H), 9.21 (d, 1H), 9.95(brs, 1H).
MS:274.9(M+1)

1-(4-(3H-imidazo [4,5-b]pyridin-2-yl)phenyl)hydrazine(4)

Compound 2-(4-bromophenyl)-3H-imidazo [4,5-b]pyridine (3) (0.001 m mole0 a pinch of PTSA And hydrazine hydrate (0.001 m mole0 were taken into a RB flask. The contents were refluxed
For 3-4 hrs. the reaction mixture was washed with ice cold water and the solid obtained was Purified.
IR (K Br) : 3323.35 cm^{-1}, 3280.92 cm^{-1} (NH), 3024.38 cm^{-1} (C-H aromatic), 1697.36cm^{-1} (C=N), 1136.07 cm^{-1} (C-N).
^{1} H NMR in DMSO-d_6: 4.52(drs, 3H),7.73 (dd,4H), 8.08 (dd,1H), 8.84 (d, 1H),9.25 (d, 1H),12.41(brs, 1H)
MS:226.0(M+1)

1-(4-(3H-imidazo [4,5-b]pyridin-2-yl)phenyl)-2-arylidenehydrazines (5a-i)

1-(4-(3H-imidazo [4,5-b]pyridin-2-yl)phenyl)hydrazine **(5)** (0.001m mole) and aldehyde (0.001 M mole) in Ethanol containing a few drops of pyridine are refluxed for 5-6 hours. It was then cooled, concentrated and poured into crushed ice and filtered. The solid thus obtained was purified by recrystallization from ethanol.

1-(4-(3H-imidazo [4,5-b]pyridin-2-yl)phenyl)-2-phenylidenehydrazines (5a)

IR (K Br) : 3380.92 cm^{-1} (NH), 3184.38 cm^{-1} (C-H aromatic), 1656.85 cm^{-1}, (C=N),1166.93 cm^{-1} (C-N).

^{1} H NMR in DMSO-d_6 : 7.15-7.31 (m, 6H),7.61-7.80 (m, 6H), 7.95 (dd,1H), 8.40 (d, 1H), 9.18 (brs, 1H), 9.50 (brs, 1H)
MS: 313 (m+)

1-(4-(3H-imidazo [4,5-b]pyridin-2-yl)phenyl)-2-(3-chlorophenylidene)hydrazine (5b)

^{1} H NMR in DMSO-d_6 : 7.17-7.32 (m, 6H),7.63-7.82 (m, 6H), 7.98 (dd,1H), 8.38 (d, 1H), 9.62 (brs, 1H).
MS: 348 (m+1)

1-(4-(3H-imidazo [4,5-b]pyridin-2-yl)phenyl)-2-(4-chlorophenylidene)hydrazine (5c)

^{1} H NMR in DMSO-d_6 : 7.16-7.32 (m, 5H),7.60-7.81 (m, 6H), 7.96 (dd,1H), 8.40 (d, 1H), 9.20 (brs, 1H), 9.61 (brs 1H)
MS: 348 (m+1)

1-(4-(3H-imidazo [4,5-b]pyridin-2-yl)phenyl)-2-(2-chlorophenylidene)hydrazine (5d)

^{1} H NMR in DMSO-d_6 : 7.15-7.31 (m, 5H),7.58-7.80 (m, 6H), 7.75 (dd,1H), 8.39 (d, 1H), 9.18 (brs, 1H), 9.60 (brs 1H)
MS: 348 (m+1)

1-(4-(3H-imidazo [4,5-b]pyridin-2-yl)phenyl)-2-(4-methoxyphenylidene)hydrazine (5e)

^{1} H NMR in DMSO-d_6 : 3.82(s, 3H), 7.10-7.30 (m, 5H),7.64-7.825 (m, 6H), 7.90 (dd,1H), 8.37 (d, 1H), 9.17 (brs, 1H), 9.60 (brs 1H)
MS: 344 (m+1)

1-(4-(3H-imidazo [4,5-b]pyridin-2-yl)phenyl)-2-(3-methoxyphenylidene)hydrazine (5f)

^{1} H NMR in DMSO-d_6: 3.82(s, 3H), 7.10-7.30 (m, 5H),7.64-7.82 (m, 6H), 7.90 (dd,1H), 8.37 (d, 1H), 9.17 (brs, 1H), 9.60 (brs 1H)
MS: 344 (m+1)

1-(4-(3H-imidazo [4,5-b]pyridine-2-yl)phenyl)-2-(2-methoxyphenylidene)hydrazine(5g)

^{1}H NMR inDMSO-d6;3.80(s,3H),7.16-7.33(m,5H), 7.66-7.84(m,6H), 7.90 (dd,1H),8.39(d,1H),9.16(brs,1H),9.62(brs,1H).
MS:344(m+1)

1-(4-(3H-imidazo [4,5-b]pyridin-2-yl)phenyl)-2-(2-nitrophenylidene)hydrazine (5h)

^{1} H NMR in DMSO-d_6 : 7.26-7.40 (m, 5H),7.65-7.95 (m, 6H), 7.95 (dd,1H), 8.35 (d, 1H), 9.20 (brs, 1H), 8.35 (d, 1H), 9.20 (brs 1H), 9.70 (brs 1H) MS: 359 (m+1)

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1-(4-(3H-imidazo [4,5-b]pyridin-2-yl)phenyl)-2-(4-nitrophenylidene)hydrazine (5i)

^{1} H NMR in DMSO-d_6 : 7.25-7.42 (m, 5H),7.66-7.96 (m, 6H), 7.98 (dd,1H), 8.38 (d, 1H), 9.20 (brs, 1H), 7.71 (brs, 1H)
MS: 359 (m+1)

3-(4-(3H-imidazo [4,5-b]pyridin-2-yl)phenylamino)-2-arylthiazolidin-4-one(6a-i)

To a solution of 1-(4-(3H-imidazo[4,5-b]pyridin-2-yl)phenyl)-2-phenylidenehydrazines **(5a)** (0.001 m mole) in absolute ethanol thiglycolic acid (0.001 m mole) and anhydrous zinc chloride were refluxed for 8 hr, concentrated, cooled and poured into crushed ice, and then filtered. The solid obtained was purified by recrystalization.

3-(4-(3H-imidazo [4,5-b]pyridin-2-yl)phenylamino)-2-phenylthiazolidin-4-ones(6a)

IR (K Br) : 3442.06 cm^{-1} (NH)ˏ 2924.85 cm^{-1} (C-H aromatic), 1119.54 cm^{-1}, (C-N) .^{1} H NMR in DMSO-d_6 : 3.95 (d, 2H),5.61 (S, 1H), 7.10 (m, 5H), 7.31 (d, 2H), 7.72 (m, 3H), 7.95 (dd, 1H), 8.40 (d, 1H), 9.19 (brs, 1H), 9.52 (brs, 1H)
MS: 388.6 (m+1)

3-(4-(3H-imidazo [4,5-b]pyridin-2-yl)phenylamino)-2(3-chlorophenyl)thiazolidin-4-one(6b)

^{1} H NMR in DMSO-d_6 : 3.90 (d, 2H),5.60 (S, 1H), 7.12 (m, 4H), 7.30 (d, 2H), 7.73 (d, 2H), 7.96 (dd, 1H), 8.41 (d, 1H), 9.20(brs, 1H), 9.55 (brs, 1H)
MS: 423 (m+1)

3-(4-(3H-imidazo [4,5-b]pyridin-2-yl)phenylamino)-2(4-chlorophenyl)thiazolidin-4-one(6c)

^{1} H NMR in DMSO-d_6 : 3.92 (d, 2H),5.62 (S, 1H), 7.13 (m, 4H), 7.32 (d, 2H), 7.74 (d, 2H), 7.96 (dd, 1H), 8.42 (d, 1H), 9.21(brs, 1H), 9.60 (brs, 1H)
MS: 423 (m+1)

3-(4-(3H-imidazo [4,5-b]pyridin-2-yl)phenylamino)-2(2-chlorophenyl)thiazolidin-4-one(6d)

^{1}H NMR in DMSO-d_6 : 3.96 (d, 2H),5.61 (S, 1H), 7.14 (m, 4H), 7.32 (d, 2H), 7.75 (d, 2H), 7.96 (dd, 1H), 8.43 (d, 1H), 9.25(brs, 1H), 9.61 (brs, 1H)
MS: 423 (m+1)

3-(4-(3H-imidazo [4,5-b]pyridin-2-yl)phenylamino)-2(4-methoxyphenyl) thiazolidin-4-one(6e)

^{1} H NMR in DMSO-d_6 : 3.76 (S, 3H), 3.93 (d, 2H), 5.63 (S, 1H), 7.15 (m, 4H), 7.33 (d, 2H), 7.76(d,2H), 7.95 (dd, 1H), 9.25 (brs, 1H), 9.61 (brs, 1H)
MS: 418 (m+1)

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3-(4-(3H-imidazo [4,5-b]pyridin-2-yl)phenylamino)-2(3methoxyphenyl)thiazolidin-4-one(6f)

^{1} H NMR in DMSO-d_6 : 3.75 (S, 3H), 3.95 (d, 2H), 5.64 (S, 1H), 7.16 (m, 4H), 7.35 (d, 2H), 7.75 (d, 2H), 7.96 (dd, 1H), 8.41 (d, 1H), 9.31 (brs, 1H), 9.60 (brs, 1H)
MS: 418 (m+1)

3-(4-(3H-imidazo [4,5-b]pyridin-2-yl)phenylamino)-2(2-methoxyphenyl) thiazolidin-4-one(6g)

^{1} H NMR in DMSO-d_6 : 3.78 (S, 3H), 3.98 (d, 2H), 5.65 (S, 1H), 7.17 (m, 4H), 7.36 (d, 2H), 7.74 (d, 2H), 7.95 (dd, 1H), 8.40 (d, 1H), 9.30 (brs, 1H), 9.61 (brs, 1H)
MS: 418 (m+1)

3-(4-(3H-imidazo [4,5-b]pyridin-2-yl)phenylamino)-2(2-nitrophenyl)thiazolidin-4-one(6h)

^{1} H NMR in DMSO-d_6 : 3.97 (d, 2H), 5.66 (S, 1H), 7.16 (m, 4H), 7.35 (d, 2H), 7.73 (d, 2H), 7.96 (dd, 1H), 7.96 (dd, 1H), 8.41 (d, 1H), 9.31 (brs, 1H), 9.62 (brs, 1H)
MS: 433 (m+1)

3-(4-(3H-imidazo [4,5-b]pyridin-2-yl)phenylamino)-2(4-nitrophenyl)thiazolidin-4-one(6i)

^{1} H NMR in DMSO-d_6 : 3.96 (d, 2H), 5.65 (S, 1H), 7.15 (m, 4H), 7.34 (d, 2H), 7.72 (d, 2H), 7.95 (dd, 1H), 8.40 (d, 1H), 9.30 (brs, 1H), 9.62 (brs, 1H)
MS: 433 (m+1)

1-(4-(3H-imidazo [4,5-b]pyridin-2-yl)phenylamino)-3-chloro-4-arylazetidin-2-ones(7a-i)

To a solution of 3-(4-(3H-imidazo [4,5-b]pyridin-2-yl)phenylamino)-2(2-nitrophenyl) thiazolidin-4-one **(6)** (0.01 mole) in benzene (50 ml), chloroacetylchloride ((0.02 mole)) and triethylamine (0.02 mole) were added dropp wise with constant stirring. The reaction mixture was then refluxed for 6 hr and the excess of benzene was distilled off. Resulting mixture was poured into crushed ice, filtered and the solid obtained was purified by recrystallization from ethanol.

1-(4-(3H-imidazo [4,5-b]pyridin-2-yl)phenylamino)-3-chloro-4-arylazetidin-2-one(7a)

IR (K Br) : 3440.01 cm^{-1} (NH)ˊ 2923.74 cm^{-1} (C-H aromatic), 1126.75 cm^{-1}, (C-N) .^{1}H NMR in DMSO-d_6 : 5.05 (d, 1H), 5.50 (d, 1H), 7.22 (m, 5H), 7.70 (dd, 4H), 8.00 (dd, 1H), 8.80 (dd, 1H), 9.23 (d, 1H), 9.90 (brs, 1H), 10.30 (brs, 1H)
MS: 390 (m+1)

1-(4-(3H-imidazo [4,5-b]pyridin-2-yl)phenylamino)-3-chloro-4(3-chlorophenyl) azetidin-2-one(7b)

^{1}H NMR in DMSO-d_6 : 5.10 (d, 1H), 5.51 (d, 1H), 7.23 (m, 4H), 7.73 (dd, 4H), 8.08 (dd, 1H), 8.82 (dd, 1H), 9.20 (d, 1H), 9.91 (brs, 1H), 10.31 (brs, 1H) MS: 425 (m+1)

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1-(4-(3H-imidazo [4,5-b]pyridin-2-yl)phenylamino)-3-chloro-4(4-chlorophenyl) azetidin-2-one(7c)

^{1}H NMR in DMSO-d_6 : 5.06 (d, 1H), 5.52 (d, 1H), 7.24 (m, 4H), 7.74 (dd, 4H), 8.06 (dd, 1H), 8.81 (d, 1H), 9.19 (d, 1H), 9.92 (brs, 1H), 10.30 (brs, 1H)
MS: 425 (m+1)

1-(4-(3H-imidazo [4,5-b]pyridin-2-yl)phenylamino)-3-chloro-4(2-chlorophenyl)-azetidin-2-one(7d)

^{1}H NMR in DMSO-d_6 : 5.08 (d, 1H), 5.55 (d, 1H), 7.25 (m, 4H), 7.75 (dd, 4H), 8.10 (dd, 1H), 8.80 (d, 1H), 9.20 (brs, 1H), 9.90 (brs, 1H), 10.35 (brs, 1H)
MS: 391 (m+1)

1-(4-(3H-imidazo [4,5-b]pyridin-2-yl)phenylamino)-3-chloro-4(4-methoxyphenyl)-azetidin-2-ones(7e)

^{1}H NMR in DMSO-d_6 : 3.80 (S, 3H), 5.10 (d, 1H), 5.56 (d, 1H), 7.24 (m, 4H), 7.76 (dd, 4H), 8.08 (dd, 1H), 8.81 (d, 1H), 9.19 (d, 1H), 9.92 (brs, 1H), 10.40 (brs, 1H)
MS: 421 (m+1)

1-(4-(3H-imidazo [4,5-b]pyridin-2-yl)phenylamino)-3-chloro-4(3-methoxyphenyl)-azetidin-2-ones(7f)

^{1}H NMR in DMSO-d_6 : 3.81 (S, 3H), 5.08 (d, 1H), 5.58 (d, 1H), 7.25 (m, 4H), 7.75 (dd, 4H), 8.10 (dd, 1H), 8.80 (d, 1H), 9.20 (d, 1H), 9.90 (brs, 1H), 10.35 (brs, 1H).
MS: 421 (m+1)

1-(4-(3H-imidazo [4,5-b]pyridin-2-yl)phenylamino)-3-chloro-4(2-methoxyphenyl)-azetidin-2-ones(7g)

^{1}H NMR in DMSO-d_6: 3.80 (S, 3H), 5.10 (d, 1H), 5.60 (d, 1H), 7.26 (m, 4H), 7.76 (dd, 4H), 8.10 (dd, 1H), 8.81 (d, 1H), 9.20 (d, 1H), 9.92 (brs, 1H), 10.36 (brs, 1H)
MS: 421 (m+1)

1-(4-(3H-imidazo [4,5-b]pyridin-2-yl)phenylamino)-3-chloro-4(2-nitrophenyl)-azetidin-2-ones(7h)

^{1}H NMR in DMSO-d_6 : 5.06 (d, 1H), 5.58 (d, 1H), 7.24 (m, 4H), 7.74 (dd, 4H), 8.08 (dd, 1H), 8.80 (dd, 1H), 9.18 (d, 1H), 9.91 (brs, 1H), 10.32 (brs, 1H)
MS: 436 (m+1)

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1-(4-(3H-imidazo [4,5-b]pyridin-2-yl)phenylamino)-3-chloro-4(4-nitrophenyl)-azetidin-2-one(7i)

^{1}H NMR in DMSO-d_6 : 5.08 (d, 1H), 5.60 (d, 1H), 7.22 (m, 4H), 7.72 (dd, 4H), 8.10 (dd, 1H), 8.82 (dd, 1H), 9.20 (d, 1H), 9.92 (brs, 1H), 10.36 (brs, 1H)
MS: 436 (m+1)

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