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Synthesis of 3-((4-(*1H*-imidazo[*4,5-b*]pyridin-2-yl)phenyl)methylamino)-2-arylthiazolidin-4-ones and 4-(*1H*-imidazo[*4,5-b*]pyridin-2-yl)phenyl)-N-(5-aryl-*1H*-1,2,3-triazol-1-yl)methanamines

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ABSTRACT

2-(chloromethyl)-1H-imidazo[4,5-b]pyridinereacts with hydrazine to form 1-((1H-imidazo[4,5-b]pyridin-2-yl)methyl)hydrazine ***(2)****, which on condensation with aromatic aldehydes converts in to 1-((4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)methyl)-2-arylidenehydrazines* ***(3a-f)****. Compounds* ***3a-f*** *on reaction with thioglycolic acid and diazomethane lead to form 3-((4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)methylamino)-2-arylthiazolidin-4-ones* ***(4a-f)*** *and 4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)-N-(5-aryl-1H-1,2,3-triazol-1-yl)methanamines respectively* ***(5a-f)****.*

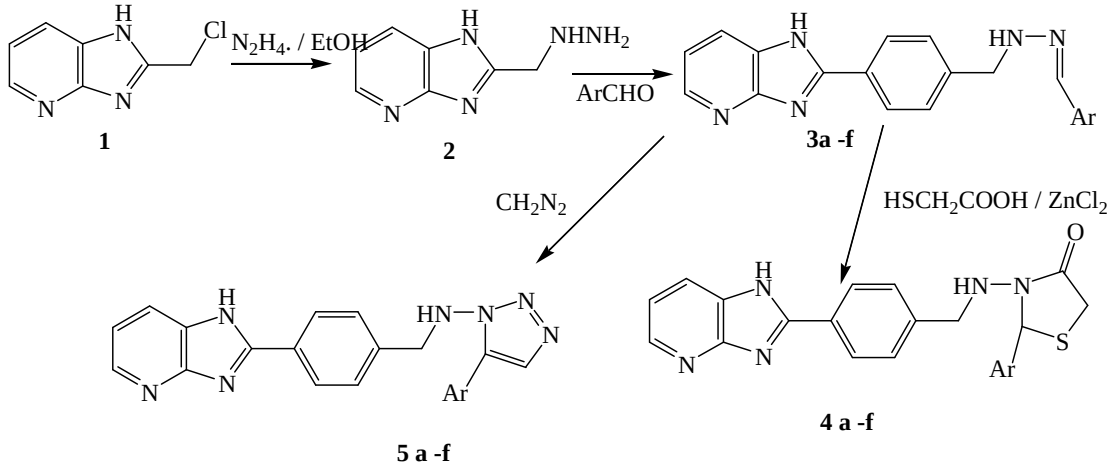
INTRODUCTION

1*H*-Imidazo[4,5-b]pyridine derivatives are important class of heterocyclic compounds[1]. Because, benzimidazole based nucleosides have been prepared and evaluated[2,3] as antiviral drugs. Thiosemicarbazones have been used as intermediates for a great variety of heterocyclic products, such as thiazolidinones, thiohydantoins, thioxopyrimidinediones. It is reported that thiazolidinones exhibit antibacterial[2], antifungal[3], anticonvulsant[4], antitubercular[5], anti-inflammatory[6], antihistaminic[7,8], cardiovascular[9] and anti-HIV[10] activities. In view of the importance of these compounds we undertook the synthesis of title compounds.

MATERIALS AND METHODS

IR spectra were recorded on potassium bromide disks on a Perkin-Elmer 383 spectrophotometer. ^{1}H NMR spectra were obtained on a Varian 400 MHz instrument with TMS as internal Standard and chemical shifts are expressed δ ppm solvent used DMSO-d_6 and Mass spectrum on a Hewlett Packard mass spectrometer operating at 70ev, TLC is performed with E. Merck precoated silica gel plates (60F-254) with iodine as a developing agent.

Scheme



Ar = 4-methylphenyl, 2-methylphenyl, 4-methoxyphenyl, 3-methoxyphenyl, 4-chlorophenyl, phenyl

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

To a solution of 2-(chloromethyl)-1H-imidazo[4,5-b]pyridine**,** (0.54mmol) in ethanol (5mL), was added hydrazine hydrate 99% (2mL) and the resulting solution was refluxed for about 5h. The reaction completion was monitored by TLC. After completion of starting material, the ethanol was evaporated completely under reduced pressure. The crude compound was recrystalised in ethyl acetate in hexane (20%) to yield the title compound as solid (83%).

^{1}H NMR (DMSO-d$_6$) δ = 8.42 (d, 1H), 7.75 (m, 1H), 7.41 (brs, 2H), 7.26 (m, 1H), 7.20 (m, 2H), 5.02 (s, 2H); Mass [M+H] = 163

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

1-((1H-imidazo[4,5-b]pyridin-2-yl)methyl)hydrazine **(2)** (0.001 m 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}H NMR (DMSO-d$_6$) δ = 13.80 (brs, 1H), 9.20 (brs, 1H), 8.41(d, 1H), 8.25 (t, 1H), 8.18 (m, 1H), 7.73 (s, 1H), 7.52 (d, 2H), 7.32 (d, 2H), 5.21 (s, 2H), 2.38 (s, 3H); Mass [M+H] = 342

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

^{1}H NMR (DMSO-d$_6$) δ = 13.78 (brs, 1H), 9.18 (brs, 1H), 8.42 (d, 1H), 8.26 (t, 1H), 8.17 (m, 1H), 7.73 (s, 1H), 7.53 (d, 2H), 7.33 (d, 2H), 5.20 (s, 2H), 2.37 (s, 3H); Mass [M+H] = 342

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

^{1}H NMR (DMSO-d$_6$) δ = 12.83 (brs, 1H), 9.10 (brs, 1H), 8.43 (d, 1H), 8.25 (t, 1H), 8.18 (m, 1H), 7.73 (s, 1H), 7.42 (d, 2H), 7.22 (d, 2H), 5.22 (s, 2H), 3.86 (s, 3H); Mass [M+H] = 358

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

^{1}H NMR (DMSO-d$_6$) δ = 12.80 (brs, 1H), 9.12 (brs, 1H), 8.44 (d, 1H), 8.26 (t, 1H), 8.19 (m, 1H), 7.78 (s, 1H), 7.42 (d, 2H), 7.22 (d, 2H), 5.22 (s, 2H), 3.87 (s, 3H); Mass [M+H] = 358

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

^{1}H NMR (DMSO-d$_6$) δ = 13.01 (brs, 1H), 9.10 (brs, 1H), 8.44 (d, 1H), 8.26 (t, 1H), 8.17 (m, 1H), 7.78 (s, 1H), 7.56 (d, 2H), 7.36 (d, 2H), 5.22 (s, 2H); Mass [M+H] = 363

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

^{1}H NMR (DMSO-d$_6$) δ = 13.32 (brs, 1H), 9.18 (brs, 1H), 8.42 (d, 1H), 8.25 (t, 1H), 8.18 (m, 1H), 7.79 (s, 1H), 7.58 (d, 2H), 7.35 (d, 3H), 5.21 (s, 2H); Mass [M+H] = 328

3-((4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)methylamino)-2-p-tolylthiazolidin-4-one (4a)
1-((4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)methyl)-2-(4-methylbenzylidene)hydrazine **(3a)** (0.001 m mole) in DMSO, diazomethane (0.001 m mole) was added and refluxed for 18 hr. The contents were cooled and poured into crushed ice, and then filtered. The solid obtained was purified by recrystalization.

^{1}H NMR (DMSO-d_6) δ = 9.38 (brs, 2H), 8.18 (d, 1H), 8.01 (m, 1H), 7.82 (d, 1H), 7.60 (s, 1H), 7.48 (d, 2H), 7.28 (d, 2H), 5.18 (s, 2H), 3.78 (s, 2H), 2.37 (s, 3H); Mass [M+H] = 416

3-((4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)methylamino)-2-(2-methylphenyl)thiazolidin-4-one (4b)
^{1}H NMR (DMSO-d_6) δ = 9.40 (brs, 2H), 8.18 (d, 1H), 8.02 (m, 1H), 7.84 (d, 1H), 7.62 (s, 1H), 7.47 (d, 2H), 7.27 (d, 2H), 5.18 (s, 2H), 3.77 (s, 2H), 2.38 (s, 3H); Mass [M+H] = 416

3-((4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)methylamino)-2-(4-methoxyphenyl)thiazolidin-4-one (4c)
^{1}H NMR (DMSO-d_6) δ = 9.52 (brs, 1H), 9.02 (brs, 1H), 8.24 (d, 1H), 8.04 (m, 1H), 7.85 (d, 1H), 7.63 (s, 1H), 7.46 (d, 2H), 7.26 (d, 2H), 5.20 (s, 2H), 3.89 (s, 3H), 3.76 (s, 2H); Mass [M+H] = 432

3-((4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)methylamino)-2-(3-methoxyphenyl)thiazolidin-4-one (4d)
^{1}H NMR (DMSO-d_6) δ = 9.53 (brs, 1H), 9.05 (brs, 1H), 8.25 (d, 1H), 8.06 (m, 1H), 7.86 (d, 1H), 7.64 (s, 1H), 7.46 (d, 2H), 7.26 (d, 2H), 5.21 (s, 2H), 3.89 (s, 3H), 3.76 (s, 2H); Mass [M+H] = 432

3-((4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)methylamino)-2-(4-chlorophenyl)thiazolidin-4-one (4e)
^{1}H NMR (DMSO-d_6) δ = 9.62 (brs, 1H), 9.10 (brs, 1H), 8.26 (d, 1H), 8.10 (m, 1H), 7.88 (d, 1H), 7.64 (s, 1H), 7.54 (d, 2H), 7.34 (d, 2H), 5.20 (s, 2H), 3.78 (s, 2H); Mass [M+H] = 437

3-((4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)methylamino)-2-phenylthiazolidin-4-one (4f)
^{1}H NMR (DMSO-d_6) δ = 9.85 (brs, 1H), 9.12 (brs, 1H), 8.24 (d, 1H), 8.12 (m, 1H), 7.98 (d, 1H), 7.66 (s, 1H), 7.55 (d, 2H), 7.35 (m, 2H), 5.21 (s, 2H), 3.78 (s, 2H); Mass [M+H] = 402

4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)-N-(5-o-tolyl-1H-1,2,3-triazol-1-yl)methanamine (5a)
To a solution of 1-((4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)methyl)-2-(4-methylbenzylidene)hydrazine **(3a)** (0.001 m mole) in DMSO, diazomethane (0.001 m mole) was added and refluxed for 18 hr. The contents were cooled and poured into crushed ice, and then filtered. The solid obtained was purified by recrystalization.
^{1}H NMR (DMSO-d_6) δ = 13.90 (brs, 1H), 9.18 (brs, 1H), 8.35 (d, 1H), 8.20 (m, 2H), 7.84 (s, 1H), 7.41 (m, 4H), 5.20 (s, 2H), 2.41 (s, 3H); Mass [M+H] = 382

4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)-N-(5-(2-methylphenyl)-1H-1,2,3-triazol-1-yl)methanamine (5b)
^{1}H NMR (DMSO-d_6) δ = 13.91 (brs, 1H), 9.20 (brs, 1H), 8.36 (d, 1H), 8.21 (m, 2H), 7.85 (s, 1H), 7.42 (m, 4H), 5.21 (s, 2H), 2.39 (s, 3H); Mass [M+H] = 382

4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)-N-(5-(4-methoxyphenyl)-1H-1,2,3-triazol-1-yl)methanamine (5c)
^{1}H NMR (DMSO-d_6) δ = 13.78 (brs, 1H), 9.19 (brs, 1H), 8.40 (d, 1H), 8.22 (m, 2H), 7.88 (s, 1H), 7.42 (d, 2H), 7.22 (d, 2H), 5.20 (s, 2H), 3.86 (s, 3H); Mass [M+H] = 398

4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)-N-(5-(3-methoxyphenyl)-1H-1,2,3-triazol-1-yl)methanamine (5d)
^{1}H NMR (DMSO-d_6) δ = 13.78 (brs, 1H), 9.19 (brs, 1H), 8.40 (d, 1H), 8.22 (m, 2H), 7.88 (s, 1H), 7.42 (d, 2H), 7.22 (d, 2H), 5.20 (s, 2H), 3.86 (s, 3H); Mass [M+H] = 398

4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)-N-(5-(4-chlorophenyl)-1H-1,2,3-triazol-1-yl)methanamine (5e)
^{1}H NMR (DMSO-d_6) δ = 13.69 (brs, 1H), 9.16 (brs, 1H), 8.42 (d, 1H), 8.24 (m, 2H), 7.90 (s, 1H), 7.60 (d, 2H), 7.40 (d, 2H), 5.23 (s, 2H); Mass [M+H] = 403

4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)-N-5-phenyl-1H-1,2,3-triazol-1-yl)methanamine (5f)
^{1}H NMR (DMSO-d_6) δ = 14.00 (brs, 1H), 9.21 (brs, 1H), 8.40 (d, 1H), 8.22 (m, 2H), 7.90 (s, 1H), 7.48 (d, 2H), 7.36 (m, 3H), 5.20 (s, 2H); Mass [M+H] = 368

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