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Der Pharma Chemica, 2014, 6(5):80-83
(http://derpharmachemica.com/archive.html)

ISSN 0975-413X
CODEN (USA): PCHHAX

A facile synthesis of 1-(4-(*1H*-imidazo[*4,5-b*]pyridin-2-yl)phenyl)-5-methyl-3-aryl-1,3,5-triazinane-2-thiones and 3-(4-(*1H*-imidazo[*4,5-b*]pyridine-2-yl) phenyl)-5-aryl-1,3,5-oxadiazinane-4-thiones

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ABSTRACT

4-(1H-imidazo[4,5-b]pyridin-2-yl)benzenamine ***(1)*** *reacts with aromatic isothiocyanates to form compound* ***2*** *which is cyclized to 1-(4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)-5-methyl-3-aryl-1,3,5-triazinane-2-thiones* ***(3a-h)*** *and 3-(4-(1H-imidazo[4,5-b]pyridine-2-yl)phenyl)-5-aryl-1,3,5-oxadiazinane-4-thiones* ***(4a-h)****. All the compounds are analysed by* ^{1}*H NMR and Mass spectra.*

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.

1,3,5-triazinan-2-ones are useful for the protection of amino groups,[4] as well as for the synthesis of polyamines,[5] poly functional aminoalcohals[4] and water soluble triazinan-2-ones are used as fertilizers.[6] Reports on the synthesis of heterocyclic 1,3,5-triazinan-2-ones[7-10] and 1,3,5-oxadiazinan-4-ones[11-13] give the importance of those compounds.

In view of the applicability of Imidazopyridines, 1,3,5-triazinan-2-ones and 1,3,5-oxadiazinan-4-ones, 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.

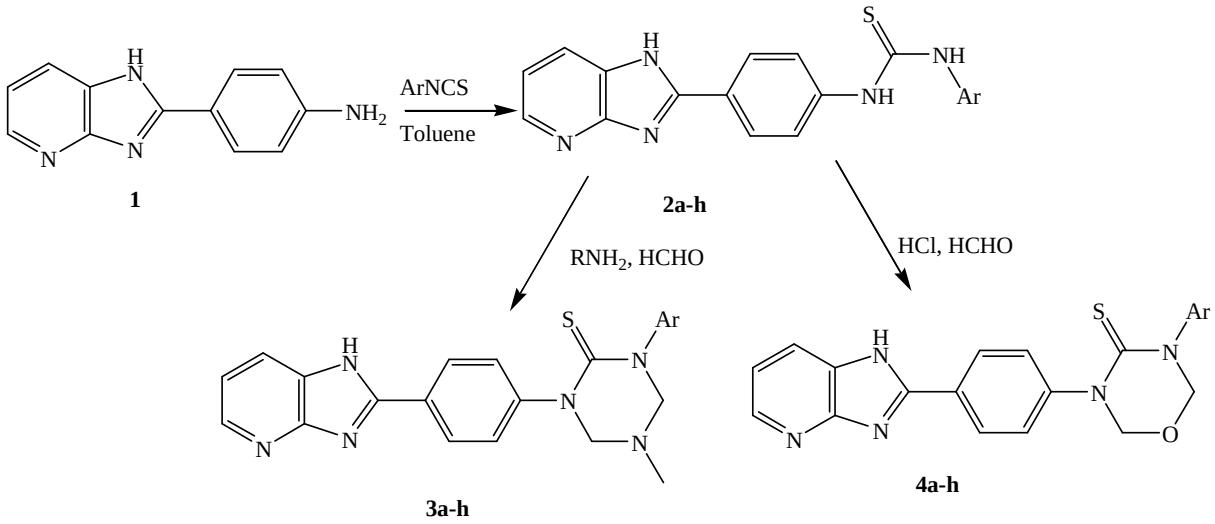
1-(4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)-3-arylthiourea
To a solution of 4-(1H-imidazo[4,5-b]pyridin-2-yl)benzenamine (0.01 mole), in dry DMF (20mL) arylisothiocyanate (0.01 mole) was added and the contents were refluxed for 4 hrs. The reaction was monitored on TLC. After the completion of reaction the content was cooled and the separated product was filtered and crystallized from EtOH.

1-(4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)-3-phenylthiourea
^{1}H NMR (DMSO-d_6) δ = 13.95 (brs, 1H), 8.61 (brs, 1H), 8.22 (s, 1H), 8.19 (d, 1H), 8.13 (m, 2H), 7.32 (m, 1H), 7.20 (d, 1H), 6.42 (t, 1H); Mass [M+H] = 346

1-(4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)-3-(4-chlorophenyl)thiourea
^{1}H NMR (DMSO-d_6) δ = 13.32 (brs, 1H), 12.02 (brs, 1H), 8.62 (brs, 1H), 8.24 (d, 2H), 8.17 (d, 1H), 7.65 (d, 2H), 7.41 (d, 1H), 7.25 (m, 1H), 7.18 (m, 2H); Mass [M+H] = 381

1-(4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)-3-(2-chlorophenyl)thiourea
^{1}H NMR (DMSO-d_6) δ = 12.99 (brs, 1H), 12.13 (brs, 1H), 8.63 (brs, 1H), 8.23 (d, 2H), 8.17 (m, 1H), 8.11 (m, 2H), 7.66 (m, 2H), 7.41 (d, 1H), 7.24 (m, 1H), 7.17 (m, 2H); Mass [M+H] = 381

Scheme



1 **2a-h** **3a-h** **4a-h**

Ar = phenyl, 4-chlorophenyl, 2-chlorophenyl, 4-methoxyphenyl, 3-methoxyphenyl, 3-hydroxyphenyl, 4-bromophenyl, 2-bromophenyl

1-(4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)-3-(4-methoxyphenyl)thiourea
^{1}H NMR (DMSO-d_6) δ = 13.62 (brs, 1H), 12.55 (brs, 1H), 8.64 (brs, 1H), 8.25 (d, 2H), 8.12 (m, 1H), 8.07 (m, 2H), 7.66 (m, 2H), 7.34 (d, 1H), 7.24 (m, 1H), 7.17 (m, 2H), 6.52 (t, 1H), 3.86 (s, 3H); Mass [M+H] = 376

1-(4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)-3-(2-methoxyphenyl)thiourea
^{1}H NMR (DMSO-d_6) δ = 13.52 (brs, 1H), 12.58 (brs, 1H), 8.66 (brs, 1H), 8.27 (d, 2H), 8.14 (m, 1H), 8.08 (m, 2H), 7.67 (m, 2H), 7.35 (m, 1H), 7.20 (d, 2H), 6.53 (t, 1H), 3.85 (s, 3H); Mass [M+H] = 376

1-(4-(1H-benzo[d]imidazol-2-yl)phenyl)-3-(3-hydroxyphenyl)thiourea
^{1}H NMR (DMSO-d_6) δ = 12.98 (brs, 1H), 12.25 (brs, 1H), 10.78 (brs, 1H), 8.68 (brs, 1H), 8.32 (d, 2H), 8.24 (m, 1H), 8.12 (m, 2H), 7.69 (m, 2H), 7.45 (m, 1H), 7.25 (d, 2H), 6.78 (t, 1H); Mass [M+H] = 362

1-(4-(1H-benzo[d]imidazol-2-yl)phenyl)-3-(4-bromophenyl)thiourea
^{1}H NMR (DMSO-d_6) δ = 13.52 (brs, 1H), 12.34 (brs, 1H), 8.64 (brs, 1H), 8.25 (d, 2H), 8.19 (d, 1H), 8.11 (m, 2H), 7.67 (d, 2H), 7.42 (d, 1H), 7.26 (m, 1H), 7.19 (m, 2H); Mass [M+H] = 425

1-(4-(1H-benzo[d]imidazol-2-yl)phenyl)-3-(2-bromophenyl)thiourea
^{1}H NMR (DMSO-d_6) δ = 13.48 (brs, 1H), 12.54 (brs, 1H), 8.65 (brs, 1H), 8.24 (d, 2H), 8.20 (d, 1H), 8.10 (m, 2H), 7.66 (d, 2H), 7.42 (d, 1H), 7.25 (m, 2H), 7.20 (m, 2H); Mass [M+H] = 425

1-(4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)-5-methyl-3-aryl-1,3,5-triazinane-2-thiones
A mixture of 1-(4-(1H-benzo[d]imidazol-2-yl)phenyl)-3-(2-bromophenyl)thiourea (0.05 mole), formaldehyde (0.1 mmoles) and methyl amine (0.05 moles) was taken in ethanol (20 mL) and refluxed for 4-6 hrs. The reaction was

monitored on TLC. After the completion of reaction it was cooled and the separated product was filtered. The crude material was passed through silica gel column and the product was eluted from 60 % ethylacetate and hexane.

1-(4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)-5-methyl-3-phenyl-1,3,5-triazinane-2-thione
^{1}H NMR (DMSO-d_6) δ = 9.82 (brs, 1H), 7.98 (d, 1H), 7.80 (d, 1H), 7.71 (m, 3H), 7.40 (d, 2H), 7.31 (d, 1H), 7.20 (m, 2H), 6.98 (t, 1H), 6.42 (d, 1H), 5.81 (s, 2H), 5.61 (s, 2H), 2.79 (s, 3H); Mass [M+H] = 401

1-(4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)-5-methyl-3-(4-chlorophenyl)-1,3,5-triazinane-2-thione
^{1}H NMR (DMSO-d_6) δ = 10.02 (brs, 1H), 7.98 (d, 1H), 8.00 (d, 1H), 7.88 (m, 3H), 7.74 (d, 2H), 7.44 (d, 2H), 7.32 (d, 1H), 7.22 (m, 1H), 6.99 (t, 1H), 6.40 (d, 1H), 5.82 (s, 2H), 5.62 (s, 2H), 2.81 (s, 3H); Mass [M+H] = 435

1-(4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)-5-methyl-3-(2-chlorophenyl)-1,3,5-triazinane-2-thione
^{1}H NMR (DMSO-d_6) δ = 10.80 (brs, 1H), 8.02 (d, 1H), 7.88 (d, 1H), 7.76 (d, 2H), 7.46 (d, 2H), 7.34 (d, 1H), 7.24 (m, 2H), 7.00 (t, 1H), 6.41 (d, 1H), 5.80 (s, 2H), 5.60 (s, 2H), 2.78 (s, 3H); Mass [M+H] = 435

1-(4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)-5-methyl-3-(4-methoxyphenyl)-1,3,5-triazinane-2-thione
^{1}H NMR (DMSO-d_6) δ = 11.12 (brs, 1H), 8.24 (d, 1H), 7.98 (d, 1H), 7.80 (d, 2H), 7.52 (d, 2H), 7.36 (d, 1H), 7.24 (m, 2H), 6.98 (t, 1H), 6.42 (d, 1H), 5.84 (s, 2H), 5.64 (s, 2H), 3.86 (s, 3H), 2.78 (s, 3H); Mass [M+H] = 431

1-(4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)-5-methyl-3-(3-methoxyphenyl)-1,3,5-triazinane-2-thione
^{1}H NMR (DMSO-d_6) δ = 11.20 (brs, 1H), 8.25 (d, 1H), 7.99 (d, 1H), 7.81 (d, 2H), 7.53 (d, 2H), 7.37 (d, 1H), 7.25 (m, 2H), 6.99 (m, 1H), 6.43 (d, 1H), 5.83 (s, 2H), 5.63 (s, 2H), 3.87 (s, 3H), 2.79 (s, 3H); Mass [M+H] = 431

1-(4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)-5-methyl-3-(3-hydroxyphenyl)-1,3,5-triazinane-2-thione
^{1}H NMR (DMSO-d_6) δ = 11.52 (brs, 1H), 10.58 (brs, 1H), 8.18 (d, 1H), 8.01 (m, 1H), 7.80 (d, 2H), 7.54 (d, 2H), 7.38 (d, 1H), 7.26 (m, 2H), 7.00 (m, 1H), 6.44 (d, 1H), 5.84 (s, 2H), 5.64 (s, 2H), 2.76 (s, 3H); Mass [M+H] = 417

1-(4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)-5-methyl-3-(4-bromoyphenyl)-1,3,5-triazinane-2-thione
^{1}H NMR (DMSO-d_6) δ = 11.15 (brs, 1H), 8.42 (d, 1H), 8.12 (m, 1H), 7.84 (d, 2H), 7.55 (d, 2H), 7.38 (d, 1H), 7.25 (m, 2H), 7.02 (m, 1H), 6.48 (d, 1H), 5.82 (s, 2H), 5.62 (s, 2H), 2.78 (s, 3H); Mass [M+H] = 479

1-(4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)-5-methyl-3-(2-bromophenyl)-1,3,5-triazinane-2-thione
^{1}H NMR (DMSO-d_6) δ = 11.24 (brs, 1H), 8.43 (d, 1H), 8.10 (m, 1H), 7.85 (d, 2H), 7.56 (d, 2H), 7.38 (d, 1H), 7.26 (m, 2H), 7.08 (m, 1H), 6.48 (d, 1H), 5.83 (s, 2H), 5.63 (s, 2H), 2.79 (s, 3H); Mass [M+H] = 479

3-(4-(1H-imidazo[4,5-b]pyridine-2-yl)phenyl)-5-aryl-1,3,5-oxadiazinane-4-thiones
1-(4-(1H-imidazo[4,5-b]pyridin-2-yl)phenyl)-3-phenylthiourea **(5)** (0.05 mole), was added with 30 % formaldehyde solution (0.1 moles) and the mixture was treated with conc. HCl (5 mL). After heating at 90-95^{O}C for 4 hrs, the reaction mixture was cooled and neutralized with NaOH. The precipitate formed was filtered and passed through silica gel column and the product was eluted from 60 % ethylacetate and hexane.

3-(4-(1H-imidazo[4,5-b]pyridine-2-yl)phenyl)-5-phenyl-1,3,5-oxadiazinane-4-thione
^{1}H NMR (DMSO-d_6) δ = 9.68 (brs, 1H), 7.82 (m, 3H), 7.74 (s, 1H), 7.65 (t, 1H), 7.41 (d, 2H), 7.30 (d, 1H), 7.21 (m, 2H), 6.98 (t, 1H), 6.62 (d, 1H), 5.98 (s, 2H), 5.78 (s, 2H); Mass [M+H] = 387

3-(4-(1H-imidazo[4,5-b]pyridine-2-yl)phenyl)-5-(4-chlorophenyl)-1,3,5-oxadiazinane-4-thione
^{1}H NMR (DMSO-d_6) δ = 9.85 (brs, 1H), 7.82 (m, 2H), 7.75 (s, 1H), 7.65 (t, 1H), 7.43 (d, 2H), 7.33 (d, 1H), 7.23 (d, 2H), 6.99 (t, 1H), 6.63 (d, 1H), 5.99 (s, 2H), 5.79 (s, 2H); Mass [M+H] = 422

3-(4-(1H-imidazo[4,5-b]pyridine-2-yl)phenyl)-5-(2-chlorophenyl)-1,3,5-oxadiazinane-4-thione
^{1}H NMR (DMSO-d_6) δ = 9.90 (brs, 1H), 8.03 (m, 2H), 7.78 (s, 1H), 7.67 (t, 1H), 7.44 (d, 2H), 7.34 (d, 1H), 7.25 (d, 2H), 7.00 (t, 1H), 6.62 (d, 1H), 6.00 (s, 2H), 5.80 (s, 2H); Mass [M+H] = 422

3-(4-(1H-imidazo[4,5-b]pyridine-2-yl)phenyl)-5-(4-methoxyphenyl)-1,3,5-oxadiazinane-4-thione
^{1}H NMR (DMSO-d_6) δ = 9.80 (brs, 1H), 8.04 (m, 2H), 7.81 (s, 1H), 7.68 (t, 1H), 7.45 (d, 2H), 7.36 (d, 1H), 7.24 (d, 2H), 6.98 (t, 1H), 6.61 (d, 1H), 5.98 (s, 2H), 5.78 (s, 2H), 3.86 (s, 3H); Mass [M+H] = 417

3-(4-(1H-imidazo[4,5-b]pyridine-2-yl)phenyl)-5-(3-methoxyphenyl)-1,3,5-oxadiazinane-4-thione
^{1}H NMR (DMSO-d_6) δ = 9.82 (brs, 1H), 8.02 (m, 2H), 7.80 (s, 1H), 7.69 (t, 1H), 7.46 (d, 2H), 7.37 (d, 1H), 7.25 (d, 2H), 6.99 (t, 1H), 6.62 (d, 1H), 5.99 (s, 2H), 5.79 (s, 2H), 3.87 (s, 3H); Mass [M+H] = 417

3-(4-(1H-imidazo[4,5-b]pyridine-2-yl)phenyl)-5-(3-hydroxyphenyl)-1,3,5-oxadiazinane-4-thione
^{1}H NMR (DMSO-d_6) δ = 10.53 (brs, 1H), 9.75(brs, 1H), 8.00 (m, 2H), 7.84 (s, 1H), 7.68 (m, 1H), 7.45 (d, 2H), 7.38 (d, 1H), 7.24 (d, 2H), 7.00 (t, 1H), 6.61 (m, 1H), 5.97 (s, 2H), 5.77 (s, 2H); Mass [M+H] = 403

3-(4-(1H-imidazo[4,5-b]pyridine-2-yl)phenyl)-5-(4-bromophenyl)-1,3,5-oxadiazinane-4-thione
^{1}H NMR (DMSO-d_6) δ = 10.05 (brs, 1H), 8.10 (m, 2H), 7.85 (m, 1H), 7.70 (m, 1H), 7.46 (d, 2H), 7.40 (d, 1H), 7.26 (d, 2H), 6.98 (t, 1H), 6.65 (m, 1H), 5.98 (s, 2H), 5.78 (s, 2H); Mass [M+H] = 466

3-(4-(1H-imidazo[4,5-b]pyridine-2-yl)phenyl)-5-(4-bromophenyl)-1,3,5-oxadiazinane-4-thione
^{1}H NMR (DMSO-d_6) δ = 10.10 (brs, 1H), 8.12 (m, 2H), 7.86 (m, 1H), 7.71 (m, 1H), 7.45 (d, 2H), 7.41 (d, 1H), 7.25 (d, 2H), 6.98 (t, 1H), 6.66 (m, 1H), 5.99 (s, 2H), 5.79 (s, 2H); Mass [M+H] = 466

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