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ECO-FRIENDLY SYNTHESIS OF IMIDAZO[4,5-B]PYRIDINE CONTAINIG-1,3,5-TRIAZINANE-2-THIONES

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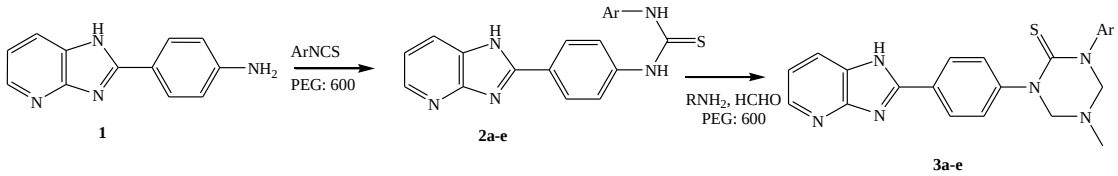
Abstract
Polyethylene glycol mediated synthesis of triazinane-2-thiones is presented. The compounds synthesied are charecterized by spectral analysis.

Introduction

Imidazopyridines are acting as structural parts of natural and synthetic bioactive molecules because of their interesting biological activities. These class of compounds are acting as precursors in variety of drugs[i-iii]. 1,3,5-triazinan-2-ones are constructive for the protection of amino groups,[iv] in addition for the preparation of polyamines,[v]poly functional amino alcohols and water soluble triazinan-2-ones are used as fertilizers.[vi] Reports on these 1,3,5-triazinan-2-ones[vii-xi] provide the significance of these compounds.

So many different conventional methods are available to prepare heterocyclic compounds;however there are most common threats to living organism. In recent past, due to chemical industries the environmental pollution has been increased predominantly. Therefore, new approaches like microwave irradiation, sonication, multi component reactions etc. have great importance.Thesetechniques are more eco-friendly methods which are in lofty claim. Therefore, avoiding the use of such solvents in chemical reactions is an effective way to decrease toxic materials to the atmosphere. In continuation to our earlier work[xii] using, polyethylene glycols, we here in report an eco-friendly synthesis of title compounds.

Scheme:



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

Results and Discussion

The solvents used in organic synthesis are most abundant, play very important role in view of their economic, safety; therefore, substitute on solvents and reinstating solvents with harmless derivative can have a huge conservation impact. We chose PEG, as green solvent. We have synthesized compounds (3a-e) under eco-friendly conditions. After working up it is observed that water andPEG are miscible, pure PEG-600 was extracted by fractional distillation which will be used in the second cycle. 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-e)**

Experimental

All the chemicals used are AR grade. The solvents were purified by regular process. The instrument used to record ^{1}H NMR spectra was Varian MR-400 MHz. Chemical shifts are mentioned in δ ppm, tetramethylsilane as internal standard. The signals were reported as q (quartet), m (multiplet), d (doublet), t (triplet), brs (broad Singlet), s (singlet), and coupling constants in Hz. The Agilent ion trap MS was used to record mass spectra.

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 (1 eq), in PEG: 600 (20mL) arylisothiocyanate (1 eq) was added and the contents were refluxed for 2-3 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 (2a)

^{1}H NMR (DMSO-d_6) δ = 6.42 (t, 1H), 6.98 (d, 2H), 7.20 (d, 2H), 7.32 (m, 1H), 7.68 (d, 2H), 8.13 (m, 2H), 8.19 (d, 1H), 8.22 (s, 1H), 8.61 (brs, 1H), 12.1 (brs, 1H), 13.95 (brs, 1H); Mass [M+H] = 346

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

^{1}H NMR (DMSO-d_6) δ =^{1}H NMR (DMSO-d_6) δ =6.92 (d, 2H), 7.18 (m, 2H), 7.25 (m, 1H), 7.41 (d, 1H), 7.65 (d, 2H), 8.17 (d, 1H), 8.24 (d, 2H), 8.62 (brs, 1H), 12.02 (brs, 1H), 13.32 (brs, 1H); Mass [M+H] = 381

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

^{1}H NMR (DMSO-d_6) δ = 7.17 (m, 2H), 7.24 (m, 1H), 7.41 (d, 1H), 7.66 (m, 2H), 8.11 (m, 2H), 8.17 (m, 1H), 8.23 (d, 2H), 8.63 (brs, 1H), 12.13 (brs, 1H), 12.99 (brs, 1H); Mass [M+H] = 381

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

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

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

^{1}H NMR (DMSO-d_6) δ = 3.85 (s, 3H), 6.53 (t, 1H), 7.20 (d, 2H), 7.35 (m, 1H), 7.67 (m, 2H), 8.08 (m, 2H), 8.14 (m, 1H), 8.27 (d, 2H), 8.66 (brs, 1H), 12.58 (brs, 1H), 13.52 (brs, 1H);

Mass [M+H] = 376

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 (1 eq), formaldehyde (2 eq) and methyl amine (1 eq) was taken in PEG: 600 (20 mL) and refluxed for 1-2 hr. 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 (3a)

^{1}H NMR (DMSO-d_6) δ =2.79 (s, 3H), 5.61 (s, 2H), 5.81 (s, 2H),6.42 (d, 1H), 6.98 (t, 1H),7.20 (m, 2H), 7.31 (d, 1H),7.40 (d, 2H), 7.71 (m, 3H),7.80 (d, 1H), 7.98 (d, 1H), 9.82 (brs, 1H); 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 (3b)

^{1}H NMR (DMSO-d_6) δ = 2.81 (s, 3H), 5.62 (s, 2H), 5.82 (s, 2H), 6.40 (d, 1H), 6.99 (t, 1H), 7.22 (m, 1H), 7.32 (d, 1H), 7.44 (d, 2H), 7.74 (d, 2H), 7.88 (m, 1H), 8.00 (d, 1H), 7.98 (d, 1H), 10.02 (brs, 1H); 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 (3c)

^{1}H NMR (DMSO-d_6) δ = 2.78 (s, 3H), 5.60 (s, 2H), 5.80 (s, 2H), 6.41 (d, 1H), 7.00 (t, 1H), 7.24 (m, 2H), 7.34 (d, 1H), 7.46 (d, 2H), 7.76 (d, 2H), 7.88 (d, 1H), 8.02 (d, 1H), 10.80 (brs, 1H); 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 (3d)

^{1}H NMR (DMSO-d_6) δ = 2.78 (s, 3H), 3.86 (s, 3H), 5.64 (s, 2H), 5.84 (s, 2H), 6.42 (d, 1H), 6.98 (t, 1H), 7.24 (m, 2H), 7.36 (d, 1H), 7.52 (d, 2H), 7.80 (d, 2H), 7.98 (d, 1H), 8.24 (d, 1H), 11.12 (brs, 1H); 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 (3e)

^{1}H NMR (DMSO-d_6) δ = 2.79 (s, 3H), 3.87 (s, 3H), 5.63 (s, 2H), 5.83 (s, 2H), 6.43 (d, 1H), 6.99 (m, 1H), 7.25 (m, 2H), 7.37 (d, 1H), 7.53 (d, 2H), 7.81 (d, 2H), 7.99 (d, 1H), 8.25 (d, 1H), 11.20 (brs, 1H); Mass [M+H] = 431

Conclusion

This paper describes the synthesis of triazinane-2-thionederivatives (**3**) using polyethylene glycol (PEG-600) as promoting reaction medium. This methodology gave good yield in less time of reaction with cleaner reaction profile.

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