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Research Article

Novel Synthesis of 2-(2-imino-4-thio-5-substitutedbiureto-1-yl)-4-(3-substituted thiocarbamido-1-yl)-6-substitutedimino-1,3,5-thiadiazine

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ABSTRACT

Novel series 2-(2-imino-4-thio-5-substitutedbiureto-1-yl)-4-(3-substituted thiocarbamido-1-yl)-6-substitutedimino-1,3,5-thiadiazine [3a(i) to 3f(iii)] have been obtained by basification of their hydrochlorides [2a(i) to 2f(iii)] in presence of ammonium hydroxide solution, which are synthesized by the interaction of 1,3-bis-(N-substitutedamidinothiocarbamido)-thiocarbamide(1a-1f) and aryl/alkylisocyanodichlorides. The latter were prepared initially by the condensation of aryl/alkylisothiocyanate with 1,3-Diformamidinothiacarbamide. The structures of all these compounds were established on the basis of IR and PMR spectrum data.

Keywords: 1,3- Diformamidinothiacarbamide, 1,3,5-thiadiazines, synthesis.

INTRODUCTION

The literature survey reveals that the heterocyclic compounds having 1,3,5-thiadiazines nucleus enhanced pharmaceutical, medicinal, agricultural and industrial values[1-2]. The synthetic applications of N-substitutedisocyanodichlorides have been investigated and shown to have enough potential in the synthesis of nitrogen and sulphur containing heterocyclic compounds[3-5] thus aim to synthesized 1,3,5-thiadiazines[6-8], reaction of aryl/alkylisocyanodichloride have been carried out with 1,3-bis-(N-substituted amidino thio carbamido)thiocarbamide in 1:1 molar ratios.

Experimental

All chemicals used were of analar grade. Aryl/alkylisothiocyanate, Aryl/alkylisocy-anodichlorides were prepared according to literature method.[9] Melting points of all synthesized compounds were determine in open capillary. IR spectra were recorded on Perkin-Elmer spectrometer in the range 4000-400 cm^{-1} in KBr pellets. PMR spectra were recorded with TMS as internal standard using $CDCl_3$ and DMSO-d_6. TLC checked the purity of the compounds on silica gel-G plates with layer thickness of 0.3 mm. and result are cited in Table 1.

RESULT AND DISCUSSION

The parent compound 1-3-Bis-(N-phenylamidinothiocarbamido) thiocarbamide**(1a-f)** was prepared by refluxing the mixture of 1,3-Diformamidinothiacarbamide (0.05mol) and phenylisothiocyanate (0.05 mol) was refluxed in carbon tetrachloride medium for 4 hr. on water bath. The compound (1a-f) was then further reacted with N-substitutedisocyanodichlorides[9] in 1:1 molar proportion in carbon tetrachloride medium for 4 hrs. During heating evolution of hydrogen chloride gas was noticed as tested with moist blue litmus paper. Cooling the reaction mixture and distilling off excess solvent needle shape crystals ware isolated. These were acidic to litmus and identified as monohydrochlorides of Synthesis of 2-(2-imino-4-thio-5-phenylbiureto-1-yl)-4-(3-phenylthio-carbamido-1-yl)-6-phenylimino-1,3,5-thiadiazine **[2a(i) to 2f(iii)].** These on

basification with aqueous ammonium hydroxide solution afforded free **bases [3a(i) to 3f(iii)]**.

1-3-Bis-(N-phenyl amidino thiocarbamido) thiocarbamide (1a)

Mixture of **(1)** (0.01 mol), phenylisothiocyanate (0.02 mol) and acetone-ethanol (50ml) were refluxed on water bath for 12 h. The mixture was filtered and filtrate during distillation yielded the crystals of 2a.Yield 72 %; m.p.270-72 ^{0}c**;** IR spectrum of compound showed ν (N-H) 3471.3cm^{-1}**,** (C-H)(Ar) 3150.0cm^{-1}**,** ν(C=N) 1642.2cm^{-1}, ν(C-N) 1253.7cm^{-1}, ν(C=S) grouping 1087.6cm^{-1}, ν(C-S) 721.7cm^{-1},ν (C=NH) grouping 1571.7cm^{-1}.The PMR spectrum of compounds showed signals due to N-H protons at δ 3.9-4.3 ppm, Ar-NH protons at δ 5.1-5.9 ppm, Ar-H protons at δ 6.3 ppm and the signal at δ 3.1-3.2 ppm is due to moisture in DMSO-d_6 and δ1.3-2.3 ppm is due to DMSO.
Similarly others compounds **1b-1f** were synthesised by above mention method.

Synthesis of 2-(2-imino-4-thio-5-phenyl biureto-1-yl)-4-(3-phenylthio-carbamido-1-yl)-6-phenylimino-1,3,5-thiadiazine [3a(i)]

1-3-Bis-(N-phenylamidinothiocarbamido) thiocarbamide (0.01M) (1a) was suspended in carbon tetrachloride medium (25ml). To this a solution of phenylisocyanodichlorides (0.01M) was added in 1:1 molar proportions. The reaction mixture was refluxed on water bath for 4 h. During heating evolution of hydrogen chloride gas was observed and tested with moist blue litmus paper. Cooling the reaction mixture and distilled off excess solvent, needle shape crystals were separated out. And crystallized from aqueous ethanol. Yield 79 %; m.p.276 ^{0}C and identified as of 2-(2-imino-4-thio-5-phenylbiureto-1-yl)-4-(3-phenylthio-carbamido- 1-yl)-6-phenylimino-1,3,5-thiadiazine hydrochloride [2a(i)], which on basification with aqueous ammonium hydroxide solution afforded free base **[3a(i)].** It was recrystallised from aqueous ethanol. Yield 72 % m.p.268 ^{0}C. IR spectrum of compound showed ν(N-H) 3273.4 cm^{-1}, ν(CH-Ar) 3118.3 cm^{-1}, ν(C=N) 1695.4 cm^{-1}, ν(C=N) imino grouping 1652.5 cm^{-1}, ν(C-N) 1181.9 cm^{-1}ν, (C=S) grouping 1063.0 cm^{-1}, ν (C–S) 726.6 cm^{1}. The PMR spectrum of compound showed signals due to Ar-NH protons at δ 7.63 ppm, N-H protons at δ 7.36 ppm and Ar-H protons at δ 6.76 ppm, NH protons at δ 3.0-3.7 ppm. The signal at δ 0.87-1.48 ppm is due to moisture DMSO-d_6. Similarly others compounds [2a(ii) to 2f(iii)] and [3a(ii) to 3f(iii)] were synthesized by above mention method.

Table 1:* Physical data and antibacterial activity of the compounds [3a(i) to 3f(iii)]

Compd.	R	R_1	Yield	m.p. (^{0}C)
[3a(i)]	Phenyl	Phenyl	72	268
[3a(ii)]	Phenyl	*p*-Chloro-phenyl	77	272
[3a(iii)]	Phenyl	Ethyl	69	256
[3b(i)]	*p*-Chloro-phenyl	Phenyl	68	273
[3b(ii)]	*p*-Chloro-phenyl	*p*-Chlorophenyl	62	279
[3b(iii)]	*p*-Chloro-phenyl	Ethyl	61	252
[3c(i)]	*p*-Tolyl	Phenyl	67	269
[3c(ii)]	*p*-Tolyl	*p*-Chlorophenyl	61	272
[3c(iii)]	*p*-Tolyl	Ethyl	64	254
[3d(i)]	Ethyl	Phenyl	67	248
[3d(ii)]	Ethyl	*p*-Chlorophenyl	71	252
[3d(iii)]	Ethyl	Ethyl	77	232
[3e(i)]	Methyl	Phenyl	73	231
[3e(ii)]	Methyl	*p*-Chlorophenyl	69	242
[3e(iii)]	Methyl	Ethyl	62	227
[3f(i)]	*t*-Butyl	Phenyl	59	264
[3f(ii)]	*t*-Butyl	*p*-Chlorophenyl	62	271
[3f(iii)]	*t*-Butyl	Ethyl	67	261

* All Compounds gave satisfactory C, H, N, and S analysis.

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