Novel Synthetic Derivatives of Substituted Amino -1, 2, 4-Thiadiazoles

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Abstract

A novel series of 3-amino-5-substituted amino-1,2,4-thiadiazoles (5a-f) and 3-substituted thiocarbamido-5-substituted amino-1,2,4-thiadiazoles (6a-f) have been obtained by the oxidative cyclization of 1-substituted-3-formamidinothiocarbamide[1] (3a-f) and 1,3-bis(substitutedthioamido)-guanidine[1] (4a-f) with bromine respectively. (3a-f) were synthesized by the interaction of guanidine (1) with various alkyl/aryl isothiocayantes (2a-f) in 1:1 molar ratio in carbon tetrachloride medium while (4a-f) were isolated by the condensation of guanidine (1) with different alkyl/aryl isothiocayantes (2a-f) in 1:2 molar ratio in ethanol-acetone medium. The structure of all these compounds was established on the basis of elemental analysis, equivalent weight and spectral data.

Keywords: Thiocarbamide, substitutedthioamidoguanidine, thiadiazoles.

Introduction

The literature survey reveals that the heteterocyclic compounds having thiadiazole nucleus enhanced pharmaceutical, medicinal, agricultural and industrial Values[2-5]. So the medicines containing thiadiazole nucleus are now used extensively in medicinal, agricultural, pharmaceutical, biotechnological faculties. These drugs have been shown to possess a diverse range of physiological activities[6-7], plant growth promoting activity, antitumor[8-9], antibacteria[10-11], amoebicial[12], antidiabetic[13] values. Some thiadiazoles were also found to be active against *S. aurues, E. coli and C. albicans*[14-16]. The synthetic application of guanidine and its derivatives have been investigated and shown to have enough potential in the synthesis of nitrogen and sulphur containing heterocycles. As a part of research presently been undertaken in these laboratories in the synthesis of nitrogen and sulphur containing compounds, it was thought interesting to investigate the chemistry of guanidine with view to develop a new route for synthesizing 1,2,4-thiadiazole by the interaction of guanidine with various alkyl/aryl isothiocyantes[17] in different reaction conditions and mediums for the isolation of 3a-f and 4a-f which on further oxidative cyclization were successfully converted into 1,2,4-thiadiazoles.

Experimental

All the chemicals used were of analytical grade, India make except guanidine (Lancaster, Germany make). Substituted isothiocyantes were prepared according to literature method[15]. Melting points of all synthesized compounds were determined in open capillary and uncorrected. IR spectra were recorded on Perkin-Elmer spectrophotometer in the range 4000-400 cm^{-1} in nujol mull as KBr pallets, PMR spectra were recorded with TMS as internal standard using $CDCI_3$ and DMSO-d_6. The purity of the compounds were checked on silica gel-G plate by TLC.

Synthesis of 3-amino-5-phenylamino-1, 2, 4-thiadiazole (5a)

In china dish, the paste of 1-phenyl-3-formamidino thiocarbamide (0.1 M) (3a) was made in chloroform. To this liquid bromine in chloroform (10%) was added with constant stirring. Initially the colour of bromine persisted. The reaction mixture was allowed to stand for 8-9 hours, when of white colour powder separated out which on crystallization from ethanol gave (5a), yield 83%, m.p. 130°C. Found (Calcd.): C, 48.48 % (50.00%), H= 3.87% (4.20%), N=29.01% (29.16%), S=15.75% (16.60%) A compound gave positive lassagine's test for nitrogen and sulphur elements. The compound did not desulphurised when boiled with alkaline plumbite solution which clearly indicate sulphur is present in cyclic form, the analytical data show molecular formula is $C_8H_8N_4S_1$, molecular weight 192 , IR spectra of compound shows v(NH) 3308.6 cm^{-1}, v(C=O) 1660.5 cm^{-1}, v(=NH) 1465.6 cm^{-1}. The PMR spectra of compound show signal due to N-H proton at δ 7.2664 ppm, Ar-H at δ 6.16054 ppm and signal at 4.00925 ppm is due to thiadiazino NH. Similarly, other compounds (5b-f) were synthesized by above mentioned methods and enlisted in Table-1.

Synthesis of 3-phenyl thiocarbamido-5-phenyl amino-1, 2, 4-thiadiazole (6a)

In china dish paste of 1, 3-bis-(phenylthioamido)-guanidine (0.1 M) (4a) was made in chloroform. To this liquid bromine in chloroform (10%) was added with constant stirring. Initially the colour of bromine disappeared the addition was continued till the colour of bromine persisted. The reaction mixture was allowed to stand for 8-9 hours, when yellow colour compound separated out. It is crystallized by ethanol to obtain (6a), yield 79%, m.p. 195 °C. Found (Calcd.): C, 54.86% (55.04%), H=3.21% (3.97%), N=20.98% (21.40%), S=17.37% (19.51%). From analytical data molecular formula is $C_{15}H_{13}N_5S_2$ and molecular weight 327. The IR spectra of compound shows v(N-H) 3383.9 cm^{-1}, v(=NH) 1573.9 cm^{-1}, v(N-N>C=S) 1179.8 cm^{-1}. The PMR spectra of the compound shows signals due to Ar-NH protons at δ 7.2704-8.18 ppm, and thiadiazolidines NH protons at δ 4.0201 ppm. Similarly, other compounds (6b-f) were synthesized from (4b-f) by above mentioned method and enlisted in Table-2.

Table-1*: Physical data of the synthesized compounds 3-Amino-5-substituted amino-1, 2, 4-thiadiazole

Compd. No.	R	Yield (%)	m.p. °C	M.W.	Molecular Formula
5a	Phenyl	83	130	192	$C_8H_8N_4S_1$
5b	p-Chlorophenyl	79	147	226	$C_8H_7N_4S_1Cl_1$
5c	p-Tolyl	68	120	206	$C_9H_{10}N_4S_1$
5d	Methyl	78	157	130	$C_3H_6N_4S_1$
5e	Ethyl	80	142	144	$C_4H_8N_4S_1$
5f	t-Butyl	63	110	177	$C_6H_{12}N_4S_1$

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

Table-2*: Physical data of the synthesized compounds 3-substituted thiocarbamide-5-substituted-1, 2, 4-thiadiazole

Compd. No.	R	Yield (%)	m.p. °C	M.W.	Molecular Formula
6a	Phenyl	87	195	327	$C_{15}H_{13}N_5S_2$
6b	p-Chlorophenyl	80	200	360	$C_{15}H_{11}N_{11}S_2Cl_2$
6c	p-Tolyl	83	182	355	$C_{17}H_{17}N_5S_2$
6d	Methyl	69	110	203	$C_5H_9N_5S_2$
6e	Ethyl	72	95	231	$C_7H_{13}N_5S_2$
6f	t-Butyl	54	124	287	$C_{11}H_{22}N_5S_2$

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

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