

Studies in the Chemistry of Some New 1,2,4-thiadiazolidine by Oxidative Cyclisation

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Abstract

Recently in this laboratory a novel series of Hector's bases (1, 2, 4-thiadiazolidine) had been synthesised. 1-substituted-3-formamidinothiocarbamides (1a-f) and 1,3-bis(N-substituted-thioamido)guanidines (1g-l) were oxidatively cyclised by using aqueous bromine as oxidizing agent in chloroform medium to synthesised yet new series of Hector's bases, viz; 3-imino-5-substituted imino-1,2,4-thiadiazolidine (2a-f) and 3-substituted thioamidoimino-5-substitutedimino-1,2,4-thiadiazolidine (2g-l), respectively. The oxidative cyclisation of (1a-l) was also carried out by making use of H_2O_2 in concentrated HCl as the oxidizing agent. The Hector's bases isolated in these reactions were characterised on the basis of conventional elemental analysis, chemical characteristics and IR and 1H -NMR spectral analysis.

Keywords: Hector's base, Oxidative cyclisation, 1-substituted-3-formamidino-thiocarbamide, 1, 3-bis(N-substituted thioamido)guanidines

1. Introduction

The first Hector's base was synthesised by Hector (1889, 1892). After Hector Hofmann and Garbail (1992), Hegershoff (1901), Kurzer (1956), Dost (1906) and Lal (1939) synthesise various series of Hector's bases and all synthesised compounds were termed and justified as Hector's bases by them. However, Sahasrabudhey (1942), Suresh (1960), Joshua (1961) investigated that all the Hector's bases which are synthesised by them are not necessarily be true Hector's bases and some were thiadiazoles and thiadiazolidines. The justification of this statement was done on the basis of gasometric studies, chemical characteristics and spectroscopic evidences (Suresh, K. S., 1959). It means that some thiadiazoles as well as thiadiazolidines are Hector's bases, but not all (For Hector's bases they must obey some typical properties (Hector D. S., 1892; Steanly, G. M., 1950; Tiwari, S. S., 1970)). The literature survey also reveals that the heterocyclic compounds having Hector's base nucleus enhance pharmaceutical, medicinal, agricultural and industrial applications. (Planka, M., 1968; Ahluwalia, U. K., 1968; Metzger, C., 1988; Zhang Ziyi, 1969) Hence medicine containing Hector's base nucleus are now used extensively in medicinal, agricultural, pharmaceutical and biotechnological faculties. These drugs were shown to possess a diverse range of physiological activities, (Budianu, C. H., 1987; McGuinness, 1988) plant growth promoting activity, antitumour, (Fernandes, 1986) herbical, (Farooq Saleem, 1987) antibacterial, (Farooq Saleem, 1989; Andotra, C. S., 1988) amoebicidal and antidiabetic (Rollas, S., 1984) properties. Very few work has been caring out on the synthesis of Hector's bases and their applications. As a part of research work being undertaken in the synthesis of nitrogen and sulphur containing heteroacycles and heterocycles having various application in drug chemistry, pharmaceutical, medicinal, agricultural, industrial and biotechnological sciences. Therefore, it was thought to investigate the reactions of cyanoguanidine with various isothiocyanates and also the reinvestigation of cyanoguanidine with substituted thiourea in hydrochloric acid to synthesise cyanoamidino-substituted-thiocarbamides (1a-f) and 1,3-diformamidino-thiocarbamide (2a)/N-substituted-formamidino(formamidino)thiocarbamide (2b-e) respectively further more the oxidative cyclisation of cyanoamidino-substituted thiocarbamides and 1,3-diformamidino-thiocarbamide (2a)/N-substituted-formamidino(formamidino)thiocarbamide with aqueous bromine in chloroform and also with H_2O_2 in concentrated hydrochloric acid gave a novel series of Hector's bases (3a-f and 4a-e) which are hitherto unknown. The present work describes suitable and somewhat direct method for the synthesis of Hector's bases. When the oxidation was carried out with H_2O_2 , the yield was comparatively poor and the greater time span required for the completion of reaction.

2. Materials and Methods

2.1 1-phenyl-3-formamidinothiocarbamide (1a)

A mixture of guanidine (0.01 M) and phenylisothiocyanate (0.01 M) and carbon tetrachloride (50 mL) was refluxed on a water bath for 2 hours. During boiling, the reaction mixture containing the suspended guanidine went into solution and after 1 hour yellowish, needle-shaped crystals gradually separated out. The reaction mixture was then again refluxed for 1 hour then filtered while hot. The new product was dried at room temperature and recrystallized from aqueous ethanol and identified as 1-phenyl-3-formamidinothiocarbamide (1a), yield 74%, m.p. 130°C. The reaction scheme was shown in Scheme-I. Similarly, other compounds (1b–f) were synthesised by above mentioned method and enlisted in Table-I.

2.2 1,3-Bis (N-phenylthioamido)guanidine (1g)

A similar procedure outlined in section 1.1 was used with some minor modifications, such as phenylisothiocyanate (0.01 M) was replaced with phenylisothiocyanate (0.02 M) Reaction yielded 67 %, m.p. was 149°C. The reaction scheme was shown in Scheme-II. Similarly, other compounds (1h–l) were synthesised by above mentioned method and enlisted in Table-II.

2.3 3-Imino-5-phenylimino-1,2,4-thiadiazolidines (2a)

In china dish the paste of 1-phenyl-3-formamidino thiocarbamide, (0.5 M) was prepared in chloroform. To this aqueous 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 4 hours at room conditions. A pale ivory powder separated out, which on crystallisation from ethanol, gave (2a), yield 83%, m.p. 130°C. The reaction scheme was shown in Scheme-III. Similarly, other compounds (2b–f) were synthesised by above-mentioned method and enlisted in Table – III.

2.4 3-Phenylthiocarbamido-5-phenylimino-1,2,4-thiadiazolidines (2g)

A similar procedure outlined in section 1.3 was used with some minor modifications, such as 1-phenyl-3-formamidino thiocarbamide was replaced with 1,3-bis-(N-phenylthioamido)guanidine Reaction yielded 79% , m.p. was 195°C. The reaction scheme was shown in Scheme-IV. Similarly, other compounds (2h–l) were synthesised by above-mentioned method and enlisted in Table – IV.

3. Instrumentation

All the chemicals used were of AnalaR grade (India make) alkyl/arylthiocyanates were prepared according to literature method (Vogel, A. Z., 1954), melting points of all synthesised compounds were determined in open capillary and uncorrected. IR-spectra were recorded on Perkin-Elmer spectrophotometer in the range 4000-400 cm^{-1} in KBr pellets. $^1\text{H-NMR}$ spectrums were recorded with TMS as internal standard using CDCl_3 and DMSO-d_6 . The purity of the compounds was checked on silica gel-G plates by TLC.

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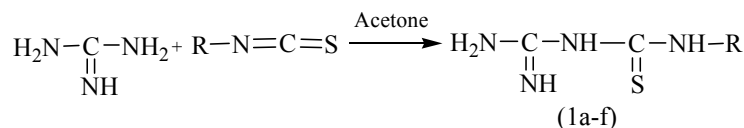
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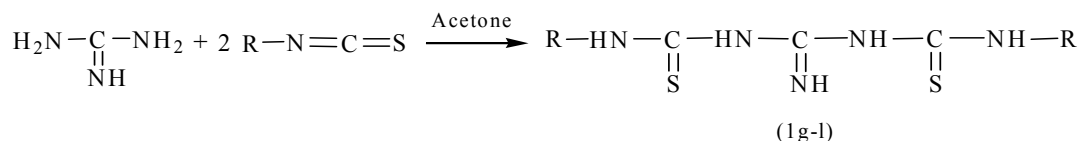
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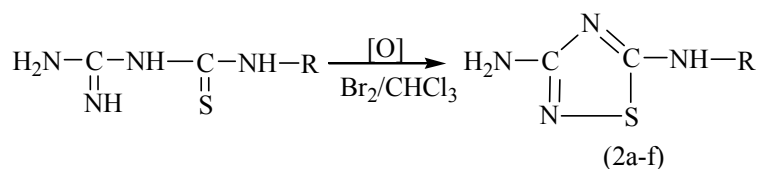
Reaction Schemes



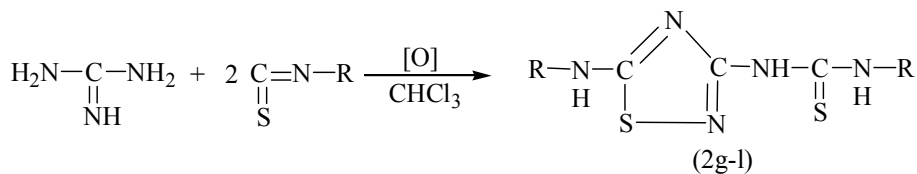
Scheme-I



Scheme-II



Scheme-III



Scheme-IV

Physical data for synthesised compounds**Table-I**

Compound No.	1-substituted-3-formamidinothiocarbamide	Yield (%)	m. p. ($^{\circ}\text{C}$)
1b	-p-Cl-phenyl-	84	142
1c	-p-tolyl-	64	204
1d	-methyl-	72	189
1e	-ethyl-	59	115
1f	-t-butyl-	67	149

Table-II

Compound No.	1,3-Bis(N-substituted thioamido)guanidine	Yield %	m.p. ($^{\circ}\text{C}$)
1h	-(N-p-Cl-phenyl thioamido)-	82	194
1i	-(N-p-tolyl thioamido)-	72	189
1j	-(N-methyl thioamido)-	82	160
1k	-(N-ethyl thioamido)-	68	172
1l	-(N-t-butyl thioamido)-	62	169

Table – III

Compound No.	N-substituted-formamidino(formamidino)thiocarbamide	Yield %	m.p. ($^{\circ}\text{C}$)
2b	-(p-Cl-phenyl)-	79	147
2c	- (p-tolyl)-	68	120
2d	- (methyl)-	78	157
2e	- (ethyl)-	80	142
2f	- (t-butyl)-	63	110

Table-IV

Compound No.	N-substituted-formamidino(formamidino)thiocarbamide	Yield %	m.p. ($^{\circ}\text{C}$)
2h	- (p-Cl-phenyl)-	80	200
2i	- (p-tolyl)-	83	182
2j	- (methyl)-	69	110
2k	- (ethyl)-	72	95
2l	- (t-butyl)-	54	124

Table-V IR spectra of synthesised compounds in (cm^{-1})

Compound	ν (N-H)	ν (C=N)	ν (>C=NH)	ν (>C-N)	ν (>C=S)	ν (>C-S)
(1a)	3393	1661	---	---	1101	517
(1g)	3387	1666	1575	1395	1178	---
(2a)	3308	1660	---	1332	1154	---
(2g)	3383	---	1566	---	1173	882

Table-V NMR spectra of synthesised compounds in (ppm)

Compound	Ar-NH	Ar-H	N-H
(1a)	δ 7.41-8.54	δ 6.85	δ 3.97
(1g)	δ 7.99-8.00	δ 6.90	δ 3.25-3.27
(2a)	---	δ 7.26	δ 4.02 and 4.00
(2g)	δ 7.26-7.79	δ 6.43-6.79	δ 4.02