SYNTHESIS OF BIS-N,N-(SUBSTITUTED ARYL-2-IMINO-1, 3-OXAZETE) THIOCARBAMIDE

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Abstract : Bis-N,N-(substituted aryl thiocarbamide) thiocarbamide 2a-e are synthesized under phase transfer catalysis, which on cyclisation with mercuric acetate furnish bis-N,N-(substituted aryl-2-imino-1,3-oxazete) thiocarbamide 3a-e.

Introduction

1,3-Oxazete /1,3-Oxazetidine derivatives are rarely known and very few 1,3-oxazetidine-2-ones are reported in the literature[1,2], which are synthesized by cycloaddition of isocyanates to C=O double bond containing substrates. This kind of compounds also shows drug activity[3]. This ring system has been suggested as a fused ring intermediate in flavins responsible for light producing intermediate in bacterial luciferase chemiluminescence[4].

Discussion

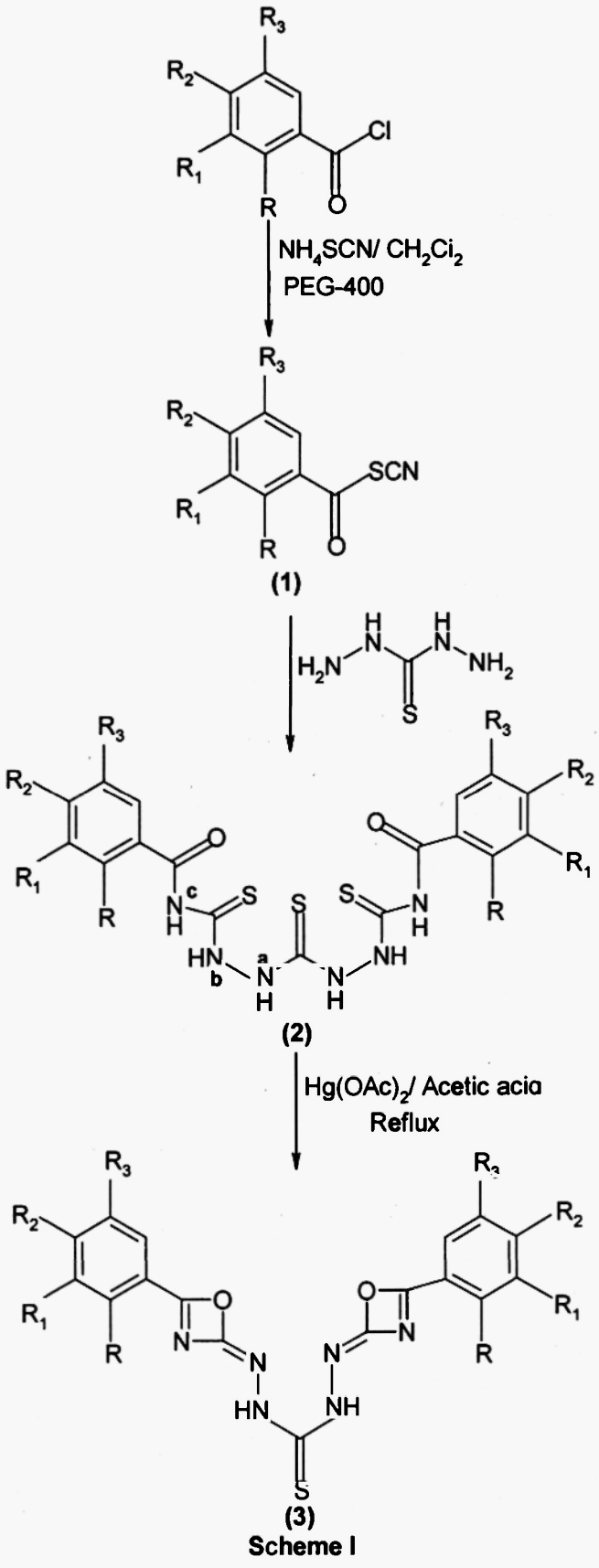
In the view of above facts, we report here in the preparation of a new series of compounds bearing 1,3-oxazete-2-imino moiety. The reaction of 4-substituted benzoyl chloride with ammonium thiocyanate at room temperature catalysed by polyethyleneglycol (PEG-400) gives 4-substituted benzoyl thiocyanate 1 as an intermediate. The compound 1 on treatment with thiocarbohydrazide[5] in situ at room temperature affords bis-N,N-(substituted aryl thiocarbamide) thiocarbamide 2a-e. This compound on further treatment with mercuric acetate in glacial acetic acid at reflux temperature undergoes intra molecular cyclisation to give bis-N,N-(substituted aryl-2-imino-1,3-oxazete) thiocarbamide 3a-e. (Scheme I)

Results & Discussion

The ^{1}H NMR of the compound 2a-e shows that the intensity of NHb proton is much higher (approximately doubled) than that of single proton and it disappears during cyclisation. This indicates that the peak intensity is not only due to NHb proton but also due to SH proton. This happens because of interchangeable tautomeric forms which are present.

Experimental

IR spectra (KBr in cm^{-1}) were recorded on Perkin-Elmer spectrum One FTIR spectrophotometer in the range of 4000-400 cm^{-1}. Melting points of all the compounds were determined in soft glass open capillaries on an electrothermal apparatus and are uncorrected. ^{1}H NMR spectra were recorded on Bruker Amx 500 MHz NMR spectrophotometer using DMSO-d_6 as solvent and TMS as an internal standard (chemical shifts in δ ppm). Mass spectra were recorded on 1100 series LC/MSD trap, Agilent. The substiuted benzoyl chlorides were prepared according to the literature procedure[6,7]. Ammonium thiocyanate, mercuric acetate, glacial acetic acid and poly ethylene glycol (PEG-400) were commercially available and used as it is.


R3
R2
R1
R
Cl
O
NH4SCN/ CH2Ci2
PEG-400
SCN
(1)
H2N
NH2
S
(2)
Hg(OAc)2/ Acetic acid
Reflux
HN
NH
(3)

Scheme I

Table I- Physical and Spectral data of compounds 2a-e and 3a-e

Sr. No.	Compd	R	R_1	R_2	R_3	Molecular Formula	M.P. (°C)	Yield (%)	Spectral data		
									IR (KBr cm^{-1})	Mass	^1H NMR DMSO d_6 / (δ ppm)
1	2a	H	H	NO_2	H	$C_{17}H_{14}N_8O_6S_3$	186-191	70	3196 (NH), 1674 (C=O), 1262 (C=S)	521.6	8.04-8.75 (m, 4H, ArH), 13.15 (s, 1H, NHa), 12.25 (s, 1H, NHb), 13.53 (s, 1H, NHc).
2	2b	H	H	H	H	$C_{17}H_{16}N_6O_2S_3$	196-200	70	3199 (NH), 1670 (C=O), 1259 (C=S),	430.8	7.5-7.99 (m, 5H, ArH), 13.54 (s, 1H, NHa), 11.88 (s, 1H, NHb), 11.84 (s, 1H, NHc).
3	2c	H	H	OCH_3	H	$C_{19}H_{20}N_6O_4S_3$	190-197	96	3132 (NH), 1671 (C=O), 1251 (C=S)	493.0	3.8 (s, 3H, OCH_3), 7.03-8.03 (m, 4H, ArH), 12.98 (s, 1H, NHa), 11.68 (s, 1H, NHb), 13.67 (s, 1H, NHc).
4	2d	F	OCH_3	F	F	$C_{19}H_{14}N_6O_4S_3F_3$	178-180	80	3214 (NH), 1669 (C=O), 1294 (C=S)	598.9	
5	2e	H	H	CH_3	H	$C_{19}H_{20}N_6O_2S_3$	206-210	75	3214 (NH), 1669 (C=O), 1294 (C=S)	459.7	
6	3a	H	H	NO_2	H	$C_{17}H_{10}N_8O_6S$	136-145	40	3195 (NH), 1680 (C=N), 1348 (C=S) 1106 (C-O)	455.4	8.08-8.472 (m, 4H, ArH), 13.22 (s, 1H, NH),
7	3b	H	H	H	H	$C_{17}H_{12}N_6O_2S$	143-149	30	3190 (NH), 1668 (C=N), 1256 (C=S), 1071 (C-O)	365.5	7.42-8.15(m, 5H, ArH), 13.334 (s, 1H, NH).
8	3c	H	H	OCH_3	H	$C_{19}H_{16}N_6O_4S$	115-120	35	3207 (NH), 1682 (C=N), 1257 (C=S) 1177 (C-O)	425.1 13.152	3.8 (s, 3H, OCH_3), 7.85-8.14 (m, 4H, ArH), (s, 1H, NH).
9	3d	F	OCH_3	F	F	$C_{19}H_{10}N_6O_4SF_3$	140-149	28		530.9	
10	3e	H	H	CH_3	H	$C_{19}H_{16}N_6O_2S$	146-153	25	3190(NH), 1676 (C=N), 1263 (C=S), 1183 (C-O)	393.1	

Bis-N,N-(4-nitrobenzoyl thiocarbamide) thiocarbamide 2a

To the solution of 4-nitro benzoyl chloride (10 gms, 0.054 mole) in methylene chloride (300 cm^3), ammonium thiocyanate (6.16 gms, 0.081 mole) and polyethylene glycol (PEG-400) (0.869 gm) were added. The mixture was stirred for 1 hr at room temperature and then thiocarbohydrazide (2.76 gms, 0.026 mole) was added to it. The reaction mixture was further stirred for two hrs. To the resulting mixture, water (217 cm^3) was added so that inorganic salt was dissolved. The slurry was filtered and the solid obtained was washed with water (160 cm^3).

The product was dried at 45-50°C for two hrs to give 70% yield. The compounds 2b-e were prepared in a similar manner and their analytical data are reported in table-I.

Bis-N, N-(4-(p-nitrophenyl)-2-imino-1, 3-oxazete) thiocarbamide 3a

A suspension of bis-N, N-(4-nitro benzoyl thiocarbamide) thiocarbamide 2a (0.5 gm, 0.0009 mole) and mercuric acetate (0.60 gm, 0.0019 mole) in glacial acetic acid (80 cm^3) was refluxed for 3-4 hrs. The resulting mixture was filtered quickly when it was hot. The filtrate was concentrated to minimum volume and poured into cold water (20cm^3). The precipitate collected by filtration was washed thrice with water (5 cm^3) and dried to furnish 40% yield of the desired product.

The compounds 3b-e were prepared in a similar manner and their analytical data are reported in table-I.

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