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Research Article

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Preparation, characterization of benzothiozine and its isomerisation in benzopyrimidine

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ABSTRACT

Several 2-arylimino-benzo (4,5-a)-2,3-dihydro-1,3, thiazin-6-one(IV) have been prepared by refluxing 1-aryl-3(1'-benzene carboxylic acid) thio carbamides (III) in ethane for 1.5 hours. These 1-aryl- 3(1'-benzene carboxylic acid)-thio carbamides(III), in turn have been prepared by refluxing different aryl isothio cyanates(II) with anthranilic acid(I) in chloroform medium. The 1,3-thiazines (IV) have been successfully isomerized into their 1,3-pyrimidine analogues (V) using 5% aqueous ethanolic sodium hydroxides solution. The 1, 3-thiazines (IV) are also converted into their benzoyl analogues (VI) by reacting them with benzoyl chloride.

Key words: thio carbamides(III), aryl isothio cyanates(II), chloroform, anthranilic acid, 1,3-thiazines (IV)

INTRODUCTION

Benzopyrimidines have found application in wide range of medicinal chemistry because of their diverse biological activities such as anti bacterial [1, 2], anti convalsant[3], anti-inflammatory[4-6], anti tumor[7-9] and anti fungal[10] activities. These chemotherapeutic application of benzopyrimidine derivatives promoted us to synthesize. Some new substituted 2-thio-3-aryl-4-oxo benzo (2,3-d) pyrimidine (V) by isomerisation of benzothiozine (IV) using alcoholic alkali.

Several method have been reported[11-14] for synthesis of benzopyrimidine derivative. However these methods suffer from drawback such as longer reaction time, use of expensive and hazards chemical along with complicated workout. The title compounds were synthesized in this communication using commonly Adrawbacks.

EXPERIMENTAL SECTION

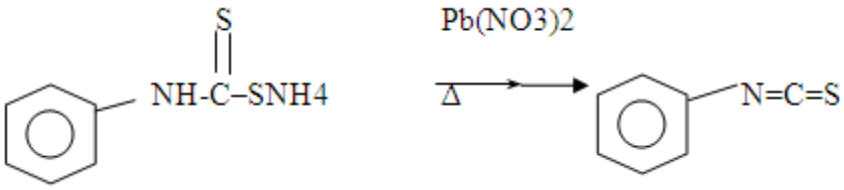
Preparation of Aryl iso thiocyanate:
Preparation of phenyl isothiocyanate by heating ammonium phenyl dithio carbamate with lead nitrate solution and water. Lastly, phenyl isothio cyanate was seperated by steam distillation process.

Similarly other substituted aryl isothiocyanate were prepared.

Table 2

	Ammonium aryl dithio carbamate		Substituted aryl isothiocyanate
1.	Ammonium phenyl dithio carbamate	1.	Phenyl iso thiocyanate
2.	Ammonium o-totyl dithio carbamate	2.	o-totyl iso thiocyanate
3.	Ammonium m-totyldithio carbamate	3.	m-totyl iso thiocyanate
4.	Ammonium p-totyl dithio carbamate	4.	p-totyl iso thiocyanate
5.	Ammonium o-chlorophenyl dithio carbamate	5.	o-chloro phenyl iso thiocyanate
6.	Ammonium p-chloro phenyldithio carbamate	6.	p-chloro phenyl iso thiocyanate

Reaction:



Reaction of anthranilic acid with aryl isothicyanate:
Formation of 1-aryl-3 (1-benzene carboxylic acid) thiocarbamides (III).

The anthanilic acid 0.01M and phenyl iso thio cyanate 0.01M were refluxed in 10ml chloroform medium for 2 hours. On distilling of solvent IIa was obtained in granular form, crystallized from ethanol, m.p. 120^{o}C (Table 1)

- **Reaction of 1-aryl-3 (1-benzene carboxylic acid) thiocarbamides (III):**

Formation of 2-arylimino-8-oxo benzo(4,5a)1,3 thiazine(IV)
2gm IIIa Was taken in R.B. flask to which 10ml ethanol was added and the contents of flask was refluxed for1 hour when IIIa underwent cyclisation to yield IVa. The solvent was distilled off and the solid obtained was recrystallised from ethanol, M.P. 202^{o}C (Table 1)

- **Isomerisation of IV into 2-thio-3-aryl-4-oxo-benzo-(2,3d)-pyrimidines(V):**

2gm Of IVa was suspended in 10ml 5% alcoholic aq. NaOH. Reaction mixture was refluxed for 1 hour when IVa was isomerized into Va. The compound was filtered and crystallized from ethanol to give 2-thio-3-phenyl-4-oxo-benzo(2,3d) pyrimidines (Va) m.p. above 300^{o}C (Table 1)

Table 1 : Synthesis of 1-aryl-3-(1-benzene carboxylic)thio carbamides(III),2-arylimino-8-oxo-benzo(4,5a) 1,3 thiazine (IV) and 2 thio-3-aryl-4-oxo-benzo(2,3d)-pyrimidine(V)

Sr. No.	Aryl isothiocyanate	1-aryl-3(1-benzenecarboxylic acid) thio-carbamides(III) m.p.^{o}c	2-arylimino-8-oxo-benzo(4,5a) 1,3 thiazine(IV) m.p.^{o}c	2-thio-3-aryl-4-oxo-benzo-(2,3d) pyrimidine(V), m.p.^{o}c	IR. Absorption band of V
1	Phenyl isothiocyanate IIa	1-phenyl-3(1-benzenecarboxylic acid) thio-carbamides(III) m.p.120^{o}c	2-phenylimino-8-oxo-benzo(4,5a) 1,3 thiazine(IV) m.p.202^{o}c	2-thio-3-phenyl-4-oxo-benzo-(2,3d) pyrimidine(V), m.p.=above300^{o}c	IR=ע NH(3245) (m^{-1}) עc=o(1660) (m^{-1})
2	o-totyl isothiocyanate IIb	1-o-totyl-3(1-benzenecarboxylic acid) thio-carbamides(III) m.p.128^{o}c	2-o-totyl imino-8-oxo-benzo(4,5a) 1,3 thiazine(IV) m.p.204^{o}c	2-thio-3-o-totyl-4-oxo-benzo-(2,3d) pyrimidine(V), m.p.=above300^{o}c	IR=ע NH(3240) (m^{-1}) עc=o(1666) (m^{-1})
3	m-totyl isothiocynate IIc	1-m-totyl-3(1-benzenecarboxylic acid) thio-carbamides(III) m.p.124^{o}c	2-m-totylimino-8-oxo-benzo(4,5a) 1,3 thiazine(IV) m.p.203^{o}c	2-thio-3-m-totyl-4-oxo-benzo-(2,3d) pyrimidine(V), m.p.=above300^{o}c	IR=ע NH(3235) (m^{-1}) עc=o(1648) (m^{-1})
4	p-totyl isothiocyanate IId	1-p-totyl-3(1-benzenecarboxylic acid) thio-carbamides(III) m.p.126^{o}c	2-p-totylimino-8-oxo-benzo(4,5a) 1,3 thiazine(IV) m.p.206^{o}c	2-thio-3-p-totyl-4-oxo-benzo-(2,3d) pyrimidine(V), m.p.=above300^{o}c	IR=ע NH(3150)(m^{-1}) עc=o(1645)(m^{-1})
5	o-chlrophenyl isothio cyanate IIe	1-o-chlorophenyl-3(1-benzenecarboxylic acid) thio-carbamides(III) m.p.123^{o}c	2-o-chlorophenylimino-8-oxo-benzo(4,5a) 1,3 thiazine(IV) m.p.200^{o}c	2-thio-3-o-chlorophenyl-4-oxo-benzo-(2,3d) pyrimidine(V), m.p.=above300^{o}c	
6	p-chlorophenyl isothio-cyanate IIf	1-p-chloro phenyl-3(1-benzenecarboxylic acid) thio-carbamides(III) m.p.112^{o}c	2-p-chlorophenylimino-8-oxo-benzo(4,5a) 1,3 thiazine(IV) m.p.201^{o}c	2-thio-3-p-chlorophenyl-4-oxo-benzo-(2,3d) pyrimidine(V), m.p.=above300^{o}c	

RESULTS AND DISCUSSION

The reaction of anthranilic acid (1) with different aryl thio cyanate (II) in chloroform media afforded -1-aryl-3(1-benzene carboxyli acid) thiocarbamides (III). The (III) on refluxing in alcohol 1.5 hours, yielded 2-aryl-imino, 8-oxo- benzo (4,5a) thiazine (IV) The benzo thiazine (IV) on isomerisation with alcoholic 5% NaOH in refluxing medium for 1 hour yielded benzopyrimidine (V). The benzopyrimidine gave the positive test of N and S elements. The Va was crystallized from ethanol, m.p. above 300^{o}C

IR= ע NH (3244cm^{-1}), ע C=O(1663cm^{-1}), ע C=N(1621cm^{-1}), ע C-N (1352 cm^{-1})

NMR = δ 2.31 (Ar-CH_3), δ 7.1-7.3 (Ar-H), δ NH (8.9)

On the basis of elemental analysis and spectral data the molecular formula of Va was established as $C_{14}H_{10}$ NOS, The other benzopyridines (Vb-Vf) were prepared by extending the above reaction to other aryl iso thiocyanates (reaction scheme 1). The M.P. and other data is recorded in the table 1.

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