

SYNTHESIS OF SOME 6-ARYLAMINO-3-AMINO-1,2,4,5-DITHIADIAZINES

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Abstract - The synthesis of some new 6-arylamino-3-amino-1,2,4,5-dithiadiazines (IIa-e) has been achieved by following a novel route.

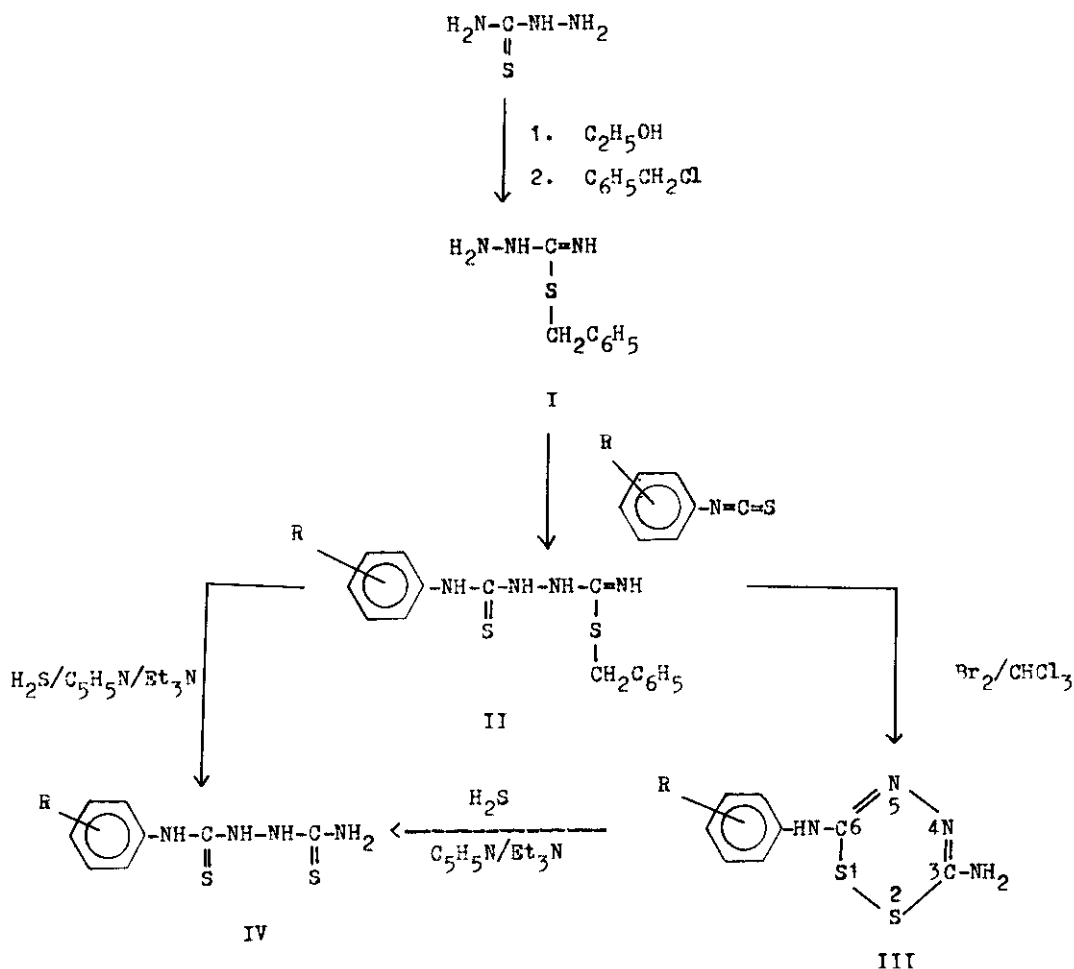
The chemistry of the oxidation products of certain substituted thiocarbamides e.g. 1,2,4-thiadiazoles, thiadiazolidines, thiadiazolines has been a well documented area^{1,2}. The reported commercial and technical utility of certain 1,2,4-thiadiazoles³ has given a boost to the research activity in the area of the synthesis of new heterocyclic systems. However, the preparation of 3,4-dihydro-3,4,6-triphenyl-3-phenylazo-1,2,4,5-dithiadiazine, the only compound of its type, has been reportedly achieved by the oxidation of the corresponding disulphide⁴.

In the light of the above observations and our continued interest in the development of simpler routes for novel heterocyclic systems⁵⁻⁷, it has been thought of sufficient interest to devise a facile synthesis of certain 6-arylamino-3-amino-1,2,4,5-dithiadiazines.

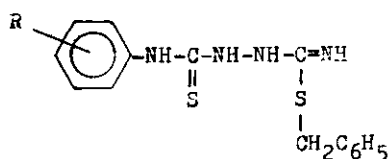
In the present paper, we report the synthesis of 5-S-benzyliso-1-aryl-2-thiohydrazodicarbonamides (II), which on oxidative debenzylation and cyclization yielded 6-arylamino-3-amino-1,2,4,5-dithiadiazines (III). Thus, the reaction of S-benzylisothiosemicarbazide (I), obtained by benzylation of thiosemicarbazide with benzyl chloride in ethanol, with phenylisothiocyanate yielded a solid product identified as 5-S-benzyliso-1-phenyl-2-thiohydrazodicarbonamide (IIa). The product IIa was oxidatively cyclised with molecular bromine to 6-phenylamino-3-amino-1,2,4,5-dithiadiazine (IIIa). Compounds IIa and IIIa, on reduction with hydrogen sulphide in pyridine-triethylamine afforded the identical 1-phenyl-2,5-dithiohydrazodicarbonamide (IVa). Following similar consecutive treatments, the remaining compounds IIb-e (Table 1), IIb-e

(Table 2) and IVb-e (Table 3) were obtained. The structures were substantiated, wherever possible, through ir, ^1H -nmr and mass spectral studies.

SCHEME 1

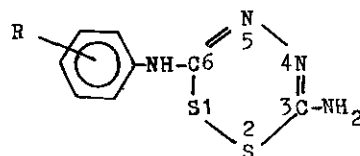


where, II-IV a, $\text{R}=\text{H}$
 b, $\text{R}=\text{CH}_3-4$
 c, $\text{R}=\text{Cl}-4$
 d, $\text{R}=\text{CH}_3\text{O}-4$
 e, $\text{R}=\text{C}_2\text{H}_5\text{O}-4$

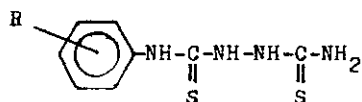
Table 1 - 5-S-Benzyliso-1-aryl-2-thiohydrazodicarbonamides (IIa-e)

Compd.	R	mp °C	Yield %	ir bands in Nujol ^{8,9}	
				$\nu_{\text{cm}^{-1}}$	assignments
IIa	H	247	46	3240 1620 1420 1150	NH C=N CH ₂ -S N-C(=S)-N
IIb	CH ₃ -4	267	52	3245 1640 1420 1160	NH C=N CH ₂ -S N-C(=S)-N
IIc	Cl-4	274	50	3240 1635 1410 1150	NH C=N CH ₂ -S N-C(=S)-N
IId	CH ₃ O-4	175	55	3250 1640 1430 1160	NH C=N CH ₂ -S N-C(=S)-N
IIe	C ₂ H ₅ O-4	158	55	3250 1640 1435 1160	NH C=N CH ₂ -S N-C(=S)-N

Table 2 - 6-Arylamino-3-amino-1,2,4,5-dithiadiazines (IIIa-e)



Compd.	R (Mol.Wt.)	mp °C	Yield %	E.I.M.S. m/z	ir in Nujol ⁸⁻¹¹		¹ H-NMR in DMSO (TMS int)	
					ν cm ⁻¹	assignment	δ ppm	assignment
IIIa	H (224)	140	74	224(M ⁺)	3500, 3420	NH	2.70(s)	2H, NH ₂
					1570	Ring C=N	6.45(br-s)	1H, NH
					1430	Ring C-S	7.30(m)	Arom-H
					480	S-S		
IIIb	CH ₃ -4 (238)	170	70	238(M ⁺)	3510, 3420	NH	2.60(s)	2H, NH ₂
					1575	Ring C=N	6.40(br-s)	1H, NH
					1440	Ring C-S	7.35(m)	Arom-H
					485	S-S		
IIIc	Cl-4 (258.5)	142	65	258(M ⁺)	3500, 3410	NH	2.78(s)	2H, NH ₂
					1560	Ring C=N	6.52(br-s)	1H, NH
					1425	Ring C-S	7.40(m)	Arom-H
					480	S-S		
IIId	CH ₃ O-4 (254)	225	75	254(M ⁺)	3550, 3440	NH	2.50(s)	2H, NH ₂
					1580	Ring C=N	6.30(br-s)	1H, NH
					1430	Ring C-S	7.10(m)	Arom-H
					495	S-S	3.53(s)	OCH ₃
IIIe	C ₂ H ₅ O-4 (268)	210	70	268(M ⁺)	3550, 3440	NH	2.60(s)	2H, NH ₂
					1600	Ring C=N	6.30(br-s)	1H, NH ₂
					1440	Ring C-S	7.15(m)	Arom-H
					490	S-S	4.30(q)	2H, CH ₂
							1.5(t)	3H, CH ₃

Table 3 - 1-Aryl-2,5-dithiohydrazodicarbonamides (IVa-e)

Compd.	R	mp °C	Yield %	ir bands in Nujol ^{8,9}	
				$\bar{\nu}$ cm ⁻¹	assignments
IVa	H	170	50	3200 1610 1200	NH C=N N-C(=S)-N
IVb	CH ₃ -4	180	52	3210 1610 1220	NH C=N N-C(=S)-N
IVc	Cl-4	182	45	3195 1595 1200	NH C=N N-C(=S)-N
IVd	CH ₃ O-4	176	55	3290 1600 1210	NH C=N N-C(=S)-N
IVe	C ₂ H ₅ O-4	179	58	3300 1620 1240	NH C=N N-C(=S)-N

EXPERIMENTAL

All melting points were determined by the open capillary tube on a Kofler hot stage apparatus and are uncorrected. S-Benzylisothiosemicarbazide (I) was prepared by benzylation of thiosemicarbazide with benzyl chloride in ethanol.

5-S-Benzyliso-1-aryl-2-thiohydrazodicarbonamides (IIa-e) .- A solution of S-benzylisothiosemicarbazide (I) (3.16 g, 0.01 M) and phenylisothiocyanate (1.35 g, 0.01 M) in benzene (50 ml) was refluxed for 4 h, and then evaporated in vacuo. The semi-solid residual product was stirred with petroleum ether (bp 40-60°C) (5 ml) and triturated with ethanol (10 ml) affording IIa, which was crystallised from ethanol, yield 1.5 g (46%), mp 260°C.

Similarly other 5-S-benzyliso-1-aryl-2-thiohydrazodicarbonamides were prepared by the condensation of S-benzylisothiosemicarbazide with different aryliso-

thiocyanates (Table 1).

6-Arylamino-3-amino-1,2,4,5-dithiadiazines (IIIa-e) .- Bromine was gradually added to a paste of 5-S-benzyliso-1-phenyl-2-thiohydrazodicarbonamide (IIa) (2 g, 0.006 M) in chloroform (1 ml) until the colour of bromine persisted. The reaction mixture warmed up considerably evolving lachrymatory fumes of benzyl bromide. Stirring was continued for 1 h at room temperature. The resultant semi-solid product was washed with ether, which on trituration with ethanol afforded the hydrobromide of 6-phenylamino-3-amino-1,2,4,5-dithiadiazine. The hydrobromide on treatment with ammonia solution yielded the corresponding free base (IIIa), which was crystallised from ethanol, yield 1 g (74%), mp 140°C. Other derivatives (IIb-e) were similarly oxidised to their corresponding dithiadiazines (IIIb-e) (Table 2).

1-Aryl-2,5-dithiohydrazodicarbonamides (IVa-e) .- The following procedures are typical to the methods used to prepare the derivatives of dithiohydrazodicarbonamides.

Method A : Reductive debenzylation of IIa-e .- 5-S-Benzyliso-1-phenyl-2-thiohydrazodicarbonamide (IIa) (3 g, 0.009 M) was dissolved in a mixture of pyridine (8 ml) and triethylamine (48 ml) and subjected to a stream of dry hydrogen sulphide for 5-6 h. The resulting reaction mixture was filtered, poured over crushed ice and acidified with 12 N hydrochloric acid, when the expected 1-phenyl-2,5-dithiohydrazodicarbonamide (IVa) got precipitated. It was filtered and crystallised from ethanol, yield 1 g (50%), mp 170°C. The remaining isothiohydrazodicarbonamides (IIb-e) were also reduced to their corresponding dithiohydrazodicarbonamides (IVb-e) (Table 3).

Method B : Reduction of IIIa-e .- Under identical conditions of reduction, 6-phenylamino-3-amino-1,2,4,5-dithiadiazines (IIIa) (2.24 g, 0.01 M) yielded 1-phenyl-2,5-dithiohydrazodicarbonamide (IVa) which was crystallised from ethanol, yield 1.57 g (70%), mp 170°C (Table 3).

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