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 (IIIa-e) has been achieved by following a novel route.

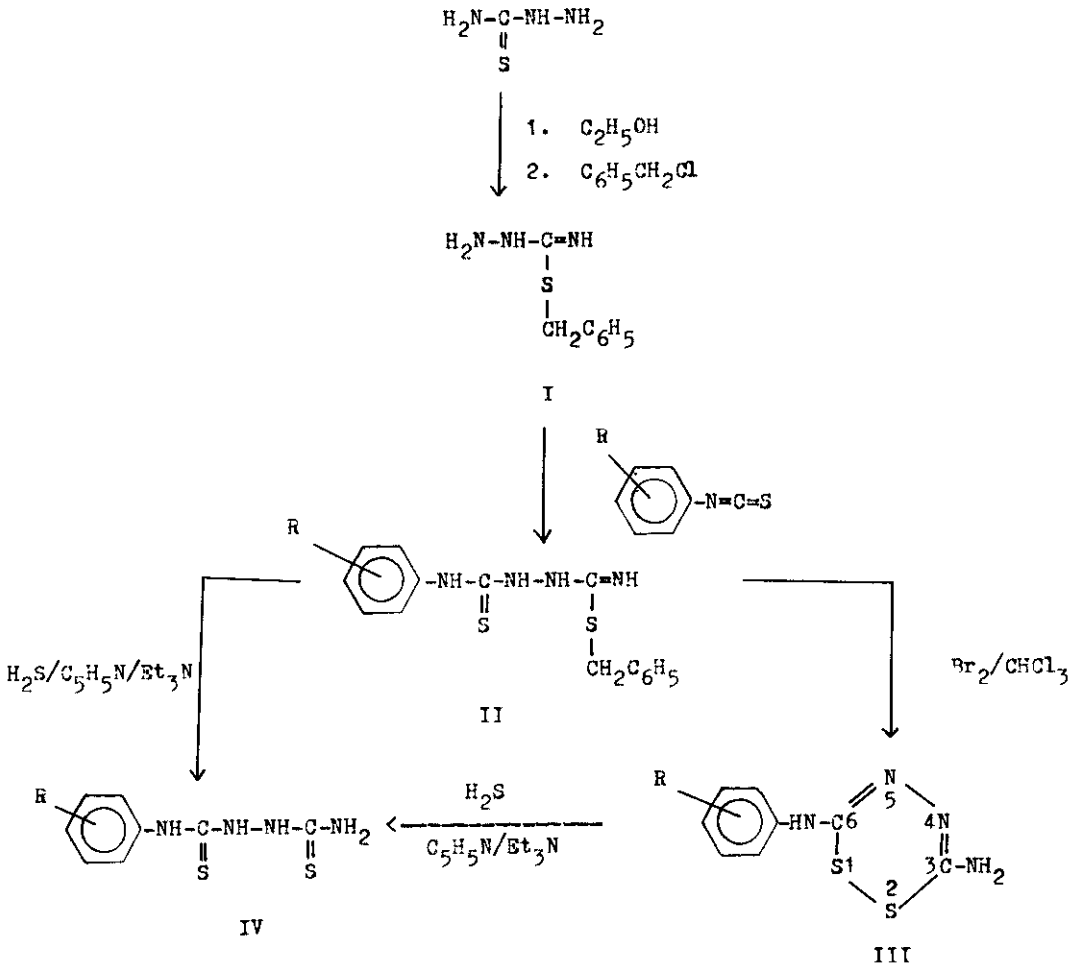
The chemistry of the oxidation products of certain substituted thiocarbamides e.g. 1,2,4-thiadiazoles, thiadiazolidines, thiadiazolines has been a well documented area[1,2]. The reported commercial and technical utility of certain 1,2,4-thiadiazoles[3] has given a boost to the research activity in the 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 disulphide[4].

In the light of the above observations and our continued interest in the development of simpler routes for novel heterocyclic systems[5-7], 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), IIIb-e

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

SCHEME 1



where, II-IV a, R=H

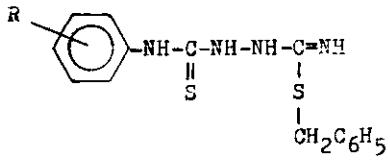
b, R=CH_3-4

c, R=Cl-4

d, R=CH_3O-4

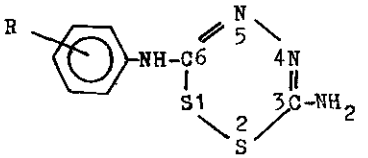
e, R=C_2H_5O-4

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



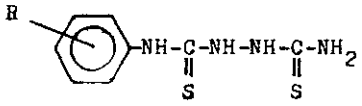
Compd.	R	mp °C	Yield %	ir bands in Nujol[8,9] ν cm^{-1}	assignments
IIa	H	247	46	3240	NH
				1620	C=N
				1420	CH_2-S
				1150	N-C(=S)-N
IIb	CH_3-4	267	52	3245	NH
				1640	C=N
				1420	CH_2-S
				1160	N-C(=S)-N
IIc	Cl-4	274	50	3240	NH
				1635	C=N
				1410	CH_2-S
				1150	N-C(=S)-N
IId	CH_3O-4	175	55	3250	NH
				1640	C=N
				1430	CH_2-S
				1160	N-C(=S)-N
IIe	C_2H_5O-4	158	55	3250	NH
				1640	C=N
				1435	CH_2-S
				1160	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] ν cm⁻¹	assignment	^{1}H-NMR in DMSO (TMS int) 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_3O-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_2H_5O-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]	
				ν 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_3O-4	176	55	3290 1600 1210	NH C=N N-C(=S)-N
IVe	C_2H_5O-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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