

Some Reactions on 4-Aryl-2-Substituted Amino-1,6-Dihydro-6-Thioxo-1,3,5-Triazines

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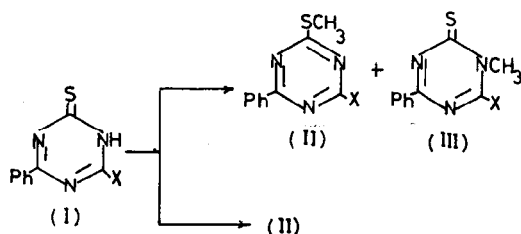
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Summary: 4-Aryl-2-substituted amino-1,6-dihydro-6-thioxo-1,3,5-triazines (IVa-c) react with methyl iodide, acrylonitrile and acetic anhydride to give 4-aryl-2-substituted amino-6-methylthio-(Va-c), 4-aryl-2-substituted amino-6-(β -cyano) ethylthio-(VIa-c), 1,3,5-triazines and 4-aryl-2-substituted amino-1-acetyl-1,6-dihydro-6-thioxo-1,3,5-triazines (VIIa-c), respectively. The structure of the products are discussed on the light of their chemical and spectroscopic properties as well as analytical data.

Introduction

The chemistry of 1,3,5-triazines had received great attention in the last years as some of their derivatives were shown to have herbicidal activity [1]. In a previous investigation [2] we reported the synthesis of some 1,3,5-triazine derivatives (IVa-c). Therefore, it seems desirable to extend the work on the 4-aryl-2-substituted amino-1,3,5-triazine derivatives (IVa-c) which have not been fully investigated, in an attempt to obtain more precise information about the course of alkylation, acrylonitrilation and acetylation.

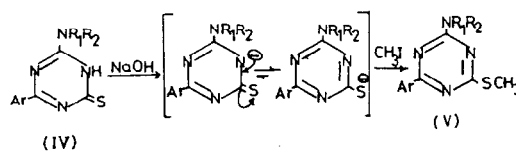
It has been reported [3] that 2-tert-butylmercapto-4-phenyl-thioxo-1,3,5-triazine (Ia) reacts with diazomethane to give a mixture of S-methyl derivative (IIa) and N-methyl derivative (IIIa) in ca.85 and 10% yield, respectively. However, treatment of the same compound with methyl iodide and sodium hydroxide gave only the S-methyl derivative (IIa). Other 2-substituted derivatives (Ib-g) gave the corresponding S-methyl derivatives on being treated with methyl iodide in presence of sodium hydroxide.



a; X = t-C₄H₉S
 b; X = C₆H₅CH₂CH₂, CH₃
 c; X = C₆H₅
 d; X = C₂H₅O
 e; X = N(CH₃)₂

Recently, it has been reported [4] that alkylation of If (X = OH) with methyl, ethyl, isoamyl iodides and benzyl chloride, in presence of sodium hydroxide, gave the corresponding S-methyl, ethyl, isoamyl and benzyl derivatives, respectively. Compound (Id; X = OC₂H₅) has been reported [3] to undergo disproportionation on being refluxed with dimethylformamide to give 4(6)-oxo-2-phenyl-1,4,5,6-tetrahydro-6(4)-thioxo-1,3,5-triazine (44%), 6-ethoxy-4-ethylmercapto-2-phenyl-1,3,5-triazine (38%) and 1,6-dihydro-2-ethylmercapto-6-oxo-4-phenyl-1,3,5-triazine (1%). However, treatment of the same compound with a mineral acid gave only If (X = OH). Oxidation of Ic with iodine in presence of triethylamine gave the corresponding disulphide. On the other hand, oxidation of Ic with hydrogen peroxide in presence of sodium hydroxide gave the O-analog, namely, 2,4-diphenyl-6-oxo-1,6-dihydro-1,3,5-triazine. Tosato [5] has shown that isomerization of trithioisocyanurates to thiocyanurates by action of heat occurs sequentially.

Treatment of IV a-c with methyl iodide in presence of sodium hydroxide, affords the corresponding S-methyl derivative (V a-c) (cf. Scheme 1):



Scheme 1

The structure of V was substantiated from (i) elemental analysis (cf. Table 1), (ii) the UV spectra showed identity and in agreement with that pre-

Table 1: Characterization data of V, VI and VII

Compound	Ar	R ₁ R ₂	m.p. °C	Yield	Mol. Formula	Found (%) (Calcd)				
						C	H	N	S	Cl
Va ₁	C ₆ H ₅	-CH ₂ -CH ₂ CH ₂ -CH ₂ -CH ₂	115	68	C ₁₅ H ₁₈ N ₄ S	62.9	5.7	19.0	11.0	--
						(62.9)	6.3	19.6	11.1	--
Va ₂	C ₆ H ₅	-CH ₂ -CH ₂ O -CH ₂ -CH ₂	112	70	C ₁₄ H ₁₆ ON ₄ S	58.0	5.3	19.4	11.3	--
						(58.3)	5.6	19.4	11.1	--
Va ₃	C ₆ H ₅	H CH ₃ CH ₂ CH ₂ CH ₂	87	72	C ₁₄ H ₁₈ N ₄ S	61.0 (61.3)	6.3 6.6	20.0 20.4	11.4 11.7	-- --
Va ₄	C ₆ H ₅	H C ₆ H ₅ CH ₂	126	71	C ₁₇ H ₁₆ N ₄ S	66.5 (66.2)	5.1 5.2	17.8 18.2	10.3 10.4	-- --
Va ₅	C ₆ H ₅	H p-CH ₃ C ₆ H ₄	128	75	C ₁₇ H ₁₆ N ₄ S	66.6 (66.2)	5.4 5.2	18.0 18.2	10.6 10.4	-- --
Va ₆	C ₆ H ₅	H p-CH ₃ OC ₆ H ₄	133	73	C ₁₇ H ₁₆ N ₄ OS	62.4	4.4	17.7	9.6	--
						(62.9)	4.4	17.3	9.9	--
Va ₇	C ₆ H ₅	H C ₆ H ₅	111	75	C ₁₆ H ₁₄ N ₄ S	65.5	4.5	18.8	10.7	--
						(65.3)	4.8	19.1	10.9	--
Vb ₁	C ₆ H ₅ CH=CH	-CH ₂ -CH ₂ CH ₂ -CH ₂ -CH ₂	114	78	C ₁₇ H ₂₀ N ₄ S	65.3	6.3	17.8	10.5	--
						(65.4)	6.4	18.0	10.3	--
Vb ₂	C ₆ H ₅ CH=CH	-CH ₂ -CH ₂ O -CH ₂ -CH ₂	130-31	76	C ₁₆ H ₁₈ N ₄ OS	61.4	5.6	17.9	9.8	--
						(61.1)	5.7	17.8	10.2	--
Vb ₃	C ₆ H ₅ CH=CH	H CH ₃ CH ₂ CH ₂ CH ₂	80	74	C ₁₆ H ₂₀ N ₄ S	63.6 (64.0)	7.0 6.8	18.6 18.7	10.8 10.7	-- --
Vb ₄	C ₆ H ₅ CH=CH	H C ₆ H ₅ CH ₂	123	75	C ₁₉ H ₁₈ N ₄ S	68.6 (68.3)	5.6 5.4	16.3 16.8	9.8 9.6	-- --
Vb ₅	C ₆ H ₅ CH=CH	H p-CH ₃ C ₆ H ₄	140	70	C ₁₉ H ₁₈ N ₄ S	68.5 (68.3)	5.3 5.4	17.0 16.8	9.7 9.6	-- --
Vb ₆	C ₆ H ₅ CH=CH	H p-CH ₃ OC ₆ H ₄	118	63	C ₁₉ H ₁₈ N ₄ OS	65.3	5.2	15.8	9.2	--
						(65.1)	5.1	16.0	9.1	--
Vb ₇	C ₆ H ₅ CH=CH	H C ₆ H ₅	137	68	C ₁₈ H ₁₆ N ₄ S	67.3	5.3	17.3	10.2	--
						(67.5)	5.0	17.5	10.0	--
Vc ₁	p-ClC ₆ H ₄	-CH ₂ -CH ₂ CH ₂	126	69	C ₁₅ H ₁₇ N ₄ Cl	56.3	5.5	17.2	10.1	10.9
						(56.2)	5.3	17.5	10.0	11.1
Vc ₂	p-ClC ₆ H ₄	-CH ₂ -CH ₂ O -CH ₂ -CH ₂	175-77	77	C ₁₄ H ₁₅ N ₄ OCl	52.0	4.6	17.3	9.9	11.1
						(52.1)	4.7	17.3	9.9	11.0
Vc _{3p}	ClC ₆ H ₄	H CH ₃ CH ₂ CH ₂ CH ₂	98	70	C ₁₄ H ₁₅ N ₄ Cl	54.9 (54.8)	5.0 4.8	18.5 18.3	10.6 10.4	12.0 11.6

Continued Table 1:

Com- pound	Ar	R ₁ R ₂	m.p. °C	Yield	Mol. Formula	Found (%) (Calcd)				
						C	H	N	S	Cl
Vc ₄	p-ClC ₆ H ₄	H C ₆ H ₅ CH ₂	134	63	C ₁₇ H ₁₅ N ₄ SCl	60.0 (59.6)	4.3 4.4	16.2 16.4	9.8 9.4	10.4 10.4
Vc ₅	p-ClC ₆ H ₄	H p-CH ₃ C ₆ H ₄	137	64	C ₁₇ H ₁₅ N ₄ SCl	59.8 (59.6)	4.4 4.4	16.3 16.4	9.3 9.4	10.3 10.4
Vc ₆	p-ClC ₆ H ₄	H p-CH ₃ OC ₆ H ₄	141	60	C ₁₇ H ₁₅ N ₄ OSCl	57.1 (56.9)	4.0 4.2	15.8 15.6	8.7 8.9	10.1 9.9
Vc ₇	p-ClC ₆ H ₄	H C ₆ H ₅	167	63	C ₁₆ H ₁₃ N ₄ SCl	58.6 (58.5)	4.2 4.0	17.0 17.1	9.7 9.7	11.0 10.8
VIa ₁	C ₆ H ₅	H CH ₃ CH ₂ CH ₂ CH ₂	118	75	C ₁₆ H ₁₉ N ₅ S	61.5 (61.3)	5.9 6.0	22.0 22.4	10.1 10.2	-- --
VIa ₂	C ₆ H ₅	H C ₆ H ₅ CH ₂	166	73	C ₁₉ H ₁₇ N ₅ S	66.0 (65.7)	4.7 4.9	20.5 20.2	9.1 9.2	-- --
VIa ₃	C ₆ H ₅	H p-CH ₃ C ₆ H ₄	175	72	C ₁₉ H ₁₇ N ₅ S	65.9 (65.7)	5.1 4.9	20.2 20.2	9.1 9.2	-- --
VIa ₄	C ₆ H ₅	H p-CH ₃ OC ₆ H ₄	156	73	C ₁₉ H ₁₇ N ₅ OS	63.1 (62.8)	4.9 4.7	19.0 19.3	9.0 8.8	-- --
VIa ₅	C ₆ H ₅	H C ₆ H ₅	157	65	C ₁₈ H ₁₅ N ₅ S	65.2 (64.9)	4.6 4.5	21.2 21.0	10.1 9.6	-- --
VIb ₁	C ₆ H ₅ CH=CH	H CH ₃ CH ₂ CH ₂ CH ₂	165	63	C ₁₈ H ₂₁ N ₅ S	63.8 (63.7)	6.3 6.2	20.8 20.6	9.4 9.4	-- --
VIb ₂	C ₆ H ₅ CH=CH	H C ₆ H ₅ CH ₂	128-29	68	C ₂₁ H ₁₉ N ₅ S	68.0 (67.6)	5.3 5.1	18.9 18.8	8.8 8.6	-- --
VIb ₃	C ₆ H ₅ CH=CH	H p-CH ₃ C ₆ H ₄	172	68	C ₂₁ H ₁₉ N ₅ S	67.7 (67.6)	5.0 5.1	19.0 18.8	8.5 8.6	-- --
VIb ₄	C ₆ H ₅ CH=CH	H p-CH ₃ OC ₆ H ₄	156-58	66	C ₂₁ H ₁₉ N ₅ OS	64.7 (64.8)	5.1 4.9	18.2 18.0	8.2 8.2	-- --
VIb ₅	C ₆ H ₅ CH=CH	H C ₆ H ₅	165	63	C ₂₀ H ₁₇ N ₅ S	67.1 (66.9)	5.0 4.7	19.2 19.5	9.0 8.9	-- --
VIc ₁	p-ClC ₆ H ₄	H CH ₃ CH ₂ CH ₂ CH ₂	109	75	C ₁₆ H ₁₈ N ₅ SCl	55.1 (55.3)	5.4 5.2	20.3 20.1	9.1 9.2	10.2 10.2
VIc ₂	p-ClC ₆ H ₄	H C ₆ H ₅ CH ₂	168	60	C ₁₉ H ₁₆ N ₅ SCl	60.0 (59.8)	4.3 4.2	18.7 18.4	8.1 8.4	9.5 9.3
VIc ₃	p-ClC ₆ H ₄	H p-CH ₃ C ₆ H ₄	173	74	C ₁₉ H ₁₆ N ₅ SCl	59.9 (59.8)	4.4 4.2	18.2 18.4	8.6 8.4	9.5 9.3
VIc ₄	p-ClC ₆ H ₄	H p-CH ₃ OC ₆ H ₄	166	65	C ₁₉ H ₁₆ N ₅ OSCl	57.6 (57.4)	4.1 4.0	17.6 17.6	8.3 8.1	8.8 8.9
VIc ₅	p-ClC ₆ H ₄	H C ₆ H ₅	186	68	C ₁₈ H ₁₄ N ₅ SCl	59.1 (58.8)	4.0 3.8	19.0 19.1	8.8 8.7	9.6 9.7

Continued Table 1:

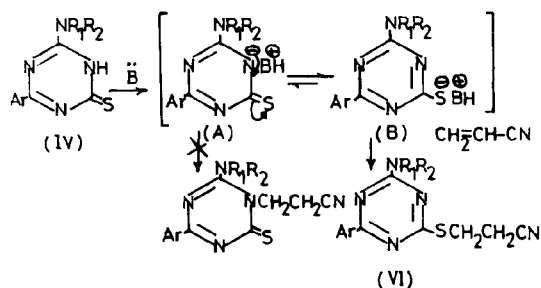
Com- pound	Ar	R ₁ R ₂	m.p. °C	Yield	Mol. Formula	Found (%) (Calcd)				
						C	H	N	S	Cl
VIIa ₁	C ₆ H ₅	H CH ₃ CH ₂ CH ₂ CH ₂	185	65	C ₁₅ H ₁₈ N ₄ OS	59.9 (59.6)	6.1 6.0	18.6 18.5	10.6 10.6	-- --)
VIIa ₂	C ₆ H ₅	H C ₆ H ₅ CH ₂	197	73	C ₁₈ H ₁₆ N ₄ OS	64.5 (64.3)	4.6 4.8	16.8 16.7	9.8 9.5	-- --)
VIIa ₃	C ₆ H ₅	H <i>p</i> -CH ₃ C ₆ H ₄	195	65	C ₁₈ H ₁₆ N ₄ OS	64.4 (64.3)	5.0 4.8	16.7 16.7	9.4 9.5	-- --)
VIIa ₄	C ₆ H ₅	H <i>p</i> -CH ₃ OC ₆ H ₄	192	65	C ₁₈ H ₁₆ N ₄ O ₂ S	61.5 (61.4)	4.7 4.5	16.1 15.9	9.1 9.1	-- --)
VIIa ₅	C ₆ H ₅	H C ₆ H ₅	199	67	C ₁₇ H ₁₄ N ₄ OS	63.6 (63.4)	4.3 4.4	17.5 17.4	10.1 9.9	-- --)
VIIb ₁	C ₆ H ₅ CH=CH	H CH ₃ CH ₂ CH ₂ CH ₂	105	63	C ₁₇ H ₂₀ N ₄ OS	62.4 (62.2)	6.2 6.1	17.3 17.1	10.0 9.8	-- --)
VIIb ₂	C ₆ H ₅ CH=CH	H C ₆ H ₅ CH ₂	169	73	C ₂₀ H ₁₈ N ₄ OS	66.6 (66.3)	4.8 5.0	15.7 15.5	8.9 8.8	-- --)
VIIb ₃	C ₆ H ₅ CH=CH	H <i>p</i> -CH ₃ C ₆ H ₄	178	65	C ₂₀ H ₁₈ N ₄ OS	66.2 (66.3)	4.9 5.0	15.6 15.5	8.6 8.8	-- --)
VIIb ₄	C ₆ H ₅ CH=CH	H <i>p</i> -CH ₃ OC ₆ H ₄	183	73	C ₂₀ H ₁₈ N ₄ O ₂ S	63.6 (63.5)	4.8 4.8	15.0 14.8	8.7 8.5	-- --)
VIIb ₅	C ₆ H ₅ CH=CH	H C ₆ H ₅	173	63	C ₁₉ H ₁₆ N ₄ OS	65.8 (65.5)	4.7 4.6	15. 16.1	99.3 9.2	-- --)
VIIc ₁	<i>p</i> -ClC ₆ H ₄	H CH ₃ CH ₂ CH ₂ CH ₂	187	65	C ₁₅ H ₁₇ N ₄ OSCl	53.6 (53.5)	5.2 5.1	16.9 16.7	9.7 9.5	10.8 10.6)
VIIc ₂	<i>p</i> -ClC ₆ H ₄	H C ₆ H ₅ CH ₂	198	77	C ₁₈ H ₁₅ N ₄ OSCl	58.3 (58.3)	4.2 4.1	15.3 15.1	8.5 8.6	9.8 9.6)
VIIc ₃	<i>p</i> -ClC ₆ H ₄	H <i>p</i> -CH ₃ C ₆ H ₄	201	73	C ₁₈ H ₁₅ N ₄ OSCl	58.5 (58.3)	4.2 4.1	15.0 15.1	8.8 8.6	9.5 9.6)
VIIc ₄	<i>p</i> -ClC ₆ H ₄	H <i>p</i> -CH ₃ OC ₆ H ₄	152	77	C ₁₈ H ₁₅ N ₄ O ₂ SCl	56.2 (56.0)	4.0 3.9	14.6 14.5	8.5 8.3	9.1 9.2)
VIIc ₅	<i>p</i> -ClC ₆ H ₄	H C ₆ H ₅	205	65	C ₁₇ H ₁₃ N ₄ OSCl	57.1 (57.2)	3.9 3.7	15.9 15.7	8.8 9.0	10.3 10.0)

Compounds Va₁-a₇, Vb₁-b₇ and Vc₁-c₇ were recrystallised from *n*-hexane. Compounds VIa-c and VIIa-c were recrystallised from benzene.

viously reported [3] for similar compounds (cf. Table 2) and (iii) acidic hydrolysis of V (a₃-a₅) gave the corresponding 4-substituted amino-6-phenyl-1,2(or 1,4)-dihydro-1,3,5-triazin-2-ones (cf. experimental) which were identical in m.p. and mixed m.p. with authentic specimens [4].

Acrylonitrile reacts with (IV a-c) in presence of pyridine, as a base, to give 4-aryl-2-substituted amino-6-(β-cyano)ethylthio-1,3,5-triazines (VIa-c). We believe that the function of pyridine, as a base, is to facilitate the conversion of IV into the intermediate pyridinium salts (A) and/or (B). Typical

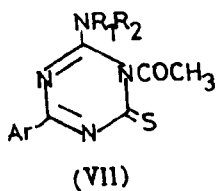
intermediate salt [4] has been isolated in the reaction of 6-phenyl-1,2,3,4(or 2,3,4,5)-tetrahydro-4-thioxo-1,3,5-triazine with amines, (cf. Scheme 2).



(B = pyridine) Scheme 2

The structure assignment of VI was based on: (i) elemental analysis (cf. Table 1), (ii) formation of 6-phenyl-4-substituted amino-1,2 (or 1,4)-dihydro-1,3,5-triazin-2-ones by acidic hydrolysis of VIa₁-a₃ (cf. experimental) indicate that the acrylonitrilation took place via the intermediate (B) rather than (A). The products of hydrolysis showed no depression on admixture with authentic specimens [4]. (iii) UV spectra showed similarities and in accordance with that reported [3] for S- substituted-1,3,5-triazines (cf. Table 2) and (iv) spot tests [6] indicated the absence of C=S function.

Acetylation of IVa-c with acetic anhydride gave the corresponding 1-acetyl derivatives (VIIa-c)



The structure of VII was assigned from: (i) elemental analysis (cf. Table 1), (ii) IR spectra exhibited bands at 1670-1640 cm⁻¹ (tert. amido C=O), (iii) the electronic spectra showed similarities with that reported [3] for thiono-1,3,5-triazine derivatives (cf. Table 2) and (iv) the C=S function in (VII) was proved by spot tests [6].

All melting points are uncorrected. Infrared and electronic spectra were measured on a Unicam SP 1200 spectrophotometer (KBr discs) and Beckman DK-2A Ratio Recording spectrophotometer (in absolute methanol), respectively.

Table 2: Electronic spectra of V, VI and VII

Compound	$\lambda_{\text{max.}}$ (nm)	$\log \epsilon_{\text{max}}$
Va ₅	260(sh.)	4.520
	255	4.538
Va ₆	265	4.367
	252	4.434
	212(sh)	4.066
Vb ₁	295	4.389
	240	4.270
	225	4.222
	218	4.213
Vb ₇	297	4.267
	277(sh.)	4.181
	225	3.886
	218	3.996
Vc ₁	250	4.426
Vc ₂	249	4.587
VIa ₂	238	4.383
VIa ₃	267(sh.)	4.567
	255	4.630
	213(sh.)	4.322
VIb ₃	300	4.048
	282(sh.)	3.964
	223(sh.)	3.738
	218	3.750
VIb ₅	300	4.546
	277(sh.)	4.435
	225(sh.)	4.228
	218	4.251
VIc ₁	265	4.635
VIIb ₃	307	4.406
	250-265	4.153
	217	4.361
VIIc ₁	250	4.305
VIIc ₃	248(sh.)	4.123
	232	4.321
	220 (sh.)	4.228

Action of methyl iodide on IV_{a-c}; Formation of 4-aryl-2-substituted amino-6-methylthio-1,3,5-triazines (V_{a-c}):

To a well stirred solution of IV (0.01 mol) in sodium hydroxide solution (0.5 N; 30 ml) and ethanol (70 ml) was added methyl iodide in dropwise. The reaction mixture was heated gently on a water-bath for 1 hr. The solution was kept for 12 hr at room temperature then diluted with water (100 ml) whereby a solid product was separated out. The product obtained was filtered, washed thoroughly with water and recrystallised from suitable solvent to give (V_{a-c}). The characterization data of V_{a-c} are given in Table 1.

Action of acrylonitrile on (IV_{a-c}); Formation of 4-aryl-2-substituted amino-6-(β-cyano)ethylthio-1,3,5-triazines (VI_{a-c}):

Triazine (IV) (0.01 mol) was added in portion-wise to a solution of acrylonitrile (3 ml), pyridine (50 ml) and water (10 ml). The reaction mixture was refluxed for 6 hr followed by reduction the original volume into its half by distillation under reduced pressure. Dilution the reaction mixture with water (150 ml) gave a solid product which was filtered, washed with water and dried. Recrystallisation the solid product from appropriate solvent afforded (VI_{a-c}) (cf. Table 1).

Action of acetic anhydride on (IV_{a-c}); Formation of 1-acetyl-4-aryl-2-substituted amino-1,6-dihydro-6-thioxo-1,3,5-triazines (VII_{a-c}):

A mixture of IV (0.01 mol) and acetic anhydride (5 ml) was heated on a water-bath for 3 hr and then cooled to room temperature. The reaction mixture was diluted with water whereby a solid

separated out. The product obtained was filtered, washed with water and dried. Recrystallisation the solid product from appropriate solvent gave VII_{a-c} (cf. Table 1).

Hydrolysis of Va_{3-a5} and VIa_{1-a3}; Formation of 6-phenyl-4-substituted amino-1,2(or 1,4)-dihydro-1,3,5-triazin-2-ones [4]:

To a solution of V or VI (0.01 mol) in acetone (100 ml) was added aqueous sulphuric acid (1N; 10 ml). The reaction mixture was heated on a water-bath for 1 hr, left over-night at room temperature and poured on ice-cold water (150 ml), whereby a solid was separated out. Authentic samples [4] were prepared and shown by m.p. and mixed m.p. experiments to be identical with these products.

References

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