2-SUBSTITUTED 7-AMINO-1,2,4-TRIAZOLO[1,5-*a*]-[1,3,5]TRIAZINES

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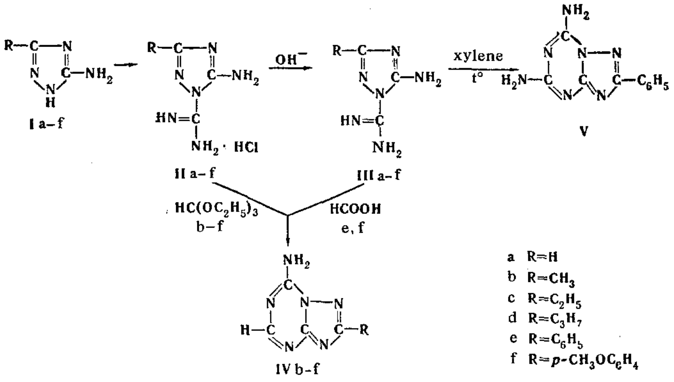
3-Substituted 5-amino-1-guanyl-1,2,4-triazoles have been obtained which, on reaction with orthoformic ester or 100% formic acid, form 2-substituted 7-amino-1,2,4-triazolo[1,5-*a*]-[1,3,5]triazines.

The reaction of 3-substituted 5-amino-1,2,4-triazoles (I) with 1-guanyl-1,2,3-benzotriazole hydrochloride [1] has given hydrochlorides of 3-substituted 5-amino-1-guanyl-1,2,4-triazoles (II).

The hydrochlorides II and the corresponding free bases (III) have been used for the synthesis of amino derivatives of aza analogs of adenine – 7-amino-1,2,4-triazolo[1,5-*a*]-[1,3,5]triazines (IV). Of the latter only one representative was previously known [2] – IV (R = H), obtained from N,N'bis(1,2,4-triazol-3-yl)formamidine and calcium cyanamide in dimethylformamide.

The aminotriazolotriazines IV are formed by the reaction of the aminoguanyltriazole hydrochlorides II with ethyl orthoformate (with the exception of R = H) or, in the case of R = aryl, by the reaction of the hydrochlorides II or the bases III with ~100% formic acid. The bases III (R = alkyl) give only the corresponding amino-5-formyltriazoles with formic acid. The reaction of the bases III with ethyl orthoformate formed mixtures of reaction products which have not been separated completely.



When IIIe was boiled in xylene or amyl alcohol, the 5,7-diaminotriazolotriazine V was isolated, this having been obtained previously [3] by the reaction of 5-amino-3-phenyl-1,2,4-triazole with dicyandiamide.

EXPERIMENTAL

Hydrochloride of 5-amino-1-guanyl-1,2,4-triazoles (IIa-f) (Table 1). An equimolar amount of 1-guanyl-1,2,3-benzotriazole was added to a solution of an aminotriazole in ethanol (IIa, e, f) or in a mixture of ethanol and ethyl acetate (1 : 3 – IIb; 1 : 4 – IIc, d), and the mixture was boiled for 20 min. After cooling, the hydrochloride II precipitated.

5-Amino-1-guanyl-1,2,4-triazoles (IIIa-f) (Table 1). The bases IIIc, e, f, precipitated from aqueous solutions of the hydrochlorides II on treatment with an equimolar amount of sodium carbonate. For the isolation of IIIa, b, d, the neutral solution was evaporated and the residue was extracted with absolute ethanol.

7-Amino-1,2,4-triazolo[1,5-*a*]-[1,3,5]triazines (IVb-f) (Table 2). Compounds IIb-f were boiled with ethyl orthoformate for 1 hr. Compounds IVe and f were formed by boiling the corresponding II or III in ~100% formic acid for 4 hr

Table 1. 5-Amino-1-guanyl-1,2,4-triazoles (III) and Their Hydrochlorides (II)

Compound	R	Mp, °C	Empirical formula	Found, %				Calculated, %				Yield, %
				C	H	N	Cl	C	H	N	Cl	
IIa	H	202—203[a]	$C_3H_6N_6 \cdot HCl$	21,81	4,54	51,57	22,34	22,17	4,35	51,68	21,81	60
IIb	CH_3	194—195[a]	$C_4H_8N_6 \cdot HCl$	26,94	5,24	b	20,11	27,20	5,15	47,58	20,08	62
IIc	C_2H_5	182[c]	$C_5H_{10}N_6 \cdot HCl$	31,55	5,89	43,28	19,02	31,50	5,83	44,07	18,60	44
IId	*n*-C_3H_7	180[d]	$C_6H_{12}N_6 \cdot HCl$	34,85	6,56	40,92	18,08	35,19	6,42	41,06	17,33	36
IIe	C_6H_5	210[e]	$C_9H_{10}N_6 \cdot HCl$	44,82	4,69	35,86	—	45,30	4.66	35,20	—	40
IIf	*p*-$CH_3OC_6H_4$	242[e]	$C_{10}H_{12}N_6O \cdot HCl$	44,39	4,82	30,92	—	44,70	4,89	31,26	—	58
IIIa	H	137[f]	$C_3H_6N_6$	28,49	4,79	b	—	28,57	4,81	66,62	—	55
IIIb	CH_3	154[g]	$C_4H_8N_6$	34,46	5,94	b	—	34,28	5,77	59,95	—	50
IIIc	C_2H_5	153[h]	$C_5H_{10}N_6$	38,30	6,42	b	—	38,96	6,55	54,49	—	70
IIId	*n*-C_3H_7	96[i]	$C_6H_{12}N_6$	42,50	7,52	50,52	—	42,85	7,21	49,95	—	40
IIIe	C_6H_5	165[h]	$C_9H_{10}N_6$	53,18	5,49	42,38	—	53,45	5,00	41,55	—	90
IIIf	*p*-$CH_3OC_6H_5$	204—205[h] (decomp.)	$C_{10}H_{12}N_6O$	51,57	5,13	b	—	51,72	5,22	36,17	—	85

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[a] From a mixture of methanol and ether. [b] The determination of nitrogen gave a high value (by 1-2%). [c] From propanol. [d] From a mixture of ethanol and ethyl acetate. [e] From methanol. [f] From ethanol. [g] From a mixture of ethanol and petroleum ether. [h] From water. [i] From benzene.

Table 2. 7-Amino-1,2,4-triazolo[1,5-*a*]-[1,3,5]triazines (IV)

Compound	R	Mp, °C	Empirical formula	Found, %			Calculated, %			Yield, %
				C	H	N	C	H	N	
IVb	CH_3	272[a]	$C_5H_6N_6$	39,22	4,19	56,38	40,00	4,04	55,96	85
IVc	C_2H_5	219—221[b]	$C_6H_8N_6$	43,76	4,72	51,40	43,84	4,92	51,18	75
IVd	*n*-C_3H_7	195[b]	$C_7H_{10}N_6$	46,72	5,82	47,14	47,18	5,67	47,15	80
IVe	C_6H_5	338—339[c]	$C_{10}H_8N_6$	56,98	4,14	39,31	56,60	3,81	39,59	95
IVf	*p*-$CH_3OC_6H_4$	341[c]	$C_{11}H_{10}N_6O$	54,13	4,53	34,80	54,56	4,17	34,67	90

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[a] From ethanol. [b] From water. [c] From dimethylformamide (decomp.).

5,7-Diamino-2-phenyl-1,2,4-triazolo[1,5-*a*]-[1,3,5]triazines (V). A mixture of 0.5 g of IIIe and 5 ml of acetic acid was boiled for 2 hr. The crystals that deposited after cooling were washed with 2 ml of acetic acid, giving 0.2 g of V, mp 375-376°C [3].

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