crystallized from a suitable solvent or distilled. The hydrochloride salts were prepared by dissolving the base in EtOH or Et_2O and adding ethanolic HCl.

1,2-Dihydro-3H-imidazo[1,5-*a*]indol-3-ones (Table IV). Procedure C. Reaction of the 2-(Aminomethyl)indole with N,N'-Carbonyldiimidazole.—A solution or suspension of 0.02 mole of the dry 2-(aminomethyl)indole in 40 ml of dry THF or C_6H_6 was cooled and a solution of 3.87 g (0.022 mole) of 92% N,N'-carbonyldiimidazole in 40 ml of THF was added. The mixture was allowed to stand at room temperature for 18–20 hr and then heated on the steam bath for 1–4 hr. The solvent was distilled using a rotating evaporator and the residue was warmed with about 50 ml of H_2O. The product was filtered off and washed with H_2O (if solid) or extracted into C_6H_6. The C_6H_6 layer was washed with H_2O and concentrated. Cyclization was usually incomplete, and further purification was obtained by crystallization of the base or salt from a suitable solvent or by partition chromatography. The salts were obtained by dissolving the base in Et_2O or EtOH and adding ethanolic HCl or excess maleic acid.

Procedure D. By Aminoalkylation of the 1,2-Dihydro-3H-imidazo[1,5-*a*]indol-3-one.—A solution or suspension of 0.01 mole of the 1,2-dihydro-3H-imidazo[1,5-*a*]indol-3-one in 30 ml of diglyme was added dropwise to a suspension of 0.011 mole of 50% NaH (in mineral oil) in 20 ml of diglyme. The mixture was stirred for 30–60 min and a solution of 0.012 mole of the dialkylaminoethyl chloride in 20 ml of diglyme was added. The reaction mixture was heated at reflux temperature for 5 hr, filtered while hot, and concentrated. The residue was dissolved in dilute HCl and extracted with C_6H_6 to remove nonbasic impurities. The aqueous layer was treated with excess 5 *N* NaOH and extracted with C_6H_6. The C_6H_6 layer was washed (H_2O), dried ($MgSO_4$), and concentrated. The residue was converted to the hydrochloride salt and recrystallized from a suitable solvent.

Procedure E. 7-Chloro-2-piperidinomethyl-1,2-dihydro-3H-imidazo[1,5-*a*]indol-3-one Hydrochloride.—A mixture of 1.03 g (0.005 mole) of 7-chloro-1,2-dihydro-3H-imidazo[1,5-*a*]indol-3-one, 0.50 ml (0.005 mole) of piperidine, 0.40 ml (0.005 mole) of 37% HCHO, and 40 ml of EtOH was heated on the steam bath for 2 hr. Some insoluble material was filtered off and the mother liquor was concentrated. The residual oil was dissolved in 5 ml of EtOH, and 1.5 ml of 3 *N* ethanolic HCl was added. The precipitate was filtered off and recrystallized from MeOH.

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Synthesis and Diuretic Activity of 2-Amino-4-arylamino-6-mercapto-*s*-triazines and Related Derivatives

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Arylbiguanides and CS_2 reacted in the presence of KOH to give the title compounds along with isomeric 1-aryl-2-thioammelines. The 6-mercapto-*s*-triazines were further converted to the corresponding 6-alkylmercapto and 6-hydroxy derivatives. In general, these compounds showed mild diuretic activity when fed orally to rats, while 2-amino-4-*m*-fluoroanilino-*s*-triazine and a few others showed good diuresis and natriuresis.

We have reported[2] earlier the significant diuretic, saluretic, and antikaluretic activity of 2-amino-4-*m*-chloroanilino-*s*-triazine (III, R = *m*-Cl) in rats and dogs. Unfortunately, these results could not be extrapolated to humans except in some cases of Cor pulmonale where interesting diuretic activity was noted.[3] Accordingly, our attempts were directed at the modification of the parent molecule. Since several mercapto-*s*-triazoles exhibit significant diuretic activity,[4] and the SO_2NH_2 group is degraded to mercapto in the body,[5] it seemed worthwhile to incorporate mercapto and related groups in III, in search for better diuretics. The present paper deals with the synthesis and evaluation of several 2-amino-4-arylamino-6-mercapto-*s*-triazines and related compounds.

Chemistry.—N-Phenylthioammeline was prepared by Welcher and coworkers[6] by the extension of Rathke's method[7] for thioammeline involving the condensation of dicyandiamide with ammonium thiocyanate in the presence of HCl. Recently, Kurzer and Pitchfork[8] have shown that the product obtained from phenyldicyandiamide and ammonium thiocyanate was not the 2-amino-4-anilino-6-mercapto-*s*-triazine (II, R = H) but was hexahydro-4,6-diimino-1-phenyl-*s*-triazine-2-thione, *i.e.*, 1-phenyl-2-thioammeline (I, R = H), which they prepared by the condensation of biguanide and phenyl isothiocyanate. We have studied an alternate route, *viz.*, the extension of Rackmann's method[9] for thioammeline wherein biguanide is treated with CS_2 (Scheme I).

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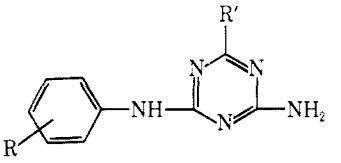
Table I
2-Amino-4-arylamino-6-substituted s-Triazines



No.	R	R'	Crystn solvent[a]	Yield, %	Mp, °C	Formula	Analyses	Optimal responsive dose, mg/kg[c]	Diuretic act.[b] Urine vol	Na^+	K^+	Cl^-
1	H	SH	E_{50}	12.7	267–268 dec[d]	$C_9H_9N_5S$	C, H, N	13.0	106	65.5	181	215
2	H	OH	E–HCl	40	>315[e]	$C_9H_9N_5O$	C, H, N	20.0	116.6	135.7	193.4	277
3	H	SC_2H_5	B	51	166–168	$C_{11}H_{13}N_5S$	N, S	*f*				
4	H	$SCH_2CH{=}CH_2$	E	92	158–159	$C_{12}H_{13}N_5S$	N, S	20.0	116.6	714.2	218.7	339
5	H	S-*n*-C_3H_7	E	65	179–180	$C_{12}H_{15}N_5S$	N, S	6.0	81.6	207	112.5	215
6	H	S-*n*-C_4H_9	B	63	169–170	$C_{13}H_{17}N_5S$	N	*f*				
7	H	S-*i*-C_4H_9	B	48	190–191	$C_{13}H_{17}N_5S$	S; N[g]					
8	H	SCH_2CH_2OH	E–B	89	162–163	$C_{11}H_{13}N_5OS$	N	20.0	95.8	128.6	181.2	215.9
9	H	$SCH_2C_6H_5$	B–H	78	180–182	$C_{16}H_{15}N_5S$	N, S	20.0	141.7	450	403.2	494
10	2-Cl	SH	E_{80}	8.0	240–242 dec	$C_9H_8ClN_5S$	C, H, N	20.0	95.8	92.8	106.2	169.2
11	2-Cl	OH	E–HCl	44	295–296 dec	$C_9H_8ClN_5O\cdot HCl\cdot H_2O$	C, H, N	12.5	95.5	96.4	148	266.8
12	2-Cl	$SCH_2CH{=}CH_2$	E	86	140	$C_{12}H_{12}ClN_5S$	N, S	2.0	111.2	615.1	216.8	223.8
13	2-Cl	SCH_2CH_2OH	B–H	93	119	$C_{11}H_{12}ClN_5OS$	N, S	3.0	98	463	184.3	184
14	2-Cl	$SCH_2C_6H_5$	B	78	180–181	$C_{16}H_{14}ClN_5S$	N	20.0	124	293	303.2	308.2
15	3-Cl	H	W	70	250–252 dec[h]	$C_9H_8ClN_5\cdot HCl$	N	10.0	244.4	1650	176.6	585
16	3-Cl	SH	C	16.8	268–270 dec	$C_9H_8ClN_5S$	C, H, N	0.2	157.0	143	212	185
17	3-Cl	OH	E–HCl	52	284–285 dec	$C_9H_8ClN_5O\cdot HCl\cdot H_2O$	N	13.0	112	257.3	155	331
18	3-Cl	SC_2H_5	B–H	61	174–175	$C_{11}H_{12}ClN_5S$	N, S	*f*				
19	3-Cl	$SCH_2CH{=}CH_2$	E_{50}	90	158–159	$C_{12}H_{12}ClN_5S$	C, H, N	4.0	141	300	142.5	431
20	3-Cl	S-*n*-C_3H_7	B	72	178–179	$C_{12}H_{14}ClN_5S$	N, S	*f*				
21	3-Cl	S-*n*-C_4H_9	B	74	168–169	$C_{13}H_{16}ClN_5S$	C, H, N	*f*				
22	3-Cl	S-*i*-C_4H_9	B	63	178–179	$C_{13}H_{16}ClN_5S$	C, H, N	*f*				
23	3-Cl	SCH_2CH_2OH	E–B	82	141–142	$C_{11}H_{12}ClN_5OS$	C, H, N	20.0	139.5	193	151.9	359
24	3-Cl	$SCH_2C_6H_5$	B	81	180–182	$C_{16}H_{14}ClN_5S$	N, S	20.0	102.0	135.4	212.2	221
25	4-Cl	H	E	78	256–258[i]	$C_9H_8ClN_5$	N	10.0	283.3	497	232.5	370
26	4-Cl	SH	C	11	293–294 dec	$C_9H_8ClN_5S$	C, H, N	20.0	166	43	156.2	184.4
27	4-Cl	OH	E–HCl	64	300	$C_9H_8ClN_5O\cdot HCl\cdot H_2O$	N	20.0	163.5	250	231.8	328
28	4-Cl	SCH_3	E	72	220–222	$C_{10}H_{10}ClN_5S$	N	*f*				
29	4-Cl	SC_2H_5	E	83	221–222	$C_{11}H_{12}ClN_5S$	N, S	*f*				
30	4-Cl	$SCH_2CH{=}CH_2$	B	89	197–198	$C_{12}H_{12}ClN_5S$	N, S	13.0	85.6	71.4	181.2	228
31	4-Cl	S-*n*-C_3H_7	E	79	221–222	$C_{12}H_{14}ClN_5S$	N, S	*f*				
32	4-Cl	S-*n*-C_4H_9	B	87	209–211	$C_{13}H_{16}ClN_5S$	N, S	*f*				
33	4-Cl	SCH_2CH_2OH	E	96	201–202	$C_{11}H_{12}ClN_5OS$	N	5.0	86.4	85.8	156.2	219
34	4-Cl	$SCH_2C_6H_5$	B	82	200–201	$C_{16}H_{14}ClN_5S$	C, H, N	14.0	103	157.0	247.5	323.9
35	4-Cl	$SCH_2COOC_2H_5$	B–H	53	175–177	$C_{13}H_{14}ClN_5O_2S$	N	*f*				
36	2-Me	SH	E	17	245–246 dec	$C_{10}H_{11}N_5S\cdot HCl\cdot 0.5H_2O$	C, H, N	6.0	166	171.4	247.5	354.2
37	2-Me	OH	E–HCl	43	275 dec	$C_{10}H_{11}N_5O\cdot HCl\cdot H_2O$	N	3.0	132	150	181.2	323.9
38	2-Me	$SCH_2CH{=}CH_2$	E	76	149–150	$C_{13}H_{15}N_5S$	C, H, N	10.0	182.6	214	247.5	269.5
39	2-Me	SCH_2CH_2OH	E–B	79	161–162	$C_{12}H_{15}N_5OS$	N[j]	3.5	97	171.5	134.3	215.8
40	2-Me	$SCH_2C_6H_5$	B	73	159–160	$C_{17}H_{17}N_5S$	N	14.0	104.6	149.8	240.1	277.5
41	3-Me	SH	E_{80}	31.7	263–264 dec	$C_{10}H_{11}N_5S$	C, H, N	20.0	166.6	114.5	243.8	347
42	3-Me	OH	E–HCl	53	258–259	$C_{10}H_{11}N_5O\cdot HCl\cdot 0.5H_2O$	N	20.0	166.6	132.8	172.4	328.1
43	3-Me	SC_2H_5	B	80	146–147	$C_{12}H_{15}N_5S$	N, S	*f*				
44	3-Me	$SCH_2CH{=}CH_2$	E	93	140–142	$C_{13}H_{15}N_5S$	C, H, N	12.0	141	118.5	212.5	266.6
45	3-Me	SCH_2CH_2OH	E	82	120–122	$C_{12}H_{15}N_5OS$	N, S	*f*				
46	3-Me	$SCH_2C_6H_5$	B–H	84	145–146	$C_{17}H_{17}N_5S$	C, H, N	11.0	122.4	54.4	245.1	254
47	4-Me	H	E	65	269–270[k]	$C_{10}H_{11}N_5\cdot HCl$	N	5.0	205.7	1212.0	168.6	231.2
48	4-Me	SH	E_{80}	20.8	266 dec	$C_{10}H_{11}N_5S$	C, H, N	2.0	95.5	100	96.5	198.5
49	4-Me	OH	E–HCl	69	>300[k]	$C_{10}H_{11}N_5O$	C, H	13.0	107.8	142.8	195	256.2
50	4-Me	SC_2H_5	B	85	195–196	$C_{12}H_{15}N_5S$	N, S	*f*				

TABLE I (*Continued*)

No.	R	R′	Crystn solvent[a]	Yield, %	Mp, °C	Formula	Analyses	Optimal responsive dose, mg/kg[c]	Diuretic act.[b] Urine vol	Na⁺	K⁺	Cl⁻
51	4-Me	$SCH_2CH{=}CH_2$	B	88	192–193	$C_{13}H_{15}N_5S$	N, S	*f*				
52	4-Me	S-*n*-C_3H_7	B–H	81	198–199	$C_{13}H_{17}N_5S$	C, H, N	*f*				
53	4-Me	S-*n*-C_4H_9	E	84	188–189	$C_{14}H_{19}N_5S$	N	*f*				
54	4-Me	S-*i*-C_4H_9	E–B	67	170–171	$C_{14}H_{19}N_5S$	N, S	13.0	89.3	178.3	143.5	210.5
55	4-Me	SCH_2CH_2OH	E	87	194–196	$C_{12}H_{15}N_5OS$	N, S	*f*				
56	4-Me	$SCH_2C_6H_5$	B	78	186–187	$C_{17}H_{17}N_5S$	N, S	13.0	96.6	42.9	192	169.4
57	2-MeO	SH	E_{80}	6.4	264–266 dec	$C_{10}H_{11}N_5OS$	N	14.0	85.1	114.2	91.4	134.0
58	2-MeO	OH	E–HCl	46	275–277 dec	$C_{10}H_{11}N_5O_2 \cdot HCl$	N	6.0	106.8	130.2	182.4	238.5
59	2-MeO	$SCH_2C_6H_5$	B	72	158–159	$C_{17}H_{17}N_5OS$	N	2.0	112.1	249.9	156.2	210
60	3-F	H	E	67	207–208	$C_9H_8FN_5$	N	6.0	261	1142	191	555
61	3-F	SH	E_{50}	17.6	258–260 dec	$C_9H_8FN_5S \cdot H_2O$	C, H, N	*f*				
62	3-F	SCH_2CH_2OH	B	79	144	$C_{11}H_{12}FN_5OS$	C, H, N	*f*				
Hydrochlorothiazide								2.5	166.6	1000	250	538.5

[a] E, EtOH; E_{80}, 80% EtOH; E–HCl, EtOH + HCl; B, C_6H_6; H, *n*-C_6H_{14}; W, H_2O; C, methyl Cellosolve. [b] Expressed as percentage of control values. [c] Dose arrived at by method described by Modi, *et al.*[15] [d] Lit.[8] mp 263–265° dec; picrate, mp 216–217°. *Anal.* Calcd for $C_9H_9N_5S \cdot C_6H_3N_3O_7$: N, 25.00. Found: N, 25.16. [e] Was obtained as hydrated hydrochloride, mp 280–285° dec. *Anal.* Calcd for $C_9H_9N_5O \cdot HCl \cdot H_2O$: N, 27.18. Found: N, 26.26. For $C_9H_9N_5O \cdot HCl \cdot 2H_2O$, S. L. Shapiro and C. G. Overberger [*J. Am. Chem. Soc.*, **76**, 97 (1954)] found mp 127–130° and F. Kurzer and E. D. Pitchfork [*J. Chem. Soc.*, 1886 (1967)] found mp 132–134° (base mp >365°). While drying at 175° *in vacuo* it lost both H_2O and HCl; picrate sinters at 252°, mp 262–264° (Kurzer and Pitchfork found mp 262–265°). [f] Not screened. [g] N: calcd, 25.45; found, 24.91. [h] Reported earlier.[2c] [i] Chlorazanil. [j] N: calcd, 25.27; found, 25.80. [k] Base liberated by NaOH.

The condensation of phenylbiguanide with CS_2 in the presence of alcoholic KOH proceeded with evolution of H_2S and gave 2-amino-4-anilino-6-mercapto-*s*-triazine (II, R = H). It gave S-alkyl derivatives by reacting with alkyl bromides. Another product, insoluble in cold dilute NaOH, was also isolated from the same reaction mixture. This compound was found to be identical with compound I (R = H) obtained by Welcher's method. Both I and II were not interconvertible by treatment with acid, alkali, boiling in C_6H_6, or pyridine. Although S-allyl or S-methyl derivatives of I also could be prepared and isolated as their hydrohalide salts, the corresponding bases were found unstable and decomposed during attempts of crystallization from organic solvents such as EtOH and Et_2O.

Since we were primarily interested in the study of mercapto-*s*-triazines (II) and their conversion to S-alkyl, sulfamoyl, and hydroxy derivatives, various substituted phenylbiguanides were condensed with CS_2 to obtain the desired II. All of these compounds gave the expected stable S-alkyl derivatives when treated with alkyl halides and on treatment with Raney nickel afforded the corresponding desulfurized products (III) identical in all respects with the corresponding compounds obtained by the interaction of appropriate arylbiguanides with formic acid. The mercapto-*s*-triazines (II) on treatment with H_2O_2 under alkaline conditions gave the corresponding 2-amino-4-arylamino-6-hydroxy-*s*-triazines. They also gave disulfide derivatives by the action of iodine[10,11] or sodium nitrite.[11] The attempt at transformation of SH in II to SO_2NH_2 by the usual method[12] did not work and instead products devoid of sulfur were obtained. Such failures have also been noted by Roblin and Clapp.[13] The 1-aryl-2-thioammelines formed simultaneously with the desired II were obtained in all cases. These were also purified and studied for their diuretic activity.

All these compounds have been listed along with their physical constants in Tables I and II.

Pharmacological Results.—The results indicate that 2-amino-4-arylamino-6-substituted *s*-triazines, in general, possess only mild diuretic activity except 2-amino-4-anilino-6-allylmercapto-*s*-triazine (**4**) which was significantly saluretic. Another compound which showed very good diuretic activity in the present study was 2-amino-4-*m*-fluoroanilino-*s*-triazine (**60**) which was better than hydrochlorothiazide (at their respective optimal dose levels) but did not equal the corresponding *m*-chloroanilino derivative (**15**).

Structure–Activity Relationship.—The study of the diuretic activity in rats given in Tables I and II shows that from among the compounds studied by us, **25**, **60**, **15**, **66**, **47**, **38**, **26**, **36**, **41**, and **42** had an activity better than or comparable to hydrochlorothiazide as far as water diuresis was concerned, the order of activity being in descending order. If the saluratic activity is compared, the order of activity is **15**, **47**, **60**, **4**, and **25**.

According to earlier reports[14,15] 2-amino-4-*p*-chloroanilino-*s*-triazine (**25**) was the most active and 2-amino-4-*p*-tolylamino-*s*-triazine (**47**) had lower diuretic activity[14] than **25**. Our experiments confirm this as true only insofar as water diuresis is concerned, but on taking into consideration the electrolyte excretion it is seen that **47** is more active than **25**. In compounds with H in the 6 position of the triazine, the order of activity as a function of substitution in phenyl is *m*-Cl > *m*-F >

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Scheme I

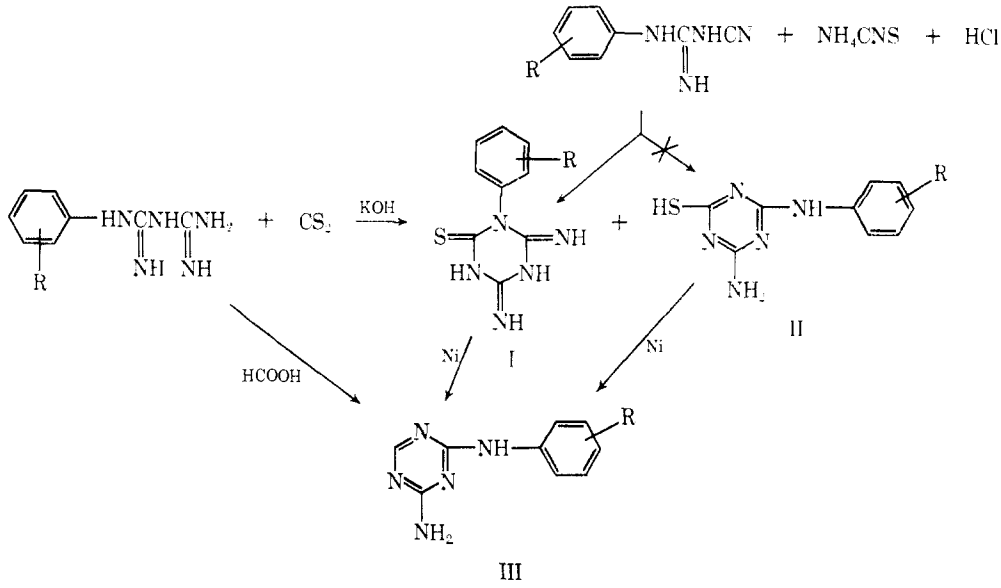
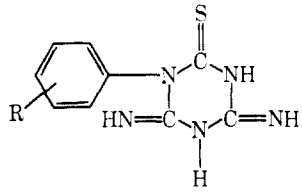


Table II

1-Aryl-2-thioammelines



No.	R	Yield, %	Mp, °C[a]	Formula	Analyses	Optimal responsive dose, mg/kg	Diuretic act.[f] Urine vol	Na^+	K^+	Cl^-
63	H	17.6	290 dec[b,c]	$C_9H_9N_5S$	C, H, N	12.0	85	292.8	171.2	262
64	2-Cl	21.2	277–278 dec	$C_9H_8ClN_5S$	C, H, N	4.5	116.6	378.5	275	336
65	3-Cl	31.2	284–285 dec	$C_9H_8ClN_5S$	C, H, N	20.0	128	143	150	138
66	4-Cl	21.5	285–286 dec[d]	$C_9H_8ClN_5S$	C, H, N	2.0	217	118.4	218.5	200
67	2-Me	20.2	269–270 dec	$C_{10}H_{11}N_5S$	N, S	20.0	105	494	181.2	336
68	3-Me	20.5	273 dec	$C_{10}H_{11}N_5S$	N, S	8.0	124.5	207	227.8	225
69	4-Me	26.2	289–290 dec[e]	$C_{10}H_{11}N_5S$	N, S	6.0	98	92.5	232.6	254
70	2-MeO	36.8	273–274 dec	$C_{10}H_{11}N_5OS$	C, H, N	[f]				
71	3-F	25.8	263–265 dec	$C_9H_8FN_5S$	N	[f]				

[a] Purified through HCl and NaOH and subsequently suspended in hot EtOH except methyl Cellosolve for **63** and Me_2CO for **65**. [b] Lit.[8] mp 287–288°. [c] Picrate, mp 228–229°. *Anal.* Calcd for $C_9H_9N_5S \cdot C_6H_3N_3O_7$: N, 25.00. Found: N, 24.72. [d] Picrate, mp 252–253°. [e] Lit.[9] mp 299–300°. [f] Expressed as percentage of control values.

p-CH_3 > *p*-Cl. Furthermore, the K^+ excretion with *m*-Cl (**15**), *m*-F (**60**), and *p*-CH_3 (**47**) was much less than with the *p*-Cl derivative (**25**).

Replacement of H in position 6 of the triazine with either SH, OH, or S-alkyl considerably reduced both diuretic and saluretic activity. The order of activity in descending order is H > S-alkyl > OH > SH. Kagawa and Van Arman[15] also had observed that substitution at position 6 by $COOC_2H_5$ and $CH_2N(CH_3)_2$ in active compounds caused a loss in activity.

It is also seen that the alkylation of the SH grouping by allyl, β-hydroxyethyl, or benzyl improved the saluretic action. 2-Amino-4-anilino-6-allylmercapto-*s*-triazine (**4**) showed powerful saluretic action which was greatly reduced by the nuclear substitution in the benzene ring in contrast to the series with R′ = H where it is observed that such nuclear substituents enhanced the saluretic activity. Similarly, benzylmercapto derivatives also lost their diuretic activity with substitution in the phenyl ring. With mercapto or β-hydroxyethylmercapto series, however, such nuclear substitution enhanced the activity.

Experimental Section[16]

Pharmacological Method.—Albino rats (male) weighing about 180–200 g were taken in a group of four in each cage and four or more such groups were taken for each test dose. Prior to the experiment, the rats were allowed food and water *ad libitum*. During the experiment each group of four animals was housed in an improved metabolism cage described by Modi, *et al.*[17] One group was used as untreated control and received orally the vehicle only consisting of 0.5 ml of 2% starch solution. Another group received hydrochlorothiazide (2.5 mg/kg) as

(16) The melting points were taken in capillary tubes with a partial immersion thermometer and are uncorrected. Where analyses are indicated only by symbols of the elements, the analytical results obtained for these elements were within ±0.4% of the theoretical values.

(17) K. N. Modi, N. N. Shah, and U. K. Sheth, *Arch. Intern. Pharmacodyn.*, **144**, 61 (1963).

reference standard suspended in the vehicle. The other groups received the various test compounds in the same vehicle. Since the dose–response curve is found to be parabolic, the dose selected for each of the test compounds was the optimal responsive dose as determined in previous experiments by the method of Modi, *et al.*[18] The urine was collected for 24 hr, its volume was measured, and the concentrations of Na^+ and K^+ (by Eel flame photometer) and Cl^- (by titration) were determined. The results are calculated as the mean of four test groups and expressed as the percentage of those in the control groups and are given in the tables.

Intermediates.—*o*-Chlorophenylbiguanide,[19] *m*-chlorophenylbiguanide,[20] *p*-chlorophenylbiguanide,[19] *m*-fluorophenylbiguanide,[21] *o*-tolylbiguanide,[20] and *m*-tolylbiguanide[20] were prepared by the condensation of the requisite arylamines with dicyandiamide using aqueous medium. Phenylbiguanide[22] and *o*-methoxyphenylbiguanide[23] were prepared by using pyridine as solvent[22] while *p*-tolylbiguanide[20] was prepared by fusion of the mixture of *p*-toluidine hydrochloride and dicyandiamide.

2-Amino-4-arylamino-*s*-triazines were obtained from the arylbiguanide hydrochlorides by refluxing with formic acid.[14]

2-Amino-4-anilino-6-mercapto-*s*-triazine (1).—To a mixture of phenylbiguanide (88.5 g, 0.5 mole) and alcoholic KOH (26.4 g of 85%, 0.4 mole, in 500 ml), 40 ml of CS_2 was added. The orange-colored reaction mixture was stirred mechanically and refluxed for 14 hr with additional amounts of CS_2 (10 ml) at intervals of 4 hr. During the entire course of the reaction, evolution of H_2S was detected by lead acetate paper. The reaction mixture was then cooled in ice–water and the solid was collected by filtration (product A). The filtrate on neutralization with HCl afforded the desired alkali-soluble compound **1** which was purified by redissolving in alkali and neutralizing to pH 6.5 with HCl; crystallized from 80% EtOH, yield 13.95 g, (12.7%), mp 267–268° dec (lit.[8] 263–265° dec), hydrochloride mp 195–200° dec, picrate mp 216–217° dec (lit.[8] 206–207° dec).

Product A was purified by dissolving in dilute HCl and reprecipitating with NaOH. It was crystallized from methyl Cellosolve to get 1-phenyl-2-thioammeline, yield 19.38 g (17.6%), mp 290° dec. 1-Phenyl-2-thioammeline (**63**) was also prepared by the method of Welcher and coworkers,[6] mp 286–288° dec (lit.[8] 286–288° dec). Both of these were found identical in all respects including ir spectra.

All of the 2-amino-4-arylamino-6-mercapto-*s*-triazines and the 1-aryl-2-thioammelines were similarly obtained and are recorded in Tables I and II, respectively.

1-*p*-Chlorophenyl-2-thioammeline (66) was also obtained from *p*-chlorophenyldicyandiamide[24] according to Welcher's method[6] for N-phenylthioammeline, mp 283–285°, yield 43.5%. *Anal.* ($C_9H_8ClN_5S$) N. It was soluble in very dilute HCl but insoluble in cold dilute NaOH.

2-Amino-4-anilino-6-allylmercapto-*s*-triazine (4).—To a filtered solution of 2-amino-4-anilino-6-mercapto-*s*-triazine (1.1 g, 0.005 mole) in 25 ml of 0.5 *N* NaOH was added allyl bromide (0.67 g, 0.0055 mole) and the resulting mixture was stirred for 10 min. After 1 hr the solid that separated was collected by filtration, washed (H_2O), and dried.

All the S-alkyl derivatives were obtained as described above.

2-Amino-4-anilino-6-hydroxy-*s*-triazine Hydrochloride (2).—2-Amino-4-anilino-6-mercapto-*s*-triazine (1.1 g, 0.005 mole) was dissolved in 15 ml of aqueous 0.7 *N* NaOH. To this, H_2O_2 (5 ml of 15%) was added dropwise with continuous stirring. The temperature was not allowed to exceed 45°. After 30 min the reaction mixture was neutralized with HCl and the solid was filtered, washed (H_2O), and crystallized (EtOH–HCl) to give fine needles of **2**, dried at 150° *in vacuo*.

All of the 2-amino-4-arylamino-6-hydroxy-*s*-triazines were prepared by following this method.

Action of Raney Nickel on 2-Amino-4-anilino-6-mercapto-*s*-triazine.—2-Amino-4-anilino-6-mercapto-*s*-triazine (0.55 g, 0.0025 mole) was finely powdered and suspended in saturated $NaHCO_3$ (50 ml). Raney nickel (W_6, 4.5 g) was added to it. The mixture was refluxed for 4 hr and filtered hot. The filtrate after neutralization with HCl was evaporated to dryness. The residue was treated with EtOH and filtered. The filtrate on evaporation gave 163 mg (37.5%) of 2-amino-4-anilino-*s*-triazine, mp 229–231°. It was recrystallized from EtOH, mp 233–234°. The mixture melting point with the compound prepared by treating phenylbiguanide with formic acid was not depressed. *Anal.* ($C_9H_9N_5$) N.

Action of Raney Nickel on 1-Phenyl-2-thioammeline.—1-Phenyl-2-thioammeline (500 mg) was suspended in 50 ml of EtOH containing about 2.8 g of Raney Ni (W_6). The reaction mixture was refluxed for 3 hr when an almost clear solution was obtained. It was then cooled to room temperature and filtered, and the filtrate was evaporated to dryness. The residue was crystallized (EtOH); one obtains 2-amino-4-anilino-*s*-triazine, 142 mg (32.6%), mp 231–232°. A mixture melting point with an authentic sample was not depressed. *Anal.* Calcd for $C_9H_9N_5$: N, 26.92. Found: N, 27.34. The picrate melted at 241–243°; a mixture melting point with the authentic picrate was not depressed.

Bis(2-amino-4-anilino-6-*s*-triazinyl) Disulfide.—To a solution of 2-amino-4-anilino-6-mercapto-*s*-triazine (1.4 g) in aqueous NaOH (50 ml of 0.4 *N*) 1 *N* I_2–KI solution was added dropwise with stirring keeping the temperature at 15–20°. The addition was stopped when no further decolorization of I_2 was observed. The mixture was left at room temperature for 15 min and the separated white solid was filtered, washed (H_2O), and crystallized (MeOH) to give the product as a dihydrate (0.75 g, 54%), mp 225–226°. It was insoluble in dilute HCl or NaOH. *Anal.* ($C_{18}H_{16}N_{10}S_2 \cdot 2H_2O$) N. After drying at 110° *in vacuo*, it showed a correct analysis for C, H, N.

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