(20.9%) of a grey tinted hydrate of disodio-1,1-di-*N*-nitrosohydroxylaminobutane was isolated.

Anal. Calcd. for $C_4H_{16}N_4Na_2O_6$: C, 20.00; H, 4.17; N, 23.3; Na, 19.17. Found: C, 19.90; H, 4.68; N, 23.9; Na, 19.16.

Acknowledgment. We are indebted to Miss Virginia Barber for infrared absorption data and Mrs. Ann Wise for the preparation of some aldoximes.

ERIE, PA.

[CONTRIBUTION FROM THE ORGANIC RESEARCH LABORATORIES OF U. S. VITAMIN AND PHARMACEUTICAL CORP.]

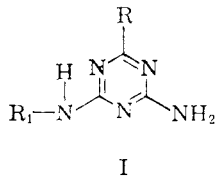
Guanamines. VIII. 6-(Substituted Phenyl)guanamines

SEYMOUR L. SHAPIRO, VINCENT A. PARRINO, AND LOUIS FREEDMAN

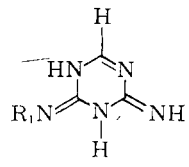
Received October 17, 1960

A series of 2-substituted amino-4-amino-6-phenyl- (and substituted phenyl)-*s*-triazines has been synthesized and the influence of structural variation on the ultraviolet absorption spectra reported.

Diuretic activity in a series of guanamines I, R = H, was ascribed to the tautomer II; whereas with homologs of I, R = alkyl, noted ineffectiveness was associated with equilibria which diminished the population of forms such as II.[1]



I

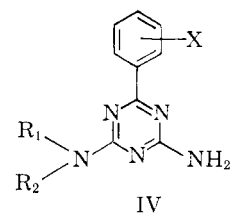


II

To challenge this concept, aryl variants of R envisioned as capable of stabilizing II were prepared (Table I), in the hope that an increase in the absolute concentration of forms such as III, rather than an unfavorable equilibrium concentration would enhance diuretic activity.[2]

Most of the compounds were prepared by condensation of the requisite acid chloride[3] with the substituted biguanide.[4] For compounds 5–12 reaction of the biguanide in methyl salicylate as a solvent, under controlled heating was the method of choice. The reduction of compound 23 to 2-amino-4-*n*-amylamino-6-*m*-aminophenyl-*s*-triazine was effected using rhodium-on-carbon.[5] On testing as a diuretic this compound was inactive while the other compounds were too insoluble for evaluation of their pharmacological properties.

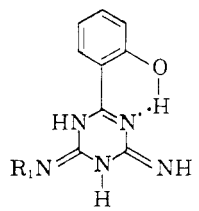
Spectral characteristics of these compounds indicate that the 6-phenyl group of IV could interact with the triazine nucleus as an unhindered biphenyl,[6] although the R_1R_2N— group can influence



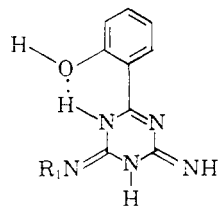
IV

X = H, *o*-OH, *o*-OCH_3, *m*-NO_2, *m*-NH_2

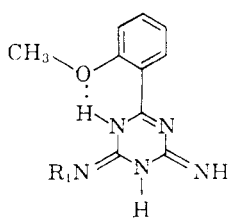
co-planarity of the 6-position substituent.[7] The role of the azomethine linkage in heteroaromatics, as imparting a pseudocarbonyl function,[8] could be



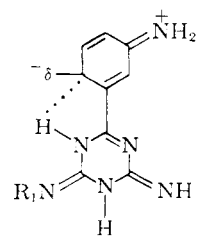
IIIa



IIIb



IIIc



IIId

(1) S. L. Shapiro, V. A. Parrino, K. Geiger, S. Kobrin, and L. Freedman, *J. Am. Chem. Soc.*, **79**, 5064 (1957).

(2) S. J. Angyal and C. L. Angyal, *J. Chem. Soc.*, 1461 (1952).

(3) S. L. Shapiro, V. A. Parrino, and L. Freedman, *J. Am. Chem. Soc.*, **81**, 3996 (1959).

(4) (a) S. L. Shapiro, V. A. Parrino, E. Rogow, and L. Freedman, *J. Am. Chem. Soc.*, **81**, 3725 (1959) for arylbiguanides; (b) S. L. Shapiro, V. A. Parrino, and L. Freedman, *J. Am. Chem. Soc.*, **81**, 3728 (1959) for alkyl and aralkylbiguanides.

(5) S. L. Shapiro, K. Weinberg, T. Bazga, and L. Freedman, *J. Am. Chem. Soc.*, **81**, 5146 (1959).

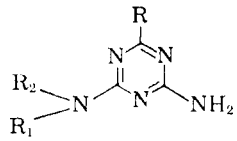
(6) H. Gilman, *Org. Chemistry*, Vol. III, John Wiley & Sons, Inc., New York, N. Y., 1953, p. 172.

(7) S. L. Shapiro, V. A. Parrino, and L. Freedman, *J. Org. Chem.*, **25**, 379 (1960).

(8) (a) S. L. Shapiro, E. Isaacs, V. A. Parrino, and L. Freedman, *J. Org. Chem.*, **26**, 68 (1961); (b) J. T. Thurston, F. C. Schaefer, J. R. Dudley, and D. Holm-Hansen, *J. Am. Chem. Soc.*, **73**, 2992 (1951); (c) J. M. McManus and R. M. Herbst, *J. Org. Chem.*, **24**, 1462 (1959); (d) R. Levine and S. Raynolds, *J. Org. Chem.*, **25**, 530 (1960).

TABLE I

GUANAMINES[a]



No.	R_1	M.P.[b]	S[c]	Yield,[d] %	Formula	Carbon Calcd.	Carbon Found[e]	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found
	R = C_6H_5—										
1[aa]	CH_3—	165–166	A	38	$C_{11}H_{13}N_5$	61.4	61.1	6.1	6.3	32.5	32.9
2	n-C_5H_{11}—	100–102	B	74	$C_{14}H_{19}N_5$					27.2	26.7
3	[f]	149–151	A	28	$C_{14}H_{17}N_5$	66.9	66.6	6.7	7.0		
4	C_6H_5—	198–199	B	55	$C_{15}H_{13}N_5$	68.4	68.3	5.0	4.8	26.6	26.6
	R = o-OH—C_6H_4—										
5[aa]	CH_3—	187–188	A	37	$C_{11}H_{13}N_5O$	57.1	57.5	5.7	6.1	30.3	30.4
6	C_3H_5[g]	164–165	A	30	$C_{12}H_{13}N_5O$	59.3	59.0	5.4	5.4	28.8	28.7
7	n-C_4H_9—	176–177	A	36	$C_{13}H_{17}N_5O$	60.2	60.4	6.6	6.8	27.0	26.9
8	n-C_5H_{11}—	148–150	A	33	$C_{14}H_{19}N_5O$	61.5	61.9	7.0	7.1	25.6	25.3
9	$C_6H_5CH_2CH_2$—	164–166	A	34	$C_{17}H_{17}N_5O$	66.4	66.1	5.6	5.3	22.8	22.6
10[aa]	$C_6H_5CH_2$—	154–155	A	36	$C_{17}H_{17}N_5O$	66.4	66.0	5.6	5.8	22.8	22.9
11	C_6H_5—	221–223	A	18	$C_{15}H_{13}N_5O$	64.5	65.0	4.7	4.8		
12	p-ClC_6H_4—	249–251	A	18	$C_{15}H_{12}ClN_5O$	57.4	57.0	3.9	4.1	22.3	22.3
	R = o-CH_3O—C_6H_4—										
13[aa]	CH_3—	223–224	B	28	$C_{12}H_{15}N_5O$	58.8	58.5	6.2	5.9		
14	C_3H_5—[g]	162–164	B	39	$C_{13}H_{15}N_5O$					27.2	26.9
15	n-C_4H_9—	174–175	A	55	$C_{14}H_{19}N_5O$	61.5	61.6	7.0	6.8		
16	n-C_5H_{11}—	191–192	A	68	$C_{15}H_{21}N_5O$	62.7	63.0	7.4	7.4		
17	i-C_5H_{11}—	195–196	B	56	$C_{15}H_{21}N_5O$	62.7	62.1	7.4	7.3		
18[aa]	$C_6H_5CH_2$—	154–155	B	61	$C_{18}H_{19}N_5O$	67.3	67.0	6.0	6.0	21.8	22.1
19	$C_6H_5CH_2CH_2$—	195–196	A	50	$C_{18}H_{19}N_5O$	67.3	67.2	6.0	5.9	21.8	22.1
20[h]	C_6H_5—	187–191	A	38	$C_{16}H_{15}N_5O$	65.5	65.2	5.2	5.3		
21	p-ClC_6H_4—	228–231	C	48	$C_{16}H_{14}ClN_5O$					21.4	20.9
	R = m-NO_2—C_6H_4—										
22[aa]	CH_3—	222–224	B	25	$C_{11}H_{12}N_6O_2$	50.8	50.9	4.7	4.7		
23	n-C_5H_{11}—	122–123	B	47	$C_{14}H_{18}N_6O_2$	55.6	55.9	6.0	6.2	27.8	28.2
24	[f]	165–167	B	38	$C_{14}H_{16}N_6O_2$	56.0	55.7	5.4	5.1		
25	C_6H_5—	212–213	B	41	$C_{15}H_{12}N_6O_2$	58.4	58.6	3.9	4.0	27.3	27.1

[a] R_2 is hydrogen unless otherwise indicated; [aa] R_2 is methyl. [b] Melting points are not corrected. [c] S = recrystallizing solvent; A = ethanol-water; B = acetonitrile; C = Methyl Cellosolve–water. [d] Yields are reported as recrystallized product. [e] Analyses are by Weiler and Strauss, Oxford, England. [f] R_1R_2N— = piperidino. [g] C_3H_5— = allyl. [h] The picrate, melted 202–206° (ethanol-hexane). *Anal.* Calcd. for $C_{12}H_{18}N_8O_8$: C, 50.9; H, 3.5; N, 21.5. Found: C, 51.2; H, 3.5; N, 21.2.

reflected herein as benzamidine or benzamide spectra. The tautomeric variants of IV, reflected by III above, may also influence or be the predominant form. The spectra have been detailed in Table II.

The influence of the 6-position substituent is manifest as R is varied as hydrogen, methyl, and phenyl in I. Relative to I, R = H (R_1 = aromatic), R = CH_3 affords pronounced bathochromic and hyperchromic effects,[9] although this effect is modified when the free amino group is replaced by the dimethylamino group (compounds 31 and 32) and a new chromophore is obtained at about 236 mμ. When R_1 is aliphatic, substitution of R = methyl for R = hydrogen gives a hypsochromic shift ($\Delta\lambda_{max}$ = 7 mμ) with no significant effect on the extinction coefficient (see compounds 28, 29).[10]

With R = phenyl, the band at about 238 mμ (compounds 1–3) indicates that the principal electronic path is through the phenyl ring, co-acting with the triazine nucleus.[11] The spectral character is clearly distinct from 2,4-diamino-6-phenyl-s-triazine[11] with compounds 1–3 showing nearly twice the absorbance and a hypsochromic effect relative to this compound. This may be associated with decreasing population of the imino form[11a] (see compounds 1 and 3 *vs.* 2) with the more fully substituted compounds. With compound 4 the bathochromic effect, relative to compounds 1–3, is

(9) C. G. Overberger and S. L. Shapiro, *J. Am. Chem. Soc.*, **76**, 1855 (1954) (see compound 1 *vs.* 4, 8, and 9, Table II of this reference).

(10) Ref. 1, shows a comparable R = H analog of compound 28 (n-butyl deriv.) λ_{max} 263 (3.80), and of compound 29, λ_{max} 263 (4.13).

(11) (a) P. B. Russell, G. H. Hitchings, B. H. Chase, and J. Walker, *J. Am. Chem. Soc.*, **74**, 5403 (1952) report λ_{max} 249 (25.0) (ethanol); (b) F. C. Nachod and E. A. Steck, *J. Am. Chem. Soc.*, **70**, 2819 (1948) report λ_{max} 244 (18.6) (95% ethanol).

TABLE II

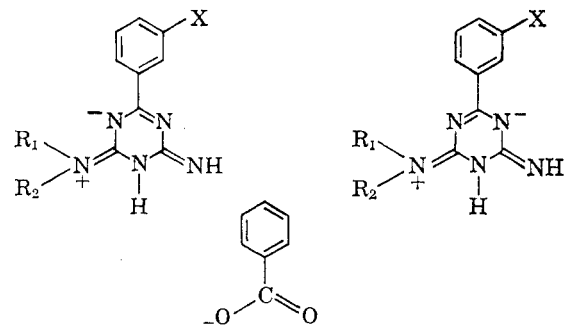
ULTRAVIOLET ABSORPTION SPECTRA[a]

No.[b]	λ_{max} ($\epsilon \times 10^{-3}$)[b,c]
1	237 (29.2); 270–290 (3.9)
2	237 (25.2); 276–290 (3.8)
3	240 (34.6); 270–288 (4.2)
4	255 (36.2); 292–303 (6.6)
5	248 (19.9); 313 (7.7)
6	251 (15.5); 315 (7.2)
7	251 (17.6); 314 (6.9)
8	250 (18.0); 314 (7.1)
9	250 (18.4); 315 (7.1)
10	248 (21.6); 313 (7.8)
11	257 (33.3); 314 (11.6)
12	262 (35.4); 292–315 (13.9)
13	276 (6.2)
14	276 (5.7)
15	276 (6.0)
16	276 (5.9)
17	276 (6.2)
18	278 (6.9)
19	275 (6.0)
20	254 (24.6); 275–281 (16.2)
21	258 (26.7); 276–287 (19.9)
22	232 (42.2); 260–278 (8.8)
23	229 (38.8); 256–275 (8.9)
24	235 (46.0); 257–288 (8.4)
25	255 (39.7)
26[da]	260 (3.7)
27[db]	256 (3.7)
28[dc]	256 (3.7)
29[dd]	257 (4.2)
30[de]	258 (4.9)
31[df]	236 (21.8); 257 (21.6)
32[dg]	227 (30.4); 259–270 (6.0)
A[e]	236 (9.0); 267 (11.8); 283–304 (8.5)
A[f]	238 (15.7); 269 (14.0); 336 (8.9)
B[g]	233 (7.6); 301 (3.9)
B[f]	239 (7.3); 326 (5.9)
C[h]	234 (7.5); 302 (3.8)
C[f]	213–217 (6.4); 296 (3.8)
D[i]	232 (40.0)

[a] The spectra were established in methanol with a Beckman recording spectrophotometer, Model DK. Compounds 5–12 were also evaluated in 0.1*N* sodium methoxide in methanol, and gave spectra identical to those found with methanol. [b] Numbers correspond to compound numbers in Table I. [c] Where a range for the maximum is shown, the extinction coefficient is calculated at the center of the shoulder. [d] Compounds 26–32 are derivatives of acetoguanamine and have been described by S. L. Shapiro, E. Isaacs, V. Parrino, and L. Freedman, *J. Org. Chem.*, **26**, 68 (1961); the 2-substituted amino group is identified below, and unless otherwise stated the 4-substituent is amino; [da] dimethylamino; [db] allylamino; [dc] *n*-amylamino; [dd] β-phenethylamino; [de] *N*-methylbenzyl; [df] 2-anilino-4-dimethylamino; [dg] 2-(2,6-dimethylanilino)-4-dimethylamino. [e] Salicylanilide. [f] Solvent for compound immediately above was 0.1*N* sodium methoxide. [g] Salicylamide. [h] Salicylic acid. [i] 2-Amino-4-*n*-amylimino-6-*m*-aminophenyl-*s*-triazine hydrochloride hydrate.

ascribable to a preferred path involving coaction of the anilino group with the triazine nucleus.[7]

Compounds 22–25 (R = *m*-nitrophenyl) afforded small hyper- and hypsochromic effects relative to compounds 1–4. This enhancement of the "anomaly" to 2,4-diamino-6-phenyl-*s*-triazine with the more electron-deficient phenyl ring having *m*-nitro substitution and the noted hyperchromicity, suggest that the predominant absorbing species may be the dipolar ion, form V, in analogy to the benzoate resonance.[12,13]



V. X = H, NO_2

The I, R = *o*-hydroxyphenyl (compounds 5–12), spectra compare with salicylic acid and allied structures[14,15] which have bands at about 237 and 308 mμ. The compounds of this series have these bands shifted bathochromically and hyperchromically, and the identity of the spectral characteristics obtained in methanol or 0.1*N* sodium methoxide suggest that formula IIIa most closely describes the key chromophore.[16]

In turn, the spectra of I, R = *o*-methoxyphenyl group (compounds 13–21), are distinguished from I, R = phenyl to a degree in excess of that predictable on steric hindrance. Additionally, they do not resemble[14] the *o*-hydroxyphenyl series, which indicates that the principal absorbing species is distinct from that classified for these groups, and which is suggested as form IIIc. The aryl R_1NH— variants in this group (compounds 20, 21) have an additional strong band at about 255 mμ reflecting the coaction of the anilino group with the triazine ring, whereas the characteristic band for this series at about 276 mμ is sublimated as a shoulder.

EXPERIMENTAL

2-Amino-4-anilino-6-m-nitrophenyl-s-triazine (Compound 25). A mixture of 4.43 g. (0.025 mole) of phenylbiguanide in 25 ml. of acetonitrile and 2.5 ml. (0.025 mole) of 40% sodium hydroxide in 10 ml. of water at 0° was treated with stirring and continued cooling with 4.62 g. (0.025 mole) of *m*-nitrobenzoyl chloride. After storage at 20° for 24 hr. the reaction mixture was decanted into 100 ml. of water, and the product 5.25 g. (68%) m.p. 209–211°, separated.

Compounds 1–4, 13–24 were similarly prepared using the appropriate biguanide and acid chloride, with an additional

(12) (a) W. F. Forbes and M. B. Sheratte, *Can. J. Chem.*, **33**, 1829 (1955); (b) W. J. Horton and D. E. Robertson, *J. Org. Chem.*, **25**, 1016 (1960).

(13) (a) H. E. Ungnade and R. W. Lamb, *J. Am. Chem. Soc.*, **74**, 3789 (1952); (b) H. H. Freedman, *J. Am. Chem. Soc.*, **82**, 2454 (1960).

(14) C. M. Moser and A. K. Kohlenberg, *J. Chem. Soc.*, 804 (1951).

(15) H. E. Ungnade, E. E. Pickett, L. Rubin, and E. Youse, *J. Org. Chem.*, **16**, 1318 (1951).

(16) R. S. Baichwal, R. M. Baxter, S. I. Kandel, and G. C. Walker, *Can. J. Biochem. and Physiol.*, **38**, 245 (1960) suggest involvement of hydrogen bonding in salicylanilides.

equivalent of sodium hydroxide when the biguanide hydrochloride was used.

2-Amino-6-o-hydroxyphenyl-4-β-phenethylamino-s-triazine (Compound 9). A mixture of 4.8 g. (0.02 mole) of β-phenethylbiguanide hydrochloride in 15 ml. of methanol was treated with 5 ml. (0.02) mole of 23% sodium methoxide in methanol. The sodium chloride formed was separated and the filtrate on evaporation gave a residue of the biguanide free base which was granulated under pentane. The biguanide was suspended in 5 ml. (excess) of methyl salicylate and heated in an oil bath maintained at 115° for 20 min. with noted evolution of basic fumes. When cool, the formed sirup was granulated under pentane to give 5.49 g. (81%) of crude product.

Compounds 5–12 were similarly prepared.

Hydrogenation of compound 23. A mixture of 2.23 g. (0.0074 mole) of the compound in 2.46 ml. of 3*N* hydrochloric acid and 250 ml. of methanol, and 0.5 g. of 5% rhodium-on-carbon was hydrogenated in the Parr hydrogenator at 20° at an initial pressure of 62.5 lbs. of hydrogen. Within 10 min. the theoretical hydrogen (3 equivalents for reduction of nitro to amine group) was absorbed. After removal of the catalyst and evaporation of the solvent, there was obtained 2.17 g. (90%) of yellow crystals of 2-amino-4-*n*-amylamino-6 *m*-aminophenyl-*s*-triazine hydrochloride hydrate, m.p. 73–79°; recrystallized (water), m.p. 79–80°.

Anal. Calcd. for $C_{14}H_{23}ClN_6O$: C, 51.5; H, 7.1; N, 26.7. Found: C, 51.5; H, 7.2; N, 27.4.

The dipicrate melted at 201–203° (acetonitrile).

Anal. Calcd. for $C_{26}H_{24}N_{12}O_{14}$: C, 43.0; H, 3.3; N, 23.2. Found: C, 43.2; N, 3.8; N, 23.2.

Acknowledgment. The authors wish to thank M. Blitz and D. Farkas for the ultraviolet absorption spectra.

YONKERS 1, N. Y.

[CONTRIBUTION FROM RESEARCH AND DEVELOPMENT DIVISION, SPENCER CHEMICAL CO.]

Vinyl Isocyanurates. Preparation of Alkenyl Isocyanurates by Trimerization or Cotrimerization of Isocyanates

ERIC C. JUENGE AND WILLIAM C. FRANCIS

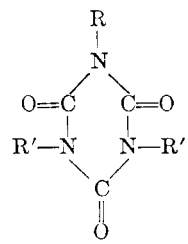
Received January 3, 1961

Trivinyl isocyanurate was obtained from the trimerization of vinyl isocyanate. Cotrimerizations of vinyl or allyl isocyanates with alkyl or aryl isocyanates yielded the corresponding unsymmetrically substituted isocyanurates. Effects of catalysts and reactant ratios on the trimerization reactions were studied.

A number of examples are to be found in the literature describing the preparation of isocyanurates by trimerization of aromatic and aliphatic isocyanates.[1,2] The trimerization of cyanic acid to form cyanuric acid is also known.[3] No examples could be found for the preparation of alkenyl isocyanurates by this type of reaction. The most nearly analogous method for the synthesis of an unsaturated derivative is that involving reaction of potassium isocyanate with allyl chloride to produce triallyl isocyanurate.[4]

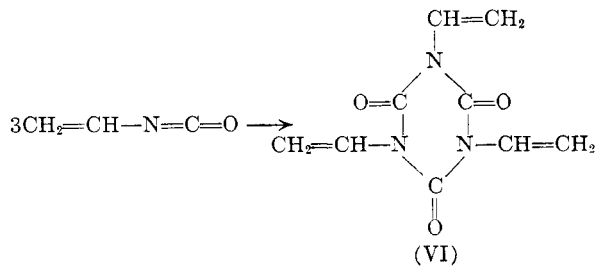
Vinyl isocyanurate is reported to result from cleavage of triallyl isocyanurate in the presence of a phenol.[5] The product was not fully described or characterized, and we were not able to repeat this reaction in our laboratory. The syntheses of di- and triallyl compounds have been effected by reaction of cyanuric acid with allyl chloride in aqueous caustic.[6] The mono- and diallyl derivatives are reported to be obtained from reaction of the triallyl compound with phenol and aromatic solvents in the presence of various catalysts.[7] Isocyanurates bearing both saturated and unsaturated aliphatic substituents have not been reported.

We have found that mixed trisubstituted isocyanurates of the following types can be prepared by base-catalyzed cotrimerization of the appropriate isocyanates.



I. R = $-CH=CH_2$; R′ = $-C_4H_9$
II. R = $-CH_2-CH=CH_2$; R′ = $-C_2H_5$
III. R = $-C_2H_5$; R′ = $-CH_2-CH=CH_2$
IV. R = $-C_4H_9$; R′ = $-CH=CH_2$
V. R = $-C_6H_5$; R′ = $-CH=CH_2$

Homotrimerization of vinyl isocyanate has also provided the novel trivinyl isocyanurate (VI) in good yield:



(VI)

(1) A. W. Hofman, *Ber.*, **18**, 765 (1885); I. C. Kogon, U. S. Pat. 2,838,511 (1958).

(2) E. M. Smolin and L. Rapoport, *Heterocyclic Compounds*, Interscience, New York, 1959, p. 104; Australian Pat. 45,955 (1959).

(3) P. Klason, *J. prakt. Chem.*, (2), **33**, 129 (1886).

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