The evaporation of the methanolic mother liquors gave sirupy 1H-2,3,4,5-tetrahydro-1,4-benzodiazepine, VIIIa, which showed the following infrared absorption: strong 2980 cm.$^{-1}$ (methylene group); 3400 cm.$^{-1}$ (—NH— group). It was dissolved in 10 ml. of methanol. Ether saturated with hydrochloric acid was added causing precipitation of VIIb; m.p. 243-244°, after recrystallization from methanol–acetone, yield 2 g. Infrared absorption: 3000–2400 cm.$^{-1}$ (ammonium salt bands). Ultraviolet absorption: λ_{max} 220 mμ (ε 2700); 242–243 (7450); 287–291 (1800).

Anal. Calcd. for $C_9H_{12}N_2 \cdot 2HCl$: C, 48.88; H, 6.38; N, 12.67; Cl, 32.06. Found: C, 49.19; H, 6.58; N, 12.67; Cl, 31.55.

o-Aminohippurylmethylamide (IX) from III.—The suspension of 1 g. of III in 1000 ml. of methanol was saturated for 5 hr. at 60° with methylamine, when a clear solution was obtained. After evaporation, the residue was crystallized from acetone, giving 600 mg. of IX, m.p. 170–174°. Infrared absorption: 3450 and 3320 cm.$^{-1}$ (—NH_2 and —NH—); 1656 and 1642 cm.$^{-1}$ (—C=O groups). Ultraviolet absorption: λ_{max} 213 mμ (ε 25,800); 250–251 mμ (ε 7800); 330–332 mμ (ε 3800).

Anal. Calcd. for $C_{10}H_{13}N_3O_2$: C, 57.95; H, 6.32; N, 20.28. Found: C, 58.51; H, 6.50; N, 20.17.

Anthranilic (X) Acid from III.—The solution of 1 g. of III in 10 ml. 70% sulfuric acid was heated 15 min. at 140° and poured on ice. The mixture was made alkaline with concentrated aqueous sodium hydroxide. Addition of acetic acid precipitated X, m.p. 143–145°, which showed the same infrared spectrum as commercial anthranilic acid.

Acknowledgment.—Appreciation is expressed to Dr. A. Steyermark for the analyses, to Dr. V. Toome and S. Traiman for the spectra.

Synthesis of the *s*-Triazine System. VI.[1] Preparation of Unsymmetrically Substituted *s*-Triazines by Reaction of Amidine Salts with Imidates

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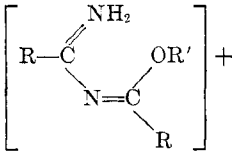
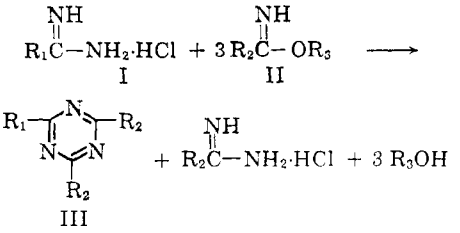
A wide variety of unsymmetrically substituted *s*-triazines are obtained by the reaction of amidine salts with the lower aliphatic imidates. The predominant product generally has one substituent radical derived from the amidine and two from the imidate reactant. The reaction occurs at a useful rate at ordinary temperatures and under conditions which are only weakly basic.

The cotrimerization of two alkyl imidates in the presence of an acidic catalyst is a convenient and sometimes practical route to a variety of interesting unsymmetrically substituted *s*-triazines.[1] However, this is inherently a random process and we have continued to search for more selective synthetic methods. The proposed mechanism for the imidate trimerization reaction[2] suggested that an intermediate "dimer" was involved which had the structure



It seemed possible that reaction of an amidine salt with an imidate might also lead to such a structure.[3] If so and if further reaction with a second imidate molecule took place as would be expected, this process would permit control of introduction of unlike R—groups into the final *s*-triazine product. Thus, the group introduced with the amidine reactant could be different from the two groups introduced as the imidate. This paper reports the development of this proposition into a widely applicable method for the synthesis of unsymmetrically substituted *s*-triazines.

Somewhat fortuitously, the reaction studied first was that of 2-methylpseudourea hydrochloride (I, R = CH_3O) with ethyl acetimidate. This work at once proved the feasibility of the method and demonstrated that the stoichiometry approached that expected for the reaction,[5]

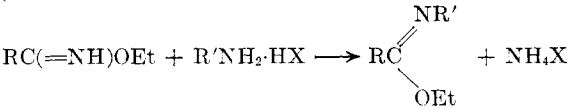


On this basis the yield of 2-methoxy-4,6-dimethyl-*s*-triazine (III. R_1 = CH_3O, R_2 = CH_3) averaged 73%. About 10% of trimethyl-*s*-triazine was obtained and acetamidine hydrochloride was re-

(1) Paper V. F. C. Schaefer, *J. Org. Chem.*, **27**, 3362 (1962).

(2) F. C. Schaefer and G. A. Peters, *ibid.*, **26**, 2778 (1961).

(3) Such a reaction would be analogous to the following, of which several examples are known[4]:



(4) R. Roger and D. G. Neilson, *Chem. Rev.*, **61**, 179 (1961).

(5) The ammonium chloride eliminated at some point in the desired reaction inevitably converts an equivalent amount of imidate to amidine salt.[6]

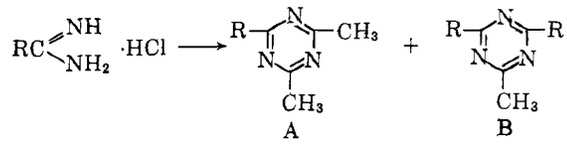
covered in about 90% yield. Consequently, in most of the subsequent work the reactant ratio used has been 1:3. The reaction mixture was usually held at room temperature until further change was negligible as judged by infrared examination. It was helpful with relatively insoluble amidine salts to dissolve part of the salt in a little methanol or ethanol and add the imidate gradually. Some reactions were exothermic; others were deliberately heated to speed the process. In only a few cases has maximization of the yield been attempted by extensive variation of the reaction conditions. The results are summarized in Table I.

The general conclusions from the results presented in Table I are as follows: 1. It is clear that the reaction is widely applicable when ethyl or methyl acetimidate or propionimidate is the imidate reactant. Yields of the expected unsymmetrically substituted s-triazine in the range of 50–90% are obtained with a great variety of amidine salts when the theoretical reactant ratio is used.

2. As anticipated, the formation of substantial amounts of the simple trimer (trimethyl- or triethyl-s-triazine) sometimes reduces the yield considerably. As the reaction proceeds the product amidine salt becomes an increasingly serious competitor of the starting amidine salt for the available imidate. Consequently, it is inevitable that some of the symmetrically trisubstituted s-triazine related to the imidate will be formed. To the extent of this side reaction, the starting amidine salt remains unchanged, and in some cases it might be advisable to use a larger proportion of imidate reactant. This would generally be economical since these simple imidates are readily prepared. It would be most effective if a substantial part of the by-product amidine were removed from the reaction sphere by crystallization.

3. If there were no selectivity in the reaction of the starting and by-product amidine salts with the imidate, the product mixture would contain an unattractively large amount of the imidate trimer if high conversion of the starting amidine were attempted. Fortunately, judging from the results obtained, the salt of the less basic amidine seems to react faster. Thus practically all complex amidine salts react well with an alkyl acetimidate or propionimidate without unfavorable competition from the strongly basic alkaneamidine by-product. A further favorable factor is the crystallization of acetamidine hydrochloride which often occurs as reaction of an amidine hydrochloride with ethyl acetimidate proceeds.

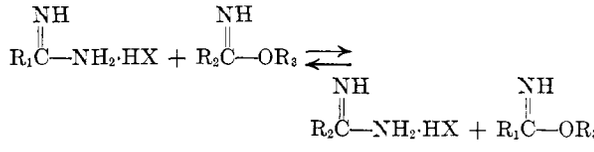
4. The formation of considerable amounts of the alternative unsymmetrical s-triazines has proved to be surprisingly common. It appears that the initial example with 2-methylpseudourea hydrochloride was an exceptionally clean reaction, 2-methoxy-4,6-dimethyl-s-triazine being the only unsymmetrical product found. The reactions with aromatic amidine salts, including 2-guanylpyridine hydrochloride, are also quite clean and in some other cases only the expected product was isolated. Occasionally in the latter, however, relatively low yields might indicate that a second product had not been recovered. The aliphatic and substituted aliphatic amidines in general gave rather low selectivity as the following compilation of product ratios indicates (reaction with ethyl acetimidate):



A B

	Mole Ratio			
R	$C_6H_5CH_2$	$(CH_3)_2CH$	$(EtO)_2CH$	CH_2OH
A/B	5.8	7.5	4.6	5.2
R	CH_3CHCl	CH_2Cl	EtO_2C	
A/B	3.8	6.0	6.0	

It is probable that this by-product formation is related to the following interchange reaction which has been observed:



This interchange apparently takes place to a greater degree with the less basic amidines, *e.g.* 2-chloropropionamidine and 1-carbethoxyformamidine in which cases the corresponding imidates were recovered, and has two results. First, the generated imidate can now partly replace the original imidate in the trimerization reaction and thus cause formation of the alternative unsymmetrically substituted s-triazine. Secondly, the less basic imidates are in general less reactive[2] and may remain in considerable amount at the "end" of the reaction. This scrambling of the starting reagents may be a relatively slow process and probably is minimized when the cotrimerization reaction is fast. In other cases it may be advisable to use less than the theoretical 3:1 imidate–amidine ratio and not attempt high conversion of the starting amidine salt.

5. Attempts to use imidates other than those derived from the lower aliphatic nitriles gave poor results except with formamidine salts. It is known from our work on imidate trimerization[2] that the higher aliphatic imidates give progressively lower yields of s-triazines and that other imidates are relatively sluggish reagents. A further drawback in their use in the present work is their poor solvent power for amidine salts. This has necessitated dilution of the reaction mixtures with methanol or ethanol, probably further impeding s-triazine formation. Imidates tried included II, R_2 =

TABLE I. PREPARATION OF UNSYMMETRICALLY SUBSTITUTED s-TRIAZINES

III IV

Reactants[a] R1	R2	Reaction conditions: Time, hr.	Temp., °C.	Work-up procedure	s-Triazine products: Structure	Yield, %[b]	Properties
C_6H_5[c]	CH_3[d]	1	60	[e]	III	55	B.p. 93–96°/1.5 mm.[f]
		+ 18	R.T.				F.p. 34°[g]
4-ClC_6H_4[h]	CH_3	2	30–45	[i]	III	88	M.p. 131–133°[j]
		+ 0.5	80				
4-$NO_2C_6H_4$[k]	CH_3	3.5[l]	60[m]	[n]	III	60	M.p. 161–163°[o]
		+ 18	R.T.				
2-C_5H_4N[k]	CH_3	0.5	50	[p]	III	81	B.p. 145–154°/1 mm.
		+ 4 days	R.T.				M.p. 55.5–57°[q]
$C_6H_5CH_2$[r]	CH_3	5 days	R.T.	[p]	III	58	B.p. 107°/2 mm.[s]
							$n^{26.5}D$ 1.5480
					IV	20	B.p. 170°/2 mm.[t]
$(CH_3)_2CH$[u]	CH_3	0.5[v]	80[m]	[p]	III	45	B.p. 176–179°[w]
		+ 18	R.T.		IV	12	
R[x]	CH_3	8 days	R.T.	[y]	III	50	B.p. 96°/2 mm.[z]
							$n^{24.6}D$ 1.4579
$(C_2H_5O)_2CH$[aa]	CH_3	2 days	R.T.	[p]	III	45	B.p. *ca.* 150°/15 mm.[bb]
					IV	*ca.* 20	B.p. *ca.* 185°/18 mm.[cc]
CH_3CHCl[k]	CH_3	4	15	[y]	III	50	B.p. 99–102°/24 mm.[dd]
		+ 18	R.T.				$n^{28.5}D$ 1.4901
					IV	26	B.p. 130–135°/24 mm.[dd]
							$n^{27.5}D$ 1.5046
CCl_3[ee]	C_2H_5[d]	20[v]	25–30[m]	[p]	III	64	B.p. 160–175°/38 mm.[ff]
$CHCl_2$[gg]	CH_3[hh]	4 days	R.T.	[p]	III	40	B.p. 117°/18 mm.[ii]
					IV	11	B.p. *ca.* 165°/7 mm.
							M.p. 84–86°[jj]
CH_3O[ee]	CH_3	0.5	80	[y]	III	73	B.p. 80°/3 mm.
		+ 1.5	80–25				F.p. 43.5°
CH_3S[kk]	CH_3	2	80	[e]	III	42	B.p. 73°/4 mm.
		+ 18	R.T.				M.p. 56–57°[ll]
CH_3S[kk]	C_2H_5	1	40[m]	[e]	III	56	B.p. 123°/17 mm.[mm]
		+ 18	R.T.				F.p. 35.5°
CH_3O[nn]	C_2H_5	1.5	80	[oo]	III	52	B.p. 58–64°/0.75 mm.
							$n^{20}D$ 1.4765
C_2H_5OCO[pp]	CH_3	0.5	50	[p]	III	39	B.p. 135–137°/17 mm.[qq]
		+ 4 days	R.T.				F.p. 38°
					IV	13	B.p. *ca.* 180°/9 mm.
CH_3CHOH[rr]	$(CH_3)_2CH$[d]	72[v]	R.T.	[p]	III	37	B.p. *ca.* 140°/20 mm.[ss]
		+ 1.5	80				
H[tt,uu]	CH_3	3.5	65–75[vv]	[p]	III, IV	[ww]	
		+ 18	R.T.				
H[tt,xx]	CH_3	1.5[v]	35–40[vv]	[p]	III, IV	[pp]	
		+ 18	R.T.				
H[tt]	C_2H_5	2.0[v]	40–60[vv]	[p]	III	[yy]	B.p. 175°; 59°/10 mm.[zz]
					IV		$n^{25}D$ 1.4692
							B.p. 144.5°[aaa]
							$n^{25}D$ 1.4748
H[bbb]	R[ccc]	5[l]	70[ddd]	[eee]	III	53	B.p. 147–153°/1.5 mm.[fff]
							$n^{20}D$ 1.4540
					IV	*ca.* 5	B.p. *ca.* 110°/2 mm.

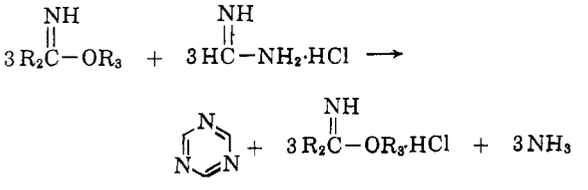
[a] Reactant ratio (imidate/amidine salt) is 3:1 except as noted. [b] Yields based on amidine reactant. [c] See ref. 7. [d] See ref. 2. [e] Diluted with water, extracted product with ether, dried, and distilled. [f] *Anal.* Calcd. for $C_{11}H_{11}N_3$: C, 71.33; H, 5.99; N, 22.69. Found: C, 71.70; H, 6.33; N, 22.64. [g] Ch. Grundmann, *et al.*, *Ber.*, **86**, 181 (1953), gives m.p. 36–37°. [h] The amidine hydrobromide was used. See F. C. Schaefer and A. P. Krapcho, *J. Org. Chem.*, **27**, 1255 (1962). [i] Diluted with water to crystalline product. [j] Recrystallized from ethanol. *Anal.* Calcd. for $C_{11}H_{10}ClN_3$: C, 60.14; H, 4.59; N, 19.13. Found: C, 59.89; H, 4.74; N, 18.96. [k] See ref. 6. [l] Methanol used as solvent, 20–50 cc. per mole of amidine. [m] The imidate was added over a 0.5-hr. period. [n] Diluted with ethanol to crystallize product. [o] Recrystallized from acetonitrile. *Anal.* Calcd. for $C_{11}H_{10}N_4O_2$: C, 57.38; H, 4.38. Found: C, 57.48; H, 4.21. [p] Diluted with ether, filtered, and distilled. [q] Recrystallized from ether. *Anal.* Calcd. for $C_{10}H_{10}N_4$: C, 64.50; H, 5.41. Found: C, 64.95; H, 5.72. [r] See ref. 8. [s] *Anal.* Calcd. for $C_{12}H_{13}N_3$: N, 21.09. Found: N, 21.23. Mass spectrometric analysis confirmed the identification and showed the product to be quite pure. [t] *Anal.* Calcd. for $C_{18}H_{17}N_3$: C, 78.52; H, 6.23; N, 15.26. Found: C, 77.82; H, 6.37; N, 15.68. Mass spectrometric analysis showed that small amounts of 2,4-dimethyl-6-benzyl- and 2,4,6-tribenzyl-*s*-triazine were present. [u] See ref. 9. [v] Ethanol used as solvent, 30–50 cc. per mole of amidine. [w] The products were difficult to separate by distillation. Yields are based on VPC analysis of distilled fractions. [x] R = $(CH_3)_2$-

TABLE I (*Continued*)

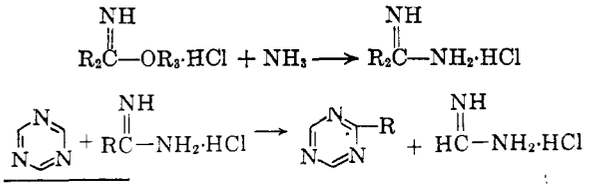
$CHCH_2OCH(CH_3)OCH(CH_3)$—; prepared by the method of ref. 6, m.p. 87–90°. *Anal.* Calcd. for $C_9H_{21}ClN_2O_2$: C, 48.10; H, 9.42. Found: C, 47.49; H, 9.29. [v] Filtered and distilled as completely as possible. Redistilled to separate products. [z] *Anal.* Calcd. for $C_{13}H_{23}N_3O_2$: C, 61.63; H, 9.15; N, 16.59. Found: C, 62.10; H, 9.27; N, 17.35. [aa] prepared in 74% yield from the nitrile by the method of ref. 6; m.p. 81–82°. *Anal.* Calcd. for $C_6H_{15}ClN_2O_2$: Cl, 19.41. Found: Cl, 19.34. [bb] *Anal.* Calcd. for $C_{10}H_{17}N_3O_2$: C, 56.85; H, 8.11; N, 19.89. Found: C, 56.32; H, 8.05; N, 20.35. [cc] N.m.r. examination indicated this fraction was approx. a 1:1 mixture of IV and 2,4,6-tris(diethoxymethyl)-s-triazine. [dd] See ref. 1. [ee] See ref. 10. [ff] Mass spectrometric analysis indicated the product to be 95 mole % as indicated with 5 mole % of 2-ethyl-4,6-bis(trichloromethyl)-s-triazine. [gg] Prepared from the nitrile by the method of ref. 6. The sirup obtained was used as such. Attempts to purify the compound resulted in conversion to 2,4,6-tris(dichloromethyl)-s-triazine. See H. Schroeder and Ch. Grundmann, *J. Am. Chem. Soc.*, **78**, 2447 (1956). [hh] Methyl acetimidate was used. It was prepared as described for the ethyl ester in ref. 2. [ii] *Anal.* Calcd. for $C_6H_7Cl_2N_3$: C, 37.52; H, 3.67; N, 21.88. Found: C, 37.82; H, 3.81; N, 22.34. [jj] Recrystallized from heptane. *Anal.* Calcd. for $C_6H_5Cl_4N_3$: C, 27.61; H, 1.93; N, 16.10; Cl, 54.35. Found: C, 27.85; H, 2.08; N, 16.03; Cl, 54.38. [kk] Hydroiodide salt was used; H. L. Wheeler and H. F. Merriam, *Am. Chem. J.*, **29**, 478 (1903). [ll] Recrystallized from ether; only trace impurities were found by mass spectrometry. [mm] *Anal.* Calcd. for $C_8H_{13}N_3S$: C, 52.43; H, 7.14; N, 22.93; S, 17.49. Found: C, 52.67; H, 7.21; N, 22.94; S, 17.34. [nn] This experiment was carried out by Dr. W. E. Taft and Miss H. M. Krazinski of the Lederle Laboratories Division. [oo] Filtered and distilled; purified product by partial freezing. *Anal.* Calcd. for $C_8H_{13}N_3O$: C, 57.46; H, 7.83; N, 25.13. Found: C, 57.78; H, 8.08; N, 24.97. [pp] See Experimental. [qq] *Anal.* Calcd. for $C_8H_{11}N_3O_2$: C, 53.03; H, 6.12; N, 23.19. Found: C, 52.99; H, 6.12; N, 23.21. [rr] See ref. 11. [ss] The product was nearly pure by mass spectrometric and VPC analysis. Higher boiling by-products were not isolated. [tt] The imidate/amidine ratio was 1.5. [uu] Formamidine acetate[15] was used; E. C. Taylor and W. A. Ehrhart, *J. Am. Chem. Soc.*, **82**, 3138 (1960). [vv] The imidate was added gradually during this period. [ww] The combined yields was 50%. The mole ratio of III to IV was 0.6, as determined by mass spectrometry. [xx] See ref. 12. [yy] The combined yield was 54%. The mole ratio of III to IV was 2.1. These data are based on mass spectrometric analysis of the distilled mixture. Fractional distillation gave the analytical samples. [zz] *Anal.* Calcd. for $C_5H_7N_3$: C, 55.03; H, 6.47; N, 38.15. Found: C, 55.01; H, 6.64; N, 38.41. See ref. 13. [aaa] *Anal.* Calcd. for $C_5H_7N_3$: C, 55.03; H, 6.47; N, 38.15. Found: C, 55.01; H, 6.64; N, 38.41. See ref. 13. [bbb] The imidate/amidine ratio was 1.0. [ccc] See [z] for structure of R; the methyl imidate[6] was used. [ddd] Two liquid phases; stirred vigorously. [eee] Separated upper mobile phase and distilled. [fff] *Anal.* Calcd. for $C_{19}H_{35}N_3O_4$: C, 61.46; H, 9.54; N, 11.67. Found: C, 61.76; H, 9.55; N, 11.37.

CN, COOEt, C_6H_5, and $CH(CH_3)OCH(CH_3)$-$OCH_2CH(CH_3)_2$. In these cases little reaction was detected.

6. The reactions of imidates with formamidine salts probably belong in a special category. It could well be that formamidine base is liberated and converted rapidly to s-triazine,

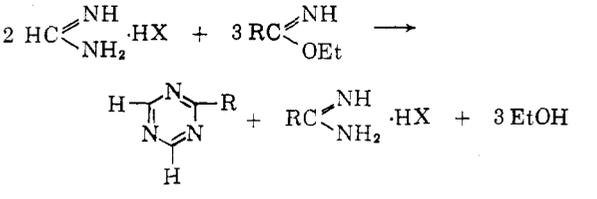


This would be similar to the use of a tertiary amine for conversion of formamidine hydrochloride to s-triazine.[13] However, the imidate salt would undoubtedly be in turn converted to the amidine salt which could react readily with s-triazine,[10]

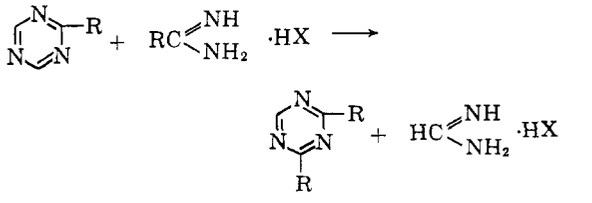


Such a roundabout scheme is not necessarily required, but it does accommodate the fact that the normally sluggish imidate, II, R_2 = $CH(CH_3)OCH(CH_3)OCH_2CH(CH_3)_2$, reacts quite well with formamidine hydrochloride.

The reactions of formamidine salts with ethyl acetimidate and propionimidate seem to show that at low temperature the over-all reaction tends to follow the stoichiometry of the equation,



This "abnormal" result tends to support the view that s-triazine is an intermediate. At higher temperature the major product is the disubstituted s-triazine. This is best interpreted as the result of reaction of the monoalkyl-s-triazine with by-product amidine salt. It has previously been



shown that acetamidine base will convert mono- to dimethyl-s-triazine[10]; we have now found that monomethyl-s-triazine reacts with acetamidine hydrochloride at 70° at a substantial rate giving

(6) F. C. Schaefer and G. A. Peters, *J. Org. Chem.*, **26**, 412 (1961).
(7) A. Pinner, "Die Imidoäther und ihre Derivate," Robert Oppenheim (Gustav Schmidt), Berlin, Germany, 1892, p. 152.
(8) Ref. 7, p. 187.
(9) Ref. 7, p. 126.
(10) F. C. Schaefer and G. A. Peters, *J. Am. Chem. Soc.*, **81**, 1470 (1959).
(11) Ref. 7, p. 132.
(12) Ref. 7, p. 93.
(13) F. C. Schaefer, I. Hechenbleikner, G. A. Peters, and V. P. Wystrach, *J. Am. Chem. Soc.*, **81**, 1466 (1959).

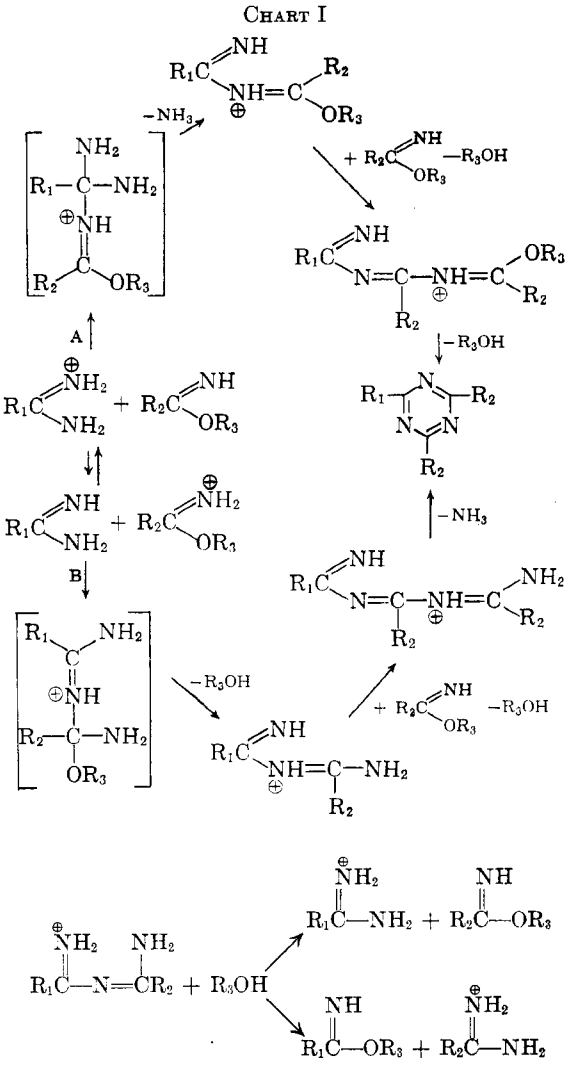
dimethyl-*s*-triazine and even a small amount of trimethyl-*s*-triazine.[14]

7. The reaction proceeds at room temperature at a useful rate. The reaction system also is only weakly basic. These features make it possible to employ sensitive reactants without much danger of degradation. This distinction from many heterocycle syntheses has been a common feature of much of our work with amidines and imidates.

Two distinct paths are conceivable for the reaction. The first (A) is analogous to that proposed for the trimerization of imidates. The alternative (B) is analogous to reaction of an imidate with an ammonium salt to give an amidine salt (see Chart I). The low reactivity of acetamidine hydrochloride toward methyl benzimidate is significant in regard to this question. Comparison of this result with the easy reaction of benzamidine hydrochloride with ethyl acetimidate suggests that the combination of a relatively weakly basic amidine and a relatively strongly basic imidate will give the best reaction. This would be the case if the initial step of the process involves transfer of the proton from the amidinium ion to the imidate and subsequent nucleophilic attack by the amidine at the electron-deficient carbon atom of the imidate conjugate acid.[15] This is the key step in path B of Chart I. It is clear that a favorable relationship of imidate–amidine basicity obtains in the reaction of practically any amidine salt with a simple aliphatic imidate. However, salts of strongly basic amidines would be less likely to react with relatively weakly basic imidates.[16]

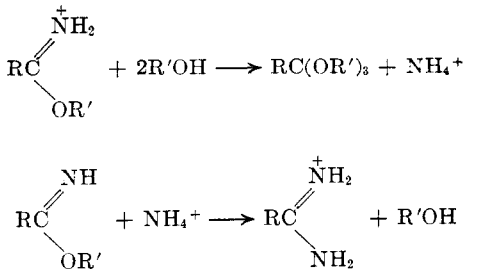
The imidate–amidine interconversion which is observed in many reactions may go through the same dimer (or trimer) intermediate as is involved in the triazine-forming reaction:

CHART I



However, the interchange does not in itself confirm the path B for the trimerization reaction.

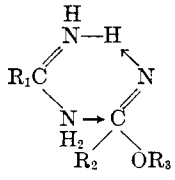
It is now apparent that the trimerization of an imidate by an acid catalyst could also be considered to follow path B. In this case preliminary alcoholysis of the imidate would lead to the amidine reactant:



This reaction is invariably observed to some degree,[2] and in view of the present work it is probably a contributor to the over-all result of imidate trimerization in some cases. However, the relatively easy trimerization of those imidates which

(14) This result explains the earlier observation[13] that pyrolysis of a mixture of formamidine and propionamidine hydrochlorides produces a larger amount of by-product triethyl-*s*-triazine than can be obtained from propionamidine hydrochloride alone.

(15) Alternatively, a concerted process involving a six-centered cyclic transition state can be visualized:



(16) Illustrative pK_A values for several imidates are the following: $CH_3C(=NH)OEt$, 7.6; $C_6H_5C(=NH)OEt$, 6.2; $EtO_2C-CH_2C(=NH)OEt$, 5.2; $EtO_2C-C(=NH)OEt$, 3.0; $CCl_3C(=NH)OCH_3$, 0.1. These data are from the work of C. A. Streuli of these laboratories, published in part in *Anal. Chem.*, **31**, 1652 (1959). The pK_A values for several amidines are: $CH_3C(=NH)NH_2$, 12.5[17]; $C_6H_5C(=NH)NH_2$, 11.6[18]; $3\text{-}C_5H_4N-C(=NH)NH_2$, 9.65.[19]

(17) G. Schwartzenbach and K. Lutz, *Helv. Chim. Acta*, **23**, 1162 (1940).

(18) A. Albert, R. Goldacre, and J. Phillips, *J. Chem. Soc.*, 2240 (1948).

(19) J. N. Baxter and J. Cymerman-Craig, *ibid.*, 1490 (1953).

are sluggish in the reaction with amidines cannot be accounted for in this way.

Experimental[20]

General.—All of the products reported gave infrared spectra fully consistent with the assigned structures. In practically all cases, the products, III and IV, from any reactant pair could be easily distinguished from one another by characteristic infrared absorption bands in the 750–850-cm.$^{-1}$ region.

Illustrations of the preparative procedures are described in detail below.

2-Methoxy-4,6-dimethyl-s-triazine.—Addition of 94 g. (1.02 moles) of 95% ethyl acetimidate to 37.8 g. (0.341 mole) of 2-methylpseudourea hydrochloride caused a moderately exothermic reaction. The temperature rose spontaneously to the boiling point in 10 min. The mixture was held at gentle reflux by cooling and, after the reaction subsided, was allowed to cool naturally for 1.5 hr. The crystalline product, acetamidine hydrochloride (25 g., m.p. 165–170°) was separated by filtration and the filtrate was fractionally distilled. After a forerun of 2,4,6-trimethyl-s-triazine (10% yield), the methoxy compound was distilled at about 80° at 3 mm.; yield, 34.6 g. (73%); f.p. 43.5°. The distillation residue (8 g.) was nearly pure acetamidine hydrochloride.

Anal. Calcd. for $C_6H_9N_3O$: C, 51.78; H, 6.52; N, 30.20. Found: C, 51.51; H, 6.76; N, 30.12.

2-(1-Chloroethyl)-4,6-dimethyl- and 2,4-Bis(1-chloroethyl)-6-methyl-s-triazine.[1]—A mixture of 196 g. (1.25 moles) of 2-chloropropionamidine hydrochloride and 430 cc. of 93% ethyl acetimidate (3.76 moles) was held at about 15° for 4 hr. It was then allowed to stand at room temperature overnight. The somewhat impure acetamidine hydrochloride which crystallized during this time was filtered (120 g., nominally 1.25 moles), and the filtrate was stripped at atmospheric pressure to remove most of the low-boiling material present. The residue was distilled as completely as possible at low pressure to separate the products from some nonvolatile residue (probably amidine salts). The distillate was then fractionated carefully to get maximum separation of the by-products 2,4,6-trimethyl-s-triazine (b.p. 155–156°) and 2,4-bis(α-chloroethyl)-6-methyl-s-triazine (b.p. 130–135°/24 mm.). A small amount of ethyl α-chloropropionimidate[6] was also present, boiling at about the same temperature as trimethyl-s-triazine. The product, 2-(1-chloroethyl)-4,6-dimethyl-s-triazine, b.p. 99–102°/24 mm., was thus recovered in high purity, none of the bis(α-chloroethyl) compound being detectable by mass spectroscopy. This material weighed 106 g., 49.5% yield; $n^{28.5}$D 1.4901, f.p. 23°. From the same distillation 2,4-bis(α-chloroethyl)-6-methyl-s-triazine was obtained in 26.5% yield.

2-Methyl- and 2,4-Dimethyl-s-triazine.[21]—Formamidine hydrochloride (0.60 mole) was stirred with 20 cc. of ethanol and held at 35–40° (slightly exothermic) while 0.90 mole of ethyl acetimidate was added over a period of 2 hr. The reactants were then allowed to stand overnight at room temperature. The partly crystallized mixture was diluted with ether and after brief standing was filtered. The recovered acetamidine hydrochloride, m.p. 165–170°, weighed 51 g. (90%). The ether solution was concentrated and the residue distilled. Material boiling at 115–155° was collected (24.2 g.) and analyzed by mass spectrometry. It was found that the product mixture consisted of: s-triazine, 0.0075 mole; methyl-s-triazine, 0.156 mole; dimethyl-s-triazine, 0.076 mole; trimethyl-s-triazine, 0.0024 mole. This corresponds to a yield of 65% of methyl- plus dimethyl-s-triazine based on the formamidine hydrochloride used.

The combined products from several similar experiments were fractionally distilled through a 2-ft. column packed with glass helices to obtain the mono- and dimethyl-s-triazine[18] in pure form. A center fraction of 2-methyl-s-triazine (b.p. 124.0–124.3°, n^{25}D 1.4767, f.p. 4°)[22] was analyzed by mass spectrometry and found to be 98.7% pure and to contain 1.0% 2,4-dimethyl-s-triazine and 0.2% s-triazine.

1-Carbethoxyformamidine Hydrobromide.—Ethyl cyanoformate was prepared by dehydration of ethyl oxamate with phosphorus pentoxide. Ethyl 1-carbethoxyformimidate hydrochloride was prepared from the nitrile by the Pinner method[7] and was converted to the free base with aqueous carbonate. 1-Carbethoxyformamidine hydrobromide was obtained in 88% yield by reaction of the imidate with ammonium bromide in ethanol[6]; m.p. 107–109°.

Anal. Calcd. for $C_4H_9BrN_2O_2$: Br, 40.6. Found: Br, 40.3.

(20) Melting points were determined by the capillary method and are uncorrected. Microanalyses were carried out in these laboratories under the direction of Dr. J. A. Kuck. Infrared spectra were interpreted by Mr. N. B. Colthup. Mass spectrometric analyses were obtained out by Mr. A. H. Struck and Miss R. Herberich. Nuclear magnetic resonance spectra were interpreted by Dr. J. E. Lancaster.

(21) This experiment was carried out by J. H. Ross.

(22) Ch. Grundmann and E. Kober, *J. Org. Chem.*, **21**, 641 (1956), reported m.p. 50.0–50.5° for a recrystallized and sublimed sample.