25–50 mm. pressure as the residue temperature was slowly raised to 110°. The distillate was collected in a receiver cooled with solid carbon dioxide. A total of 7.8 g. of s-triazine was crystallized from the distillate by chilling after dilution with petroleum ether; yield 79%. The presence of an additional 7% yield was demonstrated by recovery of an equivalent amount of 2-phenyl-s-triazine after addition of benzamidine hydrochloride to the mother liquor.[27]

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(27) F. C. Schaefer and G. A. Peters, *J. Am. Chem. Soc.*, **81**, 1470 (1959).

[CONTRIBUTION FROM THE STAMFORD LABORATORIES, CHEMICAL RESEARCH DEPARTMENT, AMERICAN CYANAMID CO.]

Synthesis of the *s*-Triazine System. IV.[1] Preparation of Monosubstituted *s*-Triazines by Reaction of *s*-Triazine with Imidates

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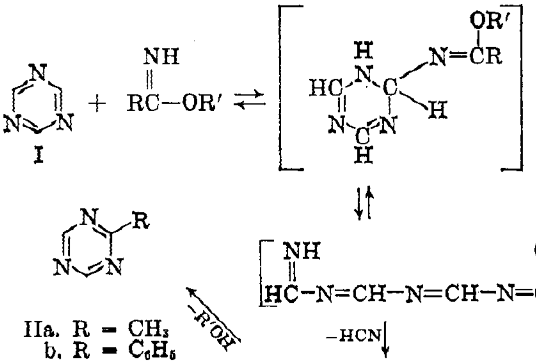
The reaction of imidates with s-triazine is shown to be a useful method for the preparation of monosubstituted s-triazines.

In an earlier paper[2] the preparation of monosubstituted s-triazines by the reaction of s-triazine (I) with amidines was reported. A reaction path closely related to that proposed for this process could also be envisioned for the reaction of I with imidates. It would similarly involve opening of the triazine ring and recyclization with inclusion of the reagent residue as outlined below. The cyclization step for the present case corresponds with that postulated for the trimerization of imidates to s-triazines.[1]



Our present results show that reaction of I with imidates can indeed give useful yields of monosubstituted s-triazines (II) despite several well known competing side reactions.[3] However, the relative ease of these side reactions is markedly dependent on the nature of the nitrile residue in the imidate. We therefore feel that to a considerable degree each imidate presents a separate problem and in this work have not gone beyond successful demonstration of a few examples of the reaction. The present work should encourage evaluation of this method for the preparation of specific monosubstituted s-triazines as interest may arise.

Reaction of s-triazine with ethyl acetimidate to form 2-methyl-s-triazine (IIa) has been studied in greatest detail. It was readily demonstrated that IIa is obtained under a variety of conditions. Process variables were evaluated roughly by semiquantitative analysis of the reaction mixtures by infrared spectroscopy. A limited number of the reaction mixtures which appeared to have been prepared under efficient conditions were worked up by distillation. The mixture of triazines recovered was finally analyzed by mass spectroscopy to obtain yield data. Instructive experiments from this work are summarized in Table I.

At 80° I and ethyl acetimidate reacted slowly in the absence of catalysts, but although all imidate was destroyed in twenty-two hours only a 20% yield of IIa was obtained. Both acetonitrile and 2,4,6-trimethyl-s-triazine were by-products. Although reaction at 25° was much slower, the yield of IIa was about 75%. Ethanol which is produced in the reaction must act as a catalyst for the formation of IIa. When a small amount was present at the start an induction period was avoided. A further benefit obtains in such case because the diluent alcohol inhibits trimerization of the imidate to 2,4,6-trimethyl-s-triazine.[1] Water also showed a slight catalytic influence and substantially aided reaction in added ethanol at 25°.

Water and alcohol may act as acids in catalyzing the desired reaction, probably participating in the ring-opening step. Therefore, the use of stronger acids was considered. Used alone, acetic acid accelerated the trimerization of ethyl acetimidate at the expense of the desired reaction, but in the presence of diluent ethanol use of acetic acid led to a

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(1) Paper III, F. C. Schaefer and G. A. Peters, *J. Org. Chem.*, **26**, 2778 (1961).

(2) F. C. Schaefer and G. A. Peters, *J. Am. Chem. Soc.*, **81**, 1470 (1959).

(3) We have discussed in reference 1 the conditions favoring the principal side reactions: (a) trimerization of the imidate, (b) dissociation of the imidate to nitrile and alcohol, (c) acid-catalyzed alcoholysis of the imidate to orthoester and concurrent formation of amidine salt, and (d) decomposition of the imidate salt to amide.

TABLE I

REACTION OF ETHYL ACETIMIDATE WITH s-TRIAZINE

Molar Ratio, Imidate/s-Triazine	Solvent and/or Catalyst per Mole s-Triazine	Reaction Conditions		Yield of Products, %[a]	
		Time, hr.	Temp.	*MT*[b]	*DMT*[c]
1.5	None	172	45	75[d]	
1.6	40 cc. ethanol	8	80	66[e,f]	18[e]
2.0	50 cc. ethanol	168	25	[g]	
3.0	1.0 cc. water + 60 cc. ethanol	260	25	90[d]	
2.0	0.25 mole acetic acid + 40 cc. ethanol	[h]		50[e,i]	16[e,i]
3.0	3.0 moles HCl[j]	4	45–75[k]	50[e]	8[e]

[a] Yields are based on formation of one mole of substituted s-triazine per mole of s-triazine used. [b] 2-Methyl-s-triazine (IIa). [c] 2,4-Dimethyl-s-triazine. [d] MT yield is estimated from infrared data. [e] Yields are based on mass spectroscopic analysis of the distilled triazine fraction. [f] Recovery of starting s-triazine was 26%. [g] MT was just detectable by infrared. [h] The imidate was added in 90 min. at 50°. The mixture was held at 50° for 1 hour longer and overnight at 25°. [i] Yields are corrected for 35% recovery of s-triazine. 2,4,6-Trimethyl-s-triazine was obtained in 48% yield based on the imidate used. [j] The imidate hydrochloride was used. [k] The temperature was raised slowly.

50% yield of IIa. Ethyl acetimidate hydrochloride reacted fairly satisfactorily with I on warming, but a large excess of the salt had to be used since much was lost by decomposition to acetamide and by alcoholysis.

The formation of 2,4-dimethyl-s-triazine in these reactions in a ratio of about 1 mole to 3–4 moles of IIa is reminiscent of the results in reaction of I with acetamidine.[2] Formation of the disubstituted triazine may be due to attack of the imidate on one of the transient intermediates in the desired reaction before recyclization to IIa has occurred, or I may react with the linear dimeric or trimeric intermediate in the trimerization of ethyl acetimidate.[1]

Results obtained with ethyl propionimidate and ethyl 2-phenylacetimidate were similar to those with ethyl acetimidate. In both cases appreciable amounts of disubstituted triazines were recovered with the desired products. The yields were encouraging for single experiments.

Aromatic imidates also may be employed satisfactorily. Methyl benzimidate gave very little reaction with I at 100°, but when ethanol was added slow reaction occurred. Acetic acid catalyst increased the rate of reaction appreciably and led to a 94% yield of 2-phenyl-s-triazine (IIb). On the other hand, only benzamide was obtained when reaction of I with ethyl benzimidate hydrochloride was attempted. Reaction of I with methyl *m*-nitrobenzimidate in boiling ethanol in the presence of acetic acid gave 2-*m*-nitrophenyl-s-triazine (IIc) in good yield. 2-*p*-Nitrophenyl-s-triazine (IId) was prepared similarly from ethyl *p*-nitrobenzimidate, but this reaction was relatively sluggish suggesting that methyl imidates may generally be more useful than the ethyl homologs.

The yields mentioned in this paper are arbitrarily based on formation of one mole of product per mole of I used. In at least one case the yields of IIa and 2,4-dimethyl-s-triazine totalled over 100% on this basis. We are, therefore, uncertain of the stoichiometry of the reaction. However, yield data reported in this way may be easily compared with similar data for the s-triazine-amidine reaction. Such a comparison indicates little choice between the two processes on the basis of yield.

EXPERIMENTAL[4]

Reaction of ethyl acetimidate with s-triazine (I). Reaction mixtures consisting of I, ethyl acetimidate, or ethyl acetimidate hydrochloride, and such additives as ethanol, water, or acetic acid when they were used were held at selected temperatures and aliquots were periodically examined by infrared spectroscopy. The usual scale of operation was 0.10 mole of I. The reactions were continued until either the imidate content was negligibly low, as judged by the absorption band at 1640 cm.$^{-1}$, or I was essentially gone as judged by the characteristic bands at 675 and 710 cm.$^{-1}$ The molar ratio of IIa to I present at each observation was determined semiquantitatively from the optical density at the characteristic 2-methyl-s-triazine frequencies (695 and 835 cm.$^{-1}$) compared to the s-triazine absorption bands. This method was standardized with mixtures of the pure compounds. From these data the yield of IIa was estimated on the assumption that I was consumed only in the desired reaction.

The calculated values reliably showed the variation with reaction time and the final values were probably accurate within ±10%. 2,4-Dimethyl-s-triazine could be detected by its characteristic band at 780 cm.$^{-1}$ if present to the extent of about 3 mole per cent of the total triazine content, but estimation of the amount present was unsatisfactory. It was still less easy to estimate the amount of 2,4,6-trimethyl-s-triazine present because of the relatively weak absorption of this compound (characteristic bands at 755, 930, 1040 cm.$^{-1}$).

When the yield appeared to be substantial, the solutions were distilled and the triazine fraction boiling at 105–150° was analyzed by mass spectroscopy. In this way the difficulty of quantitative separation of the four possible triazines on the small experimental scale was avoided. Yields derived from the analytical data agreed well with the estimates based on infrared data and substantiated the validity of this approximate method for our purposes. The results of the most instructive experiments are summarized in Table I.

2-Ethyl-s-triazine (IIe). A mixture of 16.5 g. (0.12 mole) of 72% ethyl propionimidate,[1] 6.5 g. (0.080 mole) of I, and 10 cc. of ethanol was heated at 80° for 4.5 hr. Distillation

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(4) Melting points are uncorrected. Microanalyses were carried out under the direction of Dr. J. A. Kuck. Infrared spectra were obtained and interpreted by Dr. J. E. Lancaster. Mass spectroscopic analysis were carried out under the supervision of Mr. A. H. Struck.

then yielded 4.3 g. (50%) of slightly impure IIe, b.p. 50–65° at 35 mm. and 0.8 g. (7%) of 2,4-diethyl-*s*-triazine, b.p. 65–80° at 35 mm. Identification of these products was confirmed by comparison with infrared spectra of the authentic materials prepared by the reaction of formamidine hydrochloride with propionamidine hydrochloride.[5]

2-Benzyl-s-triazine (IIf). Ethyl 2-phenylacetimidate[6] (9.8 g., 0.060 mole) was added during 30 min. to a mixture of 3.2 g. (0.040 mole) of I, 0.30 g. of acetic acid, and 2.0 cc. of ethanol which was held at 50°. The reagents were then heated for 45 min. at 80°. Crystallization on cooling gave 0.30 g. of formamidine acetate, m.p. 157–158° (lit.[7] m.p. 162–164°). Distillation of the mother liquor yielded 2.4 g. (38%) of IIf, b.p. 135–145° at 25 mm. (lit.[2] b.p. 100–105° at 2 mm.), and recrystallization of the residue from methanol gave 0.65 g. (7%) of 2,4-dibenzyl-*s*-triazine, m.p. 71–73° (lit.[2] m.p. 80–82°). Infrared comparison showed that these products were essentially identical with authentic samples prepared by the reaction of 2-phenylacetamidine hydrochloride with I[2].

2-Phenyl-s-triazine (IIb). *s*-Triazine (4.05 g., 0.050 mole) was heated with 14 g. (0.10 mole) of 97% methyl benzimidate at 100–110° for 20 hr. Following this no IIb was detectable by infrared. Ethanol (2.5 cc.) was then added and the mixture was heated at reflux for 4 hr. A small amount of IIb was then evident. Addition of 0.10 cc. of acetic acid and 8 hr. longer at 80° caused marked reduction in the imidate content of the solution, which was then diluted with water and extracted with ether. Evaporation of the ether and distillation of the residue gave 5.6 g. of IIb, b.p. *ca.* 105° at 2 mm., m.p. 62–64° (lit.[2,8] m.p. 63–65°), and 1.5 g. of less pure material as still holdup. The crude yield was thus 0.047 mole or 94%. The product was identical with authentic material by infrared comparison.

2-m-Nitrophenyl-s-triazine (IIc). A reaction mixture consisting of 8.9 g. of 93% methyl *m*-nitrobenzimidate[9] (0.046 mole), 3.80 g. (0.047 mole) of I, 0.60 g. (0.010 mole) of acetic acid, and 10 cc. of ethanol was heated at reflux for 3 hr. Essentially pure IIc crystallized as the reaction mixture cooled; yield, 7.6 g. (82%), m.p. 122–128°. Recrystallization from toluene gave material melting at 127–129° which was identical with IIc prepared by reaction of I with *m*-nitrobenzamidine hydrochloride.[2,11]

2-p-Nitrophenyl-s-triazine (IId). A mixture of 8.2 g. of 79% ethyl *p*-nitrobenzimidate[12] (0.033 mole), 3.0 g. (0.037 mole) of I, 0.45 cc. (0.0075 mole) of acetic acid, and 7 cc. of ethanol was heated at reflux for 3 hr. Crystals formed as the reaction proceeded. Filtration of the crude product and washing with ethanol gave 4.5 g., m.p. approx. 160°. Extraction of the solid with toluene left a slight amount of insoluble by-product. Fractional crystallization of the extract yielded 2.8 g., m.p. 166–168° (42%). Recrystallization from cyclohexane or toluene raised the melting point to 167–169°.

Anal. Calcd. for $C_9H_6N_4O_2$: C, 53.46; H, 2.99; N, 27.72. Found: C, 53.70; H, 2.95; N, 27.43.

Dilution of the ethanolic mother liquor from the reaction mixture with water caused crystallization of 3.4 g., m.p. 50–60°. Titration of this material showed it to be 71% ethyl *p*-nitrobenzimidate (40% recovery).

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(5) F. C. Schaefer, I. Hechenbleikner, G. A. Peters, and V. P. Wystrach, *J. Am. Chem. Soc.*, **81**, 1466 (1959).

(6) A. Pinner, *Die Imidoäther und ihre Derivate*, Robert Oppenheim (Gustav Schmidt), Berlin, Germany, 1892, p. 155. The imidate distilled at 110–112° at 22 mm. without apparent decomposition.

(7) E. C. Taylor and W. A. Ehrhart, *J. Am. Chem. Soc.*, **82**, 3138 (1960).

(8) Ch. Grundmann, H. Ulrich, and A. Kreutzberger, *Ber.*, **86**, 181 (1953).

(9) Methyl *m*-nitrobenzimidate was prepared by the general procedure of ref. 10. Recrystallization of the crude product from ether gave material which was 93% pure by titration, m.p. 50–51°.

(10) F. C. Schaefer and G. A. Peters, *J. Org. Chem.*, **26**, 412 (1961).

(11) The melting point of pure IIc was omitted from reference 2. The analytical sample was recrystallized from aqueous acetonitrile and had m.p. 129–130°.

(12) A. Pinner and F. Gradenwitz, *Ann.*, **298**, 47 (1897).

[CONTRIBUTION FROM THE ORGANIC CHEMICALS DIVISION, RESEARCH DEPARTMENT, MONSANTO CHEMICAL CO.]

Unsymmetrically Substituted Melamines

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Unsymmetrically substituted melamines have been prepared from cyanuric chloride by successive reaction with three different amines. The procedure is quite general. Most of these new compounds are liquids and were found to possess a rather high degree of thermal stability.

In the course of a search for thermally stable compounds, particularly those with wide liquid ranges, our attention was turned to melamine and its derivatives. These substances should be inherently stable as many of them possess very high melting points and melt without decomposition.[1–3] Furthermore, the *s*-triazine nucleus is similar to the very stable benzene ring.

Increasing substitution on the three exocyclic nitrogen atoms of melamine results in a corresponding lowering of melting points.[4] We proposed that the completely unsymmetrical melamines in which the three substituted amino groups are all different should have relatively low melting points and might even be liquids at room temperature. Nineteen of these compounds have been synthesized and the majority are liquids (*cf.* Table I).

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(3) E. M. Smolin and L. Rapaport, *s-Triazines and Derivatives*, Interscience, New York, 1959.

(4) Ref. 3, p. 371.