homolysis of the O–O bond in *t*-butyl perbenzoates and benzoyl peroxides in a manner formally identical with that already postulated for neighboring sulfur and iodine. The 2,2-diphenylvinyl group is a better neighboring group than iodide (see Table III) but not so effective as the phenylthio group in anchimeric acceleration of perester O–O bond homolysis. Substituent effects are compatible with the postulated dipolar transition state involving a five-membered ring with a concentration of positive charge on the neighboring group involved in the displacement on oxygen and a negative charge on the oxygen leaving group (see structures XIV or XIX).

Acknowledgment.—We are indebted to the Rohm and Haas Company for a fellowship to T. W. K., 1960–1961. We thank the Alfred E. Sloan Foundation for a fellowship for J. C. M., 1962–1964. This research was supported in part by a grant from the U. S. Army Research Office, Durham, North Carolina.

Chlorination and Bromination of Alkyl *s*-Triazines

FRED C. SCHAEFER AND JOSEPH H. ROSS

Exploratory Research Department, Central Research Division, American Cyanamid Company, Stamford, Connecticut

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Liquid-phase chlorination or bromination of alkyl *s*-triazines produced exclusively α-substitution by an acid-catalyzed process regardless of the halogenation reagent used. Nuclear halogenation of mono- and dialkyl *s*-triazines does not compete. Special emphasis has been given to the development of synthetic procedures using elementary chlorine and bromine for the preparation of mono- and polyhalogenation products from trimethyl- and triethyl-*s*-triazine. The chemistry of the wide variety of products has been explored to provide an insight into their potentialities as reactive intermediates.

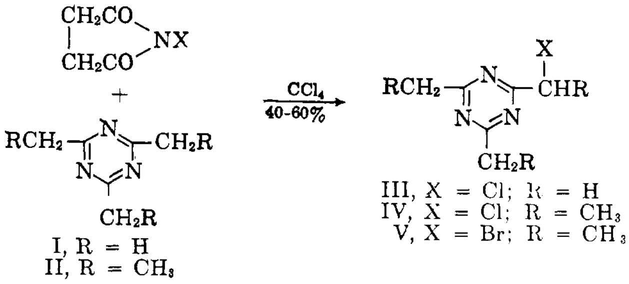
Perhaps the most promising opportunities for exploitation of the newly available alkyl *s*-triazines[1-3] lie in the study of their halogenation products. The work reported here was undertaken to explore the range of compounds which could be obtained in preparatively useful processes. Principal attention has been given to the particularly practical use of 2,4,6-trimethyl-*s*-triazine (I) and 2,4,6-triethyl-*s*-triazine (II) as substrates for chlorination or bromination, and a surprising number of different types of products has been obtained in good yield. Somewhat less work has been done with 2-alkyl *s*-triazines where unsubstituted nuclear positions are available and might have been competitive sites for halogenation. An exploratory study of the chemistry of the halogenation products was also carried out.

A substantial amount of work on the synthesis of chloro- and bromoalkyl *s*-triazines has been reported, but the bulk of this deals with compounds prepared by synthesis of the *s*-triazine system from reagents containing the halogenated alkyl group.

Only a very small number of references report the direct halogenation of an alkyl *s*-triazine group.[4] The work of Reinhardt and Schiefer, who prepared mono- and dibrominated and -chlorinated derivatives from 2-ethyl-4,6-diphenyl-*s*-triazine by direct halogenation is particularly pertinent to the present study.[5] Also significant is the reaction of 2,4-dichloro-6-methyl-*s*-triazine with elemental chlorine under rather strenuous conditions to give 2-trichloromethyl-4,6-dichloro-*s*-triazine.[6]

The halogenation of alkyl groups attached to electron-withdrawing substituents has received a great deal of attention in recent years.[7,8] The experimental work in this field provides an excellent basis for the selection of reaction procedures. The literature did not permit prediction of the reactivity of alkyl *s*-triazines, but combined with the present findings gives a satisfactory basis for interpretation of the results.

Monochlorination and Bromination.—N-Chloro- and N-bromosuccinimide (NBS) were used as halogenating agents in the initial experiments because of their wide applicability for the monosubstitution of methyl aromatics.[7,9,10] Reactions under conventional conditions were sluggish, but 2-chloromethyl-4,6-dimethyl-*s*-triazine (III), 2-(1-chloroethyl)-4,6-diethyl-*s*-triazine (IV), and 2-(1-bromoethyl)-4,6-diethyl-*s*-triazine (V) were obtained in moderate yield. Bromination of I with NBS was impractically slow. Small amounts of dihalogenation products were also obtained in these reactions, but it is clear that loss of the desired compounds through side reactions was the major obstacle to higher yields. It was found that III itself is surprisingly stable to N-chlorosuccinimide (NCS).



I, R = H
II, R = CH_3

III, X = Cl; R = H
IV, X = Cl; R = CH_3
V, X = Br; R = CH_3

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

(2) F. C. Schaefer, *ibid.*, **27**, 3362 (1962).

(3) F. C. Schaefer, *ibid.*, **27**, 3608 (1962).

(4) Reaction of N-bromosuccinimide with 2-methyl-4,6-bisphenylamino-*s*-triazine is reported to give the bromomethyl derivative [H. K. Reimschuessel and N. T. McDevitt, *J. Am. Chem. Soc.*, **82**, 3756 (1960)]. However, it is clear from the published infrared spectrum that the product is in fact 2-(*p*-bromophenylamino)-4-methyl-6-phenylamino-*s*-triazine. See related work by C. G. Overberger and S. L. Shapiro, *ibid.*, **76**, 93, 1061 (1954).

(5) H. Reinhardt and E. Schiefer, *Chem. Ber.*, **90**, 2643 (1957).

(6) E. Kober and C. Grundmann, *J. Am. Chem. Soc.*, **81**, 3769 (1959).

(7) See C. Walling, "Free Radicals in Solution," John Wiley and Sons, Inc., New York, N. Y., 1957, Chapter 8.

(8) (a) B. R. Brown, D. L. Hammick, and B. H. Thewlis, *J. Chem. Soc.*, 1145 (1951); (b) B. R. Brown, D. L. Hammick, B. H. Thewlis, and D. J. Walbridge, *ibid.*, 1369 (1953); (c) G. M. Bennett and G. H. Willis, *ibid.*, 1960 (1928).

(9) (a) C. Djerassi, *Chem. Rev.*, **43**, 271 (1948); (b) B. H. Walker, *J. Org. Chem.*, **25**, 1047 (1960); (c) H. Gershon, K. Dittmer, and R. Braun, *ibid.*, **26**, 1874 (1961).

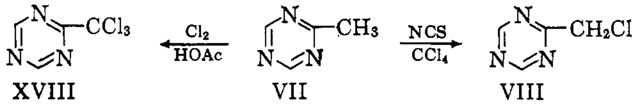
(10) (a) N. P. Buu-Hoi, *Ann.*, **556**, 1 (1944); (b) A. Hirschberg and P. E. Spoerri, *J. Org. Chem.*, **26**, 2356 (1961).

Although these experiments were moderately successful, various considerations suggested that the reactions might be following predominantly an acid-catalyzed path. If such were the case, no apparent advantage could be gained with the elegant selective halogenating reagents. We therefore concentrated on the use of elemental chlorine and bromine.[11]

Direct chlorination and bromination of several alkyl *s*-triazines has proven to be an easy process. Reactions are rapid at moderate temperatures and yields of monohalogenated products have been at least equal to those obtained with N-halosuccinimides. A particular improvement was the synthesis of 2-bromomethyl-4,6-dimethyl-*s*-triazine (VI) in 50% yield. Acetic acid is an excellent medium, but successful reactions have also been carried out in chloroform or carbon tetrachloride.

Chlorination of I with an equimolar amount of chlorine in acetic acid at 55° gave mono- and dichlorinated products in approximately a 1:1 ratio. It was both interesting and useful to find that the presence of an equimolar amount of sodium acetate in the reaction mixture shifted this product ratio to 1.7:1.0 with consequent greater conversion of I. In this case the yield of III was 54% based on unrecovered I.[12] Monobromination, however, was not appreciably influenced by the presence of sodium acetate.

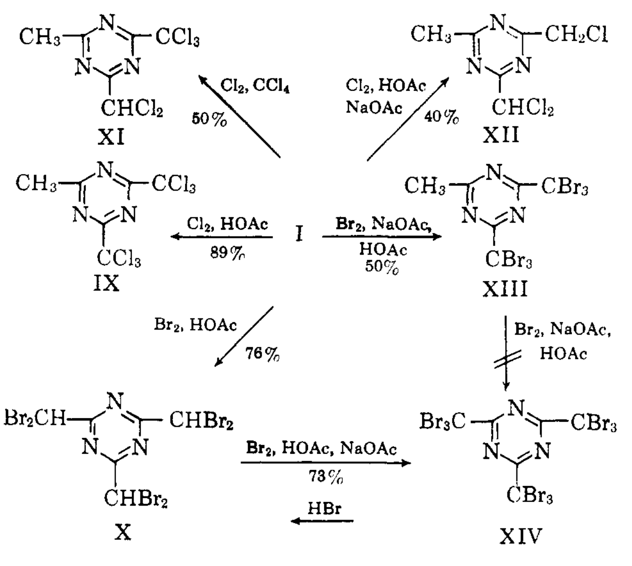
Chlorination of 2-methyl-*s*-triazine (VII) with NCS was sluggish but gave 2-chloromethyl-*s*-triazine (VIII) in low yield. 2-Ethyl-*s*-triazine and 2-isopropyl-*s*-triazine reacted with chlorine in hot carbon tetrachloride to give the α-chloroalkyl derivatives. In none of these cases was nuclear chlorination detectable.[13]



The halogenation of an ethyl substituent could not safely be assumed to occur exclusively at the α-carbon although this has been found to be the case. Successful reactions with I demonstrated that α-substitution was possible, but the published work on alkane nitriles and similar compounds suggested that β-attack would be probable if a free-radical mechanism were involved.[7] Reinhardt and Schiefer had reported the preparation of 2-(1-haloethyl)-4,6-diphenyl-*s*-triazines,[5] but these authors believed that dihalogenation gave the 1,2-dihaloethyl compounds. In the present work we have used n.m.r. spectroscopy and independent syntheses to obtain unequivocal proof of exclusive α-substitution in all cases, regardless of the degree of halogenation, and incidentally have found Reinhardt and Schiefer's products to be the 2-(1,1-dihaloethyl)-4,6-diphenyl-*s*-triazines.

CHART I

POLYHALOGENATION PRODUCTS FROM 2,4,6-TRIMETHYL-*s*-TRIAZINE



Polychlorination and Bromination.—The end products of the reactions of alkyl *s*-triazines with excess chlorine or bromine are strongly dependent on the reaction system used. A wide variety of products may be obtained in excellent yield. It appears that glacial acetic acid is a particularly useful reaction medium, probably acting as an acid catalyst, and substantially different results can be obtained in many cases through the inclusion of sodium acetate in the reaction mixture. Reactions are much the same in chloroform or carbon tetrachloride but are much slower.

The principal products derivable by polyhalogenation of I are indicated in Chart I.

Also useful was the formation of 2-dichloromethyl-4,6-dimethyl-*s*-triazine (XIX) and 2,4-dimethyl-6-trichloromethyl-*s*-triazine (XXII) as the major products when I reacted with about 1.7 moles of chlorine in acetic acid. By recycling by-product III and unchanged I, compounds XIX and XXII could be prepared as a mixture in high yield. By recycling XIX also, compound XXII could be obtained quite practically.

It is striking that 2-methyl-4,6-bis(tribromomethyl)-*s*-triazine (XIII) is the major product of bromination in the presence of sodium acetate, although a small amount of 2,4,6-tris(tribromomethyl)-*s*-triazine (XIV) was also isolated. It was not possible to brominate XIII further under these conditions. On the other hand, X was easily further brominated to XIV in the presence of sodium acetate.

Several additional halogenation products of I were isolated in the course of the work and are described in the Experimental section.

Bromination of II in hot acetic acid gave a nearly quantitative yield of 2,4,6-tris(1,1-dibromoethyl)-*s*-

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[11] NCS probably is equivalent to free chlorine in any case [P. S. Goldfinger, P. A. Gosselain, and R. H. Martin, *Nature*, **168**, 30 (1951); K. B. Wiberg and L. H. Slaugh, *J. Am. Chem. Soc.*, **80**, 3033 (1958)].

[12] Such experiments which make evident the effects of variables on the relative rates of the successive reactions, should not be taken as optimized synthetic procedures. The relative and absolute yields of these products depend upon the extent to which conversion of I is carried. For the preparation of III, most practical results might be obtained by running the reaction at the most selective conditions to relatively low conversion and recycling unconverted I.

[13] Nuclear halogenation of the *s*-triazine ring, a highly "deactivated" system toward electrophilic reagents,[14] would be expected to be difficult if observable at all. Nevertheless, Grundmann and Kreutzberger[15] have demonstrated the formation of polyhalogenation products from *s*-triazine itself. The remarkably easy nuclear chlorination of 2-methyl- and 2,5-dimethylpyrazine reported recently[10, 16] further illustrates our inability to predict with confidence the course of such reactions. Perhalides may well occur as intermediates with unforeseeable consequences.[15,17]

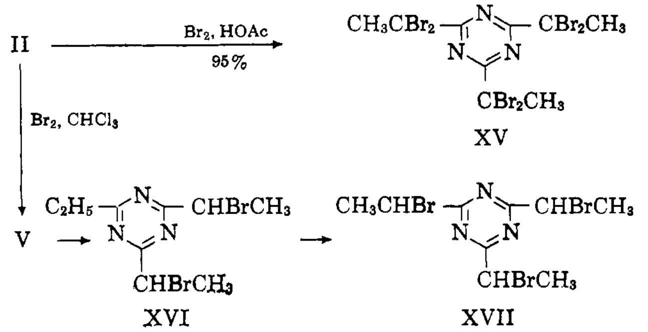
[14] L. Paoloni, *Gazz. chim. ital.*, **84**, 729 (1954).

[15] C. J. Grundmann and A. Kreutzberger, *J. Am. Chem. Soc.*, **77**, 44 (1955); U. S. Patent 2,777,847 (1957).

[16] H. Gainer, M. Kokorudz, and W. K. Langdon, *J. Org. Chem.*, **26**, 2360 (1961).

[17] (a) R. D. Brown and R. D. Harcourt, *J. Chem. Soc.*, 3451 (1959); (b) J. Eisch, *Chem. Ind.* (London), 1449 (1959).

triazine (XV). The course of this reaction is indicated by the fact that reaction of II with an equimolar amount of bromine in chloroform gave in addition to V isolable amounts of 2,4-bis(1-bromoethyl)ethyl-*s*-triazine (XVI) and 2,4,6-tris(1-bromoethyl)-*s*-triazine (XVII), but that no 1,1-dibromoethyl derivative was detectable.

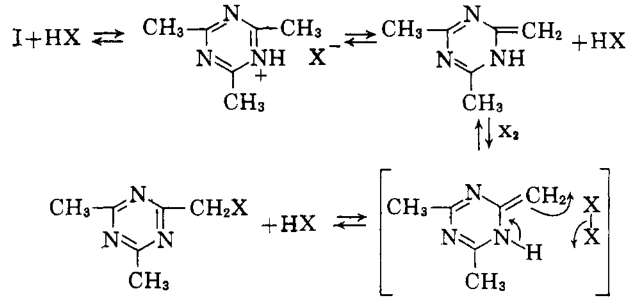


The expected product, 2-trichloromethyl-*s*-triazine (XVIII), was obtained from VII under conditions for exhaustive chlorination. Similarly the 2-(1,1-dihaloethyl)-*s*-triazines were obtained in our early work by bromination or chlorination of 2-ethyl-*s*-triazine. The yields were low in these cases, but probably can be substantially improved.

The use of n.m.r. spectroscopy was of invaluable assistance in establishing the structures of several products. The most significant features of the spectra for this purpose were the chemical shifts established as characteristic of the protons of the CH_3-, CH_2X-, and CHX_2 groups which have τ-values in the ranges 7.02–7.52, 4.15–4.56, and 3.45–3.57, respectively, measured using 10% solutions of the compounds in carbon tetrachloride.

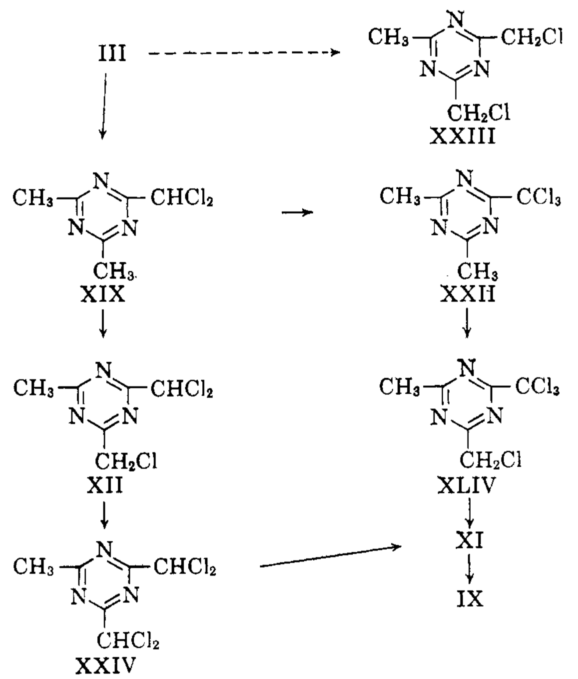
The Mechanism of the Halogenation Reactions.—Several observations support the conclusion that free-radical processes take little part in these halogenation reactions. The reactions are essentially unaffected by ultraviolet illumination or radical catalysis but are strongly responsive to hydrohalide concentration or the presence of a base. Moreover, easy substitution at the position α to the strongly electronegative *s*-triazine ring to the exclusion of β-substitution is contrary to the observed orientation in established free-radical halogenations of other polar molecules.[7] An ionic mechanism such as these observations seem to demand and which is consistent with numerous other aspects of the reactions can be formulated along lines closely related to ketone halogenation and to the work of Brown and Hammick on quinaldine and the picolines.[8]

Regardless of the reaction conditions, the predominant halogenation process is believed to proceed by acid catalysis, perhaps following an induction period in which a slow radical reaction generates the acid. The alkyl *s*-triazine, I for example, is presumably converted to an enol analog which reacts with a halogen molecule to give the halomethyl-*s*-triazine hydrohalide, a process conveniently represented as analogous with the model for acid-catalyzed ketone bromination proposed by Newman.[18]



As a consequence of the greater acidity of the chloromethyl group, the predominant dichlorination product is 2-dichloromethyl-4,6-dimethyl-*s*-triazine (XIX) under all conditions tried. However, bromination differs in that conditions of relatively high hydrogen bromide concentration tend to cause 2,4-bis(bromomethyl)-6-methyl-*s*-triazine (XX) to be the major, if not exclusive, product. This is the result of the reversibility of the dibromomethyl-*s*-triazine formation in the presence of hydrogen bromide which causes thermodynamic rather than kinetic control of the product distribution.[19] If sodium acetate is present during the reaction, the hydrogen bromide is removed and the isomeric dibromination products, XX and 2-dibromomethyl-4,6-dimethyl-*s*-triazine (XXVI), are produced in about equal amounts.

Examination of the product mixtures obtained in reactions of I with varying amounts of chlorine has made it possible to identify the predominant sequence of chlorination steps in the presence of hydrogen chloride.



It is very clear from several experiments that the dichloro isomer, XIX, is favored over 2,4-bis(chloromethyl-*s*-triazine (XXIII) by a factor of at least ten. Further chlorination gives principally XXII, but an appreciable amount of XII is also formed despite the much greater acidity of the dichloromethyl group compared with an unsubstituted methyl group. This may be taken as evidence of appreciable steric inhibition of the XIX → XXII step. Compound XXII

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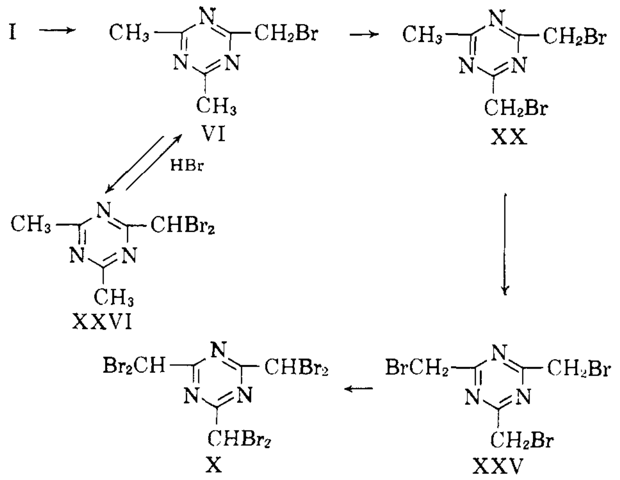
(18) M. S. Newman, *J. Am. Chem. Soc.*, **73**, 4993 (1951).

(19) The analogous situation in acid-catalyzed bromination of ketones has been studied by F. Kröhnke, *et al.*, [*Ber.*, **69**, 615,921 (1936); **86**, 1559 (1953)]. In contrast, chlorination is substantially irreversible (see ref. 26).

shows more resistance to higher chlorination than does XII and can be obtained in substantial amount. Further chlorination of IX at 60° in acetic acid saturated with hydrogen chloride proceeded at a barely perceptible rate.

Bromination of I has a much stronger tendency to give at each stage the product of least "positive halogen" character.



Reaction stops at X because tribromomethyl groups are unstable in the presence of hydrogen bromide. Reaction of XIV with hydrogen bromide does, in fact, cause reduction to X.[20] Bromination of II proceeds similarly.

When chlorination of I in acetic acid is carried out in the presence of sodium acetate, the hydrogen chloride is removed as formed. Continued reaction then depends on the relatively weak catalytic effect of acetic acid rather than responding autocatalytically to a developing hydrogen chloride concentration. The reduced reaction rate is not of importance, however, except at high chlorination stages. A more important and useful consequence is a greater selectivity in the reaction as the weaker acid has less tendency to protonate the weaker *s*-triazine bases.[21] This causes an increase in the rate of chlorination of I with respect to III and is responsible for the increase in the molar ratio of mono- to dichlorination products which obtains when reaction of I with an equimolar amount of chlorine is carried out in the presence of sodium acetate. The effect is slightly greater when a threefold excess of acetate is used. In those reactions where chloroform or carbon tetrachloride was used as the medium, the starting *s*-triazine itself probably played a role analogous to that of sodium acetate in the acetic acid system. Separation of insoluble hydrohalide salts usually occurred, the reactions were sluggish, and the products were those typical of weak acid catalysis.

An additional effect of the sodium acetate is found in the ratio of the isomeric dichlorination products, XIX–XXIII, obtained when it is used. Reaction of I with an equimolar amount of chlorine in acetic acid in the absence of sodium acetate gave these by-products in a ratio of greater than 10:1. When 1 equiv. of sodium acetate was present, this ratio was about 7:1, and with 3 equiv. it was strongly reduced to 2:1. These results suggest that the acetate ion plays a part in the reaction as a basic cocatalyst, possibly facilitating the enolization step.[22] The slightly greater crowding at the chloromethyl group in III compared to a methyl group could cause the observed reduction in selectivity. The same argument can be made in connection with the more dramatic effect on the XII–XXII ratio at the trichlorination stage.

When exhaustive bromination of I was carried out in acetic acid in the presence of sodium acetate, the reaction led nearly exclusively to XIII, which is quite analogous to the work of Hammick and others,[8] with methylpyridines, quinaldines, and 2-methylquinoxaline. This result, when the reducing activity of hydrogen bromide is eliminated, is evidently equivalent to that obtained in chlorination.

The very sluggish chlorination of I to give IX in an acetic acid–sodium acetate system and the complete failure of an attempt to brominate the residual methyl group in XIII under similar conditions are reflections of the low catalytic activity of acetic acid with the less basic, highly halogenated compounds. Ready bromination of X to XIV under the same conditions is easily seen to be consistent with the expected much higher proton lability in X.

The Reactivity of 1-Haloalkyl *s*-Triazines.—The strongly electronegative character of the *s*-triazine ring is responsible for striking differences between the chemistry of the 1-haloalkyl *s*-triazines and that of the superficially similar benzyl halides. The ability of the nucleus to stabilize an α-anion is apparent in the positive halogen character of the 1-monohaloalkyl compounds, which are readily reduced by an acidic acetone solution of sodium iodide.[23]

On the other hand, reactions of SN1 type which require stabilization of a positive charge at the α-position have not been observed.[24] Such reactivity would be expected to be inhibited by the highly electrophilic character of the carbon atoms of the *s*-triazine ring.[14] Perhaps this inhibition of ionization of an α-halogen atom is responsible for the complete absence of an elimination reaction when V reacted with ethanolic potassium hydroxide. The sole product was 2-(1-ethoxyethyl)-4,6-diethyl-*s*-triazine (XXVII). Nuclear magnetic resonance spectroscopy was used to show that the product was not the isomeric 2-(2-ethoxyethyl)-*s*-triazine which could arise by base-catalyzed addition of ethanol to the expected 2,4-diethyl-6-vinyl-*s*-triazine (XXVIII). It seems reasonable to interpret this reaction as the result

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[20] C. Broche [*J. prakt. Chem.*, [2]**50**, 97 (1894)] reported the preparation of XII by trimerization of tribromoacetonitrile with hydrogen chloride or hydrogen iodide. The melting point given was 129°. This compound was undoubtedly X, found in this work to melt at 129–131°; authentic XIV has m.p. 158–159°.

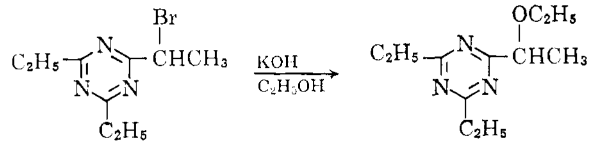
[21] This interpretation has no established precedent in ketone halogenation where the kinetics have been studied with strong acid catalysis and ketone–acid equilibration specifically discounted as a rate-determining factor [L. Zucker and L. P. Hammett, *J. Am. Chem. Soc.*, **61**, 2785, 2791 (1939)].

[22] This is probably particularly important in the absence of a stronger acid catalyst. In the bromination of ω,ω-dibromoquinaldine under similar conditions, sodium acetate has been shown not to be involved in a rate-determining step.[14b] This difference may be ascribed to the greater protonation in acetic acid of the quinaldine derivative compared to the *s*-triazines concerned.

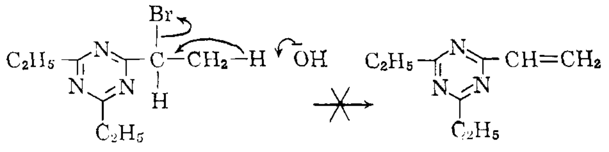
[23] S. L. Shapiro and C. G. Overberger, *J. Am. Chem. Soc.*, **76**, 97 (1954).

[24] Attempted silver ion-catalyzed hydrolysis of IX and other polyhalogenated compounds in aqueous acetic acid or ethanol were unsuccessful under conditions which are useful with α-halo derivatives of quinaldine,[8a] α-picoline,[8a] and 4-methylpyrimidine.[25] With silver nitrate incomplete halide elimination took place, but destruction of the product by the liberated nitric acid ensued. With silver acetate no reaction was obtained.

[25] H. Bredereck, W. Jentzsch, and G. Morlock, *Chem. Ber.*, **93**, 2405 (1960).



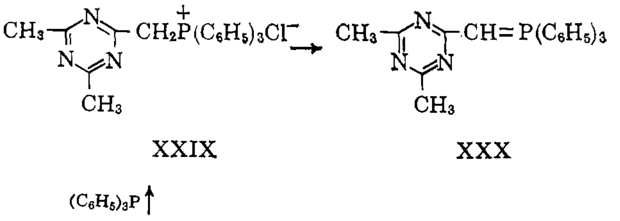
V XXVII



XXVIII

of inability of the *s*-triazine substituent to stabilize the transition state for bimolecular elimination.[26]

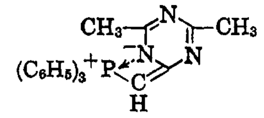
This reaction of V with ethanolic hydroxide takes place readily at room temperature and is an example of normal SN2 reactivity.[27] Other examples were demonstrated in the displacement of bromide ion from V by acetate ion to give 2-(1-acetoxyethyl)-4,6-diethyl-*s*-triazine, the easy reaction of 2-bromomethyl-4,6-dimethyl-*s*-triazine with pyridine to give the quaternary salt, and the reaction of 2-chloromethyl-4,6-dimethyl-*s*-triazine (III) with triphenylphosphine to give the salt XXIX.



XXIX XXX

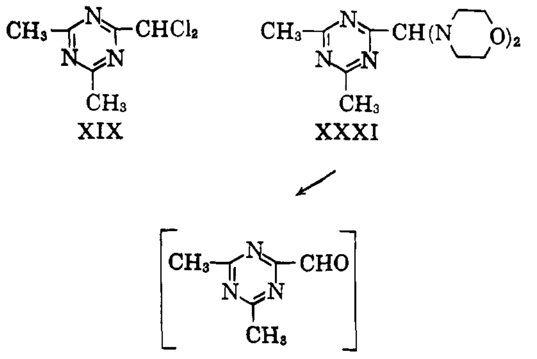
III

The quaternary phosphonium salt XXIX had somewhat exceptional properties. Its infrared spectrum exhibited a band at 2420 cm.$^{-1}$, believed to be the C–H stretching frequency of the acidic methylene group. This is the lowest frequency that was observed in a large group of triphenylphosphonium salts which included acylmethyl derivatives.[28] The position of this band can presumably be taken as a measure of the acidity of the methylene group. This indication is confirmed by the great ease of conversion of XXIX to the ylid XXX by aqueous sodium carbonate.[29] An unexpected result of n.m.r. study of XXX was evidence that the two methyl groups were not equivalent. Measurements at both 40 and 60 Mc. showed this was not a case of long range splitting due to the phosphorus atom. This result has led to the suggestion that the unsymmetrical structure XXXa may have considerable stability. Reaction of XXX with *p*-dimethylaminobenzaldehyde was extremely sluggish, although the formation of a small amount of 2,4-dimethyl-6-(*p*-dimethylaminostyryl)-*s*-triazine was demonstrated.



XXXa

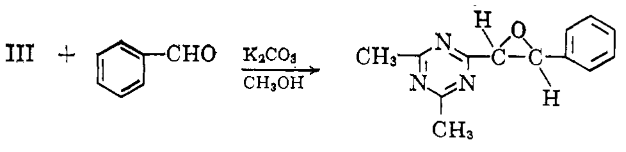
Reaction of XIX with morpholine took place readily under the conditions used by Kerfanto with a variety of dihalomethyl compounds[30] to give 2,4-dimethyl-6-dimorpholinomethyl-*s*-triazine (XXXI). Hydrolysis of this product apparently proceeded normally but 4,6-dimethyl-2-*s*-triazinecarboxaldehyde (XXXII) was not recovered, probably because of solvation and high solubility in water.[31] However, XXXI is a useful generator of the aldehyde and reacted readily with thiosemicarbazide and with 2,4-dinitrophenylhydrazine to give the expected aldehyde derivatives.



XIX XXXI

XXXII

2-Choromethyl-4,6-dimethyl-*s*-triazine (III) reacted normally with benzaldehyde under the conditions of the Darzens condensation[32] to give *trans*-2-(4,6-dimethyl-2-*s*-triazinyl)-3-phenyloxirane (XXXIII).[33]



XXXIII

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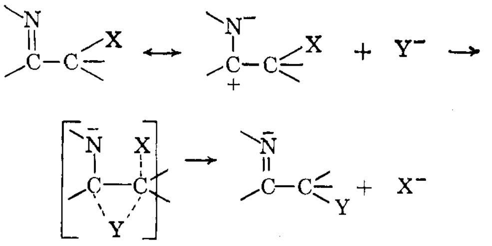
[26] C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 420.

[27] By analogy with α-halonitriles and carbonyl compounds, enhanced SN2 reactivity would be expected in these *s*-triazine derivatives over benzyl halides because of neighboring group participation in the transition state.



It seems unnecessary to invoke an α-elimination and carbene mechanism for any of these reactions, although the potentiality for such processes in the mono- and dihalomethyl-*s*-triazines appears to be substantial.

[28] Unpublished work of Mr. N. B. Colthup and Mrs. I. Chenzoff.

[29] This is comparable to the preparation of triphenylphosphinebenzoylmethylene by F. Ramirez and S. Dershowitz [*J. Org. Chem.*, **22**, 41 (1957)].

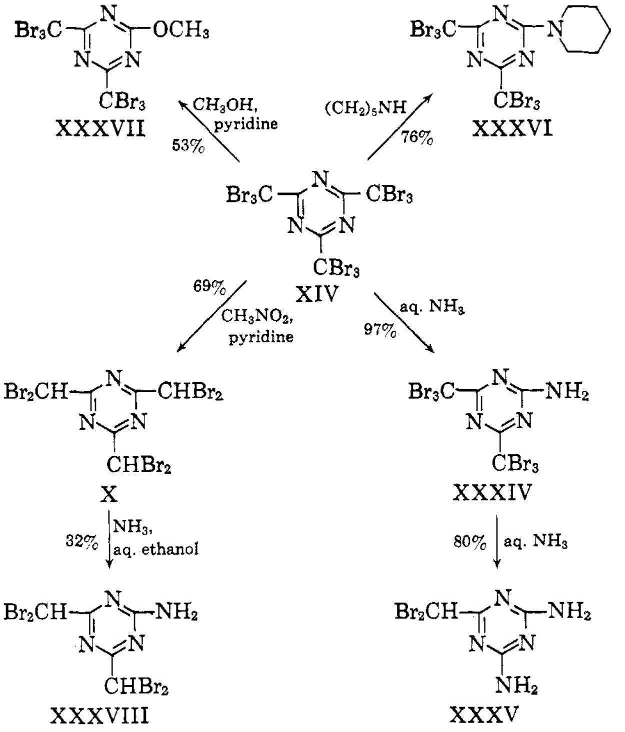
[30] M. Kerfanto, *Compt. rend.*, 493 (1962).

[31] E. Kober and C. Grundmann, *J. Am. Chem. Soc.*, **80**, 5547 (1958).

[32] (a) M. S. Newman and B. J. Magerlein, *Org. Reactions*, **5**, 413 (1949); (b) E. Kleucker, *Ber.*, **55**, 1634 (1922).

[33] The stereochemistry of such reactions has recently been discussed [see H. Kwart and L. G. Kirk, *J. Org. Chem.*, **22**, 116 (1957), and H. Dahn and L. Loewe, *Chimia* (Aarau), **11**, 98 (1957)].

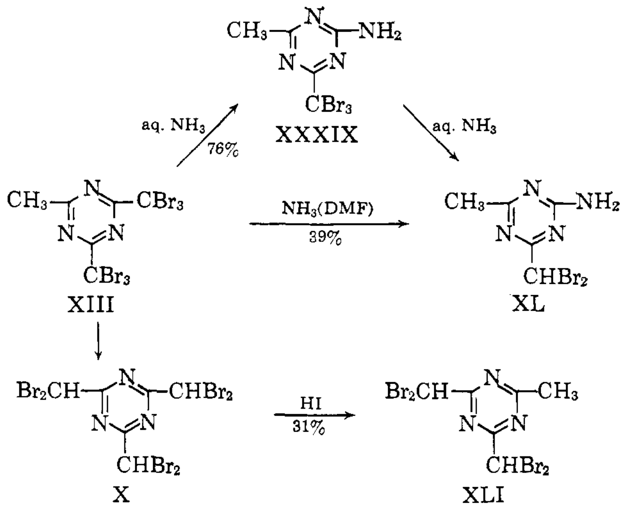
Several publications during recent years[34] have greatly enlarged much earlier reports of the reactivity of trichloromethyl-*s*-triazines. We have now found comparable reactivity in the tribromomethyl-*s*-triazines although a more complex situation arises because of easy reduction to the dibromomethyl compounds in some circumstances. Reaction of 2,4,6-tris(tribromomethyl)-*s*-triazine (XIV) with aqueous ammonia to displace one substituent is very fast at room temperature, producing the monoamine XXXIV. Further reaction was slower and accompanied by reduction, giving a high yield of 2,4-diamino-6-dibromomethyl-*s*-triazine (XXXV) as the final product. Reaction of XIV with 2 equiv. of piperidine in methoxyethanol gave only the monopiperidino-*s*-triazine, XXXVI. Displacement of a single tribromomethyl group from XIV by boiling methanol in the presence of pyridine gave XXXVII, although pyridine apparently does not catalyze such reactions with 2,4,6-tris(trichloromethyl)-*s*-triazine.[34c]



Attempts to displace a tribromomethyl group from XIV with the anions of nitromethane or malonitrile in the presence of pyridine led instead to the reduced product, *i. e.*, 2,4,6-tris(dibromomethyl)-*s*-triazine (X). Reaction of this compound with ammonia in aqueous ethanol gave the monoamine XXXVIII in low yield. 2,4,6-Tris(1,1-dibromoethyl)-*s*-triazine was unreactive toward ammonia or amines.

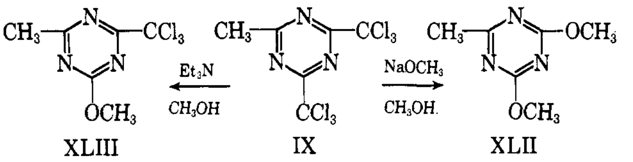
The reactions of XIII with aqueous ammonia were comparable to those observed with XIV. Displacement of one tribromomethyl group gave XXXIX and subsequent reduction gave a small amount of XL. The latter was obtained in substantial yield by reaction of XIII with ammonia in hot dimethylformamide (DMF).

An extreme example of the oxidation–reduction reactions which can occur with these polybromides is found in the unexpected reaction of XIII with dimethylformamide and 2,4-diamino-6-methyl-*s*-triazine to give X. Compound X also was reduced rapidly in a remarkable fashion by sodium iodide and acetic acid in acetone to give 2,4-bis(dibromomethyl)-6-methyl-*s*-triazine (XLI). Prolonged treatment with this reagent at room temperature caused complete reduction to I.



Reports of the efficient use of hexachloroacetone for generation of dichlorocarbene[35] led us to evaluate 2-methyl-4,6-bis(trichloromethyl)-*s*-triazine (IX) for this purpose under similar conditions. Some dichlorocarbene was obtained by reaction with sodium methoxide in cyclohexene, but the yield was only about 5%, the major product being 2-methyl-4,6-dimethoxy-*s*-triazine (XLII).

Compound XLII was also obtained by methoxide-catalyzed methanolysis of IX. The intermediate XLIII was obtained by adaptation of the method of Kober.[34c]



Experimental[36]

2-Chloromethyl-4,6-dimethyl-*s*-triazine (III). Chlorination of I with N-Chlorosuccinimide.—A mixture of 5.0 g. (0.040 mole) of I, 5.6 g. (0.040 mole) of NCS, 0.72 g. (0.003 mole) of benzoyl peroxide, and 50 ml. of carbon tetrachloride was heated at reflux for 4 hr. Filtration gave a 92% yield of succinimide. Distillation of the filtrate gave 2.3 g. of recovered I and 3.5 g. of crude III, b.p. 92–120° (20 mm.), *ca.* 60% yield based on unrecovered I. Redistillation gave a fraction boiling at 97–98° (20 mm.), $n^{25}D$ 1.5032. This was 94.5 mole % III as judged by mass spectrometry. It was essentially identical with III prepared by reaction of chloroacetamidine hydrochloride with ethyl acetimidate.[3]

Chlorination of I with Chlorine in Acetic Acid.—Chlorine (68 g., 0.96 mole) was passed into a solution of 123 g. (1.0 mole) of I in 500 ml. of glacial acetic acid at 50–55° during 1.0 hr. Anhydrous sodium acetate (1.0 mole) then was added, and the mix-

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(34) (a) A. Kreutzberger, *J. Am. Chem. Soc.*, **79**, 2629 (1957); (b) H. Schroeder, *ibid.*, **81**, 5658 (1959); (c) E. Kober, *J. Org. Chem.*, **25**, 1728 (1960).

(35) (a) P. K. Kadaba and J. O. Edwards, *ibid.*, **25**, 1431 (1960); (b) F. W. Grant and W. B. Cassie, *ibid.*, **25**, 1433 (1960).

(36) Melting points are uncorrected. Microanalyses were carried out in these laboratories under the direction of Dr. J. A. Kuck and Dr. J. H. Deonarine. Gas–liquid chromatographic separations were carried out on a silicone column. The cooperation of Dr. R. Feinland and his associates was helpful in this aspect of the work.

TABLE I

COMPOSITION OF PRODUCT MIXTURES FROM CHLORINATION OF I IN ACETIC ACID[a]

Component of mixture	Molar ratio of chlorine to I				Molar ratio of chlorine to sodium acetate to I			
	1.0	1.3	1.7	2.5	1:1:1	1:3:1	3:3:1	4.8:9:1
I	60	46	8[b]	3	37	29		
III	19	22	29	18	37	43		
XIX	20	19	29	43	21	18	9	
XXIII		1	1	4	3	8	18	
XXII	1	11	27	16	1.4	2	9	
XII		1	5	9	<1		46	15
XXIV				3			10	14
XLIV			1	2			7	29
XI				2				28
IX								14

[a] Approximate mole % based on g.l.c. and mass spectrometry data. Acetic acid was present in all samples, but the data have been normalized to show only the s-triazine ratios. [b] An indefinite amount of I was codistilled with the acetic acid and not recovered.

ture was cooled overnight. The acetic acid solution was subsequently filtered from precipitated sodium chloride and distilled. Analysis of the total distillate by mass spectrometry gave data showing 54% recovery of starting I, a 38% yield of III (27 g.), a 39% yield of dichlorinated material (35 g.), and a 2% yield of trichloride. These yields are based on unrecovered I; the yield of III based on starting I was 17%.

Purification of III was difficult because of the close boiling points of the by-products. However, the bulk of this compound was recovered as a fraction boiling at 111–112° at 24 mm., $n^{26}\mathrm{D}$ 1.5037, which was estimated to be 97% pure by mass spectrometry. Examination of the higher boiling fractions and comparison with authentic samples[3] by g.l.c. proved that the dichlorination product was almost exclusively 2-dichloromethyl-4,6-dimethyl-s-triazine (XIX), b.p. 123–125° at 24 mm. A distilled fraction, b.p. *ca.* 129° at 24 mm., rich in **2,4-dimethyl-6-trichloromethyl-s-triazine** (XXII) crystallized on standing. The crystals were washed with petroleum ether (b.p. 30–60°) and recrystallized from methanol or hexane to give analytically pure material, m.p. 72–74°.

Chlorination of I with Chlorine in Acetic Acid Containing Sodium Acetate.—Chlorine (40 g., 0.56 mole) was passed into a mixture of 68.5 g. (0.55 mole) of I, 45.1 g. (0.55 mole) of sodium acetate, and 150 ml. of glacial acetic acid over a period of 1 hr. while the temperature was held at 55–60°. The precipitated sodium chloride was filtered after the mixture had been chilled, and the solution was distilled. After a forerun containing only the bulk of the acetic acid, the remainder was distilled rapidly as completely as possible giving a mixture which was analyzed by g.l.c. and mass spectrometry. The yields of monochloride (III) and dichloride (XIX plus XXIII) were approximately 54% (30 g.) and 31% (22 g.), respectively, based on unrecovered I.

The yield of III based on starting I was 35% in this experiment, with 35% recovery of I. When a threefold excess of sodium acetate was used, the yield of III was 38% on the same basis and 27% of I was recovered.

Dichlorination of Trimethyl-s-triazine.—A mixture of 40.6 g. (0.33 mole) of I, 122 g. of acetic acid, and 6 g. of acetic anhydride was treated with chlorine at 55–60° until the weight increase was 42 g. Escape of hydrogen chloride was apparent toward the end of the reaction. The mixture was cooled to room temperature and 0.8 mole of sodium acetate was added slowly with cooling. After time to complete separation of the resulting sodium chloride, the mixture was diluted with an equal volume of ether and filtered. The insoluble salts were found to contain 0.60 equiv. of chloride ion, corresponding to 21.9 g. of hydrogen chloride in the reaction mixture. Taking this into account, the weight gain on chlorination corresponded to 1.7 moles of chlorine reacted per mole of I.

The filtrate from the reaction mixture was distilled after addition of 10 ml. of methanol. After a forerun containing most of the acetic acid, a 62-g. fraction was obtained, b.p. 70° (130 mm.). The distillation residue was negligible. Mass spectrometry and g.l.c. data (see Table I) showed the yields of the major products to be as follows (based on starting I): III, 22%; XIX, 22%; and XXII, 20%.

Trichlorination of Trimethyl-s-triazine.—Chlorine was passed over a stirred mixture of 40.6 g. (0.33 mole) of I, 81.2 g. (0.99 mole) of anhydrous sodium acetate, 122 g. of acetic acid, and 6 g. of acetic anhydride held at 55–60° until 69 g. (0.97 mole) had been absorbed (2.5 hr.). After cooling to room temperature the mixture was diluted with an equal volume of ether, and the insoluble salts were removed by filtration. The solution was treated with 10 ml. of methanol and distilled. A fraction was obtained, b.p. 78 (130 mm.)–135° (5 mm.), which weighed 78 g.; there was virtually no residue. This crude product, containing a small amount of acetic acid, was analyzed by mass spectrometry and by g.l.c. with the results shown in Table I. The indicated yield of **2-chloromethyl-4-dichloromethyl-6-methyl-s-triazine (XII)** was 40% based on starting I.

Separation of the products by fractional distillation was very difficult because of the closeness of their boiling points and because of decomposition during prolonged distillations. With the aid of a 24-in. spinning band column, 25 g. of XII of over 85% purity was separated, b.p. 123–125° (3.5 mm.). Material of higher purity was obtained by very slow distillation, b.p. 157° (18 mm.), but loss due to decomposition was substantial. A sample of 97% purity for mass spectrometry standardization was obtained by preparative g.l.c. The structure was confirmed by n.m.r. spectroscopy.

Miscellaneous Experiments on the Chlorination of I in Acetic Acid.—In Table I are collected data on the compositions of product mixtures obtained when the amounts of chlorine and sodium acetate used per mole of I were varied over a wide range. The reaction temperature was 50–60° and concentrations were in the range used in the preparations described above. Table II gives additional analytical data.

2-Methyl-4,6-bis(trichloromethyl)-s-triazine (IX).—Chlorine was passed into a stirred solution of 123 g. (1.00 mole) of I in 500 ml. of acetic acid at 45° until approximately 6.3 moles had reacted; the weight gain was corrected for dissolved hydrogen chloride which was determined by Volhard titration. The reaction mixture was then diluted with ice–water. The crude product was washed with water and air-dried to yield 295 g. (89%), m.p. 86–88°. Recrystallization from hexane raised the melting point to 95–96°, lit.[37] m.p. 96°. The n.m.r. spectrum of this compound consisted of a single peak at τ 7.02.

The mother liquors from several such crystallizations were combined and distilled to obtain a small amount of **2-chloromethyl-4,6-bis(trichloromethyl)-s-triazine**, b.p. 120–125° (0.1 mm.), m.p. 63–64° (from methanol).

Anal. Calcd. for $C_6H_2Cl_7N_3$: C, 19.78; H, 0.55; Cl, 68.13; N, 11.54. Found: C, 19.92; H, 0.90; Cl, 68.34; N, 11.63.

This compound was difficult to remove from IX by crystallization. It was convenient to avoid the problem by treating the crude product with excess sodium iodide in hot acetone containing a little acetic acid. This accomplishes reduction of any monochloromethyl groups to methyl[23] and gives a crude product melting at 93–95°.

In a similar preparation, most of the product IX, was crystallized from the acetic acid directly, and the mother liquor was distilled. Examination of the high boiling fraction (b.p. 140–190° at 3 mm.) by g.l.c. and mass spectrometry showed that hepta-, octa-, and nonachloro derivatives were present, totaling approximately 5–8% yield.

2-Dichloromethyl-4-methyl-6-trichloromethyl-s-triazine (XI).—Chlorine was bubbled for 2.5 hr. through a refluxing solution of 9.7 g. of I in 30 ml. of carbon tetrachloride under illumination

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(37) C. Grundmann, G. Weisse, and S. Seide, *Ann.*, **577**, 77 (1952).

TABLE II

ANALYTICAL DATA FOR NUMBERED COMPOUNDS

Structure	Formula	Calcd., % C	H	N	X	Found, % C	H	N	X
IV	$C_9H_{14}ClN_3$	54.13	7.07		17.76	54.17	7.13		17.53
V	$C_9H_{14}BrN_3$	44.27	5.79	17.21	32.73	44.31	5.97	17.48	32.79
VI	$C_6H_8BrN_3$	35.66	3.99	20.80	39.55	35.47	4.08	20.93	39.74
VIII	$C_4H_4ClN_3$	37.06	3.11	32.43	27.36	37.49	3.31	32.59	27.51
X	$C_6H_3Br_6N_3$	12.08	0.51	7.04	80.37	12.28	0.50	7.28	80.02
XIII	$C_6H_3Br_6N_3$[a]	12.08	0.51	7.04	80.37	12.32	1.31	7.30	79.0
XIV	$C_6H_3Br_9$	8.65	0.00	5.04	86.31	8.84	0.10	5.10	85.95
XV	$C_9H_9Br_6N_3$	16.92	1.42	6.58	75.08	16.53	1.47	6.87	74.87
XVI	$C_9H_{13}Br_2N_3$	33.46	4.06	13.01	49.48	33.44	4.61	12.96	49.18
XVII	$C_9H_{12}Br_3N_3$	26.89	3.01	10.54	59.64	26.72	2.64	10.36	59.72
XX	$C_6H_7Br_2N_3$	25.66	2.51	14.96	56.89	26.01	2.21	14.96	56.93
XXII	$C_6H_6Cl_3N_3$	31.81	2.67	18.55		31.95	2.79	18.65	
XXIV	$C_6H_5Cl_4N_3$	27.61	1.93		54.35	27.86	2.11		54.90
XXVI	$C_6H_7Br_2N_3$	25.66	2.51	14.96	56.89	25.24	2.56	14.60	56.13
XXIX	$C_{24}H_{23}ClN_3P \cdot C_6H_6$	72.3	5.82	8.43		71.35	5.85	8.40	
XXX	$C_{24}H_{22}N_3P$	75.17	5.78	10.96	(P, 8.09)	75.12	5.78	11.10	(P, 8.18)
XXXI	$C_{14}H_{23}N_5O_2$	57.32	7.90	23.87		57.72	8.29	23.91	
XXXIII	$C_{13}H_{13}N_3O$	68.71	5.76	18.49		68.68	5.61	18.11	
XXXIV	$C_5H_2Br_6N_4$	10.05	0.34	9.38		10.58	0.96	9.95	
XXXV	$C_4H_5Br_2N_5$	16.98	1.78	24.76	56.49	17.96	1.89	24.26	54.60
XXXVI	$C_{10}H_{10}Br_6N_4$	18.04	1.51	8.42	72.03	18.15	1.80	8.71	70.80
XXXVII	$C_6H_3Br_6N_3O$	11.76	0.49	6.86	78.27	11.94	0.80	6.32	79.05
XXXVIII	$C_5H_4Br_4N_4$	13.65	0.92	12.74	72.69	13.91	1.06	12.41	72.70
XXXIX	$C_5H_5Br_3N_4$	16.64	1.40	15.53	66.44	16.90	1.86	16.18	65.09
XL	$C_5H_6Br_2N_4$	21.30	2.14	19.87	56.69	21.45	2.43	19.82	56.27
XLI	$C_6H_5Br_4N_3$[b]	16.42	1.15	9.58	72 85	17.29	1.69	9.55	71.74
XLII	$C_6H_9N_3O_2$	46.44	5.85	27.08		46.16	6.05	27.42	

[a] Mol. wt.: calcd., 596.60; found, 529, 580. [b] Mol. wt.: calcd., 438.78; found, 451.8.

from a Hanovia Type 16200 ultraviolet lamp. The reaction mixture was added to excess aqueous sodium bicarbonate and extracted with methylene dichloride. Distillation of a portion of the extract gave a colorless oil, b.p. 80–96° (0.1 mm.), from which a 7% yield of 2,4-bis(dichloromethyl)-6-methyl-s-triazine (XXIV) was crystallized, m.p. 82–86°. The crude product extracted by methylene dichloride was reduced with sodium iodide-acetic acid in acetone[23] to remove monochloromethyl groups. It was then washed with aqueous sodium bisulfite, extracted with ether, and treated with excess concentrated aqueous ammonia in a little ethanol.[38] **2-Amino-4-dichloromethyl-6-methyl-*s*-triazine** crystallized directly from the reaction mixture; the crude yield was 50%, m.p. 160–170°, based on the original I used. After recrystallization from ethanol the product melted at 173–174°. The n.m.r. spectrum of this compound was essentially identical with that of XL.

Anal. Calcd. for $C_5H_6Cl_2N_4$: Cl, 36.74; N, 29.03. Found: Cl, 37.09; N, 28.97.

Collected samples of 2,4-bis(dichloromethyl)-6-methyl-s-triazine (XXIV) from similar examples were recrystallized from ethanol and hexane for analysis, m.p. 86–87°. This compound was unaffected by aqueous alcoholic ammonia under the conditions above and did not react with acidified sodium iodide.

2-Bromomethyl-4,6-dimethyl-*s*-triazine (VI).—A solution of 1.0 mole of I in 500 ml. of glacial acetic acid was held at 60° while 1.0 mole of bromine was added dropwise during 15 min. The mixture was then cooled to 25° and 1.0 mole of sodium acetate was added. The precipitated salt was removed by filtration and the filtrate was distilled. Analysis of the total distillate by g.l.c. indicated approximately a 20% recovery of I and 50 and 12% yields of VI and XX, respectively, based on unrecovered I. Virtually no XXVI was obtained. Fractional redistillation gave 80 g. (0.40 mole) of VI, b.p. 93–95 (10 mm.), $n^{25}D$ 1.5304. Mass spectrometry showed this material to be 99.5% pure.

A 26-g. fraction of higher bromination products boiling at 61–126° at 0.5 mm. was also obtained. Partial crystallization of this material gave 17 g. of XX, m.p. 54–57°.

When bromination was carried out under the conditions above but with an equimolar amount of sodium acetate present, VI was obtained in about the same yield, 46% based on starting I. However, both XX and XXVI were obtained, their respective fields being 9 and 12%.

Bromination of 2-Bromomethyl-4,6-dimethyl-*s*-triazine.—Reaction of VI with 0.5 mole of bromine per mole in boiling carbon tetrachloride gave a mixture of the isomeric dibromo compounds. There was some decomposition during the isolation procedure, but the ratio of recovered XXVI to XX was approximately 4:1. Perhaps this does not correctly represent the original product ratio.

2-Dibromomethyl-4,6-dimethyl-*s*-triazine (XXVI) boiled at 74–75° (0.2 mm.), $n^{27.5}D$ 1.5652, m.p. 20°. This compound was confirmed by its n.m.r. spectrum.

2,4-Bis(bromomethyl)-6-methyl-*s*-triazine (XX) had b.p. *ca.* 100° (0.5 mm.), m.p. 58–59° from ethanol or hexane. The n.m.r spectrum of this compound was consistent with the structure assigned.

2,4,6-Tris(dibromomethyl)-*s*-triazine (X).—Bromine (180 ml., 3.5 moles) was added in 45 min. to 62 g. (0.50 mole) of I in 600 ml. of acetic acid at 60°. The resultant mixture was filtered cold and the product was washed with acetic acid and ethanol and dried in air to yield 230 g. (76%), m.p. 125–129°. Recrystallization from acetonitrile gave m.p. 129–131°, lit.[39] m.p. 127–129°.

2-Methyl-4,6-bis(tribromomethyl)-*s*-triazine (XIII).—A mixture of 61.5 g. (0.50 mole) of I, 410 g. (5.0 moles) of sodium acetate, and 1000 ml. of acetic acid was heated to 70°, and 225 ml. (5.0 moles) of bromine was added gradually (65 min.). The mixture was heated for an additional hour at 90°, cooled, diluted with water, and allowed to stand overnight. The crystalline product was washed with water and air-dried, yielding 210 g., m.p. 120–150°. Recrystallization from acetonitrile gave 105 g., m.p. 157–158.5° (35% yield). Examination of the mother liquors by infrared showed that XIII and 2,4,6-tris(tribromomethyl)-s-triazine (XIV) were both present in substantial amount. After tedious recrystallizations XIV was isolated in approximately 6% yield, m.p. 152–155° and an additional 15% of XIII was recovered.

The n.m.r. spectrum of XIII showed a single proton peak which had very nearly the same chemical shift (τ 7.04) as that for 2-methyl-4,6-bis(trichloromethyl)-s-triazine.

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[38] This reactivity of the trichloromethyl-s-triazine structure is well defined by A. Kreutzberger [*J. Am. Chem. Soc.*, **79**, 2629 (1957)]. We find that XXIV is inert under these conditions.

[39] E. Ghigi, *Gazz, chim. ital.*, **71**, 641 (1941).

On long standing, the aqueous acetic acid solution from the reaction mixture deposited crystals of 2-acetoxymethyl-4,6-bis-(tribromomethyl)-*s*-triazine, m.p. 142–144° (from cyclohexane).

Anal. Calcd. for $C_8H_5Br_6N_3O_2$: C, 14.68; H, 0.77; Br, 73.24; N, 6.42. Found: C, 15.01; H, 1.00; Br, 72.8; N, 6.43.

2,4,6-Tris(tribromomethyl)-*s*-triazine (XIV).—A mixture of 216 g. (0.36 mole) of X, 178 g. (2.17 moles) of sodium acetate, and 1450 ml. of acetic acid was stirred at 109°, and 84 ml. (1.63 moles) of bromine was added over a period of 20 min. Heating was continued for an additional hour. The product which crystallized rapidly was collected after cooling, washed with acetic acid and water, and air-dried. The crude yield was approximately quantitative, m.p. 140–160°. Recrystallization from acetonitrile gave a 73% yield of material melting at 156–159°. The analytical sample had m.p. 158–159° (heptane).

N.m.r. and infrared examination of XIV confirmed the absence of hydrogen atoms.

Reduction of 2,4,6-Tris(tribromomethyl)-*s*-triazine.—Hydrogen bromide was passed into a solution of XIV in chloroform at 25° for 6 hr. Bromine production was evident. The solution was evaporated and the residue was triturated with petroleum ether. The crystalline product was then washed with ethanol and air-dried. The yield of 2,4,6-tris(dibromomethyl)-*s*-triazine, m.p. 119–125°, was 50%. This material was essentially identical with analytically pure X by infrared examination.

2-(1-Chloroethyl)-4,6-diethyl-*s*-triazine (IV).—Chlorine (0.10 mole) was passed into a solution of 0.10 mole of II in 30 ml. of carbon tetrachloride at 60–65°. After a brief holding period, the mixture was cooled and run into an excess of aqueous bicarbonate. The organic phase was separated, dried with potassium carbonate, and rapidly distilled as completely as possible. Analysis of the total distillate by g.l.c. showed approximately 17% recovery of II and a 58% yield of IV. Dichlorination products amounted to 10%. Yields are based on unrecovered II.

Distillation of a larger quantity of similar crude IV gave material boiling at 70° (1 mm.), n^{25}D 1.4850.

2-(1-Bromomethyl)-4,6-diethyl-*s*-triazine (V).—Bromine (1.0 mole) was added dropwise during 1.5 hr. to a solution of 1.0 mole of II in 500 ml. of chloroform. The mixture was held at gentle reflux during most of the addition. There was no apparent evolution of hydrogen bromide, and the solution remained clear. (Reaction in carbon tetrachloride led to a gummy mass.) The reaction mixture was treated with aqueous carbonate, and the organic phase was separated. Distillation after drying gave 35 g. (0.21 mole) of recovered II, b.p. 68–72° (7 mm.), and 122 g. (0.50 mole) of V, b.p. 98–100° (4 mm.), n^{25}D 1.5065.

From the higher boiling fractions were recovered 37 g. (0.11 mole) of **2,4-bis(1-bromoethyl)-6-ethyl-*s*-triazine (XVI)**, b.p. *ca.* 95° (0.22 mm.), n^{25}D 1.5412; and 3.0 g. of **2,4,6-tris(1-bromoethyl)-*s*-triazine (XVII)**, b.p. *ca.* 110° (0.2 mm.). The latter compound crystallized on cooling and after recrystallization from petroleum ether melted at 53.5–55°.

No material having a $-CBr_2CH_3$ group could be detected in the fractions containing the dibromo compound above by n.m.r. spectroscopy.

2,4,6-Tris(1,1-dibromoethyl)-*s*-triazine (XV).—To a solution of 83 g. (0.50 mole) of II in 500 ml. of acetic acid at 42° was added 105 ml. of bromine. Because reaction did not begin spontaneously, a small portion of the reaction mixture was removed and heated to about 70°. This caused a vigorous reaction, after which the material was returned to the main portion where exothermic reaction began quickly. The temperature rose spontaneously to 70° and hydrogen bromide was evolved liberally. The remainder of 205 ml. of bromine (4.0 moles) was added in portions over the following hour, the temperature remaining at 65–70°. The mixture was filtered after cooling, and the product was washed with acetic acid, ethanol, and water. The crude material weighed 302 g. (95%), m.p. 122–126°. Recrystallization from acetonitrile, ethanol, and heptane gave an analytical sample melting at 133–134°.

2-Chloromethyl-*s*-triazine (VIII).—2-Methyl-*s*-triazine and N-chlorosuccinimide (0.08 mole each) were heated in 100 ml. of boiling carbon tetrachloride in the presence of benzoyl peroxide (2.5 mmoles added in several portions) for 10 hr. Reaction was incomplete. The solution was then cooled and filtered. Fractional distillation gave 2.3 g. of VIII, b.p. 43–46° (0.5 mm.), in 22% yield. This material was identical by infrared comparison with VIII prepared by reaction of 2-chloroacetamidine hydrochloride with *s*-triazine.[40] This compound is a severe skin irritant and has poor storage stability.

2-(1-Chloro-1-methylethyl)-*s*-triazine was prepared by passing 0.20 mole of chlorine into a solution of 0.40 mole of 2-isopropyl-*s*-triazine[41] in 200 ml. of carbon tetrachloride at 65–78°. The yield was 20 g., 64% based on chlorine, b.p. 70–74° (10 mm.), n^{25}D 1.4965.

Anal. Calcd. for $C_6H_8ClN_3$: C, 45.72; H, 5.12; Cl, 22.50; N, 26.66. Found: C, 45.71; H, 5.57; Cl, 22.20; N, 26.76.

2-Trichloromethyl-*s*-triazine[42] (XVIII) was obtained in 22% yield by reaction of VII with excess chlorine in acetic acid containing acetic anhydride at 100°.

2-(1-Chloroethyl)-*s*-triazine and 2-(1,1-dichloroethyl)-*s*-triazine were obtained in approximately 10 and 18% yields, respectively, when 0.5 mole of chlorine per mole was passed into a carbon tetrachloride solution of 2-ethyl-*s*-triazine at 50–70° over a 1-hr. period.

2-(1-Chloroethyl)-*s*-triazine boiled at 93° (29 mm.), n^{25}D 1.5047. Its infrared spectrum was identical with that of a sample prepared in 37% yield by the reaction of *s*-triazine with 2-chloropropionamide hydrochloride.[42]

2-(1,1-Dichloroethyl)-*s*-triazine boiled at 83–84° (10 mm.), n^{24}D 1.5195. This product was spectroscopically identical with a sample obtained in 24% yield as a by-product from the reaction of *s*-triazine with 2-chloropropionamidine hydrochloride. Gas-liquid chromatography showed the compound to be approximately 96% pure. Its identity was confirmed by mass spectrometry and n.m.r. spectroscopy.

2-(1,1-Dibromoethyl)-*s*-triazine was recovered in 9% yield after reaction of 2-ethyl-*s*-triazine with bromine in hot acetic acid, b.p. 110–112° (10 mm.), n^{24}D 1.5803.

Anal. Calcd. for $C_5H_5Br_2N_3$: C, 22.50; H, 1.88; Br, 59.88; N, 15.74. Found: C, 23.02; H, 2.04; Br, 59.31; N, 15.31.

2-(1-Ethoxyethyl)-4,6-diethyl-*s*-triazine (XXVII).—Reaction of V (22.8 g., 0.092 mole) with an equivalent amount of potassium hydroxide in ethanol at 25–35° for 2 hr. gave about 90% of the theoretical amount of potassium bromide. Distillation of the solution gave as the major fraction 7.4 g., b.p. *ca.* 122° (15 mm.), n^{25}D 1.4728. Mass spectrometric analysis indicated that this was chiefly 2-(1-ethoxyethyl)-4,6-diethyl-*s*-triazine with some of the original bromide present; 2,4-diethyl-6-vinyl-*s*-triazine could not be detected. Examination by n.m.r. spectroscopy confirmed that this material was a 3:1 mixture of XXVII and V. In further confirmation of this result, **2-(2-ethoxyethyl)-4,6-diethyl-*s*-triazine** was prepared by reaction of 2,4-diethyl-6-vinyl-*s*-triazine[43] with ethanol containing a catalytic amount of sodium ethoxide, b.p. 120–125° (12 mm.). The structure of this product and its nonidentity with XXVII were established by infrared spectroscopy, n.m.r. examination, and mass spectrometry (*ca.* 99% purity indicated).

2-(1-Acetoxyethyl)-4,6-diethyl-*s*-triazine.—A mixture of 299 g. (1.23 moles) of V, 151 g. (1.84 moles)of anhydrous sodium acetate, 307 ml. of glacial acetic acid, and 25 ml. of acetic anhydride was heated at reflux for 18 hr. After hot filtration to remove the precipitated potassium bromide (94%), potassium iodide (12 g., 0.073 mole) was added and the mixture was heated at 90° for 30 min. to reduce residual V to triethyl-*s*-triazine (the acetate and V are very difficult to separate by distillation). Water and ether were then added, and the mixture was neutralized with sodium hydroxide and sodium carbonate. The ether phase was separated, dried, and distilled. The product acetate, collected at 139–146° (19 mm.), weighed 180 g. (68.5%). Redistillation gave material boiling at 96.0–96.5° (3 mm.), $n^{25.5}$D 1.4670.

Anal. Calcd. for $C_{11}H_{17}N_3O_2$: C, 59.17; H, 7.68; N, 18.82. Found: C, 59.27; H, 7.82; N, 18.64.

Mass spectrometric analysis showed the product to be free of compound V.

(4,6-Dimethyl-2-*s*-triazinyl)methylpyridinium Bromide.—Reaction of VI with a 50% excess of pyridine in acetone solution at room temperature for 4 hr. gave a 70% yield of the crystalline pyridinium salt, m.p. 199–202°. Recrystallization from acetonitrile gave material melting at 204–206°.

Anal. Calcd. for $C_{11}H_{13}BrN_4$: C, 46.99; H, 4.66; N, 19.93; Br, 28.42. Found: C, 47.36; H, 4.78; N, 19.62; Br, 28.71.

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(40) Prepared by Dr. K. R. Huffman using the general method of ref. 42.

(41) Prepared by the general method of ref. 42, b.p. 153°, n^{25}D 1.4684. *Anal.* Calcd. for $C_6H_9N_3$: C, 58.51; H, 7.37; N, 34.12. Found: C, 58.40; H, 7.27; N, 34.05.

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

(43) The synthesis of this compound will be reported separately.

(4,6-Dimethyl-2-*s*-triazinyl)methyltriphenylphosphonium Chloride (XXIX).—Reaction of 9.5 g. (0.060 mole) of III with 15.7 g. (0.060 mole) of triphenylphosphine in 35 ml. of benzene at room temperature for 4 days gave the phosphonium salt in approximately 90% yield. The product was adequately purified by washing with benzene. It tended to retain the solvent strongly, however. It was extremely soluble in more polar solvents such as acetonitrile and chloroform. A sample dried *in vacuo* at 65° melted at 195–198° if heated normally, but melted with gas evolution and resolidification if placed in a melting point bath at 180°.

(4,6-Dimethyl-2-*s*-triazinyl)methylenetriphenylphosphorane (XXX).—A mixture of 6.2 g. (0.012 mole) of XXIX (benzene complex), 2.0 g. (0.019 mole) of sodium carbonate, 15 ml. of water, and 20 ml. of benzene was stirred for 1.5 hr. The benzene phase then was separated, dried, and evaporated. The residue, 5.0 g. (88%), was recrystallized from ethyl acetate, m.p. 161.5–163°.

2,4-Dimethyl-6-(*p*-dimethylaminostyryl)-*s*-triazine.—A mixture of 12.3 g. (0.10 mole) of I, 14.9 g. (0.10 mole) of *p*-dimethylaminobenzaldehyde, 1 g. of potassium hydroxide, and 50 ml. of methanol was allowed to stand for 2 days. The crystals which separated, 17 g., m.p. 128–135°, were recrystallized from acetonitrile and from benzene to give analytically pure material, m.p. 143–145°; the crude yield was 67%.[44]

Anal. Calcd. for $C_{15}H_{18}N_4$: C, 70.63; H, 6.94; N, 21.68. Found: C, 70.83; H, 7.13; N, 22.03.

A mixture of equimolar amounts of XXX and *p*-dimethylaminobenzaldehyde in tetrahydrofuran gave no detectable reaction in 4 days at room temperature. After 3 days at reflux a slight amount of triphenylphosphine oxide was detectable by infrared. Thereafter, the solvent was evaporated and the residue was heated for 6 hr. at 160–170°. Extraction of the reaction mixture with ether left substantially pure triphenylphosphine oxide undissolved. The ether-soluble material contained considerable 2,4-dimethyl-6-(*p*-dimethylaminostyryl)-*s*-triazine as was determined by infrared comparison with an authentic sample.

2,4-Dimethyl-6-dimorpholinomethyl-*s*-triazine (XXXI).—A mixture of 13 g. of approximately 85% XIX (*ca.* 0.07 mole) and 50 ml. of morpholine was heated for 2 hr. on the steam bath. It then was allowed to cool slowly, and the crystallized morpholine hydrochloride was filtered out. The solution was distilled to remove essentially all unchanged morpholine, and the residue was extracted with ether. Evaporation of the ether solution gave 10.3 g. of crude XXXI, m.p. 106–115 (*ca.* 50% yield). Recrystallization from hexane raised the melting point to 121–123°.

4,6-Dimethyl-2-*s*-triazinecarboxaldehyde 2,4-dinitrophenylhydrazone was obtained by boiling a mixture of XXXI and a slight excess of 2,4-dinitrophenylhydrazine in ethanol for 2 hr., m.p. 235–237° from benzene.

Anal. Calcd. for $C_{12}H_{11}N_7O_4$: C, 45.42; H, 3.50; N, 30.91. Found: C, 45.77; H, 3.60; N, 30.56.

4,6-Dimethyl-2-*s*-triazinecarboxaldehyde thiosemicarbazone was prepared by refluxing an ethanol solution of equivalent amounts of XXXI and thiosemicarbazide for 6 hr., m.p. 230–232° from ethanol.

Anal. Calcd. for $C_7H_{10}N_6S$: C, 39.99; H, 4.79; N, 39.98; S, 15.25. Found: C, 39.90; H, 4.51; N, 39.82; S, 14.86.

2-(4,6-Dimethyl-2-*s*-triazinyl)-3-phenyloxirane (XXXIII).—A mixture of 10.0 g. of 2-chloromethyl-4,6-dimethyl-*s*-triazine of 80% purity ($\approx$0.051 mole), 5.4 g. (0.051 mole) of benzaldehyde, 7 g. of anhydrous potassium carbonate, and 20 ml. of methanol was stored at room temperature for 3 days with occasional shaking. The mixture then was filtered and the solution was evaporated. The residue was extracted with ether, and the extract was re-evaporated to a sirup. Extraction of this material with petroleum ether left undissolved a small amount of gum. The extract was again evaporated as completely as possible, leaving a residue of 11.3 g. which crystallized readily when refrigerated. The crystals were washed with a small amount of petroleum ether to remove some unchanged benzaldehyde and other minor impurities. The crude product weighed 7.0 g., m.p. *ca.* 50°. Lower melting material (4.0 g.) recovered from the wash solution was estimated to be 75–80% pure by infrared spectroscopy. The total yield was approximately 90%.

A sample of XXXIII recrystallized from hexane melted at 55–60°.

In the n.m.r. spectrum of this product which was in full accord with the assigned structure, the oxirane proton resonances at τ 5.71 and 6.20 showed a coupling of 2.9 c.p.s., characteristic of a *trans* configuration.[45] Examination of the less pure fractions showed that the oxirane content was identical with this pure compound and therefore exclusively of the *trans* configuration.

2-Amino-4,6-bis(tribromomethyl)-*s*-triazine (XXXIV).—2,4,6-Tris(tribromomethyl)-*s*-triazine (8.3 g.) was covered with 25 ml. of concentrated aqueous ammonia and the reactants were ground together with a stirring rod. After 5 min. the mixture was filtered, and the solid was washed with water and with petroleum ether. The product weighed 5.8 g. (97%), m.p. 202–208. Recrystallization from toluene or acetonitrile gave m.p. 218.5–219.5°. The n.m.r. spectrum of this product showed only the resonance of an amino-*s*-triazine group at τ 1.23.

This compound has been reported to melt at 184–185° by Broche.[20] Although the analytical data given were excellent, it is probable that his product was XXXVIII.[46]

2,4-Diamino-6-dibromomethyl-*s*-triazine (XXXVI).—A mixture of 12.1 g. (0.020 mole) of XXXIV and 60 ml. of concentrated ammonia was allowed to stand for 30 hr. The recovered solid (80% yield) was recrystallized from butanol, m.p. 220° dec. (lit.[46] m.p. 223°). Analytical data on this product were very erratic, merely showing the approximate composition.

The n.m.r. spectrum of a solution of this product in deuterated dimethyl sulfoxide had a strong peak at the chemical shift characteristic of the dibromomethyl-*s*-triazine group.

2-Piperidino-4,6-bis(trisbromomethyl)-*s*-triazine (XXXVI).—Reaction of 0.012 mole of XIV with 0.024 mole of piperidine in 70 ml. of methoxyethanol was allowed to proceed for 10 min. The mixture was then diluted with water, chilled, and filtered. The crystals obtained had m.p. 164–165° dec., 6.1-g. (76%) yield. Recrystallization from acetonitrile gave m.p. 166° dec.

2-Methoxy-4,6-bis(tribromomethyl)-*s*-triazine (XXXVII).—A mixture of 5.0 g. of XIV, 5 ml. of pyridine, and 100 ml. of methanol was heated under reflux for 3 hr. The solution was then concentrated and diluted with water to obtain 2.7 g. (53%) of crystals, m.p. 116–119°. Recrystallization from hexane gave m.p. 122.5–123°.

Reduction of XIV to X.—A mixture of 1.0 g. of XIV, 25 ml. of nitromethane, and 2 ml. of pyridine was allowed to stand for 16 hr. at room temperature. Dilution with 50 ml. of methanol and 100 ml. of water caused crystallization of 0.5 g. of X, m.p. 130–132° (69%).

Malononitrile plus pyridine in ether reacted similarly with XIV Without the basic catalyst, no reaction occurred between XIV and boiling nitromethane.

When hydrogen bromide was passed into a solution of 8.3 g. of XIV in 20 ml. of chloroform for 6 hr. at room temperature, bromine was liberated and X was recovered in 50% yield.

2-Amino-4,6-bis(dibromomethyl)-*s*-triazine (XXXVIII).—Concentrated aqueous ammonia (250 ml.) was added at room temperature to a solution of 15 g. of X in 500 ml. of ethanol. After 15 min., 3 l. of water was added and the precipitated product was filtered. The crude material, 4.2 g., was recrystallized from ethanol, giving 3.5 g. (32%), m.p. 171–173°.

2-Amino-4-methyl-6-tribromomethyl-*s*-triazine (XXXIX).—Reaction of 5.0 g. of XIII with 100 ml. of aqueous ammonia for 7 hr. gave 3.6 g., m.p. 155–180°. Extraction of this material with boiling chloroform left 1.0 g. undissolved. This was found by infrared examination to be a mixture of 2,4-diamino-6-methyl-*s*-triazine[47] and XL. From the chloroform extract, 2.3 g. of XXXIX was obtained, m.p. 153–158°, 76% yield. Recrystallization from methanol and from acetonitrile gave material melting at 157–160°.

The n.m.r. spectrum of this compound exhibited proton resonances attributable to amino- and methyl-*s*-triazine groups with very weak peaks at the chemical shifts characteristic of XL.

2-Amino-4-dibromomethyl-6-methyl-*s*-triazine (XL).—Ammonia was passed through a solution of 5.0 g. of XIII in 10-ml. of dimethylformamide for 1 hr. without heating (25–60°) and then for 1 hr. at 100°. The mixture then was filtered and the filtrate

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[44] This synthesis was carried out by Mrs. G. P. Papp.

[45] C. A. Reilly and J. D. Swalen, *J. Chem. Phys.*, **32**, 1378 (1960).

[46] A. Ostrogovich prepared 2,4-diamino-6-dibromomethyl-*s*-triazine (XXXV) and 2,4-diamino-6-tribromomethyl-*s*-triazine by bromination of 2,4-diamino-6-methyl-*s*-triazine with bromine in acetic acid. His melting point of 210° for the tribromo derivative similarly refutes Broche's reported preparation of this compound, m.p. 300° [*Bull. soc. sci. Bucharest*, **14**, 49 (1905); *Chem. Zentr.*, **II**, 1358 (1905)].

[47] M. Nencki, *Ber.*, **7**, 775 (1874).

was diluted with 25 ml. of water. The precipitated product weighed 0.9 g. (39%), m.p. 193° dec. Recrystallization from methoxyethanol raised the melting point to 201° dec.

The n.m.r. spectrum of this compound in dimethyl sulfoxide-d_6 was essentially identical with that of 2-amino-4-dichloromethyl-6-methyl-*s*-triazine.

Isomerization of XIII to X.—A mixture of 6.0 g. of XIII, 1.2 g. of 2,4-diamino-6-methyl-*s*-triazine, and 25 ml. of dimethylformamide was heated for 45 min. at 100°. Water then was added to the point of beginning crystallization. The crude product obtained was triturated with methoxyethanol which left 1.0 g., m.p. 126–130°, identified by infrared comparison as X.

Reduction of X to XLI.—A solution of 15 g. (0.025 mole) of X in 100 ml. of acetone was added to 150 g. (1.0 mole) of sodium iodide in 50 ml. of acetic acid and 500 ml. of acetone. After 6 min. at room temperature the reaction mixture was added to 25 g. of sodium bisulfite in 1 l. of ice–water. By extraction with ether, 7.2 g. of a dark oil was recovered. This was crystallized in part from ethanol, giving 3.4 g. of crude XLI, m.p. 79–85° (31% yield). Recrystallization from cyclohexane raised the melting point to 87–88.5°.

The n.m.r. spectrum of this compound was consistent with the structure XLI, although there was evidence for a minor amount of an impurity containing $-CH_2Br$.

2,4-Dimethoxy-6-methyl-*s*-triazine (XLII).—A solution of 16.5 g. (0.050 mole) of IX and 5.4 g. (0.10 mole) of sodium methoxide in 115 ml. of methanol was stored at room temperature for 60 hr. Only 1.2 g. of sodium chloride was obtained. The solution was saturated with carbon dioxide to precipitate the residual alkoxide, was filtered, and then was evaporated as completely as possible. The residue was extracted with an ether–petroleum ether mixture from which 4.7 g. of crystals were recovered, m.p. 45°. Recrystallization from hexane raised the melting point to 62–64°; the crude yield was 61%.

2-Methoxy-4-methyl-6-trichloromethyl-*s*-triazine (XLIII).—A mixture of 15 g. of IX, 18 ml. of triethylamine, and 75 ml. of methanol was heated at reflux for 6 hr. The solvent then was evaporated, and the residue was extracted with ether. The ether solution was distilled, giving 5.5 g. of product boiling at about 120° (6 mm.). The product was shown to be the expected[34c] XLIII by n.m.r. spectroscopy. (About 5% of the dimethoxy derivative XLII was found as an impurity.) The yield of XLIII was 45%.

Dichlorocarbene from IX.—A solution of 33.0 g. (0.10 mole) of IX in 50 g. of cyclohexene was added dropwise to a stirred suspension of 10.8 g. (0.20 mole) of sodium methoxide in 32 g. of cyclohexene at 5–10° over a period of 2 hr. Stirring was continued for 3 hr. longer at 5–10° and for 18 hr. at room temperature. The black mixture then was filtered and the low-boiling material was distilled. Analysis of the distillate by g.l.c. showed that about 25% of the theoretical yield of chloroform was present. The less volatile material (9 g.) then was distilled at low pressure. The fraction boiling at 65–75° (8 mm.) weighed 2.0 g. and was found to contain about 50% 2,2-dichlorobicyclo[4.1.0]heptane by mass spectrometry and g.l.c. The yield of this product was only 3–5%. The major product, *ca.* 4.5 g., b.p. 80–90° (5 mm.), m.p. 65–67°, was 2-methyl-4,6-dimethoxy-*s*-triazine (XLII).

N.m.r. Examination of Halogenation Products from 2-Ethyl-4,6-diphenyl-*s*-triazine.—2-Ethyl-4,6-diphenyl-*s*-triazine was mono- and dichlorinated and brominated as described by Reinhardt and Schiefer, and the four products were found to have the melting points reported.[5] The n.m.r. spectra of the two monohalides showed the expected quartet and doublet resonances for the methine and methyl groups, respectively, of the $-CHXCH_3$ structure. The n.m.r. spectra of the two dihalides showed single resonances due to the $-CX_2CH_3$ group rather than the complex pattern that would result from the $-CHXCH_2X$ structure. Thus there is no doubt that only α-halogenation of the ethyl group is significant.

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Reactions of Benzaldehyde with *o*-Nitroaniline[1]

GARDNER W. STACY, BRUCE V. ETTLING,[2] AND ANTHONY J. PAPA

Department of Chemistry, Washington State University, Pullman, Washington

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When benzaldehyde and *o*-nitroaniline (I) are heated under reflux in toluene for varying lengths of time, not only is the anticipated product N-benzylidene-*o*-nitroaniline (II) formed but also N,N-benzylidenedi(*o*-nitroaniline) (III). Prolonged reaction time effects heterocyclization to give 1-hydroxy-2-phenylbenzimidazole (V) and 2-phenylbenzimidazole (IV). The structure of V was substantiated by its reduction to IV and by an alternate synthesis from N-benzyl-*o*-nitroaniline. Some intermediate conversions of interest were observed. The Schiff base II added *o*-nitroaniline to form III. Also, both II and III react with benzaldehyde to give V.

The reaction of aromatic aldehydes with aromatic amines usually proceeds without complication to form Schiff bases.[3] We have examined a case, however, where several subsequential reactions of interest occurred and found that control of experimental conditions was important in governing the outcome.

When *o*-nitroaniline was heated with an excess of benzaldehyde in toluene, the Schiff base, N-benzylidene-*o*-nitroaniline (II), was in fact obtained as the major product (see Chart A[4]); however, its separation and purification from the reaction mixture was made difficult by the presence of small amounts of N,N-benzylidenedi(*o*-nitroaniline) (III) and 1-hydroxy-2-phenylbenzimidazole (V).

N-Benzylidene-*o*-nitroaniline (II) on standing at room temperature will react with traces of moisture to form III (presumably the process involves initial hydrolysis to benzaldehyde and *o*-nitroaniline with subsequent addition of the latter to unchanged II). However, II is stable at 0° and may be stored at this temperature without evidence of transformation to III.

N,N-Benzylidenedi(*o*-nitroaniline) (III) was obtained as the sole product when benzaldehyde was heated with excess *o*-nitroaniline. Crude III displayed odd behavior on attempted purification. Recrystallization from several solvents gave materials of variable melting point. Although examination of these modi-

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(2) In part abstracted from a thesis submitted by B. V. Ettling in partial fulfillment of the requirements for the degree of Doctor of Philosophy, Washington State University, June, 1958. Public Health Service Research Fellow of the National Institute of Neurological Diseases and Blindness, 1956-1958.

(3) R. W. Layer, *Chem. Rev.*, **63**, 489 (1963).

(4) Unless otherwise indicated the reactant is benzaldehyde.