PHOTOCHEMISTRY OF BIOACTIVE COMPOUNDS

I. Solution-Phase Photochemistry of Asymmetric Triazin-5-(4H)-Ones

II. Solution-Phase Photochemistry of Symmetrical Triazines

Thesis for the Degree of Ph. D.
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This is to certify that the

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I. Solution-Phase Photochemistry of
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II. Solution-Phase Photochemistry of Symmetrical Triazines

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Brian E. Pape

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Matthew Zabik
Major professor

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ABSTRACT

PHOTOCHEMISTRY OF BIOACTIVE COMPOUNDS

I. Solution-Phase Photochemistry of Asymmetric Triazin-5-(4H)-Ones.

II. Solution-Phase Photochemistry of Symmetrical Triazines

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The photolysis of 4-amino-6-R-3-(methylthio)-*as*-triazin-5-(4H)-ones (R = cyclohexyl, *t*-butyl, isopropyl) in carbon tetrachloride, benzene, methanol, water, or in the crystalline state, yields the respective 5-hydroxy-6-R-3-(methylthio)-1,2,4-triazine as the major product. Minor reactions proceed by routes which include desulfurization and oxidation. Reaction mechanisms are considered.

Photolysis of 2-fluoro and 2-bromo-4,6-bis(ethylamino)-*s*-triazine in methanol and water at 253.7 and 300 nm yielded the 2-methoxy and 2-hydroxy analogs as the major products. Photolysis of the 2-iodo-*s*-triazine analogs of atrazine, propazine, and simazine in methanol, ethanol, and *n*-butanol at 300-360 nm yielded the respective 2-alkoxy and 2-hydroxy compounds as the major product(s). Reaction mechanisms are considered. Consideration of thermal, photochemical, and spectroscopic data are suggestive of the participation of a Chugaev-type cyclic transition state in the photochemical dealkylation of *s*-triazines. Photolysis of 2-azido-4-ethylamino-6-methylthio-*s*-triazine in methanol at 253.7 and 300 nm yielded 2-amino-4-ethylamino-6-methylthio-*s*-triazine, 2-amino-4-ethylamino-*s*-triazine, and 2-azido-4-ethylamino-*s*-triazine. The observation of a "sensitized" photodecomposition of 4,6-bis(isopropylamino)-*s*-triazine is reported.

PHOTOCHEMISTRY OF BIOACTIVE COMPOUNDS

I. Solution-Phase Photochemistry of Asymmetric Triazin-5-(4H)-Ones.

II. Solution-Phase Photochemistry of Symmetrical Triazines.

By

Brian E. Pape

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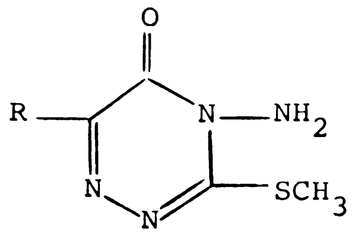
Part II. Solution-Phase Photochemistry of Symmetrical Triazines

PART I. SOLUTION-PHASE PHOTOCHEMISTRY OF ASYMMETRIC TRIAZIN-5-(4H) ONES

INTRODUCTION

A number of 4-amino-6-alkyl substituted-3-(methylthio)-*as*-triazin-5-(4H)-ones were previously tested for herbicidal activity by Vero Beach Laboratories, Inc., and are currently being developed by Chemagro Corp. (Kansas City, Mo.) under license. Representatives of this class of compounds included in this investigation of photochemical reactivity include: BAY 94337 [4-amino-6-*t*-butyl-3-(methylthio)-*as*-triazin-5-(4H)-one] (I), BAY 88410 [4-amino-6-isopropyl-3-(methylthio)-*as*-triazin-5-(4H)-one] (II), and BAY 86791 [4-amino-6-cyclohexyl-3-(methylthio)-*as*-triazin-5-(4H)-one] (III).



Asymmetric heterocyclic nitrogen compounds have been the subject of extensive investigation (Paquette, 1968; Smolin and Rapoport, 1959). Even a superficial review of the literature indicated several plausible reaction pathways that might be operative in the photodecomposition of I-III: expulsion of molecular nitrogen with the formation of the intermediate biradical; desulfurization of the carbon-three methylthio group; oxidation of a hetero atom; reduction of or addition to the carbonyl function; dimerization; and addition to the unsaturated ring (Calvert and Pitts, 1966; Crosby, 1969; Mustafa, 1964; Neckers, 1967; Pape and Zabik, 1970; Plimmer, *et al.*, 1969).

EXPERIMENTAL

Materials and Methods

Herbicides

Compounds I-III were obtained from Chemagro as technical material and were recrystallized from benzene to greater than 99% purity. Alternatively, they may be recrystallized from 1,2-dichloroethane. Final purification may be accomplished by tlc using silica gel and benzene-ethyl ether (1:1) or chloroform-acetone (9:1). Chemical authenticity was supported by ir, mass, and nmr spectra.

Solvents

All solvents were of analytical grade. Water was distilled, degassed, deionized, and had a pH of approximately 6.8.

Photochemical Equipment

All photolyses were done in a Rayonet Photochemical Reactor (The Southern N. E. Ultraviolet Co.) fitted with lamps having a peak energy output at 300 and 350 nm (Catalog No. N.P.R.-3000, -3500, respectively). All irradiations were done through borosilicate glass. Solutions were magnetically stirred, with solution temperatures maintained at approximately 25° C.

Analytical Equipment

Thin-layer chromatography (tlc) was done on precoated silica gel (HF-254) plates, with chloroform-acetone (9:1) or benzene-ethyl ether (1:1). Column chromatography was done on silicic acid AR 100 mesh (Mallinckrodt), using chloroform-acetone (9:1). Gas-liquid partition chromatography (glpc) analyses were accomplished using a 3% OV-1 or 1% SE-30 liquid phase on Gas-Chrom Q (Applied Science Laboratories), with an isothermal temperature range of 160-200° C.

All melting points were uncorrected. Infrared (ir) and ultraviolet (uv) spectra were determined with a Perkin-Elmer 337 and Beckman DB-G grating spectrophotometer, respectively. Nuclear magnetic resonance (nmr) spectra were recorded using a Varian A-60 high resolution instrument. Samples were dissolved in deuterated chloroform-d_1 or acetonitrile-d_3, with tetramethylsilane as an internal standard. Mass spectra were obtained with an LKB 9000 gas chromatograph-mass spectrometer. Spectra obtained by direct or indirect (1% SE-30 liquid phase on 60/80 mesh Gas-Chrom Q; 6 ft. x 1/8 in. i.d.; isothermal temperature 150-200° C.; ionization voltage 70 eV) introduction were essentially identical.

Elemental analyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Mich.

Photochemical Procedures

Photolysis of 4-Amino-6-Alkyl Substituted-3-Methylthio)-As-Triazin-5-(4H)-Ones (I, II, III) in Carbon Tetrachloride, Benzene, Methanol, and Water.

Photolysis of saturated solutions of I-III in carbon tetrachloride (0.25 g./100 ml. solvent) at > 290 nm resulted in reaction, and precipitation of the respective major photoproduct (IV-VI). With short irradiation time, i.e., four hours or ~ 10% conversion of I-III, product yield was greater than 90%. Prolonged photolysis (> 72 hours) resulted in multiple products (with total conversion of I-III, yield of IV-VI exceeded 60%.

Reactions were stopped with the total disappearance of I-III; solvent was removed under partial vacuum; and the amorphous residue was dissolved in chloroform-acetone (9:1). This solution was chromatographed on a silicic acid column [chloroform-acetone (9:1)]. Fractions were analyzed by glpc and tlc; pure product fractions were reduced under vacuum; and final drying was done in a drying pestle.

Comparative analysis of aliquots of starting material, photolysis solutions, and isolated photoproducts by glpc and tlc showed the product to be stable under these chromatographic procedures. Solutions of I-III held in the dark were determined to be stable over time.

Photolysis of I-III in Other Solvents

Photolysis of I-III in benzene, methanol, and water yielded essentially identical results: conversion of I-III to appropriate major product identical to that formed in carbon tetrachloride. Photolysis in water required the extraction of product with ethyl ether or chloroform.

Photolysis of I-III in the Crystalline State

Compounds I-III were dissolved in ethyl ether and distributed over the inside surface of a borosilicate flask (using rotation and air stream). Irradiation through glass resulted in a photo-reaction, with formation of a major product identical to those isolated from solution-phase reactions.

RESULTS AND DISCUSSION

Elemental Analyses and Melting Points

Elemental analyses showed that the major photoproducts of I-III had lost the equivalent of NH (Table 1).

Thin-Layer Chromatography and Gas-Liquid Partition Chromatography

Tlc and glpc behavior of starting materials and photolysis products (Table 2) suggested that the major isolated products (IV-VI) were more polar than their respective precursors [refer to Pape and Zabik (1970) for behavior correlations noted for series of carbon-two substituted *s*-triazine analogs].

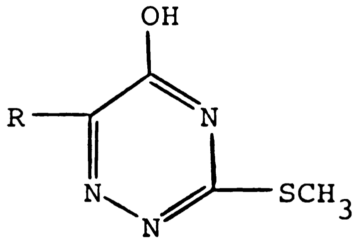
Mass Spectrometry

The mass spectra of these photoproducts are characterized by a molecular ion 15 m/e units below their respective starting material: the even mass number and isotopic abundance supported the loss of NH. Although, in each case, the base peak appeared at m/3 69 and suggested a common molecular genesis, the fragmentation pattern was insufficient to determine whether rearrangement of the heterocyclic ring had occurred (Figure 1).

Infrared Spectroscopy

The ir spectra of I-III and their respective products exhibited striking dissimilarities: loss of primary amine stretching vibrations in the 3300 cm^{-1} region; increased absorption and complexity in the 1600-1700 cm^{-1} region of the ir--suggestive of an intramolecularly bonded carbonyl or enol function; and appearance of an intense absorption between 2500-3000 cm^{-1}, strikingly similar to the observed enol-keto tautomerism occurring in the ir spectra of 2-hydroxy-s-triazines (Padgett and Hamner, 1958; Pape and Zabik, 1970) (Figure 2).

These data suggested the 1,2,4-triazine ring system (VII) as the photoproduct.

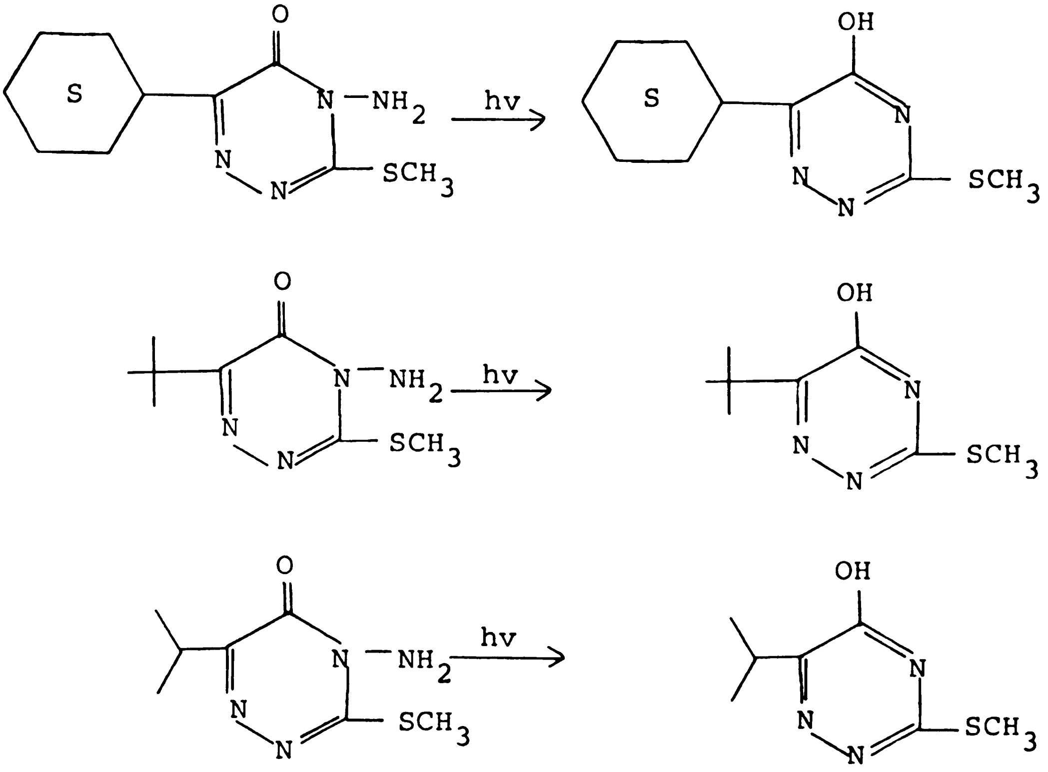


VII

Nuclear Magnetic Resonance Spectra

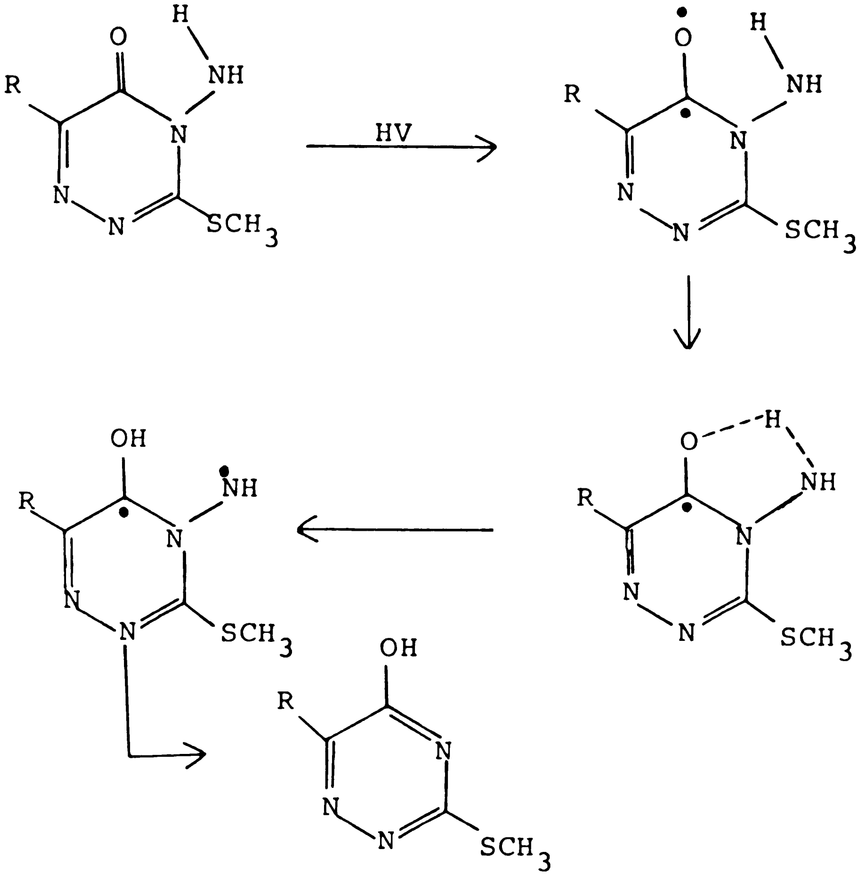
The nmr spectra of I-III and products (Table 3) supported the proposed structural system by the absence of a primary amine (2H) signal and the relatively unaltered chemical shifts of the SCH_3 and alkyl functions in product spectra. The absence of a one hydrogen signal for the enol-keto tautomer is attributed to exchange.

These data allowed the assignment of structures to the respective photoproducts of I-III as 5-hydroxy-6-t-butyl-3-(methylthio)-1,2,4-triazine (IV), 5-hydroxy-6-isopropyl-3-(methylthio)-1,2,4-triazine (V), and 5-hydroxy-6-cyclohexyl-3-(methylthio)-1,2,4-triazine (VI).



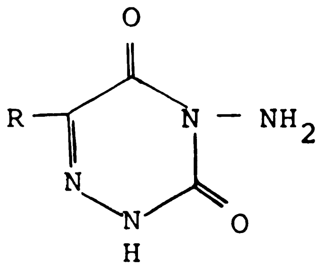
Reaction Mechanism

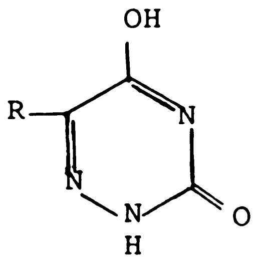
One attractive reaction pathway for the conversion of I-III → IV-VI involves an intramolecular hydrogen abstraction, mechanistically analogous to the gamma-hydrogen abstraction of aliphatic ketones (Calvert and Pitts, 1966). This would involve excitation of the carbonyl, via some unelucidated excited state, to yield a "biradical." This radical would then abstract an amine hydrogen <u>via</u> an intramolecular five-membered cyclic transition state, followed by electron shift, with elimination of NH to yield product.

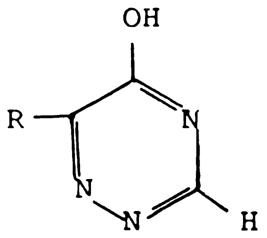


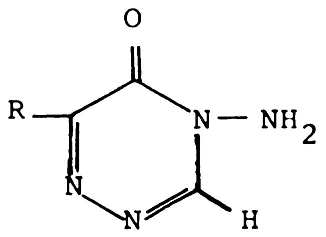
Minor Photoproducts

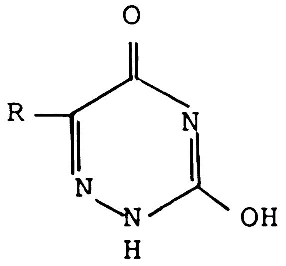
Chromatographic and mass spectral data suggest that the minor photoproducts formed after prolonged irradiation of I-III or IV-VI in solution or as a solid consist of compounds whose formation is explicable in terms of hetero atom oxidations, intramolecular rearrangements, and desulfurization. Although not definitely identified, reaction mechanisms leading to such product multiplicity are based on reported literature and structural/photochemical analogies.

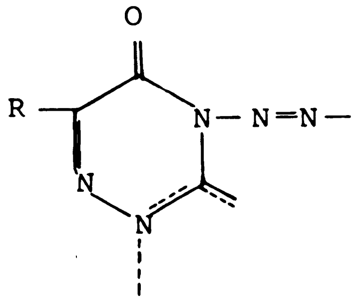












Formation of the "dicarbonyl" analogs of I-III may proceed via a sulfone or sulfoxide intermediate formed by photo-oxidation of the methylthio group [Plimmer, et al., 1969, postulated that the unstable sulfone or sulfoxides of 2-methylthio-s-triazines would yield their 2-hydroxy analogs]. The cyclic hydroxylated ketones might then be formed by the competitive elimination of NH from the "dicarbonyl," analogous to I-III → IV-VI. Hydroxy or keto desulfurization products may be formed *via* an elimination mechanism similar to that reported for *s*-triazines (Plimmer, *et al*., 1969; Pape and Zabik, 1970. Other pathways may include dimerization *via* amine hydrogen abstraction to yield azo compounds (Rosen, *et al*., 1970) and head-head or head-tail dimerization products (Neckers, 1967). At present, there is no analytical evidence to support the occurrence of these latter products.

TABLE 1.--Elemental analyses and melting points of photoproducts.

Photoproduct Analysis	Carbon		Hydrogen		Nitrogen		Sulfur		°C
	Calcd	Found	Calcd	Found	Calcd	Found	Calcd	Found	Determined
$C_8H_{13}N_3OS$(IV)	48.21	48.16	6.59	6.57	21.01	21.00	16.01	16.10	194[a]
$C_7H_{11}N_3OS$(V)	45.38	45.26	6.00	5.95	22.69	22.80	17.30	17.24	142[b]
$C_{10}H_{15}N_3OS$(VI)	53.24	53.20	6.72	6.65	18.63	18.60	14.21	14.18	193[a]

[a] Decomposition prior to melting.

[b] Slight decomposition with melting.

TABLE 2.--Thin-layer chromatographic and gas-liquid partition chromatographic data for asymmetric triazin-5-(4H)-ones and photoproducts.

Compound	TLC Data		GLPC Data	
	Solvent System[a]	Relative R_f (1 = 1.00)[f]	Column[b]	Retention Time, Min
I	A	1.00	A	3.3
	B	1.00	B	3.7
II	A	.81	A	2.7
	B	.76	B	3.0
III	A	.92	A	11.8
	B	.87	B	--
IV	A	.66	A	3.5
	B	.54	B	4.2
V	A	.56	A	3.6
	B	.35	B	4.4
VI	A	.71	A	--
	B	.41	B	--

[a] Solvent system: (A) = chloroform/acetone (9:1 v/v). (B) = benzene/ethyl ether (1:1 v/v).

[b] Column: (A) = 3% OV-1 liquid phase on 80/100 Mesh gas-Chrom Q; 6 ft. stainless steel column - 1/8 in. i.d.; carrier gas flow 25 ml/min helium; flame ionization detection.

(B) = 1% SE-30 liquid phase on 60/80 mesh Gas-Chrom Q; 6 ft. borosilicate glass column-1/8 in. i.d.; carrier gas flow 40 ml/min helium; electron ionization detection.

TABLE 3.--Nuclear magnetic resonance (nmr) data of asymmetric triazin-5-(4H)-one photoproducts.[a]

Compound	NMR Solvent	$-SCH_3$	$-NH_2$	-ALKYL
I	$CDCl_3$	7.25(3H)(s)	4.85(2H)(s)	8.40(9H)(s)
II	$CDCl_3$	7.35(3H)(s)	4.85(2H)(s)	8.60(6H)(d) 6.55(1H)(m)
III	$CDCl_3$	7.38(3H)(s)	4.95(2H)(s)	8.30(11H)(m)
IV	CD_3CN	7.78(3H)(s)		9.0(9H)(s)
V	CD_3CN	7.80(3H)(s)		9.17(6H)(d) 7.15(1H)(m)
VI	CD_3CN	7.70(3H)(s)		(8.85)(11H)(m)

[a] Nmr chemical shifts expressed in tau (τ) values, relative to tms.

(s) = singlet, (d) = doublet, (m) = multiplet

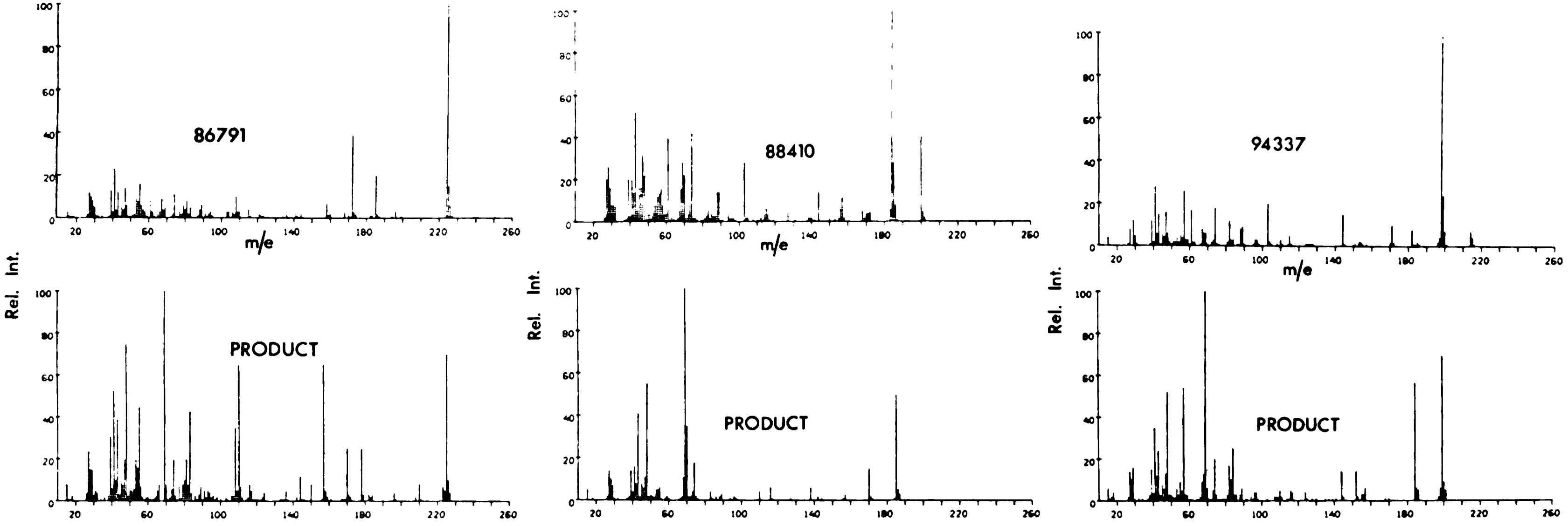


Figure 1.--Mass spectra of *as*-triazin-5-(4H)-ones and respective photo-products

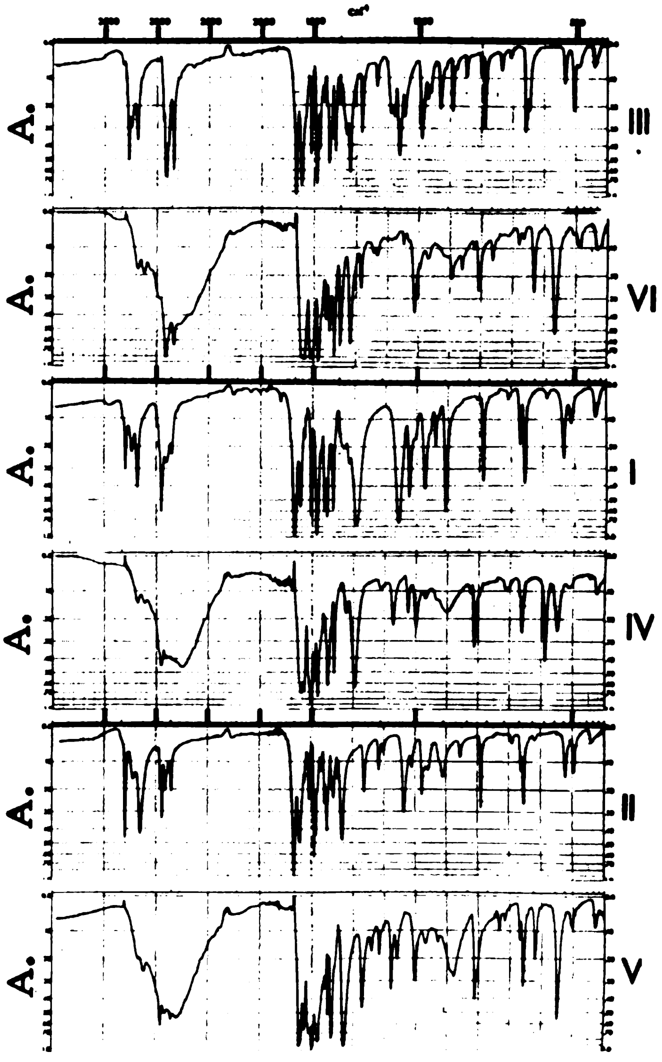


Figure 2.--Infrared spectra of as-triazin-5(4H)-ones I-III and respective photoproducts IV-VI

CONCLUSIONS

The photolysis of I-III under a wide range of reaction conditions and at wavelengths greater than 290 mn indicates the potential environmental significance of such non-biological degradations. Determination of photoproduct formation and residual level in the field would dictate toxicological evaluations and analytical procedures necessary to studies of its occurrence and ecological "burden." These particular triazinone photoproducts ("deaminated" compounds) are considerably less effective biologically than their corresponding parent compounds (Waggoner, 1971).

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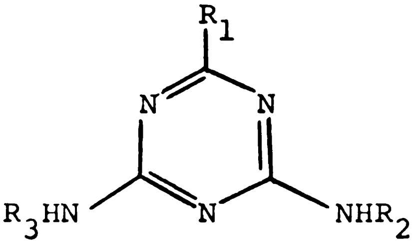
PART II. SOLUTION-PHASE PHOTOCHEMISTRY OF SYMMETRICAL TRIAZINES

INTRODUCTION

The photochemistry of *s*-triazines (Table 1) has only recently been investigated in detail. Earlier investigations have demonstrated that photodecomposition occurs in natural sunlight. In addition, changes in the uv spectra of photolysed solutions and decreases in the phytotoxicity of the unidentified product mixtures have been reported (Comes and Timmons, 1965; Jordan, *et al*., 1963, 1965). Jordan, *et al*., 1970, summarized the literature on *s*-triazine photodecomposition to that date.

Recently, Plimmer and co-workers studied the photolysis of III and IX at 220 nm in methanol solution by combined glpc-mass spectrometry. Simazine (III) yielded IX, XV, and XVIII, and other methylated products: possibly involving methylation of a ring nitrogen. Photolysis of IX yielded XVIII and methylated products (Plimmer, personal communication). Plimmer, *et al*. (1969) also reported the conversion of XXII to XV as the result of irradiation of the solid material.

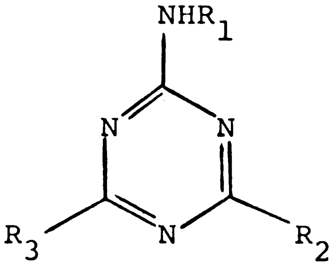
TABLE 1.--Authentic s-triazines and photoproducts.



S-triazine	Designation	Substituents		
		R_1	R_2	R_3
Atrazine	(I)	Cl	C_2H_5	C_3H_7
Propazine	(II)	Cl	C_3H_7	C_3H_7
Simazine	(III)	Cl	C_2H_5	C_2H_5
Hydroxy-Atrazine	(IV)	OH	C_2H_5	C_3H_7
Hydroxy-Propazine	(V)	OH	C_3H_7	C_3H_7
Hydroxy-Simazine	(VI)	OH	C_2H_5	C_2H_5
Atratone	(VII)	OCH_3	C_2H_5	C_3H_7
Prometone	(VIII)	OCH	C_3H_7	C_3H_7
Simetone	(IX)	OCH	C_2H_5	C_2H_5
Iodo-Atrazine	(X)	I	C_2H_5	C_3H_7
Iodo-Propazine	(XI)	I	C_3H_7	C_3H_7
Iodo-Simazine	(XII)	I	C_2H_5	C_2H_5
	(XIII)	H	C_2H_5	C_3H_7
	(XIV)	H	C_3H_7	C_3H_7
	(XV)	H	C_2H_5	C_2H_5
Fluoro-Simazine	(XVI)	F	C_2H_5	C_2H_5
Bromo-Simazine	(XVII)	Br	C_2H_5	C_2H_5
	(XVIII)	OCH_3	H	C_2H_5

TABLE 1.--Continued.

S-triazine	Designation	Substituents		
		R_1	R_2	R_3
Ametryne	(XX)	SCH_3	C_2H_5	C_3H_7
Prometryne	(XXI)	SCH_3	C_3H_7	C_3H_7
Simetryne	(XXII)	SCH_3	C_2H_5	C_2H_5



	(XXIII)	C_3H_7	SCH_3	N_3
	(XXIV)	C_3H_7	SCH_3	NH_2
	(XXV)	C_3H_7	H	NH_2
	(XXVI)	C_3H_7	H	N_3

Recent investigations in this laboratory (Pape and Zabik, 1970) have demonstrated the generality of the photochemical solvolysis of 2-chloro-s-triazines in alcohols and water between 253.7 and 300 nm. Photolysis of I, II, and III in methanol and in water yielded VII, VIII, IX, and IV, V, VI, respectively. These and other product studies were initially suggestive of a carbonium ion mechanism. The irradiation of 2-methylthio-s-triazines XX, XXI, and XXII in hydrocarbon, alcoholic, or aqueous solution resulted in the formation of the 4,6-di(alkylamino)-s-triazines XIII, XIV, and XV, respectively. Solvent participation reactions indicated an intramolecular elimination with hydrogen transfer. Our studies of changes in uv spectra of 2-chloro-s-triazines under laboratory conditions at 280 nm are identical to those reported by Comes and Timmons (1965) and Jordan, et al. (1963 and 1965) in sunlight and support the conversion of these triazines to their 2-hydroxy analogs under field conditions. The purpose of the present investigation was to extend the knowledge of the photochemistry of substituted triazines.

Objectives of these photochemical studies included: (1) the study of 2-fluoro-4,6-bis(ethylamino)-s-triazine, 2-bromo-4,6-bis(ethylamino)-s-triazine, and 2-iodo-s-triazines in methyl alcohol and in water; (2) the photolysis of 2-azido-4,6-methylthio-s-triazine; and (3) preliminary investigation of the significance of photochemical "sensitization" on the fate of the s-triazine system. The more detailed investigation of the solution-phase photolysis of 2-iodo-s-triazines X, XI, and XII was extended as part of a study of mechanistic photochemistry: to determine the kinetic and product specificity influences of the carbon-two substituents (2-F, Cl, Br, I and 2-OCH_3, OH, H) of symmetrical triazines. The directions and implications of considerations of the mechanism of s-triazine N-dealkylation have been influenced by collaborations with Z. D. Tadic and S. K. Ries who have recently completed work on the thermal reactions of *s*-triazines (Tadic and Ries, 1971).

EXPERIMENTAL MATERIALS AND METHODS

S-Triazines

Authentic s-triazines I-III, IV-VI, VII-IX, XX-XXII, XVI, and XVII were supplied by Geigy Agricultural Chemicals, Ardsley, New York. S-triazines XIII-XV were prepared photochemically (Pape and Zabik, 1970). The 2-l-s-triazines X-XVII were supplied by Tadic and Ries, and were purified to greater than 99.5% purity by column chromatography on 100 mesh silicic acid [chloroform-acetone (9:1)]. Compound XXIII was provided by CIBA Agrochemical Company, and was recrystallized from methanol until greater than 99% purity was obtained. Identity was confirmed by ir and mass spectra.

Solvents

Solvents were of analytical grade. Water used in photolysis reactions was distilled and had a pH of approximately 6.5.

Chromatography

Column and thin-layer chromatographic (tlc) separations of products were accomplished on silicic acid (AR, 100 mesh) and silica gel, respectively. The chromatographic solvent system was chloroform-acetone (9:1).

Gas-liquid partition chromatography (glpc) was achieved on a six ft stainless steel column, packed with 5% Carbowax 20-M on 60/80 mesh Gas Chrom Q (Applied Science Laboratories, Inc., State College, Pa.). Column temperatures ranged from 150-220° C. (isothermal conditions) and the carrier gas flow was 40 ml per minute (prepurified helium).

Instrumentation

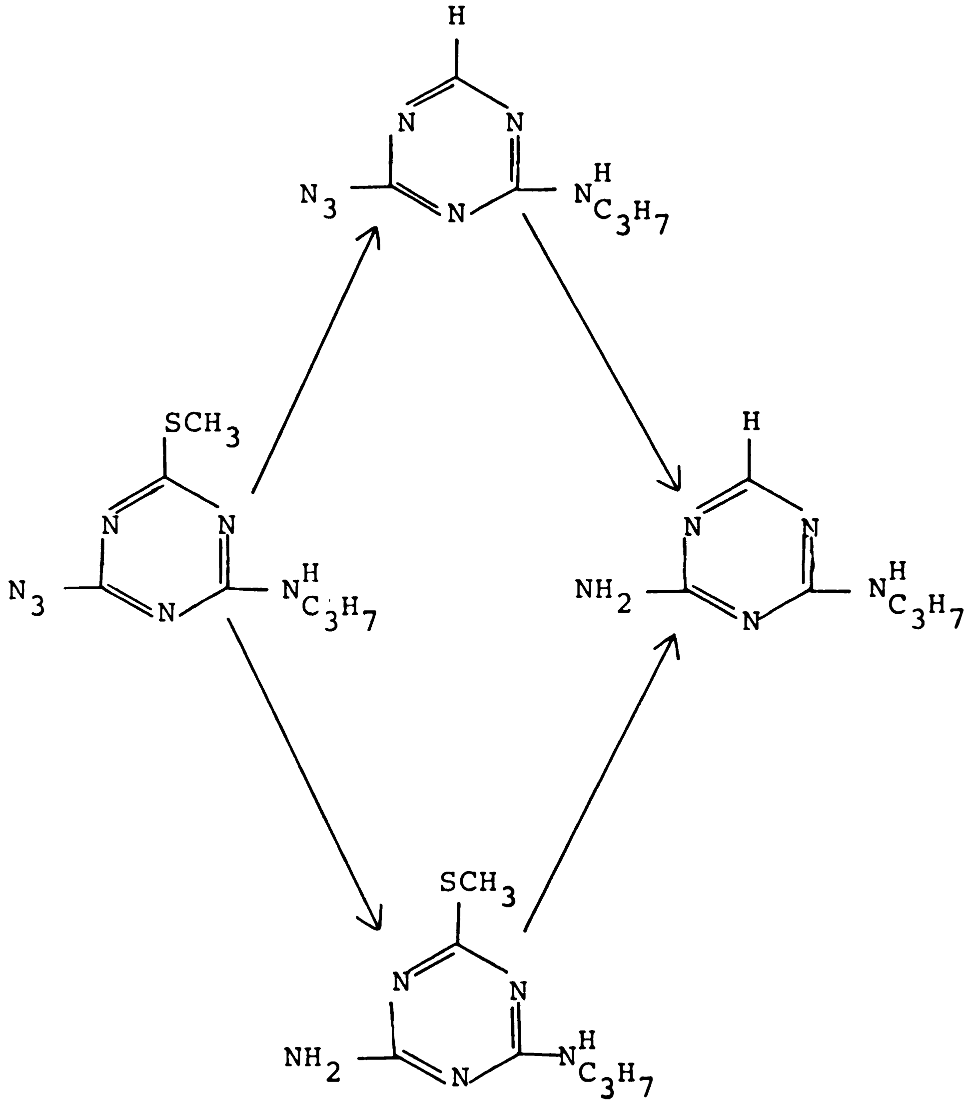
Infrared (ir) spectra were determined with a Perkin-Elmer 337 grating spectrophotomer. Ultraviolet (uv) spectra were obtained with a Beckman model DB-G instrument. The nmr spectra were obtained on a Varian A-60 high resolution spectrometer, using deuterated chloroform, with tms as an internal standard. Analysis by glpc-mass spectrometry was conducted on a LKB 9000 gas chromatograph-mass spectrometer. A 6 ft borosilicate glass column of 3% SE-30 liquid phase on 100 mesh Gas-Chrom Q was used for indirect introduction of samples. Column flow was 40 ml per minute; and operating temperature ranged from 150-220° C. (isothermal).

RESULTS AND DISCUSSION

2-Azido-4-Isopropylamino-6-Methylthio-S-Triazine

Irradiation of XXIII in methanol at 253.7 or 300 nm yielded 2-amino-isopropylamino-6-methylthio-*s*-triazine (XXIV), 2-amino-4-isopropylamino-*s*-triazine (XXV), and 2-azido-isopropylamino-*s*-triazine (XXVI), and unidentified volatile sulfur compounds. The evolution of molecular nitrogen was noted during these reactions. The identity of photoproducts XXIV, XXV, and XXVI was based on ir and mass spectra (for functional group ascriptions and spectral correlations, refer to Pape and Zabik, 1970; Plimmer, *et al.*, 1969; and Padgett and Hamner, 1958). Prolonged photolysis resulted essentially in the total conversion of XXIII to XXV, indicating that XXIV and XXVI are intermediates in the formation of XXV. The photolysis of XXIII to XXIV, and of XXVI to XXV, appears to be quite facile--understandable due to the strong driving force afforded by the loss of molecular nitrogen (Calvert and Pitts, 1966).

The photolysis of XXIII in carbon tetrachloride yielded only XXVI. There was no elimination of N_2, with the formation of XXIV or XXV. This is consistent with the inavailability of a source of reducing hydrogen, and also suggests that the elimination of the equivalent of CH_2S with the formation of XXVI is an intramolecular photoprocess. Such an intramolecular process is also consistent with the data of Plimmer, <u>et al</u>. (1969) which showed that the irradiation of prometryne (XXI) deposits yielded 4,6-bis-(isopropylamino)-<u>s</u>-triazine (with the elimination of the equivalent of CH_2S).



"Sensitized" Reactions

The irradiation of 4,6-bis(isopropylamino)-*s*-triazine (XIV) in acetone--a triplet sensitizing solvent which also may participate *via* hydrogen abstraction--at 300 nm resulted in a photoreaction. The identification of products and the generality of such "photosensitized" conversion of *s*-triazines at wavelengths greater than 290 nm are being investigated.

2-Fluoro and 2-Bromo-S-Triazines

The photolysis of XVI and XVII in a mixture of methanol and water (1:1) at 253.7 or 300 nm yielded the 2-methoxy and 2-hydroxy analog (simetone and hydroxysimazine) as the major products. The 2-hydroxy analog precipitated from solution upon concentration of the final reaction mixture, while the 2-methoxy analog was isolated by column chromatography. Their ir spectra were identical to authentic standards.

2-Iodo-S-Triazines

Photolysis of solutions of 2-I-*s*-triazines X, XI, and XII (~1 mg/ml) in dry methanol, ethanol, and *n*-butanol at 300-360 nm resulted in a progressive discoloration of solution to a deep brown and the precipitation of a crystalline product, purified by filtration and solvent washing. These precipitated photoproducts of X-XII were determined to be their respective 2-OH analogs IV, V, and VI (based on comparison of their ir spectra with authentic samples). The formation of I_2 was suggested by uv spectroscopy, and confirmed by titration with sodium thiosulfate. The presence of the respective 2-OCH_3 analogs (VII, VIII, and IX in methanol reactions) and the 2-ethoxy and 2-*n*-butoxy analogs formed in their respective alcohols was confirmed by glpc-mass spectrometry. Analysis of alkyl halides (RI) was not attempted.

These initial studies suggested the possibility of a primary photochemical process resulting in the formation of the appropriate 2-alkoxy compound, with its subsequent hydrolysis by HI to yield the 2-OH products. The participation of a solvent-cage/radical-pairing phenomenon in these processes was suggested by the absence of any detectable 2-H compounds in the methanol reactions of X-XII. Data suggest that the cleavage of the primary products--the aromatic ethers (2-OR)--was not an important photochemical process.

The photochemistry of HI, CH_3I, and *n*-C_4H_9I is well documented (Calvert and Pitts, 1966). Excitation of HI involves promotion of a non-bonding halogen electron to a higher dissociative state ($\Phi \cong 1.0$ at 253.7 nm). The solution-phase photolysis of alkyl iodides is also characterized by dissociation ($RI + \underline{hv} \rightarrow R^{\ddagger}$ 1), where $R^{\ddagger}$ is translationally and/or vibrationally excited ("hot")--i.e., that for the light and heavy dissociative fragments formed photochemically, most of the kinetic energy must be carried by the light fragment. It might be speculated that the formation of IV-VI from X-XII could occur as the result of two photochemical processes: formation of the appropriate 2-alkoxy product, and its subsequent attack by a "hot" H‡ radical formed upon the photodissociation of HI. Other experimental evidence does not support such a mechanism.

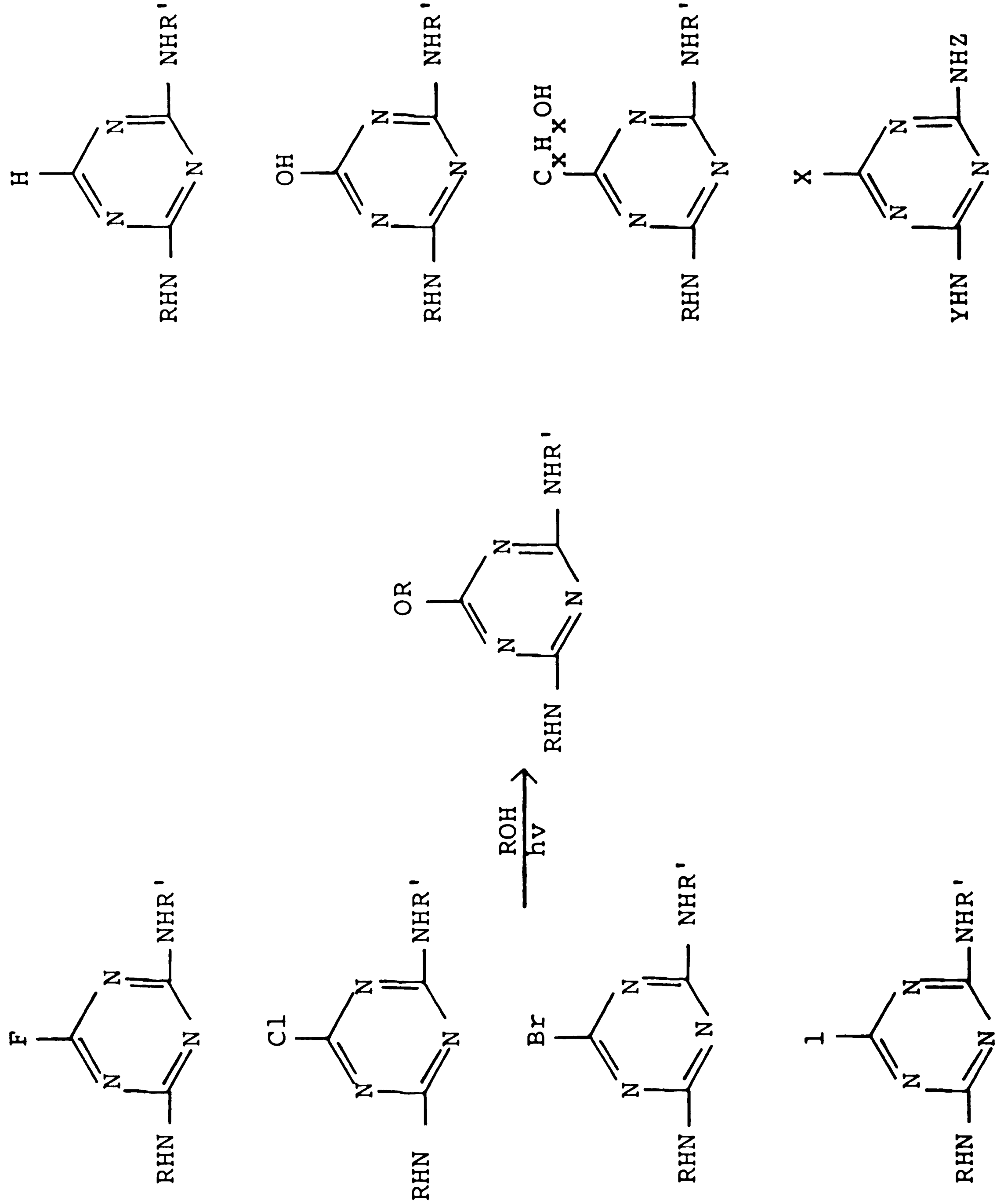
In another experiment, a solution of XI (~.001 mg/ml) in glass distilled cyclohexane was photolyzed at 300-360 nm to yield V (25%), XIV (70%), and bicyclohexane (determined by glpc-mass spectrometry). This data is not consistent with the exclusive participation of a carbonium ion mechanism: formation of V is explainable in terms of a simple solvolysis reaction with a trace of water; but XIV would not be expected if a true carbonium ion mechanism were operative: in such a dilute solution it is quite unlikely that chemical reduction of XI by HI would be significant. The operation of a competitive mechanism is suggested by this data. That the solvolysis reaction in alcoholic solution is preferred to protein abstraction in a hydrocarbon medium has recently become evident in rate studies (Pape and Zabik, unpublished data). Indeed, in a binary solvent system (cyclotexane saturated with methanol) XI yields only V and VII on photolysis.

Photolysis of XI was also carried out under different conditions during this investigation. Photolysis in

CCl_4 solution yielded unidentified products which were separated on tlc: quite likely, some of these included 2-H (XIV) and 2-X dimerization products. Again, these data support a competitive, free radical mechanism. Irradiation of crystalline XI proceeded with discoloration. No products were identified.

The nature of the leaving group appears to be critical to the rate-determining step. Iodine is an excellent leaving group, and the photolysis of X-XII proceeds much more rapidly and at longer wavelengths than I-III.

Based on the multiplicity of product formation and the well documented photochemistry of HI and alkyl halides, the product-formation reaction of the 2-iodo-*s*-triazines is viewed as a free radical/competitive-pathway mechanism which may involve radical coupling, hydrogen abstraction, and photochemical participation in the initial (intermediate) product decay, as well as chemical hydrolysis and radical trapping. An exclusive free radical photochemical process of the decay of X-XII would involve the homolytic cleavage of the triazine carbon-iodine bond to yield the respective radicals (proceeding *via* some unelucidated excited state). These two radicals would then have three alternatives: (1) recoupling to yield X-XII; (2) diffusion out of the solvent-cage to escape recoupling--necessarily followed by requisite attack on solvent or solute, most probably *via* hydrogen abstraction; or (3) hydrogen abstraction and radical coupling within the solvent-cage.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The fact that no XIV was detected in the photolysate of XI in methanol suggests the participation of a "secondary" radical-coupling/solvent-cage mechanism, where $I\cdot$ would abstract the hydroxyl hydrogen from methanol to yield $HI + \cdot OCH_3$; with $\cdot OCH_3$ and the carbon radical of the triazine ring then coupling to yield VII-IX. It is, of course, possible that $\cdot OCH_3$ could attack X-XII to yield VII-IX (analogous to the base catalyzed solvolysis of 2-halo-s-triazines in alcohols). Formation of V during the photolysis of XI is then explicable in terms of the chemical or photochemical ($H^{\ddagger}$) hydrolysis of VIII: although it is intuitively more attractive to consider the hydrolysis to be chemical under these reaction conditions, kinetic experiments are underway to remove this ambiguity. The homolytic, free radical decay of X-XII, and participation in competitive pathways is required in the CCl_4 solution-photolysis of XI. The formation of XII-XV is explicable in terms of the chemical reduction of X-XII by HI, or trapping of the triazinyl radical by HI (Calvert and Pitts, 1966). The radical may also be trapped by iodine (an even more efficient trapping agent than HI): iodine formation arising from the photodissociation of HI and alkyl halides. Under condensed-phase conditions, $H^{\ddagger}$ may participate in the reduction of X-XII or in the cleavage of VII-IX to yield products.

The photolysis of X-XII to yield IV-VI and VII-IX in methanol might be expected to proceed *via* a mechanism analogous to that of the 2-chloro-*s*-triazines--i.e., those data having been suggestive of a heterolytic cleavage of the carbon-chlorine bond to yield the carbonium ion. However, the multiplicity of these X-XII reactions in longer chain alcohols, in CCl_4, and in the crystalline state necessitates a free radical pathway.

2-Chloro-S-Triazines

Irradiation of solutions of I-III in *n*-butanol, *n*-octanol, and *n*-decanol at greater than 290 nm (borosilicate glass) and analysis of the photolysate by combined glpc-mass spectrometry demonstrated the formation of multiple triazine photoproducts: such product multiplicity requires a free radical mechanism. The glpc data indicated that the complexity of the product mixture increased with the length of the carbon chain of the alcoholic solvent used in the reaction. The dechlorinated and carbon-two *n*-alkoxy products of I-III have been definitively identified in these reactions. The classical mass spectral fragmentation patterns exhibited by these long-chain *n*-alkoxy-*s*-triazines is striking (Figure 1). Other products have glpc characteristics and mass spectra suggestive of hydroxylated alkyl and ring-substituted addition products. The photolysis of XVI-XVII under similar conditions yielded essentially identical results.

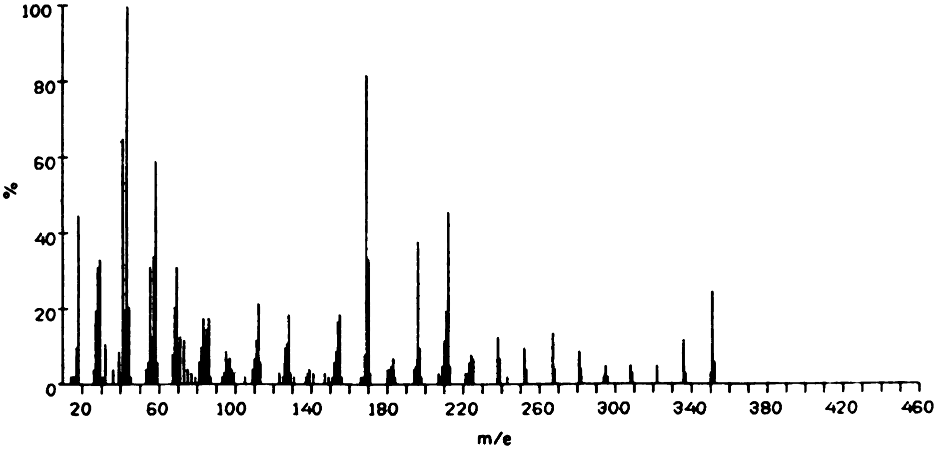
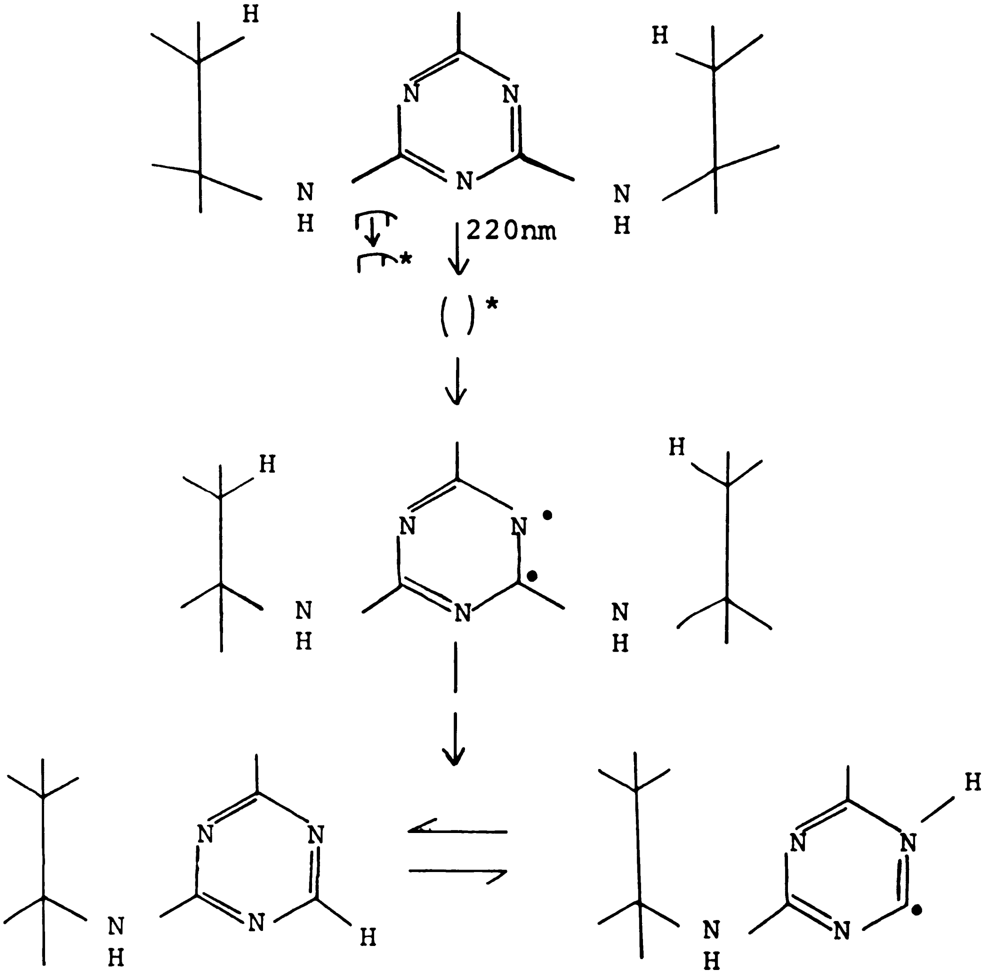


Figure 1.--Graphical representation of mass spectrum of 2-n-decoxy-4,6-bis (isopropylamino)-s-triazine (70eV)

The original interpretation of the photolytic data of I-III in methanol: (1) no evolution of HCl and (2) VII-IX as the major mechanistic product, which suggested the ionic mechanism, must be reinterpreted in terms of these new data. These original data are explicable in terms of (1) solubilities of HCl in alcohol solution; (2) formation of the hydrochloride salt of the 4,6-di(alkylamino) groups of I-III or VII-IX; and (3) a selective radical-coupling/solvent-cage preference for the formation of the carbon-two methoxy product, analogous to that noted in the reactions of X-XII.

Photochemical Dealkylation

An interesting correlation has been noted between the uv spectroscopy and photochemistry of s-triazines and recently noted thermal dealkylation reactions (Tadic and Ries, 1971). Tadic and Ries propose a cyclic transition state (Chugaev reaction) in these monomolecular dealkylations of 2-F, Cl, Br, I, OCH_3-4, 6-di(alkylamino)-s-triazines. The results of Plimmer (1969), which demonstrated the occurrence of N-dealkylation reactions at 220 nm are consistent with the participation of an analogous cyclic transition state: (see Chugaev-type reaction mechanism, p. 45). S-triazines have λ max in the 220 nm region of the uv--ascribed to a $\pi \rightarrow \pi^*$ transition of C=N of the ring (Pape and Zabik, 1970). A six-membered cyclic transition state would favor such a reaction.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CONCLUSIONS

Consideration of the uv spectroscopic data of our earlier study and comparison with data of the *s*-triazine photoconversions reported by others in natural sunlight suggests that the hydroxylation of 2-chloro-*s*-triazines to yield the 2-hydroxy analogs occurs in sunlight. The present investigation indicates that the products of *s*-triazines formed upon photolysis depends not only on the nature of the carbon-two substituent, but also upon subsequent photochemical/chemical reactions. The conversion of X-XII to IV-VI, apparently proceeding *via* an alkoxy intermediate (VII-IX), indicates the generality of these photolytic solvolyses of 2-halo-*s*-triazines in alcoholic solvents. Further studies are indicated to elucidate the role of solvent participation and competitive mechanisms. The participation of a Chugaev-type cyclic transition state in the photochemical N-dealkylation reactions of a variety of *s*-triazines is suggested by uv, photochemical, and thermal data. The kinetics and excited states of these N-dealkylations are being investigated. The facile photodecomposition of XXIII is expected to occur under field conditions to yield XXIV, XXV, XXVI, N_2, and volatile sulfur compounds. The hydrogen substitution at carbon-six appears to be intramolecular. The photochemical "sensitization" of the *s*-triazine ring is indicated as a possible avenue for the further degradation of metabolic and photolytic products (2-hydroxy and 2-H analogs).

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