Date: December 15, 1951

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Title of Study: The Reaction of 1,3,5-Trisubstituted Hexahydro-1,3,5-triazines with Carbon Disulfide.

Number of Pages in Study: 58

Under Direction of What Department: Chemistry

Scope of Study: The original purpose of the investigation was to determine whether N,N'-disubstituted methylenediamines would react with carbon disulfide and then with formaldehyde in a manner analogous to the corresponding N,N'-disubstituted ethylenediamines. The ethylenediamines react with carbon disulfide to give the inner salts of N-alkyl-N-(β-alkylaminoethyl)dithiocarbamic acids. These salts, when treated with formaldehyde, react to form 3,6-disubstituted hexahydro-1,3,6-thiadiazepine-2-thiones. These seven-membered heterocyclic compounds may be thermally decomposed to 1,3-disubstituted-2-imidazolidinethiones. The investigation was later shifted to the reaction of 1,3,5-trisubstituted hexahydro-1,3,5-triazines with carbon disulfide, which produced compounds of the type sought. The pyrolysis of these reaction products was also studied.

Findings and Conclusions: The N,N'-disubstituted methylenes investigated did not react in the manner expected. The methylenediamines used were aryl substituted, since the alkyl substituted homologs are not stable. Attempts to prepare N,N'-disubstituted methylenediamines resulted in the formation of cyclic 1,3,5-trisubstituted hexahydro-1,3,5-triazines. It was found that these compounds react with carbon disulfide to produce 3,5-disubstituted tetrahydro-1,3,5-thiadiazine-2-thiones. These latter substances were the compounds expected from the reaction of disubstituted methylenediamines with carbon disulfide and formaldehyde. The homologs prepared are: ethyl, isopropyl, cyclohexyl, β-phenylethyl, benzyl, phenyl, p-tolyl and p-phenetyl. This class of compounds has been previously reported in the literature, but none of the homologs prepared, with the exception of the ethyl, is recorded. These substances were decomposed by pyrolysis and in the cases of the isopropyl, cyclohexyl, β-phenylethyl, p-tolyl, and p-phenetyl homologs, the products were 1,3,5-trisubstituted hexahydro-1,3,5-triazine-2-thiones. This class of compounds has not been reported in the literature.

ADVISER'S APPROVAL J. A. Shotton

by Ernest M. Hodnett

THE REACTION OF 1,3,5-TRISUBSTITUTED HEXAHYDRO-1,3,5-TRIAZINES WITH CARBON DISULFIDE

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by

A. MERRILL SCHNITZER

Master of Science
Oklahoma Agricultural and Mechanical College
Stillwater, Oklahoma
1949

Submitted to the Department of Chemistry
Oklahoma Agricultural and Mechanical College
In Partial Fulfillment of the Requirements
for the Degree of
DOCTOR OF PHILOSOPHY
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ACKNOWLEDGMENT

The author wishes to express his sincere gratitude to Dr. J. A. Shotton, under whose direction and guidance this work has been done, and to other members of the Department of Chemistry for their suggestions and helpful criticism.

He also wishes to acknowledge the financial aid rendered by the Oklahoma A. and M. College in the form of a graduate fellowship in the Chemistry Department.

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INTRODUCTION

The original purpose of this investigation was to determine whether N,N'-disubstitutedmethylenediamines would undergo reactions analogous to those of the corresponding N,N'-disubstitutedethylenediamines when treated with certain reagents. N,N'-dialkylethylenediamines react with carbon disulfide and formaldehyde to give heterocyclic compounds that are active vulcanization accelerators.

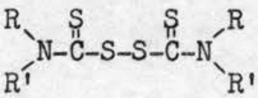
Although some methylenediamines are stable enough to be isolated and kept for considerable periods, most of these compounds are unstable and tend to polymerize or decompose to give more stable compounds. The methylenediamines investigated did not give the desired reactions.

It was found in the course of the investigation that the cyclic trimers of substituted methyleneimines (Azomethines, Schiff bases), the 1,3,5-trisubstitutedhexahydro-1,3,5-triazines, react with carbon disulfide to give products of the type desired. A survey of the literature showed that this type of reaction has been mentioned only briefly. Several of these cyclic trimers were prepared and treated with carbon disulfide, and the reaction products, as well as the compounds resulting from their thermal decomposition, were investigated.

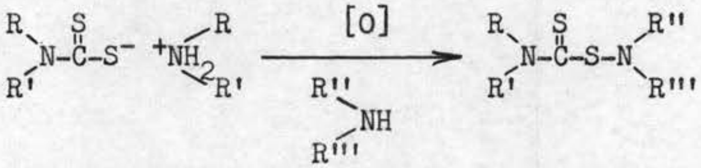
HISTORICAL

The reaction of dialkylmonoamines and carbon disulfide has been widely studied, largely because the products are useful as vulcanization accelerators. The reaction produces the dialkylammonium salts of dialkyldithiocarbamic acids:

These salts may be oxidized to thiuram disulfides:



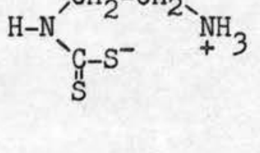
In the presence of primary or secondary amines, the product may be dithiocarbamylsulfenamides (1):



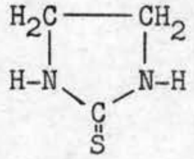
which may be thermally decomposed, losing an atom of sulfur, to yield tetrasubstituted thioureas.

Donia, Shotton, Bentz, and Smith (2) found that, in general, the reactions of N,N'-dialkylethylenediamines with carbon disulfide are analogous to the reactions of the dialkylmonoamines. However, the ethylenediamines yield cyclic products, owing to the connection between the two nitrogen atoms.

Hofmann (3) first reported the reaction of ethylenediamine with carbon disulfide to yield N-(β-aminoethyl)dithiocarbamic acid (shown here in the dipolar ion form):

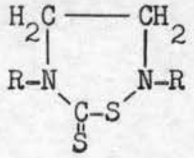


He thermally decomposed this acid and obtained hydrogen sulfide and 2-imidazolidinethione:



which may be considered as a cyclic derivative of thiourea.

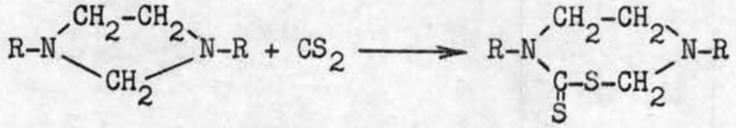
Other investigators have extended these reactions to N-substituted-ethylenediamines. Donia, et al., (2) prepared a series of N-alkyl-N-(β-alkylaminoethyl)dithiocarbamic acid inner salts by the reaction of N,N'-dialkylethylenediamines with carbon disulfide. They found that these salts could be oxidized in alkaline solution with iodine-potassium iodide reagent to give 2,5-dialkyltetrahydro-1,2,5-thiadiazine-6-thiones:



which may be considered to be cyclic dithiocarbamylsulfenamides. These compounds can be thermally decomposed, with the loss of sulfur, to the same 2-imidazolidinethiones as are obtained by decomposing the dithiocarbamic acid inner salts. It was found that the stability of the tetrahydrothiadiazine ring is related to the size of the alkyl substituents attached to the nitrogen atoms. The isopropyl compound is less stable than the cyclohexyl compound, and the ethyl compound is quite unstable, being obtained only in low yields.

Donia and co-workers (4) also studied the reactions of N,N'-dialkyldiamines with carbon disulfide. These reactions were found to be analogous to those of the dialkylmonoamines, except that ring compounds were formed. These investigators prepared a series of 1,3-imidazolidines by condensation of formaldehyde and other aldehydes with N,N'-dialkylethylenediamines.

Treatment of the 1,3-dialkylimidazolidines with carbon disulfide in ether or alcohol results in the formation of 3,6-dialkylhexahydro-1,3,6-thiadiazepine-2-thiones:



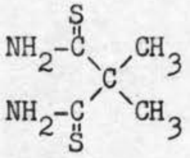
These compounds are relatively unstable, and treatment with dilute ammonia water effects removal of the methylene group to form N-alkyl-N-(β-alkylaminoethyl)dithiocarbamic acid inner salts. They are decomposed also by heat or on standing at room temperature, with the splitting out of thioformaldehyde and the formation of 1,3-dialkyl-2-imidazolidinethiones.

Delepine (5) treated the cyclic trimer of methylamine and formaldehyde, 1,3,5-trimethylhexahydro-1,3,5-triazine, with carbon disulfide and obtained a compound that he called "dimethylformocarbothialdine", m.p. 96°C., in the belief that it was an isomer of "carbothialdine".

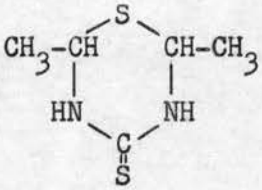
The compound long known as "carbothialdine" was first prepared through the action of carbon disulfide on acetaldehyde-ammonia by Redtenbacher and Liebig (6), and was thought to be related to the thialdines. The thialdines, which are 1,3,5-dithiazines, result from the action of hydrogen sulfide on aldehyde-ammonias. "Carbothialdine" was also prepared by Mulder (7) by condensing acetaldehyde with ammonium dithiocarbamate or trithiocarbonate. This compound is thermally unstable, and the decomposition point has been reported as 120° by Cohn (8) and 135° by Ainley and co-workers (9). It is difficult to purify, owing to rapid decomposition in solvents, including water and alcohols. It is soluble in dilute acids, though again with decomposition. Claus (10) found that iodine, nitrous acid, or mercuric chloride also cause the compound to decompose, with the formation of ammonium thiocyanate, acetaldehyde, ammonia, and carbon disulfide.

Guareschi (11) found that ferric thiocyanate is formed when "carbothialdine" is treated with ferric chloride; but that oxidation with ferric chloride in dilute acids, or with chlorine water, produces thiuram disulfide, indicating that the dithiocarbamate structure is present within the molecule. Mulder (7) and Levi and Gimignani (12) found that on treatment with heavy-metal salts, dithiocarbamic acids containing aldehyde residues are formed.

Several structures have been proposed for "carbothialdine" and its homologs. Without chemical evidence, Hlasiwetz (13) suggested the structure:

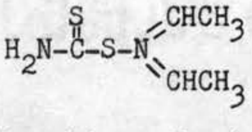


and the name "thiuram carbomethyl" by analogy with the thiuram disulfides. Claus (10) supported the structure:



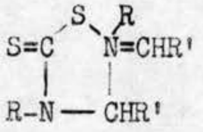
He believed that the formation of thiocyanates in the decomposition reactions indicated that a thiourea-type structure was present, but this is not necessarily true, since aqueous ammonium dithiocarbamate gives ammonium thiocyanate upon standing.

Mulder (7) proposed the structure:

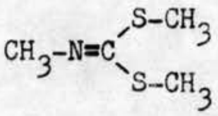


to account for the ease of formation of metallic dithiocarbamates upon treatment of "carbothialdine" with heavy metal salts. This formula was accepted by Guareschi (11), Levi and Gimianini (12), and Levi (15).

Delepine (5) suggested still another structure for "carbothialdine" to account for the formation of the dimethyl homolog that he prepared. His suggested formula is:

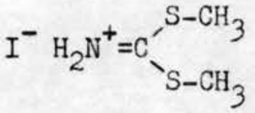


in which R = H and R' = CH_3 for "carbothialdine" itself, and R = CH_3 and R' = H for the "dimethyl" homolog. This formula was accepted by Marks (28) and Powers (29). The Mulder formula could not hold for "dimethylformocarbothialdine", since this compound must have a methyl group on each nitrogen. The dimethyl compound reacts with methyl iodide to give di(methylthio)-N-methylmethyleneimine:



$$CH_3-N=C\begin{matrix} \diagup S-CH_3 \\ \diagdown S-CH_3 \end{matrix}$$

Levi and Gimignani found that "carbothialdine" itself reacts with methyl iodide to give di(methylthio)methylenimine hydroiodide:

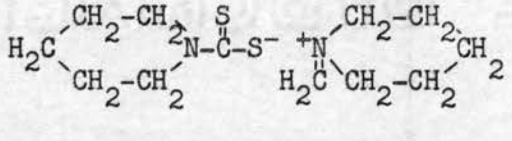


$$I^- \; H_2N^+=C\begin{matrix} \diagup S-CH_3 \\ \diagdown S-CH_3 \end{matrix}$$

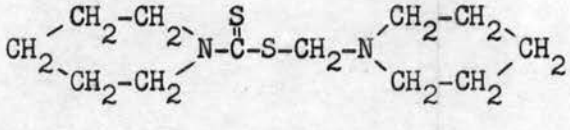
Di(methylthio)methyleneimine is usually obtained by methylation of ammonium dithiocarbamate.

Bodendorf (14) obtained a compound, m.p. 106-107°C., from formaldehyde and methylammonium N-methyldithiocarbamate, which he called "2,4-dimethyl-2-methylenecarbothialdine". He assumed that this was the same compound as that prepared by Delepine, and Ainley and co-workers (9) proved the assumption correct. These investigators do not consider any of the proposed formulas shown above for "carbothialdine" as being satisfactory, since they all fail in some respect. Neither the formula of Hlasiwetz nor that of Claus are in accord with the methods of formation and reactions of "carbothialdine" that have been reported. The formula of Mulder, which has been accepted by Levi, is not satisfactory for the dimethyl analog prepared by Delepine. Furthermore, this formula would require salt-like properties, since it contains a pentavalent nitrogen atom.

Levi(15) treated piperidinium N,N-cyclopentamethylenedithiocarbamate with formaldehyde and obtained a compound, m.p. 61°C., which he called piperidylmethyleneammonium pentamethylenedithiocarbamate, and which would have the structure:

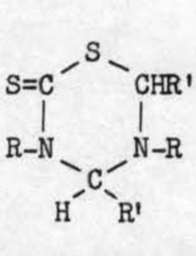


This compound, according to the above structure, is ionic, and would have the same salt-like properties as would "carbothialdine" if Mulder's formula were correct. Delepine's proposed structure also contains a pentavalent nitrogen atom, and would require ionic properties for "carbothialdine". Actually neither Levi's compound nor "carbothialdine" appears to be ionic in nature. Donia and co-workers (4) have shown by conductivity measurements that Levi's compound is not electrovalent, but covalent, and they propose the structure:

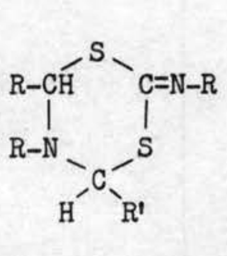


Ainley and co-workers suggested that the formula for "carbothialdine" and its homologs, based on chemical evidence, must be one of two possibilities:

(A)

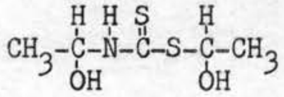


(B)



They suggest that the formation of "carbothialdine" from acetaldehyde, ammonia, and formaldehyde proceeds through a dihydroxy intermediate, either:

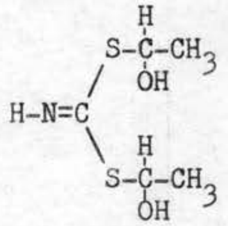
(A')



$CH_3-\underset{OH}{\overset{H}{C}}-\overset{H}{N}-\overset{S}{\overset{\|}{C}}-S-\underset{OH}{\overset{H}{C}}-CH_3$

or

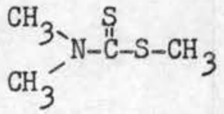
(B')



Either of these intermediates could, on condensation with ammonia, cyclize to give the final heterocyclic compound. Intermediate (A') would produce structure (A), whereas intermediate (B') would produce structure (B). These authors attempted to differentiate between the two structures that they propose for "carbothialdine" by chemical methods. Attempts were made to convert the lactone sulfur of structure (A) into oxygen by treatment with mercuric oxide, but in all cases decomposition occurred. Since chemical methods failed to distinguish between the possibilities, ultraviolet absorption spectra were used.

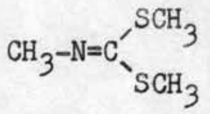
They compared the absorption spectra of methyl dimethyldithiocarbamate:

(C)



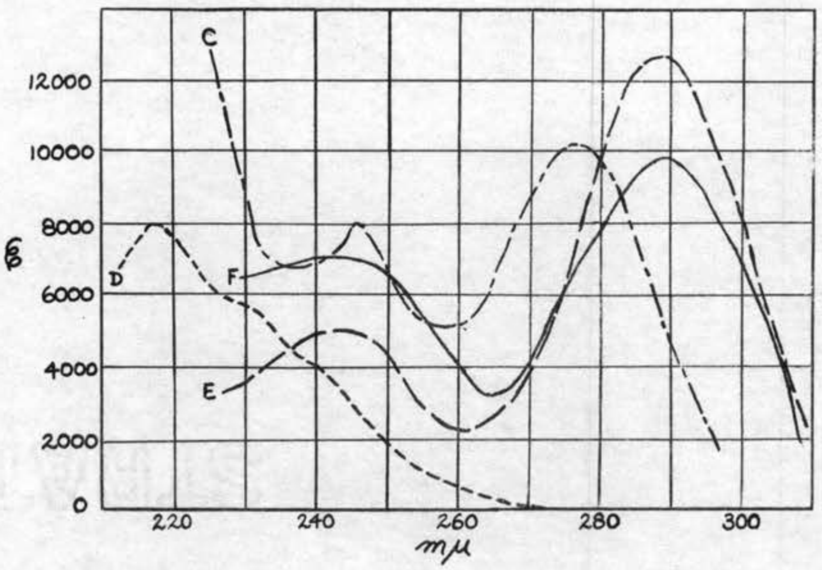
which they claim would be analogous to their proposed structure (A) for "carbothialdine", and di(methylthio)-N-methylmethyleneimine:

(D)



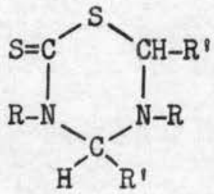
which would be analogous to proposed structure (B), with the absorption spectra of "carbothialdine" and "dimethylformocarbothialdine".

It was found that "carbothialdine", "dimethylformocarbothialdine", and methyl dimethyldithiocarbamate (C) gave similar curves, with a marked peak in the range 276-289 mμ, and a smaller peak at about 245 mμ. Di-(methylthio)-N-methylmethyleneimine (D) gave only a low general end absorption in this range. The curves obtained are shown below:



(C) Methyl dimethyldithiocarbamate (E) "Carbothialdine"
(D) Di(methylthio)-N-methylformimine (F) "Dimethylformocarbothialdine"

From this information, these investigators conclude that the correct structure for "carbothialdine" and its homologs is the proposed structure (A), which is:



"Carbothialdine" would have R = H, and R' = CH_3, while "dimethylformocarbothialdine" would have R = CH_3 and R' = H. These investigators name these compounds 2-thio-4,6-dimethyltetrahydro-1,3,5-thiadiazine and 2-thio-3,5-dimethyltetrahydro-1,3,5-thiadiazine respectively. The compounds listed as prepared by these authors are:

2-thio-3-phenyl-5-methyltetrahydro-1,3,5-thiadiazine -- m.p. 148°
2-thio-3-α-naphthyl-5-methyltetrahydro-1,3,5-thiadiazine -- m.p. 160-61°
2-thio-3-(p-hydroxyphenyl)-5-methyltetrahydro-1,3,5-thiadiazine-- m.p. 163-64°
2-thio-3-(3'-chloro-4'-hydroxyphenyl)-5-methyltetrahydro-1,3,5-thiadiazine -- m.p. 146°
2-thio-3-(p-dimethylaminophenyl)-5-methyltetrahydro-1,3,5-thiadiazine -- m.p. 168-69°
2-thio-3-phenyl-5-(β-diethylaminoethyl)tetrahydro-1,3,5-thiadiazine -- m.p. 103-4°

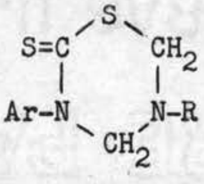
2-thio-3-phenyl-5-(β-hydroxyethyl)tetrahydro-1,3,5-thiadiazine
-- m.p. 136° (probably impure)

Two general methods of preparation are given by Ainley and co-workers for synthesis of these 3-aryl-5-alkyl homologs:

> METHOD I. The barium salt of the aryldithiocarbamic acid was precipitated by addition of barium chloride to a solution of the ammonium salt, followed by double decomposition with the sulfate of the aliphatic amine. The barium sulfate was removed, formaldehyde added, and the precipitated product recrystallized.
>
> METHOD II. In the case of the aminophenols, the starting point was the sodium aryldithiocarbamate, which was prepared from the sodium salt of the aminophenol.

It was found that, in some cases, the alkylammonium salt of the aryldithiocarbamic acid (prepared by direct reaction of the arylamine, carbon disulfide, and alkylamine) would react with formaldehyde to give the desired product in good yield.

Some of the above 2-thio-3-aryl-5-alkyltetrahydro-1,3,5-thiadiazines, along with other homologs, have been tested as insecticides by Davies and Sexton (16). Homologs investigated, other than the listed compounds, are: 3-phenyl-5-propyl; 3-phenyl; 3-phenyl-5-ethyl; 3-phenyl-5-butyl; 3-phenyl-5-isobutyl; 3-phenyl-5-cyclohexyl; 3-(p-tolyl)-5-methyl; 5,5'-ethylenebis(3-phenyl); 5,5'-hexamethylenebis(3-phenyl); 3-(p-chlorophenyl)-5-methyl; 3-methyl-5-ethyl; 5,5'-ethylenebis(3-methyl); and 3,5-diethyl. Gudgeon, Harland, and Sexton (17) and Harland and Sexton (18) have obtained patents for the use of compounds of the type:



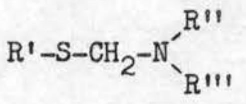
as insecticides, where Ar = various aryl groups, including substituted aryl groups, and R = alkyl or cycloalkyl groups, including those containing hydroxyl radicals.

The reaction products of primary and secondary amines, aldehydes, and carbon disulfide have been patented by numerous individuals as vulcanization accelerators, although in most instances, the products have not been characterized or identified. Scott has patented as accelerators the compounds formed by the reaction of formaldehyde and the condensation product of three moles of acetaldehyde and two moles of aniline (19); the carbon disulfide derivatives of the reaction products of secondary amines and aldehydes (20); the products obtained from the action of formaldehyde on the condensation product of aniline and "a straight-chain aldehyde containing a plurality of carbon atoms" (21); the carbon disulfide derivative of the reaction product of diethylamine and paraformaldehyde (22); the carbon disulfide derivative of the reaction product of piperidine and furfural (23); and the reaction product of carbon disulfide and the product formed by treating a secondary amine, such as dibenzylamine, with an aldehyde, such as paraformaldehyde (24).

Moore (25) patented a stabilized emulsion of the carbon disulfide derivative of the reaction product of a secondary aliphatic amine, such as piperidine, and an aliphatic aldehyde such as formaldehyde, for use as a vulcanization accelerator.

Sibley (26) patented as an accelerator the product obtained by treating a mono-N-alkylcyclohexylamine, such as N-methyl- or N-ethylcyclohexylamine, with an aldehyde such as formaldehyde, using a molar ratio of 2:1, and further treating this product with carbon disulfide.

Sloan (27) has patented an accelerator which he identifies as carbamyl diethylaminomethyl sulfide or other compounds of the general formula:

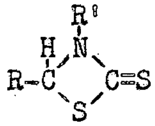


$$R'\text{-}S\text{-}CH_2\text{-}N\begin{matrix} R'' \\ R''' \end{matrix}$$

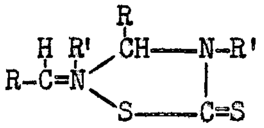
in which R' is a thiocarbamyl group and R'' and R''' are hydrocarbon radicals, not more than one of which is aromatic. The method of preparation was not indicated.

Marks (28) has patented accelerators made from equimolar proportions of aldehydes, amines, and carbon disulfide. These compounds were indicated as being dimethylene-1,3-thiaimines of the type:

(G)



He also claimed accelerators prepared from two moles of aldehyde, two moles of amine, and one mole of carbon disulfide, which he called "carbothialdines". The structure for these compounds is given as:



This is the structure proposed by Delepine for "carbothialdine". Accelerators of this type were also claimed to have been made via the ammonium dithiocarbamate and via the anhydro-aldehyde-amine. Aldehydes that are indicated are formaldehyde, acetaldehyde, propionaldehyde, butyraldehyde, and benzaldehyde; and the amines mentioned are methyl, ethyl, hydroxyethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, aniline, and o- and p-toluidine. It is also indicated that molar ratios of aldehyde, amine, and carbon disulfide may be 1:1:1, 2:1:1, 2:2:1, or 4:2:1 for preparing accelerators.

Powers (29) obtained a patent, assigned to the same company as was Marks', making many of the same claims as did Marks. However, Powers named the four-membered heterocyclic compounds (E) as "N-alkyl-(or aryl-) α-mercapto-alkyl-dithio-carbamolactones", considering them as being the lactones of N-alkyl-(or aryl-)α-mercapto-alkyl-dithiocarbamic acids. He claims the same reagents as did Marks. He lists six different "carbothialdines" and six "dithiocarbamolactones", although he does not give the physical properties or analytical data for these compounds, nor does he describe how he arrived at the structures that are indicated. Powers also patented the product obtained by treating the dithiocarbamate from carbon disulfide and an aromatic amine with an aldehyde (30). In addition, he patented the dark, high-boiling, viscous liquids or resinous solids he obtained by causing to react, in the absence of substantial quantities of added acid, aldehydes, amines, and carbon disulfide, and removing water by vacuum distillation (31). The structure of these compounds was not indicated.

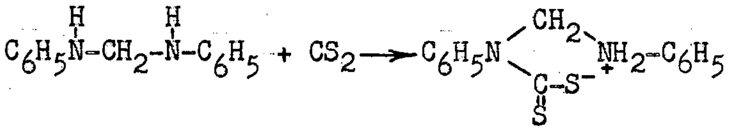
Twiss and Jones (32) patented the accelerator made when an aldehyde, other than formaldehyde, and a secondary amine are blended into the rubber mixture to be vulcanized, and carbon disulfide is added. The structure of the products was not given.

Lichty (33) patented accelerators made from formaldehyde and dithiocarbamic acids. A preference was expressed for dithiocarbamates derived from secondary amines containing at least one aliphatic (including cycloaliphatic) and one substituted or unsubstituted radical, such as benzyl, β-phenethyl, tetrahydrofurfuryl, or furfuryl. An equimolar or excess amount of formaldehyde was used.

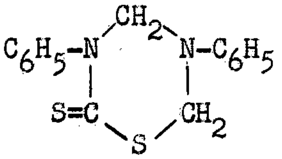
DISCUSSION

I. PREPARATION OF DISUBSTITUTED METHYLENEDIAMINES AND REACTIONS WITH CARBON DISULFIDE AND FORMALDEHYDE

It was hoped that when methylenedianiline was treated with carbon disulfide, the following reaction would occur:

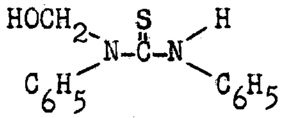


This reaction would be analogous to that reported for dialkylethylenediamines by Donia, Shotton, Bentz, and Smith (2). The product, N-phenyl-N-(phenylaminomethyl)dithiocarbamic acid, when treated with formaldehyde, should give the cyclic compound:



if it reacts as do the disubstituted ethylenediamines.

Methylenedianiline was prepared by the reaction of aniline with formaldehyde in a basic aqueous solution, after the method of Eberhard and Weltner (34). Treatment of this compound with carbon disulfide in cold acetone or alcohol gave no precipitate; a precipitate would be expected if the inner salt had formed. When the solution was heated and then cooled, a compound precipitated in the form of white, shiny plates, and melted at 150.8-151.8° after recrystallization. This substance, when heated with formalin, dissolved, and another compound, also in the form of white shiny plates, appeared upon cooling of the solution. This material melted at 125.5-126.5°, with the evolution of a gas, which was found to be formaldehyde. It was not possible to recrystallize this compound, due to the ease with which it decomposed. The carbon disulfide reaction product proved to be thiocarbanilide, which was formed as a result of decomposition during heating. Grignard (35) states that reactions between amines and carbon disulfide, which would be expected to give dithiocarbamic acids, often give thiourea derivatives. The formaldehyde-thiocarbanilide reaction product was not characterized, since it was not a compound of the type sought. However, on the basis of carbon-hydrogen analyses and its ease of liberation of formaldehyde, it was thought to be the monomethylol derivative of thiocarbanilide:



The treatment of methylenedianiline with carbon disulfide and then with formaldehyde, without heating, was investigated. In the presence or absence of solvents at ice bath temperatures a white solid mixture precipitated. Part of this precipitate was soluble in acetone and part insoluble. The bulk of the soluble material was the cyclic trimer of N-phenylmethyleneimine, 1,3,5-triphenylhexahydro-1,3,5-triazine, $(C_6H_5N{=}CH_2)_3$, although a small amount of a compound melting at 169-170° was recovered after several recrystallizations. This higher-melting material was later determined to be the desired heterocyclic compound; however, the yield by this method of preparation was very low. The insoluble material was a higher polymeric form of N-phenylmethyleneimine. Both the trimer and the higher polymer have been studied by Miller and Wagner (36).

It was thought that the ammonium salt of N-phenyl-N-(phenylaminomethyl)dithiocarbamic acid might react with formaldehyde to give the desired product. The preparation of this salt was attempted by the action of ammonium hydroxide and carbon disulfide on methylenedianiline in solution, but when this reaction was attempted at ice bath temperatures, ammonium

N-phenyldithiocarbamate formed, due to decomposition of the methylenedianiline. If the solution was allowed to stand or if it was heated, hydrogen sulfide was eliminated and thiocarbanilide formed.

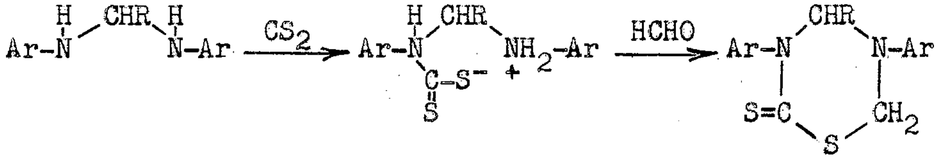
Both primary and secondary aliphatic amines react with carbon disulfide in alcoholic solutions to give alkyl- or dialkyldithiocarbamic acids, which combine with more of the amine to form salts. With aromatic amines a similar reaction does not occur unless aqueous ammonia or a metallic hydroxide is added. Under these conditions a salt of an aryldithiocarbamic acid is formed; otherwise, in the absence of these reagents there is no reaction in the cold, but when the solution is heated, hydrogen sulfide is eliminated, and a symmetrical disubstituted thiourea is formed. Fry and Culp (37) reported that in the case of secondary amines, hydrogen sulfide may not be eliminated, and thiuram disulfide derivatives will be formed. Sidgwick (38) states that the difference in the ease of formation of the dithiocarbamic acids is probably due to the weaker basic nature of the aromatic amines in comparison with the aliphatic amines. Methylenedianiline did not form an internal dithiocarbamic salt, probably due to the influence of the phenyl groups on the nitrogen atoms. It seemed desirable to try diamines that were less aromatic in nature.

Ethylidenedianiline, 1,1-(N,N'-diphenyl)diaminoethane, was prepared by treating aniline with acetaldehyde in an aqueous solution according to Eibner (39), and was treated with carbon disulfide and formaldehyde in cold solution in the same manner as was the methylene homolog. As with the methylene compound, the products of the reaction were the cyclic trimer and higher polymer of N-phenylmethyleneimine. None of the desired sulfur-containing substance was obtained. When ethylidenedianiline was heated with carbon disulfide in solution decomposition occurred, and thiocarbanilide was obtained as before.

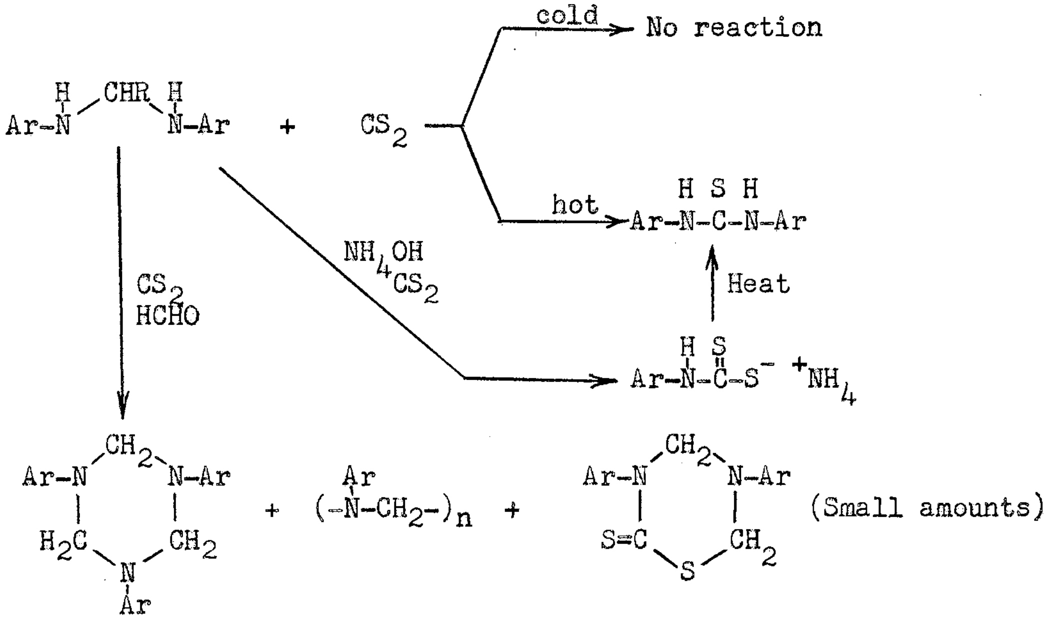
Propylidenedianiline was prepared by the action of propionaldehyde on aniline according to the method of Eibner (40). Attempts to obtain the dithiocarbamic acid of this compound by reaction with carbon disulfide were not successful. The attempted preparation of the ammonium salt of this acid resulted in decomposition of the starting material, and only ammonium N-phenyldithiocarbamate was recovered. The direct action of formaldehyde and carbon disulfide on propylidenedianiline again did not yield the desired type product.

Ethylidenedi-p-toluidide was prepared by treating an aqueous suspension of p-toluidine with acetaldehyde. Treatment with carbon disulfide gave no dithiocarbamic salt, and treatment with carbon disulfide and formaldehyde did not produce the desired type of heterocyclic compound.

The reactions that were attempted, using diarylmethylenediamines are:



The products that were identified indicate that the reactions actually were:

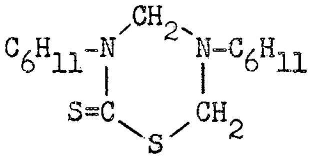


In the cases of diamines in which R = alkyl, treatment with carbon disulfide and formaldehyde apparently caused them to decompose, since no hexahydrotriazines were recovered containing an alkyl group on a carbon atom. It appeared that aryl-substituted methylenediamines would not give satisfactory yields of the desired 3,5-disubstituted tetrahydro-1,3,5-thiodiazine-2-thiones when treated with carbon disulfide and formaldehyde.

II. PREPARATION OF 1,3,5-TRIALKYLHEXAHYDRO-1,3,5-TRIAZINES AND REACTION WITH CARBON DISULFIDE

Although N,N'-dicyclohexylmethylenediamine had not been reported in the literature, an attempt was made to prepare this compound by the reaction of cyclohexylamine and methylene dichloride, in a manner similar to that used to prepare N,N'-dialkylethylenediamines by Donia and co-workers (2). A solid compound in the form of white needles was recovered, and after purification, melted at 72.2-72.8°. A small amount of a crystalline material melting at 96-98° was also isolated, but not identified. In addition, a high-boiling, very viscous, amber-colored substance was obtained, which would not crystallize from alcohol or acetone solutions. The crystalline material melting at 72.2-72.8° was found to be 1,3,5-tricyclohexylhexahydro-1,3,5-triazine, rather than the N,N'-dicyclohexylmethylenediamine that was desired. The high-boiling, amber-colored substance was not characterized, but it was believed to be a polymeric material. The cyclic trimers of the methyleneimines can be prepared in many cases by the reaction of amines and formaldehyde, and since recovery of the product is simpler and less time consuming, this method was used for subsequent preparations of this compound and other homologs. Aldehydes of molecular weight above that of formaldehyde tend to give products other than the cyclic trimers when treated with primary amines. The reactions of aldehydes and amines have been reviewed by Sprung (41).

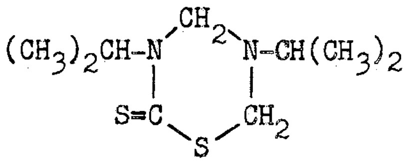
The 1,3,5-tricyclohexylhexahydro-1,3,5-triazine was treated at room temperature with carbon disulfide, but no reaction occurred. When refluxed in acetone or alcohol, however, the reagents did react, and a white, crystalline compound was obtained which melted after recrystallization at 145.8-146.2°. This compound was believed to be of the type desired, and to have the following structure:



Evidence in support of this structure is given later. This compound may be named 3,5-dicyclohexyltetrahydro-1,3,5-thiadiazine-2-thione. A review of the literature revealed only one instance in which the reaction of carbon disulfide and a methyleneimine trimer had been described, that of the N-methyl compound, which was reported by Delepine (5). The reaction has been briefly mentioned elsewhere by Davies and Sexton (16), Marks (28), and Powers (29).

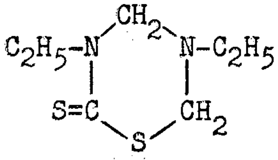
An attempt was made to prepare 1,3,5-tricyclohexyl-2,4,6-trimethylhexahydro-1,3,5-triazine by the action of acetaldehyde on cyclohexylamine. None of this material was obtained, however. The preparation of 1,3,5-tricyclohexyl-2,4,6-triethylhexahydrotriazine by the action of propionaldehyde on cyclohexylamine was attempted, but again none of the desired product was recovered.

1,3,5-Triisopropylhexahydro-1,3,5-triazine was prepared by the action of formaldehyde on isopropylamine in aqueous solution. This compound was refluxed with carbon disulfide in acetone and a white crystalline compound was obtained. After recrystallization, this material melted at 124.8-125.4°. This compound was found to be the desired product, 3,5-diisopropyltetrahydro-1,3,5-thiadiazine-2-thione:



1,3,5-Tributylhexahydro-1,3,5-triazine was prepared by the action of formaldehyde on n-butylamine in aqueous solution. This compound was refluxed with carbon disulfide in acetone solution, but no solid could be recovered. An attempt was made to purify the oily liquid from the reaction by distillation at reduced pressure, but decomposition occurred and none of the desired product could be recovered. This product was not characterized since it could not be purified. However, thioformaldehyde was split out during the distillation attempt, which indicated that the desired cyclic compound might have been present, since this type of thermal decomposition was observed for the cyclohexyl and isopropyl compounds.

1,3,5-Triethylhexahydro-1,3,5-triazine was prepared by the action of formaldehyde on an aqueous solution of ethylamine. Refluxing this compound with carbon disulfide in acetone produced a white crystalline solid, melting at 73.4-74.9° after recrystallization. This solid was 3,5-diethyltetrahydro-1,3,5-thiadiazine-2-thione:



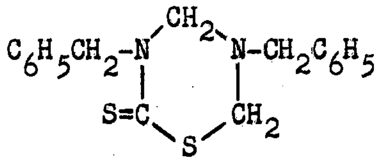
Ethanolamine was treated with formaldehyde in aqueous solution. The reaction product, b.p. 109-111° (6mm.), was refluxed with carbon disulfide in acetone solution. None of the desired product was recovered, and only a foul-smelling, dark-colored, water-soluble liquid was obtained.

n-Hexylamine was treated in aqueous solution with formalin, and the resulting product was refluxed for several hours in alcoholic solution with carbon disulfide, and a reaction was indicated by the formation of an oil.

It was not possible to purify the product due to decomposition of the oil when distilled, even under reduced pressure, and thioformaldehyde was formed as in the case of the butyl analog. Attempts to obtain crystals from the oil were unsuccessful.

II. PREPARATION OF 1,3,5-TRI(ARALKYL)HEXAHYDRO-1,3,5-TRIAZINES AND REACTION WITH CARBON DISULFIDE

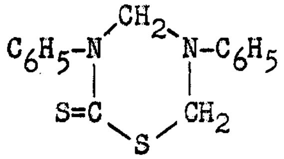
An aqueous solution of benzylamine was treated with formaldehyde and the oil that formed was refluxed with carbon disulfide in acetone. None of the desired product was obtained, but only a brown, foul-smelling oil. This substance was not identified due to its extremely disagreeable odor. In some cases, the type of compound sought may be made by treating the amine salt of the substituted dithiocarbamic acid with two moles of formaldehyde: this procedure was used to prepare the benzyl homolog. Benzylammonium N-benzyldithiocarbamate was treated with formaldehyde and 3,5-dibenzyltetrahydro-1,3,5-thiadiazine-2-thione was obtained. The melting point of this compound is 101.8-102.6° and its structure is:



An aqueous suspension of β-phenylethylamine was treated with formaldehyde to produce 1,3,5-tri(β-phenylethyl)hexahydro-1,3,5-triazine. This compound was refluxed with carbon disulfide in acetone solution and a white crystalline compound was obtained. This material, after purification, melted at 107.8-108.6° and was found to be 3,5-di(β-phenylethyl)tetrahydro-1,3,5-thiadiazine-2-thione. This compound was also prepared by the alternate method of treating β-phenylethylammonium β-phenylethyldithiocarbamate with formaldehyde.

[V. PREPARATION OF 1,3,5-TRIARYLHEXAHYDRO-1,3,5-TRIAZINES AND REACTION WITH CARBON DISULFIDE

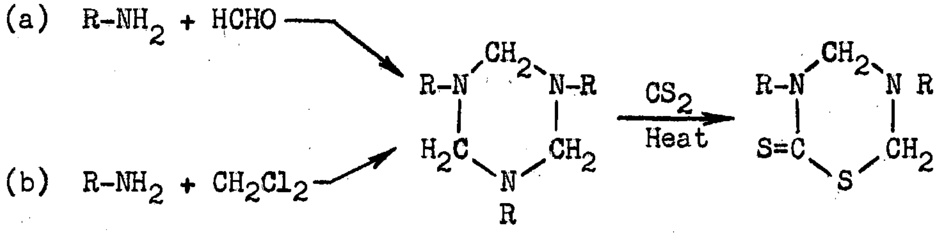
1,3,5-Triphenylhexahydro-1,3,5-triazine was prepared from aniline and formaldehyde, and separated from the insoluble polymeric side product formed from the aniline and formaldehyde. Attempts were made to cause this cyclic trimer to react with carbon disulfide, but no product was obtained. The addition of acid to the reaction mixture was tried in an attempt to bring about reaction, since these cyclic trimers are not stable in acidic media, but the desired results were not obtained. The reaction was attempted in a sealed tube at elevated temperatures, but without success. An alternate method of preparation was then used. Aniline was treated with carbon disulfide in cold acetone solution, and then formaldehyde was added. The product, after separation from side-reaction products, is a white solid m.p. 172.8-173.6°. This compound is 3,5-diphenyltetrahydro-1,3,5-thiadiazine-2-thione:



1,3,5-Tri(p-tolyl)hexahydro-1,3,5-triazine was prepared from p-toluidine and formaldehyde, and refluxed with carbon disulfide in acetone but no reaction occurred. Attempts to carry out this reaction in a sealed tube at elevated temperatures resulted only in decomposition, and the product obtained was N,N'-di(tolyl)thiourea. The alternate method of preparation, consisting of the treatment of p-toluidine with carbon disulfide and then with formaldehyde in cold acetone solution, was used to prepare the desired compound, 3,5-di(p-tolyl)tetrahydro-1,3,5-thiadiazine-2-thione. This compound is a white crystalline solid, melting at 101.8-102.6°.

A cold alcoholic solution of p-phenetidine was treated with formaldehyde to prepare 1,3,5-tri(p-phenetyl)hexahydro-1,3,5-triazine. This compound was refluxed for three hours with carbon disulfide in acetone solution. A white crystalline solid was recovered from this reaction; the solid melts at 156.2-157.0° and was found to be 3,5-tri(p-phenetyl)tetrahydro-1,3,5-thiadiazine-2-thione. Thus, the cyclic trimer of N-(p-ethoxyphenyl)-methyleneimine ($C_2H_5OC_6H_4N{=}CH_2$) reacted with carbon disulfide, while the corresponding phenyl and p-tolyl compounds did not react. This thione was also prepared by the alternate method.

The preparation of 1,3,5-trisubstituted hexahydro-1,3,5-triazines and their reaction with carbon disulfide may be shown by:



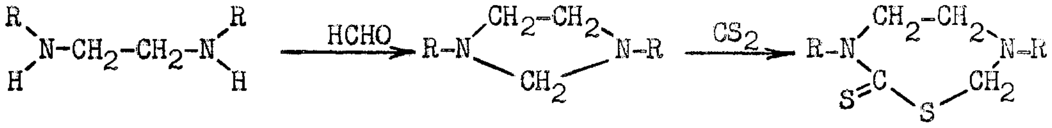
The final product is a 3,5-disubstituted tetrahydro-1,3,5-thiadiazine-2-thione.

The reaction with carbon disulfide does not proceed in all cases, although it appears to go with greater ease with alkyl and aralkyl compounds than with aryl compounds. A reflux period of about fifteen minutes is sufficient for the alkyl and aralkyl compounds, and a longer period may cause decomposition.

The 3,5-disubstituted tetrahydro-1,3,5-thiadiazine-2-thiones of high-molecular weight are more stable than those of low molecular weight. The ethyl compound becomes discolored and develops a somewhat disagreeable odor after a few days; the isopropyl compound discolors at a slower rate while the higher homologs, such as cyclohexyl, are stable for extended periods.

V. PROOF OF STRUCTURE OF 3,5-DISUBSTITUTED TETRAHYDRO-1,3,5-THIADIAZINE-2-THIONES

Donia and co-workers (4) found that treatment of ethylenediamines with formaldehyde and then with carbon disulfide proceeds:

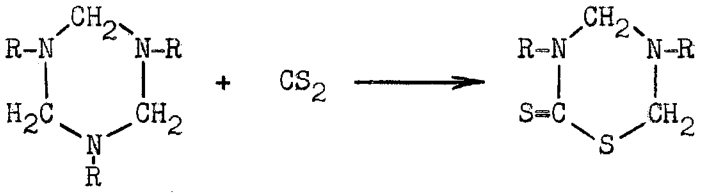


N,N'-Dialkylethylenediamines

1,3-Dialkylimidazolidines

3,6-Dialkylhexahydro-1,3,6-thiadiazepine-2-thiones

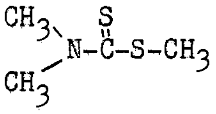
By analogy with the reaction of the above diamine-formaldehyde product with carbon disulfide, it would be expected that the treatment of 1,3,5-trisubstituted hexahydro-1,3,5-triazines with carbon disulfide would proceed:



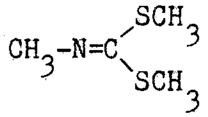
(I)

The treatment of the trisubstituted hexahydrotriazines with carbon disulfide gave evidence of reaction when R = alkyl or aralkyl; but did not go when R = phenyl or p-tolyl. The reaction proceeded when R = p-phenetyl, but required a long reflux period. Donia and co-workers noted that 1,3-diphenylimidazolidine gave no reaction with carbon disulfide. It thus appears that the aryl compounds are less reactive toward carbon disulfide than the alkyl in both of the above cases.

A survey of the literature revealed that Ainley and co-workers (9) also proposed this type structure (I) for some aryl-alkyl compounds which they prepared from alkylammonium N-aryldithiocarbamates and formaldehyde. They believe this structure to be in accordance with the methods of preparation that may be used and with observed reactions, whereas the other formulas that have been advanced are inadequate. In addition, they believe that ultraviolet spectra of these substances offers further evidence for structure (I). The spectra of their compounds were compared with that of methyl dimethyldithiocarbamate (II) and di(methylthio)-N-methylmethyleneimine (III).



$(CH_3)_2N-C(=S)-S-CH_3$ (II)

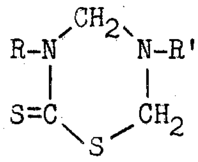


$CH_3-N=C(SCH_3)_2$ (III)

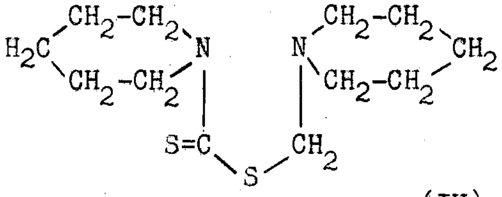
These investigators found that methyl dimethyldithiocarbamate has a spectrum very similar to those of their compounds, indicating structure (I). Marked absorption peaks were noted in the range 276 mμ to 289 mμ and subsidiary peaks around 245 mμ. These compounds were named as 2-thio-3-aryl-5-alkyltetrahydro-1,3,5-thiadiazines, but may be more properly called 3-aryl-5-alkyltetrahydro-1,3,5-thiadiazine-2-thiones.

The products from the reaction of 1,3,5-trisubstituted hexahydro-1,3,5-triazines and carbon disulfide gave absorption curves with marked peaks in the range 290-295 mμ and secondary peaks in the range 245-249 mμ. Furthermore, these curves (plate 1) have the same general form as those given by Ainley for his compounds, which indicates that these compounds all possess the same type structure.

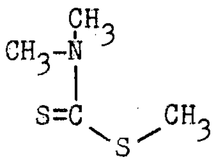
It was felt that piperidylmethyl N,N-cyclopentamethylenedithiocarbamate (IV) would provide a more satisfactory basis for comparison with the compounds thought to possess structure (I) than does methyl dimethyldithiocarbamate. This standard (IV) contains a chain structure of nitrogen, sulfur, and carbon atoms more nearly like the proposed structure than does methyl dimethyldithiocarbamate (II), as may be seen by examination of the formulas:



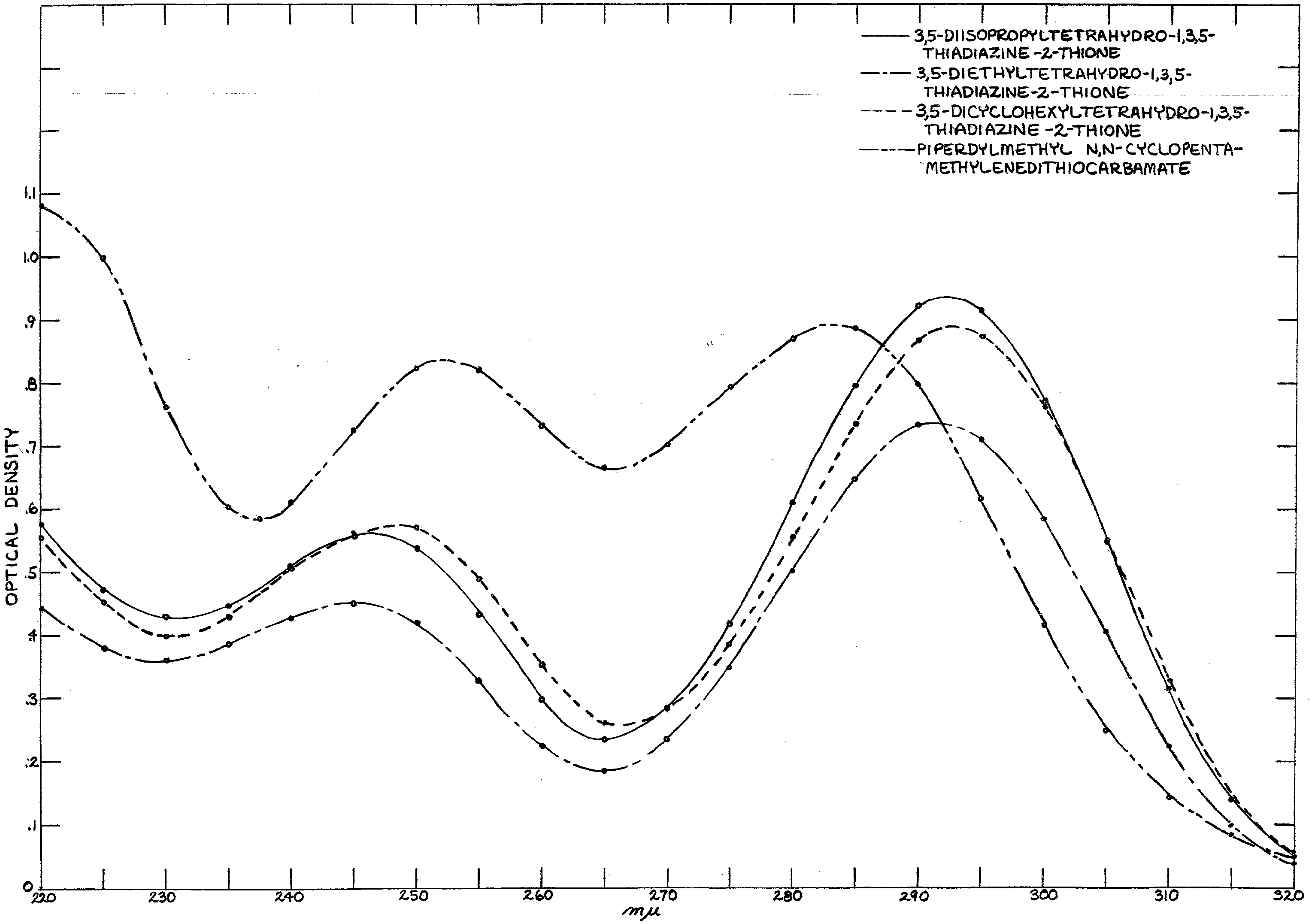
(I)



(IV)



(II)


3,5-DIISOPROPYLTETRAHYDRO-1,3,5-THIADIAZINE-2-THIONE
3,5-DIETHYLTETRAHYDRO-1,3,5-THIADIAZINE-2-THIONE
3,5-DICYCLOHEXYLTETRAHYDRO-1,3,5-THIADIAZINE-2-THIONE
PIPERDYLMETHYL N,N-CYCLOPENTAMETHYLENEDITHIOCARBAMATE
OPTICAL DENSITY
1.1
1.0
.9
.8
.7
.6
.5
.4
.3
.2
.1
0
220
230
240
250
260
270
280
290
300
310
320
mμ

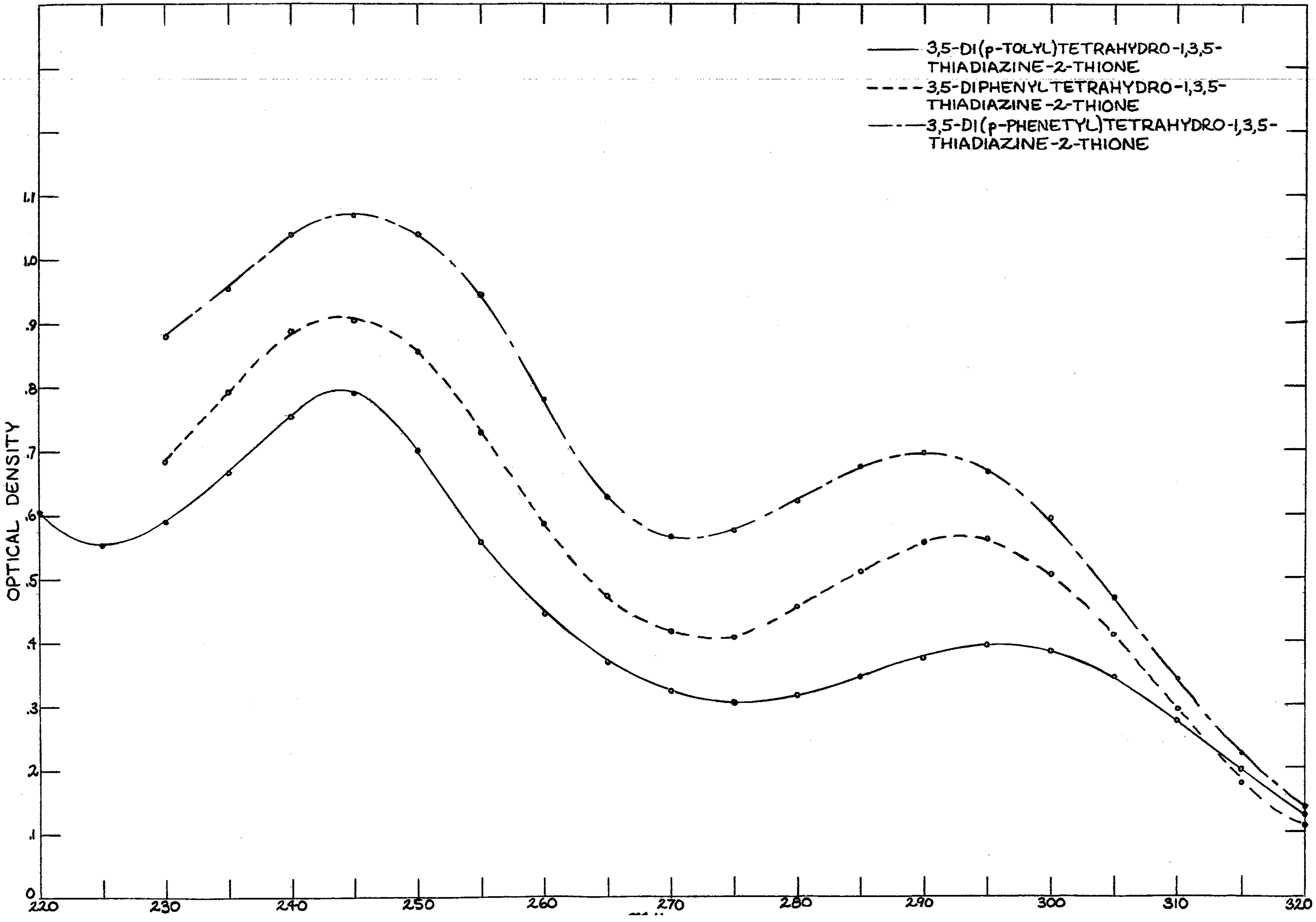
The absorption curves for piperidylmethyl N,N-cyclopentamethylenedithiocarbamate (IV) and the 3,5-dialkyltetrahydro-1,3,5-thiadiazine-2-thiones that were prepared are shown on plate 1. The three compounds with the the proposed structure (I) have similar curves, with maximum absorption peaks in the range of 291-293 mμ, and smaller peaks in the range of 245-249 mμ. The linear standard (IV) has a curve of the same general form, except that the two absorption peaks are more nearly the same height, and are closer together.

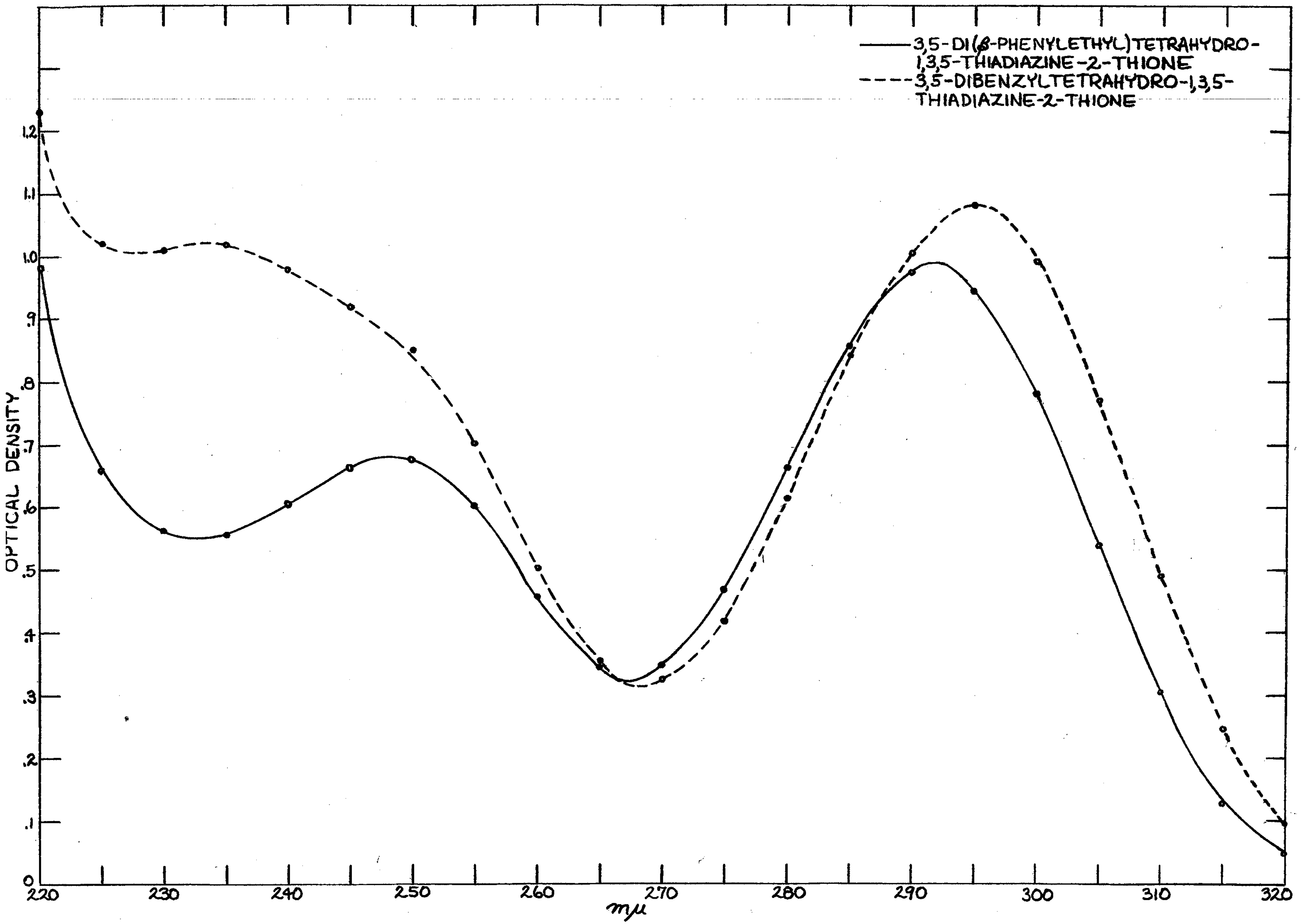
The absorption curve given by Ainley (9) for methyl dimethyldithiocarbamate (II) shows a maximum absorption at about 275 mμ, which is not as near the maxima of the experimental compounds as is that of the standard (IV). However the subsidiary peak of the methyl dimethyldithiocarbamate appears at 245 mμ, which is closer to those of the experimental compounds than to that of compound (IV).

The absorption curves of the 3,5-diaryltetrahydro-1,3,5-thiadiazine-2-thiones (plate 2) are reversed from those of the alkyl homologs, with the maximum absorption near 245 mμ, and the subsidiary peak in the region of 290-296 mμ. This is probably due to the presence of the benzene ring, which is a chromophore, and capable of altering the absorption of chromophores already present, as well as absorbing in the ultraviolet region itself.

The 3,5-diaralkyltetrahydro-1,3,5-thiadiazine-2-thiones give curves (plate 3) which appear to be somewhat intermediate between those of the alkyl and aryl homologs. The β-phenylethyl compound has an absorption curve nearly identical with those of the alkyl homologs, while the benzyl compound gives a curve approaching those of the aryl homologs. This is as would be expected, since the benzene ring is nearer the thiadiazine ring in the benzyl compound than in the β-phenylethyl compound and should be

PLATE 2 - ABSORPTION CURVES OF ARYL HOMOLOGS




3,5-DI(β-PHENYLETHYL)TETRAHYDRO-1,3,5-THIADIAZINE-2-THIONE
3,5-DIBENZYLTETRAHYDRO-1,3,5-THIADIAZINE-2-THIONE
OPTICAL DENSITY
0
.1
.2
.3
.4
.5
.6
.7
.8
.9
1.0
1.1
1.2
220
230
240
250
260
270
280
290
300
310
320
mμ

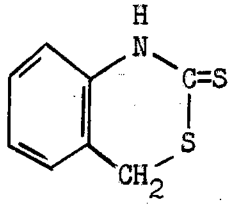
more aromatic in nature. Brode (48) states that a $-CH_2-$ linkage between two chromophores acts as an insulator, and that a $-CH_2-CH_2-$ linkage is even more effective.

These 3,5-disubstituted tetrahydro-1,3,5-thiadiazine-2-thiones formed precipitates when treated with heavy metal salts such as mercuric chloride or silver nitrate, and also with ferric chloride. These products were not studied, but this type reaction is characteristic of compounds of this type.

Treatment of the lower homologs of the 3,5-disubstituted tetrahydro-1,3,5-thiadiazine-2-thiones with ammonium hydroxide caused decomposition in a manner similar to that observed by Donia and co-workers for the ethylene analogs of these compounds, the 3,6-dialkylhexahydro-1,3,6-thiadiazepine-2-thiones, and also for the linear analogs, the dialkylaminomethyl dialkyldithiocarbamates. The products formed are formaldehyde and dithiocarbamate salts.

Hofmann (47) desulfurized thiocarbanilide to produce carbanilide with mercuric oxide in hot alcoholic solution: a similar reaction was attempted for these compounds. Treatment of 3,5-dicyclohexyltetrahydro-1,3,5-thiadiazine-2-thione with mercuric oxide under varied conditions did not produce a detectable amount of material containing a carbon-oxygen double bond.

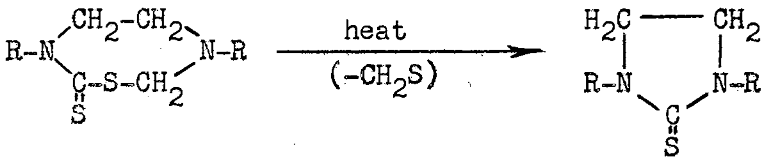
Kitamura (42) reported that alkaline hydrogen peroxide was very effective for oxidizing an aliphatic carbon-sulfur double bond to a carbon-oxygen double bond in structures such as:



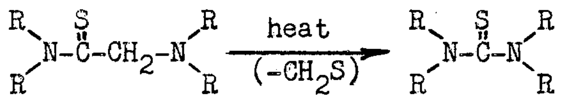
He found that this reagent was effective in cases where mercuric oxide, bromine, potassium permanganate, or nitric acid failed to react. Attempts were made to oxidize 3,5-dicyclohexyltetrahydro-1,3,5-thiadiazine-2-thione using alkaline hydrogen peroxide, but in every instance the starting material was recovered unchanged. This compound has no hydrogen atom attached to a nitrogen atom, however, and in the mechanism for this type of oxidation proposed by Kitamura (43), a hydrogen atom must be present.

VI. DECOMPOSITION OF 3,5-DISUBSTITUTED TETRAHYDRO-1,3,5-THIADIAZINE-2-THIONES

Donia and co-workers (4) reported that 3,6-dialkylhexahydro-1,3,6-thiadiazepine-2-thiones may be thermally decomposed to give 1,3-dialkyl-2-imidazolidinethiones:

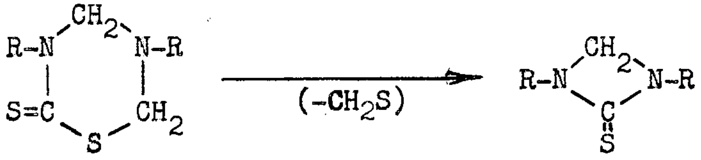


The thermal decomposition of dialkylaminomethyldialkyldithiocarbamates results in the formation of tetraalkylthioureas:



In both cases the resulting products may be considered as tetrasubstituted thiourea derivatives.

By analogy with the above reactions, it would be expected that the thermal decomposition of 3,5-disubstituted tetrahydro-1,3,5-thiadiazine-2-thiones would result in the formation of a compound containing a thiourea residue. The following reaction might be expected on strong heating of these compounds:



3,5-Diisopropyltetrahydro-1,3,5-thiadiazine-2-thione was thermally decomposed by the gentle boiling of a molten sample. Thioformaldehyde was obtained (1.8 moles per mole of starting material), in addition to an acetone-soluble portion. A white crystalline solid, m.p. 99.4-100.2°, was recovered from the acetone solution.

3,5-Dicyclohexyltetrahydro-1,3,5-thiadiazine-2-thione was similarly decomposed, and thioformaldehyde was again obtained in addition to an acetone-soluble portion. A white crystalline compound melting at 158.2-160° was isolated from the acetone-soluble mixture.

When pyrolysis of the ethyl analog of the above compounds was attempted thioformaldehyde was obtained, indicating that the desired reaction may have occurred, but attempts to isolate a solid material similar to the above decomposition products were not successful.

3,5-Dibenzyltetrahydro-1,3,5-thiadiazine-2-thione was boiled gently for three minutes, but no thioformaldehyde was evident. A soluble material was obtained, which melted at 157-157.8°, in addition to unchanged starting compound.

The β-phenylethyl homolog of these compounds was pyrolyzed, but no thioformaldehyde formed, and no solid could be recovered from the oil that remained.

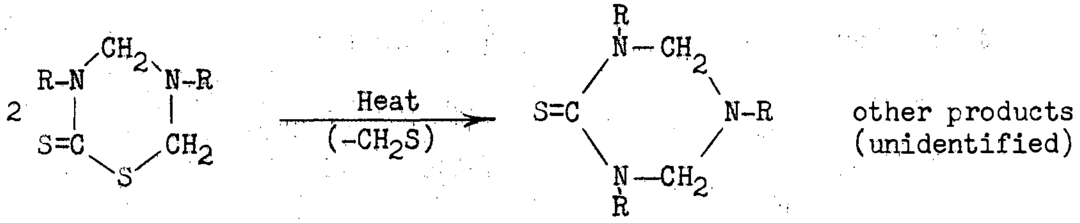
Heating of the phenyl homolog caused the formation of thioformaldehyde, in addition to 1,3,5-triphenylhexahydro-1,3,5-triazine. No soluble sulfur-containing solid could be recovered from the oily decomposition mixture.

Pyrolysis of 3,5-di(p-tolyl)tetrahydro-1,3,5-thiadiazine-2-thione produced a very low yield of an acetone-soluble solid, melting at 150.5-152°, but no thioformaldehyde was noted.

The thermal decomposition of the p-phenetyl homolog produced thioformaldehyde, in addition to an acetone-soluble crystalline material melting at 173-174.2°.

II. STRUCTURE OF THERMAL DECOMPOSITION PRODUCTS OF 3,5-DISUBSTITUTED TETRAHYDRO-1,3,5-THIADIAZINE-2-THIONES

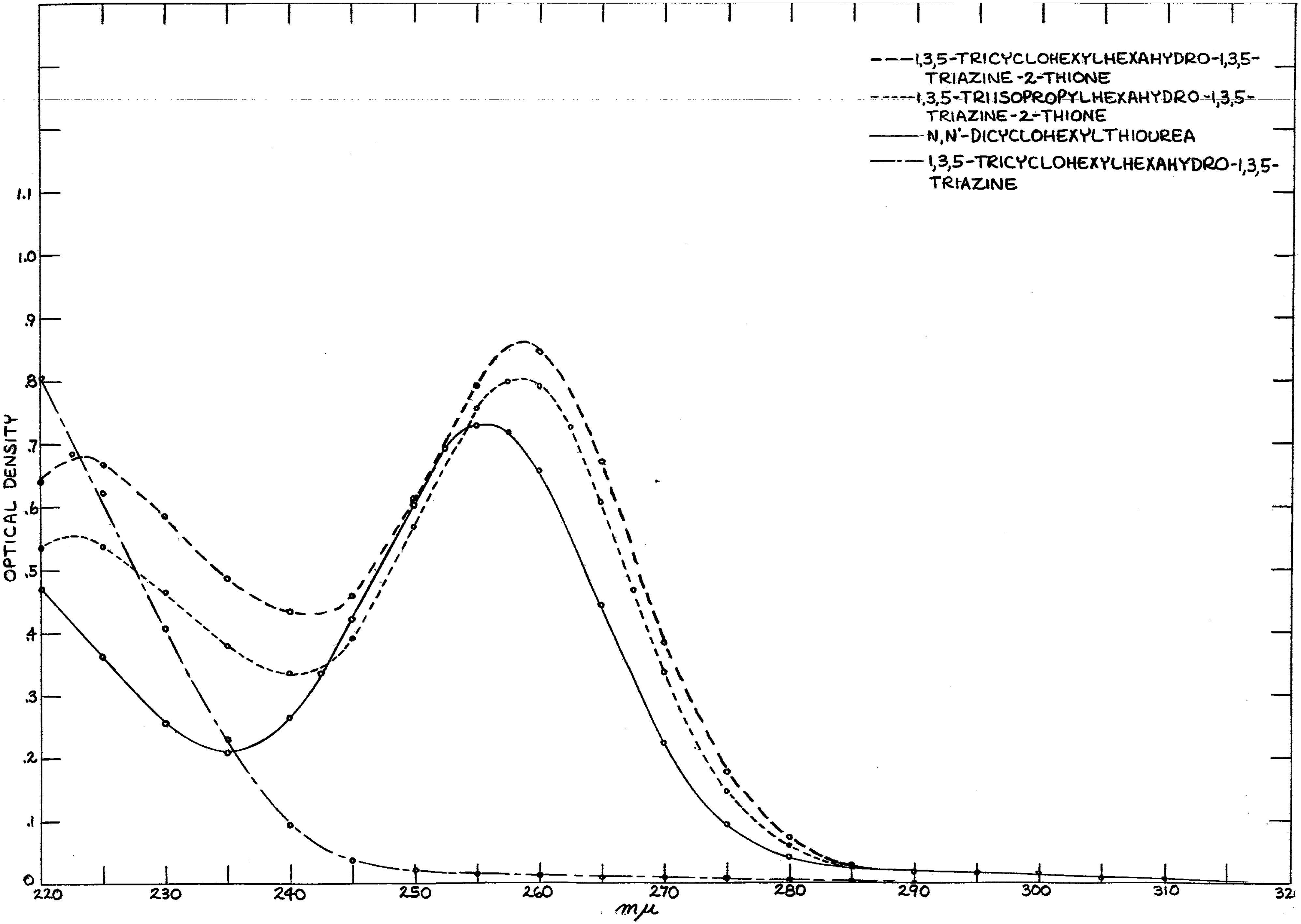
Analytical data for the crystalline solids that were obtained from the thermal decomposition of the cyclohexyl, isopropyl, p-tolyl, p-phenetyl, and benzyl homologs of the 3,5-disubstituted tetrahydro-1,3,5-thiadiazine-2-thiones did not correspond to the calculated values for the four-membered ring compounds that might be expected. On the basis of analytical data and molecular-weight determinations of the compounds obtained, and the fact that a thiourea-type linkage would be expected as a result of splitting out of thioformaldehyde, the reaction that occurred appeared to be:



(V)

The proposed thermal products (V) would be named as 1,3,5-trisubstituted hexahydro-1,3,5-thiadiazine-2-thiones.

In order to obtain evidence in support of the proposed structures, ultraviolet absorption spectra were utilized. The spectra of the alkyl homologs (the cyclohexyl and isopropyl compounds) were compared with that of N,N'-dicyclohexylthiourea and of 1,3,5-tricyclohexylhexahydro-1,3,5-triazine. The curves for these compounds are shown on plate 4. The 1,3,5-tricyclohexylhexahydro-1,3,5-triazine absorption curve drops rapidly from 220 mμ to 240 mμ, and then slowly approaches zero. The absorption curve of N,N'-dicyclohexylthiourea drops from 220 mμ to 235 mμ, then rises to a maximum at 256 mμ, and then drops rapidly to 280 mμ. The two experimental compounds have similar curves with maxima near 259 mμ and smaller peaks near 223 mμ, and these curves are similar to that of N,N'-dicyclo-

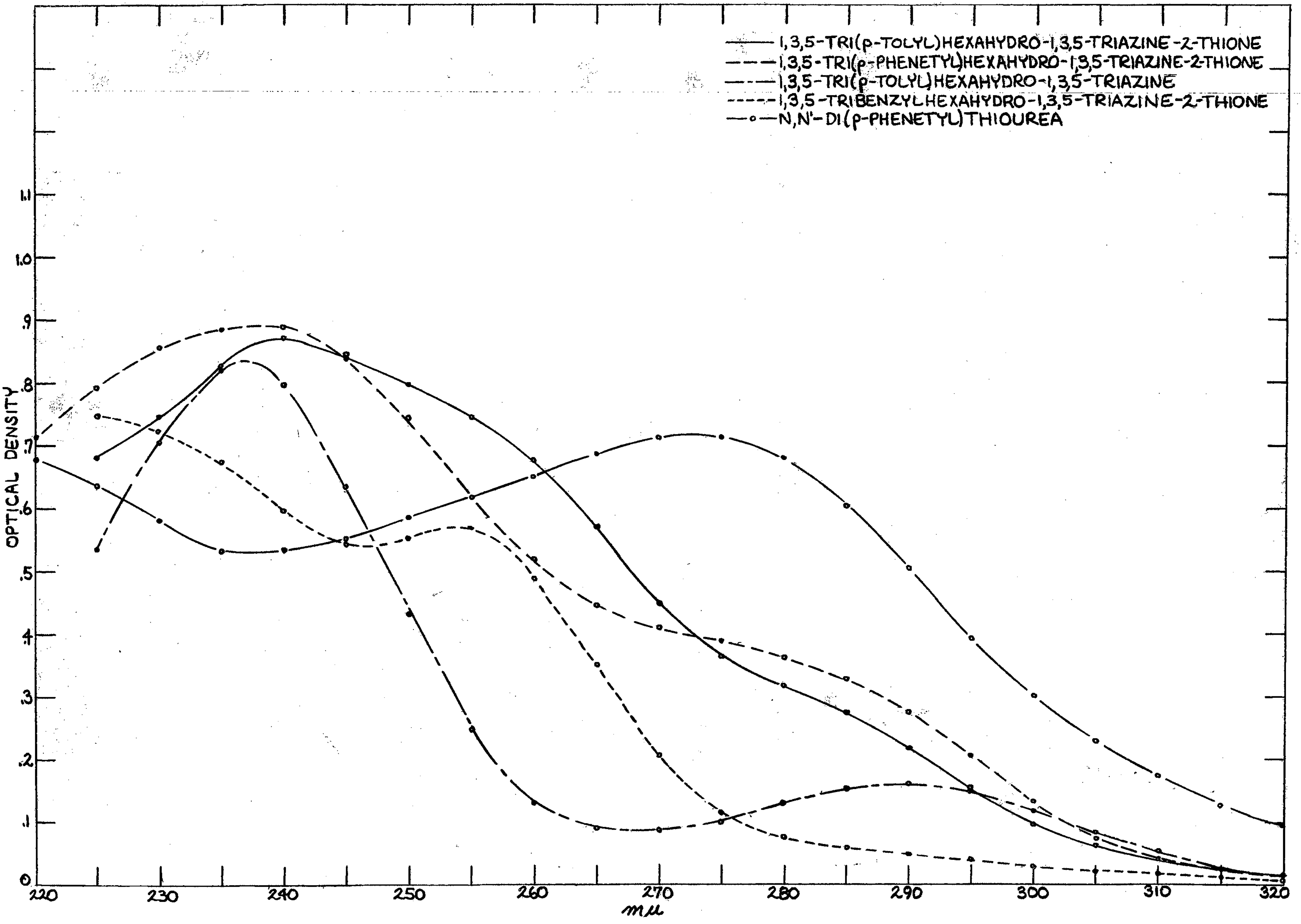


---- 1,3,5-TRICYCLOHEXYLHEXAHYDRO-1,3,5-TRIAZINE-2-THIONE
------ 1,3,5-TRIISOPROPYLHEXAHYDRO-1,3,5-TRIAZINE-2-THIONE
—— N,N'-DICYCLOHEXYLTHIOUREA
—·— 1,3,5-TRICYCLOHEXYLHEXAHYDRO-1,3,5-TRIAZINE
OPTICAL DENSITY
1.1
1.0
.9
.8
.7
.6
.5
.4
.3
.2
.1
0
220
230
240
250
260
270
280
290
300
310
32
mμ

hexylthiourea. On the basis of these absorption data it appears that the alkyl compounds under consideration contain a thiourea type linkage $(\sqsupset N-\overset{\overset{S}{\|}}{C}-N\sqsubset)$ and a triazine ring as predicted. Clow and Helmrich (49) found that N,N-dialkylthioureas gave curves only slightly different from those of N,N,N',N'-tetraalkylthioureas, and furthermore, the curves that these investigators give for tetramethyl- and tetraethyl- thiourea correspond closely to those obtained for the experimental compounds.

The absorption curves of the aryl pyrolysis products (plate 5) show considerable variation from those of the alkyl thermal products, while the benzyl homolog gives a curve that appears to be intermediate between these two types. The *p*-tolyl and *p*-phenetyl pyrolysis products give curves that differ somewhat from each other, probably due to the difference in the weighing effects of the methyl and ethoxy groups on the benzene ring. These curves vary considerably from that of N,N'-di-*p*-phenetylthiourea, indicating that the triarylhexahydrotriazine structure must exert more influence on the ultraviolet absorption of the molecule than does the trialkylhexahydrotriazine structure in the case of the alkyl analogs. Indeed, the absorption curve of 1,3,5-tri(*p*-phenetyl)hexahydro-1,3,5-triazine (plate 5) shows that this compound absorbs more strongly in the ultraviolet region studied than does the alkyl homolog, 1,3,5-tricyclohexylhexahydro-1,3,5-triazine (plate 4).

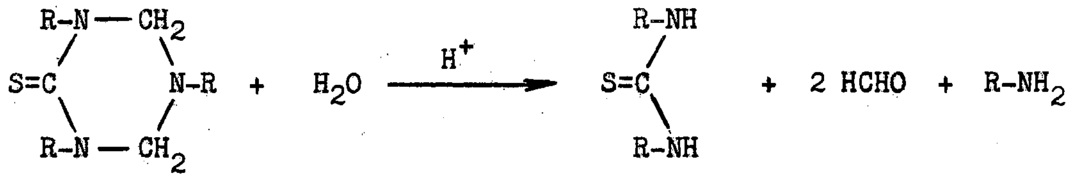
Brode (48) states that if the chromophores in a molecule are widely separated, each may exhibit its characteristic absorption spectrum, but that the close proximity or conjugation of chromophores results in changes in absorption that are not easily predicted. Although it would be difficult to predict the form of the absorption curve resulting from a combination of the substituted thiourea and trisubstituted hexahydrotriazine structures, especially since they overlap within the molecule, it appears that the


1,3,5-TRI(p-TOLYL)HEXAHYDRO-1,3,5-TRIAZINE-2-THIONE
1,3,5-TRI(p-PHENETYL)HEXAHYDRO-1,3,5-TRIAZINE-2-THIONE
1,3,5-TRI(p-TOLYL)HEXAHYDRO-1,3,5-TRIAZINE
1,3,5-TRIBENZYLHEXAHYDRO-1,3,5-TRIAZINE-2-THIONE
N,N'-DI(p-PHENETYL)THIOUREA
OPTICAL DENSITY
1.1
1.0
.9
.8
.7
.6
.5
.4
.3
.2
.1
0
220
230
240
250
260
270
280
290
300
310
320
mμ

combination of these effects might give curves of the type observed for the aryl pyrolysis products. The fact that the benzyl homolog absorbs in a manner intermediate between the aryl and alkyl pyrolysis products further indicates that both the aryl and alkyl compounds have the same type structures, and that the difference in the curves is due to the presence of the aromatic rings in the *p*-tolyl and *p*-phenetyl homologs. Clow and Helmrich (49) have noted that a $-CH_2-$ group at least partially detaches the chromophores in aryl substituted thioureas, and this must be the case with the benzyl pyrolysis product.

Attempts were made to convert the carbon-sulfur double bond of these compounds to carbon-oxygen double bonds by oxidation with mercuric oxide in a manner similar to that used by Hoffman (47) for thiocarbanilide, but no oxidation occurred. Alkaline hydrogen peroxide was also used as described by Kitamura (42), but again no oxidation occurred.

The 1,3,5-trisubstituted hexahydro-1,3,5-triazines are hydrolyzed in acid solutions to give formaldehyde and substituted amines. It might be expected that the 1,3,5-trisubstituted hexahydrotriazine-2-thiones would hydrolyze in the following manner:



Acidic hydrolysis of 1,3,5-tricyclohexyltetrahydro-1,3,5-triazine-2-thione produced N,N'-dicyclohexylthiourea, formaldehyde, and cyclohexylamine, indicating that the above reaction must have occurred and that the proposed structure for these pyrolysis products is correct.

EXPERIMENTAL

I. PREPARATION OF METHYLENEDIAMINES AND REACTIONS WITH CARBON DISULFIDE AND FORMALDEHYDE

A. Preparation of Methylenedianiline

The method used was similar to that of Eberhard and Weltner (34). One hundred and eighty-six grams (2.0 moles) of aniline, 65 ml. of ethanol, and 40 g. of potassium hydroxide were treated with 77 g. of formalin on a hot water bath. The reaction was carried out in a 3-necked flask equipped with stirrer and reflux condenser. Oily droplets separated, which gradually solidified. The crystals were filtered and washed four times with cold alcohol. The crystals were white, and melted at 62-64°. The yield was 53 g. or 13% of the theoretical amount.

B. Attempted Preparation of N-Phenyl-N-(phenylaminomethyl)dithiocarbamic Acid Inner Salt

Fifteen grams of methylenedianiline in cold acetone solution was treated with an excess of carbon disulfide. No precipitate formed on standing, so the mixture was refluxed for several minutes, then evaporated to one-quarter of the original volume, and on cooling a precipitate formed. Recrystallization from acetone gave white, shiny plates, m.p. 150.8-151.8°. A mixed melting point with thiocarbanilide showed no depression, indicating that this compound was thiocarbanilide.

Analysis: Calculated for $C_{13}H_{12}N_2S$: C, 68.4; H, 5.3.

Found: C, 68.8; H, 6.03.

C. Reaction of Thiocarbanilide with Formaldehyde

Before the identity of the methylenedianiline-carbon disulfide product was determined, a 5 g. portion was treated with an excess of formalin and heated. The hot solution was filtered, and crystals appeared on cooling. Attempts to recrystallize this material from various solvents were unsuccessful, owing to decomposition. In every case the starting material and formaldehyde appeared. The crude product melted at 125.5-126.5° with the evolution of formaldehyde. This compound was not definitely identified, but was believed to be the monomethylol derivative of thiocarbanilide.

Analysis: Calculated for $C_{14}H_{14}N_2S$: C, 65.1; H, 5.47.

Found: C, 64.7; H, 6.48.

D. Reaction of Methylenedianiline with Carbon Disulfide and Formaldehyde

An excess of carbon disulfide was added to a cold solution of methylenedianiline in acetone, and after standing ten minutes, formalin was added. The mixture was allowed to stand one-half hour, and then water was carefully added. The solid that formed was filtered and extracted with hot acetone. The insoluble material from this extraction gave no melting-point depression with the high polymer of N-phenylmethyleneimine prepared by the method of Miller and Wagner (36). The bulk of the soluble material melted at 140°, and gave no melting-point depression when mixed with the cyclic trimer of N-phenylmethyleneimine. A small amount of substance containing nitrogen and sulfur and melting at 169-170° was recovered from the soluble material. There was not enough of this compound available to allow analysis.

E. Reaction of Methylenedianiline with Carbon Disulfide and Ammonium Hydroxide

Molar equivalent amounts of carbon disulfide and ammonium hydroxide were added to a cold solution of methylenedianiline, and the mixture was placed in a refrigerator overnight. Crystals formed, and the odor of hydrogen sulfide was noticeable. The crude solid started melting at 134° and melted over a range of several degrees. This material was thought to be thiocarbanilide, and a mixed melting point with a pure sample gave no depression.

The reaction was repeated, and the yellowish-white solid which formed was removed as soon as it precipitated. It was washed with cold ether, dried, and melted at 98-99° with decomposition. A mixed melting point with ammonium N-phenyldithiocarbamate showed no depression.

F. Preparation of Ethylidenedianiline

This compound was prepared by treating aniline with formaldehyde as described Eibner (39). An aqueous solution of aniline (0.98 mole) was treated dropwise with acetaldehyde (0.49 mole) with cooling. The resulting oil was separated from the aqueous layer and dried over potassium carbonate.

G. Reaction of Ethylidenedianiline with Carbon Disulfide and Formaldehyde

Crude ethylidenedianiline was dissolved in acetone and carbon disulfide was added. After standing five minutes, formalin was added and the mixture cooled. The solid that formed was filtered out, and the crude material melted at 138-172°. This material was extracted with hot acetone and the acetone-soluble fraction, after recrystallization from ether, melted at 139-141°. The insoluble portion, after repeated washing with dioxane, melted at 212-216°. These materials were believed to be the cyclic trimer and higher polymer respectively, of N-phenylmethyleneimine, and mixed melting points with these compounds gave no depression.

H. Preparation of Propylidenedianiline

This compound was prepared by treating aniline with propionaldehyde after the method of Eibner (40). An aqueous solution of aniline (0.82 mole) was treated dropwise with propionaldehyde (0.41 mole) with cooling. The resulting oil was separated from the aqueous layer and dried over potassium carbonate.

I. Reactions of Propylidene Dianiline

Treatment of the diamine with carbon disulfide and ammonium hydroxide yielded a yellowish solid, m.p. 99°, which was found to be ammonium

N-phenyldithiocarbamate. Treatment of the diamine in cold acetone solution with carbon disulfide gave no evidence of reaction, and the addition of formaldehyde gave an alcohol-soluble fraction and an alcohol-insoluble fraction. These compounds were the cyclic trimer and higher polymer of N-phenylmethyleneimine, as proved by mixed melting points.

J. Preparation of Ethylidenedi-p-toluidine

The method used was that described by von Pechmann and Ansel (44). Two-tenths of a mole of p-toluidine was suspended in 200 ml. of water containing 3.5 g. of potassium hydroxide, and 0.1 mole of acetaldehyde was added dropwise. The mixture was stirred and maintained at 0° during the addition and for 45 minutes thereafter.

K. Attempted Reaction of Ethylidenedi-p-toluidine with Carbon Disulfide and Formaldehyde

A solution of the crude diamine in acetone was treated with an excess of carbon disulfide, but no precipitate formed. Some of the amine was treated directly with carbon disulfide in the absence of a solvent, but no evidence of reaction was observed. Formaldehyde was then added and the mixture allowed to stand overnight. Attempts to obtain crystals from the resultant oil were unsuccessful.

II. PREPARATION OF 1,3,5-TRIALKYLHEXAHYDRO-1,3,5-TRIAZINES AND REACTION WITH CARBON DISULFIDE

A. Reaction of Cyclohexylamine with Methylene Chloride

Seven-tenths mole of cyclohexylamine was placed in a 3-necked flask equipped with stirrer and reflux condenser, and 0.38 mole of methylene chloride was added dropwise. The mixture was refluxed for five hours after the addition was completed, and then allowed to stand overnight. The solid mixture was treated four times with excess 40% sodium hydroxide solution, and the oily layer that formed was dried over potassium carbonate, and distilled to remove excess cyclohexylamine. Part of the amine came over as an azeotrope with water, b.p. 94-95°, and the temperature then rose to 138°. A solid appeared in the still pot, which gave a positive test for halogen, indicating that it probably was a hydrochloride salt. The mixture was again treated with 40% potassium hydroxide, dried, and distilled. The pressure was reduced and the material boiling in the range 46-110° (4 mm.) was collected. This material was dissolved in acetone, cooled, and a white crystalline solid was obtained, which after recrystallization melted at 72.2-72.8°. This compound was found to be 1,3,5-tricyclohexylhexahydro-1,3,5-triazine.

Analysis: Calculated for $C_{21}H_{39}N_3$: C, 75.75; H, 11.8; Mol. wt. 333.5.
Found: C, 75.34; H, 12.6; Mol. wt. 327.

In addition to this compound, a crystalline solid was isolated from an acetone solution of the fraction boiling at 238° (4 mm.). This substance melted at 96-98°, but was not identified. A still higher-boiling fraction was obtained, b.p. 253° (3 mm.), but no crystalline solid could be obtained from this dark brown, highly viscous substance.

B. Preparation of 1,3,5-Tricyclohexylhexahydro-1,3,5-triazine by Reaction of Cyclohexylamine and Formaldehyde

One and fifteen-hundredths moles of cyclohexylamine was dissolved in 250 ml. of water and 1.2 moles of formaldehyde (as formalin) was added dropwise with stirring and cooling. An oil appeared, which slowly solidified in the form of white needles. These were isolated by filtration, washed with cold water, and melted at 72-73°. This compound was the same as that prepared by the reaction of cyclohexylamine and methylene chloride. The yield was 105 g., which is 82% of the theoretical amount.

C. Preparation of 3,5-Dicyclohexyltetrahydro-1,3,5-thiadiazine-2-thione

One hundred and five grams (0.383 mole) of 1,3,5-tricyclohexylhexahydro-1,3,5-triazine was dissolved in acetone, an excess of carbon disulfide added, and the mixture refluxed for one-half hour. The mixture turned light brown, and upon cooling, a precipitate formed. After being twice recrystallized from an acetone-water mixture, the white, shiny plates melted at 145.8-146.2°. This material was not soluble in dilute hydrochloric acid. The yield, after one recrystallization, was 65 g., which is 56.6% of the theoretical amount.

Analysis: Calculated for $C_{15}H_{26}N_2S_2$: C, 60.36; H, 8.78; N, 9.39; S, 21.47; Mol. wt., 298.46.

Found: C, 60.47; H, 9.15; N, 9.18; S, 21.84; Mol. wt., 302.

D. Attempted Preparation of 1,3,5-Tricyclohexyl-2,4,6-trimethylhexahydro-1,3,5-triazine

Sixty milliliters (0.496 mole) of cyclohexylamine was dissolved in 500 ml. of water, and 25.3 ml. (0.45 mole) of acetaldehyde was added dropwise with stirring at room temperature. On standing several hours, an oil appeared, which was separated from the water and dried three times over solid potassium hydroxide while being cooled in an ice bath. This material was then distilled twice at reduced pressure. The fraction boiling at 68-72° (41 mm.) was collected. It had an index of refraction of n_{23}^{D} = 1.4565, and an odor similar to that of green bananas.

A precipitate formed immediately upon the addition of carbon disulfide, which indicated that the compound was not the desired hexahydrotriazine. This solid was cyclohexylammonium cyclohexyldithiocarbamate, m.p. 144-45°, as proved by mixed melting points.

The liquid product from the cyclohexylamine-acetaldehyde reaction was not characterized since it was not the desired compound.

E. Preparation of 1,3,5-Triisopropylhexahydro-1,3,5-triazine

Two hundred and seventy-five milliliters of isopropylamine (3.23 moles) was dissolved in 250 ml. of water, and 283 g. of formalin was added dropwise with stirring. The temperature was maintained at 20°, and stirring was continued for 30 minutes after the addition was complete. The mixture was then allowed to stand overnight. The water layer was removed, twice extracted with ether, and the ether extracts added to the oil layer. The combined extracts and oil were dried by treating twice with potassium hydroxide and once with potassium carbonate. The mixture was distilled twice, and the fraction boiling at 115-122° (11 mm.) was collected. The yield was 144.9 g. (0.68 mole), or 63% of the theoretical amount.

F. Preparation of 3,5-Diisopropyltetrahydro-1,3,5-thiadiazine-2-thione

The hexahydrotriazine was dissolved in acetone, carbon disulfide added, and the mixture was refluxed for one-half hour. Cooling and the addition of water caused crystals to form. After recrystallization from acetone, the melting point was 124.8-125.4°. The yield was 62.2 g. (0.285 mole), or 42% of the theoretical amount.

Analysis: Calculated for $C_9H_{18}N_2S_2$: C, 49.5; H, 8.3; N, 12.88; S, 29.37; Mol. wt., 218.38.

Found: C, 49.7; H, 8.7; N, 13.29; S, 29.36; Mol. wt., 224.

An attempt was made to prepare this compound by the alternate method of treating the amine with carbon disulfide, and then treating the resultant dithiocarbamic acid with formaldehyde, but a dark brown, foul-smelling oil was formed, and attempts to obtain crystals from this oil were unsuccessful.

G. Preparation of 1,3,5-Tributylhexahydro-1,3,5-thiadiazine

Seventy-four grams (1.0 mole) of *n*-butylamine was dissolved in 500 ml. water, and a slight excess of formaldehyde (as formalin) added dropwise with stirring, while the temperature was maintained between 15° and 20°. Stirring was continued for 30 minutes after the addition was complete. The oil layer that formed was removed, treated with solid potassium hydroxide, the resulting aqueous layer removed, and the oil dried over potassium carbonate overnight. The material was distilled at reduced pressure and the fraction boiling at 132-134° (4-5 mm.) was collected as product. The yield was 49 g. (58%).

H. Attempted Preparation of 3,5-Dibutyltetrahydro-1,3,5-thiadiazine-2-thione

The 1,3,5-tributylhexahydro-1,3,5-triazine was dissolved in acetone, carbon disulfide added, and the mixture refluxed for 1½ hours. Attempts to obtain crystals from the resulting mixture were unsuccessful, and only an oil was received. Distillation at 115 mm. was attempted, but decomposition occurred, so the pressure was lowered to 7 mm., and the material came over between 61° and 150°. Decomposition again occurred, with thioformaldehyde being split out during the distillation. The distillation was attempted at 2 mm., but decomposition still occurred, and the material distilled in the range 70-125°. Further attempts to purify the foul-smelling product were not made.

I. Preparation of 1,3,5-Triethylhexahydro-1,3,5-triazine

One hundred grams (0.734 mole) of 33% ethylamine was treated dropwise with 62.5 g. of formalin, while being stirred and maintained at 10°. The solution was treated three times with solid potassium hydroxide, and the oil layer that formed was removed after each treatment. The aqueous layer was then extracted with ether, and the oil layers and ether extract combined. This material was treated with solid potassium hydroxide and agitated for one hour. The resulting aqueous layer was removed, and the treatment with solid base and separation of the aqueous layer repeated. The material was dried overnight over potassium carbonate, and then distilled. The fraction boiling at 92-97° (11 mm.) was collected as product. The yield was 32.0 g., or 25% of the theoretical amount.

J. Preparation of 3,5-Diethyltetrahydro-1,3,5-thiadiazine-2-thione

Thirty-two grams (0.187 mole) or 1,3,5-triethylhexahydro-1,3,5-triazine was dissolved in acetone, carbon disulfide added, and the mixture refluxed for 45 minutes. The mixture became dark brown and developed a disagreeable odor, indicating that the reflux period was too long and that some decomposition had occurred. The addition of a few drops of water and cooling caused the formation of a precipitate, which after recrystallization from acetone melted at 73.4-74.9°. The yield was 10.5 g., or 29.5% of the theoretical amount.

Analysis: Calculated for $C_7H_{14}N_2S_2$: C, 44.17; H, 7.4; S, 33.70; Mol. wt., 190.33.

Found: C, 44.45; H, 8.25; S, 33.8; Mol. wt., 200.

K. Reaction of Ethanolamine with Formaldehyde and Carbon Disulfide

Sixty-six grams (1.07 moles) of ethanolamine was dissolved in 190 ml. of water, cooled, and 91.5 g. of formalin added dropwise with stirring. The water was distilled at 60 mm., then the pressure was reduced to 6 mm., and the fraction boiling at 109-111° collected. This material was dissolved in four parts of acetone, carbon disulfide added, and the mixture refluxed for 30 minutes. The mixture became dark red and developed a disagreeable odor. The acetone was distilled from the mixture, and the remainder of the material distilled at reduced pressure. The temperature rose continuously during distillation, and the distillate had a foul odor. It became discolored on standing several days, and attempts to obtain crystals were unsuccessful.

L. Reaction of n-Hexylamine with Formaldehyde

Five grams (0.05 mole) of redistilled n-hexylamine was dissolved in

50 ml. of alcohol and 10 ml. of formalin added with agitation, while cooling in an ice bath. After standing two hours, carbon disulfide was added, and the mixture refluxed for two hours. An oil layer separated, indicating that a reaction had occurred, but attempts to obtain crystals from acetone or alcohol solutions of the oil were unsuccessful. The oil was allowed to stand for four weeks but no crystals formed. This liquid was distilled at 10 mm. pressure, and came over between 110° and 135°; however decomposition occurred, and thioformaldehyde was formed. Further attempts to purify the material were not made.

An attempt to prepare the desired 3,5-dihexyltetrahydro-1,3,5-thiadiazine-2-thione by the alternate method of adding carbon disulfide and then formaldehyde to an alcoholic solution of the amine resulted in the evolution of hydrogen sulfide and the formation of N,N'-dihexylthiourea.

I. PREPARATION OF 1,3,5-TRI(ARALKYL)HEXAHYDRO-1,3,5-TRIAZINES AND REACTION WITH CARBON DISULFIDE

A. Preparation of 1,3,5-Tribenzylhexahydro-1,3,5-triazine

Nine and seven-tenths grams (0.91 mole) of benzylamine was dissolved in 250 ml. of water and treated dropwise with an excess of formalin with stirring and ice cooling. The mixture was stirred for two hours after the addition was complete and then allowed to stand overnight. The water layer was removed and extracted with benzene, and the combined oil and extract treated with potassium hydroxide. The product, which distilled at about 240° at atmospheric pressure though with some decomposition, was distilled at reduced pressure. The distillate was dissolved in acetone, an excess of carbon disulfide added, and refluxed for 30 minutes. The product was a viscous brown oil with a foul odor, and attempts to obtain crystals from this oil were not successful, and shorter reflux periods also failed to produce the desired type product.

The desired compound was prepared by the alternate method. Ten and seven-tenths grams (0.1 mole) of benzylamine in 70 ml. of cold alcohol was treated with 3.8 g. (0.05 mole) of carbon disulfide. The dithiocarbamate salt was filtered out, washed with cold alcohol, then suspended in 200 ml. alcohol and treated with an excess of formalin. The soluble product was recovered from the alcohol, and after recrystallization melted at 101-102°. The yield was 12 g., or 76% of the theoretical amount.

Analysis: Calculated for $C_{17}H_{18}N_2S_2$: C, 64.91; H, 5.77; S, 20.39;

Mol wt., 314.46.

Found: C, 65.12; H, 7.2; S, 20.42; Mol. wt., 322.

C. Preparation of 1,3,5-Tri(β-phenylethyl)hexahydro-1,3,5-triazine

β-Phenylethylamine (4.37 g., 0.036 mole) was suspended in 35 ml. of water, an excess of formalin added slowly with stirring and ice cooling, and the mixture allowed to stand overnight in a refrigerator. The oil layer was removed and the aqueous layer extracted twice with petroleum ether. The combined oil and extracts were dried over potassium carbonate and distilled. The material boiling at 210-225°, a viscous yellow liquid with a characteristic odor, was collected as product. The amount obtained was 4.06 g., or 84.5% of the theoretical yield.

D. Preparation of 3,5-(β-phenylethyl)tetrahydro-1,3,5-thiadiazine-2-thione

A solution of 4.06 g. (0.01 mole) of 1,3,5-tri(β-phenylethyl)hexahydro-1,3,5-triazine in acetone was treated with an excess of carbon disulfide, and the mixture refluxed for 20 minutes. The mixture was poured into an evaporating dish, the solvent and excess carbon disulfide evaporated, and the solid obtained was recrystallized from acetone. The product was in the form of white needles, melting at 107-108.5°. The yield was 1.5 g., which is 44% of the theoretical amount.

This compound was also made by the alternate method of treating the amine with carbon disulfide, and then causing the resulting dithiocarbamate to react with formaldehyde.

Analysis: Calculated for $C_{19}H_{22}N_2S_2$: C, 66.63; H, 6.47.

Found: C, 66.34; H, 8.9.

IV. PREPARATION OF 1,3,5-TRIARYLHEXAHYDROTRIAZINES AND REACTION WITH CARBON DISULFIDE

A. Preparation of 1,3,5-Triphenylhexahydro-1,3,5-triazine

The method used was that of Miller and Wagner (36). Redistilled aniline (25.5 g., 0.274 mole) was treated with an excess of formalin. The soluble trimer, melting at 140-141°, was separated from the insoluble higher polymer with acetone.

B. Reaction of 1,3,5-Triphenylhexahydro-1,3,5-triazine with Carbon Disulfide

Some of this compound was dissolved in acetone, carbon disulfide added, and refluxed for ten minutes. Only the starting material, in addition to some of the insoluble higher polymer of aniline and formaldehyde formed during the heating, was recovered. The reaction was again attempted, but the mixture was refluxed for four hours. The results were as before. The reaction was tried again, and 3 drops of 6 N hydrochloric acid were slowly added to about 50 ml. of the refluxing mixture. The acid caused the cyclic trimer to decompose, and no sulfur-containing product was received.

The reaction was attempted in a sealed tube, which was heated at 92° in a water bath for one-half hour. No reaction occurred, and the starting material was recovered. The sealed-tube reaction was tried again, and the heating period was extended to 2½ hours, but none of the desired product was obtained. The sealed-tube reaction again attempted, and this time the tube was heated in an oil bath at 125° for 2½ hours. After removing the acetone and carbon disulfide, a viscous yellow oil remained. Repeated attempts to obtain crystals from acetone or alcohol solutions of this material were unsuccessful.

C. Preparation of 3,5-Diphenyltetrahydro-1,3,5-thiadiazine-2-thione by Alternate Method

Seventy-one grams (0.76 mole) of redistilled aniline was dissolved in 250 ml. of alcohol, and 29 g. (0.38 mole) of carbon disulfide was slowly added, while stirring the mixture and cooling in an ice bath. After ten minutes, 66 g. (0.76 mole) of formalin was slowly added with agitation. An oil formed, which gradually solidified. The mixture was warmed (not all of the solid dissolved), filtered, and cooled. The crystals which formed in the liquor were filtered off, and the filtrate was used to extract the original solid four more times, the soluble material being recovered and removed each time. An insoluble material remained, which appeared to be the high polymer of aniline and formaldehyde. The soluble material melted over the range of 135-160°, indicating that some of the cyclic trimer of aniline and formaldehyde (m.p. 140-141°) might be present. This material was recrystallized from acetone, and then melted at 169-171°. A second recrystallization raised the melting point of the white needles to 172.8-173.6°. The weight of the product (once recrystallized) was 5.1 g., which represents a 4.7% yield.

Analysis: Calculated for $C_{15}H_{14}N_2S_2$: C, 62.89; H, 4.9; S, 22.38.

Found: C, 62.61; H, 5.68; S, 22.14.

D. Preparation of 1,3,5-Tri(p-tolyl)hexahydro-1,3,5-triazine

The method used was that described by Miller and Simons (45). Redistilled p-toluidine (21.4 g., 0.2 mole) was treated with an excess of formalin in cold alcoholic solution. After 30 minutes the solid was filtered off, washed with cold alcohol, and dried under vacuum.

E. Reaction of 1,3,5-Tri(p-tolyl)hexahydro-1,3,5-triazine with Carbon Disulfide

An unweighed amount of this compound was dissolved in acetone, carbon disulfide added, and the mixture refluxed for ten minutes, but no reaction occurred, and the starting materials were recovered.

The reaction was tried again with the reflux period extended to three hours, but the starting materials were again recovered.

The reaction was attempted in a sealed tube. The mixture was heated for one hour at 125°, then poured into an evaporating dish and the acetone and excess carbon disulfide evaporated. The solid remaining was washed with cold alcohol and recrystallized twice from acetone. The crystals were yellowish-white, and melted at 178-179.2°. This compound was believed to be N,N'-di(p-tolyl)thiourea, m.p. 178-179°. (Literature value).

F. Preparation of 3,5-Di(p-tolyl)tetrahydro-1,3,5-thiadiazine by Alternate Method

Redistilled p-toluidine (20.4 g., 0.19 mole) was dissolved in 125 ml. of acetone, chilled to ice bath temperature, and 11 ml. (0.19 mole) of carbon disulfide added. After standing five minutes, 16.25 ml. (0.19 mole) of formalin was added, and the mixture was agitated occasionally for one hour. It was then placed in a refrigerator overnight, during which time the mixture developed an orange color and a disagreeable odor. The acetone and excess carbon disulfide was evaporated, the viscous oil taken up in acetone, water added, and the solution placed in a refrigerator for two days. The crystals that formed were filtered and recrystallized from acetone, and melted at 131.2-132.6°.

Analysis: Calculated for $C_{17}H_{18}N_2S_2$: C, 64.93; H, 5.77; S, 20.39.

Found: C, 64.97; H, 6.24; S, 20.42.

G. Preparation of 1,3,5-Tri(p-phenetyl)hexahydro-1,3,5-triazine

The method of preparation was similar to that of Wagner (46). Redistilled p-phenetidine (27.4 g., 0.2 mole) in 150 ml. of cold alcohol was treated with 12.5 ml. carbon disulfide and allowed to stand for 10 minutes. Twenty-three grams of formalin was added, with agitation and cooling. Water was added until an oil formed, the mixture was then warmed to dissolve the oil, and upon cooling, whitish-yellow needles formed. After recrystallization twice from acetone, the melting point was 156.2-157°, and the yield was 10 g., or 13.4% of the theoretical amount.

V. PROOF OF STRUCTURE OF 3,5-DISUBSTITUTED TETRAHYDRO-1,3,5-THIADIAZINE-2-THIONES

A. Ultraviolet Absorption of 3,5-Dicyclohexyltetrahydro-1,3,5-thiadiazine-2-thione

A small sample (2.3 mg.) of this material was dissolved in 20 ml. of Phillips "spectro-grade" isooctane, and 0.7 ml. of this solution was placed in 5.5 ml. more of this solvent. This represents a concentration of 0.00009 mole per liter. The optical density of this solution was determined, using a Beckman Model DU Spectrophotometer, for the range of 220-320 $m\mu$. The data are plotted on plate 1.

B. Ultraviolet Absorption of 3,5-Diisopropyltetrahydro-1,3,5-thiadiazine-2-thione

A 50.3 mg. portion of this compound was placed in 40 ml. of "spectro-grade" isooctane, but it appeared that only about half of the material dissolved. Two-tenths milliliters of this solution was diluted with 5.0 ml. of the solvent and the optical density determined as before. If about half of the material had gone into solution, the concentration would have been of the order of 0.00011 mole per liter. The curve for the data obtained is shown on plate 1.

C. Ultraviolet Absorption of 3,5-Diethyltetrahydro-1,3,5-thiadiazine-2-thione

Three and one-tenth milligrams of this compound was placed in 20 ml. of "spectro-grade" isooctane, but not all dissolved. One milliliter of this solution was diluted with 5.5 ml. of the isooctane and the optical density was determined through the range 220-320 mμ. The concentration would have been 0.00012 mole per liter if all of the material had gone into solution. The data obtained are plotted on plate 1.

D. Ultraviolet Absorption of 3,5-Dibenzyltetrahydro-1,3,5-thiadiazine-2-thione

A few crystals (2.9 mg.) of this compound was dissolved in 20 ml. of "spectro-grade" isooctane, and then 1.0 ml. of this solution was placed in about 9 ml. of the solvent, and the optical density determined as with the other homologs. The concentration of the solution analyzed about .00005 mole per liter. The data are plotted on plate 3.

E. Ultraviolet Absorption of 3,5-Di(β-phenylethyl)tetrahydro-1,3,5-thiadiazine-2-thione

Two and six-tenths milligrams of this compound was placed in 20 ml. of "spectro-grade" isooctane, but not all of the solid dissolved. The ultraviolet spectrum of this solution was determined, and is plotted on plate 3.

F. Ultraviolet Absorption of 3,5-Diphenyltetrahydro-1,3,5-thiadiazine-2-thione

A small sample (2.1 mg.) of this compound was placed in 20 ml. of the isooctane, but it did not all dissolve. The absorption of this solution was weak, since the solubility was very low. The above amount of this compound was dissolved in 20 ml. of 95% ethyl alcohol, and one ml. of this solution diluted to about 9 ml. This represents a concentration of about 0.00004 mole per liter. The results are plotted on plate 2.

G. Ultraviolet Absorption of 3,5-Di(p-tolyl)tetrahydro-1,3,5-thiadiazine-2-thione

Two and three-tenths milligrams of this material was placed in 20 ml. of isooctane, but not all dissolved. Seven-tenths milliliters of this solution was diluted to 5 ml., and the optical density determined for the range of 220-320 mμ. The data are plotted on plate 2.

H. Ultraviolet Absorption of 3,5-Di(p-phenetyl)tetrahydro-1,3,5-thiadiazine-2-thione

Two and eight-tenths milligrams of this material was placed in 20 ml. of isooctane, but the solubility was too low to give satisfactory absorption. The same amount of this substance was dissolved in 20 ml. of 95% ethyl alcohol, then one ml. of this solution was diluted to about 8 ml. The absorption was determined, and the results are plotted on plate 2.

I. Reaction of 3,5-Disubstituted Tetrahydro-1,3,5-thiadiazine-2-thiones with Metallic Salts

The dicyclohexyl homolog in alcohol was treated with aqueous mercuric chloride and a water-insoluble, alcohol-insoluble, white precipitate formed. Treatment of the dicyclohexyl homolog with silver nitrate produced a black precipitate, and treatment with ferric chloride also produced a black precipitate.

J. Attempted Oxidation of 3,5-Dicyclohexyltetrahydro-1,3,5-thiadiazine-2-thione

The method of Kitamura (42) was attempted. Two grams of the compound was suspended in 10% potassium hydroxide, and 30% hydrogen peroxide added slowly over a period of four hours with vigorous stirring. The mixture was stirred overnight, more hydrogen peroxide added, and stirring continued for four hours. The mixture was then allowed to stand for two days. The precipitate was recrystallized from acetone, and melted at 145-146°, indicating that it was the starting material and that no oxidation had occurred.

K. Attempted Oxidation of 3,5-Dicyclohexyltetrahydro-1,3,5-thiadiazine-2-thione with Mercuric Oxide

One and eight-tenths grams (0.006 mole) of this compound was dissolved in ether, 2 g. of mercuric oxide added, and the mixture allowed to stand for five days with occasional agitation. The mixture was filtered, cooled, and the crystals that formed melted at 140-42°. A mixed melting point with the starting compound showed no depression, indicating that no oxidation had occurred.

The oxidation was attempted by placing the reagents in acetone and refluxing for two hours, but the starting organic compound was recovered unchanged.

L. Treatment of 3,5-Disubstituted Tetrahydro-1,3,5-thiadiazine-2-thiones with Ammonium Hydroxide

A one-gram sample of 3,5-diisopropyltetrahydro-1,3,5-thiadiazine-2-thione was suspended in water and ammonium hydroxide and allowed to stand overnight. The solid went into solution, and evaporation of the water and ammonia left a white crystalline solid, which was found to be isopropylammonium N-isopropyldithiocarbamate.

A one-gram sample of the ethyl homolog was placed in ammonium hydroxide and heated gently. The solid reacted and went into solution like the isopropyl homolog.

The cyclohexyl homolog was treated with ammonia as above, but reacted at a much lower rate, requiring several days to dissolve.

I. THERMAL DECOMPOSITION OF 3,5-DISUBSTITUTED TETRAHYDRO-1,3,5-THIADIAZINE-2-THIONES

A. Pyrolysis of 3,5-Diisopropyltetrahydro-1,3,5-thiadiazine-2-thione

Two and one-tenth grams (0.0096 mole) of this compound was placed in a flask equipped with a reflux condenser, and heated to 175°. Within a period of three or four minutes, a solid appeared in the molten mass. The heating was discontinued, the mass cooled and extracted with acetone. The dull yellow, insoluble, amorphous material gave a positive test for sulfur, a negative test for nitrogen, and melted at 226-228°, with decomposition. This material was thioformaldehyde, and 0.81 g. (0.0173 mole) was obtained. The acetone-soluble material was recrystallized twice from acetone, and melted at 99.4-100.2°. This material was thought to be 1,3,5-triisopropylhexahydro-1,3,5-triazine-2-thione.

Analysis: Calculated for $C_{12}H_{25}N_3S$: C, 59.21; H, 10.35; S, 13.17; Mol. wt., 243.40.

Found: C, 59.29; H, 11.32; S, 13.06; Mol. wt., 236.

B. Pyrolysis of 3,5-Dicyclohexyltetrahydro-1,3,5-thiadiazine-2-thione

Fifteen grams of this material was placed in a flask equipped with a reflux condenser, and gently boiled for 5 minutes. A solid (thioformaldehyde) appeared in the molten mass during the heating. After cooling, the resulting material was extracted with acetone. A soluble compound was obtained from the acetone extract, which after recrystallization twice from acetone, had a melting point of 158.2-160°. This compound was believed to be 1,3,5-tricyclohexylhexahydro-1,3,5-triazine-2-thione.

Analysis: Calculated for $C_{21}H_{37}N_3S$: C, 69.35; H, 10.26; S, 8.82; Mol. wt., 363.59.

Found: C, 69.65; H, 10.70; S, 8.75; Mol. wt., 365.

C. Pyrolysis of 3,5-Diethyltetrahydro-1,3,5-thiadiazine-2-thione

A sample of this compound was melted and gently boiled for 3 minutes, but no thioformaldehyde appeared. The material was recrystallized from acetone and melted at about 73°, indicating that the starting material had been recovered.

The decomposition was again attempted, but the boiling was continued for 5 minutes. No thioformaldehyde was obtained, and a dark brown oil remained. Attempts to obtain crystals from the oil or from alcohol or acetone solutions were unsuccessful.

The decomposition was tried again, with a two-minute boiling period. Some thioformaldehyde was obtained in addition to a soluble substance, but the only solid recovered from the acetone extract proved to be the starting material.

D. Pyrolysis of 3,5-Dibenzyltetrahydro-1,3,5-thiadiazine-2-thione

Six grams of this material was boiled gently for three minutes, then it was taken up in acetone, but no thioformaldehyde was detected. The crystals recovered from the solution started melting at 93°, indicating that some starting material was present. This solid was recrystallized twice from acetone, and then melted at 157-157.8°. The yield was 0.25 g. This compound was believed to be 1,3,5-tribenzylhexahydro-1,3,5-triazine-2-thione.

Analysis: Calculated for $C_{24}H_{25}N_3S$: C, 74.36; H, 6.51

Found: C, 74.37; H, 7.68.

E. Pyrolysis of 3,5-Di(β-phenylethyl)tetrahydro-1,3,5-thiadiazine-2-thione

A small sample of this compound was boiled gently for two minutes and then extracted with acetone. The insoluble thioformaldehyde present was removed by filtration, and attempts were made to obtain a solid from the soluble portion, but only an oil was obtained.

F. Pyrolysis of 3,5-Diphenyltetrahydro-1,3,5-thiadiazine-2-thione

Six grams (0.018 mole) of this compound was boiled gently for 7 minutes, then cooled, extracted with acetone, and the thioformaldehyde filtered from the solution. A solid, m.p. 141-142°, was recovered from the solution and a mixed melting point with 1,3,5-triphenylhexahydro-1,3,5-triazine showed no depression. No sulfur-containing solid was recovered from the solution.

G. Pyrolysis of 3,5-Di(p-tolyl)tetrahydro-1,3,5-thiadiazine-2-thione

Four and one-tenth grams (0.013 mole) was boiled gently for 6 minutes, then taken up in acetone. No thioformaldehyde was evident as all of the material was soluble. A very small amount (about 0.02 g.) of a white crystalline solid was recovered from the solution, m.p. 150.5-152°.

H. Pyrolysis of 3,5-Di(p-phenetyl)tetrahydro-1,3,5-thiadiazine-2-thione

Five grams (0.013 mole) of this compound was boiled gently for two minutes, extracted with acetone, the thioformaldehyde filtered from the solution and the soluble solid recovered. After recrystallization twice from alcohol, the melting point was 173-174.2°. The yield was 0.14 g. This compound was thought to be 1,3,5-tri(p-phenetyl)hexahydro-1,3,5-triazine-2-thione.

Analysis: Calculated for $C_{27}H_{31}O_3N_3S$: C, 67.90; H, 6.53.
Found: C, 67.72; H, 7.56.

II. PROOF OF STRUCTURE OF 1,3,5-TRISUBSTITUTED HEXAHYDRO-1,3,5-TRIAZINE-2-THIONES

A. Ultraviolet Absorption of 1,3,5-Trialkylhexahydro-1,3,5-triazine-2-thiones and Standards

Small unweighed samples of these compounds were dissolved in isooctane, and the concentrations adjusted until the absorptions fell within the desired range. The optical densities of these solutions were determined on a Beckman

Model DU Spectrophotometer, and the results are plotted on plate 4. The following compounds were studied:

1,3,5-Triisopropylhexahydro-1,3,5-triazine-2-thione
1,3,5-Tricyclohexylhexahydro-1,3,5-triazine-2-thione
N,N'-Dicyclohexylthiourea
1,3,5-Tricyclohexylhexahydro-1,3,5-triazine

B. Ultraviolet Absorption of 1,3,5-Triaryl- and 1,3,5-Triaralkylhexahydro-1,3,5-thiadiazine-2-thiones and Standards

Small unweighed samples of these compounds were dissolved in the proper solvent, and the concentrations adjusted to give absorptions that were within the desired range. The *p*-tolyl homolog was dissolved in isooctane, while the other compounds were dissolved in 95% ethyl alcohol, and the optical densities were determined. The results are plotted on plate 5. The compounds studied were:

1,3,5-Tri(*p*-tolyl)hexahydro-1,3,5-triazine-2-thione
1,3,5-Tri(*p*-phenetyl)hexahydro-1,3,5-triazine-2-thione
1,3,5-Tribenzylhexahydro-1,3,5-triazine-2-thione
N,N'-Di(*p*-phenetyl)thiourea
1,3,5-Tri(*p*-tolyl)hexahydro-1,3,5-triazine

C. Attempted Oxidation of 1,3,5-Tricyclohexylhexahydro-1,3,5-triazine-2-thione

Two grams of this compound was suspended in 15 ml. of 10% sodium hydroxide and 5 ml. of 30% hydrogen peroxide added in small portions over a period of 2 hours, while the mixture was stirred. The mixture was allowed to stand overnight, and then 3 ml. more peroxide was added. The solid was filtered, washed with water, and melted at 157-159°. A mixed melting point with the original compound showed no depression, indicating that no oxidation had occurred.

D. Acidic Hydrolysis of 1,3,5-Tricyclohexylhexahydro-1,3,5-triazine-2-thione

One-half gram of this compound was suspended in 20 ml. of water, 5 ml. of dilute hydrochloric acid added, and the mixture refluxed for 30 minutes. The solid remaining was filtered, recrystallized from alcohol, and melted at 178-80°. A mixed melting point was taken with N,N'-dicyclohexylthiourea, and the mixture melted at 176-79°, indicating that this solid was the disubstituted thiourea. During the reflux period, the odor of formaldehyde was detected, and the filtrate from the reflux gave a positive test for aldehydes with Schiff's reagent. The filtrate was made basic with sodium hydroxide, treated with benzoyl chloride, and the resulting solid recrystallized from alcohol. This product melted at 146.8-147.8°, indicating that cyclohexylamine was formed during the hydrolysis. The melting point of N-cyclohexylbenzamide is reported to be 149°.

SUMMARY

The reactions of 1,3,5-trisubstituted hexahydro-1,3,5-triazines with carbon disulfide have been studied. The principal products of these reactions are crystalline 3,5-disubstituted tetrahydro-1,3,5-thiadiazine-2-thiones for the ethyl, isopropyl, cyclohexyl, β-phenylethyl, and p-phenetyl homologs. The n-butyl and n-hexyl homologs appear to react, but the products are liquids, and attempts to purify these materials were not successful. The benzyl, phenyl, and p-tolyl homologs do not react in a similar manner under the experimental conditions that were used; however, an alternate procedure was used to prepare the desired 3,5-disubstituted tetrahydro-1,3,5-thiadiazine-2-thiones. This class of compounds has been reported previously but the following homologs that were prepared are not recorded in the literature: isopropyl, cyclohexyl, β-phenylethyl, benzyl, phenyl, p-tolyl, and p-phenetyl. Additional evidence for the 3,5-disubstituted tetrahydro-1,3,5-thiadiazine-2-thione structure was obtained, to supplement that given in the literature.

The 3,5-disubstituted tetrahydro-1,3,5-thiadiazine-2-thiones were thermally decomposed, and crystalline pyrolysis products were obtained for the isopropyl, cyclohexyl, β-phenylethyl, p-tolyl, and p-phenetyl homologs. These products are believed to be 1,3,5-trisubstituted hexahydro-1,3,5-triazine-2-thiones, since evidence in support of this structure was obtained. This class of compounds has not been previously reported in the literature.

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HEXAHYDRO-1,3,5-TRIAZINES WITH CARBON
DISULFIDE

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He entered the naval service in the fall of 1943, attended the Naval Reserve School at the United States Naval Academy, and received a commission as Ensign in the Naval Reserve in December of 1943. In January of 1944, he was married to Winona Maddox. He attended the Naval Diesel Engineering School at Penn State College, State College, Pa., in the spring of 1944, and was then assigned to the USS LST 681, which served in the Pacific area.

After his discharge from the navy in the spring of 1946, he attended the summer session at Northwestern State College, and that fall he entered Oklahoma A. and M. College. In the fall of 1947 he was appointed a Graduate Fellow in the Chemistry Department, and served in that capacity for four years. He received a Master's degree in June of 1949. He has two children, Steven Merrill and Janine Kay.