3-1975

Photochemical behavior of some nitrogen heterocyclics

James Wesley Harris

PHOTOCHEMICAL BEHAVIOR OF SOME NITROGEN HETEROCYCLICS

A THESIS

SUBMITTED TO THE DEPARTMENT OF CHEMISTRY

OF THE GRADUATE SCHOOL OF

THE UNIVERSITY OF RICHMOND

IN PARTIAL FULFILLMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

MASTER OF SCIENCE

Stuart C Clough

W. Allan Pozzuto

James E. Worsham, Jr.

Wm E. Trout, Jr.

BY

JAMES WESLEY HARRIS, JR.

William H Myers

Richard W. Taylor

MAY, 1975

to my parents

TABLE OF CONTENTS

ACKNOWLEDGMENTS

I would like to express my deepest appreciation and utmost respect to Dr. Stuart C. Clough who suggested this problem. His constructive criticism always provided the needed improvement, and his never ending wit provided the enjoyment which makes life more bearable.

In addition, I want to gratefully acknowledge and express my appreciation to Mr. Ashby F. Johnson, Jr. and Mr. John B. Forehand, who provided their expertise and time in performing the 60 MHz nuclear magnetic resonance spectra and the mass spectral analyses, respectively, and their employer, A. H. Robins Company, who allowed them to use the instrumentation to do so.

My thankfulness also goes to Dr. Jerry Whidby, who gave his time and expertise to do the 100 MHz nuclear magnetic resonance spectra, and his employer, Philip Morris, Incorporated, who provided the instrumentation to do so.

Finally, I want to thank the University of Richmond who helped sponsor my research with a Faculty Research Grant.

ABSTRACT

The compounds, 3,6-dimethoxypyridazine, 1,2-dimethyl-3,6(1H,2H)-pyridazinedione, and 6-methoxy-2-methyl-3(2H)-pyridazinone, were prepared by using reported preparations. Their photochemistry was investigated and compared to the thermal chemistry and photochemistry of maleic hydrazide.

HISTORICAL

Since colonial times when John Rolfe harvested his first crop of tobacco in 1612, farmers have been attempting to increase the yield (pounds/acre) of tobacco by a variey of agricultural techniques. Growers of bright tobacco soon realized that a significant increase in yield could be had if tobacco plants were decapitated (topped) when they reached maturity. Topping is usually done at the time or before the plant begins to flower and is accomplished by breaking or cutting off the top or crown of the plant at about the third branch below the seed head.[1]

By removing this enormous metabolic sink, the plant response normally includes an enlargement of upper leaves, which leads to an increase in cured leaf body, and an increase in the growth of the root system. The increased root activity leads to an increase in the amount of nicotine content in a topped plant, since the nicotine content is proportional to the root activity. The enlargement of the leaves would mean they have thicker cell walls and more cellular contents leading to an increase in the cured leaf body.[2]

However, when the grower removes the source of apical dominance from the plant, he encounters a new problem resulting from stimulated growth of lateral branches, more commonly known as "suckers." There are usually two suckers present

in each leaf axil, and sometimes a third sucker may be present in the axils of the upper leaves. The first sucker attached to the plant has a well organized meristem including one or two leaf primordia and several young immature leaves. This sucker stem is somewhat elongated and if the plant is topped, rapid elongation of this first sucker of the upper three or four axils results. Gradually, these suckers re-establish partial apical dominance and suppress not only the growth of other suckers, but unfortunately the further development of the primary leaves.

The second sucker, which is much less developed but has a meristem and three or four leaf primordia, is attached to the leaf petiole. Topping causes little additional development of the second sucker, but if the first suckers are removed from the upper leaf axils, rapid development of the second suckers will occur in those same axils, and first suckers in the middle of the plant will begin to develop rapidly. Even if suckers present on the upper part of the plant are removed, growth of the lower suckers occurs. The plant wants to continue to develop suckers to maintain some semblance of apical dominance so long as auxillary buds are present and capable of growth. Therefore, the manual removal of suckers during a growing season is a recurring and demanding process.

Modern chemical control of tobacco suckers was first conceived during a lecture on apical dominance in a beginning botany course at North Carolina State University. When

indole-acetic acid was applied to the cut stump of a decapitated plant, that plant acted similarly to a plant with an intact top. This observation lead a student to question whether a chemical method could control suckers on topped tobacco plants.[2]

At first, various synthetic plant hormones were tried, but such side effects as adventitious root initiation and distorted plant growth were very undesirable.[2] The chemical technique of using the hormones was put aside, and the search was continued for a chemical compound that would control suckers on the topped tobacco plants. In 1949 Schoene and Hoffman reported that maleic hydrazide (1) would temporarily inhibit the growth of a plant with little visible harm to the plant itself.[3] Then, in 1952 Petersen reported maleic hydrazide was effective in controlling tobacco suckers.[4] Its usefulness spread widely in the tobacco growing areas, and today, more than 90% of the U. S. bright tobacco crop is treated with maleic hydrazide.

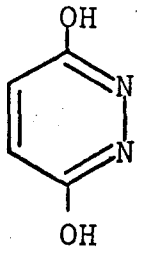
Maleic hydrazide eliminated the tedious hand operation of removing suckers, and it increased crop yield when compared to hand suckered crops, because of its ability to better control suckers. Several additional benefits were realized by the grower. The plants did not wilt as readily after treatment should dry weather conditions follow because there is an increase in the plant's moisture-holding capacity.[5] There has been speculation that as metabolites accumulated due to increased sucker control,

there may be an accumulation of hydrophilic substances. These are probably responsible for the increase in moisture-holding capacity. It has also been reported that treated plants were less susceptible to brown spot disease (Alternaria longipes), and late season buildup of hornworm populations (Manduca sexta) were reduced because of the reduction in tender tissue which is used as a habitat.[2]

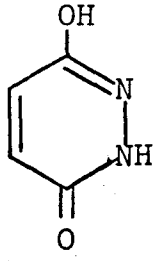
However, what may benefit the grower, may not benefit the manufacturer and consumer. Maleic hydrazide treatment causes undesirable changes in the cured leaf. There is a decrease in the filling capacity due to the fact that where good sucker control occurs, leaves will ripen more slowly, and thereby remain longer on the plant. The slower ripening will result in thicker and heavier leaves, which means the leaves would have thicker cell walls and more cellular contents.[2] After curing, this results in a product that is less springy; consequently, the filling capacity would be reduced. It has also been reported that there are decreases in the alkaloids, including nicotine, and the ash content after treating with maleic hydrazide.[5] In addition, maleic hydrazide treated tobacco is usually lacking in color and there is the "MH-effect," which is the bronzing of the leaves while still on the growing plant. This effect may cause the grower to believe his plants are mature, and he may harvest the leaves before they are fully ripe.[2]

Maleic hydrazide is normally applied to the tobacco plant as the diethanolamine salt in concentrations of approximately 30% (MH-30) or as a solution of the potassium salt (Royal MH-30)[6], both resulting in the application of approximately 170 mg/plant of maleic hydrazide.[2] Since it is sprayed on the plant, significant quantities of it are left on and in the leaves, and this residue causes major changes in both the chemical and physical properties of the leaf. Because this residue may ultimately be inhaled by the consumer, it was deemed of interest to study the photochemical and thermal behavior of this suckering agent.

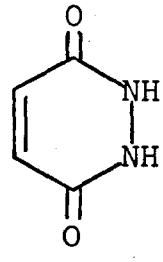
Maleic hydrazide is capable of existing in three possible tautomeric forms (1a, 1b, and 1c):



1a

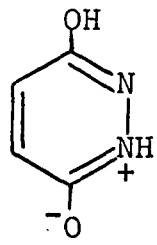


1b



1c

Ottersen concluded from his X-ray study on 4,5-dichloro-3,6-pyridazinedione (2) that the solid state structure of 1 corresponded to tautomer 1b. The basis of the structure assignment was the different carbon-nitrogen and carbon-oxygen bond lengths, and the location of hydrogen atoms on the oxygen and nitrogen. Also resonance stabilization of the heterocycle was evident even though the double bonds were more localized in 2 than in pyridazine.[7] It had been previously pointed out that 1b would permit resonance stabilization of the heterocycle.[8] The orbital of the single bonded nitrogen with the unshared pair of electrons could overlap giving a resonance structure (3) with an sp^2 - hybridized N-atom.

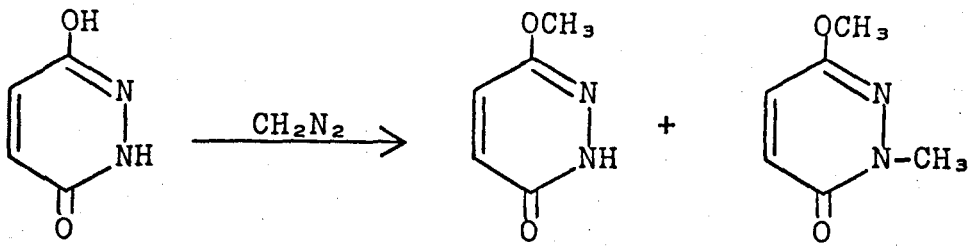


3

However, in solution, there is much evidence that 1 exists in at least two tautomeric forms, 1b and 1c, 1b being the predominant tautomer.

Arndt concluded from the reaction of 1 with diazomethane that there was evidence for 1 existing predominantly as tautomer 1b in solution. In this reaction, 6-methoxy-3(2H)-pyridazinone (4) formed rapidly, and 6-methoxy-2-methyl-3(2H)-pyridazinone (5) subsequently

formed more slowly.[8]

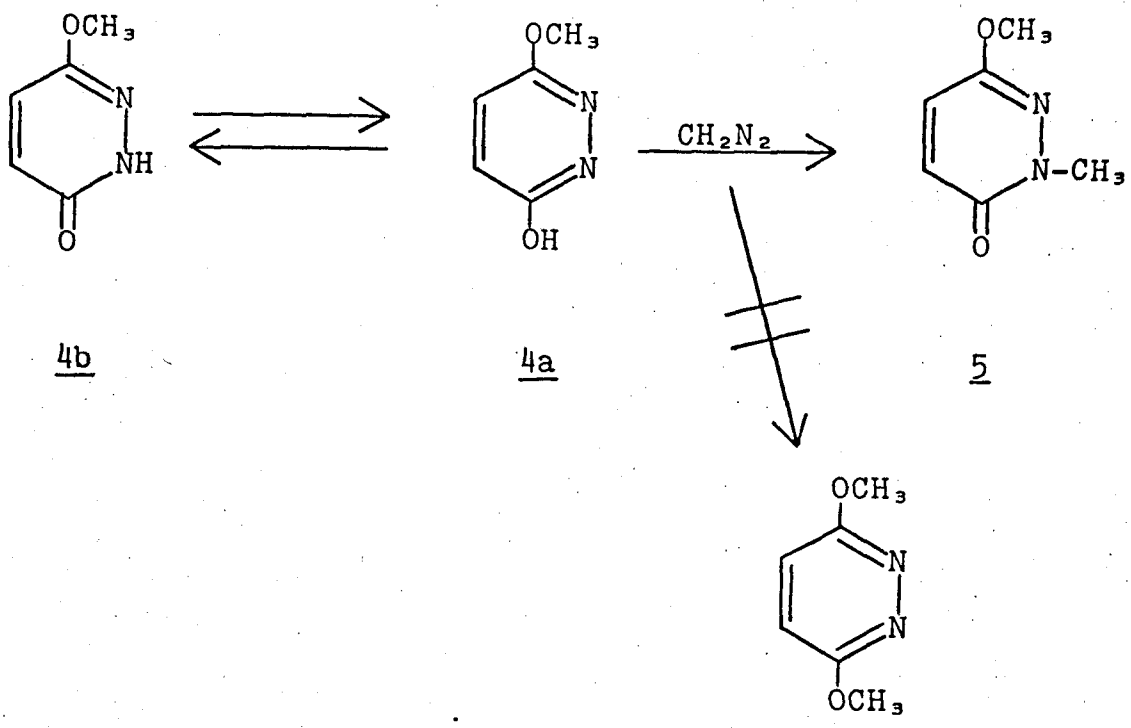


1b 4b 5

Miller and White, using uv spectroscopy and chemical methods as probes, undertook a study involving 1 and several of its methyl derivatives also to determine the major tautomer present in solution.[9]

6-methoxy-3(2H)-pyridazinone (4)
6-methoxy-2-methyl-3(2H)-pyridazinone (5)
3,6-dimethoxypyridazine (6)
6-hydroxy-2-methyl-3(2H)-pyridazinone (7)
1,2-dimethyl-3,6(1H,2H)-pyridazinedione (8)

Firstly, they ruled out tautomer 1a on the basis of the reaction of 4 with excess diazomethane. The reaction gave 5, but no 6.

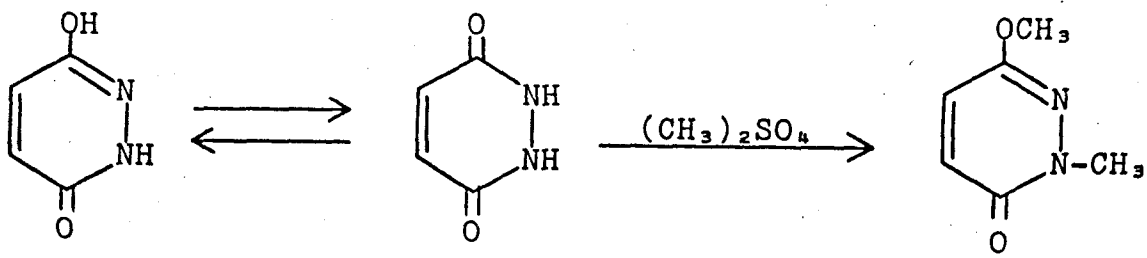


4b 4a 5

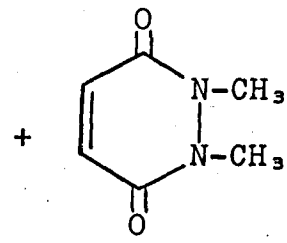
6

Then by comparing the uv spectra, pKa values, and chemical reactivities of 1 with the same data for the methyl derivatives, Miller and White also concluded that 1 exists predominantly as tautomer 1b.

However, when 1 is reacted with $(CH_3)_2SO_4$, it apparently yields 5 and 8.[10]



1b 1c 5

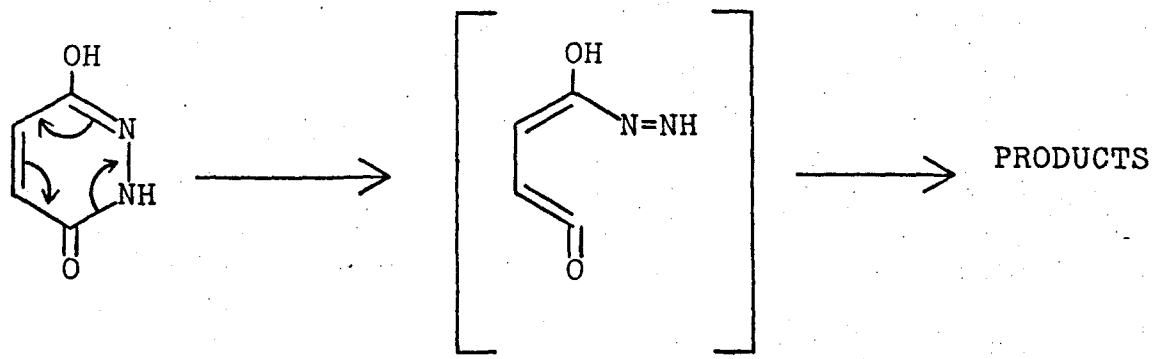


8

Therefore, in solution, 1 does seem to exist as an equilibrium mixture of two tautomeric forms, 1b and 1c, with the uv spectra suggesting that the equilibrium greatly favors 1b. This fact is also consistent with Katritzky's interpretation of 1's proton magnetic resonance spectrum.[11] He concluded that fast proton exchange (conversion of 1b to 1c and vice versa) caused the discrepancy between the interpretation of the nmr spectrum, reported by Gompper and Altreuther as favoring 1c as the predominant tautomer,[12] and other spectral and chemical evidence which favors 1b. No one has reported any evidence that 1a is of any importance in solution.

In 1958 Crafts et al.,[13] and in 1961 Mitchell[14] reported that 1 was stable to light, a factor of obvious significance in its utilization, even though Crafts had observed differences between greenhouse and field trials. Because of these differences, Stoessl reinvestigated the excited state behavior of 1 in 1964. He found it to be photo-labile and identified a number of the breakdown products: nitric acid (12.5%), formic acid (7.5%), succinic acid (18.8%), maleic acid (8.3%), and fumaric acid (22.6%).[15]

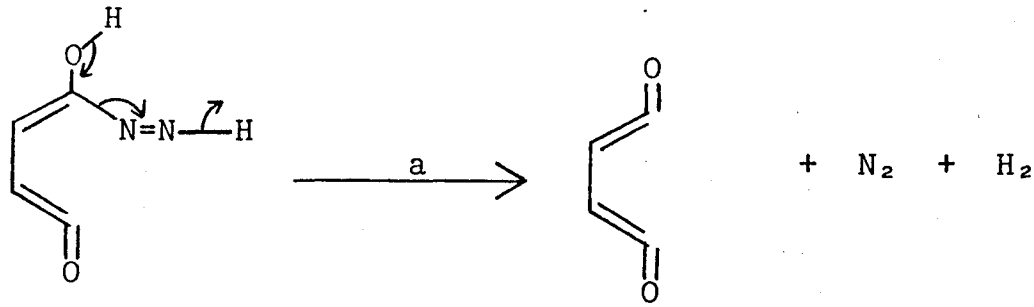
From what is known concerning the important tautomeric form of 1 in solution and from the nature of the identified products, Stoessl proposed that the pathway of photolysis could be analogous to that of six-membered carbocyclic dienes, which are known to undergo photochemical electrocyclic ring opening to trienes.[16]



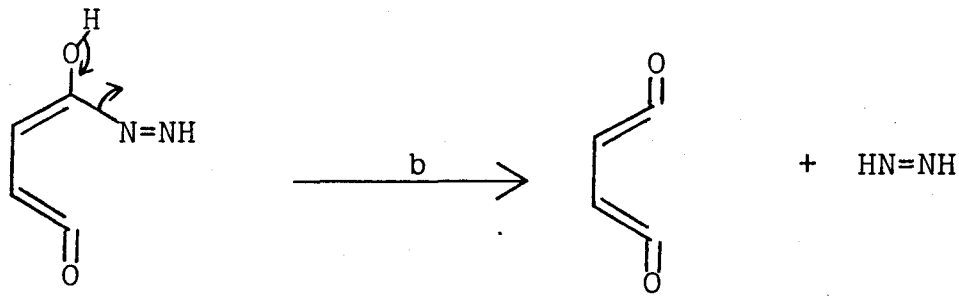
1b 9

The intermediate (9) could decompose in a number of ways (a, b, or c) in which diimide could, but need not, be involved. The products would be succinic acid (via the ketene) and nitrogen, together with either hydrogen or the

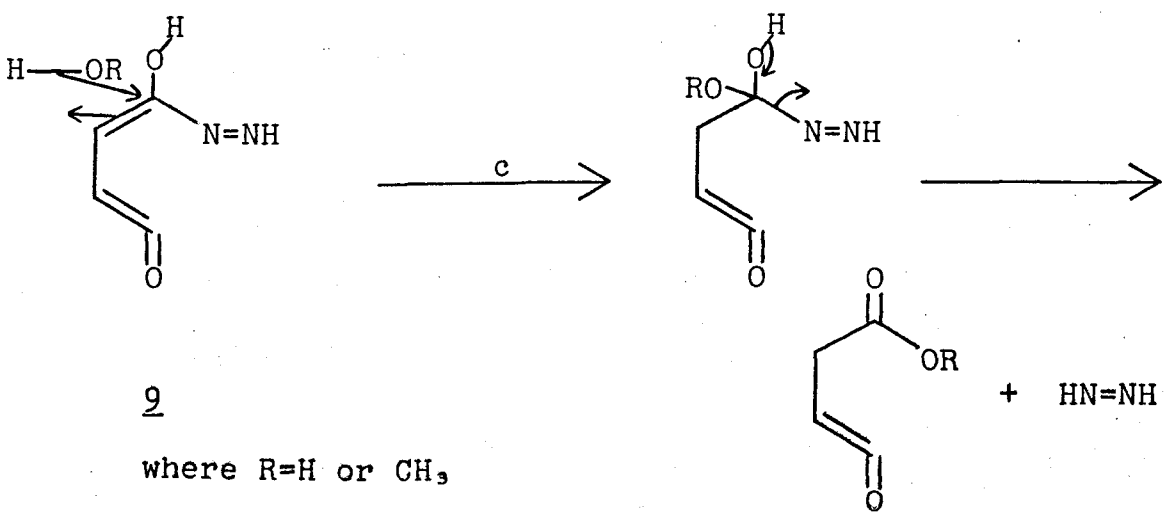
products of a hydrogen transfer to one or several acceptors.



9



9

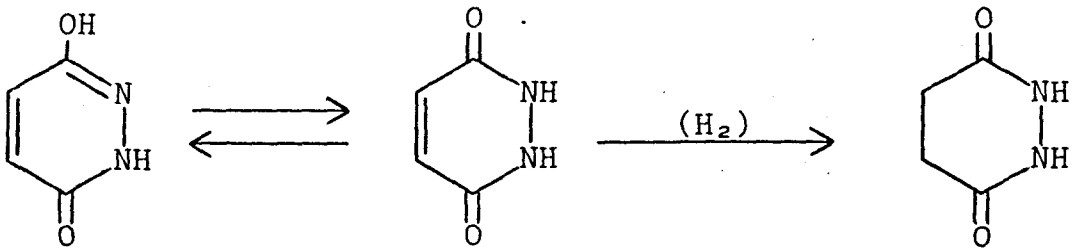


9

where R=H or CH_3

Stoessl irradiated aqueous solutions of 1 in sealed, evacuated vessels. He found that hydrogen was liberated only in traces or not at all in some runs. Based on the evidence that little or no hydrogen was formed, and that nitrogen (40%), carbon dioxide (1.5%), and succinic acid (25%) were isolated, he discarded pathway a as a mechanism of formation of the photolysis products, but the possibility of hydrogen transfer still remained.

Stoessl then proposed that 1 might act as a hydrogen acceptor.



1b 1c 1o

He showed that the expected product, cyclic succinhydrazide (1o), was one of the photolysis products by comparing chromatographic properties with the authentic compound, but only in a yield of approximately 3% based on photolyzed 1.

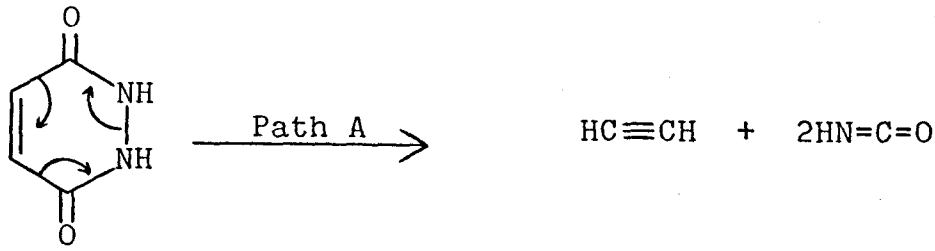
Stoessl then attempted to prove the intermediacy of ketenes by irradiating 1 in dry methanol. The experiment produced some dimethyl succinate in a very low yield (0.45%)

along with 10 and nitrogen.® No dicarboxylic acids or the dimethyl esters of fumaric and maleic acids were detected. Therefore, Stoessl's work only gave, at the most, tentative support to his mechanism, and no further evidence as to which pathway (a, b, or c) his intermediate followed in decomposing to products.[17]

In addition to 1's photolytic characteristics, Clough et al.,[18] and Patterson et al.,[19] have investigated its thermal behavior above 450°C. Because it is used extensively in the tobacco fields of the U. S. as a sucker-inhibiting agent,[2,6] concern about the fate of residual 1 in a cigarette is very real. There is additional interest in its thermal behavior because of the possibility that Germany, which imports more than 100 million pounds of U. S. tobacco leaf each year, might ban the use of 1 or set tolerance levels for it or for its thermal degradation products in the manufactured product or in the smoke.[20]

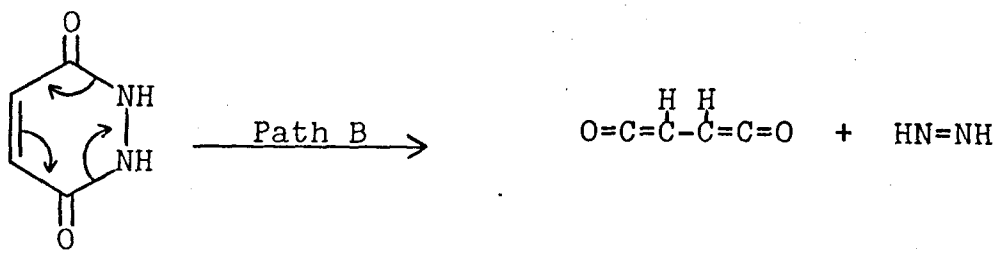
Clough proposed that 1 might thermally fragment in either of two ways. Path A is the thermally allowed 2+2+2 cyclo-reversion mechanism leading to acetylene and two moles of isocyanic acid.

®According to Stoessl, the low yield resulted from unavoidable losses during the work-up. He wrote that " more than 67% of the ester was lost in an appropriate control experiment." [17]



1c

The second thermally allowed path (B) is a 4+2 cycloreversion which would yield diimide and bis-ketene.



1c

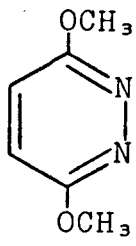
Reasonably strong evidence, including trapping experiments, for the formation of bis-ketene and isocyanic acid was presented which suggested that both fragmentation paths were thermally operative and accounted for essentially all of the primary products observed.

In addition, it is worthy to note the similarity in the thermal and photochemical fragmentations in the maleic hydrazide system. Path B of Clough *et al.*, forms the same two products, diimide and bis-ketene, as Stoessl's mechanism *b via* the decomposition of intermediate 9.

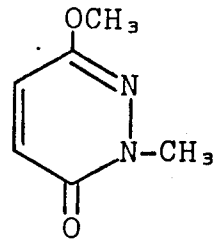
Also Stoessl's mechanism a will give bis-ketene, and mechanism c gives diimide plus a ketene.

STATEMENT OF THE PROBLEM

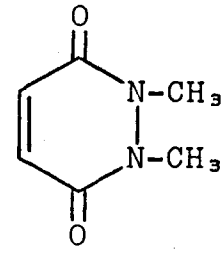
Both Stoessl's photochemical studies and Clough's thermal studies, however, are ambiguous by nature of the substrate. Because of the equilibrium between the tautomeric forms of 1, it is not clear which form(s) is (are) responsible for the transformations observed. Therefore, a goal of this research is to undertake a photochemical study of each of the methyl derivatives (6, 5, and 8) corresponding to the tautomers of 1.



6



5



8

Methyl substitution as shown should preclude tautomerization, and since each individual methyl derivative represents one of the tautomeric forms of 1, each should offer precise chemistry which will allow the definition of the chemical behavior of that particular tautomer via the isolation and identification of the photolysis products. With the identification of the photolysis products from each derivative a reaction mechanism might be proposed which

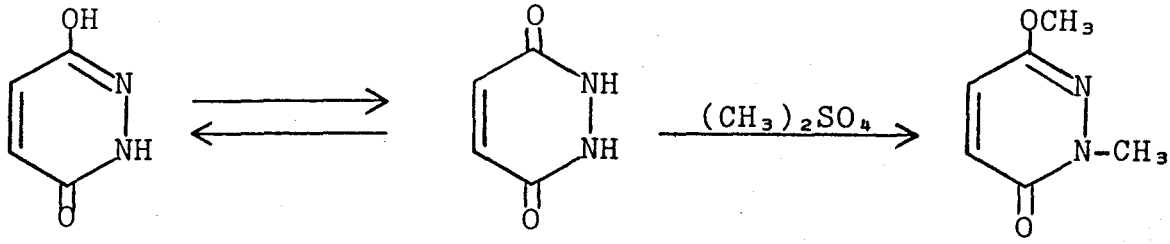
may or may not be consistent with Stoessl's or Clough's mechanisms. In the opinion of this author, a ring system, which is as commercially important and biologically active as the pyrazinedione ring system (of which 1 is the parent compound) deserves to have its chemical behavior in both the ground and excited states well understood.

DISCUSSION

Syntheses

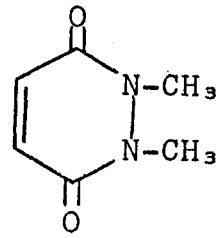
Each of the three methyl derivatives of maleic hydrazide (5, 6, and 8) was prepared by the procedures of Przezdziecki and Chrzaszczewska[10] with only a modification in the procedure for the preparation of 5 and 8.

Compounds 5 and 8 were prepared by reacting 1 with dimethyl sulfate at 140°C.



1b 1c 5

+



8

After two hours of heating, water and then solid sodium carbonate were added to the reaction mixture to give a saturated solution of sodium carbonate, and this obtained mixture was extracted with chloroform. The chloroform extract was dried ($MgSO_4$) and rotary evaporated to a solid. This solid was then placed in a vacuum sublimation apparatus, and the temperture kept at 90°C until all of 5 had sublimed. Compound 5 was removed from the apparatus, and then the temperature was raised to 120°C where 8 sublimed.

Przezdziecki and Chrzaszczewska claimed separation of the two derivatives by crystallization from chloroform. According to their procedure, the chloroform extract of the saturated solution of sodium carbonate was concentrated and the precipitate was filtered off. This precipitate was redissolved in chloroform to which ether was added until crystallization started. The precipitate was filtered off, dried, and was found to be 8. Finally, they evaporated the chloroform filtrate and obtained 5. No matter how this author tried, a clean separation of the two derivatives using chloroform could not be achieved. In our hands, fractional sublimation was found to be a more convenient method of separating the two derivatives.

The third derivative, 6, was easily prepared by following Przezdziecki and Chrzaszczewska's procedure. 3,6-Dichloropyridazine was heated with sodium methylate in a sealed tube to form 6 and sodium chloride. The sodium chloride was filtered off, the methanol rotary evaporated,

and 6 was crystallized from water.

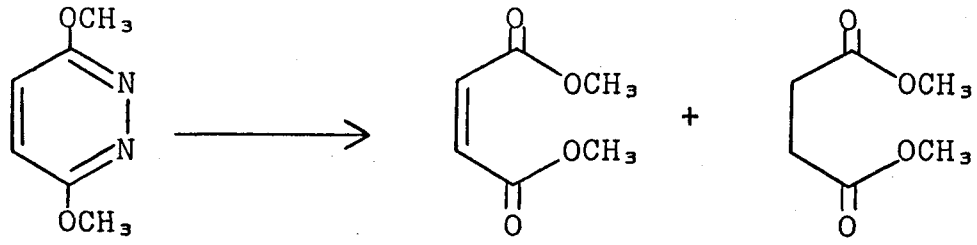
Photochemistry

The photochemistry of the isomers 5, 6, and 8 were investigated separately. It was expected that either 5 or 8 or both would undergo photoinduced fragmentation paralleling that of maleic hydrazide as reported by Stoessl. It was further expected that isomer 6 would probably not parallel the photochemical behavior of maleic hydrazide and indeed might well be either relatively unaffected by uv irradiation or generate Dewar pyridazines as observed in the analogous photochemistry of pyridine and benzene.[21] Our results were not exactly in accord with these initial predictions and are discussed below.

Photochemistry of 3,6-Dimethoxypyridazine (6)

Compound 6 (λ_{max}^{EtOH} 287 nm, ε 2295) was irradiated in methanol through a Pyrex filter using a Hanovia 550 watt mercury arc lamp. Extended irradiation (108 hours) resulted in the formation of only trace amounts of seven products which were separated by gas chromatography. Most of the starting material was recovered apparently unchanged. Of the seven products only three were formed in amounts sufficient for structural assignments to be made. Of these only two, dimethyl succinate and dimethyl maleate, have been identified. The third product, an oil, has not been identified to date, although it is of particular interest to

us because it is formed as a major product in the irradiation of 5. The compound will be designated I (for interest).



6

+ I + 4 Trace Products

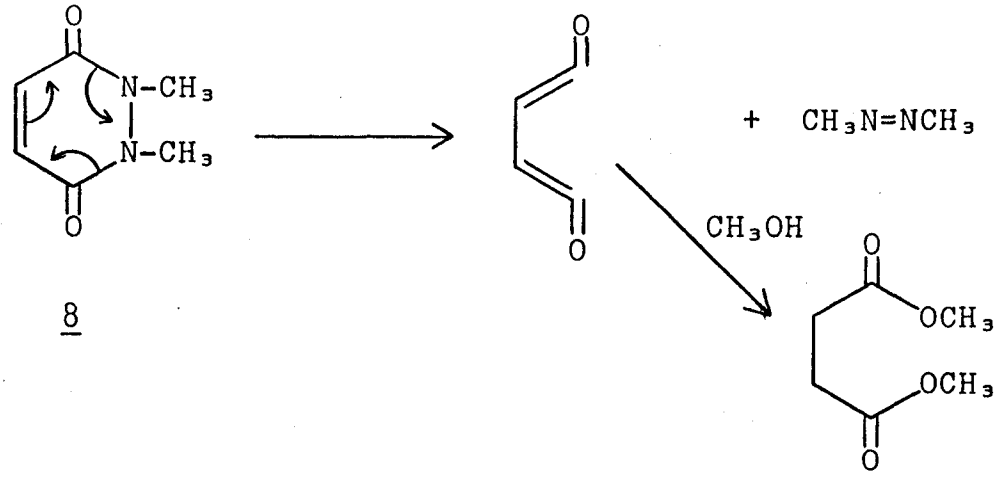
We have attempted to identify I by interpretation of its spectral properties. The infra-red spectrum shows no absorption in the NH or OH region but shows absorption at 2850-3000 cm^{-1}, indicative of the presence of an sp^3 C-H stretch. There was no detectable absorption at energies greater than 3000 cm^{-1} suggesting the absence of an sp^2 C-H stretch in the molecule. There were two strong bands in the carbonyl region, one at 1790 cm^{-1} which may well be due to a methyl ester, and another at 1735 cm^{-1} which could be the result of either a C=O or C=N stretch.

The 100 MHz nmr spectrum, run in $CDCl_3$, was complicated because of difficulties in obtaining a pure sample. It showed weak singlets at δ 7.10 and 7.50 which did not integrate sensibly and are assumed to result from impurities. More interesting were the three complex multiplets at δ 2.95, 3.60, and 4.60, and additionally what appears to be the superposition of several singlets at δ 3.90 which are

assumed to be similar methyl groups (OCH_3 or NCH_3). Because the spectrum is complex and contains significant impurities, the integration we have obtained is not believed to be meaningful. The mass spectral fragmentation pattern is also complex suggesting that the aromatic ring has been destroyed, and the molecular ion is believed to be present at either m/e 212 or m/e 184.

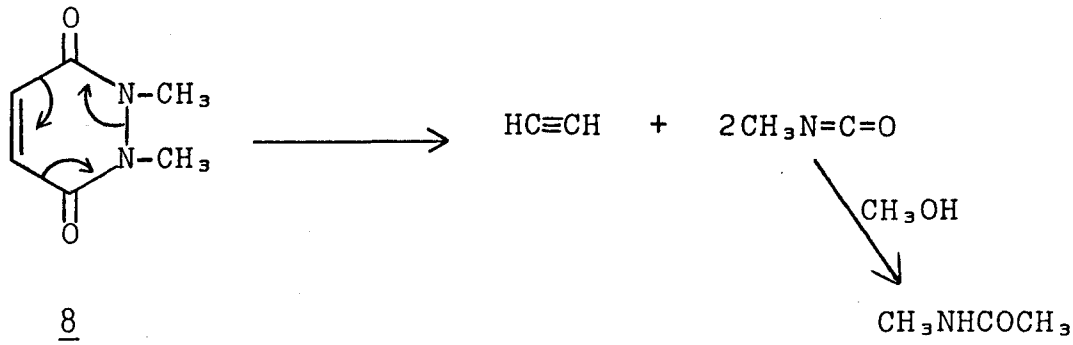
Photochemistry of 1,2-Dimethyl-3,6(1H,2H)-pyridazinedione (8)

Two modes of cleavage are available for this compound. A 4+2 cycloreversion could produce bis-ketene and azomethane. Under the reaction conditions employed, azomethane (bp 1.5°C)[22] would be a gas and consequently would be lost in work-up. Bis-ketene, if generated in methanol, should react to form dimethyl succinate. It is worth noting that substituted bis-ketenes have been shown to be intermediates in the photolyses of substituted cyclobutenediones, and some have actually been observed directly by Chapman and his co-workers[23] and also by Obata and Takizawa[24] using infra-red spectroscopy at subambient temperatures. Bis-ketene itself has also been implicated in the thermal fragmentation of maleic hydrazide as discussed in the historical section, and it is for this reason that it is highly suspected as an intermediate in this investigation.



8

An alternate photofragmentation path is a 2+2+2 cycloreversion which would produce methyl isocyanate and acetylene.®



8

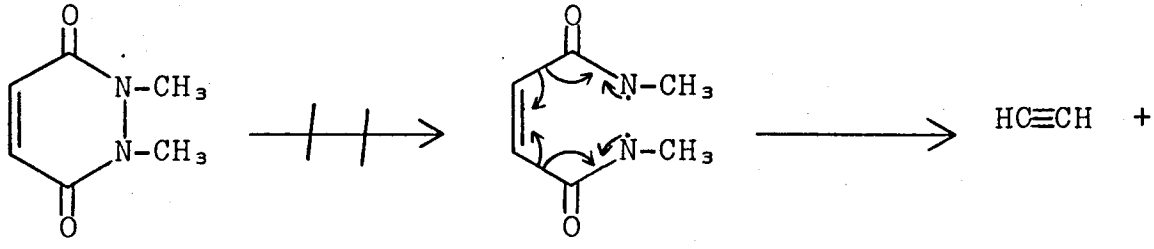
®The photochemically induced cycloreversions indicated, if concerted, would have to be antarafacial with respect to one component. We have no evidence for suggesting that the reactions we are dealing with are concerted and thus do not intend to imply that they are. They are discussed in this terminology for convenience only.

Any methyl isocyanate produced should also react with methanol to form N-methyl methylcarbamate. The acetylene would be lost in our work-up.

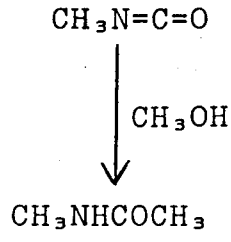
When 8 (λ_{max}^{EtOH} 335 nm, ε 2701) was irradiated through a Pyrex filter for an extended period of time a very slow photoreaction occurred. Only one product was observed in the photoreaction. It was subsequently separated from residual starting material and isolated by gas chromatography and identified as dimethyl succinate by comparisons of retention time (gc), ir spectra, and nmr spectra of an authentic sample. This observation was interpreted as suggestive evidence for the 4+2 cyclo-reversion generating bis-ketene. With this thought in mind efforts were then expended towards the trapping of bis-ketene which was believed to have been produced. The photoreaction was thus run in the presence of n-butyl-amine. Amines are significantly more reactive as nucleo-philes towards ketenes than alcohols and should trap the bis-ketene, if present, to form N-n-butylsuccinimide.[25] The n-butylamine was chosen because it has been used in earlier work to trap bis-ketene which had been generated thermally.[18] The result of this experiment was the forma-tion, as expected, of N-n-butylsuccinimide. This was identified by comparison of retention time (gc) and ir spectra with an authentic sample of N-n-butylsuccinimide prepared according to a procedure similar to that of Dufield *et al.*[26] Significantly, n-butylamine does not produce

N-n-butylsuccinimide when treated with dimethyl succinate under our reaction conditions. At present this is the extent of the evidence in hand to support the presence of bis-ketene and thus the 4+2 cycloreversion. No attempt has been made to document the presence of azomethane at this time.

All efforts to demonstrate the involvement of the 2+2+2 cycloreversion, which might reasonably be expected to occur <u>via</u> a diradical process initiated by cleavage of the N-N bond was to no avail.



8

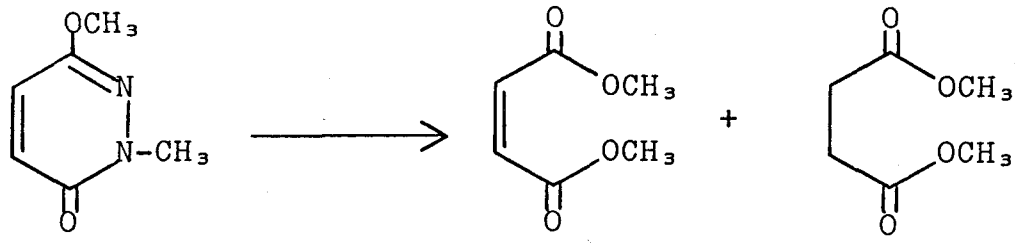


Authentic N-methyl methylcarbamate was synthesized by reaction of $CH_3N=C=O$ with CH_3OH and gas chromatograph conditions were optimized for the potential spotting of this compound. At no time was there any indication of the presence of this compound, and thus there was no evidence for this competing path. This observation contrasts dramatically with the thermal behavior described

for maleic hydrazide itself. It is also interesting to note that no dimethyl maleate or fumarate was observed in the photolysate. Although extremely slow, this is apparently a rather clean photoreaction.

Photochemistry of 6-Methoxy-2-methyl-3(2H)-pyridazinone (5)

Compound 5 (λ_{max}^{EtOH} 310 nm, ε 2712) was irradiated in methanol for extended periods of time (144 hours). This resulted in the formation of only trace amounts of thirteen products, which were separated by gas chromatography. Most of the starting material was recovered apparently unchanged, and of the thirteen products only three were formed in amounts sufficient for structural assignments to be made.



5 + I + 10 Products

Recovered starting material and dimethyl succinate were readily identified (gc, ir, nmr, and mass spect). A second component was at first believed to be 1,2-dimethoxyethylene because of the 100 MHz nmr spectrum obtained by the FT technique on a sample trapped from the gas chromatograph. However, when the retention time of this component

was compared to those of both cis and trans-1,2-dimethoxyethylene, prepared by the procedure of Kokubo et al.,[27] this was found not to be the case. Further investigation (ir, nmr, and mass spect) showed this component to be dimethyl maleate. The third major product was not identified but has already been described as I, formed in the photolysis of 6.

This photoreaction, like that of 6, is very inefficient. However, when the anhydrous methanol solution of 5 was acidified with HCl and photolyzed, photodecomposition was relatively rapid and formation of I occurred almost exclusively. The enhancement of the photoefficiency is considered to be of considerable significance as will be discussed in the following section. Precisely how significant awaits the structure assignment of I.®

®Control experiments demonstrated that 5, 6, and 8 showed no decomposition after three weeks in methanol in the absence of uv light.

SUMMARY

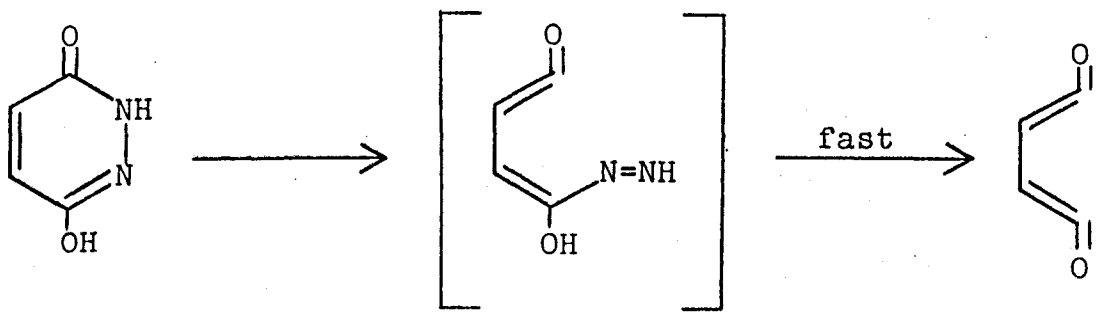
If tautomer 1c was important in the photoinduced fragmentation of maleic hydrazide, one would expect 8 to undergo a similar fragmentation with a similar quantum yield. Indeed, since photoinduced tautomerization, a possible route for radiationless decay, was precluded by methyl substitution, one might even expect the fragmentation of 8 to be more efficient. Although the products of the photolyses of maleic hydrazide and 8 were very similar, the efficiency of the reactions differed considerably. Instead of observing a more efficient photoreaction, the opposite was noted. This suggests to us that tautomer 1c was not the tautomer which directed the fragmentation of maleic hydrazide.

The photolysis of 8 is nicely rationalized as the result of a 4+2 cycloreversion to form bis-ketene and azomethane. The reaction is clean and no evidence was found to suggest the involvement of any competing 2+2+2 cycloreversion. This is in direct contrast to the thermal fragmentation of maleic hydrazide in which both 4+2 and 2+2+2 cycloreversions apparently competed rather effectively.

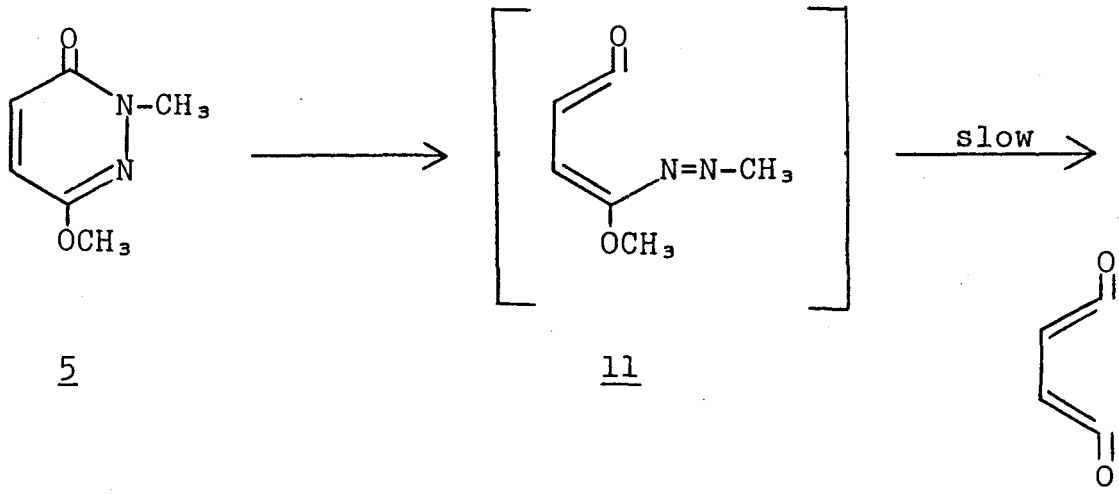
Compound 6 was not expected to undergo any photoinduced fragmentation paralleling that of maleic hydrazide nor to produce any products remotely similar to any of the other

two isomers. However, it did undergo photoinduced fragmentation, producing dimethyl maleate, dimethyl succinate, and I along with four trace products. Surprisingly, 6 was more efficient at generating I than was 5. Without the identification of I, no logical explanation can be offered explaining why 6 gave the products it did.

If tautomer 1b was the tautomer which directed the photoinduced decomposition of maleic hydrazide, one would expect 5 to give similar products (i.e., dimethyl maleate, dimethyl succinate, and azomethane). One can argue that the quantum yield for formation of these products should be similar to or less than that observed in the photolysis of maleic hydrazide. Intermediate 9, presumably formed in the irradiation of maleic hydrazide, should be able to undergo facile proton transfer and elimination of diimide to form bis-ketene and subsequent products, whereas the similar methyl transfer and elimination of azomethane from intermediate 11, possibly generated in the irradiation of 5, should be rather slow.



1b 9

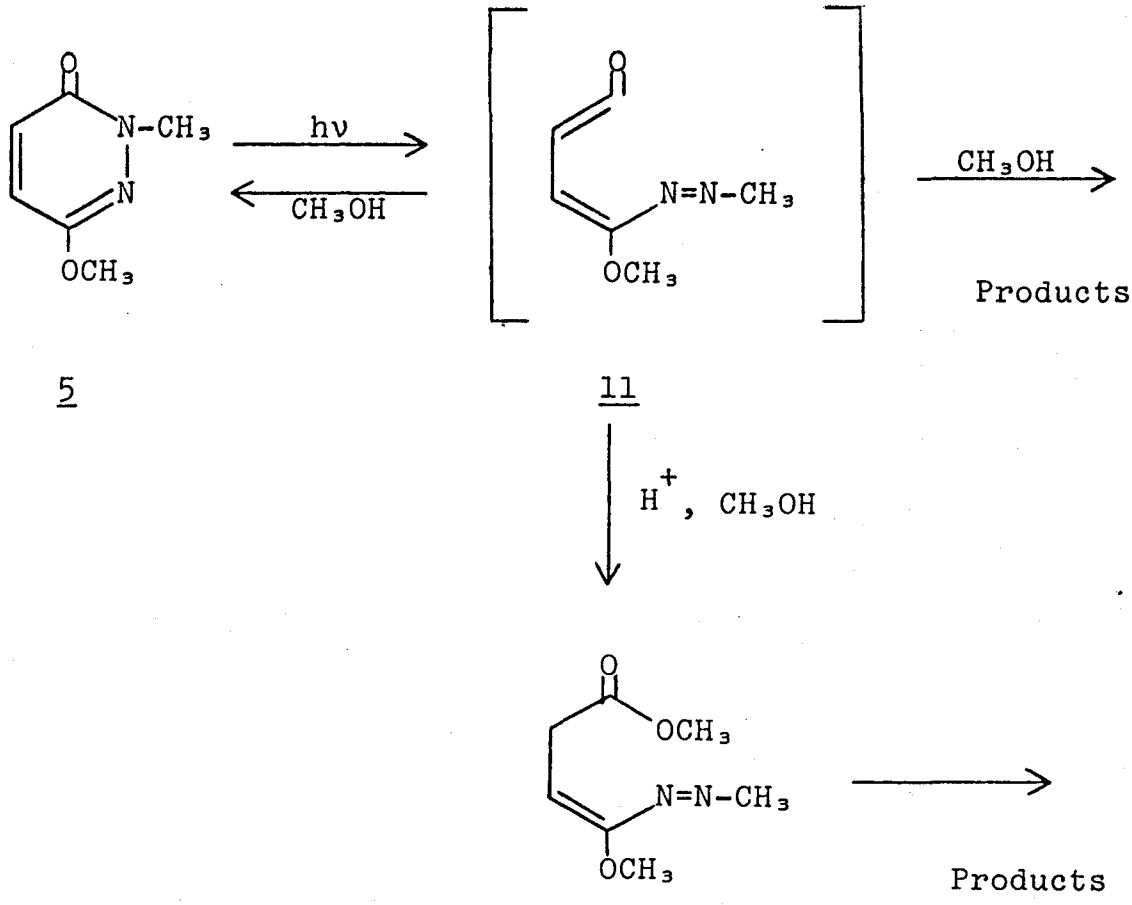


5 11

Indeed, dimethyl succinate might arise from intermediate 11 directly without involvement of the bis-ketene. In any case, intermediate 11 should be relatively stable to decomposition (compared to 9) and could undergo a thermally allowed 2+2+2 electrocyclic ring closure[16] to reform starting material, thus greatly decreasing the overall photoefficiency of the reaction. Competing with this reversibility is any other chemistry which might result from intermediate 11.

Irradiation of 5 did produce dimethyl maleate and dimethyl succinate. In addition there were many trace products and a significant amount of I. The efficiency of the reaction was low by comparison to the corresponding reaction of maleic hydrazide, as was expected. If the proposed mechanism involving the reversible formation of intermediate 11 is operative, it should be possible to devise an experiment capable of trapping this labile

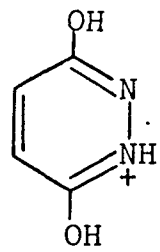
compound. For this reason 5 was photolyzed in anhydrous methanol in the presence of HCl. The reaction of alcohols with ketenes is known to be acid catalyzed.[28] We expected to see similar products formed with a significant increase in the efficiency of the reaction because acid catalyzed nucleophilic attack on the ketene would be expected to be faster than thermal ring closure to 5.



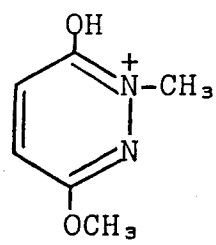
The result of this experiment was the significant improvement in photoefficiency as expected and the formation of I as the major product. Thus it appears that the photochemistry of 5 parallels the photochemistry of maleic hydrazide in terms of product distribution and photoefficiency, and thus tautomer 1b is

likely the photochemically active tautomer of maleic hydrazide. However, until we can assign a structure for I, we can not draw firm support for this mechanism on the basis of this experiment. Overall we have results which are nicely rationalized by claiming acid catalyzed interception of intermediate 11, but unfortunately there may be an alternate explanation.

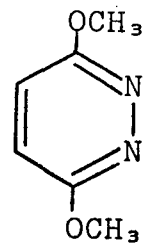
Barlin has shown that the structure of protonated pyridazinones are as shown below.[29]



It should be noted that there is a similarity between protonated 5 and 6 in the bonding in the ring.



Protonated 5



6

It may be that protonation sufficiently alters the electron distribution of 5 to make possible a new competing reaction, one which is similar to that observed for 6. It is believed

that the assignment of a structure to I will be sufficient to differentiate between these two explanations.

EXPERIMENTAL

Melting points were determined on a Thomas Hoover Capillary Melting Point Apparatus. All melting points are uncorrected and recorded in °C.

Boiling points were recorded as the temperature at which the sample distilled in °C, are uncorrected, and are recorded at atmospheric pressure unless reported otherwise.

The infra-red spectra were recorded on Perkin-Elmer instruments, Model 710 and Model 21.

The nuclear magnetic resonance spectra were recorded at 100 MHz with a Varian Associates XL-100 pulsed-Fourier transform or frequency swept high resolution 23.5-kG spectrometer. The nmr spectra at 60 MHz were obtained with a Varian Associates A-60 Recording Spectrometer. The nmr date are presented as follows: chemical shift (splitting pattern®, number of hydrogens, assignment). Chemical shifts are expressed in parts per million relative to internal tetramethylsilane in deuterated chloroform.

Molecular weights were determined by mass spectrometry. The mass spectra were recorded on a Hitachi Perkin-Elmer

---

®s=singlet, d=doublet

Mass Spectrometer, Model RMU-6H, at 70 ev. The fragments are reported as m/e.

Ultraviolet spectra and data were obtained with a Beckmann Acta C III Spectrophotometer, using 1 cm matched quartz cells.

Irradiations were carried out using either a 450-W Hanovia high pressure mercury arc lamp, centered in an internal water-cooled quartz immersion well with a Pyrex filter, or a 550-W Hanovia high pressure mercury arc lamp, centered in an internal water-cooled Pyrex immersion well.

A Varian Associates Aerograph Gas Chromatograph, Model 90-P, was used for analyzing reaction products and for trapping samples.

1,2-Dimethyl-3,6(1H,2H)-pyridazinedione (8) and 6-Methoxy-2-methyl-3(2H)-pyridazinone (5)

These compounds were prepared by a modified procedure of Przezdziecki and Chrzaszczewska.[10]

Dimethyl sulfate (20 g, 0.16 mol) was added to maleic hydrazide (1) (11.2 g, 0.1 mol) in a 250 ml flask fitted with a reflux condenser, a thermometer, and a magnetic stirrer, and the resulting mixture was heated to a temperature of 140-150°C for 2 hours with continuous stirring. The reaction was allowed to cool to room temperature, 20 ml of water was added, and solid sodium carbonate was spooned in until the mixture was saturated. Then the mixture was extracted with 100 ml of chloroform. The chloroform extract was dried ($MgSO_4$) and rotary evaporated to a solid. The solid was placed in a vacuum sublimation apparatus and the temperature was kept at 90°C (2 mm) until all of 5 had sublimed. Compound 5 was removed from the apparatus and then the temperature was raised to 120°C (2 mm) where 8 sublimed.

Resublimation of 5 yielded 2.96 g (26.4%) of colorless needles: mp 61-63°C (Lit. 65-66°C)[10]; ir ($CHCl_3$, Model 710) 2950 (CH) and 1660 cm^{-1} (C=O); nmr ($CDCl_3$, 60 MHz) δ 3.69 (s, 3, NCH_3), 3.87 (s, 3, OCH_3), 6.97 (s, 2, CH=CH); uv (ethanol) 310 nm (ϵ 2712); molecular weight 140.

Also resublimation of 8 yielded 3.01 g (26.9%) of yellow prisms: mp 134-135°C (Lit. 137-138°C)[10]; ir ($CHCl_3$,

Model 710) 1585 and 1630 cm^{-1} (C=O); nmr ($CDCl_3$, 60 MHz) δ 3.68 (s, 6, NCH_3), 6.95 (s, 2, CH=CH); uv (ethanol) 335 nm (ϵ 2701); molecular weight 140.

3,6-Dimethoxypyridazine (6)

This compound was prepared by the procedure of Przezdziecki and Chrzaszczewska[10], using 3,6-dichloropyridazine (14.9 g, 0.1 mol) and sodium methylate [previously prepared by dissolving metallic sodium (4.6 g, 0.2 mol) in 100 ml of methanol].

Recrystallization of 6 from 50 ml of water yielded 10.8 g (73%) of a white solid: mp 104-106°C (Lit. 108°C)[10]; ir ($CHCl_3$, Model 710) 2920 (CH) and 1590 cm^{-1} (C=N); nmr ($CDCl_3$, 60 MHz) δ 4.08 (s, 6, OCH_3), 6.95 (s, 2, CH=CH); uv (ethanol) 287 nm (ϵ 2295); molecular weight 140.

N-n-Butylsuccinimide

This compound was prepared by a modified procedure of Dufield *et al.*[26]

15 ml of a solution of sodium ethylate (previously prepared by dissolving 2.3 g of sodium in 50 ml of ethanol) was added to a flask equipped with a reflux condenser. Succinimide (3.0 g, 0.033 mol) was added to the flask and the resulting mixture was refluxed for 15 min to obtain a homogenius solution. n-Butyl bromide (3.0 g, 0.022 mol) was then added and the solution was refluxed overnight.

The ethanol was removed by heating the solution on a steam bath and the resulting residue, when distilled, yielded 2.0 g (66%) of N-n-butylsuccinimide: bp 102-105°C (0.5 mm) [Lit. 110-120°C (0.8 mm)[26]]; ir ($CHCl_3$, Model 710) 2950 (CH) and 1695 cm^{-1} (C=O).

N-Methyl Methylcarbamate

Methyl isocynate (5.7 g, 0.1 mol) was poured into a 25 ml flask equipped with a reflux condenser, a thermometer, a magnetic stirrer, and an addition funnel. Methanol (3.2 g, 0.1 mol) was placed in the funnel and added dropwise over a period of 15 min. The solution refluxed for approximately 3 min at 37°C.

After the solution stopped refluxing, it was distilled and yielded 6.7 g (75%) of N-methyl methylcarbamate: bp 104-106°C (40 mm); ir ($CHCl_3$, Model 710) 3375 (NH), 2980 (CH), 1730 (C=O), and 1555 cm^{-1} (C-O); nmr ($CDCl_3$, 60 MHz) δ 2.80 (d, 3, $C\underline{H}_3N$), 3.70 (s, 3, $OC\underline{H}_3$), and 5.20 (m, 1, $N\underline{H}$).

1,2-Dimethoxyethylene

This compound was prepared by the procedure of Kokubo *et al.*[27] 6 g of 1,2-dimethoxyethylene were obtained: bp 104-108°C (Lit. 95-105°C)[27]; ir ($CHCl_3$, Model 710) 2840, 2940 (CH) and 1660 cm^{-1} (C-O); gas chromatograph analysis using a 21' X 0.25" column of 7% QF-1 on Johns Manville Chromosorb G (DMCS/AW) at 150°C gave a composition of 97% *cis* isomer and 3% *trans* isomer of the distillate.

Irradiation of 3,6-Dimethoxypyridazine (6)

A solution of 500 mg (3.6 mmol) of 6 in 250 ml of methanol was irradiated for 108 hours using a 550-W Hanovia high pressure mercury arc lamp centered in a Pyrex well. The solution turned cloudy white after 72 hours of irradiation. After 108 hours most of the solvent was removed by rotary evaporation leaving a white oil. The oil was analyzed by vpc using a 18' X 0.25" column of 10% Carbowax 20,000 on Johns Manville Chromosorb Q at 170°C. The chromatogram showed the presence of 7 products (retention times: 1.0, 3.75, 4.9, 6.5, 7.0, 9.6, and 22 min; and yields: 0.20, 0.17, 0.26, 0.74, 0.78, 0.26, and 2.25%, respectively), plus methanol (retention time-1.5 min) and 6 (retention time-2 min), more than 95% of which was found to be unchanged.

The compounds with retention times of 6.5, 7.0, and 22 min were the major products and are the only ones that have been identified. The other products have not been identified due to the difficulty of acquiring sufficient material to work with.

The compound with a retention time of 6.5 min was identified as dimethyl maleate by trapping samples from the detector port of the gas chromatograph to be used for ir, nmr, and mass spectral analyses: ir ($CHCl_3$, Model 710) 1735 (C=O) and 1600 cm^{-1} (C=C); nmr ($CDCl_3$, 100 MHz) δ

6.26 (s, 2, $\underline{H}C=C\underline{H}$), 3.64 (s, 6, $OC\underline{H}_3$); molecular weight 144.

The compound with a retention time of 7.0 min was identified as dimethyl succinate by comparison of gas chromatograph retention time to an authentic sample. In addition, it was trapped and its identity was further confirmed by comparison to the ir of an authentic sample: ir ($CHCl_3$, Model 710) 1730 cm^{-1} (C=O). Further, a sample was trapped for nmr and mass spectral analyses: nmr ($CDCl_3$, 100 MHz) δ 2.53 (s, 4, $C\underline{H}_2C\underline{H}_2$), 3.64 (s, 6, $OC\underline{H}_3$); molecular weight 146.

The third component with a retention time of 22 min has not been identified to date, and has been designated I. Its infra-red spectrum showed no absorption in the NH or OH region and no detectable absorption at energies greater than 3000 cm^{-1}. However, it did show absorptions at 2850-3000 cm^{-1}, and there were two strong bands in the carbonyl region, one at 1790 cm^{-1} and another at 1735 cm^{-1}. The 100 MHz nmr spectrum, run in $CDCl_3$, was complicated because of difficulties in obtaining a pure sample. It showed weak singlets at δ 7.10 and 7.50, complex multiplets at δ 2.95, 3.60, and 4.60, and what appeared to be the superposition of several singlets at δ 3.90. The mass spectral fragmentation pattern was complex suggesting that the aromatic ring had been destroyed, and the molecular ion was believed to be present at either m/e 212 or m/e 184.

Irradiation of 1,2-Dimethyl-3,6(1H,2H)-pyridazinedione (8)

A solution containing 500 mg (3.6 mmol) of 8 in 150 ml of methanol was irradiated for 144 hours using a 450-W Hanovia high pressure mercury arc lamp equipped with a Pyrex filter. The solution turned light yellow after 72 hours of irradiation. Removal of most of the solvent by rotary evaporation left a light yellow oil. The oil was analyzed by vpc using a 21' X 0.25" column of 7% QF-1 on Johns Manville Chromosorb G (DMCS/AW) at 240°C. The chromatogram showed the presence of one product only (approximately 0.5% conversion, retention time-8 min), plus methanol (retention time-3.5 min), and 8 (retention time-13.5 min). The product was identified as dimethyl succinate based on retention time as compared to an authentic sample. In addition, it was trapped and its identity was further confirmed by comparison to the ir and nmr of an authentic sample: ir ($CHCl_3$, Model 710) 1730 cm^{-1} (C=O); nmr ($CDCl_3$, 100 MHz) δ 2.53 (s, 4, $C\underline{H}_2C\underline{H}_2$), 3.64 (s, 6, $OC\underline{H}_3$).

Irradiation of 1,2-Dimethyl-3,6(1H,2H)-pyridazinedione (8) in the Presence of n-Butylamine

A solution containing 500 mg (3.6 mmol) of 8 and 3 ml of n-butylamine in 150 ml of methanol was irradiated for 144 hours using a 450-W Hanovia high pressure mercury arc lamp equipped with a Pyrex filter. The solution turned yellow-green after 36 hours of irradiation. Removal of most of the solvent by rotary evaporation left a yellow-green oil. The oil was analyzed by vpc using a 21' X 0.25" column of 7% QF-1 on Johns Manville Chromosorb G (DMCS/AW) at 230°C. The chromatogram showed the presence of three products (retention times: 7, 9.5, and 11.5 min, respectively), plus n-butylamine (retention time-3 min), methanol (retention time-4.5 min), and 8 (retention time-15 min), more than 95% of which was found to be unchanged. The major product was identified as N-n-butylsuccinimide based on retention time (7 min) as compared to an authentic sample. Also, it was trapped and its identity was further confirmed by comparison to the ir of an authentic sample: ir ($CHCl_3$, Model 710) 2950 (CH) and 1695 cm^{-1} (C=O).

The products with the retention times of 9.5 and 11.5 min have not been identified because of the difficulty of acquiring sufficient material to work with.

Irradiation of 6-Methoxy-2-methyl-3(2H)-pyridazinone (5)

A solution containing 500 mg (3.6 mmol) of 5 in 150 ml of methanol was irradiated for 144 hours using a 450-W Hanovia high pressure mercury arc lamp equipped with a Pyrex filter. The solution turned light yellow after 96 hours of irradiation. After 144 hours most of the solvent was removed by rotary evaporation leaving a light yellow oil. The oil was analyzed by vpc using a 18' X 0.25" column of 10% Carbowax 20,000 on Johns Manville Chromosorb Q at 200°C. The chromatogram showed the presence of 13 products (retention times: 1.0, 3.0, 3.4, 3.75, 4.3, 5.6, 5.75, 6.75, 7.3, 8.0, 9.2, 12.5, and 18 min), plus methanol (retention time-1.5 min), and 5 (retention time-16 min), more than 95% of which was found to be unchanged.

The compounds with retention times of 5.6, 5.75, and 18 min were the major products and are the only ones that have been identified. The other products have not been identified due to the difficulty of acquiring sufficient material to work with.

The compound with a retention time of 5.6 min was identified as dimethyl maleate by trapping samples from the detector port of the gas chromatograph to be used for ir, nmr, and mass spectral analyses: ir ($CHCl_3$, Model 710) 1735 (C=O) and 1600 cm^{-1} (C=C); nmr ($CDCl_3$, 100 MHz) δ

6.26 (s, 2, $\underline{H}C=C\underline{H}$), 3.64 (s, 6, $OC\underline{H}_3$); molecular weight 144.

The compound with a retention time of 5.75 min was identified as dimethyl succinate by comparison of gas chromatograph retention time to an authentic sample. In addition, it was trapped and its identity was further confirmed by comparison to the ir of an authentic sample: ir ($CHCl_3$, Model 710) 1730 cm^{-1} (C=O). Further, a sample was trapped for nmr and mass spectral analyses: nmr ($CDCl_3$, 100 MHz) δ 2.53 (s, 4, $C\underline{H}_2C\underline{H}_2$), 3.64 (s, 6, $OC\underline{H}_3$); molecular weight 146.

The third component with a retention time of 18 min has not been identified to date, and has been designated I. Its infra-red spectrum showed no absorption in the NH or OH region and no detectable absorption at energies greater than 3000 cm^{-1}. However, it did show absorptions at 2850-3000 cm^{-1}, and there were two strong bands in the carbonyl region, one at 1790 cm^{-1} and another at 1735 cm^{-1}. The 100 MHz nmr spectrum, run in $CDCl_3$, was complicated because of difficulties in obtaining a pure sample. It showed weak singlets at δ 7.10 and 7.50, complex multiplets at δ 2.95, 3.60, and 4.60, and what appeared to be the superposition of several singlets at δ 3.90. The mass spectral fragmentation pattern was complex suggesting that the aromatic ring had been destroyed, and the molecular ion was believed to be present at either m/e 212 or m/e 184.

REFERENCES

1. " Tobacco in the United States," United States Department of Agriculture Consumer and Marketing Service, U. S. Government Printing Office, Washington, D. C., 1966.

2. Seltmann, H., Invited Papers, 5th International Tobacco Scientific Congress, 19, 77 (1970).

3. Schoene, D. L., and Hoffmann, O. L., Science, 109, 588 (1949).

4. Petersen, E. L., Agr. Jour., 44, 332 (1952).

5. Moseley, J. M., Tob. Sci., 3, 73 (1959).

6. Collins, W. K., Hawks, S. N., Jr., and Kittrell, B. U., Tob. Sci., 14, 86 (1970); ibid., 15, 106 (1971).

7. Ottersen, T., Acta Chem. Scand., 27 (3), 797 (1973).

8. Arndt, F., Angew. Chem., 61, 397 (1949).

9. Miller, O. M., and White, R. W., Can. J. Chem., 34, 1510 (1956).

10. Przezdziecki, Z., and Chrzaszczewska, A., Lodz. Towarz. Nauk. Wydzial III, Acta Chim., 10, 109 (1965).

11. Katritzky, A. R., and Waring, A. J., Chem. Ind. (London), 695 (1962).

12. Gompper, R., and Altreuther, P., Z. Analyt. Chem., 170, 205 (1959).

13. Crafts, A. S., Currier, H. B., and Drever, H. R., Hilgardia, 27 (22), 723 (1958).

14. Mitchell, L. C., J. Assoc. Offic. Agr. Chemists, 44 (4), 643 (1961).

15. Stoessl, A., Chem. Ind. (London), 580 (1964).

16. Dauben, W. G., Pure. Appl. Chem., 9, 539 (1964); Courtot, P., and Rumin, R., Bull. Soc. chim. France, 3665 (1969); Courtot, P., and Rumin, R., Tetrahedron Letters, 1849 (1970); Vogel, E., Grimne, W., and Dinne, E., ibid., 391 (1965); Padwa, A., Brodsky, L., and Clough, S. C., Chem. Comm., 417 (1971).

17. Stoessl, A., Can. J. Chem., 43, 2430 (1965).

18. Clough, S. C., Kang, J. C., Johnson, W. R., and Osdene, T. S., Chem. Ind. (London), 323 (1973).

19. Patterson, J. M., Issadorides, C. H., Groutas, V. C., and Smith, W. T., Jr., Chem. Ind. (London), 337 (1972).

20. Tobacco Reporter, 99 (3), 25 (1972).

21. Van Tamelen, E. E., Pappas, S. P., and Kirk, K. L., J. Am. Chem. Soc., 93 (23), 6092 (1971); Wilzbach, K. E., and Rausch, D. J., ibid., 92 (7), 2178 (1970).

22. Handbook of Chemistry and Physics, 53rd Edition, Weast, R. C., Editor-in-Chief, Chemical Rubber Co., Cleveland, Ohio, C131 (1972-1973).

23. Chapman, O. L., McIntosh, C. L., and Barber, L. L., Chem. Comm., 1162 (1971).

24. Obata, N. and Takizawa, T., Chem. Comm., 587 (1971).

25. March, Jerry, Advanced Organic Chemistry-Reactions, Mechanisms, and Structures, McGraw-Hill Book Company, New York, New York, 288, 499 (1968).

26. Duffield, P. M., Budzikiewicz, H., and Djerassi, C., J. Am. Chem. Soc., 87 (13), 2913 (1965).

27. Kokubo, T., Iwatsuki, S., and Yamashita, Y., Macromolecules, 1 (6), 482 (1968).

28. Murai, K. and Akazome, G., Kogyo Kagaku Zasshi, 62, 1251 (1959).

29. Barlin, G. B., J. Chem. Soc. Perkin II, 1199 (1974).

BIOGRAPHICAL SKETCH

James Wesley Harris, Jr. was born June 28, 1949 in Richmond, Virginia. In June, 1967, he graduated from Henrico High School and entered the University of Richmond where he received the degree of Bachelor of Science in June, 1971, with a major in chemistry. In September, 1971, he enrolled in the Graduate School of the University of Richmond to continue his study for the degree of Master of Science. He is a member of Phi Beta Kappa, Gamma Sigma Epsilon, and the American Chemical Society.