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# The Reaction of Pyridine with Sulfur Dioxide in Benzoyl Chloride

(55 letters)

# THE REACTION OF PYRIDINE WITH SULFUR DIOXIDE IN BENZOYL CHLORIDE

by

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# INTRODUCTION

At the turn of the present century, a number of investigations concerning the action of benzoyl chloride on certain inorganic salts had been reported (1,2). In the cases of potassium oxalate, sodium nitrite and sodium carbonate, benzoic anhydride was one of the main reaction products. Moreover, the reactions took place with particular ease in pyridine but no rationale for this catalysis was given. When the reaction was subsequently applied to sodium hydrosulfite (sodium dithionite; $Na_2S_2O_4$) by two German chemists, A. Binz and T. Marx, benzoyl disulfide ($C_6H_5CO\text{-}S\text{-}S\text{-}CO\text{-}C_6H_5$) was formed as well as the anhydride (3). However, two colored compounds in addition were produced when the reaction was carried out in pyridine. These latter compounds were also formed using anhydrous sodium sulfite but not the hydrated form. They were best prepared by bubbling sulfur dioxide gas into a mixture of pyridine and benzoyl chloride at ice temperature followed by treatment with strong sodium hydroxide solution.

The first of these colored compounds, a scarlet-red substance which was precipitated in the form of needles by sodium hydroxide, was soluble in pyridine and glacial acetic acid. When recrystallized from hot methanol, it melted at about 259°. On drying at 120°, the scarlet-red modification was converted to a darker ruby-red form but the visible spectra of both modifications taken in alcohol were reported to be identical but were not published. Complete combustion of the compound was difficult, and determination of the molecular

weight by the cryoscopic technique was considered to be, at best, an approximation. On the basis of an average molecular weight of 202 and of the analytical data, the authors assigned the empirical formula $C_{11}H_{10}N_2S$. They proposed no structure for the compound.

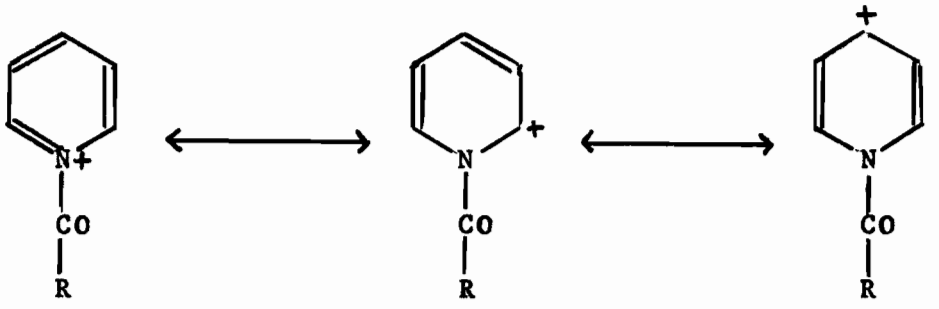
The second of these colored compounds was a yellow substance, of high molecular weight, which was provisionally assigned the formula $C_{23}H_{16}O_6N_4S_4$. It was not dissolved by the ordinary laboratory solvents, but was transformed into the aforementioned red compound by warming with sodium hydroxide.

There is no well-known parallel for this reaction to suggest a structure for the red and yellow compounds. It is not easy to see why the sulfur of sulfur dioxide undergoes reduction under the mild conditions of the reaction, nor is the role of benzoyl chloride apparent. Consequently, it may be profitable to review the reactions of pyridine in the presence of benzoyl chloride and other halides.

## A. Reactions of Acylpyridinium Halides

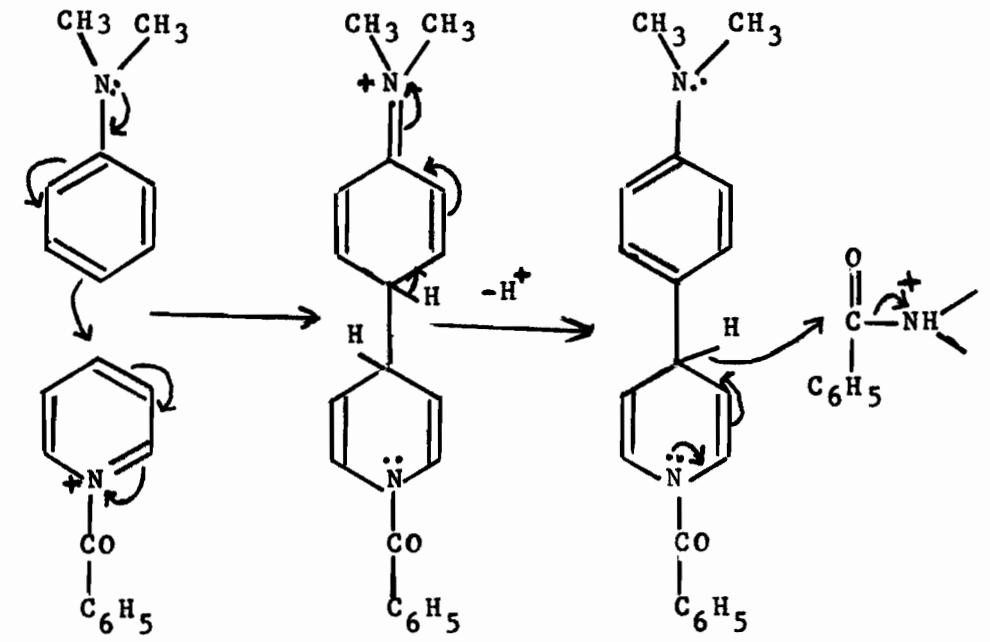
A variety of acyl chlorides react with pyridine and its homologues but the quaternary 1-acylpyridinium halides have rarely been isolated; in general, their formation has been deduced from the structures of the products isolated from the reaction mixture. These quaternary halides of pyridine are easily hydrolyzed and, if the conditions are carefully controlled, high yields of acid anhydrides may be obtained (4). Numerous examples in the literature establish the

reactivity at the 2 and 4 positions of the pyridine nucleus because of the canonical forms of the resonance hybrid shown below:

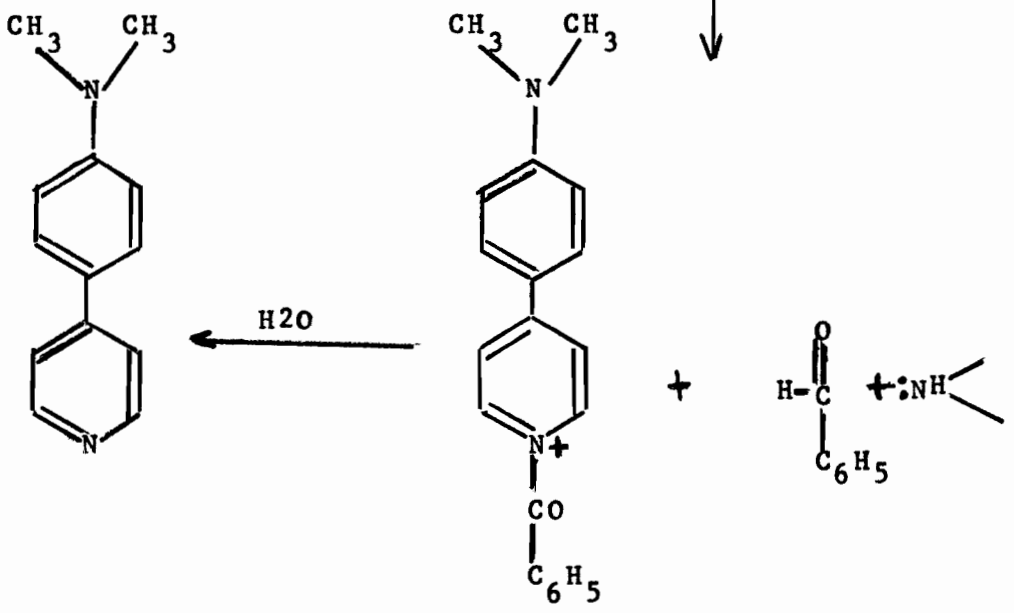



I II III

Koenigs and Ruppelt (5) and later McEwen et al (6) obtained 4-(p-dimethylaminophenyl)-pyridine by addition, at room temperature, of dimethylaniline to a mixture of benzoyl chloride and pyridine. Presumably, the reaction takes place through the intermediate formation of a 1,4-dihydro compound which then releases a hydride ion to reduce a benzoyl group to benzaldehyde, and gives the 4-phenylpyridine derivative. The rate of formation of the intermediate is probably slow compared to the rate of its further reaction.

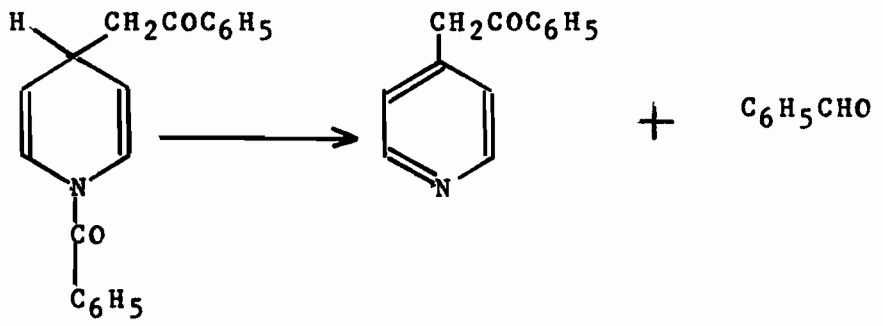


IV V VI



VIII VII

Ghigi (7) has demonstrated a similar attack at the 4-position of the acylpyridinium ring by the α-methylene group of a ketone. Acetophenone reacts with benzoyl chloride and pyridine at room temperature to form slowly the intermediate 1,4-dihydro adduct and, finally, the 4-phenacyl pyridine.

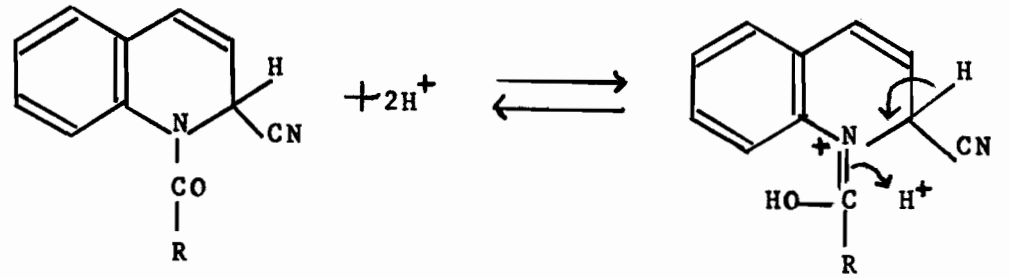



IX X

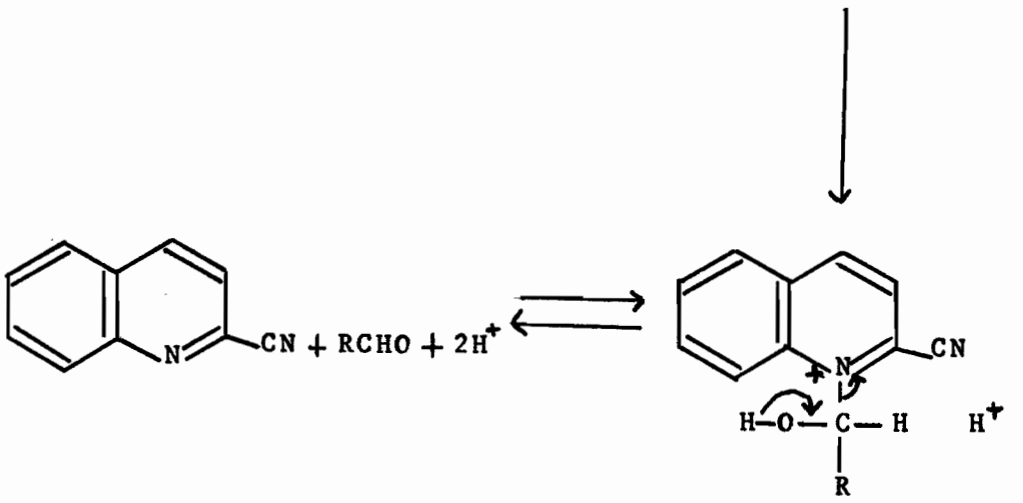
At present, a well-known reaction of acyl quaternary heteroaromatic bases is the so-called Reissert reaction for the preparation of an aldehyde from an acid chloride. The acyl halide is first converted to a Reissert compound, a 1-acyl-2-cyano-1,2-dihydroquinoline, by reaction with quinoline and aqueous potassium cyanide solution (or potassium cyanide in liquid $SO_2$), or with liquid hydrogen cyanide in benzene. The Reissert compound is then converted to an aldehyde and quinaldic acid by reaction with concentrated hydrochloric acid. The reaction can be applied to isoquinoline but not to pyridine.

The mechanism of the reaction has been investigated by McEwen and Hazlett (8). Coordination of a proton with the amide oxygen of the Reissert compound (XI) gives the conjugate

acid (XII). The complex (XIII) is formed by simultaneous loss of a proton from the 2-position of the quinoline ring and gain of a proton by the original carbonyl carbon atom. Dissociation of (XIII) then occurs to give the aldehyde and quinaldonitrile (XIV) which is hydrolyzed to quinaldic acid.



XI XII

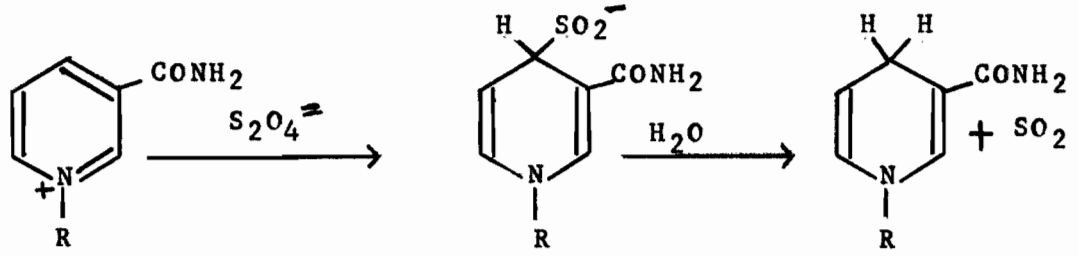


XIV XIII

B. Partial Reduction to Dihydro and Tetrahydro Pyridine

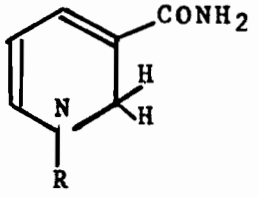
The number of examples of successful reductions of pyridine and its derivatives to the dihydro and tetrahydro stage is small, largely because of the readiness of the partially reduced structures to polymerize, oxidize and rearrange. However, Karrer and his co-workers (9) have studied the action of sodium

hydrosulfite on a number of nicotinamide quaternary salts and have, in many cases, actually isolated the corresponding 1,4-dihydro isomers which were oxidized with more difficulty than the 1,2-dihydro forms and fluoresced blue. During the hydrosulfite reduction of nicotinamide quaternary salts, an intermediate yellow color, attributable to the formation of a sulfinic acid, is produced. This intermediate, though stable in alkaline medium, rapidly breaks down in neutral or acid solution to give the 1,4-dihydro-nicotinamide (10).




XV XVI XVII

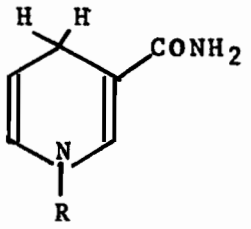
At these low pH values, protonation at the 4-position was visualized as accompanying loss of $SO_2$. The structure of the hydrosulfite reduction product was unequivocally demonstrated by isotopic tracer studies on nicotinamide compounds containing deuterium. The 1,2-dihydro and 1,6-dihydro-1-alkyl nicotinamides have also been isolated and exhibit widely differing ultraviolet spectra when compared with one another and with the 1,4-dihydro system:



1,2-dihydro

$\lambda$ max = 425 m$\mu$ (estimated)

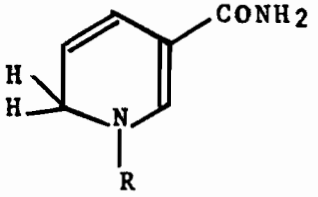
XVIII



1,4-dihydro

$\lambda$ max = 360 m$\mu$ ($H_2O$)

XIX



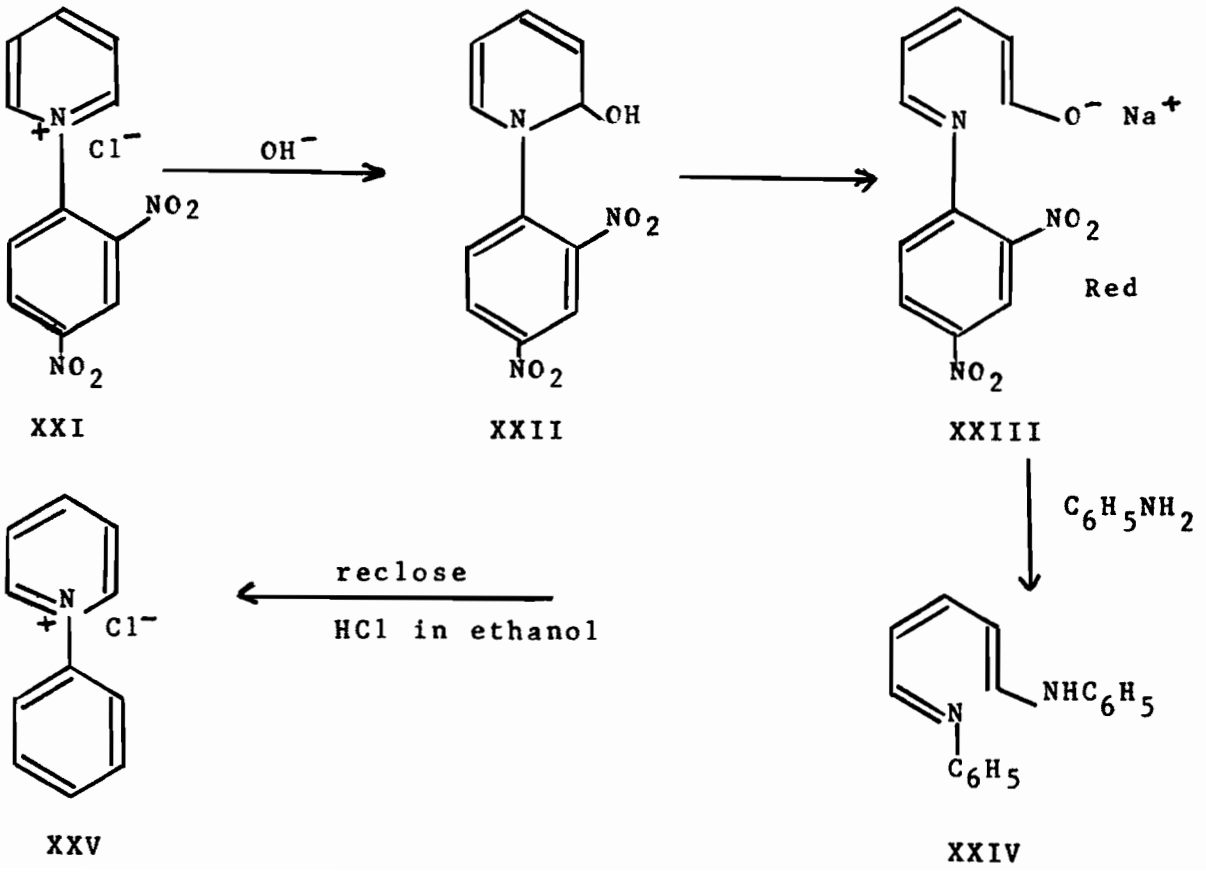
1,6-dihydro

$\lambda$ max = 270 m$\mu$
360 m$\mu$ ($H_2O$)

XX

C. Ring Opening Reactions

The pyridine ring will often open with astonishing ease when quaternized by certain reagents. Zincke and his co-workers (11,12,13,14) found that 1-(2,4-dinitrophenyl) pyridinium salts gave a derivative of glutaconaldehyde by rupture of the ring:

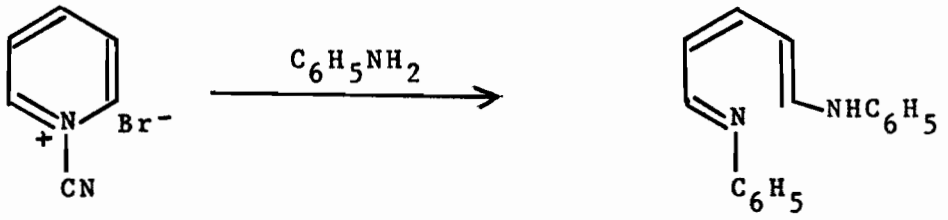



XXI XXII XXIII

XXIV XXV

The anionic charge is stabilized by resonance and this may partly account for the ease of ring opening, not encountered with 1-alkylpyridinium halides.

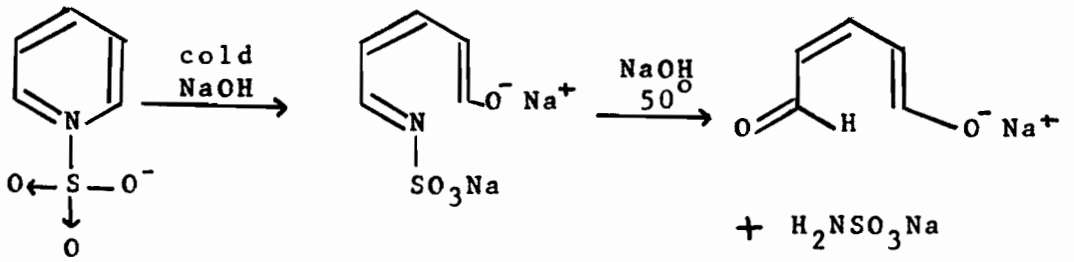
König (15,16) discovered similar reactivity in the adduct of pyridine and cyanogen bromide. He prepared from the quaternary compound and aniline the known glutaconaldehyde dianil.




XXVI XXVII

Although the reaction is successful with many substituted pyridines, it may be sterically hindered in 2,6-disubstituted pyridines, and inhibited by electronegative substituents operating to impede the quaternization step.

The opening of the pyridine ring, brought about by the addition of such compounds as sulfur trioxide, chlorosulfonic acid and ethyl chlorosulfonate, has been extensively studied by Baumgarten (17,18). On treating the adduct with strong aqueous sodium hydroxide, the sodium salt of glutaconaldehyde precipitates from solution. Sodium bisulfite similarly results in cleavage of the pyridine ring but only after considerable contact time (19).




XXVIII XXIX XXX

It is evident, then, that the ring opening reactions have at least one feature in common; the presence of quite strongly electron-withdrawing groups at the ring nitrogen. It accordingly seems unlikely, though it is not impossible, that ring opening is involved in the Binz and Marx reaction.

## EXPERIMENTAL

### A. Reagents

(1) Pyridine, Fisher certified reagent, infrared spectroanalyzed

(2) 2-Picoline, Reilly Chemical Co., minimum assay 98%, freshly distilled b.p. $126^{\circ}$-$129^{\circ}$

(3) 2,4-Lutidine, Reilly Chemical Co. (85%)

(4) 2-Methyl-5-Ethylpyridine, Reilly Chemical Co.

(5) Isoquinoline, Fisher certified reagent, highest purity

(6) Benzoyl chloride, Fisher certified reagent, high purity, b.p. $196^{\circ}$-$197^{\circ}$

(7) Sulfur dioxide gas, (anhydrous), Matheson

(8) Sodium sulfite, (anhydrous), Anachemia reagent grade, minimum assay 97.0%

### B. Reaction of Pyridine with Sulfur Dioxide in Benzoyl Chloride to form Compound A

The following procedure is essentially that of Binz and Marx (3):

Anhydrous sulfur dioxide gas was bubbled into an ice-cold mixture of pyridine (dried over KOH) (100 ml.) and benzoyl chloride (56 ml.), in an inert atmosphere, for 1½ hours. Yellow crystals formed during the addition but gradually dissolved in the reaction mixture, which became deep red after several minutes. After the addition, the mixture was slowly distilled under reduced pressure until the pot temperature reached $100^{\circ}$. (Heating to $140^{\circ}$ as suggested by Binz and Marx was found to cause extensive charring of the pot residue). At this point, approximately

1/3 of the liquid had distilled over. White hygroscopic crystals which formed in the distillate were subsequently identified as pyridine hydrochloride, m.p. 82°. The pot mixture was thoroughly cooled in ice and 50% aqueous potassium hydroxide solution (200 ml.) was cautiously added under vigorous stirring. A small amount of red compound precipitated along with a large amount of white solid. The former was removed by continuous extraction of the solid in a Soxhlet assembly with methyl ethyl ketone (300 ml.) in which it was slightly soluble. The solvent was removed in vacuo leaving a scarlet-red crystalline substance (350 mg.) which, when recrystallized from a 3:1 mixture of methyl ethyl ketone and pyridine, melted at 259°-262° (decomposition). When the scarlet-red compound was dried in vacuo over $P_2O_5$, it was converted to a darker ruby-red modification having the same melting point and exhibiting no depression when mixed with the scarlet-red species.

The yellow substance of Binz and Marx, m.p. 246°, was not isolated.

The analytical data for compound A are presented in Table I.

Some difficulty was encountered in the early analyses because nitrogenous chars were formed during the combustion. The results of analyst A are, therefore, looked upon with some skepticism and no formula was assigned on the basis of these data. The formula $C_{23}H_{18}N_4S_2O$, assigned on the basis

of the data of analyst B, gives corresponding percentages of carbon (64.2), hydrogen (4.2), nitrogen (13.0) and sulfur (14.9).

Table I

Analytical Data for Compound A

| Analyst | %C | %H | %N | %S | %O (by difference) | Formula assigned |
|---|---|---|---|---|---|---|
| Binz and Marx | 65.35 | 4.95 | 13.86 | 15.84 | 0 | $C_{11}H_{10}N_2S$ |
| A* | 61.13 | 5.16 | 7.85 | 13.77 | 12.09 | |
| B† | 64.79 | 4.24 | 12.74 | 14.34 | 3.89 | $C_{23}H_{18}N_4S_2O$ |

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Montreal, P.Q.,
Canada.

† Dr. A. Bernhardt,
433 Mülheim (Ruhr),
Höhenweg 17,
West Germany.

Because of the limited solubility of the compound (less than 1%) in the common organic solvents, the molecular weight could not be determined by the accurate vapor pressure osmometric method. Similarly, the Rast cryoscopic method could not be used because the compound decomposed in hot camphor to afford a dark, almost opaque solution.

In the course of their investigations on the action of benzoyl chloride on a mixture of pyridine and sulfur dioxide, Binz and Marx reported a substantially greater

yield of the red compound (6 grams per 50 ml. of pyridine) than the amount obtained in the present work (350 mg. per 100 ml. of pyridine).

In the present work, efforts to increase the yield by changing the order of addition proved fruitless. Though all three components are necessary for the formation of the colored substance, the order of addition is seemingly irrelevant, provided only that the sodium hydroxide solution is the last addendum. Conducting the reaction at room temperature and at $40^{\circ}$ also did not increase the yield.

Under milder conditions of alkalinity, the quantities of the red compound formed were reduced to about 1/5 of that obtained using 50% potassium hydroxide solution. Saturated aqueous sodium carbonate and concentrated aqueous ammonia solutions afforded approximately 70 mg. of compound A per 100 ml. of pyridine, thus demonstrating that a strong base is needed.

In order to assess the role of benzoyl chloride, several other aromatic acid chlorides were employed in the Binz and Marx reaction. In the cases of m-bromobenzoyl chloride and o-chlorobenzoyl chloride in pyridine, red products were obtained which, after recrystallization, melted at $259^{\circ}$-$262^{\circ}$ (decomposition). Mixed melting points and infrared and visible spectra indicated these products to be identical to that obtained using benzoyl chloride and pyridine. Elemental analyses showed that no halogen

had been incorporated into the molecule. Thus, it appears that the acid chlorides act as condensing agents and do not become incorporated themselves in the product. The use of p-toluenesulfonyl chloride and α-naphthoyl chloride, in place of benzoyl chloride, gave no isolable colored product although, in the latter case, trace amounts of the red compound were indicated. Aliphatic acid chlorides led only to the formation of dark intractable tars.

C. Measurement of the Dissociation Constant of Compound A

The substance (compound A) was submitted to conditions of increasing acidity and the $pK_{BH^+}$ determined according to the following relation:

$$pK_{BH^+} = pH + \log \frac{[BH^+]}{[B]}$$

The ratio of $\frac{[BH^+]}{[B]}$ is determined spectrophotometrically from the equation:

$$\frac{[BH^+]}{[B]} = \frac{D_B - D}{D - D_{BH^+}}$$

where $D_B$, D and $D_{BH^+}$ are the optical densities of the neutral form (in $H_2O$), the mixture of neutral and protonated forms, and the completely protonated form (in 15% HCl), respectively, in solutions of the same stoichiometric concentration.

FIGURE I

The Spectrophotometric Measurement

of the

$pK_{BH^+}$ of Compound A

Spectra were taken on a Perkin-Elmer Model 350

Spectrophotometer

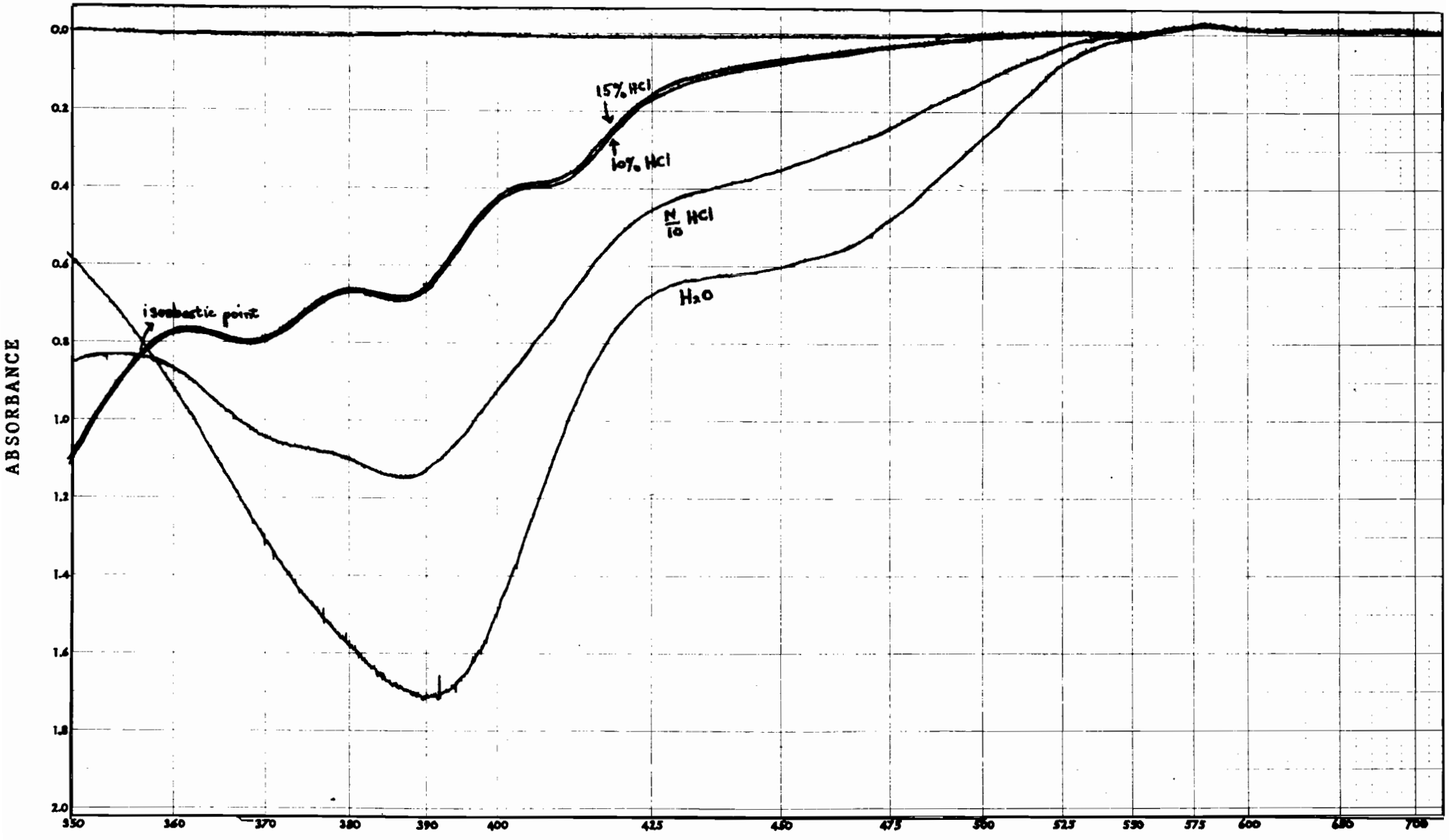

ABSORBANCE
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4
1.6
1.8
2.0
15% HCl
10% HCl
N/10 HCl
H₂O
isosbestic point
350
360
370
380
390
400
425
450
475
500
525
550
575
600
650
700
WAVELENGTH (MILLIMICRONS)

FIGURE I

D. Attempted Reaction of Pyridine, Benzoyl Chloride and Sodium Sulfite

Pure dry pyridine (20 ml.) was added to a mixture of benzoyl chloride (23 ml.) and anhydrous sodium sulfite (20 g.) according to the procedure of Binz and Marx but no observable reaction ensued, and the red and yellow substances reported by Binz and Marx were not obtained.

E. Reaction of 2-Picoline with Sulfur Dioxide in Benzoyl Chloride to form Compound B

The same procedure as used to isolate compound A was employed here. Distillation of the mixture under reduced pressure at 100°, as was used in this case, gave a lesser amount of distillate than in the case with pyridine. On treating the pot residue with strong aqueous alkali, under efficient ice-cooling, compound B was obtained as a blue-red substance (450 mg. of compound B was obtained per 100 ml. of 2-picoline). When recrystallized from a 3:1 mixture of methyl ethyl ketone and pyridine, compound B melted from 201° -203°. Calc. for $C_{24}H_{16}N_4S_4$: C, 59.0; H, 3.3; N, 11.5; S, 26.1%. Found by Analyst B: C, 58.86; H, 3.40; N, 11.37; S, 26.10%.

F. Reaction of 2,4-Lutidine with Sulfur Dioxide in Benzoyl Chloride to form Compound C

When the modified Binz and Marx procedure given for compound A was applied to 2,4-lutidine, the deep red color characteristic of the reaction was observed. However, the solid red compound, precipitated during the strong caustic

treatment, was very unstable to light and could therefore only be isolated in an apparently oxidized form as brown crystals, m.p. 294°-297° (decomposition) from acetone. The analytical data (Found by Analyst B: C, 47.10; H, 3.23; N, 2.53; S, 2.69%) show an oxygen content of 44.45%, indicating an extraordinarily high incorporation of oxygen into the molecule.

G. Reaction of 2-Methyl-5-Ethylpyridine with Sulfur Dioxide in Benzoyl Chloride to form Compound D

This case was similar to that described in the previous section. The compound was initially precipitated as a red colored substance but was rapidly converted by exposure to air and light, to a dark, almost coal-black, product m.p. 289°-294° (decomposition) from acetone. The analysis (Found by Analyst B: C, 60.94; H, 4.92; N, 7.56; S, 13.25%) indicates an oxygen percentage composition of 13.33%. There is no obvious reason to explain the difference between this and the foregoing case.

H. Reaction of Isoquinoline with Sulfur Dioxide in Benzoyl Chloride to form Compound E

Anhydrous sulfur dioxide was bubbled into an ice-cold mixture of pure isoquinoline (50 ml.) and pure benzoyl chloride (28 ml.) for 1½ hours. The solution acquired a deep red color during the addition. The solution was then distilled under reduced pressure at 80° until approximately 1/5 of the liquid had distilled over. Strong potassium hydroxide solution (100 ml.) was then added to the pot

residue and the red compound extracted from a Soxhlet assembly with methyl ethyl ketone (300 ml.). Removal of the solvent in vacuo and addition of ethyl acetate to the residue precipitated 250 mg. of a scarlet-red compound which melted at 255°-257° (decomposition), when recrystallized from a 3:1 mixture of methyl ethyl ketone and pyridine. Calc. for $C_{38}H_{24}N_4S_2O_5$: C, 67.0; H, 3.7; N, 8.2; S, 9.5%. Found by Analyst B; C, 66.55; H, 3.72; N, 8.08; S, 10.93%.

## I. Visible Spectra

The visible spectra of compounds A,B and E taken on a Perkin-Elmer model 350 spectrophotometer, appear in Figures 2,3 and 4. They exhibit several features of interest summarized in Table III.

Table III

Visible Spectral Characteristics of Compounds A,B and E

| Compound | Solvent | $\lambda$ max | color of solution |
|---|---|---|---|
| $A^+$ (Figure 2) | $H_2O$ | 390 mμ<br>455 mμ (shoulder) | yellow |
| | ethanol | 412 mμ<br>480 mμ (shoulder) | orange |
| | methyl ethyl ketone | 448 mμ<br>520 mμ (shoulder) | red |
| B (Figure 3) | ethanol | 542 mμ<br>425 mμ (shoulder) | blue-red |
| E (Figure 4) | ethanol | 462 mμ<br>370 mμ (shoulder) | red |

FIGURE 2

The Visible Spectra of Compound A
in Water, Ethanol, and
Methyl Ethyl Ketone

Spectra were taken on a Perkin-Elmer Model 350
Spectrophotometer

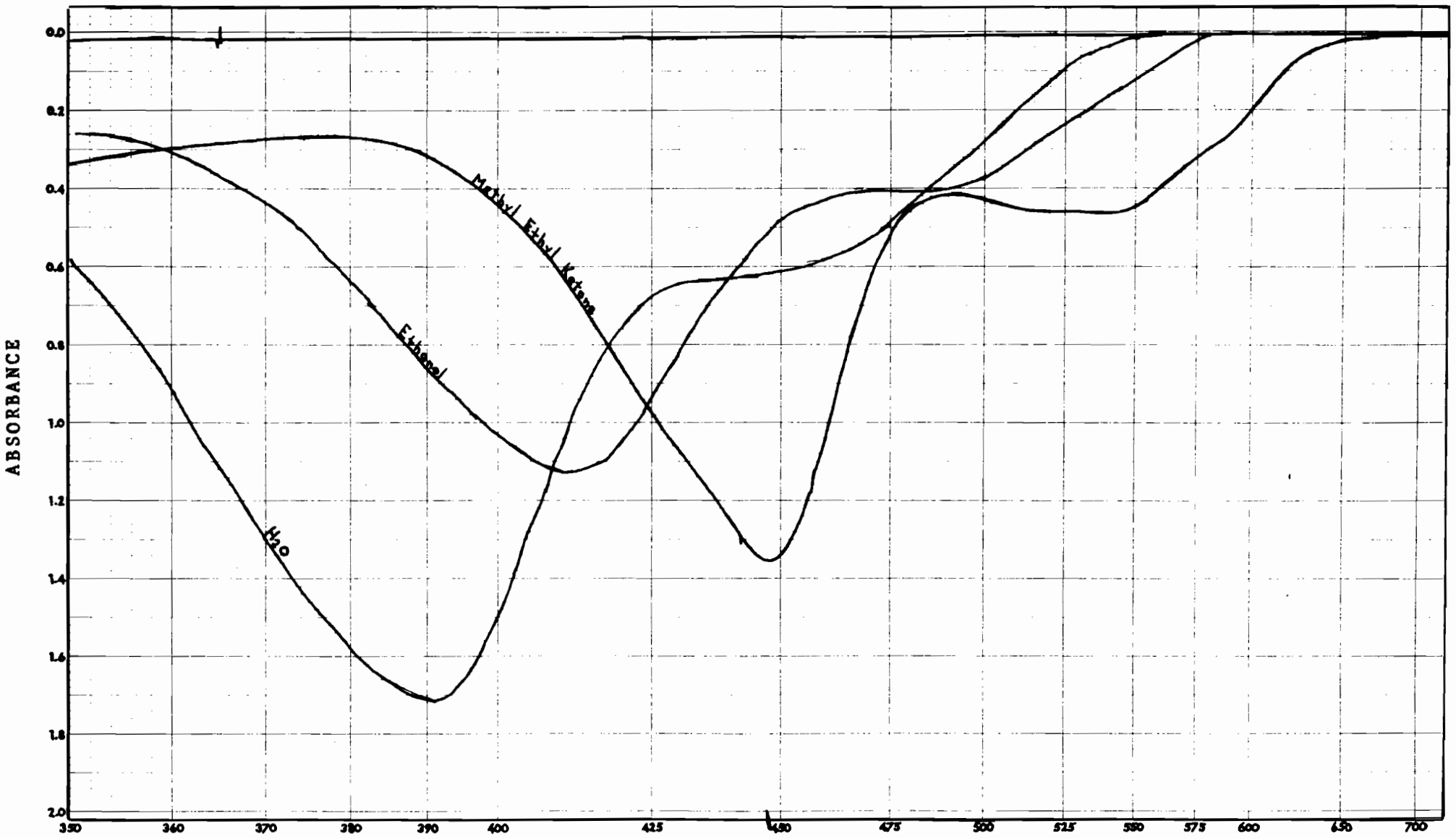

ABSORBANCE
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4
1.6
1.8
2.0
350
360
370
380
390
400
425
450
475
500
525
550
575
600
650
700
Methyl Ethyl Ketone
Ethanol
H2O
WAVELENGTH (MILLIMICRONS)

FIGURE 2

FIGURE 3

The Visible Spectrum of Compound B

in Ethanol

Spectrum was taken on a Perkin-Elmer Model 350

Spectrophotometer

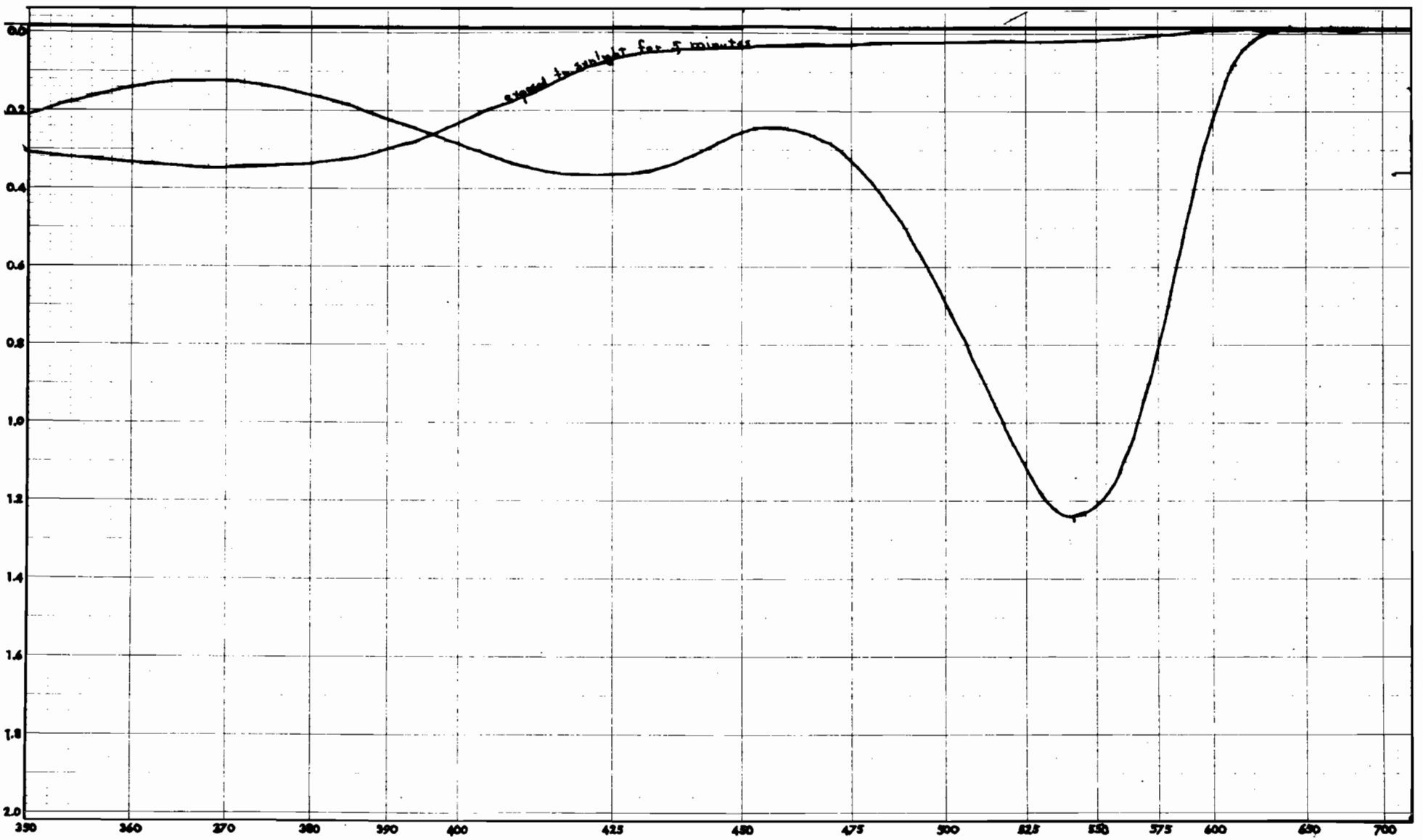

ABSORBANCE
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4
1.6
1.8
2.0
350
360
370
380
390
400
425
450
475
500
525
550
575
600
650
700
WAVELENGTH (MILLIMICRONS)

FIGURE 3

FIGURE 4

The Visible Spectrum of Compound E

in Ethanol

Spectrum was taken on a Perkin-Elmer Model 350

Spectrophotometer

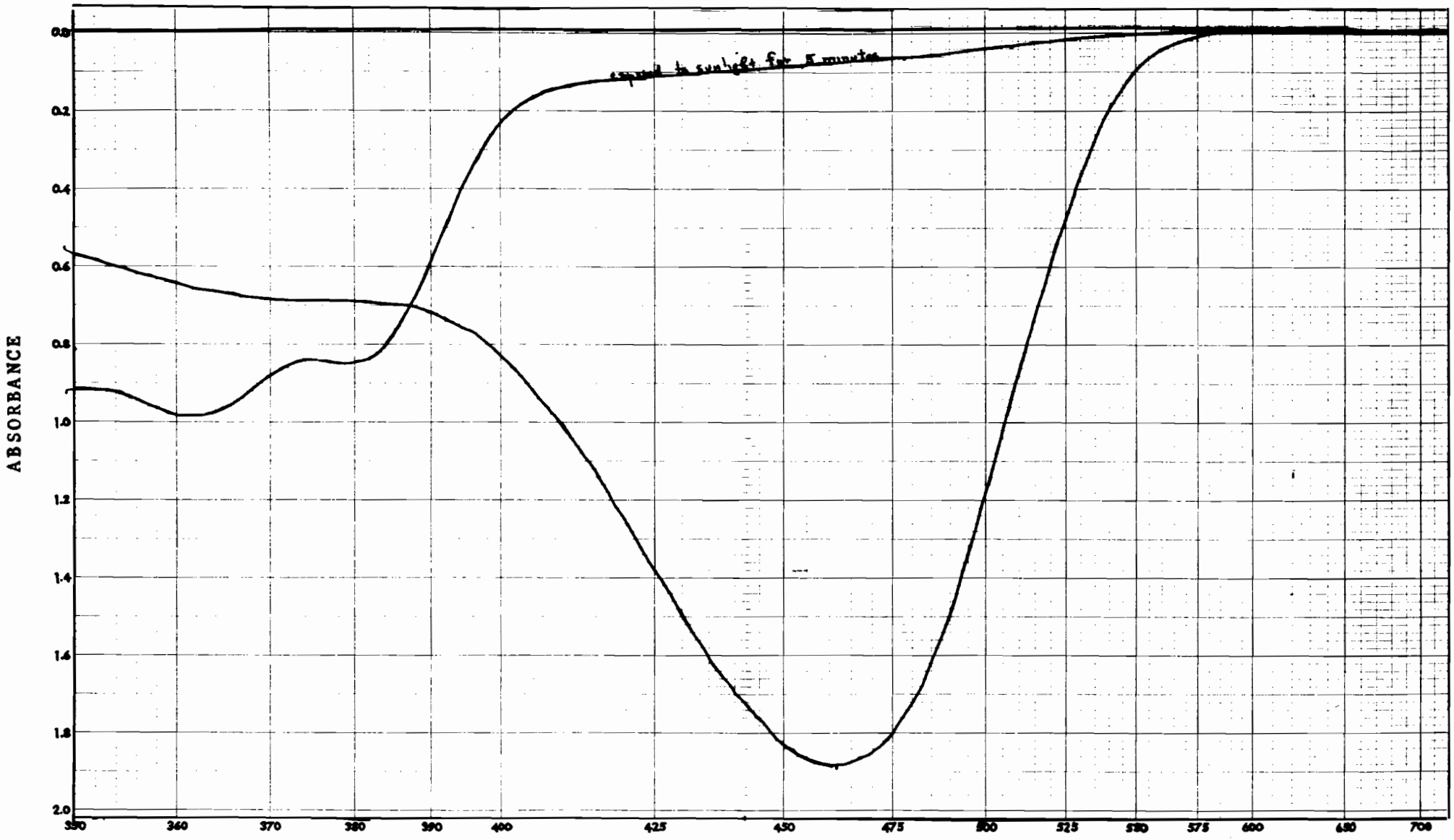

exposed to sunlight for 5 minutes
ABSORBANCE
0.0
0.2
0.4
0.6
0.8
1.0
1.2
1.4
1.6
1.8
2.0
350
360
370
380
390
400
425
450
475
500
525
550
575
600
650
700
WAVELENGTH (MILLIMICRONS)

FIGURE 4

* Because of their rapid oxidation in air, compounds C and D gave no significant absorption in this region of the spectrum.

† The three solutions are not of the same stoichiometric concentration.

As is evidenced in Figure 2, the $\lambda$max value undergoes a systematic shift to shorter wavelength when compound A is put into more strongly hydrogen-bonding solvents.

The three compounds studied are all unstable and fade, usually quite rapidly, when exposed to strong light. Compound B undergoes photochemical decomposition in 5 minutes when exposed to sunlight, the solution becoming almost completely colorless from a deep red-blue. Observation of the spectrum (Figure 3) shows that only a broad envelope absorption in the region 350 m$\mu$ to 390 m$\mu$ remains. Analogously, the $\lambda$max of compound E in ethanol shifts from 462 m$\mu$ to give two less intense but broad peaks at 362 m$\mu$ and about 380 m$\mu$ (Figure 4 and 5) when exposed to sunlight or ordinary white light from a 150 watt source.

Kinetic studies on the rate of decomposition of both the latter compound (Figure 5) and compound A (Figure 6) indicate that only one photochemical product is obtained in each case as the curves clearly pass through an isosbestic point. The $\lambda$max of compound A in ethanol shifts from 412 m$\mu$ to give two less intense peaks, one at 405 m$\mu$ and the other at about 380 m$\mu$ though, in this case, the photochemical decomposition is appreciably slower than in the previous two instances.

FIGURE 5

Change in the Visible Spectrum of Compound E in Ethanol with Time of Exposure to Ordinary White Light from a 150 Watt Source

Spectra were taken on a Beckman Model DU Spectrophotometer

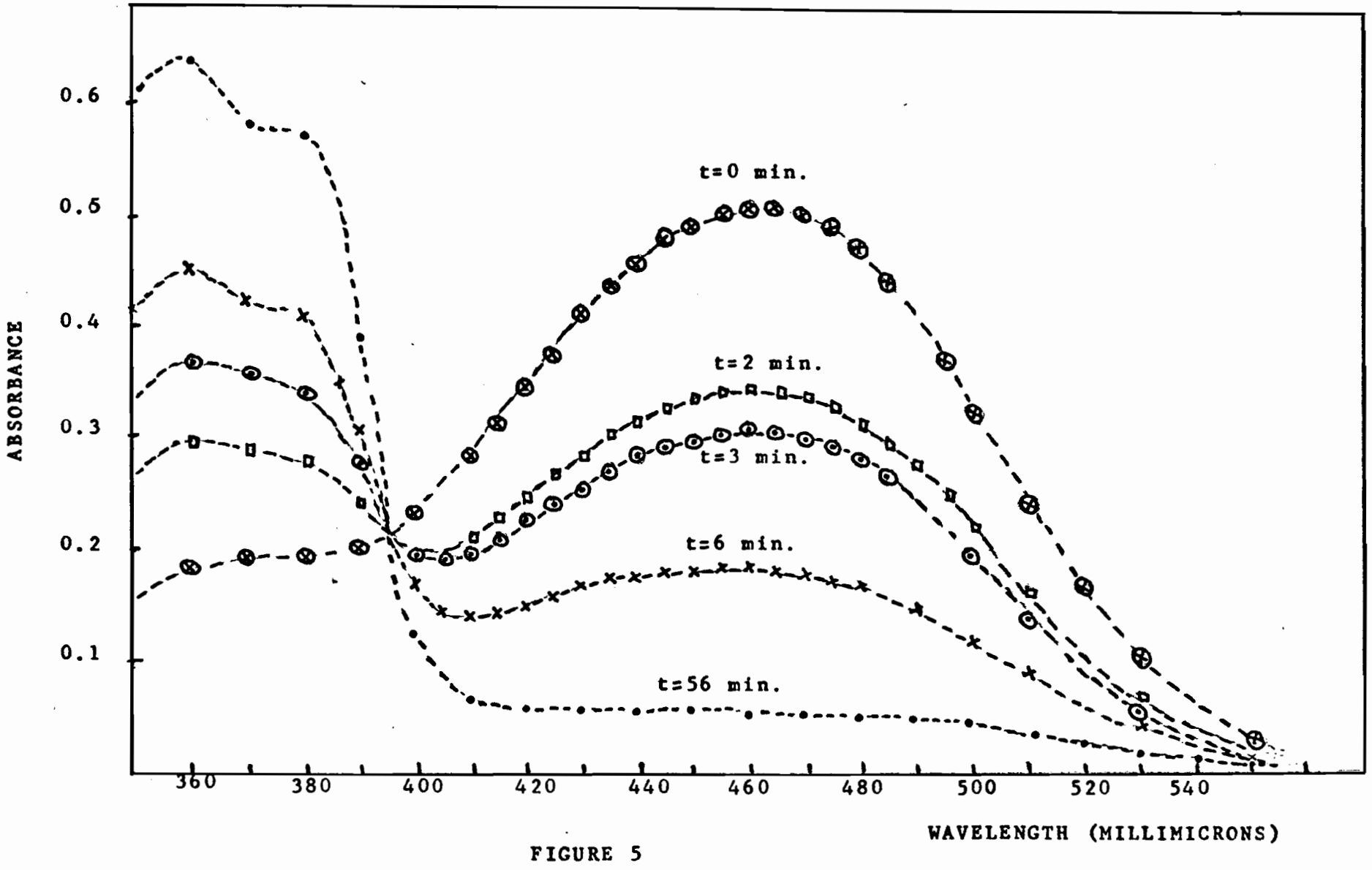

ABSORBANCE
0.6
0.5
0.4
0.3
0.2
0.1
t=0 min.
t=2 min.
t=3 min.
t=6 min.
t=56 min.
360
380
400
420
440
460
480
500
520
540
WAVELENGTH (MILLIMICRONS)

FIGURE 5

FIGURE 6

Change in the Visible Spectrum of Compound A in Ethanol with Time of Exposure to Ordinary White Light from a 150 Watt Source

Spectra were taken on a Beckman Model DU Spectrophotometer

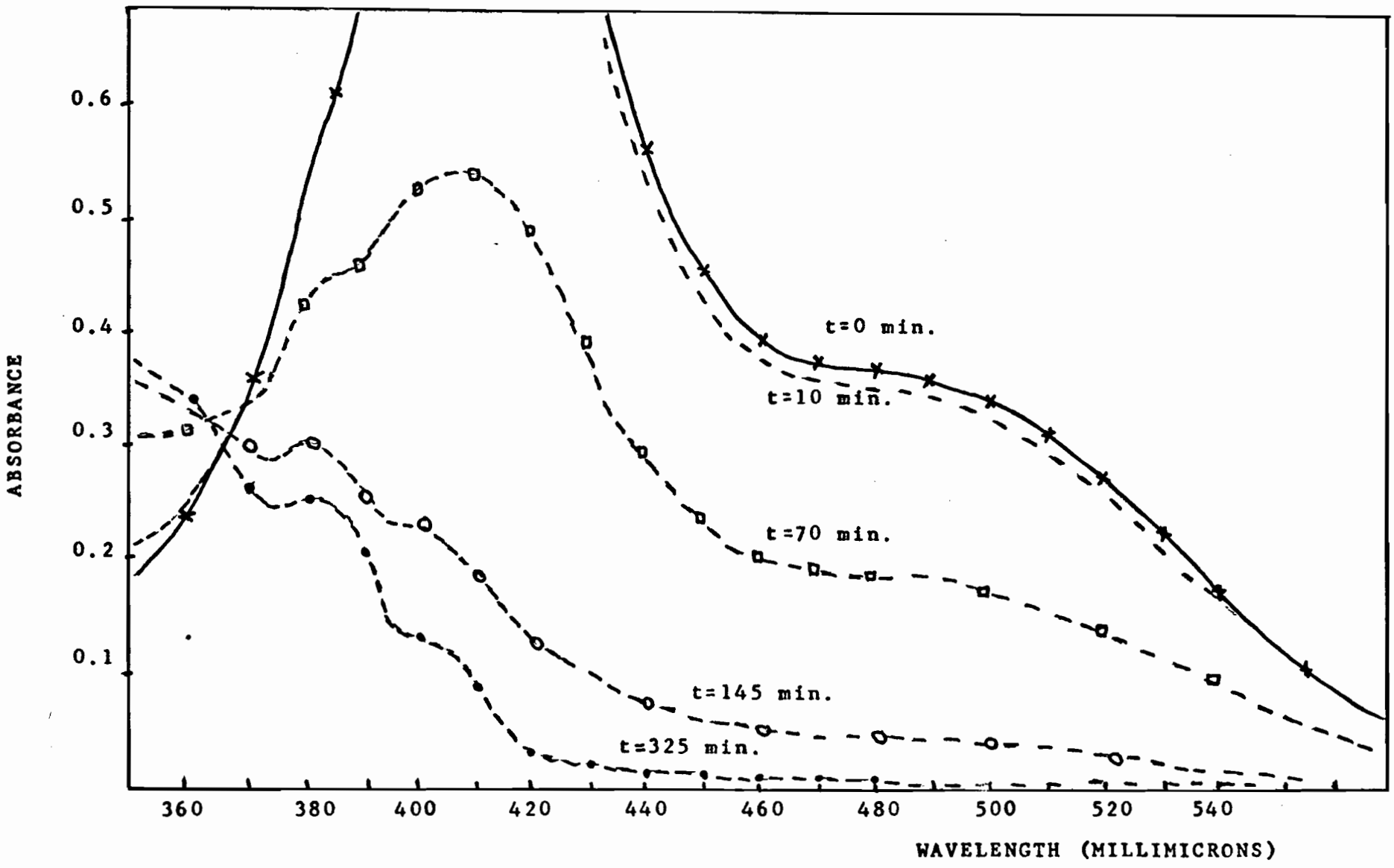

ABSORBANCE
0.6
0.5
0.4
0.3
0.2
0.1
t=0 min.
t=10 min.
t=70 min.
t=145 min.
t=325 min.
360
380
400
420
440
460
480
500
520
540
WAVELENGTH (MILLIMICRONS)

FIGURE 6

## J. Ultraviolet Spectra of Photo-oxidized Products

The ultraviolet spectra of the compounds obtained by photo-oxidation of A,B,C,D and E, recorded on a Beckman model DU spectrophotometer, are given in Figures 7,8,9,10 and 11. The data are reproduced below in Table IV.

Table IV

Ultraviolet Spectral Characteristics of Compounds from Photo-oxidation of A,B,C,D and E

| Compound | $\lambda$ max | Solvent |
|---|---|---|
| A | 230 mμ<br>270 mμ (weak)<br>320 mμ<br>335 mμ | ethanol |
| B | 225 mμ<br>270 mμ | ethanol |
| C | 220 mμ<br>270 mμ (weak) | ethanol |
| D | 235 mμ<br>335 mμ (weak) | ethanol |
| E | 215 mμ<br>242 mμ<br>280 mμ | ethanol |

FIGURE 7

The Ultraviolet Spectrum of the Photo-oxidation Product of Compound A in Ethanol

Spectrum was taken on a Beckman Model DU Spectrophotometer

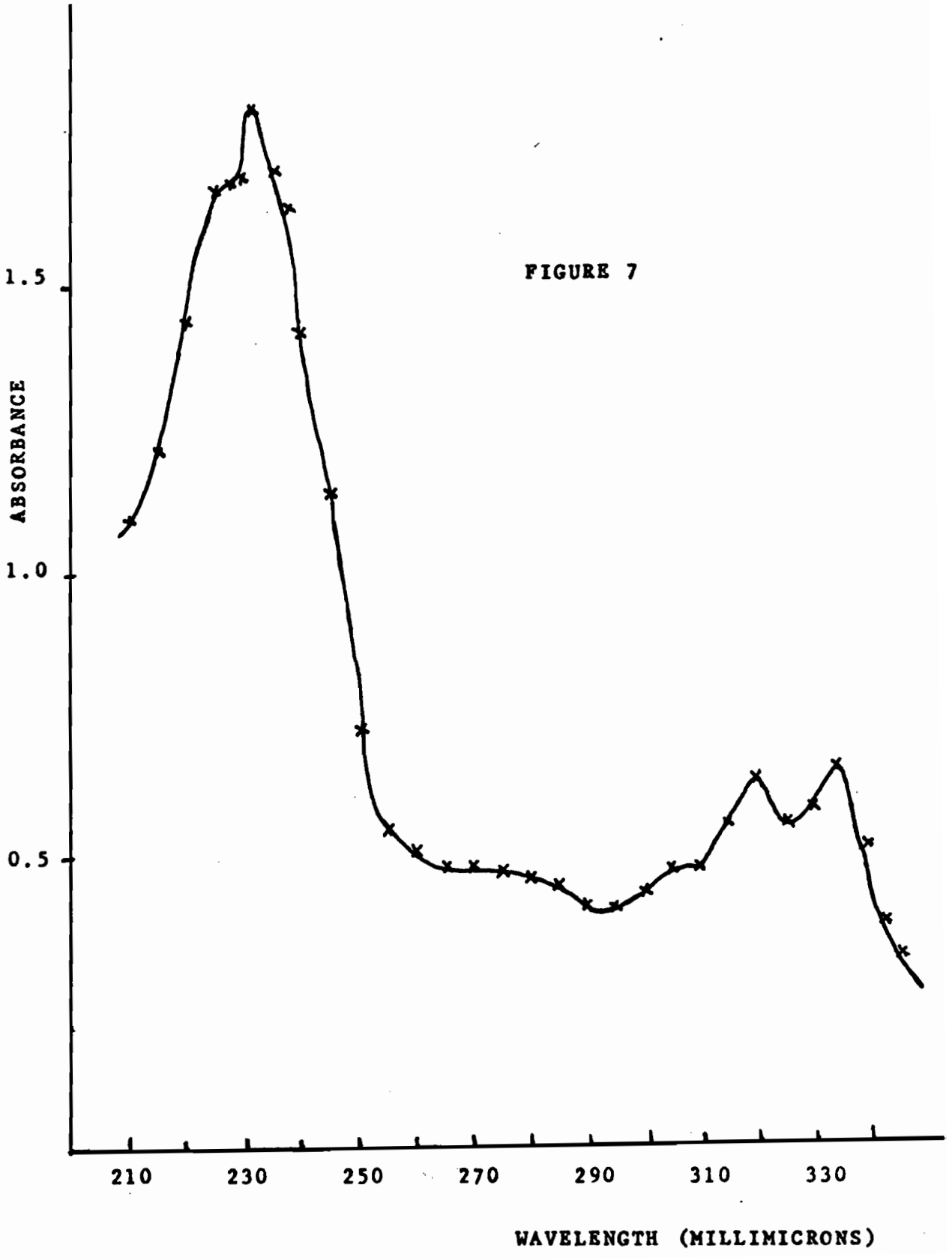

1.5
1.0
0.5
ABSORBANCE
210
230
250
270
290
310
330
WAVELENGTH (MILLIMICRONS)

FIGURE 7

FIGURE 8

The Ultraviolet Spectrum of the Photo-oxidation Product of Compound B in Ethanol

Spectrum was taken on a Beckman Model DU Spectrophotometer

FIGURE 8

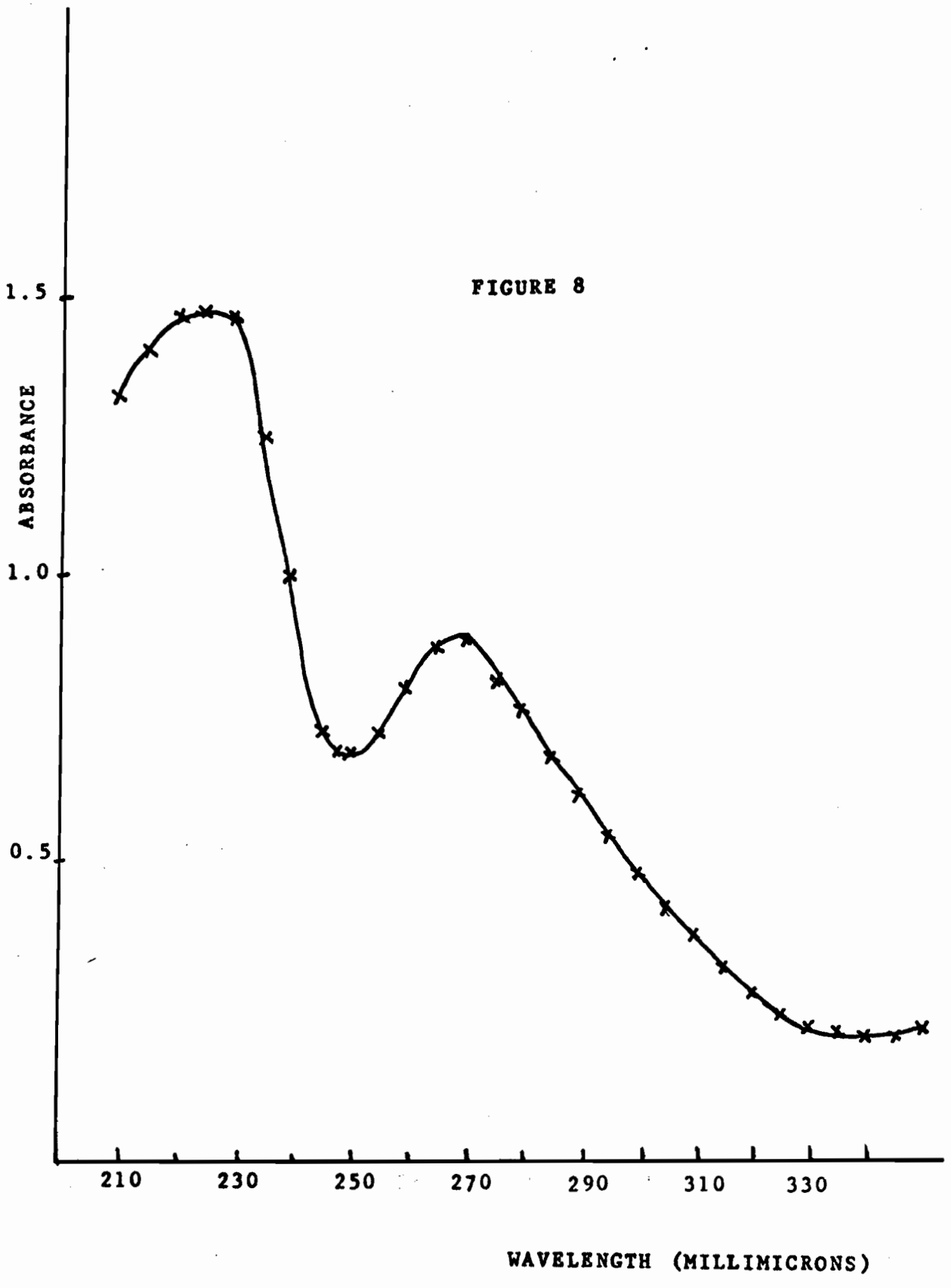

1.5
1.0
0.5
ABSORBANCE
210
230
250
270
290
310
330
WAVELENGTH (MILLIMICRONS)

FIGURE 9

The Ultraviolet Spectrum of the Photo-oxidation Product of Compound C in Ethanol

Spectrum was taken on a Beckman Model DU Spectrophotometer

FIGURE 9

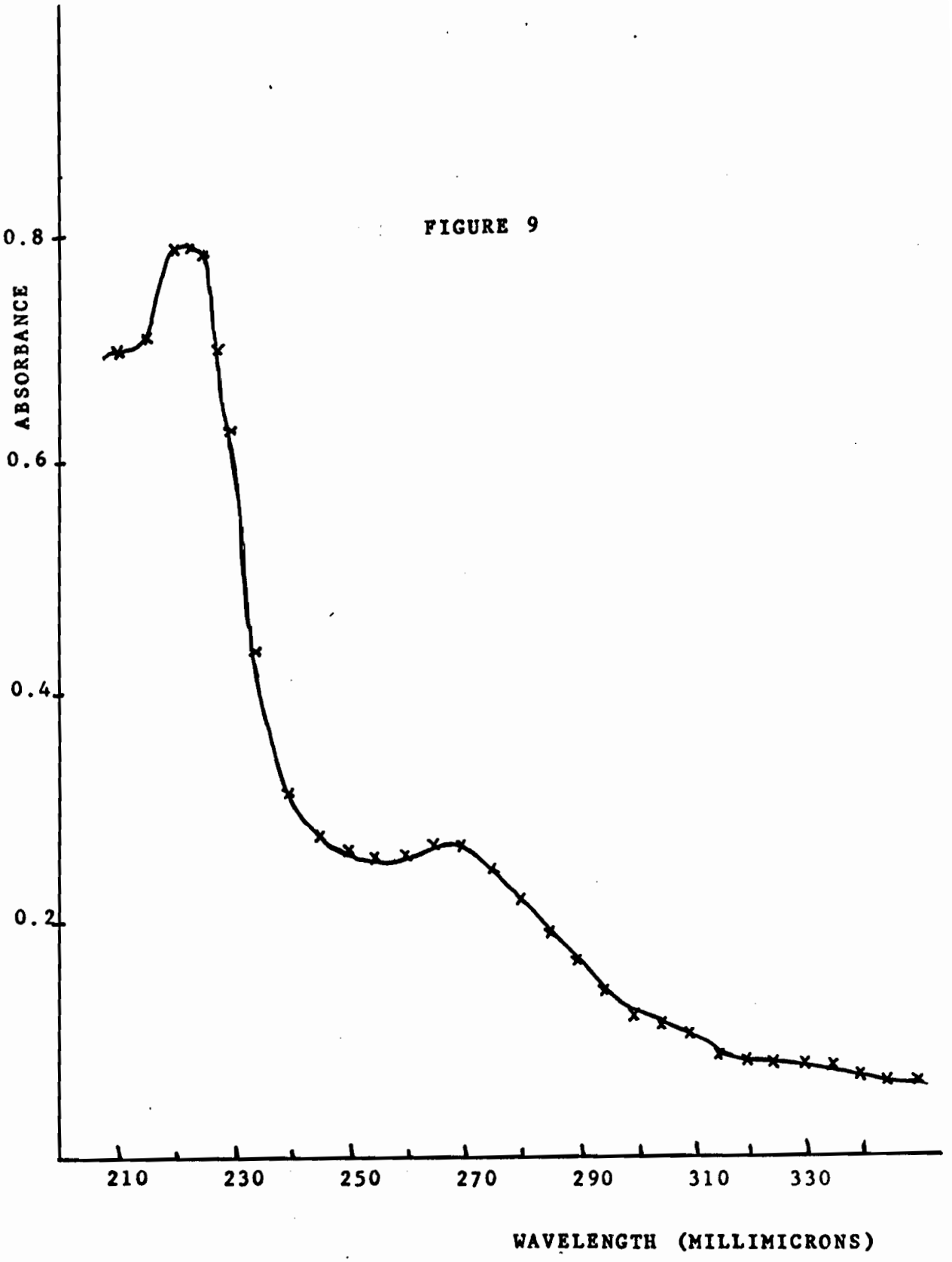

0.8
0.6
0.4
0.2
ABSORBANCE
210
230
250
270
290
310
330
WAVELENGTH (MILLIMICRONS)

FIGURE 10

The Ultraviolet Spectrum of the Photo-oxidation Product of Compound D in Ethanol

Spectrum was taken on a Beckman Model DU Spectrophotometer

FIGURE 10

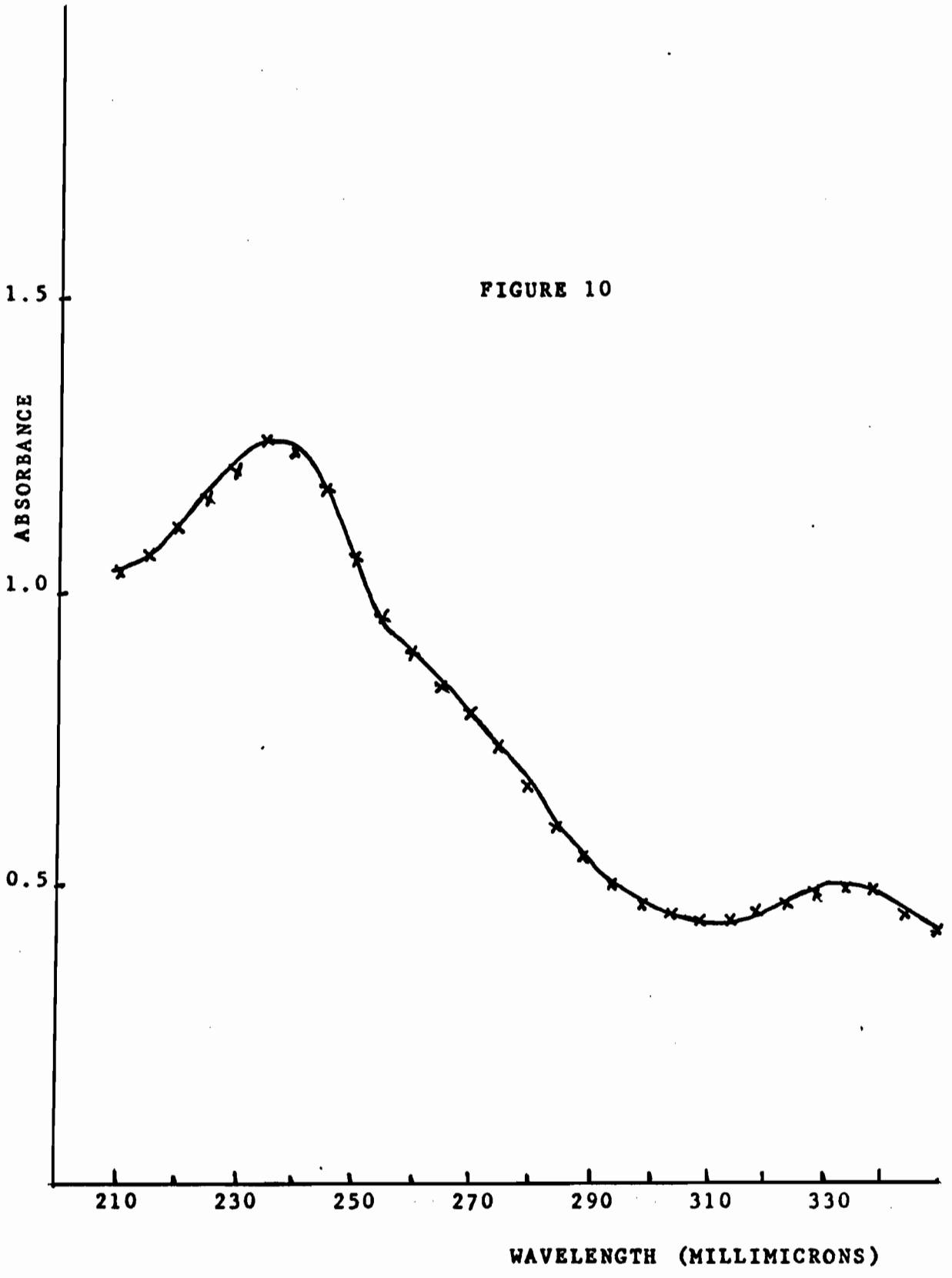

1.5
1.0
0.5
ABSORBANCE
210
230
250
270
290
310
330
WAVELENGTH (MILLIMICRONS)

FIGURE 11

The Ultraviolet Spectrum of the Photo-oxidation Product of Compound E in Ethanol

Spectrum was taken on a Beckman Model DU Spectrophotometer

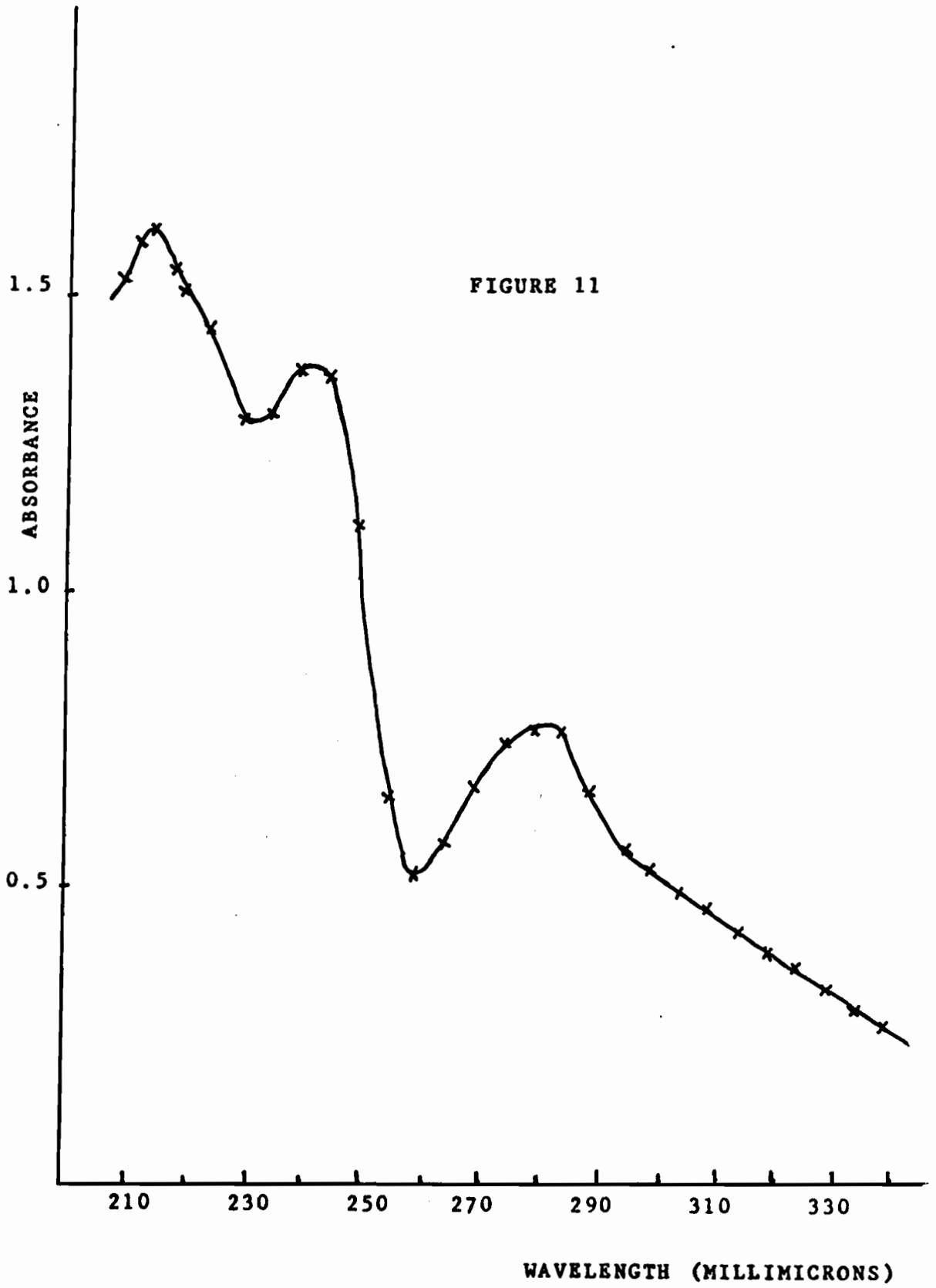

1.5
1.0
0.5
ABSORBANCE
210
230
250
270
290
310
330
WAVELENGTH (MILLIMICRONS)

FIGURE 11

K. Infrared Spectra

All infrared spectra were taken on a Perkin-Elmer Infracord spectrophotometer using the potassium bromide disc technique. The spectra of compounds A,B,C,D and E appear in Figures 12,13,14,15,16.

L. Nuclear Magnetic Resonance Spectra

The nuclear magnetic resonance spectra of compounds A,B and E were taken in trifluoroacetic acid on a high frequency Varian 60 mc. model. They appear in Figures 17,18,19.

FIGURE 12

The Infrared Spectrum of Compound A

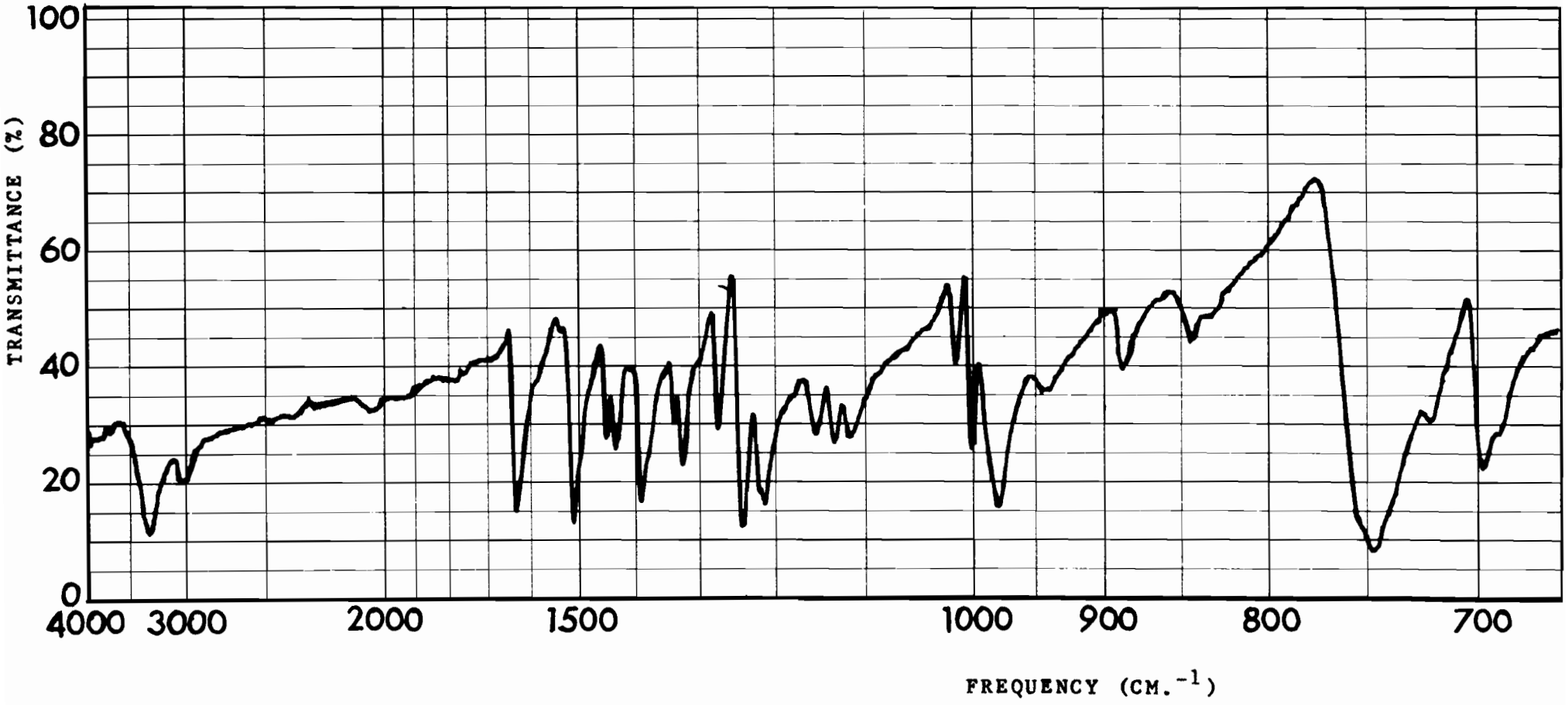

100
80
60
40
20
0
TRANSMITTANCE (%)
4000
3000
2000
1500
1000
900
800
700
FREQUENCY (CM.$^{-1}$)

FIGURE 12

FIGURE 13

The Infrared Spectrum of Compound B

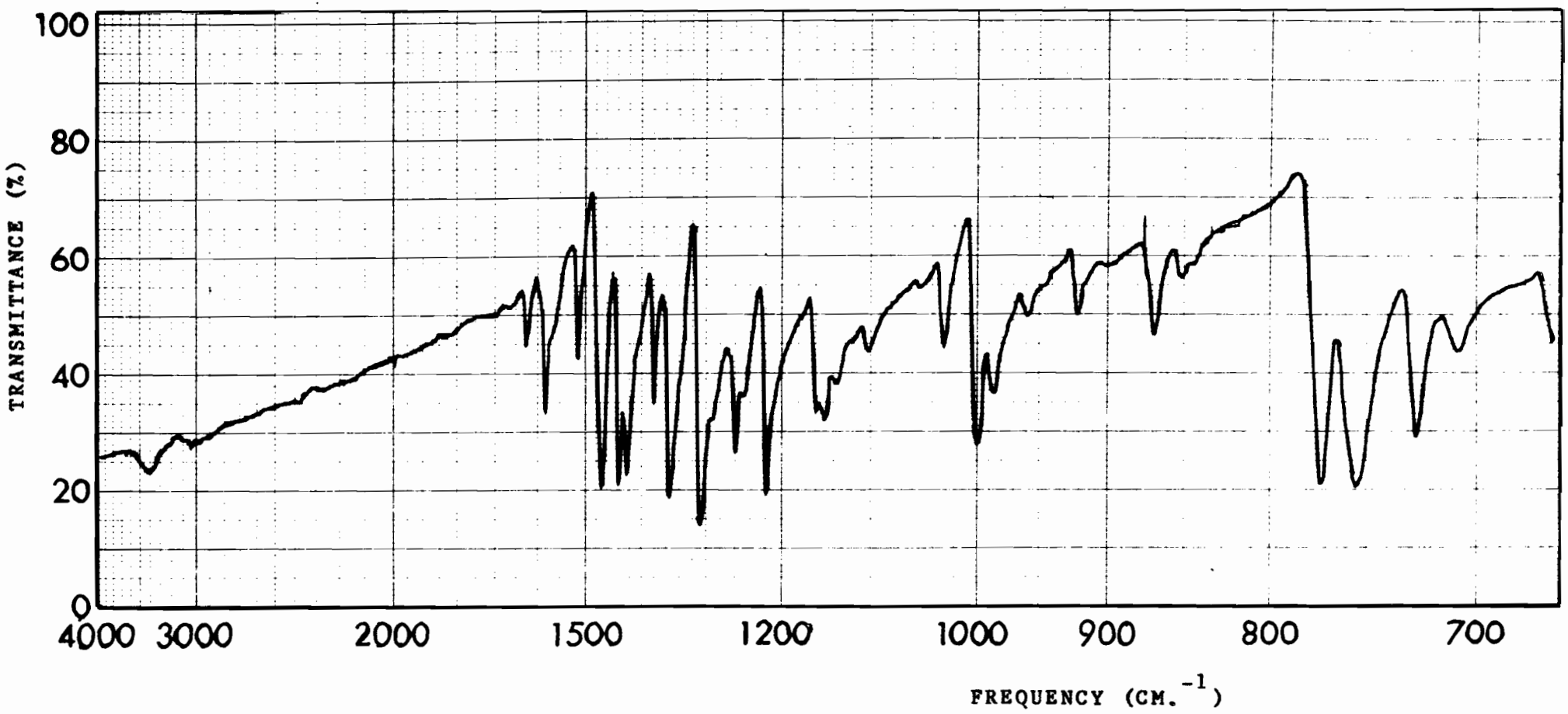

100
80
60
40
20
0
TRANSMITTANCE (%)
4000
3000
2000
1500
1200
1000
900
800
700
FREQUENCY (CM.$^{-1}$)

FIGURE 13

FIGURE 14

The Infrared Spectrum of Compound C

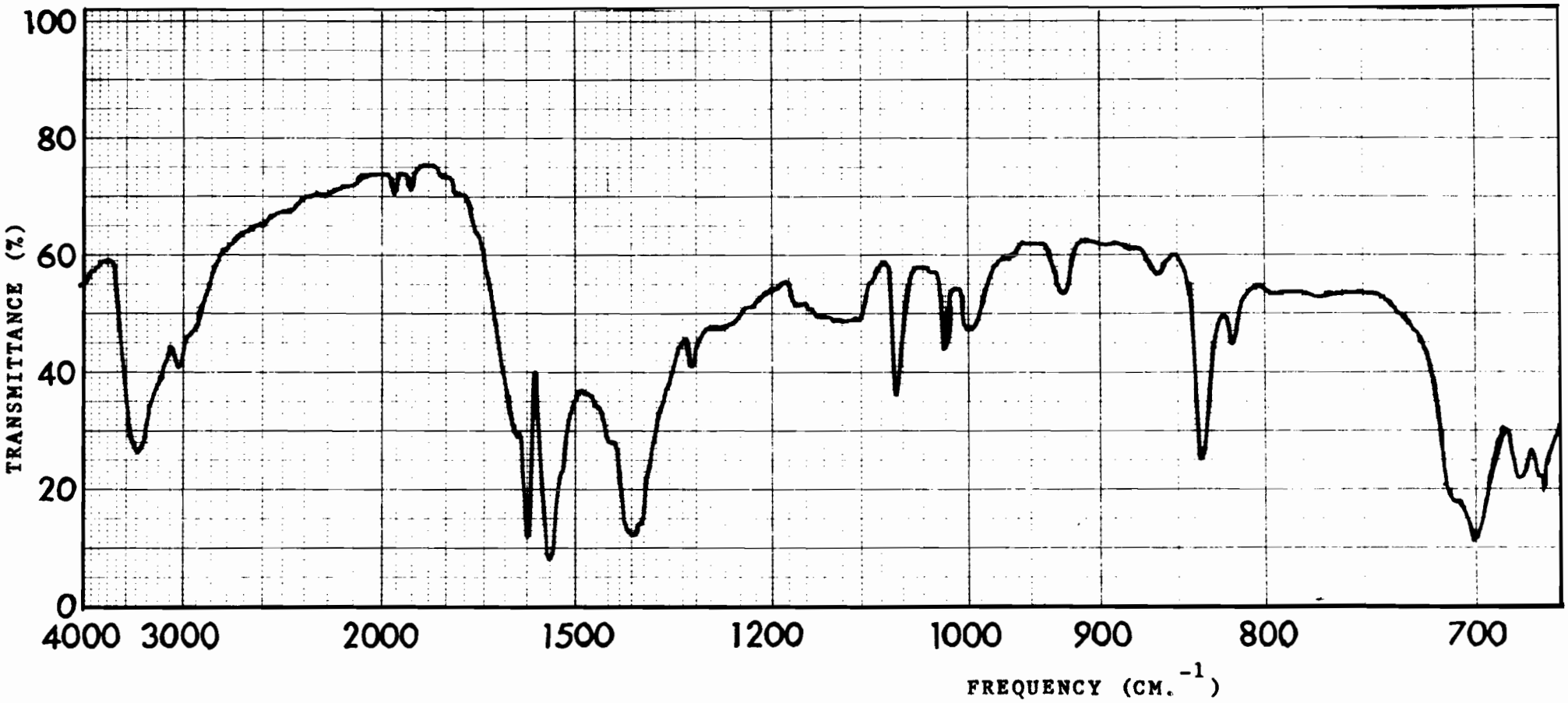

100
80
60
40
20
0
TRANSMITTANCE (%)
4000
3000
2000
1500
1200
1000
900
800
700
FREQUENCY (CM.$^{-1}$)

FIGURE 14

FIGURE 15

The Infrared Spectrum of Compound D

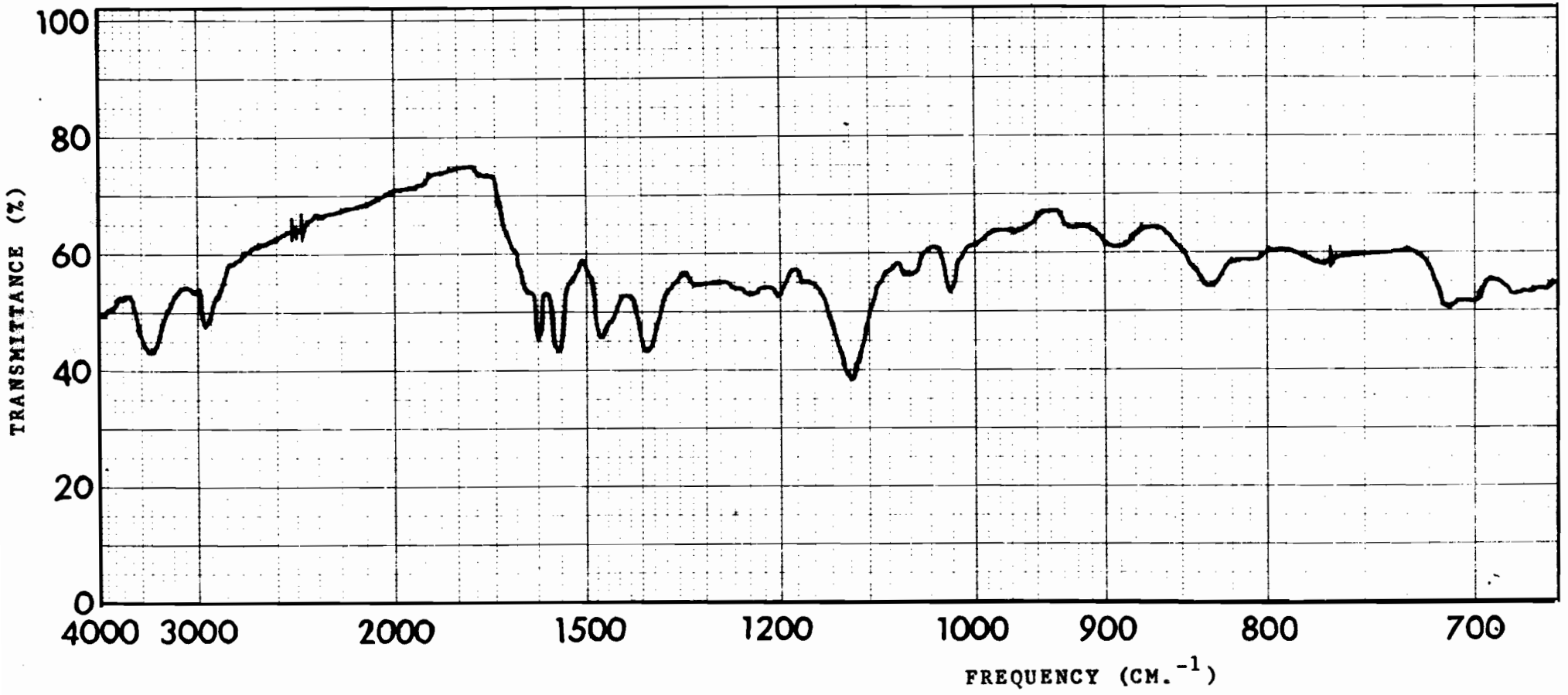

100
80
60
40
20
0
TRANSMITTANCE (%)
4000
3000
2000
1500
1200
1000
900
800
700
FREQUENCY (CM.$^{-1}$)

FIGURE 15

FIGURE 16

The Infrared Spectrum of Compound E

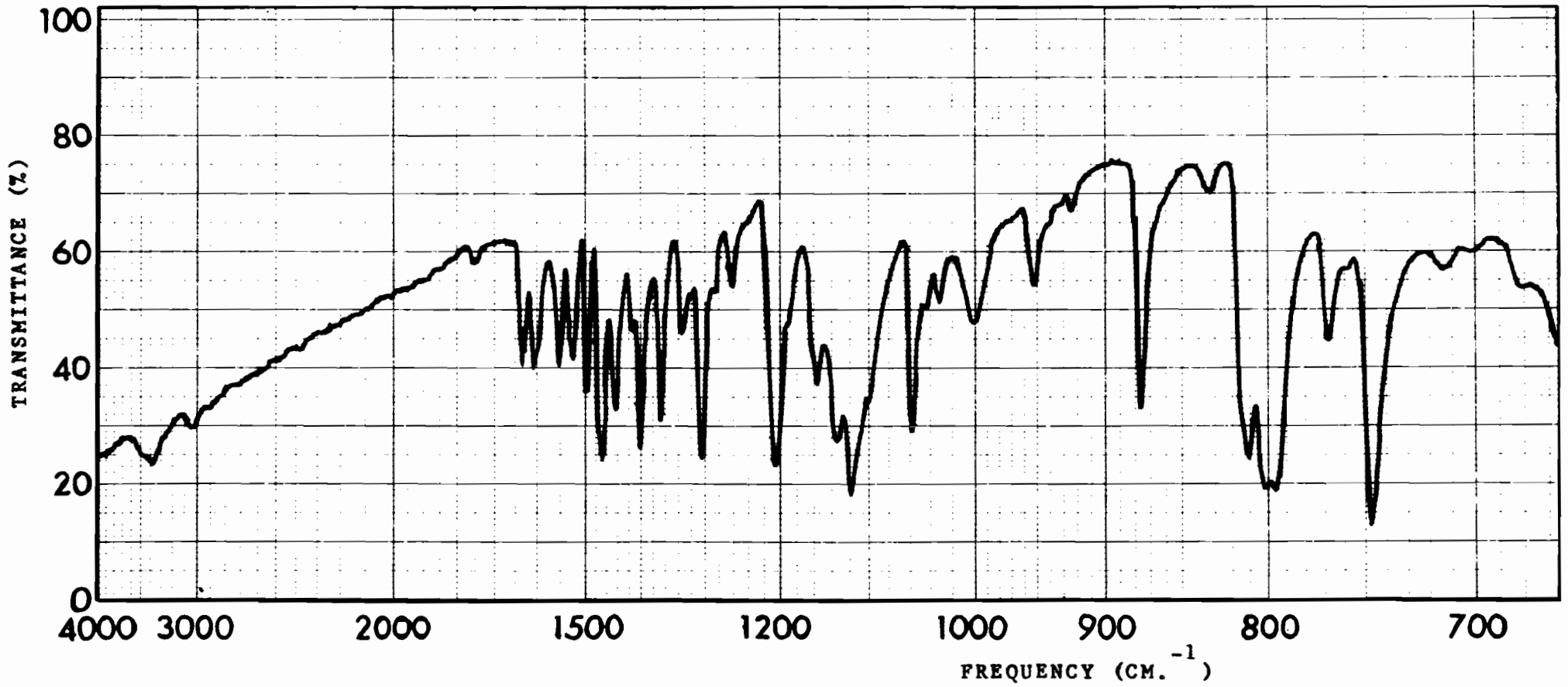

100
80
60
40
20
0
TRANSMITTANCE (%)
4000
3000
2000
1500
1200
1000
900
800
700
FREQUENCY (CM.$^{-1}$)

FIGURE 16

FIGURE 17

The Nuclear Magnetic Resonance Spectrum

of Compound A

FIGURE 17

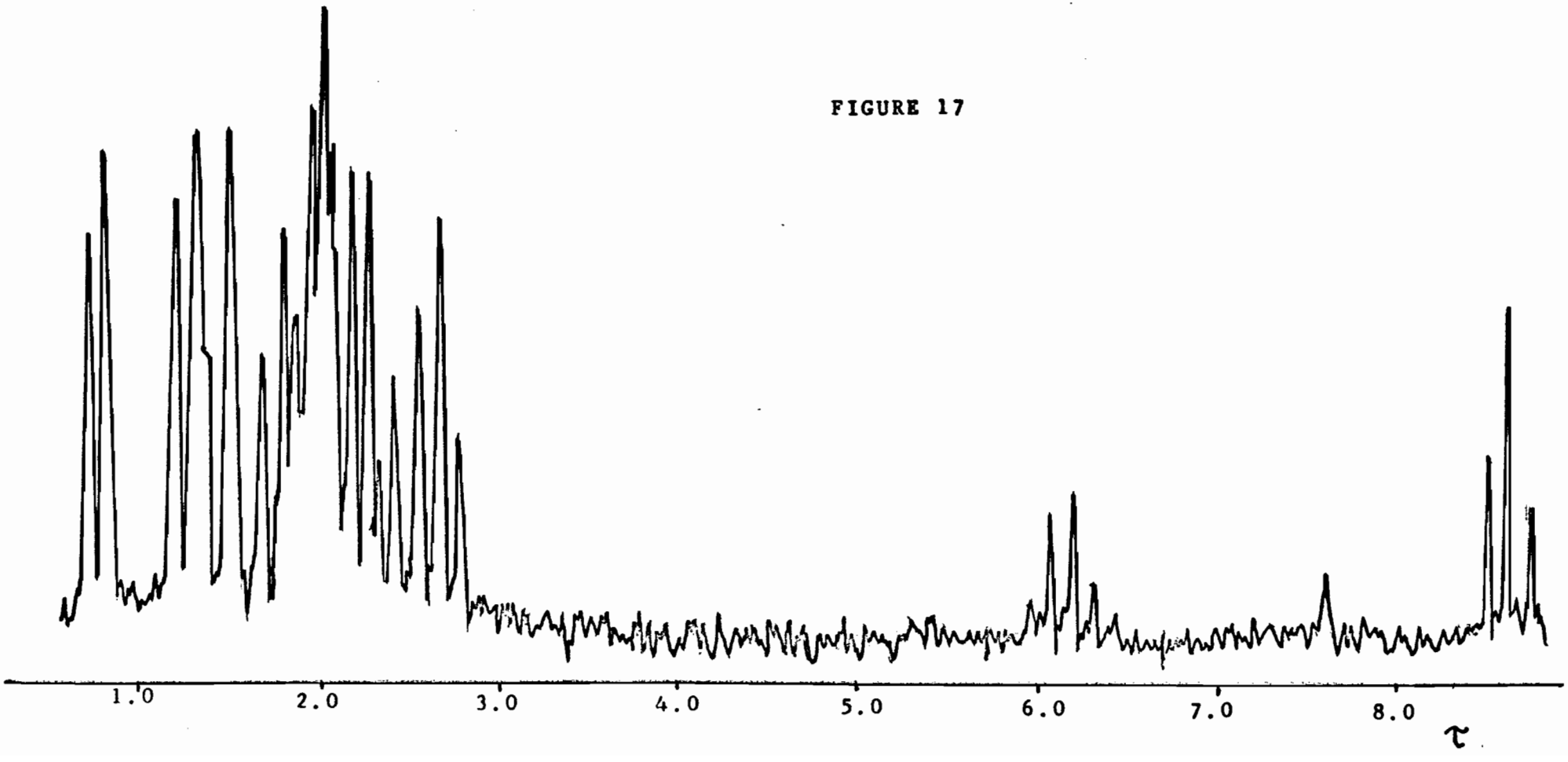


FIGURE 18

The Nuclear Magnetic Resonance Spectrum

of Compound B

FIGURE 18

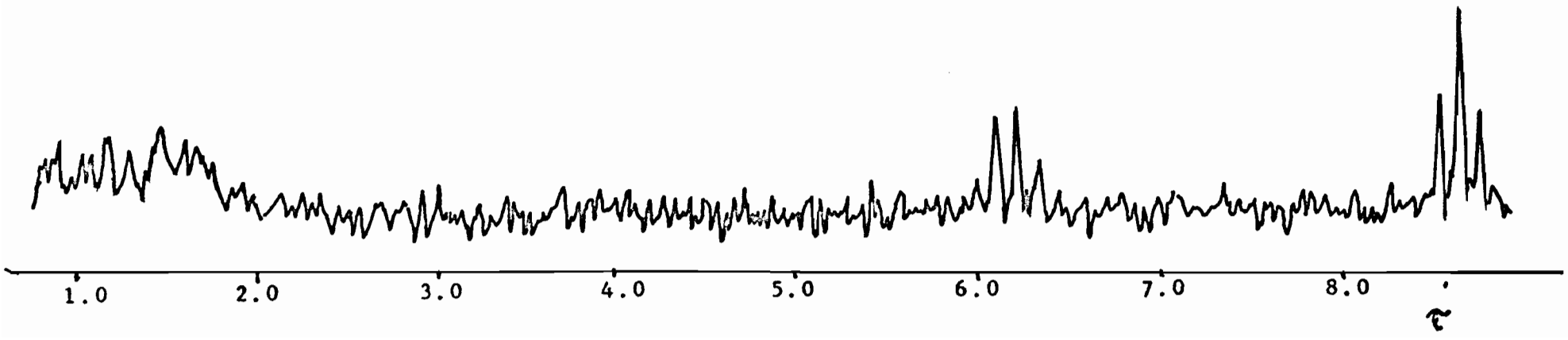
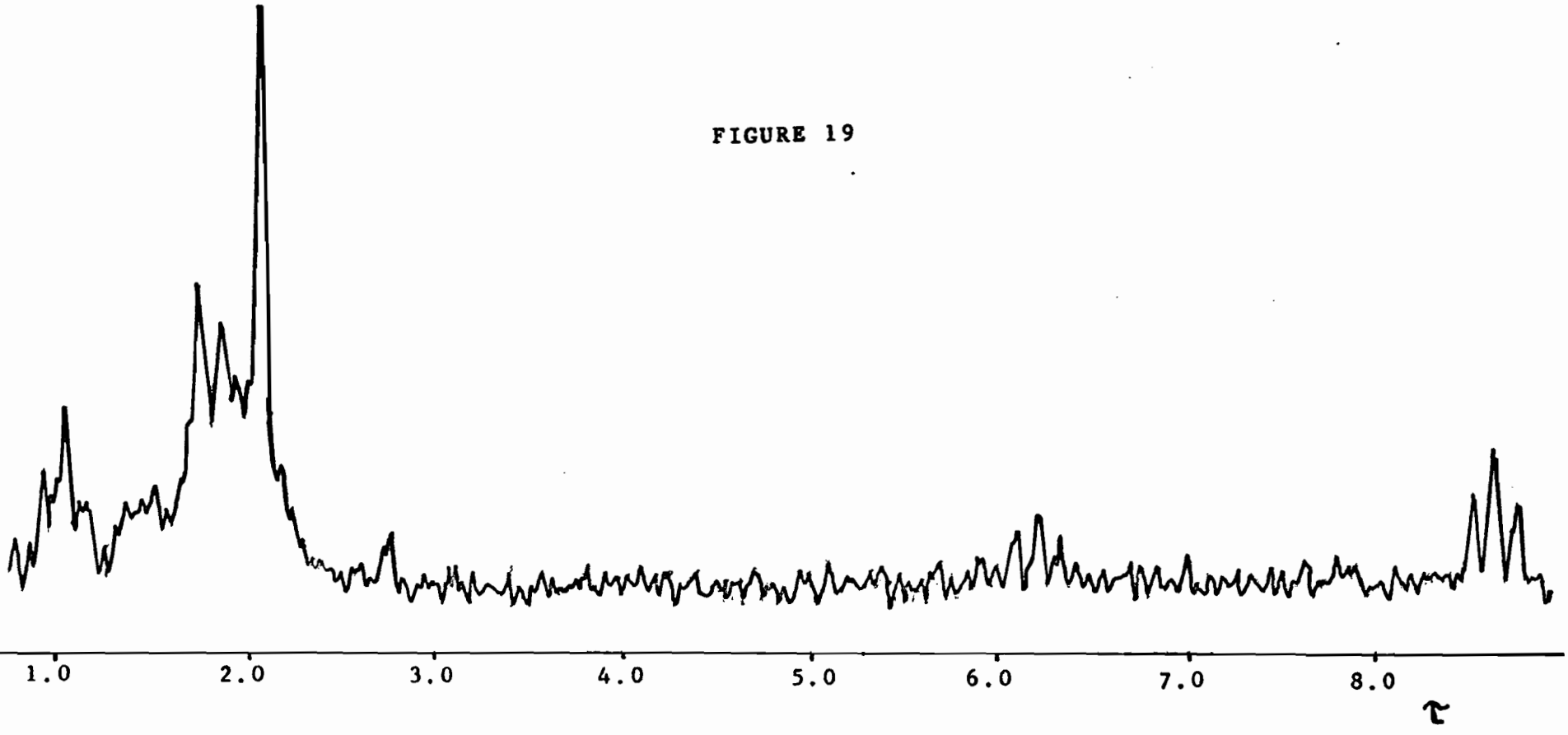


FIGURE 19

The Nuclear Magnetic Resonance Spectrum

of Compound E

FIGURE 19

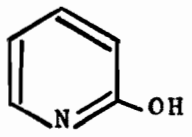


## RESULTS AND DISCUSSION

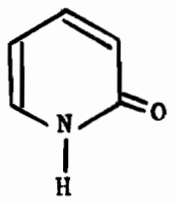
The data reported in the preceding section of this thesis strongly suggest a similarity between the compounds obtained from the Binz and Marx reaction, and the pyridinols and pyridinethiols. The chemistry of the former class of compounds has been well documented in recent years:

The 3-pyridinol possesses similar reactivity to phenolic compounds in that it readily undergoes a variety of electrophilic substitutions. It exists mainly in the zwitterionic form, thus making it only slightly less basic than pyridine itself (Table V).

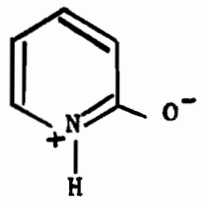
In the case of the 2- and 4-pyridinols, spectral studies have shown that, of the two main tautomeric forms possible, the pyridone structure is the favored one, the ratio of lactam to lactim form in the 2-isomer being 340:1, and in the 4-isomer 2200:1, or roughly 6.5 times greater than for the 2-isomer.



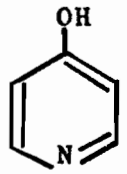

XXXI



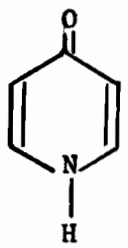

XXXII



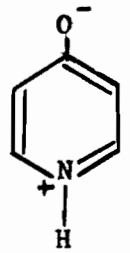

XXXIII




XXXIV



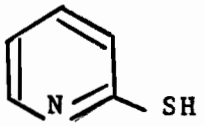

XXXV



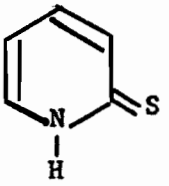

XXXVI

Thus, N-alkylation takes place with relative facility in these compounds. $pK_{BH^+}$ measurements (see Table V) have indicated a value of 0.75 for the 2-pyridinol and 3.27 for the 4-pyridinol, entirely in consonance with the conclusion that the pyridone is the predominant form with appreciable resonance contribution from the dipolar forms XXXIII and XXXVI respectively, decreasing the electron density about the ring nitrogen.

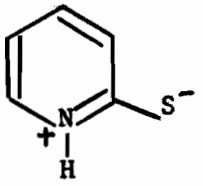
The situation with the 2- and 4-pyridinethiols is entirely analogous. Jones and Katritzky (20) measured the $pK_{BH^+}$ values of these compounds and compared them to their oxygen analogues. As shown in Table V, the dissociation constant for the 2-pyridinethiol is -1.07 and that of the 4-pyridinethiol 1.48.



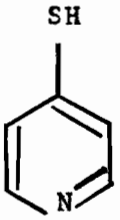

XXXVII



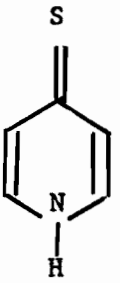

XXXVIII



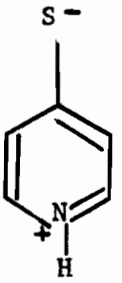

XXXIX




XL




XLI




XLII

The sulfur analogs are thus less basic than their hydroxy counterparts, and the forms carrying the hydrogen atom on nitrogen are more preferred in mercapto than in hydroxy-N-heterocycles. Later work by Albert and Barlin (21) has corroborated this view.

It is immediately seen, therefore, that compound A synthesized in the present work, is of the same order of basicity as the 2- and 4-pyridinols and pyridinethiols though the evidence favoring either the $\alpha$ or $\gamma$ form in the latter case is not conclusive. It is certain, however, that the electron density about the nitrogen atom has been greatly reduced by the introduction of a sulfur-containing group capable of electron withdrawal. Thus, the compound is quite soluble only in strong acids and the yellow HCl salt (m.p. $185^{\circ}$-$186^{\circ}$), formed by passing dry hydrogen chloride through a tube containing the red neutral form, readily dissociated on contact with moisture.

Table V

Dissociation Constant Values for Pyridinols, Mercaptopyridines and other Pyridine Compounds

| Compound | $pK_{BH^+}$ |
|---|---|
| pyridine | 5.23 |
| 2-pyridinol | 0.75 |
| 2-pyridinethiol | -1.07 |
| 3-pyridinol | 4.86 |
| 4-pyridinol | 3.27 |
| 4-pyridinethiol | 1.48 |
| pyridine-N-oxide | 0.79 |

The ultraviolet spectra of both the 2- and 4-hydroxy and mercaptopyridines have been reported (21,22). Their main characteristics are given in Table VI below.

Table VI

Ultraviolet Spectral Characteristics of Pyridinols and Pyridinethiols

| Compound | $\lambda$max | Solvent |
|---|---|---|
| 2-pyridinol | 227 mμ<br>297 mμ | methanol |
| 2-pyridinethiol | 273 mμ<br>345 mμ | ethanol |
| 3-pyridinol | 245 mμ<br>283 mμ | methanol |
| 4-pyridinol | 256 mμ | ethanol |
| 4-pyridinethiol | 231 mμ<br>275 mμ<br>327 mμ | ethanol |

When these data are compared to the ultraviolet spectral data for the compounds in Table IV, it is immediately seen that there is a marked similarity between 4-pyridinethiol and compounds formed from compounds A and B by photo-oxidation.

The infrared spectra of the 2- and 4-pyridones substantiate the finding of the overwhelming preponderance of the lactam form, indicated earlier by ionization constant measurements. The spectrum of 2-pyridinol shows an intense carbonyl absorption at 1650 $cm.^{-1}$ as well as a strong N-H stretching mode at about 3100 $cm.^{-1}$. The spectrum of the 4-isomer is similar, while the 3-pyridinol exhibits the expected features of a lactim structure, strong O-H stretching vibration at about 3500 $cm.^{-1}$ but no N-H band. Spinner (23,24) has studied the spectra of the corresponding 2- and 4-pyridinethiols and has concluded that, in each case, the thione form is present in both the solid state and in solvents of low polarity. Three features in the infrared spectrum enable one to differentiate between the mercapto form and the thioamide form; these are the presence or absence of a strong absorption in the range 1630-1600 $cm.^{-1}$ due to a skeletal stretching vibration of C=C and C=N bonds which do not form part of an aromatic skeleton, a strong thiocarbonyl stretching band near 1150 $cm.^{-1}$ ($\pm$70 $cm.^{-1}$) and the N-H stretching mode at about 3200 $cm.^{-1}$.

In the present work, most of these bands are observed in the compounds studied (Figures 12,13,14,15,16). The N-H stretching mode is found at about 3300 $cm.^{-1}$, which is at a slightly higher frequency than reported for the pyridinethiols. The absorption due to the skeletal stretching appears in all cases (except C and D) at 1630 $cm.^{-1}$ and is a band of medium intensity when compared to other peaks in

the spectrum. The band between 1100 cm.$^{-1}$ and 1200 cm.$^{-1}$, indicative of a thiocarbonyl group, is particularly weak in the cases of compounds A and C but slightly more intense in the other three cases. From the information gleaned from these spectra, it is quite certain that the nitrogen centre has acquired a hydrogen atom through some process, possibly tautomeric. This supports the view, expressed earlier from the dissociation constant measurement, that the compounds bear a resemblance to the 2- and 4-pyridinethiols, though undisputable evidence for the presence of the thiocarbonyl group is lacking.

The nuclear magnetic resonance spectra of compounds A, B and E, taken in trifluoroacetic acid (Figures 17,18,19), exhibit certain features which are not easily explained. In compound A, there is a multiplet of 16 lines in the range of 0.7 to 2.8$\tau$, a quartet of low intensity at 6.2$\tau$ and a triplet band at 8.65$\tau$. The latter two peaks would seem to imply an ethyl group attached to the ring but it is possible that a small residue of methyl ethyl ketone, trapped as a clathrate during the recrystallization step, is responsible for this absorption though the spectrum of the ketone taken in the same solvent shows resonance at about 5.8$\tau$ and 8.6$\tau$ as well as from the methyl group adjacent to the carbonyl group. Compound B shows absorption peaks comparable to that of compound A while compound E is different in the 1.0 to 2.5$\tau$ region, as would be expected from the presence of a benzene nucleus.

## CONCLUSION

Unequivocal elucidation of the structure of compounds from the Binz and Marx reaction is difficult. There are, nevertheless, certain implications in the evidence presented in this thesis.

The possibility of a ring opening reaction of the type described by Zincke and his co-workers would seem to be precluded by the spectral data which suggest the presence of a pyridine ring, probably partially reduced. The infrared spectra indicate the presence of an N-H bond and a C=C linkage which lies exo to the aromatic system, though the existence of a thiocarbonyl group is doubtful. Ultraviolet and visible spectral data point to a structure in which the mobility of the electrons permit a relatively facile photo-oxidation resulting in the observed fading when its dilute solution is exposed even to ordinary white light.

Thus, a fairly long conjugated system must be assumed to account for the red color. However, much more evidence is required before a plausible structure can be advanced. In the meantime, the following points have been established by the work presented in this thesis:

1. The formation of a red compound from the reaction of pyridine with sulfur dioxide in benzoyl chloride (the Binz and Marx reaction) has been confirmed.
2. Although benzoyl chloride is required for this reaction it does not become incorporated in the product.

3. Other heterocyclic compounds related to pyridine react in similar fashion with sulfur dioxide in benzoyl chloride to give colored compounds.
4. Solutions of the compounds are bleached by exposure to visible or ultraviolet light, by what appears to be a photo-oxidation reaction.

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