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The Synthesis, Characterization and Reactions of 1,2-dihydro-2-thiono, 3,1-Benzoxazin-4-one and its Isomer the 3,1-benzothiazine-2 (1H), 4-dione

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The Synthesis, Characterization and Reactions
of 1,2-dihydro-2-thiono,3,1-Benzoxazin-4-one
and its isomer the 3,1-benzothiazine-2(1H),
4-dione.

This paper submitted in fulfillment of the
requirements of Chemistry 30.

Dr. Roger P. Staiger, Advisor

Submitted by:

Joan Louise Davis

May 31, 1967

Approved by:

Roger P. Staiger

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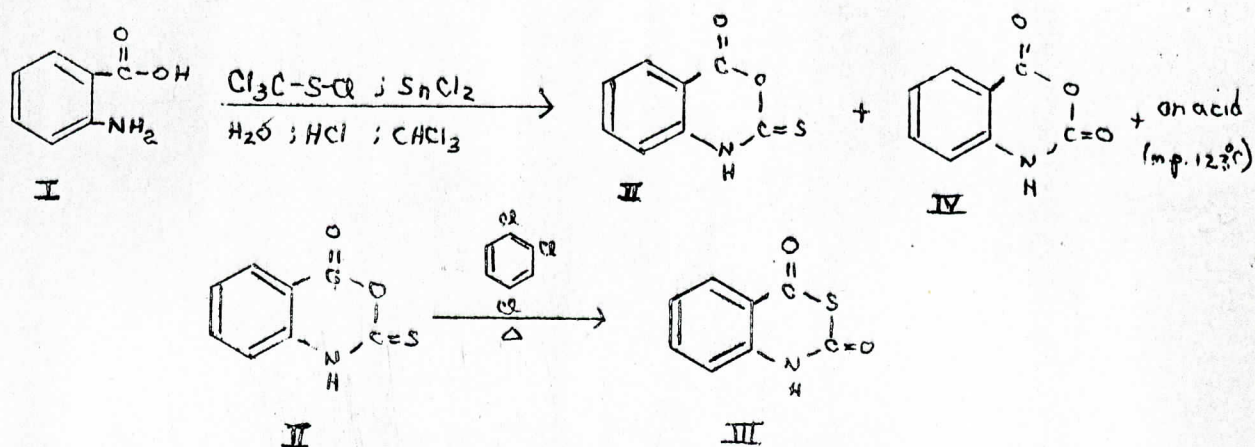
INTRODUCTION

The objective of this research was to prepare 1,2-dihydro-2-thiono-3,1-benzoxazin-4-one (thioisatoic anhydride) and an isomer, the 3,1-benzothiazine, 2(1H),4-dione. The structures of these isomers have been elucidated by chemical and infrared spectrophotometric methods.

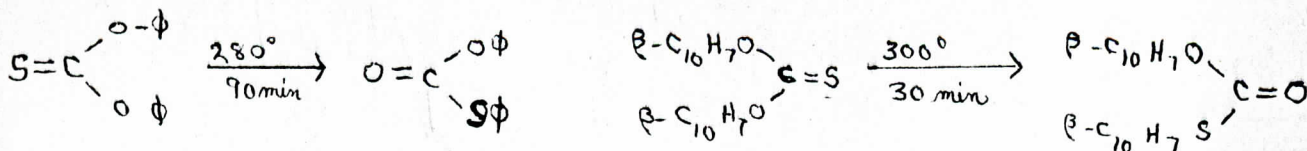
The reactions of thioisatoic anhydride with sodium hydroxide, ammonia, a series of diprotic amines, and methyl iodide have been investigated. The products of the reactions have been characterized. It appears that the mechanism of the reaction of thioisatoic anhydride with various nucleophiles is analogous to those reported for Isatoic Anhydride with some minor differences.

HISTORICAL

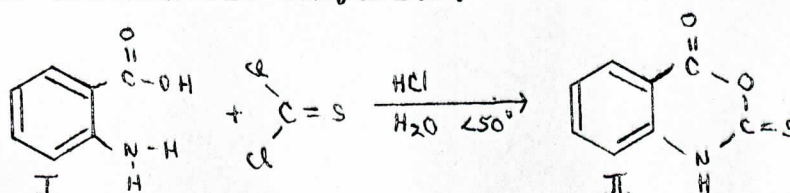
The chemical literature reports one preparation of thioisatoic anhydride by J. R. Marshall¹, using trichlorosulphenylchloride, stannous chloride dihydrate, and anthranilic acid (I) in an aqueous hydrochloric acid-chloroform medium. After purification of the product from ethyl acetate and acetone a product was obtained melting between 230-235°C with the evolution of hydrogen sulfide gas. This material was described as thioisatoic anhydride (II). It was reported that the infrared spectrum showed a strong absorption peak at a frequency of 1785 cm⁻¹. Along with the product were isolated some isatoic anhydride (IV) and an uncharacterized sulfur-free acid. Marshall also reported that thioisatoic anhydride could be isomerized by heating in boiling 1,2,4-trichlorobenzene to 3,1-benzothiazine-2(IH),4-dione (III), which when purified from acetone melted at 226-235°C turning to a red liquid with gas evolution. The reactions were presented as:



An isomerization of the above type has been reported by Schonberg and Vargha² with the C=S being transformed to the C-S-C in the conversion of diphenyl thiocarbonate to thiocarbonate:



A second method of preparation of thioisatoic anhydride (II) is described in a personal communication of the unpublished work of Charles Wade at the University of Delaware. This preparation is similar to that for the preparation of isatoic anhydride described by Fegley³ substituting thiophosgene for phosgene. Wade's procedure of synthesis requires the suspension of anthranilic acid (I) (29.7g.-0.217moles) in water (217ml) and concentrated hydrochloric acid (27.3ml). Thiophosgene (25g.= 16.6ml= 0.217moles) is added dropwise, with stirring, at a temperature not exceeding 50°C. The product separates and after cooling, is filtered, dried in a vacuum over calcium chloride, and purified from spectrograde dioxane under anhydrous conditions. Yield 35g (90%theo.) with a m.p. of 203-204°C. Although no structure was presented it was assumed to be thioisatoic anhydride.



Analytical data available:

	<u>Compound</u>	<u>M.P. (°C)</u>	<u>%C</u>	<u>%H</u>	
Marshall	II	230-235	53.7	2.70	Found
Marshall	III	226-235	53.5	2.70	Found
Wade	II	203-204	53.18	2.76	Found
			53.6	2.79	Theo.

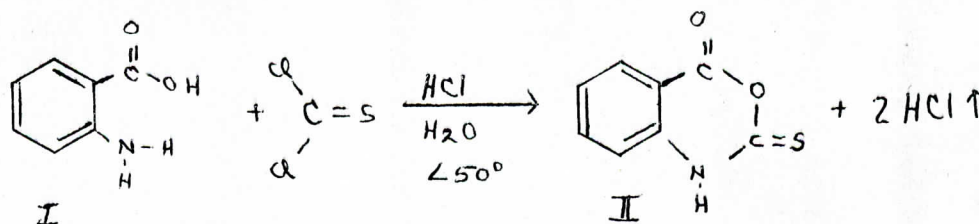
The obvious discrepancies of these results for the two methods of synthesis raised speculation about the validity of both works. This research attempts to clarify the situation.

EXPERIMENTAL

SYNTHESIS OF THIOISATOIC ANHYDRIDE (II) or 1,2-DIHYDRO-2-THIO-3,1-BENZOXAZIN-4-ONE

After careful consideration of the reported methods of preparation of thioisatoic anhydride (II), the procedure by Wade was selected because it appeared to yield a better product and it paralleled the synthesis of isatoic anhydride (IV) described by Wagner and Fegley.³

Reaction:

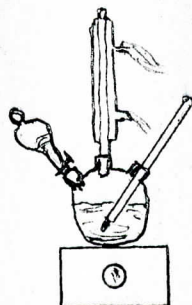


Apparatus: The following instruments were used to make the physical measurements unless otherwise noted:

Thomas Hoover melting point apparatus.

Perkin-Elmer Infracord Model-137.

The apparatus for synthesis consisted of a 500ml round-bottom 3-neck flask with standard taper joints equipped with a magnetic stirrer, separatory funnel, a thermometer and a condenser.



Procedure 1: Anthranilic acid (II) (29.7g= 0.217moles), water (217ml) and 12M HCl (27 ml) were added to the 500 ml flask. The mixture was stirred until all of the anthranilic acid dissolved. Thiophosgene (25g.= 16.6ml= 0.217moles) was added dropwise to the

vigorously stirred reaction mixture at a rate of approximately one drop/3sec. The total time of the addition was $2\frac{1}{2}$ hours.

After the first few drops of the thiophosgene had been added, red oily droplets appeared in the flask. A solid precipitate formed approximately five minutes after the initial introduction of the thiophosgene. The temperature remained at 30°C for the first half hour. At this time a layer of red liquid was present at the upper surface, and a yellow-gray precipitate was suspended in the lower reaction mixture. The temperature rose gradually to 40°C and remained constant for the duration of the reaction. Stirring was continued one-half hour after the complete addition of the thiophosgene. The product remained suspended in the reaction mixture two days before filtration. The mixture was filtered onto a Buckner funnel, washed with water, and placed in a vacuum desiccator over calcium chloride to dry. The product possessed a pungent odor similar to H_2S . A yield of 32.6g (84% theo.) was obtained. The crude product had a m.p. range of $185\text{-}187^{\circ}\text{C}$. Purification from dioxane, acetone, and acetone-water, yielded white needles, which melted at $203\text{-}204^{\circ}\text{C}$ with gas evolution. This is in agreement with the m.p. data reported by Wade. An infrared spectrum (IR#2a) shows a strong absorption peak at 5.7u which is characteristic of the anhydride $\overset{\text{O}}{\parallel}\text{C}-\text{O}$ stretch. By comparison the spectrum of isatoic anhydride (IV) shows the $\overset{\text{O}}{\parallel}\text{C}-\text{O}$ stretch at 5.75u (IR#4). The -NH peak appears at 3.4u, shifted to longer wavelength by the influence of the neighboring $\text{C}=\text{S}$. This latter group shows three characteristic absorption peaks between 8.33 and 9.52u.

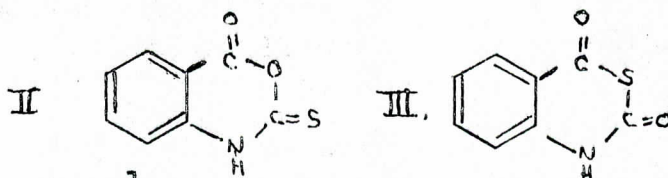
Procedure 2. Anthranilic acid (I) (14.85g. = 0.1085moles), water (108.5ml) and 12M HCl (13.5ml) were added to a 500ml flask. The

mixture was stirred until the anthranilic acid dissolved. Thiophosgene (12.5g.= 8.3ml= 0.1085moles) was added dropwise. Total time of the addition was 1-3/4 hours. The appearance of the reaction mixture was the same as procedure 1.

The solution with suspended precipitate was allowed to stir overnight. The precipitate was filtered onto a Buckner funnel, washed with water, and placed in a vacuum desiccator to dry. Purification from acetone yielded thioisatoic anhydride (II) with a m.p. of 204-205°C. The infrared spectrum of the crude product differed from that of the crude product of procedure 1 by the presence of a -NH peak at 2.85u. The spectra of the recrystallized compounds were identical.

On the evidence of the method of preparation, m.p., and infrared spectra, structure II was assigned to the above material.

A request to Marshall at Nottingham, England, for spectral data for the two isomers (II and III),



reported in his paper¹ resulted in the receipt of a sample of the product he called thioisatoic anhydride (II). The sample consisted of yellow needles. The m.p. redetermined, gave a value of 220-235°C. An infrared spectrum of Marshall's product (IR#2b) when compared with the spectra of II and III (IR's 2a and 3) showed peaks characteristic to both products. An inspection of IR#2a revealed significant absorption peaks at 5.7u, 6.123u, and 6.57u. An inspection of IR#3 reveals absorption peaks at 6.05u, 6.18u, and 6.4u. The strong peak at 5.7u had disappeared. By superimposing the spectra of

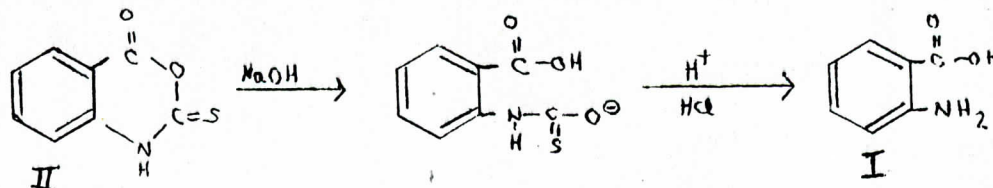
Marshall's II (IR#2b) first on IR#2a, then on IR#3, it was shown to contain all of the above mentioned absorption peaks. A comparison of the fingerprint region (7.0-15u) of these spectra, likewise indicated a mixture of peaks in Marshall's compound.

It was then concluded that II reported by Marshall was actually a mixture of II and III. The melting point of his II (230-235°C) had a range of 9°, overlapping with the range of II. The sharp m.p.'s reported for II and III prepared by the procedures described above, and the 35° difference in m.p.'s of the two compounds, in addition to the spectral differences, indicated a complete separation of products.

REACTIONS OF THIOISATOIC ANHYDRIDE (II)

FORMATION OF ANTHRANILIC ACID (I)

Reaction:

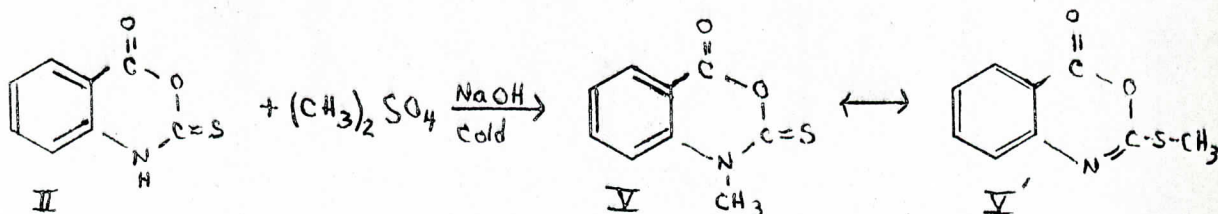


Thioisatoic anhydride (II) (0.5g) was stirred into 10% NaOH(10ml). The material dissolved with some evidence of gas evolution. After filtration the reaction mixture was made slightly acidic with 3M HCl. An insoluble precipitate separated which upon recrystallization melted at 144-145°C. An IR(#1b) of this material, and its m.p. agreed with the m.p. and spectrum (IR#1a) for anthranilic acid (I), received from Maumee Chemical Company.

FORMATION OF 2 METHYLTHIO-3,1-BENZOXAZIN-4-ONE (V)

Procedure 1.

Reaction:

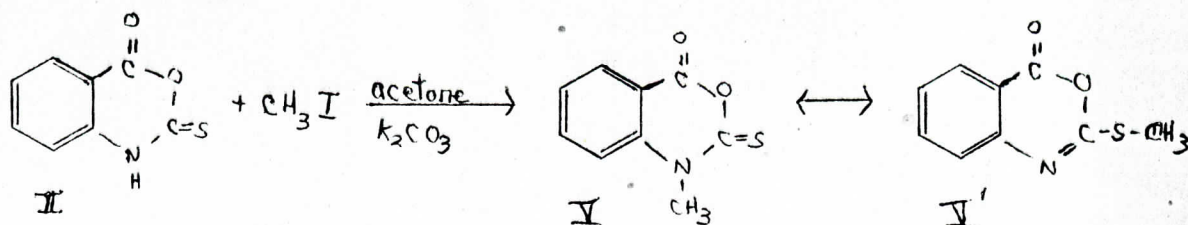


Thioisatoic anhydride (II) (1g.) was dissolved in 0.2N NaOH (20ml). A molar excess of dimethyl sulfate (.7ml) was added dropwise to the solution from a pipet. The solution was kept in an ice bath to maintain a low temperature. After 15 minutes the solution became cloudy. A phase separation was observed, the product of the reaction being a pale white oil. Attempted triturations with acetone and ether yielded no solid product. The oil was allowed to stand several weeks. The oil, at the end of this period was placed in methanol, a solvent for dimethyl sulfate. Upon addition of water to the solution, a white

crystalline compound separated and was filtered by gravity. The compound had a m.p. range of 202-212°C, and the IR (#5a) indicated that the impurity was excess dimethyl sulfate.

Procedure 2

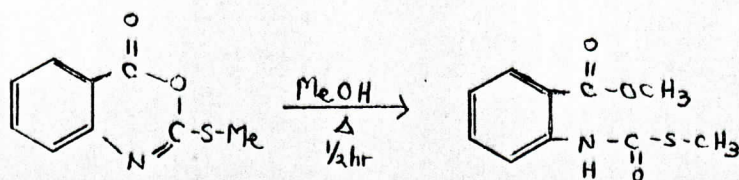
Reaction:



Similar to Marshall's procedure¹, thioisatoic anhydride (II) (2.7g.) was mixed with potassium carbonate (1.56.) and methyl iodide (1.5ml). The reaction solution was then refluxed for 1-3/4 hours. Upon cooling a precipitate fell out of solution. The yellow-white precipitate was filtered onto a Buckner funnel while the strong odor of sulfur dioxide was detected. The crude product had a m.p. range of 75°. It was hypothesized that not all of the thioisatoic anhydride (II) had reacted, and that the product was a mixture. Recrystallizations from dioxane, and acetone-water, yielded the methyl derivative with a m.p. of 102-103°C. This compares favorably with the m.p. of 106.5-.108.5°C reported for this compound by Marshall. He also proposed the isomeric form V. An infrared spectrum (IR#5b) was taken and revealed characteristic shifts due to the introduction of the -CH₃ group.

FORMATION OF METHYL N-O-METHOXYCARBONYLPHENYLTHIOCARBAMATE (VI)

Reaction:

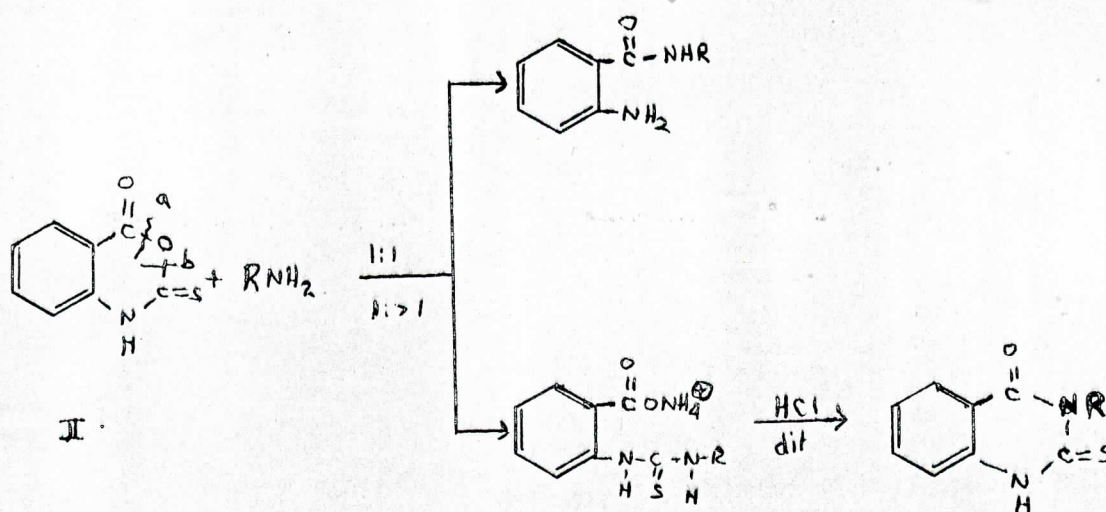
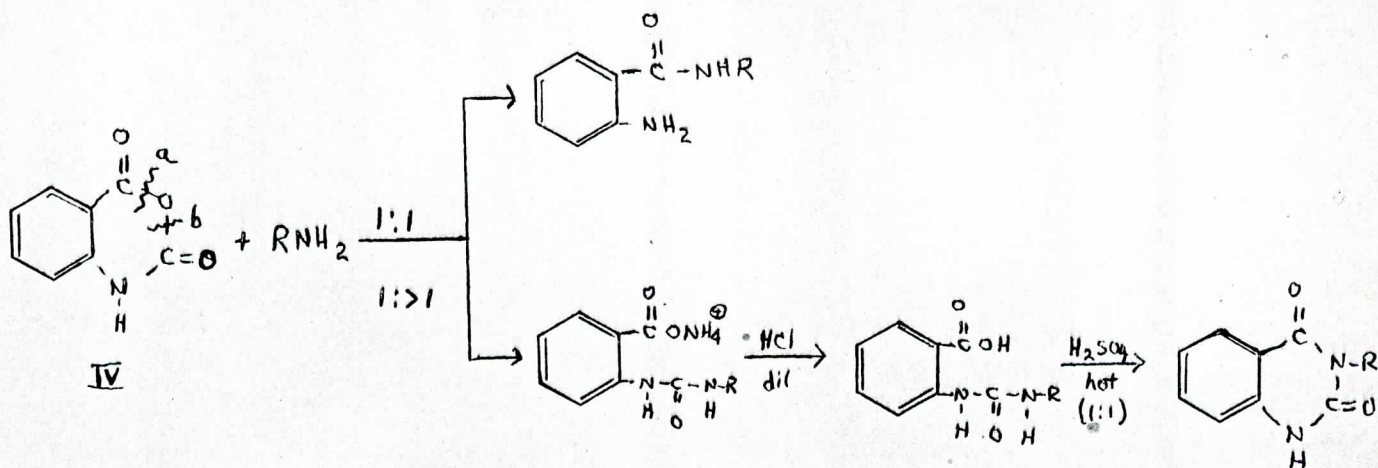


Approximately following Marshall's procedure, methanol(10ml) was added to a 20ml beaker containing 2-methylthio-3,1-benzoxazin-4-one (Vb) prepared by procedure 2 above. The reaction mixture was placed on a steam bath and boiled for thirty minutes maintaining a constant level of methanol. The reaction mixture was allowed to cool, and a cream colored oil was separated from the supernate liquid. It was placed on a watch glass, triturated with acetone and ether in an attempt to obtain a solid product. After three unsuccessful attempts to obtain the solid product, the oil was allowed to stand for one week. Over this period of time, fine white needles separated from the oil. Sufficient needles were isolated to obtain a m.p. of 88-90°C using a Fischer-Johns melting point apparatus.

FORMATION OF 2-THIONO BENZOYLENE UREAS

Proposed Reaction Mechanism.

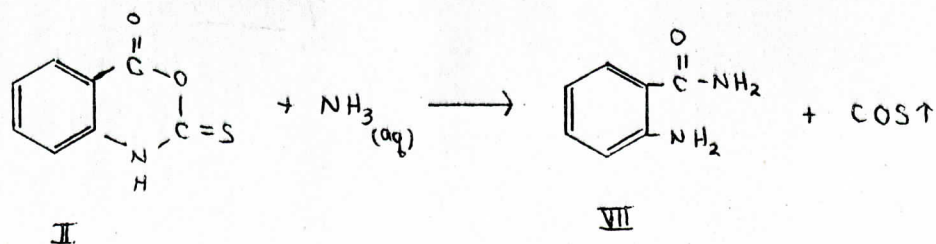
The reaction mechanism of thioisatoic anhydride with various concentrations of primary amines appeared to be analogous to that for isatoic anhydride IV.



When equimolar quantities of thioisatoic anhydride and amine were reacted, a ring cleavage occurred at point a/ and yielded anthranilamides as products. When a greater than equal molar quantity of the amine was reacted, the ring cleavage occurred at point b/. and the ammonium salt of the o-ureidobenzoic acid was present in solution. Upon acidification with dilute HCl, the o-thioureidobenzoic acid was not isolated, but rather the ring closed species, the 2-thiono benzoylene urea. With isatoic anhydride, the o-ureidobenzoic acid was isolated, and the stronger acid H₂SO₄ was required to cause a ring closure. When the 2-thiono benzoylene urea derivatives are reacted with hot sulfuric acid (1;1) a decomposition product was obtained but was not characterized.

FORMATION OF ANTHRANILAMIDE (VII) (o- amino benzanide)

Reaction:

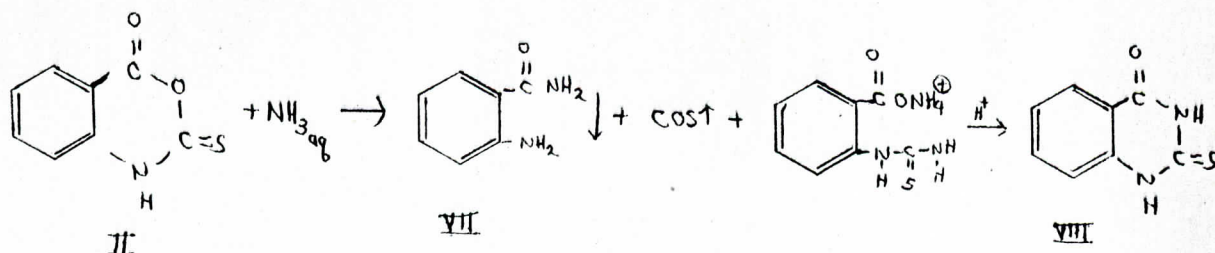


Equimolar quantities of thioisatoic anhydride (II) and aqueous ammonia were reacted. The resulting clear solution was allowed to stand in an ice bath for 15 minutes at which time the anthranilamide precipitated out of the solution. The product was filtered and dried. A m.p. of 108-110°C, agreed with the reported value of 108°C. An IR(#8) was taken and compared favorably with a reference infrared spectrum for a sample from the Maumee Chemical Company Pure Compound File.

FORMATION OF 2-THIONO-BENZOYLENE UREA (VIII)

Procedure 1.

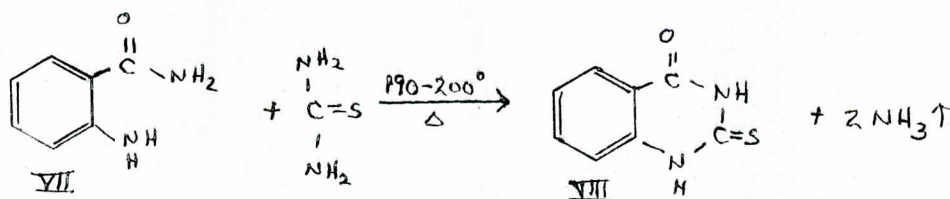
Reaction:



Thioisatoic anhydride (2.75g) was added to conc. aqueous NH_3 (10ml). The reaction mixture was allowed to sit for 15 minutes in an ice bath. The solution was then filtered and the filtrate was made slightly acidic with 3M HCl. A tan precipitate, insoluble in an acid media, settled out. Recrystallizations from methanol yielded a white compound (VIIIa) melting at 272-275°C. An IR (#8a) was taken and was considerably different from the starting material (II).

Procedure 2.

Reaction:



Anthranilamide (VII) (27.2g=0.2moles) and thiourea (15.2g=0.2moles) were mixed in a beaker. The reactants were heated with stirring to 190°C at which time they appeared as a brown paste. The temperature of the paste was slowly raised to 200°C, and solidification occurred. After cooling the solid was broken up and suspended in 200ml of water. 10% NaOH was added until all of the solid had dissolved. After filtration, the filtrate was acidified with 3M HCl. The m.p. of the crude material was 315-318°C. Recrystallization from dioxane yielded a product with a m.p. of 316-318°C. An IR (#8b) was obtained. This product, the 2-thiono benzoylene urea agreed in m.p. with that reported in work done by Moyer and Staiger.⁵

An elemental analysis of their reference compound agreed well with the calculated values:

	<u>%C</u>	<u>%H</u>	<u>%S</u>	Emperical formula
Theo	53.9	3.37	17.95	$C_8H_6ON_2S$
Found	53.54	3.17	17.67	

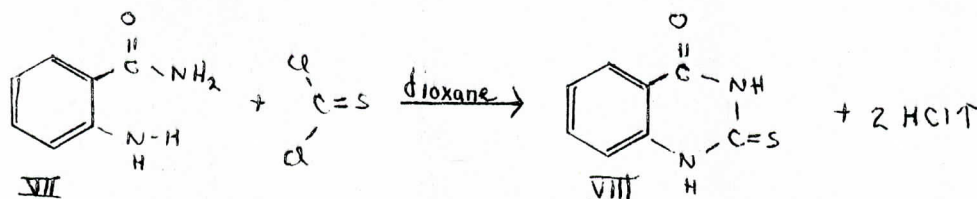
On the basis of m.p., it was concluded that VIIIb was the 2-thiono benzoylene urea.

Recrystallization of the crude product from methanol yielded a product melting of 306-308°C. The IR (#8c) shows definite shifts of peaks with respect to spectra #8b. An elemental analysis was performed by Galbraith Laboratory Inc.:

	<u>%C</u>	<u>%H</u>	Emperical formula
Theo	53.9	3.37	$C_8H_6ON_2S$
Found	53.86	3.45	

Procedure 3.

Reaction:



Anthranilamide (VII) (13.65g=0.1moles) was dissolved in dioxane(50ml). To this reaction mixture, thiophosgene (13.65g=7.6ml= 0.1moles) was added dropwise with stirring. The thiophosgene reacted immediately to form a precipitate. The reaction mixture was stirred for several additional minutes, and the precipitate was separated by filtration.

Several different solvents were used for recrystallization and three different products were obtained, each with a different infra-red spectrum.

<u>Compound and IR #</u>	<u>M.P. °C</u>	<u>Solvent</u>
8d	315-318	dioxane, MeOH (25°C)
8e	254-255	dioxane, MeOH (hot)
8f	230-232	insol dioxane, MeOH (hot)

An elemental analysis for VIIIe yielded an unexplained % for carbon.

	<u>%C</u>	<u>%H</u>	<u>Emperical formula</u>
Theo	53.9	3.37	$C_8H_6ON_2S$
Found	67.52	3.59	

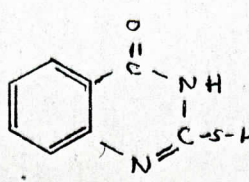
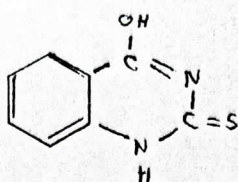
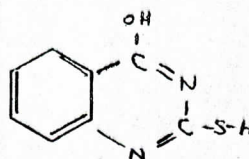
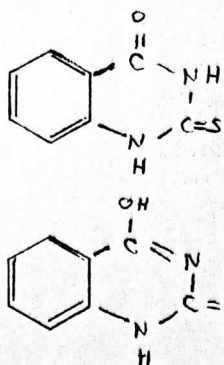
Summary: The preparations of the 2-thiono benzoylene urea by a variety of synthetic routes instead of yielding one product yielded a series of compounds with different m.p.'s and different IR's. An examination of the literature yielded two additional compounds reported as VIII, but having still different melting point values.

<u>Compound 8</u>	<u>M.P. °C</u>
a	272-275
b	315-318
c	306-308
d	315-318
e	254-255
f	230-232

Literature

Moyer & Staiger ⁵	315-318
Rupe ⁶	280-281 ; 284
Davis ⁷	305-310

It is hypothesized that the several compounds prepared are tautomers. Four possible structures can be proposed:

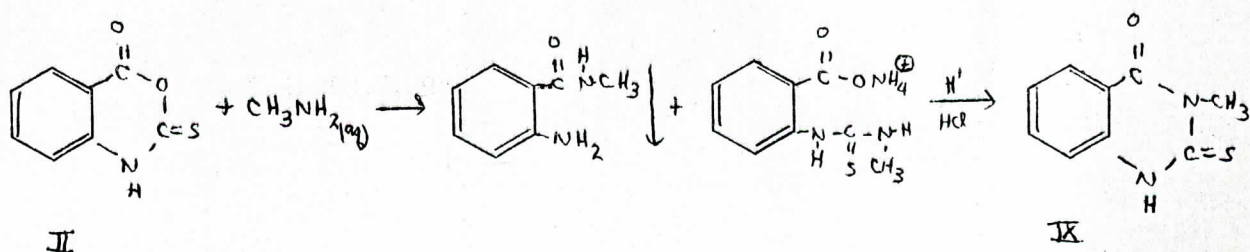


The tautomeric shifts could be caused by the method of preparation, solvent used for crystallization, presence of acid or base, or the temperature of the reaction mixture. 0.5 g. of VIIIb was placed in methanol and sodium hydroxide for five days in an attempt to effect a tautomeric shift. The IR (#8g.) showed the appearance of a peak at 2.95u. The rest of the spectrum was the same.

FORMATION OF 2-THIONO-3 METHYL BENZOYLENE UREA (IX)

Procedure 1.

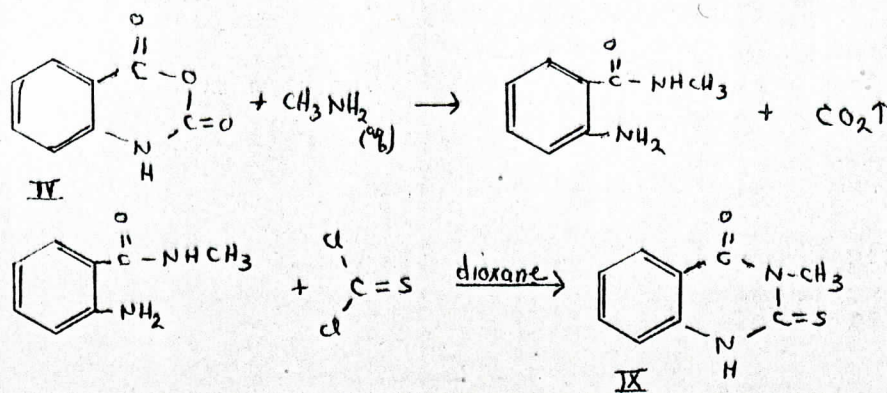
Reaction:



Thiosatoic anhydride (II) (1g) was stirred into methylamine (10ml of 30% soln.). Gas evolution was observed. The reaction mixture was allowed to stand for approximately 15 minutes, after which it was filtered. The filtrate was carefully acidified yielding a tan precipitate. The crude product was recrystallized three times, yielding a white product melting at 260-263°C. IR (#9a). This m.p. agreed favorably with that of a reference compound prepared by Moyer and Staiger at Ursinus⁸, m.p. 264-266°C after five recrystallizations from methanol. The IR (#9a) is superimposable with that of the reference compound (IR #9).

Procedure 2

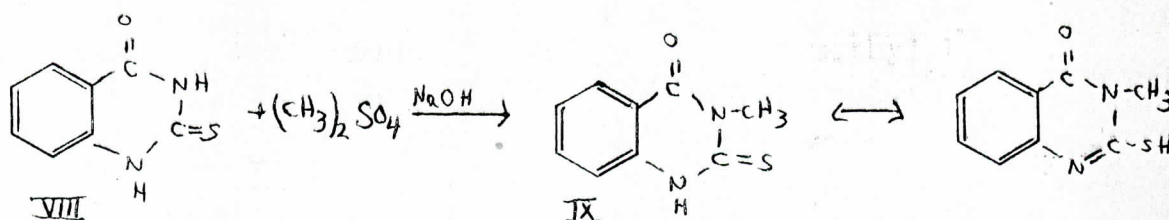
Reaction:



Equimolar quantities of isatoic anhydride (IV) and methylamine were stirred together. After 15 minutes, the methyl anthranilamide was collected by filtration. It was dissolved in dioxane (15ml), and thiophosgene (2ml) was added dropwise to the reaction mixture with stirring. The reaction occurred immediately with the formation of a yellow precipitate. The crude product was separated by filtration, recrystallized from methanol. The m.p. range was observed to be 260-263°C. An IR(#9b) was taken and was identical with the reference spectrum (#9). While the product still contained some impurities causing the m.p. range, the product is the 2-thiono-3 methyl benzoylene urea.

Procedure 3.

Reaction:

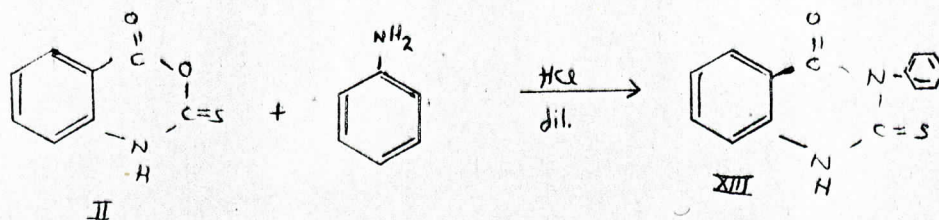
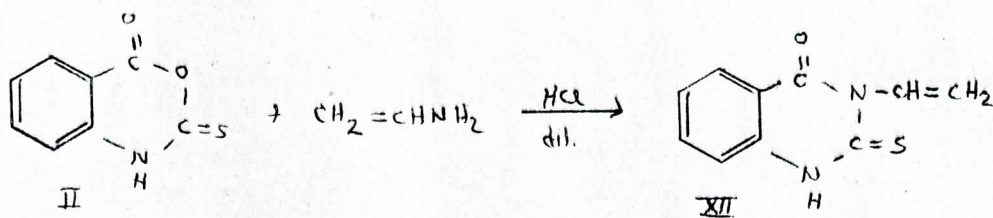
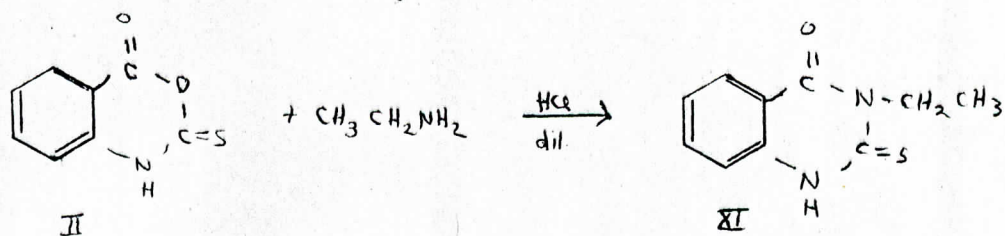
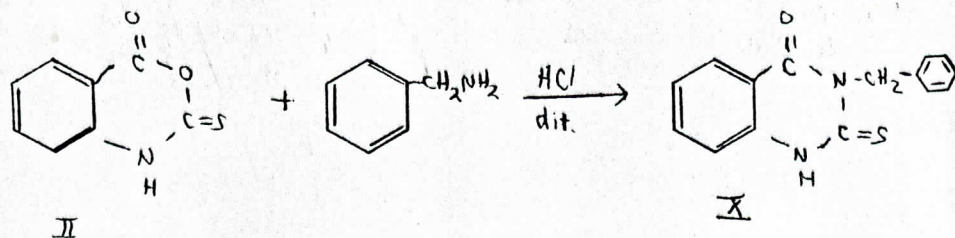


2-Thiono benzoylene urea (VIIIb) (1g) was dissolved in 10% NaOH (50ml). Dimethyl sulfate(1.5g.= 0.7ml) was added with stirring. After a period of 15 minutes an oil was separated from the supernate liquid and when treated with methanol, white needles fell out of solution. The m.p. was found to be greater than 347°C determined on a Townson and Mercer Type V Melting Point Apparatus. An IR (9c) was taken which revealed very broad absorption peaks.

Compound 9b (0.5g.) was placed in alcoholic methanol for several days. The m.p. of the product (#9d) was greater than 347°C and its infrared spectrum (#9d) revealed wide absorption bands. It is also possible that the sodium salt of the isomeric structure was the isolated product.

FORMATION OF: 2-THIONO-3-BENZYL BENZOYLENE UREA (COMPOUND X)
2-THIONO-3-ETHYL BENZOYLENE UREA (COMPOUND XI)
2-THIONO-3-ALLYL BENZOYLENE UREA (COMPOUND XII)
2-THIONO-3-PHENYL BENZOYLENE UREA (COMPOUND XIII)

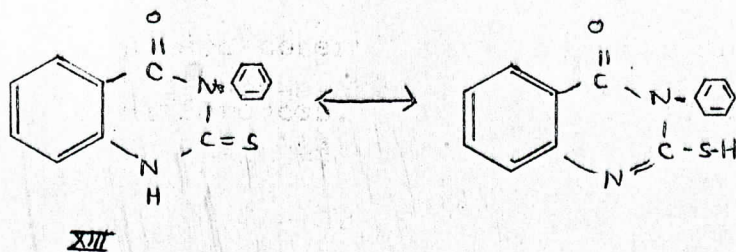
Reactions:



Thioisatoic anhydride (II) (0.5g.) was stirred into 15 ml of benzyl amine, ethyl amine, allyl amine, and aniline respectively, with gas evolution. The reaction mixtures were then allowed to sit for 15 minutes and then filtered. Each was then made slightly acidic with 3M HCl. The products of the several reactions were recrystallized from methanol.

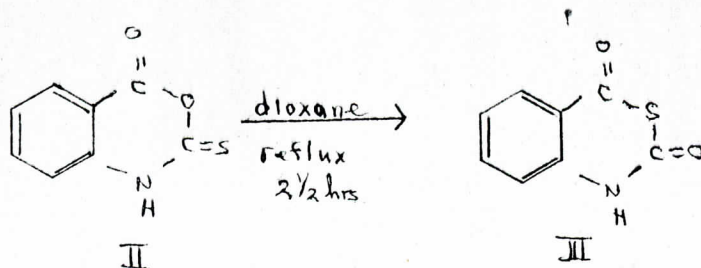
COMPOUND	M.P. (°C)	#RECRYSTALLIZATIONS	I.R.#
X (Benzyl)	180-225 195-210	1 2	10
XI (Ethyl)	190 part 215-217	crude	11
XII (Allyl)	150-175 160-168	1 2	12
Literature ⁹	197-200		
XIII (Phenyl)	115-117 116-117	1 2	13a
Literature ¹⁰	303-304d		

No conclusion can be drawn about the preparation or unsuccessful preparation of the above compounds. A reference spectrum (#13) was available for the 2-Thiono-3-phenyl benzoylene urea. Definite shifts in the absorption peaks were observed. A tauteric shift could account for the I.R. and m.p. differences. The following structures have been postulated:



SYNTHESIS OF 3,1-BENZOTHIAZINE, 2(1H)-4-DIONE (III)

Reaction:



Procedure: Thioisatoic anhydride (II) (1.0g.) was placed in dioxane (10ml) and refluxed for 2½ hours. Upon cooling white needles separated. A melting point range of 228-234°C was observed. A fractional crystallization was performed in acetone, knowing the ratio of solubility of II and III in acetone to be 1:15 and 1:85, as reported by Marshall. The first crop of ppt. was filtered and dried in air. It had a melting point of 237-238°C melting to a red liquid.

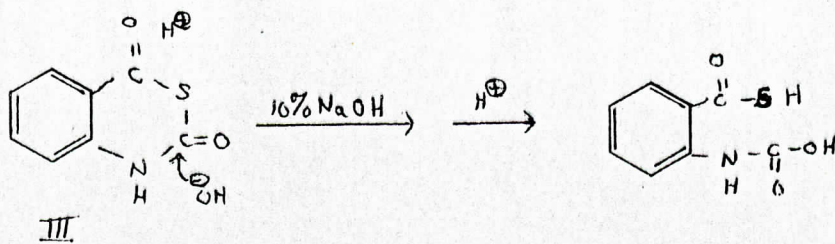
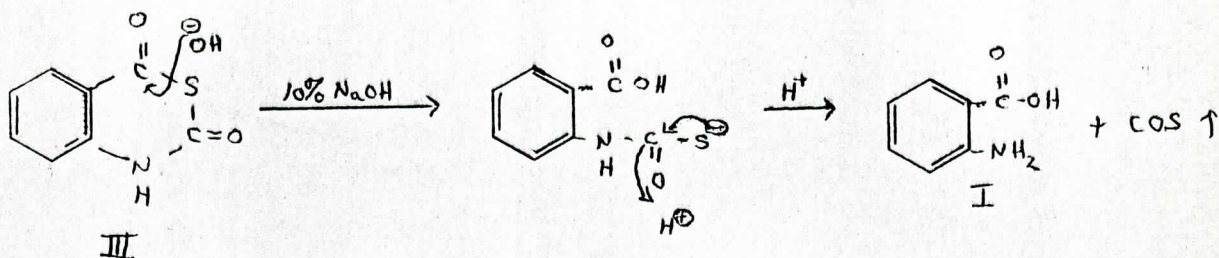
The infrared spectrum IR #3 differs from IR #2a. The strong anhydride peak at 5.7u has disappeared, and the -S- group appears at 14.08u with a shifting of the carboxyl to 6.05 and 6.15. Elemental analysis by Galbraith Laboratories Inc. shows good agreement with the theoretical values.

	<u>%C</u>	<u>%H</u>	Empirical formula
Theo	53.6	2.79	C ₈ H ₅ O ₂ NS
Found	53.76	2.80	

REACTIONS OF COMPOUND III (3,1-BENZOTHIAZINE 2(IH-)-4-DIONE

The reactions of Compound III with ammonia, methylamine, and NaOH yielded products that could not be characterized. The products with ammonia and methylamine, both with equimolar concentrations and with an excess of the amine yielded tars. However the reaction with NaOH yielded a product with a m.p. range of 130-170°C. An IR (#14) was taken. No gas evolution was observed during the course of the reaction.

The proposed reactions are:



FUTURE WORK

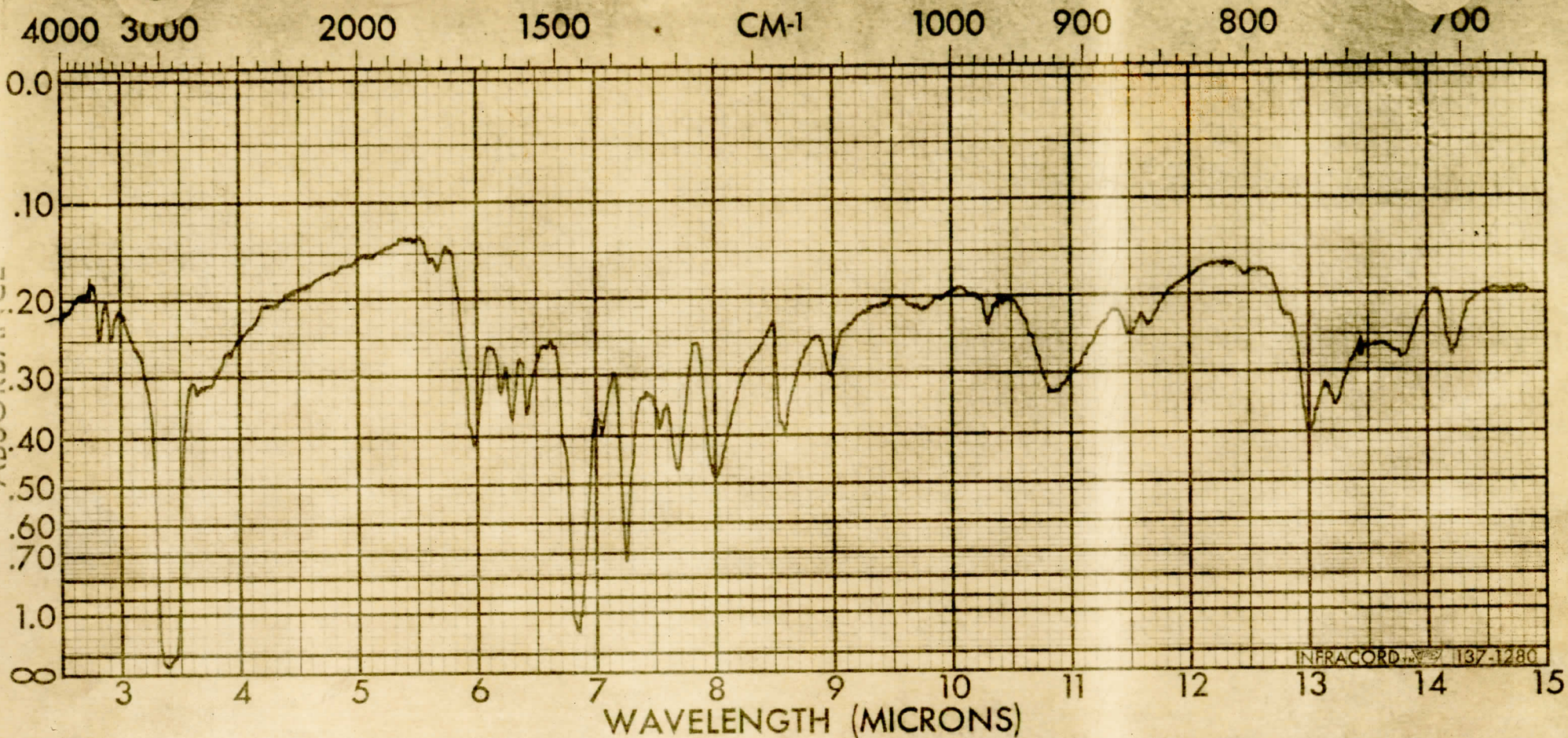
The chemistry of thioisatoic anhydride (II) being relatively new, the course of this research points out numerous new problems and projects.

- 1) Methods could be devised to increase the yield of III. The reactions of III could be investigated.

- 2) The 2- thiono- benzoylene (VIII) urea appears to undergo tautomeric shifts. Investigation should be conducted to determine if these shifts are responsible for the divergent results. This problem would probably involve chromatographic rather than spectrophotometric methods to identify the various isomers. Shifts have also been observed in the 2- thiono-3-benzoylene ureas.

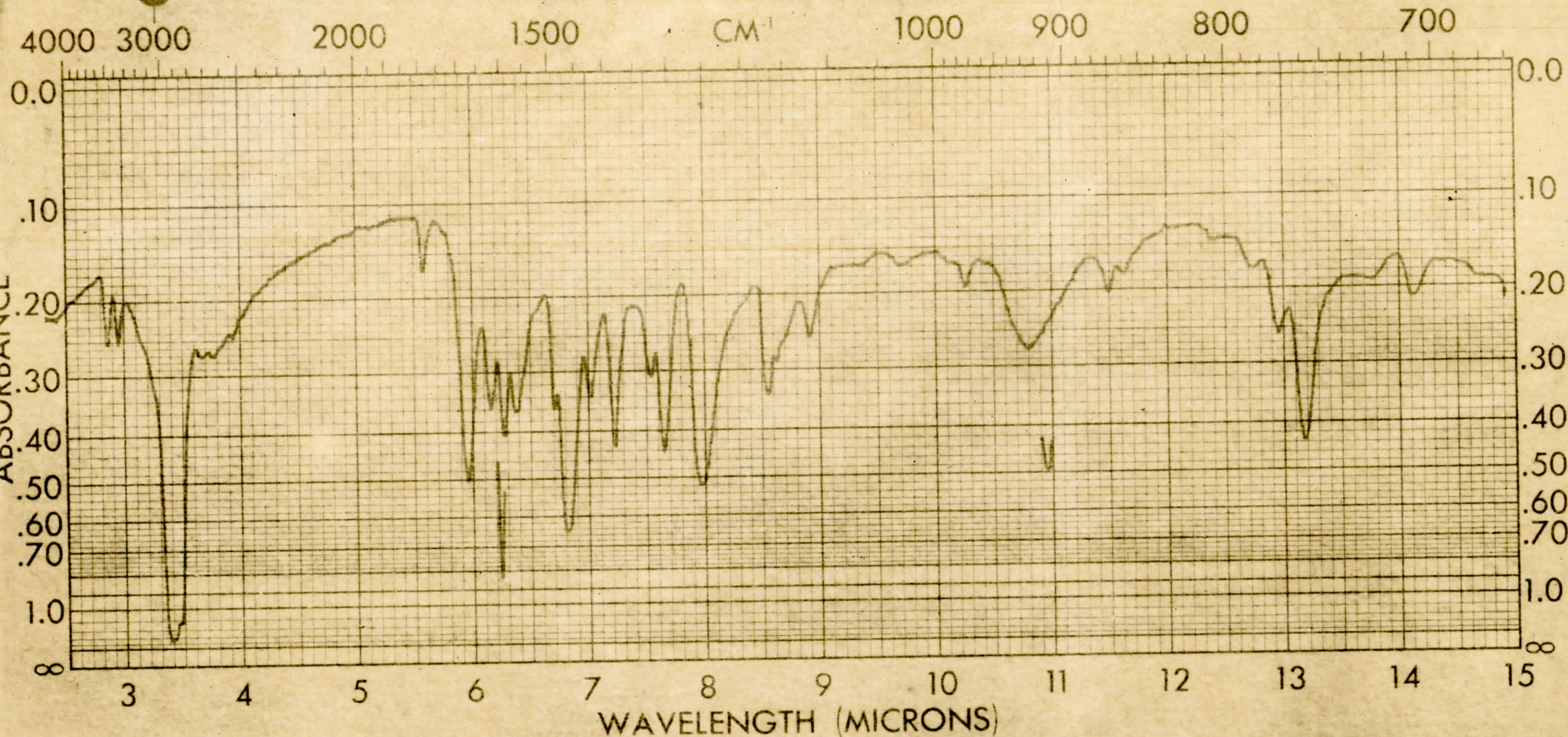
FOOTNOTES

1. Marshall, J.C.S., 171, 938-40 (1965)
2. Schonberg and Vargha, Ber, 1930, 63, 178-79
3. Fegley and Wagner, Organic Synthesis, Coll., Vol III, 488
4. Heilbron, Dictionary of Organic Compounds, Vol
5. Moyer, Staiger, Exp. #395 4-14-60 (Ursinus College)
6. Rupe, Beilstein 24, 199, 379
7. Davis, J.A.C.S. 56, 715-21 (1934)
8. Moyer and Staiger, Exp 321(3) 11-1-61 (Ursinus College)
9. Staiger, Exp 421(4) 5-10-60 (Ursinus College)
10. Freundler, Beilstein, 24, 380



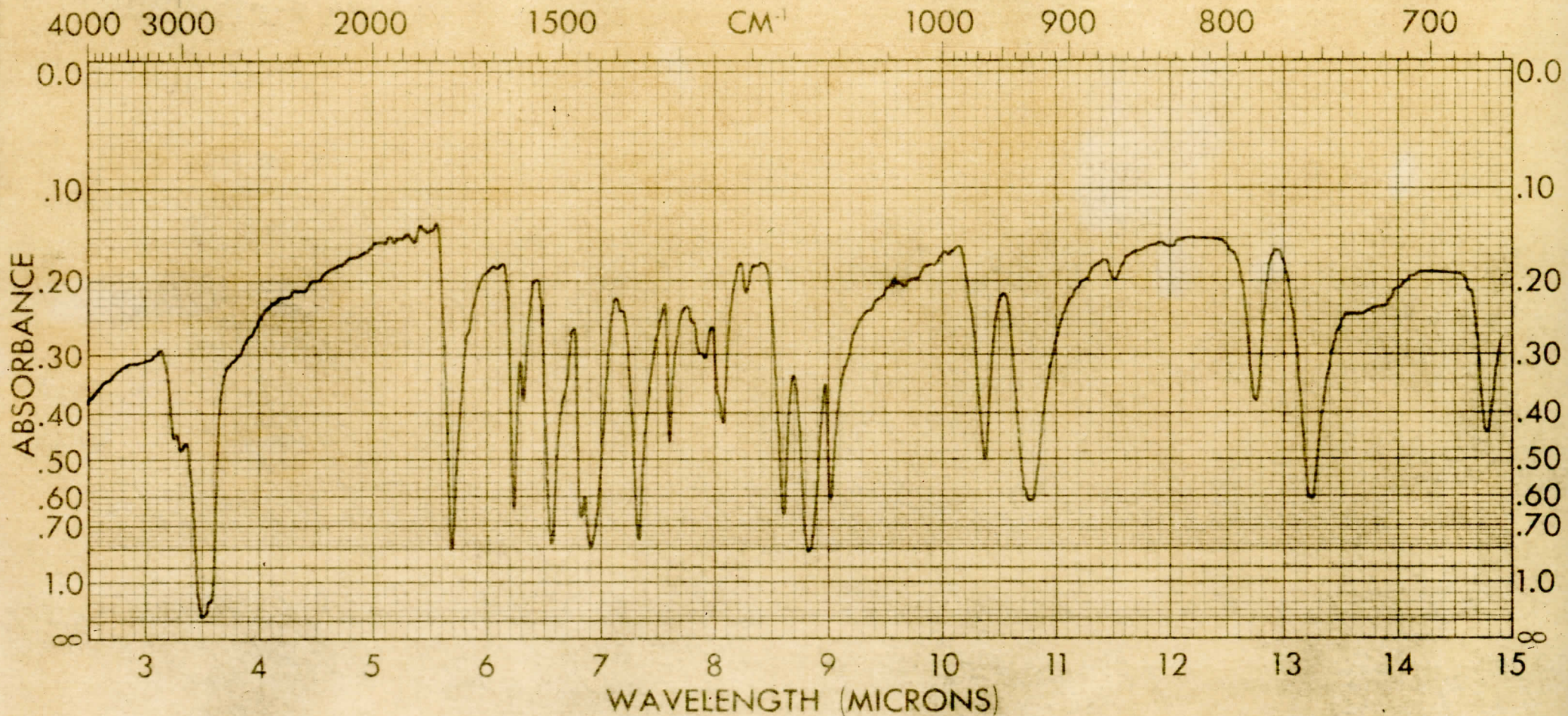
SPECTRUM NO. <u>1a</u>	ORIGIN <u>Maumee Chem. Co.</u>	LEGEND	REMARKS
SAMPLE <u>Anthranilic Acid</u>	<u>Sample 311A 12/30/60</u>	1.	
<chem>Nc1ccc(cc1)C(=O)O</chem>	PURITY <u>As received</u>	2.	
PHASE	DATE <u>12/19/61 4:00 PM</u>		
THICKNESS	OPERATOR <u>RPS</u>		

SPECTRUM NO. 1a
SAMPLE



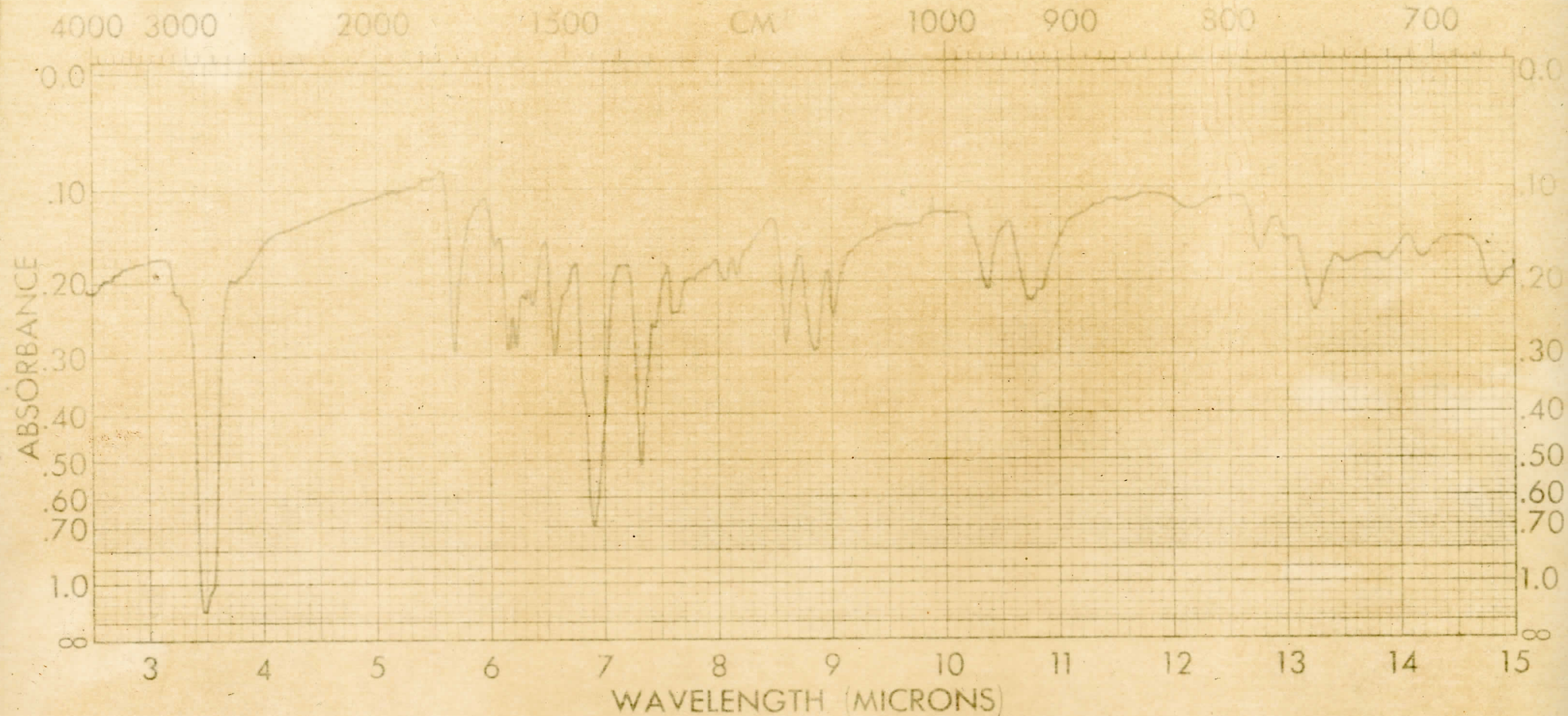
SPECTRUM NO. <u>16</u>	ORIGIN _____	LEGEND _____	REMARKS _____
SAMPLE <u>I</u>		1. _____	<chem>Nc1ccc(O)cc1</chem> + NaOH + HCl → <chem>Nc1ccc(O)cc1</chem>
<chem>Nc1ccc(O)cc1</chem>	PURITY <u>m.p. 144-145° (40)</u>	2. _____	
<u>anthranilic acid</u>	PHASE _____	DATE <u>5-8-67 9:30</u>	
	THICKNESS <u>Demount cell</u>	OPERATOR <u>J.L.D.</u>	
	<u>Nujol Mull</u>		

SPECTRUM NO. 16
SAMPLE



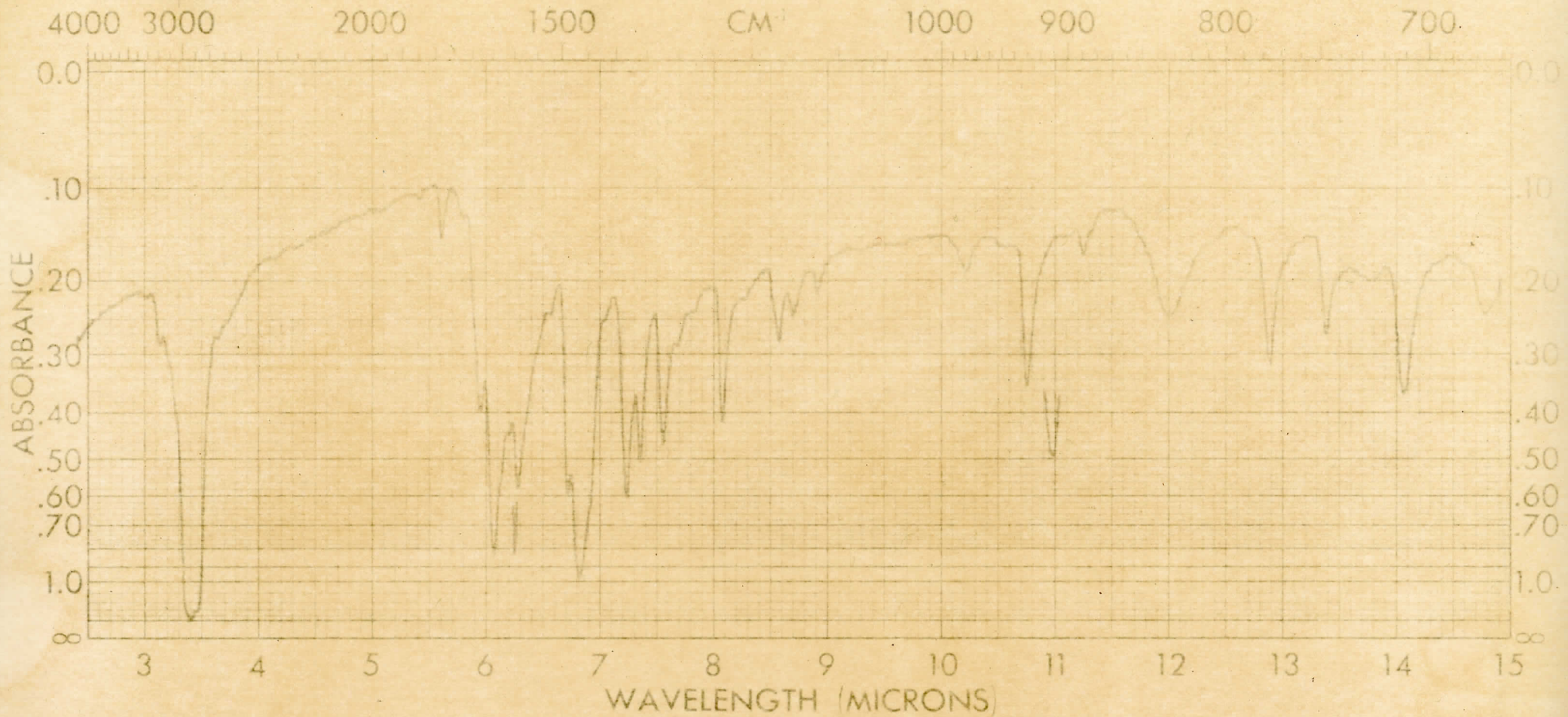
SPECTRUM NO.	ORIGIN	LEGEND	REMARKS
2a			
SAMPLE II [+5]			
<chem>O=C1OC(=O)C1</chem>	Cradith SA.		Twice RX Sample from Acetone-water, Good
Thiostaric anhydride	PURITY Rx-tissue Gran	1.	MP (195) 203-4 with Gas Evolution showing plate
	2% Acetone-water	2.	Yellow liquid. Agrees well with Data Supplied by Charles Wade who reports MP 203-5°C
	PHASE MP (195) 203-4	DATE 11/30/66	
	THICKNESS Nujol Mull	OPERATOR RPS	

SAMPLE SPECTRUM NO. 2a



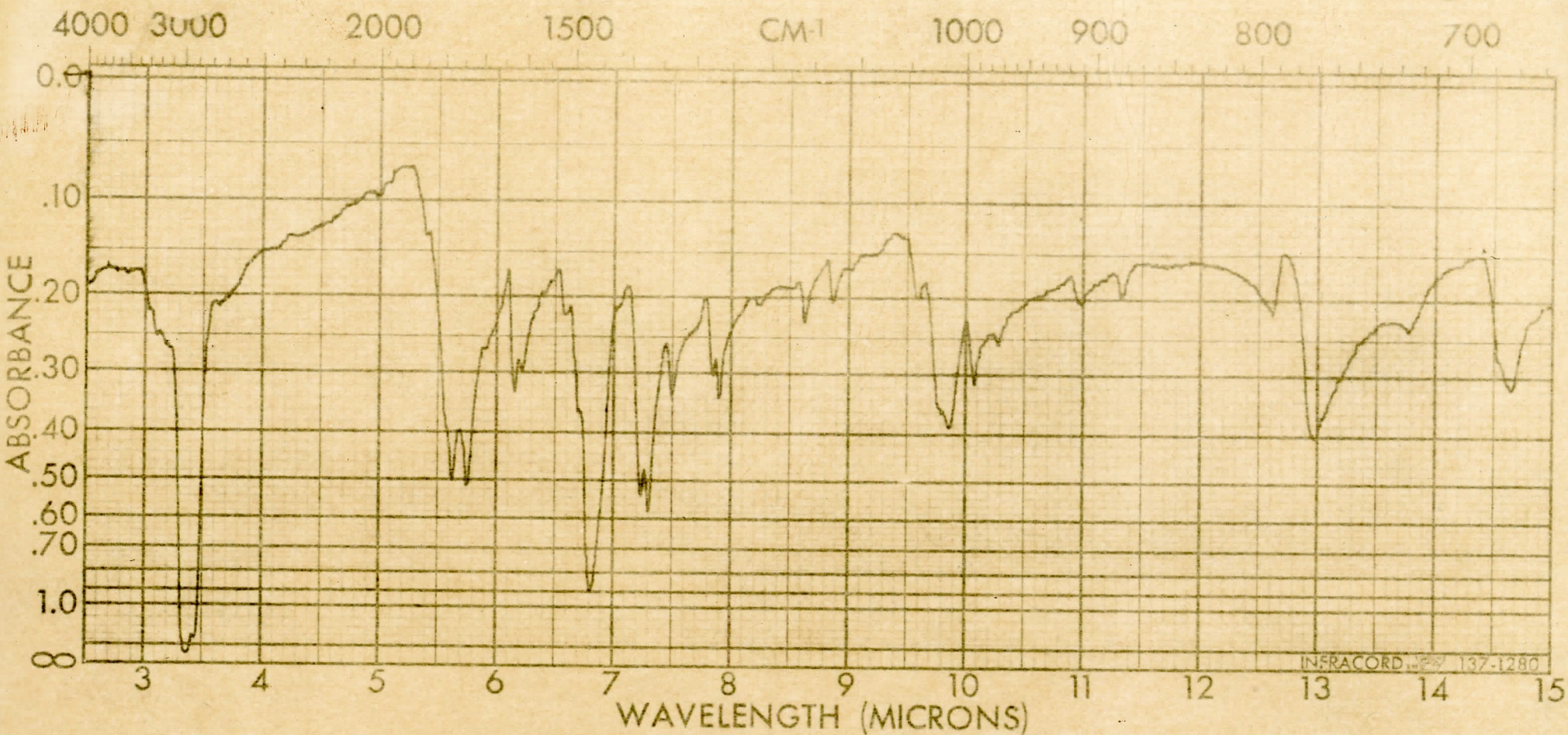
SPECTRUM NO.	ORIGIN	LEGEND	REMARKS
26			
SAMPLE <i>Comp II</i>		1.	<i>Sample sent by Marshall</i>
<chem>C1=CC=NC=C1</chem>	PURITY	2.	<i>from Boots Pure Drug Comp.</i>
	PHASE <i>mp 220-235°</i> <i>Densit cell</i>	DATE <i>2-7-67</i>	<i>Nottingham, England.</i>
	THICKNESS <i>Nyal Mull</i>	OPERATOR <i>J.L.D.</i>	

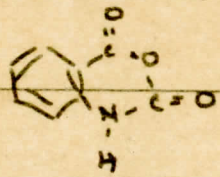
SAMPLE SPECTRUM NO. 26



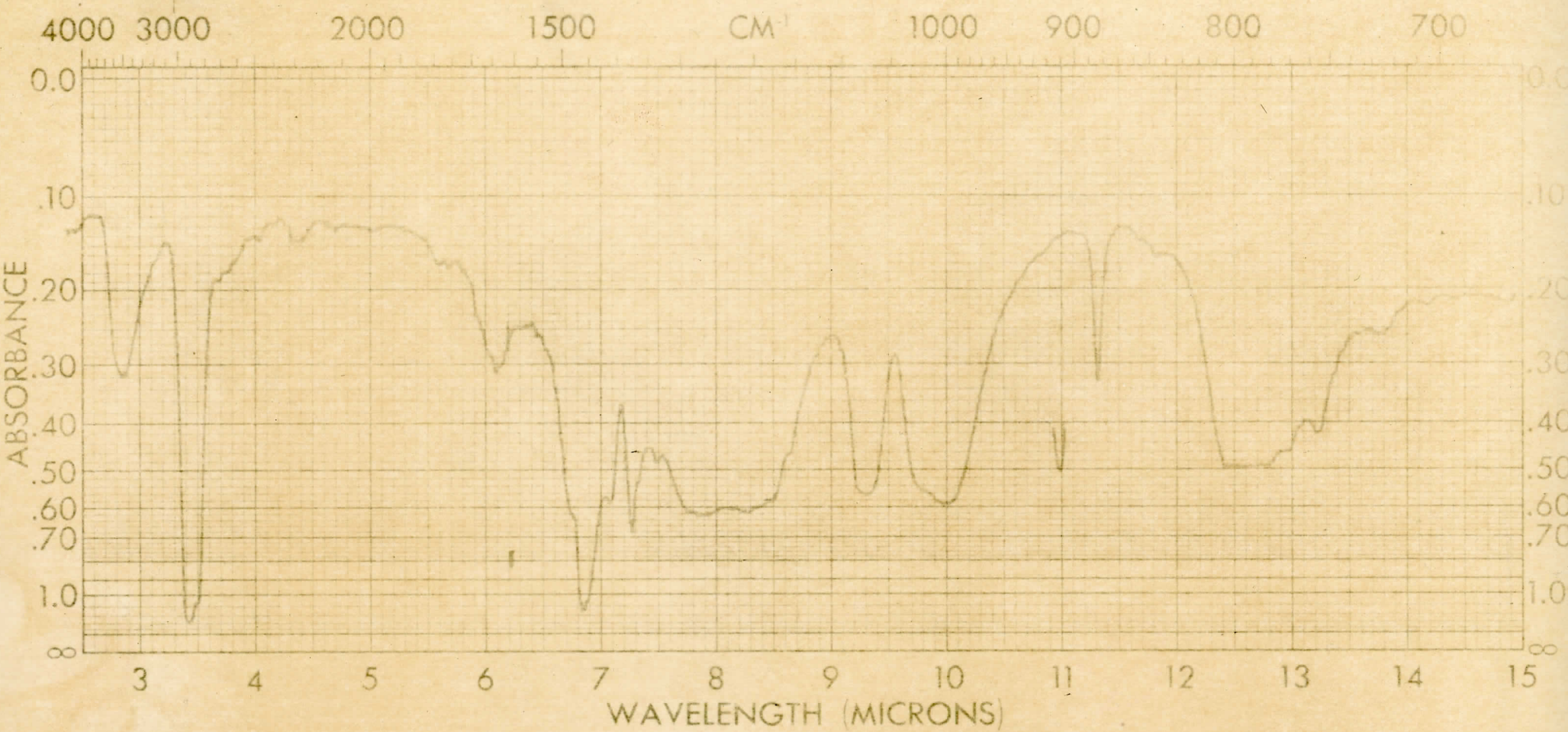
SPECTRUM NO. <u>3</u>	ORIGIN	LEGEND	REMARKS
SAMPLE <u>III</u>		1.	analysis: calc C 53.6%
<chem>O=C1NC2=CC=CC=C2S1</chem>	PURITY <u>white needles</u> <u>Rx: acetone</u>	2.	Found: C 53.76%
<u>3,1-benzothiazine 2,1,1-dione</u>	PHASE <u>m.p. 238-237°</u> <u>Dismount cell</u>	DATE <u>4-6-67</u>	H <u>2.40%</u>
	THICKNESS <u>Nujol Malt</u>	OPERATOR <u>J.L.D.</u>	

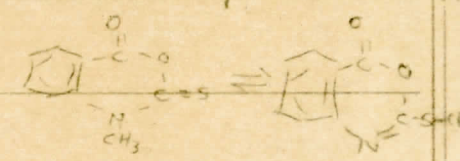
SAMPLE SPECTRUM NO. 3



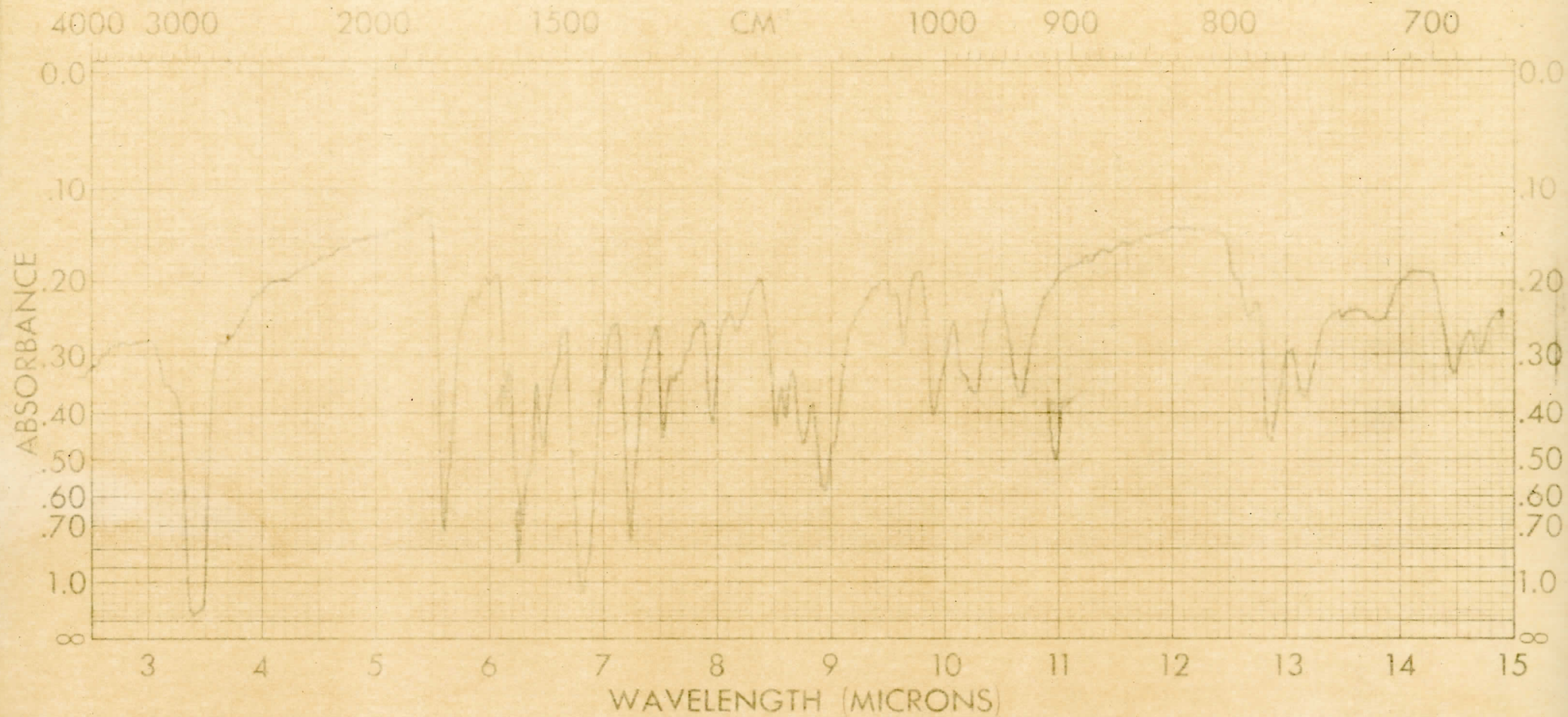
SPECTRUM NO. <u>4</u>	ORIGIN <u>Maurer tech.</u>	LEGEND	REMARKS
SAMPLE <u>Isatoic Anhydride</u>		1.	
<u>II</u> 	PURITY <u>Rx-MeOH</u> <u>MP 230 244.5 d</u>	2.	
	PHASE <u>N-Jol M-11</u>	DATE <u>10/18/61 1:00 PM</u>	
	THICKNESS <u>Demand cell</u>	OPERATOR <u>RPS</u>	

SPECTRUM NO. 4
SAMPLE



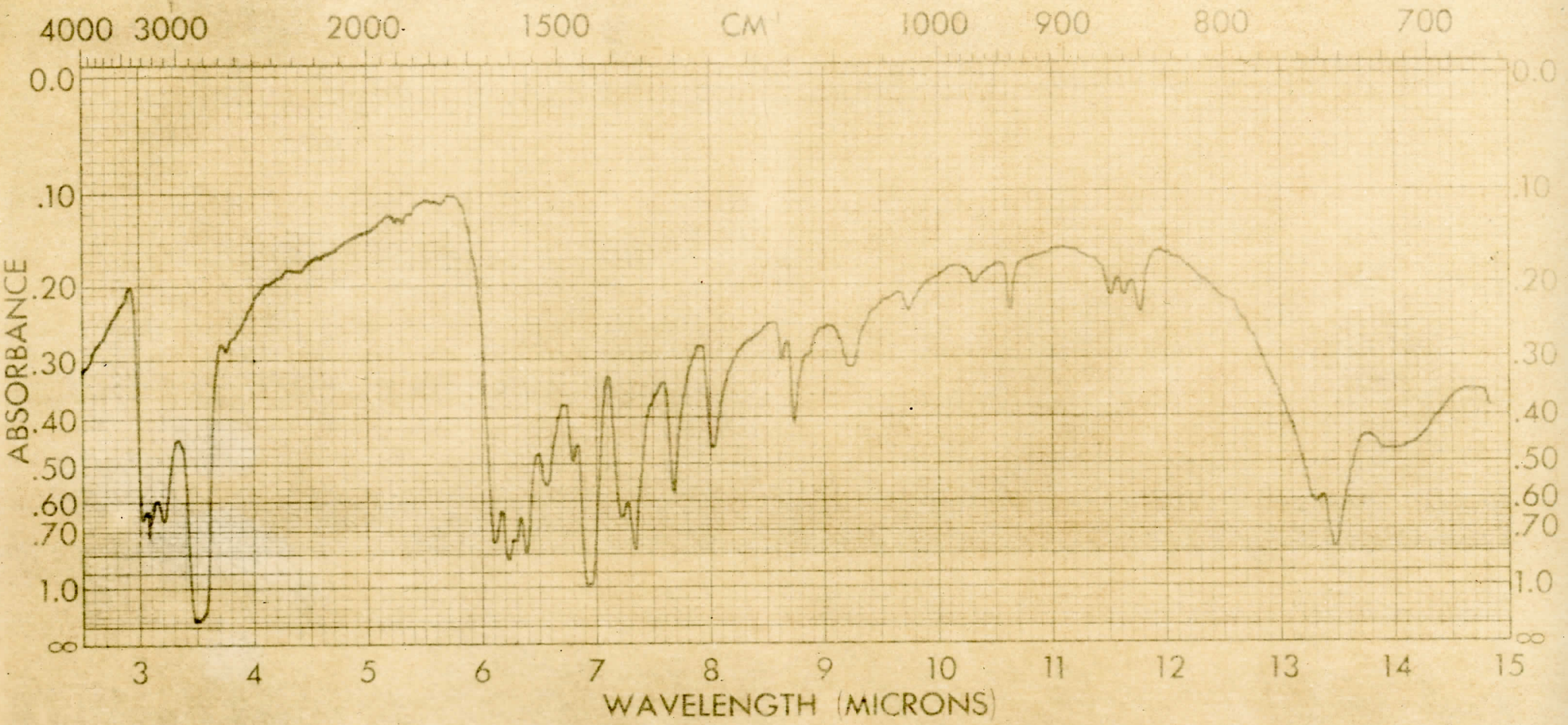
SPECTRUM NO.	ORIGIN	LEGEND	REMARKS
5a			
SAMPLE <u>Va</u>		1.	tautomeric shift?
<u>2-Methylthio-3,1-benzoxazin</u>	PURITY <u>mp range 202-212°C</u>	2.	
	PHASE <u>Demount cell</u>	DATE <u>2-10-67</u>	
	THICKNESS <u>Nujol Mull</u>	OPERATOR <u>J.L.D.</u>	

SAMPLE SPECTRUM NO. 5a



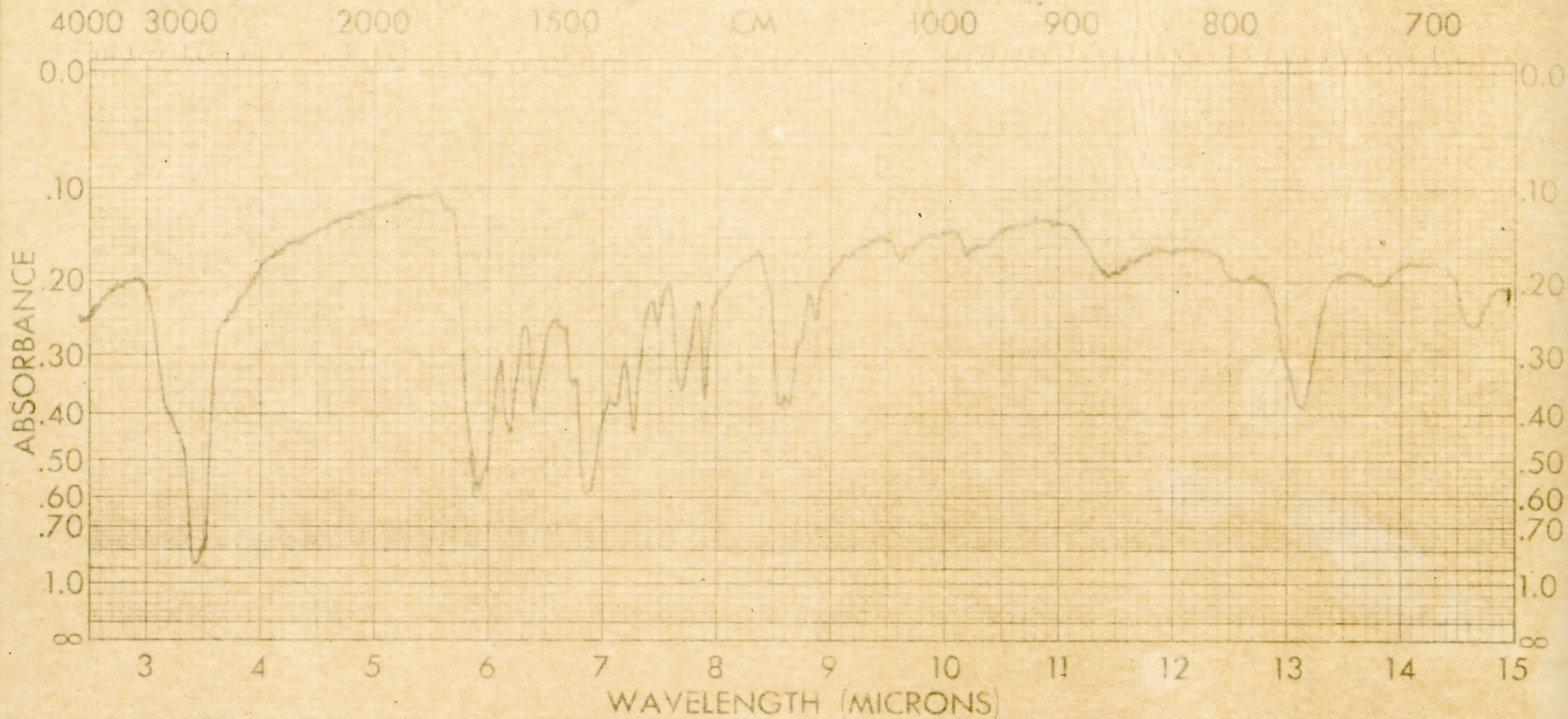
SPECTRUM NO. 56	ORIGIN	LEGEND	REMARKS
SAMPLE <chem>CC1=CC=C(C=C1)C(=O)OC</chem> Vb	PURITY m.p. 102-103°C	1.	
<chem>CC1=CC=C(C=C1)C(=O)OC</chem> 2 methylthio 3,1-benzoxin	PHASE 2 Rx : acetone - H09 Demount cell	DATE 5-2-67	
THICKNESS Nujol Mull	OPERATOR J.L.D.		

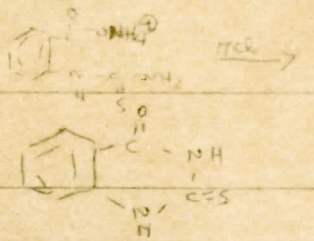
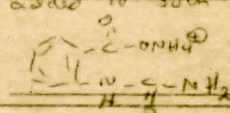
SAMPLE SPECTRUM NO. 56



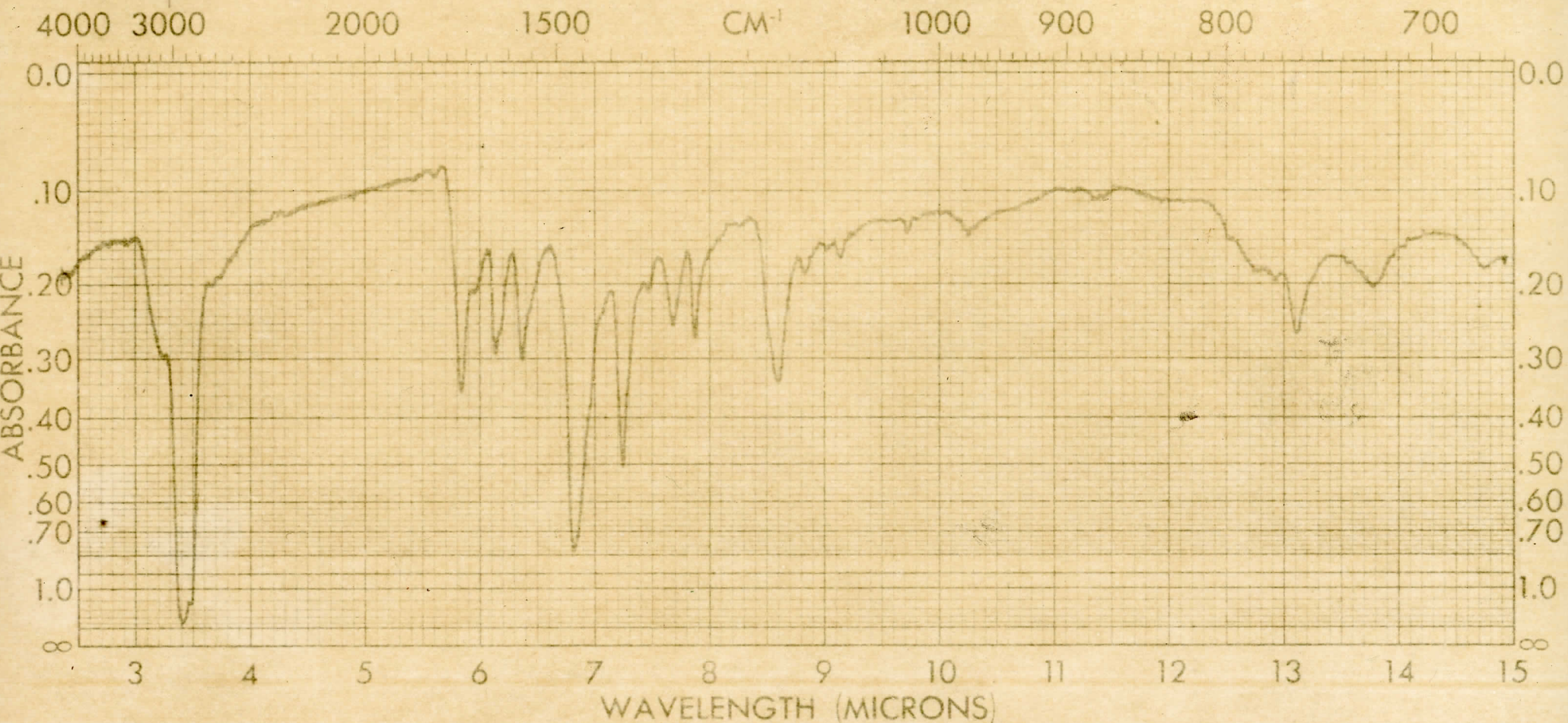
SPECTRUM NO. 7	ORIGIN	LEGEND	REMARKS
SAMPLE Antaronamide	treatment at Once thru 1h with Ammonia water	1.	Compare with S.R. Gagliardi for Infrared Antaronamide - Pure Compound File # 485
<chem>NC(=O)C1=CC=CC=C1N</chem> VII	PURITY RX - Hot Water off yellow - light yellow Cryst.	2.	
	PHASE MP 70 108-110	DATE 11/30/66	
	THICKNESS Nujol Mull Densat Cell	OPERATOR RPS	

SAMPLE SPECTRUM NO. 7



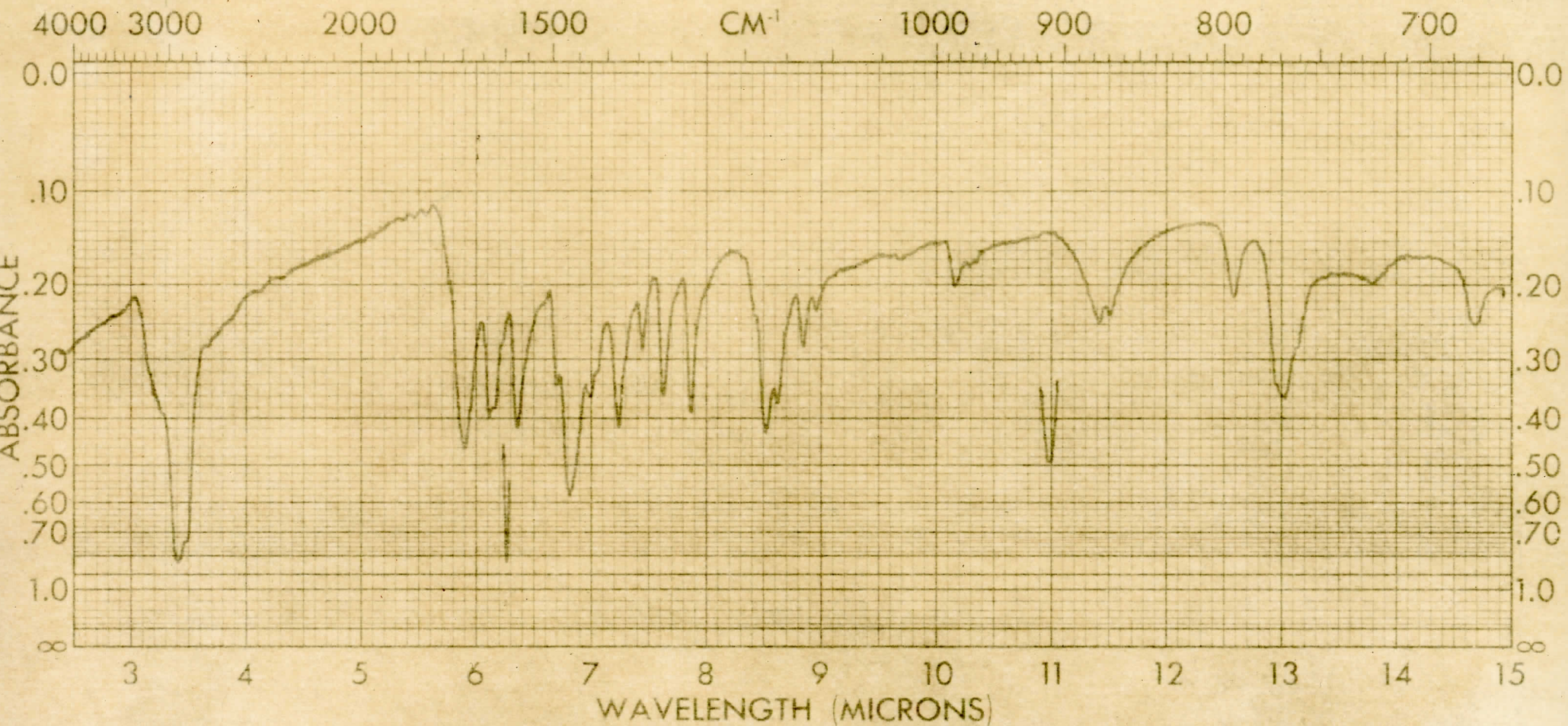
SPECTRUM NO.	ORIGIN	LEGEND	REMARKS
8a			
SAMPLE VIII a 	PURITY crude prod - mp range Rx MeOH - white crystals	1. 2.	Pop 2-27-67 HCl (dil) was found to cause a ring closure rather than produce o-thioisobenzamide when added to soln containing
2 Thiois benzamide mesa	PHASE (250) Shuk & Debn 255 Math 272-2725 Dover int Cell	DATE 2-28-67	
	THICKNESS Nyal Mull	OPERATOR JLD	

SAMPLE SPECTRUM NO. 8a



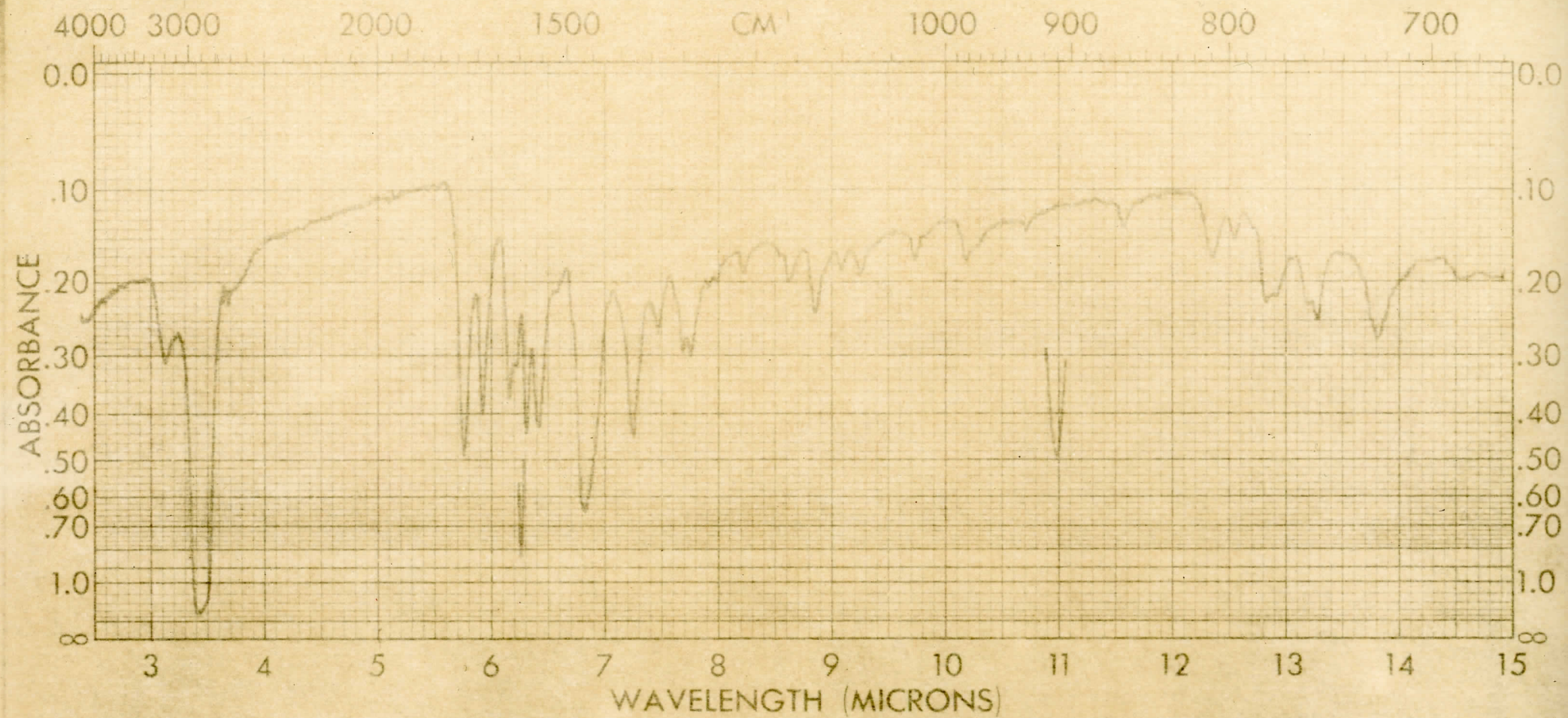
SPECTRUM NO. 86	ORIGIN	LEGEND	REMARKS
SAMPLE 2- Thieno -		1.	Synthesized by procedure
Benzoylurea <chem>C(=O)Nc1ccccc1</chem>	PURITY R _x hot Diogen	2.	of Ex # 395 (3) 4/1/60
	PHASE mp 316-318 (310) Dumont Cell	DATE 2-27-67	
	THICKNESS Nujol Mulli	OPERATOR J.L.D.	

SPECTRUM NO. 86
SAMPLE



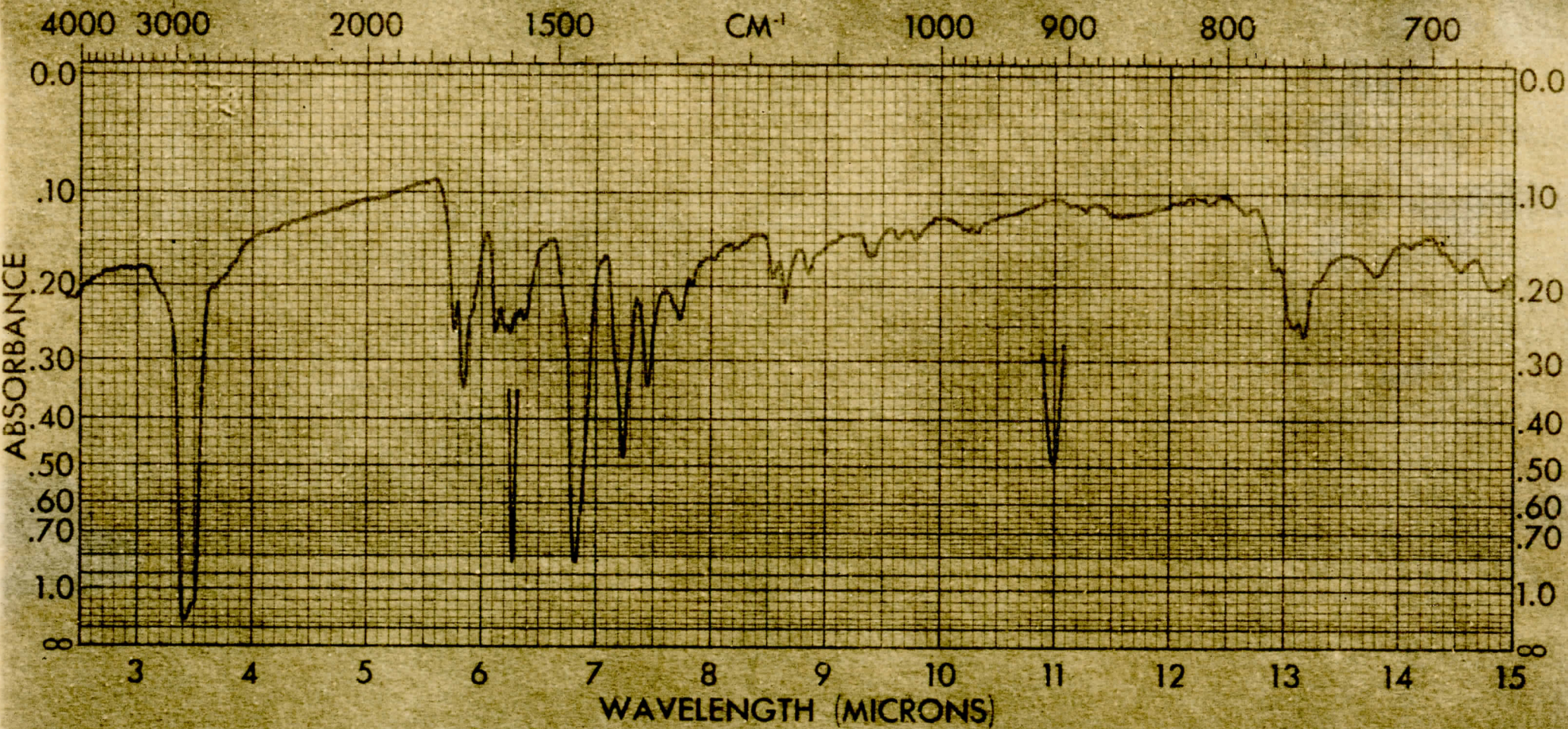
SPECTRUM NO. <u>80</u>	ORIGIN	LEGEND	REMARKS <u>Ex 315</u>
SAMPLE <chem>C1=CC=C(C=C1)C(=O)O</chem>		1.	wash lower \subset MeOH. Than HOT
	PURITY <u>mp 306-308°C</u>	2.	MeOH cooled, double wt H_2O .
	PHASE <u>Damocet cell</u>	DATE <u>3-6-67 9:30 AM</u>	yellow crystals
	THICKNESS <u>Nujol mass</u>	OPERATOR <u>JLD</u>	analysis c <u>53.9</u> <u>53.86</u> H <u>3.32</u> <u>3.45</u>

SPECTRUM NO. 80
SAMPLE



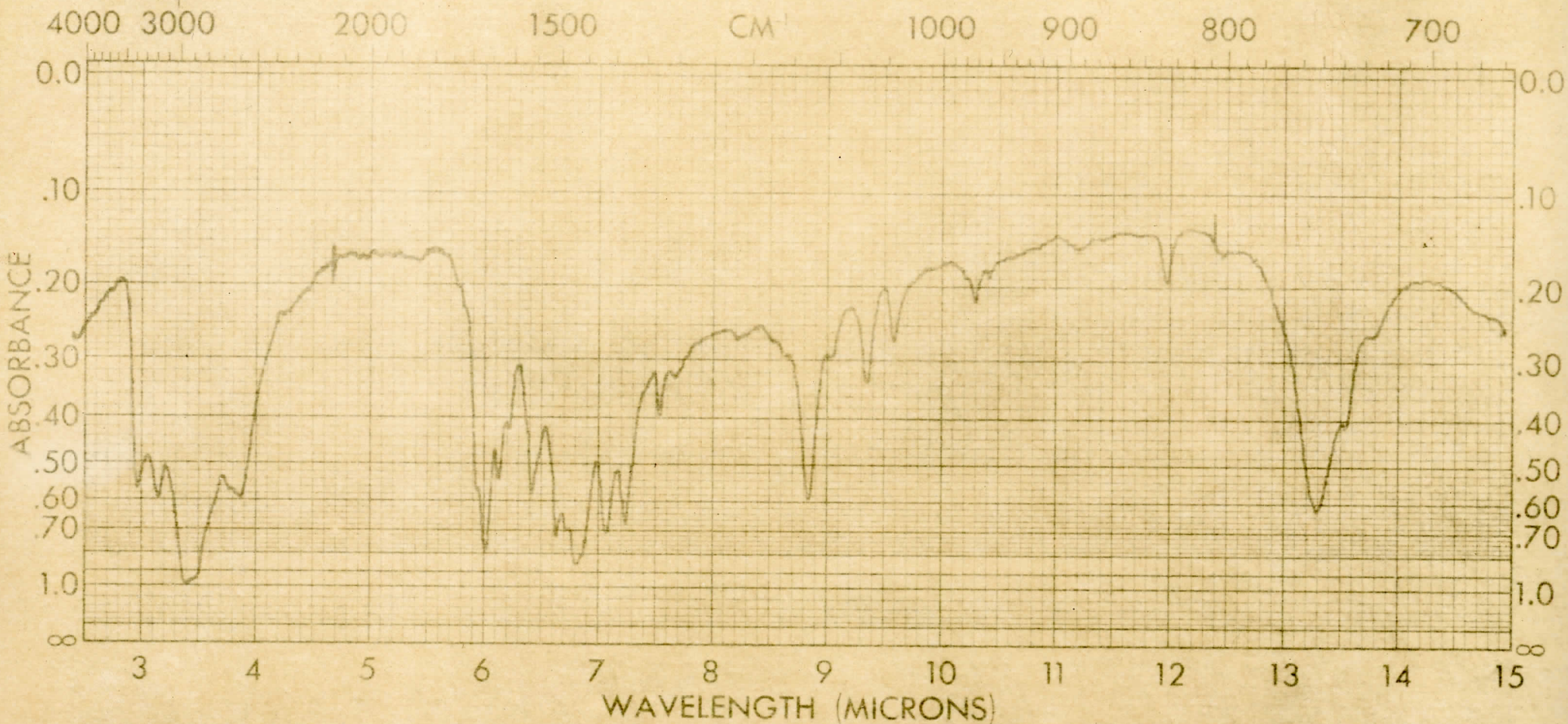
SPECTRUM NO.	ORIGIN	LEGEND	REMARKS
8d			
SAMPLE <chem>C1=CC=C(C=C1)C(=O)N</chem>	PURITY m.p. 315-318d	1.	yellow comp
	PHASE	2.	wash with MeOH bnt
	THICKNESS demount cell Nujol Mull	DATE 4-3-67 10:15	moel in hot MeOH
		OPERATOR J. L. D.	Prep: <chem>C1=CC=C(C=C1)C(=O)N</chem>

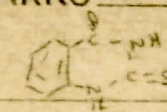
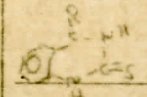
SAMPLE SPECTRUM NO. 8d



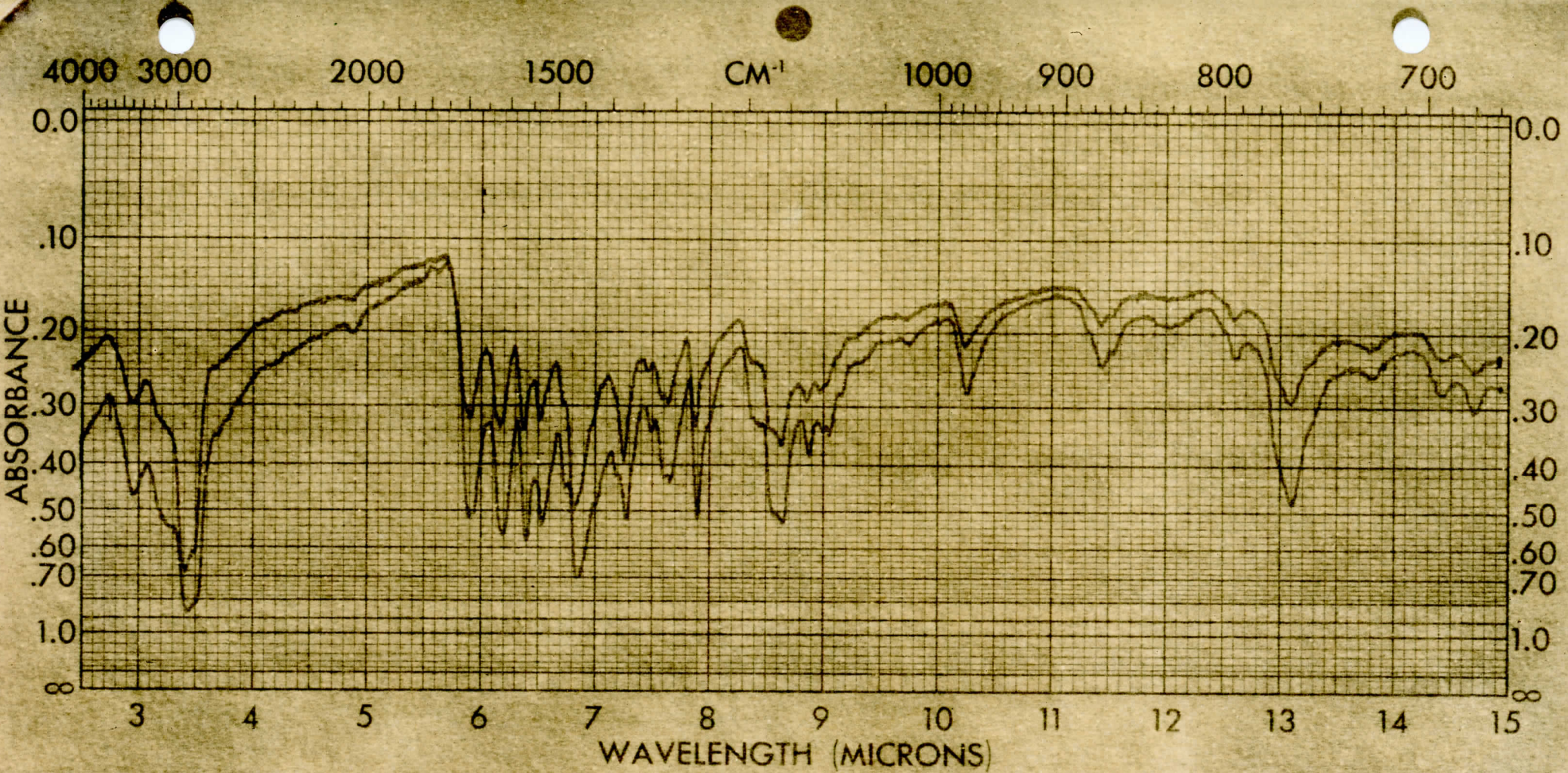
SPECTRUM NO. <u>82</u>	ORIGIN _____	LEGEND _____	REMARKS <u>Exp: $\frac{1}{2} \text{H} + \frac{1}{2} \text{CO}_2$</u>
SAMPLE <u>2-thiouracil benzene</u>	PURITY <u>m.p. 254-255 °C</u>	1. _____	<u>white comp. sol. diene</u>
<chem>C1=NC(=O)NC(=O)N=C1</chem>	PHASE _____	2. _____	<u>Rx hot MeOH</u>
THICKNESS <u>NaCl Mull</u>	DATE <u>4-3-67 10:00 AM</u>		<u>analysis</u>
	OPERATOR <u>J.L.D.</u>		<u>%C</u> <u>%H</u>
			<u>Theo</u> <u>53.9</u> <u>3.57</u>
			<u>Found</u> <u>67.02</u> <u>3.59</u>

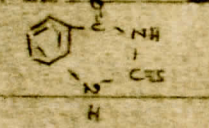
SPECTRUM NO. 82
SAMPLE



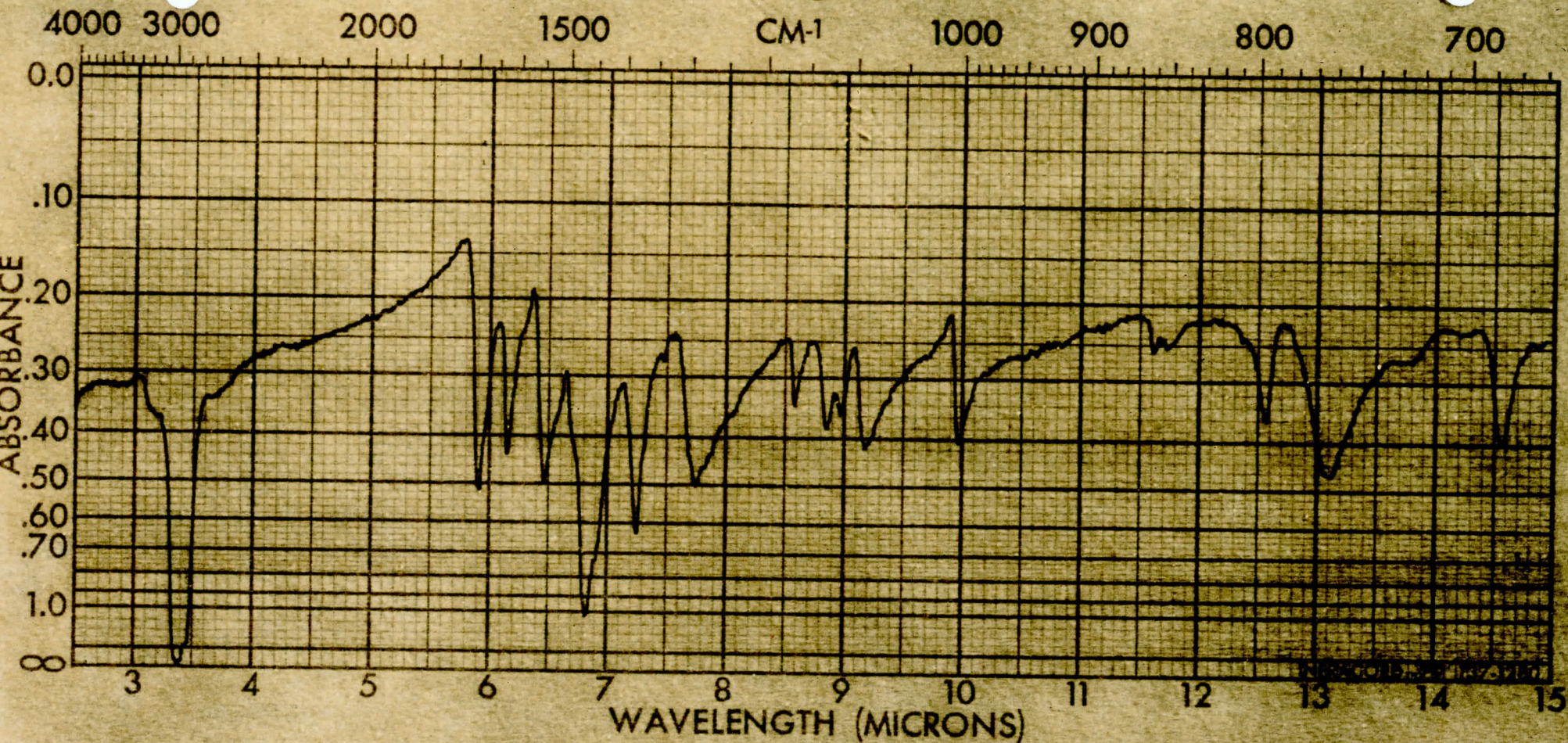
SPECTRUM NO. <u>8F</u>	ORIGIN _____	LEGEND _____	REMARKS _____
SAMPLE <u>VIII</u>		1. _____	<chem>Rx</chem>  in Hot
<u>2 Thoms benzoylone urea</u>	PURITY <u>Rx MeOH mp 230-232</u>	2. _____	digane. This is sample that about go into soln
	PHASE _____	DATE <u>3-3-67 10.00</u>	 prep 3/2/67 by
	THICKNESS <u>Demoval cell Nujol Mull</u>	OPERATOR <u>J.L.W.</u>	reactor of anthran alamide $\bar{c} \begin{matrix} u \\ u \end{matrix} - \bar{c} - \bar{c} - \bar{c}$

SAMPLE SPECTRUM NO. 8F



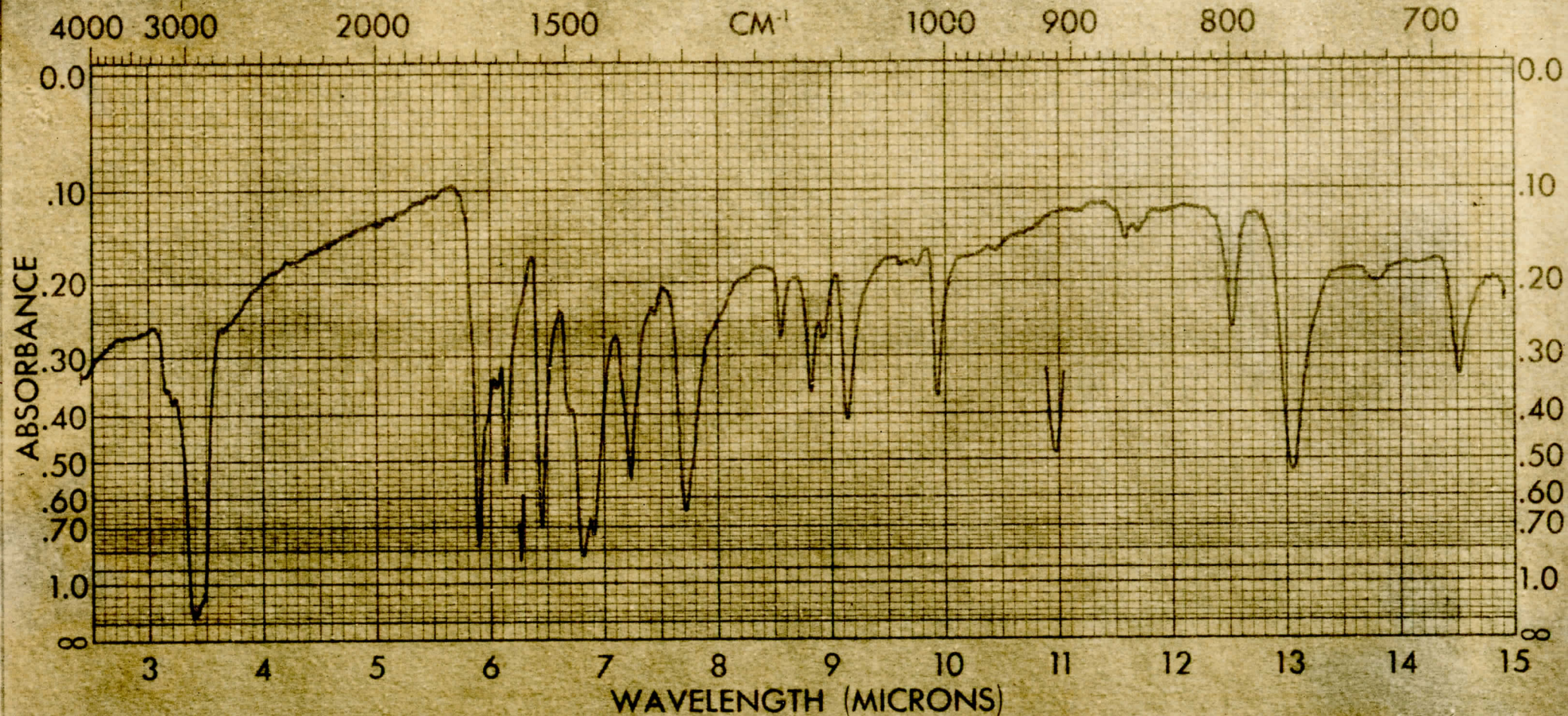
SPECTRUM NO. <u>89</u>	ORIGIN _____	LEGEND _____	REMARKS <u>prep Exp 395</u>
SAMPLE <u>VIII</u>	PURITY _____	1. _____	<chem>C1=CC=C(C=C1)C(=O)N</chem> $+ MeOH + NaOH$
	PHASE _____	2. _____	<u>Soln sat for 5 days</u>
THICKNESS <u>Diamond cell</u>	DATE <u>3-21-67</u>	OPERATOR <u>J.L.O.</u>	<u>attempt to determine isotermic shift</u>

SPECTRUM NO. 89
SAMPLE



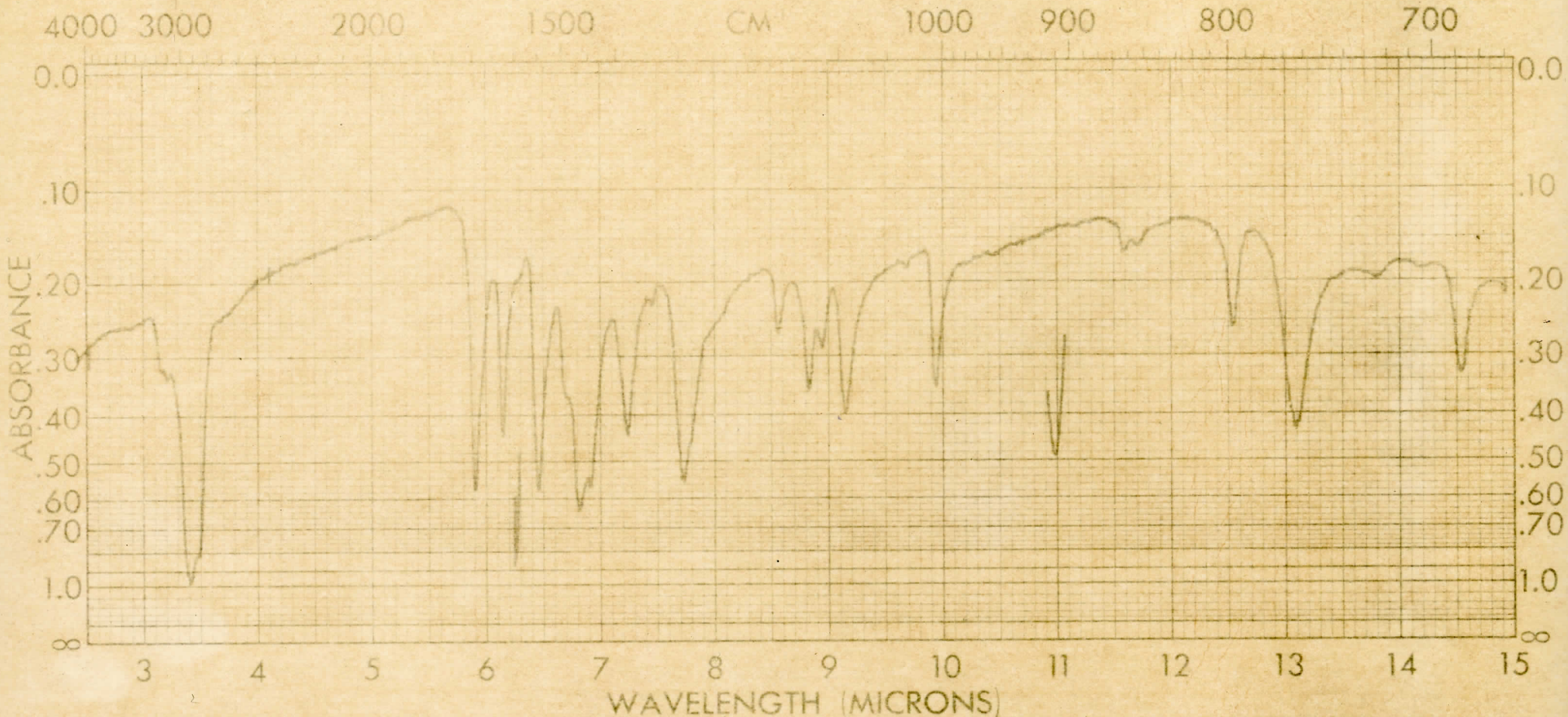
SPECTRUM NO. <u>21 (9)</u>	ORIGIN <u>Exp # 321 (3)</u>	LEGEND	REMARKS									
SAMPLE <u>2-thiono-3-methyl</u> <u>Benzoylurea</u>	<u>4/1/61</u>	1. <chem>Cc1ccc(cc1)C(=O)NC(=S)N</chem>	Analysis									
Benzoylurea <chem>Cc1ccc(cc1)C(=O)NC(=S)N</chem>	PURITY <u>Rx-MeOH</u>	2. <chem>Cc1ccc(cc1)C(=O)NC(=S)N</chem>	<table border="1"> <thead> <tr> <th></th> <th>Theo</th> <th>Found</th> </tr> </thead> <tbody> <tr> <td>C</td> <td>25.9</td> <td>25.17</td> </tr> <tr> <td>H</td> <td>4.17</td> <td>4.09</td> </tr> </tbody> </table>		Theo	Found	C	25.9	25.17	H	4.17	4.09
	Theo	Found										
C	25.9	25.17										
H	4.17	4.09										
IX	MP <u>100</u> <u>267-266</u> <u>Fine white needles</u>	DATE <u>1/2/62</u> <u>3:00 PM</u>	Ret. for - Davis - in R. <u>3/15/67</u>									
	PHASE <u>Nujol Mull</u>	OPERATOR <u>RPS</u>	<u>copy - PURE</u>									
	THICKNESS <u>Diamond Cell</u>		<u>Cpd. File</u>									

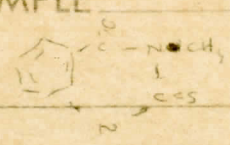

SPECTRUM NO. 21
SAMPLE



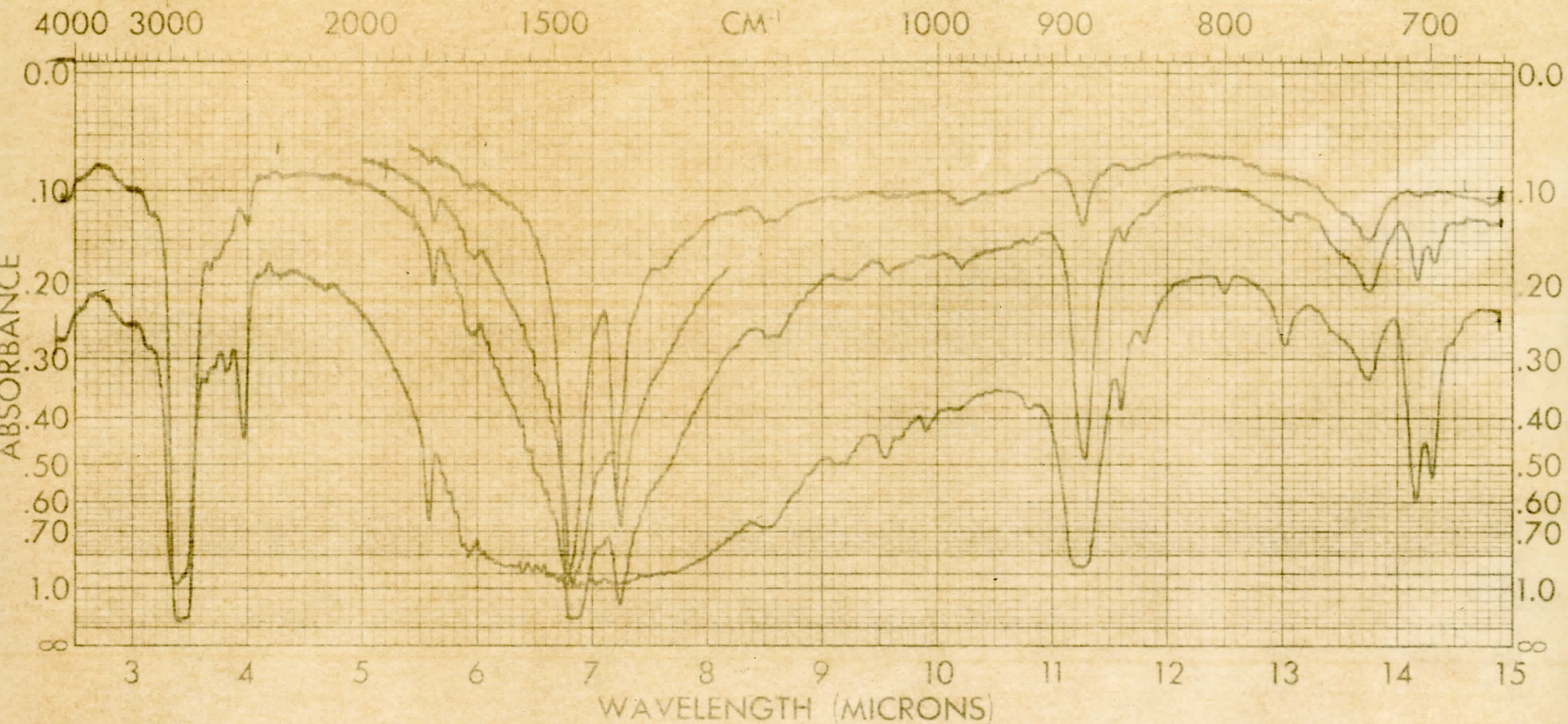
SPECTRUM NO.	ORIGIN	LEGEND	REMARKS
9a			
SAMPLE <chem>CN1CCCC1</chem> 2-Ethano-3-methyl iminoisoindole	PURITY <i>mp 250-253°</i>	1.	<i>This I.R. + excess CH₃NH₂ + HCl</i>
	PHASE <i>white crystals</i>	2.	<i>I.R. agrees with copy-pure Cpd file of 2-there 3-methyl iminoisoindole</i>
	THICKNESS <i>1/2 mm</i>	DATE <i>3-13-67</i>	
		OPERATOR <i>J.L.D.</i>	

SAMPLE SPECTRUM NO. 1A



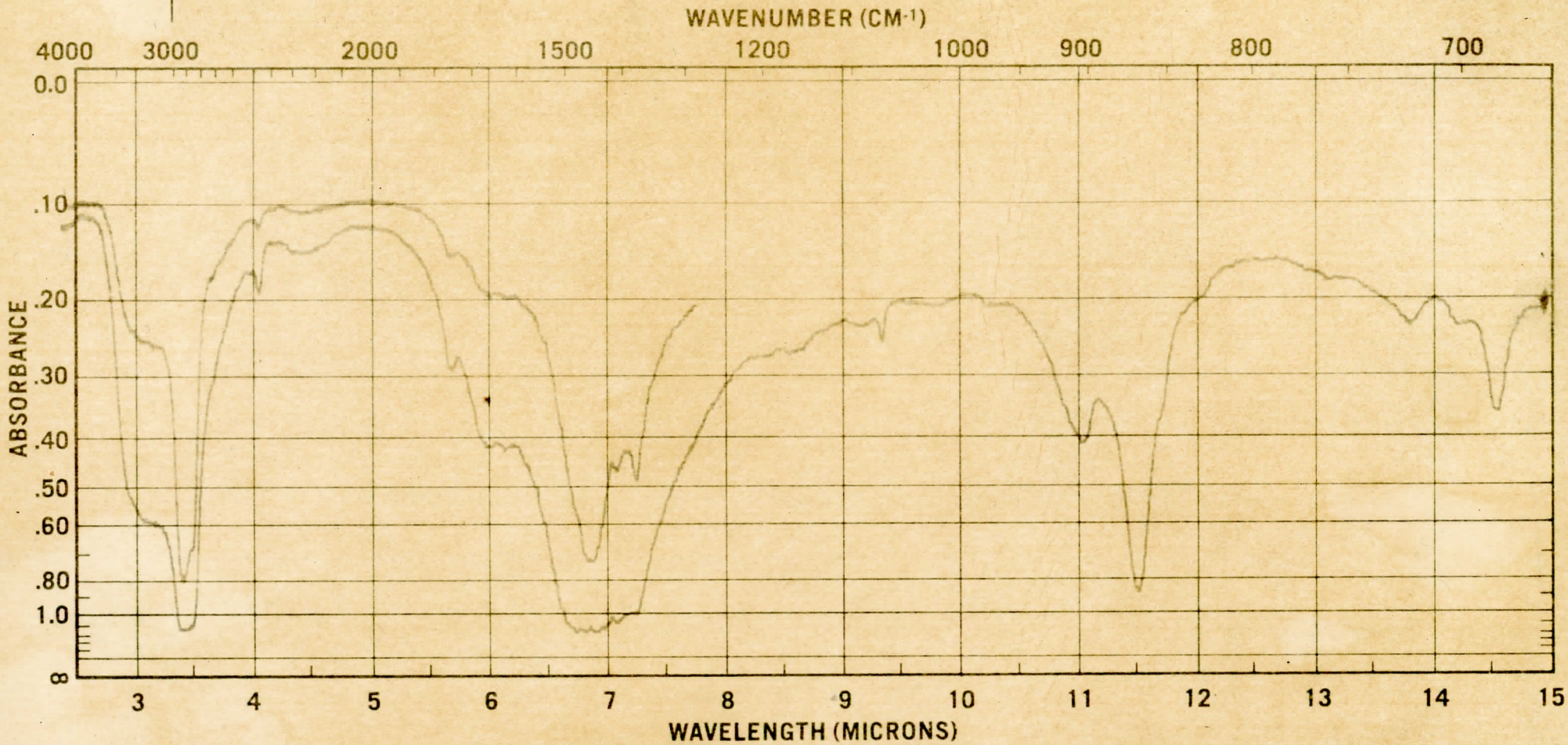
SPECTRUM NO. 96	ORIGIN	LEGEND	REMARKS I.R. + CH ₃ NH ₂ →
SAMPLE 	PURITY <i>Rx Mech</i> mp. 240-255° red lig m.p. (22. Mech) 259-263° mp (32. Mech) 260-263°	1. 2.	 prob impure. impurity prob α-C=O
2 Thioxo - 3 - methyl benzoylamine	PHASE Demount cell	DATE 3-13-67 10:00 AM	I.R. agrees E copy - pure Cpd F.G. (1-2-62 R.P.S.)
THICKNESS	Nujol mull	OPERATOR J.L.D.	

SAMPLE SPECTRUM NO. 96



SPECTRUM NO. 9c	ORIGIN	LEGEND	REMARKS
SAMPLE IV		1.	<chem>CN(C)C1=CC=CC=C1</chem> ↔ <chem>CN(C)C1=CC=C(C=C1)S</chem>
2-Thione-3-methyl benzopyrone sua	PURITY (85) up to 347° d.d. not melt	2.	
	PHASE Dismant all	DATE 3-14-67	
	THICKNESS Nujol Mull	OPERATOR J.L.D.	Thiophene group <chem>C1=CC=C(C=C1)S</chem> + <chem>CN(C)C1=CC=C(C=C1)S</chem>

SAMPLE SPECTRUM NO. 9c



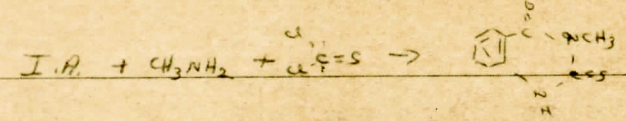
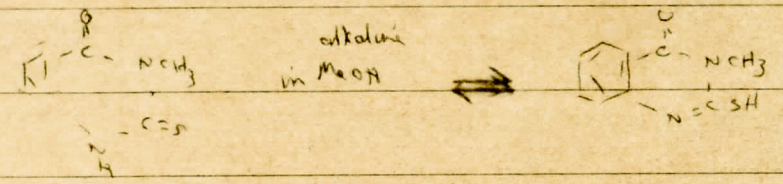
NUMBER 9d

DATE 3-16-67 PATHLENGTH _____

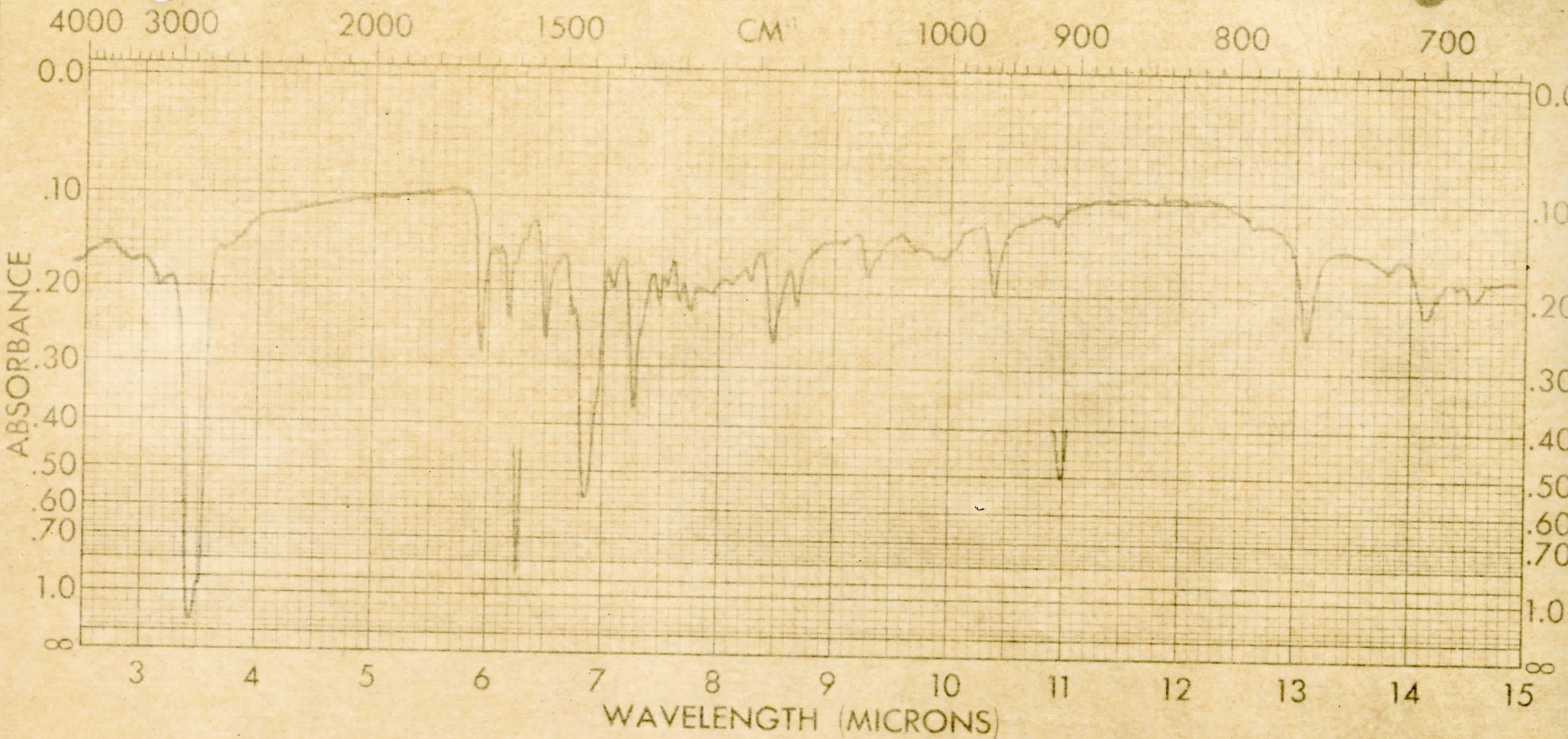
SAMPLE 2-thio-3-methyl benzoylurea

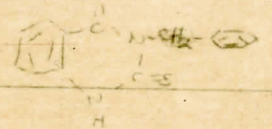
ANALYST J.L.D.

NOTES

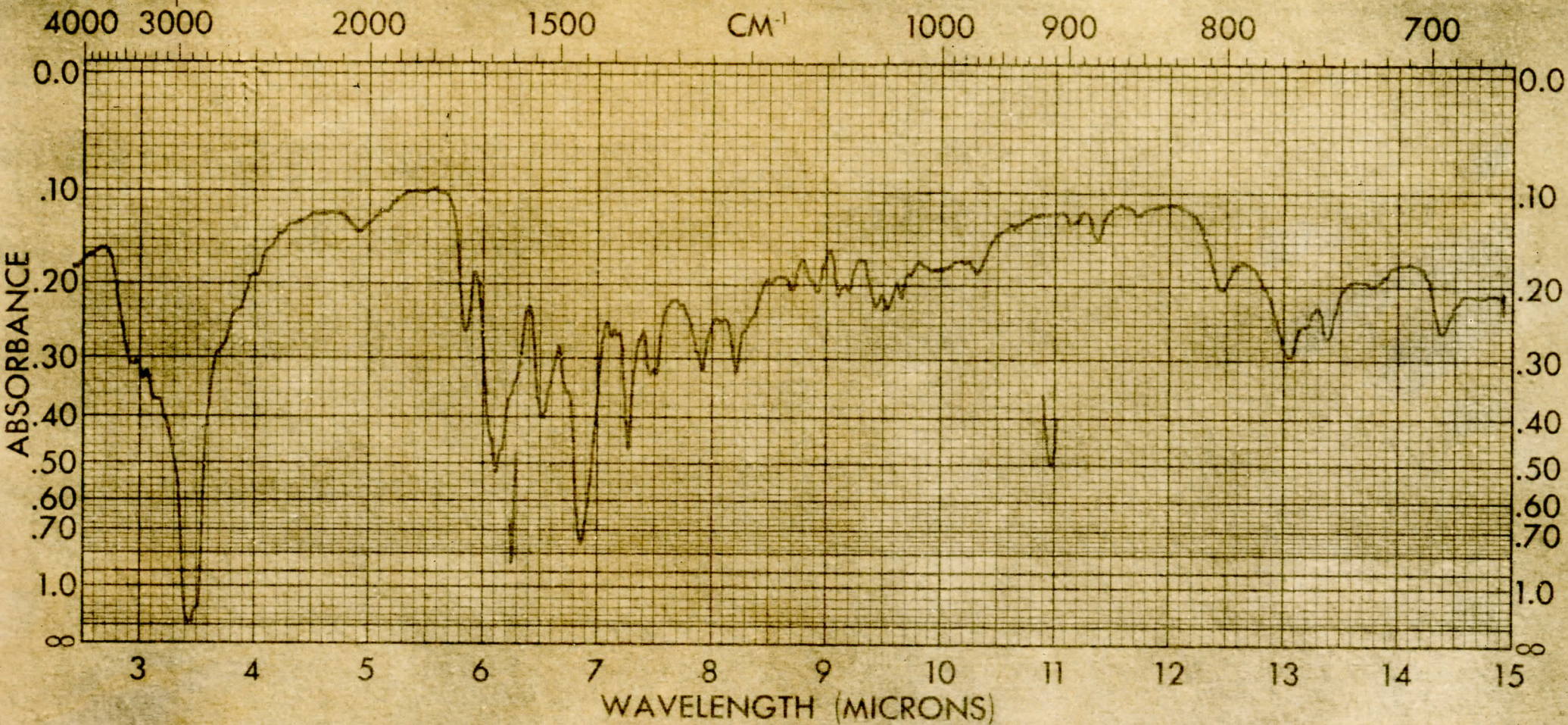


up to 347°C. did not melt.



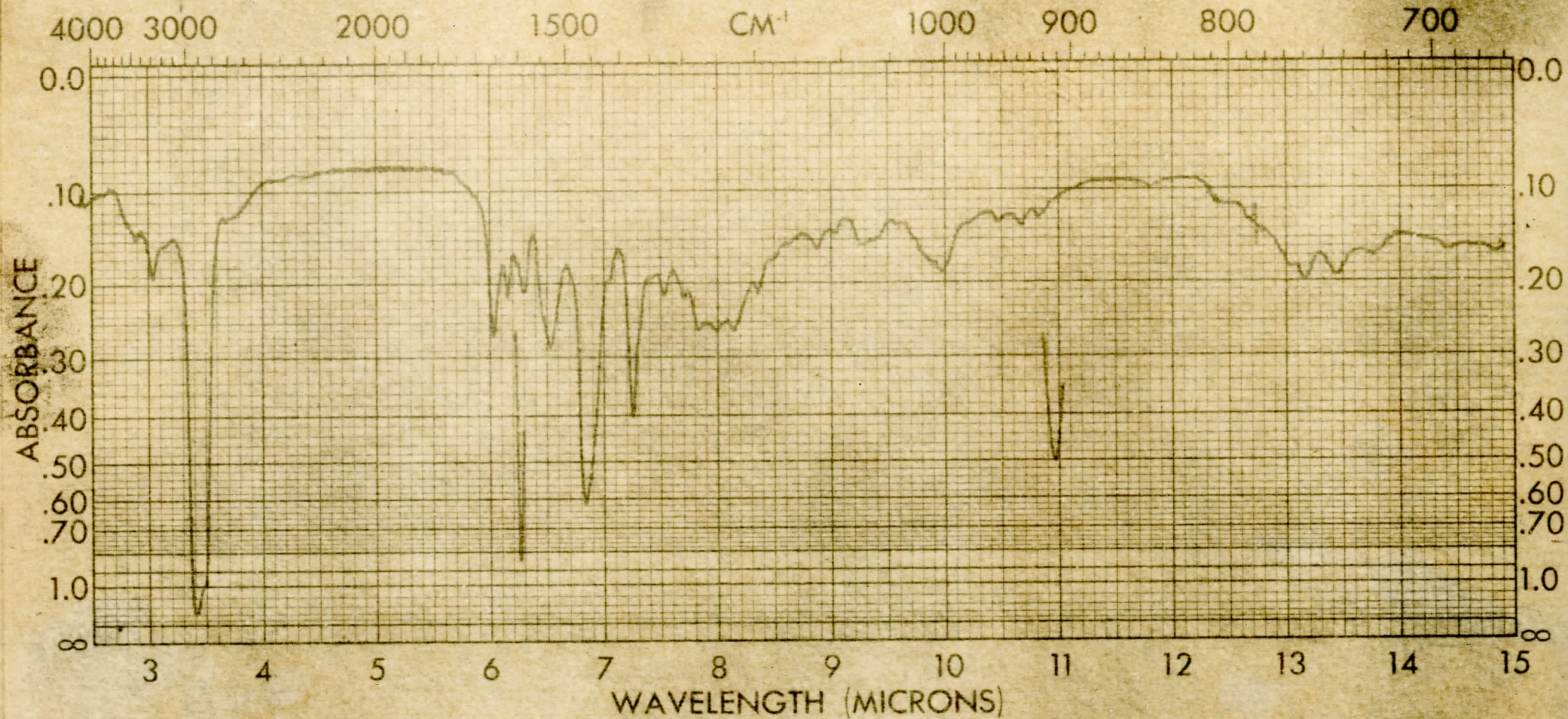
SPECTRUM NO. <u>10</u>	ORIGIN _____	LEGEND _____	REMARKS _____
SAMPLE <u>X.</u>		1. _____	
	PURITY <u>Rx 2 MeOH</u>	2. _____	
<u>2-thiureido-3-benzoyl benzoylurea</u>	<u>mp. 195-210°C</u>	DATE <u>5-22-67</u>	
	PHASE <u>Dismount cell</u>	OPERATOR <u>J.L.D.</u>	
	THICKNESS <u>Nujol Mull</u>		

SPECTRUM NO. 10
SAMPLE



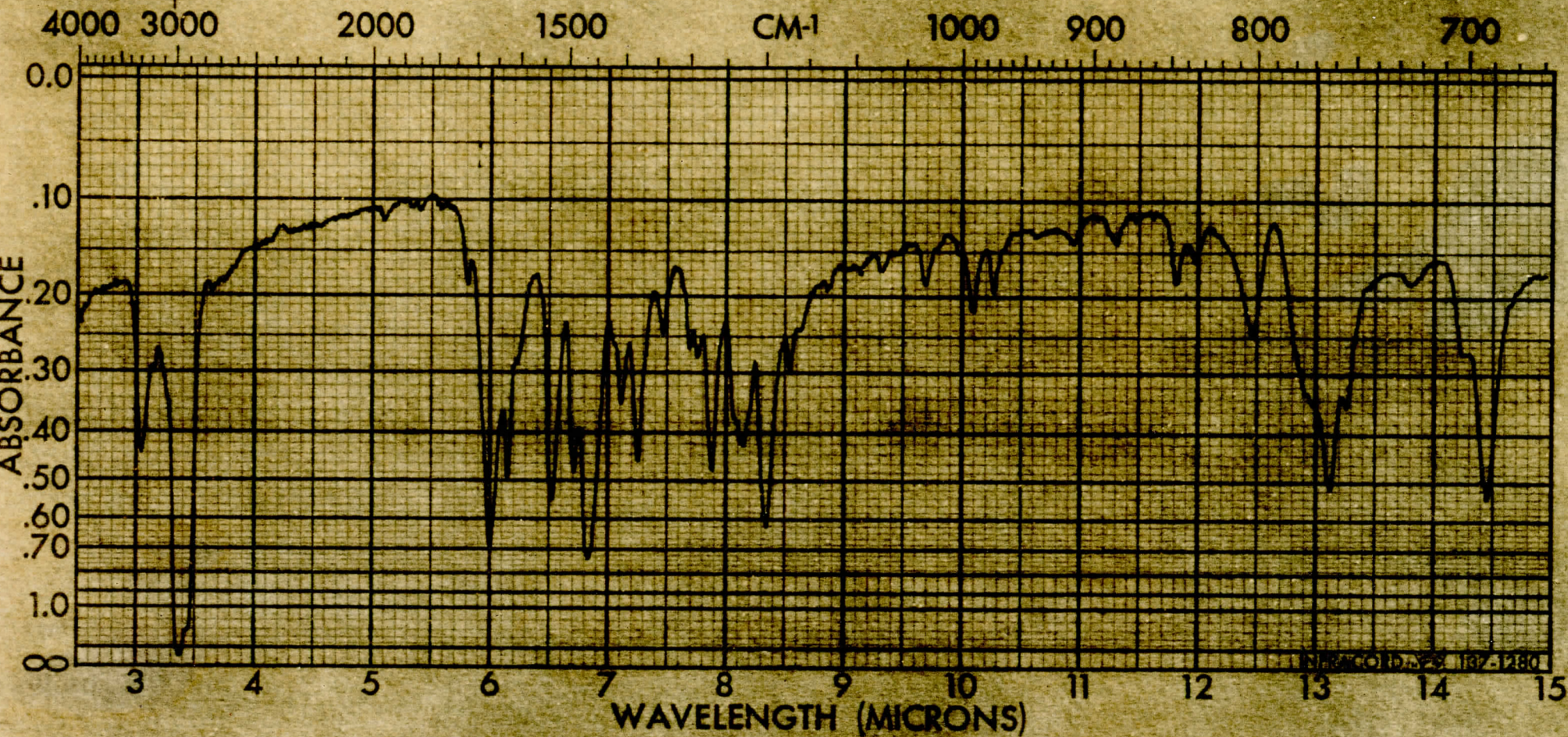
SPECTRUM NO. <u>11</u>	ORIGIN _____	LEGEND _____	REMARKS _____
SAMPLE <u>XI</u>		1. _____	
<chem>CCN(C)C(=S)C1=CC=CC=C1</chem> 2-thio-3-ethyl benzoylurea <u>urea</u>	PURITY <u>mp. part 190</u> <u>215-217</u>	2. _____	
	PHASE <u>Demount cell</u>	DATE <u>5-10-67</u>	
	THICKNESS <u>Neq. of Hall</u>	OPERATOR <u>J.L.O.</u>	

SPECTRUM NO. 11
SAMPLE



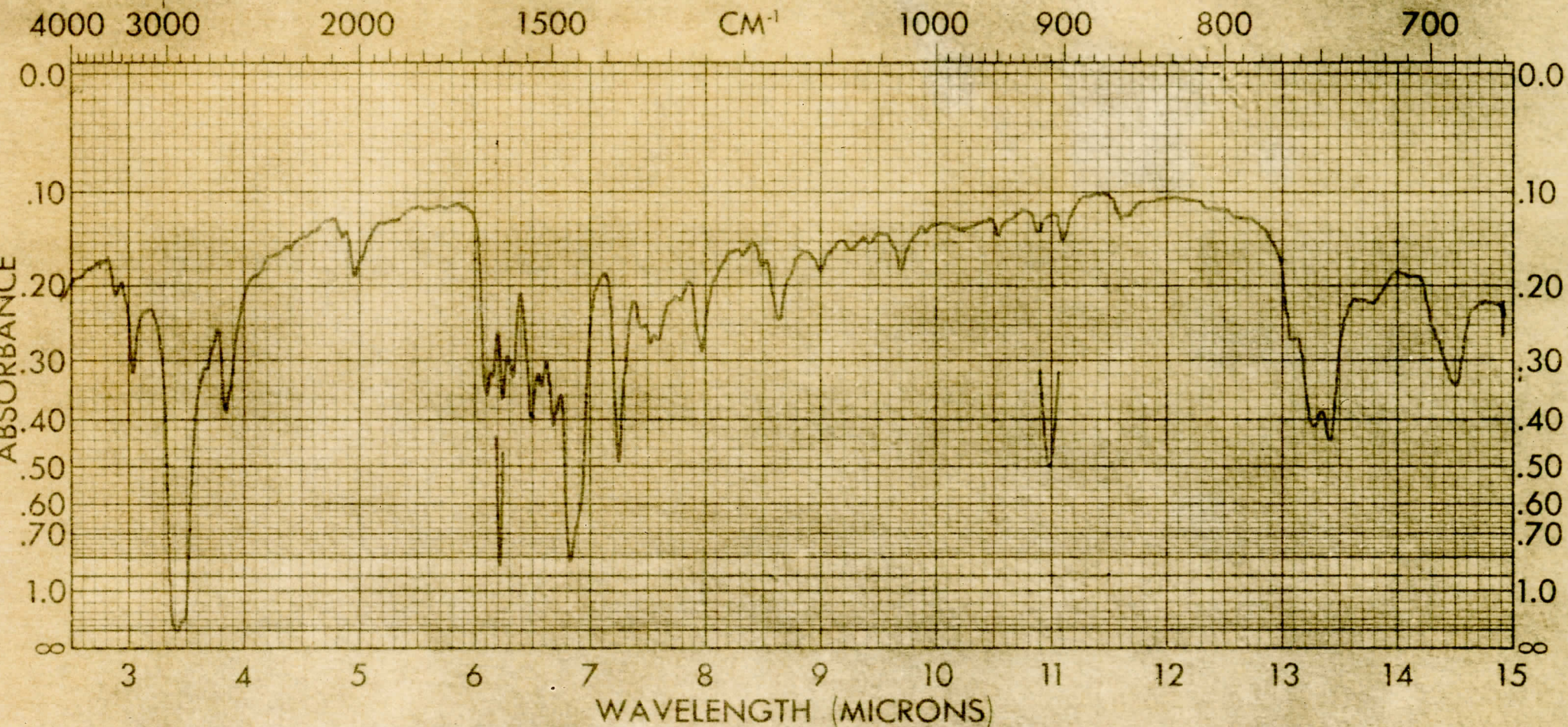
SPECTRUM NO. <u>12</u>	ORIGIN _____	LEGEND _____	REMARKS _____
SAMPLE		1. _____	
<chem>C1=CC=C(C=C1)C(=O)N=CC=C</chem>	PURITY <u>Rx2Meth</u> <u>mp 160-168</u>	2. _____	
2-thione -3-allyl benzoylurea <u>usa</u>	PHASE _____	DATE <u>5-19-67</u>	
	THICKNESS <u>Demount cell</u> <u>Nujol Mull</u>	OPERATOR <u>J.L.B.</u>	

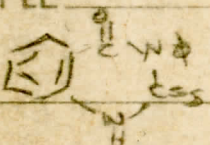
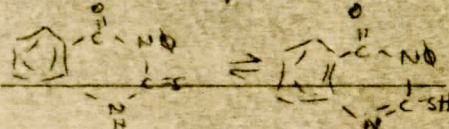
SAMPLE SPECTRUM NO. 12



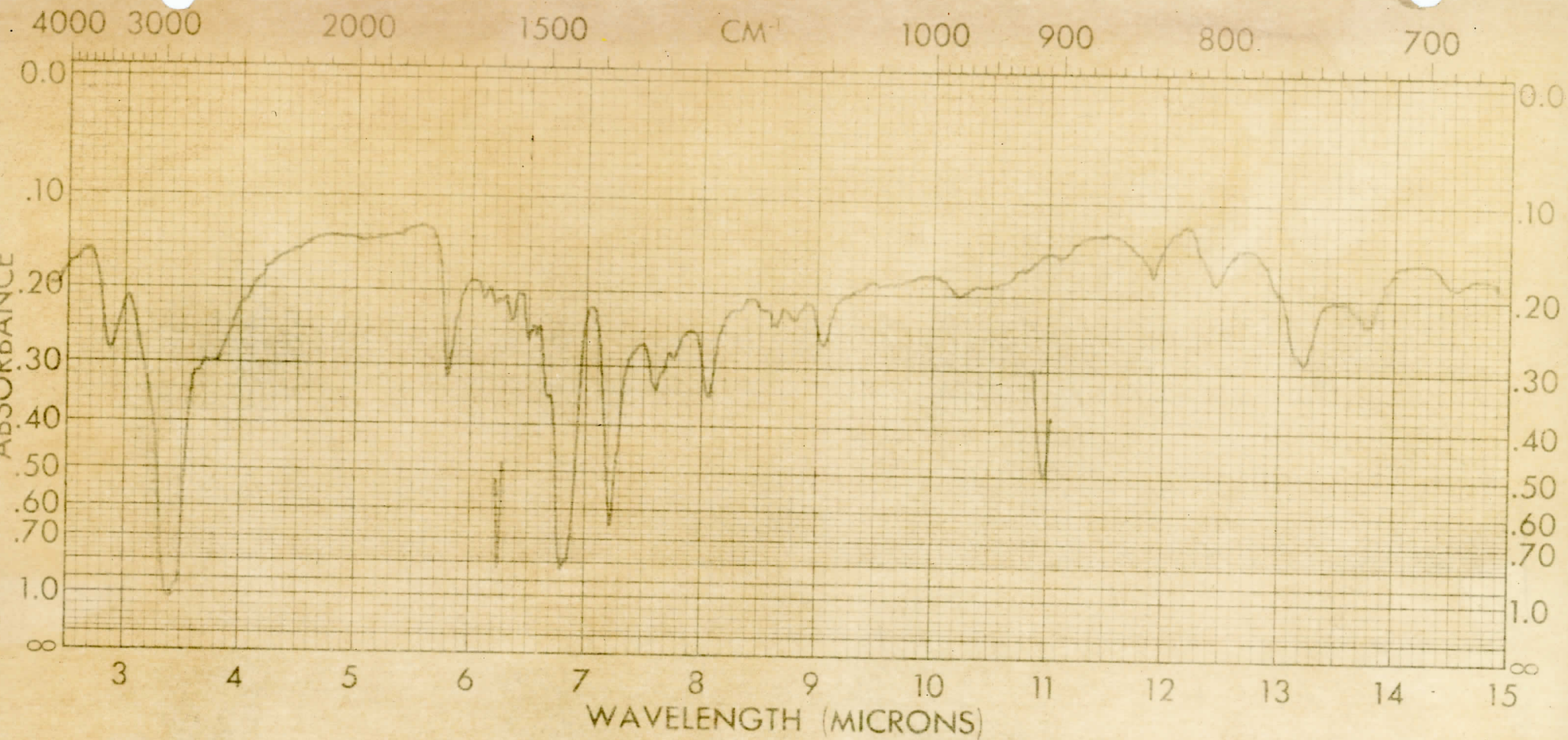
SPECTRUM NO. # 1 (13)	ORIGIN Exp. # 321 (2)	LEGEND	REMARKS
SAMPLE 2-thione-3-phenyl benzoylurea Benzoylurea	"1/61		Ref - Baileys 24 370
<chem>O=C1NC(=O)C2=CC=CC=C12</chem>	PURITY Rx - Thion white crystals MP (20) 303-4	1.	
PHASE Nujol Mull	DATE 1/2/62 3:20 PM	2.	COPY TO PURE Cpd. FILE
THICKNESS Densit Cell	OPERATOR RPS		

SPECTRUM NO. 13
SAMPLE



SPECTRUM NO. <u>13a</u>	ORIGIN _____	LEGEND _____	REMARKS _____
SAMPLE	<i>Rx121760H</i>	1. _____	<i>tautomeric shift</i>
	PURITY <i>m.p. 116-117°C</i>	2. _____	
	PHASE _____	DATE <i>5-11-67</i>	
	THICKNESS <i>Demount Cell</i>	OPERATOR <i>J. L. D.</i>	
	<i>Nujol Mull</i>		

SPECTRUM NO. 13a
SAMPLE



SPECTRUM NO.	ORIGIN	LEGEND	REMARKS
SAMPLE XIV		1.	<chem>C1=CC=C(C=C1)C(=O)O</chem> + NaOH + HCl →
	PURITY m.p. range 130°-170°C	2.	
	PHASE	DATE 5-12-67	
	THICKNESS <i>Demount cell</i> <i>Napyl Mull</i>	OPERATOR J.L.D.	

SPECTRUM NO. 14