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Preparation of 1, 2, 3-Trimethylbenzene

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PREPARATION OF 1, 2, 3-TRIMETHYLBENZENE

by

JOHN HORACE PEELING

A thesis presented to the Department of Chemistry of Union College in partial fulfillment of the requirements for the degree of Bachelor of Science with a Major in Chemistry.

By John H. Peeling

Approved By Howard E. Shaffer

Dated: May 12th, 1961.

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ACKNOWLEDGMENT

I would like to express my sincere gratitude to Dr. Howard E. Sheffer of the Union College Chemistry Department for his advice and constant assistance throughout this experiment.

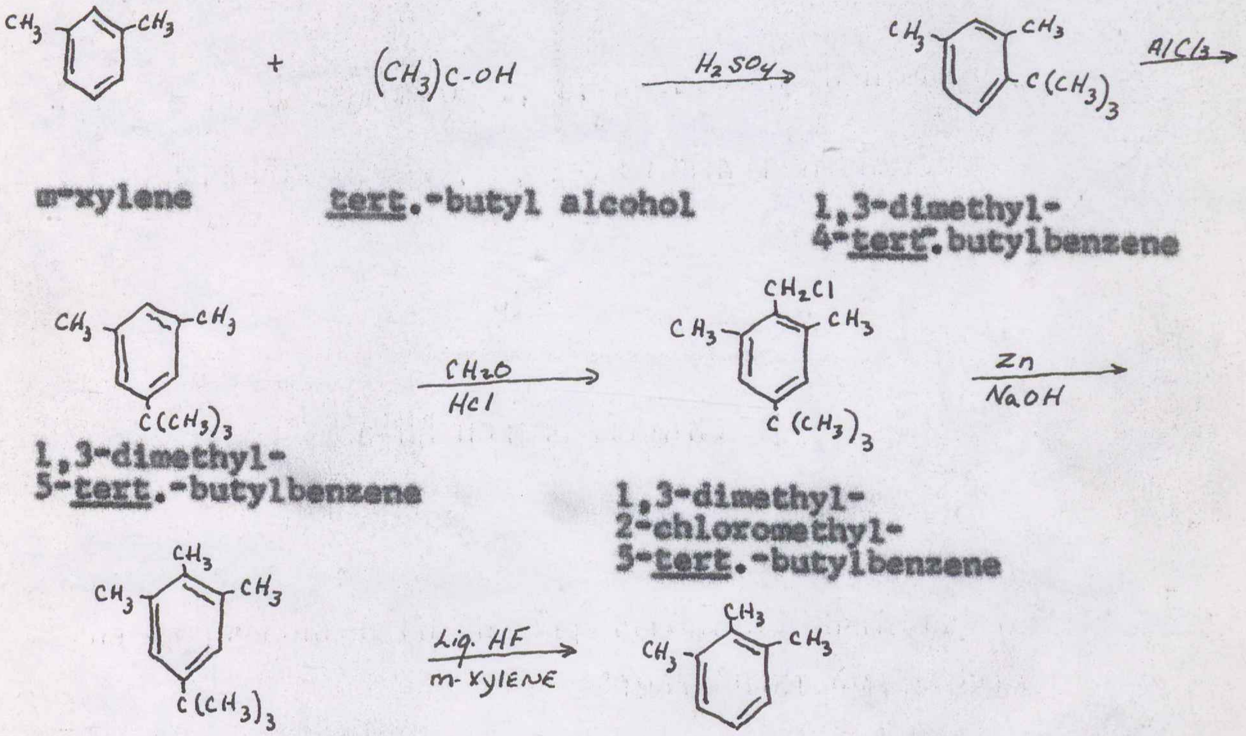
INTRODUCTION

The purpose of this project is the synthesis 1, 2, 3-trimethylbenzene or hemimellitene as an intermediate for further research. The synthesis was carried out using two different approaches.

One problem which came up in the first step of the synthesis turned out to be a small research project itself. The literature showed that *tert*.-butyl alcohol alkylated m-xylene to yield 1, 3-dimethyl-4-*tert*.-butylbenzene; whereas we found evidence for the reaction giving a product with properties similar to the product obtained by reacting *tert*.-butyl chloride with m-xylene. This latter product is probably 1, 3-dimethyl-5-*tert*.-butylbenzene. Infared spectroscopy, vapor phase fractometry, refractive indices, nitrations, cooling curves and oxidations proved these products to be identical except for purity. A comparison of these methods showed that *tert*.-butyl chloride gave higher yields and a higher decree of purity.

Planned Synthesis of 1, 2, 3-trimethylbenzene

Method #1 - Peeling



m-xylene

<u>tert</u>.-butyl alcohol

1,3-dimethyl-
4-<u>tert</u>".butylbenzene

1,3-dimethyl-
5-<u>tert</u>.-butylbenzene

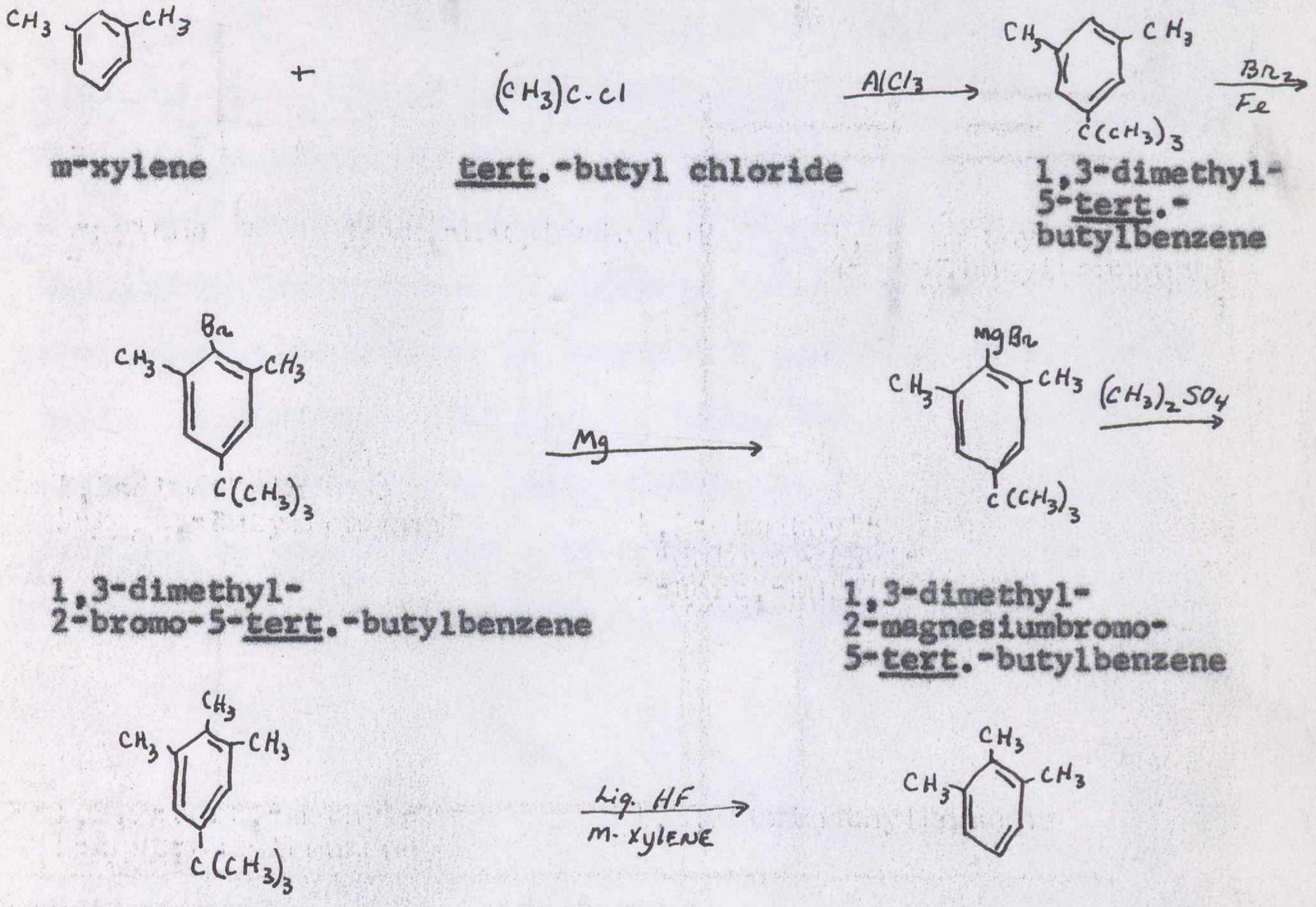
1,3-dimethyl-
2-chloromethyl-
5-<u>tert</u>.-butylbenzene

1,2,3-tert.-methyl-
5-<u>tert</u>:butylbenzene

1,2,3-trimethylbenzene

Planned Synthesis 1,2,3-trimethylbenzene

Method #2 - Nigriny



m-xylene

tert.-butyl chloride

1,3-dimethyl-5-tert.-butylbenzene

1,3-dimethyl-2-bromo-5-tert.-butylbenzene

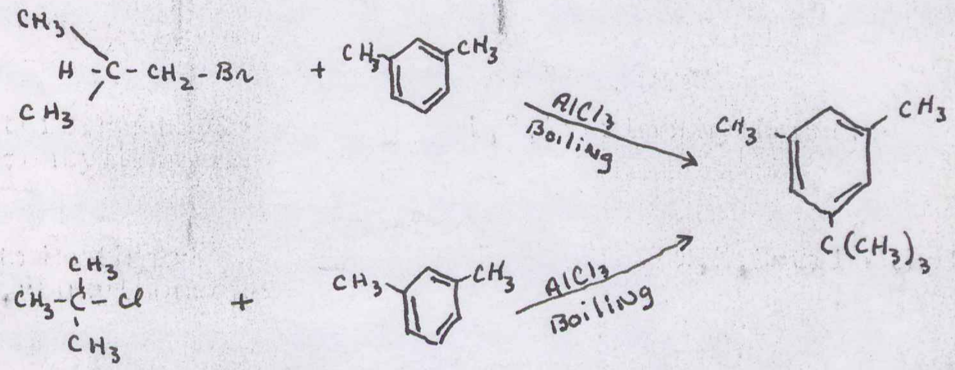
1,3-dimethyl-2-magnesiumbromo-5-tert.-butylbenzene

1,2,3-trimethyl-5-tert.-butylbenzene

1,2,3-trimethylbenzene

HISTORICAL

Baur (1) in 1891 did the initial work on this reaction with the synthesis of 1,3-dimethyl-5-tert.-butylbenzene. He was able to synthesize the 1,3,5 isomer in two ways. The first way involved the boiling of m-xylene with isobutylbromide in the presence of aluminum chloride. After repeated factional distillations he obtained a colorless liquid which boiled at 200-202°c (747 m.m.). Using the same procedure except for substituting tert. -butyl chloride for isobutylbromide, he obtained the same liquid boiling at the same temperature. The two methods are shown as follows:



He was able to prove the structure of this 1,3,5 isomer by oxidizing with chromic acid and by nitrating with fuming nitric acid. In oxidizing he found two acids formed. In one case he formed 3,5-dimethylbenzoic acid C_6H_3 $(CH_3)_2$ COOH which melted at 166°c and in another case he formed trimesic acid C_6H_3 $(COOH)_3$. He deducted that both acids have the symmetrical structure 1,3,5 and therefore the butylxylene is symmetrical.

Nitrating with fuming nitric acid and sulfuric acid in a waterbath, he formed the trinitro-derivative which after recrystallization from alcohol yielded yellow-white needle crystals melting at 110°c. The nitrogroups take the 2,4,6 positions on the ring. Nitrating in a glacial acetic acid solution with fuming nitric acid forms the mononitro derivative which after recrystallization from alcohol yielded white crystals melting at 85°c.

In 1932, Smith and Cass (4) worked with the trimethylbenzenes. They found that trimethylbenzenes could be made easily by just refluxing m-xylene with aluminum chloride. However, methylation using methyl chloride and aluminum chloride, yielded no 1,2,3-trimethylbenzene.

Wirth (13) in 1936 was able to make 1,3,-dimethyl-5-_tert_.-butylbenzene using _tert_.-butyl chloride with m-xylene. He reacted m-xylene with _tert_.-butyl chloride in the presence of aluminum chloride in less than 2% of the amount of _tert_.-butyl chloride, while keeping the temperature below 30°c during the entire reaction. This method was used by Nigriny.

In 1939, Nightingale and Smith (8) carried out the synthesis of 1,3-dimethyl-4-_tert_.-butylbenzene using m-xylene and _tert_.-butyl alcohol in the presence of concd. sulfuric acid. Aluminum chloride was used to convert the 1,3,4 isomer to the 1,3,5 isomer. This method was used and is and is described in the experimental section of this thesis.

Maurice J. Schlatter (11) carried out the synthesis of 1,3-dimethyl-5-<u>tert</u>.-butylbenzene using m-xylene and <u>tert</u>.-butyl chloride in the presence of aluminum chloride. Next, he chloromethylated using formaldehyde and hydrochloric acid giving 1,3-dimethyl-2-chloromethyl-5-<u>tert</u>.-butylbenzene. The next step was to reduce the chloromethylated product with zinc dust and sodium hydroxide giving 1,2,3-trimethylbenzene. The final and crucial step was the removal of the <u>tert</u>.-butyl group. This was done using liquid anhydrous hydroflouric acid and m-xylene for equilibration.

THEORY

Introduction of the *tert*.-butyl group in the first step is the basis for the whole synthesis because it blocks not only the position it occupies, but the two adjacent positions as well. The *tert*.-butyl group is easily introduced and removed from aromatic nuclei without disturbing other alkyl substituents (11). It also activates the nucleus towards further substitution except in those positions adjacent to it.

According to the procedure outlined by Kirrman and Graves (6) the 1,3-dimethyl-4-alkylbenzenes can be prepared from m-xylene and an alcohol in the presence of 70-85% sulfuric acid. This method is applicable only when alkyl group is secondary or tertiary. 1,3-dimethyl-4-*tert*.-butylbenzene treated with aluminum chloride isomerizes to 1,3-dimethyl-5-*tert*.-butylbenzene.

In the chloromethylation there is only one position open and that is position two. The chloromethyl derivative is easily reduced leaving only the removal of the *tert*.-butyl group before the hemimellitene is obtained.

EXPERIMENTAL

1,3-dimethyl-4-tert.-butylbenzene (8)

The pure m-xylene (750cc) and tert.-butyl alcohol (110 cc) were mixed and the flask placed in an ice bath. A mixture of 1050 cc concentrated sulfuric acid and 220 cc of water was added during a two hour period while the solution was stirred mechanically. The stirring was continued for eighteen hours at room temperature. The xylene layer, was separated, washed repeatedly with water and dilute alkalai, dried and distilled using a column with an ordinary water condenser. There was no exothermic reaction noted or detected during the whole reaction. The first batch was distilled and gave the following results:

FRACTION NO.	BOILING RANGES, °c
1	138-142
2	142-180
3	180-210
4	210-222
5	222-232

Since separation was not achieved with an Engler flask, a sponge packed and asbestos wrapped fractionating column (1' x 3/4'') was used. A heater was also wrapped about the column to keep the column at the same temperature of the vapors distilling over. This column gave the following results after refractionating the first set of fractions:

FRACTION NO.	BOILING RANGES, °c	WT. OF FRACTIONS, GRAMS
1A-1	139	118.4
1A-2	139-142	8.6
1A-3	142-200	198.2
1A-4	200-210	56.4
1A-5	210-240	13.4

The second batch was prepared the same way as the first batch and stripped of excess xylene with the sponge packed column. The fraction 1A-4 of the first batch was added to the second batch and both distilled in a 4' x 1/2" column packed with 1/32" stainless steel helices. The following fractions were taken:

FRACTION NO.	BOILING RANGES, °c	WT. OF FRACT., g.	REFRACTIVE INDEX n_D^{25}
2B-1	197-200	0.9	1.4910
2B-2	200-203	2.3	1.4920
2B-3	203-206	5.5	1.4925
2B-4	206-208	22.6	1.4933
2B-5	208-209	23.7	1.4930
2B-6	209-240	14.2	1.4938
Residue	240-	16.7	

Variac settings for all fractions; pot-66 volts column 86 volts.

Since fractions no. 2B-4 and 2B-5 had refractive indices close to the 1,3,5 isomer 10 grams of each were weighed out and distilled in a concentric tube column (75 theoretical plates) for further separation. The following results were obtained: See next page

The fractionation was carried out over a three day period. The column was put on total reflux when unattended. Although the column was on total reflux, some vapors did get over as shown in fraction No. 4.

The following notification will be used for identifying samples throughout this thesis.

1,2,3 etc.-batch No.

A-1' x 3/4" sponge packed column

B-4' x 1/2" 1/32" stainless steel helices packed column

C- concentric tube column (75 theoretical plates)

RESULTS AND DISCUSSION

The following methods were used to prove the structufe of the 1,3,4 isomer. This is where deviations from the physical contents of the 1,3,4 isomer occurred. It also showed the similarity of my product with the exception of purity, to Nigriny's supposedly pure 1,3,5 isomer.

1. cooling curves

cooling curves were made for my sample 2C-3 and Nigriny's sample 5 from the concentric tube column. The samples were used and mixed first in a 1:1 ratio and then in a 3:1 ratio.

Date	Time	Head Temp.	Pot Temp.	Col. Variac	Rt Variac	Reflux Ratio Setting*	Fract. No.	Wt.	N_D25
2/15/61	1:25 pm	205	208	116	56	1:1	2C-1	.2g	
	2:30pm	207	208	130	60	1:1	2C-1		1.4880
	3:10 pm	208.2	208	130	60	5:1	2C-2	1.2g	1.4916
	3:15 pm	208.5	208	130	60	5:1	2C-3	9.3	1.4931
2/16/61	12:45 pm	208.7	209	130	60	5:1	2C-4	6.3	1.4937
2/20/61	7:30 am	211.8	216	130	60	Total	2C-4		
							2C-5	.2	1.4941
							Residue	1.4	

* These are only the set reflux ratios. The actual ratios were in the order of approximately 100:1.

GRAPH #1

Sample 2C-3

Time (sec)	Temp. °c
0	-18.0
15	-19.0
30	-21.0
45	-22.0
60	-23.0
75	-23.0
90	-23.0
105	-23.0
120	-23.5
135	-24.0
150	-24.5
165	-26.0
180	-26.5

GRAPH #2

1:1

Time (sec)	Temp. °c
0	3.0
15	-3.0
30	-7.0
45	-13.0
60	-17.0
75	-19.5
90	-17.5
105	-17.8
120	-18.0
135	-18.2
150	-19.0
165	-20.5

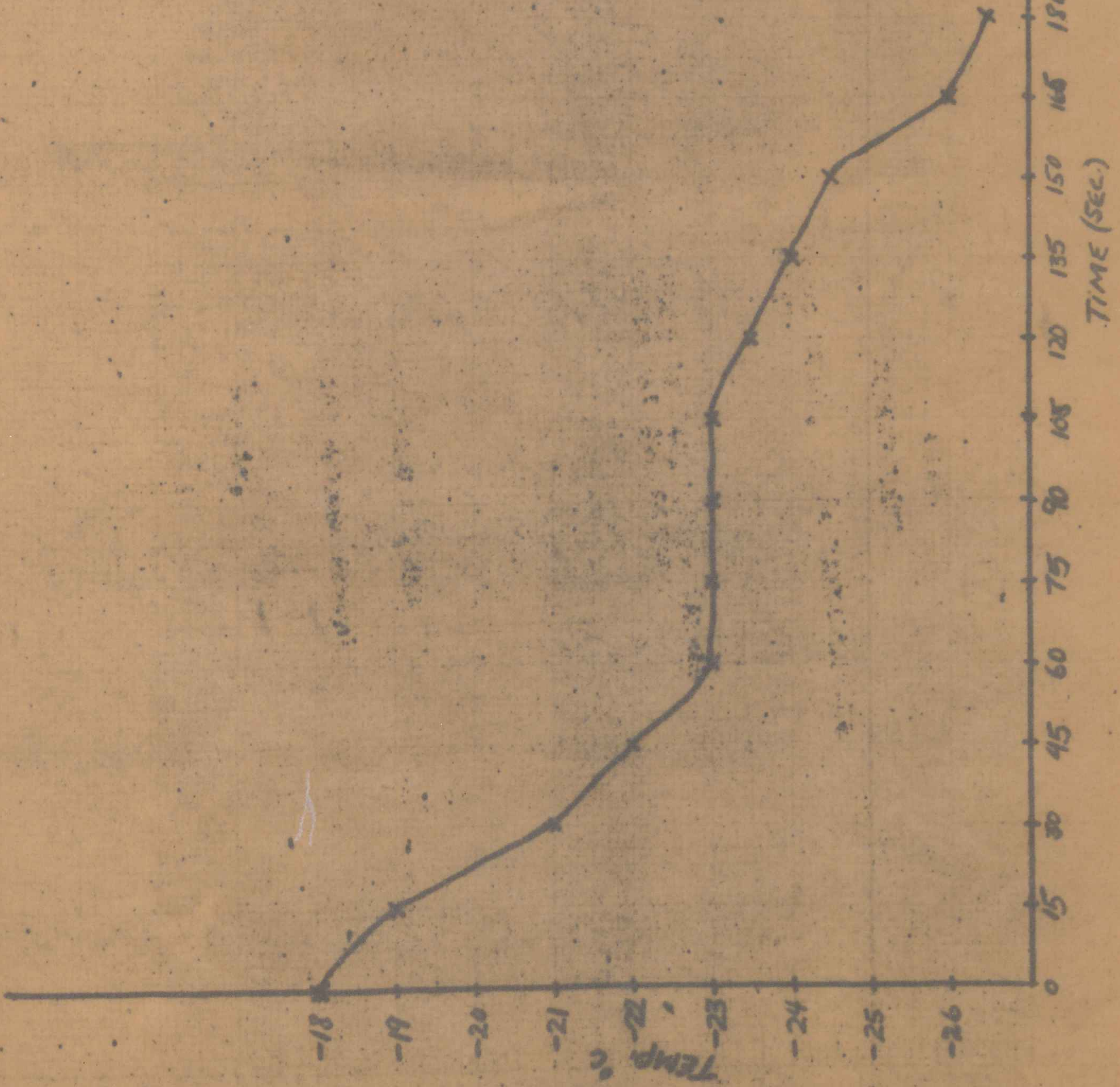
GRAPH #3

3:1

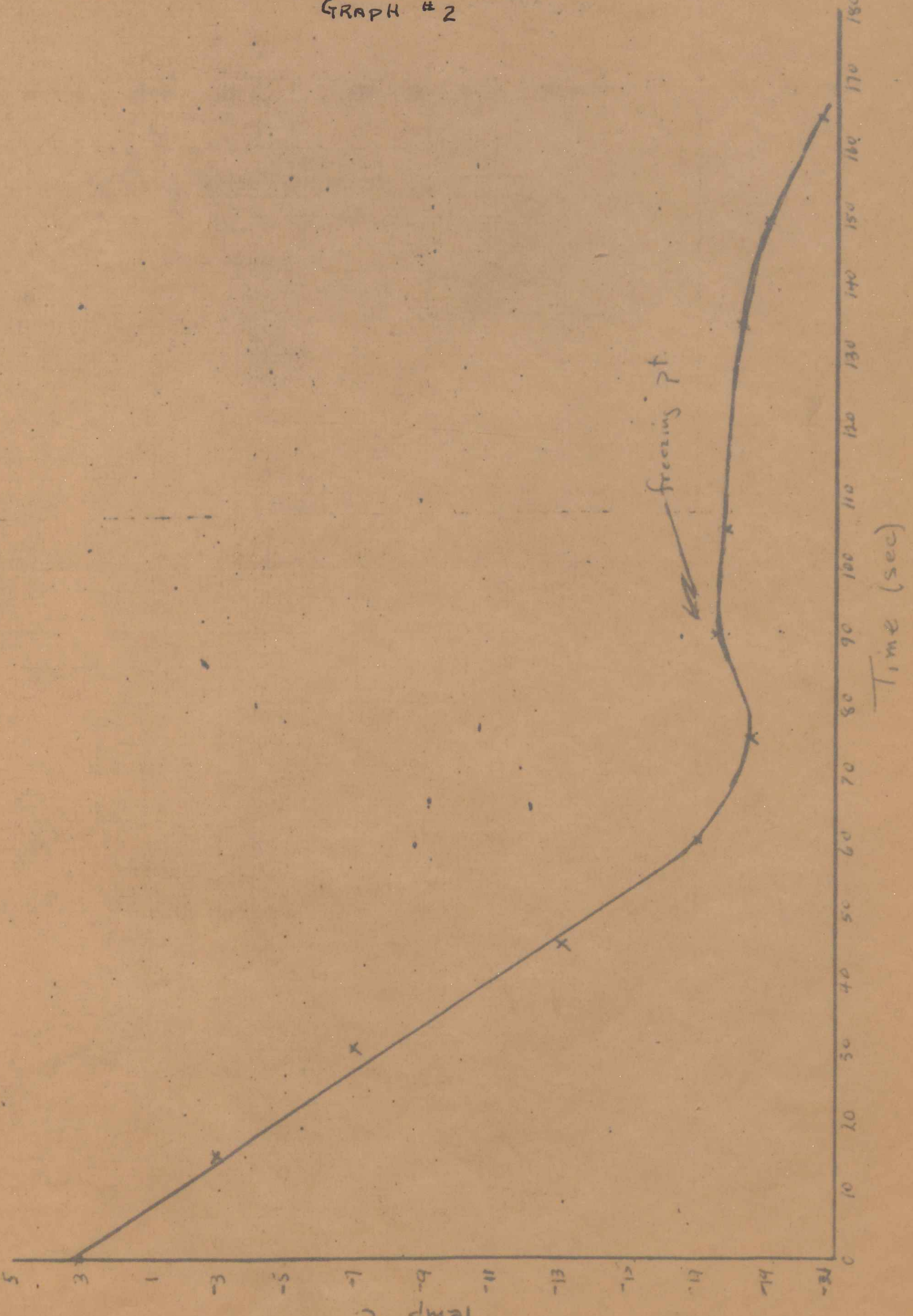
Time (sec)	Temp. °c
0	-19.0
15	-20.5
30	-22.5
45	-21.2
60	-21.3
75	-22.7
90	-25.0
105	-27.0
120	-29.3
135	-30.5
150	-31.0
165	-31.0
180	-29.2
195	-27.0
210	-24.7
225	-23.2
240	-22.7
255	21.5
270	-21.2
285	-21.2
300	-19.5

Sample 2C-3 shows a melting point of -23.0°c from the graph(See Graph #1.) This is quite far from the reported

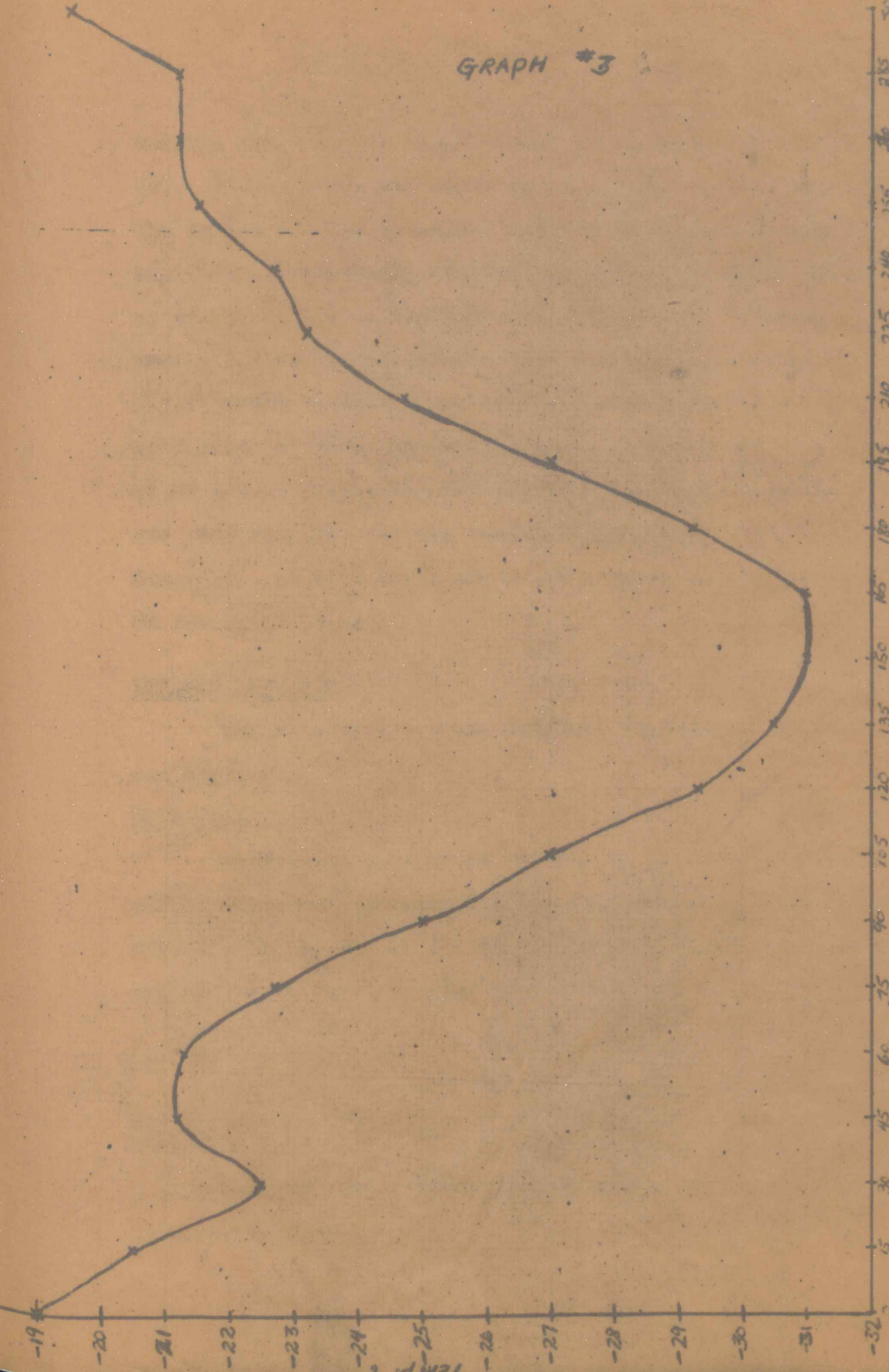
GRAPH #1


-18
-19
-20
-21
-22
-23
-24
-25
-26
TEMP. °C
0
15
30
45
60
75
90
105
120
135
150
165
180
TIME (SEC.)

GRAPH #2


freezing pt
Time (sec)
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
Temp °C
5
3
1
-3
-5
-7
-9
-11
-13
-15
-17
-19
-21

GRAPH #3


TIME (SEC.)
0
15
30
45
60
75
90
105
120
135
150
165
180
195
210
225
240
255
270
285
300
-19
-20
-21
-22
-23
-24
-25
-26
-27
-28
-29
-30
-31
-32

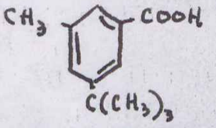
melting point of the 1,3,4 isomer which melts at -31.0°c (8). The 1,3,5 isomer melts at -21.5° (8) which shows that the sample 2C-3 is primarily 1,3,5 with a small amount of impurity which lowered the melting point. Graph #2 shows my sample 2C-3 with Nigriny's in a 1:1 ratio. Nigriny's pure 1,3,5 melted at -17.0°. The 1:1 ratio melted at -17.8° which shows that my product is essentially the same as Nigriny's but a little less pure. However, as th e amount of my sample increases, the amount of impurity increases, and this accounts for the lower melting point (-21.2°) in Graph #3. This is still above the literature melting point of the 1,3,5 isomer.

INFARED SPECTRUM

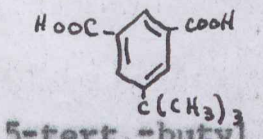
The same spectrum was obtained for both my sample and Nigriny's.

OXIDATIONS

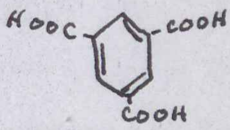
Oxidations were tried by Nigriny using both dichromate and permanganate as oxidizing agents. Several trials were run on both my samples and Nigriny's with hopes of obtaining any of the following acids:



5-*tert.*-butyl-3-methyl-
1-benzoic acid

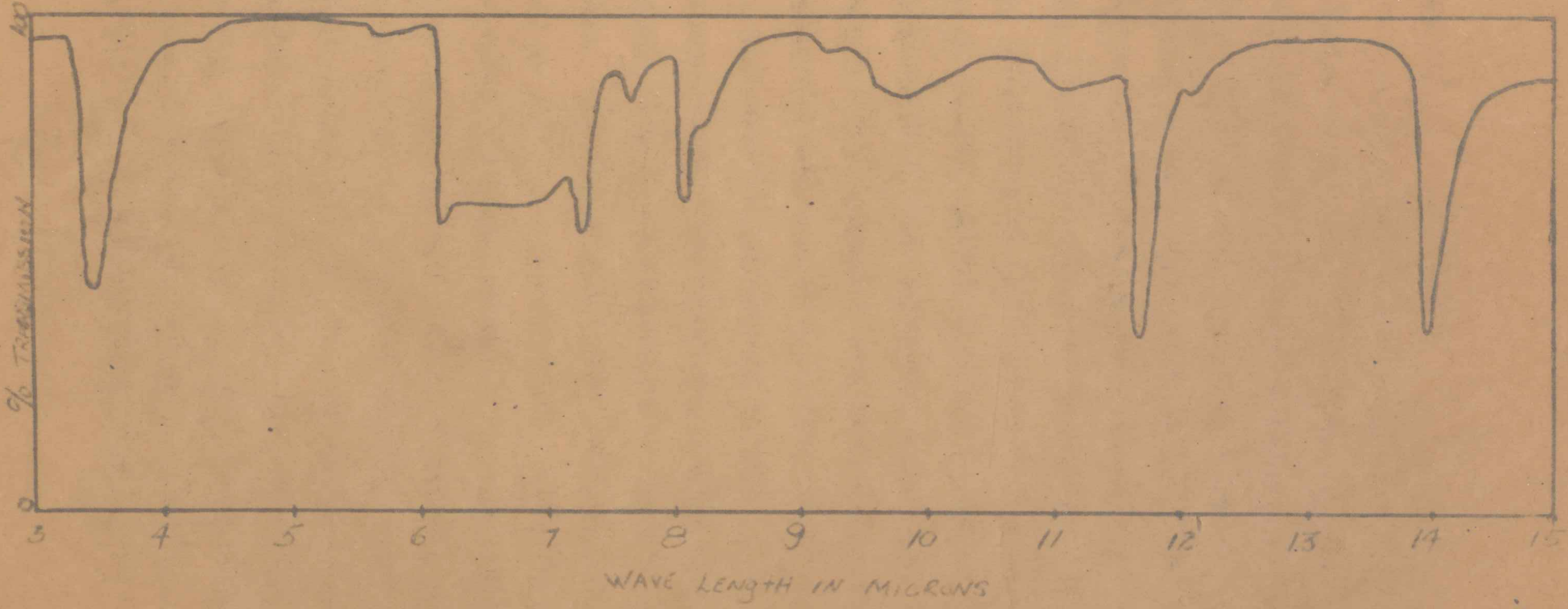


5-*tert.*-butyl
isothallic acid



trimesic
acid

Although many trials were run, none of the above acids could be isolated.



Sample: 2C-3-

1,3 dimethyl 5 t-Butyl Benzene

MONONITRATION (2)

The nitration was run on sample 2C-3 using a method similar to the nitration of mesitylene. The reaction was carried out on the micro scale using a 50 cc three necked flask equipped with a mechanical stirrer, a thermometer and a dropping funnel. Exactly 2.68 grams of the sample was placed in the flask along with three grams of acetic anhydride. The reaction mixture was cooled bdow 10°c in an ice bath. A solution of 1.575 grams of fuming nitric acid in 1 gram of glacial acetic acid and 1 gram of acetic anhydride was added, with stirring, over a period of forty minutes while the temperature was kept between 15° and 20°c.

After the addition of the nitric acid solution was complete, the reaction mixture was allowed to sit overnight at room temperature. The flask was warmed with stirring in a water bath to 50°c and maintained at this temperature for ten minutes. The cooled reactions were then poured slowly into 30 cc of ice water and stirred. About 15 grams of sodium chloride was added and the aqueous layer was decanted and extracted with 200 cc of ether. The ether layer was added to the mononitro residue and this etheral solution was washed with 30 cc portions of 10% sodium hydroxide until the water extract was distinctly alkaline. The ether was evaporated off using a steam bath. The residue was steam distilled and the product collected. The crystals were recrystallized from methanol. The crystals melted

79° - 81°c. The yield was 25%.

Sample 2C-3

REACTANT	WT. USED	MOLES
Acetic Anhydride	2.17 g	0.0217
Sample 2C-3	2.00	0.0123
Nitric Acid (fuming)	1.17	0.0186
Acetic Acid	2.00	0.0123
Acetic Anhydride	0.73	0.0072

Yield- 0.50 g   0.50/2 x 100 = 25%
M.P. 79°-81°c

Heiber, a chemistry 12 student, did the mononitration using the same procedure but different amounts of reactants. He also obtained a yield of 25%. He carried out three crystallizations with the final crystallization giving a M.P. of 63°-79°c.

Sample 2C-3

REACTANT	WT. USED	MOLES
1,3,5 isomer	2.68 g	0.0166
Acetic Anhydride	3.00 g	
Nitric Acid (fuming)	1.575	0.025
Acetic Acid	1.000 g	
Acetic Anhydride	1.000 g	

Yield- 0.83 g   0.83/2.68 x 100 = 25%

PRODUCT	M.P. RANGE °c
1st cryst. - 0.97 g	47°-70°
2nd cryst. - 0.89 g	53°-77°
3rd cryst. - 0.83 g	63°-79°

The Journal of Organic Chemistry (3) describes mononitration as a way of proving the structure of the 1,3,5 isomer. The nitration in this article was carried out using the same instructions I used. They got a yield of 66% and a product which melted at 84°-85°.

Since my yield of mononitration product is low the most that I can say is that there is 1,3,5 isomer present. The question of the purity of the sample will have to be shown by other methods of analysis such as vapor phase chromatography.

REFRACTIVE INDICES

The literature values of the refractive indices were taken as a possible means of identification. The refractive index at 25°c for the 1,3,4 isomer is 1.4909. The refractive index at 25°c for the 1,3,5 isomer is 1.4935. The fraction 2B-1, n_D^{25} - 1.4910 was thought to be the 1,3,4 isomer but results from the vapor phase proved that it was the 1,3,5 isomer with some m-xylene (n_D^{25} - 1.4951.) The m-xylene does not account for the low refractive index of sample 2B-1. There might possibly be some tert.-butyl alcohol

(n_D^{25}-1.3858). This is probably very unlikely. Those fractions above the refractive index of the 1,3,5 isomer had small amounts of high boiling impurities which showed up on vapor phase also.

GAS CHROMATOGRAPHY

Chromatographic methods have been used since 1951. The theory of separation is based on the fact that the material to be separated distributes itself between two phases, one of which is mobile. The stationary phase is either a liquid or a solid and the moving phase is a liquid or a gas. Gas Chromatography is so named because the mobile phase is a gas (10).

Gas Chromatography separates mixtures by retarding various components of the mixture in the stationary phase. These various components are retarded in the column by their interaction with the stationary phase. Each component remains in the column for a certain period of time, called retention, before it passes through the rest of the column and reaches the detector. The difference in partition coefficients is the basis for gas-liquid chromatography and the difference in absorbtion coefficients is the basis for gas-solid chromatography.

The carrier gas (mobile phase) used should be almost completely inert to the stationary phase. It should also be different from the vapors of samples being separated. A gas of low density and high thermal conductivity gives the best sensitivity. Carrier gases used are hydrogen, helium and nitrogen. Both hydrogen and helium are the best, because they meet the above standards. Helium is most commonly used because of the explosive nature of hydrogen.

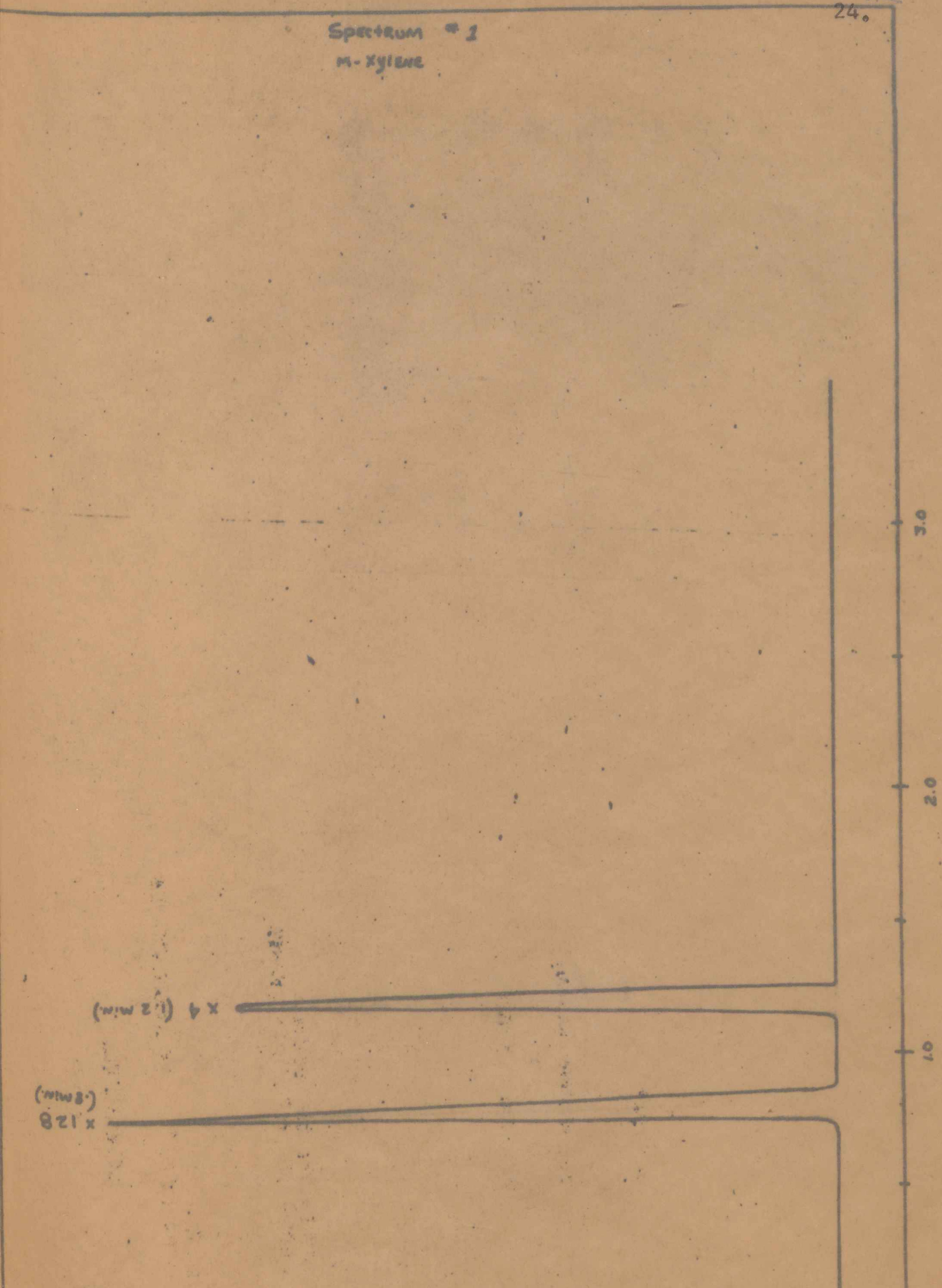
There are many choices which could be used for the stationary phase. Generally, the fixed phase which is involatile at operating temperature is best. Although high molecular weight substances should be appropriate here, low-molecular wieght substances have low viscosites which increase column efficiency. Therefore, a compromise between both factors (high molecular weight and low viscosity) must be effected.

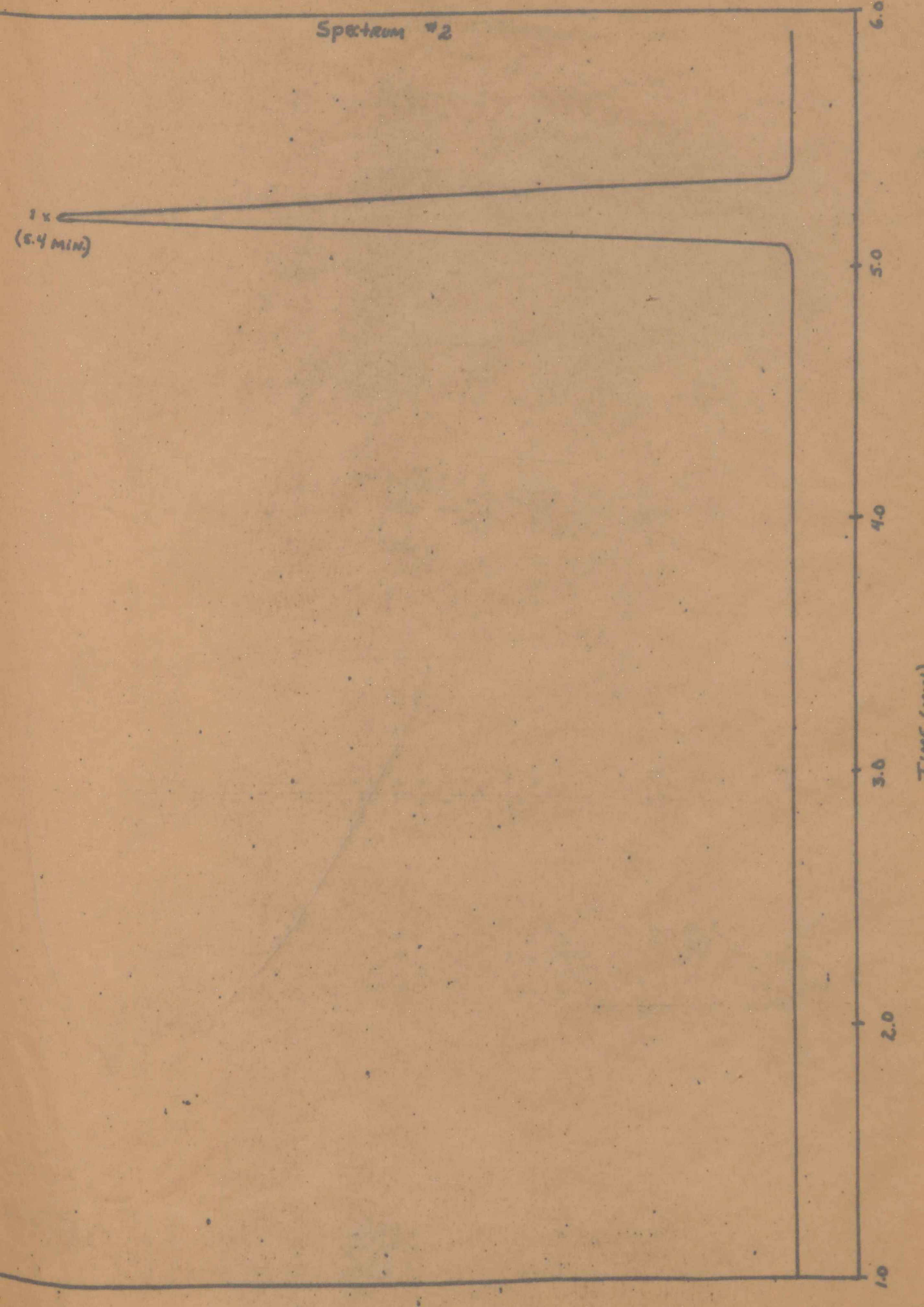
After the vapors have passed through the column, they reach the detector which analyzes them and records the results on paper. The detector should have (1) as high sensitivity as possible (2) quick response so as to detect all changes in vapor concentration and (3) linear response. It should not destroy or absorb any vapors in case they are to be trapped out after passing through the detector.

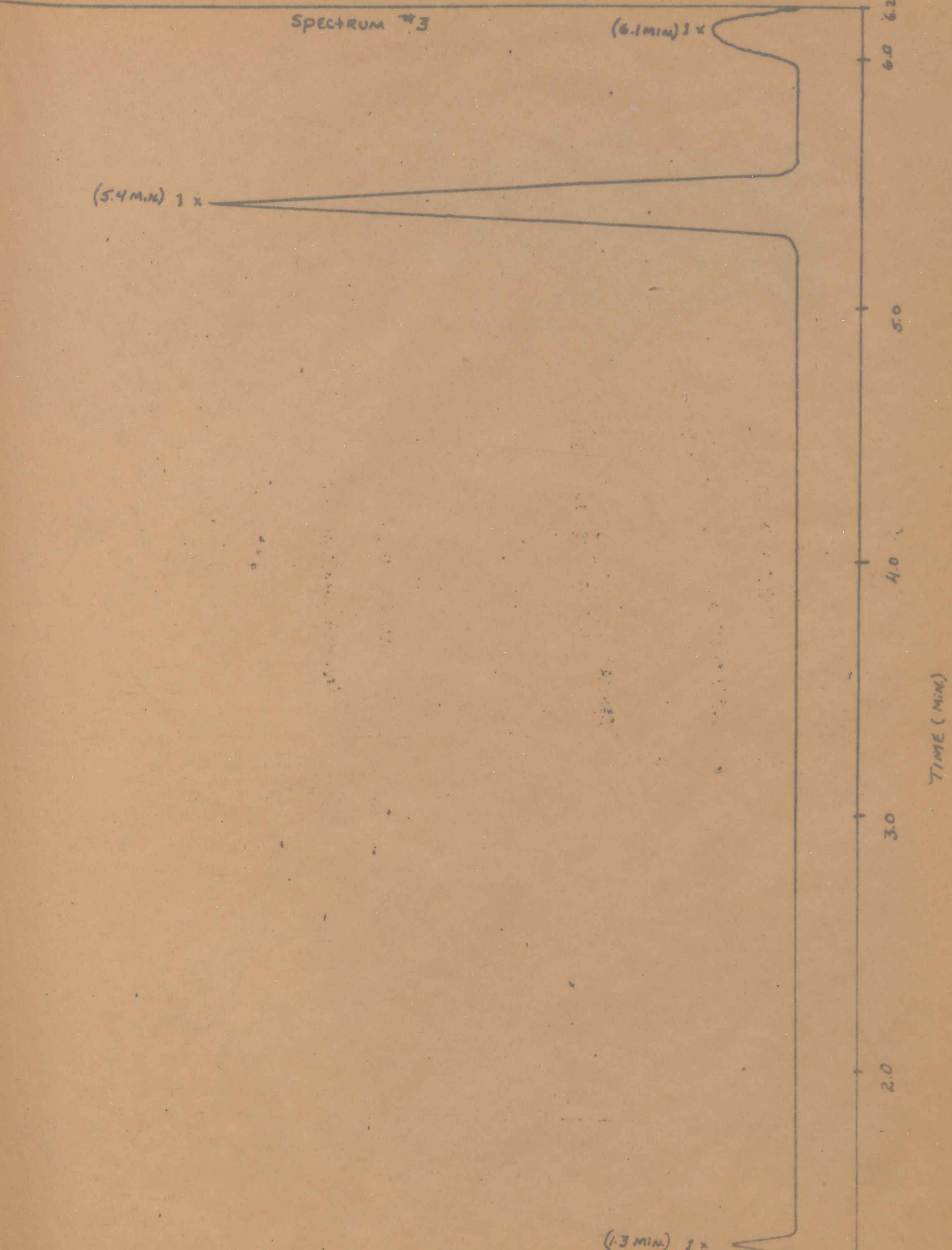
Qualitative results are obtained by comparing the retention time of an unknown substance with literature retention times of known substances run at the same flow, temperature, and type of column. The flow should be kept constant since it effects the retention time. The temperature is more important since a 1° change in temperature will cause a change in retention time in the order of 5%.

The Perkin - Elmer vapor fractometer (model 154-D) was used to analyze the results. Column R (Ucon polyglycol LB-550-x) was used. This column is a moderately polar general purpose column for medium temperature ranges

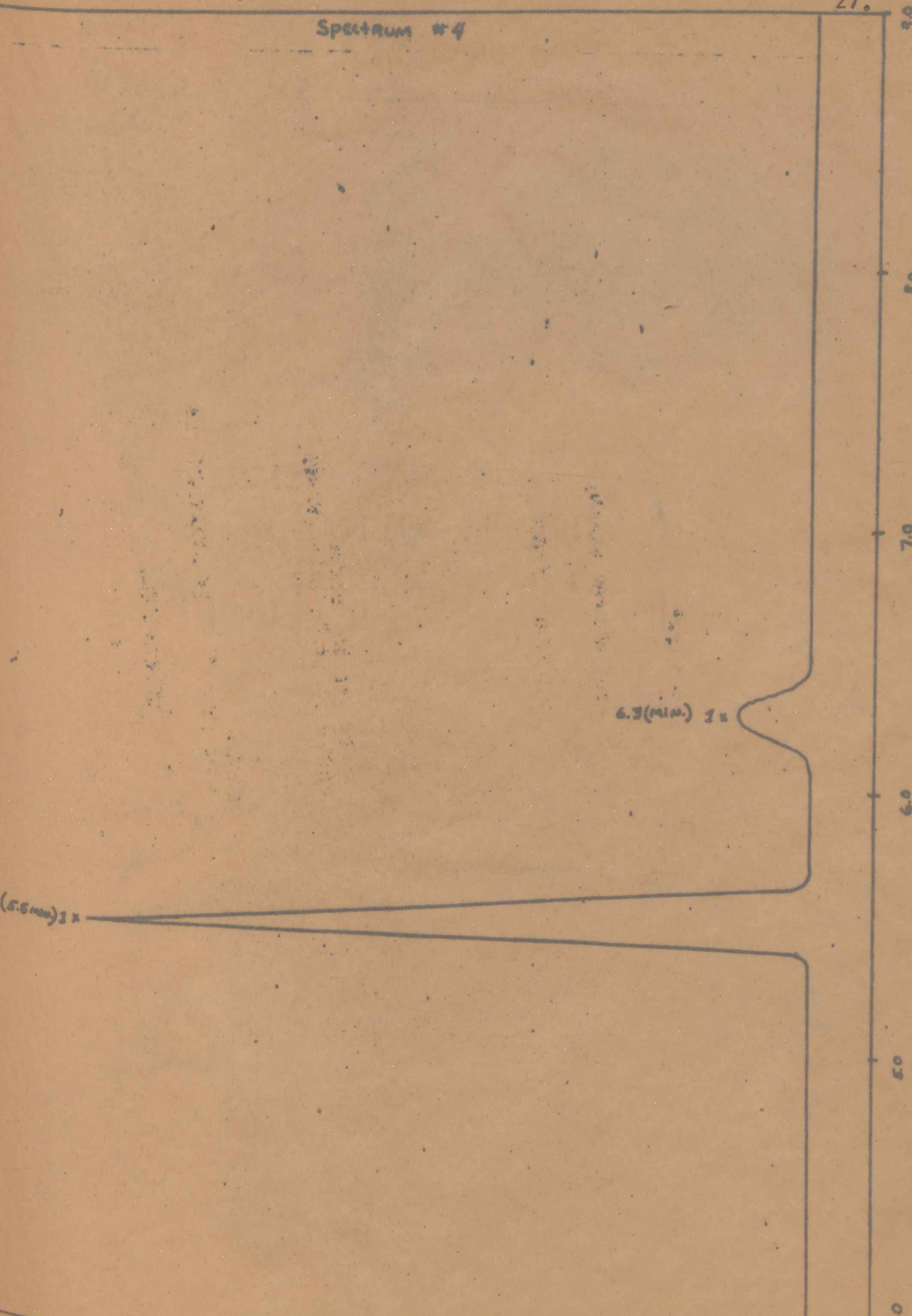
Spectrum #1
m-xylene

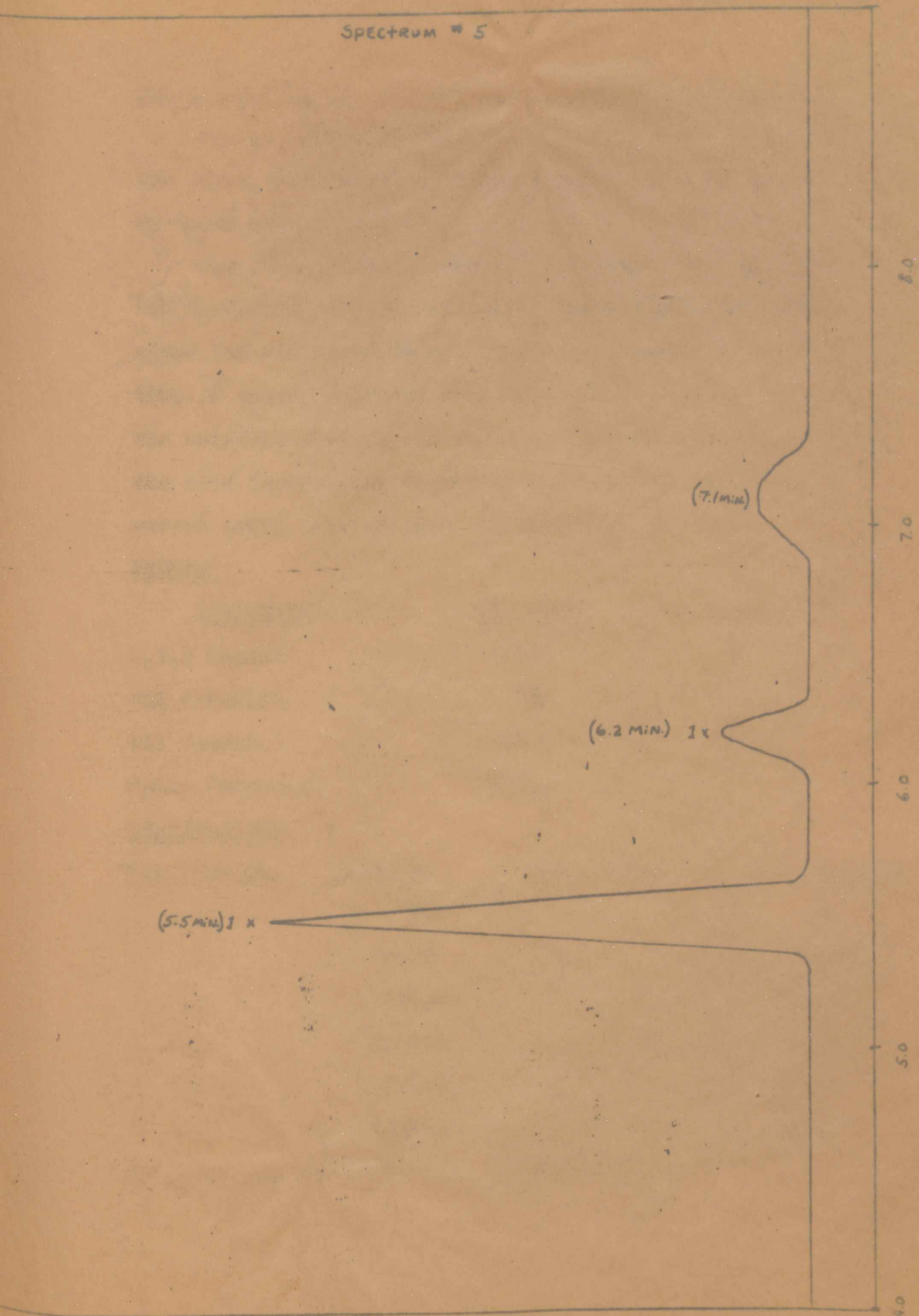



Spectrum #2
1 x
(5.4 MIN)
6.0
5.0
4.0
3.0
2.0
1.0
TIME (MIN)


SPECTRUM #3
(6.1 MIN) 1 x
(5.4 MIN) 1 x
(1.3 MIN) 1 x
6.2
6.0
5.0
4.0
3.0
2.0
1.2
TIME (MIN.)

Spectrum #4




SPECTRUM # 5
(7.1 MIN)
(6.2 MIN.) 1 x
(5.5 MIN) 1 x
8.0
7.0
6.0
5.0
4.0
TIME (MIN)

CHLOROMETHYLATION of 1,3-dimethyl-5-tert.-butylbenzene

Two methods were used for the chloromethylations, the first carried out by Carpenter (12) and the second by Nauta and Dienske (7).

One mole (162g) of the 1,3,5 isomer, 75 g of 40% formalin, and 200g of concd. hydrochloric acid were mixed and warmed to 50°c. Then with constant stirring, 400g of concd. sulfuric acid was added. After 5 3/4 hrs. the reaction mixture was cooled. The layers were separated, the acid layer being discarded and the oily layer was washed until free of acid and distilled in vacuo.

RESULTS

REACTANTS	WT. USED	MOLES
1,3,5 isomer	162g	1
40% formalin	75g	1
HCl (concd.)	200 g	2
H_2SO_4 (concd.)	400 g	

DISTILLATION

FRACTION NO.	TEMP.°c	PRESSURE,mm	WT. OF FRACT.g
1	- 93	1	
2	94-95	1	34.5
3	95-100	1	58.1
4	100-112	1	2.6
5	115-123	1	1.5
6	123-240	1	10.7

MP (fraction #6) -28°   yield -10.7g

In the second method of the mole (162g) of the 1,3,5 isomer was mixed with 583 g of concd. hydrochloric acid and 75g of 40% formalin. The reaction mixture was stirred for twelve hours during which time a steady stream of anhydrous hydrogen chloride gas was passed through it. The mixture was kept at 35° throughout the whole reaction. After twelve hours the reaction mixture was cooled, separated and the oily distilled in vacuo. Two vacuum distillations were carried out since the first column did not give the desired fractionation. The second column consisted of 1' x 3/4" packed with 1/32" stainless stell helices.

RESULTS AND DISCUSSION:

REACTANTS	WT. USED g.	MOLES
1,3,5 isomer	162	1.0
HCl	583	19.6
40% formalin	75	1.0

1st DISTILLATION

FRACT. NO.	TEMP.°c	PRESS.
1	85-100	3mm
2	100-112	3mm
3	112-120	3mm
4	120-144	3mm

2nd DISTILLATION

All the above fractions were redistilled in the second vacuum set up which was described above.

FRACT. NO.	TEMP. °c	PRESS	WT.
1	- 120	40 mm	29.4
2	120-150	38 mm	19.1
3	150-180	32 mm	19.0

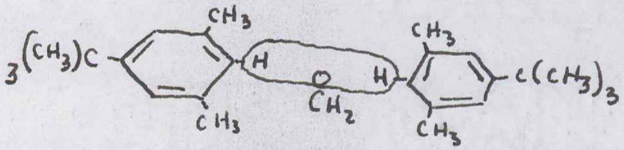
The remaining residue (fraction #4) was removed and distilled at atmospheric pressure.

FRACT. NO.	TEMP.°c	WT.
4-1	180-218	8.6
4-2	218-242	3.5
4-3	242-	3.5

There was no yield out of a possible yield of about 116 g. reported by (5).

In the first method fractions 1,2, 3 were almost pure 1,3,-dimethyl 5-tert.- butylbenzene. Samples 4 and 5 were in the intermediate range. The product was collected in the last fraction (fraction #6). This soon crystallized to form white needle-like crystals. The actual melting point is 27° (12) and its boiling range is 120-121 at mm (12).

In the second method all fractions in the first distillation were contaminated with the 1,3,5 isomer which was the reason for switching over to the second column. Fractions 1-3 of the second distillation were primarily the 1,3,5 isomer. No crystals were formed in any fraction. The crystals obtained were from the liquid being distilled. These were formed in the flask overnight, and taken out before the liquid was heated. The residue which boiled in a range of about 300-400°c was a viscous oil which formed crystals on standing. Since this was a condensation reaction, formaldehyde helped to join two rings:



These methods of preparation were followed exactly and therefore the yields should be much better than they were. I can think of no reason why they did not produce.

SUMMARY:

This experiment has shown (1) that there is a discrepancy in the literature as far as isomers obtained and (2) that the Friedel Crafts reaction using aluminum chloride gave the highest yields and the highest degree of purity. Proof of structure would have been more conclusive if we had some 1,3,4 isomer. There is no explanation why the chloromethylations did not give better yields. Since the proof of structure took a long period of time the end product, 1,2,3-trimethylbenzene, was not obtained.

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