THE PREPARATION OF CERTAIN ESTERS OF 2-THIOPHENE CARBOXYLIC ACID

A THESIS

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Master of Science in Chemistry

by

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THE PREPARATION OF CERTAIN ESTERS OF

2-THIOPHENE CARBOXYLIC ACID

Approved:

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Acknowledgement is also hereby made to the Socony-Vacuum Oil Company, Inc., for their cooperation in furnishing a quantity of 2-acetyl thiophene to be used in this problem and to the Chemists of that organization for information pertaining to their previous experience with the compound.

PREFACE

This investigation was conducted in conjunction with academic work pursuant to receiving a degree of Master of Science in Chemistry under the auspices of the Education Program of the United States Air Force, which is administered by the United States Air Force Institute of Technology, Civilian Institutions Division, with headquarters at Wright-Patterson Air Force Base, Dayton, Ohio.

The writer is very appreciative of the opportunity to further his education and better equip himself as an officer in the United States Air Force through this program.

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THE PREPARATION OF CERTAIN ESTERS OF

2-THIOPHENE CARBOXYLIC ACID

CHAPTER I

INTRODUCTION

Much interest has been shown previously in finding useful derivatives of thiophene compounds. Recently this interest has centered around finding useful derivatives for 2-acetyl thiophene, which is the starting compound in this investigation.

It was theorized that 2-acetyl thiophene, being much the same structurally as acetophenone, should have the same general chemical characteristics and have similar chemical reactivity as the latter. Since acetophenone is easily oxidized to benzoic acid, it was felt that the 2-acetyl thiophene could be just as easily converted to its acid, 2-thiophene carboxylic acid, and this acid in turn used to prepare esters by reacting it with the various alcohols.

A complete literature survey was made and the assumptions cited above were found to be factual. As was expected, Beilstein[1] cited several references for methods of preparing 2-thiophene carboxylic acid by various means. One of the methods cited was that of Curtius and Thyssen[2] by oxidizing 2-acetyl thiophene with sodium permanganate.

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[1]Beilstein, 18, p. 289 (1934).

[2]T. Curtius and H. Thyssen, J. prakt. Chem. (2) 65, pp. 6-7, (1902).

It will be noted later (Chapter III, Experimental) that the results using this method were not satisfactory and another method was exploited.

The reading also indicated that the preparation of only one ester of 2-thiophene carboxylic acid had been reported, that being the Ethyl Ester.[3] Therefore, it was decided that an attempt would be made to prepare a series of the esters and compare their physical properties.

The following recorded data pertaining to 2-thiophene carboxylic acid and the ethyl ester was found:

> 2-Thiophene Carboxylic Acid, alpha-Thiophenic acid, Thenoic Acid: $C_5H_4O_2S$, MW 128, needles from water mp 126-7° C, very soluble hot water, ethyl alcohol, and ether; sparingly soluble in petroleum ether; has irritating odor. Ethyl Ester: $C_7H_8O_2S$, MW 156; bp 218° C, 115° C/25 mm, 96° C/18 mm; density 1.162 at 16° C.[4]

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[3] Ibid.

[4] Heilbron, Dictionary of Organic Compounds, p. 758 (1946).

CHAPTER II

PURPOSE OF THIS INVESTIGATION

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As stated in Chapter I, this problem was entered into with the object being to prepare a number of the esters of 2-thiophene carboxylic acid and compare the physical constants of the pure products.

Since 2-acetyl thiophene is the "parent" compound, the first step in the experimental portion of the investigation deals with the preparation of the 2-thiophene carboxylic acid by oxidation of 2-acetyl thiophene. It might be mentioned that the acid is available on the market, but the price is almost prohibitive at this time, especially if large quantities are to be used in research.

Aside from the aspects of Chemistry involved with respect to technique and acceptable processes, the writer has placed a great emphasis on the practical aspects of the investigation. Such things as economy of materials and using available equipment without ordering higher priced and more satisfactory pieces has been practiced. Furthermore, the importance of purity of the products and accurate physical constants have been placed above high yields. In other words, at times high yields have probably been sacrificed to insure obtaining pure products with constants worthy of publication. It is felt that if accurate results are reported, methods can be improved and yields increased in future investigations.

CHAPTER III

EXPERIMENTAL

CHAPTER III

EXPERIMENTAL

The Preparation of 2-Thiophene Carboxylic Acid

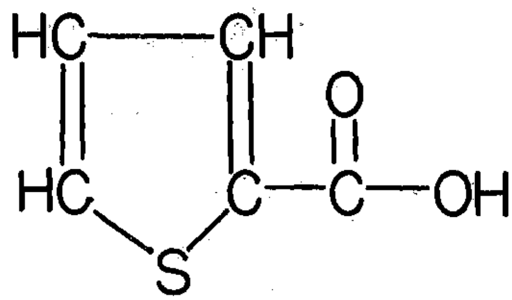

Figure 1

In the preliminary experimental work an attempt was made to utilize the method of preparation as cited by Curtius and Thyssen.[5]

A 3-liter 3-neck flask was fitted with an efficient electric stirrer and a dropping funnel. Twelve grams (0.3 mole) of sodium hydroxide was dissolved in one liter of water in the flask. To the sodium hydroxide solution 11.5 grams of 2-acetyl thiophene was added, forming an immiscible solution. Since the sodium permanganate was not available, an equivalent amount of potassium permanganate was dissolved in one liter of water and admitted dropwise through the dropping funnel with stirring. This solution consisted of 68.3 grams (0.43 moles) of potassium permanganate dissolved in the one liter of water.

The process included allowing the reaction mixture to stand over-

[5]Curtius and Thyssen, loc. cit.

night and then heating on a water bath until all green color disappeared. The solution was filtered and hydrochloric acid was added to the solution until only weakly alkali. The solution was then evaporated to about 250 cc and, after cooling, a mixture of 9 grams of 30% hydrogen peroxide and 8 grams of water was added. The mixture was then warmed for four hours on a water bath and acidified with hydrochloric acid. Upon cooling the 2-thiophene carboxylic acid precipitated out, but the yield and purity was very poor.

Other attempts using the same procedure produced equally poor results. A search was begun for a better method of preparation.

Through Dr. E. Emmit Reid, word was received that industrial chemists at the Socony-Vacuum Oil Co., Inc., had experienced considerable success preparing the acid by using a method analogous to that reported by Newman and Holmes[6] for the preparation of beta-naphthoic acid. It was decided to try this method in hopes of finding a successful method of acid preparation. The method entailed oxidation of a ketone by using a freshly prepared sodium hypochlorite solution according to the following reaction:

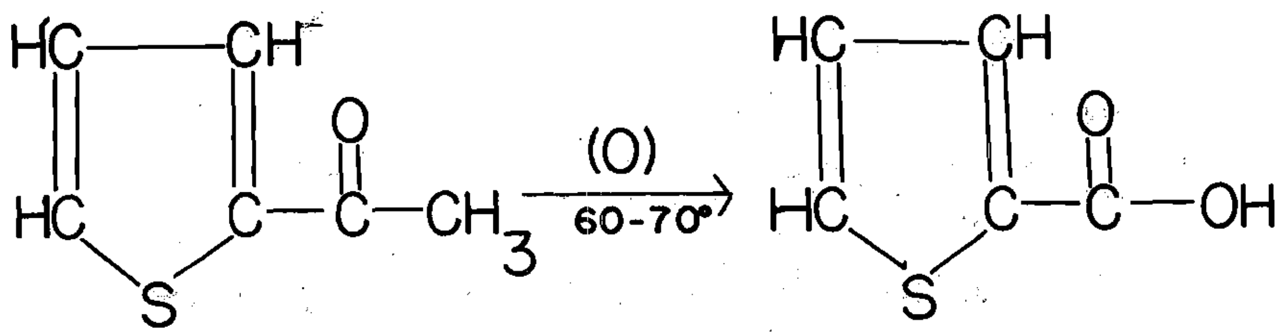

Figure 2

[6] M. S. Newman and H. L. Holmes, Organic Synthesis, Coll. Vol. II, p. 428 (1943).

In the sodium hypochlorite oxidation of the 2-acetyl thiophene, a 3-liter, 3-neck flask was fitted with an efficient stirrer, a thermometer, and a delivery tube. Into the flask was placed 218 grams (5.45 moles) of sodium hydroxide and 300 cc of water to effect solution. The solution was allowed to cool to room temperature and 1250 grams of cracked ice was added to the flask. The reaction apparatus was placed under the hood and a tank of commercial chlorine gas was connected to the delivery tube into the flask. Chlorine gas was bubbled in with stirring and maintaining the temperature at zero degrees until a gain in weight of 161 grams was noted by occasionally weighing the flask and contents. The ice originally added was sufficient to maintain the zero temperature. The delivery tube was then replaced by a dropping funnel and the solution warmed to 55° C. To the mixture, 63 grams (0.5 mole) of 2-acetyl thiophene was added dropwise over a period of 30-40 minutes with stirring and maintaining the temperature at 60-70° C. The mixture was stirred 30 minutes longer after addition of the 2-acetyl thiophene and any excess sodium hypochlorite was destroyed by adding a solution of 50 grams of sodium sulfite in 200 cc of water. The solution was tested with starch-iodide paper to make certain that all chlorine was gone. The solution was then cooled to room temperature, placed in a 4-liter beaker and carefully acidified with concentrated hydrochloric acid. A nice, white precipitate of 2-thiophene carboxylic acid precipitated out with violent foaming upon acidification. Constant stirring should be maintained during the careful acidification.

Yields using this method were very high (over 90%), and the purity of the compound as denoted by the melting point was very good, being sufficiently pure not to require any type of purification. The melting point of the product was found to be 126-128° C as compared with a literature value of 126-127° C.

Several batches of 2-thiophene carboxylic acid were prepared by this method to provide a supply of the acid with which to prepare the esters.

This concluded the preliminary experimental work and efforts were concentrated on the preparation of the various esters.

The General Method of Esterification

The general method of esterification introduced by E. Fischer[7] was chosen as the method of ester synthesis to be used in this research problem. This method consists of the refluxing of an acid with excess alcohol in the presence of about 3% of dry hydrogen chloride or sulfuric acid as a catalyst. It was decided to use dry hydrogen chloride as the catalyst.

Figure 3, page 9 following, indicates a type reaction for esterification using the Fischer method.

[7]Louis Feiser and Mary Feiser, Organic Chemistry, p. 178, (1944).

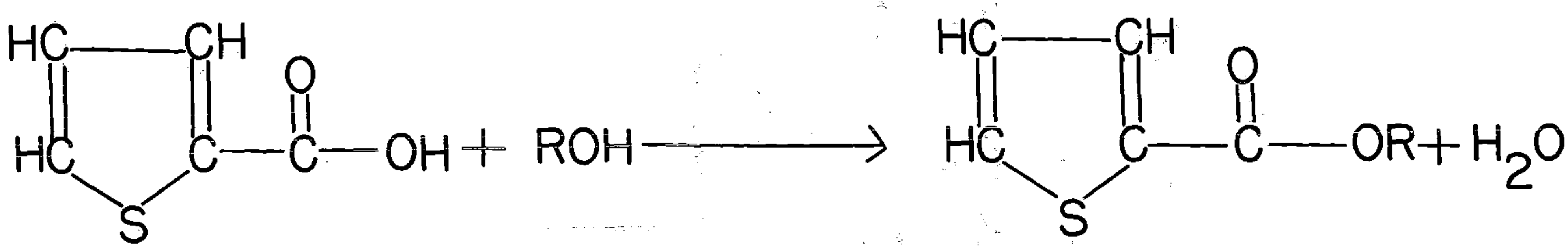

Figure 3

The Preparation of the Ethyl Ester of 2-Thiophene Carboxylic Acid

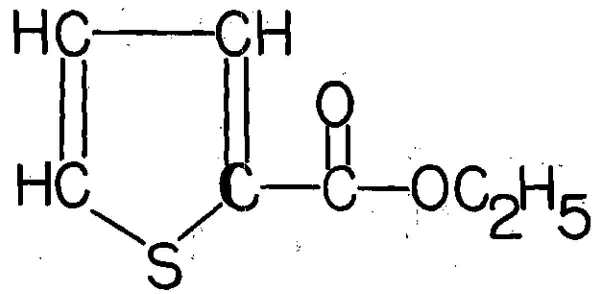

Figure 4

It was decided to prepare the ethyl ester first since it had been previously prepared[8] and some physical constants were available.[9] In doing this, an indication of the probable future success of the investigation could be ascertained and any glaring errors in technique could be worked out before attempting to prepare the unknown esters.

This being the first attempt, the reaction apparatus was relatively crude. It will be noted later that as subsequent preparations were made, the apparatus was constantly improved as a result of the knowledge gained through experience.

The reaction apparatus consisted of a 200 ml 3-necked pyrex flask fitted with a delivery tube, a reflux condenser, and a thermometer. A Bunsen burner was used as a source of heat and a water trap was fitted to the reflux condenser to safely carry away any excess hydrogen chloride

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[8]Curtius and Thyssen, loc. cit.

[9]Heilbron, loc. cit.

gas driven off.

The hydrogen chloride gas was produced by dropping concentrated hydrochloric acid into concentrated sulfuric acid. A safety trap was placed between the hydrogen chloride generator and the reaction flask.

In an effort to conserve starting materials, it was decided to conduct this experiment in small quantities. 0.05 moles (7 grams) of the 2-thiophene carboxylic acid was placed in the reaction flask with an excess of ethyl alcohol (25 grams). Since only about 3% dry hydrogen chloride is required to catalyze the reaction[10] the reaction mixture was saturated with the gas by bubbling it through the delivery tube prior to refluxing the mixture. The delivery tube was then replaced by a rubber stopper and heat applied.

The temperature of the refluxing mixture was noted periodically and stabilization of this temperature after four hours refluxing was assumed to indicate that the reaction was near completion.

The mixture was steam distilled with the distillate coming over as a colorless oil-water immiscible mixture. The distillate was then "salted out" with a saturated sodium chloride solution and extracted with ether. The ether solution was washed with a 5% solution of sodium bicarbonate until basic to litmus and then washed with water. The ether layer was dried over anhydrous sodium sulfate.

The ether was distilled off and the remaining product was distilled under 23 mm pressure, coming over at 111-113° centigrade. The literature lists the boiling point as 115° under 25 mm pressure.

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[10]Feiser, loc. cit.

The product is a clear, light brown, slightly oily liquid with a very pleasant odor. Redistillation under more reduced pressure caused the slight color to disappear.

The yield was calculated as 34.2% of the theoretical, but it must be again pointed out that high yields have been sacrificed for high purity. Furthermore, working in such small quantities would obviously result in decreased yields through mechanical losses.

From this "pilot" experiment the following conclusions were drawn:

(1) The method is successful and adaptable to this investigation.

(2) Larger quantities must be used to give larger yields facilitating determination of physical constants.

The Preparation of the Methyl Ester of

2-Thiophene Carboxylic Acid

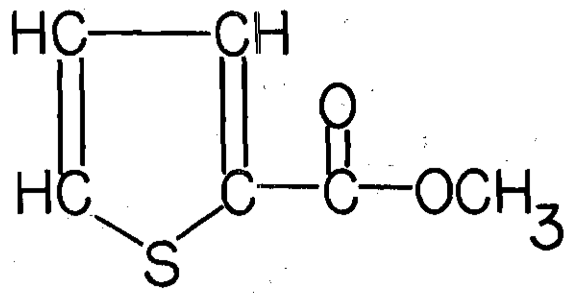

Figure 5

This experiment marks the first attempt in this investigation to prepare an ester of 2-thiophene carboxylic acid not previously prepared or recorded in literature. It also marks the first modification of equipment and technique as a result of experience.

Larger quantities of the starting material were used which necessitated the use of a larger reaction flask. In this instance a three liter 3-neck flask was used and was fitted with a delivery tube, reflux condenser, and thermometer. The reflux condenser was connected to a water trap to eliminate the excess hydrogen chloride gas.

Commercially prepared hydrogen chloride gas was used in preference to generator-produced gas to saturate the reaction mixture and a controllable electric heating source of the trade name "Ful-Kontrol" replaced the Bunsen burner as a heat source.

2-Thiophene carboxylic acid in the amount of 0.25 mole (32 grams) was placed in the reaction vessel with an excess of methyl alcohol (2.5 moles or 62 grams).

Heat was applied to the mixture causing refluxing. Again the reflux temperature was noted periodically and stabilization of this temperature taken as an indication of completion of reaction. The temperature stabilized after five hours refluxing.

Steam distillation, "salting out", ether extraction, drying, and vacuum distillation was carried out as indicated on pages 11 and 12.

The pure product distilled at 102° centigrade under a reduced pressure of 20 mm as a clear, colorless, slightly oily liquid with a very pleasant odor almost identical to the odor of methyl salicylate (oil of wintergreen).

A yield of 81.4% of the theoretical was obtained. Other physical constants will be treated in detail in Chapter IV.

The Preparation of the Propyl Ester of 2-Thiophene Carboxylic Acid

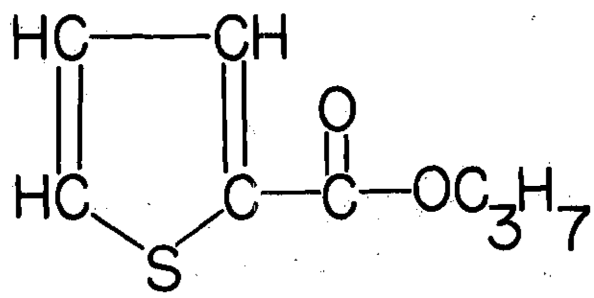

Figure 6

The same modified apparatus as described in the preparation of the methyl ester (page 13) was used in this preparation. Again commercially prepared hydrogen chloride gas was used as the catalyst.

2-Thiophene carboxylic acid in the amount of 0.25 mole (32 grams) was placed in the three liter reaction flask with an excess of n-propyl alcohol (2.5 moles or 122 grams).

Stabilization of the reflux temperature was again used as an indication of the completeness of the reaction. After six hours refluxing this temperature stabilized.

Steam distillation, "salting out," ether extraction, drying, and vacuum distillation was carried out as indicated on pages 11 and 12.

The pure product distilled at 126-128° under a reduced pressure of 20 mm and at 130° at a reduced pressure of 25 mm. Other physical constants will be considered in detail in Chapter IV.

A yield of 42% of the theoretical was obtained.

The Preparation of the Butyl Ester of 2-Thiophene Carboxylic Acid

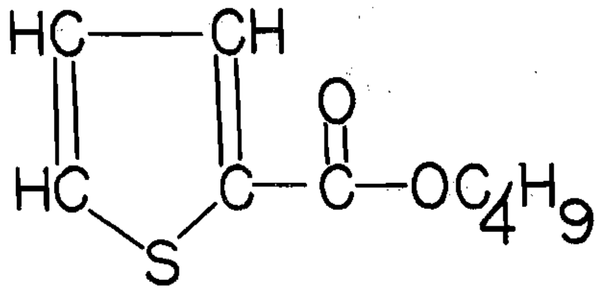

Figure 7

The same modified apparatus as described in the preparation of the methyl ester (page 13) was used in this preparation. Commercially prepared hydrogen chloride gas was used as a catalyst.

2-Thiophene carboxylic acid in the amount of 0.25 mole (32 grams) was placed in the three liter 3-neck flask with an excess of n-butyl alcohol (2.5 moles or 185 grams).

Stabilization of the reflux temperature used as an indication of the completeness of the reaction. After fourteen hours refluxing this temperature stabilized.

Steam distillation, "salting out," ether extraction, drying, and vacuum distillation was carried out as indicated on pages 11 and 12.

The pure product distilled at 134.5° under a reduced pressure of 20 mm. Other physical constants will be discussed in detail in Chapter IV.

A yield of 46.3% of the theoretical was obtained.

The Preparation of the Amyl Ester of

2-Thiophene Carboxylic Acid

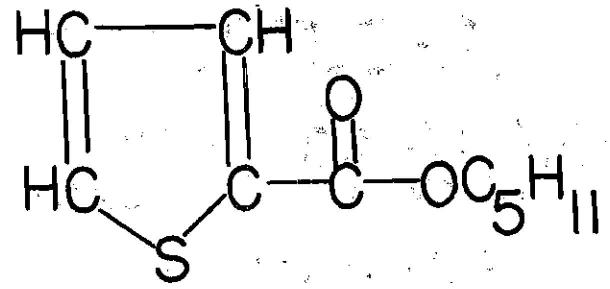

Figure 8

The same modified apparatus as described in the preparation of the methyl ester (page 13) was used in this preparation. Commercially prepared hydrogen chloride was used as a catalyst.

2-Thiophene carboxylic acid in the amount of 0.25 mole (32 grams) was placed in the reaction flask with an excess of n-amyl alcohol (2.5 moles or 220 grams).

Stabilization of the reflux temperature was used as an indication of the completeness of the reaction. After eight hours refluxing this temperature stabilized.

Steam distillation, "salting out," ether extraction, drying, and vacuum distillation was carried out as indicated on pages 11 and 12. It might be mentioned that the products became more difficult to steam distill as the series was ascended on the basis of larger R-groups.

Due to excessive bumping when distilling under reduced pressure, it was difficult to obtain a constant boiling point at 20 mm pressure considered accurate enough to report. The reader is referred to

Chapter IV. In the determination of physical constants discussed in this chapter, extreme care and the best possible technique with modifications of apparatus was used.

Bumping of the distillation mixture has been a problem in all the previous reduced pressure distillations and has become worse as the higher members of the series were prepared. The use of boiling chips used in conjunction with a capillary tube introduced below the surface of the liquid and fitted with a short section of rubber tubing and pinch clamp at the top did not suitably reduce the bumping.

Increasing tendency to decompose under reduced pressures of 20-25 mm previously used for distillation of the product has been noted. A lower pressure above the distillation mixture will be used.

A boiling point of 116.5° under a reduced pressure of 4 mm was obtained.

The yield of the pure product was 26.5% of the theoretical.

The Preparation of the Hexyl Ester of 2-Thiophene Carboxylic Acid

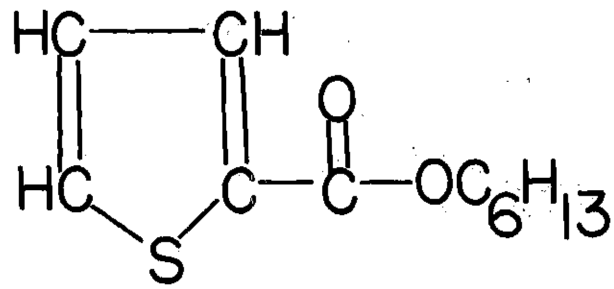

Figure 9

The reaction apparatus was greatly modified for this preparation. A 500 ml 1-neck pyrex flask with ground glass fitting was used for the reaction vessel. To this was fitted a Dean-Stark distilling tube receiver calibrated in 1/8 cc's to receive 10 cc of liquid from the reflux condenser, anything in excess of this amount returning to the reaction flask. To the top ground glass fitting of the distilling tube receiver was fitted a finger-type condenser with a matching ground glass fitting. This condenser served as the reflux condenser and to it was connected a water trap to safely carry away any excess hydrogen chloride driven off. A 500 ml heating mantle and a controllable variac were used as a source of heat.

2-Thiophene carboxylic acid in the amount of 0.25 mole (32 grams) was placed in the reaction flask with an excess of n-hexyl alcohol (1 mole or 102 grams).

The reaction mixture was saturated with commercially prepared hydrogen chloride gas prior to assembling the reaction apparatus.

The distilling tube receiver served as an excellent means of indicating when the reaction was complete. The refluxing mixture vapors rose and struck the cold finger of the condenser. The vapors then condensed and the liquid dropped into the receiver. The water present being heavier than the un-reacted alcohol fell to the bottom of the receiver forming a two layer system. The receiver being calibrated, it was very easy to note when the calculated amount of water formed in the reaction had deposited itself in the receiver.

Steam distillation was exceedingly difficult. Large volumes of water (steam) appeared to come over with very little product. This observation was found to be correct when the extraction process was carried to completion and a yield of only 8.7% of the theoretical was obtained. This was considered too low to be acceptable and another technique was deemed necessary.

It was postulated that since only acid and alcohol are used in this synthesis, since the acid is very soluble in water, and since the excess alcohol is distilled off at a lower temperature than the product, it would be feasible to dilute the reaction mixture with water after completion of the reaction, thus dissolving any unreacted acid. Then it was felt that the steam distillation process could be eliminated and the diluted final reaction mixture extracted with ether. The theory was that the unreacted acid impurity in very dilute water solution would be separated with the water layer of the ether extraction; the unreacted alcohol being separated out with the ether layer and later distilled off.

The preparation was attempted again with this postulation in mind. The usual steps were carried out as indicated above except that upon completion of the reaction, the reaction mixture was diluted with water and ether extraction carried out at this point.

The ether portion was then dried over anhydrous sodium sulfate, the ether distilled off, and the crude product vacuum distilled under 4 mm pressure.

The postulation was found to be valid since a yield of 29.8% of the theoretical was obtained and the product was proved to be that desired and in pure form (see Chapter IV, Determination of Physical Constants and Chapter V, Identification of the Esters).

The pure product has a boiling point of 131° at 4 mm pressure. More complete physical constants will be presented in Chapter IV.

Possibly the separation and purification of the products of esterification formed when the acid and longer chained alcohols are reacted warrants further investigation. However, this technique of separation and purification seems to offer one solution and a suitable method until such investigation can be carried out.

The Preparation of the Heptyl Ester of

2-Thiophene Carboxylic Acid

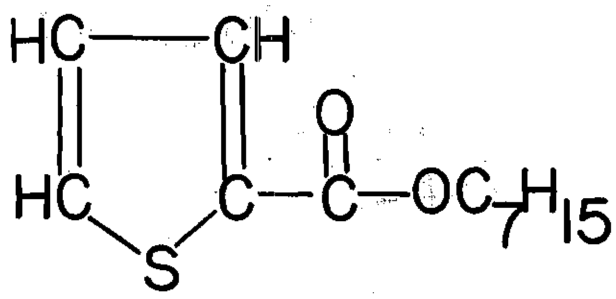

Figure 10

The same improved apparatus and modified technique as discussed in detail in the report of the preparation of the hexyl ester (pages 19-21) were used in this preparation.

2-Thiophene carboxylic acid in the amount of 0.25 mole (32 grams) and an excess of n-heptyl alcohol (1 mole or 117 grams) were placed together in the reaction flask. The mixture was saturated with dry hydrogen chloride prior to assembling the apparatus.

When the water collected in the distilling tube receiver indicated that the reaction was complete, the reaction mixture was diluted with water and ether extraction effected. The ether layer was dried over anhydrous sodium sulfate, the ether then distilled off, and the crude product distilled under reduced pressure.

This preparation also seemed to validate the postulation made in the previous preparation since a yield of 47.3% of the theoretical was obtained using this technique. The product was later proved to be that desired and was proven pure (see Chapter IV, Determination of Physical

Constants, and Chapter V, Identification of the Esters).

The pure product has a boiling point of 145° under 4 mm of pressure. More complete physical constants will be discussed in Chapter IV.

CHAPTER IV

DETERMINATION OF PHYSICAL CONSTANTS

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DETERMINATION OF PHYSICAL CONSTANTS

Boiling Point Determinations

The purpose of these determinations was to obtain accurate boiling points under reduced pressure that would be valid and worthy of publication.

As experienced previously, one of the biggest problems in these distillations was the elimination or control of bumping in the distilling flask. To overcome this, a 50 ml Claisen type distilling flask was used. Into the flask were placed boiling chips and loosely packed glass wool sufficient to fill the bulb of the flask. These precautions proved successful.

The vacuum distillation apparatus was fitted with a fraction cutter which facilitated isolation of the pure product.

A pressure of 4 mm was the lowest that could be obtained with the apparatus available. It was at this pressure that the distillations were made and the boiling points recorded.

Table I lists the boiling points for the various esters prepared. Figure 12 is a graph of the boiling points plotted against the R-group of the parent alcohol used in making each particular ester. It will be noted that the boiling points of the esters, members of a series, all fall on a smooth curve.

TABLE I

Boiling Points

of the Esters of 2-Thiophene Carboxylic Acid Prepared

ESTER	BOILING POINT (4 mm. Pressure)
Methyl	72.0° C
Ethyl	79.0° C
Propyl	90.0° C
Butyl	103.5° C
Amyl	116.5° C
Hexyl	131.0° C
Heptyl	145.0° C

Figure 11

BOILING POINT vs. R GROUP of ESTER

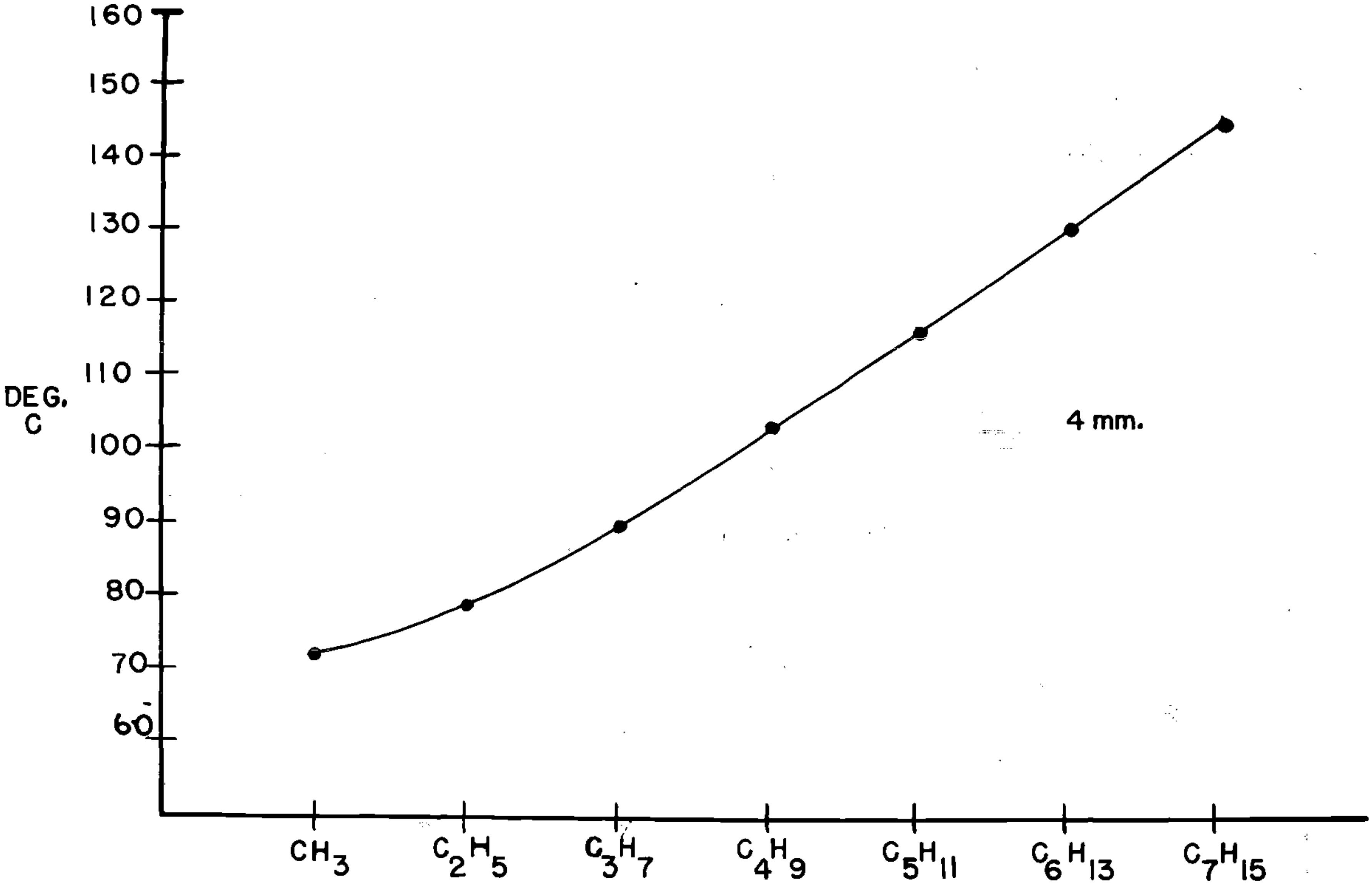

Figure 12

Density Determinations

The purpose of these determinations was to establish densities of the esters at a specified temperature that would be valid, worthy of publication, and of the accuracy required for use in molar refraction calculations.

A constant temperature bath maintained at 25° C was utilized to measure the densities at a constant specified temperature.

Each individual density was calculated by using the following formula:

$$\frac{\text{Wt. of specified vol. of water at } 25^\circ}{\text{Wt. of equal vol. of ester at } 25^\circ} = \frac{\text{Density of water at } 25^\circ}{\text{Density of ester at } 25^\circ}$$

Table II lists the densities for the various esters prepared. Figure 14 is a graph of the densities plotted against the R-group of the parent alcohol used in making each particular ester.

TABLE II

Densities

of the Esters of 2-Thiophene Carboxylic Acid Prepared

ESTER	DENSITY AT 25° C
Methyl	1.22070
Ethyl	1.16000
Propyl	1.11954
Butyl	1.08870
Amyl	1.06466
Hexyl	1.03035
Heptyl	1.00054

Figure 13

DENSITY vs. R GROUP of ESTER

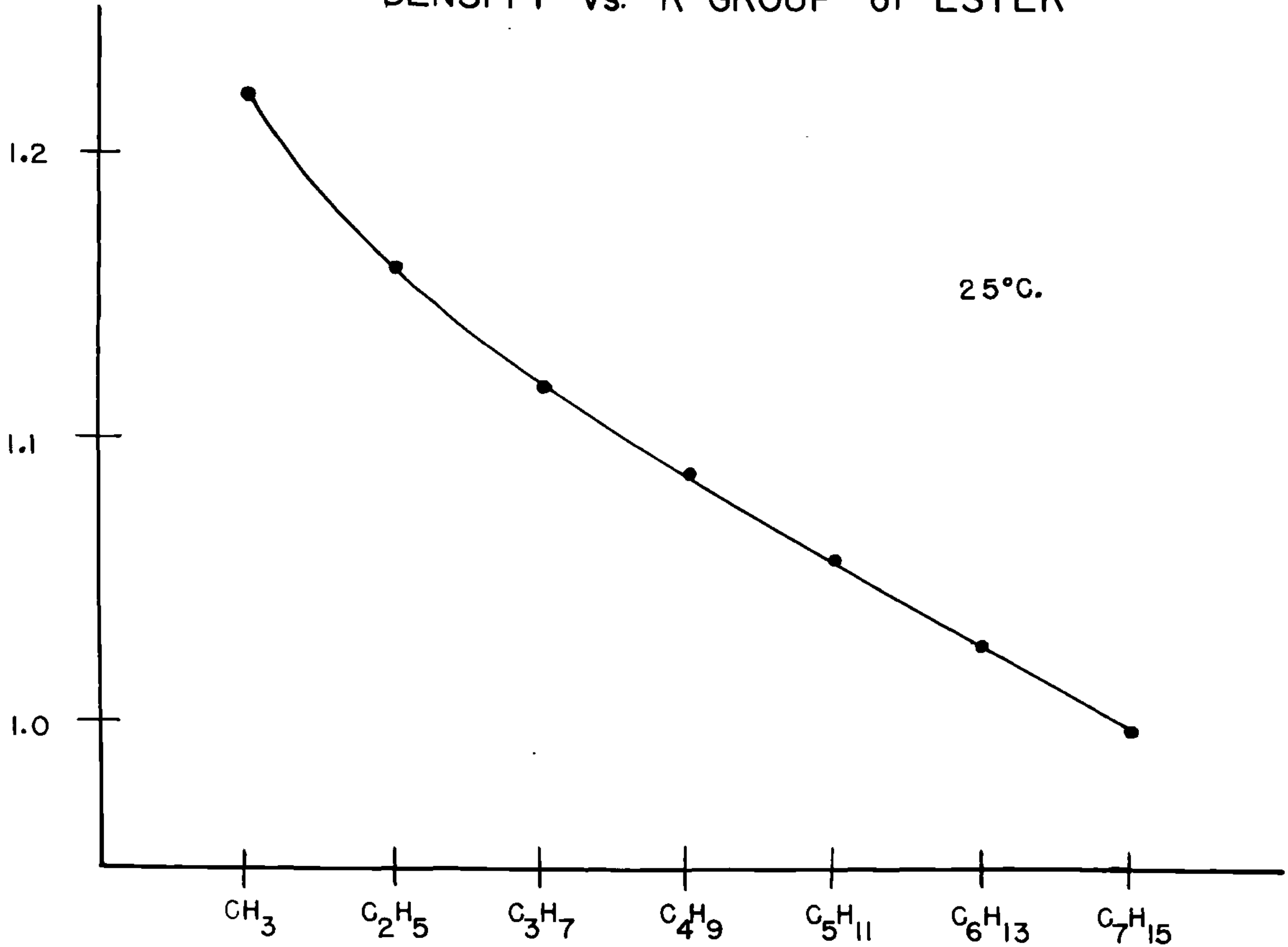

Figure 14

Refractive Index Determinations

The purpose of these determinations was to establish refractive indices of the esters prepared that would be valid, worthy of publication, and of the accuracy required for molar refraction calculations.

The refractive indices were determined at a constant temperature of 25° C so that the data would correspond to and could be used with the densities determined at the same temperature in connection with molar refraction determinations.

A refractometer in conjunction with a constant temperature bath and centrifugal pump to circulate the water through the instrument was used for the determinations.

Table III lists the refractive indices for the various esters prepared. Figure 16 is a graph of the refractive indices plotted against the R-group of the parent alcohol used in making each particular ester. It will be noted that the points of the graph fall on a smooth curve with two exceptions. It is felt that the discrepancy of the two points not falling on the curve is probably due to the fact that the determinations of the refractive indices are much more accurate than the graph paper permits plotting; i.e., refractive indices are read with extreme accuracy to the fourth decimal place, whereas graph paper does not permit plotting with this accuracy. Repetition of the determinations on these two esters checked the results obtained. In addition, it is felt that the molar refraction calculations involving these experimental values (Chapter V) verifies the validy of the values.

TABLE III

Refractive Indices

of the Esters of 2-Thiophene Carboxylic Acid Prepared

ESTER	REFRACTIVE INDEX	
	25°C	20°C
Methyl	1.5393	1.5418
Ethyl	1.5238	1.5261
Propyl	1.5158	1.5181
Butyl	1.5105	1.5130
Amyl	1.5047	1.5072
Hexyl	1.4956	1.4979
Heptyl	1.4891	1.4914

Figure 15

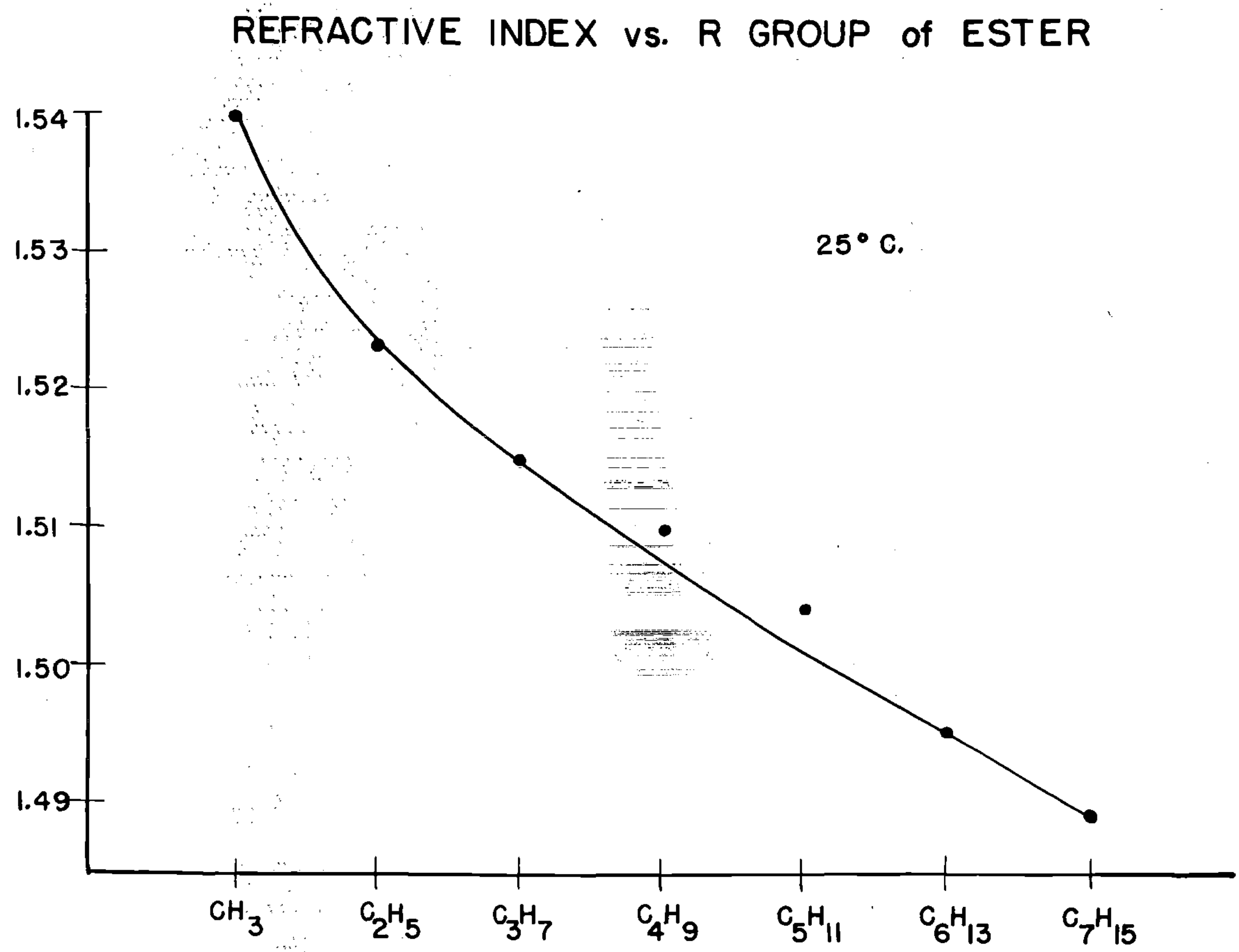
REFRACTIVE INDEX vs. R GROUP of ESTER
25° C.
1.54
1.53
1.52
1.51
1.50
1.49
CH3
C2H5
C3H7
C4H9
C5H11
C6H13
C7H15

Figure 16

CHAPTER V

IDENTIFICATION OF THE ESTERS

CHAPTER V

IDENTIFICATION OF THE ESTERS

General

Two separate and distinct methods of identification were used to identify the esters prepared. These methods were:

(1) Calculation of the experimental molar refraction and comparison with theoretical molar refraction.

(2) Calculation of the molecular weights using saponification data and comparison with theoretical molecular weight.

The following pages contain a discussion of these methods of identification and the tabulation of the results obtained.

Molar Refraction

The calculation of the theoretical and experimental molar refractions for the esters prepared was carried out according to the method discussed by Glasstone.[11]

In the calculation of the theoretical molar refractions, the following atomic refraction equivalents for the D-line were used:

Carbon........................	2.42 cc
Hydrogen......................	1.10 cc
Oxygen (in CO group)..........	2.21 cc
Oxygen (in ether linkage).....	1.64 cc
Sulfur........................	8.00 cc
Double Bond...................	1.73 cc

In the calculation of the experimental molar refractions for the esters prepared, the following formula was used:

$$M.R. = \frac{n^2 - 1}{n^2 + 2} \cdot \frac{M}{d}$$

M.R. is molar refraction
n is refractive index
M is molecular weight
d is density

Obviously, it is important that the refractive index and density used in the calculation must be obtained at the same temperature. In these calculations, the temperature was 25° C.

Table IV is a compilation of the theoretical and experimental molar refractions for the esters prepared.

It will be noted that in each case the experimental value is approximately equal to the theoretical value.

[11] S. Glasstone, <u>The Elements of Physical Chemistry</u>, pp. 157-8 (1946)

TABLE IV

Molar Refractions

of the Esters of 2-Thiophene Carboxylic Acid Prepared

Ester	Molar Refraction Theoretical	Experimental
Methyl	36.43 cc	36.08 cc
Ethyl	41.05 cc	41.13 cc
Propyl	45.67 cc	45.59 cc
Butyl	50.29 cc	50.64 cc
Amyl	54.91 cc	55.13 cc
Hexyl	59.53 cc	60.08 cc
Heptyl	64.15 cc	65.14 cc

Figure 17

Saponification of the Esters

For the saponification of the esters an alcoholic solution of sodium hydroxide approximately 0.5 N was prepared. To insure saponification under comparable conditions, four reflux condensers were set up with Bunsen burners as a source of heat. For each run, four 200 ml Erlenmeyer flasks were washed and dried in an oven. After drying, the flasks were removed and allowed to cool. One flask was used as a "blank" in each run, and into this flask was placed 30 ml of the alcoholic sodium hydroxide solution, 20 ml of 95% ethyl alcohol, and two drops of phenolphthalein. Into each of the other three flasks carefully weighed samples of the ester being saponified were placed. An amount of sample approximately equal in weight to 1/100 the molecular weight of the ester was used in each case except as noted later. After the samples had been weighed, 30 ml of the alcoholic NaOH was added to each flask from the burette. Ethyl alcohol in the amount of 20 mls and 2 drops of phenolphthalein were also added to each flask. The blank and three samples were then attached to the reflux condensers and refluxed gently for the same length of time. After the refluxing had been accomplished, the flasks were removed, 50 mls distilled water added, the flasks cooled, and the solutions titrated with an HCl solution of approximately the same normality as the alcoholic NaOH solution (in this case 0.474 N).

By using the following formula, the experimental molecular weight for each sample was calculated:

$$\text{M.W.} = \frac{\text{Wt. of sample} \times 1000}{(\text{cc blank} - \text{cc sample}) \times \text{Na}}$$

In the formula above, cc blank is the amount of acid used in neutralizing the blank, cc sample is the amount of acid used in neutralizing the sample, and Na is the normality of the acid.

The saponifications of the methyl, propyl, butyl, and amyl esters were easily accomplished in one to two hours and the calculated molecular weights were in very close agreement with the theoretical values.

Some difficulty was encountered in the saponification of the hexyl and heptyl esters when the method described above was used. It was found that the molecular weights calculated for the individual samples were not in very close agreement and were generally high. It was decided that this discrepancy could be possibly attributed to one of the following causes:

(1) Incomplete saponification

(2) Slightly impure samples

In an effort to obtain results more nearly in agreement with the theoretical, the weight of the sample was reduced one-half (1/200 the molecular weight of the ester), and the same amount of alcoholic NaOH was used (30 ml). In addition, the reflux time was extended to 4 hours in the case of the hexyl ester and 5 hours in the case of the heptyl ester. This modification of saponification technique improved the results greatly, but still did not bring them as close to the theoretical molecular weights as in the case of the first four esters (see Chapter VI for further discussion).

Table V lists the theoretical molecular weights as compared to the calculated molecular weights using saponification equivalents.

TABLE V

Theoretical and Calculated Experimental Molecular Weights of the Esters of 2-Thiophene Carboxylic Acid Prepared Using Saponification Equivalents

	Molecular Weight	
Ester	Theoretical	Calculated (Average)
Methyl	142.0	142.7
Propyl	170.0	169.9
Butyl	184.0	184.4
Amyl	198.0	198.6
Hexyl	212.0	217.0
Heptyl	226.0	237.0

Figure 18

CHAPTER VI

GENERAL DISCUSSION OF THE RESULTS OF THE INVESTIGATION

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In general, the results of this investigation were very gratifying to the writer and are believed to be accurate. Great care and every possible precaution was used to insure accurate results.

It is felt that the boiling points and densities are accurate as indicated by the curves plotted. The methyl, propyl, butyl, and amyl esters are believed to be 100% pure and the data related to these esters are believed to be beyond question.

As a result of the difficulty encountered in obtaining the desired results in saponification of the hexyl and heptyl ester, some questions arise concerning these two esters. This difficulty might indicate that the curve for the refractive indices (Figure 16) might correctly be drawn through the butyl and amyl points instead of the hexyl and heptyl points.

The hexyl and heptyl esters might rightfully not be 100% pure as the procedure for preparation had to be altered for these esters eliminating the steam distillation step. If this is the case, the calculations in connection with the saponification indicate that these particular esters are 96-98% pure, which is considered acceptable purity for an organic compound prepared synthetically.

It is the intention of the writer to continue the investigation of the esters of 2-thiophene carboxylic acid in the near future. If this desire becomes a reality, the hexyl and heptyl esters will be investigated thoroughly in an attempt to perfect a method of preparation of the pure compounds and to either verify the physical constants obtained or correct same. After this is accomplished, an attempt will be made to prepare higher esters of the series.

CHAPTER VII

SUMMARY

CHAPTER VII

SUMMARY

In this investigation, the methyl, propyl, butyl, amyl, hexyl, and heptyl esters of 2-thiophene carboxylic acid were prepared. According to a literature search made prior to starting the problem, the esters named above had not been before prepared and were not reported in literature.

Complete physical constants were determined for the esters prepared, and a two-method scheme of identification was carried out.

It is the anticipation and desire of the writer to carry on further research in the synthesis of the esters of 2-thiophene carboxylic acid in the very near future.

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