REARRANGEMENT STUDIES IN DEHYDRATIONS OF

CARBON-14 LABELED PHENYLETHANOLS

By

ROBERT STEPHEN JONES

Bachelor of Science

Oklahoma State University

Stillwater, Oklahoma

1957

Submitted to the faculty of the Graduate School of
the Oklahoma State University in partial
fulfillment of the requirements
for the degree of
MASTER OF SCIENCE
May, 1961

REARRANGEMENT STUDIES IN DEHYDRATIONS OF

CARBON-14 LABELED PHENYLETHANOLS

Thesis Approved:

[signature]
Thesis Adviser

[signature]

[signature]
Dean of the Graduate School

ii

ACKNOWLEDGMENT

TABLE OF CONTENTS

LIST OF TABLES

INTRODUCTION

This work was undertaken in order to establish whether or not the styrene-α-C^{14} and styrene-β-C^{14} produced in the course of other work of interest (10) were actually labeled in the desired positions.

Some question has been raised as to the correctness of the above proposition by the results and interpretations of work done on many phenylethyl and related systems by several groups of workers. Varied techniques have been employed to show carbon atom rearrangements in a variety of solvolysis and dehydration reactions. The object of the present work has been to discover by means of carbon-14 tracer techniques if carbon atom positional rearrangements occur under the conditions of two dehydration reactions of particular interest since one of them is catalyzed by a base and one by an acid.

Rearrangements in Phenethyl and Related Systems

Examples: Using a series of substituted phenethyl p-toluenesulfo-
nates in solvolysis reactions, Winstein and coworkers obtained varying
degrees of rearrangement with each combination of ester and solvent.
They were able to find the rearrangements because a completely different
compound resulted as the product of solvolysis of the p-toluenesulfonate
ester. For example:

Pinacol rearrangement (21)

$$\phi - \underset{\underset{CH_3}{\overset{|}{O}}}{\overset{\overset{\phi}{\overset{|}{\,}}}{C}} - \underset{\underset{SO_2}{\overset{|}{O}}}{\overset{\overset{H}{\overset{|}{\,}}}{C}} - H \quad \xrightarrow[\text{80\% dioxane}]{\overset{\overset{O}{\overset{\parallel}{\,}}}{K-O-C-CH_3}} \quad \phi - \underset{\underset{O}{\overset{\parallel}{\,}}}{C} - \underset{\underset{\phi}{\overset{|}{\,}}}{\overset{\overset{H}{\overset{|}{\,}}}{C}} - H \quad + CH_3OH$$

(with p-toluenesulfonyl group bearing CH₃-substituted benzene ring)

$$+ \; SO_3H$$

(p-toluenesulfonic acid, CH₃ on ring)
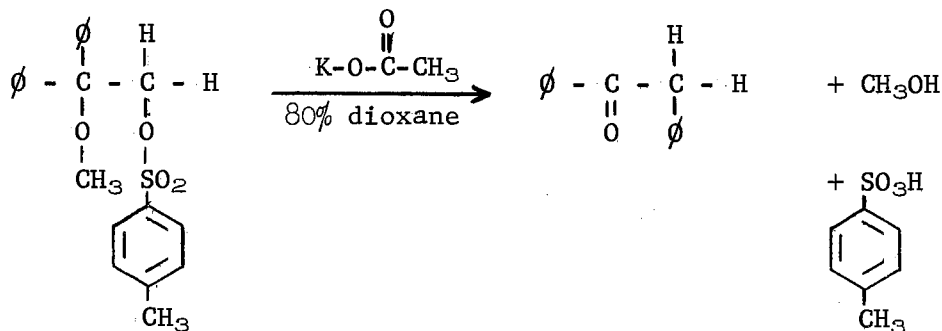
Wagner-Meerwein rearrangement (22)

$$CH_3 - \underset{\underset{CH_3}{\overset{|}{\,}}}{\overset{\overset{CH_3}{\overset{|}{\,}}}{C}} - \underset{\underset{O}{\overset{|}{\,}}}{\overset{\overset{H}{\overset{|}{\,}}}{C}} - \phi \quad \xrightarrow{\overset{\overset{O}{\overset{\parallel}{\,}}}{H-O-C-CH_3}} \quad CH_3 - \underset{\underset{O=C}{\overset{|}{\,}}}{\overset{\overset{CH_3}{\overset{|}{\,}}}{C}} - \underset{}{\overset{\overset{CH_3}{\overset{|}{\,}}}{C}} - \phi \;+\; SO_3H$$

(SO₂ attached to CH₃-substituted benzene ring on left; CH₃ groups with O=C–CH₃; p-toluenesulfonic acid on right)
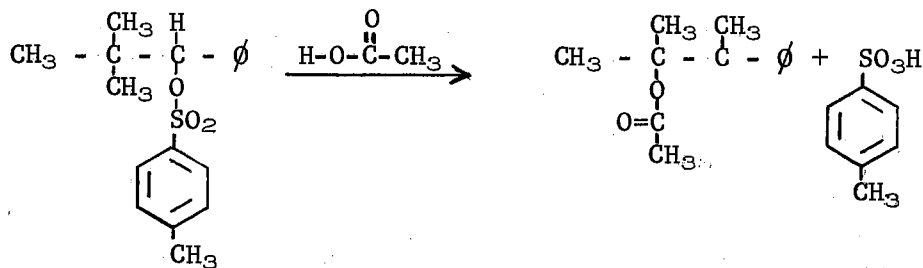
With the aid of carbon-14 tracer techniques, Collins, et al.
have shown similar rearrangements in solvolyses and also in dehydra-
tions with a strong dehydrating agent. For example:

$$\underset{\phi}{\overset{\overset{\displaystyle H \quad OH}{|} \quad |}{\phi_2C} - \overset{*}{C}H} \quad \xrightarrow[\text{xylene}]{P_2O_5} \quad \overset{(50\%)}{\phi_2C} = \underset{\phi}{\overset{*}{C}H}$$

$$\text{and} \quad \overset{(50\%)}{\phi_2\overset{*}{C}} = \underset{\phi}{CH} + H_2O \qquad (1)$$
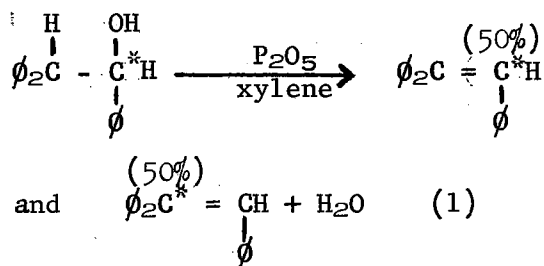
Of more immediate importance to the present study are the researches that have been done on the simple β-phenethyl system. Lee and coworkers (16) made the p-toluenesulfonate of 2-phenylethanol-1-C^{14} and subjected this ester to solvolysis with a series of solvents of increasing acid strength. The resulting products were oxidized to benzoic acid with potassium permanganate and assayed for carbon-14. The extent of rearrangement of carbon-14 from the 1-carbon to the 2-carbon position in each solvent is shown in Table I. These data on rearrangement were verified by Saunders, et al. (19) with the use of deuterium tracer techniques.

TABLE I

EXTENT OF CARBON-14 REARRANGEMENT IN SOLVOLYSIS REACTIONS

OF THE p-TOLUENESULFONATE OF 2-PHENYLETHANOL-1-C^{14}

Solvent	Extent of Carbon-14 Rearrangement from 1- to 2-Carbon Position
Ethanol	0.3%
Glacial Acetic Acid	5.5%
90% Formic Acid	40 %
Anhydrous Formic Acid	45 %

Proposed Mechanisms: In all the above cases where rearrangements occur the reactions proceed at least partially by a unimolecular mechanism. That is to say, carbonium ions are formed as intermediates.

It appears that phenyl group migration takes place in the rearrangements and Winstein (20) has postulated that predominant "phenyl participation" is important, and has accumulated kinetic data in support of this contention. An S_N1 reaction intermediate which has met with some favor is the "phenonium ion," a carbocyclic three-membered carbonium ion including a phenyl group which could lend some stability to the structure through resonance. Cram (6) was the first to find definite evidence for such an intermediate in a specific system. He obtained sound stereochemical evidence in the acetolysis of optically active and racemic mixtures of the p-toluenesulfonate of 3-phenyl-2-butanol. Some resonance forms of the intermediate are shown here.
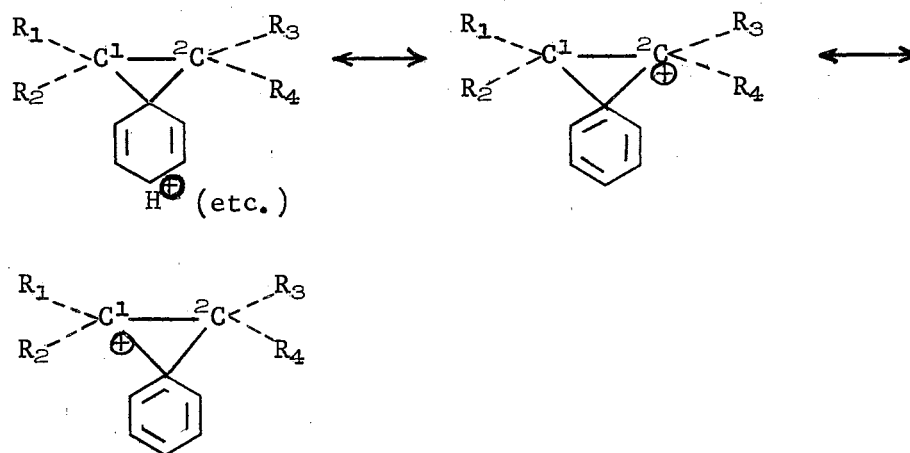
This intermediate has at one time or another met with acceptance at the hands of nearly all workers with related systems. However, in two important instances "phenonium ion" intermediates have been shown to be incompatible with experimental data by stereochemical considerations (4, 22). As a result of this later work the tendency has since been to favor the "classical" open carbonium ions in all instances where convincing proof is lacking in support of the bridged intermediate.

Possibility of Rearrangements in Dehydrations of 1- and 2-Phenylethanol

In the previously reported rearrangements caused by dehydrations the catalysts responsible were of strongly acid character. A high percentage of rearrangement resulted from the solvolysis of the p-toluenesulfonate of 1,2,2-triphenylethanol with formic acid which went completely to 1,1,2-triphenylethylene with elimination (1). Dehydrations of several carbinols with phosphorous pentoxide in anhydrous xylene yielded olefins with 50% rearrangement of carbon-14 labels (1, 5).

The possibility that rearrangements may be caused by dehydrating agents of other than strong acid character has, however, not been excluded. In view of the propensity of phenylethyl systems and substituted variations for rearranging under rather varied conditions, one should be cautious about making the assumption that no rearrangement occurs until it has been shown that this is so.

Two dehydrating agents were used in other work of interest (14). One, potassium bisulfate, was used in catalytic amounts to dehydrate 1-phenylethanol, and the other, potassium hydroxide, was used in much larger proportions to dehydrate 2-phenylethanol. It is possible that such reagents could cause a dehydration to proceed by the E1 or unimolecular elimination mechanism through a carbonium ion intermediate which is the mechanism favored for all cases where rearrangements occur. The behavior of the two agents may be different since one is a strong base and the other the salt of a fairly strong acid.

INTRODUCTION TO EXPERIMENTAL WORK

Styrene-β-C^{14}

Synthesis: Styrene-β-C^{14} was prepared from 2-phenylethanol-1-C^{14} by dehydration with potassium hydroxide in the presence of sulfur as a polymerization inhibitor. The dehydration reaction is represented by the following equation:

$$\emptyset - CH_2 - \overset{*}{C}H_2OH \xrightarrow[S]{KOH} \emptyset - CH = \overset{*}{C}H_2 + H_2O$$
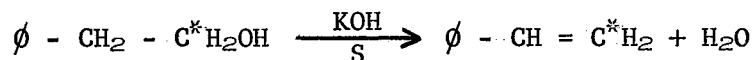
By means of preliminary runs it was found that up to 85% yields of styrene were readily obtained. In order to obtain such high yields it was necessary to wrap the exposed parts of the distilling head between reaction flask and condenser with heating tape and to increase the temperature of the oil bath gradually from 150° to 180° at which temperature the reaction flask was maintained for four hours. Styrene and water distilled as they were formed. As they are immiscible, the styrene was separated from the water with a micro-pipette and was pure enough for polymerization without further purification.

Oxidation: As a means of discovering whether any rearrangement of the side chain carbon atoms had occurred, labeled styrene-β-C^{14} was oxidized to benzoic acid. If rearrangement had occurred, some of the radioactive carbon would appear in the benzoic acid. If no rearrangement had occurred, the benzoic acid would be free from radioactivity. The equation for the oxidation is given below:

$$\emptyset - CH = \overset{*}{C}H_2 \xrightarrow[NaOH]{KMnO_4} \emptyset\text{-}CO_2H + \overset{*}{C}O_2$$
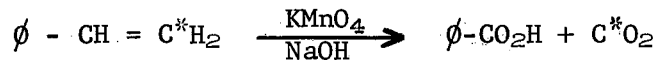
The permanganate oxidation was done under basic conditions because benzoic acid is soluble in base and can be separated from the manganese dioxide byproduct which is insoluble in base by filtration. The filtrate is then acidified, the benzoic acid precipitates, and is collected by suction filtration.

The oxidation was done at water reflux temperature with magnetic stirring because Hurd, et al. (12) have reported that under mild conditions, permanganate oxidation of styrene results in only a 7% yield of benzoic acid and a 55% yield of mandelic acid. This acid represents the halfway point in the oxidation of styrene to benzoic acid. When the reaction was done at 100° with magnetic stirring, yields of 50 - 60% benzoic acid were obtained.

Styrene-α-C^{14}

Synthesis: Styrene-α-C^{14} was prepared from 1-phenylethanol-1-C^{14} by dehydration with potassium bisulfate in the presence of hydroquinone as a polymerization inhibitor. The equation is shown below:

$$\phi - C^*HOH - CH_3 \xrightarrow[\text{hydroquinone}]{\text{KHSO}_4} \phi - C^*H = CH_2$$
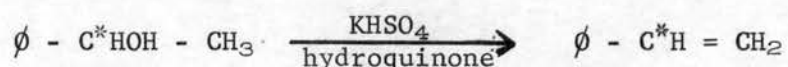
It was necessary to raise the reaction mixture to a higher temperature than with the 2-phenylethanol in order to get good yields. Yields ran between 60 - 78%. The styrene obtained was of high purity, about 99.94 - 99.95% with most of the impurity a small amount of water since the styrene and water distilled over together and had to be separated with a micro-pipette.

Polymerization: In the case of the styrene-α-C^{14} it was decided to use a high-conversion polystyrene polymer to determine the activity of the monomer. The reason for this was that it was anticipated that

the benzoic acid would have a high activity comparable with that of the styrene and the alcohol instead of a very low one as in the case of the styrene-α-C^{14}, and that the method of assay would have to be changed from a liquid scintillation spectrometer to a vibrating reed electrometer. The latter instrument is more precise, but also more limited as to the physical state of materials that can be assayed with it. It is very difficult to obtain good analyses with liquid samples, therefore it was essential to have solid samples for the assays.

It was determined that the most rapid and best procedure for obtaining a high-conversion polystyrene was to use a cationic initiator in a solvent. Reaction rates for cationic polymerizations do not increase appreciably with an increase in temperature so the polymerization was done at room temperature. 1,2-Dichloroethane was selected as a suitable solvent and anhydrous stannic chloride as a good initiator. Since, according to Pepper (17), the rate of polymerization is proportional to the square of the styrene concentration, and the molecular weight of polymer is proportional to the styrene concentration, a low concentration of stannic chloride with respect to that of monomer and solvent was used.

The polymerization proceeded rapidly at first, until the amount of dissolved polymer became so great that it swelled and absorbed all the solvent. The mixture was allowed to stand for some time after this occurred in order to insure as high a conversion as possible. To recover the polymer, sufficient acetone was added to dissolve the swollen mass and this acetone solution poured into a large excess of methanol, whereupon the polymer precipitated as a white flocculent material. It was collected by suction filtration and dried overnight on

a vacuum line while being heated with an infra-red lamp. An 84% conversion to white powdery polystyrene was obtained. There is no kinetic isotope effect associated with cationic polymerization of styrene-α-C^{14} so a conversion of 84% is sufficiently high for the purposes of this work (10).

<u>Oxidation</u>: Yields of 50 - 60% were obtained in the oxidations of styrene-β-C^{14} and were adequate for dealing with the synthesis of that isomer because the product benzoic acid from those oxidations retained only a negligible amount of carbon-14. In the case of styrene-α-C^{14}, however, two runs produced benzoic acid of relatively high activity although precision obtained with the liquid scintillation spectrometer was not good enough to warrant comparison between the carbinol, styrene, and benzoic acid. In view of the possibility of a kinetic isotope effect occurring during the permanganate oxidation of the styrene, it was desired to find a means of obtaining higher yields of benzoic acid in order to minimize the effect such an isotope effect might have on depressing the relative activity of the benzoic acid.

It was thought that the rigorous conditions (i.e., 100°) might have caused some of the benzoic acid to be oxidized further into fragments which caused the loss of some product. Accordingly a technique was developed in which the oxidation was run at room temperature, but on a mechanical shaker which would continually keep the styrene in contact with the oxidizing agent. The reaction was done in a Pyrex test tube fitted with a cap with standard taper ground glass joint which was kept tightly closed. The reaction was allowed to continue for a period of about six weeks to insure as complete reaction as possible, and was then quenched by reducing the remaining excess perman-

ganate with formaldehyde.

A crude yield of about 113% was obtained after an ether extraction of several hours. This crude benzoic acid contained a small amount of mandelic acid, ϕ-CHOH-CO$_2$H, which is a hygroscopic material soluble in both ether and water. To eliminate this material, the product was again dissolved in ether and thrice extracted with water. Even this did not completely remove it, but upon recrystallization from hot water benzoic acid melting at 120.5 - 122° was obtained showing that the product was now pure.

Radioactivity Assay of Carbon-14 Labeled Compounds

Liquid Scintillation Counter: All the radioactivity assays made during the study of styrene-β-C^{14} were done on a Tri-Carb Model 314 Liquid Scintillation Spectrometer. Samples of about 100 mg. each were weighed into standard-size vials on an analytical balance, and dissolved in about 21 ml. of a toluene solution containing primary and secondary scintillators. After these vials had been allowed to come to the temperature at which assays were run (about -10°) they were placed in a socket between two photomultiplier tubes which registered the flashes of phosphorescence caused by each carbon-14 beta particle in the sample.

The absolute counting efficiency of the liquid scintillation spectrometer varies from day to day and is affected greatly by the chemical nature of the sample. Differences of 10 - 15% in counting efficiency between different solutes are not uncommon because of the fact that each compound has a characteristic "quenching" effect upon the phosphorescence excited by beta particles. Because of these inherent defects, this method of counting is effective only for comparing samples

of the same chemical composition, or samples of high activity with those
of very low activity. The latter was the type of comparison needed in
this case so liquid scintillation counting proved very convenient for
determining the extent of rearrangement in the production of styrene-β-C^{14}
from 2-phenylethanol-1-C^{14}.

Vibrating Reed Electrometer: A much more precise although more
time-consuming method of carbon-14 assay was resorted to in the study
of the preparation of styrene-α-C^{14} by dehydration of 1-phenylethanol-1-C^{14}.
Solid samples of 5 - 10 mg. each were weighed into small platinum boats on
a micro-balance. The samples were then transferred to a wet combustion
apparatus and oxidized to carbon dioxide with hot Van Slyke's solution (18).
The radioactive carbon dioxide was flushed out with ordinary carbon dioxide
and expanded into an evacuated stainless steel ionization chamber. The
radioactivity assays were then made on an Applied Physics Corporation
Vibrating Reed Electrometer, Model 30.

Although some variation from day to day and some erratic behavior
were encountered with this method of counting, in general precise data
were obtainable. A major disadvantage was that liquid samples could not
be uniformly handled by the wet combustion procedure. The precision
obtained with liquid samples was not good enough for the purposes of
this study. Fortunately, however, the styrene could be readily converted
into solid polymer and benzoic acid is a solid.

EXPERIMENTAL DATA

Styrene-β-C^{14}

Preparation of Styrene-β-C^{14}: In this reaction, the elements of water were removed from 2-phenylethanol-1-C^{14} by the action of solid potassium hydroxide at an elevated temperature. The reaction product, styrene-β-C^{14}, along with water was removed from unreacted alcohol by distillation as it was formed.

A mixture of 2.0113 g. of the radioactive alcohol, 1.8 g. of solid potassium hydroxide pellets, and about 0.05 g. of powdered sulfur was placed in a 20-ml. round-bottom flask which was then immersed in a silicone oil bath. A distilling head and condenser was fitted to the reaction flask and the surface of the distilling head wrapped with heating tape to promote rapid distillation.

The silicone oil bath was heated to 180° at which temperature it was maintained for four hours. Styrene began to collect as distillate after about 30 minutes of heating, and styrene and water distilled over until the reaction flask was almost dry at the end of four hours. The styrene layer was removed from the water layer of the distillate with a micro-pipette giving 1.4394 g. of styrene (yield 84%).

Benzoic Acid from Styrene-β-C^{14}: In the oxidative degradation of styrene to benzoic acid, a weighed amount of styrene was oxidized with an equivalent amount of basic permanganate at 100° with constant stirring. The balanced equation used to determine the necessary proportion of

potassium permanganate is given below:

$$3 \, \phi - CH = CH_2 + 10 \, KMnO_4 \xrightarrow{\text{NaOH}} 3 \, \phi - \overset{\overset{\displaystyle O}{\displaystyle \|}}{C} - OK + 10 \, MnO_2$$

$$+ \, 3 \, K_2CO_3 + 4 \, H_2O + KOH$$
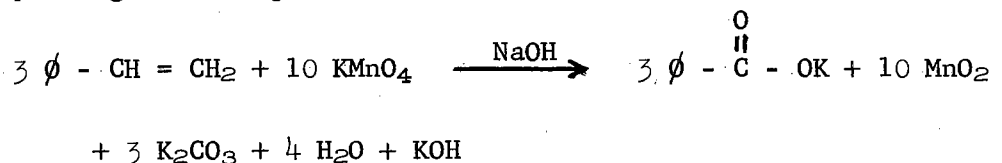
From this equation the required ratio of the weight of potassium per-
manganate to styrene was calculated to be 5.06 g. potassium permanganate/g.
styrene.

A mixture of 1.1733 g. of styrene, 15 ml. of water, 1 g. of sodium
hydroxide, and the calculated amount of 5.95 g. of potassium perman-
ganate was placed in a 20-ml. round-bottom flask. The flask was equipped
with a reflux condenser and a magnetic stirrer and placed in a 115-volt
heating mantle connected into a variable transformer for heat control.

The reaction mixture was heated at water reflux temperature until
the reaction had subsided and the purple and green colors of the perman-
ganate and manganate ions had disappeared, being vigorously mixed all
the while with a magnetic stirrer and Teflon-coated "pill." The heating
was then halted and the manganese dioxide residue was removed by filtration
while the solution was still warm. After the reaction vessel and precip-
itate were twice washed with hot water the combined filtrate and washings
were acidified with 3 ml. of concentrated hydrochloric acid. The result-
ing fluffy white precipitate was collected by suction filtration and
washed with cold water; 0.8466 g. of benzoic acid were obtained for a
yield of 61.5%. The melting point was 119 - 120° before purification.

Styrene-α-C^{14}

Preparation of Styrene-α-C^{14}: In this reaction water was removed
from 1-phenylethanol-1-C^{14} by the action of solid potassium bisulfate at

elevated temperatures (3). Styrene and water were removed from the unreacted alcohol by distillation as they formed.

A mixture of 3.1849 g. of the radioactive alcohol, 0.02 g. of solid potassium bisulfate, and 0.02 g. of hydroquinone as a polymerization inhibitor was placed in a 20-ml. round-bottom flask which was immersed in a silicone oil bath. To the reaction flask was attached a distilling head and condenser. The distilling head was wrapped with heating tape to promote rapid distillation.

The bath was heated to 150 - 160° until an initial period of vigorous boiling had subsided. The temperature was then raised to 192° and kept there until distillate stopped coming over. The reaction proceeded for about three hours. Styrene-α-C^{14} (2.2175 g.) was separated from the water layer by micro-pipette giving a yield of 78%. The refractive index of this styrene showed it to be identical with 99.94 - 99.95% pure styrene (2). The concentration of water dissolved in the styrene was less than 0.01%.

Benzoic Acid-Carboxyl-C^{14} from Styrene-α-C^{14}: Since about 60% yields were the best obtainable with the oxidation procedure used on styrene-β-C^{14}, a different procedure was adopted in an attempt to obtain higher yields of benzoic acid. In this procedure room temperature was maintained, constant mechanical shaking was utilized, and an excess of potassium permanganate was used.

A mixture of 0.2411 g. of styrene, 1.33 g. of potassium permanganate amounting to a 9% excess, 1 g. of sodium hydroxide, and 10 ml. of water was placed in a large Pyrex test tube equipped with a ground glass joint. A glass stopper was tightly secured to the reaction tube with rubber bands and it was placed on a mechanical shaker set for high speed. The

vigorous shaking was continued for a period of six weeks because there is a tendency for heterogeneous permanganate oxidations of styrene to stop at mandelic acid unless pushed (12).

At the end of six weeks the reaction was quenched by the addition of 5 ml. of formaldehyde which rapidly reduced the remaining permanganate ions. The mixture was then acidified with concentrated hydrochloric acid causing the suspended manganese dioxide to dissolve and a large amount of fluffy white precipitate to form. All of the solution and precipitate was then transferred to a continuous ether extraction apparatus along with ether washings of the reaction tube. One hundred milliliters of ether was added, a water reflux condenser attached and the system heated for four days. The ether phase was then evaporated under the hood. The recovered product weighed 0.319 g. (crude yield = 113%). The melting point of the material was 119 - 120°. The product contained some water which was due to the presence of a small percentage of mandelic acid, a hygroscopic byproduct soluble in both water and ether.

In order to purify the crude benzoic acid, it was redissolved in ether, filtered, and extracted three times with water. The ether phase was then evaporated and the solid residue recrystallized from hot water. The resulting benzoic acid-carboxyl-C^{14} was pure, its melting point being 121 - 122°.

Polymerization of Styrene-α-C^{14}: The cationic polymerization of styrene-α-C^{14} was based on a procedure given by Pepper (17) in which styrene was polymerized in the presence of anhydrous stannic chloride with 1,2-dichloroethane as the solvent.

A solvent-catalyst solution was prepared by dissolving 0.1209 g. of stannic chloride in 12.5436 g. of freshly redistilled 1,2-dichloro-

ethane. The concentration of this catalyst solution was 0.00964 g. of stannic chloride per gram of 1,2-dichloroethane. One and a half milliliters of this solution was mixed with 0.3362 g. of styrene-α-C^{14}. The polymerization was run in a stoppered 20-ml. glass vial placed in a dessicator at room temperature. After 15 minutes the reaction mixture was cloudy, indicating that the polymerization was proceeding rapidly. After 24 hours one drop of the solution was added to one ml. of methanol causing immediate precipitation to occur, showing that the polymerization was well advanced. At the end of two months (1,656 hours) the reaction mixture was a swollen yellow-tinged solid, the polymer at high conversion having absorbed all the solvent.

Thirteen milliliters of acetone was added to the swollen solid mass of polystyrene, the vial capped and replaced in the dessicator until solution was complete. The acetone-polymer solution was then poured into a large excess of methanol resulting in the formation of a large amount of white flocculent precipitate. The precipitate was allowed to settle for an hour, after which it was filtered by suction through a fine frit. The methanol filtrate was perfectly clear indicating that essentially all the polymer had been collected. The fritted filter containing the swollen polymer was then placed on a vacuum line under a few millimeters of mercury pressure and heated with an infra-red lamp to drive out all remaining solvent. A yield of 0.2784 g. of white powdery polystyrene resulted for a conversion of 84%.

RESULTS

Carbon-14 Radioactivity Assays

Liquid Scintillation Spectrometer: All the radioactivity assays concerning styrene-β-C^{14} and one concerning styrene-α-C^{14} were made on a liquid scintillation spectrometer. Readings were obtained in terms of counts/minute directly from the scalar built into the instrument. These values were readily converted to specific activity in terms of counts/minute millimole.

In each case the activities shown are the mean of a series of five counts of five minutes duration. Two channels were used, a "red" and a "green" one. These represented different window widths or discriminator settings for the two photomultiplier tubes in the instrument. The value used to calculate the specific molar activity for comparison between compounds was always taken from the channel giving the higher reading.

Vibrating Reed Electrometer: The remaining assays needed to evaluate the behavior of the reaction producing styrene-α-C^{14} from 1-phenylethanol-1-C^{14} were done on a vibrating reed electrometer after the samples were oxidized to carbon dioxide. Readings were obtained from the strip chart of the recording potentiometer in millivolts (mv.), which were converted to microcuries/millimole (μc./mmole) with the aid of the following constants:

1.39×10^{-16} coulombs/disintegration (for carbon-14 in carbon

dioxide)

3.7×10^{10} disintegrations/second for one curie

1.0 x 10^{10} ohms (resistance of electrometer)

From the above constants a value of 0.01945 μc./mv. is obtained.

The activities used in calculating specific activities were averages from two or more assays of each solid product. The individual assays of benzoic acid and polystyrene were alternated to minimize errors caused by slow drifts in the vibrating reed electrometer. The individual activity measurements given are averages of several converted millivolt readings obtained from the strip chart.

Styrene-β-C^{14}

Two runs were made in the study of the synthesis of styrene-β-C^{14}. The carbon-14 assay data for the first run are shown in Table II.

The settings on the instrument were:

    High voltage tap No. 5

    Channel selector No. 2

    Window width for red channel = 10 - 50

    Window width for green channel = 50 - 100

TABLE II

RADIOASSAYS FOR RUN NO. 1 IN STUDY OF STYRENE-β-C^{14}

Compound	Observed Activity, counts/5 minutes		Specific Activity, counts/min. mmole
	Red	Green	Red
2-Phenylethanol-1-C^{14}	523,435	231,526	98,900
Benzoic acid	564	197	127.6
Background	43	29	

The benzoic acid has only 0.129% of the activity present in the 2-phenylethanol-1-C^{14}. The benzoic acid from this run had not been

purified well, so some of the carbon-14 shown to be present was probably due to impurities.

The benzoic acid from the second run was twice recrystallized from a basic solution resulting in a 2° rise in melting point. Therefore, the product was purer than that from the first run. The data are shown in Table III. Instrument settings were the same as before.

TABLE III

RADIOASSAYS FOR RUN NO. 2 IN STUDY OF STYRENE-β-C^{14}

Compound	Observed Activity, counts/5 minutes		Specific Activity, counts/minute mmole	
	Red	Green	Red	Green
2-Phenylethanol-1-C^{14}	448,854	177,877	109,162	43,259
Styrene-β-C^{14}	294,404	106,194	112,492	40,577
Benzoic acid	157	92	39	22
Background	54	33		

The benzoic acid has only 0.0357% of the activity present in the 2-phenylethanol and 0.0347% of the activity present in the styrene-β-C^{14}. Further data from this run are given in Table IV.

Instrument settings were:

High voltage tap No. 7

Channel selector No. 2

Window width for green channel = 50 - 100

The benzoic acid has 0.043% of the activity present in the 2-phenylethanol-1-C^{14} and 0.046% of the activity present in the styrene-β-C^{14}. Another series of counts gave a value of 0.0475% of the activity retained in the benzoic acid.

TABLE IV

FURTHER DATA ON RUN NO. 2 IN STUDY OF STYRENE-β-C^{14}

Compound	Activity, counts/5 minutes Green	Specific Activity, counts/minute mmole Green
2-Phenylethanol-1-C^{14}	508,483	123,643
Styrene-β-C^{14}	302,014	115,275
Benzoic acid	588	53
Background	371	

Styrene-α-C^{14}

The products of the first run made in the study of the synthesis of styrene-α-C^{14} were assayed by liquid scintillation counting. The results are given in Table V.

Instrument settings were:

    High voltage tap No. 7

    Channel Selector No. 2

    Window width for red channel = 10 - 50

    Window width for green channel = 50 - 100

TABLE V

RADIOASSAYS FOR RUN NO. 1 IN STUDY OF STYRENE-α-C^{14}

	Activity, counts/5 minutes		Specific Activity, counts/minute mmole	
	Red	Green	Red	Green
1-Phenylethanol-1-C^{14}	220,290	679,835	43,834	135,286
Benzoic acid-carboxyl-C^{14}	204,290	420,280	49,660	102,138
Background	150	410		

Here the benzoic acid has retained 75.5% of the activity in the 1-phenylethanol-1-C^{14} according to the data for the green or higher counting channel. Unfortunately, however, in such a situation as this, where the activities of the two compounds are of the same order of magnitude, liquid scintillation counting is not sufficiently precise. This unreliability stems from the "quenching" properties of the compounds on the scintillator solution. Not enough is known about them in general to permit quantitative comparisons to be made between different labeled compounds of similar activity.

For the above reason carbon-14 assays of the second run in the study of the synthesis of styrene-α-C^{14} were made on a vibrating reed electrometer. The data for the second run are shown in Table VI.

TABLE VI

RADIOASSAYS FOR RUN NO. 2 IN STUDY OF STYRENE-α-C^{14}

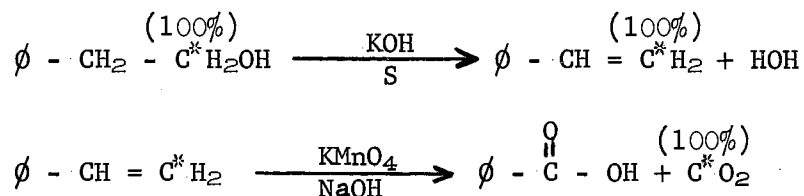| Polystyrene of 84% Conversion μc./mmole		Benzoic Acid-carboxyl-C^{14} μc./mmole
2.81		2.37
2.70		2.38
2.76	mean	2.38

The benzoic acid-carboxyl-C^{14} has retained 86.1% of the carbon-14 activity present in the styrene. Enough precision was obtained in these assays to enable a valid comparison between the polystyrene and the benzoic acid. A significant difference in activity was found supporting the data obtained through liquid scintillation counting.

DISCUSSION OF RESULTS

Interpretation of Results

Dehydration of 2-Phenylethanol-1-C^{14} by Means of Potassium Hydroxide:

The results of the radioactivity assays run on 2-phenylethanol-1-C^{14}, the

styrene-β-C^{14} produced from it by dehydration with potassium hydroxide,

and the benzoic acid obtained by degradative oxidation of the styrene

show that no appreciable amount of carbon-14 was retained in the benzoic

acid. It follows that essentially all of the carbon-14 contained in the

styrene was in the position beta to the benzene ring.

$$\phi - CH_2 - \overset{*}{C}H_2OH \quad \overset{(100\%)}{} \quad \xrightarrow[S]{KOH} \quad \phi - CH = \overset{(100\%)}{\overset{*}{C}H_2} + HOH$$

$$\phi - CH = \overset{*}{C}H_2 \quad \xrightarrow[NaOH]{KMnO_4} \quad \phi - \overset{O}{\overset{\|}{C}} - OH + \overset{(100\%)}{\overset{*}{C}O_2}$$

The above equations show the determined position of carbon-14 tracer

atoms in the styrene. An average of three assays shows the relative amount

of radioactivity contained in the benzoic acid to be 0.042% of that contained

in the styrene-β-C^{14}. Well within experimental error, then, it can be

stated that no rearrangement of side-chain carbon atoms occurs in the high

temperature dehydration of 2-phenylethanol by the action of the strong

base, potassium hydroxide.

Dehydration of 1-Phenylethanol-1-C^{14} by Means of Potassium Bisulfate:

According to the data obtained by liquid scintillation counting of 1-phenyl-

ethanol-1-C^{14} and the benzoic acid-carboxyl-C^{14} resulting from degradative oxi

dation of styrene-α-C^{14} prepared from the alcohol, the benzoic acid contained

75.5% of the activity present in the starting product. These data would

indicate a side-chain carbon atom positional rearrangement of 24.5%,

but it seemed unwise to place much reliance upon these liquid scintilla-

tion counting data.

Further data were obtained from assays by the vibrating reed electro-

meter on styrene-α-C^{14} (in polymer form) and benzoic acid-carboxyl-C^{14}

resulting from degradative oxidation of monomeric styrene-α-C^{14}. These

data showed that the benzoic acid-carboxyl-C^{14} retained 86.1% of the

carbon-14 activity present in the styrene. This would correspond to a

side-chain carbon atom rearrangement of 13.9% in the dehydration reaction

catalyzed by potassium bisulfate.

$$\phi - \overset{(100\%)}{C^*HOH} -CH_3 \xrightarrow[\text{hydroquinone}]{KHSO_4} \phi - \overset{(86\%)}{C^*H} = CH_2 + \phi - CH = \overset{(14\%)}{C^*H_2} + HOH$$

$$\phi - \overset{(86\%)}{C^*H} = CH_2 + \phi - CH = \overset{(14\%)}{C^*H_2} \xrightarrow[\text{NaOH}]{KMnO_4} \phi - \overset{(86\%)}{\underset{O}{\overset{\|}{C^*}}} - OH + \overset{(14\%)}{C^*O_2}$$
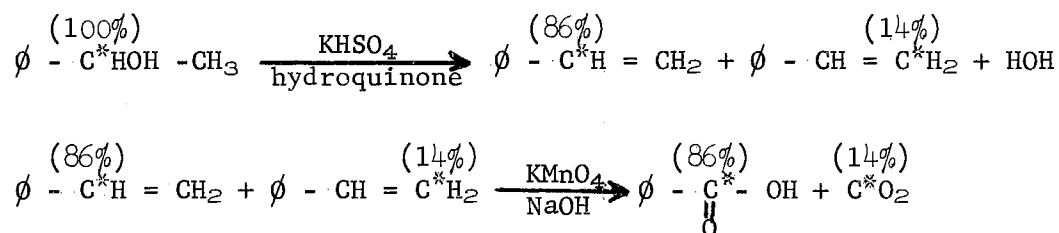
The above equations show the extent of observed carbon-14 positional

rearrangement that occurred during the high temperature dehydration of

1-phenylethanol by the action of potassium bisulfate, the salt of a

strong acid. The indication of a rearrangement furnished by the liquid

scintillation counting data agrees qualitatively with the information

gained by the use of the wet oxidation and vibrating reed measurement

technique. However, the data obtained from the latter technique, being

more precise and much more likely to be accurate, must exclusively be

used to form a quantitative opinion of the extent of rearrangement.

Possible Reaction Mechanisms

There are two generally accepted mechanisms by which olefin elim-

ination reactions proceed: the bimolecular elimination (E2), a concerted one-step process; and the unimolecular elimination (E1), a two-step process with a slow rate-determining step and a very fast step.

Bimolecular Elimination: The E2 mechanism is a widely occurring one in which a strong nucleophilic agent attacks and removes a hydrogen atom from a position beta to a nucleophilic group which also splits off at the same time (13). In the general equation the attacking nucleophile is represented as Y and the leaving nucleophilic group as X. The curved arrows represent the shift of electrons by inductive effect which aids the leaving group to split off.
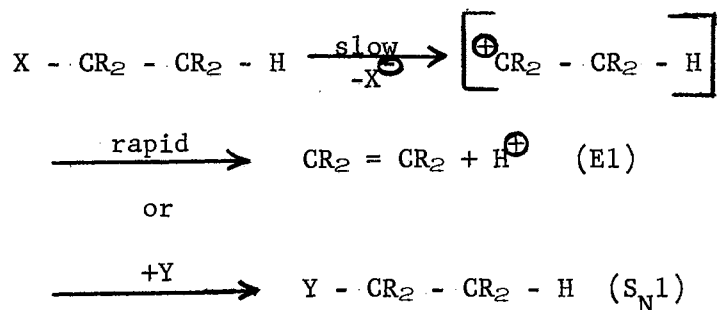
$$Y + H - \underset{\beta}{CR_2} - \underset{a}{CR_2} - X \longrightarrow YH + CR_2 = CR_2 + X \quad (E2)$$
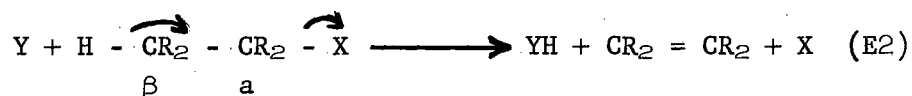
This type of reaction mechanism is characterized by second-order kinetics, first-order each in substrate and in base, showing that the rate of elimination is dependent upon the concentration of base (11). In general, E2 eliminations are favored over $S_N 2$ substitutions (the corresponding mechanism of substitution which usually occurs concurrently with the elimination reaction) by the following factors: (a) branching of the carbon skeleton at either the α- or β-carbon atoms, (b) the action of strong bases at high concentrations, (c) nonpolar solvents, and (d) high temperatures (9). E2 reactions are catalyzed by bases and tend to predominate over the competing E1 mechanism under basic conditions.

Unimolecular Elimination: The E1 mechanism is also an important one for olefin-forming eliminations; it has been established for a number of alkyl halides and sulfonium salts (13), and is almost certainly the path by which acid-catalyzed dehydrations of many alcohols proceed (9). The reaction proceeds in two steps: a slow one in which an electrophilic

agent removes an electronegative group X from the molecule resulting

in a positively charged carbonium ion which then reacts quite rapidly

either to lose a β-hydrogen atom with the formation of an olefin or to

regain some nucleophilic group Y. The carbonium ion acts to stabilize

itself as best it can by shifting electrons and the locality of the posi-

tive charge to the most stable position or positions, frequently causing

a rearrangement of the carbon skeleton of the molecule in the process.

$$X - CR_2 - CR_2 - H \xrightarrow[-X^{\ominus}]{slow} \left[\overset{\oplus}{C}R_2 - CR_2 - H \right]$$

$$\xrightarrow{rapid} CR_2 = CR_2 + H^{\oplus} \quad (E1)$$

or

$$\xrightarrow{+Y} Y - CR_2 - CR_2 - H \quad (S_N 1)$$

Approximate first order kinetics are characteristics of E1 elimina-

tions, first order in substrate and independent of the concentration of

the attacking reagent. This mechanism is commonly encountered in cases

where the substrate may yield a relatively stable carbonium ion, i.e.

when the α-carbon atom is secondary or tertiary and, more particularly,

when an α-phenyl or α-vinyl group is present. E1 eliminations are favored

over $S_N 1$ substitutions (the corresponding mechanism of substitution which

occurs simultaneously with the elimination) by the following factors:

(a) solvents of high polarity, (b) the addition of non-common ions to

the solution, and (c) high temperatures. The ratio of the rates of

$S_N 1/E1$ reactions are roughly independent of the nature of the leaving

group and the concentration of base present, except that with high base

concentrations E2 elimination tends to replace E1 elimination (9).

Probable Mechanisms in Cases Studied

The experimental data obtained for the two cases studied make possible

a rather clear-cut decision as to whether E1 or E2 reaction mechanisms
are to be assigned to the respective cases. The complete absence of
carbon atom rearrangement in the strong-base-catalyzed dehydration of
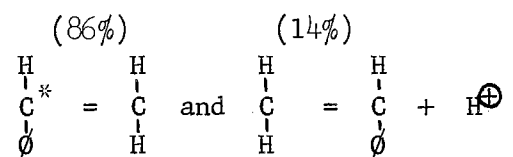2-phenylethanol-1-C^{14} argues heavily in favor of the E2 mechanism for
this reaction. The occurrence of a carbon atom rearrangement in the acid-
catalyzed dehydration of 1-phenylethanol-1-C^{14} argues as strongly in favor
of the E1 mechanism for that reaction.

Base-Catalyzed Dehydration of 2-Phenylethanol-1-C^{14}: The fact that
a weight of potassium hydroxide similar to the weight of 2-phenylethanol-
1-C^{14} was needed for good yields agrees with the second-order kinetics
characteristic of E2 mechanisms. The advanced temperatures necessary
and the rather low polarity of the alcohol also conform to what is known
about the conditions required for E2 reactions. An equation showing the
reaction mechanism follows in a straightforward manner from the previously
shown general equation. On the basis of the experimental data it is safe
to say that the potassium-hydroxide-catalyzed dehydration of 2-phenyl-
ethanol proceeds by the concerted E2 mechanism of olefin elimination.

$$OH^{\ominus} + H - \underset{\phi}{CH} - \overset{*}{C}H_2 - OH \rightleftarrows H_2O + \underset{\phi}{CH} = \overset{*}{C}H_2 + OH^{\ominus}$$
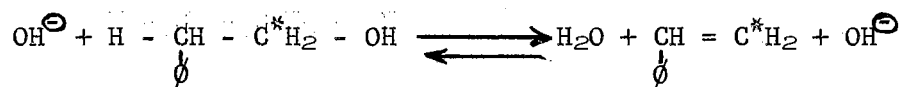
Acid-Catalyzed Dehydration of 1-Phenylethanol-1-C^{14}: In this case
a true catalytic amount of potassium bisulfate (0.02 g. compared with
2-3 g. of the alcohol) was adequate to furnish good yields of styrene.
This agrees well with the general rule that E1 eliminations proceed
independently of the concentration of attacking reagent. Any dissocia-
tion of the potassium bisulfate catalyst would provide non-common ions
to the solution which process accelerates unimolecular reactions and, in
addition the presence of the α-phenyl group should tend to stabilize the

carbonium ion intermediates formed in the process. The demonstration
of positional carbon atom rearrangement is most convincing evidence in
favor of the El mechanism, since this type of rearrangement is common
and is characteristic of reactions proceeding through carbonium ion inter-
mediates.

In proposing carbonium ion transition states one must take into
account two theoretical possibilities, the bridged intermediate or
"phenonium" ion and the "classical" open carbonium ion transition state.
In both of these it is necessary to envisage hydride ion transfer before
there can be phenyl group migration. The latter is necessary of course,
as the positions of the side-chain carbon atoms in styrene are determined
in relation to the phenyl group and there must be a change of the phenyl
group from one carbon atom to the other for one to observe a rearrange-
ment. Equations are shown here representing both schemes.

Elimination via the "classical" open carbonium ion intermediate:

Elimination via the bridged "phenonium" ion intermediate:

$$(86\%) \qquad (14\%)$$

$$\overset{\underset{\phi}{|}}{\overset{|}{C}}{}^{*} \; = \; \overset{\underset{H}{|}}{\overset{|}{C}} \quad \text{and} \quad \overset{\underset{H}{|}}{\overset{|}{C}} \; = \; \overset{\underset{\phi}{|}}{\overset{|}{C}} \; + \; H^{\oplus}$$

From the available data it is impossible to say which carbonium

ion path is taken so both are given as possible intermediates in the

El elimination of water from 1-phenylethanol-1-C^{14} under acid catalysis.

CONCLUSIONS

The present theoretical knowledge of physical organic chemistry applicable to this work utilizes reaction conditions, kinetic rate data, and isotopic tracer methods to elucidate the mechanisms by which reactions proceed. In this work, the base and acid versions of dehydration reactions of 2- and 1-phenylethanol, respectively, were studied. The following conclusions were drawn from a comparison of reaction conditions and experimentally observed carbon-14 tracer rearrangements with theoretical considerations.

(1) No carbon atom positional rearrangement occurs during the dehydration of 2-phenylethanol by the action of solid potassium hydroxide at advanced temperatures. This lack of rearrangement together with characteristic reaction conditions indicates that the E2 bimolecular mechanism of elimination predominates completely in this base-catalyzed reaction.

(2) A definite small positional rearrangement of side-chain carbon atoms occurs in the dehydration of 1-phenylethanol by the action of solid potassium bisulfate at advanced temperatures. A rearrangement of this type is characteristic of reactions proceeding via unimolecular reactions. The fact that there is not a complete rearrangement indicates that a bimolecular mechanism probably plays some part. It is concluded that this acid-catalyzed reaction proceeds mainly through the E1 unimolecular elimination mechanism with a minor contribution from the competing E2 bimolecular elimination mechanism.

29

SUMMARY

Carbon-14 isotopic tracers were used to discover if side-chain positional rearrangements occur in dehydration reactions at high temperatures of 2-phenylethanol-1-C^{14} and 1-phenylethanol-1-C^{14} catalyzed by potassium hydroxide and potassium bisulfate, respectively. Each carbon-14 labeled alcohol was heated in the presence of the dehydration catalyst and a suitable polymerization inhibitor, water and carbon-14 labeled styrene distilling over as they were formed. The radioactive styrenes were oxidized to benzoic acid to determine whether the carbon tracers were in the α- or β-carbon positions. Styrene-α-C^{14} was also polymerized with a cationic initiator to obtain a high conversion solid polymer for radioactivity assay purposes.

The radioactivity assays were done by two different methods. 2-Phenylethanol-1-C^{14}, the styrene-β-C^{14} produced from it, and the benzoic acid obtained from the styrene by degradative oxidation were assayed by means of liquid scintillation counting. Styrene-α-C^{14} (in polymer form) and the benzoic acid-carboxyl-C^{14} prepared from it were assayed by wet combustion to carbon dioxide and analysis on a vibrating reed electrometer.

Carbon-14 positional rearrangements observed were: 0% in the base-catalyzed dehydration, and 13.9% in the acid catalyzed reaction. Mechanisms for the two reactions were deduced from the comparison of experimental results with theoretical considerations, and structures for the transition states or intermediates were proposed.

BIBLIOGRAPHY

1. W. A. Bonner and C. J. Collins, _J. Am. Chem. Soc._, 75, 5372-9 (1953).

2. R. H. Boundy and R. F. Boyer, "Styrene, its Polymers, Copolymers and Derivatives," ACS Monograph No. 115, Reinhold Publishing Company, 1952.

3. L. A. Brooks, _J. Am. Chem. Soc._, 66, 1295 (1944).

4. C. J. Collins and W. A. Bonner, _J. Am. Chem. Soc._, 77, 92-9 (1955).

5. C. J. Collins, D. N. Ness, R. H. Mayor, G. M. Toffel and A. R. Jones, _J. Am. Chem. Soc._, 75, 397-402 (1953).

6. D. J. Cram, _J. Am. Chem. Soc._, 71, 3863-70 (1949).

7. H. B. Dykstra, _J. Am. Chem. Soc._, 56, 1625 (1934).

8. W. S. Emerson, _Chem. Revs._, 45, 183 (1949).

9. E. S. Gould, "Mechanism and Structure in Organic Chemistry," Henry Holt and Company, N. Y., p. 472-507, 1959.

10. E. M. Hodnett and A. W. Jensen, _J. Polymer Sci._, XLIII, 183-191 (1960).

11. E. D. Hughes, C. K. Ingold, S. Masterman and B. J. MacNulty, _J. Chem. Soc._, 1940, 899.

12. C. D. Hurd, R. W. McNamee and F. O. Green, _J. Am. Chem. Soc._, 61, 2979 (1939).

13. C. K. Ingold, "Structure and Mechanism in Organic Chemistry," George Banta Publishing Company, Menasha, Wisconsin, p. 419-472, 1953.

14. A. W. Jensen, Ph.D. Thesis, Oklahoma State University (1958).

15. R. E. Kirk and D. F. Othmer, "Encylcopedia of Chemical Technology," Interscience, N. Y., 13, 119-45, 1954.

16. C. C. Lee, G. P. Slater and J. W. T. Spinks, _Can. J. Chem._, 35, 1417 (1957).

17. D. C. Pepper, _Trans. Faraday Soc._, 45, 404, (1949).

18. V. R. Raaen and G. A. Ropp, _Anal. Chem._, 25, 174 (1953).

19. W. H. Saunders, Jr., S. Asperger and D. H. Edison, _J. Am. Chem. Soc._, 80, 2421-4 (1958).

20. S. Winstein and R. Heck, _J. Am. Chem. Soc._, 78, 4801 (1956).

21. S. Winstein, C. R. Lindegren, H. Marshall and L. L. Ingraham, _J. Am. Chem. Soc._, 75, 147 (1953).

22. S. Winstein and B. K. Morse, _J. Am. Chem. Soc._, 74, 1133 (1952).

VITA

Robert Stephen Jones

Candidate for the Degree of

Master of Science

Thesis: REARRANGEMENT STUDIES IN DEHYDRATIONS OF CARBON-14 LABELED
    PHENYLETHANOLS

Major Field: Organic Chemistry

Biographical:

    Personal data: Born August 18, 1935, Oskaloosa, Iowa.

    Undergraduate study: Bachelor of Science Degree, Oklahoma State
        University, Stillwater, Oklahoma, 1954-1957.

    Professional Experience: Graduate Teaching Assistant at Oklahoma
        State University, Stillwater, Oklahoma, 1957-1959.