I. STEREOCHEMISTRY OF THE REACTION OF D(+)-2,3-EPOXYBUTANE WITH ALCOHOLS

II. THE COORDINATION REACTION BETWEEN SILVER ION AND ALKYNES

III. SOME RELATIONSHIPS OF STEROLS TO PLANT GROWTH

Thesis by
George Kenneth Helmkamp

In Partial Fulfillment of the Requirements
for the Degree of
Doctor of Philosophy

California Institute of Technology
Pasadena, California
1953

ACKNOWLEDGMENTS

I wish to express my thanks to Professor Howard J. Lucas for the valuable suggestions, encouragement and criticism received during this research program.

The theoretical considerations and mathematical development of the evaluation of the empirical argentation constants, K_1 and K_2, were made according to the suggestions of Forrest L. Carter. I wish also to acknowledge the fact that much of the oxidation procedure and design of equilibration equipment was made with the cooperation of Mr. Carter.

ABSTRACT

PART I.

The reaction between D(+)-2,3-epoxybutane and alcohols is accompanied by a Walden inversion. The 3-methoxy-2-butanol prepared in this manner is an <u>erythro</u>-isomer, for <u>meso</u>-2,3-dimethoxybutane can be prepared from it by the Williamson synthesis.

PART II.

Permanganate oxidation under alkaline conditions has been employed as a method for the quantitative determination of aqueous solutions of 3-hexyne.

3-Hexyne and several homologs (methyl groups in the 1-, 2- and 5-positions) have been synthesized. Argentation constants for these have been evaluated by means of their solubilities in aqueous solutions of silver ion at constant ionic strength.

PART III.

A survey has been made concerning the effect of various steroidal substances on growth of pea embryos. A strong inhibition was noted in the presence of testosterone. Estrone and saponins tended to enhance early growth.

TABLE OF CONTENTS

PART I

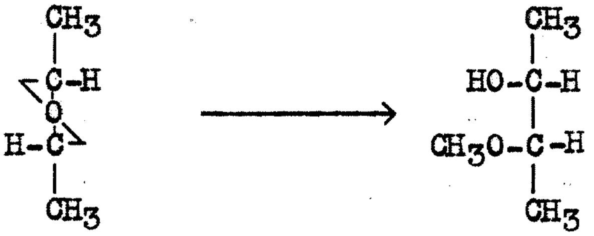
STEREOCHEMISTRY OF THE REACTION OF D-(+)-2,3-EPOXYBUTANE WITH ALCOHOLS

INTRODUCTION.

D(+)-2,3-Epoxybutane has proved to be a highly useful compound for the study of the stereochemical aspects of reactions of the epoxide ring. As will be outlined below, several types of *trans*-openings of the ring have been observed, and, in fact, no reactions involving *cis*-opening of this particular ring are known.

The assumptions for the basis of the present investigation of the proof of the direction of opening of the epoxide ring by alcohols arise as follows:

1. Ring opening will be *trans*, leading to an optically active mono-ether of *meso*-2,3-butanediol.



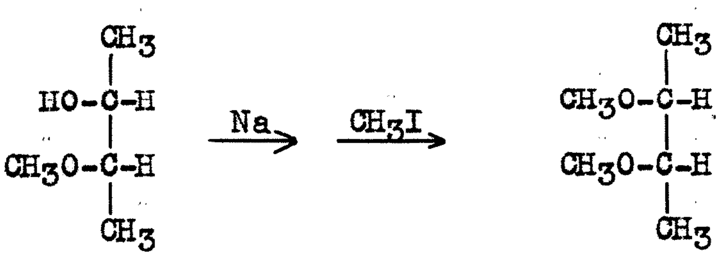
(1)

D-(+)-2,3-Epoxybutane

L-*erythro*-3-methoxy-2-butanol

2. The *erythro*-3-methoxy-2-butanol obtained in this manner, could then be readily converted into a *meso*-diether by the Williamson synthesis, resulting in loss of optical activity.

The loss of optical activity at this point would not necessarily be due to the single inversion shown in equation 1.

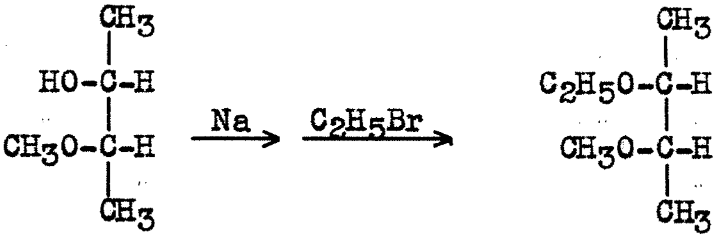


(II)

L-erythro-3-Methoxy-2-butanol

meso-2,3-Dimethoxybutane

3. If, in the Williamson synthesis, methyl iodide is replaced by ethyl bromide, the resulting compound is no longer a meso-modification. If the resulting diether then retains optical activity, it will have been satisfactorily demonstrated that racemization cannot be solely responsible for loss of optical activity during formation of the diethers.



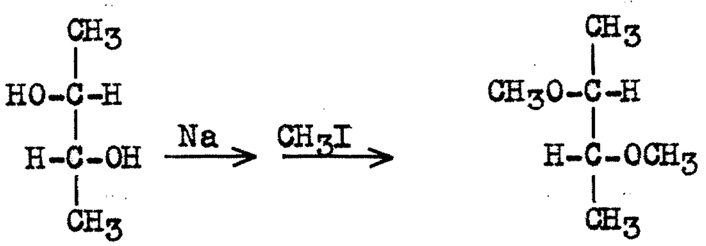
(III)

L-erythro-3-Methoxy-2-butanol

D-erythro-3-Ethoxy-2-methoxybutane

4. Diethers can be prepared from D(-)-2,3-butanediol through the Williamson synthesis. A comparison of the physical constants of the erythro-dimethyl ether with those of the known diether of the D-series will further confirm whether the former is truly meso or merely a DL modification or a mixture.

Preparation of diethyl ethers of the D-series will serve the same purpose.



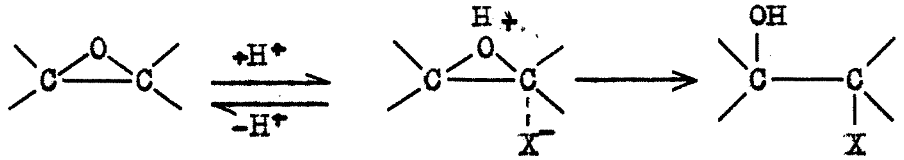
(IV)

D(-)-2,3-Butanediol D-2,3-Dimethoxybutane

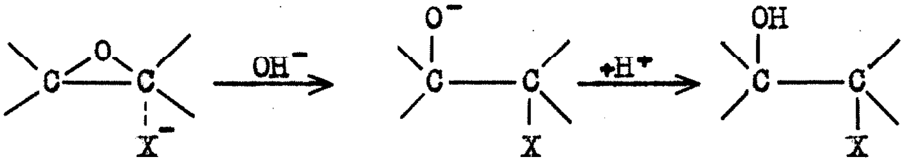
LITERATURE SURVEY.

A comprehensive survey of the mechanism and stereochemistry of the opening of the epoxide ring was made by Winstein and Henderson in 1950 (1). In consideration of this, it should suffice to include in this thesis only those pertinent facts which are directly associated with the problem at hand.

Opening of the epoxide ring proceeds by a nucleophilic attack on carbon with displacement of the oxygen atom. The reaction may be either acid- or base-catalyzed. The respective mechanisms are given by equations V and VI (1).



(V)



(VI)

The first reaction (eq. V), involving the conjugate acid as an intermediate, is ordinarily much more rapid than the base-catalyzed reaction (2). However, the reverse may be true in those cases where a base may convert the attacking species into a more highly nucleophilic agent. This may be illustrated in the case of the reaction between phenols and oxides, in which the phenolate ion is highly superior to phenol as the attacking species.

The use of an aliphatic alcohol as the nucleophilic attacking reagent is the subject of particular concern here. The reaction may be made under neutral, acidic or basic conditions . Here again, the reaction involving the conjugate acid is best from considerations of reaction rate.

Winstein and Henderson (3) have suggested that the 2-methoxycyclohexanol prepared from cyclohexene oxide is trans. The proof follows from two considerations. First, cyclohexene oxide must be cis because of the steric impossibility of the existence of a trans form. Secondly, the monomethyl ether of 1,2-hexanediol is assumed to be trans by virtue of a comparison of its physical properties with those of a compound of known configuration. The constants compare favorably with those of a monoether of the 1,2-cyclohexanediol which does not form a compound with acetone. Boeseken (4) has shown that only one modification of 1,2-cyclohexanediol undergoes this reaction, and this must then be the cis-form.

The stereochemical aspects of the opening of the epoxide ring of 2,3-epoxybutane have been well characterized.

A nucleophilic attack by water on optically active trans-2,3-epoxybutane (5) leads to optically inactive meso-2,3-butanediol, whereas cis-2,3-butanediol gives rise to the DL modification of the glycol. Similarly, acetic acid (6), hydrohalic acids (7, 8, 9) and ammonia (10) induce a trans-opening of the ring.

The reaction of cis- and trans-2,3-epoxybutane with methanol has been carried out by Winstein and Henderson (11). However, they have merely assumed trans-opening of the ring by analogy with the reactions mentioned above. The conclusion is undoubtedly well-founded, but unequivocal proof still rests in the use of optically active modifications of 2,3-epoxybutane.

In the course of the present investigation, there were numerous instances in which it was necessary to employ the Williamson synthesis for the preparation of ethers of alcohols. In all cases, it has been assumed that no inversion takes place during this reaction. It will be pointed out later in the discussion that there is no ambiguity in this assumption, as demonstrated by a series of reactions.

It is known that normally the Williamson reaction proceeds by an S_N2 mechanism (12). Thus, second order kinetics has been observed for the reaction of sodium eugenoxide with alkyl halides (13). Also, complete inversion of optically active 2-chloro- or 2-bromo-octane has been observed when either of these react with sodium alkoxides (14).

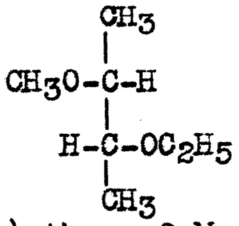
Ordinarily, racemization of the alcohol is assumed to be negligible during the Williamson synthesis, but Doering and Aschner (15) have shown that *levo*-phenylmethylcarbinol and *levo*-2-methylbutanol racemize in the presence of ketones. They concluded that stereochemical equilibration of alcohols is accomplished through an oxidation-reduction mechanism.

NOMENCLATURE.

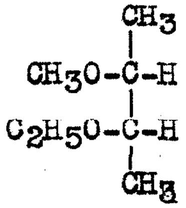
Since there are two centers of asymmetry in the 2,3-butanediol molecule, it became necessary to decide on a system of nomenclature.

The designation of both the *erythro*- and *threo*-forms as either D or L has been chosen to conform with the nomenclature used by Lucas and Garner (16) for the 2,3-disubstituted butanes. These authors have chosen carbon atom C-3 as the point of reference, in conformance with carbohydrate nomenclature (17). Thus, the highest numbered asymmetric carbon atom determines the family.

Consideration of the 2-methoxy-3-ethoxybutanes is illustrative.



D(-)-*threo*-2-Methoxy-3-ethoxybutane



L(+)-*erythro*-2-Methoxy-3-ethoxybutane

EXPERIMENTAL.

D(-)-2,3-Butanediol. The D(-)-2,3-butanediol used as a starting material for the syntheses was obtained from the National Research Council of Canada through the courtesy of Dr. G. A. Ledingham, Director and Drs. A. C. Neish and J. A. Wheat.

All of the optical isomers of 2,3-butanediol are produced by bacterial fermentation. The levo-form is produced by Aerobacillus polymyxa (18, 19), and a mixture of meso- and dextro-isomers arise through the use of Aerobacter aerogenes (20).

The following optical properties (table 1) were obtained for the active glycol, with comparative values found by Lucas and Garner (16) for material obtained from the Northern Regional Research Laboratory, Peoria, Ill.

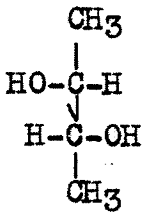
TABLE 1

Optical Properties of D(-)-2,3-Butanediol

Glycol	$\alpha^{25}D$	$[\alpha]^{25}D$
Crude (Canadian)	-12.45°	
Crude (Regional Laboratory)	-12.4°	
Distilled (Canadian)	-12.87°	-13.06°
Distilled (Regional Laboratory)	-13.00°	-13.19°

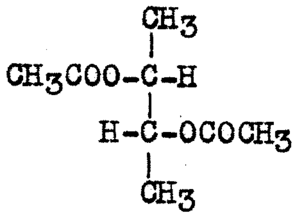
The glycol used in this investigation was distilled through a 30 cm. column packed with glass helices. The fraction which was retained was collected over a 0.1° range, and it must then be concluded that there is contamination with either 1% <u>meso</u>-glycol or with 0.5% <u>dextro</u>-glycol.

<u>D(+)-2,3-Diacetoxybutane</u>. This compound was prepared according to the method of Lucas and Garner (16).



$$\begin{array}{c} CH_3 \\ | \\ HO-C-H \\ | \\ H-C-OH \\ | \\ CH_3 \end{array}$$

D(-)-2,3-Butanediol



$$\begin{array}{c} CH_3 \\ | \\ CH_3COO-C-H \\ | \\ H-C-OCOCH_3 \\ | \\ CH_3 \end{array}$$

(VII)

D(+)-2,3-Diacetoxy-
butane

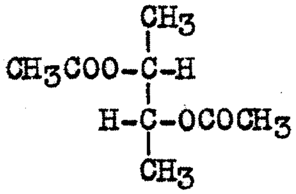
To 180 g. (2 moles) of redistilled D(-)-2,3-butanediol and 800 g. (10 moles) of pyridine in a two-liter flask were added 448 g. (4.4 moles) of acetic anhydride. The temperature was kept below 40° by means of an ice bath during the 45 minutes required for the addition. The mixture stood overnight at room temperature. Pyridine and acetic acid were removed by distillation at 100 mm., and the 2,3-diacetoxybutane was distilled at 14 mm.; b. 86.8-87.4°, $\alpha^{25}D$* +13.62°, yield 331 g. (95%). Lit., $\alpha^{25}D$ +14.10° (16).

No further purification was attempted because it was shown (16) that this had no effect on the purity of the epoxide prepared from this material.

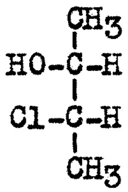
<u>L(+)-erythro-3-Chloro-2-butanol.</u> This compound was prepared according to the method given by Lucas and Gould (8).

---

*All observed rotations were made using pure liquids in a one decimeter polarimeter tube.



$$\begin{array}{c} CH_3 \\ | \\ CH_3COO-C-H \\ | \\ H-C-OCOCH_3 \\ | \\ CH_3 \end{array}$$



$$\begin{array}{c} CH_3 \\ | \\ HO-C-H \\ | \\ Cl-C-H \\ | \\ CH_3 \end{array}$$

(VIII)

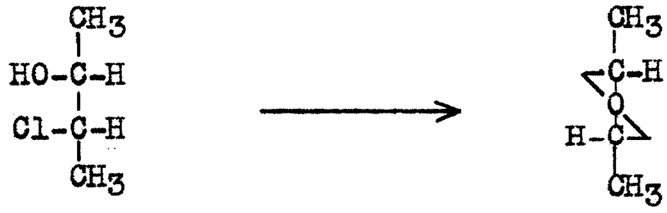
D(+)-2,3-Diacetoxybutane L(+)-*erythro*-3-Chloro-2-butanol

A mixture of 261 g. (1.5 moles) of D(+)-2,3-diacetoxybutane and 380 g. of reagent grade hydrochloric acid (37%) was placed in a one-liter ampoule and cooled to about -20°. Dry hydrogen chloride gas was passed into the mixture until 143 g. (4 moles) had been added. The ampoule was then sealed and allowed to stand at room temperature for 14 days. The contents were then poured over 700 g. of technical sodium bicarbonate with stirring. The solid residue was removed by filtration and washed with 500 ml. of isopropyl ether. This ether was used to wash the aqueous phase and then it was combined with the original organic phase. The total organic material was washed with 5% sodium bicarbonate solution, cooled with dry ice and filtered through crushed dry ice.

The reaction product contained both the expected chlorohydrin and some 3-chloro-2-acetoxybutane. It was unnecessary to separate the two products, for both are converted to the same epoxide in the subsequent reaction.

After the isopropyl ether was removed by distillation, two main fractions were obtained by fractional distillation. The first was collected from 65-66.5° (44 mm.); $\alpha^{25}D$ +8.48°; yield 115 g. The second was collected from 72-74.5° (35 mm.); $\alpha^{25}D$ +10.98°; yield 43.6 g. The combined yield was 90%.

D(+)-2,3-Epoxybutane.



(IX)

L(+)-*erythro*-3-Chloro-2-butanol D(+)-2,3-Epoxybutane

A one-liter, 3-necked flask was placed in a hot water bath and fitted with a mercury-sealed stirrer, a dropping funnel and a condenser leading to a receiver in an ice-hydrochloric acid bath at about -15°.

A solution of 265 g. technical potassium hydroxide in 135 ml. water was placed in the flask and heated to about 90°. While maintaining this temperature, the mixed chlorohydrin and chloroacetoxy compounds from the previous reaction were added over a period of 1½ hours.

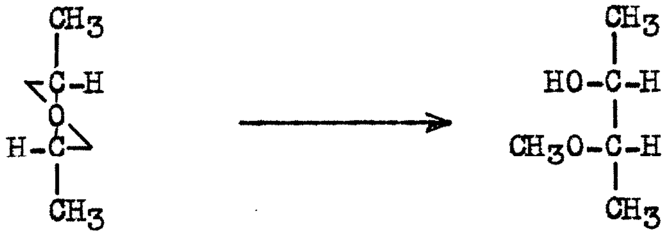
The product which distilled from the reaction mixture was dried with anhydrous potassium carbonate, filtered and distilled through a 30 cm. column packed with helices: b. 52.8-53.5° (748 mm.); $\alpha^{25}D$ +45.61°; yield, 67.7 g., 59.5% from the glycol. Repeated fractional distillation yielded a product with a maximum rotation of +46.44°. Lit., b. 53.5-53.7° (745 mm.); $\alpha^{25}D$ +47.23° (16). This represents an optical purity of about 98.3% when compared with the best value observed by previous investigators, +47.23° (16). In view of this, it shall be assumed that the maximum optical purity of compounds prepared from this epoxide will be 98%.

L(+)-*erythro*-3-Methoxy-2-butanol. Base catalyzed opening of the epoxide ring of D(+)-2,3-epoxybutane proved to be quite slow. The method attempted was essentially that of Chitwood and Freure (21).

A small piece (o.1 g.) of clean sodium was dissolved in 40 g. (1.25 moles) of methanol which had been distilled from over sodium methoxide (b. 64.8-64.9°). The mixture was placed on a steam cone and refluxed during the addition over 45 minutes of 9.04 g. (0.125 moles) of D(+)-2,3-epoxybutane. After the addition, a slow reflux rate was maintained for 2½ hours. Fractional distillation yielded no significant amount of material boiling above the boiling point of methanol.

A similar attempt was made using one mole of methanol containing 0.3 g. sodium hydroxide and 7.2 g. (0.10 mole) of epoxide. The mixture was refluxed for 2½ hours, then again for one hour after standing overnight. Fractional distillation yielded unreacted epoxide, methanol and a fraction of a gram of higher boiling material; b. 82.5° (125 mm.).

The acid catalyzed reaction (11), in contrast to the above results, proceeded quite smoothly and rapidly.



(X)

D(+)-2,3-Epoxybutane L(+)-erythro-3-Methoxy-2-butanol

To a solution of three drops of concentrated sulfuric acid in 32 g. (1 mole) of anhydrous methanol, was added 7.2 g. (0.10 mole) of the epoxide with stirring. The reaction was sufficiently exothermic to initiate refluxing. After the addition was complete (about 30 minutes), the solution was refluxed for one-half hour and allowed to stand overnight. After the acid had been neutralized with potassium carbonate, most of the methanol was removed by distillation through a semi-micro distilling tube. Refractionation of the foreruns and of the main fraction yielded 8.36 g. of L(+)-<u>erythro</u>-3-methoxy-2-butanol (84%): b. 79.1-79.3° (117 mm.); $n^{25}D$ 1.4098; $d^{25}4$ 0.9064; $\alpha^{25}D$ +18.05°; $[\alpha]^{25}D$ +19.92°; MR_D 28.46 (calc'd 28.45). Lit.; b. 132.3-132.5° (748 mm.); $n^{25}D$ 1.4107 (11).

Analysis. Calc'd for $C_5H_{12}O_2$: C, 57.66; H, 11.62. Found:* C, 57.33; H, 11.28.

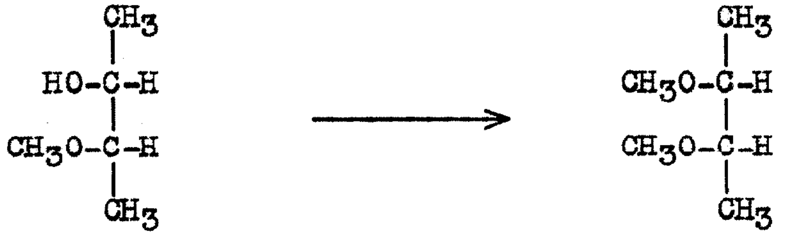
---

*Unless otherwise indicated, all analyses were made by Dr. A. Elek, 4763 W. Adams Boulevard, Los Angeles 16, California.

The reaction was repeated: yield, 79%, with an optical purity of the crude product of 99%, based on the best value of $\alpha^{25}D$ obtained previously.

It is obvious from the above results, that the base catalyzed reaction between 2,3-epoxybutane and methanol is considerably slower than the acid catalyzed reaction. This difference has been noted to a much less degree in the case of the reaction of propylene oxide with methanol (21). In the case of propylene oxide, the reaction time of the base catalyzed reaction is about one-half that of the acid catalyzed reaction. Yields were equivalent in both instances (70-80%).

meso-2,3-Dimethoxybutane.



(XI)

L(+)-*erythro*-3-Methoxy-2-butanol

meso-2,3-Dimethoxybutane

To 30 ml. of anhydrous ethyl ether were added 2.3 g. (0.10 mole) of sodium shavings and 5.20 g. (0.050 mole) of L(+)-*erythro*-3-methoxy-2-butanol. After 24 hours, hydrogen evolution had virtually ceased, leaving a clear reddish solution along with the excess sodium. The sodium was removed and an excess of methyl iodide, 10.6 g. (0.075 mole), was added. Fairly rapid formation of sodium iodide started after a few minutes. The mixture was heated under a reflux condenser for two hours and allowed to stand for three hours. The ether was removed by distillation, water was added to dissolve the sodium iodide, and the aqueous phase was shaken twice with portions of the ether previously removed. All of the ether phases were combined and dried with potassium carbonate. Distillation was carried out at 750 mm.: b. 107.3-108.0°; $\alpha^{25}D$ -0.03°; crude yield, 3.79 g. (64%). The optical rotation indicated possible contamination with methoxybutanol to an extent of less than 0.5%.

Refractional distillation through a semi-micro distilling tube was made after the addition of metallic sodium which in the molten state reacted with unchanged starting material: b. 108.0° (750 mm.); $\alpha^{25}D$ 0.00°; $n^{25}D$ 1.3890; $d^{25}4$ 0.8435; MR_D 33.13 (calc'd, 33.19).

Analysis. Calc'd for C_6H14O_2: C, 60.97; H, 11.94. Found: C, 61.06; H, 11.71.

L(+)-erythro-3-Ethoxy-2-butanol. The procedure was identical with that used for the preparation of the methoxy homolog, except that the time required for the reaction of epoxybutane with ethanol was about twice as long as with methanol. Yields were 80% and 83% in successive reactions when the reactants were refluxed for two hours and allowed to stand for two days. Physical constants: b. 83.5° (109 mm.); $n^{25}D$ 1.4106; $d^{25}4$ 0.8866; $\alpha^{25}D$ +23.53°; $[\alpha]^{25}D$ +26.54°;

MR_D 33.07 (calc'd, 33.08).

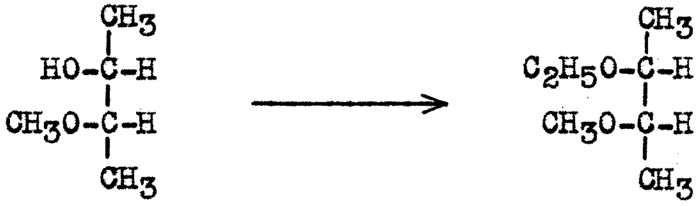
Analysis. Calc'd for $C_7H_{16}O_2$: C, 60.97; H, 11.94. Found: C, 61.01; H, 11.96.

meso-2,3-Diethoxybutane. The procedure was similar to that used for the preparation of *meso*-2,3-dimethoxybutane. The reactants, ethyl iodide and sodium 3-ethoxy-2-butoxide, were refluxed for 16 hours and allowed to stand overnight before isolation of the product: crude yield, 77%; $\alpha^{25}D$ +5.75°. This represents an optical purity of 76% based on contamination with unreacted starting material and on the best value of rotation after purification.

Three successive fractional distillations from sodium metal were necessary to prepare an optically pure material: b. 138.0° (745 mm.); $n^{25}D$ 1.3936; $d^{25}4$ 0.8190; $\alpha^{25}D$ +0.01°; $[\alpha]^{25}D$ +0.01°; MR_D 42.67 (calc'd, 42.43).

Analysis. Calc'd for $C_8H_{18}O_2$: C, 65.70; H, 12.41. Found: C, 65.92; H, 12.49.

D(-)-*erythro*-2-Methoxy-3-ethoxybutane.



$$\begin{array}{r}CH_3\\ HO-C-H\\ CH_3O-C-H\\ CH_3\end{array} \longrightarrow \begin{array}{r}CH_3\\ C_2H_5O-C-H\\ CH_3O-C-H\\ CH_3\end{array} \qquad (XII)$$

L(+)-*erythro*-3-Methoxy-2-butanol

D(-)-*erythro*-2-Methoxy-3-ethoxybutane

The Williamson procedure was used as described previously: yield of crude product, 60%. Physical constants: b. 124.0° (746 mm.); $n^{25}D$ 1.3918; $d^{25}4$ 0.8281; $\alpha^{25}D$ -6.32°; $[\alpha]^{25}D$ -7.63°; MR_D 38.00 (calc'd, 37.81).

<u>Analysis</u>. Calc'd for $C_7H_{16}O_2$: C, 63.59; H, 12.20. Found: C, 63.54; H, 12.08.

<u>L(+)-erythro-2-Methoxy-3-ethoxybutane.</u>

(XIII)

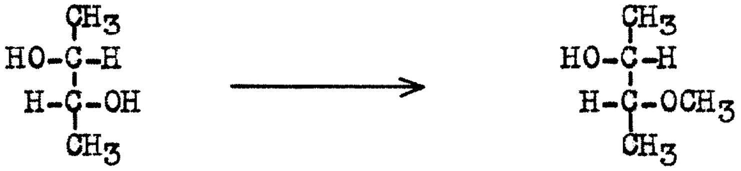
L(+)-erythro-3-Ethoxy-2-butanol   L(+)-erythro-2-Methoxy-3-ethoxybutane

The Williamson synthesis was used as described previously: yield of crude product, 70%; $\alpha^{25}D$ +6.45°.

On repeated fractional distillation of the crude product, the observed rotation first dropped to +6.14°, then rose to a maximum value: b. 123.8° (747 mm.); $n^{25}D$ 1.3917; $d^{25}4$ 0.8284; $\alpha^{25}D$ +6.34°; $[\alpha]^{25}D$ +7.65°; MR_D 37.98 (calc'd, 37.81).

<u>Analysis</u>. Calc'd for $C_7H_{16}O_2$: C, 63.59; H, 12.20. Found: C, 63.50; H, 12.17.

<u>D(-)-threo-3-Methoxy-2-butanol.</u>



(XIV)

D(-)-2,3-Butanediol   D(-)-threo-3-Methoxy-2-butanol

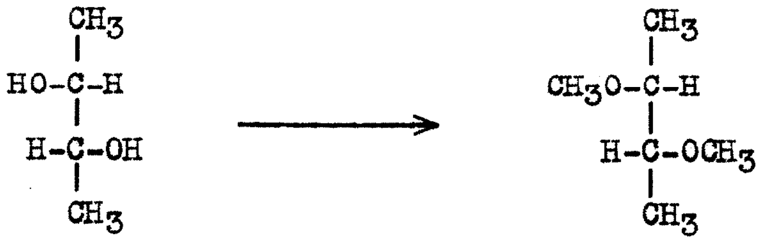
After preliminary attempts to prepare this compound in an ether solution had been found to be unsatisfactory, the following procedure was adopted, and it yielded excellent results.

D(-)-2,3-Butanediol was freed from water by distillation at reduced pressure. To 76 g. (0.85 mole) of the glycol was added 2.6 g. (0.11 mole) of clean sodium shavings. After the reaction was complete, the reaction flask was fitted with a reflux condenser, and 22 g. (0.15 mole) of redistilled methyl iodide was added with swirling. The flask and contents were warmed with an infra-red lamp, inducing a spontaneous temperature rise to 85°. After the initial reaction had subsided, as shown by a temperature drop, the temperature was maintained at about 50° for five hours. After standing two days, the reaction mixture still remained homogeneous, and the monoether was removed by distillation at 100 mm. pressure. The fraction boiling below 82° was collected. There was no indication, in either the distillate or the dry-ice trap on the distillation column, of any low-boiling diether. After removal of the monoether, the pressure was reduced and the excess glycol was recovered: b. 81.7-82.0° (15 mm.); $\alpha^{25}D$ -13.0°. In this and in subsequent analogous reactions, there was no indication that racemization of the glycol had taken place.

Fractional redistillation of the monoether was made in a semi-micro distilling tube: b. 74.5° (113 mm.); $n^{25}D$ 1.4067; $d^{25}4$ 0.8983; $\alpha^{25}D$ -24.25°; $[\alpha]^{25}D$ -26.24°; MR_D 28.52 (calc'd, 28.46); yield, 10.1 g. (86%). Lit.:[11] b. 126.4-126.5°; $n^{25}D$ 1.4074.

Analysis. Calc'd for $C_5H_{12}O_2$: C, 57.66; H, 11.62. Found: C, 57.78; H, 11.63.

D(+)-2,3-Dimethoxybutane.



$$\begin{array}{c} CH_3 \\ | \\ HO-C-H \\ | \\ H-C-OH \\ | \\ CH_3 \end{array} \longrightarrow \begin{array}{c} CH_3 \\ | \\ CH_3O-C-H \\ | \\ H-C-OCH_3 \\ | \\ CH_3 \end{array} \qquad (XV)$$

D(-)-2,3-Butanediol

D(+)-2,3-Dimethoxybutane

In the attempt to prepare the monomethyl ether of butanediol by a procedure involving ethyl ether as a solvent, enough D(+)-2,3-dimethoxybutane was formed to obtain physical constants and analyses.

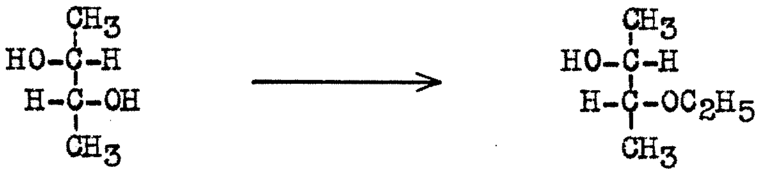
To a solution of 18.0 g. (0.20 mole) of redistilled D(-)-2,3-butanediol in 50 ml. ethyl ether was added 4.8 g. (0.21 mole) of clean sodium shavings. The reaction flask was protected with a calcium chloride drying tube and was allowed to stand for 30 hours. Over this period of time, it was necessary to regularly crush the solid which formed on the surface of the sodium in order to expose fresh metal. The mixture was heated under reflux and 42 g. (0.30 mole) of methyl iodide were added dropwise. The heating was continued for five hours and the reaction mixture was allowed to stand for two days. After most of the ether had been removed by distillation, sufficient water was added to dissolve the sodium iodide.

The ether phase was separated, combined with an ether extract of the aqueous phase, dried with potassium carbonate, filtered and distilled. Three major fractions were isolated. The first was the diether fraction: b. 52.5-57.5° (127 mm.); $\alpha^{25}D$ +0.75°; yield, 3.6 g. (15%). The second was monoether: b. 74-79° (127 mm.); $\alpha^{25}D$ -15.6°; yield, 2.1 g. (10%). The final fraction was unreacted starting material.

Repeated fractional distillation of the diether from over sodium in a semi-micro distilling tube yielded the pure product: b. 111.0° (746 mm.); $n^{25}D$ 1.3905; $d^{25}4$ 0.8464; $\alpha^{25}D$ +2.76; $[\alpha]^{25}D$ +3.26; MR_D 33.13 (calc'd, 33.19).

Analysis. Calc'd for $C_6H_{14}O_2$: C, 60.97; H, 11.94. Found: C, 61.03; H, 11.86.

D(-)-*threo*-3-Ethoxy-2-butanol.



(XVI)

D(-)-2,3-Epoxybutane

D(-)-*threo*-3-Ethoxy-2-butanol

To 60 g. (0.75 mole) of redistilled D(-)-2,3-butanediol were added 2,4 g. (0.11 mole) of sodium shavings. After the sodium had dissolved, an excess of ethyl iodide, 28 g. (0.18 mole), was added to the still hot solution (85°). A temperature of about 85° was maintained for about one hour by means of an infra-red lamp. The reaction mixture remained homogeneous to this point.

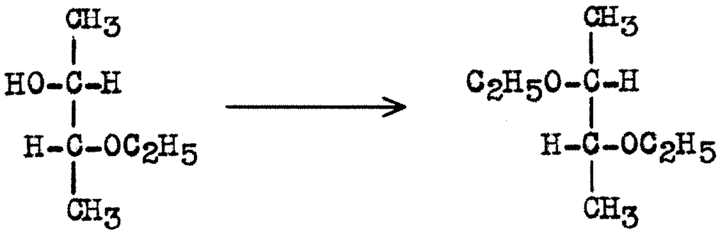
The monoether was removed from the excess glycol by distillation at reduced pressure: b. 82.3-83.6° (131 mm.); $\alpha^{25}D$ -32.40°; crude yield, 10.7 g. (87%). Two redistillations through a semi-micro distilling tube were necessary to obtain a pure product: b. 93.7° (173 mm.); $n^{25}D$ 1.4072; $d^{25}4$ 0.8773; $\alpha^{25}D$ -32.77°; $[\alpha]^{25}D$ -37.35°; MR_D 33.17 (calc'd, 33.08).

Analysis. Calc'd for $C_6H_{14}O_2$: C, 60.97; H, 11.94. Found: C, 61.03; H, 11.81.

Excess glycol was recovered from the reaction residue by distillation at 7 mm.: yield, 47.3 g.; b. 69.0-69.7°; $\alpha^{25}D$ -12.82°; $[\alpha]^{25}D$ -12.99°. Thus, about 93% of the original glycol was accounted for, and again there was no evidence of significant loss of optical activity.

D(-)-*threo*-2,3-Diethoxybutane.

The procedure was similar to that employed for the synthesis of *meso*-2,3-diethoxybutane: yield of crude product, 44%; $\alpha^{25}D$ -4.11°.



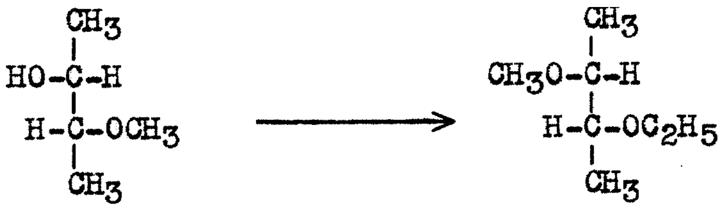
(XVII)

D(-)-threo-3-Ethoxy-2-butanol D(-)-2,3-Diethoxybutane

The crude product was purified by distillation from over sodium metal in a semi-micro fractionating tube: b. 139.8° (747 mm.); $n^{25}D$ 1.3956; $d^{25}4$ 0.8267; $\alpha^{25}D$ -4.07; $[\alpha]^{25}D$ -4.94; MR_D 42.63 (calc'd, 42.43).

Analysis. Calc'd for $C_8H_{18}O_2$: C, 65.70; H, 12.41. Found: C, 65.67; H, 12.22.

D(-)-threo-2-Methoxy-3-ethoxybutane.



(XVIII)

D(-)-threo-3-Methoxy-2-butanol D(-)-threo-2-Methoxy-3-ethoxybutane

The synthetic procedure was similar to that employed for meso-2,3-diethoxybutane.

The yield of crude product was not calculated because of an error in weighing. The diether was purified by distillation from over sodium metal: b. 126.2° (745 mm.); $n^{25}D$

1.3936; d^{25}_4 0.8333; α^{25}_D -0.12°; $[\alpha]^{25}_D$ -0.14°; MR_D 37.92 (calc'd, 37.81).

Analysis. Calc'd for $C_7H_{16}O_2$: C, 63.59; H, 12.20. Found: C, 63.85; H, 12.15.

Derivatives of Monoethers.

Pertinent information on these derivatives is given in Table 2.

DISCUSSION AND INTERPRETATION OF RESULTS.

It was pointed out by Prof. H. J. Lucas (22) that the physical constants of 2,3-disubstituted butanes exhibited some interesting relationships.

A comparison of refractive indices and densities (Table 3) reveals that in the monoether series, the *erythro*-isomers have the higher values, whereas in the diether series the *threo*-isomers have the higher values.

It was also of interest to compare the boiling points of the various pairs of compounds. In order to do this, it was necessary to correct the boiling points of two of the compounds for different pressures.

Extensive data on the vapor pressure of pure compounds at various pressures is given by Stull (23). Information for the disubstituted butanes was not available, but data was found for a compound quite similar in boiling point and in structure.

The vapor pressure, P, of a pure liquid as a function

TABLE 2

Derivatives of Monoethers

Ether	Deriv.	M.p., °C	Carbon, %		Hydrogen, %		Nitrogen, %	
			Calc'd	Found	Calc'd	Found	Calc'd	Found
L(+)-*erythro*-3-Methoxy-2-butanol	a	131-132[c]					5.13	5.55
	b	56-58					9.39	9.57
L(+)-*erythro*-3-Ethoxy-2-butanol	a	78-80	71.05	71.11	7.37	7.32		
D(-)-*threo*-3-Methoxy-2-butanol	a	93-94					5.13	5.46
D(-)-*threo*-3-Ethoxy-2-butanol	a	73-74	71.05	71.06	7.37	7.36		

[a] α-Naphthylurethan, prepared according to the directions of T. L. Shriner and R. C. Fuson, "Identification of Organic Compounds," 3rd Ed., John Wiley and Sons, Inc., New York, N. Y., 1948, pp. 163-164.

[b] 3,5-Dinitrobenzoate.

[c] Previous value for DL-isomer (11), 111-112°.

TABLE 3

Boiling Points of Ethers

Compound	n^{25}_D	d^{25}_4	B.p., obs.		B.p., calc'd.	
			°C.	P, mm.	°C.	P, mm.
L(+)-*erythro*-3-Methoxy-2-butanol	1.4098	0.9064	79.2	117		
D(-)-*threo*-3-Methoxy-2-butanol	1.4067	0.8983	74.5	113	75.9	117
L(+)-*erythro*-3-Ethoxy-2-butanol	1.4106	0.8866	83.5	109		
D(-)-*threo*-3-Ethoxy-2-butanol	1.4072	0.8773	93.7	173	82.4	109
meso-2,3-Dimethoxybutane	1.3890	0.8435	108.0	750		
D(-)-*threo*-2,3-Dimethoxybutane	1.3905	0.8464	111.0	746		
meso-2,3-Diethoxybutane	1.3936	0.8190	138.0	745		
D(+)-*threo*-2,3-Diethoxybutane	1.3956	0.8267	139.8	747		
D(-)-*erythro*-2-Methoxy-3-ethoxybutane	1.3918	0.8281	124.0	747		
D(-)-*threo*-2-Methoxy-3-ethoxybutane	1.3936	0.8333	126.2	745		

of the absolute temperature, T, is given by equation XIX.

$$\log P = A + B/T \qquad (XIX)$$

A plot of log P vs. 1/T is linear, and in order to make the necessary correction in a boiling point, it must be assumed that the slope, B, will be constant for similarly constituted compounds with molecular weights and boiling points in the same range.

In order to correct the boiling points of 3-methoxy-2-butanol and 3-ethoxy-2-butanol, the vapor pressure data for 4-methyl-2-pentanol was chosen (23). It was necessary to correct the boiling point of the methoxy compound from 113 mm. to 117 mm. and of the ethoxy compound from 173 mm. to 109 mm. These changes are so small that the method employed is probably valid to the accuracy desired.

4-Methyl-2-pentanol

$$\log P = 8.510 - 2300/T \qquad (XX)$$

D(-)-threo-3-Methoxy-2-butanol

$$\log P = 8.657 - 2300/T \qquad (XXI)$$

D(-)-threo-3-Ethoxy-2-butanol

$$\log P = 8.506 - 2300/T \qquad (XXII)$$

A comparison of boiling points is given in Table 3.

Similar relationships of physical constants have been noted previously, but not until now has the significance of a potential bond-forming hydrogen atom been noted. For example, the following erythro-compounds have the higher values of refractive index and density: 3-bromo-2-butanol (7), 3-chloro-2-butanol (8), 2,3-butanediol, 2,3-butanediamine (10), 3-amino-2-butanol (10), and _cis_-2,3-buteneimine (10). The following _threo_-compounds have the higher values: 2,3-dibromobutane (6, 24, 25), 2,3-diacetoxybutane (25), 2,3-dichlorobutane (8), 2-chloro-3-iodobutane (9), and 2-bromo-3-iodobutane (9).

Fisher-Taylor-Hirschfelder models were constructed of the alkoxybutanols in order to visualize any phenomena which could lead to the observed effects.

The models of the _erythro_- and _threo_-3-methoxy-2-butanols were oriented into a most probable position, i.e., in such a manner that there was free rotation of the methyl groups and also a maximum distance between like groups. The illustrations, Figure 1, made of these models are not drawn to scale, but are rather shown in such a manner to present relative positions of the atoms.

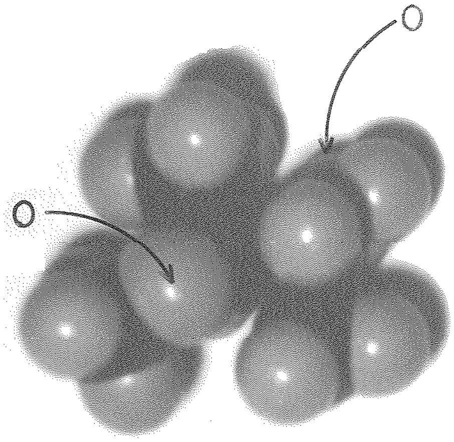
The _threo_-compound (II) is readily oriented in such a manner that there exists a possibility for intramolecular hydrogen bonding. The _erythro_-isomer (I) tends to assume a most probable orientation in which the hydroxyl group is opposite the methoxyl group, and the hydroxyl hydrogen is directed away from the molecule. In this case, there is excellent opportunity for intermolecular bonding. Associated with this would be an increase in boiling point, refractive index and density.

Probable orientations, again according to models, are shown for erythro- and meso-dimethoxybutanes (Figure 4).

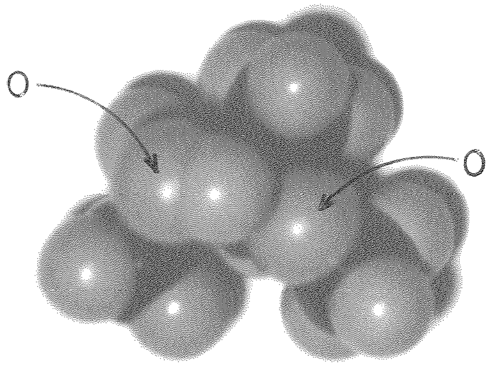
In these two instances the two oxygen atoms of the meso-form (IV) are projected from the asymmetric carbon atoms in an opposite sense, whereas, in the threo-form (III) they are projected in more nearly the same sense. In other words, the picture of the threo-form (III) shows both oxygen atoms projecting above the plane of the paper. Consequently, the threo-isomer should exhibit a greater dipole moment and physical constants (boiling point, refractive index and density) than the meso-modification.

The same argument, based on molecular models, has been found to apply to the 3-halo-2-butanols.

In one case, that of 3-bromo-2-acetoxybutane, the physical data is conflicting (6), owing in part to a very small spread between values. An exception is noted in the case of 2,3-epoxybutane, of which the cis-isomer (erythro) has the higher values (5, 7). This is again demonstrable by atomic models, in which orientation is predetermined by the rigid three-membered ring. In the cis-isomer, both of the methyl groups are on the same side of the ring, whereas, in the trans-isomer, they are opposed. The former then exhibits a possibility for a higher dipole moment and a resulting increase in boiling point, refractive index and density.

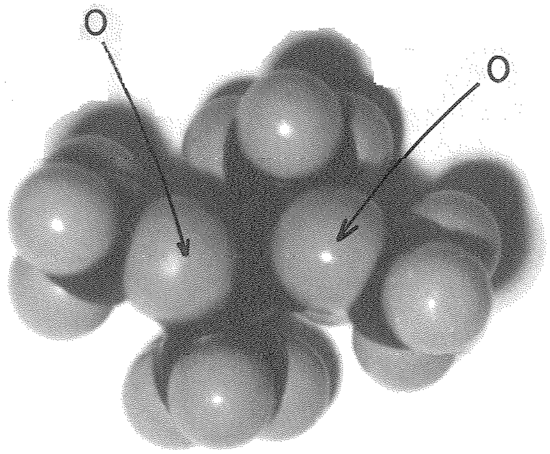


(I) *erythro*-3-Methoxy-2-butanol

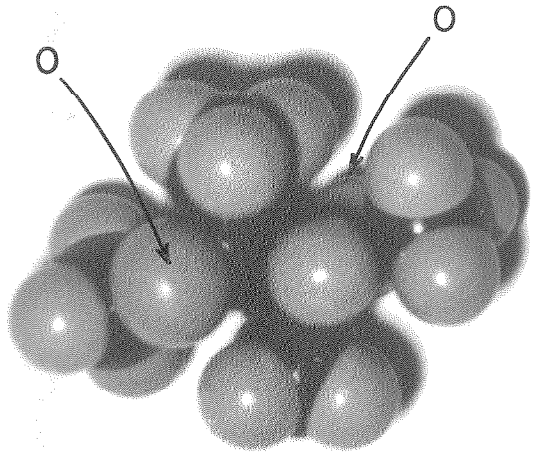


(II) *threo*-3-Methoxy-2-butanol

Figure 3



(III) *threo*-2,3-Dimethoxybutane



(IV) *meso*-2,3 Dimethoxybutane

Figure 4

STEREOCHEMICAL RESULTS.

The stereochemical aspects of the reaction between D(+)-2,3-epoxybutane and alcohols have followed the expected pattern.

The monoether resulting from a nucleophilic attack by methanol on D(+)-2,3-epoxybutane possesses optical activity. The 2,3-dimethoxybutane made from this monoether by way of the Williamson synthesis is optically inactive.

The situation is identical when ethyl groups are substituted for methyl groups.

A second series of reactions (equations 12 and 13) further substantiates the conclusions drawn regarding the optical purity of the products. If the loss of optical activity of the symmetrical diethers was due to causes other than the result of one complete inversion in the initial reaction, it would necessarily follow that the unsymmetrical diethers (equations 12 and 13) would be inactive by virtue of the same reasons.

This is not the case, for the antipodes D(-)-erythro-2-methoxy-3-ethoxybutane and L(+)-erythro-2-methoxy-3-ethoxybutane have optical rotations of opposite sign and of the same magnitude.

The conclusion that the inactive diethers have the meso-configuration is strengthened by the preparation of diastereomeric diethers (also monoethers) from D(-)-2,3-

butanediol by the Williamson synthesis. These all have the D-threo-configuration, the same as that of the glycol. They all have physical properties different from the corresponding erythro-isomers, and in addition the symmetrical threo-diethers possess optical activity. This also lends support to the conclusion that the inactivity of the erythro-isomers cannot be ascribed to racemization, but must arise from internal compensation.

REFERENCES

1. R. C. Elderfield, "Heterocyclic Compounds," Vol. I, John Wiley & Sons, Inc., New York, 1950, pp. 27-42.

2. J. N. Bronsted, M. Kilpatrick and M. Kilpatrick, J. Am. Chem. Soc., 51, 428 (1929).

3. S. Winstein and R. B. Henderson, J. Am. Chem. Soc., 65, 2196 (1943).

4. J. Boeseken, Rec. trav. chim., 47, 683 (1928).

5. C. E. Wilson and H. J. Lucas, J. Am. Chem. Soc., 58, 2396 (1936).

6. S. Winstein and H. J. Lucas, ibid, 61, 1581 (1939).

7. S. Winstein and H. J. Lucas, ibid, 61, 1576 (1939).

8. H. J. Lucas and C. W. Gould, Jr., ibid, 63, 2541 (1941).

9. H. J. Lucas and H. K. Garner, ibid, 72, 2145 (1950).

10. F. H. Dickey, W. Fickett and H. J. Lucas, ibid, 74, 944 (1952).

11. S. Winstein and R. B. Henderson, ibid, 65, 2196 (1943).

12. E. R. Alexander, "Ionic Organic Reactions," John Wiley & Sons, Inc., New York, 1950, p. 213.

13. S. S. Woolf, J. Chem. Soc., 1937, 1173.

14. E. D. Hughes, C. K. Ingold and S. Masterman, ibid, 1937, 1200.

15. W. von E. Doering and T. C. Aschner, J. Am. Chem. Soc., 71, 838 (1949).

16. H. J. Lucas and H. K. Garner, ibid, 70, 990 (1948).

17. Report of the Committee on Carbohydrate Nomenclature, Chem. Eng. News, 26, 1623 (1948).

18. A. C. Neish, Can. J. Res., 23b, 10 (1945).

19. G. E. Ward, O. G. Pettijohn, L. B. Lockwood and R. D. Coghill, J. Am. Chem. Soc., 66, 541 (1944).

20. G. S. Walpole, Proc. Roy. Soc. London, 83B, 272 (1911).

21. H. C. Chitwood and B. T. Freure, J. Am. Chem. Soc., 68, 680 (1946).

22. G. K. Helmkamp and H. J. Lucas, ibid, 74, 951 (1952).

23. D. R. Stull, Ind. Eng. Chem., 39, 517 (1947).

24. R. T. Dillon, W. G. Young and H. J. Lucas, J. Am. Chem. Soc., 52, 1953 (1930).

25. S. Winstein and R. E. Wood, ibid, 62, 548 (1940).

PART II

THE COORDINATION REACTION BETWEEN SILVER ION AND ALKYNES

A. INTRODUCTION.

The research program which was carried out was based on the previous work of H. J. Lucas and W. S. Dorsey (1) at the California Institute of Technology. It had been found that 3-hexyne would coordinate with silver ion in aqueous solution, and methods were devised to evaluate argentation constants for two coordination reactions (equations I and II).

$$Ag + B\text{ (3-hexyne)} \longrightarrow AgB \qquad (I)$$

$$Ag + AgB \longrightarrow Ag_2B \qquad (II)$$

The overall plan of this problem was to reevaluate the argentation constants of 3-hexyne by means of a different analytical or theoretical approach, and then to apply this technique to the study of alkynes containing various substituents <u>alpha</u> to the triple bond.

It seemed advisable to first consider variations in the analytical procedure which was used for the quantitative determination of 3-hexyne. Previously, a two-phase, liquid-liquid equilibration method (2, 3) was used to evaluate the argentation constants. The quantitative method for the analysis of 3-hexyne in both the organic (CCl_4) and aqueous phases was the bromination procedure of Lucas and Pressman

(4). The techniques involved proved to be quite tedious, for the aqueous phase contained only very small amounts of alkyne. Consequently, rigorous exclusion of oxygen from the system was necessary because of a rapid reaction between oxygen and the alkyne in the aqueous phase.

The bromination procedure had been pictured as a relatively simple, stepwise addition of bromine to the triple bond, which could be controlled so that the reaction did not proceed beyond the addition of one molecule of bromine per molecule of 3-hexyne. However, the reaction was apparently more complicated, for Dorsey found that the product isolated from such a reaction was a mixture. An analysis showed only a very small amount of bromine.

In spite of the fact that the bromination procedure led to satisfactory results in the case of 3-hexyne, it did not seem advisable to apply it to the determination of more complicated alkynes, either unsymmetrical ones or those less soluble in water.

B. QUANTITATIVE DETERMINATION OF 3-HEXYNE BY PERMANGANATE OXIDATION.

Oxidation of the Carbon-Carbon Triple Bond. The carbon-carbon triple bond is subject to oxidative cleavage in somewhat the same manner as the double bond. Alkaline permanganate (5), acidic dichromate and nitric acid (6) can all by used to oxidize a disubstituted acetylene (I, figure 4) to the carboxylic acid stage (III) with formation of an intermediate alpha-diketone (II). In addition, nitric acid oxidation was found to lead to the formation of aliphatic acids (IV) with one less carbon atom than those acids (III) which resulted from simple oxidative rupture of the triple bond.

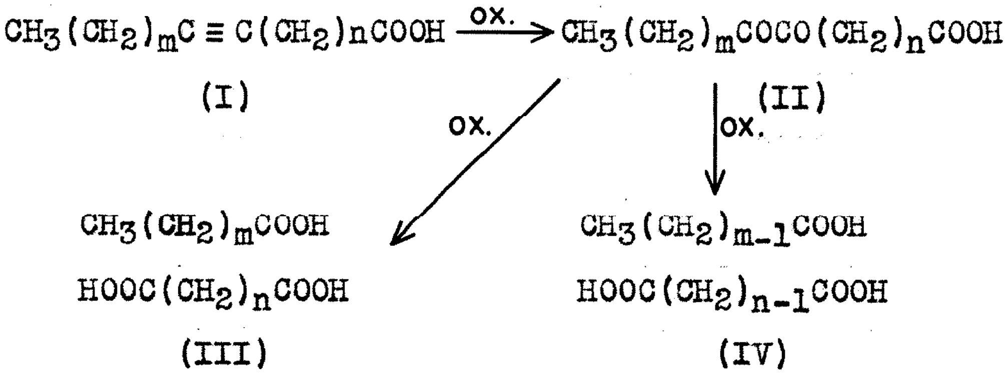


Figure 1. Known Oxidation Products of Acetylenic Compounds.

Oxidative Analytical Procedure. An analytical procedure based on permanganate oxidation seemed easiest to adapt to the present investigation. In order to minimize errors resulting from the analysis of extremely small quantities of alkyne, it was decided to change the distribution system also.

In the distribution system, one quantitative determination could be eliminated if the organic phase were pure alkyne. In effect, this procedure would then involve merely the measurement of solubility of the alkyne in aqueous solutions of silver ion at constant ionic strength.

The principal assumption to be made at this point was that silver ion and silver nitrate-alkyne complexes were insoluble in the pure alkyne under the conditions of the experiments. A specific experiment was run to verify this assumption. Equal parts of 3-hexyne and 1 f. silver nitrate were shaken for five minutes in the absence of both light and air. A 0.50 ml. portion of the organic phase was removed and evaporated to dryness. No residue remained.

The alkyne chosen for a preliminary investigation was 3-hexyne. This was used not only because of its availability but also because of its symmetry. With 3-hexyne, an unsymmetrical reaction would lead to a minimum of reaction products. Furthermore, solubility measurements and argentation constants were available (1) for comparative purposes.

Reagents and Apparatus.

1. 3-Hexyne. A few ampoules of 3-hexyne remained from those prepared by Dorsey (1), but the main source of material was the Farchan Research Laboratories.

The 3-hexyne as received from Farchan was washed five times with a 5% ferrous ammonium sulfate solution containing ammonium thiocyanate. Considerable amounts of peroxides were present because the mixture became quite warm during the first washing. The 3-hexyne was dried over potassium carbonate and transferred rapidly to a 30 cm., helix-packed column which was being flushed with dry nitrogen. The column vent was then protected with a glass "tee" through which nitrogen* was flowing.

In order to eliminate changing receivers during the distillation, no water was admitted to the column condenser until a constant boiling point was reached. The very small amount of forerun, b. 80.0-80.3° (746 mm.), was vented into a hood. After the main portion of distillate had been collected, the receiver was removed and stoppered while directing a rapid stream of nitrogen across the mouth. The receiver was then kept in a desiccator flushed with nitrogen.

Table 1

Physical Constants of 3-Hexyne

Source	$n^{25}D$	$n^{20}D$	B.p., °C
Farchan	1.4090^a	1.4116^a	80.5-80.6 (746 mm.)
Dorsey (1)	1.4089		80.0-80.3 (744 mm.)
Literature (7)		1.4115	81 (760 mm.)
Literature (8)		1.4110	

^{a}Calculated, using $n^{21.5}D = 1.4108$ and $dn/dt = 0.0005237$ (9).

2. Ampoules. Glass ampoules for the storage of alkynes were prepared from 5-6 mm. tubing. The ampoule neck was drawn down to a capillary which would admit a No. 22 hypodermic needle, and the bulb was blown to a diameter of 5 to 15 mm. The total amount of glass was kept below about

---

*All of the nitrogen used here and in subsequent experiments was dry and was sold as 99.9% pure.

0.6 g. so that the ampoule could be easily crushed. Figure 2 illustrates an ampoule of normal size.

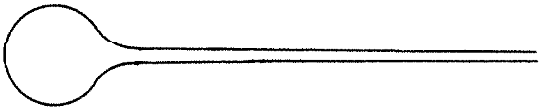


Figure 2. Ampoule for Storing Alkynes (Drawn to Scale).

Colored lengths of glass thread were inserted into the ampoules for identification.

For filling the ampoules in the absence of air, two techniques were used. In the first, the ampoules were placed in a wide-mouthed bottle with a loosely-fitting stopper or screw cap. The bottle and contents were placed in a desiccator which was evacuated and flushed with nitrogen four times. The bottle of ampoules, freshly distilled alkyne and other necessary equipment were transferred to a dry-box with a nitrogen atmosphere. The ampoules were filled using a hypodermic syringe, taking care not to wet the neck of the ampoule while removing the needle. If the ampoules were soft glass, they were sealed with a hot nichrome wire. If they were pyrex, the tip was plugged with a small piece of modeling clay and the ampoule was sealed after removal from the dry-box.

The second filling technique was used more extensively. When an alkyne was distilled in an atmosphere of nitrogen, the receiving flask was stoppled. Two three-inch, No. 22

hypodermic needles were attached to a source of pure nitrogen. The first was inserted into the flask of alkyne to maintain a slight pressure during removal of samples. The second was placed in a vertical position so that an ampoule could be placed over the end for flushing with nitrogen be-filling. The ampoule was filled with 3-hexyne from a hypodermic syringe and was sealed immediately.

Three weighings were made on each ampoule, the first just before filling, the second after filling (including the capillary tip removed during sealing) to determine the weight of the contents, and the third after discarding the capillary tip. The last weight was used as a check for leaks when the ampoule was used.

3. <u>Standard 1.00 f. Silver Nitrate and Potassium Nitrate</u>. Reagent grade silver nitrate and potassium nitrate were dried for 24 hours at 115°. The dried compounds were used directly to prepare 1.00 <u>f</u>. solutions at 25.0°. The prepared solutions were kept in 3-liter erlenmeyer flasks, each fitted with a delivery tube and a 3-way stopcock for introducing nitrogen. Light was excluded from the silver nitrate solution by wrapping the flask in aluminum foil.

Immediately after preparation, the flask and contents were flushed for three hours with a stream of nitrogen, with intermittent agitation of the contents. Evaporation of water from the stock solution was kept at a minimum by first passing the nitrogen through a gas-washing bottle containing some stock solution.

4. Standard Potassium Permanganate and Oxalic Acid Solution. Standard permanganate solutions were prepared by the method of Pierce and Haenisch, using arsenious oxide as the primary standard. Oxalic acid solutions were then standardized using the prepared permanganate solution (10).

5. n-Heptane. n-Heptane (Phillips Petroleum Co., 99.5 mole % minimum) was freed of oxidizable materials by shaking it with 30% fuming sulfuric acid, several times with distilled water, twice with neutral potassium permanganate solution and again thoroughly with water. The procedure was then repeated. The n-heptane was dried with potassium carbonate and distilled through a short Vigreux column.

6. Thermometers. All thermometers were calibrated at total immersion against U. S. Bureau of Standards thermometers. In addition, the thermometers which were associated with individual distillation columns were calibrated empirically against the boiling points of various liquids. In general, the following liquids were used: ethyl ether, acetone, methanol, carbon tetrachloride, benzene, n-heptane, acetic acid and n-butyl ether.

7. Large Equilibration Flask. The equilibration flask, fitted with a modified Lucas-Eberz pipette, is shown in Figure 3.

8. Modified Lucas-Eberz Pipette. This was a pipette

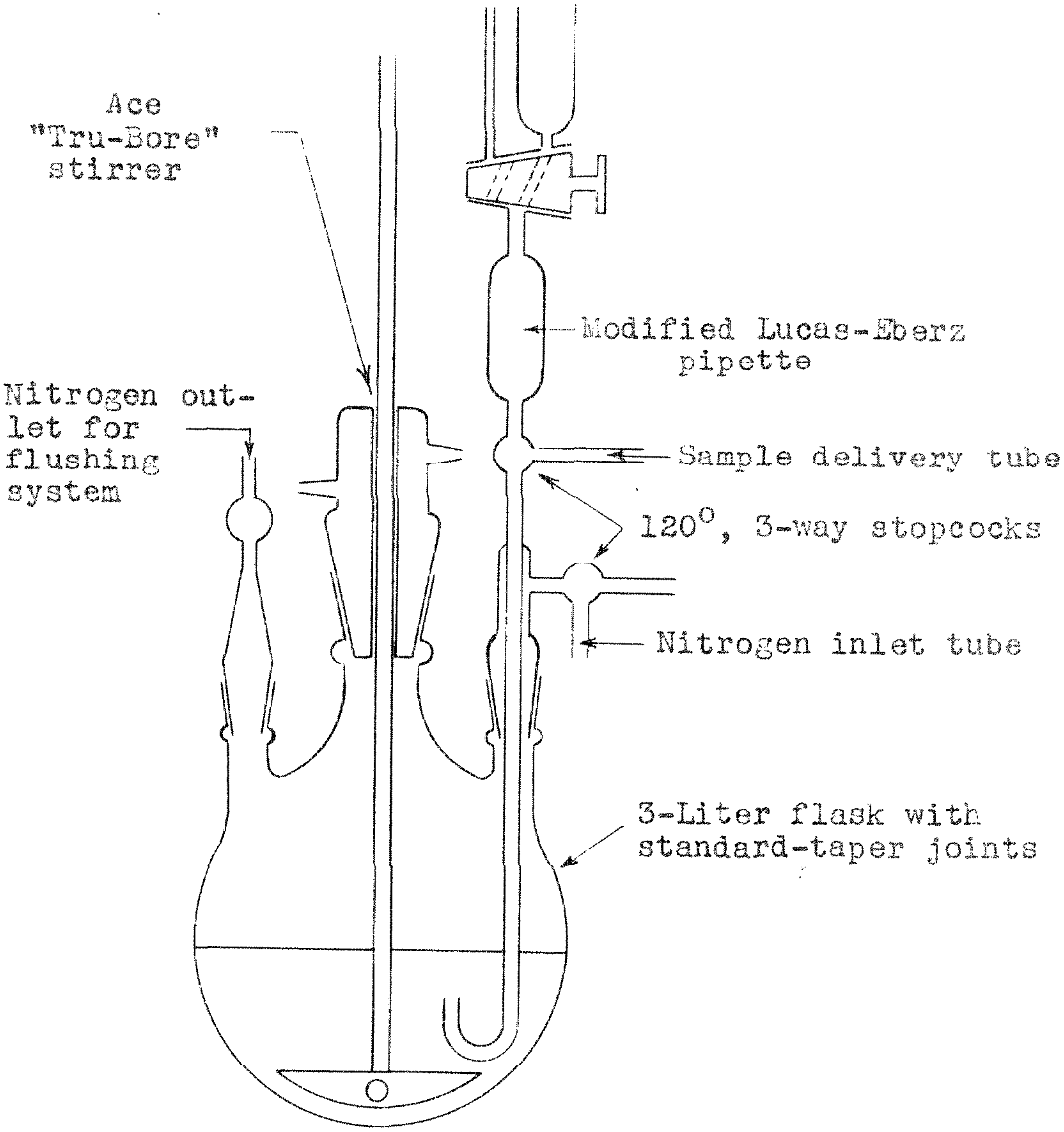


Figure 3

Large Equilibration Flask and Sampling Pipette

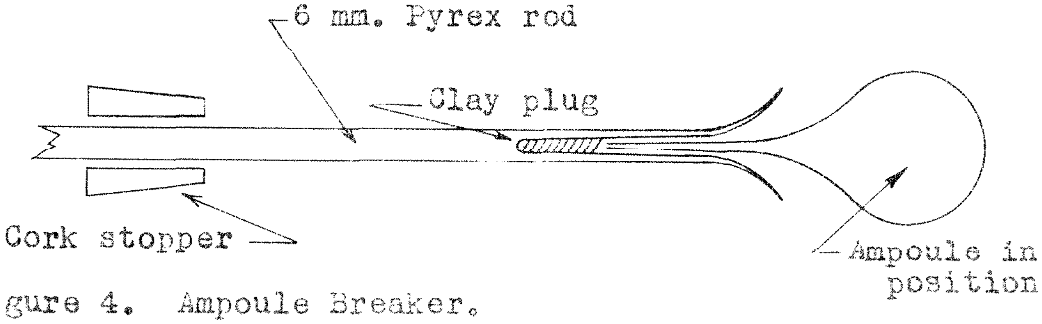


Figure 4. Ampoule Breaker.

calibrated to contain, with a reservoir for rinsing. The modification involved attachment of a 120° stopcock on the delivery tube so that it could be used with the large equilibration flask (figure 3). The pipette was calibrated with standard potassium permanganate solution by titration with standard oxalic acid solution.

9. Volumetric Glassware. Burettes were calibrated by weight of water delivered. "Retested" pipettes were used as received from the manufacturer.

10. Ampoule Breaker. This piece of apparatus was prepared to break ampoules of 3-hexyne below the surface of the solution held by the large equilibration flask. The breaker consisted of a long glass rod fitted loosely in a cork stopper which was of an appropriate size to replace the nitrogen outlet tube in the equilibration flask. One end of the glass rod was sealed to a short piece of glass tubing containing a small plug of modeling clay (Figure 4) which served to hold an ampoule.

11. Constant Temperature Bath. The bath was a standard E. H. Sargent model, number S-84805. The mercury-metal regulator maintained a range of ±0.02°, and the accuracy of the empirical setting was ±0.1°.

12. Nitrogen. The nitrogen used was guaranteed by the vendor to have a purity in excess of 99.9%. It was used as received. Nitrogen pressure was controlled to a maximum

of about 40 mm. mercury by using a small mercury regulator (Figure 5).

13. Small Equilibration Flask and Sampling Pipette. These are illustrated by Figure 6. The pipette was modelled after a Lucas-Eberz pipette, but modified by using a standard-taper male joint for the delivery tip.

Preliminary Investigation. It was found that the presence of silver nitrate or potassium nitrate had no significant effect on the oxidation-reduction reaction between potassium permanganate and oxalic acid under standard conditions. The oxidation of 3-hexyne was studied to determine whether any conditions could be found which could be used for quantitative determinations in the presence or absence of these inorganic reagents.

In order to best evaluate an oxidation procedure, it was necessary to prepare oxygen-free standard solutions of 3-hexyne in water. This was done by very nearly the same method used by Dorsey (1).

Since the ampoules of 3-hexyne which had previously been prepared contained from 0.5 to 1.0 g. of alkyne, it was necessary to use a 2-liter volumetric flask to dissolve all of the 3-hexyne.

The techniques involved in the preparation of standard samples of 3-hexyne in water involved several precautions. Boiling, distilled water was poured into a pre-warmed 2-liter

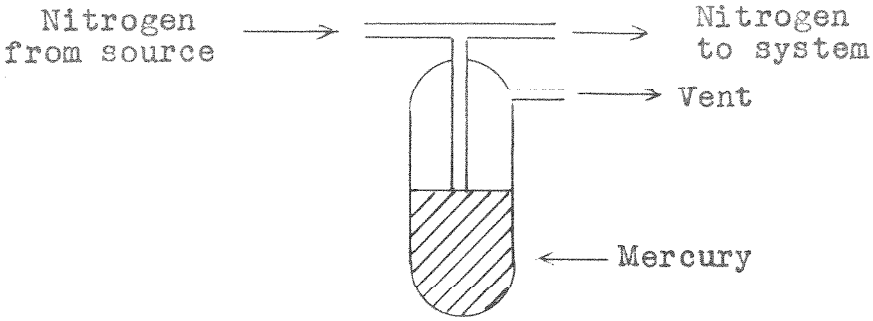


Figure 5

Nitrogen-pressure Regulator

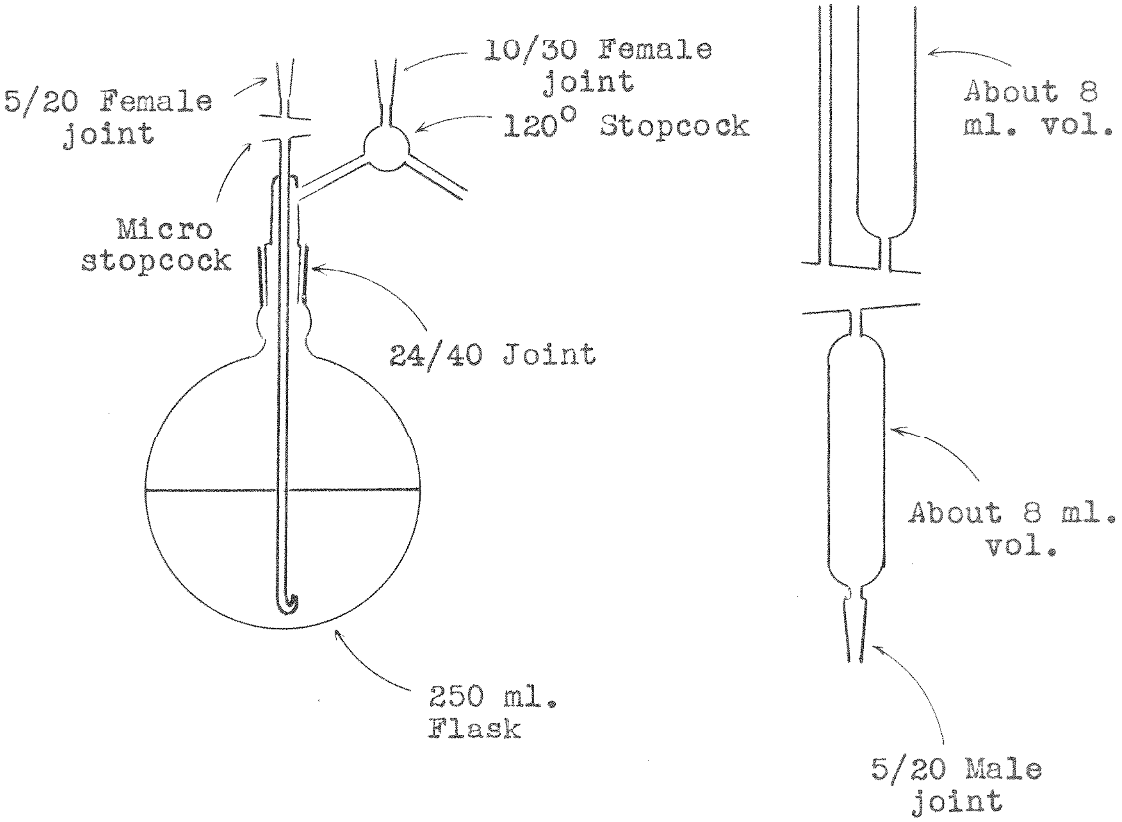


Figure 6

Equilibration Flask and Lucas-Eberz Pipette volumetric flask to near the calibration line. Pure nitrogen was bubbled through the solution while it was being cooled to room temperature. An ampoule of 3-hexyne was weighed for comparison with its original check weight, and it was then inserted into an ampoule breaker (Figure 4) without any clay plug. The ampoule and holder were inserted into the volumetric flask. The flask was tilted far enough on its side so that, when the ampoule was crushed, the light organic material could not rise into the neck of the flask. As the ampoule breaker was being removed, it was washed with a very small portion of boiled, distilled water. All parts of the ampoule remained in the flask. The flask was stoppered immediately and inverted. It was shaken in the inverted position until all of the 3-hexyne had dissolved, and it was then placed in a constant temperature bath at 25.0° for one-half hour. The flask was filled to correct volume and the contents were equilibrated by inverting the flask back and forth twenty times.

Standard samples in glacial acetic acid or n-heptane were prepared in the same manner, except that it was possible to use smaller volumetric flasks.

Standard samples were not kept for more than about one hour after the flasks had been opened for withdrawing a series of aliquots.

An 0.0218 f., oxygen-free solution of 3-hexyne in n-heptane was prepared by the method just described, using 0.0896 g. of 3-hexyne for a final volume of 50 ml.

Samples of this standard solution were shaken with aqueous potassium permanganate under varying conditions of temperature, shaking time, pH and concentration of silver ion. The results were too inconsistent to be considered quantitatively useful.

For a more convenient method of preparing solutions of either known or constant concentration, saturated solutions were considered. Dorsey (1) had given a value for the solubility of 3-hexyne in water at 25.0° (0.00305 mole/liter) and such a saturated solution would be convenient to use to determine optimum conditions for the oxidation procedure.

It would be well to point out at this time that the solubility value given by Dorsey differed considerably from the final value which we eventually obtained.

Preparation of Saturated Solutions of 3-Hexyne. Two liters of glass-distilled water were placed in the large equilibration flask (Figure 3). The water was boiled for fifteen minutes and the flask and contents were cooled to 25.0° in the constant temperature bath. During this heating and cooling, a stream of nitrogen was kept flowing through the flask.

The nitrogen flow was increased while the left stopcock (Figure 3) was being replaced with an ampoule of 3-

hexyne held in the ampoule breaker (Figure 4). The ampoule was crushed against the side of the flask, and the standard fitting was replaced. The mixture was stirred vigorously for one hour and was then allowed to settle for one hour before sampling.

At this point, about one or two ml. excess 3-hexyne were present in the equilibration flask. Under the conditions of equilibration just outlined, the settling was complete after about twenty minutes (as shown by subsequent oxidation methods), but the two phases were nevertheless allowed to remain undisturbed for one hour. During preliminary investigations, a saturated solution was used for two or three days, but after the oxidative procedure had been developed, the solutions were discarded after about four hours.

Neutral Oxidation of Water Solutions of 3-Hexyne. The oxidation of 3-hexyne could presumably proceed to several different extents (equations III through VI).

$$5\ CH_3CH_2C{\equiv}CCH_2CH_3 + 4\ MnO_4^- + 12\ H^+ \longrightarrow$$

$$5\ CH_3CH_2COCOCH_2CH_3 + 4\ Mn^{++} + 6\ H_2O \qquad (III)$$

(4e change per molecule of 3-hexyne).

$$5\ CH_3CH_2C{\equiv}CCH_2CH_3 + 6\ MnO_4^- + 18\ H^+ \longrightarrow$$

$$10\ CH_3CH_2COOH + 6\ Mn^{++} + 4\ H_2O \qquad (IV)$$

(6e change).

$$5\ CH_3CH_2C \equiv CCH_2CH_3 + 12\ MnO_4^- + 36\ H^+ \longrightarrow$$
$$5\ CH_3CH_2COOH + 5\ CH_3COOH + 5\ CO_2 +$$
$$12\ Mn^{++} + 18\ H_2O \qquad (V)$$

(12 e change).

$$5\ CH_3CH_2C \equiv CCH_2CH_3 + 18\ MnO_4^- + 54\ H^+ \longrightarrow$$
$$10\ CH_3COOH + 10\ CO_2 + 18\ Mn^{++} + 32\ H_2O \qquad (VI)$$

(18e change).

The oxidation was expected to proceed to the extent indicated by equation IV, and the preliminary experiments were based on this and on the solubility found by Dorsey (1).

Procedure 2-56.*

1. An excess of standard permanganate was introduced by pipette into a 250 ml. iodometric flask. This excess was based on the expected solubility value of 3-hexyne, on the size of sample of the saturated solution of 3-hexyne, and on the extent to which we expected the 3-hexyne to be oxidized. On this basis, the excess ordinarily amounted to about 10%.

2. A measured volume of the saturated water solution of 3-hexyne was added to the iodometric flask. The flask was stoppered quickly and shaken vigorously. The shaking was repeated several times during a 20-minute period.

3. The stopper of the iodometric flask was washed down with water, the contents of the flask were heated to above 60°, and 15 ml. 6n sulfuric acid and a measured excess of

---

*Research Notebook Number 2, p. 56.

standard oxalic acid solution were added. The excess oxalic acid was back-titrated with permanganate.

4. For comparison purposes, the following calculation was made for each oxidation:

$$\underline{n} = \frac{(\text{Vol. KMnO}_4 - \text{blank})(\text{Norm.}) - (\text{Vol. ox.acid})(\text{Norm.})}{\text{Vol. 3-Hexyne Solution}} \qquad \text{(VII)}$$

After the extent of oxidation is established, the molar concentration of 3-hexyne can be calculated by dividing $\underline{n}$ by the electron change taking place during the oxidation of the molecule.

Results. On the basis of the assumptions made concerning solubility and extent of oxidation, insufficient amounts of permanganate were used in the initial experiments. In a series of about 50 trials, each using more permanganate than the previous one, the value of "$\underline{n}$" increased to a constant value of about 0.064. This represented a considerable increase over the expected value, 0.018.

The oxidation was repeated, both in the presence and absence of a small amount of silver ion (Table 2).

In observing the values of "$\underline{n}$" (Table 2), it became obvious that the value for silver-free oxidation was very nearly 3/2 that for the oxidation in the presence of silver ion. If Dorsey's solubility value could now be assumed correct, the oxidation in the absence of silver ion must proceed according to equation VI, and in the presence of silver ion according to equation V.

Table 2

Neutral Oxidation of Saturated Water
Solutions of 3-Hexyne

Conditions	n	n/12[a]	n/18[b]
No silver ion added	0.0625		0.00348
No silver ion added	0.0630		0.00350
Plus 1 ml. 1 f. $AgNO_3$	0.0417	0.00348	
" 1 ml. " "	0.0429	0.00357	
" 2 ml. " "	0.0437	0.00364	
" 5 ml. " "	0.0430	0.00358	

[a]From equation V. [b]From equation VI.

In observing these relationships, we concluded that the next logical step would involve the study of standard solutions. An oxygen-free, standard solution of 3-hexyne in water was prepared and samples were oxidized by the usual procedure. Results are given in Table 3.

Table 3

Neutral Oxidation of a Standard Solution
of 3-Hexyne, 0.002605 f.

Conditions	n	n/6[a]	n/4[b]
No salts added	0.0160	0.00267	
	0.0155	0.00258	
	0.0149	0.00248	
	0.0157	0.00262	
KNO_3 added	0.0123	0.00205	0.00307
	0.0121	0.00202	0.00302
$AgNO_3$ added	0.0081	0.00135	0.00202
	0.0085	0.00142	0.00212

[a]From equation IV. [b]From equation III.

In the neutral oxidation without added supplementary materials, the reaction proceeded essentially to the propionic acid stage. Although the average value of the experimental concentration of 3-hexyne was 99% of the theoretical value, the deviation between samples was of the order of ±5%.

If either potassium nitrate or silver nitrate were added to the permanganate before oxidation, the results were low. In the latter case, the solution which remained after neutralization of the permanganate had a yellow color and an odor reminiscent of biacetyl. This then could account for the low values of "n". It is interesting at this point to note that this condition of color and odor was not present during the oxidation of saturated solutions of 3-hexyne.

Procedure 2-67. Procedure 2-56 was modified to a small extent. The reaction mixture, after 30 minutes shaking, was transferred quantitatively to a wide-mouth erlenmeyer flask containing a warm (above 60°) mixture of standard oxalic acid acidified with dilute sulfuric acid.

Standard Solutions of 3-Hexyne in Acetic Acid. An oxygen-free, 0.00957 f. solution of 3-hexyne in glacial acetic acid was prepared by the usual method. Oxidation of aliquots of this solution by permanganate proceeded to the same extent with or without added potassium or silver nitrate. The quantitative deviations of six samples were not more than

±1%. However, assuming that the reaction yielded only the diketone, the results were 6% high.

Another standard solution was prepared, using acetic acid which had been treated with permanganate and distilled. The results were similar to those of the previous sample, with indication of the formation of a larger proportion of propionic acid.

Standard Solution of 3-Hexyne in Water. An 0.00173 f. solution of 3-hexyne in water was prepared and oxidized by the usual procedure. These results are presented in Table 4.

Table 4

Oxidation of an 0.00173 f. Solution of 3-Hexyne in Water

Conditions	No. of Runs	n/6[a]	n/4[b]
KNO_3 Added	3	0.00186±.00002	0.00279±.00002
$AgNO_3$ Added	3		0.00195±.00003

[a] From equation IV. [b] From equation III.

Since the oxidation of 3-hexyne was quite sensitive to conditions of saturation of the alkyne in the aqueous phase, it was now necessary to work only with solutions used in experimental procedures.

Isolation of 3,4-Hexanedione. The following materials were placed in a 500 ml., glass-stoppered flask.

150 ml. 1.00 f. $AgNO_3$
50 ml. 0.5 n. $KMnO_4$
200 ml. H_2O
0.3771 g. 3-hexyne.

The flask was shaken for 40 minutes at room temperature. Additional permanganate solution was added as needed to maintain a purple color. The purple color was then discharged by adding an excess of oxalic acid. The reaction mixture was extracted with four 25 ml. portions of ether. The first ether extract was bright greenish-yellow, and the last was colorless.

The combined ether extracts were dried with magnesium sulfate and evaporated to a small volume, leaving a highly-colored yellow liquid.

An oxime was prepared by the pyridine method given by Shriner and Fuson (11). This was recrystallized twice from methanol-water: m. 187.5-188.6°. Lit.: oxime of 3,4-hexanedione, m. 185° (12).

A solution of the oxime in methanol formed an orange precipitate with a solution of nickel chloride, indicating the presence of an alpha-dioxime.

Semicarbazone (13): m. 266-267° (decomp.). Lit.: m. 270° (decomp.) (12).

These results confirm the presence of considerable quantities of 3,4-hexanedione.

Saturated Solutions of 3-Hexyne at Ionic Strength 1 μ: Neutral Oxidation. The temperature of the equilibrating bath was set at 28° to facilitate control during abnormally high day temperatures.

During a series of oxidations of saturated solutions of

3-hexyne in 1.00 f. potassium nitrate, both 250 ml. and 125 ml. iodometric flasks were used. It was found that low results were obtained with the use of flasks having a large air space over the reaction mixture (Table 5).

Table 5

Effect of Flask Size on Oxidation of 3-Hexyne

Flask, ml.	No. of Runs	n
125	5	0.0351±0.0012
250	4	0.0301±0.0007

The results still remained too inconsistent. The oxidation under alkaline conditions was studied.

Alkaline Oxidation. Smaller equilibration flasks (Figure 6) were used in order to facilitate handling.

A description of the procedure follows, with references to Figure 7.

1. An ampoule of 3-hexyne (a) was placed into a thoroughly clean, 250 ml. equilibration flask (b). The flask was assembled using a minimum of silicone grease at the joints.

2. The equilibration flask was evacuated. After wrapping it in towels, it was shaken or swirled to rupture the ampoule.

3. The equilibration flask (b) was attached to the stock solution flask (c) by means of the delivery tube (d) which then was evacuated.

4. The desired volume of either or both silver nitrate

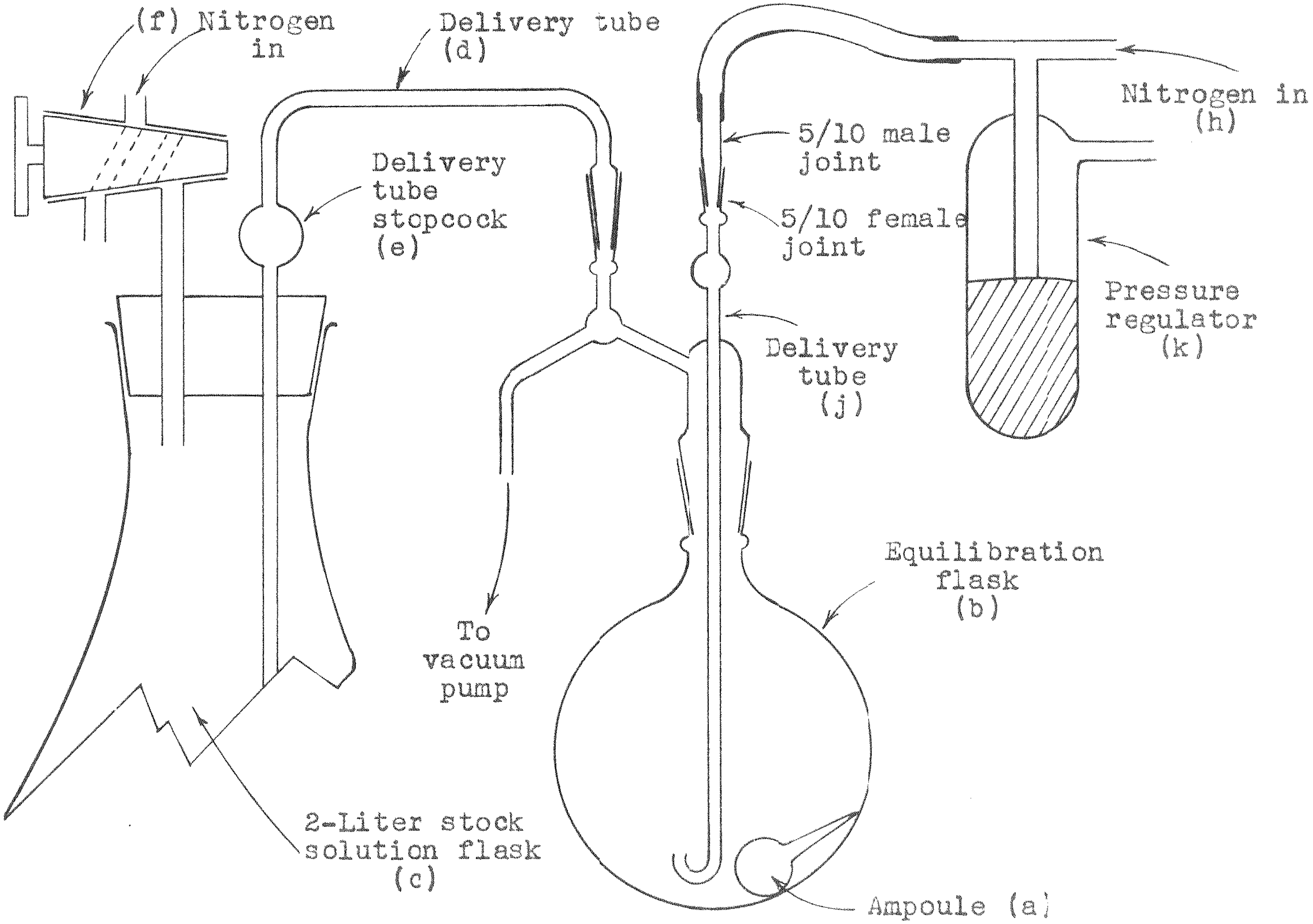


Figure 7. Use of Small Equilibration Flask.

and potassium nitrate stock solution was introduced into the equilibration flask and all stopcocks were closed. Nitrogen was added to the stock solution flask through stopcock (f) to a small positive pressure.

5. A 5/10 male joint (g) was attached to the nitrogen line (h). The line was flushed with nitrogen and was connected to the female 5/10 joint (i) on the delivery tube (j) of the equilibration flask. Nitrogen was slowly introduced into the equilibration flask until a small positive pressure was attained (limited to about 30 mm. mercury by the small pressure regulator (k)). This method of introducing nitrogen insured the removal of any free alkyne from the delivery tube.

6. The equilibration flask and contents (two liquid phases) were cooled to about 15° to bring an excess of alkyne into solution (the solubility of 3-hexyne increases with a decrease in temperature over the range employed). A saturated solution was readily obtained by warming the flask and contents to equilibration temperature.

7. The flask and contents were swirled for five minutes and were placed in a constant temperature bath at $25.0 \pm 0.1^{\circ}$. Over a 30 minute period, the contents were swirled for one-half minute intervals every five minutes. After allowing the phases to separate for at least one hour, the material was ready for sampling.

Oxidation Procedure. The procedure was identical with 2-67 except that the flask was shaken mechanically for 40 minutes during the reaction. Appropriate volumes of 5% sodium hydroxide were added to the reaction flask before introducing the alkyne solution.

An 0.00173 f. solution of 3-hexyne in water was prepared, using 0.2845 g. of 3-hexyne for two liters of solution. Oxidation reactions were run on both this and on saturated solutions of 3-hexyne in 1.00 f. potassium nitrate. Results are given in Table 6.

Table 6

Alkaline Oxidation of 3-Hexyne in Water

Solution	No. of Runs	n	n/6
0.00173 f.	4	0.0109 ± 0.0002	0.00182
Sat'd. in 1 f. KNO_3	3	0.0617 ± 0.0007	0.0103
Sat'd. in 1 f. KNO_3	3	0.0609 ± 0.0005	0.0102

At this point, the oxidation procedure was reproducible to a sufficient degree to continue the study further. The method was applied to saturated solutions of 3-hexyne in aqueous silver nitrate solutions.

The amount of potassium permanganate to be used was based on the coordination data of Dorsey (1) and on the previous observation that the oxidation proceeded about 2/3 as far in the presence of silver ion as in its absence. Contrary to the expected behavior, the value of "n" was found to be larger than in the absence of silver ion, instead of being about two-thirds. It was obvious that the calculated excess of permanganate was actually insufficient. After the amount of permanganate had been appropriately increased to the point where further excess remained unreduced, the value of "n" was determined for a series of solutions of different concentrations of silver ion at an ionic strength of unity. These results are given in both tabular (Table 7) and graphically (Figure 8).

Solubility of 3-Hexyne at Ionic Strength 1.00 μ. As a result of the previous investigation, conditions were established for obtaining consistent results in the analysis of 3-hexyne.

If "n" is plotted as a function of the concentration of silver ion (Figure 8), a smooth curve is obtained. Only the value of "n" at zero silver ion concentration shows any major deviation.

If the plot is extrapolated to zero silver, the n-axis intercept is 0.120, which is twice the experimental value, 0.061. Consequently, the oxidation in the presence of silver ion required twice as much permanganate as the oxidation in the absence of silver ion.

Considering equations III through VI (pp. 48-49), which show various possible extents of oxidation of 3-hexyne, there is only one combination in which one reaction requires twice as much permanganate as the other. This involves

Table 7

Oxidation of Saturated Solutions of 3-Hexyne in the Presence of Silver Ion

(Ag_t), moles/l.	No. of Runs	<u>n</u>
0.0000	5	0.061 ± 0.001
0.0083	6	0.139 ± 0.002
0.0195	3	0.165 ± 0.001
0.0295	3	0.187 ± 0.002
0.0402	3	0.214 ± 0.001
0.0520	3	0.236 ± 0.002
0.0640	3	0.270 ± 0.002
0.0875	5	0.311 ± 0.004
0.1400	3	0.417 ± 0.003

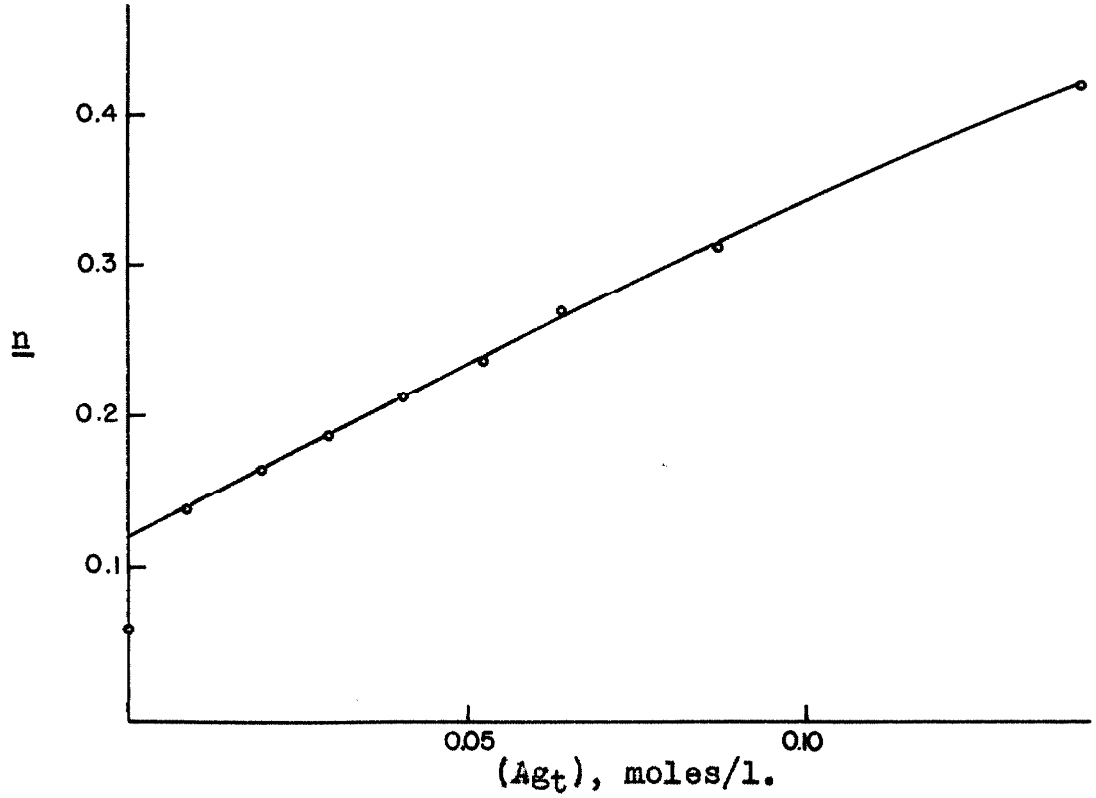


Figure 8. Variation of <u>n</u> with Silver Ion Concentration.

equation IV, yielding propionic acid, and equation V, yielding equal parts of propionic and acetic acids.

When measurements were made at silver ion concentrations above about 0.2 _f_., the reaction became quite sensitive to pH. If a high pH was maintained by the use of sodium hydroxide in excess of the amount needed to precipitate silver oxide, the reaction tended to proceed to the same extent as the oxidation conducted at silver ion concentrations below 0.2 _f_. If, however, insufficient sodium hydroxide was added, or if the pH of the solution was maintained at about 9 by means of a phosphate buffer, the reaction required only about one-half as much permanganate. The results tended to become more variable as the concentration of silver ion increased.

In order to substantiate the evidence concerning the extent of oxidation, a series of runs were made under varying conditions of pH. The values of "_n_" were tabulated and plotted as before (Table 8, Figure 9).

Isolation of Oxidation Products of 3-Hexyne. The reaction mixtures which remained after titration were combined according to the value of "_n_". The first group of samples included all of those with a value of "_n_" which lay on or near the lower line in Figure 9. The second group was comprised of samples with maximum values of "_n_", corresponding to the upper line.

Table 8

Effect of pH on the Oxidation of 3-Hexyne

Conditions	(Ag_t) moles/l.	No. runs	Approx. pH	n
Excess NaOH	0.224	3	11	0.57
Phos. buffer	0.224	3	9	0.24
Acet. buffer	0.224	2	5	0.12
Excess NaOH	0.250	1	11	0.62
Phos. buffer	0.250	2	9	0.28
Acet. buffer	0.250	2	5	0.23
Excess NaOH	0.429	3	11	1.06
Insuff. NaOH	0.429	1	9	0.88
Phos. buffer	0.429	3	9	0.51

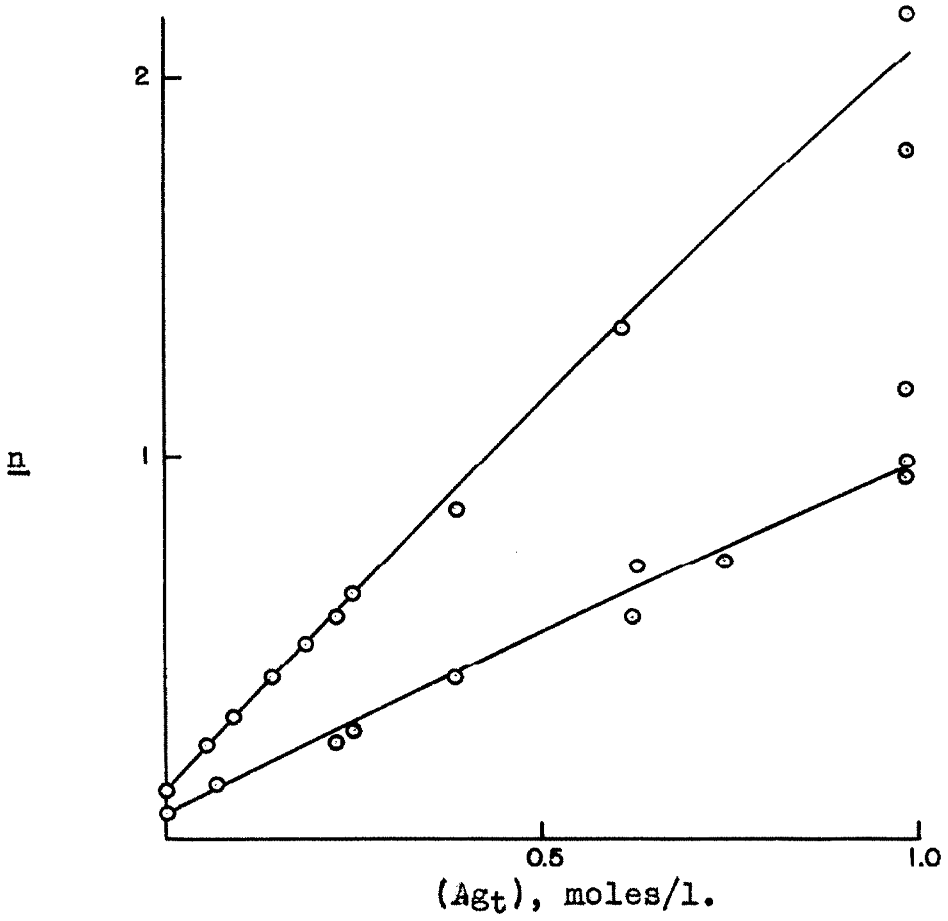


Figure 9. Values of n at Various Concentrations of Silver Ion.

After about two liters of either of the two reaction mixtures had been collected, it was made strongly alkaline by adding solid sodium hydroxide. After evaporating the solution to about 150 ml., it was made strongly acidic with 12 n. sulfuric acid. The mixture was steam distilled. The steam distillate was carefully neutralized to a phenolphthalein end-point with dilute sodium hydroxide solution. This was evaporated to dryness in a tared evaporating dish and dried for 12 hours at 115°. The solid was dissolved in water and diluted to 25.0 ml.

A p-phenylphenacyl ester was then prepared (14) from the material in solution, using an equivalent amount of p-phenylphenacyl bromide. The isolated ester was dissolved in benzene-ligroin, 1:1, boiled with Norite and filtered. The filtrate was diluted to 25.0 ml. with solvent, and this solution was used for chromatographic isolation (15) of the esters.

Portions of the prepared solution of esters were placed on a #2 chromatographic column containing 3:1 silicic acid-celite as adsorbent. These were developed with 1:1 benzene-ligroin at 15-20# pressure. Progress of the bands was observed by fluorescence under an ultra-violet lamp. Isolated bands fluoresced blue, but overlapping portions of bands gave a white fluorescence.

After individual zones were isolated from the extruded column, they were eluted with acetone, and the acetone solutions were freed from traces of suspended solids by centrifugation.

The solutions were evaporated from tared evaporating dishes to obtain the weight of ester. The ester was then crystallized from methanol-water for determination of melting points.

Lower line (Figure 9): one zone formed; m. 101.0-101.7°. Lit.: m. for the ester of propionic acid, 102° (14).

Upper line (Figure 9): two zones formed, but with some overlap. These were separated as well as possible, eluted and placed on separate columns for further purification.

Each fraction developed into two zones, one major and the other minor. Both upper and both lower zones were combined before eluting.

Table 9

Isolation of Oxidation Products of 3-Hexyne

Zone	Recovery, g.	M.p., °C	Mixed m.p., °C
Upper	0.1339	109.3-110.4[a]	109.6-110.8[b]
Lower	0.1284	100.3-101.7[c]	-----

[a] Lit.: p-phenylphenacyl ester of acetic acid, m. 111° (14).
[b] Mixed melting point with ester of acetic acid.
[c] Lit.: p-phenylphenacyl ester of propionic acid, m. 102° (14).

The molar ratio of acetate/propionate was 1.10. The chromatographic separation was repeated on a separate portion of the stock solution. The first development resulted in two well-defined zones: upper, 0.0144 g. acetate; lower, 0.0122 g. propionate; molar ratio, acetate/propionate, 1.24.

The results of the chromatographic isolation confirm the prediction that in the absence of silver ion, a saturated solution of 3-hexyne is oxidized to propionic acid by alkaline permanganate. Furthermore, in the presence of silver ion, the oxidation proceeds to the extent that approximately equivalent amounts of acetic and propionic acids are formed.

It seems probable that each molecule of 3-hexyne was broken unsymmetrically to form acetic and propionic acids. If one-half of the molecules were yielding propionic acid and the other half acetic acid, it should have been possible to find conditions in which the oxidation proceeded essentially to the acetic acid stage. The half-and-half stage seemed to be a maximum extent of oxidation.

Summary. The use of the permanganate oxidation technique as an analytical tool for the determination of 3-hexyne is quite limited.

The oxidation has been found to proceed to various extents, and there are several conditions which must be imposed in order that the final products of the reaction can be predicted. These conditions include such factors as pH, presence of silver ion andconcentration of the 3-hexyne (saturated solution or below saturation). A tabular summary of results is given on page 67, in Table 10.

The most reliable data was obtained by alkaline oxidation of 3-hexyne either in the absence of silver ion (equation IV) or in the presence of silver ion at concentrations below 0.2 f. Duplicability of results was possible to within ±2% in most instances. However, quantitative deviations of as great as 20% were noted in comparing data from oxidation and spectrophotometric determinations.

Table 10

SUMMARY OF RESULTS OF VARIOUS OXIDATIONS OF 3-HEXYNE

1. Standard solutions of 3-hexyne (below saturation).

Conditions of Oxidation; Supplements.	Principle Reaction	3-Hexyne Found, % of Amount Taken[a]
Initially neutral	b	99±5
Initially neutral	b	107±2
Initially neutral plus silver ion	c	112±3
Standard solution in acetic acid	c	106±1
Standard solution in acetic acid plus silver ion	c	106±2
Alkaline	b	105±2
Alkaline plus silver ion	d	93±2
Acetate buffer, pH 5	b	100±1
Alkaline plus silver ion	d	94±1

2. Saturated aqueous solutions of 3-hexyne at unit ionic strength.

Conditions	Principle reaction
Initially neutral	b
Initially neutral plus silver ion	c
Alkaline	b
Alkaline plus silver ion	e
Phosphate buffer, pH 9, plus silver ion	b
Acetate buffer, pH 5, plus silver ion	c (inconsistent)
Acidic plus silver ion	c (inconsistent)

[a] Based on the equation in the previous column.
[b] From equation IV.
[c] From equation III.
[d] From equation VI.
[e] From equation V.

C. SYNTHESIS OF ACETYLENIC COMPOUNDS.

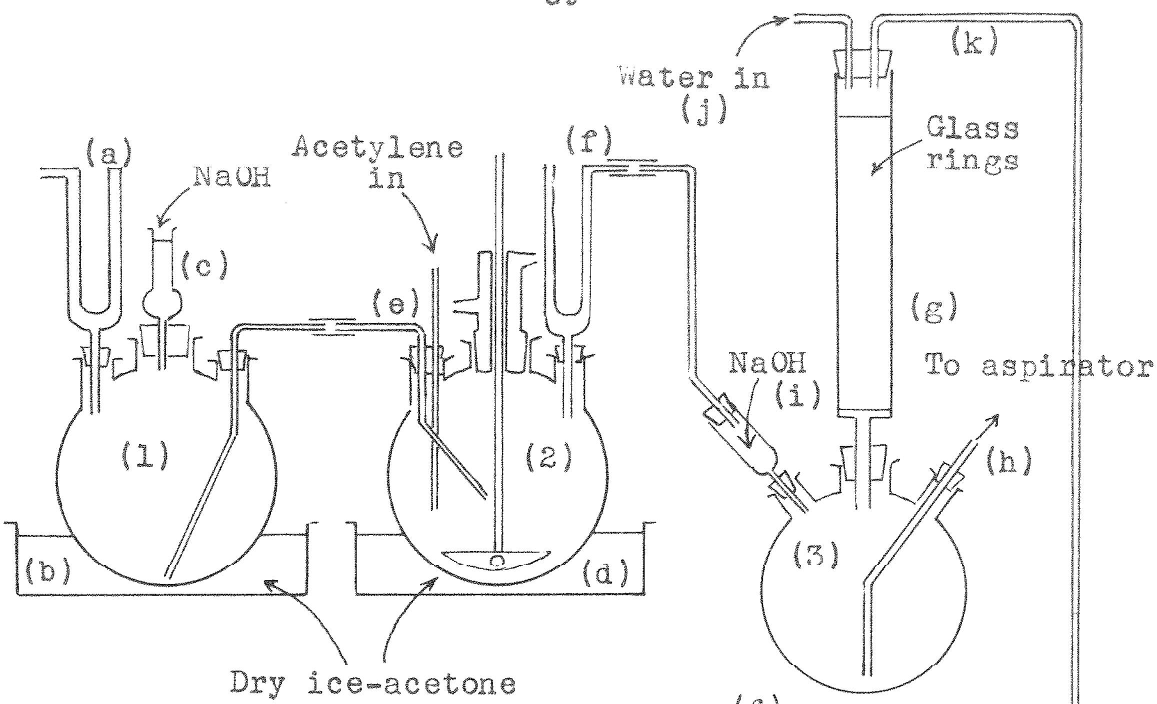
1-Butyne.

The alkylation of acetylene was based on work of Vaughn, Hennion, Vogt and Nieuwland (16), but extensive modifications were made in the purification system (Figure 10). In the following description, the letters and numerals in parentheses refer to the apparatus shown in Figure 10.

About one liter of liquid ammonia was introduced through a dry ice reflux condenser (a) into a 3-necked, 3-liter flask (1) which was cooled by a dry ice-acetone bath (b). The flask vent was protected with a sodium hydroxide drying tube (c). Throughout the experiment, all liquid ammonia solutions were protected in a similar manner.

Clean sodium metal was cut into cubes about one centimeter thick, and 59 g. (2.6 moles) of these were added to the liquid ammonia in about four portions. Meanwhile, about 1.5 liters of ammonia were being collected in a second flask (2), which was equipped with an "Ace Tru-Bore" broad-blade stirrer and a dry ice reflux condenser (f).

Commercial acetylene was scrubbed twice with 98% sulfuric acid and introduced below the liquid ammonia surface in flask (2). The liquid temperature was kept as low as possible with the dry ice bath (this had been transferred from flask (1)). The contents of flask (2) were stirred throughout all of the operations involving this flask.



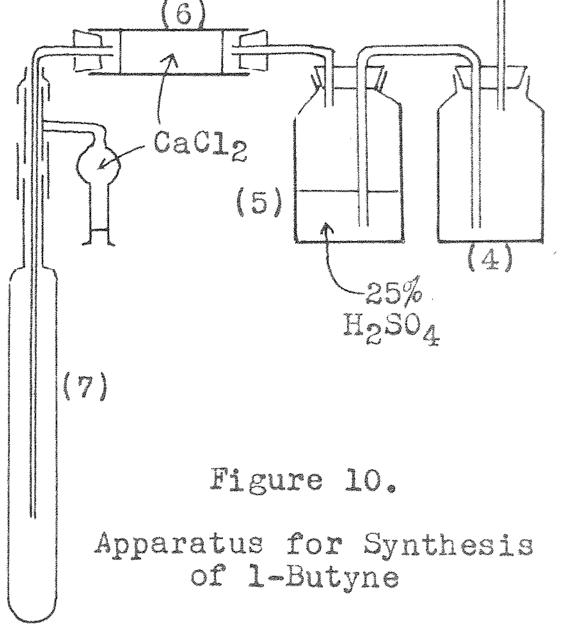


Figure 10.

Apparatus for Synthesis of 1-Butyne

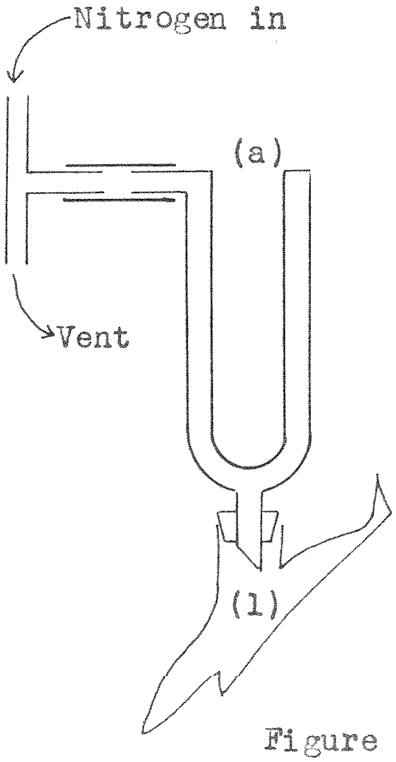


Figure 11. Method for Transfer of Solutions of Sodium

After 15 minutes of acetylene addition, the blue solution of sodium from flask (1) was transferred slowly to flask (2) by means of nitrogen pressure (Figure 11). The rate of addition was controlled so that the contents of flask (2) never became completely blue. The addition of acetylene was continued for about 15 minutes after all of the sodium solution had been added and the color had been discharged.

If sodium metal remained in the first flask, it was necessary to transfer a small amount of liquid back and forth from the second flask. The additional blue color was then discharged as before.

The transfer tubes (e) were replaced by a dropping funnel containing 153 ml. (2 moles) of ethyl bromide. The cooling bath was lowered and the liquid ammonia was allowed to come to the boiling point. The ethyl bromide was added over a period of two hours and this was followed by two additional hours of stirring.

The ammonia absorption system consisted of a 40x4 cm. Rashig tower (g) packed with glass rings made from 6-8 mm. glass tubing. The column was connected to a 2-liter, 3-necked flask (3) equipped with a water withdrawal tube (h) and a gas inlet tube (i). The top of the column was fitted with a tap water inlet tube (j) and an outlet tube (k) for scrubbed gases. The outlet gases were then led through a trap (4), a scrubber containing 25% sulfuric acid (5), a calcium chloride drying tower (6), and finally into an ampoule (7) cooled in dry ice and acetone.

After the reaction of ethyl bromide was complete, the coolant was removed from the dry ice reflux condenser (f) and the contents of flask (2) were allowed to pass through the absorption system. Vigorous boiling of the ammonia solution was promoted by placing a hot plate about six inches below the flask.

Water was introduced into the Rashig tower (g) at such a rate that the tower remained hot to within about four inches of the top of the packing. Excess aqueous ammonia solution was withdrawn from flask (3) as often as convenient, using a water aspirator.

When essentially all of the ammonia had evaporated from flask (2), 150 ml. of water were added to the residue and the mixture was warmed to about 40° with a water bath. The system was flushed for about 20 minutes with a slow stream of nitrogen.

The ampoule (7) containing the product was removed and placed under a reflux condenser containing ice and concentrated hydrochloric acid (about -20°). A boiling chip was introduced into the ampoule and the contents were allowed to reflux without application of heat. After the vigorous boiling had subsided, indicating the removal of a major portion of the dissolved acetylene, the ampoule was cooled, sealed and weighed.

The yields in four successive syntheses were 79%, 83%, 93% and 94%. Significant amounts (about 10%) of 3-hexyne, b. 72-83° (750 mm.), were found in the first two synthetic products. The other two were comparatively free from higher boiling material. No further purification was attempted.

Isopropylacetylene.

Isoamylene was synthesized by passing isoamyl alcohol over 10-16 mesh alumina at about 500° (17). Over a period of 4½ hours, 203 g. (2.3 moles) of the alcohol were passed over 40 g. alumina to yield 142 g. of crude alkene. The alkene was shaken for one hour with an equal volume of 60% sulfuric acid and distilled.

The combined isoamylene from several dehydration runs, 213 g. (3.0 moles), was dissolved in a mixture of 600 ml. dry carbon tetrachloride and 30 ml. of dry ethanol. The solution was cooled to about -5° and 453 g. (2.84 moles) of bromine in 300 ml. dry carbon tetrachloride were added over a four-hour period. The maximum temperature reached during the reaction was -1°. The excess carbon tetrachloride was stripped off on a steam cone andthe product was distilled at reduced pressure: b. 62.5-65.0° (15 mm.); yield of dibromide, 604 g. (86%).

The dibromide was dehydrobrominated in two steps. A preliminary attempt to remove two molecules of hydrogen bromide simultaneously was unsuccessful.

Into a 3-necked flask fitted with a mechanical stirrer and a dropping funnel were placed 80 ml. ethylene glycol and 450 g. (8 moles) powdered potassium hydroxide. The flask and contents were heated in an oil bath to about 150° and then 538 g. (2.37 moles) 1,2-dibromo-3-methylbutane were introduced with stirring.

The volatile products were condensed with a short Liebig condenser and collected. The system was protected by a dry ice and acetone trap to collect any isopropylacetylene which formed.

As the dibromide was being added, the temperature of the bath was raised to about 170° and maintained there until addition was complete. Additional ethylene glycol was added as needed to facilitate stirring and the temperature was brought gradually to 230°. The total time required for the addition of the dibromide was 4½ hours. After this, the mixture was stirred and heated for an additional hour. The product was mainly monobromoisopentene (only about 2 ml. of liquid collected in the dry ice trap): yield, 350 g. (99%). No attempt was made to purify the crude product.

The second molecule of hydrogen bromide was eliminated with the use of sodamide. A 3-liter, 3-necked flask was fitted with a "Tru-Bore" stirrer, a dry ice reflux condenser and a sodium hydroxide drying tube. About 1.5 liters of liquid ammonia were introduced and then 140 g. (8 moles) of sodium metal in the form of one centimeter cubes were added in three portions. During each addition a small amount of ferric chloride was also added.

After all of the blue color had been discharged, one liter of mineral oil was added and the excess ammonia was evaporated with vigorous stirring. The reaction flask was then attached to an ammonia-scrubbing train as shown in Figure 10.

The temperature of the sodamide suspension was raised to 160-170° by means of an oil bath, and 370 g. of crude monobromoisopentene were added over a period of 1½ hours. The reaction apparently proceeded as rapidly as the monobromide was added, for immediately after the addition was complete there was no further heating of the Raschig tower.

The heating bath was dropped, and after the mixture had cooled, 200 ml. of water were introduced slowly with vigorous stirring. The system was flushed with a small stream of nitrogen during the addition of water to aid in carrying the alkyne through the scrubbing system. The flask was warmed to 100° on a steam cone and steam was introduced into the residue to drive over any residual alkyne. The system was flushed again with nitrogen, and the water scrubber, acid scrubber and drying tube were successively warmed to about 50° with either a water bath or an infra-red lamp.

The ampoule contained 121.5 g. (73% from the monobromide) of the crude alkyne. Before use, this was distilled through a 30 cm. column packed with helices: b. 25.8-26.6° (745 mm.); yield from isoamyl alcohol, about 45%.

<u>tert</u>-Butylacetylene.

The synthesis of <u>tert</u>-butylacetylene was carried out according to the general scheme given by Ivitzky (18).

$$(CH_3)_2C(OH)C(OH)(CH_3)_2 \xrightarrow{H^+} (CH_3)_3COCH_3 \qquad (VIII)$$

$$(CH_3)_3COCH_3 \xrightarrow{PCl_5,\ 0^\circ} (CH_3)_3CCl_2CH_3 \qquad (IX)$$

$$(CH_3)_3CCl_2CH_3 \xrightarrow{KOH,\ 150^\circ} (CH_3)_3CC\equiv CH \qquad (X)$$

Pinacolone was synthesized in 80% yield from piancol according to the procedure given in Organic Syntheses (19).

The pinacolone was converted to the <u>gem</u>-dichloride with phosphorous pentachloride. A 3-necked, 1-liter flask was fitted with a reflux condenser, dropping funnel and mechanical stirrer. An ice-water bath was placed around the flask and 250 g. (1.2 moles) of finely powdered phosphorous pentachloride was added. While stirring, 101 g. (1.15 moles) of pinacolone were added over a period of two hours. The stirring was continued for one hour at 0° and for nine hours at room temperature. The reaction mixture was poured over about 750 g. of cracked ice. A white solid and an oily liquid formed. The solid was isolated and air dried, and the liquid was separated and distilled. The combined yield of the mono- and di-chlorides was 56%.

A total of 135 g. (0.87 mole) of crude dichloride and

23 g. (0.19 mole) of monochloride were shaken with 450 g. of powdered potassium hydroxide in a one-liter flask. Sixty ml. of absolute ethanol were added and the pasty mass was mixed by shaking.

The flask was fitted to a reflux condenser with a distillation head at the upper end. An oil bath was placed around the reaction flask and heated to 135°. The temperature was gradually raised to 240° over a nine-hour period, maintaining a convenient reflux by controlling the water through the condenser below the distillation head.

The product was collected from 38-50° and was then distilled: b. 37.5-38.4° (747 mm.); yield, 50.7 g. (58%).

<u>2-Heptyne</u>.

1-Hexyne* was redistilled: b. 69.5-71.5° (750 mm.). This was used as the starting material for the synthesis of 2-heptyne.

$$C_4H_9C \equiv CH \xrightarrow{C_2H_5MgBr} C_4H_9C \equiv CMgBr \xrightarrow{(CH_3)_2SO_4} C_4H_9C \equiv CCH_3 \qquad (XI)$$

Ethyl Grignard reagent was prepared from 27.5 g. (0.25 mole) ethyl bromide and 6.1 g. (0.25 mole) magnesium in dry ether. The reagent was decanted through glass wool into a 500 ml. flask fitted with a mechanical stirrer, condenser and dropping funnel. Calcium chloride drying tubes were attached to all vents.

---

*Student preparation, according to Lucas and Pressman (20).

A solution of 17.9 g. (0.216 mole) of 1-hexyne in 50 ml. dry ether was added at a rate which maintained a low rate of reflux. The mixture was refluxed until gas evolution had ceased and then for an additional hour. One mole of freshly distilled dimethyl sulfate was added over a 20 minute period with vigorous stirring. The mixture was treated with 25 ml. of dilute sulfuric acid and 100 ml. of water. The ether layer was isolated, dried with anhydrous potassium carbonate and distilled. The fraction boiling 106-110° (750 mm.) was collected: crude yield, 14 g. (67%).

The crude material was carefully fractionated through a 30 cm. heligrid column: b. 110.0-110.6° (747 mm.); $n^{25}D$ 1.4196; $d^{25}4$ 0.7440. Lit.: b. 109° (721 mm.) (21); $n^{25}D$ 1.4199 (21); b. 107-111° (16); $n^{25}D$ 1.4220 (16).

Calculation of molar refractions of acetylenic compounds will be given in another portion of this thesis.

<u>2-Methyl-3-hexyne</u>.

The alkylation of isopropyl acetylene was carried out according to the procedure of Thorn, Hennion and Nieuwland (22).

$$(CH_3)_2CHC\equiv CH \xrightarrow{C_2H_5MgBr} (CH_3)_2CHC\equiv CMgBr \xrightarrow{(C_2H_5)_2SO_4}$$

$$(CH_3)_2CHC\equiv CCH_2CH_3 \qquad \text{(XII)}$$

Ethyl Grignard was prepared from 14.6 g. (0.6 mole) magnesium and 65 g. (0.6 mole) dry ethyl bromide in 200 ml. dry ether. The mixture was cooled to about 0° and 34 g. (0.5 mole) isopropyl acetylene was distilled into the stirred solution. After the reaction had subsided, the mixture was refluxed for one hour.

A solution of 124 g. (0.8 mole) freshly distilled diethyl sulfate in an equal volume of dry ether was added with stirring to the Grignard reagent. After this addition, the solution was refluxed for two hours and allowed to stand overnight. The product was decomposed with dilute hydrochloric acid.

The ether phase was separated, washed twice with 25 ml. portions of 5% potassium carbonate and dried over anhydrous potassium carbonate. The product was isolated by fractional distillation through a small Weston column: b. 88.5-93.0° (750 mm.); yield, 9.5 g. (19.8%).

The crude product was purified by careful fractionation through a 30 cm. heligrid column: b. 93.0-93.3° (746 mm.); $n^{25}D$ 1.4089; $d^{25}4$ 0.7173. Lit.: b. 94-95°; $d^{20}4$ 0.7264; $n^{20}D$ 1.4114 (23).

2,2-Dimethyl-3-hexyne.

The procedure employed was that given by Hennion and Banigan (24) for introducing a *tert*-butyl group into a 1-alkyne.

$$\mathrm{CH_3CH_2C\equiv CH \xrightarrow{C_2H_5MgBr} CH_3CH_2C\equiv CMgBr \xrightarrow{(CH_3)_2CO} CH_3CH_2C\equiv CC(CH_3)(OH)CH_3} \qquad \mathrm{(XIII)}$$

Over a 45 minute period, 58 g. (1.0 mole) of dry, redistilled acetone was added to a Grignard reagent prepared from 0.92 mole 1-butyne and 0.92 mole ethyl magnesium bromide. After refluxing the mixture for one hour, the product was decomposed with 18 g. of water in 40 ml. methanol. To this was added 100 ml. water and sufficient 7% hydrochloric acid to dissolve the precipitated solid.

The ether layer was separated and combined with two ether washings of the aqueous phase. The combined ether solutions were dried and filtered, and the ether was removed by distillation through a short Vigreux column.

The 2-methyl-3-hexyn-2-ol was isolated by fractional distillation at reduced pressure: b. 51.0-51.8° (12 mm.); yield, 80 g. (78%).

The crude product was carefully distilled through a 30 cm. column packed with helices: b. 53.4-54.3° (15 mm.); $n^{25}D$ 1.4389; $d^{25}4$ 0.8547; yield, 71.4 g. (69%).

<u>Analysis</u>. Calc'd for $C_7H_{12}O$: C, 74.95; H, 10.78. Found: C, 74.86; H, 10.89.

$$CH_3CH_2C \equiv CC(CH_3)(OH)CH_3 \longrightarrow CH_3CH_2C \equiv CCCl(CH_3)_2 \quad \text{(XIV)}$$

A 1-liter, 3-necked flask was fitted with a mechanical stirrer and was placed in an ice bath. Fifteen g. of anhydrous calcium chloride, 100 ml. ligroin and 49.3 g. (0.44 mole) 2-methyl-3-hexyn-2-ol were added. Anhydrous hydrogen chloride was passed into the flask for five hours. During this time the contents were kept near 0° and were stirred continuously.

The organic phase was decanted from the calcium chloride sludge and was combined with two 20 ml. portions of ligroin which had been used to wash the sludge and rinse the reaction flask. The combined ligroin fractions were washed with anhydrous potassium carbonate until free of hydrogen chloride. The ligroin was removed by distillation at 250 mm.

Isolation of the 2-chloro-2-methyl-3-hexyne was made by fractional distillation through a small Weston column: b. 72-79° (100 mm.); crude yield, 88%.

Two grams of the crude product were refractionated through a semi-micro distilling tube to obtain physical constants: b. 78.5° (100 mm.); $n^{25}D$ 1.4479; $d^{25}4$ 0.9054.

<u>Analysis</u>. Calc'd for $C_6H_{11}Cl$: Cl, 27.15. Found: Cl, 26.66.*

$$CH_3CH_2C \equiv CCCl(CH_3)_2 \xrightarrow{CH_3MgI} CH_3CH_2C \equiv CC(CH_3)_3 \qquad (XV)$$

Methyl Grignard reagent was prepared from 13 g. (0.55 mole) magnesium and 71 g. (0.50 mole) methyl iodide in 200 ml. dry ether. The solution was transferred to another 1-liter flask with nitrogen pressure and through a glass wool plug.

The reaction flask was fitted with a reflux condenser, a mechanical stirrer and a dropping funnel containing 48.5 g. (0.37 mole) 2-chloro-2-methyl-3-hexyne in 75 ml. dry ether. The ether solution of the chloro compound was added

---

*All analyses for chlorine were made by F. Geiger, Chaffey College, Ontario, California.

to the Grignard reagent at a rate of one drop every five seconds with continuous stirring. After standing overnight, the mixture was refluxed for three hours and was then cooled to 0° with an ice bath. The product was decomposed by adding 100 ml. 10% hydrochloric acid with stirring.

The two phases were separated and the ether phase was combined with 15 ml. of ether used to extract the aqueous phase. The ether solution was dried and the ether was removed by distillation.

2,2-Dimethyl-3-hexyne was isolated by distillation and purified by fractional distillation through a 30 cm., helix-packed column: b. 57.2-57.3° (155 mm.); $n^{25}D$ 1.4085; $d^{25}{}_4$ 0.7188; yield, 10.3 g. (25%).

<u>Analysis</u>. Calc'd for C_8H_{14}: C, 87.19; H, 12.81. Found: C, 87.31; H, 12.91.

<u>2,2,5-Trimethyl-3-hexyne</u>.

$$(CH_3)_2CHC \equiv CMgBr \xrightarrow{(CH_3)_2CO} \xrightarrow{H_2O} (CH_3)_2CHC \equiv CC(OH)(CH_3)_2 \qquad (XVI)$$

The acetylenic Grignard was prepared as described previously from 51 g. (0.75 mole) isopropylacetylene. Acetone was dried and distilled, and 51 g. (0.88 mole) in an equal volume of dry ether was added dropwise to the Grignard reagent. After the mixture was refluxed for one hour, the ether phase was separated and dried with anhydrous potassium carbonate. Most of the ether was removed by flash distillation.

After removal of a small amount of forerun, 2,5-dimethyl

3-hexyn-2-ol was recovered by fractional distillation at reduced pressure: b. 57.7-58.8° (15 mm.); crude yield, 81.3 g (86%).

A small amount of the crude material was used for purification for evaluation of physical constants: b. 59.0° (15 mm.); $n^{25}D$ 1.4331; $d^{25}4$ 0.8367.

Analysis. Calc'd for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.14; H, 11.24.

$$(CH_3)_2CHC \equiv CC(OH)(CH_3)_2 \xrightarrow{\text{Dry HCl}} (CH_3)_2CHC \equiv CCCl(CH_3)_2 \qquad \text{(XVII)}$$

The synthetic procedure for preparing 2-chloro-2,5-dimethyl-3-hexyne was identical with that used to prepare 2-chloro-2-methyl-3-hexyne.

From 73.4 g. of the alkynol were obtained 67.5 g. (80%) of the crude chloro compound: b. 80-81½° (100 mm.).

Ten grams of the crude product was refractionated three times for evaluation of physical constants: b. 91.5° (100 mm.); $n^{25}D$ 1.4400; $d^{25}4$ 0.8778.

Analysis. Calc'd for $C_8H_{13}Cl$: Cl, 24.51. Found: Cl, 24.74.

$$(CH_3)_2CHC \equiv CCCl(CH_3)_2 \xrightarrow{CH_3MgI} (CH_3)_2CHC \equiv C(CH_3)_3 \qquad \text{(XVIII)}$$

After 62.9 g. (0.43 mole) of the chloro compound had reacted with methyl magnesium bromide, the ether phase was isolated, dried and distilled. Two main fractions were isolated after the ether was removed.

Table 11

Products Isolated from Reaction XVIII

B.p., °C	P, mm.	Yield, g.	$n^{25}D$	$d^{25}4$
103-112	747	21.5	-----	----
71-74	100	18.2	1.447	0.73

The boiling point of the first fraction was of the magnitude expected for 2,2,5-trimethyl-3-hexyne. This fraction was redistilled twice through a 30 cm. heligrid column: b. 110.0-110.2° (747 mm.); $n^{25}D$ 1.4084; $d^{25}4$ 0.7124; yield, 18.3 g. (34%).

Analysis. Calc'd for C_9H_{16}: C, 87.01; H, 12.98. Found: C, 86.92; H, 13.10.

The higher-boiling fraction was redistilled twice through efficient columns, but the boiling point range remained at about two degrees with no significant plateau appearing. The molecular weight by Victor Meyer method* was 137±2. The molecular weight of $C_{10}H_{20}$ would be 140.

Di-tert-butylacetylene.

The exact procedure of Hennion and Banigan (24) was followed. This corresponds to the method used for the synthesis of 2,2-dimethyl-3-hexyne given in this thesis. The tert-butylacetylene Grignard reagent was prepared from 26 g. (0.31 mole) of tert-butylacetylene and about 0.4 mole ethyl magnesium bromide. After the reaction with 23.3 g. (0.4

---

*Molecular weight determination by F. Geiger, Chaffey College, Ontario, California.

mole) acetone, the 2,5,5-trimethyl-3-hexyn-2-ol was isolated by the usual procedure: b. 80-81° (50 mm.); yield, 37 g. (83%).

A small portion of the alkynol was purified for evaluation of physical constants: b. 85.0° (60 mm.); $n^{25}D$ 1.4282; $d^{25}4$ 0.8167. Lit.: b. 85° (60 mm.); $n^{38}D$ 1.4222; d^{38} 0.8064; f.p. 32.0-31.8° (24). After the purified sample had stood overnight, it crystallized: m. 30-31½°.

An additional 10 g. of the alkynol was prepared by the same procedure: yield, 71%.

2-Chloro-2,5,5-trimethyl-3-hexyne was prepared from 37 g. (0.26 mole) of 2,5,5-trimethyl-3-hexyn-2-ol: b. 76-82° (100 mm.); yield, 38.8 g. (89%). Lit.: b. 81-81½° (100 mm.) (24).

The coupling reaction between this chloro compound and methylmagnesium bromide was carried out as in the two previous reactions. The yield of di-tert-butylacetylene from 38.8 g. (0.24 mole) of 2-chloro-2,5,5-trimethyl-3-hexyne was 22.2 g. (65%): b. 106-111° (730 mm.).

The product was redistilled from a small Weston column in a nitrogen atmosphere: b. 110.9-111.5° (746 mm.); $n^{25}D$ 1.4036; $d^{25}4$ 0.7074. Lit.: b. 111.1° (730 mm.); $n^{25}D$ 1.4026; d^{25} 0.7080.

1-Bromo-1-butyne.

$$CH_3CH_2C\equiv CH \xrightarrow{KOBr} CH_3CH_2C\equiv CBr \qquad (XIX)$$

1-Bromo-1-butyne was synthesized according to the procedure of Strauss, Kollek and Heyn (25).

A sodium hypobromite solution was prepared from 92 g. potassium hydroxide, 750 ml. water and 83 g. bromine in a glass-stoppered Pyrex bottle. The solution was kept near 0° during addition of bromine to the potassium hydroxide solution. After nitrogen was bubbled through the solution for about 20 minutes, 28 g. (0.52 mole) butyne was added, and the bottle was tightly closed with a lightly greased stopper.

The mixture was shaken mechanically at room temperature for six hours and was then allowed to stand overnight. The organic phase had separated well and most of it was removed from the bottom of the reaction bottle by means of a pipette. The remainder was extracted with two 25 ml. portions of ether.

The combined organic phases were dried over magnesium sulfate, filtered and distilled: b. 88.8-89.8° (749 mm.); yield, 58.9 g. (85%). The crude product was then redistilled through a semi-micro distilling tube: b. 91.5° (745 mm.); $n^{25}D$ 1.4599; $d^{25}4$ 1.3912. Lit.: b. 90-91° (26).

The product was redistilled in a nitrogen atmosphere and was transferred to ampoules with as little contact with air as possible. After several days in the ampoules, the colorless product had turned red, but no further discoloration or decomposition was noted over a period of several months.

3-Hexyn-2-ol.

$$CH_3CH_2C \equiv CH \xrightarrow{C_2H_5MgBr} CH_3CH_2C \equiv CMgBr \xrightarrow{(CH_3)CHO} CH_3CH_2C \equiv CCH(OH)CH_3 \qquad (XX)$$

3-Hexyn-2-ol was prepared according to the general procedure given by Thompson, Burr and Shaw (27).

Ethylmagnesium bromide was prepared from 29 g. (1.2 moles) magnesium and 110 g. (1.0 mole) ethyl bromide in 300 ml. ether. The dropping funnel on the reaction flask was replaced by a 10 mm. glass tube connected to an ampoule of 1-butyne. The flask vent was protected by a dry ice and acetone reflux condenser. While the mixture in the reaction flask was being stirred mechanically, 43.7 g. (0.81 mole) 1-butyne was allowed to distil into the reaction flask. The mixture was allowed to stand three hours.

Acetaldehyde was prepared by distillation from 52.8 g. (0.40 mole) paraldehyde in the presence of p-toluenesulfonic acid. The distillate was added to the reaction flask over a period of 75 minutes. The product was refluxed for one hour after addition and was allowed to stand overnight. One mole of water (30% in methanol) was added slowly with vigorous stirring.

The ether layer was decanted. Ice-cold, 7% hydrochloric acid was added to the aqueous suspension until it was neutral, and the remaining ether was separated and added to the main organic phase. The combined ether solutions were dried with anhydrous potassium carbonate and stored under dry nitrogen for later distillation.

Ether was removed by flask distillation. When the temperature of the residual liquid reached 60°, the material was transferred to a smaller flask and was distilled through a 40 cm. Vigreux column at reduced pressure: b. 55-60° (15 mm.).

The crude product was then redistilled through a 40 cm., helix-packed column in a nitrogen atmosphere: b. 57.2-58.1° (14 mm.); $n^{25}D$ 1.4446; $d^{25}4$ 0.8727; yield, 55.2 g. (56.3%).

<u>Analysis</u>. Calc'd for $C_6H_{10}O$: C, 73.43; H, 10.27. Found: C, 73.62; H, 10.28.

Two derivatives were prepared.

1. <u>alpha</u>-Naphthylurethane (28): m. 90-91°. <u>Analysis</u>. Calc'd for $C_{17}H_{17}O_2N$: C, 76.38; H, 6.41. Found: C, 76.68; H, 6.48.

2. 3,5-Dinitrobenzoate (29): m. 136-137°. <u>Analysis</u>. Calc'd for $C_{13}H_{12}O_6N_2$: C, 53.43; H, 4.14. Found: C, 53.48; H, 4.06.

A repeat synthesis of 3-hexyn-2-ol from 0.80 mole of 1-butyne yielded 0.62 mole (78%) of the alkynol: b. 72-76° (38 mm.).

<u>3-Hexyn-2-one</u>.

$$CH_3CH_2C\equiv CMgBr \xrightarrow{(CH_3CO)_2O} CH_3CH_2C\equiv CCOCH_3 \qquad (XXI)$$

The Grignard of 1-butyne was prepared as usual (0.90 mole), and was added, with vigorous stirring, to 102 g. (one mole) acetic anhydride in an equal volume of dry ether. The addition required one hour, and the products were refluxed for an additional hour before decomposition of the product with 150 ml. water.

Two ether washings of the aqueous phase were combined with the original ether phase. These were dried with anhydrous potassium carbonate, filtered and distilled: b. 58.7-60.5° (35 mm.); yield, 20 g. (23%).

The crude product was refractionated through a small Weston column: b. 75.0-75.9° (73 mm.); $n^{25}D$ 1.4376; $d^{25}4$ 0.8747; yield, 15.9 g. (18%). Lit.: b. 77.0-78.5° (73 mm.); $n^{25}D$ 1.4371 (26).

Two derivatives were prepared.

1. Semicarbazone (30): m. 115-116°. Analysis. Calc'd for $C_7H_{11}ON_3$: N, 27.43. Found: N, 27.53.

2. 2,4-Dinitrophenylhydrazone (31): m. 143-144°. Analysis. Calc'd for $C_{12}H_{12}O_4N_4$: N, 11.29. Found: N, 11.34.

Methyl 2-heptynoate.

2-Heptynoic acid was purchased from Farchan Research Laboratories and was purified by treating it with 5% ferrous sulfate containing a small amount of ammonium thiocyanate. This was followed by distillation: b. 121.6-121.8° (10 mm.); $n^{25}D$ 1.4572. Lit.: b. 122° (10 mm.); $n^{20}D$ 1.4619 (32).

The methyl ester of 2-heptynoic acid was prepared by

Fischer esterification as given by Zoss and Hennion (32). A 100 ml. flask with a side arm and a thermometer well was fitted with a reflux condenser protected at the top with a "tee" through which a small stream of nitrogen was flowing. After the system had been thoroughly flushed with nitrogen, 32 g. (1.0 mole) anhydrous methanol, 1.2 g. 98% sulfuric acid and 25 g. (0.20 mole) 2-heptynoic acid were introduced and the side arm was stoppered. The mixture was refluxed with a small flame, and the temperature of the flask contents was observed by means of a thermometer in the well. After refluxing for one hour, the temperature had become constant. After one additional hour of refluxing, the products were cooled and added to 50 ml. of alkaline (1% NaOH) half-saturated sodium chloride solution in a 100 ml. separatory funnel and shaken.

The aqueous phase was removed and the treatment of the organic phase with sodium chloride solution was repeated. The organic phase was dried overnight over anhydrous magnesium sulfate. The liquid was decanted from the drying agent and the latter was washed with two small portions of methanol. The combined methanol solutions were distilled at reduced pressure through a small Weston column: b. 76.2-78.5° (10 mm.); yield, 21.8 g. (79%).

The product was refractionated: b. 78.2-78.6° (10 mm.); $n^{25}D$ 1.4428; $d^{25}4$ 0.9290. Lit.: b. 72° (10 mm.); $n^{20}D$ 1.4455; d^{20} 0.932 (32).

Methyl *beta*-ketoheptanoate.

$$\mathrm{CH_3CH(OH)(CH_2)_3CH_3 \xrightarrow{ox.} CH_3CO(CH_2)_3CH_3} \qquad \mathrm{(XXII)}$$

$$\mathrm{CH_3CO(CH_2)_3CH_3 \xrightarrow{Na} \xrightarrow{CO_2} \xrightarrow{H^+} HOOCCH_2CO(CH_2)_3CH_3} \qquad \mathrm{(XXIII)}$$

$$\mathrm{CH_3(CH_2)_3COCH_2COOH \xrightarrow{CH_2N_2} CH_3(CH_2)_3COCH_2COOCH_3} \qquad \mathrm{(XXIV)}$$

The general procedure given by Levine and Hauser (33) was followed.

2-Hexanone was prepared from 2-hexanol by dichromate oxidation (34): b. 125-127° (750 mm.); yield, 70%.

Sodamide was prepared from 14.4 g. (0.63 mole) sodium and a small crystal of ferric chloride in 300 ml. liquid ammonia.

Over a five minute period, 50 g. (0.50 mole) 2-hexanone was added to the suspension of sodamide in ammonia. A water-jacketed condenser was attached to the reaction flask and the ammonia was evaporated as rapidly as possible (about 20 minutes), maintaining a total volume in the reaction flask of about 300 ml. by the addition of dry ether. When the ether began to reflux, the contents of the flask were poured over about five moles of crushed dry ice. The flask was rinsed with ether and this was added to the dry ice reaction mixture.

After the reaction products had reached room temperature, water and ether were added very cautiously until two nearly clear phases had formed. The aqueous phase was neutralized by pouring it over a mixture of 30 ml. 98% sulfuric acid in 200 g. crushed ice.

The organic phase and two ether washings of the aqueous phase were combined and dried over sodium sulfate. The ether solution was decanted from the drying agent and treated with about 20% excess of an ethereal solution of diazomethane (as indicated by evolution of nitrogen).

The excess diazomethane was destroyed by the addition of glacial acetic acid. A major portion of the ether was removed by flash distillation at reduced pressure, and the crude ester was recovered by distillation at 8 mm.; b. 68-70°; yield, 8.45 g. (28%).

The methyl 2-heptynoate was purified by distillation through a semi-micro distilling tube: b. 83.2-83.5° (10 mm.); $n^{25}D$ 1.4250; $d^{25}4$ 0.9858.

Analysis. Calc'd for $C_8H_{14}O_2$: C, 60.74; H, 8.92. Found: C, 60.78; H, 9.02.

A 2,4-dinitrophenylhydrazone was prepared (35): m. 106-107°. Analysis. Calc'd for $C_{14}H_{18}O_6N_4$: N, 16.56. Found: N, 16.71.

Thionyl bromide.

Thionyl bromide was prepared from thionyl chloride by the method of Elderfield et. al. (36).

$$SOCl_2 \xrightarrow{HBr} SOBr_2 \qquad (XXV)$$

Hydrogen bromide was prepared by adding bromine to refluxing tetralin. The hydrogen bromide gas was bubbled through 150 g. practical grade thionyl chloride for two hours at -5° to 0°. The product was distilled through a

30 cm. Vigreux column, collecting the fraction boiling from 63-69° (40 mm.); yield, 226 g. (80%).

D. MOLAR REFRACTIONS OF ACETYLENIC COMPOUNDS.

Molar refractions for all synthetic acetylenic derivatives were determined by use of the Lorenz-Lorentz equation. These experimental values were then compared with the refractions calculated by two different methods.

Hennion and Banigan (37) have studied the refractions of twenty different purified acetylenic hydrocarbons reported in literature. They found that by assigning values to carbon atoms and to the triple bond by the usual methods, considerable discrepancies appear between found and calculated values.

By using data from the twenty alkynes they were able to get exceptionally close agreements by assigning individual values to carbon atoms in various positions in the alkyne.

Thus, the following values were obtained (37):

Carbon Atom	Molar Refraction Contribution
Triple-bonded atom	3.240
Alpha to triple bond	2.779
Beta to triple bond	2.605
Gamma to triple bond	2.436
All others	2.418

No contribution was assigned the triple bond, and the hydrogen value remained 1.100. Using this data, the maximum deviation obtained by Hennion and Banigan (37) was 0.5%.

In Table 12 are presented all of the molar refraction values determined for the products synthesized during the course of this investigation. Columns I, II and III show respectively the observed refractive index, density and molar refraction for each compound. Column IV gives the calculated value for the molar refractions using the standard atomic and triple bond contributions. Column V gives the molar refractions calculated by means of the method proposed by Hennion and Banigan (37).

Our observed values of molar refractions of the hydrocarbons agreed very well with the values calculated according to the method of Hennion and Banigan. Di-<u>tert</u>-butylacetylene showed a deviation of 0.6%, but for all other values the deviations were below 0.3%.

The observed values for the alkynols were consistently higher than the calculated values, but the deviations remained below 0.5% in all cases.

The "allylic-type" chloro compounds exhibited some exaltation. The deviations in three instances were +0.69, +0.70 and +0.64. These are sufficiently consistent that it should be possible to employ a special value for the contribution of an <u>alpha</u>-chlorine atom to the molar refraction of acetylenic compounds. An average of the three deviations could be added to the normal contribution of chlorine, 5.968, to give a new value, 6.65. More cases would have to be observed to add one more significant figure.

No abnormality was observed for 1-bromo-1-butyne, but considerable exaltation is present when a carbonyl group is conjugated with the triple bond as in the case of 3-hexyn-2-one or methyl-2-heptynoate.

Table 12

Molar Refractions of Acetylenic Compounds

Compound	I $n^{25}D$	II $d^{25}4$	III MR, obs.	IV Stnd.	V New
3-Hexyne	1.4090	0.7185	28.26	27.91	28.25
2-Heptyne	1.4196	0.7440	32.68	32.52	32.70
2-Methyl-3-hexyne	1.4089	0.7173	33.14	32.52	33.05
2,2-Dimethyl-3-hexyne	1.4085	0.7188	37.86	37.14	37.86
2,2,5-Trimethyl-3-hexyne	1.4084	0.7124	42.70	41.76	42.66
Di-_t_-butylacetylene	1.4036	0.7074	47.75	46.38	47.47
3-Hexyn-2-ol	1.4446	0.8727	29.90	29.43	29.77
2-Methyl-3-hexyn-2-ol	1.4389	0.8647	34.51	34.05	34.63
2,5-Dimethyl-3-hexyn-2-ol	1.4338	0.8357	39.21	38.67	39.38
2,5,5-Trimethyl-3-hexyn-2-ol	1.4282	0.8167	44.09	43.29	44.19
1-Bromo-1-butyne	1.4599	1.3912	26.18	26.44	26.23
2-Chloro-2-methyl-3-hexyne	1.4479	0.9054	38.61	37.39	37.82
2-Chloro-2,5-dimethyl-3-hexyne	1.4400	0.8778	43.43	42.01	42.73
2-Chloro-2,5,5-trimethyl-3-hexyne	1.4343*	0.8585*	48.17	46.63	47.53
Methyl 2-heptynoate	1.4428	0.9290	39.99	38.80	38.97
3-Hexyn-2-one	1.4367	0.8747	28.83	27.92	28.26

*Data from Hennion and Banigan (24).

E. QUANTITATIVE DETERMINATION OF ALKYNES BY SPECTROPHOTOMETRIC METHODS.

Introduction. Since the quantitative results of the determination of 3-hexyne by oxidative methods were generally unreliable, and since the method was not suited for more complex alkynes, it became necessary to investigate further methods of analysis.

A Perkin-Elmer, automatic recording, infra-red spectrophotometer was available in the Crellin laboratories. The instrument was reported capable of analyses of two- to five-component systems with errors of less than ±0.5%.

The spectrophotometer could be used for the analysis of alkynes containing any functional group, and consequently it was a logical choice for further investigation.

Effect of Silver Ion on Solubility of Various Compounds. Several acetylenic compounds containing functional groups (-OH and $-COOCH_3$) were available through Farchan Research Laboratories, and synthetic procedures were available for introducing or incorporating halogens, keto groups and nitrile groups along with the triple bond. In order to determine the effect of these groups on the reaction of silver ion with a triple bond, it became necessary to insure that these groups themselves did not coordinate or react with aqueous silver ion.

1. The hydroxyl group. One gram of reagent grade

cyclohexanol was dissolved in water and diluted to 50.0 ml. in a volumetric flask. The concentration of this solution was 0.203 f.

Two-ml. samples of this solution were transferred to iodometric flasks containing 15.00 ml. of 0.548 n. potassium permanganate and 15 ml. of 6n sulfuric acid. The mixture was warmed to about 50° for thirty minutes with shaking and the excess permanganate was titrated with a standard solution of oxalic acid. Two identical samples were run. Considering the reaction to proceed to the adipic acid stage, the concentrations found were 0.235 f. and 0.231 f.

The duplicability in this instance was more important than the extent of oxidation, for the method was to be applied to the oxidation of saturated solutions of cyclohexanol in both potassium nitrate and silver nitrate solutions.

An excess (about 4 ml.) of cyclohexanol was placed in each of two separatory funnels containing respectively 30 ml. of 0.1 f. potassium nitrate and 30 ml. of 0.1 f. silver nitrate. These were shaken vigorously several times over a thirty minute period and then allowed to settle overnight. The aqueous phases were separated and two-ml. samples were pipetted into a measured excess of standard permanganate. The oxidation was carried out as before. The amount of permanganate consumed in each instance varied by only about 1%. Duplicate determinations showed no significant change.

It was tentatively assumed that silver ion had no effect on the solubility of cyclohexanol at constant ionic strength.

2. The ester group. Methyl caproate was prepared by Fischer esterification, using 25 g. (0.22 mole) caproic acid, 40 g. (1.1 moles) methanol and 1.2 g. 98% sulfuric acid. The solution was refluxed for two hours and then mixed with 50 ml. alkaline (1% NaOH), half-saturated sodium chloride.

The organic phase was separated, dried and distilled: b. 70.6-72.0° (50 mm.); $n^{25}D$ 1.4032; yield, 22.4 g. (81.5%). Lit.: b. 53-54° (20 mm.); $n^{23.1}D$ 1.4038 (38).

Since quantitative measurements were to be made by infra-red spectrophotometric methods, purified carbon tetrachloride would be required for extractant and solvent.

Two liters of reagent grade carbon tetrachloride were placed in a 2-liter, round-bottomed flask. Chlorine gas was bubbled slowly into the liquid (hood) for ten minutes, leaving the solution typically bright greenish-yellow. The flask was stoppered lightly and placed in direct sunlight. After standing for three days in intermittent sunlight, the solution was shaken twice with aqueous sodium bisulfite, twice with 5% sodium hydroxide and twice with distilled water. Anhydrous magnesium sulfate was used to dry the treated carbon tetrachloride. After filtration, the treated product was distilled at atmospheric pressure. The water-carbon tetrachloride azeotrope was discarded and the product was collected over a 0.5° range, 76.5-77.0° (750 mm.); $n^{25}D$ 1.4568.

A solution of five ml. methyl caproate in 50 ml. purified carbon tetrachloride was divided into four portions for separate treatment as follows:

a. Control.

b. Shaken with anhydrous potassium carbonate, allowed to settle overnight.

c. Shaken with an equal volume of aqueous silver nitrate (0.2 *f.*), separated in a separatory funnel, transferred to a glass-stoppered flask containing anhydrous potassium carbonate, and allowed to stand overnight.

d. Same as (c), but using 0.2 f. potassium nitrate in place of the silver nitrate.

Optical density measurements of each of these solutions were made with the Perkin-Elmer spectrophotometer, using the carbon-hydrogen band at approximately 3.45 microns. The following is a description of the technique employed for making optical measurements.

a. Carbon tetrachloride was placed in the "blank" cell and control solution was placed in the sample cell of the instrument (both cells, 0.05 mm. light path). The position of maximum absorption was determined by allowing the instrument to run slowly over the range 3.3-3.6 microns. In this instance, the point was 3.457 microns.

b. The sample cell was drained, flushed with five-ml. portions of carbon tetrachloride twice, dried with a stream of dry nitrogen and filled with purified carbon tetrachloride. With both cells in the light paths, the instrument was set at 3.457 microns and balanced to 100% transmission.

c. The sample cell was removed, drained, dried with nitrogen, filled with an appropriate sample and placed in position in the instrument. The instrument was run slowly over the range 3.3-3.6 microns, and the maximum optical density was recorded.

The results using the four prepared samples are given in Table 13.

Table 13

Relative Solubility of Methyl Caproate in Aqueous Solutions

Sample	Optical Density
a. Control	0.401
b. Dried with potassium nitrate	0.402
c. Treated with silver nitrate and dried	0.401
d. Treated with potassium nitrate and dried	0.403

From these results, it was concluded that there was no appreciable adsorption of methyl caproate from carbon tetrachloride solution by anhydrous potassium carbonate. Also, at constant ionic strength, the presence of silver ion had no observable effect on the solubility of methyl caproate in water. Furthermore, a satisfactory distribution for extraction purposes is indicated.

In order to verify the fact that the silver ion is without effect on the solubility of methyl caproate in water, a saturated solution of the ester was prepared in 0.200 f. silver nitrate and in 0.200 f. potassium nitrate. After the solutions had stood overnight, the excess organic phase was removed. Five-ml. portions of each of the aqueous phases was shaken with 3.00 ml. of carbon tetrachloride in 15 ml. separatory funnels. The stopper and stopcock of the funnels were ungreased, but were wet with carbon tetrachloride by placing a drop at the exposed edge of the joint immediately after fitting together the two ground glass surfaces. A portion of the carbon tetrachloride phase was transferred to a 2-ml., glass-stoppered volumetric flask containing a small amount of anhydrous potassium carbonate, The flask was stoppered and shaken. Optical density measurements on these dried solutions were made as before. The results are given in Table 14.

Table 14

Relative Solubility of Methyl Caproate in Potassium Nitrate and Silver Nitrate Solutions

Sample	Optical Density
Treated with potassium nitrate	0.030
Treated with silver nitrate	0.030

At this point, it became apparent that cells with longer light paths were necessary. However, within the limit of accuracy of all of the measurements, there was no indication that silver ion increased the solubility of methyl caproate at constant ionic strength.

3. Nitriles. Commercial *n*-butyronitrile was purified by fractional distillation through a small Weston column: b. 116.4-116.7° (750 mm.); $n^{25}D$ 1.3818. Lit.: b. 117.9° (760 mm.) (39); $n^{25}D$ 1.3820 (40).

Optical density measurements of solution of *n*-butyronitrile in *n*-heptane were made with the Beckmann DU spectrophotometer in the region 212 to 320 millimicrons. In order to obtain satisfactory readings, it was necessary to maintain slit widths at a maximum (2 mm.). The instrument behaved very erratically at the low range, so for comparitive purposes, 216.5 millimicrons was arbitrarily chosen for preliminary studies.

Into a 250 ml. equilibration flask was placed 150 ml. of an 0.200 *f*. solution of potassium nitrate. *n*-Butyronitrile was added in small portions with swirling until no more would dissolve. One-half ml. excess nitrile was added and the assembly was placed in a constant temperature bath at 25.0°. The mixture was equilibrated by swirling the solution several times during a four hour period.

The equilibration procedure was repeated, using an 0.200 *f*. solution of silver nitrate in place of the potassium nitrate.

After the mixtures had settled for 1½ hours, 15 ml. samples were pipetted into small separatory funnels containing 10.0 ml. n-heptane. These were shaken for several minutes, then the aqueous phase was drawn off. The organic phase was transferred to a glass-stoppered flask containing a small amount of anhydrous drying agent (sodium sulfate or magnesium sulfate). The optical density of these solutions was checked in the Beckmann DU instrument at 216.5 millimicrons, 2.0 mm. slit width (Table 15).

Table 15

Relative Solubility of n-Butyronitrile in Potassium Nitrate and Silver Nitrate Solutions

Salt	Salt conc.	Optical Density
Potassium nitrate	0.200 f.	0.604
Silver nitrate	0.200 f.	0.710[a]
Silver nitrate	0.200 f.	0.212[b]

[a] First extraction. [b] Second extraction.

These results indicate an increased solubility of n-butyronitrile in the presence of silver ion. An extraction procedure for this compound is not efficient, and direct measurements on the aqueous solutions are not feasible because of interference of the nitrate ion absorption at this particular wave length.

Direct Solubility Measurements of Nitriles. During the preparation of a saturated solution of n-butyronitrile, it was observed that a very small rise in temperature caused a saturated solution to become cloudy. Using this phenomenon, it was possible to make direct solubility measurements of n-butyronitrile in aqueous solutions.

Two 5-ml. burettes were filled with the nitrile. No lubricant was used on the stopcocks. Two 50-ml. burettes were filled respectively with 1.00 f. silver nitrate and potassium nitrate.

A measured volume of 1.00 f. silver nitrate and/or 1.00 f. potassium nitrate was pipetted into a 25 ml., glass-stoppered mixing cylinder. A slight excess of n-butyronitrile (in excess of the amount needed to saturate the solutions, as indicated by preliminary measurements) was introduced by means of the micro burette. In order to obtain precise measurements, it was necessary to read the micro burette immediately before and immediately after removing some nitrile.

The cylinder was stoppered using a stopper coated very lightly with silicone grease. The cylinder and contents were cooled to about 10° by means of an ice bath. The contents were swirled to bring the nitrile into solution and then the cylinder was shaken thoroughly (not vigorously) and placed in a constant temperature bath at 25.0°. When a second phase formed, as indicated by cloudiness, the cylinder was removed and cooled, and additional aqueous solution was added from one of the 50 ml. burettes. The process was repeated until no second phase appeared after 20 minutes at

25.0°.

Two major precautions were necessary, The first involved care in adding additional aqueous phase near the end point. Changes were discernible when the total volume was increased by only about 0.5%. The second precaution involved care in differentiating between formation of two liquid phases and formation of gas bubbles as the temperature rose.

The results of solubility measurements will be described along with those of n-valeronitrile and n-capronitrile.

n-Valeronitrile (Eastman White Label) was shaken with 2% sulfuric acid, isolated and dried over anhydrous magnesium sulfate. After filtration, the product was fractionally distilled in a 30 cm., helix-packed column: b. 139.4° (750 mm.); $n^{25}D$ 1.3951. Lit.: b. 141.3° (760 mm.) (39); $n^{25}D$ 1.3950 (40).

n-Capronitrile (Eastman White Label) was washed with 2% sulfuric acid, dried over sodium sulfate, filtered and fractionally distilled through a 30 cm., helix-packed column: b. 87.6-87.8° (64 mm.); $n^{25}D$ 1.4051. Lit.: b. 86.8° (60 mm.) (41); $n^{25}D$ 1.4049 (40).

Solubility of Nitriles in Aqueous Solutions of Potassium Nitrate and Silver Nitrate. The solubilities of the three nitriles (n-butyro-, n-valero- and n-capro-nitrile) was determined at various silver ion concentrations, maintaining the ionic strength of the solutions near unity.

The concentrations of silver ion and of nitrile were calculated on the assumption that the volumes of organic and aqueous phases were additive. This was probably valid in the case of the valero- and capro-nitriles, but relatively large amounts of n-butyronitrile were soluble at high concentrations of silver ion.

The concentration of the nitrile was plotted as a function of the silver ion concentration (Table 16, Figure 12), and a mathematical expression was obtained by the method of least squares (equation XXVI).

Similar data were obtained for n-valeronitrile (Table 17, Figure 13, equation XXVII) and n-capronitrile (Table 18, Figure 14, equation XXVIII).

From the behavior of the solubility of n-butyronitrile in the presence of silver ion, it is necessary to postulate the formation of a strong complex involving two molecules of nitrile and one of silver ion. When the concentration of silver ion is unity, the solubility of n-butyronitrile has increased by 1.35 moles/liter over the value at zero silver ion concentration.

Let us assume two equations (XXIX and XXX) and two constants (XXXI and XXXII):

$$Ag^+ + B \rightleftharpoons AgB^+ \qquad \text{(XXIX)}$$

$$AgB^+ + B \rightleftharpoons AgB_2^+ \qquad \text{(XXX)}$$

Table 16

Solubility of n-Butyronitrile in Aqueous Solutions

(Ag_t), moles/l.	(Nitrile), moles/l.	(Nitrile, moles/l., Calc'd, Equation XXVI
0.000	0.446	0.446
0.136	0.582	0.581
0.234	0.690	0.688
0.457	0.959	0.960
0.665	1.250	1.251
0.860	1.569	1.559
0.940	1.688	1.693
0.350		0.824
0.550		1.084
0.750		1.382

$$(\text{Nitrile}) = 0.446 + 0.935\,(Ag_t) + 0.418\,(Ag_t)^2 \qquad (\text{XXVI})$$

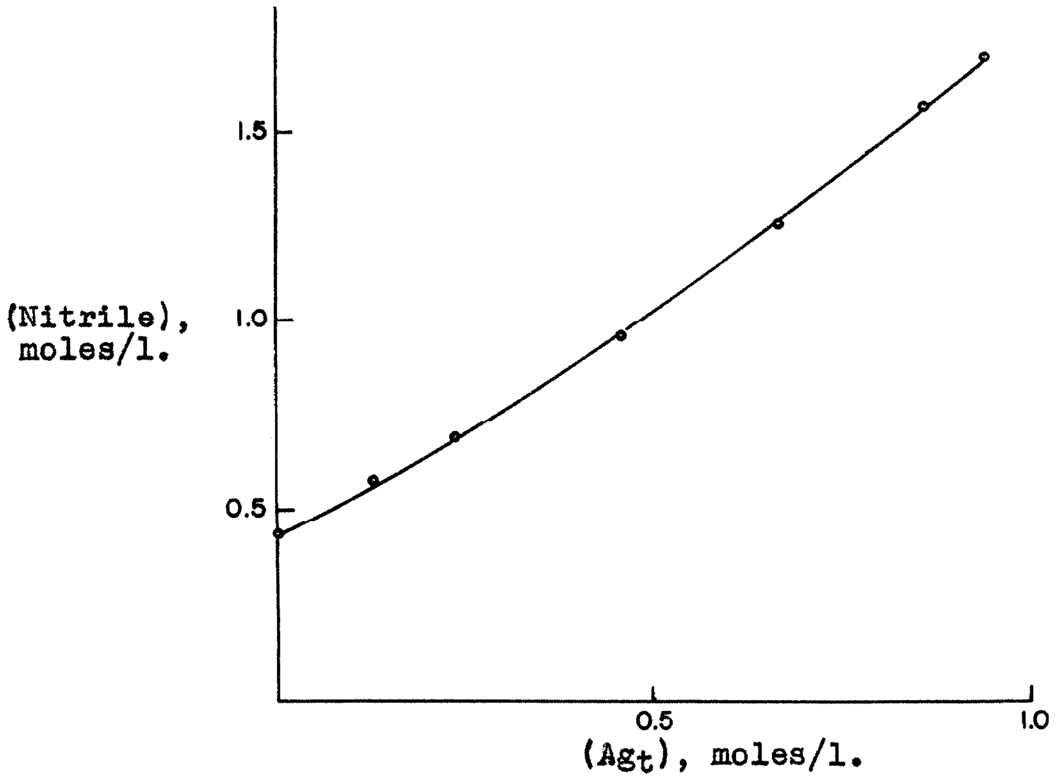


Figure 12. Solubility of n-Butyronitrile in Aqueous Solutions.

Table 17

Solubility of n-Valeronitrile in Aqueous Solutions

(Ag_t), moles/l.	(Nitrile), moles/l.	(Nitrile), moles/l., Calc'd, Equation XXVII
0.000	0.123	0.123
0.145	0.174	0.176
0.159	0.184	0.181
0.294	0.231	0.232
0.495	0.312	0.312
0.513	0.321	0.319
0.687	0.392	0.393
0.799	0.440	0.442
0.947	0.510	0.508

$$(\text{Nitrile}) = 0.123 + 0.355\,(Ag_t) + 0.055\,(Ag_t)^2 \qquad \text{(XXVII)}$$

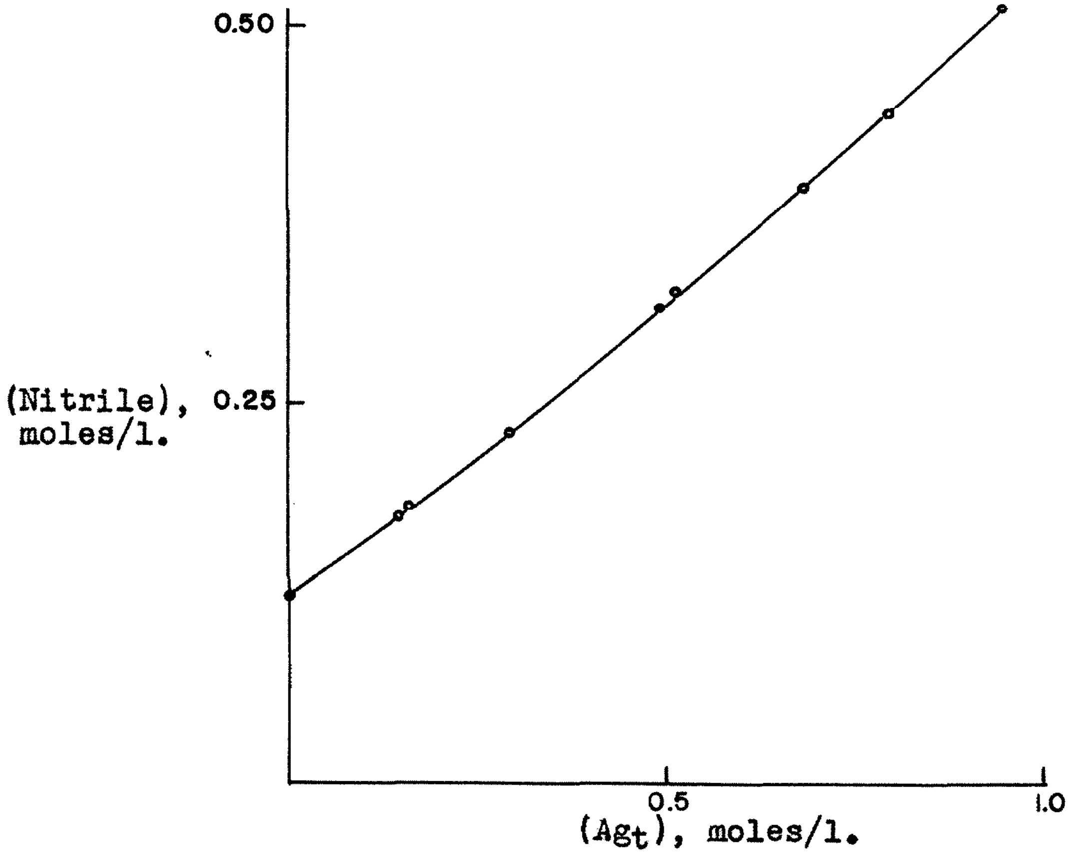


Figure 13. Solubility of n-Valeronitrile in Aqueous Solutions.

Table 18

Solubility of n-Capronitrile in Aqueous Solutions

(Ag_t), moles/l.	(Nitrile), moles/l.	(Nitrile), moles/l., Calc'd, Equation XXVIII
0.084	0.042	0.042
0.172	0.050	0.050
0.343	0.068	0.067
0.504	0.084	0.083
0.714	0.107	0.107
0.973	0.137	0.138

$$(\text{Nitrile}) = 0.0345 + 0.0870\,(Ag_t) + 0.020\,(Ag_t)^2 \qquad \text{(XXVIII)}$$

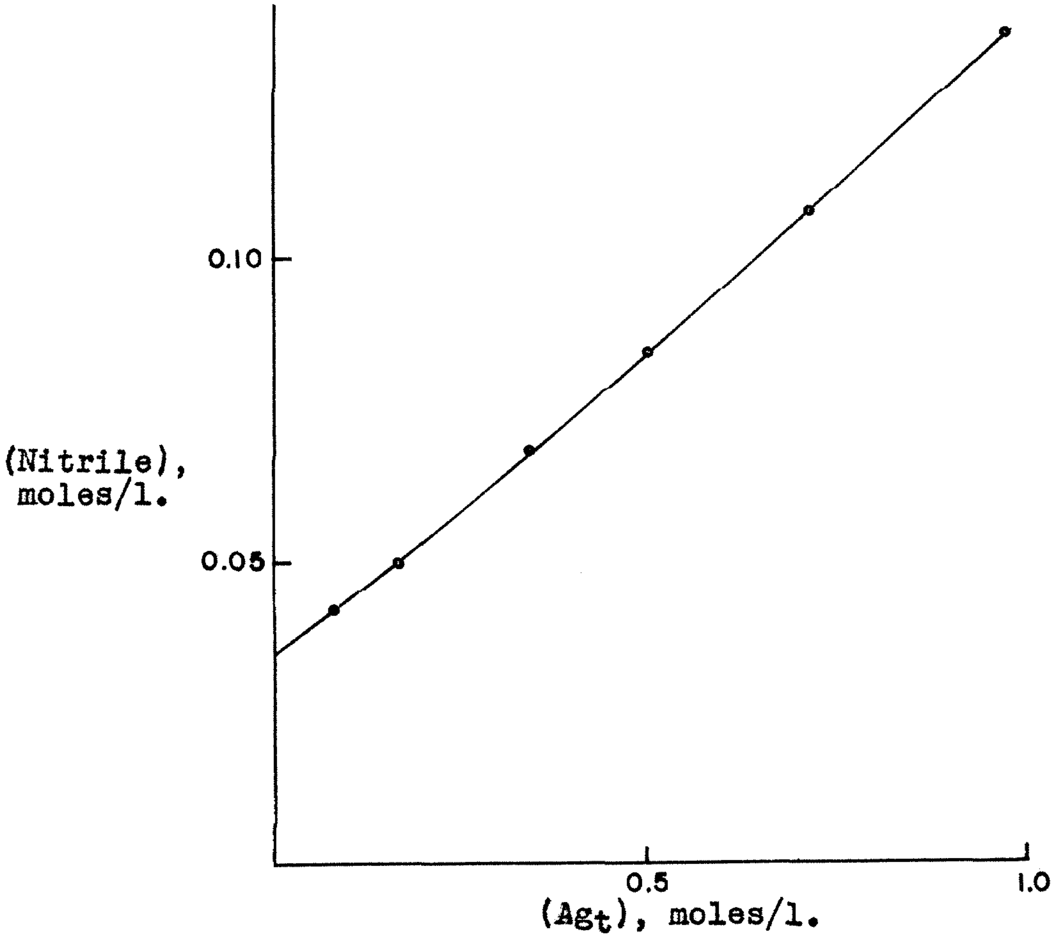


Figure 14. Solubility of n-Capronitrile in Aqueous Solutions.

$$K_1 = \frac{(AgB^+)}{(Ag^+)(B)} \qquad \text{(XXXI)}$$

$$K_2 = \frac{(AgB_2^+)}{(AgB^+)(B)} \qquad \text{(XXXII)}$$

Under these conditions, the following relationships hold:

$$(Ag_t) = (Ag^+) + (AgB) + (AgB_2) \qquad \text{(XXXIII)}$$

$$(B_t) = (B) + (AgB) + 2(AgB_2) \qquad \text{(XXXIV)}$$

$$(B_t) = (B) + K_1(Ag^+)(B) + 2K_1K_2(Ag^+)(B)^2 \qquad \text{(XXXV)}$$

The last expression (equation XXXV) indicates that the total concentration of nitrile in solution under these conditions should vary linearly with the concentration of the silver ion. The variance with observed facts can be explained by the fact that under the experimental conditions the ionic strength of the solutions is varying considerable as the silver ion concentration is increased. It is also quite possible that there exists an additional coordination reaction involving two silver ions and one molecule of nitrile.

Distribution Measurements. In an attempt to further evaluate the coordination reaction between silver ion and nitriles, distribution measurements for *n*-valeronitrile were made using carbon tetrachloride and aqueous phases.

A Beer's law plot was made for *n*-valeronitrile in carbon tetrachloride, using the carbon-hydrogen absorption band at 3.44 microns. Spectrophotometric measurements were made as described previously, using a 1.0 mm. cell (Table 19, Optical Density of Solutions of n-Valeronitrile in Carbon Tetrachloride

(Nitrile), moles/l.	Optical Density, 3.44 u, 1.0 mm. cell
0.117	0.055
0.325	0.134
0.526	0.211
0.770	0.290

Table 19

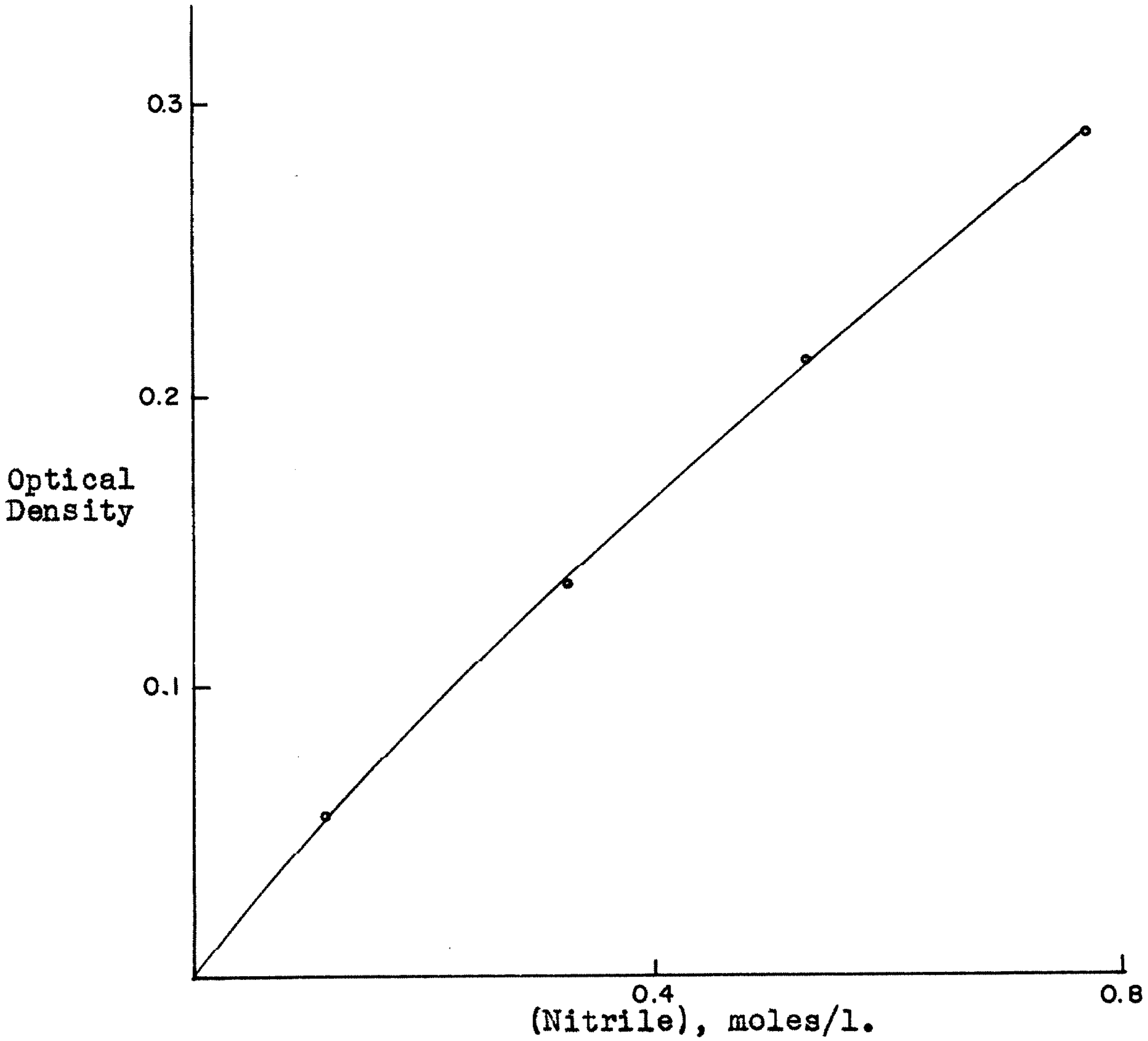


Figure 15. Optical Density of Solutions of n-Valeronitrile in Carbon Tetrachloride.

Figure 15).

The distribution coefficient of n-valeronitrile between carbon tetrachloride and 1.00 f. potassium nitrate solution was determined at 25.0°.

Five ml. of a solution of n-valeronitrile in carbon tetrachloride (about 0.5 f.) and 50 ml. 1.00 f. potassium nitrate were shaken intermittently over a three hour period at 25.0°. After standing overnight at this temperature, the phases were shaken thoroughly every fifteen minutes for one hour.

The aqueous phase was separated and an aliquot was shaken for two hours with a relatively large measured volume of carbon tetrachloride. The extraction procedure was repeated with fresh carbon tetrachloride.

The original organic phase and both of the extraction phases were dried separately with anhydrous magnesium sulfate, and optical density measurements were made on each at 3.44 microns (1.0 mm. cell).

The distribution coefficient, K_d, was calculated after converting optical densities to concentrations and calculating the total concentration of nitrile in the original aqueous phase. Results are given in Table 20.

$$K_d = \frac{(\text{Nitrile})_{\text{org.}}}{(\text{Nitrile})_{\text{aq.}}} \qquad \text{(XXXVI)}$$

The distribution measurements were repeated, using silver nitrate and potassium nitrate solutions at an ionic strength of unity instead of 1.00 f. potassium nitrate. However, before the aqueous phase was extracted with carbon tetrachloride, sufficient 5 f. potassium cyanide was added to dissolve the silver cyanide which precipitated.

The following notations were used:

(B_t) = concentration of nitrile in aqueous phase, moles/liter.

(B_c) = concentration of nitrile in carbon tetrachloride phase, moles/liter.

$(B_o) = (B_c)/K_d = (B_c)/34$ = concentration of uncomplexed nitrile in aqueous phase, moles/liter.

(Ag_t) = concentration of silver ion before equilibration, moles/liter.

$(B_{com}) = (B_t) - (B_o)$ = concentration of complexed nitrile in aqueous phase, moles/liter.

$(Ag^+) = (Ag_t) - (B_{com})$ = concentration of uncomplexed silver ion, moles/liter.

$\underline{K} = (B_{com})/(Ag^+)(B_o)$ = coordination constant if the reaction involved only the reaction between one molecule of nitrile and one silver ion.

If we plot the arbitrary value of $\underline{K}$ versus total concentration of silver ion, $\underline{K}$ apparently approaches infinity as total silver approaches zero. This is distinctly different from the situation involving the coordination reactions between silver ion and 3-hexyne (1). In the case of the alkyne, the value of $\underline{K}$ approaches some finite value as the concentration of silver ion approaches zero.

Since the evaluation of coordination constants between nitriles and silver ion was only of incidental importance to the thesis problem, the study was discontinued.

Table 20

Distribution Data for *n*-Valeronitrile

(B_t)	(B_c)	(B_o)	(Ag_t)	(B_{com})	(Ag^+)	K
0.0185	0.258	0.0076	0.100	0.0109	0.089	16.1
0.0200	0.258	0.0076	0.200	0.0124	0.188	8.7
0.0380	0.483	0.0140	0.250	0.0240	0.226	7.6
0.0320	0.273	0.0080	0.500	0.0240	0.476	6.3
0.0610	0.540	0.0160	0.500	0.0450	0.455	6.2
0.0850	0.643	0.0190	0.750	0.0660	0.684	5.1
0.0540	0.338	0.0099	1.000	0.0441	0.956	4.7
0.1010	0.642	0.0190	1.000	0.0820	0.918	4.7
0.00112	0.380		0.000			34[a]
0.00112	0.389		0.000			35[a]

[a] $K = K_d$ (equation XXXVI).

4. Phenol. The solubility of phenol in aqueous solutions of silver ion was determined by the visual phase change technique. It was found that phenol was miscible with 1 f. silver nitrate in all proportions.

5. Conclusions. Since a coordination reaction was apparent between silver ion and nitriles, it would be impossible to study coordination of an alkyne substituted with a nitrile group.

The aliphatic hydroxyl group and methyl ester group exhibited no significant coordination reaction with silver ion in aqueous solutions.

3-Hexyn-2-ol and methyl 2-heptynoate were synthesized for a study of their coordination reactions.

Analytical Procedure for Determination of Alkynes in Aqueous Solutions. The following section deals with the manipulations and the mechanics of making quantitative measurements of alkynes in aqueous solutions at ionic strength of unity. The equilibration procedure was similar to that described previously (pp. 55-57).

1. Beer's law plot. One, two, three, five and ten ml. pipettes and twelve 25 ml. volumetric flasks were calibrated for use with carbon tetrachloride at 25.0°. The maximum deviation for any piece of apparatus from its assigned volume was 0.2%.

An ampoule containing a predetermined amount of acetylenic compound was weighed to insure that there had been no leakage during storage. The ampoule was scratched several times with a carborundum chip and was placed in a 125 ml., glass-stoppered flask. The flask and contents were weighed to the nearest 0.01 g.

The ampoule was broken with a stirring rod, and about 75 ml. of purified carbon tetrachloride was quickly introduced, making certain that the stirring rod had been washed free of alkyne. The flask was stoppered and weighed to determine the amount of carbon tetrachloride added.

The flask and contents were placed in a constant temperature bath at 25.0° for one hour with intermittent swirling. Definite volumes of the stock solution were transferred to calibrated volumetric flasks by means of calibrated delivery pipettes and were diluted to volume at 25.0°.

Optical density measurements were made as described in a subsequent description, and the results were plotted as moles/liter of alkyne versus optical density.

2. Equilibration. An ampoule of alkyne (0.4 to 1 g. of material) was weighed for comparison with previous check weight to determine whether the ampoule had been leaking. This was done to insure that the alkyne had not been in contact with oxygen.

The ampoule was scratched once with a carborundum chip, then placed in an appropriate equilibration flask. The flask was evacuated, flushed with dry nitrogen and reevacuated. It was then shaken or swirled vigorously until the ampoule had been ruptured.

The flask was connected to a stock solution bottle (1.00 $\underline{f}$. silver nitrate or 1.00 $\underline{f}$. potassium nitrate) and the transfer line was evacuated (Figure 8, p. 56). The desired amount of stock solution was transferred to the flask, leaving a two-phase system. The flask was covered with aluminum foil to exclude light and was brought to a slight, positive pressure (about 30 mm. mercury) by introducing dry nitrogen through the sample delivery tube.

The flask was placed in an ice bath for about five minutes, then the contents were swirled vigorously for two minutes. The organic materials were more soluble in the cold solution than in the 25° solution. The flask was then placed in the equilibration bath at 25.0°. After 30 minutes the contents were swirled for one minute. The swirling was repeated six times at five minute intervals. The flask was then allowed to remain in the bath for one hour before sampling.

3. Concentration of Silver Nitrate. About five ml. of the saturated aqueous solution was removed from the equilibration flask through the delivery tube by means of nitrogen pressure. This solution served to flush the delivery tube, and was discarded.

A sample was then removed with a Lucas-Eberz pipette and transferred to a porcelain casserole. The sample was washed from the pipette with about 30 ml. of wash water.

A measured excess of standard potassium chloride solution was added to the casserole, and the excess chloride ion was titrated with a standard solution of silver nitrate, using a chromate endpoint.

4. Concentration of Alkyne in the Aqueous Phase. An appropriate volume of carbon tetrachloride, adjusted to give a final optical density of 0.2 to 0.5, was introduced into a 50 ml. mixing cylinder along with sufficient 5 *f*. potassium cyanide to prevent precipitation of any silver on addition of sample. The cylinder and contents were cooled to about 10° to prevent loss of volatile products on addition of sample.

At the time of sampling, the small equilibration flask contained two phases. These consisted of about 100-200 ml. of aqueous solution and about 0.5 g. of undissolved alkyne. A sample was drawn from the equilibration flask with a Lucas-Eberz pipette, and was transferred rapidly to the mixing cylinder. The sample was followed by about 20 ml. of water for rinsing the pipette. When the room temperature was above 25°, speed was essential in transferring the sample because of the tendency of the alkyne to come out of solution as the temperature increased.

The mixing cylinder was shaken mechanically for 30 minutes. Most of the aqueous phase was removed with a water aspirator in a hood, and the remaining material was transferred to a 20 ml. separatory funnel with an ungreased stopper and stopcock. If the aqueous phase was not removed as indicated in the previous paragraph, it would pour from the cylinder first and wet the restricted part of the separatory funnel. This prevented removal of the carbon tetrachloride phase without drawing off some water.

The isolated carbon tetrachloride solution was transferred to a 15 ml., glass-stoppered centrifuge tube containing about 0.5 g. of freshly dried magnesium sulfate. This was shaken for five minutes then allowed to settle. If magnesium sulfate tended to remain suspended, a small plug of glass wool was forced down through the solution. In several instances, centrifugation was effective.

The carbon tetrachloride solution of alkyne was now ready for spectrophotometric measurements. These were made as soon as possible to prevent concentrations from changing by evaporation of the solvent.

5. Infra-red Technique. The Perkin-Elmer infra-red spectrophotometer was turned on at least 15 minutes before use.

"Optical Density" recording paper was placed on the drum, and purified carbon tetrachloride was introduced into each of two 1.0 mm. cells.

With the cells in position in the instrument, the appropriate zero transmission, amplifier balance, 100% transmission and "gain" adjustments were made.

In all instances, the carbon-hydrogen peak at about 3.4 microns was used for measurements.

With carbon tetrachloride in both cells, the instrument was run slowly from about 3.2 microns to about 3.6 microns. The pen was then removed from the recording paper and the instrument was reversed to approximately the original wave length setting.

The sample cell was removed, drained and dried with a stream of dry nitrogen. The cell was then filled with sample. About two ml. of sample was flushed through the cell before the protective caps were placed in position.

The cell was replaced in the instrument and the pen was placed in recording position. The instrument was again run slowly past the point of maximum optical density.

The sample cell was removed and connected to a hypodermic syringe containing the same sample. This additional amount was introduced, forcing the previous sample out in front of it. The drum of the spectrophotometer was adjusted to a new position, and repeat measurements were made on both sample and blank.

The cells were removed. The sample cell was drained then dried with a stream of nitrogen.

A typical recording is shown in Figure 16.

Arbitrary positions were chosen for setting the recording paper, because optical densities were obtained from equivalent positions for the blank and the sample. The op-

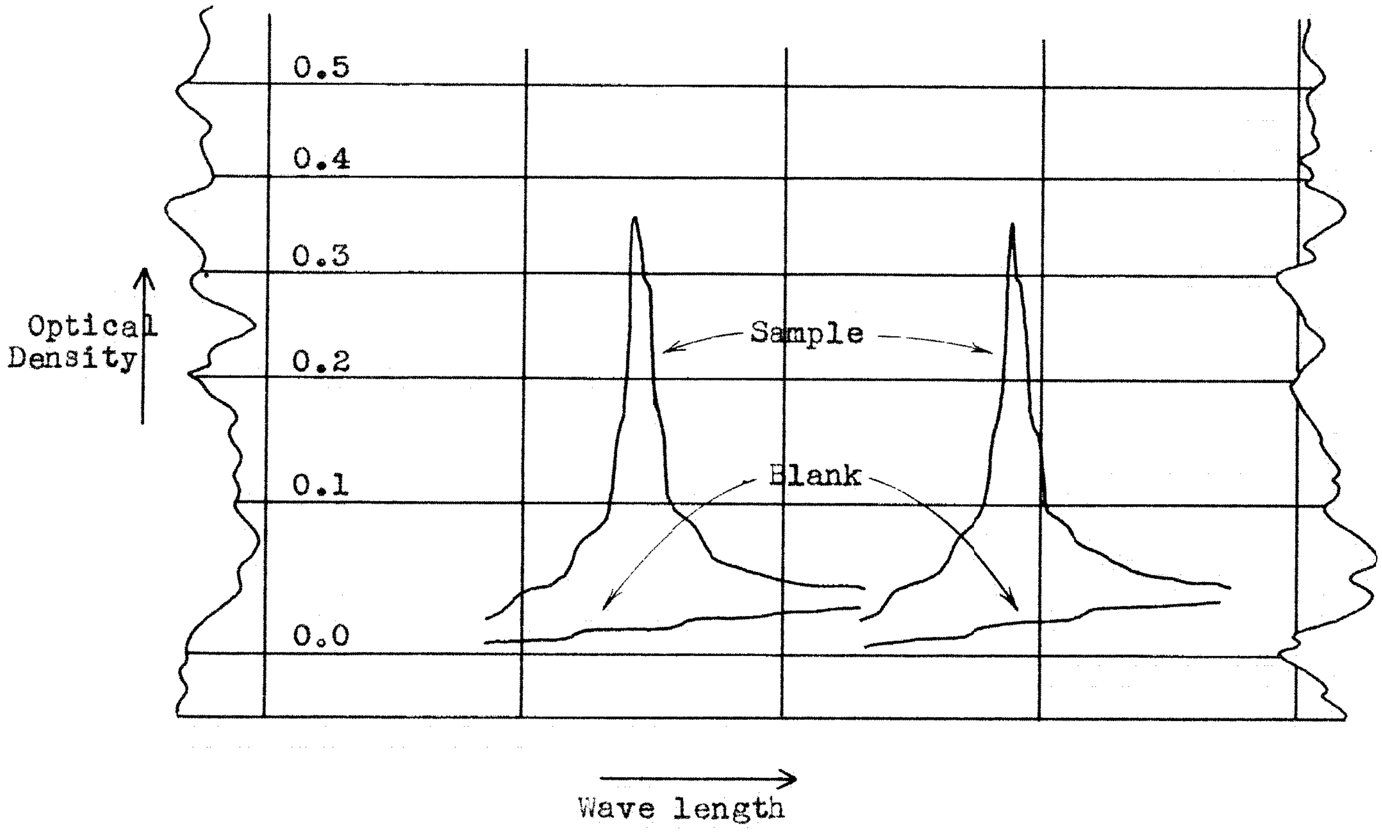


Figure 16. Optical Density Recording.

tical density of the blank was calculated at the wave length at which the sample showed a maximum absorption peak. This optical density was then subtracted from the maximum optical density shown by the sample, and calculations were made from the resulting value.

Methyl 2-Heptynoate. A Beer's law plot was prepared for methyl 2-heptynoate using the carbon hydrogen peak at 3.439 microns with a 1.0 mm. cell (Figure 17).

Saturated aqueous solutions of methyl 2-heptynoate in 1.00 f. potassium nitrate were extracted with about 1½ volumes of carbon tetrachloride, and optical density measurements were made on the organic solutions. The results were unsatisfactory because the optical density readings were below 0.1. If less extractant was used, two or more extractions were necessary to keep the accuracy within a 1% limit.

The carbonyl peak of the ester was stronger, so another Beer's law plot was prepared at 5.810 microns (Figure 18).

Saturated aqueous solutions of the ester in 1.00 f. potassium nitrate were extracted with about 1½ volumes of carbon tetrachloride, and optical density measurements were made using the carbonyl peak (Table 21).

The aqueous phases remaining after extraction were combined, and 22 ml. of this combination was reextracted with 10.0 ml. of carbon tetrachloride. Optical density measurements indicated that the ester was present to the extent of about 0.00001 mole/liter after the first extraction.

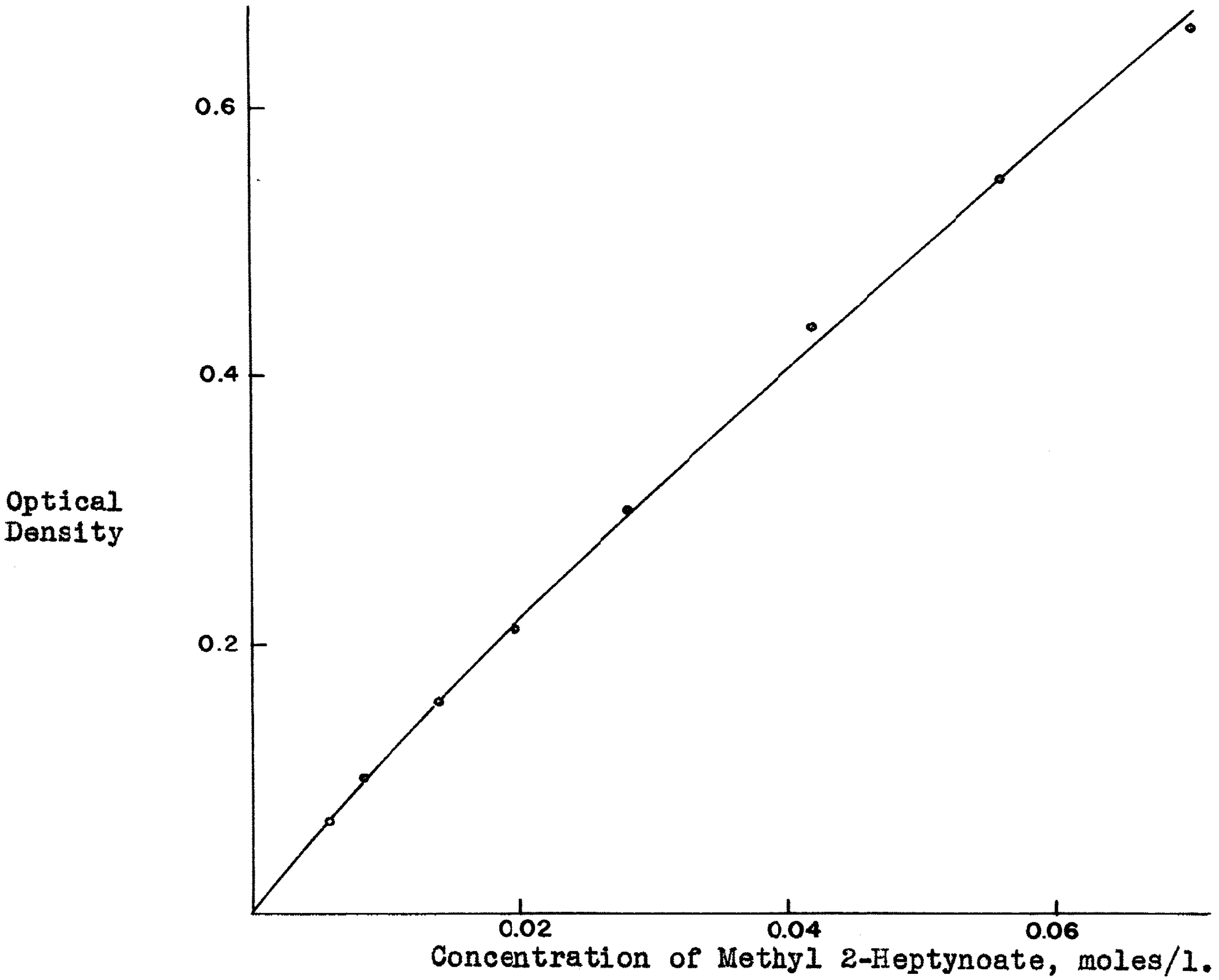


Figure 17. Optical Density of Methyl 2-Heptynoate in Carbon Tetrachloride: 3.439 microns, 1.0 mm. cell.

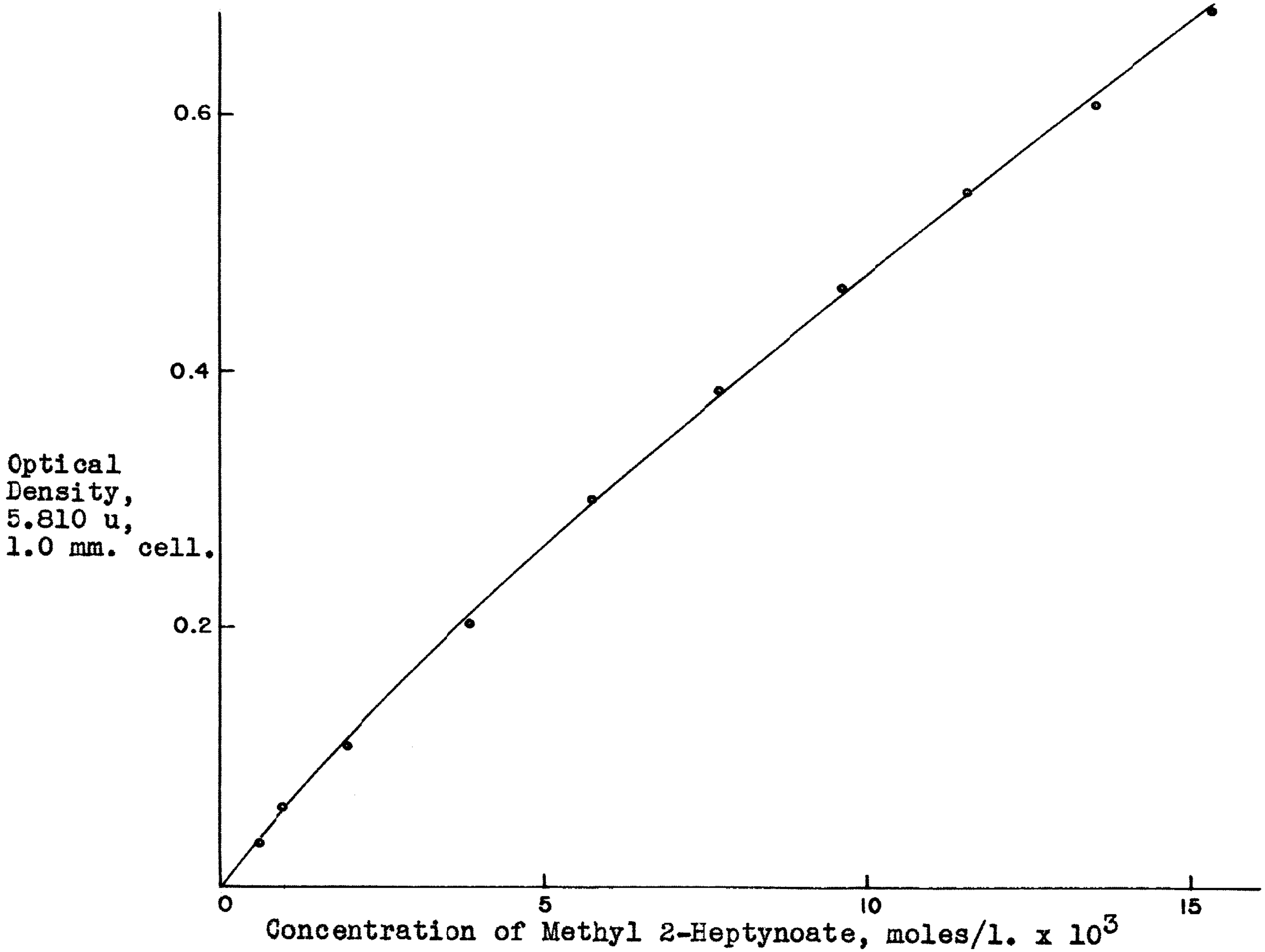


Figure 18. Optical Density of Methyl 2-Heptynoate in Carbon Tetrachloride.

Table 21

Solubility of Methyl 2-Heptynoate in 1.00 f.

Potassium Nitrate at 25.0°

CCl_4, ml.	Aqueous sol'n, ml.	Optical density	Conc. ester, CCl_4	moles/liter Aqueous
10.00	7.52	0.139	0.00253	0.00336
10.00	7.74	0.140	0.00256	0.00331

Equilibration mixtures were prepared using varying concentrations of silver ion at constant ionic strength. The results were very inconsistent and it soon became obvious that a time factor was involved. When the equilibration flask was opened after three days at 25°, considerable amounts of a viscous liquid and a dark precipitate were present.

The last sample which had been extracted from the equilibration mixture was saved, and an infra-red spectrum was run from 2.5 to 7.5 microns (Figure 19).

The triple bond peak at 4.5 microns had almost disappeared and extensive changes had taken place in the region in which the carbonyl peak absorbs.

Decomposition Product of Methyl 2-Heptynoate. In order to isolate sufficient material for identification purposes, two ampoules of methyl 2-heptynoate were placed in an equilibration flask along with about 30 ml. of 1.0 f. silver nitrate solution. The flask was evacuated until the aqueous solution had boiled for several minutes. The flask was filled

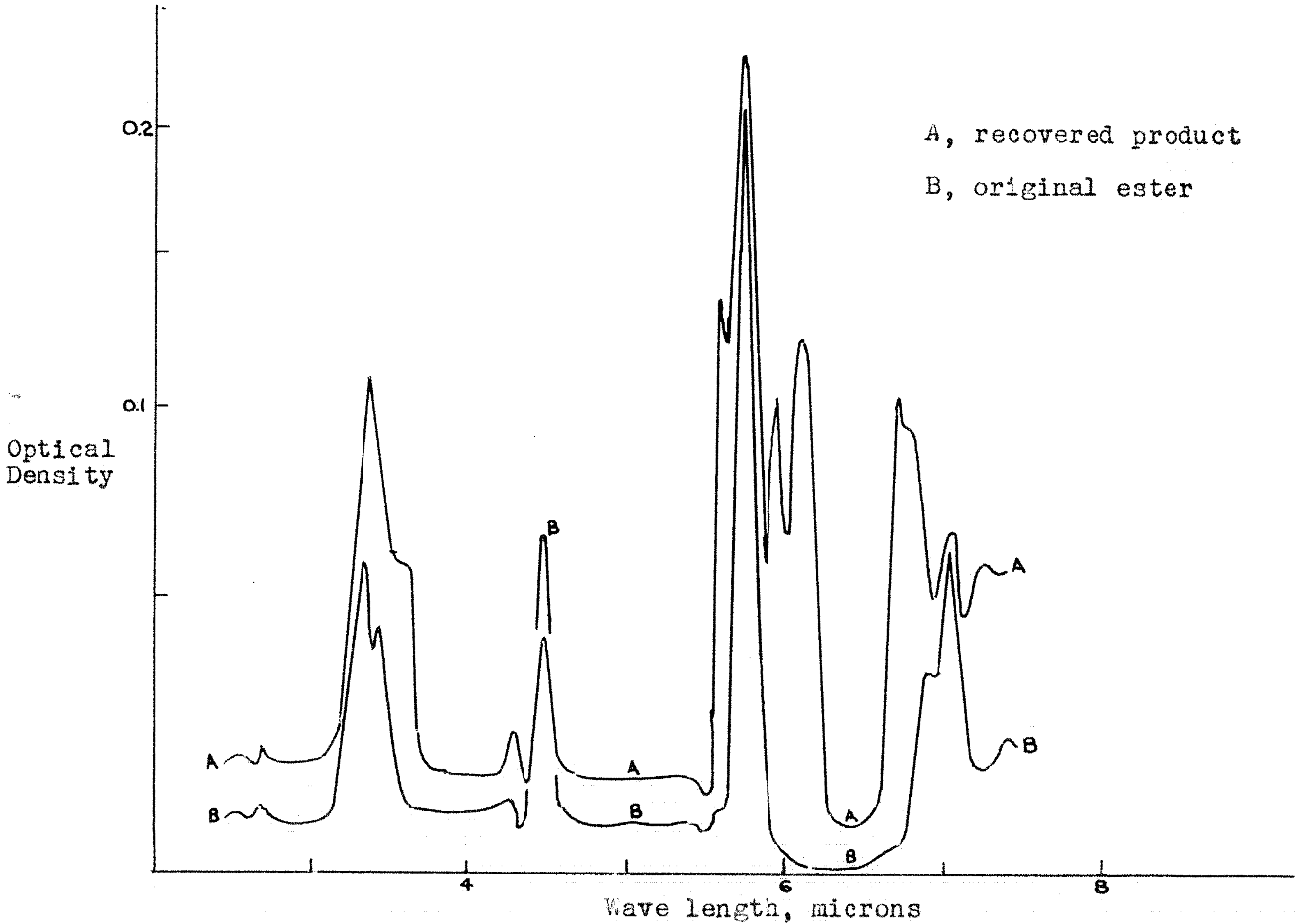


Figure 19. Infra-red Spectrum of Hydration Product of Methyl 2-Heptynoate

with dry nitrogenand the contents were swirled vigorously without rupturing the ampoules. The evacuation procedure was repeated three times, then the flask was wrapped in aluminum foil and the ampoules were broken by shaking the flask. After one day, the organic phase had become oily and slightly discolored. No free silver was apparent.

After two days, the organic phase was a purple, viscous oil. The flask was opened, and 30 ml. of ether were added to dissolve the organic material. The aqueous phase was separated and washed twice with 25 ml. portions of ether. All of the ether phases were combined, dried with anhydrous magnesium sulfate and distilled. After the ether had been removed, the pressure was reduced: b. 71-74$\frac{1}{2}^{\circ}$ (9 mm.); yield, 2.0 g. from 3.7 g. of the original ester.

A 2,4-dinitrophenylhydrazone was prepared from a portion of the isolated product and was recrystallized several times from ethanol: m. 106.2-106.8°.

An ampoule of methyl 2-heptynoate was broken under a dilute, acidic solution of mercuric acetate. After three days the organic phase was removed by extraction with ether. The ether was evaporated and a 2,4-dinitrophenylhydrazone was prepared from the residue: m. 105-107°.

The most likely hydration product of methyl 2-heptynoate should be methyl beta-ketoheptanoate, so this oompound was synthesized according to the procedure of Levine and Hauser (42). The 2,4-dinitrophenylhydrazone melted at 106-

107°; mixed melting point with the hydration product derivative, 106-107° (see synthetic section for analyses).

The results indicate that silver ion induces hydration of the triple bond containing an adjacent carbomethoxy group. The hydration proceeds in the direction expected from electronic interpretations of the effect of the ester group.

<u>3-Hexyn-2-ol, Distribution coefficient</u>. An ampoule of 3-hexyn-2-ol was broken under oxygen-free conditions in an equilibration flask containing about 80 ml. 1.00 <u>f</u>. potassium nitfate and about an equal volume of carbon tetrachloride. A small positive pressure of nitrogen was introduced into the flask, and it was then placed in a constant temperature bath at 25.0°. The flask and contents were swirled intermittently for three hours to effect equilibration.

After the phases had been allowed to separate completely, 75 ml. of the aqueous phase was transferred to a 100 ml. mixing cylinder containing 20.0 ml. carbon tetrachloride and about 20 g. sodium sulfate. These were shaken mechanically for 30 minutes. The organic phase was separated and dried over magnesium sulfate.

Two additional extractions were made of aliquot portions of the aqueous phase.

Optical density measurements were made on all of the carbon tetrachloride phases, with appropriate dilutions as shown in the second column of Table 22 (Beer's law plot in

Figure 20).

Table 22

Distribution of 3-Hexyn-2-ol Between Carbon Tetrachloride and 1.00 f. Potassium Nitrate

Sample	Dilution[a]	Alkynol, moles/l.[b]	Alkynol, moles/l.[c]
Original CCl_4	1:10	0.295	-----
First extraction	1:20	0.422	0.113
Second extraction	none	0.024	0.007
Third extraction	none	0.003	0.001

[a] Some samples were diluted to keep within a reasonable range of optical density.
[b] Original carbon tetrachloride phase.
[c] Amount removed from the original aqueous solution.

The total concentration of alkynol present in the original aqueous phase was 0.121 moles/l. (calculated from the three extractions). The distribution coefficient, K_d, was

$$\underline{K}_d = 0.295/0.121 = 2.44 \qquad \text{(XXXVII)}$$

This distribution coefficient eliminated the possibility that an extraction procedure would be convenient for quantitative determination by spectrophotometric means of 3-hexyn-2-ol in aqueous solution.

<u>3-Hexyn-2-ol, Decomposition Product.</u> A portion of the 3-hexyn-2-ol extracted from the aqueous solution was used for an infra-red spectrum. The spectrum was compared with the spectra of pure 3-hexyn-2-ol and some alkynol extracted from an aqueous silver nitrate solution (Figure 21).

A comparison of the spectra indicate that in the presence of silver ion the alkynol is either hydrated or oxidized

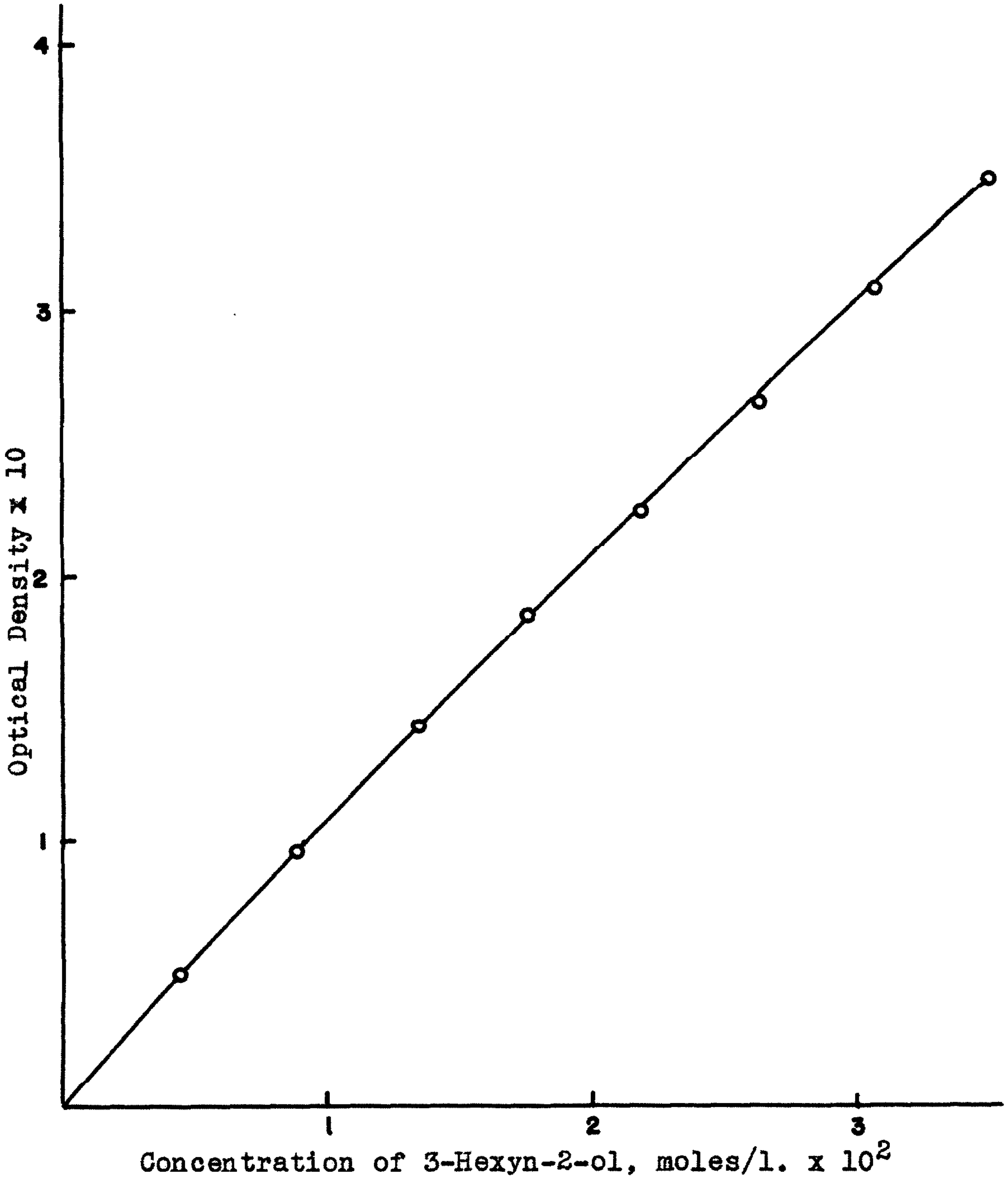


Figure 20. Optical Density of Solutions of 3-Hexyn-2-ol in Carbon Tetrachloride: 9.230 u, 1.0 mm. cell.

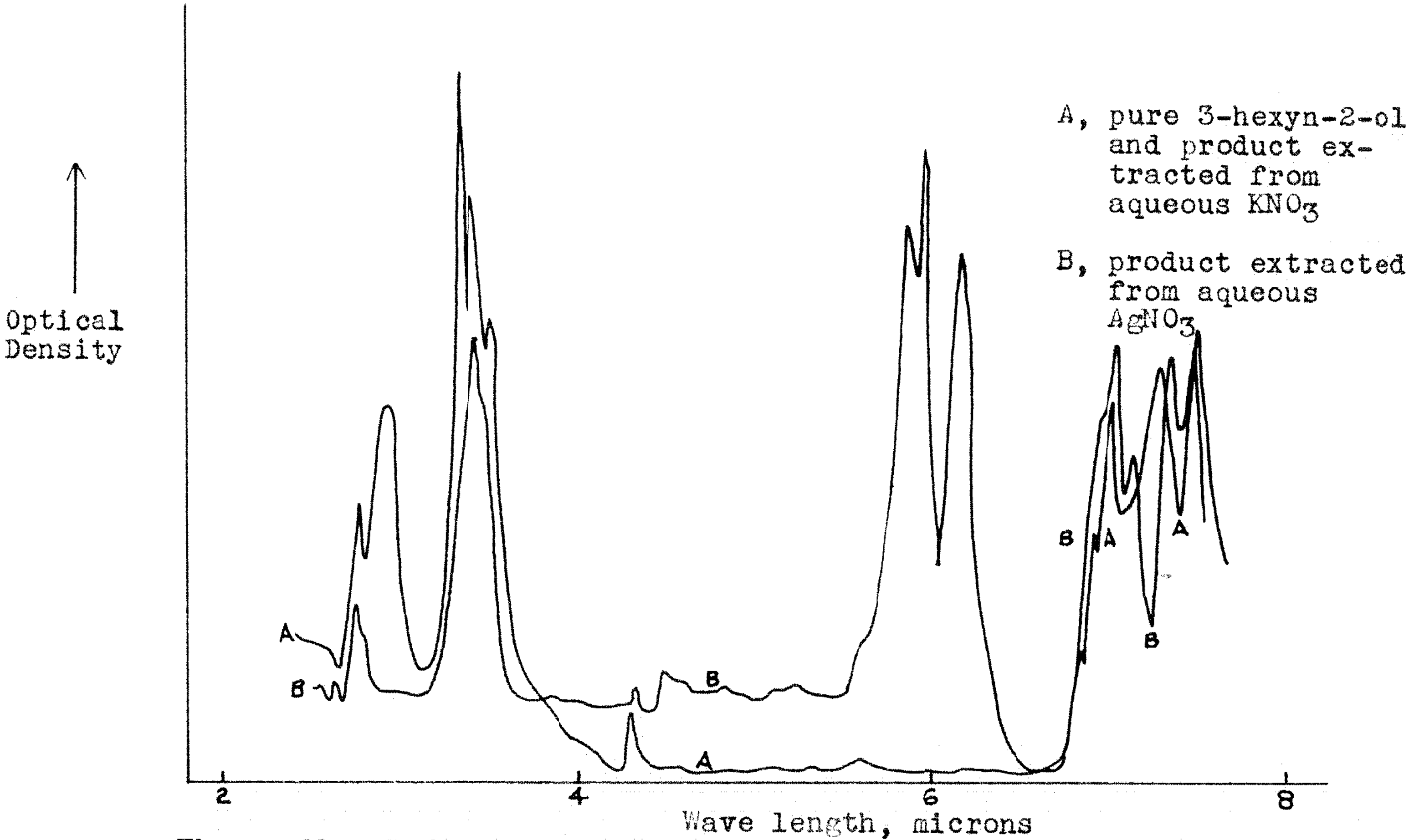


Figure 21. Infra-red Spectrum of 3-Hexyn-2-ol and Hydration Product.

or both. This is indicated by the appearance of a strong carbonyl peak and by a decrease in intensity of the hydroxyl peak.

In order to insure that the reaction is not catalyzed by traces of oxygen, two more samples were prepared, one in the absence of oxygen and the other in the presence of oxygen.

An ampoule of 3-hexyn-2-ol and 35 ml. 1.0 f. silver nitrate were sealed into a large ampoule (Figure 22). The ampoule was evacuated using a water aspirator, then the stopcocks were closed and the contents of the ampoule were boiled for a short time. The stopcocks were opened to the aspirator system and the boiling was continued for one minute. Dry nitrogen was introduced into the ampoule and the pressure was brought to about five pounds. The ampoule was closed and shaken five minutes and allowed to stand overnight. The evacuation, boiling and shaking procedure was repeated twice. The ampoule was then evacuated until the solution began to boil. The stopcocks were closed and the small ampoule containing the alkynol was broken by vigorous shaking. The entire piece of equipment was then covered with aluminum foil to exclude light.

After four hours the sample showed signs of decomposition by formation of a finely-divided gray precipitate. After 24 hours, the ampoule was inverted and 25 ml. carbon tetrachloride was introduced into bulb (A) (Figure 22).

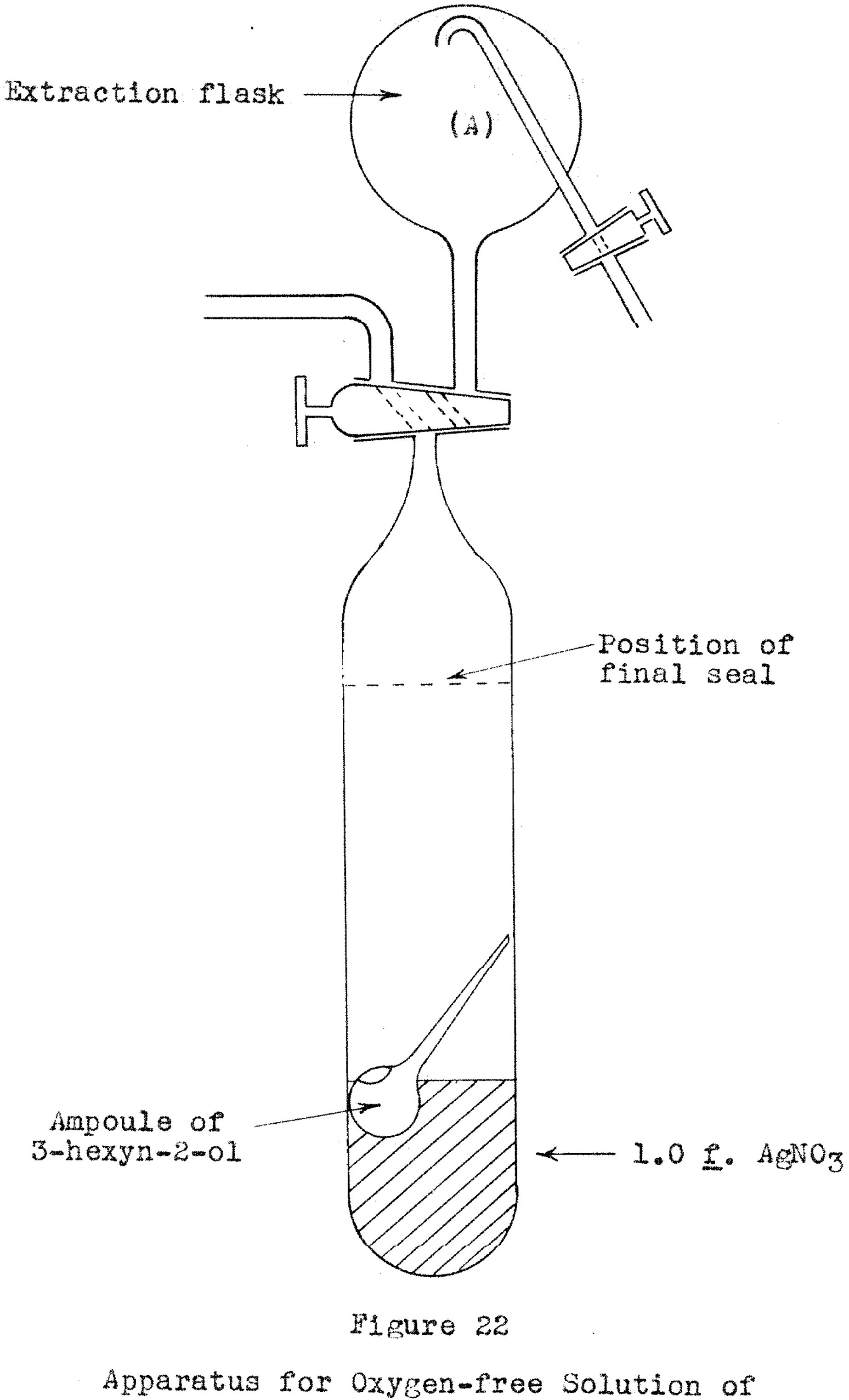


Figure 22

Apparatus for Oxygen-free Solution of
3-Hexyn-2-ol in 1.0 f. Silver Nitrate

A slow stream of nitrogen was bubbled through the carbon tetrachloride for ten minutes. The carbon tetrachloride was heated to boiling and the nitrogen stream was discontinued. As soon as the carbon tetrachloride vapors began to leave the flask, the stopcocks were closed and the heating was discontinued. With the apparatus inverted, the aqueous solution was allowed to enter the bulb containing the carbon tetrachloride. The mixture was shaken for five minutes and the carbon tetrachloride phase was isolated and dried with magnesium sulfate.

A second ampoule of 3-hexyn-2-ol was broken in a glass-stoppered bottle containing 35 ml. 1.0 f. silver nitrate in the presence of air. The bottle was covered with aluminum foil and was allowed to stand for 24 hours. Decomposition products appeared at about the same rate as in the oxygen-free sample. The aqueous phase was extracted as in the previous sample.

The concentrations of product in each of the two prepared samples were adjusted so that the optical density at 3.4 microns was about 0.2, then the entire spectrum was run from 2.5 to 11.5 microns (Figure 23).

The difference between the two curves was negligible. In view of the rapid reaction of 3-hexyn-2-ol and methyl 2-heptynoate in aqueous silver nitrate solutions, further work was directed toward the synthesis and study of disubstituted

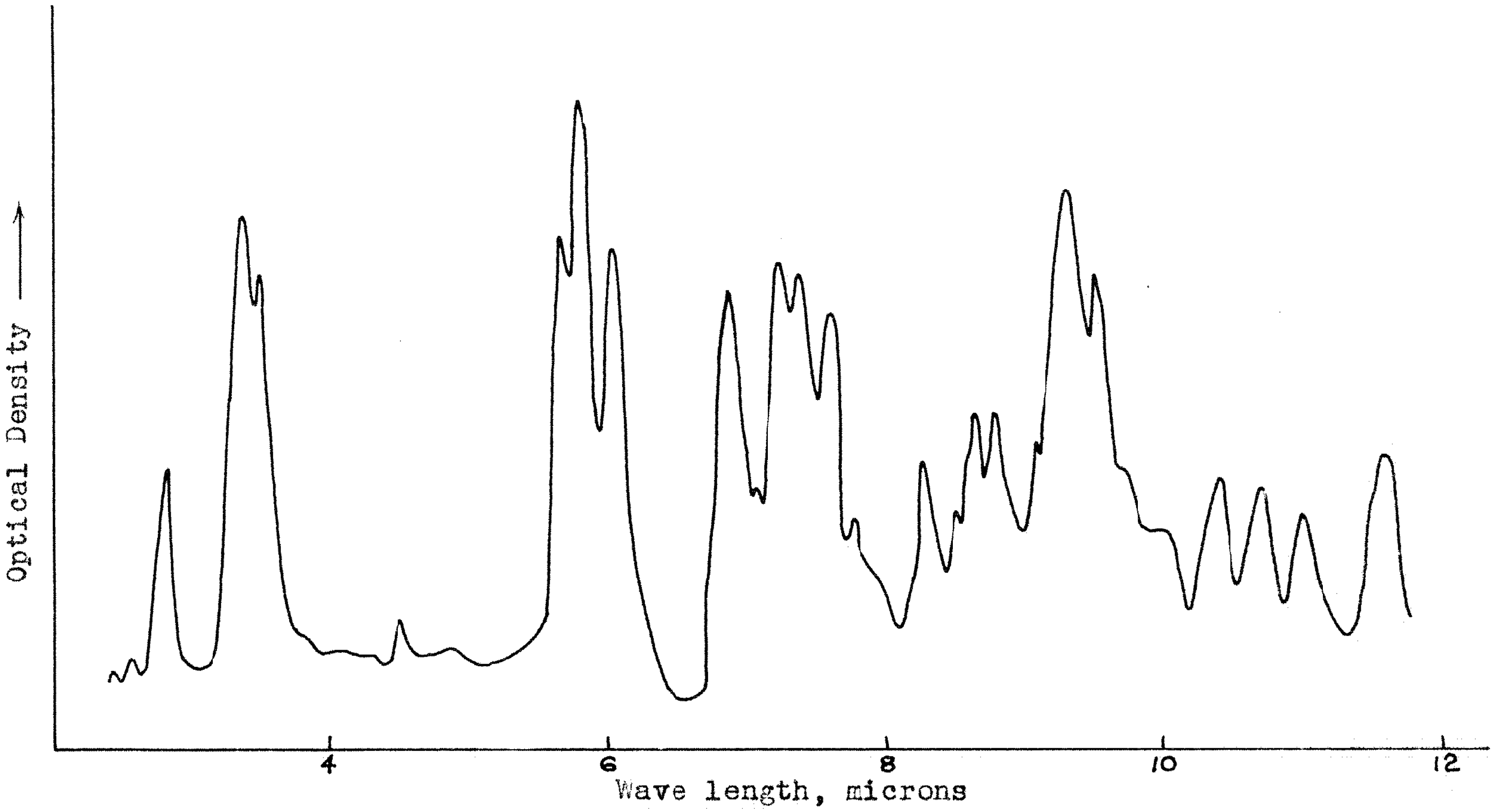


Figure 23. Absorption Spectrum of Hydration Products of 3-Hexyn-2-ol Extracted from Aqueous Silver Nitrate in the Presence or in the Absence of air.

alkyl acetylenes.

Solubility of Acetylenic Hydrocarbons in Aqueous Silver Nitrate and Potassium Nitrate Solutions. Solubility measurements of various acetylenic hydrocarbons in silver nitrate and/or potassium nitrate solutions at constant ionic strength were determined by the procedure previously outlined.

An extraction procedure for the determination of aqueous solutions of 3-hexyne was practical, for Dorsey (1) found a distribution coefficient of over 500 for 3-hexyne between 1.00 *f*. potassium nitrate and carbon tetrachloride at 25.0°. All of the additional hydrocarbons used for this study had higher molecular weights than 3-hexyne and no additional functional groups were present. From these facts, it was concluded that the distribution coefficient for the remaining hydrocarbons would be at least as favorable for a similar type of quantitative determination.

The compounds studied were 3-hexyne, 2-heptyne, 2,2-dimethyl-3-hexyne, 2-methyl-3-hexyne, 2,2,5-trimethyl-3-hexyne and di-*tert*-butylacetylene.

In the extraction procedure used for the analysis of aqueous solutions, the ratio of the volumes of saturated aqueous solution to carbon tetrachloride extractant was adjusted so that subsequent optical density measurements were in the vicinity of 0.2 to 0.5. In the case of the highly insoluble 2,2,5-trimethyl-3-hexyne and di-*tert*-butylacetylene it was necessary to use about 100 ml. of aqueous solution and only five to ten ml. of carbon tetrachloride.

In preparing a Beer's law plot for each alkyne, at least two different series of points were made using material from different ampoules. This eliminated the possibility of a weighing error in determining the weight of the contents of an ampoule.

In the following section, Tables 23 through 30 give the solubilities of the various alkynes along with the solubilities calculated from a mathematical expression for concentration of alkyne as a function of the total silver concentration (second degree equation calculated by a method of least squares). The corresponding mathematical expression is given below each table (equations XXXVIII through XLV). In addition, Figures 24 through 31 present a graphical illustration of the same solubility effect.

Table 23

3-Hexyne, solubility in aqueous silver nitrate solutions, t = 25.0°, ionic strength = 1.00.

(Ag_t), moles/l.	(B_t) found, moles/l. x 10^4	(B_t) calc'd, moles/l. x 10^4
0.000	68	76
0.108	199	204
0.128	233	228
0.272	405	408
0.318	478	469
0.338	496	496
0.531	756	761
0.761	1102	1098
1.000	1475	1483

$$(B_t) = 0.00758 + 0.1157(Ag_t) + 0.0250(Ag_t)^2 \qquad \text{(XXXVIII)}$$

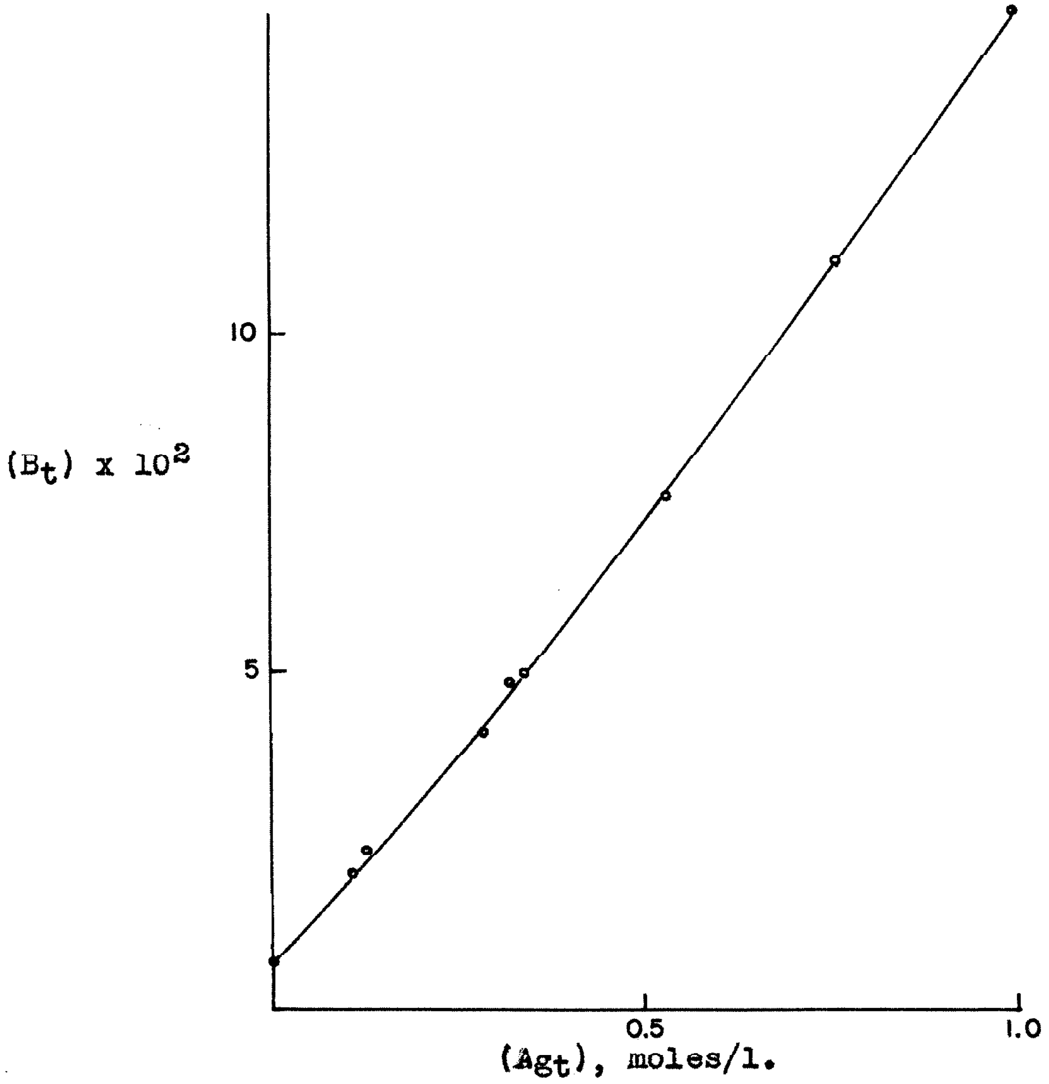


Figure 24. 3-Hexyne solubility, t=25.0°, u=1.00.

Table 24

3-Hexyne, solubility in aqueous silver nitrate solutions, t = 35.0°, ionic strength = 1.00.

(Ag_t), moles/l.	(B_t) found, moles/l. x 10^4	(B_t) calc'd, moles/l. x 10^4
0.000	64	60
0.074	129	126
0.190	244	244
0.307	361	361
0.360	408	415
0.548	619	617
0.730	822	818
0.752	843	844
1.000	1135	1136

$$(B_t) = 0.00599 + 0.0940(Ag_t) + 0.0136(Ag_t)^2 \qquad \text{(XXXIX)}$$

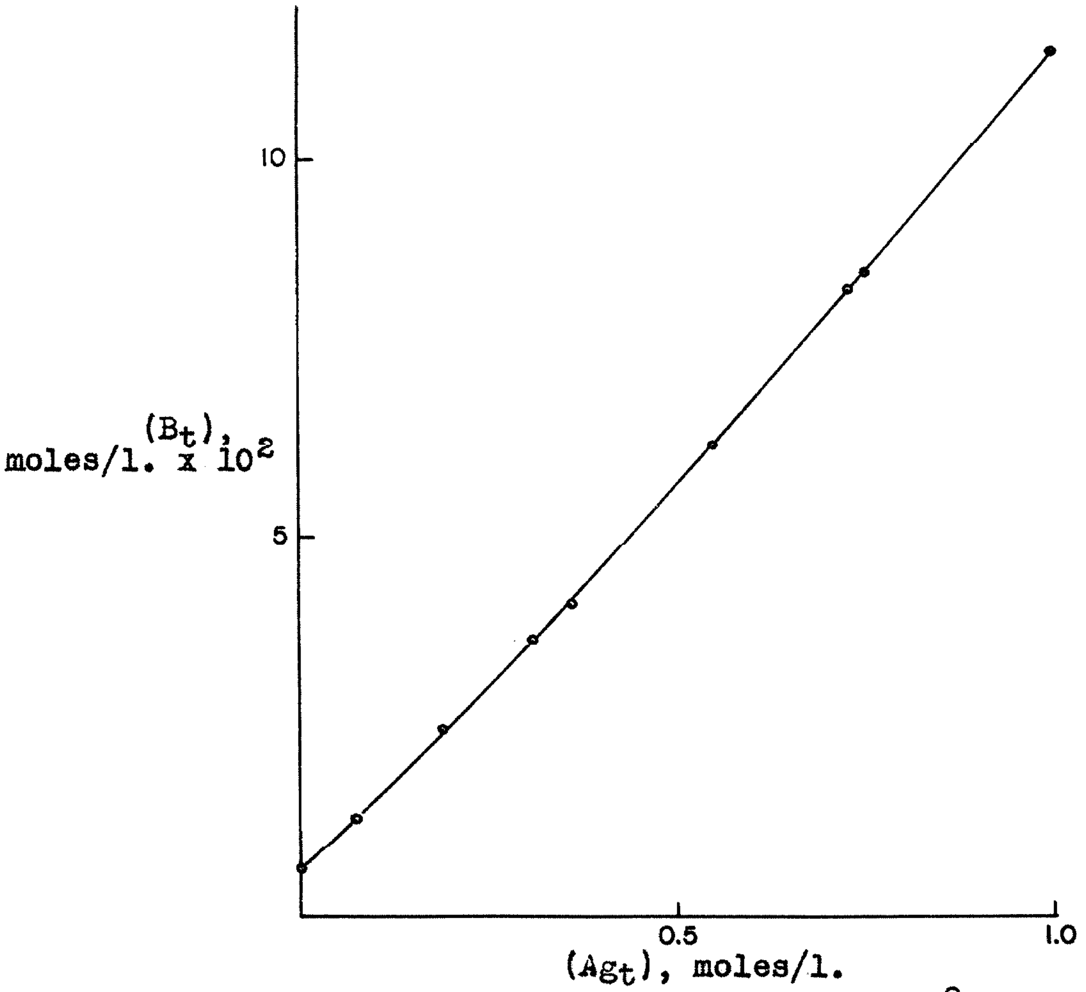


Figure 25. 3-Hexyne solubility, t=35.0°, u=1.00.

Table 25

2-Heptyne, solubility in aqueous silver nitrate solutions, t = 25.0°, ionic strength = 1.00.

(Ag_t), moles/l.	(B_t) found, moles/l. x 10^5	(B_t) calc'd, moles/l. x 10^5
0.000	170	165
0.146	474	478
0.290	795	805
0.290	807	805
0.441	1115	1136
0.528	1345	1381
0.585	1501	1525
0.786	2028	2057
1.000	2674	2667

$$(B_t) = 0.00170 + 0.0200(Ag_t) + 0.00470(Ag_t)^2 \qquad \text{(XL)}$$

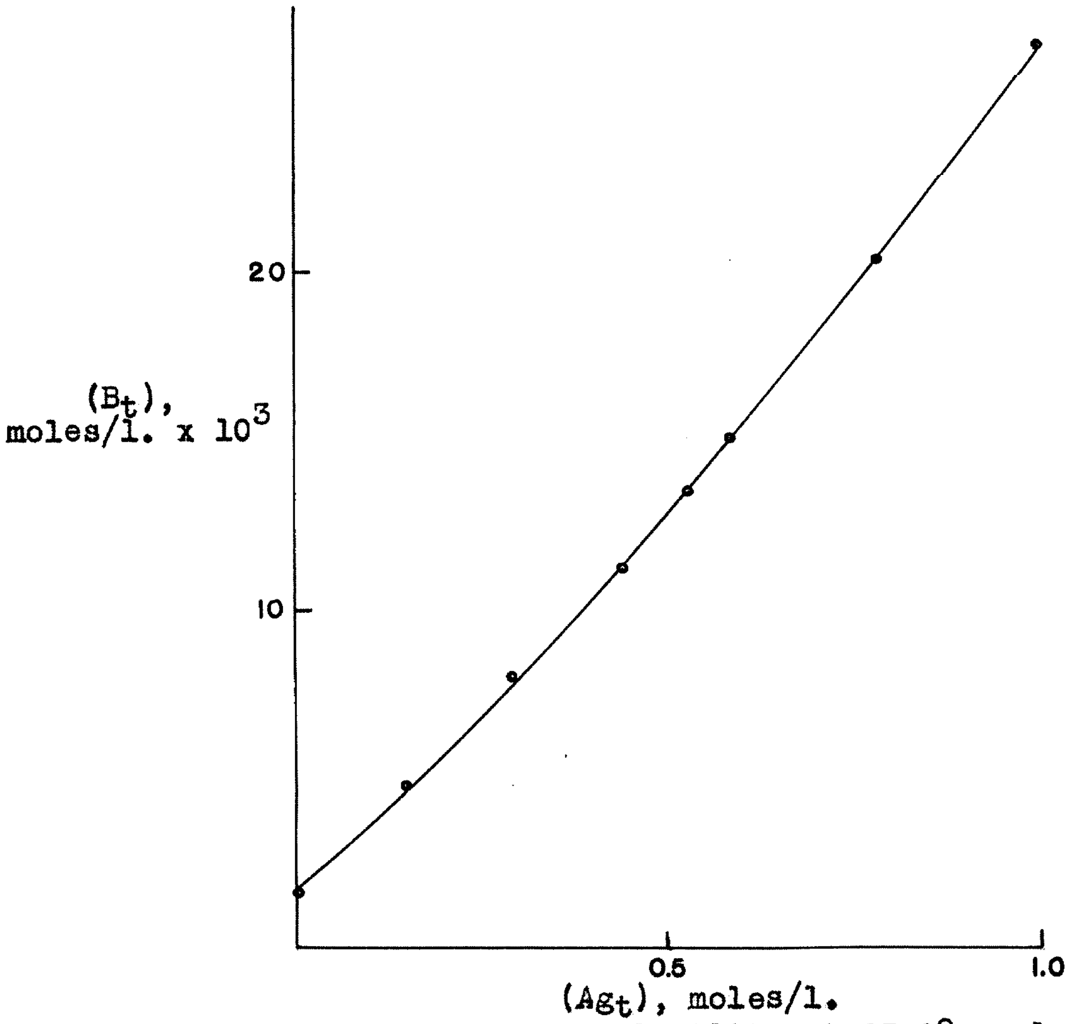


Figure 26. 2-Heptyne solubility, t=25.0°, u=1.00.

Table 26

2-Methyl-3-hexyne, solubility in aqueous silver nitrate solutions, $t = 25.0^{\circ}$, $u = 1.00$

(Ag_t), moles/l.	(B_t) found, moles/l. x 10^5	(B_t) calc'd, moles/l. x 10^5
0.000	180	188
0.096	553	565
0.175	895	886
0.358	1670	1663
0.675	3090	3128
0.675	3120	3128
1.000	4800	4791

$$(B_t) = 0.00188 + 0.03856(Ag_t) + 0.00747(Ag_t)^2 \qquad \text{(XLI)}$$

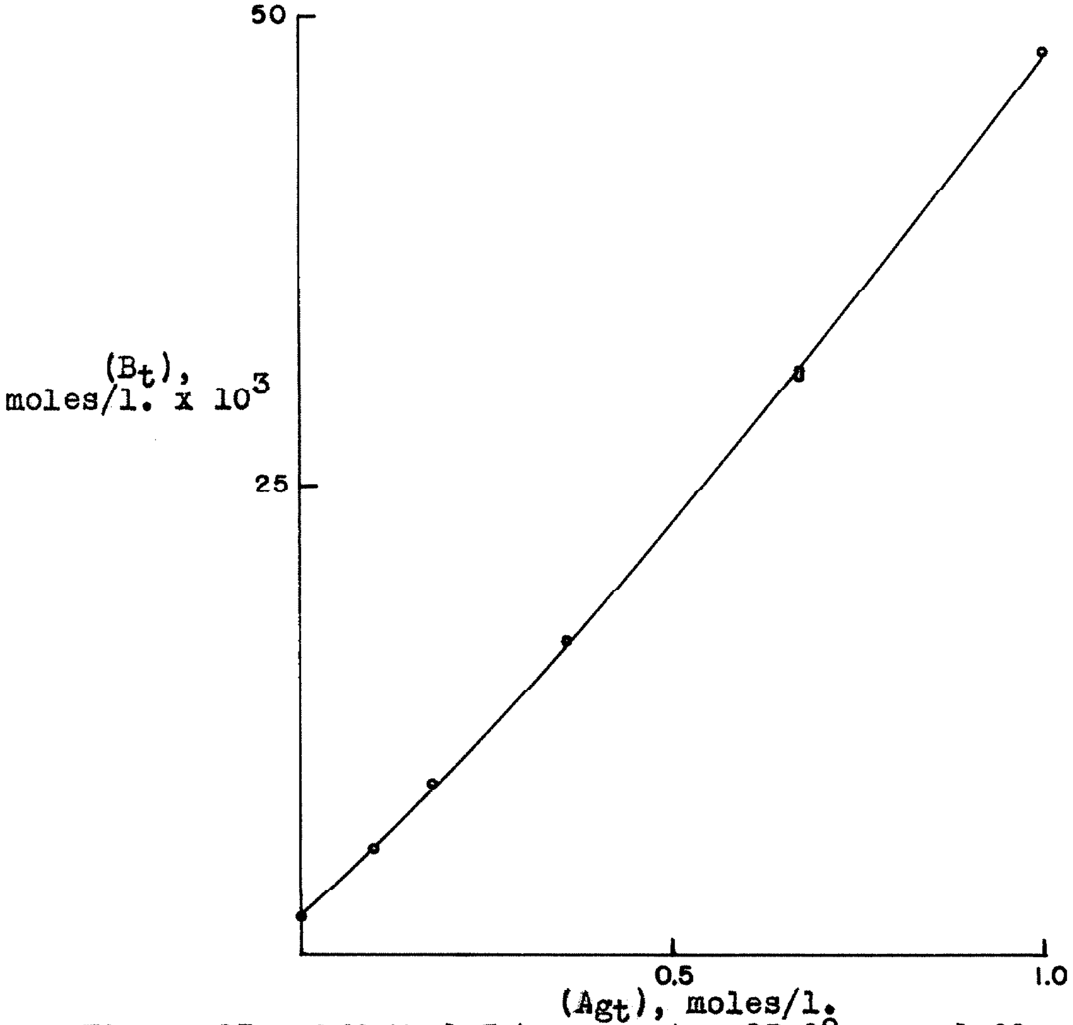


Figure 27. 2-Methyl-3-hexyne, $t = 25.0^{\circ}$, $u = 1.00$.

Table 27

2,2-Dimethyl-3-hexyne, solubility in aqueous silver nitrate solutions, t = 25.0°, u = 1.00

(Ag_t), moles/l.	(B_t) found, moles/l. x 10^5	(B_t) calc'd, moles/l. x 10^5
0.000	72	68
0.165	284	289
0.360	564	567
0.579	900	899
0.707	1111	1104
0.927	1470	1472

$$(B_t) = 0.00068 + 0.01302(Ag_t) + 0.00230(Ag_t)^2 \qquad \text{(XLII)}$$

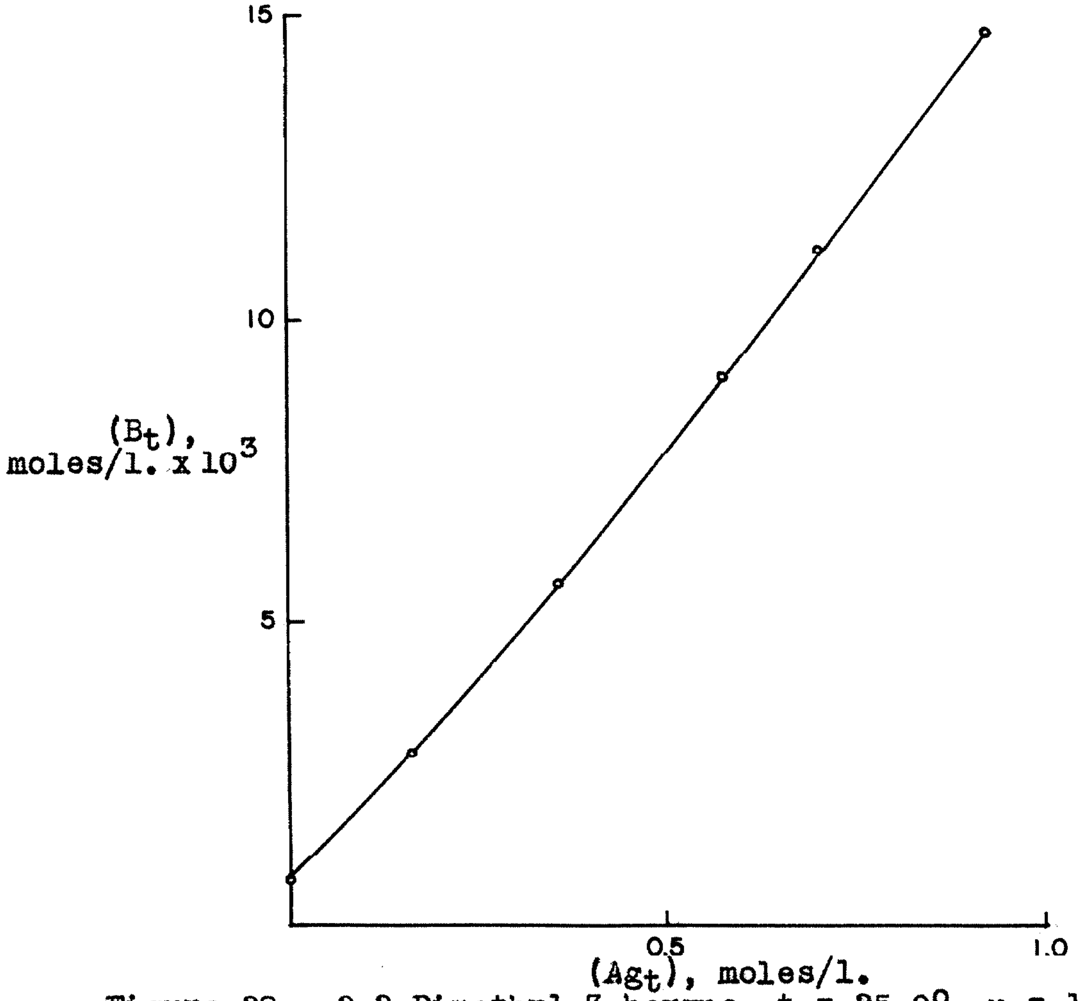


Figure 28. 2,2-Dimethyl-3-hexyne, t = 25.0°, u = 1.00.

Table 28

2,2,5-Trimethyl-3-hexyne, solubility in aqueous silver nitrate solutions, $t = 25.0^{\circ}$, $u = 1.00$

(Ag_t), moles/l.	(B_t), found, moles/l. x 10^6	(B_t) calc'd, moles/l. x 10^6
0.000	241	226
0.127	885	907
0.284	1746	1761
0.380	2340	2316
0.641	3860	3860
1.000	6120	6122

$$(B_t) = 0.000226 + 0.005255(Ag_t) + 0.000641(Ag_t)^2 \qquad \text{(XLIII)}$$

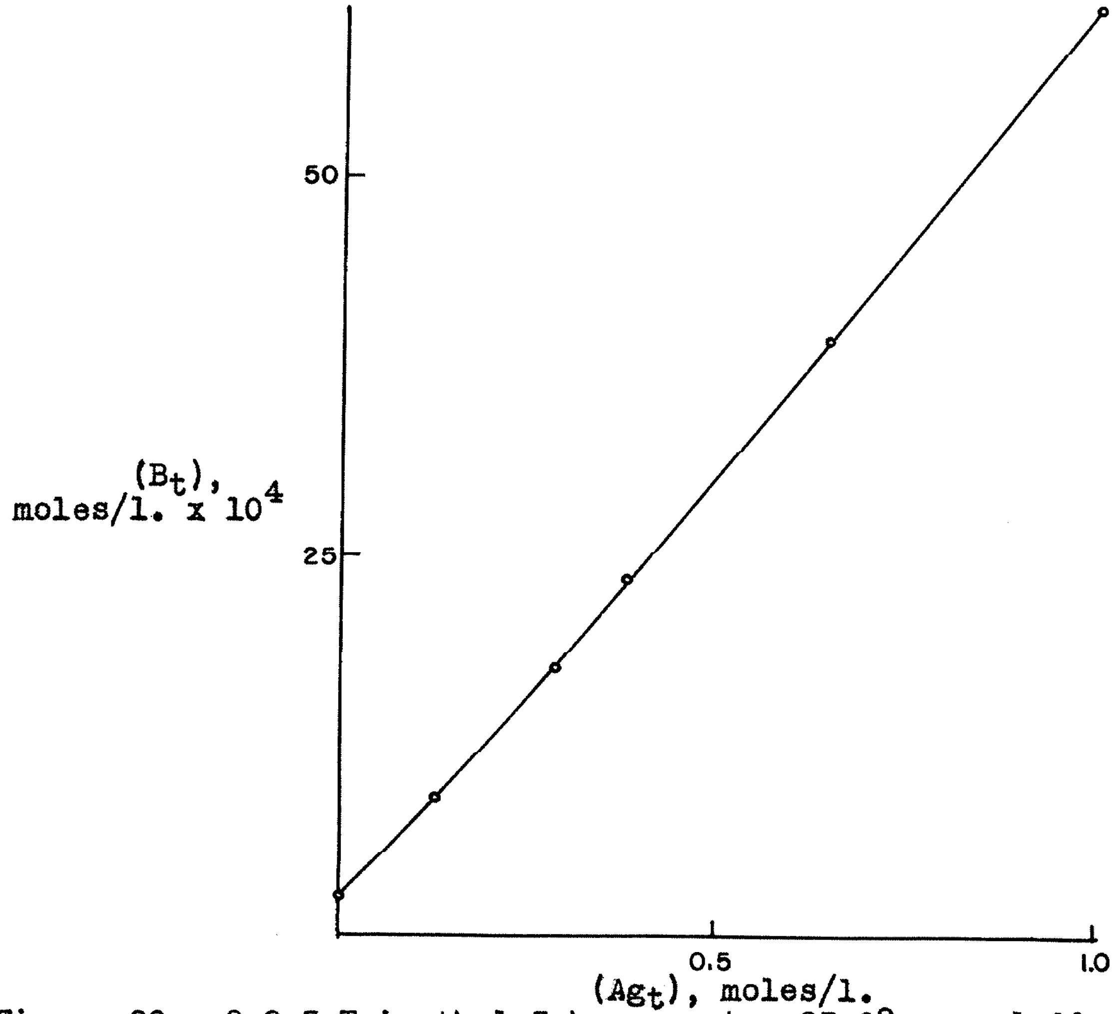


Figure 29. 2,2,5-Trimethyl-3-hexyne, $t = 25.0^{\circ}$, $u = 1.00$.

Table 29

Di-tert-butylacetylene, solubility in aqueous silver nitrate solutions, t = 25.0°, u = 1.00

(Ag_t), moles/l.	(B_t) found, moles/l. x 10^6	(B_t) calc'd, moles/l. x 10^6
0.000	147	149
0.217	568	584
0.368	914	914
0.395	955	974
0.446	1082	1093
0.483	1217	1180
0.651	1637	1591
0.733	1798	1801
0.793	1970	1959
1.000	2533	2533

$$(B_t) = 0.000149 + 0.001900(Ag_t) + 0.000484(Ag_t)^2 \quad \text{(XLIV)}$$

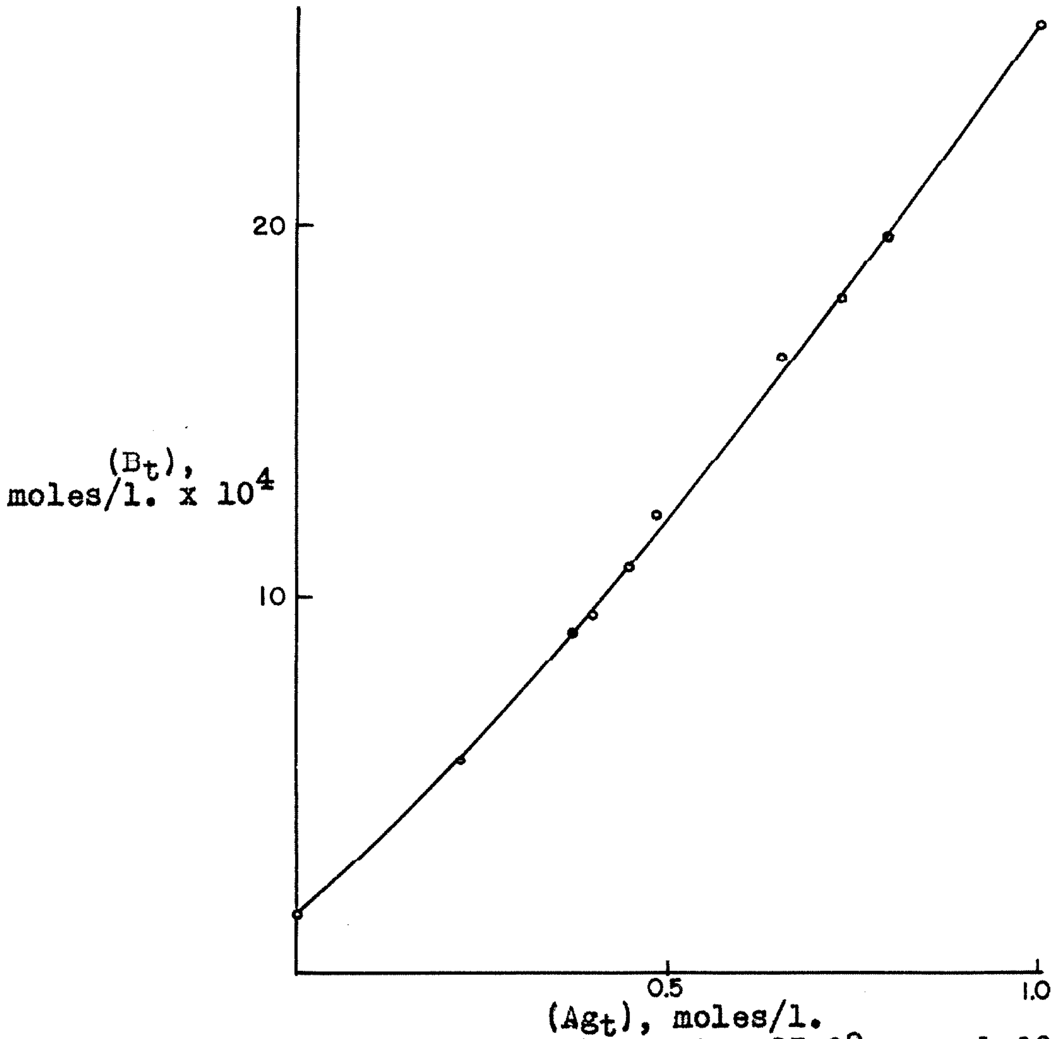


Figure 30. Di-tert-butylacetylene, t = 25.0°, u = 1.00.

Table 30

Di-tert-butylacetylene, solubility in aqueous silver nitrate solutions, t = 35.0°, u = 1.00

(Ag_t), moles/l.	(B_t) found, moles/l. x 10^6	(B_t) calc'd, moles/l. x 10^6
0.000	77	78
0.055	148	159
0.163	332	323
0.293	537	532
0.436	778	773
0.521	895	917
0.707	1293	1264
1.000	1838	1848

$$(B_t) = 0.000078 + 0.001454(Ag_t) + 0.000316(Ag_t)^2 \qquad (XLV)$$

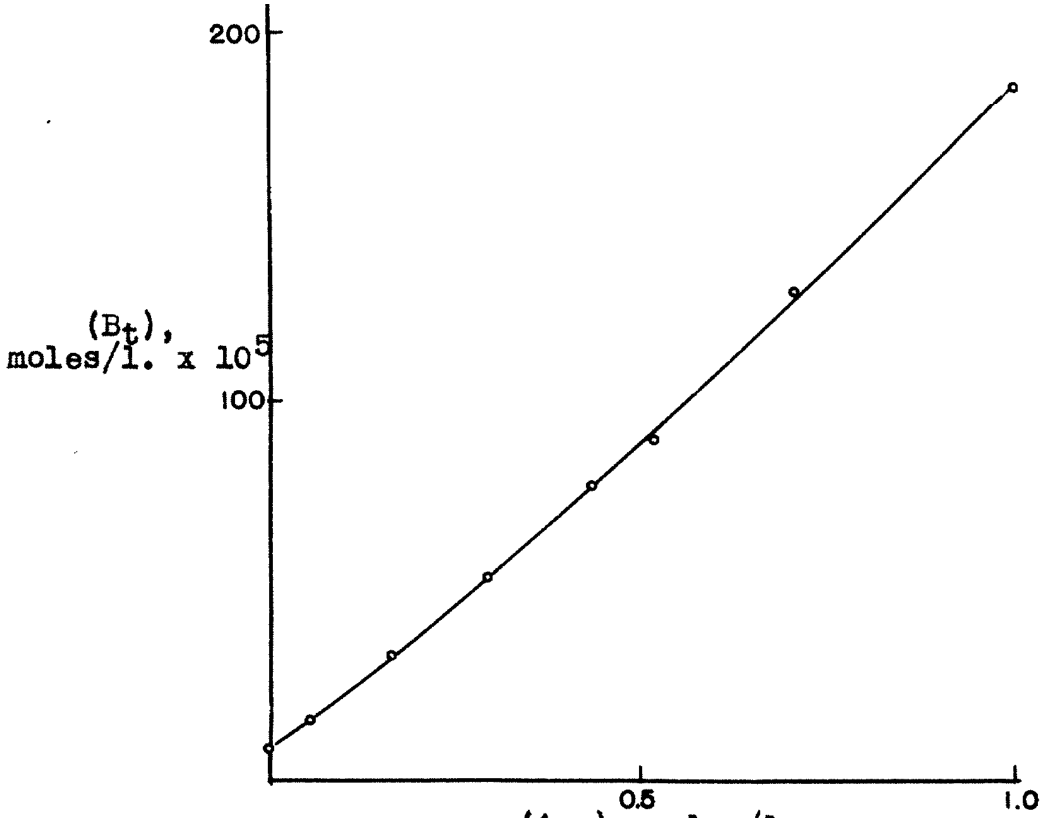


Figure 31. Di-tert-butylacetylene, t = 35.0°, u = 1.00.

F. CALCULATION OF ARGENTATION CONSTANTS.

Mathematical Considerations. The notation used throughout this thesis is that of Eberz, Welge, Yost and Lucas (43).

B = alkyne.

(B_t) = total concentration of alkyne in aqueous phase, moles/liter.

(B) = concentration of uncomplexed alkyne in aqueous phase, moles/liter.

(Ag_t) = total silver concentration in aqueous phase, moles/liter.

(Ag^+) = concentration of free silver ion in aqueous phase, moles/liter.

(AgB) = concentration of species $Ag^+{\cdot}B$ in aqueous phase, moles/liter.

(Ag_2B) = concentration of species $Ag_2^{++}{\cdot}B$ in aqueous phase, moles/liter.

In the mathematical treatment of results, it was assumed that two coordination equations were operative (equations XLVI and XLVIII). These were based oh Dorsey's interpretation of the coordination reaction between silver ion and 3-hexyne (1).

$$Ag^+ + B \rightleftharpoons AgB^+ \qquad \text{(XLVI)}$$

$$\underline{K}_1 = \frac{(AgB)}{(Ag^+)(B)} \qquad \text{(XLVII)}$$

$$AgB^+ + Ag^+ \rightleftharpoons Ag_2B^{++} \qquad \text{(XLVIII)}$$

$$\underline{K}_2 = \frac{(Ag_2B)}{(Ag^+)(AgB)} \qquad \text{(LIX)}$$

The total concentrations of alkyne and silver ion can be given as a function of argentation constants, uncoordinated silver ion and uncoordinated alkyne (equations L through LIII).

$$(B_t) = (B) + (AgB) + (Ag_2B) \qquad \text{(L)}$$

$$(B_t) = (B) + \underline{K}_1(Ag^+)(B) + \underline{K}_1\underline{K}_2(Ag^+)^2(B) \qquad \text{(LI)}$$

$$(Ag_t) = (Ag^+) + (AgB) + 2(Ag_2B) \qquad \text{(LII)}$$

$$(Ag_t) = (Ag^+) + \underline{K}_1(Ag^+)(B) + 2\underline{K}_1\underline{K}_2(Ag^+)^2(B) \qquad \text{(LIII)}$$

With the current method of equilibration, the values (Ag_t), (B_t) and (B) are known. The solubility of 3-hexyne in 1.00 f. potassium nitrate, (B), is assumed to be constant when potassium ion is partially or completely substituted by silver ion.

Using equations LI and LIII, the solubility, (B_t), of 3-hexyne can be calculated in terms of (B), (Ag_t), $\underline{K}_1$ and $\underline{K}_2$ (equation LIV).

$$(B_t) = (B) + (Ag_t)/2 - \frac{[\underline{K}_1(B)-1]\left[\underline{K}_1(B)+1-\sqrt{[\underline{K}_1(B)+1]^2 + 8\underline{K}_1\underline{K}_2(B)(Ag_t)}\,\right]}{8\underline{K}_1\underline{K}_2(B)} \qquad \text{(LIV)}$$

By differentiation of equation LIV:

$$\frac{d(B_t)}{d(Ag_t)} = \frac{1}{2} + \frac{\underline{K}_1(B)-1}{\left[(\underline{K}_1(B)+1)^2 + 8\underline{K}_1\underline{K}_2(B)(Ag_t)\right]^{1/2}} \qquad \text{(LV)}$$

At $(Ag_t) = 0$, equation LV reduces to equation LVI.

$$\left[\frac{d(B_t)}{d(Ag_t)}\right]_{(Ag_t)=0} = \frac{\underline{K}_1(B)}{1 + \underline{K}_1(B)} \qquad \text{(LVI)}$$

By plotting the experimental values of the solubility of 3-hexyne at various concentrations of silver ion, the value of $\underline{K}_1$ can be calculated. The slope at zero silver ion concentration and the intercept, (B), are either known or can be determined from a second degree mathematical expression for the curve. The second argentation constant, $\underline{K}_2$, can then be obtained directly from equation LIV.

The constants evaluated in this manner were useful only in a comparative manner for all activity effects were ignored.

An approach to a thermodynamic constant was possible with the help of the assumption that no appreciable amount of silver ion or silver ion-alkyne complex dissolved in the organic phase. This was substantiated by experiment.

Equal parts of 1.0 $\underline{f}$. silver nitrate solution and 3-hexyne were shaken for five minutes (absence of air and light). A portion of the 3-hexyne was carefully transferred to a tared crucible and evaporated to dryness. No residue remained (as indicated by no change in weight of the crucible.

As a consequence, the activity of the free (unassociated) alkyne in the aqueous solution was at or near unity. The aqueous solution was in equilibrium at all times with pure alkyne.

The activity coefficients of silver ion and of the silver ion-alkyne complex approach unity as the concentration of the silver ion approaches zero.

With use of these points, the following calculations were made:

1. The constant for the coordination reaction between

one silver ion and one molecule of alkyne is given by equation XLVII.

$$\underline{K}_1 = \frac{(AgB)}{(Ag^+)(B)} \qquad \text{(XLVII)}$$

2. In the previous evaluation of the first argentation constant, (B) was expressed in terms of molar concentrations. Equation LVI was used to determine $\underline{K}_1$, for $d(B_t)/d(Ag_t)$ was known from the least squares equations.

Under these conditions, the concentrations or activities of silver ion and silver-ion-alkyne complex do not enter into the expression. If (B), moles/liter, is replaced by unity (activity), $\underline{K}_1$ should then be a thermodynamic constant. This new constant will be termed $\underline{K}_0$.

3. In order to evaluate $\underline{K}_0$, it was necessary only to multiply $\underline{K}_1$ by (B).

Calculations of Constants from Oxidation Data. The analytical data obtained by an oxidation procedure (Table 7, Figure 8, p. 60) were fairly reliable in the region of 0.0 to 0.2 $\underline{f}$. silver nitrate.

Using a method of least squares for determining the mathematical expression for the data given in Table 7 ($\underline{n}/6$ for zero silver concentration and $\underline{n}/12$ for other concentrations), equation LVII was obtained.

$$(B_t) = 0.100 + 0.1987(Ag_t) - 0.170(Ag_t)^2 \qquad \text{(LVII)}$$

The experimental value of $\underline{K}_1$, evaluated according to equation LVI was 24.9. The value found by Dorsey (1) was

19.2.

The rate of change of slope of equation LVII was reverse that expected from the theoretical considerations of equation LIV. However, considering the complexity of the oxidation of 3-hexyne, it was not surprising to have noted deviations from the expected pattern.

Calculations of Constants from Spectrophotometric Data. The results obtained by means of spectrophotometric analyses were much more consistent with the expected behavior of the coordination reactions.

The values of $\underline{K}_1$ and $\underline{K}_2$ (Table 31) were quite similar for most of the alkynes. There was no obvious trend in the constants which could be attributed to successive introduction of methyl groups into the 2- and 5-positions of 3-hexyne.

Attempts to evaluate ΔH for the coordination reaction by means of variation of $\underline{K}_1$ with temperature led to anomalous results.

These values of $\underline{K}_1$ were then transformed into the corresponding $\underline{K}_0$ values according to the method outlined on page 149. The results are given in Table 32.

With the introduction of each successive methyl group into the alpha-position of 3-hexyne, the value of $\underline{K}_0$ decreased by very nearly a factor of three.

The values of $\underline{K}_2$ corresponding to $\underline{K}_0$ were impossible to calculate in a similar manner. The second thermodynamic con-

Table 31

Argentation Constants of Various Acetylenic Hydrocarbons

Compound	t, °C	K_1	K_2
3-Hexyne	25.0	17.3	0.36
3-Hexyne	35.0	17.3	0.21
2-Heptyne	25.0	11.9	0.26
2-Methyl-3-hexyne	25.0	20.5	0.28
2,2-Dimethyl-3-hexyne	25.0	19.1	0.30
2,2,5-Trimethyl-3-hexyne	25.0	23.4	0.34
Di-*tert*-butylacetylene	25.0	12.8	0.53
Di-*tert*-butylacetylene	35.0	18.6	0.33

Table 32

Argentation Constants of Various Acetylenic Hydrocarbons

Compound	t, ^{o}C	$(B)^{a}$	$\underline{K}_1$ [b]	$\underline{K}_o$ [c]
3-Hexyne	25.0	0.00758	17.3	0.131
3-Hexyne	35.0	0.00599	17.3	0.103
2-Heptyne	25.0	0.00171	11.9	0.0204
2-Methyl-3-hexyne	25.0	0.00188	20.5	0.0386
2,2-Dimethyl-3-hexyne	25.0	0.00068	19.1	0.0130
2,2,5-Trimethyl-3-hexyne	25.0	0.000226	23.4	0.00529
Di-*tert*-butylacetylene	25.0	0.000149	12.8	0.00191
Di-*tert*-butylacetylene	35.0	0.000078	18.6	0.00145

[a] Concentration of free alkyne, moles/liter.

[b] Calculated from equation LVI.

[c] Evaluated according to the method given on p. 149.

stants required information concerning the behavior of the activity coefficients of finite values of the concentration of silver ion and of silver ion-alkyne complexes.

In the case of 3-hexyne and of di-*tert*-butylacetylene, values of $\underline{K}_o$ were determined for two different temperatures. Then by means of the van't Hoff isobar (equation LVIII), the heat of reaction in solution was calculated (Table 33).

$$\ln \frac{(\underline{K}_o)_{T2}}{(\underline{K}_o)_{T1}} = \frac{\Delta H}{R} \left[\frac{T_2 - T_1}{T_1 T_2} \right] \qquad \text{(LVIII)}$$

Table 33

Heat of Coordination Reactions

Compound	$\underline{K}_{o25}/\underline{K}_{o35}$	ΔH, Kg.cal.
3-Hexyne	1.27	-4.38
Di-*tert*-butylacetylene	1.32	-5.03

These results are comparable to those obtained for the reaction of silver ion with alkenes (44), Table 34.

Table 34

Compound	$\underline{K}_{o0}/\underline{K}_{o25}$	ΔH, Kg.cal.
2-Methyl-2-butene	2.53	-6.01
Cyclohexene	2.45	-5.80

Throughout this thesis, the coordination reaction has been represented as involving free silver ion and alkyne. The reaction could be better represented as involving silver ion with two molecules of water of hydration and alkyne.

According to Winstein and Lucas (44), the energy of the bond between silver ion and the unsaturated bond in question is probably somewhat greater than 6 kg.cal., for to the ΔH of the reaction shown in equation XLVI must be added the ΔH of the reaction shown in equation LIX.

$$H_2O + H_2O\cdot Ag^+ \rightleftharpoons (H_2O)_2Ag^+ \qquad \text{(LIX)}$$

Accuracy of Results. The factors which were considered in determining the accuracy of argentation constants by spectrophotometric means were (a) the instrument, (b) change in composition of solutions during handling, (c) reaction of alkynes with oxygen, (d) low solubilities at low silver ion concentrations, (e) unsatisfactory distribution coefficients for extraction procedures, (f) hydration of the triple bond and (g) error in slope in equation LVI due to invalid assumptions in the use of the method of least squares.

a. The instrument. Noticeable shifts in the balance point of the instrument could be noted over periods of time of less than a minute. This effect was eliminated by taking blank readings both before and after sample readings. If any discrepancies occurred, the optical density measurements were repeated.

The accuracy of the wave length setting mechanism was not better than ±0.005 microns. If the absorption peak used for determination of optical density was quite narrow, it was necessary to scan a short spectral region with each sample and record the maximum absorption observed.

If these precautions were observed, the accuracy and duplicability were probably within ±0.5%, the value given by the manufacturer.

b. Change in Composition of Solutions During Handling. The drying agents used for carbon tetrachloride solutions of alkynes had no observable effect on the concentration of the solute.

The container for all solutions was chosen so that there was a minimum of air space above the solution. Transfer of a carbon tetrachloride solution from one container to another had no observable effect on the optical density. This error was probably smaller than instrumental errors.

c. Reaction of Alkynes with Oxygen. Dorsey (1) observed that aqueous solutions of alkynes reacted very rapidly with dissolved oxygen. He had been dealing with solutions of very low concentrations, and traces of oxygen were quite significant. During the present investigation, oxygen was excluded by a method similar to the one used by Dorsey. However, concentrations of alkynes were much greater (5 to 50 times) than those used previously, and the percentagewise effect of oxygen would be reduced proportionately. Solutions of alkynes in carbon tetrachloride were exposed to air in a closed flask for 24 hours without effect on optical density measurements.

d. Low Solubilities at Zero Silver Ion Concentration. The major problem encountered here was keeping the optical densities of the carbon tetrachloride solutions (from the extraction process) within the range of best accuracy of the spectrophotometer (0.2 to 0.5). The accuracy of this determination will reflect on the accuracy of the least squares curve obtained from a series of determinations; however, see (g).

e. Distribution coefficients. This point was evaluated previously. It might be added that the extraction procedure was aided by the addition of potassium cyanide to the aqueous phase before extraction. This would make the distribution coefficient for alkynes between carbon tetrachloride and the aqueous solution greater. The maximum error contribution was of the order of 0.2%.

f. Hydration of the triple bond. After 3-hexyne had been in the presence of aqueous silver nitrate under experimental conditions for several hours, the absorption spectrum of the extracted material began to show a small absorption peak at 5.82 microns. This coincided precisely with a carbonyl peak of 3-hexanone.

A semi-quantitative, two-component, spectrophotometric analysis indicated the presence of about 1% 3-hexanone in the 3-hexyne after 15 hours, and about 3½% after 47 hours. Over this period of time, the concentration of 3-hexanone appeared to vary linearly with time.

In all of the equilibration procedures, the alkynes were in the presence of aqueous silver nitrate solution for three to five hours. On the basis of the data given above, the maximum amount of hydration which occurred was about 0.4%.

The infra-red spectrum of di-<u>tert</u>-butylacetylene exhibited the same phenomenon. No quantitative determinations were made, but the carbonyl peak appeared at about the same rate as the peak for 3-hexyne.

Up to this point, the variations in determination of the alkyne have been considered. It has been assumed that the quantitative analysis of silver is precise relative to the analysis of alkyne.

g. Method of least squares. All of the curve fitting was made on the assumptions that the curve was of second degree, that the error in (Ag_t) was negligible with respect to the error in (B), and that the error in (B) was constant over the entire range of silver ion concentration. The last assumption was probably valid when (Ag_t) was over 0.2 moles/liter, because, in all of the extraction procedures, an attempt was made to adjust the ratio of saturated aqueous solution to carbon tetrachloride extractant so that optical density measurements were of the same magnitude. This was often impractical when (Ag_t) was very low, and consequently these results were less accurate.

The experimental data for the evaluation of the argentation constants for 3-hexyne at 25.0° was chosen for a typical analysis of error. Nine points $(n = 9)$ were used for curve-fitting by the method of least squares.

Since the evaluation of $\underline{K_o}$ was made from $d(B)/d(Ag_t)$ at $(Ag_t) = 0$ (equation LVI, when $(B) = 1$), it was necessary to determine the relationship between the accuracy of this slope and the accuracy of the values of (B).

If $d(B)/d(Ag_t)$ (termed $\underline{b}$ hereafter) is solved as a function of the summations used in the method of least squares, equation LX is obtained.

$$\underline{b} = \frac{A\Sigma y + B\Sigma yx + C\Sigma yx^2}{D} \qquad \text{(LX)}$$

$x = (Ag_t)$. $\quad y = (B)$. $\quad n = 9$.

$A = \Sigma x^2 \Sigma x^3 - \Sigma x \Sigma x^4$. $\quad B = n\Sigma x^4 - (\Sigma x^2)^2$.

$C = \Sigma x \Sigma x^2 - n\Sigma x^3$.

$D = 2\Sigma x \Sigma x^2 \Sigma x^3 - (\Sigma x)^2 \Sigma x^4 - (\Sigma x^2)^3 + n\Sigma x^2 \Sigma x^4$

$\quad - n(\Sigma x^3)^2$.

By differentiation of $\underline{b}$ (assuming no error in x):

$$\Delta\underline{b} = \frac{\pm n\Delta yA \pm \Delta yB\Sigma x \pm \Delta yC\Sigma x^2}{D} \qquad \text{(LXI)}$$

$$= \frac{\Delta y\sqrt{n^2A^2 + (\Sigma x)^2B^2 + (\Sigma x^2)^2C^2}}{D} = 1.2\Delta\underline{y} \qquad \text{(LXII)} \; \text{(LXIII)}$$

By substituting the appropriate summations into equation LXII, a relationship between error in $\underline{y}$ and error in $\underline{b}$ can be obtained (equation LXIII) for the 3-hexyne system. The most probable error in $\underline{y}$, according to the previous discussion, will be about ±2.1%. This results in a ±2.5% error in $\underline{b}$. The first argentation constant, $\underline{K_o}$ varies directly with $\underline{b}$ (equation LXIV), so the error remains about ±2.5%.

$$\underline{b} = \underline{K_o}/(1 + \underline{K_o}) \quad \text{or,} \quad \underline{K_o} = \underline{b}/(1 - \underline{b}). \qquad \text{(LXIV)}$$

REFERENCES

1. W. Smith Dorsey, Ph.D. Thesis, California Institute of Technology, Pasadena, California, 1950.

2. W. F. Eberz, H. J. Welge, D. M. Yost and H. J. Lucas, J. Am. Chem. Soc., 59, 45 (1937).

3. S. Winstein and H. J. Lucas, ibid., 60, 836 (1938).

4. H. J. Lucas and D. Pressman, Ind. Eng. Chem., Anal. Ed., 10, 140 (1938).

5. K. Hazura and A. Grüssner, Monats., 9, 947 (1888).

6. A. W. Johnson, "Acetylenic Compounds," Vol. II, Edward Arnold & Co., London, 1950, p. 80.

7. A. L. Hennee and K. W. Greenlee, J. Am. Chem. Soc., 67, 484 (1945).

8. K. N. Campbell and L. T. Eby, ibid., 63, 2683 (1941).

9. G. Egloff, "Physical Constants of Pure Hydrocarbond," Vol. I, A. C. S. Monograph No. 78, Reinhold Publishing Corporation, New York, 1939, p. 366.

10. W. C. Pierce and E. L. Haenisch, "Quantitative Analysis," 3rd ed., John Wiley & Sons, New York, 1948, p. 214.

11. R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," 3rd ed., John Wiley & Sons, Inc., New York, 1948, p. 202.

12. E. Urion, Compt. rend., 191, 263 (1930).

13. R. L. Shriner and R. C. Fuson, op. cit., p. 170.

14. N. L. Drake and J. Bronitsky, J. Am. Chem. Soc., 52, 3715 (1930).

15. J. G. Kirchner, A. N. Prater and A. J. Haagen-Smit, Ind. Eng. Chem., 18, 31 (1946).

16. T. H. Vaughn, G. F. Hennion, R. R. Vogt and J. A. Nieuwland, J. Org. Chem., 2, 1 (1937).

17. J. F. Norris and R. Reuter, J. Am. Chem. Soc., 49, 2624 (1927).

18. P. Ivitzky, Bull. soc. chim., (4) 35, 357 (1924).

19. "Organic Syntheses," Coll. Vol. I, John Wiley & Sons, Inc., New York, 1941, p. 462.

20. H. J. Lucas and D. Pressman, "Principles and Practice in Organic Chemistry," John Wiley & Sons, Inc., New York, 1949, p. 162.

21. J. H. Wotiz and F. A. Miller, J. Am. Chem. Soc., 71, 3441 (1949).

22. S. D. Thorn, G. F. Hennion and J. A. Nieuwland, ibid., 58, 796 (1936).

23. L. S. Dedusenko, Trudy Khim Inst. Azerbaidzham. Filiala Akad. Nauk, 4, No. 1, 15 (1940); Khim. Referat. Zhur., 4, No. 9, 53 (1941); C. A., 37, 1697 (1943).

24. G. F. Hennion and T. F. Banigan, Jr., J. Am. Chem. Soc., 68, 1202 (1946).

25. F. Strauss, L. Kollek and W. Heyn, Ber., 63B, 1868 (1930).

26. M. J. Murray and F. F. Cleveland, J. Chem. Phys., 12, 156 (1944).

27. A. F. Thompson, Jr., J. G. Burr, Jr., and E. N. Shaw, J. Am. Chem. Soc., 63, 186 (1941).

28. R. L. Shriner and R. C. Fuson, op. cit., p. 163.

29. R. L. Shriner and R. C. Fuson, op. cit., p. 165.

30. R. L. Shriner and R. C. Fuson, op. cit., p. 170.

31. R. L. Shriner and R. C. Fuson, op. cit., p. 171.

32. A. O. Zoss and G. F. Hennion, J. Am. Chem. Soc., 63, 1151 (1941).

33. R. Levine and C. R. Hauser, ibid., 66, 1768 (1944).

34. H. J. Lucas and D. Pressman, op. cit., p. 286.

35. H. J. Lucas and D. Pressman, op. cit., p. 290.

36. R. C. Elderfield, W. J. Gensler, F. Brody, J. D. Head, S. C. Dickerman, L. Wiederhold, III, C. B. Kremer, H. A. Hageman, F. J. Kreysa, J. M. Griffing, S. M. Kupchan, B. Newman and J. T. Maynard, J. Am. Chem. Soc., 68, 1581 (1946).

37. G. F. Hennion and T. F. Banigan, Jr., ibid., 68, 1381 (1946).

38. P. Heinanen, Chem. Zentr., 1944, II, 14.

39. J. Timmermans and Y. Delcourt, J. chim. phys., 31, 85 (1934).

40. A. Dorinson and A. Q. Ralston, J. Am. Chem. Soc., 66, 361 (1944).

41. D. R. Stull, Ind. Eng. Chem., 39, 517 (1947).

42. R. Levine and C. R. Hauser, J. Am. Chem. Soc., 66, 1769 (1944).

PART III

SOME RELATIONSHIPS OF STEROLS TO PLANT GROWTH

This portion of the thesis is presented as it was submitted to the Journal of Plant Physiology for publication.

Some Relationships of Sterols to Plant Growth[1]

by

George Helmkamp and James Bonner

---

[1] This work was made possible by generous samples of pure compounds from the following individuals: Dr. W. G. Bywater, S. B. Penick & Co.; Dr. Karl Folkers, Merck & Co., Inc.; and Dr. Abraham White, Chemical Specialties Co. Inc.

Introduction. In spite of the universal occurrence of steroids in plants, the role of these materials remains quite unknown. That steroids possess physiological activity for the higher plant was in fact demonstrated only after the discovery of estrogenic principles in plants in 1926-1927 by Loewe and Spohr (1), Dohrn, Faure, Poll and Blotevogel (2), Loewe, Lange and Spohr (3), and Loewe (4).

The status of our knowledge of the influence of the animal steroid hormones on the vegetative growth and reproductive development of plants has been extensively reviewed by Löve and Löve (5). There appear to be several well established examples of the influence of estrogenic materials on vegetative growth. Effects on flowering appear to be generally secondary to this effect. Hylmö (6) has however demonstrated an influence of estrone and of testosterone on sexual expression in spinach, and Löve and Löve (5) have been able to suppress either anther or gynecium growth in Melandrium by application of estrone or testosterone respectively.

In addition to the effects which estrone exerts when applied directly to intact plants, there are additional instances of effects of estrone on growth of isolated plant parts or tissues. Such effects have been observed by Kögl and Haagen-Smit (7) and by Bonner and Axtman (8) with isolated pea embryos, by Fiedler (9) with isolated root tips of corn, by Weyland (10) with Allium cepa roots, and by Gioelli (11) with cultures of carrot root. In all of these instances additions of estrone to the culture medium have served to cause a general increase in growth rate. That the synthetic estrogen, diethylstilbesterol can replace estrone in promotion of plant growth has been established by Zollikofer (12).

The effects of testosterone treatment of higher plants, other than the influence on sex expression noted above, have been quite varied. v. Euler (13), for example, found that inhibition of seedling development resulted when seeds of Lepidium sativum or Hordeum vulgare were treated with testosterone at concentrations of 0.01% as well as with estrone. Similarly, Glaser and Ranftl (14) found testosterone harmful to growth of hyacinth bulbs while David and Gouzon (15) found testosterone to be without effect on the species studied by them.

Certain microorganisms are influenced by additions of steroids to the nutrient medium. The Rhodotorula sugari and R. glutinis, two of several yeasts investigated by Weber (16) responded (particularly in the presence of Zn) with increased growth to applications of estrone, estradiol benzoate or testosterone. Nekam and Polgar (17) found growth retardation of Trichophyton crateriform and Staphylococcus aureus by estrone, but growth arrest by either androsterone or testosterone.

No function nor physiological activity has as yet been found for the universally distributed phytosterols and mycosterols so far as plants are concerned although these substances have of course found extensive use in the synthesis of products which have hormone or vitamin activity in higher animals.

The saponins constitute a group of steroids of wide but sporadic occurrence in the plant kingdom. Balansard and Pellessier (18-24) in a series of papers published between 1943 and 1945 have shown that saponins include substances capable of eliciting plant growth responses. These authors used various concentrations (10 to 1000 mgm. per ml.) of quillaja, polygala, saponaria and sapindus saponins. The growth rate of isolated wheat embryos was approximately doubled by optimal concentrations of saponin, although higher concentrations were toxic. Saponin applications also brought about increased rate of development of shoots and roots by begonia leaves. The treatment of seeds of cereals and tomato with dilute solutions of saponins accelerated germination and increased subsequent growth rate. The application of dilute saponin solutions to tomato roots resulted, however, in growth inhibitions, preceded in some instances by a short period of increased growth. Seeds of peas absorbed water more rapidly in the presence of saponins. Balansard, Pellessier and Conil (25) found similar effects of saponin on water absorption by seeds of corn, with a subsequent more rapid germination. v. Euler (13) germinated seeds of *Lepidium sativum* and *Hordeum vulgare* in the presence of digitonin, quillaja saponin, or sodium cholate but found only growth inhibitions due apparently to the use of excessively high concentrations.

In the present work we propose to present a survey of the physiological activity of a wide variety of steroids. The comparison is based on effects on the growth of isolated pea embryos in aseptic culture, according to the method of Kögl and Haagen-Smit (7) and Bonner and Axtman (8).

Materials and Methods.-- All of the experiments were conducted with excised embryos of pea, variety Alaska. The methods of sterilization and culture were identical with those of Bonner and Axtman (8). The culture medium was that prescribed by Bonner and Addicott (26) for growth of pea roots[I], except that the agar medium contained 2 per cent rather than 4 per cent sucrose and the culture vessels were 75 x 250 mm. pyrex

---

[I] The basal medium contained $Ca(NO_3)_2 \cdot 4H_2O$ 170 mg./l.; $MgSO_4 \cdot 7H_2O$ 21 mg./l.; KNO_3 85 mg./l; KCl 61 mg./l.; KH_2PO_4 20 mg./l.; ferric tartrate 1.5 mg./l.; agar, 1%; sucrose 2%.

test tubes. The plants were grown at 25° C. in the dark. Approximate measurements of stem growth were made weekly for three weeks, and after four weeks the plants were removed from the culture tubes for measurement of final stem and root lengths. The individual stems and roots of each group were then separated for dry weight measurements. Twenty embryos were cultured and grown in each experiment for each treatment. The number of plants finally harvested in each group was approximately 18 since an occasional embryo either failed to develop or formed adventitious roots or shoots due to injury at excision. These individuals were discarded.

Accessory substances were added to the culture medium in water, ether or alcohol solutions, and controls were prepared using comparable amounts of pure solvents. The addition of ether was without significant effect. Alcohol, however, tended to increase growth somewhat after two weeks. Several compounds, principally the esterified compounds, precipitated from the cold medium, and hence concentrations were limited in these cases by a solubility factor.

The results, as recorded in the tables below, are given as per cent of the growth of the control. Additional notations indicate statistical significance of growth in the individual treatments from growth in the unsupplemented basal medium.

The growth of the individual control series was quite uniform as between successive experiments. Table 1 presents the average growth measurements for eleven control groups.

<u>Principal</u> <u>Experimental</u> <u>Results</u>.-- In preliminary experiments several groups of embryos were cultured in the presence of nonsteroidal accessory substances in order to arrive at as optimal a medium as possible for this variety of pea. The results of these experiments are given in Table 2.

Vitamin B_1, at 1.0 mg./liter, and casein hydrolysate, 100 mg./l. increased root growth significantly. Nicotinic acid, pantothenic acid, ascorbic acid and adenine were substantially inactive. Vitamin B_6, at 1.0 mg./l. inhibited shoot growth, and biotin above 0.01 mg./l. was markedly inhibitory either alone or in the presence of the B vitamins mentioned above. As a consequence of these results, none of these accessory substances was used in the culture medium.

Estrone, in accordance with the earlier findings, exhibited considerable activity in increasing growth of pea embryos, increasing stem growth by a maximum of 20 per cent at its optimum concentration of 1 mg./l.

Testosterone on the contrary was highly inhibitory, exerting a growth depressing effect which disappeared only at concentrations of 0.01 mg./l. and below. Two other compounds of the animal sex hormone series, dihydroxyestrin and methyl androstenediol, were also slightly inhibitory and in common with others of the steroids tested showed inhibitory action to an extent which approached statistical significance.

Cortisone, in concentrations of 1 and 10 mg./l. greatly inhibited shoot growth although only the higher concentration inhibited growth of the root.

Of the further typically animal sterols summarized in table 4 all were ineffective or inhibitory to growth of pea embryos at all concentrations tested. Thus cholesterol, from two different sources, caused small and somewhat irregular inhibition, particularly of root growth. Cholic acid inhibited both shoot and root growth at low concentration, desoxycholic acid was less effective, and a-hyodesoxycholic acid was inhibitory only at relatively high concentrations.

The steroids most active in promotion of growth of pea embryos have been found among the saponins. The present results summarized in table 5 roughly parallel those of Balansard and Pellessier (7) in which the rate of growth of wheat embryos was nearly doubled by saponin application. In contrast to the work with wheat, however, no growth inhibition by saponins was noted with pea embryos, even in concentrations as high as 50 mg./l. Optimum growth of stems occurs in all cases near 10 mg./l. Root response in general followed the response in stem growth.

The saponin preparations used included 3 commercial samples of relatively crude material containing mixtures of materials as well as one chemically defined compound, diosogenin saponin. The latter was fully as effective in promoting pea embryo growth as the crude materials.

The remaining compounds tested for effectiveness on the growth of pea embryos were plant products, naturally occurring or synthetically modified. These included a sitosterol preparation, stigmasterol hydrate and acetate, diosgenin acetate, dehydrodiosgenin acetate, hecogenin acetate, $\Delta^{9,11}$ hecogenin acetate and ergosterol. Results with these materials are summarized in table 6. All were either ineffective or slightly inhibitory over the concentration ranges tested.

Discussion:-- It has been shown in the data presented above that the promotion of pea embryo growth by sterols and related materials possesses a definite chemical specificity. Of all of the sterols and sterol derivatives tested in the present investigation, only one, estrone, caused significant increases in growth. This material has not only been previously shown to be effective in the pea embryo test but to influence the growth of other higher plant tissues and species as well. It is particularly noteworthy that the well known plant sterols ergesterol, stigmasterol, and sitosterol were found to be without growth promoting effect.

That the growth promotion of pea embryos by estrone is attended by a marked chemical specificity is stressed by the fact that the closely related dihydroxyestrin was found to be totally ineffective. In addition, the growth promotion of pea embryos by estrone finds its counterpart in the relatively specific growth inhibition exerted by testosterone. This material in concentrations as low as 0.1 mg./l., was found to bring about significant reduction in embryo growth. Growth reductions of a less striking nature were caused by a variety of other materials. It is nevertheless striking that the most effective growth inhibitor in these experiments is testosterone just as estrone is the most striking growth promoter.

The steroidal saponins constitute another group of substances with marked growth promoting effects on cultured pea embryos. That growth promotion by saponins is not due to their possible content of estrone is indicated by the fact that in one instance, that of diosgenin saponin, a presumably pure material was found to bring about growth promotion. It is still quite uncertain, however, whether promotion of growth is actually exerted through a mechanism similar to that affected by the sterols proper. It might, for example, be possible that saponins with their marked surface properties affect in some unknown manner the wetting or other relations to water of embryos and seedlings in culture. Still, the growth promotions brought about in these experiments by the steroidal saponins are striking and deserve further chemical attention.

Do the growth promotions and growth inhibitions by sterols and steroidal materials described in this paper and in earlier work have any relation to the normal growth of the plant? This question we cannot answer because we do not know now such elementary facts as whether or not sterols and steroidal materials are transported within the plant so that they might then act in hormonal capacities. Neither do we have any insight into the biochemical role of sterols and steroidal materials. That sterols may indeed play significant physiological roles is, however, suggested by the occurrence of estrogenic substances in plant material coupled with the fact that such estrogenic substances as estrone can be shown as in the present case to possess specific physiological activity for higher plants.

Summary.-- The embryos of mature pea seeds respond by increased growth when they are supplied in aseptic culture with certain sterols or steroidal materials. Of the seventeen sterols and steroids tested, only one, estrone, possessed the activity of significantly increasing growth of pea embryos in culture. Other compounds and in particular, testosterone, were highly effective in inhibition of growth. Naturally occurring plant sterols such as ergosterol, stigmasterol and sitosterol were without effect on pea embryo growth. The steroidal saponins both in crude preparation and in chemically pure form exert marked effects in increasing the growth of excised pea embryos.

Kerckhoff Laboratories of
Biology

California Institute of
Technology

Pasadena, California

Table 1

Average growth of 11 control series of excised pea embryos in unsupplemented basal medium. Growth in dark at 25° C. Initial length of stem approx. 2 mm.

Stem length, (mm.) after:

1 week	2 weeks	3 weeks	4 weeks
17.7 ± 2.4	32.1 ± 4.5	43.3 ± 5.1	56.0 ± 9.0

Root length, (mm.) after:

4 weeks
56.9 ± 9.9

Table 2

Growth responses of excised pea embryos to varied accessory factors. Measurements after 4 weeks.

Accessory Substance	Conc., mg./l.	Growth in length. % of Control	
		Stem	Root
Vitamin B_1	1	93	133*
Vitamin B_6	1	81*	89
Biotin	0.1	10**	7**
"	0.01	94	110
"	0.001	103	102
Casein Hydrolyzate	100	89	121*

*Significant at 5 per cent level

**Significant at 1 per cent level

Table 3

Growth responses of excised pea embryos to steroid animal hormones. Measurements after 4 weeks.

Accessory Substance	Conc., mg./l.	Growth in length % of control		Dry weight, % of control	
		Stem	Root	Stem	Root
Estrone	10.0	102	108	93	99
	1.0	120*	115	118	114
	0.1	104	96	107	99
	0.01	100	106	106	125
Testosterone propionate	10.0	35**	90	56	77
	1.0	75**	85	89	83
	0.1	75**	90	84	93
	0.01	104	104	106	103
Dihydroxy estrin	10.0	87	94	83	89
	1.0	90	85	83	105
Methyl-androstenediol	1.0	83	81	97	107
Cortisone	10.0	15**	25**	-	-
	1.0	78**	112	92	116

*Significant at 5 per cent level

**Significant at 1 per cent level

Table 4

Growth responses of excised pea embryos to cholesterol and related animal sterols. Measurements after 4 weeks.

Accessory Substance	Conc., mg./l.	Growth in length % of control		Dry weight, % of control	
		Stem	Root	Stem	Root
Cholesterol	10.0	93	87	101	88
	1.0	100	108	98	106
	0.1	90	80**	88	87
	0.01	85	87	96	99
Cholic acid	0.1	78*	80**	83	82
	0.01	76*	86	90	93
Desoxycholic acid	0.1	96	90*	91	97
	0.01	82	88	83	89
a-Hyodesoxycholic acid	10.0	69**	68**	82	70
	1.0	104	80*	106	88

*Significant at 5 per cent level

**Significant at 1 per cent level

Table 5

Growth responses of excised pea embryos to Saponins.

Measurements after 4 weeks.

Accessory Substance	Conc., mg./l.	Stem length % of control	Root length % of control	Dry wt., Stem	% of control Root
Saponin, Merck Sample 1	50.0	92	115	107	110
	20.0	98	104	103	103
	10.0	124*	100	118	105
	10.0	126*	111	107	114
	1.0	106	102	102	96
	1.0	115	106	105	117
Saponin, Merck Sample 2	10.0	140**	143**	120	125
	1.0	119*	91	105	105
Saponin Penick	10.0	117*	98	104	104
	1.0	134**	132*	117	124
Diosgenin saponin	10.0	143**	147**	120	136
	1.0	113	123	110	135

*Significant at 5 per cent level

**Significant at 1 per cent level

Table 6

Growth responses of excised pea embryos to typical plant sterols.

Measurements after 4 weeks.

Accessory Substance	Conc., mg./l.	Growth in length. % of control		Dry wt., % of control	
		Stem	Root	Stem	Root
Ergosterol	10.0	89	72*	82	86
	1.0	91	94	89	83
Sitosterol	10.0	79	111	86	91
	1.0	87	102	85	90
Diosgenin acetate	10.0	102	98	106	95
	1.0	82*	96	93	91
Stigmasterol acetate	10.0	90	110	100	103
	1.0	96	96	101	98
Stigmasterol hydrate	10.0	94	93	94	94
	1.0	85	91	85	94
Hecogenin acetate	10.0	96	104	98	98
	1.0	96	102	100	100
$\Delta^{9,11}$ Hecogenin acetate	10.0	91	94	88	90
	1.0	80	85	84	82
Dehydrodiosgenin acetate	10.0	104	104	100	98
	1.0	98	116	97	106

*Significant at 5 per cent level

Literature Cited

1. S. Loewe and E. Spohr, Akad. d. wiss. Wien, Anzeiger 63, 167-169 (1926); after A. Löve and D. Löve, Arkiv för Botanik 32A, No. 13, 1-60 (1945).
2. M. Dohrn, W. Faure, H. Poll, and W. Tokokinine Blotevogel, Med. Klinik 22, 1417-1419 (1926); after A. Löve and D. Löve, Arkiv for Botanik 32A, No. 13, 1-60 (1945).
3. S. Loewe, F. Lange, and E. Spohr, Biochem. Zeitschr. 160, 1-26 (1927).
4. S. Loewe, Internat. Kongr. f. Sexualforsch. I, 113-116 (1927); after A. Löve and D. Löve, D. Arkiv för Botanik 32A, No. 13, 1-60 (1945).
5. A. Löve and D. Löve, Arkiv. för Botanik 32A, No. 13, 1-60 (1945).
6. B. Hylmö, Botan. Notiser 1940, 389-394; C. A. 35, 7460 (1941).
7. F. Kögl and A. J. Haagen-Smit, Z. Physiol. Chem. 243, 209-226 (1936).
8. J. Bonner and G. Axtman, Proc. Nat. Acad. Sci. 23, 453-457 (1937).
9. H. Fiedler, Zeitschr. f. Botanik 30, 385-436 (1936).
10. H. Weyland, Z. Krebsforsch. 56, 148-164 (1948); C. A. 44, 194h (1950).
11. F. Gioelli, Arch. Sci. Biol. (Italy) 28, 311-316 (1942).

12. C. Zollikofer, Schweiz. Z. Biochem. 1, 1-9 (1942); Biol. Abst. 19, 20018 (1945).

13. H. v. Euler, Arkiv Kemi, Mineral., Geol. A22, No. 14 (1946).

14. E. Glaser and F. Ranftl, Z. Geburtschülfe u. Gynäkol. 124, 113-125 (1942); C. A. 44, 4970c (1950).

15. R. David and B. Gouzon, Rev. Sci. 77, 579-583 (1939); Chem. Zentr. 1940, II, 357.

16. A. P. Weber, Compt. Rend. Acad. Sci. Paris 202, 517-519 (1936); Chem. Zentr. 1938, I, 2563.

17. L. Nekam and P. Polgar, Acta Dermato-Venereol. 30, 200-205 (1950); C. A. 44, 7934d (1950).

18. J. Balansard and F. Pellessier, Compt. Rend. Soc. Biol. 137, 454 (1943).

19. J. Balansard and F. Pellessier, Compt. Rend. Soc. Biol. 137, 455 (1943).

20. J. Balansard and F. Pellessier, Compt. Rend. Soc. Biol. 137, 461-462 (1943).

21. J. Balansard and F. Pellessier, Compt. Rend. Soc. Biol. 137, 523-525 (1943).

22. J. Balansard and F. Pellessier, Compt. Rend. Soc. Biol. 137, 763-764 (1943).

23. J. Balansard and F. Pellessier,Compt. Rend. Soc. Biol. 138, 622-623 (1944).

24. J. Balansard and F. Pellessier, Compt. Rend. Soc. Biol. 139, 1098-1100 (1945).

25. J. Balansard, F. Pellessier, and S. Conil, Compt. Rend. Soc. Biol. 140, 140-142 (1946).

26. J. Bonner and F. Addicott, Bot. Gaz. 99, 408-411 (1937).

PART IV. PROPOSITIONS.

1. No optical isomers have been observed for compounds of the type RR'CXY, where R is a deuterated analog of R'. The approach to this problem has been through attempts to resolve potential racemic modifications such as α-pentadeuteriophenylbenzylamine[a].

It is proposed that an optically active compound could be made by replacing CH_3I with CD_3I in equation II, p. 2 of this thesis. The optical antipode could be prepared by treating D(+)-2,3-epoxybutane with CD_3OH (equation I, p. 1) followed by methylation via the Williamson synthesis.

[a] G. R. Clemo and G. A. Swan, J. Chem. Soc., 1939, 1960.

2. It is proposed that an attempt should be made to prepare derivatives of disubstituted acetylenic hydrocarbons with 2,4-dinitrobenzenesulfenyl chloride.[a] It is believed that too little attention is paid to methods for the characterization of liquids other than the use of the unwieldy methods of density, boiling point and refractive index.

[a] N. Kharasch and C. M. Buess, J. Am. Chem. Soc., 71. 2724 (1949).

3. It is proposed that Grignard reagents will add across a triple bond if a strongly electronegative atom

(or group) is alpha to the triple bond. This is based on by-products formed during the reaction of 2-chloro-2-methyl-3-hexyne and homologs with methyl magnesium bromide.[a,b]

The by-products are not polymers (or even dimers) of the starting material, the boiling point range suggests the existence of a mixture (possibly cis-trans isomers), and only carbon and hydrogen are present in the molecule.

The amount of by-product formed is a function of the number of methyl groups present in the 5-position (steric hindrance to addition), and the yield may exceed that of the normal product formed by simple coupling.

[a] G. F. Hennion and T. F. Banigan, Jr., J. Am. Chem. Soc., 68, 1202 (1946).

[b] This thesis, pp. 82-83.

4. With one exception, diisopropylacetylene, all of the possible ethyl-, isopropyl- and tert-butyl-substituted acetylenic hydrocarbons have been synthesized.

Several routes are suggested for the direct or indirect introduction of an isopropyl group into acetylene.

a. A coupling reaction involving 2-bromo-3-hexyne and methyl magnesium bromide.

b. A coupling reaction involving silver or cuprous acetylide and an isopropyl halide.

c. Via dehydrohalogenation of the gem-dihalide of isopropyl isobutyl ketone.

d. By reductive dehalogenation of 2-chloro-2-methyl-4-alkyl-acetylenes with lithium aluminum anhydride.

5. A synthesis for L- and D-2-deuterobutane and for L-2,3-dideuterobutane is proposed.

The reduction of 2-tosyloxybutane with lithium aluminum hydride is expected to proceed with a Walden inversion.

If this method is combined with the method proposed by Fickett (Ph.D. Thesis, California Institute of Technology, 1950), L-2,3-dideuterobutane could be obtained.

6. A mechanism is proposed for the synthesis of thianaphthene, benzofuran and indole by cyclodehydrogenation.[a,b]

The mechanism is pictured as a nucleophilic attack by the "hetero" atom on the terminal carbon atom of an ortho vinyl group.

[a] H. Hoog, J. Verheus and F. J. Zuiderweg, Trans. Far. Soc., 35, 995 (1939).

[b] C. Hansch et. al., J. Am. Chem. Soc., 70, 1561, 2495 (1948); ibid, 71, 943 (1949); ibid, 73, 3080 (1951).

7. It is proposed that a study should be conducted concerning the coordination reaction between silver ion and a carbon-carbon multiple bond which has one side of

the point of unsaturation highly hindered. α-Pinene is suggested as a compound for possible study.

8. It is proposed that trans-glycols of cyclohexane could be induced to form cyclic acetals with acetone.

In molecular models, if 1,2-cyclohexanediol is placed in the chair form in which both hydroxyl groups are "equatorial"[a], the distance between the hydroxyl groups is identical with the distance between the same groups if they were cis (i.e., one "polar" and one "equatorial").

[a] B. Magasanik and E. Chargaff, J. Biol. Chem., 174, 173 (1948).

9. Since saponins in general augment growth of pea embryos[a,b], it is proposed that the action is physical rather than chemical. These do not act as precursors of any of the characteristic growth hormones.

[a] J. Balansard and F. Pellessier, Compt. Rend. Soc. Biol., 137, 454, 455, 461, 523, 763 (1943).

[b] This thesis, p. 163 ff.

10. In order to bring about a more-intimate contact with current literature (month by month) and to increase knowledge concerning active persons in the field of organic chemistry, and furthermore to aid in the ability of a student to express himself orally, I propose that a "current literature" seminar course be given quarterly

<u>for academic credit</u>.

With this plan, each student could be allotted one-half of one class period to present material of recent publication, which was of interest to him and/or which was connected with his research problem.