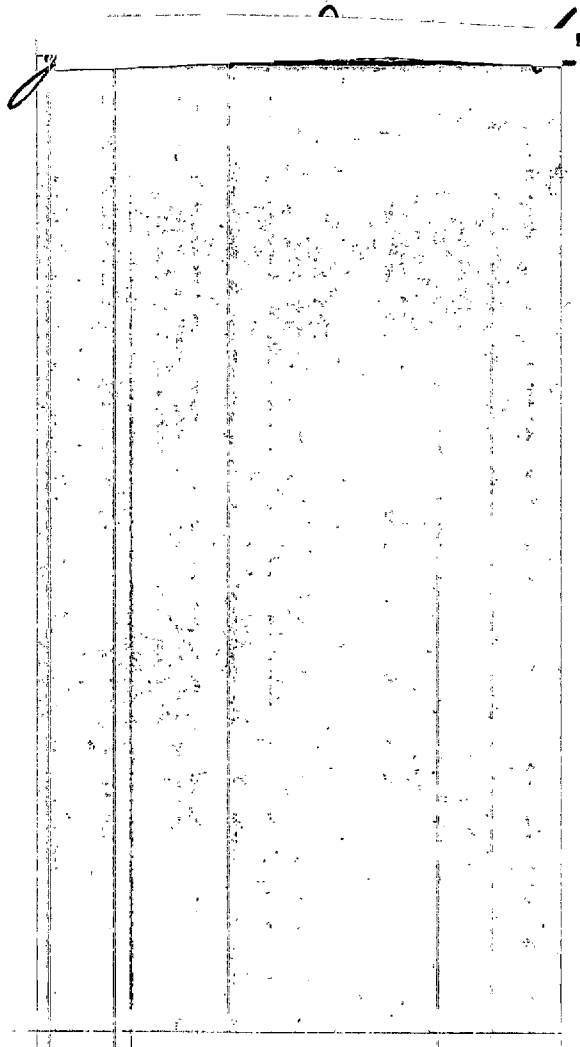


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THE SYNTHESSES OF n-OCTENOIC ACIDS

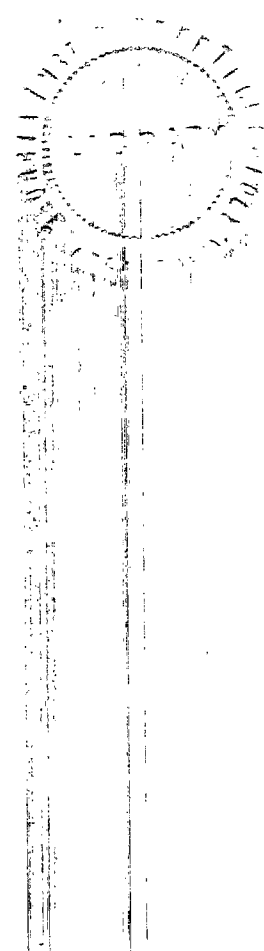
A THESIS

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the Faculty of the Graduate Division
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In Partial Fulfillment
of the Requirements for the Degree
Master of Science in Chemistry

By
James Henry Diamond

October 1956



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THE SYNTHESSES OF n-OCTENOIC ACIDS

Approved:

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Date Approved by Chairman:

Oct. 11, 1956

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ABSTRACT

The Syntheses of n-Octenoic Acids

There are eleven possible isomers of n-octenoic acid. The trans 2-, 3-, 5-; cis 2-, 5-; and 7-octenoic acids have previously been reported. The trans-4, trans-6, cis-3, cis-4, and cis-6 isomers are initially reported in this work. The previously known isomers, with the exception of cis-5-octenoic acid, were also prepared. When the refractive index, density, molecular refraction, freezing point, and melting point of the para-bromophenacyl ester of cis-trans isomers were compared, the trans isomer generally had the higher value. The infrared spectra of all trans compounds showed strong absorption at 10.35 microns. None of the cis compounds showed absorption at this wave length.

trans-Octenoic acids were prepared either directly or indirectly by the Knoevenagel condensation. The condensation of n-hexaldehyde with malonic acid in the presence of pyridine gave trans-2-octenoic acid. When triethanolamine was used instead of pyridine, trans-3-octenoic acid was formed. By utilization of this reaction with normal C₃, C₄, and C₅ aldehydes, ethylenic acids with less than eight carbon atoms were prepared. The chain length of these acids was increased, using known methods, until the desired octenoic acid was obtained.

Allyl chloride was used as the starting material in the preparation of 7-octenoic acid. The five additional carbon atoms required to give an octenoic acid were supplied as the result of two ethylene oxide additions, and one carbonation of a Grignard reagent.

The *cis*-octenoic acids were prepared by semihydrogenation of the corresponding acetylenic acid in the presence of W-5 Raney nickel. Syntheses of the requisite *n*-octynoic acids have previously been reported. However, the chromic acid oxidation of 3-octyn-1-ol was found to offer a shorter and more direct route to 3-octynoic acid than the previously described procedure.

A 25 per cent yield of 3-octyn-1-ol was obtained from ethylene oxide and 1-hexynylmagnesium bromide when standard procedures were used. A modification which consisted of replacing ether with benzene, as soon as the initial Grignard reagent was formed, increased the yield to 81 per cent. Claims for the general applicability of this modification must await further investigation.

Catalytic semihydrogenation of 2-octynoic acid was found to give predominantly *cis* olefinic acid, with some acetylenic and saturated acid as an impurity. The sodium-liquid ammonia semireduction of 2-octynoic acid gave a product with physical properties similar to octanoic acid.

New compounds reported include five previously mentioned *n*-octenoic acids, *trans*-5-heptene-1-ol, and 1-bromo-*trans*-5-heptene. A number of physical constants not previously reported have been determined for the octenoic acids and their intermediates.

CHAPTER I

PURPOSE

The purpose of this investigation was to prepare the eleven isomers of n-octenoic acid in a reasonably high state of purity and determine the physical properties of these compounds. Of these eleven isomers the trans 2-, 3-, 5-; cis 2-, 5-; and 7-octenoic acids have been reported in the literature. However, physical data is incomplete for some of the known n-octenoic acids and their precursors. This study proposed to prepare and obtain additional physical constants from these known compounds. Also the five n-octenoic acids, not previously reported, were prepared and characterized.

A secondary purpose was to study various methods of synthesizing unsaturated compounds containing less than nine carbon atoms. Some reactions of these compounds were studied.

CHAPTER II

INTRODUCTION

Saturated fatty acids ranging from C_4 to C_{26} have been identified as constituents of naturally occurring fats. However, unsaturated fatty acids with less than ten carbon atoms have not been observed in nature (1). Hence, unsaturated fatty acids with less than ten carbon atoms must be synthetically prepared.

Unsaturated fatty acids differ from saturated acids in several respects. As compared to the saturated acids, the double bond generally lowers the melting point and increases the acidity. The ethylenic linkage offers a reactive functional group which may undergo the various reactions characteristic of the double bond. With increased knowledge of polymerization techniques, some of the unsaturated acids described in this study possibly may find use as monomers or copolymers.

Methods of synthesizing unsaturated fatty acids.--Methods of synthesizing straight chain fatty acids have been reviewed by Gunstone (2). The synthetic problem may be divided into two parts: introduction of the unsaturated linkage, and positioning the $-COOH$ group at the desired location in the molecule.

With the exception of allyl chloride, very few ethylenic compounds suitable for further conversion to carboxylic acids are commercially available. 3-Pentenoic acid (3) has been prepared using 2-butenyl chloride (Shell Development Company) as the starting material. The acid was not

specifically assigned a cis or trans configuration, but the reported physical constants are similar to those reported for trans-3-pentenoic acid (4). Delaby and Lecomte (5) prepared unsaturated C₆-C₉ acids by starting with acrolein. Because of an intramolecular shift of the double bond in the sequence of reactions described by these authors, geometrical and positional isomers may have been formed.

The usual methods of producing ethylenic compounds such as dehydration of alcohols, dehalogenation of dihalides, and removal of hydrogen halide from monohalides could not be employed in this investigation since they cannot be considered unambiguous. Isomerization of the double bond may occur in the above reactions (6). Such methods must be excluded when pure cis and trans olefinic compounds are desired.

Other methods (2) of preparing olefinic acids, or unsaturated intermediates, were considered with respect to obtaining readily available starting materials and pure products. Of these, the Knoevenagel condensation seemed the most promising for preparing trans-ethylenic acids. The Knoevenagel reaction is the condensation of an aldehyde with malonic acid or diethylmalonate in the presence of an organic base, such as pyridine, to give a 2-olefinic acid. Linstead (7), in an investigation of the Knoevenagel condensation using propionaldehyde and *n*-butyraldehyde, found that with triethanolamine or dimethylaniline the condensation yielded the 3-olefinic acid exclusively. Linstead did not specifically assign either the cis or trans structure to the acids prepared by the Knoevenagel condensation. Recent investigations (8, 9, 10, 11) offer evidence that the Knoevenagel condensation yields the trans forms of 2- and 3-olefinic acids.

Newman and Wotiz (12) have reported the preparation of the six n-octynoic acids. It should be possible to convert these compounds to n-octenoic acids by partial hydrogenation. Semireduction by "chemical" methods such as sodium in liquid ammonia yields predominantly trans compounds (8, 13, 14, 15, 16). Metal-ammonia reductions have been successfully performed on acetylenic alcohols (17), carboxylic acids (8), and amines (18). However, the method failed to effect reduction of certain of the octadecynoic acids (8). A more widely used method of semireduction is catalytic hydrogenation. In contrast to "chemical" hydrogenation, catalytic hydrogenations yield predominantly cis olefins (13, 15, 16). This method has been used to prepare unsaturated acids (8, 19) and hydrocarbons (6) having a cis configuration.

Many naturally occurring olefinic compounds have a cis configuration. If one of these compounds of suitable chain length, and capable of being converted to a carboxylic acid were available, it might serve as a precursor to a cis-octenoic acid. In a review of geometrical isomerism (13), a number of reagents are listed, which may cause stereomutation of a cis compound to the generally more stable trans form. When this process (elaidinization) is attempted, cis-trans mixtures frequently result. The slight differences in physical properties of cis-trans isomers (particularly in the case of higher fatty acids) make clean separations exceedingly difficult.

In summary, there are two acceptable routes to trans olefinic acids: the Knoevenagel condensation and the sodium-liquid ammonia semireduction of acetylenic compounds. The Knoevenagel condensation gives a trans-2 or -3 olefinic acid in a reasonably high state of purity. Once

an acid having a trans double bond is formed, the chain length may be increased by utilizing sequences of known reactions until the desired octenoic acid is obtained. In the few reported (8) cases of partial reduction of acetylenic acids with sodium in liquid ammonia, a pure trans product was reported. In a preliminary experiment, reported in this thesis, 2-octynoic acid was reduced with sodium in liquid ammonia to give a product whose properties indicated a large amount of saturated material. In view of the uncertainty of the sodium-liquid ammonia reduction, and difficulty in preparing some of the octynoic acids, the Knoevenagel condensation seemed more promising for producing trans olefinic acids. The only attractive route to the cis-octenoic acids was catalytic semihydrogenation of the corresponding acetylenic acids.

CHAPTER III

EXPERIMENTAL

The Preparation of trans-2-Octenoic Acid (20, 21, 22, 23, 24)

Knoevenagel condensation.--To 52.1 grams (0.50 moles) of malonic acid in a one liter flask was added 84.6 grams (1.07 moles) of dry pyridine. After cooling to room temperature, 52.4 grams (0.52 moles) of freshly distilled n-hexaldehyde was slowly added to this mixture. The mixture was stirred until homogenous and allowed to stand at room temperature. The flask was shaken once every 24 hours. After standing 88 hours, the flask was heated eight hours on a steam bath.

The crude acid was obtained by treating the reaction mixture with cold 25 per cent sulfuric acid. Sufficient sulfuric acid was added to acidify all organic material. The aqueous layer was extracted three times with ether. Combined acid and ether extracts were heated on a steam bath to remove the ether. The acid was then converted to its sodium salt with a saturated sodium carbonate solution. Alkali insoluble material was removed and the aqueous solution extracted three times with ether to remove basic or neutral material. The sodium salt solution of the acid was acidified and extracted three times with ether. Magnesium sulfate was used to dry the acid and ether extracts. Ether was removed under reduced pressure and the acid distilled through column 1. A description of distilling columns may be found in Appendix I. Physical constants for trans-2-octenoic acid may be found in

Tables 3A, 3B, 3C, and 4. In addition to these tabulated values, Bourguet (24) reports: boiling point $143^{\circ}/15$ mm; n_D^{17} 1.461; d_4^{17} 0.944.

The sodium-liquid ammonia reduction of 2-octynoic acid.--Sodium 2-octynate was prepared by neutralizing 0.10 mole of 2-octynoic acid with methanolic sodium hydroxide to a phenolphthalein end point. Most of the methanol was removed by slight heating under vacuum. The residual salt was dried to a constant weight over sulfuric acid in a vacuum desiccator. A solution of 4.84 grams (0.25 gram atoms) of sodium in 300 ml. of liquid ammonia was prepared. To this solution, the 0.10 mole of sodium 2-octynate was added over a period of 30 minutes. Ten minutes after all the sodium salt had been added, the ammonia solution changed from dark blue to yellow. Stirring of the reaction mixture was continued an additional one and a half hours. Then 15 grams of ammonium chloride was added and stirring was continued an additional hour. The ammonia was allowed to evaporate by standing overnight. One hundred ml. of ether and one hundred ml. of water were added to the reaction mixture. The ether layer was discarded and the aqueous layer acidified with cold 35 per cent sulfuric acid. The liberated acid was taken up in three portions of methylene chloride. These extracts were dried, freed of solvent, and the residual oil distilled through column 3. Five fractions having the properties listed in Table 1 were obtained. The infrared spectra of the acid produced in the above manner did not show the characteristic trans absorption at 10.3 microns. Upon repetition of this experiment similar results were obtained.

TABLE 1

SODIUM-LIQUID AMMONIA REDUCTION OF 2-OCTYNOIC ACID

<u>Fraction</u>	<u>Boiling Point °C</u>	<u>Pressure mm</u>	<u>Refractive Index 20°C</u>
1	62-70	1.3	1.4340
2	76-82	1.2	1.4353
3	84-86	1.2	1.4452
4	75-82	0.7	1.4548
5	83-84	0.8	1.4550
<hr/>			
<u>n-Octanoic Acid</u> ¹	99	16	1.4278
<u>trans-2-Octenoic Acid</u> ²	100	1.1	1.4592
<u>2-Octynoic Acid</u> ²	101	1.2	1.4603

The Preparation of trans-3-Octenoic Acid

trans-3-Octenoic acid (5).--trans-3-Octenoic acid was prepared in a manner similar to that described by Linstead (25) for the preparation of trans-3-hexenoic acid. Freshly distilled n-hexaldehyde (1.25 moles) was added, with vigorous stirring, to a two liter flask containing 1.25 moles of triethanolamine and 1.25 moles malonic acid. Very little heat was evolved during addition of the aldehyde. Stirring was continued an additional 30 minutes. The clear, viscous, yellow liquid was shaken at least once a day for eight days. It was then heated eight hours on a steam bath.

¹Boiling point reported by Newman and Wotiz (12). Refractive index reported in present investigation.

²Physical properties reported in present investigation.

After acidifying with cold 25 per cent hydrochloric acid, the organic acid was extracted from the aqueous layer with three portions of ether. The crude acid and ether extracts were washed three times with water. After drying over magnesium sulfate, ether was removed under reduced pressure. The acid was distilled through column 1.

The Preparation of trans-4-Octenoic Acid

1-Pentanal.--1-Pentanol was oxidized to 1-pentanal in a manner similar to that of Kuhn and Grundmann (26). A two liter flask was fitted with a dropping funnel, mercury sealed stirrer, and a condenser set for downward distillation. 1-Pentanol (3.4 moles) was added to the flask and heated to boiling. An oxidizing solution of 1.15 moles of sodium dichromate dissolved in 270 grams of sulfuric acid and 600 ml. of water was added, with vigorous stirring, over a period of 75 minutes. Distillation of the reaction mixture was continued an additional 45 minutes. The organic layer of the distillate was dried over magnesium sulfate and distilled through column 1. Four different runs using a similar procedure gave yields of 18 to 21 per cent. Boiling point 99-103°; n_D^{20} 1.3948; 2,4-dinitrophenylhydrazone m.p. 98°, literature 98°.

trans-3-Heptenoic acid (9, 27).--In the manner described for trans-3-octenoic acid, trans-3-heptenoic acid was prepared by condensing 0.77 moles of 1-pentanal with 0.80 moles of malonic acid in the presence of 0.80 moles of triethanolamine. Two similar condensations gave yields of 16 and 18 per cent. Neutralization equivalent: calculated 128.2, found 129.9.

trans-3-Heptene-1-ol (17, 28).---In a typical (70) lithium aluminum hydride reduction 16.0 grams (0.42 moles) of lithium aluminum hydride (Metal Hydrides, Inc.) and 600 ml. of dry ether were placed in a two liter flask fitted with a dropping funnel, mercury sealed stirrer, and condenser. Calcium chloride drying tubes protected the condenser and dropping funnel from moisture. trans-3-Heptenoic acid, 41.5 grams (0.42 moles), dissolved in 400 ml. of dry ether, was added dropwise over a period of two hours, so as to produce gentle refluxing. The reaction mixture was stirred an additional 75 minutes after which it was decomposed, with cooling, by the addition of 250 ml. of 20 per cent sulfuric acid. Organic material was extracted with two 100 ml. portions of ether. The combined ethereal layers were dried over sodium sulfate, filtered, and ether removed by distillation. The crude alcohol was distilled through column 1. Physical constants for unsaturated alcohols are in Table 6.

1-Bromo-trans-3-heptene (17, 29).---The procedure of Crombie and Harper (30) for preparing 1-bromo-3-pentene from 3-pentene-1-ol was followed. Twenty-nine grams (0.25 moles) of trans-3-heptene-1-ol and 8.0 grams (0.10 moles) of dry pyridine were placed in a 100 ml. flask fitted with a stirrer, thermometer, and dropping funnel, and the mixture cooled in an ice bath. Then 32.5 grams (0.12 moles) of phosphorous tribromide was added over a period of three hours during which time the reaction mixture was kept at a temperature of 5° or less. The mixture was allowed to warm to room temperature by standing overnight after which the crude product was distilled from the reaction mixture under reduced pressure. When all the liquid had distilled, a bright orange residue foamed up in the dis-

tilling flask. The distillate was dissolved in ether, washed with three portions of ten per cent sodium carbonate and two portions of water, and dried over calcium chloride. After removing the ether, the crude bromide was distilled under reduced pressure through column 1. Physical constants for unsaturated bromides are in Table 7.

trans-4-Octenoic acid.--The Grignard reagent from 26.1 grams (0.15 moles) of 1-bromo-3-heptene was prepared in the usual manner, using a total of 110 ml. of ether. Dried carbon dioxide (from dry ice) was passed over the surface of the stirred Grignard reagent which was at 0°. Carbon dioxide was passed into the flask for six hours (31). The reaction mixture was decomposed with 50 ml. of water and 50 ml. of 18 per cent hydrochloric acid. After separating the ether layer from the aqueous layer, most of the ether was removed by distillation. The crude acid was purified by being converted to its sodium salt with ten per cent sodium carbonate solution. Basic or neutral material which did not dissolve in the sodium carbonate was discarded. The sodium salt solution was acidified with hydrochloric acid and extracted three times with ether. Combined acid and ether extracts were dried over magnesium sulfate. After removal of ether, the crude acid was distilled through column 1. A yield of 38 per cent was obtained.

The Preparation of trans-5-Octenoic Acid

trans-5-Octenoic acid was prepared as described by Howton and Davis (8).

trans-3-Hexenoic acid (25).--In the manner described for trans-3-octenoic acid, 2.35 moles of n-butyraldehyde was condensed with 2.34 moles of

malonic acid in the presence of 2.37 moles of triethanolamine. The crude acid was distilled through column 1. Melting point 12° ; reported (8). Melting point 14° .

trans-3-Hexene-1-ol (8).--Reduction of 1.87 moles of trans-3-hexenoic acid with 2.44 moles of lithium aluminum hydride afforded 1.59 moles of trans-3-hexene-1-ol, upon distillation through column 2. Melting point of alpha-naphthylurethan 70° .

1-Bromo-trans-3-hexene (8).--The procedure outlined in the preparation of 1-bromo-trans-3-heptene was followed. To a one liter flask was added 1.54 moles of trans-3-hexene-1-ol, 0.56 moles of pyridine, and 100 ml. of carbon tetrachloride as a solvent. The flask was cooled to 0° and phosphorous tribromide (0.63 moles) added, with stirring, over a period of four hours. The crude bromide was obtained as previously described and distilled through column 2.

Diethyl trans-3-hexenylmalonate (8).--In a typical malonic ester condensation (71), 0.99 gram atoms of sodium were dissolved in 500 ml. of absolute ethanol. To this solution was added 1.00 moles of freshly distilled diethyl malonate (boiling point $89^{\circ}/13$ mm). To the resulting solution was added 0.97 moles of 1-bromo-trans-3-hexene over a period of two hours. After refluxing two hours and standing overnight, the mixture had an orange color. No attempt was made to isolate the expected product of this reaction.

trans-3-Hexenylmalonic acid (8).--A solution of 2.05 moles potassium hydroxide in 120 grams of water was used to hydrolyze the crude ester.

After refluxing six hours, the reaction flask was fitted for downward distillation and one liter of steam volatile material collected. The residue remaining after distillation was acidified with hydrochloric acid and the crude acid removed by three ether extractions. No attempt was made to isolate a pure product.

trans-5-Octenoic acid.--Crude trans-3-hexenylmalonic acid was charged to a 500 ml. distilling flask and the system evacuated. The temperature of the flask was gradually increased and smooth evolution of carbon dioxide was evident. After decarboxylation was complete, the flask temperature increased rapidly and distillation began. After distillation was complete, the crude product was dried over calcium sulfate and charged to column 2. Yield (based on 1-bromo-trans-3-hexene) 61 per cent. Reported (8) yield 52 per cent; para-phenylphenacylate m.p. 56.5°.

The Preparation of trans-6-Octenoic Acid

trans-3-Pentenoic acid (3, 4, 25).--In a typical Knoevenagel condensation 5.20 moles of freshly distilled propionaldehyde was mixed with 5.20 moles of triethanolamine and 5.20 moles of malonic acid. The reactants were not stirred sufficiently to dissolve all the malonic acid. After standing two days a heavy white crystalline mass had formed which was assumed to be a salt of triethanolamine and malonic acid. After standing 3.5 days the mixture was heated 15 hours on a steam bath. The crystals melted readily and a gas was liberated, indicating evolution of carbon dioxide. After working up in the usual manner, a yield of only five per cent was obtained.

In an attempt to increase the yield, triethanolamine was purified by distilling under 0.5 mm pressure. Malonic acid was dried in a vacuum desiccator over phosphorous pentoxide for three days.

When 2.62 moles of freshly distilled propionaldehyde was mixed with 2.45 moles of purified triethanolamine and an equal amount of dried malonic acid, a yield of 13 per cent was obtained. The reactants were stirred immediately after mixing, until the mixture became homogenous. A larger (7.16 mole) run gave a slightly lower yield (10 per cent), due to less efficient stirring of the reactants. Reported (25), d^{20}_4 0.9852.

trans-3-Pentene-1-ol (32, 33, 34).--In a manner similar to that described for trans-3-heptenoic acid, trans-3-pentenoic acid was reduced to trans-3-pentene-1-ol. A total of 1.28 moles of acid was reduced with 1.71 moles of lithium aluminum hydride, giving 1.03 moles of trans-3-pentene-1-ol. Melting point of alpha-naphthylurethan 92-93°; reported (33) m.p. 93°.

1-Bromo-trans-3-pentene (30, 32).--In a manner previously described, trans-3-pentene-1-ol was converted to 1-bromo-trans-3-pentene. To 1.00 mole of trans-3-pentene-1-ol, 0.36 moles of dry pyridine, and 75 ml. of carbon tetrachloride was slowly added 0.41 mole of phosphorous tribromide. After distilling through column 1, 105 grams (0.71 moles) of 1-bromo-trans-3-pentene was obtained. Reported (4) d^{20}_4 1.2715.

trans-5-Heptene-1-ol.--The Grignard reagent from 0.70 moles of 1-bromo-trans-3-pentene prepared in the usual manner; a total of 500 ml. of dry ether being used. Ethylene oxide (Matheson Co.) was passed into a previously calibrated trap immersed in an ice bath. When the desired

amount of ethylene oxide had been collected, the trap was removed from the ice bath and connected to the flask containing the Grignard reagent. In this manner 47 ml. (0.94 moles) of ethylene oxide was passed over the stirred surface of the Grignard reagent. The reaction flask, fitted with a Dewar type condenser containing ice, was immersed in an ice bath. Very little reflux was observed when ethylene oxide was added. After standing overnight, 220 ml. of ether was distilled from the reaction mixture. Then 200 ml. of dry benzene was added. Distillation was continued until the effluent temperature reached 65°. The flask was then heated under reflux for 75 minutes. After cooling to room temperature, ice water, followed by cold 17 per cent hydrochloric acid, was added to the flask. This procedure was similar to those described by Huston and D'Arcy (35), and Thayer et al. (36). After separation from the aqueous layer, the crude alcohol was dried over magnesium sulfate. The solvent was removed and the alcohol distilled through column 1. Physical properties in addition to those reported in Table 6 are: d^{20} 0.8536; M_r 35.52, calculated 35.63; would not freeze after standing two hours at -73°; alpha-naphthylurethan m.p. 79.5-80°.

1-Bromo-trans-5-heptene.--The bromination was similar to those previously described. To 36.5 grams (0.32 moles) of trans-5-heptene-1-ol, 66 ml. of carbon tetrachloride, and 0.12 moles of pyridine, was added 0.15 moles of phosphorous tribromide. After working up in the usual manner and distilling through column 1, a yield of 31.8 grams was obtained.

trans-6-Octenoic acid.--The Grignard reagent from 30.1 grams (0.17 moles) of 1-bromo-trans-5-heptene was prepared in usual way. It was then

carbonated and the acid isolated as described in the preparation of trans-4-octenoic acid. The crude acid was charged to column 1 and distilled under reduced pressure, giving a yield of 52 per cent.

The Preparation of 7-Octenoic Acid

4-Pentene-1-ol (37, 38, 39).---In the first of two runs the procedure of Kharasch and Fuchs (37) was closely followed. The Grignard reagent of allyl chloride was prepared by dropping 3.51 moles of allyl chloride dissolved in 230 ml. of ether, into a stirred mixture of 3.88 grams atoms of magnesium and 770 ml. of ether. The flask was cooled in an ice bath before addition of allyl chloride. It appeared that allyl chloride was reacting with the magnesium. However, after approximately one fourth of the chloride had been added, a violent reaction occurred which resulted in some ether and product being lost. After the allyl chloride addition was complete, a white gray viscous slurry had formed. This Grignard reagent spontaneously burst into flame upon exposure to the atmosphere. Ethylene oxide (3.81 moles) was passed into the stirred and cooled Grignard reagent. After adding 500 ml. of benzene and distilling off ether until effluent temperature reached 50°, the flask was allowed to stand overnight. The mixture was worked up in the usual manner; a yield of 31 per cent being obtained upon distillation through column 1.

A second similar run was made using 4.01 moles of allyl chloride and a total of 1460 ml. of dry ether. The reaction between magnesium and allyl chloride was initiated at room temperature. Only after the reaction definitely had started was the ice bath used. Ethylene oxide was added and the reaction mixture treated as previously described. Drying over

sodium sulfate and distilling through column 1 gave a yield of 70 per cent. Melting point of alpha-naphthylurethan 61° ; reported (38) m.p. 62° .

1-Bromo-4-pentene.--In a manner described for previous brominations, 3.82 moles of 4-pentene-1-ol, 1.40 moles of pyridine, and 500 ml. ether were placed in a two liter flask. After cooling to 0° , 1.56 moles of phosphorous tribromide was added. The crude bromide was isolated and distilled through column 2.

6-Heptene-1-ol (40, 41).--The Grignard reagent from 2.76 moles of 1-bromo-5-pentene was prepared in the usual way. Ethylene oxide (3.02 moles) was added to the Grignard reagent and the mixture worked up in the usual manner. The crude alcohol was charged to column 2 and upon rectification a yield of 120 grams was obtained. Melting point of alpha-naphthylurethan 55° . Reported (41) d_4^{20} 0.8455.

1-Bromo-6-heptene (41).--To 1.02 moles of 6-heptene-1-ol, 0.37 moles of dry pyridine, and 200 ml. of dry ether, was added 0.42 moles of phosphorous tribromide. The reaction and purification were performed as in similar brominations.

7-Octenoic acid (19, 42).--The Grignard reagent from 0.73 moles of 1-bromo-6-heptene was prepared in the usual manner. It was then carbonated as described in the preparation of trans-4-octenoic acid. Purification of the crude acid was effected by conversion to its sodium salt with sodium carbonate solution. After reacidification and drying over anhydrous magnesium sulfate, the acid was charged to column 2. A yield of 37 per

cent was obtained. Reported (42): amide m.p. 75-76°. Taylor and Strong (19) report: boiling point 90-92°/1 mm; para-toluidide m.p. 56-57°.

The Preparation of cis-2-Octenoic Acid

2-Octynoic acid (43).--The Grignard reagent from 1.05 moles of ethyl bromide was prepared in the usual manner. To this Grignard reagent was slowly added 1.00 moles of 1-heptyne (Farchan Research Laboratory). After addition of 1-heptyne was complete, the mixture was refluxed two hours. Two hundred ml. of dry ether was added and carbon dioxide passed over the surface of the Grignard reagent as in previous carbonations. The crude acid was isolated, then distilled through column 2. Yield 58 per cent. Reported (43), M_r 39.89, calculated 38.68.

cis-2-Octenoic acid (24).--A 16.2 gram (0.12 mole) sample of 2-octynoic acid was catalytically semihydrogenated in the presence of five grams of an ethanolic paste of W-5 Raney nickel³ (44). The acid to be hydrogenated along with the catalyst and 100 ml. of benzene as a solvent was placed in a one liter reaction flask. Theoretical hydrogen uptake: 3.45 liters; actual hydrogen uptake 3.75 liters in 98 minutes. The apparatus shown in Figure 1 was used in this and all subsequent semihydrogenations. After removal of the catalyst by filtration, the benzene was removed under vacuum. The crude acid, which had a light green color due to dissolved nickel, was charged to column 3. Upon rectification a yield of 61 per cent was obtained. Reported (24) constants: M_r 41.12, theory 40.20.

³The Raney nickel had aged five months at room temperature.

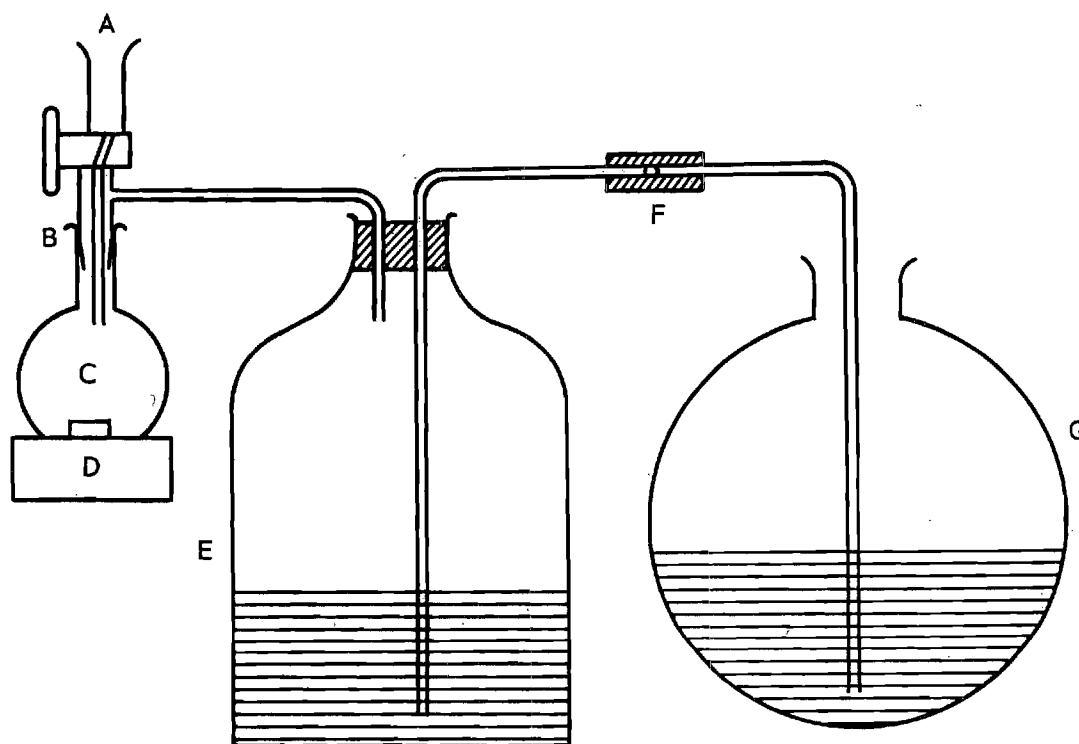


Figure 1

Hydrogenation Apparatus

Hydrogen, catalyst, and material to be hydrogenated are introduced into the system through the stopcock below funnel (A). A standard taper glass joint (B) connects the stopcock and funnel to a one liter reaction flask (C). Stirring is provided by a magnetic stirrer (D). A seven liter graduated bottle (E) contains hydrogen which is absorbed by the reactants in flask (C). Two feet of rubber tubing (F) connect the hydrogen reservoir (E) with a five liter flask (G). Flask (G) contains water which flows into bottle (E) during the course of a hydrogenation. By adjusting the height of flask (G), hydrogen pressure can be maintained at slightly greater than atmospheric pressure. The volume of hydrogen absorbed is determined by measuring the volume of water in bottle (E) at the beginning and at the end of the reaction.

The Preparation of cis-3-Octenoic Acid

1-Hexyne.--1-Hexyne (45) was prepared by the reaction of sodium acetylide (6 moles) with n-butyl bromide (6 moles) in liquid ammonia.

2-Heptyn-1-ol (12).--The Grignard reagent from 1.70 moles of ethyl bromide was prepared in 740 ml. of ether. To the stirred Grignard reagent 1.53 moles of 1-hexyne was slowly added. After refluxing four hours, the flask was cooled and gaseous formaldehyde passed over the surface of the mixture until there was no further evidence of reaction. The crude alcohol was obtained by adding ice water, then cold 20 per cent sulfuric acid to the flask. The ethereal layer was separated and dried over sodium sulfate. After removing solvent and distilling through column 2, a yield of 116 grams was obtained.

1-Bromo-2-heptyne (12).--To a solution of 116 grams (1.03 moles) of 2-heptyn-1-ol and 1.3 grams of pyridine in 300 ml. of dry ether, 106 grams (0.39 moles) of phosphorous tribromide was added at a rate sufficient to maintain refluxing. After heating and stirring two additional hours, the mixture was cooled and poured onto ice, and the organic material was extracted with ether. These extracts were washed with saturated sodium carbonate and sodium chloride, then dried over calcium chloride. The crude bromide was charged to column 2 and distilled. When this reaction was repeated at ice bath temperature, a 65 per cent yield was obtained.

1-Cyano-2-heptyne (12).--A mixture of 0.68 moles of 1-bromo-2-heptyne, 0.86 moles of dry cuprous cyanide, and 100 ml. of redistilled para-xylene was stirred and heated in an oil bath at 160°. When the temperature inside the flask reached 155°, a vigorous reaction occurred. If the

temperature dropped below 155° the reaction ceased. The spontaneous exothermic reaction Newman and Wotiz (12) report could not be duplicated. The oil bath was maintained at 160-163° for two hours. At this time there was no further evidence of reaction. After cooling, the mixture was extracted with benzene; all solids being removed by filtration. On distillation through column 2 there was obtained 51.9 grams of the nitrile. The freshly distilled nitrile was colorless, but after standing one day turned brown. Maintaining a temperature sufficiently high to cause a reaction to occur is most important.

3-Octynoic acid (12).--A stream of gaseous hydrogen chloride was passed into a solution of 0.43 moles of 1-cyano-2-heptyne in 110 ml. of methanol and 10 ml. of water until it refluxed and the temperature later dropped to 30°. The precipitated ammonium chloride was collected and the filtrate washed with 10 per cent sodium carbonate. The filtrate was concentrated by removing methanol under reduced pressure. The crude ester was hydrolyzed with 40 grams of potassium hydroxide in 90 ml. of methanol. Heat was evolved when the alkali was added. After refluxing five hours, the mixture was cooled and acidified with dilute sulfuric acid. The crude acid was removed and the aqueous layer extracted with ether. After concentration of the combined acid and ether extracts, crude acid was separated from neutral material by conversion to its sodium salt. Reacidification, drying over magnesium sulfate, and distilling through column 2 gave a yield of 12 per cent. Newman and Wotiz reported (12) a yield of 74 per cent and boiling point 120-130°/6 mm. Upon repetition of this synthesis with similar quantities, a 1.2 gram sample having n_D^{20} of 1.4543 was the purest material obtained. 3-Octynoic acid from the

TABLE 2

PROPERTIES OF 3-OCTYNOIC ACID PREPARED BY
METHOD OF NEWMAN AND WOTIZ

<u>Fraction</u>	<u>Weight Grams</u>	<u>Boiling Point °C</u>	<u>Pressure mm</u>	<u>n²⁰_D</u>
1	1.51	105	2	1.4542
2	1.38	108	1.5	1.4552
3	1.31	112	0.7	1.4576
4	2.99	135	0.8	1.4643
—	—	—	—	—
3-Octynoic ⁴ Acid	--	110	2	1.4577 (25°)

syntheses reported here had an ester like odor. The hydrolysis procedure of Newman and Wotiz could not be duplicated.

cis-3-Octenoic acid.--A 13.4 gram sample of impure 3-octynoic acid was partially catalytically hydrogenated. Theoretical hydrogen uptake to form olefinic compound: 2.8 liters; actual uptake 1.1 liters. A 2.6 gram sample with n²⁰_D 1.4461, boiling point 103°/0.7 mm; neutralization equivalent 169, was the best fraction obtained after distillation through column 3. Because of the impurity of this sample, further characterization was not warranted.

3-Octyn-1-ol (12, 45, 47), Run I.--The Grignard reagent was prepared from 1.50 moles of 1-hexyne. Ethylene oxide (1.65 moles) was added to this Grignard reagent in the manner described for trans-5-heptene-1-ol. The

⁴Physical constants reported by Newman and Wotiz (12).

crude alcohol was distilled through column 2, giving a yield of 25 per cent.

3-Octyn-1-ol, Run II.--In an attempt to prepare 3-octyn-1-ol in a higher yield, the following procedure was used.

A two liter flask was fitted with a dropping funnel, mercury seal stirrer, and an efficient condenser. The Grignard reagent from 2.51 moles of ethyl bromide, 2.66 gram atoms of magnesium, and 700 ml. of ether was prepared in the usual manner. The Grignard reagent was stirred and gently refluxed for 30 minutes. After cooling, 700 ml. of dry thiophene free benzene was added, and the condenser set for downward distillation. The flask was heated gently with stirring and a total of 700 ml. of solvent was distilled. The flask temperature was 86° and the distillate had a benzene odor at the end of the distillation. Any ether remaining with the Grignard reagent must have been held by a chemical attraction because this temperature is sufficient to cause ether to distill. At this point the Grignard reagent had a characteristic black color and very little suspended material.

The Grignard reagent was cooled in a water bath at approximately 10°. A solution of 2.00 moles of 1-hexyne in 35 ml. of benzene was added to the ethyl magnesium bromide over a period of 95 minutes. Very little reflux occurred, but a constant evolution of a gas (ethane) could be detected. The cooling bath was replaced by a heating mantle and refluxing was continued for five hours. At this point the mixture was a smooth white-gray suspension. It slowly settled upon standing, leaving a black, clear supernatant liquid. Ethylene oxide (2.82 moles) was passed onto the stirred surface of the Grignard reagent, which was

cooled in an ice bath. After two moles of ethylene oxide had been added, the mixture became gelatinous and stirring was less efficient. The mixture was allowed to warm to room temperature by standing overnight. The reaction mixture was then refluxed four hours, after which 600 ml. of solvent was distilled, with stirring, during a three hour period. After cooling to room temperature, ice water, then cold 20 per cent sulfuric acid was added. The organic layer was separated, dried over magnesium sulfate and distilled through column 2.

3-Octynoic acid.--Procedures similar to those used in oxidizing acetylenic alcohols were used (48, 49). An oxidizing solution was prepared by dissolving 1.23 moles of chromium trioxide in 370 grams of concentrated sulfuric acid and diluting with water to give 770 ml. of solution.

To 110 grams (0.86 moles) of 3 octyn-1-ol was added 160 ml. of water and 350 ml. of acetone. Three hundred ml. of acetone were required to give a homogenous solution. This solution was placed in a five liter flask fitted with a thermometer, dropping funnel, and a mercury sealed stirrer. The flask was placed in an ice bath and the oxidizing solution added over a period of four hours, during which time the temperature was kept at 5° or less. Stirring was continued an additional four hours at ice bath temperature. Organic material was extracted from the reaction mixture with ether. The ether was removed under reduced pressure and the crude acid purified by conversion to its sodium salt. Reacidification and distillation through column 2 gave a yield of 21 per cent. 3-Octynoic acid was colorless when freshly distilled, but turned yellow upon standing overnight. The yield of acid was only 2.3 per cent when water alone was used as a solvent, other conditions being unchanged.

cis-3-Octenoic acid.--A 21.5 gram (0.15 mole) sample of 3-octynoic acid was partially hydrogenated in the presence of 16 grams of an ethanolic paste of W-5 Raney nickel. Seventy ml. of benzene was used as a solvent. The theoretical hydrogen uptake was 5.05 liters; actually took up 5.04 liters in 131 minutes. The acid was isolated in the usual manner and charged to column 3. A yield of 82 per cent was obtained upon rectification.

The Preparation of cis-4-Octenoic Acid

2-Hexyn-1-ol (12).--The Grignard reagent from 1.60 moles of ethyl bromide was prepared in the usual manner. To it was added 1.50 moles of 1-pentyne (Farchan Research Laboratory). After refluxing five hours, the mixture was cooled and gaseous formaldehyde passed onto the stirred surface of the Grignard reagent until no further reaction was evident. After working up in the usual manner, a yield of 61 grams was obtained upon distillation through column 2.

1-Bromo-2-hexyne.--In a manner analogous to that used in the preparation of 1-bromo-2-heptyne, 0.62 moles of 2-hexyn-1-ol and one gram of pyridine were treated with 0.23 moles of phosphorous tribromide. After distillation through column 2, a yield of 65 grams was obtained.

4-Octynoic acid.--In a malonic ester synthesis similar to that described for trans-5-octenoic acid, 0.40 moles of 1-bromo-2-hexyne was added to an ethanolic solution of the sodium salt of diethyl malonate. No intermediate products were isolated. After hydrolysis and decarboxylation, the crude product was distilled. Twenty grams of crude acid were obtained. After three crystallizations from carbon tetrachloride a yield of 13.5 grams (24 per cent) pure acid was obtained.

cis-4-Octenoic acid.--4-Octynoic acid (0.096 moles) from the previous reaction was partially catalytically hydrogenated, using the same procedure as in previous hydrogenations. Theoretical hydrogen uptake: 2.85 liters; actual uptake, 2.98 liters in 48 minutes. After removal of solvent, the acid was charged to column 3. A 69⁵ per cent yield was obtained.

The Preparation of cis-6-Octenoic Acid

1-Chloro-4-iodobutane.--A five liter flask was fitted with a mercury sealed stirrer and condenser. Sodium iodide (6.50 moles) which had been dried overnight at 105° was placed in the flask. Dry acetone (2.9 liters) was added to the flask and after stirring for 30 minutes most of the sodium iodide had dissolved. Then 1,4-dichlorobutane⁵ (7.27 moles) was added. The mixture was stirred and refluxed 17 hours. After cooling to room temperature and removal of the solids by filtration, the acetone was distilled off, and the crude product was washed with sodium thio-sulfate, then water. After drying with calcium chloride, the crude product was distilled under reduced pressure. No attempt was made to isolate a pure product as impurities could be removed when subsequent compounds were purified. The ease with which 1-chloro-4-iodobutane decomposes makes purification difficult. A 77 per cent yield of product with boiling point 40-55°/1.2 mm. was obtained.

1-Chloro-5-hexyne (12).--The procedures described in "Organic Syntheses"¹⁷ (46) and by Vaughn et al. (50) for the preparation and use of sodium acetylide in liquid ammonia were followed. In all syntheses employing

⁵Gift from Electrochemicals Division, E.I. duPont de Nemours, Co.

liquid ammonia the reaction flask was cooled in a dry ice-acetone bath. Also a dry ice-acetone filled Dewar type condenser was attached to the flask.

Sodium acetylide was prepared by adding 3.39 gram atoms of sodium in small strips to 3.5 liters of liquid ammonia. While sodium was being added, acetylene was bubbled through the liquid ammonia solution. If a blue color developed in the liquid ammonia, addition of sodium was discontinued until the blue color was discharged. After all the sodium had been added, acetylene was bubbled through the stirred solution for 15 minutes. To this mixture was added 676 grams (3.10 moles) of 1-chloro-4-iodobutane during four hours. Stirring was continued 30 additional minutes, and the reaction mixture allowed to come to room temperature by standing overnight. One liter of ice water was slowly added to the reaction mixture. The organic layer was taken into ether, washed with dilute acid, then water, and dried over calcium chloride. The ether was removed under vacuum and rectification through column 2 gave a yield of 253 grams.

1-Chloro-5-heptyne (12).--To a solution of 255 grams (2.18 moles) of 1-chloro-5-hexyne in 2.5 liters of liquid ammonia was added 2.28 moles of sodium amide (Farchan). After stirring one hour, 340 grams (2.40 moles) of methyl iodide was added over a period of two and one half hours. After stirring an additional two hours, the mixture stood overnight. The crude chloride was worked up in a manner similar to 1-chloro-5-hexyne. Distillation through column 2 gave a yield of 129 grams.

1-Iodo-5-heptyne (12).--Dry sodium iodide (2.51 moles) was dissolved in 1.6 liters of dry acetone. To this solution was added 306 grams (2.31

moles) of 1-chloro-5-heptyne. After refluxing and stirring for 20 hours, the mixture was cooled and the salt removed by filtration. Five hundred ml. of acetone was removed by distillation and the remaining orange liquid used in the next reaction without further treatment.

1-Cyano-5-heptyne (12).--The product of the previous reaction consisting of 2.31 moles (theoretical yield) of 1-iodo-5-heptyne in 1.1 liters of acetone was diluted with 400 ml. of water. To this solution was added 221 grams (3.39 moles) of potassium cyanide (Baker's C.P.). The reaction mixture was stirred and refluxed 45 hours. At this time the flask was fitted for downward distillation and 1.2 liters of mixed solvent distilled. The yellow organic layer was removed and the aqueous layer extracted three times with ether. Combined organic material was dried over calcium sulfate. The ether was removed under vacuum and crude nitrile distilled through column 2.

6-Octynoic acid (12).--To a two liter flask with a mercury sealed stirrer and efficient condenser was added 161 grams (1.33 moles) of 1-cyano-5-heptyne. A solution of 1.54 moles of potassium hydroxide in 774 ml. of water was then added and the mixture refluxed with stirring for 56 hours. At this time the evolution of ammonia had ceased. The alkaline solution was first extracted with ether to remove neutral or alkaline organic material. Cold 18 per cent hydrochloric acid was used to acidify the aqueous layer. The resulting organic layer was separated and the aqueous layer extracted three times with ether. Crude acid and ether extracts were dried over magnesium sulfate. After most of the ether had been evaporated under reduced pressure, a slurry of crystals remained. This

crop of crystals was collected by filtration. The mother liquor was chilled and another crop of crystals removed by filtration. This procedure was repeated three additional times. After drying over calcium chloride in a vacuum desiccator, the first crop of crystals had m.p. 43.5-44°; while the last crop had m.p. 42°. A yield of 142 grams or 76 per cent was obtained.

cis-6-Octenoic acid.--The same apparatus and procedures as in previous catalytic semihydrogenations was used. A 0.143 mole sample of 6-octynoic acid along with 13 grams of an ethanolic paste of W-5 Raney nickel and 100 ml. of benzene was introduced into the reaction flask. The theoretical hydrogen uptake was 4.35 liters. Actually the sample took up 4.41 liters in 56 minutes before a break in the rate of hydrogenation occurred. Benzene was removed and the acid distilled through column 3. The hydrogenation gave a yield of 71 per cent.

Ozonization of trans-4 and trans-6-Octenoic Acids

A sample of six grams of trans-4-octenoic acid was dissolved in 80 ml. of methylene chloride and ozonized. The ozone was generated in apparatus similar to that described by Robinson (51). The ozonide was decomposed and oxidized as described by Henne and Hill (52), with a mixture of 10 grams of concentrated sulfuric acid, 12 ml. of 30 per cent hydrogen peroxide and 30 ml. of water. The volatile acid was separated by steam distillation and identified as butyric acid by its characteristic odor. The dibasic acid was crystallized from water and identified as succinic acid. Melting point 185°, literature 185°; para-bromophenacyl ester m.p. 98-99°, literature 99-100°; para-nitrobenzyl ester m.p. 88-89°, literature 88°.

In a similar manner trans-6-octenoic acid was ozonized. Acetic acid was identified by the method of Feigl (53). Acetic acid was also identified by conversion to the para-bromophenacyl ester which melted at 82-83°, literature 85°. The dibasic acid was crystallized three times from water and once from ether. It was identified as adipic acid on the basis of the following properties: melting point 149-150°, literature 151-153°; para-bromophenacyl ester m.p. 154°, literature 154°.

TABLE 3A

PHYSICAL PROPERTIES OF n-OCTENOIC ACIDS

Acid	Refractive Index (t°C)		Density (t°C)		Boiling Point °C (Pressure mm)	
	Found	Literature	Found	Literature	Found	Literature
<u>n</u> -Octanoic ^a	1.4278 (20°)	1.4285 (20°)	0.9098 (20°)	0.910 (20°)	--	238 (760 mm)
trans-2-Octenoic	1.4592 (20°)	1.4587 (20°)	0.9425 (20°)	0.9807 ^b (20°)	100 (1.1 mm)	154 (22 mm)
cis-2-Octenoic	1.4441 (20°)	1.456 (15°)	0.9234 (20°)	0.940 (15°)	89 (0.9 mm)	127 (15 mm)
trans-3-Octenoic	1.4452 (20°)	1.4456 (22°)	0.9378 (20°)	0.942 (20°)	92 (1.4 mm)	142 (19 mm)
cis-3-Octenoic	1.4433 (20°)	--	0.9352 (20°)	--	96 (0.5 mm)	--
trans-4-Octenoic	1.4441 (20°)	--	0.9313 (20°)	--	93 (1.5 mm)	--
cis-4-Octenoic	1.4417 (20°)	--	0.9301 (20°)	--	96 (0.8 mm)	--
trans-5-Octenoic	1.4452 (20°)	1.4431 (24°)	0.9345 (20°)	0.9339 (25°)	95 (1.3 mm)	86 (0.2 mm)
cis-5-Octenoic	--	1.4432 (20°)	--	0.9604 ^b (24°)	--	88 (0.4 mm)
trans-6-Octenoic	1.4454 (20°)	--	0.9422 (20°)	--	90 (1.2 mm)	--
cis-6-Octenoic	1.4441 (20°)	--	0.9378 (20°)	--	88 (0.8 mm)	--
7-Octenoic	1.4424 (20°)	1.4430 (20°)	0.9358 (20°)	0.9348 (20°)	84 (0.7 mm)	235 (706 mm)

^aEastman Kodak (white label) n-octanoic acid was used without further purification. This acid was a colorless oil having a slight fatty acid odor.

^bThis value is obviously too large.

TABLE 3B

PHYSICAL PROPERTIES OF n-OCTENOIC ACIDS

<u>Acid</u>	<u>Melting Point °C</u>		<u>Literature Reference</u>	<u>p-Bromophenacyl Ester M. P. °C</u>
	<u>Found^c</u>	<u>Literature</u>		
<u>n</u> -Octanoic	16	16	(58)	67
<u>trans</u> -2-Octenoic	7	5-6	(23)	93
<u>cis</u> -2-Octenoic	-6	--	(24)	67
<u>trans</u> -3-Octenoic	1	--	(5)	69.5
<u>cis</u> -3-Octenoic	-25	--	--	65
<u>trans</u> -4-Octenoic	-4	--	--	78
<u>cis</u> -4-Octenoic	-35	--	--	43
<u>trans</u> -5-Octenoic	-10	-9	(8)	55.5
<u>cis</u> -5-Octenoic ^d	--	--	(8)	48
<u>trans</u> -6-Octenoic	6	--	--	68.5
<u>cis</u> -6-Octenoic	-17	--	--	50
7-Octenoic	-25	--	(42)	60.5

^cMelting points below 0° were usually over a two degree range, the upper limit being that recorded.

^dNot prepared in this investigation

TABLE 3C

PHYSICAL PROPERTIES OF n-OCTENOIC ACIDS

<u>Acid</u>	<u>Molecular Refraction Found</u>	<u>Exaltation</u>	<u>Neutralization Equivalent</u>	<u>Hydrogen Uptake Moles</u>
<u>n</u> -Octenoic	40.76 ^e	0.01	144.8 ^f	--
trans-2-Octenoic	41.26 ^g	1.00	141.9 ^h	1.02 ⁱ
cis-2-Octenoic	40.91	0.65	142.6	0.91
trans-3-Octenoic	40.37	0.11	145.4	0.93
cis-3-Octenoic	40.33	0.07	140.7	0.95
trans-4-Octenoic	40.57	0.31	144.7	0.97
cis-4-Octenoic	40.43	0.17	144.3	0.81
trans-5-Octenoic	40.51	0.25	143.0	0.91
cis-5-Octenoic	39.23	-1.03	--	--
trans-6-Octenoic	40.20	-0.06	144.2	0.92
cis-6-Octenoic	40.29	0.02	143.0	0.93
7-Octenoic	40.24	-0.03	142.1	0.97

^eCalculated molecular refraction of n-octanoic acid 40.75.

^fCalculated neutralization equivalent of n-octanoic acid 144.2.

^gCalculated molecular refraction of n-octenoic acid 40.26.

^hCalculated neutralization equivalent of n-octenoic acid 142.2.

ⁱTheoretical hydrogen uptake 1.00 mole.

TABLE 4

ACIDS PREPARED BY THE KNOEVENAGEL CONDENSATION

Acid	Per Cent Yield Found Literature		Physical Properties of Acid Formed						
			Refractive Index (t°C)		Boiling Point °C (Pressure mm)		p-Bromophenacyl Ester M. P. °C		Literature Reference
			Found	Literature	Found	Literature	Found	Literature	
trans-3-Pentenoic	13	32	1.4357 (20°)	1.4354 (20°)	54 (1 mm)	93 (14 mm)	90	88	(25)
trans-3-Hexenoic	35	31	1.4397 (20°)	1.4391 (20°)	83 (2.9 mm)	110 (15 mm)	80	82	(8)
trans-3-Heptenoic	18	34	1.4410 (20°)	1.4420 (20°)	77 (0.5 mm)	85 (1 mm)	83	--	(9)
trans-3-Octenoic	35	--	1.4452 (20°)	1.4456 (22°)	92 (1.4 mm)	142 (19 mm)	69	--	(5)
trans-2-Octenoic	28	68	1.4592 (20°)	1.4587 (20°)	100 (1.1 mm)	154 (22 mm)	93	93	(23)

TABLE 5

PHYSICAL PROPERTIES OF ACETYLENIC ACIDS

Acid	Boiling Point °C (Pressure mm)		Melting Point °C		Refractive Index (t°C)		p-Bromophenacyl Ester M. P. °C		Literature Reference
	Found	Literature	Found	Literature	Found	Literature	Found	Literature	
2-Octynoic	101 (1.2 mm)	133 (10 mm)	--	5	1.4603 (20°)	1.4595 (20°)	--	--	(43)
3-Octynoic	85 (0.4 mm)	110 (2 mm)	19	18	1.4573 (20°)	1.4577 (25°)	105	--	(12)
4-Octynoic	--	121 (2 mm)	49	49	--	--	--	--	(12)
5-Octynoic ⁶	--	96 (0.3 mm)	--	8	--	1.4555 (25°)	--	64	(8)
6-Octynoic	--	116 (2 mm)	44	37	--	--	69	--	(12)

⁶Not prepared in this investigation.

TABLE 6

PHYSICAL PROPERTIES OF UNSATURATED ALCOHOLS

Alcohol	Per Cent Yield		Synthetic Method	Boiling Point °C (Pressure mm)		Refractive Index (t°C)		Literature Reference
	Found	Literature		Found	Literature	Found	Literature	
trans-3-Pentene-1-ol	81	--	Reduction of the corresponding carboxylic acid with LiAlH_4	47 (13 mm)	137 (760 mm)	1.4334 (20°)	1.4340 (20°)	(33)
trans-3-Hexene-1-ol	85	81		58 (11 mm)	53 (9 mm)	1.4389 (20°)	1.4393 (20°)	(8)
trans-3-Heptene-1-ol	83	--		66 (9 mm)	171 (760 mm)	1.4393 (20°)	1.4415 (20°)	(17)
4-Pentene-1-ol	70	60	Addition of ethylene oxide to a Grignard reagent	62 (30 mm)	76 (60 mm)	1.4300 (20°)	1.4299 (20°)	(37)
trans-5-Heptene-1-ol	49	--		77 (11 mm)	--	1.4437 (20°)	--	--
6-Heptene-1-ol	38	--		54 (2.3 mm)	105 (20 mm)	1.4395 (20°)	1.4403 (20°)	(41)
3-Octyn-1-ol	81	40		87 (9 mm)	97 (15 mm)	1.4541 (20°)	1.4542 (25°)	(47)
2-Hexyn-1-ol	41	71	Addition of HCHO to a Grignard reagent	76 (18 mm)	88 (58 mm)	1.4521 (20°)	1.4539 (17°)	(12)
2-Heptyn-1-ol	68	77		74 (6.0 mm)	98 (28 mm)	1.4544 (20°)	1.4523 (25°)	(12)

TABLE 7

PHYSICAL PROPERTIES OF BROMIDES FORMED BY THE REACTION OF PHOSPHOROUS TRIBROMIDE WITH ALCOHOLS

Bromide	Moles Alcohol per Mole PBr ₃	Solvent	Per Cent Yield		Boiling Point °C (Pressure mm)		Refractive Index (t°C)		Literature Reference
			Found	Literature	Found	Literature	Found	Literature	
1-Bromo-4-pentene	2.44	ether	72	67	124 (740 mm)	126 (760 mm)	1.4652 (20°)	1.4632 (20°)	(37)
1-Bromo-trans-3-pentene	2.41	CCl ₄	71	60	80 (152 mm)	122 (621 mm)	1.4686 (20°)	1.4695 (20°)	(4)
1-Bromo-trans-3-hexene	2.46	CCl ₄	63	41	65 (36 mm)	72 (44 mm)	1.4687 (20°)	1.4671 (24°)	(8)
1-Bromo-trans-3-heptene	2.08	none	59	58	66 (20 mm)	60 (12 mm)	1.4687 (20°)	1.4641 (25°)	(17)
1-Bromo-trans-5-heptene	2.12	CCl ₄	56	--	85 (34 mm)	--	1.4691 (20°)	--	--
1-Bromo-6-heptene	2.64	ether	71	58	73 (19 mm)	78 (20 mm)	1.4662 (20°)	--	(41)
1-Bromo-2-hexyne	2.73	ether	65	63	73 (26 mm)	98 (80 mm)	1.4901 (20°)	1.4884 (25°)	(12)
1-Bromo-2-heptyne	2.64	ether	66	72	89 (26 mm)	84 (20 mm)	1.4900 (20°)	1.4878 (25°)	(12)

TABLE 8

MISCELLANEOUS ACETYLENIC COMPOUNDS

<u>Compound</u>	<u>Per Cent Yield</u>		<u>Boiling Point °C</u> (<u>Pressure mm</u>)		<u>Refractive Index</u> (<u>t°C</u>)		<u>Literature Reference</u>
	<u>Found</u>	<u>Literature</u>	<u>Found</u>	<u>Literature</u>	<u>Found</u>	<u>Literature</u>	
1-Hexyne	63	73	72 (738 mm)	72 (740 mm)	1.3992 (20°)	1.3988 (20°)	(45)
1-Chloro-5-hexyne	70	74	144 (737 mm)	144 (760 mm)	1.4500 (20°)	--	(12)
1-Chloro-5-heptyne	43	38	82 (28 mm)	175 (760 mm)	1.4600 (20°)	1.4599 (25°)	(12)
1-Cyano-2-heptyne	67	92	81 (6 mm)	124 (56 mm)	1.4468 (20°)	1.4475 (25°)	(12)
1-Cyano-5-heptyne	57	75	60 (1.0 mm)	79 (2 mm)	1.4550 (20°)	1.4530 (25°)	(12)

CHAPTER IV

DISCUSSION

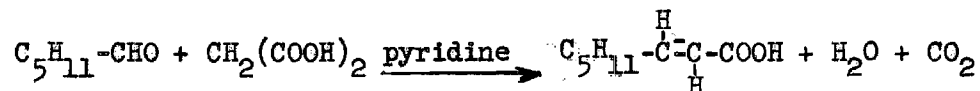
Discussion of trans-Octenoic Acids

General.--As stated in the introduction, the trans-octenoic acids were prepared through the Knoevenagel condensation. The trans-2 and -3 octenoic acids were prepared by condensing malonic acid with hexaldehyde in the presence of pyridine or triethanolamine, respectively. Other trans-octenoic acids were prepared by first forming a trans-3 acid by a Knoevenagel condensation, then reducing the acid to an alcohol with lithium aluminum hydride. The alcohol was treated with phosphorous tribromide, giving the corresponding bromide. The bromide was converted to a Grignard reagent, which was then treated in one of two ways: first, if it was desired to increase the chain length by one carbon atom, the Grignard reagent was carbonated to give a carboxylic acid; second, if it was necessary to increase the chain length by two carbon atoms, ethylene oxide was added to the Grignard reagent. The alcohol obtained thusly could be brominated, and the Grignard reagent from the bromide could be carbonated to yield a carboxylic acid.

Evidence that the acids produced by a Knoevenagel condensation, as well as the alcohols and bromides obtained from these acids, have a trans configuration is supported by the strong infrared absorption of these compounds in the 10.3 micron region.

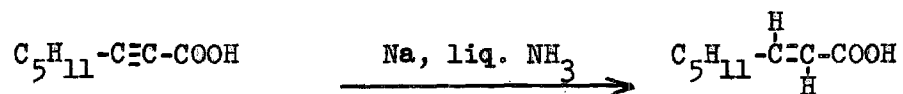
Ozonization of acids.--trans-Octenoic acids which had previously been reported were not ozonized. Since trans-4 and trans-6 octenoic acids were new compounds, they were ozonized.

trans-2-Octenoic Acid



trans-2-Octenoic acid was prepared in a typical Knoevenagel condensation. This acid was first reported by Bourguel (24) in 1929, who prepared cis-2-octenoic acid by catalytic semihydrogenation of 2-octynoic acid. Stereomutation of the cis acid was induced by exposing a quartz tube containing the cis acid and iodine, heated to 100°, to sunlight. Bourguel reported incomplete conversion to the trans isomer. However, he obtained a fraction having physical constants similar to trans-2-octenoic acid prepared by a Knoevenagel condensation. Bachman (23) first prepared trans-2-octenoic by the Knoevenagel condensation in 1933.

The following equation represents an attempted synthesis of trans-2-octenoic acid.

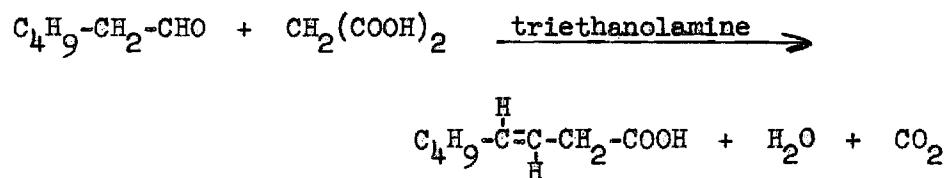


2-Octynoic acid was prepared by carbonating 1-heptynylmagnesium bromide. In order to increase its compatibility with the sodium-liquid ammonia solution, 2-octynoic acid was first converted to its sodium salt.

When the product of this reaction was characterized, it was found to consist chiefly of saturated material and did not have the characteristic trans infrared absorption at 10.3 microns. The "teflon"

stirring paddle used in this reaction was attacked by the sodium-liquid ammonia, as indicated by the black and rough surface of the paddle. There was some possibility that this rough surface may have catalyzed the hydrogenation of any olefinic acid to the corresponding saturated compound. When the experiment was repeated under the same conditions, similar results were obtained. On the basis of these two experiments, it was deemed advisable to prepare the trans-octenoic acids by the Knoevenagel condensation.

trans-3-Octenoic Acid



The present investigation is the first to report the preparation of trans-3-octenoic acid by the Knoevenagel condensation. At the present time there have been no reports of 3-olefinic acids prepared by the Knoevenagel condensation which were contaminated by position isomers.

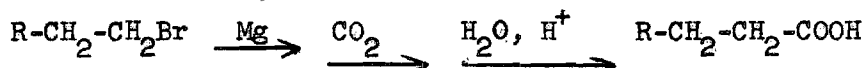
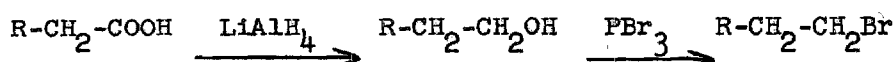
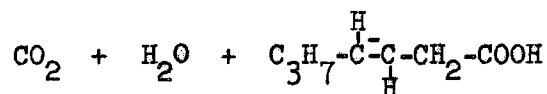
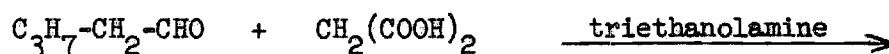
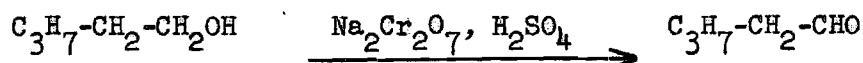
trans-3-Octenoic acid was previously reported by Delaby and Lecomte (5), who prepared a series of C₆-C₉, trans-2 and -3 olefinic acids. The following procedure was used in their preparation of trans-3-octenoic acid. Interaction of n-butylmagnesium bromide with acrolein gave 1-heptene-3-ol, an allylic secondary alcohol. This alcohol on bromination with phosphorous tribromide afforded 3-bromo-1-heptene, which underwent an allylic rearrangement to give predominantly 1-bromo-2-heptene. The bromide was then treated with cuprous cyanide, yielding

1-cyano-2-heptene. The nitrile was hydrolyzed with aqueous sodium hydroxide to give the desired acid.

The purity of the product produced by this sequence of reactions is questionable. This is due to the allylic rearrangement which must give a 100 per cent conversion to a primary bromide, if pure products are to be obtained. Delaby and Hubert (54) later repeated the above sequence of reactions to obtain 1-bromo-2-heptene. This compound was converted to a Grignard reagent and carbonated. When the crude acid was fractionated, a sample having a refractive index of 1.4453 and density of 0.865 was obtained. *trans*-3-Octenoic acid prepared in this study had a refractive index of 1.4452 and density of 0.9378. Winstein and Young (55) state that the conversion of secondary allylic alcohols into bromides by phosphorous tribromide gives, under ordinary preparative conditions, an equilibrium mixture containing mainly the primary bromide along with 10 to 20 per cent of the secondary bromide. It may be concluded from these results that the method of Delaby and Lecomte may result in an unsaturated acid contaminated by position isomers.

trans-4-Octenoic Acid

(R equals $C_3H_7-\overset{H}{\underset{H}{|C-C|}}$)

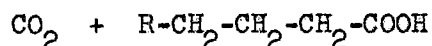
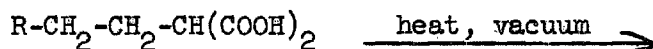
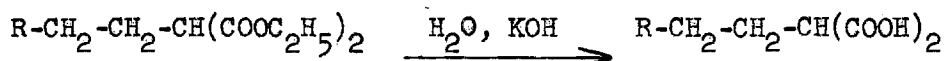
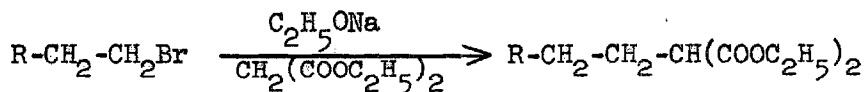
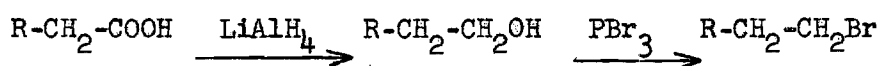
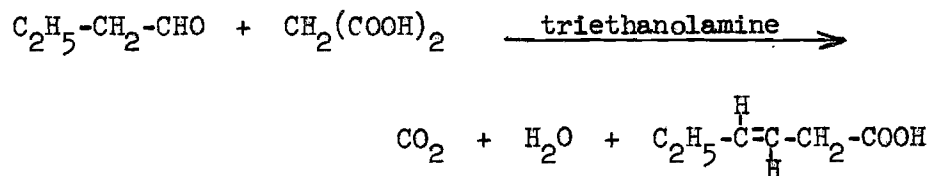


n-Valeraldehyde was prepared by the oxidation of n-amyl alcohol.

Condensation of n-valeraldehyde with malonic acid in the presence of triethanolamine gave trans-3-heptenoic acid, which was reduced to trans-3-hepten-1-ol with lithium aluminum hydride. Reaction of this alcohol with phosphorous tribromide in the presence of pyridine gave the bromide. The bromide was converted to a Grignard reagent, which was carbonated to yield trans-4-octenoic acid. When crude trans-4-octenoic acid was distilled without purification via the sodium salt, a yellow impure product resulted. After purification a colorless, reasonably pure product was obtained. During the course of a Knoevenagel condensation polymeric substances are formed which must be removed if a pure product is desired.

trans-5-Octenoic Acid

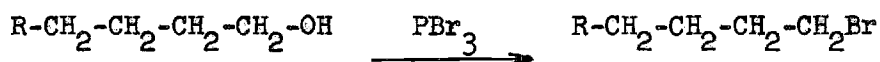
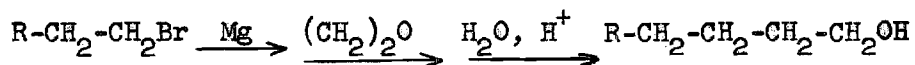
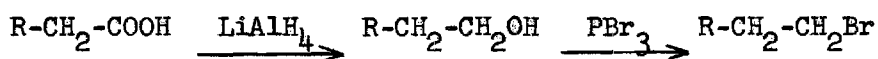
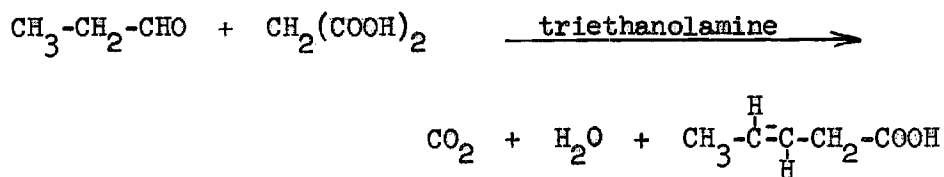
(R equals $C_2H_5-\overset{H}{\underset{H}{C}}=C-$)



trans-3-Hexenoic acid, prepared by the condensation of n-butyr-aldehyde and malonic acid in the presence of triethanolamine, was reduced to trans-3-hexene-1-ol with lithium aluminum hydride. The action of phosphorous tribromide in the presence of pyridine on this alcohol gave the bromide, which on reaction with sodiomalonic ester gave ethyl trans-3-hexenylmalonate. The corresponding free acid, which was obtained by saponification but not isolated, was readily decarboxylated by heating under vacuum to give trans-5-octenoic acid. Howton and Davis (8) were the first investigators to prepare trans-5-octenoic acid by the above sequence of reactions.

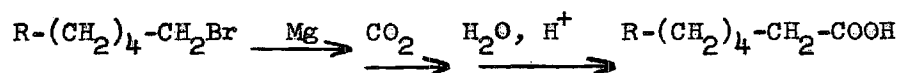
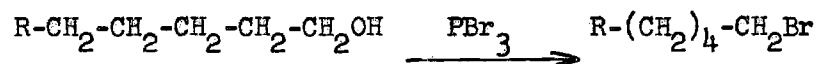
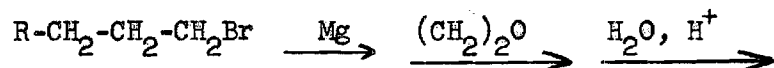
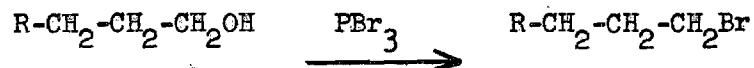
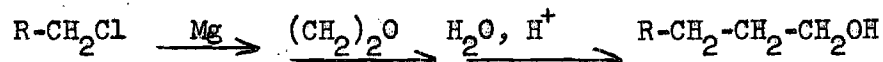
trans-6-Octenoic Acid

(R equals $\text{CH}_3-\overset{\text{H}}{\underset{\text{H}}{\text{C}}}=\text{C}-$)



trans-3-Pentenoic acid was prepared by condensing propionaldehyde with malonic acid in the presence of triethanolamine. The three carbon atoms necessary to convert trans-3-pentenoic acid to trans-6-octenoic acid were added as the result of an ethylene oxide addition and the carbonation of a Grignard reagent. Prior to this investigation trans-5-heptene-1-ol and 1-bromo-trans-5-heptene has not been reported in the literature. trans-6-Octenoic acid, a new compound, was prepared in an overall yield of 1.0 per cent based on propionaldehyde.

7-Octenoic Acid

(R equals $\text{H}_2\text{C}=\text{CH}-$)

Two synthetic routes to 4-pentene-1-ol were available. The first possibility (39), which was not utilized in this investigation, consisted of chlorinating tetrahydrofurfuryl alcohol with thionyl chloride, followed by cleavage with powdered sodium in ether, giving 4-pentene-1-ol. The method (37) used for preparing 4-pentene-1-ol in this study was somewhat shorter than the procedure just described. It consisted of preparing the Grignard reagent of allyl chloride; then adding ethylene oxide to the Grignard reagent. The Grignard reagent-ethylene oxide complex was decomposed with dilute acid, affording the desired alcohol. Kharasch and Fuchs (37) reported using 800 ml. of ether in preparing three moles of allylmagnesium chloride. Since allylmagnesium chloride is insoluble in ether, it must be used as a suspension. It was found in this investigation that 1100 ml. of ether per three moles of allyl chloride gave a smoother reaction and higher yields than did the smaller amount of ether.

4-Pentene-1-ol was treated with phosphorous tribromide and pyridine to give the bromide, which was converted to a Grignard reagent. Ethylene oxide was added to the Grignard reagent, and the resulting alcohol brominated with phosphorous tribromide in the presence of pyridine. The Grignard reagent of this bromide was formed and after carbonation yielded 7-octenoic acid.

The above method has not previously been used to prepare 7-octenoic acid. However, the preparation of this acid has been reported by two other methods. Taylor and Strong (19) prepared 7-octynoic acid and catalytically semihydrogenated it to the olefinic acid. Gol'mov (42) prepared 7-octenoic acid via a malonic ester condensation with 1-bromo-5-hexene.

Proof that 7-octenoic acid has a terminal double bond is readily obtained from its infrared absorption spectra. Absorption occurred at wave lengths characteristic of terminal olefins, but no absorption occurred at characteristic cis-trans wave lengths.

Discussion of cis-Octenoic Acids

General.--As was stated in the introduction, catalytic semihydrogenation of acetylenic compounds gives predominantly cis compounds. If any trans compounds were formed in the hydrogenations reported in this study, their concentration was too low to give any infrared absorption at 10.3 microns.

The semihydrogenations performed in this investigation resulted in cis-octenoic acids which most probably contained small amounts of the parent acetylenic compound and octanoic acid as impurities. The presence

of an acetylenic acid could be shown only in the case of cis-2-octenoic acid. Of the acetylenic acids prepared in this work, only 2-octynoic acid showed strong absorption at 4.5 microns due to the acetylenic bond. In hydrogenations of 2-octynoic acid, even when a slight (10 per cent) excess of hydrogen was taken up, the infrared spectra of the product always had definite absorption at 4.5 microns.

In this study a sharp decrease in the rate of hydrogenation, when one molecular equivalent of hydrogen was taken up, did not occur. When approximately the theoretical volume of hydrogen was absorbed, there was a gradual decrease in the rate of hydrogenation. In no instance was there a sharp "break" in the rate of hydrogenation as reported (8, 19) in previous studies. All acetylenic acids were partially reduced with W-5 Raney nickel catalyst (44) which had aged for five months at room temperature. In a preliminary experiment freshly prepared Raney nickel was used in the reduction of 2-octynoic acid. There was no observable change in the rate of hydrogenation after one molecular equivalent of hydrogen had been absorbed.

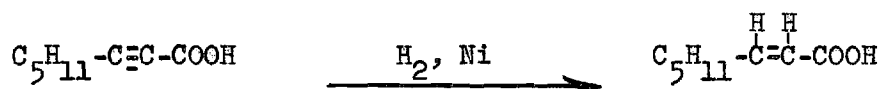
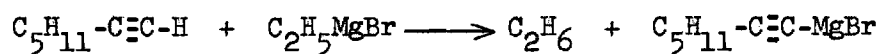
Previous studies (8, 19) report that the acetylenic acid was converted to the olefinic acid in 10 to 15 minutes, using Raney nickel as a catalyst. Much longer times (50 to 130 minutes) were required for the semihydrogenations reported here. Raney nickel is known to catalyze the hydrogenation of ethylenic compounds. Generally the rate of hydrogenation of ethylenic compounds is slower than that of acetylenic compounds. However, if the ethylenic compound is allowed to remain in contact with the catalyst and hydrogen for a sufficient period of time, some of the ethylenic compound may be reduced. Adkins and Billica (44)

found that the hydrogenation of stearolic acid over W-6 Raney nickel catalyst caused the immediate formation of the ethylenic acid, but further hydrogenation to the saturated acid occurred more slowly and was complete after about two hours. No attempt will be made here to discuss the variables, proposed mechanisms, or other aspects of catalytic semihydrogenation.

When the physical properties of the cis and trans octenoic acids are compared, certain regularities in cis-trans relationships appear. The trans isomers have a higher melting point, higher refractive index, greater density, higher melting point of para-bromophenacyl ester, and larger molecular refraction (except trans-6-octenoic acid) than the cis isomers. These relationships may be seen in Tables 3A, 3B, and 3C. These same observations were made in 1929 by Bourguel (24) for C_4-C_9 , normal, 2-olefinic acids. All eleven n-octenoic acids are colorless oils with a typical unsaturated fatty acid odor.

Ozonization of acids.--Newman and Wotiz (12) ozonized each of the six octynoic acids. Only the dibasic acids were isolated. In each case the expected acid was obtained and identified by melting point and neutralization equivalent. Each cis-octenoic acid reported in the present study was obtained by partial hydrogenation of the corresponding known octynoic acid. Isomerization of the double bond should not occur under the conditions used for semihydrogenation. Hence the cis-octenoic acids were not ozonized.

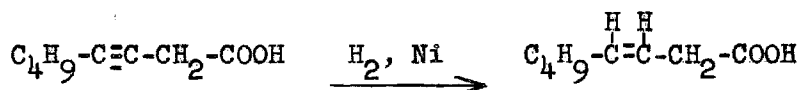
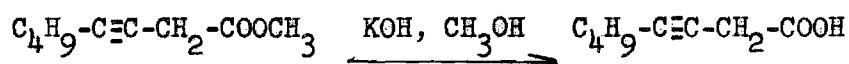
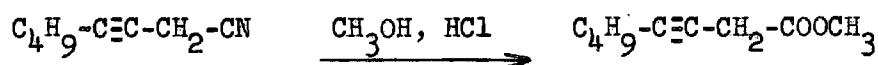
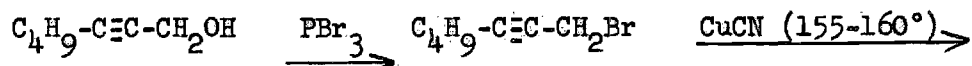
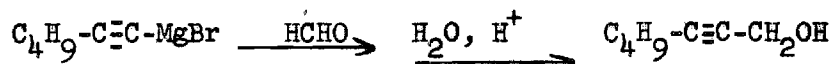
cis-2-Octenoic Acid



Previously 2-octynoic acid had been prepared by carbonation of 1-heptynyl sodium (43). Carbonation of 1-heptynylmagnesium bromide offered a somewhat simpler and slightly different approach. Bourguel (24) prepared cis-2-octenoic acid by semihydrogenating 2-octynoic acid in the presence of colloidal palladium stabilized by starch. Ethyl acetate or benzene was used as a solvent.

Several trial catalytic hydrogenations of 2-octynoic acid were run so that optimum conditions could be determined. The use of absolute ethanol as a solvent (8) resulted in a product contaminated by esters. No such complications arose when dry thiophene free benzene was used as a solvent. Benzene was easily removed from the reaction mixture and satisfactorily served as a solvent in all semihydrogenations reported here.

cis-3-Octenoic Acid

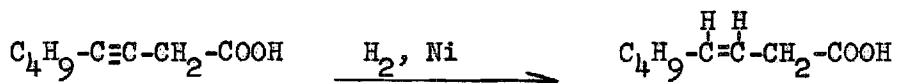
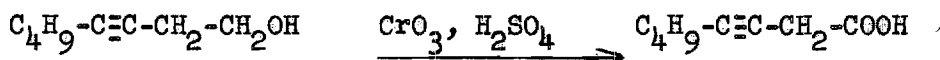
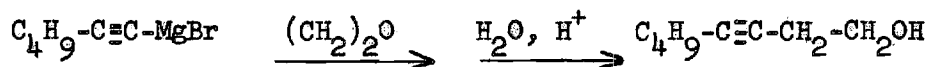


Newman and Wotiz (12) used the above sequence of reactions to prepare 3-octynoic acid. Their work was duplicated without difficulty until the preparation of 1-cyano-2-heptyne was attempted. Newman and Wotiz state that the reaction between 1-bromo-2-heptyne and cuprous cyanide became exothermic when the reactants were heated to 157°. In three separate preparations of 1-cyano-2-heptyne, during the course of the present investigation, the exothermic reaction ceased unless the reactants were maintained at 157° by continued heating. However, the nitrile could be prepared satisfactorily if the temperature was maintained at 157°. Newman and Wotiz report yields of 0 to 92 per cent for this reaction. These authors' attempts to combine 1-bromo-2-heptyne with water-acetone solutions of potassium cyanide were always fruitless.

1-Cyano-2-heptyne which could not be hydrolyzed by aqueous alkali or acids, was easily converted as described by Newman and Wotiz (12), to

the corresponding methyl ester by passing hydrogen chloride gas into a solution of the nitrile, water, and methanol. The crude ester was hydrolyzed, without further purification, by alcoholic alkali (12). The low refractive index of the product reported here indicates very little hydrolysis of the ester to acid had occurred. Newman and Wotiz reported a 74 per cent yield of acid by this procedure. A small sample of the impure 3-octynoic acid was hydrogenated. The product of hydrogenation was too impure to be worthy of characterization. Due to the low yields (12 per cent based on 1-cyano-2-heptyne) and impurity of the 3-octynoic acid prepared in this manner, a new method of synthesis was desired.

The following reactions were found to offer a route to 3-Octynoic acid.



The most unusual step in this series of reactions is the chromium trioxide oxidation of 3-octyn-1-ol. Such oxidations of normal C₄, C₅, and C₆ acetylenic primary alcohols have been reported (48, 49) to give the corresponding acetylenic acid in yields of 11 to 50 per cent. In view of the rather low yield expected from the oxidation, a method of preparing 3-octyn-1-ol in as high a yield as possible was sought.

Newman and Wotiz (12), using 1-hexyne as a starting material, and employing a liquid ammonia procedure, obtained a 21 per cent yield of 3-octyn-1-ol, boiling point 105-106°/25 mm. In the present investigation the liquid ammonia procedure was not used, but the Grignard reagent of 1-hexyne was prepared. It was then treated with ethylene oxide in the usual manner (36), giving a 25 per cent yield of 3-octyn-1-ol.

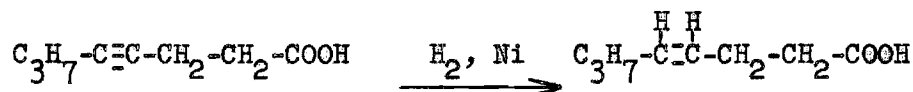
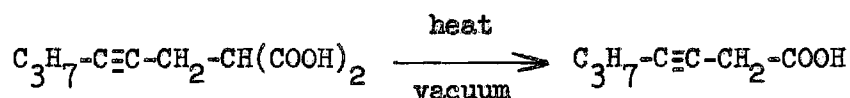
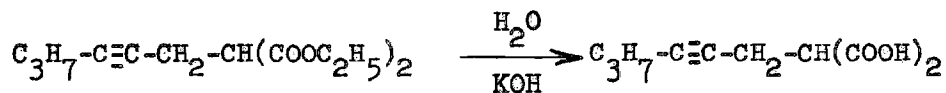
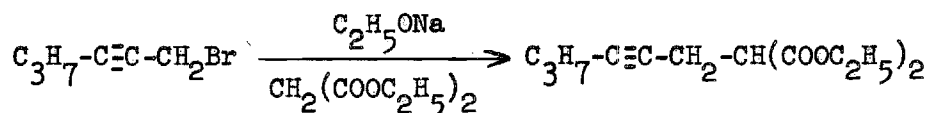
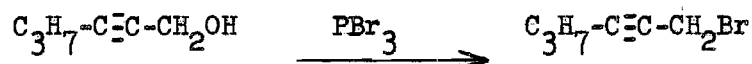
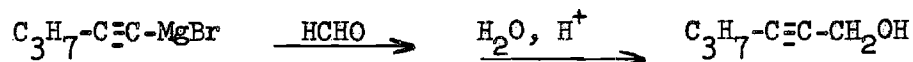
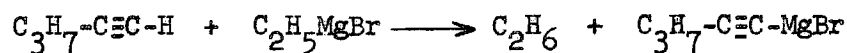
In an attempt to prepare 3-octyn-1-ol in a higher yield, standard procedures for the addition of ethylene oxide to Grignard reagents were modified. Raphael (72) states that acetylenic Grignard reagents are generally more soluble in benzene than in ether. Ethylmagnesium bromide was prepared in the usual manner. Benzene was then introduced and the mixture warmed to boil off the ether. The resulting benzene solution of ethylmagnesium bromide was treated as usual with the acetylenic compound. However, 1-hexynylmagnesium bromide was not soluble in benzene, but formed a smooth white suspension. Ethylene oxide was added to the Grignard reagent and after working up in the usual manner, a yield of 81 per cent 3-octyn-1-ol was obtained. This method differs from the usual methods of adding ethylene oxide to acetylenic Grignard reagents in only one respect: ether was replaced by benzene after ethylmagnesium bromide had been formed. This change in procedure offers several advantages. Less material will be lost by entrainment during periods of refluxing due to the lower volatility of benzene. It has been postulated (56) that the addition of ethylene oxide to Grignard reagents occurs in two steps. First a weakly bound oxonium complex is formed, which may then undergo thermal rearrangement to give $R-CH_2-CH_2-O-MgBr$. The last mentioned compound is easily hydrolyzed to $R-CH_2-CH_2OH$ and $Mg(OH)Br$. If the weakly bound oxonium complex is not heated suffi-

ciently to cause rearrangement to occur, a poor yield of the desired alcohol will be obtained. When ether is replaced by benzene a higher reflux temperature is possible; thus enabling the desired thermal rearrangement to take place. No attempt will be made here to elucidate the course of reaction between Grignard reagents and ethylene oxide. This reaction has been reviewed (56, 57). Evidence presented here seems to indicate the importance of heating the reactants sufficiently to cause the desired thermal rearrangement.

3-Octyn-1-ol was oxidized to 3-octynoic acid by dissolving the alcohol in a water-acetone solution and slowly adding a slight excess of chromium trioxide in a water-sulfuric acid solution (48, 49). Eglinton and Whiting (49) who prepared 4-pentynoic acid by chromic acid oxidation of 4-pentyn-1-ol obtained yields as indicated, using the following solvents: water, 50 per cent; acetone 36 per cent; methyl ethyl ketone, 34 per cent; and glacial acetic acid, 11 per cent. In the present investigation a 21 per cent yield of 3-octynoic acid was obtained with a water-acetone solvent, but the yield was only 2.3 per cent when water alone was used as a solvent. Thus it is evident that the yield is quite dependent on the solvent, and the optimum solvent for one oxidation may be unsuited for another.

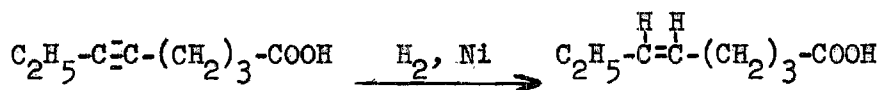
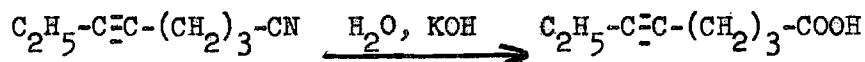
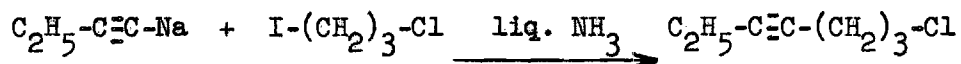
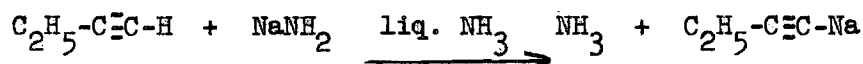
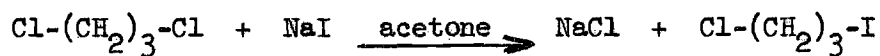
3-Octynoic acid was partially hydrogenated over Raney nickel to give cis-3-octenoic acid.

cis-4-Octenoic Acid



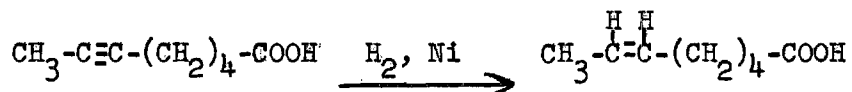
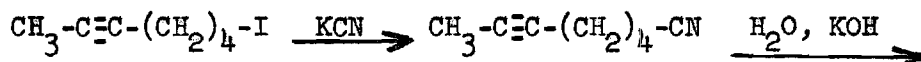
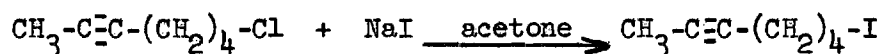
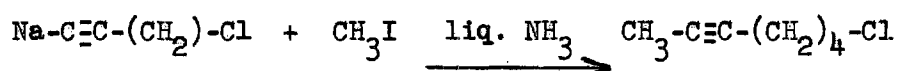
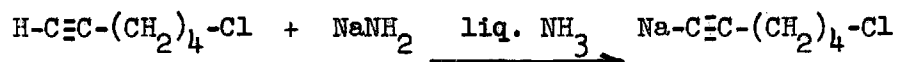
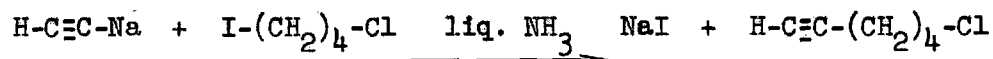
The method outlined by Newman and Wotiz (12) proved satisfactory for the preparation of 4-octynoic acid. This acid has the highest melting point (49°) of the n-octynoic acids. 4-Octynoic acid was catalytically semihydrogenated to cis-4-octenoic acid. The overall yield of cis-4-octenoic acid from 1-pentyne was four per cent.

cis-5-Octenoic Acid



The above sequence of reactions are those reported by Howton and Davis (8), but were not investigated in the present study. Newman and Wotiz (12) also have described a similar synthesis of 5-octynoic acid. Howton and Davis prepared 5-octynoic acid from trimethylene chloride in an overall yield of 11 per cent and then converted 5-octynoic acid to cis-5-octenoic acid by catalytic semihydrogenation. All the physical constants reported by Howton and Davis for cis-5-octenoic acid seem reasonable except the density (0.9604 at 20°). Other octenoic acids have densities of 0.92 to 0.94. The density reported by these authors indicates an impure sample or the size of the sample was too small to permit accurate measurements.

cis-6-Octenoic Acid



The procedure outlined by Newman and Wotiz (12) for the preparation of 6-octynoic acid was followed. Crude 6-octynoic acid, which was not distilled, was purified by crystallization from diethyl ether. 6-Octynoic acid prepared in this study had a melting point of 44°, while Newman and Wotiz report a melting point of 37°. The melting point reported here remained constant after repeated crystallizations. Homogeneity of the product reported here is shown by the slight difference in melting points of the purest and least pure sample of octynoic acid. The last batch of crystals taken from the mother liquor had a melting point of 42°. cis-6-Octenoic acid was prepared from 1,4-dichlorobutane in an overall yield of seven per cent.

CHAPTER V

RECOMMENDATIONS

The Knoevenagel condensations reported in this study gave reasonably pure trans olefinic acids, but the yields (13 to 35 per cent) were not encouraging. The low yields may partially be attributed to the tendency of aldehydes to polymerize under basic conditions. As an aid to elucidating the course of the Knoevenagel condensation, a preliminary study should be made of the products formed when aldehydes are mixed with pyridine or triethanolamine.

The need for vigorous stirring of the reactants in a Knoevenagel condensation has previously been mentioned. In selecting a mechanical stirrer, the viscosity of the reaction mixture should be considered. Perhaps the viscosity could be decreased by using an inert solvent. A homogenous reaction mixture is desired, but the differences in solvent characteristics of the reactants make the choice of a solvent difficult. Perhaps diisopropyl ether or dioxane could be used as a solvent.

The time and temperature variables of the reaction should be studied. The usual procedure is to allow the reactants to stand two to four days at room temperature, then heat the reaction mixture 12 hours on a steam bath to effect decarboxylation. It was observed that the reaction mixture changed from yellow to brown-orange upon heating at 100° for several hours. The colored material was always an impurity. Instead of allowing the reaction mixture to stand several days, the reactants could be heated on the steam bath immediately after mixing.

Another possibility would be to allow the reactants to stand two to four days; then decarboxylate at room temperature by the use of reduced pressure. Thus polymerization, which is favored by prolonged heating, should be minimized. If the vacuum were carefully controlled, little product should be lost by volatilization.

A reasonable mechanism for the formation of a 2-olefinic acid from an aldehyde, malonic acid, and pyridine has been given by Alexander (59). No such mechanism is available which will explain the difference in the reaction when triethanolamine is used instead of pyridine. It may be hypothesized that the Knoevenagel condensation in the presence of triethanolamine gives a 2-olefinic acid, which changes to the 3-isomer under the influence of triethanolamine. Kon et al. (60) have investigated the isomerization of the ethyl esters of pure 2- and 3-hexenoic acid under the influence of sodium ethoxide. It was found that either ester gave an equilibrium mixture containing approximately 90 per cent of the 2-enoic ethyl ester. It is suggested that isomerization of 2-hexenoic acid in triethanolamine be investigated to determine if triethanolamine does cause conversion to the 3-olefinic acid. Likewise the isomerization of 3-hexenoic acid in pyridine should be studied. If more than qualitative results are expected from these experiments, a method of accurately measuring the amounts of each isomer must be devised. Perhaps chromatographic methods would be capable of doing this. It is obvious from the preceding discussions that much work remains to be done before the course of the Knoevenagel condensation can be fully elucidated.

The anomalous results of the sodium-liquid ammonia reduction of 2-octynoic acid reported here warrant further investigation. These results

indicate the presence of only small amounts of trans-2-octenoic acid. The reduction of 2-octynoic acid produced primarily saturated material. Perhaps as the unsaturated linkage is moved farther from the carboxyl group the desired reduction could be accomplished. More work needs to be done before a general conclusion concerning the sodium-liquid ammonia reduction of octynoic acids can be reached.

The aged non-pyrophoric Raney nickel used in the partial hydrogenations reported here gave predominantly cis-olefinic compounds. In the case of 2-octynoic acid, traces of acetylenic acid persisted after more than one mole of hydrogen had been absorbed. Elsner and Paul (6) report the use of a nickel copper catalyst which was more selective toward ethylenic bonds than Raney nickel. Semihydrogenations should be performed in a manner such that the desired volume of hydrogen will be absorbed within 15 minutes. An unconfirmed observation of this investigation was that prolonged hydrogenations cause an increase in the amount of saturated product.

The modification reported here in the preparation of 3-octyn-1-ol from ethylene oxide and 1-hexynylmagnesium bromide resulted in the yield being increased from 25 to 81 per cent. This new procedure should be tried in the preparation of alcohols (of all types) which previously had been obtained in low yields using the old procedure. No general claims for this new procedure can be made until it has been used to prepare a wide variety of alcohols. Perhaps the role of solvent in this type reaction could be better understood if dipropyl or dibutyl ether were used instead of diethyl ether. Also, hydrocarbon solvents other than benzene should be investigated.

cis-5-Octenoic acid should be prepared so that additional physical constants could be obtained. Particular attention should be directed toward an accurate density determination. The value reported by Howton and Davis appears too large when compared with the density of other octenoic acids. If their value is correct, it indicates an anomaly.

CHAPTER VI

CONCLUSIONS

The five trans isomers of n-octenoic acid were prepared either directly or indirectly by the Knoevenagel condensation.

The cis -2, -3, -4, and -6 n-octenoic acids were prepared by catalytic semihydrogenation of the corresponding acetylenic acid.

7-Octenoic acid was prepared by increasing the chain length of allyl chloride using known reactions.

When the refractive index, density, molecular refraction, freezing point, and melting point of the para-bromophenacyl ester of cis-trans isomers were compared, the trans isomer generally had the higher value. All trans compounds showed strong infrared absorption at 10.35 microns, however cis compounds did not absorb at this wave length.

Catalytic semihydrogenation of 2-octynoic acid was found to give predominantly cis olefinic acid, with some acetylenic and saturated acid as an impurity. The sodium-liquid ammonia semireduction of 2-octynoic acid gave a product with physical properties similar to octanoic acid.

Standard procedures for the addition of ethylene oxide to 1-hexynylmagnesium bromide were modified to increase the yield of 3-octyn-1-ol from 25 to 81 per cent.

APPENDIX I

DETERMINATION OF PHYSICAL CONSTANTS

Boiling points and melting points.--The Centigrade scale was used in all temperature measurements. All boiling and melting points are uncorrected. Boiling points represent the temperature at which middle cuts distilled. Pressures below 15 mm were measured with a McLeod gauge, and pressures between 15 mm and atmospheric pressure were measured with a closed-end U tube manometer. The vacuum distillations were carried out with the column connected to a pressure regulator controlled by a manostat operating a leak valve.

Melting points for substances melting above room temperature were determined in a Thiele apparatus. Substances melting between 0° and 25° were placed in an ice bath. When solidification occurred, the sample was removed from the ice bath and the rate of warming determined. The melting point was taken as the "flat" portion of a time vs temperature curve. Substances melting below 0° were frozen in a dry ice-acetone bath, and their melting points were taken in the above manner. Two melting point determinations were made for each compound as a check on accuracy.

Refractive index.--Refractive indices were determined using a Bausch and Lomb Abbe Refractometer. A constant temperature bath was used to control the temperature of the refractometer prisms.

Density.--Density was determined using an Ace Glass (No. 5437) specific Gravity Pycnometer Tube with a 2 ml. capacity. A constant temperature

bath at 20.0° was used in all determinations. The procedure described in the literature (61) was used.

Molecular refraction.--Molecular refraction (M_r) was determined from the experimentally determined density and refractive index, using the Lorenz and Lorentz Equation,

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

in which n is the refractive index and d the density, both measured at the same temperature. M is the molecular weight of the compound.

In calculating the theoretical molecular refraction, the values of atomic refraction listed in Table 9 were used (62).

TABLE 9

ATOMIC AND MULTIPLE BOND REFRACTION CONSTANTS

<u>Structural Feature</u>	<u>Molecular Refraction in cc. per mole</u>
H	1.100
C	2.418
-CH ₂ -	4.630
C=C	1.733
Hydroxyl oxygen, O	1.525
Carbonyl oxygen, O	1.211

Neutralization equivalent.--The neutralization equivalent was determined by standard procedures (63). An 0.3 gram sample of acid was accurately weighed and dissolved in 30 ml. of ethanol. This solution was titrated

with standard 0.1 normal sodium hydroxide to a phenolphthalein end point. A blank was always run on solvent and indicator.

Hydrogen uptake.--Hydrogen uptake was determined for all octenoic acids as a means of ascertaining degree of unsaturation. The apparatus (64) consisted essentially of a 100 ml. gas burette connected to a 250 ml. reaction flask. Mercury was used as a leveling liquid, so that the pressure in the burette could be at atmospheric pressure. Magnetic stirring was used. A 0.35 to 0.45 gram sample of octenoic acid was accurately weighed. The acid, 0.035 to 0.045 grams of platinum oxide catalyst, and 40 ml. of glacial acetic acid (DuPont C. P.) were introduced into the 250 ml. flask. Hydrogen was passed through the apparatus for 10 minutes. Pressure in the apparatus was made equal to atmospheric pressure; then stirring was started. Hydrogen uptake was almost complete within 15 minutes. The reaction was allowed to continue an additional 15 minutes to be certain of completeness of reaction. Hydrogenations were run at room temperature. The reaction flask was immersed in a water bath so that a constant temperature could be maintained.

Solid derivatives.--The acids reported in this study were converted to their para-bromophenacyl esters. Standard procedures (65) were used to prepare these esters. The crude ester was crystallized from ethanol to a constant melting point.

Alpha-naphthylurethans prepared according to standard procedures (66) were used as derivatives of alcohols. The crude alpha-naphthylurethan was crystallized from petroleum ether.

Description of distilling columns.--The packed columns used in this work were of the total condensation, variable take-off type. Columns 1 and 2 were packed with glass helices of 1/8 and 1/4 inch diameter, respectively. Column 3 was packed with a tantalum spiral wire.

Column	Packed Section		Plate Value (Estimated)
	Length	Diameter	
1	36 cm.	0.9 cm.	10
2	38 cm.	1.5 cm.	7
3	40 cm.	0.3 cm.	-

APPENDIX II

DISCUSSION OF INFRARED SPECTRA

The infrared absorption spectra of all compounds synthesized in this investigation were determined. Due to space limitations, only the spectra of octenoic acids and five intermediate compounds are presented here. Wotiz and Miller (67) have published the infrared spectra of all six methyl esters of n-octynoic acid. This reference also contains spectra of acetylenic intermediates prepared in work reported here. Howton and Davis (8) have recorded the infrared spectra of 5-octynoic acid, trans-3-hexenoic acid, cis, and trans-5-octenoic acid. The infrared spectra of n-octanoic acid is well known and is included here for reference purposes only. trans-5-Heptene-1-ol is a new compound. Its spectra is included for this reason, and is typical of trans olefinic primary alcohols.

All trans olefinic compounds whose spectra were determined showed strong absorption at 10.35 microns. Bellamy (68) summarizes evidence that this band is characteristic of trans ethylenic bonds. The cis-octenoic acids absorbed rather weakly in the 14 micron range. Absorption at this wave length in unsaturated compounds may be attributed to cis ethylenic bonds (69). In cis-octenoic acids the characteristic cis absorption at 7.1 to 7.4 microns is obscured by carboxylic acid absorption at 7.0 to 7.5 microns. The absence of the 10.35 micron band in the spectra of cis octenoic acids gives evidence of the absence of trans-ethylenic bonds.

The spectra of cis-2-octenoic acid shows absorption at 4.5 microns which is characteristic of disubstituted acetylenes. This indication of an acetylenic linkage persists, even after adding more than the theoretical amount of hydrogen necessary to reduce the acetylenic acid to the olefinic acid. The 4.5 micron acetylenic absorption band in 2-octynoic acid is very strong. Hence low concentrations of this compound would give detectable absorption in this region. The 4.5 micron band is much weaker in 3-octynoic acid and altogether absent in 4-, 5-, and 6-octynoic acids. Thus if any acetylenic acid were present after partial catalytic hydrogenation of 4-, 5-, or 6-octynoic acid, the acetylenic bond could not be detected in the infrared spectra.

When molecules are altered so that an increase in polarity results, the infrared absorption is also increased. This may be seen by comparing the spectra of 3-octynoic acid and 3-octyn-1-ol. The acid shows weak acetylenic absorption at 4.5 microns, whereas the alcohol shows no absorption in the 3.7 to 6.8 micron range. The C-Br absorption (19 microns) does not appear in the spectral range shown here. By replacing the -OH of an alcohol with -Br, the intensity of C-C and C-H absorptions are increased. The bromide may absorb at wave lengths where the alcohol showed no absorption.

Absorption in the 8.0 to 8.7 micron range cannot be assigned to a particular group as listed in Table 10. Since all compounds whose spectra were determined absorbed in this region, this absorption is probably due to C-C and C-H.

APPENDIX III

INFRARED SPECTRA

The figures in this section are photographs of actual spectra. A Perkin-Elmer model 21 recording spectrophotometer equipped with sodium chloride optics and prism was used. All spectra were obtained using a slit program of "927" which gave slit widths ranging from 12 microns at a wave length of two microns to 280 microns at a wave length of 14 microns.

All figures show per cent transmission (ordinate) versus wave-length in microns (abscissa).

TABLE 10

INFRARED ABSORPTION OF VARIOUS GROUPS (69)

Wave Length (Microns)	Group Absorbing (R is alkyl)
2.8 - 3.2	O-H (primary alcohol)
3.0 - 3.1	$\equiv\text{C}-\text{H}$
3.1 - 3.7	carboxylic acids
3.3	$=\text{CH}$ -(olefinic)
3.4 - 3.5	$-\text{CH}_2-$
3.4 - 3.5	$\text{C}-\text{CH}_3$
3.5	C-H
4.7 - 4.6	$\text{R}_1-\text{C}\equiv\text{C}-\text{R}_2$
4.7 - 4.8	$\text{R}-\text{C}\equiv\text{C}-\text{H}$

TABLE 10 (Continued)

INFRARED ABSORPTION OF VARIOUS GROUPS (69)

Wave Length (Microns)	Group Absorbing (R is alkyl)
5.4	-CH=CH ₂
5.7 - 6.1	carboxylic acids
6.0 - 6.3	C = C (all types)
6.8 - 7.0	- CH ₂ -
6.8 - 7.8	C - H
6.9	C - CH ₃
6.9 - 7.3	primary alcohols
7.0 - 7.2	- CH = CH ₂
7.0 - 7.2	- CH ₂ -
7.0 - 7.5	carboxylic acids
7.1 - 7.4	R ₁ HC = CHR ₂ (cis)
7.3	C - CH ₃ , ethyl, <u>n</u> -propyl
7.5 - 8.0	primary alcohols
7.6 - 7.9	R ₁ HC = CHR ₂ (trans)
7.7 - 8.3	carboxylic acids
8.5 - 12.7	C - C
9.0 - 9.5	-CH = CH ₂
9.1 - 10.0	ethyl, <u>n</u> -propyl
9.3 - 9.8	primary alcohols
10.0 - 10.1	- CH = CH ₂
10.2 - 10.5	R ₁ HC = CHR ₂ (trans)

TABLE 10 (Continued)

INFRARED ABSORPTION OF VARIOUS GROUPS (69)

Wave Length (Microns)	Group Absorbing (R is alkyl)
10.2 - 11.1	<u>n</u> -propyl
10.5 - 11.8	carboxylic acids
11.5 - 12.2	<u>n</u> -propyl
12.1 - 14.5	$R_1HC = CHR_2$ (cis)
12.8 - 13.6	ethyl
13.2 - 14.3	<u>n</u> - propyl
13.5 - 13.9	$(-CH_2-)_4$
14.4 - 20	- CH = CH ₂
19 - 21	C - Br

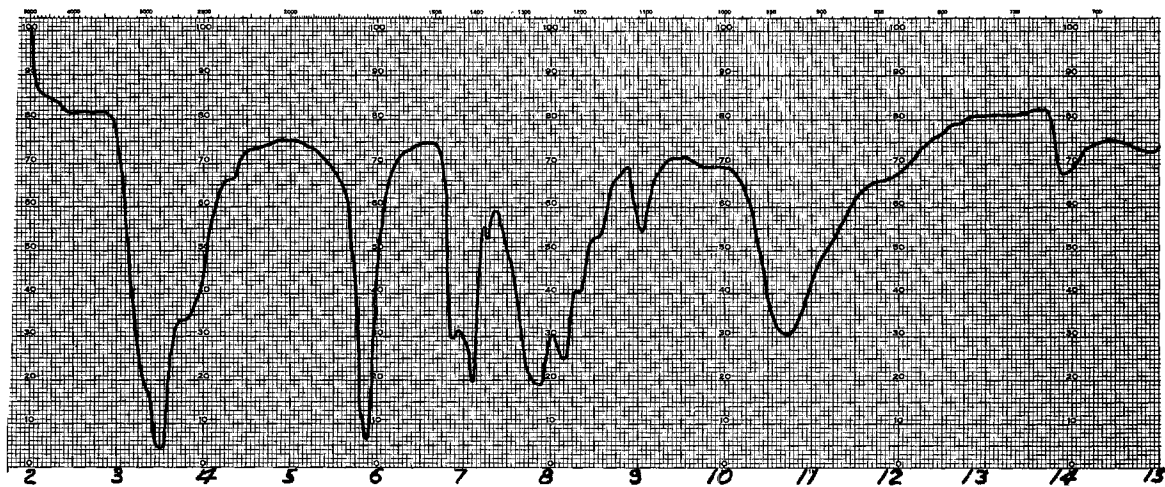


Figure 2
 n-Octanoic Acid
 Phase: liquid
 Cell Thickness¹: 0.111 vs. 0.099
 Concentration: 5.0 per cent CCl₄ solution

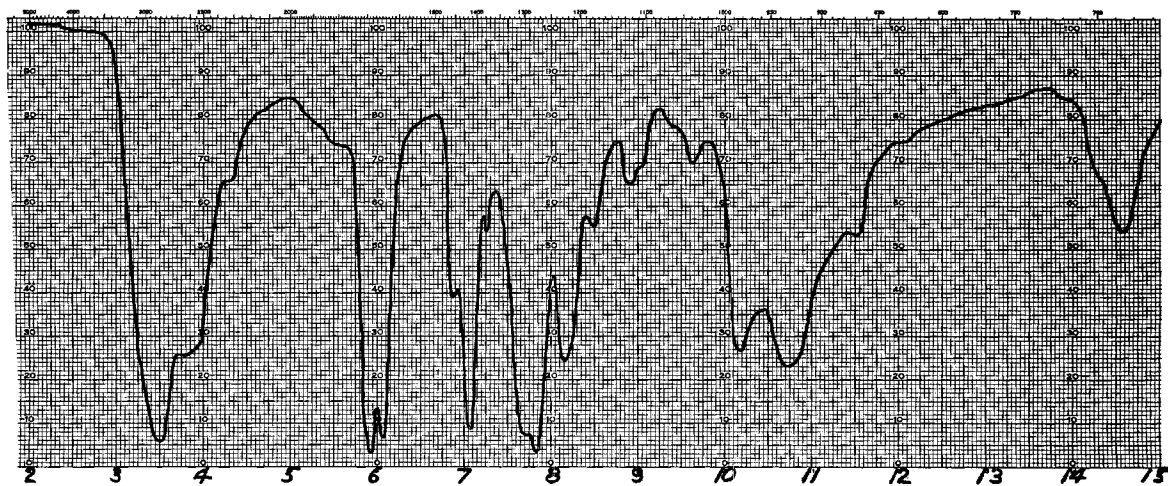


Figure 3
 trans-2-Octenoic Acid
 Phase: liquid
 Cell Thickness: 0.111 vs. 0.099
 Concentration: 5.0 per cent CCl₄ solution

¹The first number represents the thickness (millimeters) of the cell containing the sample being investigated. The second number represents the thickness of the cell containing the solvent.

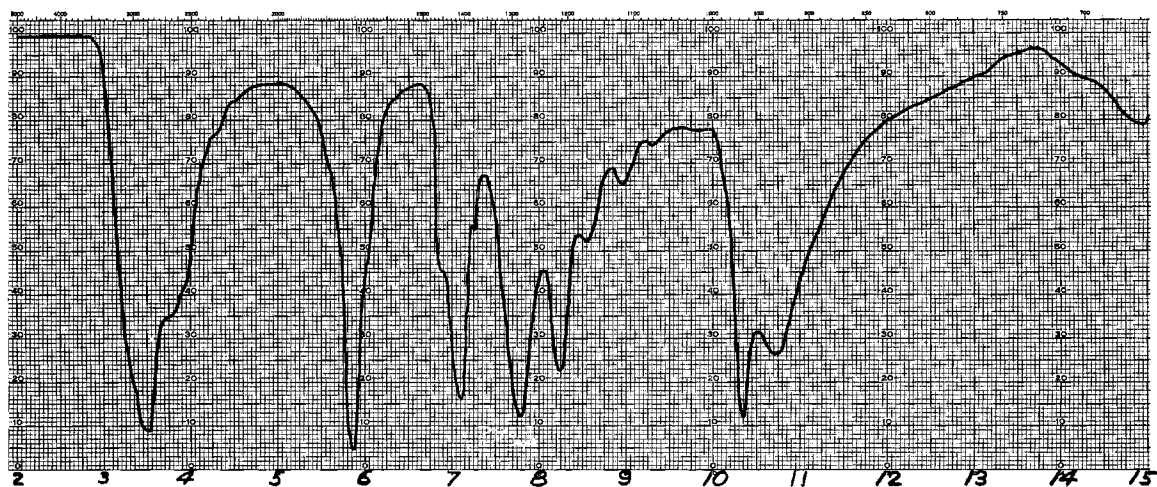


Figure 4
trans-3-Octenoic Acid
Phase: liquid
Cell Thickness: 0.111 vs. 0.099
Concentration: 5.5 per cent CCl₄ solution

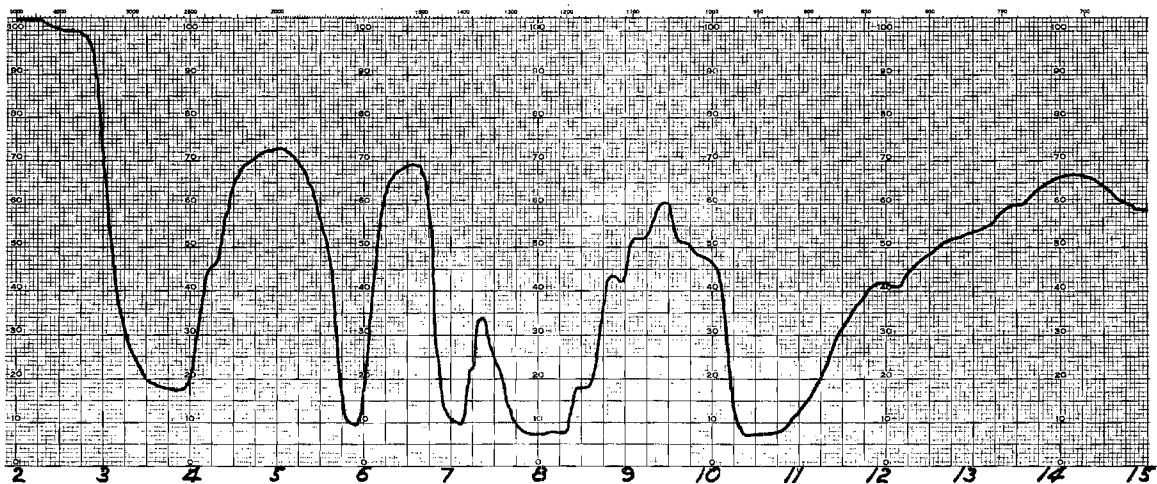


Figure 5
trans-4-Octenoic Acid
Phase: liquid
Cell Thickness: 0.025
Concentration: pure compound

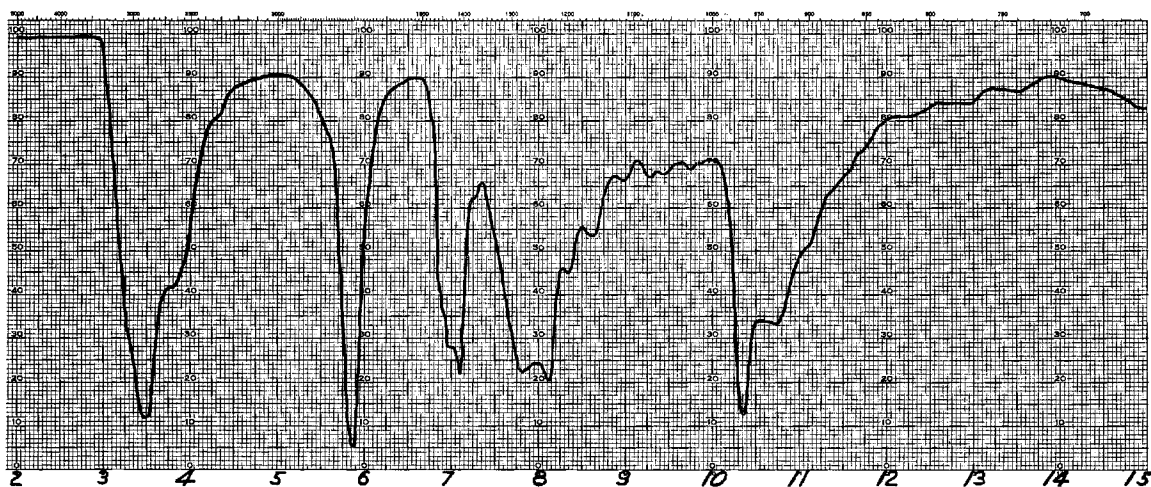


Figure 6
trans-5-Octenoic Acid
Phase: liquid
Cell Thickness: 0.111 vs. 0.099
Concentration: 5.2 per cent CCl_4 solution

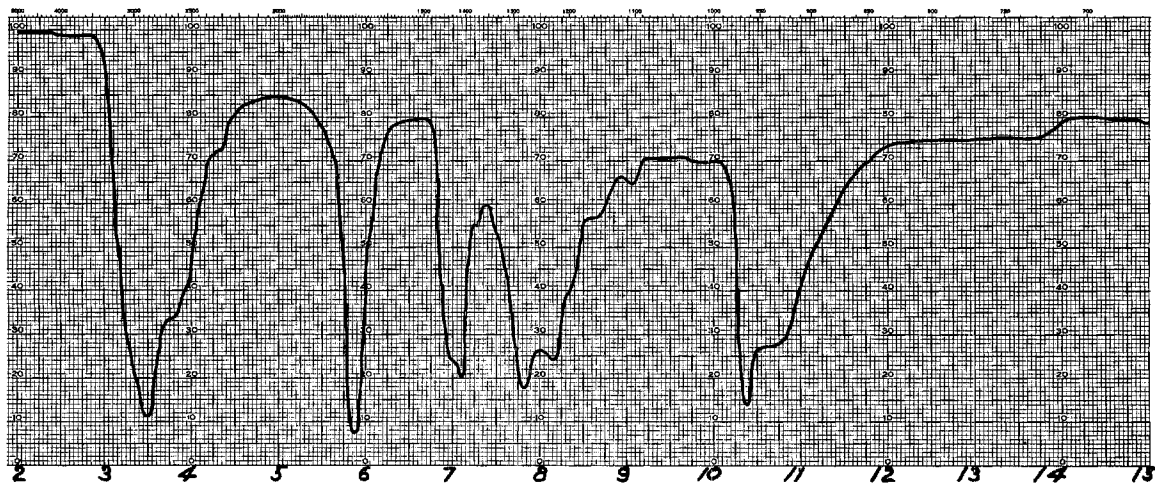


Figure 7
trans-6-Octenoic Acid
Phase: liquid
Cell Thickness: 0.111 vs. 0.099
Concentration: 5.1 per cent CCl_4 solution

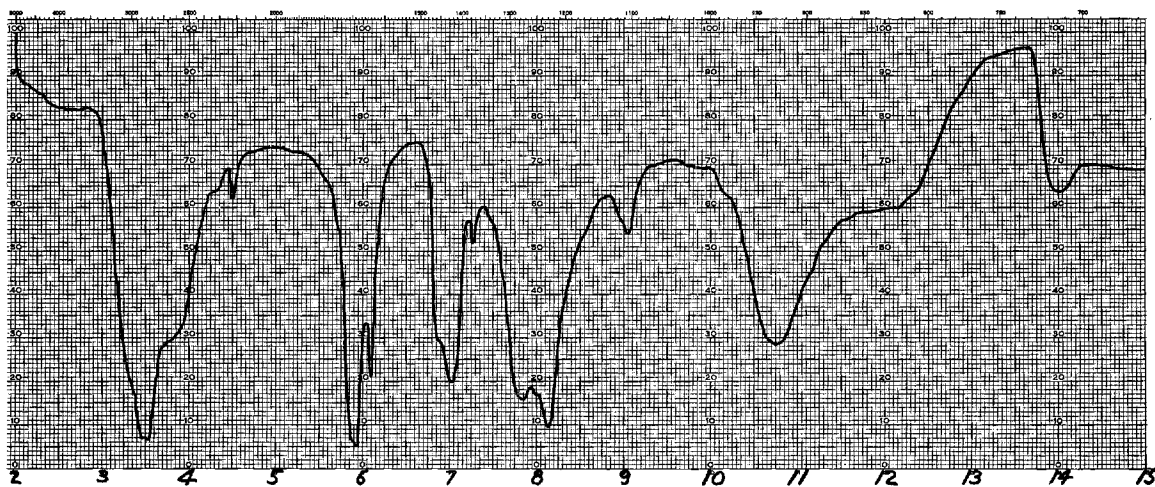


Figure 8
cis-2-Octenoic Acid
Phase: liquid
Cell Thickness: 0.111 vs. 0.099
Concentration: 5.0 per cent CCl₄ solution

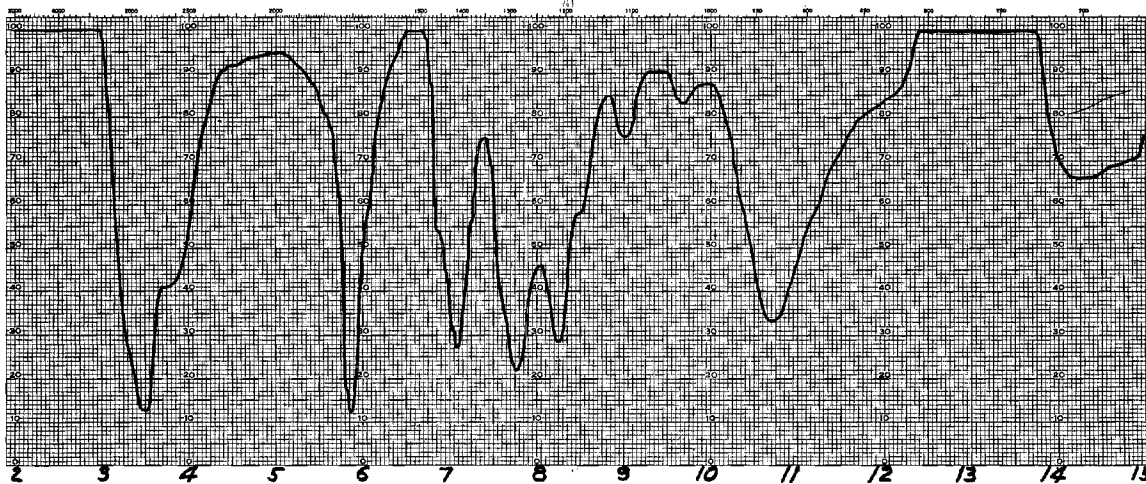


Figure 9
cis-3-Octenoic Acid
Phase: liquid
Cell Thickness: 0.111 vs. 0.099
Concentration: 5.1 per cent CCl₄ solution

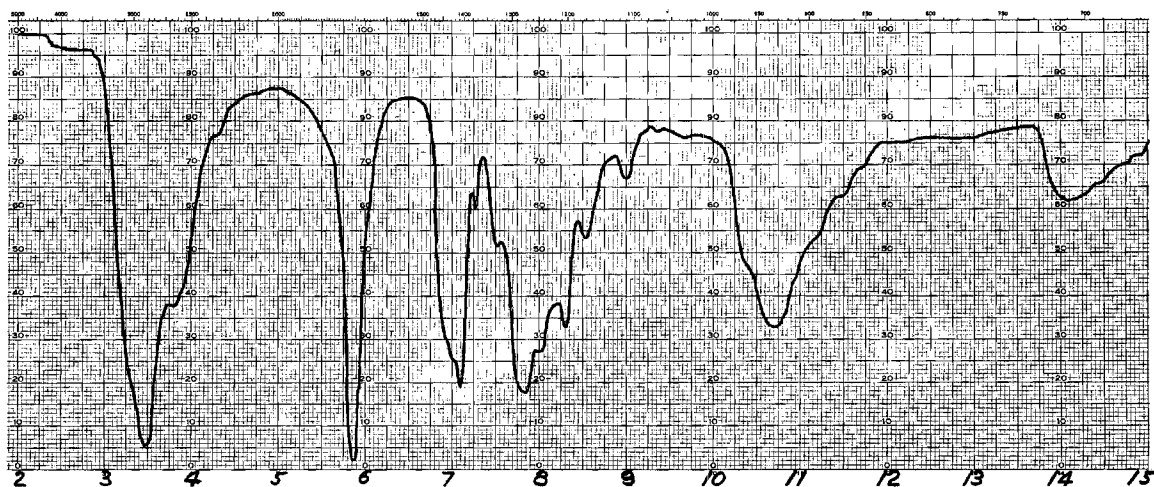


Figure 10
 cis-4-Octenoic Acid
 Phase: liquid
 Cell Thickness: 0.111 vs. 0.099
 Concentration: 5.1 per cent CCl_4 solution

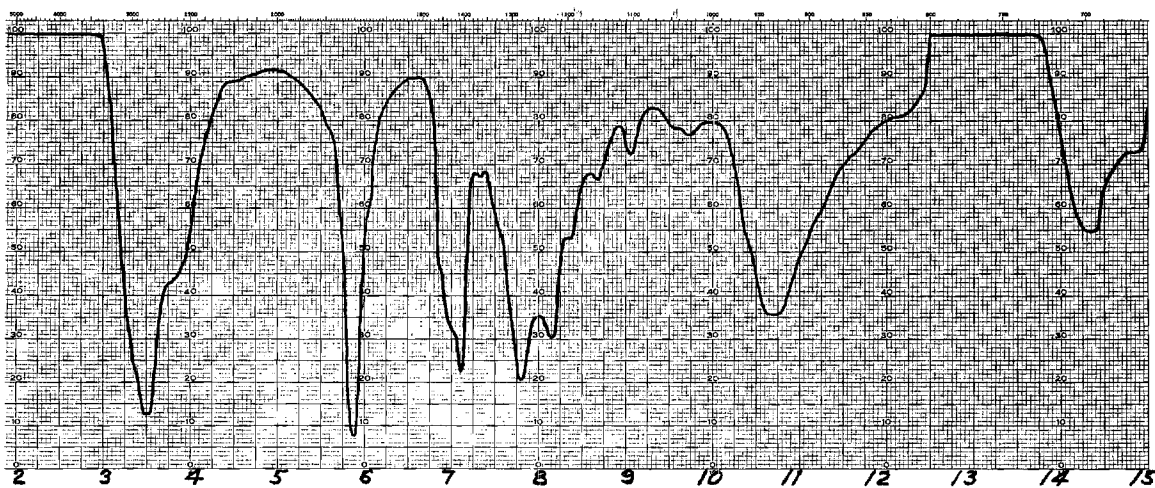


Figure 11
 cis-6-Octenoic Acid
 Cell Thickness: 0.111 vs. 0.099
 Concentration: 5.1 per cent CCl_4 solution

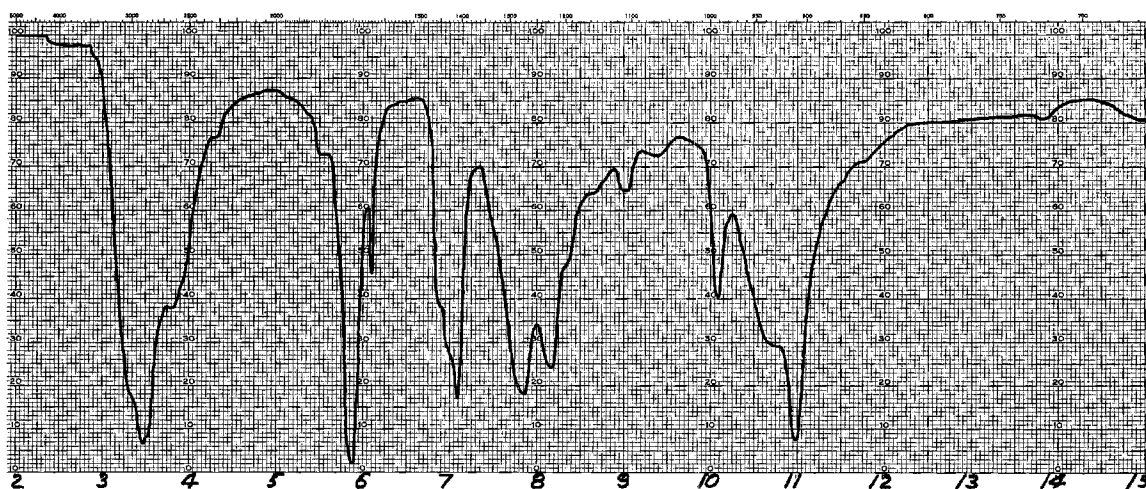


Figure 12
7-Octenoic Acid
Phase: liquid
Cell Thickness: 0.111 vs. 0.099
Concentration: 5.2 per cent CCl₄ solution

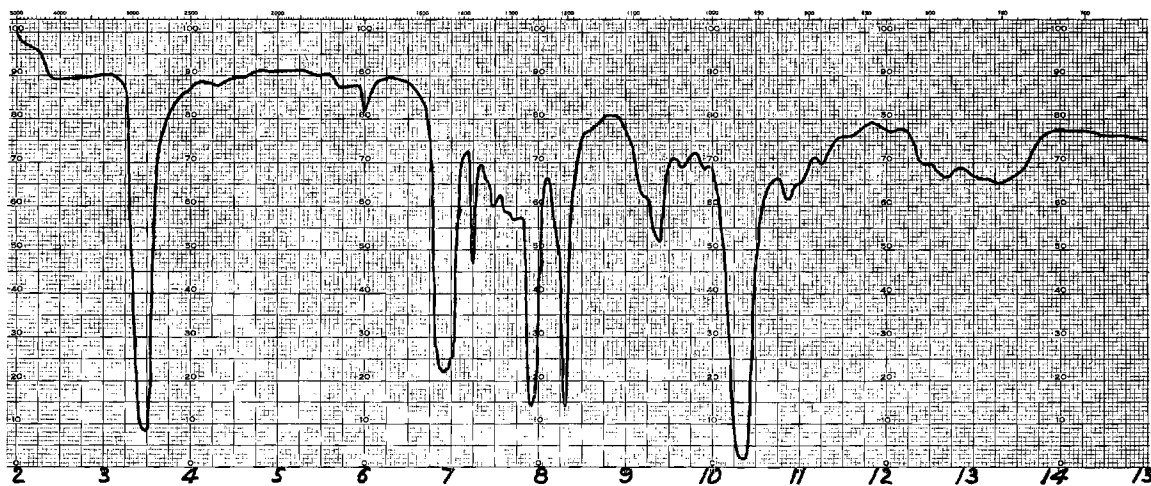


Figure 13
1-Bromo-trans-3-heptene
Phase: liquid
Cell Thickness: 0.025
Concentration: pure compound

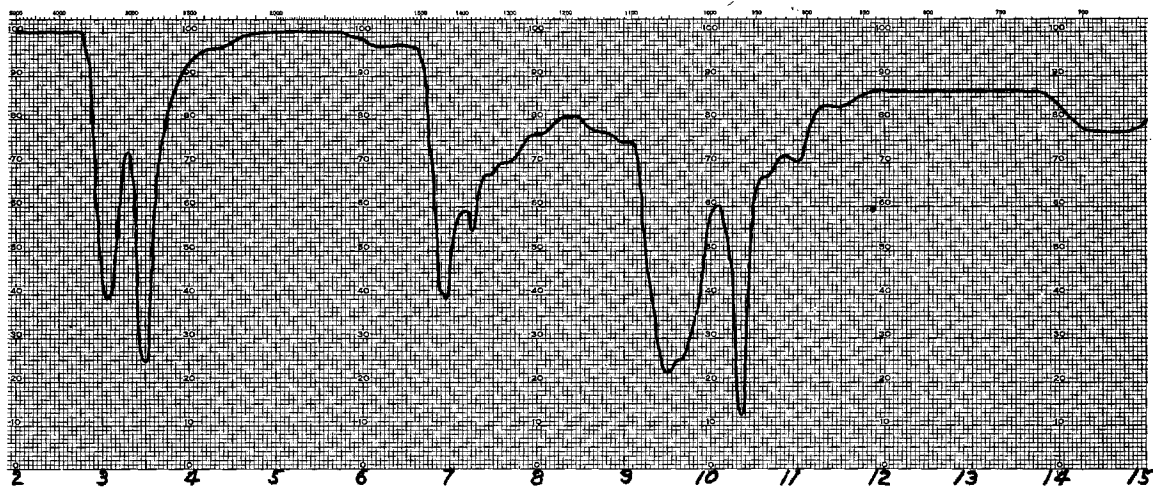


Figure 14
 trans-5-Heptene-1-ol
 Phase: liquid
 Cell Thickness: 0.111 vs. 0.099
 Concentration: 5.0 per cent CCl_4 solution

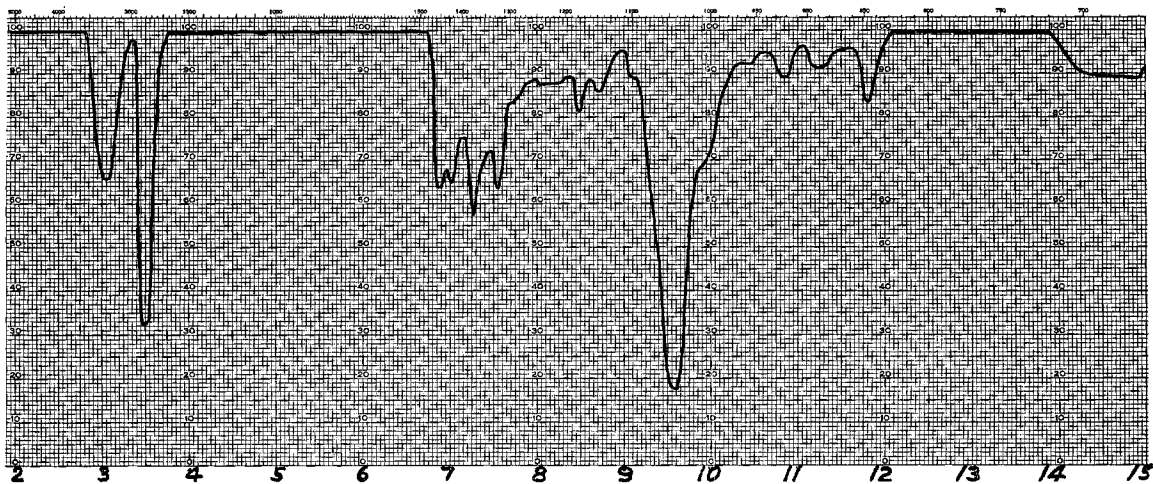


Figure 15
 3-Octyn-1-ol
 Phase: liquid
 Cell Thickness: 0.111 vs. 0.099
 Concentration: 4.9 per cent CCl_4 solution

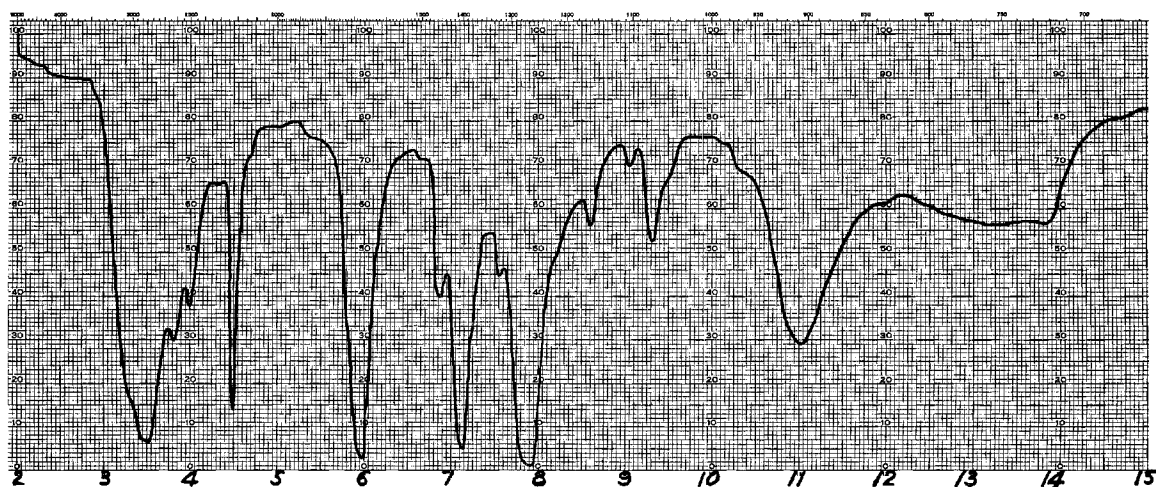


Figure 16
2-Octynoic Acid
Phase: liquid
Cell Thickness: 0.111 vs. 0.099
Concentration: 5.0 per cent CCl_4 solution

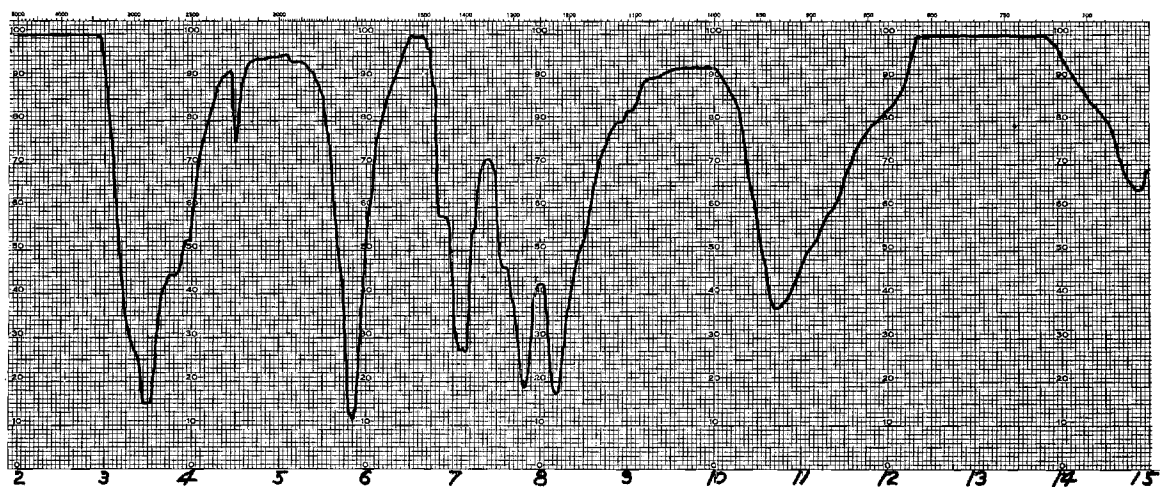


Figure 17
3-Octynoic Acid
Phase: liquid
Cell Thickness: 0.11 vs. 0.099
Concentration: 5.0 per cent CCl_4 solution

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