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Preparation of some alkynes and alkenynes

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THE PREPARATION OF SOME ALKYNES AND ALKENYNES

A thesis presented to the Committee on Graduate Studies and the Department of Chemistry of Union College, Schenectady, New York, in partial fulfillment of the requirements for the degree of Master of Science.

by Edward John Lamby III MS 1971

By Edward John Lamby
(Student's signature)

Approved by John R. Johnson
Thesis advisor

Approved by
Committee on Graduate Studies

Date 8/6/71

I dedicate this thesis
to my wife, Louise, whose untiring
devotion and patience made the pur-
suance of this project possible.

I also wish to thank the
faculty of the Chemistry Department
and in particular my mentor, John R. Sowa.

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ABSTRACT

Several new compounds have been prepared. They are: 5,5-dimethyl-3-hexyn-1-ol; 2,2,5-trimethyl-8-nonen-3-yn-5-ol; 5-bromo-2,2,5-trimethyl-8-nonen-3-yne; 5-chloro-2,2,5-trimethyl-8-nonen-3-yne; 2,2,5,5-tetramethyl-8-nonen-3-yne and 2,2,9,9-tetramethyl-3,7-decadiyne. Also 2,2,5,6,9,9-hexamethyl-5,6-bis(3-butenyl)-3,7-decadiyne was probably prepared.

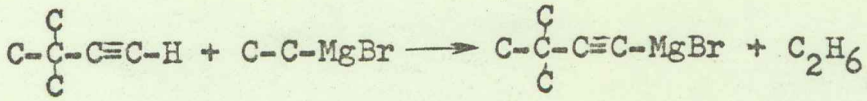
Tetrahydrofuran appears to be a better solvent than ether in acetylenic Grignard exchange reactions and in the reaction of the acetylenic Grignard with ethylene oxide. An improved method has been developed for the preparation of the 1,1-dihalodimethylbutane. Dehydrohalogenation to the alkyne has been done with potassium hydroxide in dimethyl sulfoxide, a much better method than those traditionally used.

INTRODUCTION

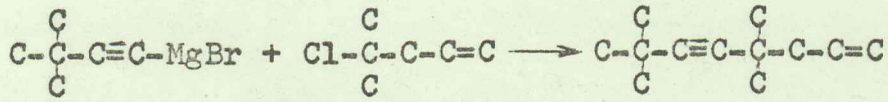
The following thesis concerns the preparation of several alkynes and their conversion to alkenynes. Alkynes are of interest because of their potential biological activity (1), general reactivity to boranes (2), complexing ability with some transition metals (3), as well as other general reactions of π-bonds (4). It was the intention of this investigation to prepare several alkynes with varying degrees of steric hindrance and evaluate the effect of this property. Double bonds were incorporated in several of these compounds to aid in the assessment.

In every synthesis, the starting material was t-butylacetylene. The commercial product is expensive, its laboratory preparation is time consuming and gives low overall yield. A new synthetic route was developed to get around most of these disadvantages, the details of which are given in the Discussion and Experimental Sections.

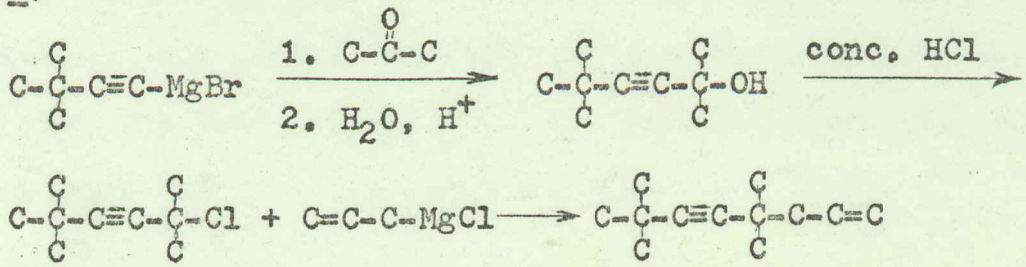
Beyond the preparation of t-butylacetylene, the most important class of reactions was the Grignard reaction. Examples of the general reaction scheme for the preparation of alkenynes is given on the following page:



Path 1.



Path 2.



REACTION I

While the above approaches appear plausible, the coupling of the halides with the Grignard reagents did not follow these paths. The product from Path 2 was 2,2,5,5,6,6,9,9-octamethyl-3,7-decadiyne. This was not expected since the 2-chloro-2,5,5-trimethyl-3-hexyne is known to couple with methylmagnesium bromide to form the di-t-butylacetylene (5). Hennion and Banigan (6) have suggested that the first approach might not be feasible.

EXPERIMENTAL

Except where noted infared spectra were run on the Perkin-Elmer Model 21 Infared Spectrometer and the NMR spectra were recorded on the Varian Associates A-60 NMR Spectrometer and were referenced to external tetramethylsilane. The VPC separations were run on the Perkin-Elmer Vapor Fractometer, Model 154. The Büchi Rotavapor-R was used for removing solvents. Temperatures are in degrees Centigrade.

Preparation of 1-Bromo-1-Chloro-3,3-Dimethylbutane (7)

To a 3-necked 500-ml round bottomed flask equipped with a condenser, addition funnel, thermometer and a teflon coated magnetic stirring bar was added 132 g (1.60 moles) of t-butyl chloride. The flask was cooled to -25° with a dry ice-acetone bath and 3.00 g of anhydrous aluminum trichloride was added. About 164 g (1.60 moles) of vinyl bromide (Dow Chemical Company) was poured from a gas cylinder which had been precooled to below 10° and added slowly to the reaction mixture over 30-45 minutes while keeping the reaction mixture between -30 to -20°. The reaction is exothermic and the temperature rises rapidly if the addition of the vinyl bromide is to fast.

After the addition of the vinyl bromide was complete, the reaction mixture was kept at -30 to -25° for 30 minutes.

It was then decanted into 50 ml of water and stirred until two colorless phases were present. The organic layer was separated, washed with 50 ml of a 10 percent aqueous sodium hydroxide and two 50-ml portions of water. The organic layer was dried overnight over potassium hydroxide.

Crude yield 306 g (95.4%). Boiling range 158-164° (literature 161-163°). NMR (δ, ppm, neat): 1.10, s(9 H); 2.55, d(2 H, J = 6Hz); 6.10, t(1 H, J = 6Hz). IR (cm^{-1}, neat) 2900(s), 1480(s), 1280(s), 1200(s), 885(s), 768(s), 755(s), 718(s), and 600(s).

Preparation of t-Butylacetylene

Three methods were used to dehydrohalogenate the 1-bromo-1-chloro-3,3-dimethylbutane. In the first two methods only the solvents were different, while in the third both the solvent and the dehydrohalogenating agent were changed.

Method 1.

Into a 1-l 3-necked round bottomed flask equipped with a stirrer, addition funnel, condensers, and thermometers (see Diagram 1) was added 100 g of powdered and dried potassium hydroxide, 100 ml of mineral oil, 25 ml of absolute ethanol, and 100 g (0.5 mole) of 1-bromo-1-chloro-3,3-dimethylbutane. The stirred mixture was heated slowly to 130° while watching for an exotherm. Initially the water flow rate in Condenser 1 was regulated so that only the t-butylacetylene distilled.

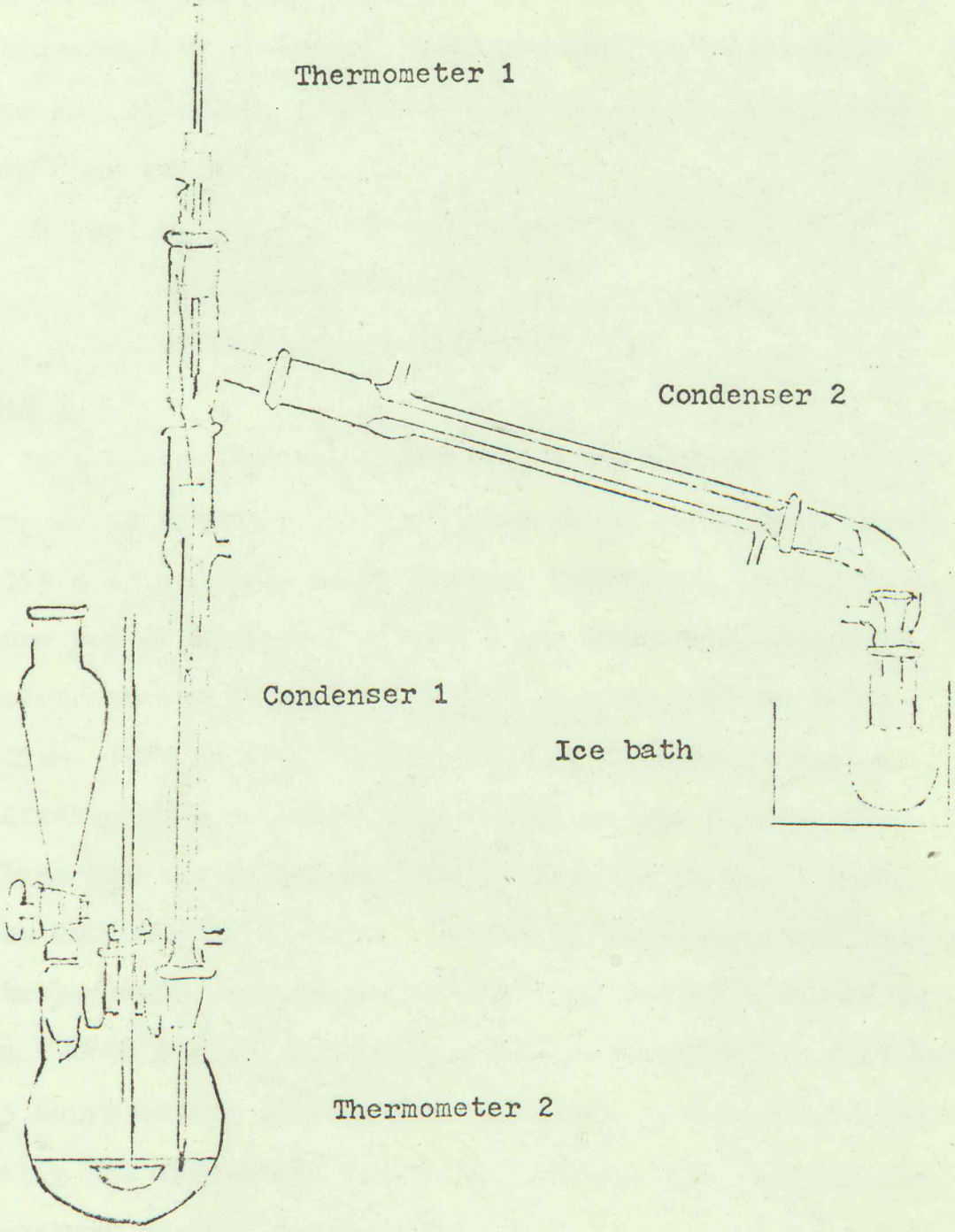

Thermometer 1
Condenser 2
Condenser 1
Ice bath
Thermometer 2

DIAGRAM I

over. The mixture was refluxed for 3 hours before turning the water off in Condenser 1 and allowing the remaining alkyne and alkene to distill over until a pot temperature of 200° was reached.

Yield: alkyne 18.3 g (44%), boiling range 36-7.5°
(literature 39-40°)
alkene approximately 40%

Method 2.

Into a 1-l 3-necked round bottomed flask equipped and set up as in Method 1 was added 300 ml of diethylene glycol and 175 g (3.1 moles) of potassium hydroxide. While the mixture was being heated to 120°, the potassium hydroxide dissolved in the diethylene glycol to give a clear brown solution. Two hundred g (1.0 mole) of 1-bromo-1-chloro-3,3-dimethylbutane was slowly added to the flask. The reaction was exothermic and the temperature rose to 140°, so the heat was turned off. As the addition was continued, the temperature dropped to 110-120° and the heat turned on again. When addition was complete, the mixture was refluxed for 3 hours before turning the water off in Condenser 1, and allowing the alkene and alkyne to distill over until a pot temperature of 200° was reached.

Yield: alkyne 43.0 g (52.2%), boiling range 36-7°
alkene 47.1 g (40.0%), boiling range 103-08°

Method 3.

Into a 500-ml 3-necked round bottomed flask set up and equipped as in Method 1 with the exception that a fractionating column was used in place of Condenser 1, was added 200 ml of dimethyl sulfoxide and 140 g (1.25 moles) of potassium t-butoxide. The stirred mixture was heated to 80°, the heat turned off, and 100 g (0.5 mole) of 1-bromo-1-chloro-3,3-dimethylbutane was added at such a rate as to maintain the head temperature at 36-40°. The reaction was extremely exothermic and the pot temperature rose to about 160°. Later, after about 50 percent of the dihalodimethylbutane was added, the heat was turned on and some of the t-butyl alcohol was forced over. After addition was complete, the alkyne and alcohol were distilled over until a pot temperature of 155° was reached.

Yield: alkyne 28.8 g (70.0%), boiling range 36-38°.

NMR (δ, ppm, neat): 1.20, s(9 H), 1.92, s(1 H).

By Dehydrohalogenation of 1-Chloro-3,3-Dimethyl-1-Butene

Method 1.

The procedure of Method 2 above was used. One mole 118.5 g) of 1-chloro-3,3-dimethyl-1-butene was used in place of 1-bromo-1-chloro-3,3-dimethylbutane. There was no reaction and essentially all of the starting material was recovered. The spectral data of the alkene is: NMR (δ, ppm,

neat); 0.80, s(9 H), 5.80, s(2 H). IR (cm^{-1}, neat); 2950(s),1650(w), 1612(s), 1463(s), 1360(s), 1300(w), 1266(s), 1195(w), 939(s), 823(s), and 795(s).

Method 2.

The procedure and set up of Method 3 above were used for the dehydrohalogenation. One mole (118.5 g) of 1-chloro-3,3-dimethyl-1-butene was used in place of the 1-bromo-1-chloro-3,3-dimethylbutane.

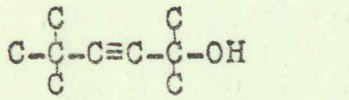
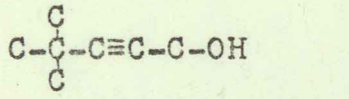
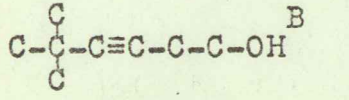
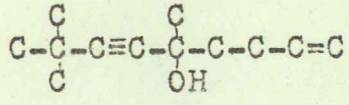
Yield: alkyne 57 g (70%), boiling range 36-38°.

Preparation of Acetylenic Alcohols (See Table I & II)

Into a round bottomed 3-necked flask equipped with an addition funnel, Dewar condenser (dry ice-acetone), thermometer, drying tube and magnetic stirrer was added 25-50 ml of anhydrous ether and the appropriate amount of magnesium. The flask was cooled using an ice bath and bromoethane (same molar amount as the magnesium) in an equal volume of anhydrous ether was added at such a rate as to maintain a gentle reflux. When addition was complete, the ice bath was removed and the mixture refluxed for 30 minutes. The Grignard reagent was cooled in an ice bath and the t-butylacetylene (same molar amount as the magnesium) in an equal volume of anhydrous ether was slowly added. The cooling bath was removed and the reaction mixture allowed to stand overnight.

The next day the acetylenic reagent, which had precipitated out of solution, was cooled using an ice bath. It was sometimes necessary to add some more anhydrous ether, usually 25-50 ml, in order to stir the slurry. Formaldehyde, ethylene oxide, or the appropriate ketone in an equal volume of anhydrous ether was added slowly. After the addition was completed, the mixture was refluxed for 1 hour, cooled, and 10 percent hydrochloric acid was added. The layers were separated and the water layer was extracted 3 times with ether. The ether extractions were combined, washed with 5 percent sodium bicarbonate, once with water, and dried over anhydrous potassium carbonate. The alkynols were purified by distillation, and identified by boiling point, NMR, and IR.

TABLE I

Alcohol	t-Butylacetylene (moles)	Reacting Agent (moles)	Boiling Point	Yield
	20.5 g(0.25)	acetone 14.5 g(0.25)	60-61° at 17 mmHg	22.0 g (62.8%)
	20.5 g(0.25)	formaldehyde[A] 8.00 g(0.267)	74-76° at 20-21 mmHg	14.0 g (50.0%)
 [B]	41.0 g(0.50)	ethylene oxide[C] 26.4 g(0.60)	84-85° at 17 mmHg	32.0 g (50.8%)
	32.9 g(0.40)	allylacetone 39.2 g(0.40)	56° at 1.1 mmHg	43.0 g (59.7%)

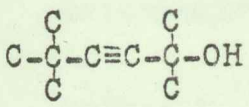
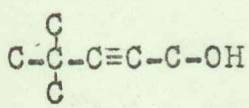
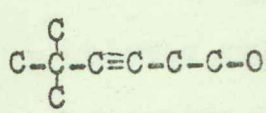
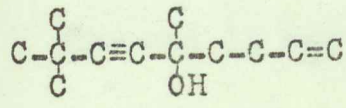
A. Formed by depolymerizing paraform and bubbled into the Grignard solution. Paraform was dried over phosphorous pentoxide for 5 days before using.

B. Tetrahydrofuran used as a solvent instead of ether. Reaction was more vigorous and the acetylenic Grignard was ready to use after 3 hours.

C. The ethylene-oxide-tetrahydrofuran solution was cooled over dry ice before using.

TABLE II

SPECTRAL DATA

Alcohol	NMR(δ, ppm)*	IR(cm^{-1})*
	1.20, s(9 H) 1.42, s(6 H) 4.24, s(1 H)	Not run
	1.10, s(9 H) 4.18, s(2 H) 4.75, s(1 H)	3310(s), 2900(s), 2248(m), 1480(s), 1368(s), 1264(s), 1197(s), 1060(s), 998(s), 832(m)
	1.10, s(9 H) 2.28, t(2 H, J = 7Hz) 3.56, t(2 H, J = 7Hz) 4.84, s(1 H)	3290(s), 2900(s), 2240(vw), 1481(s), 1468(s), 1368(s), 1262(s), 1205(s), 1048(s), 849(m)
	1.08, s(9 H) 1.28, s(3 H) 1.38-1.75, m(2 H) 1.85-2.40, m(2 H) 3.63, s(1 H) 4.58-6.00, m(3 H)	3370(s), 3070(m), 2980(s), 2870(s), 2230(m), 1649(s), 1480(s), 1460(s), 1370(s), 1275(s), 1125(s), 1000(s), 920(s), 875(s), 780(w)

*All NMR and IR spectra were run neat.

Preparation of the Haloalkynes and Haloalkenynes

(see Tables III & IV)

The haloalkynes were prepared from the corresponding alcohols with concentrated hydrochloric acid, phosphorous trichloride, or phosphorous tribromide.

Method 1.

Preparation of 2-Chloro-2,5,5-Trimethyl-3-Hexyne

Into a 250-ml 3-necked round bottomed flask was added 22.0 g (0.157 mole) of 2,5,5-trimethyl-3-hexyn-2-ol. The flask was cooled in an ice bath, 25 ml of concentrated hydrochloric acid added, stirred for 2 hours, and the layers separated. The organic layer was washed with three 20-ml portions of water and dried over anhydrous calcium chloride. NMR and IR were taken (see Table IV). Yield: 16.6 g (68.8%).

Method 2.

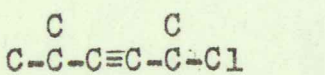
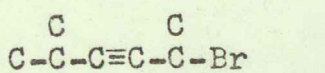
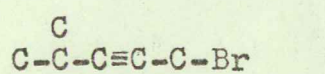
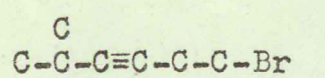
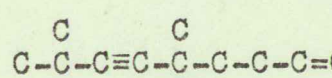
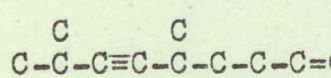
Preparation of 2-Bromo-2,5,5-Trimethyl-3-Hexyne

Into a 250-ml 3-necked round bottomed flask equipped with condenser, an addition funnel, thermometer, drying tube, and magnetic stirrer was added 15.6 g (0.11 mole) of 2,5,5-trimethyl-3-hexyn-2-ol and 50 ml of anhydrous ether. The flask was cooled in an ice bath and 13.6 g (4.8 ml, 0.05 mole) of phosphorous tribromide was slowly added over a 45 minute period. The temperature was kept below 8° during the addition. The reaction mixture was stirred for 3 hours at

2-4° before slowly adding 20 ml of water. The layers were separated and the organic layer washed with 20 ml of 5 percent aqueous sodium bicarbonate, two 20-ml portions of water, and dried over anhydrous calcium chloride.

Yield: 20.3 g (91%). A NMR was taken. Other haloalkynes and -alkenynes were prepared as above. With phosphorous trichloride the reaction time was 4 hours instead of 3. See Tables III and IV for the compounds made, their physical characteristics, and spectral data. A VPC was run on the chlorotrimethylnonenyne using a diisodecyl phthalate column, temperature 122°, 10 pounds pressure, and it showed that 2 products were present in an 8.1 to 1 ratio, the major product appeared at 47 minutes and the minor product at 29 minutes.

TABLE III

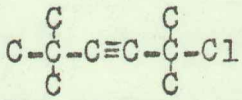
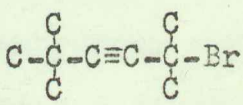
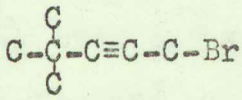
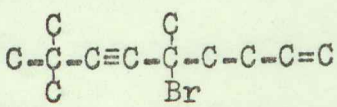
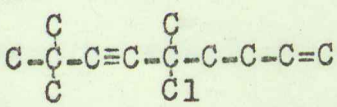
Haloalkyne or Haloalkenyne	Halogenating Agent and Procedure	Alcohol (moles)	Boiling Point	Yield
	conc. HCl, 1 25 ml	2,5,5-trimethyl- 3-hexyn-2-ol 22.0 g (0.157)	A	16.6 g (68.8%)
	PBr_3, 2 13.4 g (0.05 moles)	2,5,5-trimethyl- 3-hexyn-2-ol 15.6 g (0.11)	A	20.3 g (91.0%)
	PBr_3, 2 13.4 g (0.05 moles)	4,4-dimethyl- 2-pentyn-1-ol 14.0 g (0.125)	A	13.1 g (60.0%)
	PBr_3, 2 20.3 g (0.075 moles)	5,5-dimethyl- 3-hexyn-1ol 23.8 g (0.19)	B	--
	PBr_3, 2 17.1 g (0.06 moles)	2,2,5-trimethyl- 8-nonen-3-yn-5-ol 27 g (0.15)	B	A
	PCl_3, 2 8.50 g (0.062 moles)	2,2,5-trimethyl- 8-nonen-3-yn-5-ol 27 g (0.15)	34-5° at 0.45 mmHg	A

A. Not determined.

B. Decomposed during vacuum distillation.

TABLE IV

SPECTRAL DATA

Haloalkyne or Haloalkenyne	NMR (δ, ppm)*	IR (cm^{-1})*
	1.15, s(9 H) 1.72, s(6 H)	2920(s), 2230(m), 1458(s), 1368(s), 1280(s), 1205(s), 1115(s), 1000(s), 990(s), 796(s)
	1.09, s(9 H) 1.82, s(6 H)	
		2860(s), 2230(s), 1478(s), 1429(s), 1358(s), 1267(s), 1205(s), 967(m), 928(s), 833(s)
	See Figure I	See Figure II
	See Figure III	See Figure IV

* All NMR and IR spectra were run neat.

Preparation of 2,2,5,5-Tetramethyl-7-Octen-3-Yne

Method 1, Part 1.

Preparation of 2-Methyl-4-Penten-2-Ol

Into a 500-ml 3 necked round bottomed flask equipped with condenser, thermometer, addition funnel, drying tube, and magnetic stirrer was added 26.7 g (1.10 moles) of magnesium, 100 ml of anhydrous tetrahydrofuran and 50 ml of anhydrous ether. The flask was cooled in an ice bath and 76.5 g (1.00 mole) of allyl chloride in 25 ml of anhydrous tetrahydrofuran and 125 ml of anhydrous ether was added slowly over 6.7 hours. The temperature of the reaction was kept below 12° and was generally below 8°. The Grignard reagent precipitated out during the addition of the allyl chloride. The reaction mixture was allowed to come to room temperature and to stand overnight. The next day the Grignard reagent was cooled in an ice bath and 58 g (1.00 mole) of reagent grade acetone added over a 2 hour period. The reaction mixture was worked up in the usual manner.

Yield: 43.5 g (43.5%), boiling point 118° (literature 117-19°) (8). NMR (δ, ppm, neat): 1.17, s(6 H); 2.20, d(2 H, J = 7Hz); 4.00, s(1 H); 4.72-6.20, m(3 H). IR (cm^{-1}, neat): 3320(s), 3050(w), 2910(s), 1640(s), 1460(s), 1370(s), 1148(s), 1080(s), 996(s), 777(m).

Part II: Preparation of 4-Chloro-4-Methyl-1-Pentene

Into a 250-ml 3-necked round bottomed flask equipped with condenser, thermometer, addition funnel, drying tube and magnetic stirrer was added 20 g (0.20 mole) of 2-methyl-4-penten-2-ol and 50 ml of anhydrous ether. The flask was cooled in an ice bath and 13.7 g (8.8 ml, 0.10 mole) of phosphorous trichloride slowly added. After completed addition the reaction mixture was stirred for 2 hours before adding 20 ml of water. The layers were separated and the organic layer washed with 20 ml of 5 percent aqueous sodium bicarbonate, 20 ml of water and dried over anhydrous calcium chloride.

Yield: 16.5 g (69.7%), boiling range 34-5° at 66 mm Hg. NMR (δ, ppm, neat): 1.21, s(6 H); 2.18, d(2 H, J = 7Hz); 5.50-6.11, m(3 H). IR (cm^{-1}, neat): 3040(w), 2900(s), 1645(s), 1460(s), 1440(s), 1370(s), 1111(m), 995(s), 918(s), 833(s).

Part III: Preparation of the Tetramethyloctenyne

The t-butylacetylenic Grignard was prepared in the same manner as outlined under the Acetylenic Alcohols from 8.2 g (12.4 ml, 0.10 mole) of t-butylacetylene. The Grignard reagent was cooled in an ice bath and 11.9 g (0.10 mole) of 4-chloro-4-methyl-1-pentene slowly added. The reaction was exothermic and 2 layers separated. The layer containing the product was put on the Rotavapor-R to remove the solvent only, but all of the contents of the flask were removed.

Method 2, Experiment 1.

Into a 250-ml 3-necked round bottomed flask equipped with a condenser, thermometer, addition funnel, drying tube and magnetic stirrer was added 36 ml of 3M allylmagnesium chloride in tetrahydrofuran (Alfa Inorganics). The flask was cooled in an ice bath and 16.6 g (0.107 mole) of 2-chloro-2,5,5-trimethyl-3-hexyne in 20 ml of anhydrous tetrahydrofuran was slowly added over 1.5 hours. When addition was complete, the mixture was allowed to come to room temperature slowly before heating to 35° for 1 hour. The reaction mixture was cooled and kept overnight before working it up in the usual manner. The results are presented after Method 3.

Method 2, Experiment 2.

This experiment was the same as Experiment 1 except that the addition time of the 2-chloro-2,5,5-trimethyl-3-hexyne was added over a 6 hour period and the reaction mixture was stirred for 2 hours before allowing the reaction to come to room temperature. The remainder of the experiment was the same.

Method 2, Experiment 3.

This experiment was the same as Experiment 1 except that the 2-chloro-2,5,5-trimethyl-3-hexyne was added as quickly as possible.

Method 2, Experiment 4.

This experiment was the same as Experiment 1 except that allylmagnesium bromide was used in place of allylmagnesium chloride.

Method 3, Experiment 1.

Part 1: Preparation of Allylphenyl Ether

Into a 1-l 1-necked round bottomed flask equipped with a condenser was added 43.5 g (0.46 mole) of phenol, 300 ml of acetone, 62.1 g of potassium carbonate, 37.5 g of potassium iodide, and 41.1 g (0.54 mole) of allyl chloride. The mixture was refluxed for 8 hours and cooled to room temperature. The organic layer was filtered off and the salt washed with four 100-ml portions of ether. The ether extractions were combined with the organic layer. The ether and acetone were removed by vacuum distillation and the resulting organic layer washed with base to remove the unreacted phenol.
Yield: 43.1 g (70.0%) boiling point 92° at 47 mm Hg. (9).

Part 2: Preparation of Tetramethyloctenyne

Into a 500-ml 3-necked round bottomed flask equipped with condenser, thermometer, drying tube, nitrogen inlet tube, and magnetic stirrer was added 1.7 g (0.22 mole) of lithium wire cut into 10 mm lengths and 50 ml of anhydrous tetrahyrdofuran (10). The mixture was cooled to -15° using an ice-salt bath and 13.4 g (0.10 mole) of allylphenyl ether in

25 ml of anhydrous ether was slowly added over an 1 hour period. Allyllithium was filtered rapidly through glass-wool into a 250-ml 3-necked round bottomed flask equipped with condenser, thermometer, drying tube, nitrogen inlet tube, and magnetic stirrer and cooled to -25°. To this was slowly added 8.1 g (0.04 mole) of 2-bromo-2,5,5-trimethyl-3-hexyne in 25 ml of anhydrous ether over 25 minutes. The temperature was maintained at -30 to -25° for 1 hour and then allowed to come to room temperature. Fifty ml of water was added and the layers separated. The organic layer was dried and the solvents removed. The remaining was distilled under vacuum.

Method 3: Experiment 2.

Allyllithium was prepared in the same manner as in Experiment 1, Part 2 and transferred to another flask as outlined previously. The reaction mixture was cooled to -35° and 6.34g (0.04 mole) of 2-chloro-2,5,5-trimethyl-3-hexyne in 25 ml of anhydrous ether added over a 45 minute period. The reaction mixture was held at -50 to -30° for 1 hour before packing in dry ice and letting it stand overnight. It was worked up as in Experiment 1.

The results of the above methods were poor. Method 1 left no residue in the flask after removing the solvent on the Rotavapor-R and work along this line was dropped. Method 2 gave 2,2,5,5,6,6,9,9,-octamethyl-3,7-decadiyne.(27). The

yields in each case were less than 1 gram. The melting point was 108-110°. NMR (δ, ppm, in $CDCl_3$): 1.17, s; 1.21, s. Due to closeness of peaks, ratios could not be determined. IR (cm^{-1}, carbon tetrachloride): 2950(s), 1470(s), 1360(s), 1267(s), 1200(s), 1140(s), 988(s). A mass spectrograph ran at Sterling-Winthrop Research Institute had a parent peak at 246. Some of the more important peaks were: 231, 203 and 189. A ^{13}C Fourier Analysis ran at General Electric Research and Development Center showed the presence of t-butyl, isopropenyl, and acetylenic carbons. The material dissolved in concentrated sulfuric acid and gave an orange colored solution indicating the presence of unsaturation. The material, however, did not decolorize bromine in carbon tetrachloride.

Attempted Preparation of 2,2-Dimethyl-8-Nonen-3-Yne

Method 1 Part 1:

Preparation of 4-Penten-1-ol

4-Penten-1-ol was prepared as outlined in Hornig, C. Org. Syn., Coll. III, p. 698. The only change was the use of small chunks of potassium in place of powdered sodium. First tetrahydrofurfuryl chloride was prepared from 102 g (1.00 mole) of tetrahydrofurfuryl alcohol, 87 g (1.1 moles) of pyridine, and 125 g (1.05 moles) of thionyl chloride. Yield: 84.4 g (70.0%) boiling range 48-49° at 17 mm Hg. The 4-penten-1-ol was prepared from 44 g (1.1 moles) of

potassium in 180 ml of anhydrous ether. Yield: 30.0 g (70.0%) boiling range 133-140°.

Method 1 Part II.

Preparation of 5-Bromo-1-Pentene (10)

5-Bromo-1-pentene was prepared according to the method of Forge, Green, and Gersdorff. Thirty g (0.35 mole) of 4-penten-1-ol, 8.1 g (8.2 ml, (0.099 mole) of pyridine, and 39.3 g (13.8 ml, 0.146 mole) of phosphorous tribromide were used. Yield: 39.2 g (75.0%) boiling range 68-70° at 12 mm Hg.

Preparation of 2,2-Dimethyl-8-Nonen-3-Yne

The t-butylacetylenic Grignard was prepared in the usual manner from magnesium, 3.70 g (0.15 mole), t-butyl-acetylene, 12.3 g (0.15 mole) and allowed to stand overnight before using. The Grignard reagent was cooled in an ice bath and 5-bromo-1-pentene, 22.35 g (0.15 mole) in 22 ml of anhydrous ether was added slowly. The reaction mixture was held at 3° for two hours before allowing it to slowly warm to room temperature. The mixture was refluxed for 1 hour before cooling and worked up in the usual manner. There was no reaction.

Method 2.

Into a 250-ml 3-necked flask equipped with condenser, thermometer, addition funnel and drying tube was added 30 ml of anhydrous ether and 3.64 g (0.15 mole) of magnesium.

Twenty g (0.15 mole) of 4-bromo-1-butene (K and K Laboratories) in 20 ml of anhydrous ether was added slowly to form the Grignard reagent. When addition was complete, the reaction mixture was refluxed for 30 minutes. It was cooled in an ice bath and 25.00 g (0.15 mole) of 1-bromo-4,4-dimethyl-2-pentyne in 25 ml of anhydrous ether was added slowly. It was then reacted under the same conditions as in Method 1 before working up in the usual manner. Yield 5.00 g (28.3%) of 2,2,9,9-tetramethyl-3,7-decadiyne, boiling range 54-55.5° at 14 mm Hg. NMR (δ, ppm, neat): 1.16, s(9 H); 3.92, s(2 H). IR (cm^{-1}, neat): 2855(s), 2230(s), 1649(w), ,1478(s), 1455(s), 1360(s), 1263(s), 1205(s), 1060(m), 990(s), 833(s). NMR and IR spectra indicate that a small amount of olefin is present.

Preparation of 2,2,5,5-Tetramethyl-8-Nonen-3-Yne

Into a 250-ml 3-necked round bottomed flask equipped with Dewar condenser, thermometer, drying tube, addition funnel and magnetic stirrer was added 2.43 g (0.10 mole) of magnesium and 25 ml of anhydrous ether. The flask was cooled using an ice bath and an ice cold solution of 9.5 g (0.10 mole) methyl bromide in 10 ml of anhydrous ether added slowly. After the completed addition, the mixture was refluxed for 30 minutes. The Grignard reagent was cooled using an ice bath and 18.2 g (0.075 mole) of crude 5-bromo-2,2,5-trimethyl-8-nonen-3-yne in 10 ml of anhydrous ether slowly added. After addition was

complete the reaction mixture was refluxed for 1 hour, cooled and worked up in the usual manner.

Crude yield: 11.65 g. The material was distilled and then fractionally distilled using a glass bead column. The material remaining in the flask after the first distillation was set aside and later it was noticed that crystals had formed. (Melting point 85-89° after washing with ethanol). Yield: less than 1 g. NMR (in CCl_4): see Figure V. Yield (liquid): 2.2 g at 70-72°, 17 mm Hg. NMR (neat): see Figure VI. IR (neat): see Figure VII. Also a VPC was run using a diisodecyl phthalate column, temperature 122°, 10 pounds pressure, and it showed that 2 products were present in a 1.9 to 1 ratio, the major product appeared at 34 minutes and the minor product at 47 minutes.

DISCUSSION

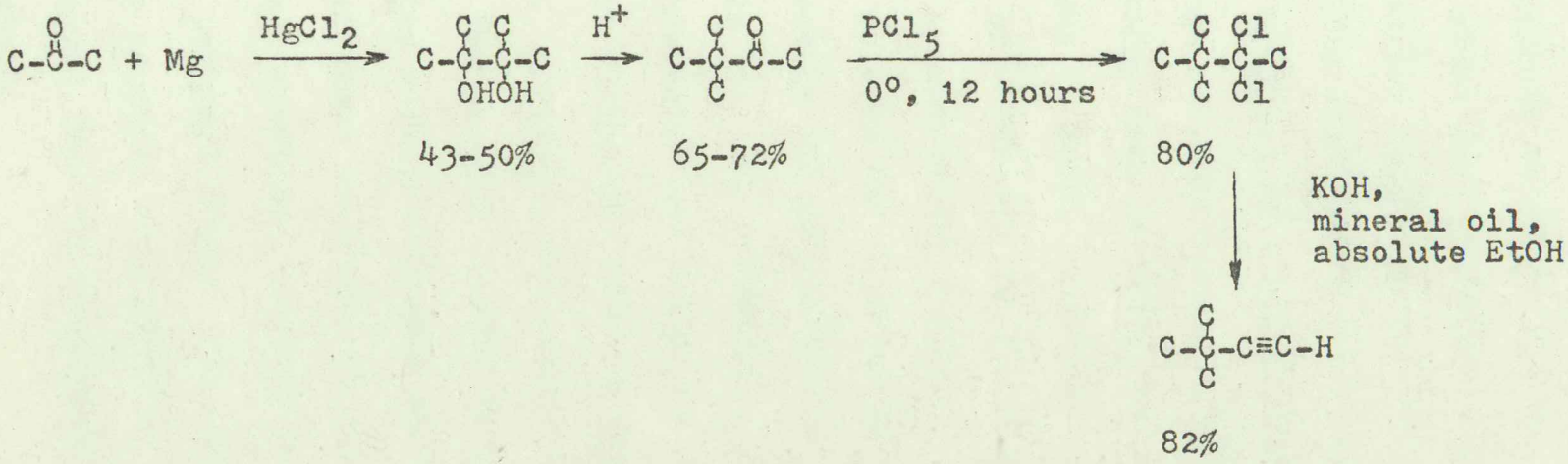
Traditionally t-butylacetylene is prepared by the halogenation of pinacolone with phosphorous pentachloride at 0° and the product dehydrohalogenated with potassium hydroxide in mineral oil and absolute ethanol for a total preparation time of about 15 hours. As indicated in Figure VIII, the overall efficiency of this method is low. A new method was developed which is also shown in Figure VIII. The dihalodimethylbutane was prepared by the method of Brändström (12), vinyl bromide being used instead of vinyl chloride. Since vinyl bromide boils at 16° versus -13.9 for vinyl chloride, the use of vinyl bromide eliminates the need to bubble a gas into the reaction. The yield in either case is about 95 percent. Sometimes the initial exotherm from the addition of the small amount of vinyl bromide to the reactants was not observed, making it necessary to add more aluminum trichloride until an exotherm was observed.

Several of the standard techniques were used to dehydrohalogenate the dihalide. None of them were very satisfactory, mainly because of the amount of the trans olefin that was formed. Since this isomer could not be dehydrohalogenated easily, other systems were considered. Of these, potassium t-butoxide in dimethyl sulfoxide was chosen and found to give good results. When this system was used to dehydrohalogenate

FIGURE VIII

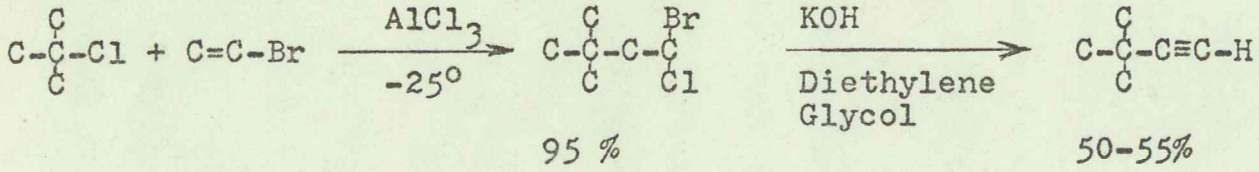
PREPARATION OF t-BUTYLACETYLENE

LITERATURE (28)



Overall efficiency 23.6%

PRESENT APPROACH



Overall efficiency 47.5%

the dihalide, the overall yield was better than 50 percent, and the overall reaction time was about 5 hours. Gordinier (13) has since used potassium hydroxide in place of the more expensive potassium t-butoxide and has found comparable results with yields sometimes exceeding 70 percent.

The Grignard of t-butylacetylene was prepared through an exchange reaction with ethylmagnesium bromide. The solvent normally used in these exchange reactions is ether and takes about 12 hours. In this study tetrahydrofuran was used in place of ether and the slightly exothermic reaction took place in approximately 3 hours. Clearly tetrahydrofuran is a better solvent for this reaction.

Generally the preparation of the alkynols went with ease. (See Table I). The literature (14) reveals that there are several syntheses involving the reaction of ethylene oxide with acetylenic Grignards, such as those made from methyl-, ethyl-, n-propyl-, n-butyl-, n-pentyl-, and n-hexylacetylene. The yield of the desired alcohol is generally 30 to 40 percent except when methylacetylenic Grignard is used. The major by-product of these reactions is the ethylene halohydrin. When the t-butylacetylenic Grignard was reacted with ethylene oxide in tetrahydrofuran, the yield was 50 percent. Since the other reaction used ether as a solvent, the higher yield might suggest that tetrahydrofuran is a better solvent for this reaction.

With the exception of 1-bromo-5,5-dimethyl-3-hexyne, 5-bromo- and 5-chloro-2,2,5-trimethyl-8-nonen-3-yne, the halogenations went well. The 1-bromo-5,5-dimethyl-3-hexyne and the 5-bromo-2,2,5-trimethyl-8-nonen-3-yne decomposed during the vacuum distillation. The halononenynes showed several peaks on the NMR spectra which could not be explained (see Figure I and III). The bromotrimethylnonenyne shows the appearance of a singlet next to the t-butyl peak and a triplet at 2.80 ppm. The NMR spectrum of the chlorotrimethylnonenyne shows several peaks which are not consistent with the structure. These peaks are at 0.95 (2 singlets), 1.54 (singlet) and 2.7 (triplet). It is not possible to separate these materials by fractional vacuum distillation. A VPC was run on the chlorotrimethylnonenyne using a diisodecyl phthalate column and it indicated that there were two products present in an 8.1 to 1 ratio. When the chlorotrimethylnonenyne was treated with aqueous silver nitrate, a white precipitate was formed, indicating the presence of the halide. At this time to propose a mechanism that would explain these peaks is difficult.

The last step of these reactions involves the coupling of a halo-compound with a Grignard reagent to form the desired product. In many cases however, the compounds coupled abnormally. Späth has concluded that these reactions are essentially a free radical process and the first step

may be represented as R-X + R'-MgX' ⟶ MgXX' + R• + R•' (15). The normal coupling product is R-R', but side reactions can occur, and in some cases the major product becomes R-R and R'-R'. Fuson has shown that in the case of the alkylation of methylmagnesium iodide with benzyl chloride the major products, which are present in equal amounts, are bibenzyl and ethane. The normal product, ethylbenzene, is only 25 percent of the yield (16). Also, when 5 mole percent of colbaltous chloride is introduced into the reaction system, the ratio of the normal to abnormal coupling can change drastically. For example, in the absence of colbaltous chloride, methylmagnesium bromide reacts with cinnamyl chloride to give an 89 percent yield of the normal product. With colbaltous chloride the yield of the normal product is 12 percent and the abnormal products is 70 percent (17).

Acetylenic Grignards also react with alkyl halides. For example, n-butyl bromide reacts with ethynlmagnesium bromide to give n-buylacetylene in 72 percent yield (18). On the other hand ethyl bromide reacts with ethynldimagnesium bromide to give 3-pentyne in 20 percent yield.(19). It should be noted that 1-heptynlmagnesium bromide does not with iodomethane at all (20). Another peculiarity is the reaction of allyl bromide with an acetylenic Grignard. Unless a catalytic amount of cuprous or cupric chloride, bromide or cyanide is added the reaction will not go (21).

In spite of Hennion's and Banigan's suggestion that acetylenic Grignards will not couple with tertiary halides, an attempt was made to couple 4-chloro-4-methyl-1-pentene with the t-butylacetylenic Grignard reagent (22). The reaction did not couple and this approach to the problem was discontinued.

The next approach to the problem was to use a method similiar to the one Hennion used in the preparation of di-t-butylacetylene in which 2-chloro-2,5,5-trimethyl-3-hexyne was reacted with methylmagnesium bromide. Allylmagnesium chloride was used in place of methylmagnesium bromide in order to form the 2,2,5,5-tetramethyl-7-octen-3-yne. The reaction was run using several different rates of addition and also using allylmagnesium bromide in place of allylmagnesium chloride, but the results were always the same. The only identifiable product was the 2,2,5,5,6,6,9,9-octamethyl-3,7-decadiyne. An NMR spectrum was recorded before the complete evaporation of the solvent and it showed the presence of allylic hydrogens. Perhaps abnormal coupling was taking place and the allylic peaks were actually 1,5-hexadiene, which boils at 60° (23), and would come off during the removal of the solvent. When allyllithium was used in place of allylmagnesium chloride, a small amount of the impure but desired product was obtained. The reaction was repeated, but since the yield was also very low, the approach to the

problem was dropped.

The most sucessful approach to the problem has been the coupling of the impure 5-bromo-2,2,5-trimethyl-8-nonen-3-yne with methylmagnesium bromide to form the 2,2,5,5-tetramethyl-8-nonen-3-yne. A crystalline product was also isolated and has not been completely identified, but it is probably 2,2,5,6,9,9-hexamethyl-5,6-bis(3-butenyl)-3,7-decadiyne. The primary evidence is the NMR (see Figure V). A VPC was run on the remaining material using a diisodecyl phthalate column and it showed that two products were present in a 1.9 to 1 ratio. An NMR spectrum of the mixture had 3 peaks in the t-butyl region (see Figure VI). This is due to the fact that the methyls of the t-butyl group are different from those in the 5,5-position and this would explain a second peak. If elimination instead of coupling had occurred, a product that might be formed is 2,2,5-trimethyl-5,8-dinonen-3-yne. The methyl group in that 5-position would be in a different environment and would explain the third peak.

An attempt was made to prepare 2,2-dimethyl-8-nonen-3-yne by the reaction between 5-bromo-1-pentene and the t-butylacetylenic Grignard. However the reaction did not go at all. This was somewhat surprising since examples of acetylenic Grignards coupling with bromoalkanes have been reported (24).

An attempt was also made to couple 1-bromo-4,4-dimethyl-2-pentyne with 3-butenylmagnesium bromide, but again the dimethylnonenyne was not obtained. Instead, 2,2,9,9-tetramethyl-3,7-decadiyne was obtained. A similiar reaction has been reported (25). For example, 1-bromo-2-butyne has been coupled with ethylmagnesium bromide to give 2-hexyne in 25 percent yield while 2,6-octadiyne, "the by-product", was obtained in 70 percent yield. The usually normal products are obtained with analogous allylic systems (26). It is not clear why 2-alkenes give one product and 2-alkynes give another.

One of the more interesting NMR spectra is that of trans-1-chloro-3,3-dimethyl-1-butene. The spectrum has two singlets, one at 0.80 ppm and the other at 5.80 in a ratio of 9 to 2. The peak at 0.80 ppm is due to the t-butyl group and the other to the olefinic hydrogens. The normal spin-spin coupling constants for olefinic hydrogens are 6-14 Hz when the hydrogens are cis and 11-18 when they are trans. Here the coupling constant is apparently 0. The inductive and field effects of the chloride seem to be counterbalancing the electron donating and field effects of the t-butyl group so that only a singlet is observed at 5.80 ppm. A weak peak on the IR at 1300 cm^{-1} indicates that the hydrogens are trans to each other. When the chlorodimethylbutene was treated with bromine in carbon tetrachloride, the singlet

at 5.80 ppm disappeared and two doublets, one at 3.39 ppm and the other at 6.40, appeared. It is also noted that this compound would not dehydrohalogenate in a potassium hydroxide-diethylene glycol system while it did when treated with potassium t-butoxide-dimethyl sulfoxide.

Clearly several questions are still unanswered. For example, why should 1-bromo-4,4-dimethyl-2-pentyne react with 3-butenylmagnesium bromide to form 2,2,9,9-tetramethyl-3,7-decadiyne and what are the side reactions from the reaction of 2,2,5-trimethyl-8-nonen-3-yn-5-ol in the presence of phosphorous tribromide or phosphorous trichloride. Several of the compounds should be tested for biological activity and investigated in the areas of hydroboration reactions and transition metal complexation.

SUMMARY

Several new compounds have been prepared. They are: 5,5-dimethyl-3-hexyn-1-ol; 2,2,5-trimethyl-8-nonen-3-yn-5-ol; 5-bromo-2,2,5-trimethyl-8-nonen-3-yne; 5-chloro-2,2,5-trimethyl-8-nonen-3-yne; 2,2,5,5-tetramethyl-8-nonen-3-yne and 2,2,9,9-tetramethyl-3,7-decadiyne. Also 2,2,5,6,9,9-hexamethyl-5,6-bis(3-butenyl)-3,7-decadiyne was probably prepared.

Tetrahydrofuran appears to be a better solvent than ether in acetylenic Grignard exchange reactions and in the reaction of the acetylenic Grignard with ethylene oxide. An improved method has been developed for the preparation of the 1,1-dihalodimethylbutane. Dehydrohalogenation to the alkyne has been done with potassium hydroxide in dimethyl sulfoxide, a much better method than those traditionally used. The NMR spectrum of trans-1-chloro-3,3-dimethyl-1-butene has only one peak in the vinyl region.

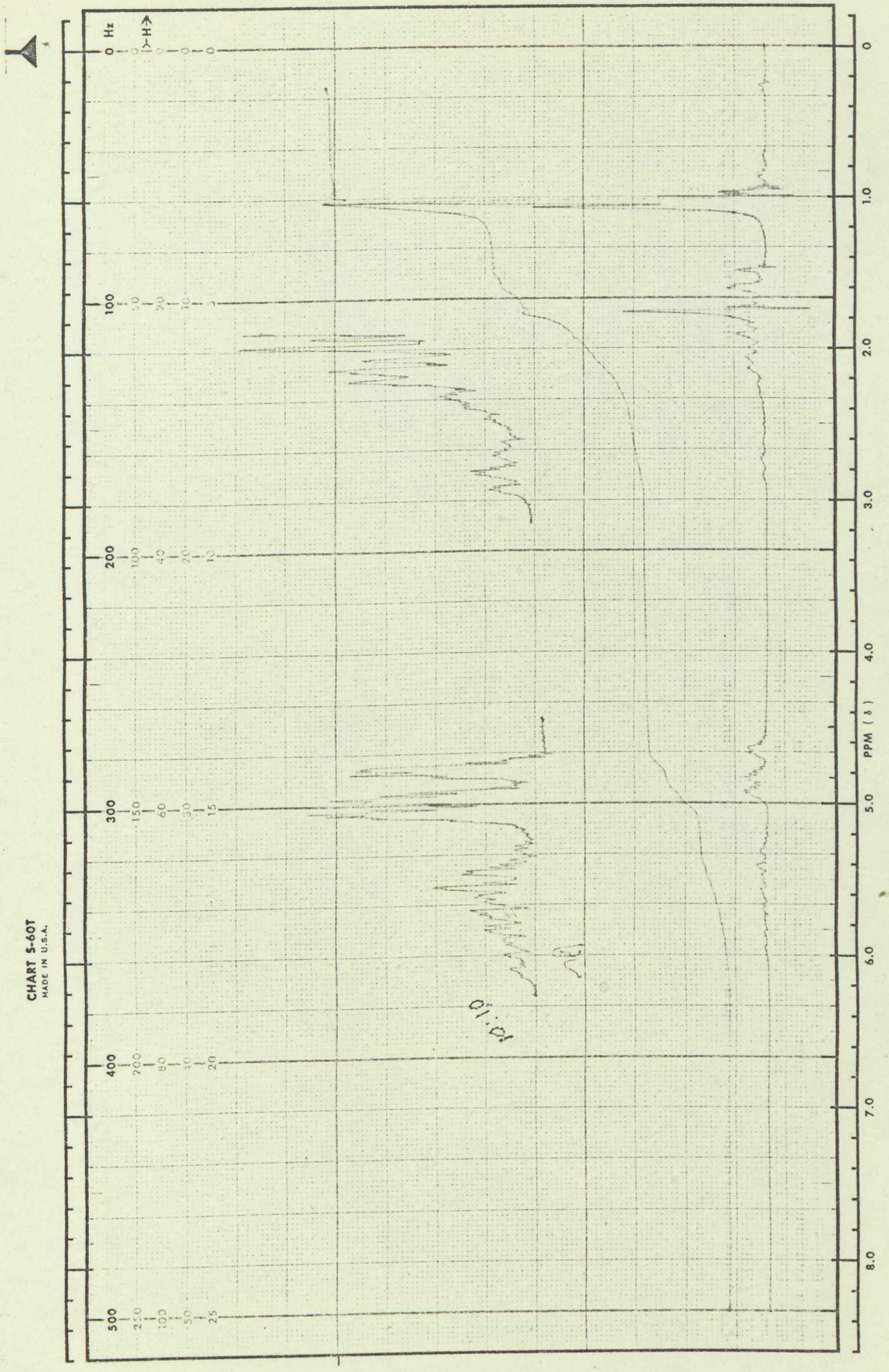


Figure I 5-Bromo-2,2,5-Trimethyl-8-Nonen-3-Yne
(Run on Varian Associate T-60)

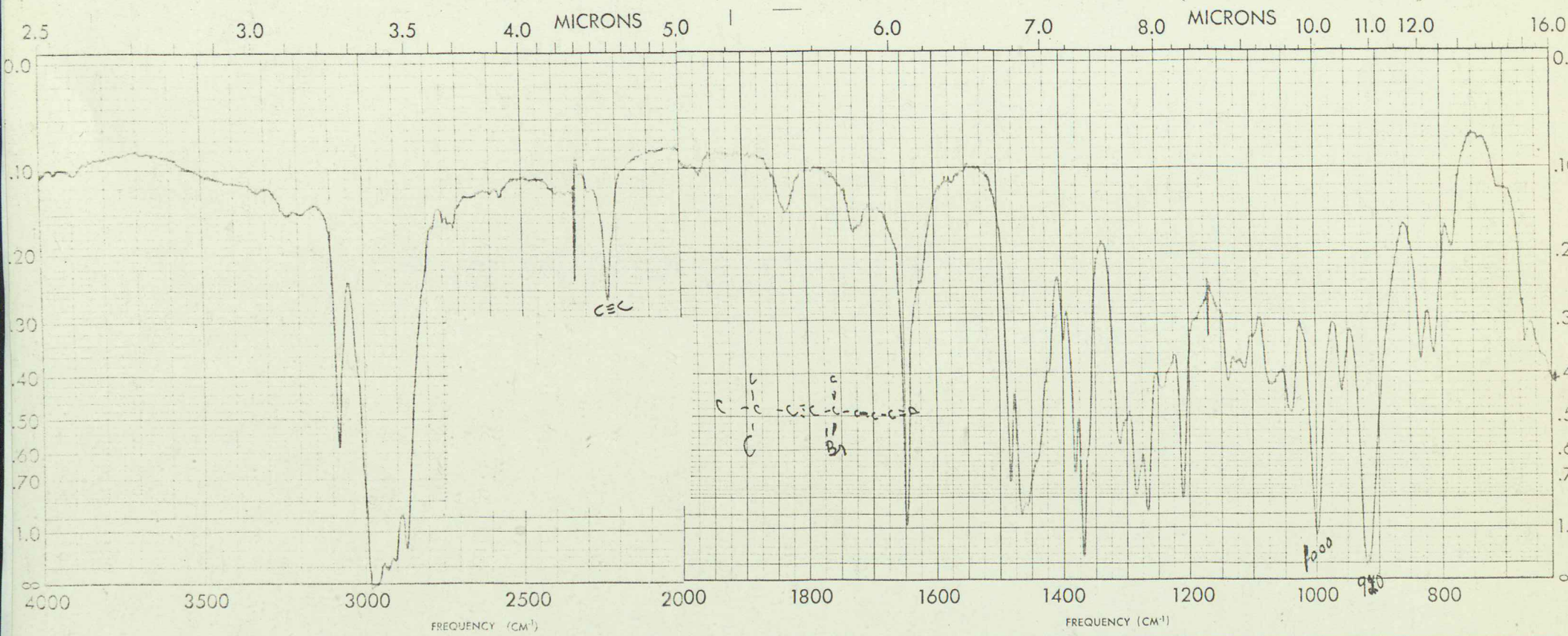


Figure II 5-Bromo-2,2,5-Trimethyl-8-Nonen-3-Yne
(Run on Perkin-Elmer 237)

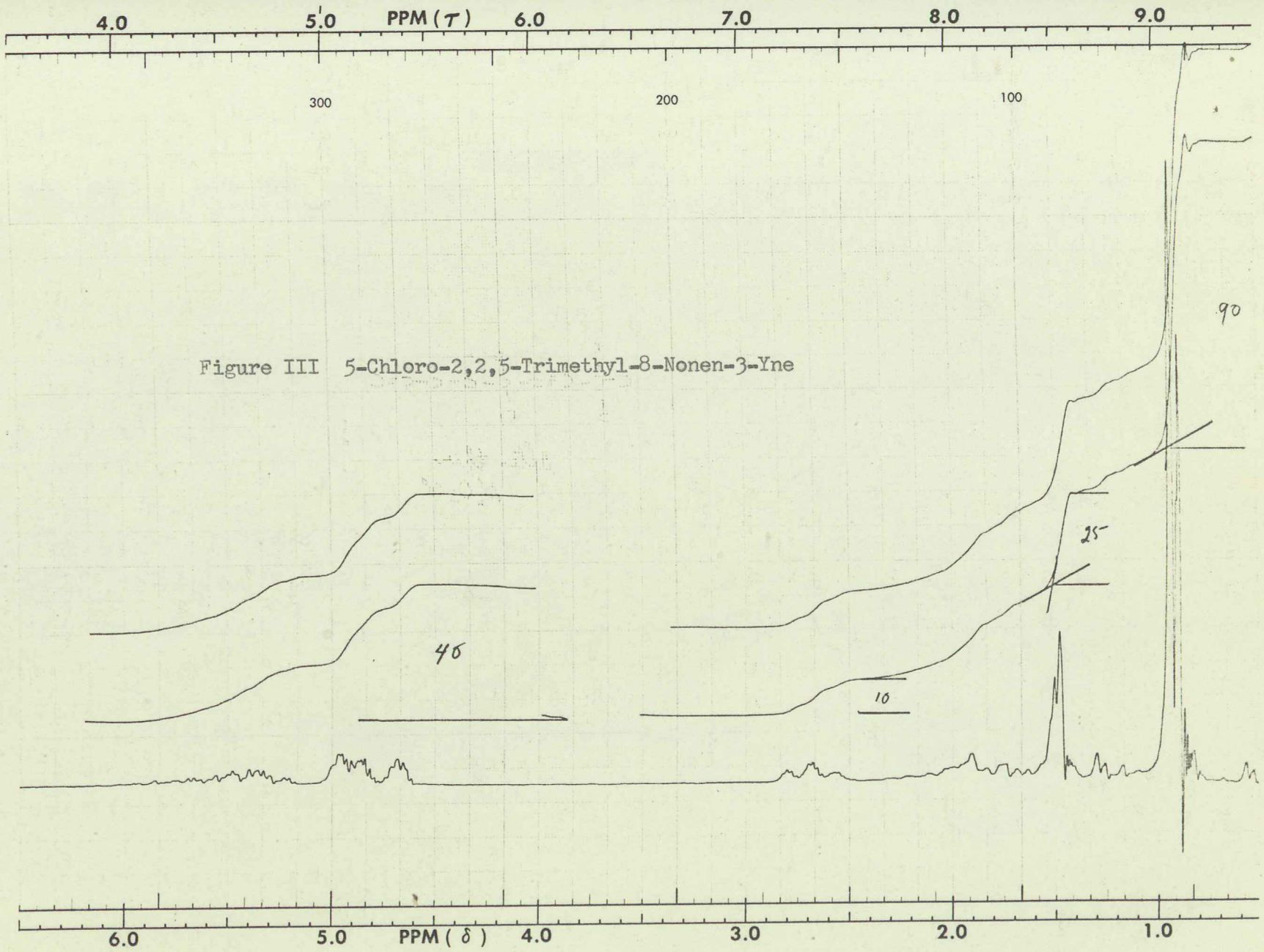


Figure III 5-Chloro-2,2,5-Trimethyl-8-Nonen-3-Yne

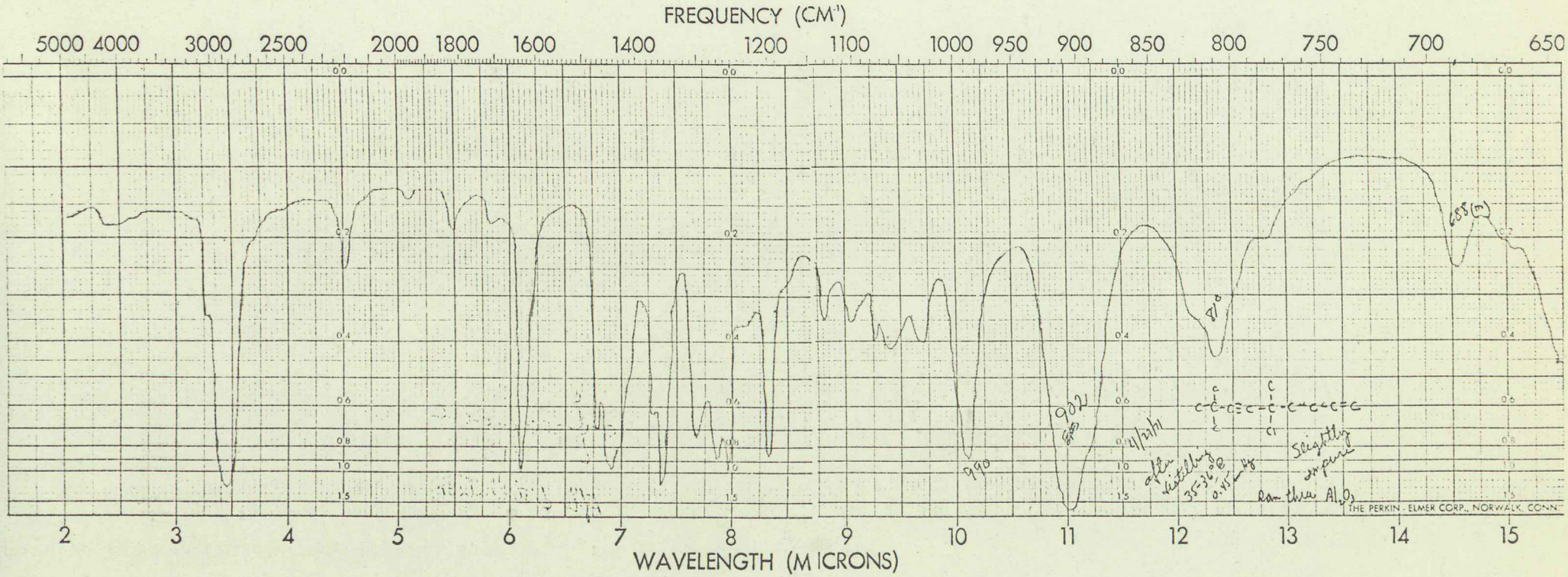


Figure IV 5-Chloro-2,2,5-Trimethyl-8-Nonen-3-Yne

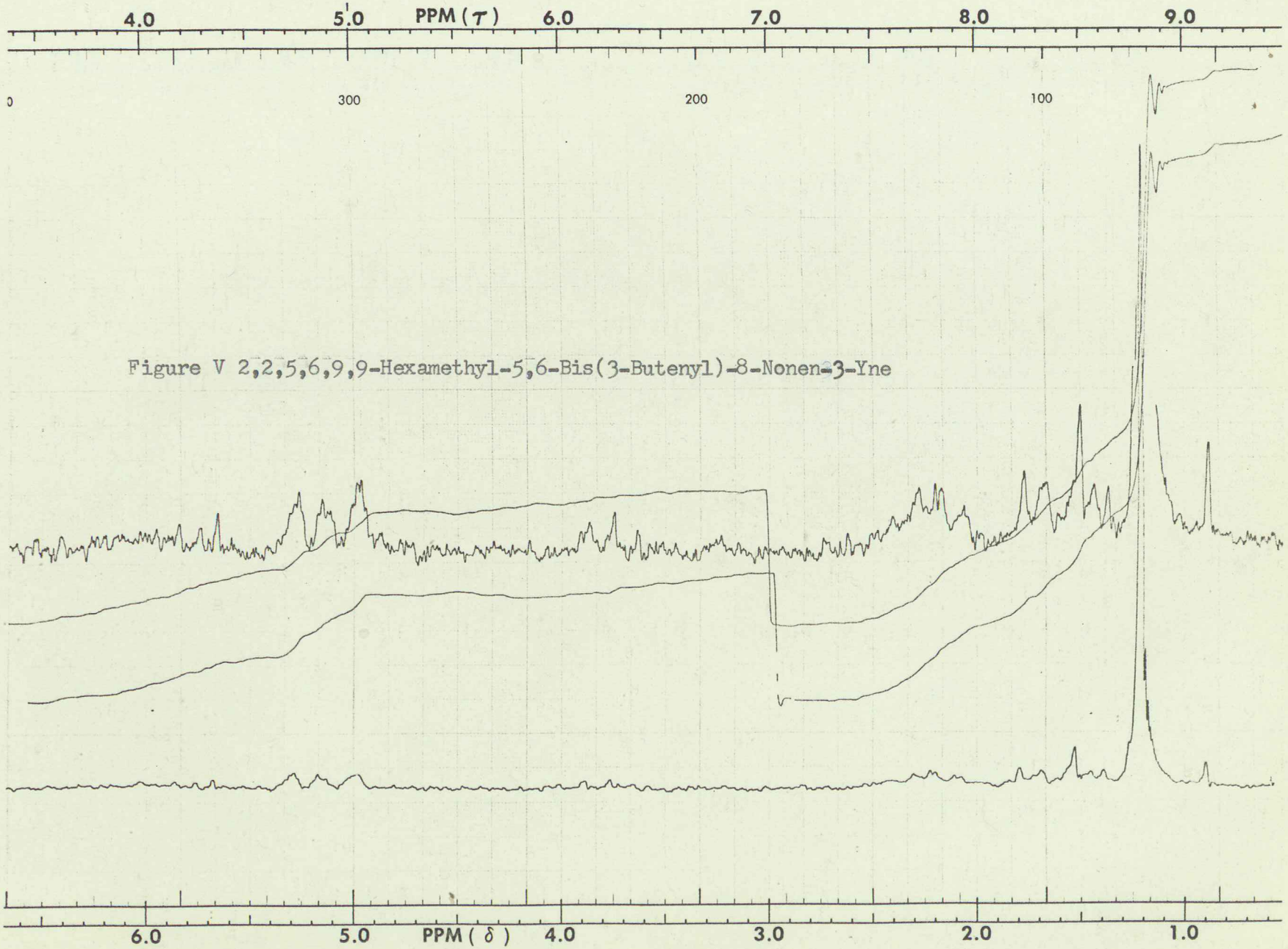


Figure V 2,2,5,6,9,9-Hexamethyl-5,6-Bis(3-Butenyl)-8-Nonen-3-Yne

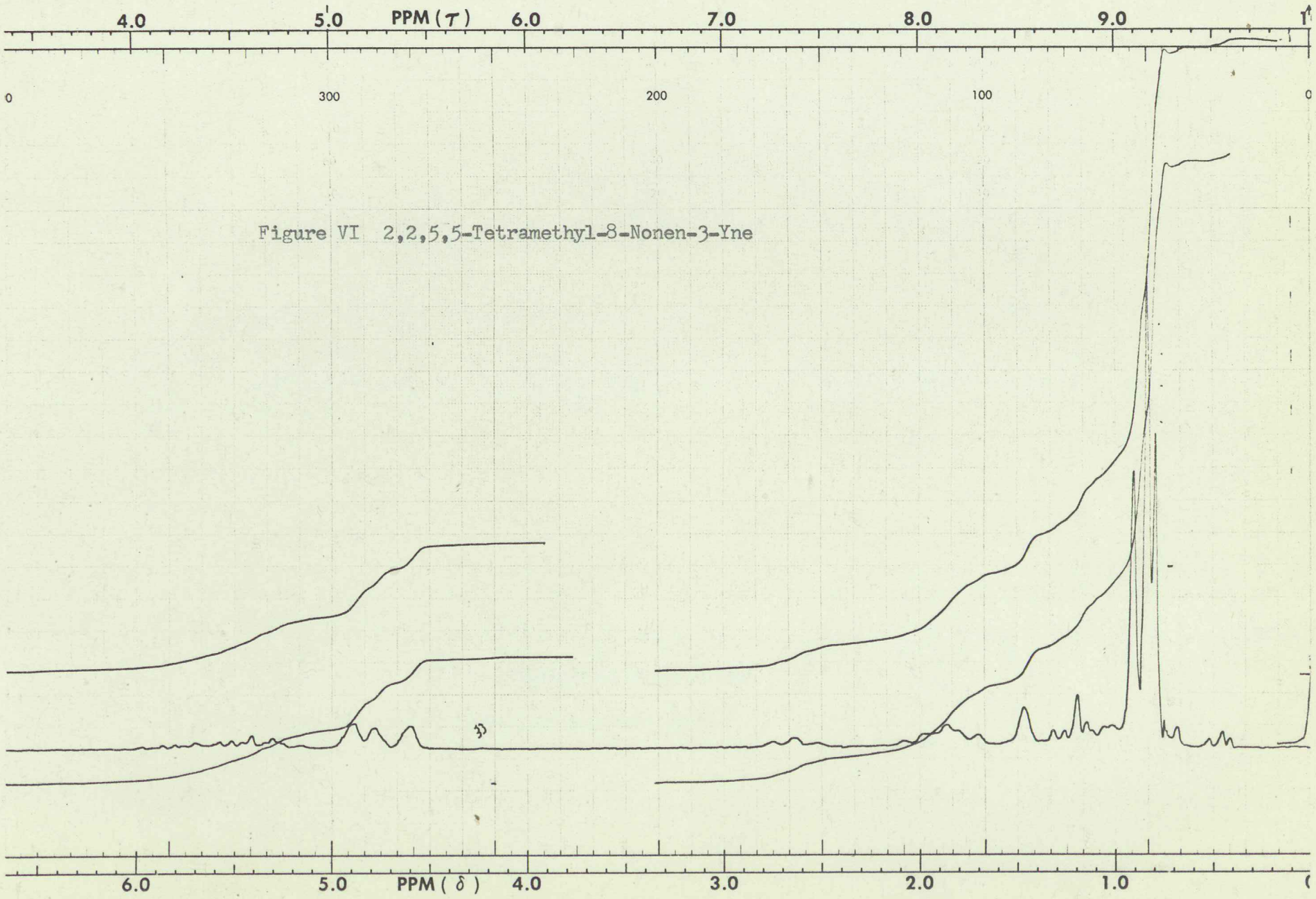


Figure VI 2,2,5,5-Tetramethyl-8-Nonen-3-Yne

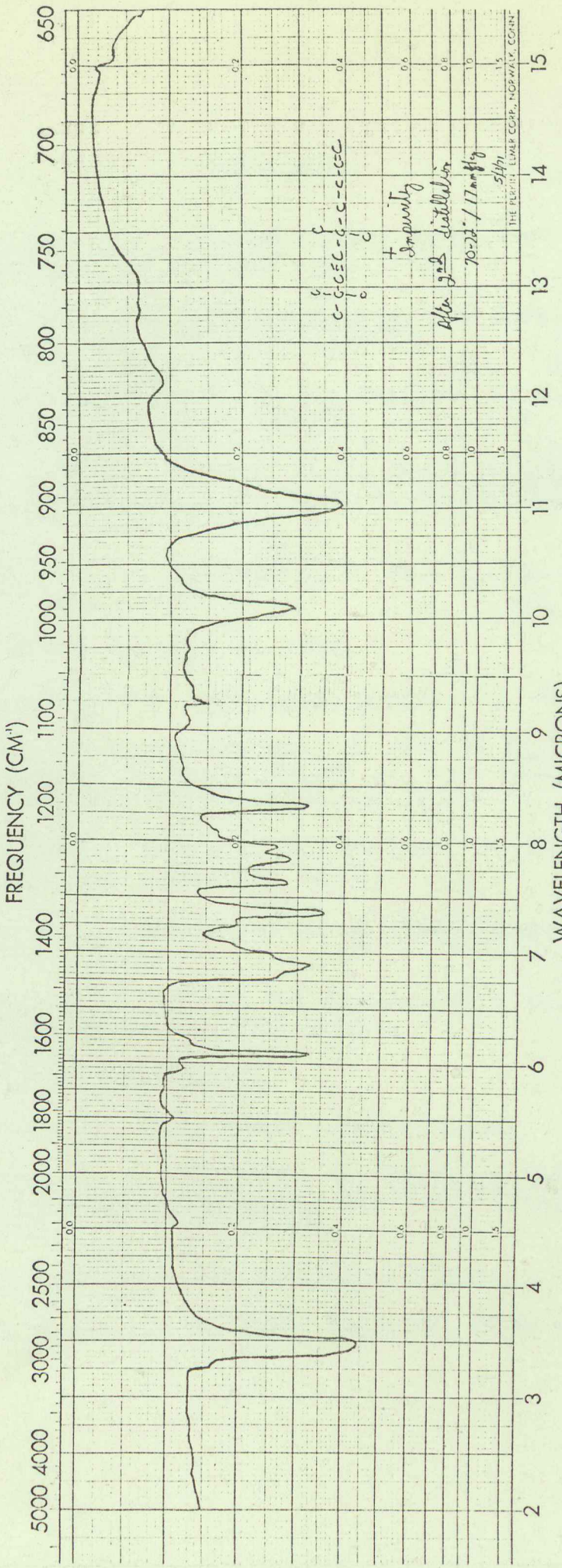


Figure VII 2,2,5,5-Tetramethyl-8-Nonen-3-Yne

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