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I. PROPARGYLATION OF ORGANIC HALIDES USING "ALLENYLLITHIUM".

II. SYNTHESIS AND SOME REACTIONS OF ARYLBORON DICHLORIDES.

III. DIRECT ALKYLATION OF ETHERS BY MEANS OF ACETYLENIC ALUMINUM REAGENTS.

IV. REDUCTIVE CYCLIZATION OF UNSATURATED KETONES.

by

Ⓒ JOSE GUILLERMO CALZADA

A THESIS

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DEPARTMENT OF CHEMISTRY

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FACULTY OF GRADUATE STUDIES AND RESEARCH

The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies and Research, for acceptance, a thesis entitled

I. PROPARGYLATION OF ORGANIC HALIDES USING "ALLENYLLITHIUM".
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IV. REDUCTION CYCLIZATION OF UNSATURATED KETONES.

submitted by JOSE GUILLERMO CALZADA in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

Supervisor

Edgar Warnhoff
External Examiner

Date 15-2-74

A MIS PADRES

A CRISTINA

ABSTRACT

It was found that "allenyllithium" was a highly efficient reagent for the direct propargylation of alkyl, benzylic and allylic halides. In addition, the intermediate lithium acetylide allowed further functionalization to the propargyl alcohol or acetylenic ester.

A general route for the preparation of arylboron dichlorides utilizing tetraaryl tin derivatives was devised. These organoboron compounds upon reaction with ethyl diazoacetate afforded high yields of ethyl arylacetates.

A new reaction was discovered in which ethers were shown to undergo alkylation in the presence of alkynylalanes and aryldiazonium salts.

The cyclization of a δ-olefinic ketone was achieved utilizing an electron transfer reagent. The reductive cyclization of unsaturated ketones was demonstrated to be a synthetically useful procedure for the preparation of complex molecules. A model for the C-D unit of gibberellic acid was synthesized.

ACKNOWLEDGEMENTS

The author wishes to thank Messrs. R. Swindlehurst and G. Bigam and their staffs for recording of the infrared and nmr spectra, Dr. A. Hogg, Mr. A. Budd, and the staff for running the mass spectra, and Mrs. D. Mahlow and Mrs. A. Dunn for determining the microanalyses.

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CHAPTER I

[illegible] NEW, VERSATILE AND DIRECT APPROACH TO PROPARGYLATION

INTRODUCTION

In the past two decades considerable effort has been dedicated to solving the problems associated with coupling reactions. Methods for coupling either a propargylic or allylic unit are especially important for the synthesis of molecules found in nature, particularly those of the isoprenoid type. In this introduction, the discussion will be limited to propargylic coupling.

Basically, there are two approaches to the "propargylation" reaction:

a) The coupling of a propargyl halide with an alkyl or an allylic organometallic,

$$R\,M(X) \;+\; XC\,H_2C{\equiv}C\text{-}H \longrightarrow RC\,H_2C{\equiv}C\text{-}H$$

M = Mg, Li, etc.

b) Coupling of an alkyl or an allylic halide with a propargyl organometallic,

$$R\,X \;+\; (X)\text{-}MC\,H_2C{\equiv}C\text{-}H \longrightarrow RC\,H_2C{\equiv}C\text{-}H$$

M = Mg, Li, etc.

Early reports on the first method, utilizing propargyl bromide and a Grignard reagent, showed that complex mixtures of allenic, acetylenic and metal halogen exchange products were formed.[1,2] Also, because of the presence of a terminal acidic proton in propargyl bromide, the acetylenic Grignard was also produced.

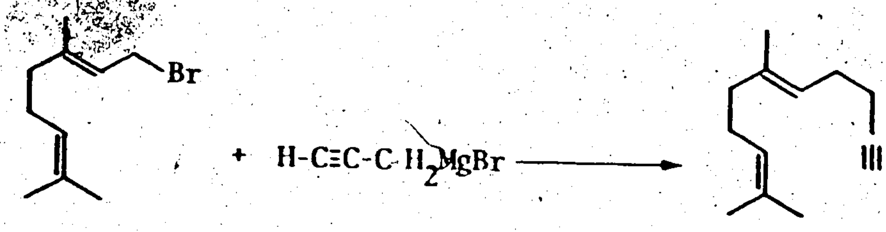
$$\mathrm{H{-}C{\equiv}C{-}CH_2Br + EtMgBr \longrightarrow C_2H_6 + C_2H_5CH{=}C{=}CH_2 + C_3H_7C{\equiv}C{-}H + BrMgC{\equiv}C{-}CH_2Br + C_2H_5Br}$$

Recently, Arens and Brandsma[3] have shown that the main product obtained when the reaction is carried out at a low temperature (-40°) is the allene.

$$\mathrm{CH_3(CH_2)_6CH_2MgBr + H{-}C{\equiv}C{-}CH_2Br \xrightarrow{90\%} CH_3(CH_2)_7CH{=}C{=}CH_2}$$

On the basis of these results, little hope exists for a successful propargylation reaction utilizing this methodology of coupling.

Preliminary work based on the second approach was also not very encouraging due to the low yields and laborious separations required. Examples of earlier attempts are shown in the following equations.[4,5]



Ref.4a

20% (impure)

$$H_2C{=}CH{-}CH_2Br + H{-}C{\equiv}C{-}CH_2MgBr \longrightarrow \underset{5\%}{H{-}C{\equiv}C{-}CH_2CH_2CH{=}CH_2} + \underset{35\%}{H_2C{=}C{=}CH{-}CH_2CH{=}CH_2}$$

Ref. 4b

Although varying the reaction conditions has somewhat improved the outcome of this approach, nevertheless the formation of allenic material has not been avoided. Moreover, the desired acetylene is extremely difficult to separate from the mixture[4a], unless it is transformed into a derivative which can be separated from the allene.

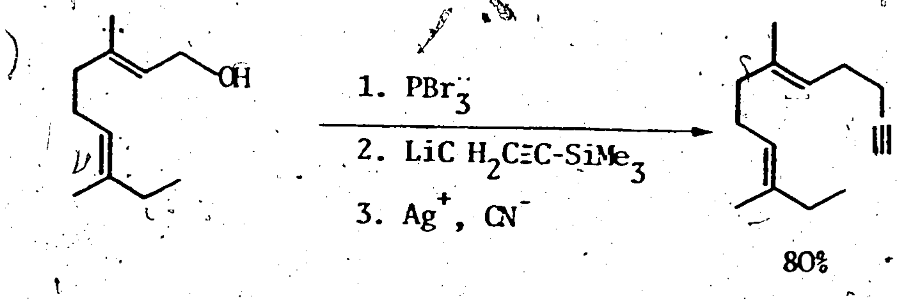
The latter method has recently been modified in two different ways.

In the first, a blocking-deblocking procedure reported by Corey and Kirst[9], the formation of the allene is minimized by making use of a new reagent, 1-trimethylsilylpropynyllithium. The trimethylsilyl group, presumably because of steric hindrance and perhaps also due to electronic factors, avoids, to a great extent, the formation of the allene. Subsequently, deblocking affords the free acetylene in good yields. The entire sequence involves the following reactions:

$$CH_3C{\equiv}C{-}Li \xrightarrow{Me_3SiCl} CH_3C{\equiv}C{-}SiMe_3 \xrightarrow[TMEDA]{n\text{-}BuLi} LiCH_2C{\equiv}C{-}SiMe_3$$

$$\xrightarrow{R{-}X} RCH_2C{\equiv}C{-}SiMe_3 \xrightarrow{Ag^+/CN^-} RCH_2C{\equiv}C{-}H$$

This method has been applied successfully in the total synthesis of several natural products. For example, an important sequence in the synthesis of Cecropia juvenile hormone is illustrated below.[19]

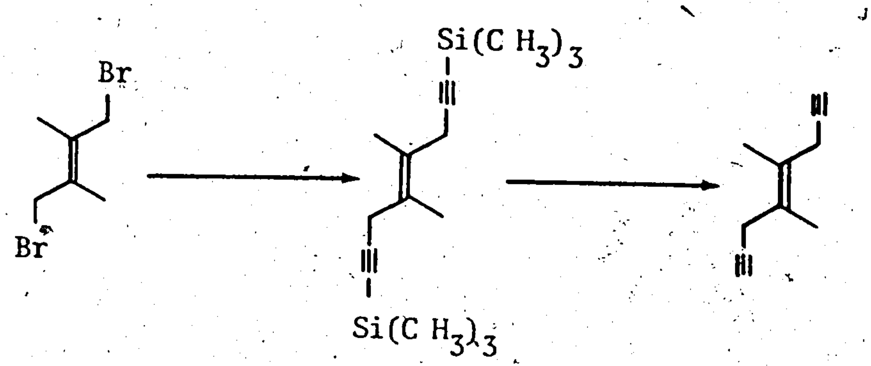


The second modification was devised by Ireland and coworkers.[10] This method utilizes both the "old" procedure (*i.e.*, reaction of the Grignard reagent of propargyl bromide with a halide) in concert with the Corey-Kirst[9] trimethylsilylation procedures. Thus, the crude alkylation reaction mixture is first treated with ethylmagnesium bromide (which acts as a base), then trimethylchlorosilane is added to form the silyl derivative of the alkyne. The separation is carried out and the propargylated product can be regenerated using the same Arens procedure utilized by Corey and Kirst.[9]

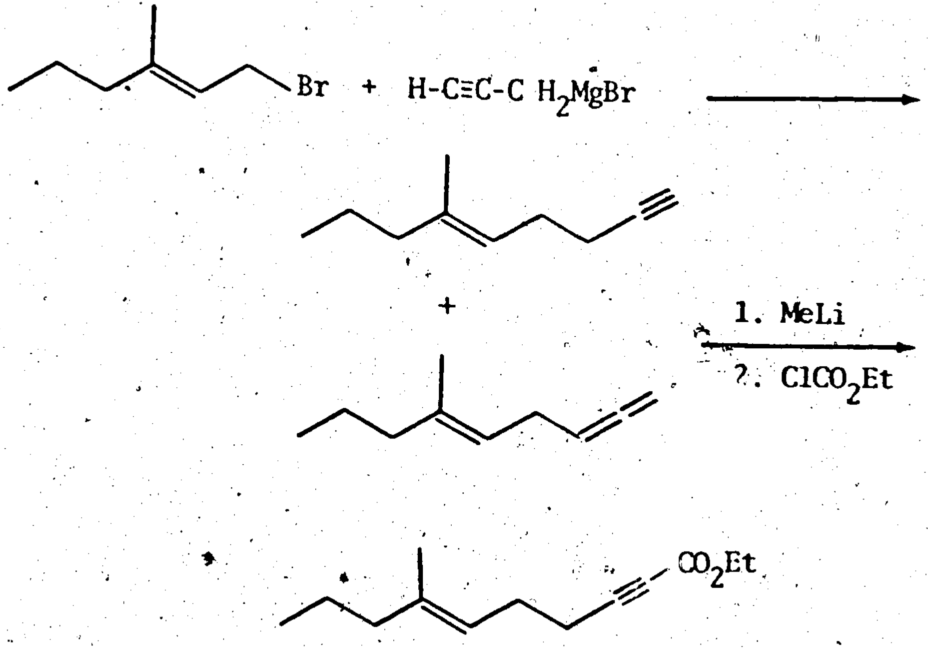
$$R\text{-}X + H\text{-}C{\equiv}C\text{-}CH_2MgBr \longrightarrow \left[R\text{-}CH_2C{\equiv}C\text{-}H + R\text{-}CH{=}C{=}CH_2\right]$$

$$\xrightarrow[2.\ Me_3SiCl]{1.\ EtMgBr} \xrightarrow{Separation} \xrightarrow[CN^-]{Ag^+} R\text{-}CH_2C{\equiv}C\text{-}H$$

One application of this method is illustrated for the synthesis of an enediyne,



This concept was also employed by Katzenellenbogen and coworkers[8] in a synthesis of the tetrahomoterpene isolated from the codling moth.



48-62%

Although some of the procedures discussed earlier have found use for propargylation, they are nonetheless multi-step processes, and it would be highly desirable to find a one step method for such a tranformation.

In 1970[11], F. Jaffe reported the formation of allenyllithium by metalation of allene using *n*-butyllithium in tetrahydrofuran. The chemical properties of this new organometallic were investigated for silation and 1,2-addition to benzophenone.

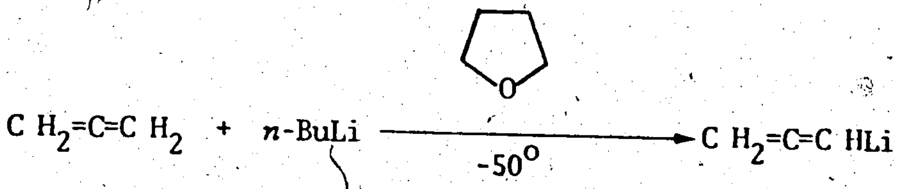
The purpose of the research undertaken here was to investigate the nature and the synthetic potential of this new organometallic compound as a possible propargylating reagent.

RESULTS AND DISCUSSION

Allene has been the subject of extensive study presumably because of its interesting molecular structure. In spite of the fact that many physical and chemical properties of allene are known, no specific investigation has been undertaken to determine the pKa of this hydrocarbon.

Prototropic rearrangements of allenes with bases such as sodium amide or potassium hydroxide[12] tend to indicate that allenic hydrocarbons possessing terminal $C{=}CH_2$ units are relatively "acidic".

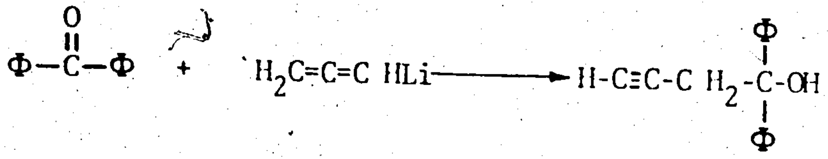
Jaffe[11] has shown that when allene is allowed to react with *n*-butyllithium in tetrahydrofuran at -50°, allenyllithium is produced, and furthermore suggested that as a result of this facile metalation, the pKa of this hydrocarbon is comparable to that of fluorene (pKa 23).



When the metalated allene was allowed to react with trimethylchlorosilane, both the allenyl and the propargyl silanes were obtained (in unstated yields).

$$CH_2{=}C{=}CHLi + Me_3SiCl \longrightarrow CH_2{=}C{=}CHSiMe_3 + H\text{-}C{\equiv}C\text{-}CH_2SiMe_3$$

Furthermore, the addition of allenyllithium to benzophenone afforded the propargylic alcohol in 70% yield.



$$\Phi-\overset{O}{\overset{\|}{C}}-\Phi + H_2C=C=CHLi \longrightarrow H-C\equiv C-CH_2-\underset{\Phi}{\overset{\Phi}{C}}-OH$$

However, no investigation was undertaken concerning the reaction of this organometallic towards alkyl or allylic halides.

The purpose of the present investigation was to explore the chemistry and synthetic scope of alkylation reactions of allenyllithium.

Metalation of allene under the same conditions reported by Jaffe[11] (tetrahydrofuran/*n*-butyllithium, -50°), followed by the addition of *n*-heptyl iodide (molar ratio of RLi/R'I = 2.5) and slow warming to room temperature led to the consumption of all the starting halide and formation of the corresponding allene (20% yield) and the acetylene (16% yield). Also, a volatile material, presumably 1-heptene was detected by glc.

$$CH_3(CH_2)_5CH_2I \xrightarrow{CH_2=C=CH_2/n\text{-}BuLi} CH_3(CH_2)_5CH_2CH_2C\equiv C-H$$

$$+ \; CH_3(CH_2)_5CH_2CH=C=CH_2$$

Apparently allenyllithium in tetrahydrofuran behaved primarily as a base and elimination rather than substitution took place preferentially.

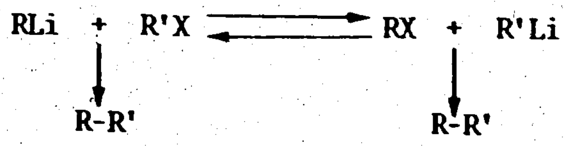
When the reaction was repeated using N,N,N',N'-tetramethylethylenediamine (TMEDA) as an additive in an ether/hexane solvent system, a similar product distribution was obtained (although not all of the starting material was consumed).

These results indicated that polar coordinating media, such as THF or TMEDA, which are known to "free" anions from the corresponding gegenanion,[13] promoted formation not only of elimination product, but rearranged allenic product as well.

As a result, a study of the metalation-alkylation of allene was next undertaken in a less polar solvent system. Ether was initially chosen as solvent, and since commercial *n*-butyllithium in hexane was being employed, a 1:1 ratio (by volume) of ether: hexane was utilized merely for convenience.

The reaction of *n*-butyllithium and allene in a different solvent system posed the problem of determining the extent of the metalation at several temperatures. It was especially important to find the point at which none of the starting *n*-butyllithium remained (*i.e.*, when the metalation was complete).

It is well known that alkyllithium compounds in the presence of alkyl or allylic halides undergo metal-halogen exchange[14]. The result is the formation of three possible products, as illustrated in the following equations:



$$\begin{tikzcd} \mathrm{RLi} + \mathrm{R'X} \arrow[r, shift left] \arrow[d] & \mathrm{RX} + \mathrm{R'Li} \arrow[l, shift left] \arrow[d] \\ \mathrm{R\text{-}R'} & \mathrm{R\text{-}R'} \end{tikzcd}$$

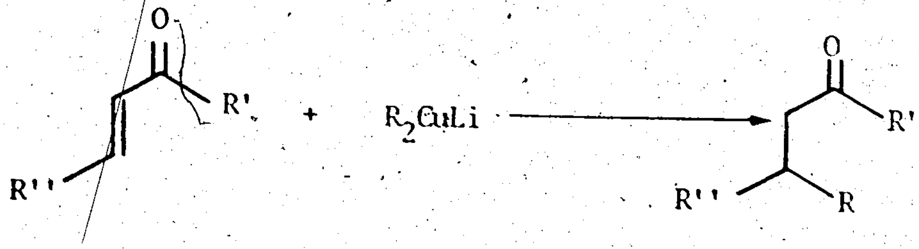
$$RLi + RX \longrightarrow R\text{-}R$$

$$R'X + R'Li \longrightarrow R'\text{-}R'$$

There are several methods available in the literature to determine the presence of alkyllithiums. Among the best known is the Gilman test[15]. However, the Gilman test does not permit the differentiation between two organolithium reagents in a mixture. Thus, it was decided to employ a method that would transform *n*-butyllithium into a derivative, and hopefully, at the same time learn more about the chemistry of allenyllithium.

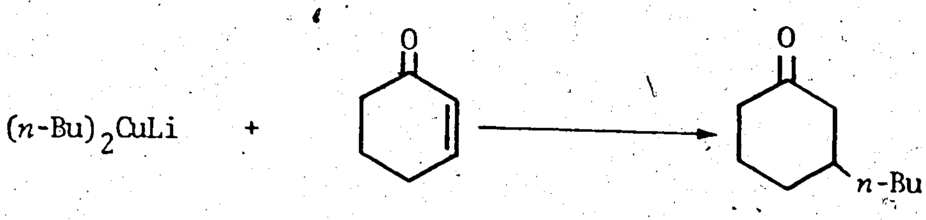
Alkyl, vinylic and aryllithium compounds readily react with cuprous iodide to form an "ate complex" (cuprate)[16]. House and coworkers have demonstrated that these cuprates react under very mild conditions with conjugated enones *via* 1,4- addition[16].

$$2\ RLi + CuI \longrightarrow R_2CuLi + LiI$$



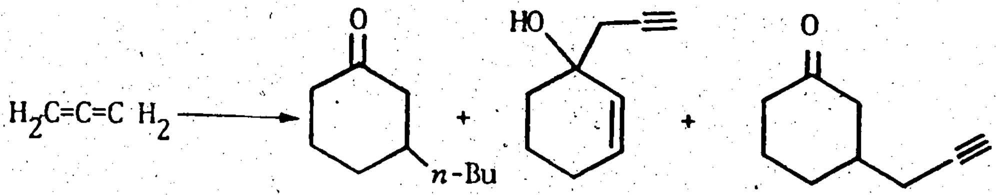
Consequently, this method was chosen for the study of the metalation of allene. If an enone such as 2-cyclohexenone were utilized, the presence of *n*-butyllithium could be detected by the formation of 3-butylcyclohexanone. At the same time, the products arising from allenyllithium would give an indication of the chemical reactivity of this organometallic.

$$2\ n\text{-BuLi} + \text{CuI} \longrightarrow (n\text{-Bu})_2\text{CuLi} + \text{LiI}$$



Allene and *n*-butyllithium were mixed at -78° in hexane/ether (1:1) and then warmed to -50°. At this point cuprous iodide was added, the mixture was stirred for 30 minutes, then cooled to -78° and treated with 2-cyclohexenone. Analysis by glc revealed the exclusive formation of 3-butylcyclohexanone, a clear indication that allene does not undergo appreciable metalation at this temperature.

The same procedure was repeated, but this time the temperature of the mixture was allowed to increase to -30°. Three products were obtained on this occasion: 3-butylcyclohexanone, 1-(2-propynyl)-2-cyclohexen-1-ol, and 3-(2-propynyl)cyclohexanone.



The formation of products containing the propargylic unit demonstrated that allene did undergo metalation under these conditions, however, the presence of 3-butylcyclohexanone indicated that the metalation of allene was incomplete.

In another run, the mixture of allene and *n*-butyllithium (-50°) was allowed to warm to -20°, whereupon a white precipitate formed. This suspension was stirred for 15 minutes at -15° and the same procedure using cuprous iodide and 2-cyclohexenone was followed. This time 3-butylcyclohexanone was absent and only the 1,2- and 1,4-addition products, resulting from propargyl group migration, were present. These results showed that under the aforementioned conditions the *n*-butyllithium was totally consumed. Subsequently these conditions were used for the alkylation reactions.

Addition of *n*-heptyl iodide to the mixture of metalated allene (at -20°, RLi/R'I = 3.1) and slowly warming the resulting mixture to room temperature resulted in the formation of 67% of 1-decyne and 23% of starting iodide. There was no evidence (ir or nmr) of allene formation.

In a repetition of this experiment, it was found that a ratio of RLi/R'I = 5 was necessary to consume all the starting halide. This resulted in the formation of 93% (glc) yield of 1-decyne (after a seven hour reaction period at room temperature).

$$CH_2{=}C{=}CH_2 \; + \; n\text{-BuLi} \xrightarrow[93\%]{n\text{-heptyl iodide}} \text{1-decyne}$$

The propargylation of benzylic and allylic halides, a most interesting problem from the synthetic point of view, was next examined.

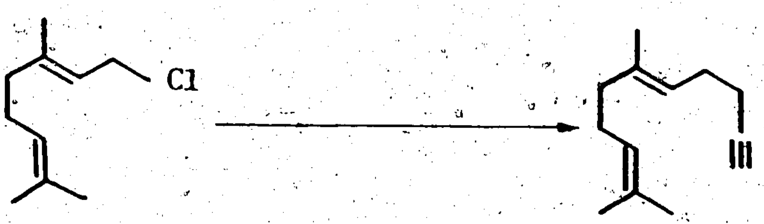
Straight chain terminal acetylenes are usually synthesized by interaction of the corresponding alkyl halide and sodium or lithium acetylide. However, attempts at coupling alkali metal acetylides with homoallylic or homobenzylic halides to produce 1,5-enynes has been proven to be generally inefficient, due to the tendency of these systems to undergo elimination[17,18,19].

The reaction of benzyl chloride with metalated allene was found to be faster than the corresponding reaction with *n*-heptyl iodide. After forty minutes, the starting material was completely consumed with concomitant quantitative transformation to 4-phenyl-1-butyne. Also, the RLi/R'X ratio, necessary to achieve this result, was considerably smaller than in the case of *n*-heptyl iodide, namely 3.5.

$$\Phi\text{-}CH_2Cl \xrightarrow{CH_2=C=CH_2/n\text{-}BuLi} \Phi\text{-}CH_2CH_2C{\equiv}C\text{-}H$$

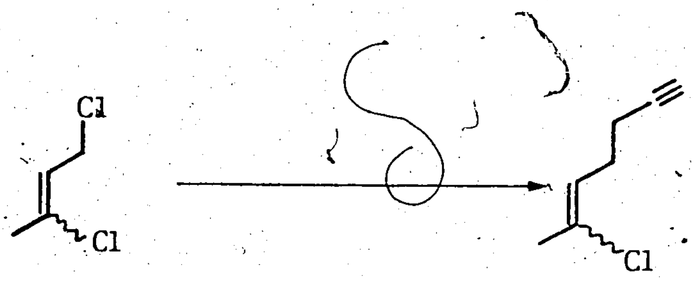
100%

Allylic halides, such as geranyl chloride, behaved in a manner comparable to benzyl chloride. No evidence of S_N2' attack, isomerization of the double bond or allene formation could be detected.



92% (isolated)

Also, 1,3-dichloro-2-butene, was propargylated in 80% (glc) yield.

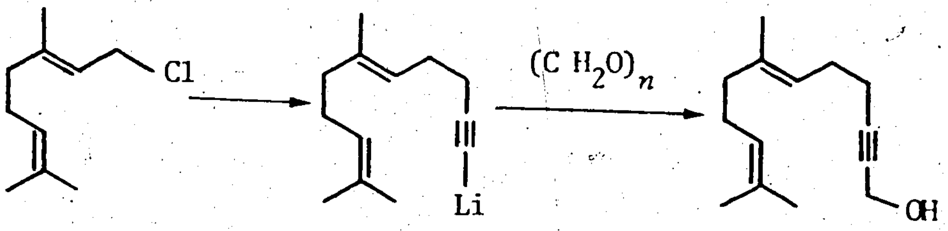


In order to ascertain whether the lithium salt or the free acetylene was present at the end of the reaction, deuterated water was used to quench the mixture using benzyl chloride as alkylating agent. Complete deuteration of the terminal acetylenic product was obtained, demonstrating that the lithium acetylide was the intermediate prior to hydrolysis.

$$\Phi\text{-}CH_2Cl \xrightarrow{CH_2=C=CH_2/n\text{-}BuLi} \Phi\text{-}CH_2CH_2C\equiv C\text{-}Li$$

$$\xrightarrow{D_2O} \Phi\text{-}CH_2CH_2C\equiv C\text{-}D$$

The attractive possibility for further functionalization of this intermediate, either by treatment with paraformaldehyde to form the corresponding propargyl alcohol or with ethyl chloroformate to give rise to the acetylenic ester, also proved to be successful. In this way, the important precursor in the synthesis of farnesol[9] and sirenin was obtained[20] in 83% yield (isolated) from geranyl chloride without isolation of intermediates.



83%

Ethyl chloroformate was employed in the propargylation of benzyl chloride and the corresponding ester was isolated in 80% yield.

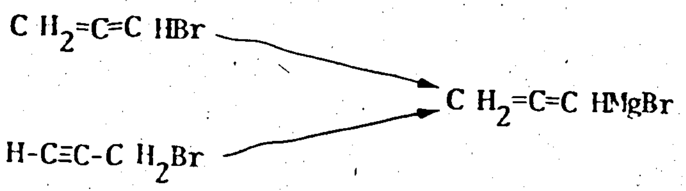
$$\Phi\text{-CH}_2\text{Cl} \longrightarrow \Phi\text{-CH}_2\text{CH}_2\text{C}\equiv\text{C-Li} \xrightarrow{\text{ClCO}_2\text{Et}} \Phi\text{-CH}_2\text{CH}_2\text{C}\equiv\text{C-CO}_2\text{Et}$$

80%

On the basis of these results, it is apparent that this new reaction represents a highly efficient, convenient procedure for effecting the direct propargylation of halides, without the usual problems experienced by other methods (allene formation, etc.) An additional advantage is the possibility of *in situ* functionalization of the terminal alkyne without isolation of intermediates.

The Nature of the Propargylating Agent

The most pertinent analogy to the present study is the particular case of the Grignard reagent formed from either propargyl bromide or allenyl bromide.

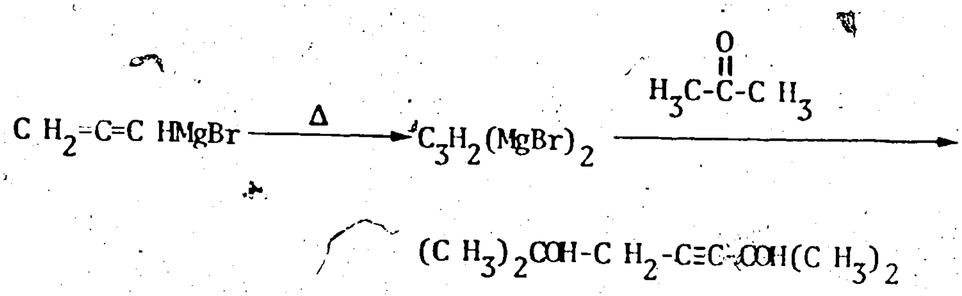


The respective Grignard reagents prepared from either halide show[21] the same infrared absorption at 1878 cm^{-1}. On this basis, the constitution of these reagents was believed to be identical and correspond to an allenic structure.

More recently, the allenyl structure has been supported by proton[6] and ^{13}C nmr spectroscopy[7]. The absorption at a very low field (208 ppm, relative to TMS, $CH_2=\overset{*}{C}=CHMgBr$) in the ^{13}C nmr spectrum unequivocably confirms the allenic structure for this Grignard reagent.

Hydrolysis of a freshly prepared "propargyl" Grignard reagent afforded an allene/propyne ratio of 4. This organometallic appears to be unstable, since either on standing or after a reflux period (in ether), the absorption band in the ir shifts from 1878 to 1950 cm^{-1}. At the same time, the ratio of allene/propyne obtained upon hydrolysis is reduced to two. Upon treatment of the reagent which was refluxed for 15 hours with acetone[2], a 94% yield of the diol was obtained.

These results have been interpreted in terms of a disproportionation of the mono- to the di-Grignard reagent[2].



$$CH_2{=}C{=}CHMgBr \xrightarrow{\Delta} C_3H_2(MgBr)_2 \xrightarrow{H_3C-\overset{\overset{O}{\|}}{C}-CH_3} (CH_3)_2COH-CH_2-C{\equiv}C-COH(CH_3)_2$$

Jaffe[11] has reported that allenyllithium shows characteristic ir absorption either at 1887 or 1894 cm^{-1} depending on the solvent in which it was prepared. Because these results were similar to those reported for the Grignard reagent of propargyl bromide, an allenic structure was assigned to the organolithium compound. However, this author did not consider that the dilithium salt of propyne also shows an absorption[22] at 1870 cm^{-1}.

A brief investigation was undertaken to determine the nature of the reagent prepared in hexane/ether (1:1), which were the conditions used for the propargylation reaction.

For this study, *n*-butyllithium was mixed with an excess of allene with ether at -78°. On warming slowly to -20° a white precipitate appeared and the suspension was stirred for a certain period of time (see Table I). Vacuum was applied to eliminate excess allene and the sample was hydrolyzed with D_2O. The gas evolved was collected and analyzed.

TABLE I

Composition of the Gas Evolved Upon Hydrolysis of Metalated Allene

Run	Time(min)	% allene	% propyne
1	10	28	72
2	30	21	79
3	60	19	81

The results of the glc-mass spectral analysis for run 2 are shown in Table II.

TABLE II

Deuterium Incorporation of Allene and Propyne from Run 2

	d_0	d_1	d_2
Propyne	-	27	73
Allene	52	48	—

A sample taken from run 3 (after 30 minutes at -20°) was evaporated *in vacuo* to dryness. A portion of the solid obtained was hydrolyzed and the gas analyzed by glc. The gas was exclusively propyne. The ir spectra of this solid (nujol) showed a strong absorption at 1890 cm^{-1}.

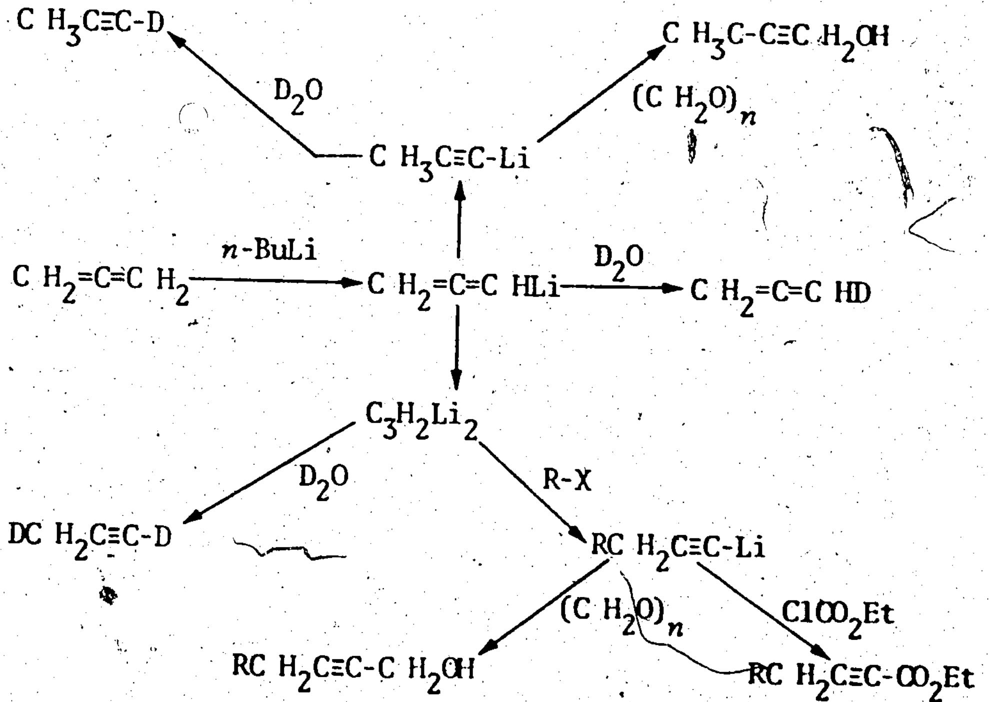
In another experiment, the metalated allene was allowed to reach 25° and held at that temperature for 45 minutes. The mixture was cooled to -20°, evacuated, then hydrolyzed with D_2O. The gas evolved was shown by glc to be 99% propyne (a trace of allene was present). The ir spectrum of the gas presented two important absorptions at 2600 and 2610 cm^{-1} which probably corresponds to DC $H_2C\equiv C$-D and C $H_3C\equiv C$-D ($\equiv$C-D stretching)[23].

These results show that there is presumably more than one species present in the mixture at -20°. The detection of allene-d_1 indicates that some allenyllithium exists, but because of the large proportion of propyne-d_2, it is concluded that the main constituent is the dilithium salt, $C_3H_2Li_2$.

The isolated lithium salt and the mixture which was allowed to warm to room temperature produced exclusively propyne upon hydrolysis. Similar behavior has been observed upon hydrolysis of the dilithium salt of propyne[7].

The detection of the allene-d_0 is probably due to the initial excess allene, since under the conditions at which the experiments were run it proved impossible to completely eliminate the excess allene. Also, it is possible that some allene-d_0 could arise by disproportionation of allenyllithium.

The presence of propyne-d_1 is explicable on the basis that allenyllithium may rearrange in part to propynyllithium. The existence of this salt was actually proved when the intermediate lithium acetylides were treated with paraformaldehyde. Small amounts of 2-butyn-1-ol could be isolated.



Although the above results are rather complex, they nonetheless indicate that allenyllithium is not a stable organometallic as originally claimed. Very likely, it rearranges to some extent to propynyllithium and mainly disproportionates to $C_3H_2Li_2$.

These observations parallel those discussed previously for allenylmagnesium bromide. The latter reagent, on standing, disproportionates to the di-Grignard reagent and in part, also rearranges to the acetylenic organometallic[7].

$$CH_2{=}C{=}CHMgBr \longrightarrow CH_3C{\equiv}C\text{-}MgBr \quad + \quad C_3H_2(MgBr)_2$$

EXPERIMENTAL

General Considerations

Infrared (ir) spectra were recorded on an Unicam SP 1000 Infrared Spectrophotometer.

Nuclear magnetic resonance (nmr) spectra were run on a Varian A-60 or HR-100 Spectrometer. Unless otherwise stated, carbon tetrachloride (CCl_4) was employed as the solvent with tetramethylsilane (TMS) as the internal reference standard. Chemical shifts are reported as δ values relative to TMS = 0. The following abbreviations were used in the text: s = singlet, d = doublet, t = triplet, and m = multiplet.

Mass spectra were recorded on an AEI Model MS-2 or Model MS-9 Spectrometer. Spectra are reported in the following fashion: *m/e* = peak mass (relative intensity).

Quantitative gas liquid chromatographic (glc) analyses were performed on Varian Aerograph Series 1200 and 1400 instruments versus a reference solution of the authentic compounds, using a column packed with 20% DEGS on Chromosorb W. Preparative gc work was performed on a Varian Aerograph A-90-P3 instrument using 20% DEGS on Chromosorb W, 10' x ¼".

Refractive indices were measured on a Bausch and Lomb Abbe - 3L Refractometer.

All operations were carried out under an atmosphere of oxygen-free nitrogen[24].

The concentration of commercial *n*-butyllithium in hexane (Foote, 1.5-1.6M) was determined by titration with 2-butanol in xylene[25]. Allene (Matheson) was more than 99% pure.

The Reaction of Allene and *n*-Butyllithium in the Presence of N,N,N',N'-Tetramethylethylenediamine Followed by the Addition of *n*-Heptyl Iodide

To a solution of *n*-butyllithium (33.1 ml, 50 mmole, 1.51M) was added a solution of TMEDA (5.81 g, 50 mmole) in 20 ml of ether, maintaining the temperature below 25°. The mixture was cooled to -50° and allene (3 ml, c a. 50 mmole) was distilled into the flask. Towards the end of the distillation a white precipitate appeared. Stirring was continued for 10 minutes and then the temperature was slowly increased to -20°. A solution of *n*-heptyl iodide (9.04 g, 40 mmole) in 20 ml of ether was added dropwise. At this temperature an aliquot was analyzed by glc (60°). Only starting material was present. The temperature was allowed to increase to 25°. After 30 minutes, the mixture was poured into ice-water and extracted with ether. The organic extract was washed with dilute hydrochloric acid, brine, and dried over Na_2SO_4. Analysis by glc showed the presence of 50% starting material. Also, 1-decyne was present in 15% (identified by peak enhancement), and another component with a very close retention time, in 20% (relative areas). Preparative glc (60°) afforded a mixture of 1-decyne and the unknown compound. This mixture showed ir absorption (liquid film) at: 3320 (C≡C-H), 2120 (C≡C), 1960 (C=C=C) and 850 cm^{-1} (C-H=C=C-H_2). Based on these spectroscopic data the allene was inferred to be 1,2-decadiene.

The Reaction of Allene and *n*-Butyllithium in Tetrahydrofuran Followed by the Addition of *n*-Heptyl Iodide

To a cooled solution (-40°)* of *n*-butyllithium in hexane ([illegible] ml, 50 mmole, 1.52M) and 30 ml of tetrahydrofuran, allene ([illegible] ml, c a. 58 mmole) was added, at -50°. No precipitate was formed at -50°. Upon cooling the mixture to -55° a white precipitate appeared. Stirring was continued for 20 minutes, then a solution of *n*-heptyl iodide (9.04 g, 40 mmole) in 15 ml of THF was added over a period of 20 minutes. The temperature was allowed to increase slowly. At -10° an aliquot was analyzed by glc (60°). Less than 5% of starting material was present. The mixture was poured into ice-water, saturated with NaCl and extracted with ether. The ether extracts were combined and washed with brine and dried over Na_2SO_4. Analysis by glc showed the presence of a volatile material with the same retention time (peak enhancement) as 1-heptene. Also, 1-decyne was present in 16% yield as well as another component that showed the same characteristics as described above (19%, relative areas).

Reaction of Allene with *n*-Butyllithium in Hexane:Ether (1:1) Solvent System

To a cooled (-78°) solution of allene (c a. 6 ml, 100 mmole) in 50 ml of ether was added 48 ml of a 1.52 M solution of *n*-butyllithium (73 mmole) in hexane over a period of 30 minutes. The solution was slowly allowed to warm (without removing the bath) to -15° (about 30 minutes) and then stirred for an additional 15 minutes (a white suspension formed).

This mixture was used for the alkylation of *n*-heptyl iodide using different RLi/R'I ratios. The results are summarized in Table III, and the best result (entry 3) is described in detail below.

TABLE III

The Reaction of Allene with *n*-BuLi

Followed by Addition of *n*-Heptyl Iodide

Entry	RLi/R'I	1-Decyne (%,glc)	*n*-Heptyl Iodide (%,glc)
1	3.1	67	23
2	3.7	83	16
3	5.0	95	0

Synthesis of 1-Decyne

To the mixture prepared above, at -15°, *n*-heptyl iodide (3.39 g, 15 mmole) in 10 ml of ether was added over a period of 15 minutes. After seven hours of stirring at room temperature, the reaction mixture was poured into ice-water and extracted with ether. The ether layers were combined, washed with brine and dried over Na_2SO_4. Glc analysis (60°) showed the formation of 95% of 1-decyne. The solution was concentrated at atmospheric pressure. Fractional distillation provided pure 1-decyne (1.83 g, 88%), bp 104-105° (92 mm) (lit.[26] bp 174°), n_D^{20} 1.4267 (lit.[26] n_D^{20} 1.4265); the nmr and ir were identical to an authentic sample.

General Preparation of the Propargylating Reagent for the Reaction with Allylic and Benzylic Chlorides

¶

To a cooled (-78°) solution of allene (c a. 4.5 ml, 75 mmole) in 35 ml of ether, 34.5 ml of 1.52M *n*-butyllithium (52.5 mmole) was added over a period of 30 minutes. The mixture was slowly allowed to warm (without removing the bath) to -15° and then stirred for 15 minutes at this temperature.

General Work-up Procedure

The reaction mixture was poured into ice-water, saturated with sodium chloride and extracted with ether. The organic extracts were combined and washed with saturated ammonium chloride solution, brine, and dried over Na_2SO_4.

Synthesis of 4-Phenyl-1-butyne

To the propargylating reagent (prepared as described above), at -15°, a solution of benzyl chloride (1.9 g, 15 mmole) dissolved in 10 ml of ether was added over a period 15 minutes. Then the temperature was slowly increased to 25°. After one hour the mixture was worked up in the usual way. Glc analysis (60°) indicated a 93% yield of 4-phenyl-1-butyne. A small sample was purified by evaporative distillation (114-115°, 66 mm). n_D^{20} 1.5229 (lit.[27] n_D^{20} 1.5212) ir (liquid film): 3300 (C≡C-H), 2120 (C≡C), 1605 (aromatic), 750, 700 cm^{-1} (monosubstitution); nmr : δ 7.18 (s, 5H) C_6H_5, 2.74 (m, 2H) C_6H_5C-H_2, 2.42 (m, 2H) C H_2C≡C H, 1.82 (m, 1H) C≡C-H. When the reaction was repeated but quenched with D_2O, the 1-deuteroalkyne was obtained, ir : 2592 cm^{-1} (C≡C-D); nmr : complete absence of the absorption at δ 1.82.

Synthesis of 5-Phenyl-2-pentyn-1-ol

A solution of benzyl chloride (1.9 g, 15 mmole) in 10 ml of ether was added dropwise to a cooled (-15°) solution of the propargylating agent (RLi = 52.5 mmole) and then the temperature was allowed to increase to 25° (without removing the cooling bath). After one hour, paraformaldehyde (2.0 g, 66 mmole, dried over P_2O_5) was added all at once and the mixture was stirred overnight. The white suspension was worked up in the usual way and the solvent was removed at atmospheric pressure. Fractional distillation of the residue afforded a low boiling fraction (50-60°/8 mm). Several components were present and the major one was isolated by preparative glc (120°). This was identified as 2-butyn-1-ol, n_D^{20} 1.4665 (lit.[28] n_D^{20} 1.4670), ir (liquid film) 3350 (OH), 2300, 2230 (C≡C), 1020 cm^{-1} (-H_2C-OH); nmr: δ 4.15 (broad singlet, 2H) CH_2OH, 3.65 (broad singlet, 1H) O-H, 1.85 (t, J = 2 Hz, 3H) CH_3. The fractional distillation was continued. At 111-112°/0.08 mm, 1.92 g (80%) of 5-phenyl-2-pentyn-1-ol was obtained, n_D^{20} 1.5484; ir (liquid film) 3300 (OH), 2290, 2230 (C≡C), 1608 (C_6H_5), 1020 (CH_2OH), 750 and 705 cm^{-1} (C_6H_5); nmr: δ 7.12 (s, 5H) C_6H_5, 4.12 (m, 2H) CH_2OH, 3.14 (partially resolved triplet) O-H, 2.72 (m, 2H) $C_6H_5CH_2$, 2.45 (m, 2H) CH_2C≡C; mass spectrum *m/e*: 160.0869 (*Calcd.*: 160.0888 for $C_{11}H_{12}O$), 159(2), 142(23), 129(12), 116(4), 91(100), 77(3), 65(19), 63(5), 51(9), 39(15), 29(5). *Anal Calcd.* for $C_{11}H_{12}O$: C, 82.46; H, 7.55. *Found*: C, 82.70; H, 7.41.

Synthesis of Ethyl 5-Phenyl-2-pentynoate

A solution of benzyl chloride (1.9 g, 15 mmole) in 10 ml of ether was added to the propargylating reagent (RLi = 52.5 mmole, prepared as described above) at -15°, over a period of 15 minutes. The mixture was warmed slowly to room temperature, and one hour later was cooled to -78°. Ethyl chloroformate (freshly distilled, 40 g, 0.37 mmole) was added dropwise over a 30 minute period. The temperature was gradually allowed to increase to 25° (3 hours). Work-up as previously described, and removal of the solvent at atmospheric pressure afforded a residue that was distilled under reduced pressure. There was obtained 2.43 g (80%) of ethyl 5-phenyl-2-pentynoate, bp 118-119° (0.4 mm); n_D^{20} 1.5210; ir (thin film) 2240 (C≡C), 1715 (C=O), 755 and 705 (C_6H_5); nmr: δ 7.17 (s, 3H) C_6H_5, 4.08 (q, J = 7 Hz, 2H) -O-C H_2, 2.62 (m, 4H) C H_2C H_2, 1.18 (t, J = 7 Hz, 3H) C H_3; mass spectrum *m/e*: 202.1001 (*Calcd.* for $C_{13}H_{14}O_2$: 202.0994), 157(12), 129(37), 91(100), 66(17), 51(10), 39(9), 29(12). *Anal Calcd.* for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. *Found:* C, 77.50; H, 6.92.

Synthesis of (E)-2,6-dimethyl-2,6-undecadien-10-yne (Homogeranylacetylene)

To a stirred suspension of the propargylating reagent (52.5 mmole, prepared as described above), at -15°, was added a solution of geranyl chloride (2.59 g, 15 mmole), in 10 ml of ether over a period of 10 minutes. Then the temperature was allowed to rise slowly to 25°. After one hour the mixture was worked up in the usual way. Elimination of the solvent was carried out at atmospheric pressure. Fractional distillation afforded 2.44 g (bp 101-103°/10 mm) of homogeranylacetylene (92%); n_D^{20} 1.4715; ir (thin film): 3320 (≡C-H), 2120 (C≡C), 1670 (C=C); nmr: δ 5.12 (m, 2H) $(CH_3)_2C{=}CH$ and $CH_2C{-}CH_3{=}CH{-}CH_2$, 1.92 - 2.3 (m, 8H) 3(C=C-C H_2) and C H_2C≡C, 1.73 (m, 1H) C≡C-*H*, 1.68, 1.64, 1.62 (s,s,s, 9H) 3(C=C-C H_3); mass spectrum *m/e*: 176.1572

(*Calcd.* for $C_{13}H_{20}$: 176.1565), 176(3), 161(10), 133(11), 105(9), 93(10), 91(19), 81(11), 79(14), 77(9), 69(13), 55(11), 53(14), 41(83), 39(23), 29(15). The nmr and the mass spectrum were in agreement with the reported literature[29] values.

Synthesis of (E)-7,11-dimethyl-6,10-dodecadien-2-yne-1-ol

A solution of geranyl chloride (2.59 g, 15 mmole) in 10 ml of ether was added (at -15°) dropwise to a suspension of the propargylating reagent (52.5 mmole, prepared as described above) over a period of 15 minutes. The temperature was allowed to increase slowly to 25°, and after one hour 2.0 g of paraformaldehyde (66 mmole, dried over P_2O_5) was added all at once. The mixture was stirred overnight and worked up in the usual way. Elimination of the solvent at atmospheric pressure afforded a residue. Distillation provided 2.55 g (83%) of the title compound (bp 115-116°/0.5 mm; bulb to bulb, 140°/0.2 mm). n_D^{20} 1.4948; ir (thin film) 3360 (OH), 2300 and 2230 (C≡C), 1675 (C=C), 1020 (C H_2O-H); nmr: δ 5.1 (m, 2H) C H_2C-C H_3=C *H*-C H_2 and (C H_3)$_2$C=C-*H*, 4.15 (broad singlet, 2H) C *H*$_2$OH, 3.18 (m, 1H) O-*H*, 1.9 - 2.3 (m, 8H) 3(C=C-C *H*$_2$) and C≡C-C *H*$_2$, 1.68, 1.63, 1.61 (s,s,s, 9H) 3(C=C-C *H*$_3$); mass spectrum *m/e*: 206.1668 (*Calcd.* for $C_{14}H_{22}O$: 206.1671, lit[30]: 206.1664), 173(5), 105(7), 91(15), 81(16), 69(100), 67(16), 53(13), 41(75), 39(20). *Anal Calcd.* for $C_{14}H_{22}O$: C, 81.50; H, 10.75. *Found:* C, 81.51; H, 10.71.

Synthesis of 2-Chloro-2-hepten-6-yne

To a stirred suspension of propargylating reagent (52.5 mmole), at -15°, a solution of 1,3-dichloro-2-butene (1.88 g, 15 mmole) in 10 ml of ether was added dropwise over a period of 15 minutes. The mixture was allowed to warm to room temperature and worked up in the usual way. Analysis by glc (60°) indicated an 80% yield of 2-chloro-2-hepten-6-yne. An analytical sample was isolated by preparative glc (60°); n_D^{20} 1.4635; ir (thin film) 3310 ($\equiv$C-H), 2130 cm^{-1} (C$\equiv$C); nmr: δ 5.55 (m, 1H) C=C H, 2.3 (m, 4H) C H_2C H_2, 2.1 (d, J = 1.7 Hz, 3H) C=C-C H_3, 1.83 (m, 1H) $\equiv$C-H; mass spectrum *m/e*: 128.0391 (*Calcd.* for $C_7H_9{}^{35}Cl$: 128.0393), 130(6), 128(18), 113(5), 93(67), 91(46), 89(100), 77(23), 65(9), 63(6), 53(97), 51(15), 43(10), 27(33). *Anal Calcd.* for C_7H_9Cl: C, 65.38; H, 7.05; Cl, 27.56. *Found:* C, 65.43; H, 6.89; Cl, 27.30.

Deuteration Experiments

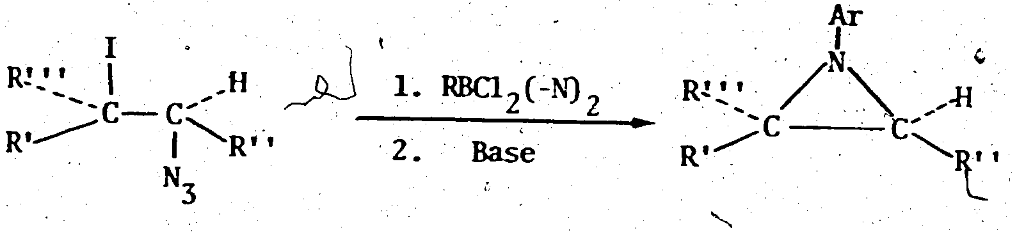
The experiments were carried out utilizing the propargylating reagent described above for the reaction with benzyl or allylic chlorides. The mixture, at -20°, was stirred for a certain length of time (see Table I, page 17). The excess allene was removed under vacuum (5 mm for 5 minutes). D_2O was added (3 ml, 0.15 mmole) and the gas was collected until the pressure equalized to atmospheric pressure. The gas was analyzed by glc (Adiponitrile 25% on Chromosorb W, 25 ft., at 25°) and mass spectrometry (8 *ev.*). The handling of the evaporated sample of propargylating reagent was conducted in a dry box. Nujol was used for the ir. determination.

CHAPTER II

SYNTHESIS OF ARYLBORON DICHLORIDES AND THEIR REACTIONS WITH ETHYL DIAZOACETATE

INTRODUCTION

Recently a great deal of interest has been devoted to the application of arylboron dichlorides in organic synthesis. H. C. Brown and coworkers[31] have demonstrated that phenylboron dichloride may be used to exclusively transfer the phenyl group upon reaction with iodoazides, and such transformations have led to efficient stereospecific synthesis of N-arylaziridines.



Unlike methods available for preparation of alkylboron dichlorides, aryldichloroboranes can not be obtained by direct hydroboration procedures. For example, Brown and Ravindram[32] have reported that olefins are readily hydroborated by dichloroborane, leading to the formation of alkylboron dichlorides in high yield.

$$RCH{=}CH_2 + HBCl_2 \longrightarrow RCH_2CH_2BCl_2$$

This manner of forming a carbon-boron bond by hydroboration is not applicable to aromatic substrates (and would imply a benzyne type of starting material); thus the target of synthesizing arylboron dichlorides has been approached primarily in three different ways:

1) The reaction between aromatic hydrocarbons and boron trichloride.
2) Halogenolysis of an oxygen-boron bond.
3) The interaction of organometallic compounds with boron trichloride.

The reaction of aromatic hydrocarbons and boron trichloride was initially reported by Pace in 1929[33]. Phenylboron dichloride was prepared by interaction of benzene and boron trichloride over palladium at 500-600°, but the yields were not reproducible.

$$\Phi\text{-}H + BCl_3 \xrightarrow[Pd]{500\text{-}600^{o}} \Phi BCl_2 + HCl$$

Replacing palladium by aluminum, Muetterties[34] was able to carry out the reaction in sealed tubes at 120-150°.

$$3\,ArH + Al + 3\,BCl_3 \longrightarrow ArBCl_2 + AlCl_3 + 1.5\,H_2$$

Phenylboron dichloride was obtained in yields of 60-80%. However, when substituted hydrocarbons were used, (*i.e.*, toluene), mixtures of the positional isomers were produced.

Boronic esters and anhydrides have also been used to prepare arylboron dichlorides by treatment with boron trichloride[35]. Although high yields have been reported in some cases, Gerrard and coworkers[36] describe this method as not being simple. For example, the reaction between boron trichloride and phenylboronic anhydride only produced yields in the order of 30-40%. Apparently the reaction is reversible, *viz.*,

$$(\Phi\text{-B=O})_3 + 3BCl_3 \rightleftarrows 3\,\Phi BCl_2 + 3BClO$$

The reaction of boronic esters and anhydrides with phosphorus pentachloride also affords arylboron dichlorides.[35] However, this method is disadvantageous in that phosphorus oxychloride forms an addition complex with phenylboron dichloride. As a result, it is difficult to separate the desired pure arylboron dihalide.

$$(\Phi\text{-B=O})_3 + 3\,PCl_5 \longrightarrow 3\,\Phi BCl_2 + 3\,POCl_3$$

$$\Phi\text{-B(OR)}_2 + 2\,PCl_5 \longrightarrow \Phi\text{-BCl}_2 + 2\,POCl_3 + 2\,RCl$$

The reaction of other organometallic compounds with BX_3 has been the method most widely utilized for preparing arylboron dihalides. Diphenyl mercury was first used by Michaelis[37,38] to prepare phenylboron dichloride; nevertheless the yield was low.

$$\Phi_2Hg + BCl_3 \longrightarrow \Phi BCl_2 + \Phi HgCl$$

More recently, Gerrard and coworkers[39] have improved and extended this reaction by using arylmercuric halides. Yields varied from 40 to 75%.

$$ArHgCl + BCl_3 \longrightarrow ArBCl_2 + HgCl_2$$

The use of organotin compounds for the synthesis of organoboron dihalides was first applied in 1959 by Bruickman and Stone.[40] Vinylboron dichloride was prepared according to the following equation:

$$(CH_2{=}CH)_4Sn + 2\,BCl_3 \longrightarrow 2\,(CH_2{=}CH)_2SnCl_2 + 2\,CH_2{=}CHBCl_2$$

This methodology has been extended for the synthesis of alkyl and arylboron dichlorides. Depending on the ratio of the tin compound to boron trichloride, two, three, or four groups can be replaced.

$$R_4Sn + 3\,BCl_3 \longrightarrow 3RBCl_2 + RSnCl_3$$

$$R_4Sn + 4\,BCl_3 \longrightarrow 4\,RBCl_2 + SnCl_4$$

In most cases a maximum of three groups can be replaced, depending on the solvent used.[41] Gerrard and his associates[36] were able to replace all four groups of tetraphenyl tin when the reaction was carried out in the absence of a solvent, but the scope of this procedure was not further explored.

$$\Phi_4Sn + 4\ BCl_3 \longrightarrow 4\ \Phi BCl_2 + SnCl_4$$

The method of Gerrard[36] (absence of solvent) seemed to be the most promising, because of the good yields and also because organotin compounds are readily available, easily stored, and can be handled in the atmosphere without appreciable oxidation or hydrolysis.

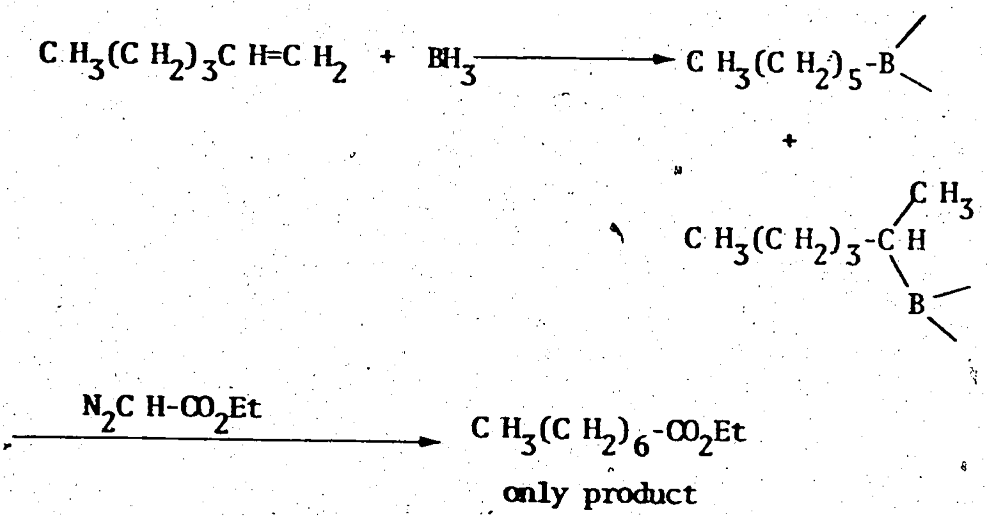
As part of the investigation undertaken here, the possibility of generalizing the method of Gerrard was examined. Indeed, the procedure proved to be widely applicable, making this method an excellent route for the preparation of arylboron dichlorides.

The reaction of organoboranes with substituted diazocompounds represents a very useful, novel procedure to obtain ketones, esters, nitriles, aldehydes and some of their α-deuterio derivatives.[42]

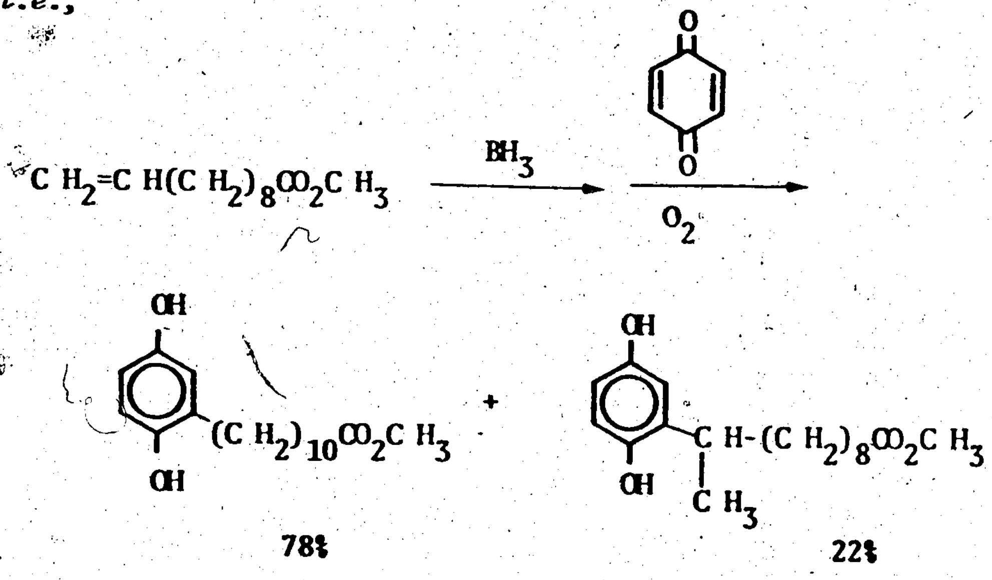
$$R_3B + N_2CHZ \longrightarrow R\text{-}CH_2Z$$

$Z = COOEt,\ CN,\ CHO,\ COR'$

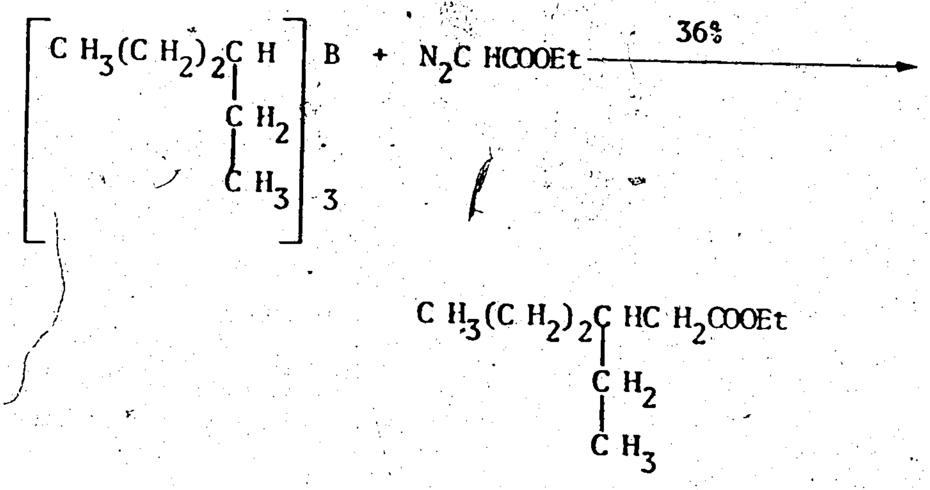
In general, organoboranes derived from terminal olefins react smoothly with diazo compounds affording very good yields of the homologated products. Moreover, the migration of a secondary alkyl group (invariably present when the organoborane is obtained by hydroboration of terminal olefins), has never been observed.



This feature represents a great advantage over other "homologation" reactions of organoboranes, in which the migration of a secondary group is preferred over that of the primary. In the latter case, the product is contaminated with up to c a. 20-25% of the undesired isomer (resulting from migration of the secondary group), *i.e.*,[43]



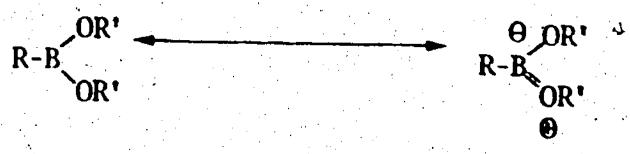
Two limitations, however, are present in the reaction of diazo compounds with organoboranes. When the borane contains bulky groups, the reaction is very slow and low yields are obtained.



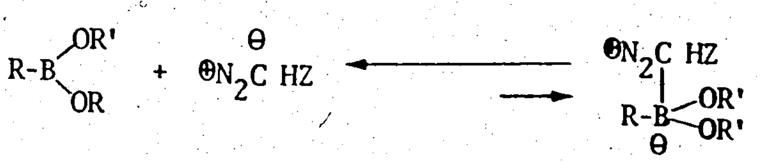
$$\left[CH_3(CH_2)_2\underset{\underset{CH_3}{|}}{\underset{CH_2}{\underset{|}{C}}}H\right]_3B + N_2CHCOOEt \xrightarrow{36\%} CH_3(CH_2)_2\underset{\underset{CH_3}{|}}{\underset{CH_2}{\underset{|}{C}}}HCH_2COOEt$$

The other limitation is a common one for reactions employing trialkylboranes, namely, that only one of the alkyl groups is utilized effectively. As a result, a maximum yield of only 33% can be achieved (based on olefin). This obviously becomes an important consideration when the alkyl groups of the organoborane are not readily available.

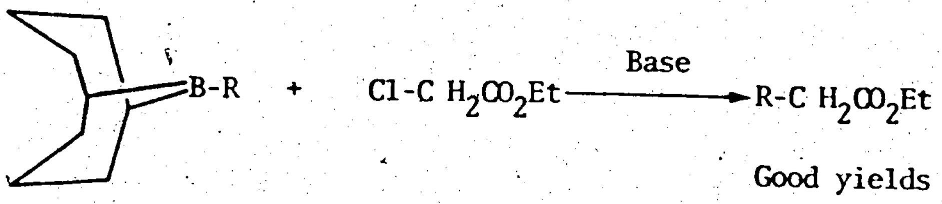
Prior attempts in our laboratory to circumvent this problem by utilizing boronic esters proved to be unsatisfactory. This is possibly due to the decreased electrophilicity of boron in these derivatives by resonance contributions of the type:



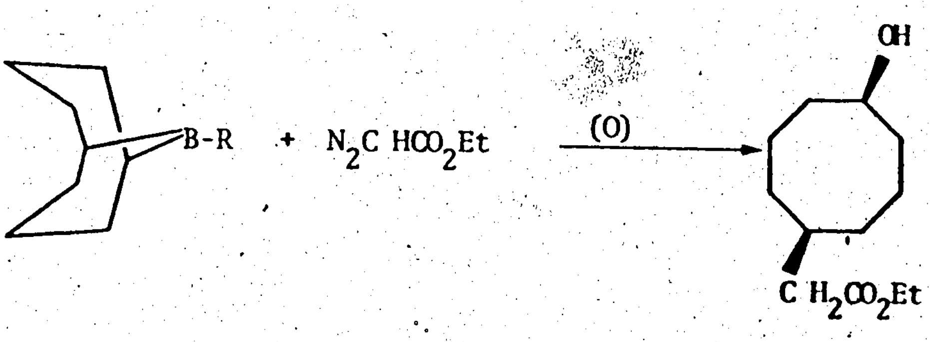
As a consequence, the boron is not electrophilic enough to initially coordinate with the diazo compound, *viz.*,[44]



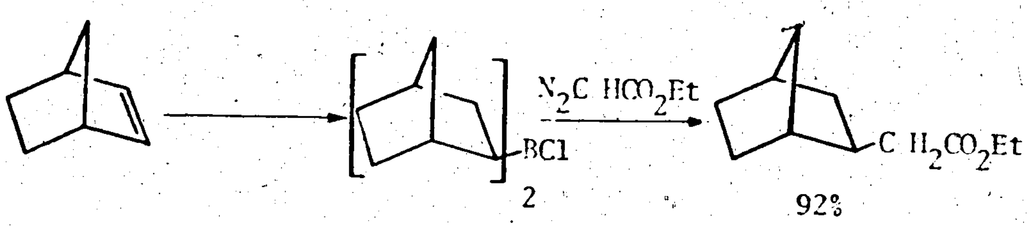
Recent developments by H. C. Brown and his group have demonstrated that the use of B-alkyl-9-boracyclo(3.3.1)nonanes overcomes the problem of effectively utilizing only one group[45], since in these derivatives, the B-alkyl rather than B-cyclooctyl bond migrates preferentially.



However, attempts to utilize this methodology for the reaction with diazo compounds resulted in the exclusive migration of the boron-cyclooctyl bond, in marked contrast with the aforementioned results[46].

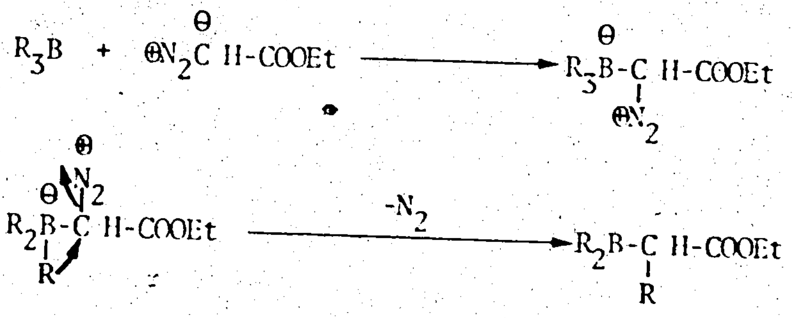


More recently, a new class of mixed organoboranes has been employed, namely, dialkylchloroboranes. These compounds react with diazo compounds under very mild conditions (-78°) and it was observed that bulky groups are also transferred efficiently. No chlorine migration was observed[47].



The high reactivity of dialkylchloroboranes was attributed to the enhanced electrophilicity of boron induced by the electronegative chlorine atom.

The reaction between organoboranes with diazo compounds is believed[42] to proceed by an initial coordination step of the borane with the diazo compound, followed by concerted migration of the alkyl group with displacement of nitrogen.

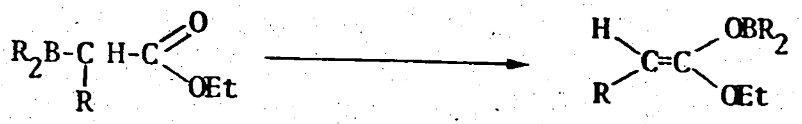


$$R_3B + \oplus N_2\overset{\ominus}{C}H\text{-}COOEt \longrightarrow R_3\overset{\ominus}{B}\text{-}\underset{\oplus N_2}{C}H\text{-}COOEt$$

$$R_2\overset{\ominus}{B}\text{-}\underset{R}{\overset{\oplus N_2}{C}}H\text{-}COOEt \xrightarrow{-N_2} R_2B\text{-}\underset{R}{C}H\text{-}COOEt$$

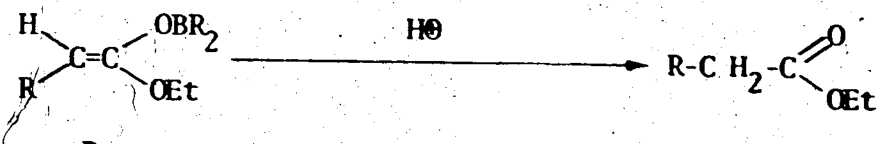
A

Pasto and Wojtkowski[48] have shown that an intermediate such as A could not be isolated from the reaction between an organoborane and a diazo ester. Instead, the rearranged product, an enol borinate B, was isolated and shown to be the intermediate prior to hydrolysis.



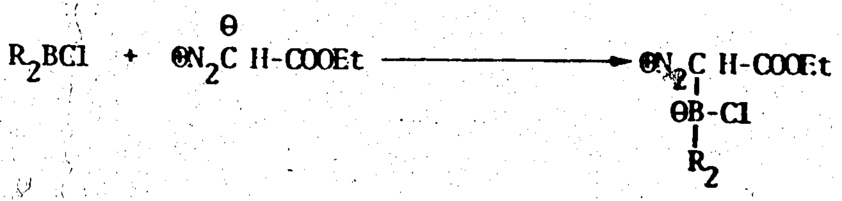
A B

Enol borinates such as B are highly sensitive to water and hydrolyze rapidly to form the corresponding ester.

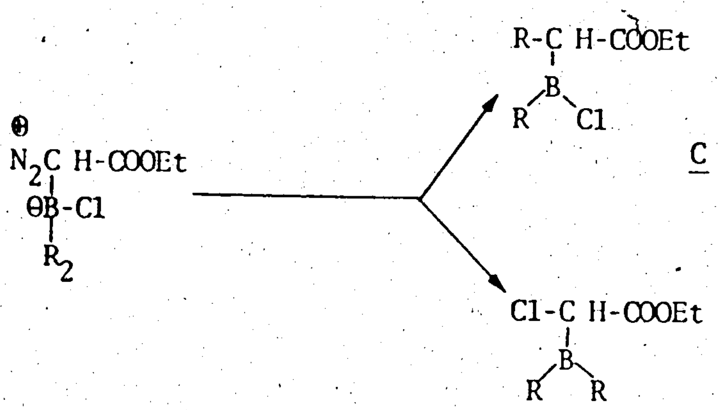


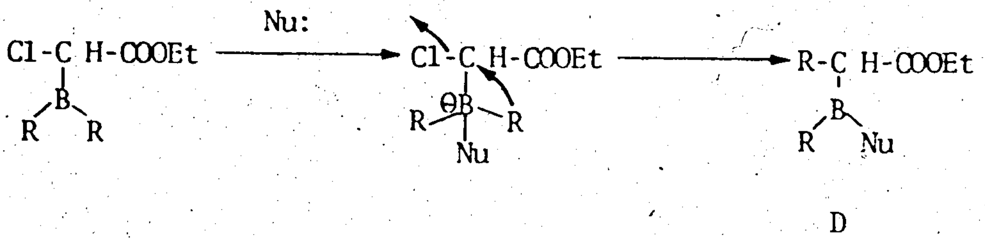
B

The reaction of dialkylchloroboranes with ethyl diazoacetate affords excellent yields of homologated esters. Although products resulting from the net migration of chlorine were not observed, this did not eliminate the possibility of an initial transfer of chlorine followed by displacement upon addition of a nucleophile, *i.e.*,

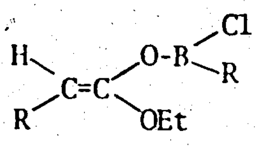


$$R_2BCl + \oplus N_2\overset{\ominus}{C}H\text{-}COOEt \longrightarrow \oplus N_2\underset{\underset{\underset{R_2}{|}}{\ominus B\text{-}Cl}}{\underset{|}{C}}H\text{-}COOEt$$

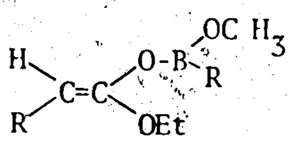




Thus, intermediates C and D or the corresponding enol borinates E and F (resulting from rearrangement of C and D[48], respectively) could also give rise to the same product upon hydrolysis. This mechanistic subtlety has not yet been resolved.

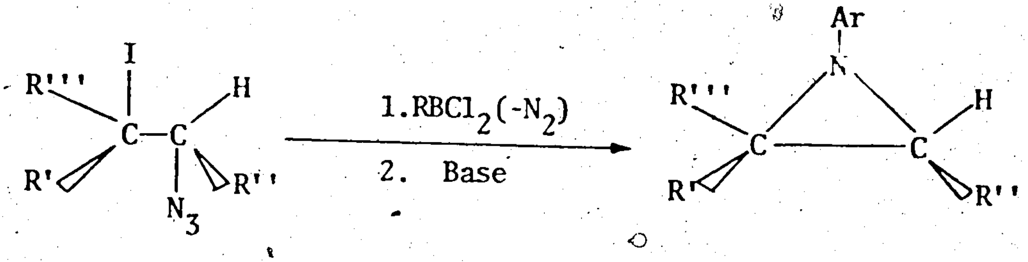


E



F

Further investigation of the synthetic utility of "mixed" boranes have led to the use of aryl and alkyl dichloroboranes. Recently[31] these reagents have been applied to the synthesis of aziridines, and have proven successful toward solving the problem of effectively utilizing only the alkyl or aryl group in a mixed organoborane.



Before any of the aforementioned work with organohaloboranes was published, preliminary results utilizing phenyl boron dichloride[49] were already obtained in our laboratories. Phenylboron dichloride was shown to react quantitatively with ethyl diazoacetate. It was then learned[50] that the Purdue group was developing a synthesis of alkyldichloroboranes with a view to studying its reactions with diazo compounds. To avoid duplication of effort, a joint study was undertaken in which our group investigated the aryl and the Purdue group the alkyldichloroboranes.

Arylboron dichlorides, now readily available in high yield by the reaction of tetraaryl tin compounds with boron trichloride in the absence of a solvent[51], were allowed to react with ethyl diazoacetate. It was found that the reactions proceeded under very mild conditions and excellent yields of ethyl arylacetates were obtained.

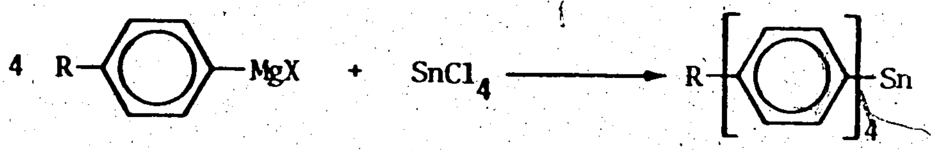
RESULTS AND DISCUSSION

Arylboron dichlorides are excellent reagents to achieve selective transfer of the aryl group upon reaction with ethyl diazoacetate.

Initially, several of the methods reported in the literature for the synthesis of arylboron dichlorides were investigated.

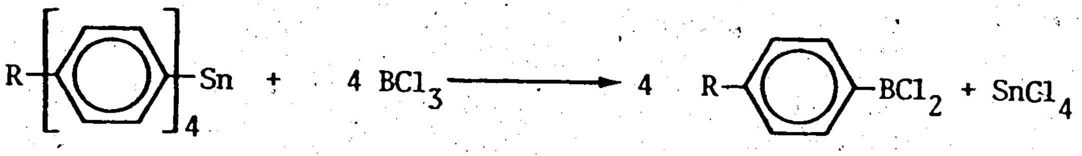
The halogenolysis of the B-O bond, utilizing boronic anhydrides and phosphorus pentachloride or boron trichloride, resulted in low yields. Also, when phosphorus pentachloride was used, complex mixtures were obtained. It was then decided to explore the generality of the method of Gerrard, which made use of tetraphenyltin and boron trichloride in the absence of solvents.

The organotin compounds were prepared utilizing the conventional method of reacting the corresponding aryl Grignard reagent with tin tetrachloride[56]. These compounds were easily purified, crystalline and stable to air.



R = CH_3, Cl, Φ

The arylboron dichlorides were prepared by mixing the tin compounds with boron trichloride at -78° and then slowly warming. At -5° an exothermic reaction took place, which was moderated by means of a cooling bath. The mixture was then refluxed and fractionally distilled under nitrogen to afford the pure arylboron dichlorides. In this manner several arylboron dichlorides were synthesized[51] (see Table III).



R = CH_3, Cl, Φ

TABLE III

Reaction of Tetraaryltin Compounds
with Boron Trichloride

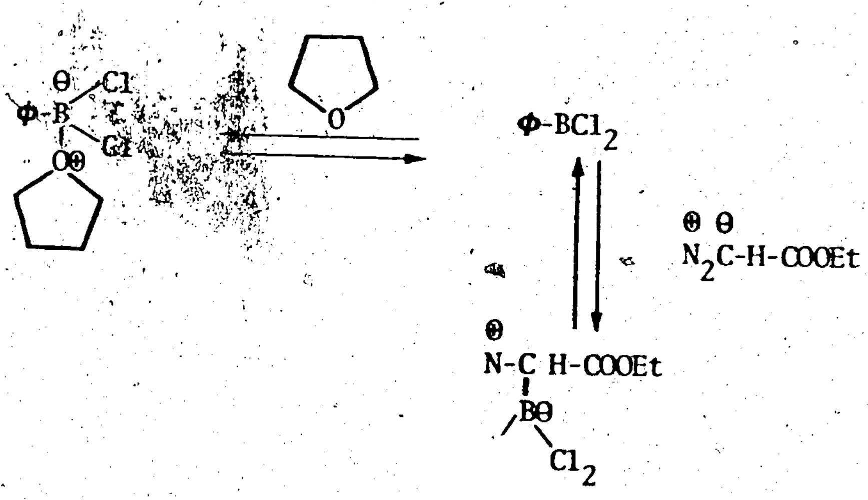
Substituent	Isolated Yield(%)
p-CH_3	70
p-Cl	85
p-Φ	78

Attention was then focused on the reaction of these compounds with ethyl diazoacetate.

Initial results obtained in our laboratories have shown that phenylboron dichloride reacts smoothly with ethyl diazoacetate in tetrahydrofuran at -20°.[49]

$$\Phi\text{-BCl}_2 + \text{N}_2\text{CH-COOEt} \xrightarrow[-20^{\circ}]{} \Phi\text{-CH}_2\text{COOEt}$$

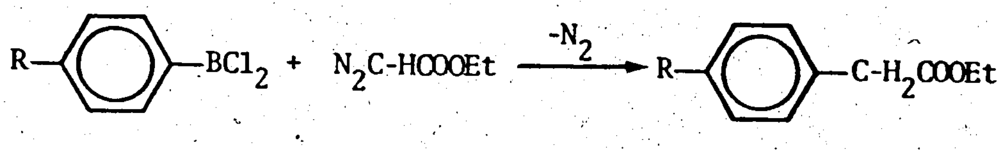
The use of tetrahydrofuran as a solvent was crucial for the success of this procedure. In diethyl ether as solvent the reaction was extremely fast and only low yields of product were obtained. The reduced reactivity in tetrahydrofuran is probably a consequence of the greater coordinating power of this solvent, which competes with the diazo ester.



When the reaction between Φ-BCl$_2$ and N$_2$CH-COOC$_2$H$_5$ was repeated under the same conditions previously reported[49] (two equivalents of ethyl diazoacetate, in tetrahydrofuran, at -20°), a 100% (glc) yield of ethyl phenylacetate was obtained. However, the isolation procedure was complicated by the fact that ethyl chloroacetate was also present in the product (arising from the decomposition of the excess ethyl diazoacetate during the work-up).

When the reaction was repeated using a moderate excess (10%) of diazo ester, the formation of ethyl phenylacetate was quantitative and ethyl chloroacetate formation was less than 5% (glc) and completely absent in the isolated product.

The reaction was then explored with several other arylboron dichlorides and the results were very similar to those obtained from phenylboron dichloride. A summary of the results is shown in Table IV.



R = CH_3, Cl, Φ, H.

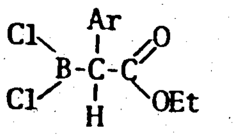
TABLE IV

Reaction of Substituted Phenylboron Dichlorides with Ethyl Diazoacetate

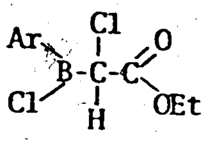
Substituents	glc yield(%)	isolated yield(%)
p-Cl	100	91
p-CH_3	100	95
p-Φ	100	91
H	100	98

Although the mechanism of this reaction has not been investigated in detail, a reasonable pathway can be formulated on the basis of the results obtained here and those observed by H. C. Brown and his group[53].

The possibility of migrating an aryl group to form G or the chlorine to give H, exists in the case of phenylboron dichlorides as it does for dialkyl or diarylboron dichlorides.

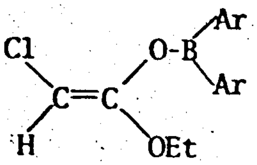


G



H

Subsequent methanolysis of the intermediate H, should result in the migration of the aryl group, formation of the enol borinate and finally the product. However, if intermediate H is unstable and rearranges to the enol borinate J



J

the product after hydrolysis would be ethylchloroacetate. Obviously, methanolysis of G or the corresponding enol borinate, would give rise to the product (allylic or benzylic carbon-boron bonds are cleaved by protic compounds[52]).

H. C. Brown and coworkers, in a parallel study with alkyldichloroboranes, found that mixtures of alkyl esters and ethyl chloroacetate are formed upon reaction with ethyl diazoacetate. Apparently the slight difference between the migratory ability of alkyl groups and chlorine, together with the fast and irreversible rearrangement to the enol borinate, afforded the aforementioned mixtures. This occurred at temperatures ranging from -78° to -25° and utilizing a variety of solvents (see Table V).

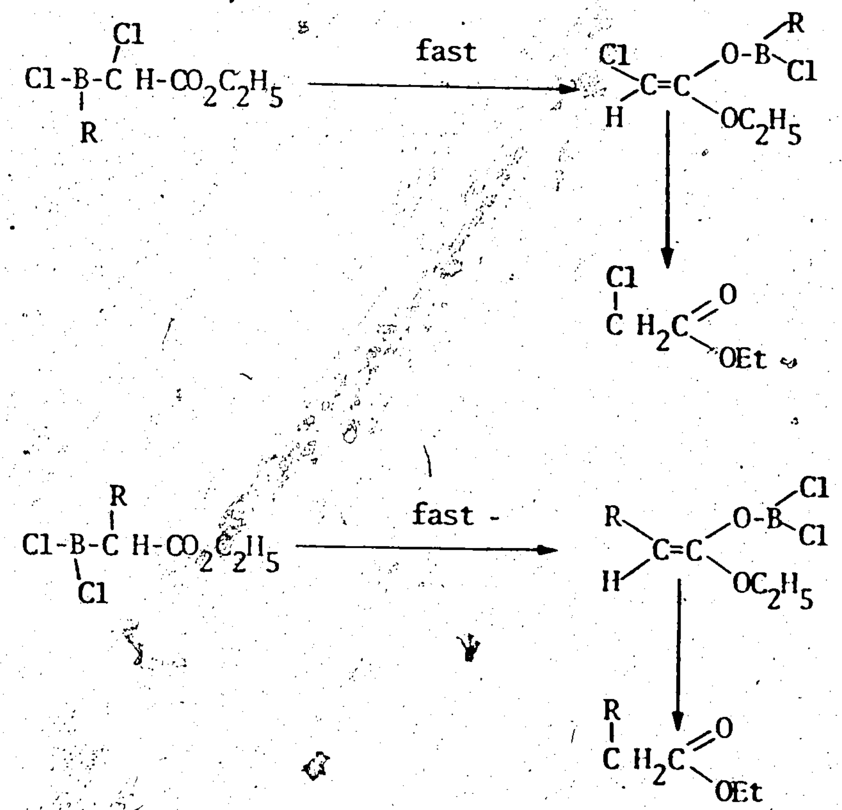


TABLE V

Reaction of Alkyldichloroboranes with Ethyl Diazoacetate in Ethyl Ether at -62^{o}

Alkyldichloroborane	"Homologated" ester, yield, %	% Ethylchloroacetate
n-Butyl	57	32
Cyclopentyl	71	22
3-Hexyl	60	26

The data in Table V together with the results obtained with arylboron dichlorides suggests that the migratory aptitude is in the order of Ar>R>Cl. Such an order for aryl *vs.* alkyl has previously been observed in the rearrangements of α-haloboronates[54].

In conclusion, the reaction of ethyl diazoacetate with arylborondichlorides provides a useful method for the synthesis of ethyl arylacetates. At the same time it represents a solution to the problem of efficiently utilizing only the organic group of a mixed organoborane.

EXPERIMENTAL

General Considerations

Mass spectra were recorded at 70 *ev.* on an AEI Model MS-9 spectrometer. Spectral data are expressed in the following manner: *m/e*: peak mass (relative intensity).

Infrared spectra (ir) were recorded using an Unicam SP 1000 Infrared Spectrophotometer. Nuclear magnetic resonance (nmr) spectra were recorded on a Varian A-60 or HR-100 Spectrometer. Unless otherwise stated, carbon tetrachloride was employed as the solvent, and chemical shifts are reported in δ values. The following abbreviations are used in the text: s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet. Gas chromatographic (glc) analyses were preformed using an Aerograph A-90 - P-3 and a Varian Aerograph Series 1200 and Series 1400 chromatograph versus a reference solution of the authentic compounds, utilizing as a column: 10% FFAP on Chromosorb W. All the reactions were carried out under an atmosphere of oxygen-free[24] nitrogen.

Synthesis of *Tetrakis* (*p*-tolyl) tin

To a solution of tin tetrachloride (14.7 ml, 33.2 g, 0.125 mole) in a mixture of 200 ml of toluene and 300 ml of tetrahydrofuran, a solution of the Grignard reagent of *p*-bromotoluene in tetrahydrofuran (250 ml, 0.5 mole, 2M solution, from 85.5 g, 0.5 mole of *p*-bromotoluene) was added at room temperature over a period of one hour. The mixture was refluxed for one hour. After cooling the mixture to 25°, 10% hydrochloric acid was added. The crude hydrolysate was filtered, and the residue was washed several times with hot toluene. The two layers were separated, and the organic layer was washed with brine and concentrated to 300 ml. On cooling, the organotin compound began to crystallize. Methanol (100 ml) was added and then the mixture was filtered, affording 44.32 g (75%) of *tetrakis* (*p*-tolyl) tin, mp 234-235° (lit.[55] mp 230°); mass spectrum *m/e*: 484.1216 (*Calcd.* for $C_{28}H_{28}{}^{120}Sn$: 484.1213). *Anal Calcd.* for $C_{28}H_{28}Sn$: C, 69.59; H, 5.84. *Found:* C, 69.68; H, 5.94.

Synthesis of *Tetrakis* (*p*-Chlorophenyl) tin

A solution of the Grignard reagent of *p*-bromochlorobenzene in ether (500 ml, 0.5 mole, 1M solution, from 95.74 g, 0.5 mole of *p*-bromochlorobenzene) was added to a solution of tin tetrachloride (14.7 ml, 3312 g, 0.125 mole) in toluene (500 ml) at room temperature. At the end of the addition (c a. 1 hour) the ether was distilled and the mixture was refluxed for two hours. The mixture was cooled to room temperature and a solution of 10% hydrochloric acid was added. The organic layer was filtered through celite and concentrated to 200 ml. Methanol (100 ml) was added, and on cooling the mixture in a Dry-Ice acetone bath, crystallization occurred. The mixture was filtered and the crystals washed with methanol to afford 41.15 g (58%) of *tetrakis*-(*p*-chlorophenyl) tin, mp 198-199° (lit.[56] mp 199°). Mass spectrum *m/e*: 563.9043 (*Calcd.* for $C_{24}H_{16}{}^{35}Cl_4{}^{120}Sn$: 563.9030). *Anal Calcd.* for $C_{24}H_{16}Cl_4Sn$: C, 51.00; H, 2.86; Cl, 25.12. *Found:* C, 51.15; H, 2.99; Cl, 24.87.

Synthesis of *Tetrakis* (*p*-biphenyl) tin

A tetrahydrofuran solution of the Grignard reagent of *p*-bromobiphenyl (500 ml, 0.5 mole, 1M solution, from 116.55 g, 0.5 mole of *p*-bromobiphenyl) was added to a solution of tin tetrachloride (11.5 ml, 26 g, 0.1 mole) in a mixture of ligroine (100 ml), and tetrahydrofuran (800 ml). The mixture was concentrated to a volume of c a. 500 ml, cooled to room temperature and poured into ice-hydrobromic acid. The white precipitate was filtered, then washed thoroughly and successively with water, methanol, chloroform and again with methanol, affording 66.50 g (90%) of *tetrakis* (*p*-biphenyl) tin, mp 260-262° (lit.[57] mp 260-262°). Mass spectrum *m/e* : 732.1824 (*Calcd.* for $C_{48}H_{36}{}^{120}Sn$: 732.1839). *Anal Calcd.* for $C_{48}H_{36}Sn$: C, 78.81; H, 4.96. *Found:* C, 79.03; H, 4.98.

Synthesis *p*-tolylboron dichloride

A 250 ml three-necked flask, fitted with a nitrogen inlet, a magnetic stirring bar and a Kjeldahl connecting bulb attached to a Dry-Ice condenser (connected to a mercury bubbler), was flushed with nitrogen and then charged with *tetrakis*-(*p*-tolyl) tin (29[illegible] g, 0.06 mole) and cooled to -78°. Boron trichloride (21.4 ml, 0.26 mole) was added and the cooling bath was allowed to warm slowly. At about -5° an exothermic reaction took place. The reaction was controlled by adding Dry-Ice to the cooling bath. Then the mixture was refluxed for five hours and fractionally distilled under nitrogen. The fraction boiling at 88-90°/11 mm (lit.[39] 92°/10 mm) afforded 28.4 g (70%) of *p*-tolylboron dichloride.

Synthesis of *p*-chlorophenylboron dichloride

Following the same procedure described above, *tetrakis* (*p*-chlorophenyl) tin (33.3 g, 0.06 mole) and boron trichloride (21.4 ml, 0.06 mole) were refluxed for 30 minutes. After distillation under reduced pressure this afforded 38.4 g (85%) of *p*-chlorophenylboron dichloride, bp 104-105°/24 mm (lit.[39] bp 70°/0.4 mm).

Synthesis of *p*-biphenylboron dichloride

No exothermic reaction was observed when the mixture of *tetrakis* (*p*-biphenyl) tin (32.26 g, 0.044 mole) and boron trichloride (16.5 ml, 0.46 mole) was warmed to 0°. After refluxing for four hours, followed by distillation under nitrogen, there was obtained 32.1 g (78%) of *p*-biphenylboron dichloride, bp 136-137°/0.6 mm. Mass spectrum *m/e*: 234.0117 (*Calcd.* for $C_{12}H_9{}^{11}B^{35}Cl_2$: 234.0115.

Anal Calcd. for $C_{12}H_9BCl_2$: C, 61.35; H, 3.86; [illegible], 30.18.
Found: C, 61.11; H, 4.20; Cl, 29.76.

General Work-up Procedure for the Reactions of Arylboron Dichlorides and Ethyl Diazoacetate

Once the nitrogen evolution was complete, methanol (5 ml) was added dropwise, keeping the temperature below -20°. Then water (5 ml) was added and the mixture poured into saturated aqueous Na_2CO_3 solution (75 ml) and extracted with ether. The ether extracts were combined and dried over Na_2SO_4.

Synthesis of Ethyl Phenylacetate

To a cooled (-25°, Dry-Ice carbon tetrachloride bath) solution of phenylboron dichloride (1.33 ml, 1.59 g, 10 mmole) in 10 ml of tetrahydrofuran, ethyl diazoacetate (1.25 g, 11 mmole) in 10 ml of THF, was added dropwise over a period of 90 minutes. A smooth evolution of nitrogen was produced (97%). At this temperature methanol (5 ml) was added dropwise, followed by water (5 ml). The mixture was worked up in the usual way and the solvent removed at atmospheric pressure. Distillation at reduced pressure afforded 1.64 g (98%) of ethyl phenylacetate, bp 85-86°/3 mm (lit.[58] bp 120-121°/20 mm), ir (thin film) 1730 (C=O), 720 cm^{-1} (C_6H_5); nmr: δ 7.4 (s, 5H) $C_6\mathit{H}_5$, 4.2 (q, J = 7 Hz, 2H) $OC\mathit{H}_2CH_3$, 3.6 (s, 2H) $C_6H_5C\mathit{H}_2$, 1.2 (t, J = 7 Hz, 3H) $C\mathit{H}_3$. The ir and nmr were identical in all respects with an authentic sample.

Synthesis of Ethyl *p*-Chlorophenylacetate

Ethyl diazoacetate (1.25 g, 11 mmole) in THF (10 ml) was added dropwise to a cooled (-25^{o}) solution of *p*-chlorophenyl dichloride (1.89 g, 10 mmole) in 10 ml of THF (1.5 hours). Nitrogen was evolved quantitatively. The mixture was quenched and worked up in the usual way. Analysis by glc showed the formation of 100% yield of ethyl *p*-chlorophenylacetate. Evaporation of the solvent and fractional distillation produced 1.80 g (91%) of a clear liquid, bp 106-107^{o}/3.5 mm, mp 31-32^{o}, (lit.[59] mp 32^{o}), ir (liquid film) 1730 (C=O), 820 cm^{-1} (p-ClC$_6$H$_4$); nmr: δ 7.2 (s, 4H) C_6H_4, 4.5 (q, J = 7 Hz, 2H) OCH_2, 3.55 (s, 2H) $-C_6H_4CH_2$, 1.2 (t, J = 7 Hz, 3H) CH_3.

Synthesis of Ethyl *p*-Tolylacetate

Ethyl diazoacetate (1.25 g, 11 mmole) in 10 ml of THF was added to a solution of *p*-tolylboron dichloride (1.98 g, 11.45 mmole) at -25^{o}. Nitrogen was evolved in 100% (1.5 hours). Work-up of the mixture in the usual way and analysis by glc showed a quantitative formation of ethyl *p*-tolylacetate. Removal of the solvent and fractional distillation afforded 2.01 g (95%) of ethyl *p*-tolylacetate, bp 96-97^{o}/3.2 mm (lit.[60] bp 240^{o}), ir (liquid film) 1730 (C=O), 810 cm^{-1} (p-CH$_3$C$_6$H$_4$-); nmr: δ 7.05 (s, 4H) C_6H_4, 4.12

(q, J = 7 Hz, 2H), OC H_2, 3.4 (s, 2H) C_6H_4C H_2, 2.28 (s, 3H) C $H_3C_6H_4$, 1.15 (t, J = 7 Hz, 3H) C H_2C H_3.

Synthesis of Ethyl *p*-biphenylacetate

To a cooled (-25°) solution of *p*-biphenylboron dichloride (2.368 g, 10 mmole) in THF (30 ml), ethyl diazoacetate (1.25 g, 11 mmole) in 10 ml of THF was added over a period of 90 minutes. Work-up of the reaction mixture and analysis by glc showed the formation of ethyl *p*-biphenylacetate in 100% yield. Evaporation of the solvent and fractional distillation (bp 135-136°/0.5 mm, lit.[61] bp: 167-168°/3.5 mm) produced 2.05 g (91%) of ethyl *p*-biphenylacetate, ir (liquid film) 1730 (C=O), 760 and 700 cm^{-1} (C_6H_5-); nmr: δ 7.5 (m, 9H) $C_6H_5C_6H_4$, 4.18 (q, J = 7 Hz, 2H) OC H_2, 3.65 (s, 2H) C H_2COO, 1.25 (t, J = 7 Hz, 3H) C H_3.

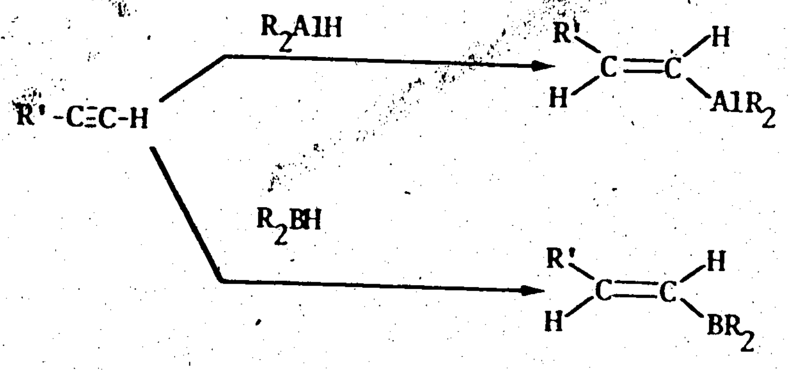
CHAPTER III

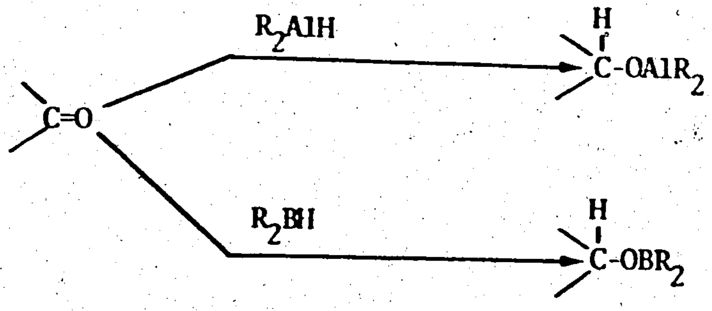
THE DIRECT ALKYLATION OF ETHERS UTILIZING ORGANOALUMINUM REAGENTS

INTRODUCTION

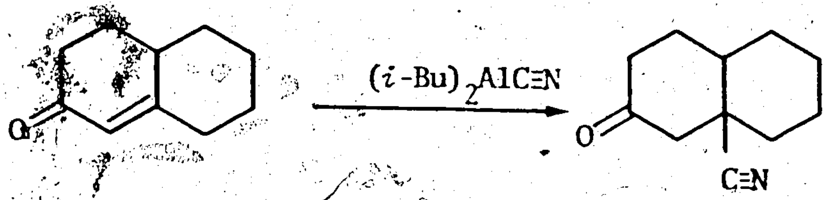
The utilization of organoaluminum compounds in organic synthesis has been steadily growing during the past few years. In many instances organoaluminum compounds display chemistry similar to that of organoboron compounds, due to the fact that aluminum and boron are in the same group in the Periodic Table.

For example, either organoaluminum hydrides or dialkylboranes react with acetylenes or ketones in the same way.

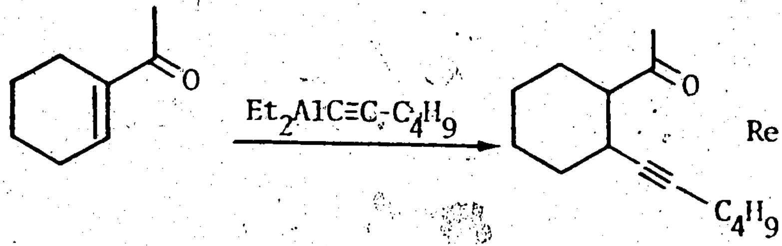




Nevertheless, several marked differences exist between these two kinds of organometallic compounds. Triorganoboranes, for example, are stable towards water, whereas triorganoaluminum compounds undergo immediate hydrolysis. One very interesting and striking difference between the chemistry of mixed alanes and boranes is the ability with which the groups attached to boron or aluminum are transferred. In aluminum reagents that ligand which possesses the highest degree of *s*-character tends to migrate, whereas the situation for mixed triorganoboranes is completely the opposite. Several examples demonstrating these characteristics are presented below:



Ref. 65



Ref. 66

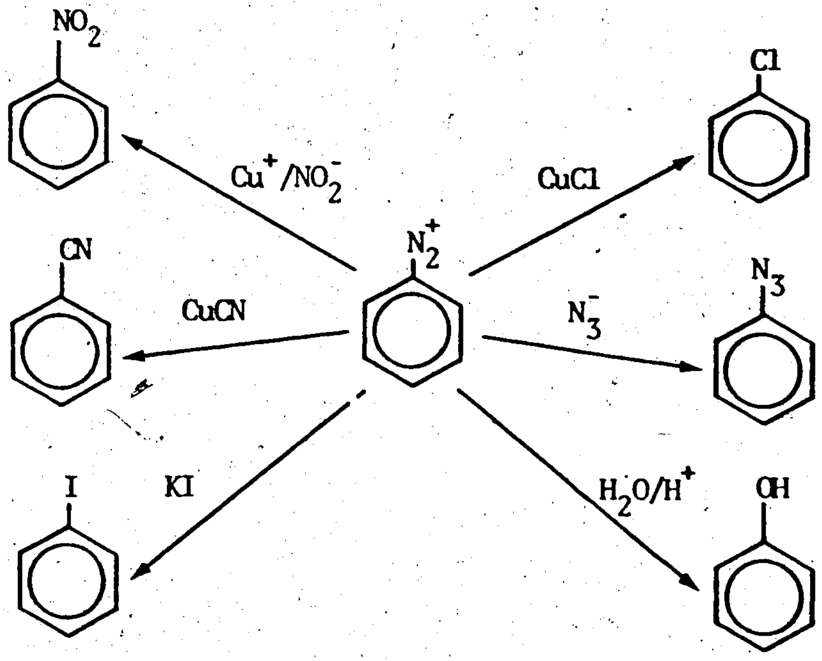
$$(n\text{-Bu})_2B\text{-}C\equiv C\text{-}C_4H_9 \xrightarrow{N_2C\ HCOOEt} n\text{-Bu-}C\ H_2COOEt$$

Ref. 67

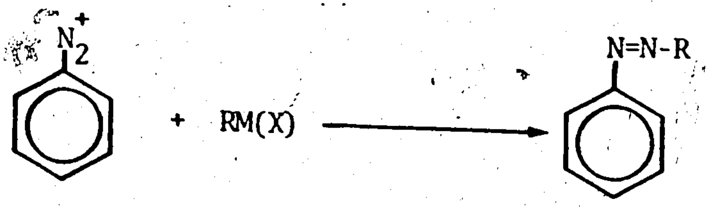
In the research undertaken here utilizing organoaluminum compounds, a new reaction was discovered, and the tendency of aluminum to transfer the group with the highest degree of *s*-character was also observed.

RESULTS AND DISCUSSION

Aryl diazonium compounds are useful synthetic intermediates. Substitution reactions employing these derivatives have made it possible to synthesize numerous classes of compounds (for example, aryl halides, phenols, aryl ethers, arylazides, aromatic nitro compounds, aryl nitriles, etc.)



Nevertheless, attempts to alkylate diazonium salts to form carbon-carbon bonds (with the exception of the nitrile synthesis mentioned above) have been uniformly unsuccessful. For example, the reaction between organomagnesium or zinc reagents with diazonium salts results in high yields of alkylation on nitrogen with formation of azo compounds[68].



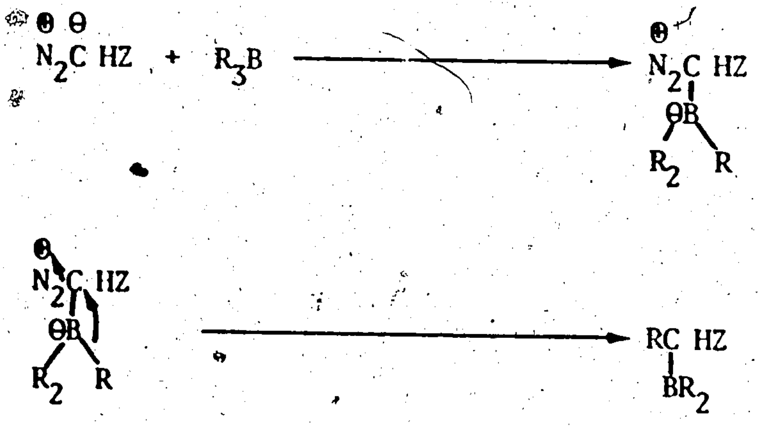
M = Zn, Mg.

The reaction between organoboranes and functional diazo-compounds represents a rather general method of preparing esters, ketones, nitriles and aldehydes[42].

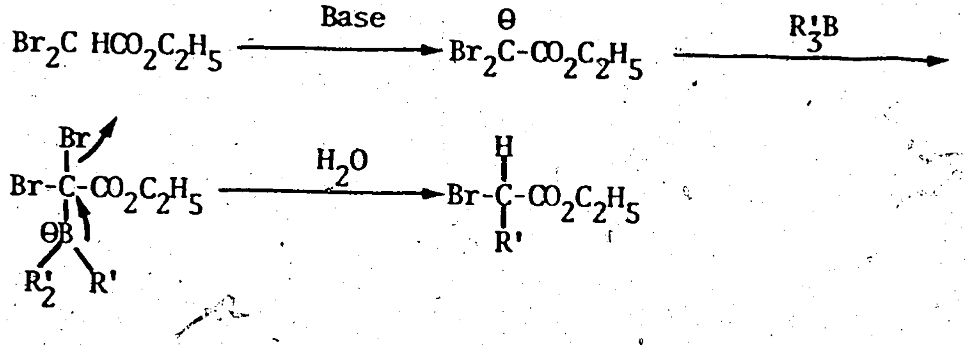
$$N_2CHZ + R_3B \longrightarrow RCH_2Z$$

Z = COOEt, COR', CHO, CN

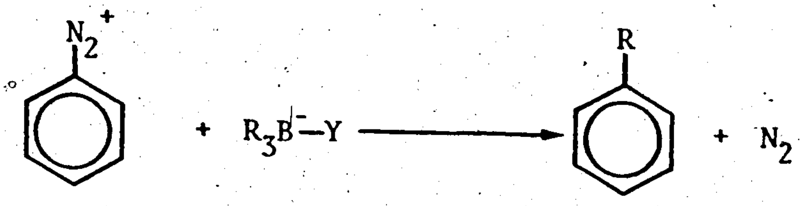
Presumably the first step in the mechanism of this reaction involves the initial coordination of the borane with the diazo-compound. Once this "ate" complex is formed, there is transfer of an alkyl group with concomitant displacement of nitrogen, *i.e.*,



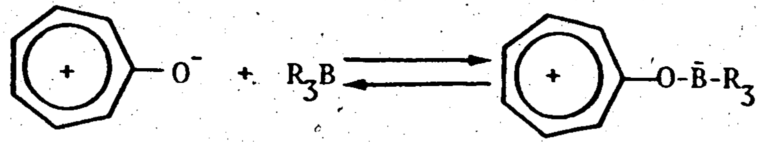
Boranes do not usually transfer ligands unless the boron atom is tetracovalent; moreover, the process takes place intramolecularly, *i.e.*,[69]



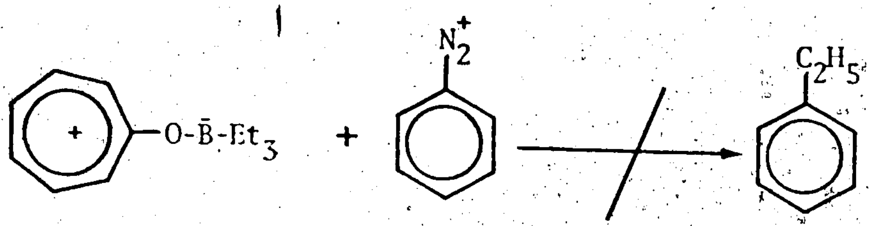
Despite the fact that diazonium salts lack a similar type of coordination site, it was of interest to explore the possibility of an organoborane achieving displacement of nitrogen if the borane was present as an "ate" complex[70].



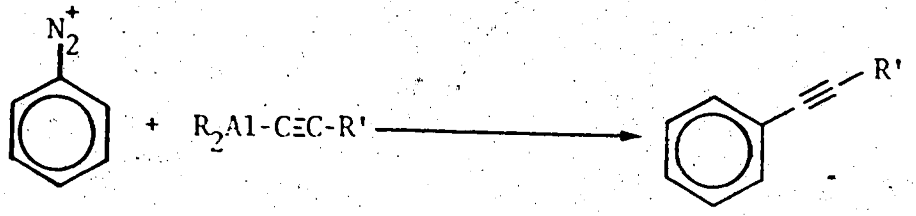
Tropone was chosen for the formation of the organoborane complex, because it is well known that the oxygen atom of tropone possesses high electron density (as a result of the tendency of this system to form a π-electron sextet[71]).



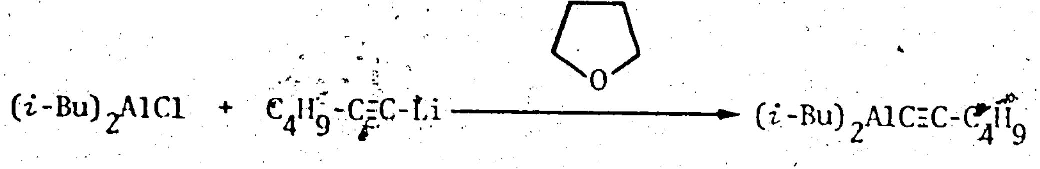
Admixture of a solution of tropone and triethylborane to a suspension of phenyldiazonium fluoroborate in tetrahydrofuran, however, did not produce any nitrogen evolution. On heating, decomposition of the diazonium salt took place, but no alkylation product was formed.



In view of the success of certain organoaluminum compounds, especially dialkylalkynylalanes to achieve alkylation (opening of epoxides[72], conjugate addition of enones[66], etc.), these reagents were next selected to explore the possibility of alkylation of diazonium salts. Preferential migration of the alkynyl moiety was anticipated due to this rather general tendency of mixed organoaluminum reagents[73].

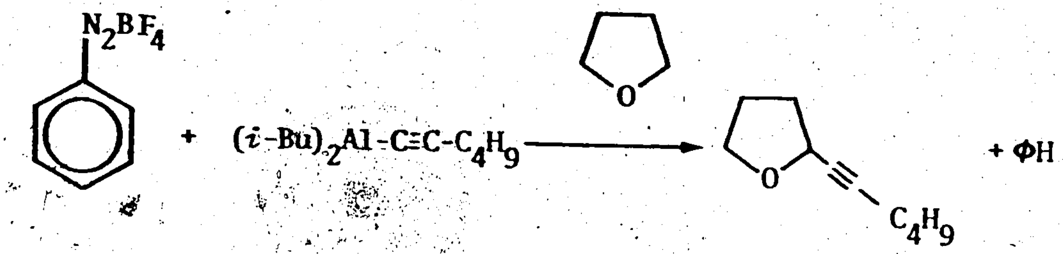


For this purpose, diisobutyl(1-hexynyl)alane was prepared by reacting diisobutylaluminum chloride with 1-hexynyllithium.

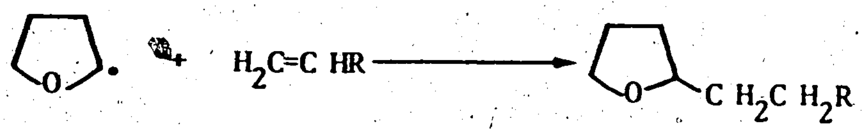


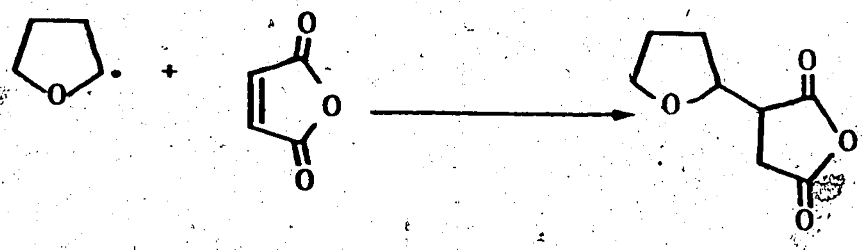
$$(i\text{-Bu})_2\text{AlCl} + \text{C}_4\text{H}_9\text{-C}\equiv\text{C-Li} \longrightarrow (i\text{-Bu})_2\text{AlC}\equiv\text{C-C}_4\text{H}_9$$

The addition of the alane solution to the suspension of phenyldiazonium fluoroborate in tetrahydrofuran at 0°, produced a smooth evolution of nitrogen. Analysis of the reaction mixture, however, did not reveal the presence of the expected alkylation product. Instead, 2-(1-hexynyl)tetrahydrofuran was produced in 63% yield, demonstrating that the solvent had participated in the reaction under these conditions. Also the presence of benzene was detected by glc.

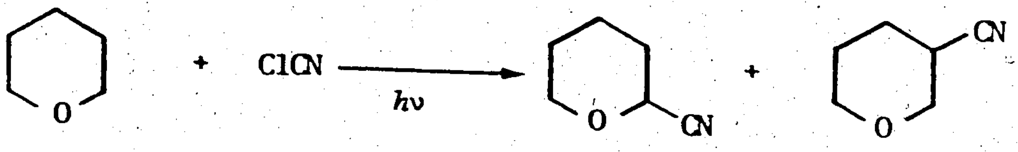


The result of this reaction presented a very interesting case in which a relatively unactivated carbon-hydrogen bond was transformed into a carbon-carbon bond in a single step. Although α-ether radicals are known to add to unsaturated molecules,[74a,b]



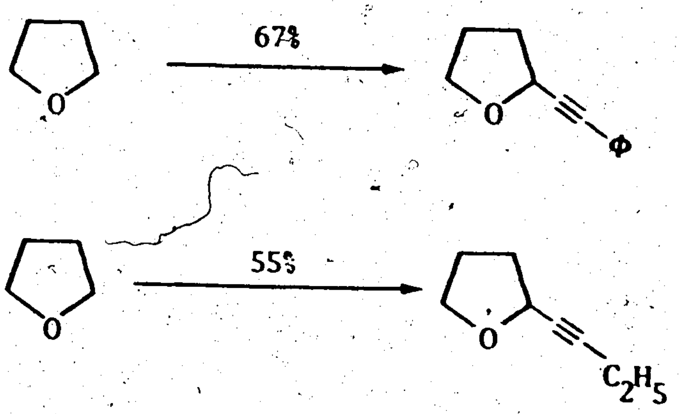


there are few examples of substitution reactions of the type C-H ⟶ C-C, in which a carbon-carbon bond is formed directly. One example is the photochemical reaction of tetrahydropyran with cyanogen chloride[75]; nevertheless, even in this instance the alkylation is not selective (*i.e.*, restricted to only the *a*-substitution product)

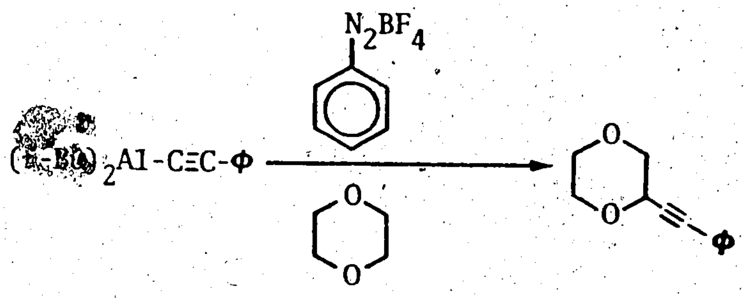


The novelty of this direct alkylation of tetrahydrofuran with organoaluminum reagents in the presence of a diazonium salt prompted a more detailed investigation into the scope of this reaction.

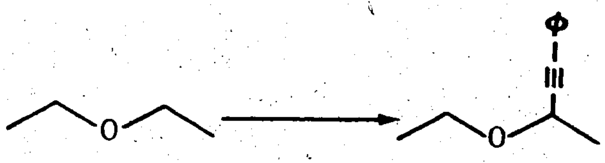
The procedure proved to be fairly general for different acetylenic moieties. Thus, phenylacetylene and 1-butyne produced alkylated products in yields of 67 and 55%, respectively, using THF as substrate.



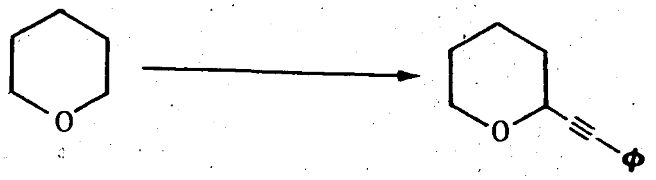
In addition to tetrahydrofuran, several other ethers were also alkylated in varying yields. The reaction of *p*-dioxane, because of its low melting point, could not be carried out at a temperature below 10°. Utilizing phenylacetylene, a 33% yield of alkylated product was obtained.

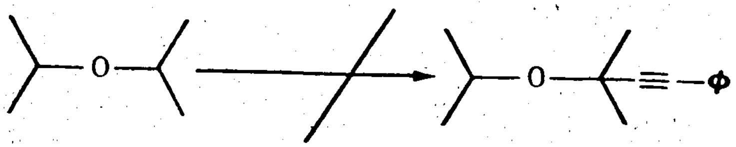


In the case of ethyl ether a smooth evolution of nitrogen was produced at 16° with the concomitant formation of 52% of alkylated product.

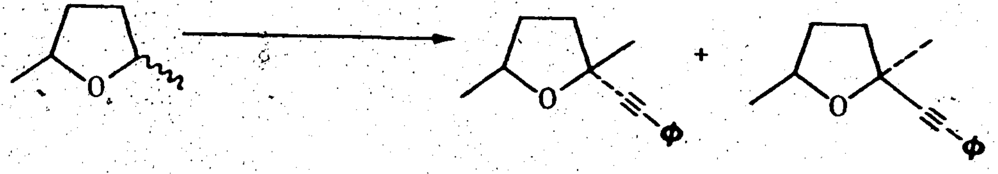


Tetrahydropyran reacted at 6° to afford a 28% yield of 2-phenylethynyltetrahydropyran. Diisopropyl ether, however, failed to provide any of the expected alkylated product.





The reaction in 2,5-dimethyltetrahydrofuran was sluggish and a great deal of "tarry" material was formed. Nevertheless, a 20% yield of a mixture of two alkylated diasteroisomeric compounds was produced.



Attempts to optimize the yields of the reaction were carried out utilizing tetrahydrofuran as the ether and phenylacetylene as the alkyne. When the reaction was carried out at 0° in the presence of two equivalents of diazonium salt, only one mole of nitrogen was evolved. On increasing the temperature, the second mole of nitrogen was liberated. The corresponding alkylated tetrahydrofuran derivative was formed in 72% yield.

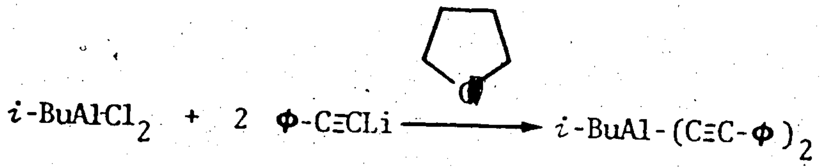
Obviously this result demonstrated that only one equivalent of diazonium salt is necessary for the reaction. By changing the reaction temperature to -20°, less tar was produced. Nevertheless practically no change in yield resulted (70%).

In all the results described thus far, the reactions were carried out utilizing the ether "reagent" as the solvent. Thus it was desirable to investigate the possibility of using the ether in equimolar amounts and conducting the reaction in an "inert" solvent. For this purpose diisobutyl(1-hexynyl)alane was generated in pentane. The solvent was evaporated by gently heating the mixture under a stream of nitrogen. The residue was dissolved in methylene chloride, a solvent which has been used successfully in certain reactions of organoaluminum compounds[76]. Upon reaction with phenyldiazonium fluoroborate in the presence of 2% of tetrahydrofuran none of the alkylate product was detected by glc. A similar result was obtained when hexane was utilized as the solvent.

The possibility of increasing the yields by means of varying the structure of the organoaluminum reagent was examined next. Diethylphenylethynylalane was synthesized by reacting diethylaluminum chloride with phenylethynyllithium. This alane proved to be less reactive towards THF than was the isobutyl analog. A temperature of 0° was required for a smooth evolution of nitrogen (compared to -30° for diisobutylphenylethynylalane). A slightly lower yield was also obtained (46%).

$$(Et)_2AlCl + \Phi C{\equiv}C\text{-}Li \longrightarrow (Et)_2AlC{\equiv}C\text{-}\Phi$$

During the course of this investigation it was observed that irrespective of the ether used, the only group observed to migrate from the mixed alane reagent was the acetylenic moiety. To investigate the possibility of using the acetylenic group more efficiently, the dialkynylalane was synthesized. Such a reagent was prepared from interaction of isobutylaluminum dichloride with the lithium salt of phenylacetylene, *i.e.*,



$$i\text{-BuAlCl}_2 + 2\ \Phi\text{-C}\equiv\text{CLi} \longrightarrow i\text{-BuAl-(C}\equiv\text{C-}\Phi)_2$$

Upon reaction of this reagent with phenyldiazonium fluoroborate at -30° in tetrahydrofuran, smooth evolution of nitrogen was observed. Nevertheless, the effect of this second alkynyl group was almost negligible, as the yield did not improve (70%).

Until now, the reaction has been shown to be extremely dependent on the ether "solvent" utilized, and the effects of temperature or the nature of the organoaluminum reagent did not appear to produce dramatic changes in the yields. One parameter that has remained constant throughout has been the phenyldiazonium salt.

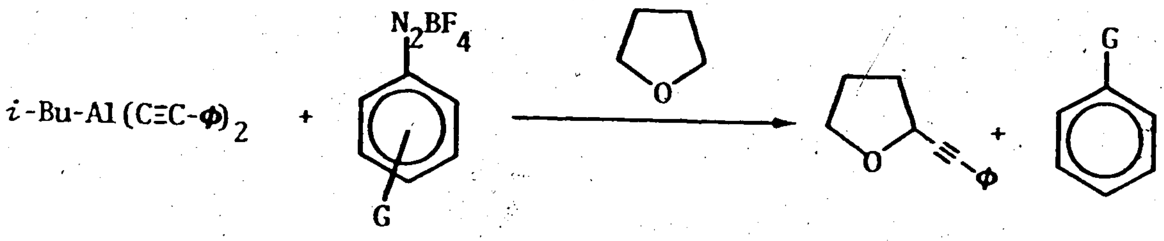
It is well known that there are marked differences in the rates of decomposition of substituted diazonium salts. Especially interesting is the enhanced reactivity of substituted diazonium salts with *meta* electron-releasing substituents. For example, the rate coefficients for the decomposition (towards solvolysis) of *m*-methoxyphenyl diazonium and *p*-methoxy salts have beer estimated as 3400 and 0.11 (sec^{-1} x 10^{7}) respectively[77]. o, there is a marked difference in the relative ease with which various substituted diazonium salts accept an electron (reduction potential). Recently, the half-wave potentials of several diazonium salts[78] has been determined and some of these values are shown in Table VI.

TABLE VI

The Half-Wave Potentials of Various Aryldiazonium Salts

Substituents	E ½ *vs.* sce.
m-Cl	+0.41
H	+0.29
m-C H_3	+0.285
p-OC H_3	+0.140
p-N(C H_3)$_2$	-0.095

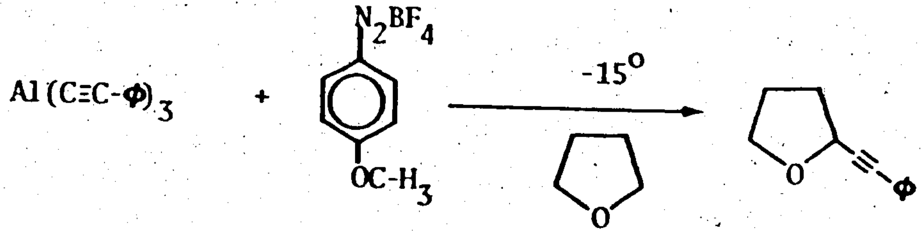
The possibility that the use of a different diazonium salt could improve the yield of the reaction was next examined. Several different salts were synthesized and their efficiency in this process was investigated utilizing isobutyldiphenylethynylalane and tetrahydrofuran as a model system.



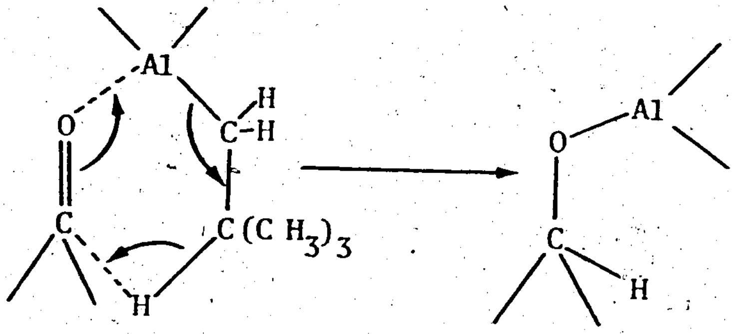
Treatment of the *meta*-chloro salt with the alane in THF afforded a 27% yield of alkylated product. The *meta*-tolyl salt gave comparable yields as the unsubstituted salt (73%).

Use of *para*-methoxybenzenediazonium fluoroborate produced a very clean reaction, resulting in an 82% yield of the propargyl ether. Also less tar formation was encountered in the reaction as compared to the other diazonium salts. A trialkynylalane was also allowed to react with the *p*-methoxy salt in THF; an 85% yield of alkylated product was formed. The trialkynylalane was prepared by interaction of three equivalents of the lithium salt of phenylacetylene and one equivalent of aluminum chloride in tetrahydrofuran.

$$3\ \Phi\text{-C}\equiv\text{C-Li} + \text{AlCl}_3 \longrightarrow \text{Al(C}\equiv\text{C-}\Phi)_3$$



It also seemed clear from the latter experiment that the hydrogen (hydride or hydrogen atom) utilized to reduce the diazonium salt ($R\text{-}N_2^{\oplus} \longrightarrow RH$), is provided by the solvent rather than the alane reagent. In the cases where the alane used had an isobutyl group, the possibility existed that the hydrogen atom could have originated from the isobutyl group. It is well known that alanes containing a β-hydrogen atom serve as reducing agents. For example, ketones can be reduced with triisobutylaluminum[64].



Once it was found that the *para*-methoxy salt afforded the best results, this salt was allowed to react with the diisobutylphenylethynylalane studied initially. Although a smooth evolution of nitrogen was not obtained until the mixture was warmed to -10° (compared to -30° for the unsubstituted salt), the alkylated product was obtained in 82% yield.

Observing the reduction potentials of the different diazonium salts summarized in Table VI, it would appear that the yields of alkylation product increase slightly as the potential becomes more negative. This suggested the possibility that a further increase in yields might be achieved by utilizing a salt with a potential lower than that of the *para*-methoxy salt.

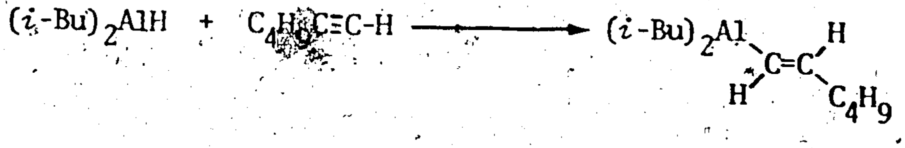
Toward this end, *p*-N,N-dimethylaminophenyldiazonium fluoroborate was synthesized and allowed to react with diisobutylphenylethynylalane in ethyl ether. At room temperature no nitrogen evolution was observed. The mixture was brought to reflux (36°), and at this temperature nitrogen was liberated; disappointingly, however, only 11% of the propargyl ether was formed.

In light of these results, *p*-methoxyphenyldiazonium fluoroborate proved to be the salt of choice (*i.e.*, gave the best yields and the cleanest reaction mixture). This salt was then used in alkylating the ethers which were tried previously utilizing the unsubstituted salt, and it was observed that better yields were obtained in all cases when the *p*-methoxy salt was employed.

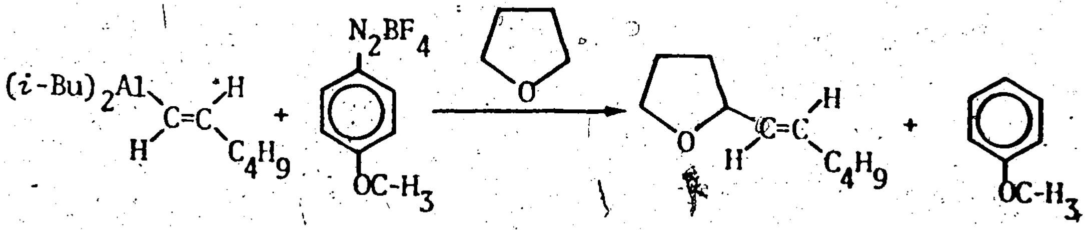
Ethyl ether reacted at 15° with diisobutylphenylethynylalane and gave rise to a 64% yield of alkylated product (*vs.* 52% using the unsubstituted salt). *p*-Dioxane afforded a 43% yield (compared with 33% obtained with the phenyldiazonium salt). The yields of alkylation product obtained from tetrahydropyran and 2,5-dimethyltetrahydrofuran, respectively, each increased by c a. 15%.

As previously mentioned, the high selectivity of these reactions allows the exclusive migration of the alkyne portion of a mixed alane. After having observed this high selectivity with acetylenic groups, it became interesting to investigate the possibility of achieving the preferential migration of a vinylic group. The ready accessibility of dialkyl-*trans*-vinylic alanes[62] made it possible not only to test the selectivity of this reaction, but also the feasibility of conserving the geometry of the double bond.

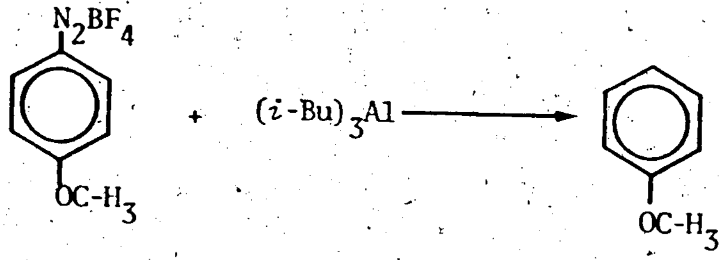
trans-Diisobutyl-1-hexenylalane was prepared by hydroalumination of 1-hexyne utilizing ligroine as a solvent[79]. The solvent was eliminated *in vacuo* and the residue was dissolved in tetrahydrofuran.



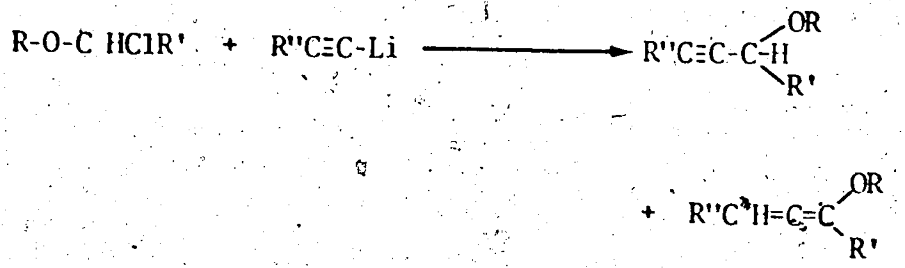
This THF solution of the mixed vinylalane was allowed to react with *p*-methoxyphenyldiazonium fluoroborate. A smooth evolution of nitrogen was produced with concomitant formation of the expected allylic ether in 38% yield (anisole was also detected (63%)). The product showed strong infrared absorption at 965 cm^{-1}, indicating that the *trans* stereochemistry was preserved during the migration. No evidence of any other transfer products (*i.e.*, isobutyl group migration) could be detected by glc.



In previous studies, there was always a group attached to aluminum with a higher degree of *s*-character than the isobutyl group. This eliminated the possibility of the isobutyl group migrating. In order to determine whether an sp^3-hybridized bond could migrate, triisobutylaluminum was allowed to react with the *p*-methoxy salt in tetrahydrofuran. Anisole was formed in 48% yield; however, no alkylation product arising from migration of an isobutyl group could be detected.



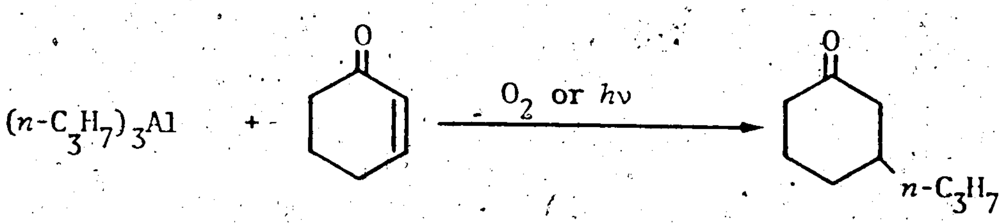
Propargyl ethers are usually prepared[80] by treatment of the corresponding α-chloroether with an appropriate lithium acetylide. The product can usually be readily isolated, but occasionally allenic material is also present due to prototropic rearrangement.



$$R\text{-}O\text{-}CHClR' + R''C\equiv C\text{-}Li \longrightarrow R''C\equiv C\text{-}C\overset{OR}{\underset{R'}{H}} + R''C^{*}H=C=C\overset{OR}{\underset{R'}{}}$$

The direct alkylation of ethers observed in the present study provides another alternative for the synthesis of propargyl ethers. In certain cases, the yields are high and the ready availability of the ethers makes this method an attractive direct procedure for obtaining these compounds. Moreover, no allene formation could be detected (nmr or ir) in any of these reactions. Obviously this method has some limitations in as much as the ether must be used as a solvent rather than in stoichiometric amounts.

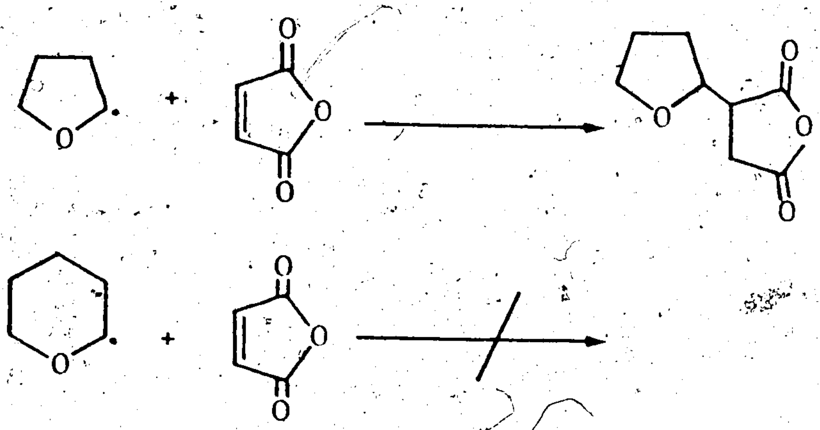
The mechanism of these reactions is as yet uncertain. Recently, Kabalka and Daley[81] have reported that the 1,4-addition of tri-*n*-propylaluminum to 2-cyclohexenone is catalyzed by molecular oxygen or UV light. This was taken as evidence that the reaction proceeds by a free radical chain process, since it was also inhibited by galvinoxyl, an efficient free-radical scavenger.



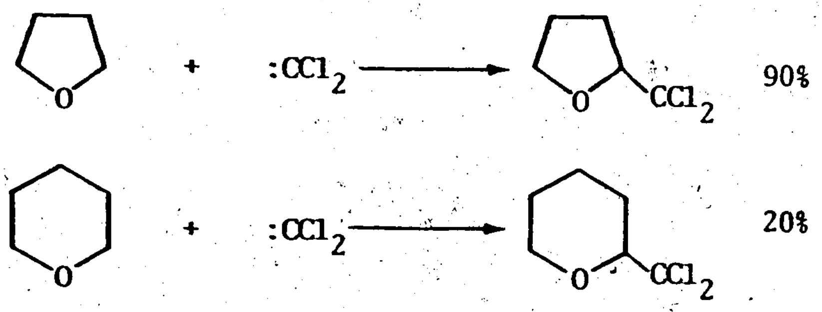
These observations suggested the possibility that some radical type process might be associated with the direct alkylation of ethers. To explore this possibility, the reaction between diisobutylphenylethynylalane and phenyldiazonium fluoroborate was conducted in the presence of 5 mole % galvinoxyl. Nevertheless, no inhibition was observed and the yield obtained of alkylated product [illegible] same as in the absence of galvinoxyl.

This result tends to indicate that the reaction does not proceed by a free radical chain process; however, the mechanism remains for future work to determine.

It has been generally observed that five membered ring ethers afford better yields and react under milder conditions than the six membered ring ethers. For instance, the radical-initiated reaction between tetrahydrofuran and maleic anhydride is a high yield process; however, tetrahydropyran fails to react analogously[74b].



Similar results have been observed for the reaction of carbenes[82] with tetrahydrofuran and tetrahydropyran respectively.

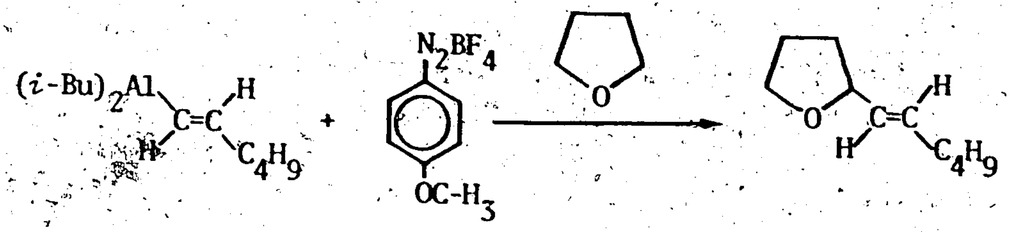


These studies parallel the results obtained in the present investigation, in which high yields of alkylated product were produced with tetrahydrofuran (60-80%), however the reactions with tetrahydropyran were less efficient (20-35%).

In conclusion, the reaction of ethers with mixed dialkylalkynylalanes in the presence of aryldiazonium salts provides a new direct process to alkylate ethers. Although the method has several limitations, the availability and low cost of the ethers makes this method an attractive procedure to prepare in a single step, propargyl ethers.

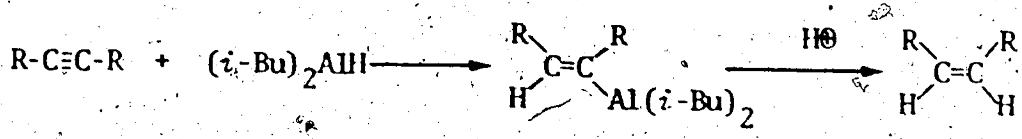
Synthesis of Allenes

During the course of this investigation, a brief study was also undertaken on the synthesis of allenes. This was prompted by the finding that the migration of vinylic groups takes place with retention of configuration. Thus, it will be recalled that diisobutyl-*trans*-1-hexenylalane, upon reaction with *p*-methoxyphenyldiazonium fluoroborate with tetrahydrofuran, afforded *trans*-2(1-hexenyl)tetrahydrofuran in 38% yield.

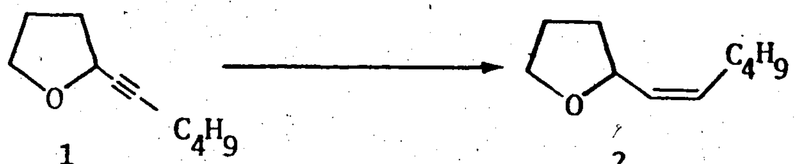


In order to independently prove the stereochemistry of this compound, it was desirable to prepare the corresponding *cis* isomer and compare the properties (glc, nmr and ir) of the two materials.

It is well known that acetylenes are readily converted into *cis* olefins upon treatment with diisobutylaluminum hydride followed by a hydrolytic work-up[62].

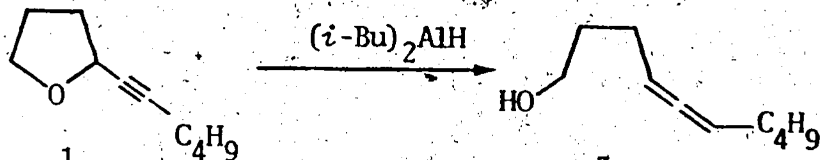


Thus, the obvious immediate precursor to *cis*-2(1-hexenyl)tetrahydrofuran 2 is 2-(1-hexynyl)tetrahydrofuran 1, readily available by the direct alkylation of THF.



1 2

However, treatment of propargylic ether 1 with diisobutylaluminum hydride utilizing ligroin as the solvent, followed by a hydrolytic work-up, failed to produce any 2. Instead, a compound possessing strong ir absorption at 3300 and 1950 cm^{-1} was obtained. Subsequently, this compound was shown to be the allenic alcohol 3, formed in 92% yield (glc).



1 3

This observation that a propargylic ether upon reaction with diisobutylaluminum hydride[87] gave rise to an allene, prompted a brief study of the scope of the process.

For this purpose the behaviour of a 1-alkoxy-2-alkyne was chosen as a model for investigation. The latter compounds are easily prepared from terminal alkynes either by treating the appropriate alkali acetylide with a chloromethyl alkyl ether, or with formaldehyde followed by an alkyl halide (Williamson synthesis).

$$RC\equiv CM \xrightarrow[\substack{1.\ CH_2O \\ 2.\ R'X}]{R'OCH_2Cl,\ or} RC\equiv C\text{-}CH_2OR'$$

M = Na, Li

Should the reaction with diisobutylaluminum hydride prove successful, a simple synthesis of terminal allenes would thus be available[88] from simple precursors.

$$R\text{-}C\equiv C\text{-}CH_2OR' \xrightarrow{i\text{-}Bu_2AlH} RCH=C=CH_2$$

The propargylic ether chosen was 1-methoxy-2-octyne, readily synthesized by treatment of the lithium salt of 1-heptyne with chloromethyl methyl ether.

$$CH_3(CH_2)_4C\equiv C\text{-}Li \quad + \quad ClCH_2OCH_3 \longrightarrow CH_3(CH_2)_4C\equiv C\text{-}CH_2OCH_3$$

A ligroine solution of 1-methoxy-2-octyne was treated at c a. 30-35^{o} with one equivalent of DIAH. After 5.5 hours, a 57% yield of 1,2-octadiene and 5% of 1-octene was detected by glc analysis (c a. 20% starting material also remained).

$$CH_3(CH_2)_4C\equiv C\text{-}CH_2OCH_3 \quad + \quad (i\text{-}Bu)_2AlH \longrightarrow$$

$$CH_3(CH_2)_4CH=C=CH_2 \quad + \quad CH_3(CH_2)_5CH=CH_2$$

Several parameters (including time, temperature, solvent and leaving group) were altered in an attempt to increase the yields of allene.

Similar results were obtained at slightly higher temperatures (c a. 50°) in ligroin solvent, and also in refluxing methylene chloride as solvent. The yield of allene could be increased (c a. 65-70%) by using methylene chloride (at reflux) and an extended reaction time (12 hours). Even under these conditions, however, starting material (c a. 15%) still remained. In an attempt to drive the reaction to completion, two equivalents of DIAH, in pentane, were used. Under these conditions, however, no allene was detected; rather, only low retention time products were detected by glc. This outcome is probably the result of subsequent reaction of the initially produced allene with DIAH, a precedented reaction[89].

It was also shown that another propargyl ether, namely, 1-methoxy-2-undecyne upon treatment with one equivalent of DIAH, in refluxing pentane, afforded 38% yield of 1,2-undecadiene. In another run utilizing 1.5 equivalents of DIAH, at room temperature (after 24 hours), 1,2-undecadiene was present in 69% (1-undecene and starting material were detected also by glc in 7 and 10% respectively).

$$CH_3(CH_2)_7C\text{-}C{\equiv}CH_2OCH_3 \xrightarrow{\text{DIAH}} CH_3(CH_2)_7CH{=}C{=}CH_2$$

$$+ \quad CH_3(CH_2)_7CH_2CH{=}CH_2$$

Repeating the reaction in ethyl ether proved to be slow. Obviously, the use of ethyl ether, due to complexation with DIAH, retarded the reaction. After 18 hours, less than 40% of allene was produced.

Next, the possibility of increasing the yields was focused on the nature of the leaving group. For this purpose a propargylic chloride, 1-chloro-2-octyne, was synthesized following the procedure of Zweifel[90]. 1-Heptyne was hydroformylated by treatment of 1-heptynyllithium with paraformaldehyde[91]. Subsequent tranformation of the propargyl alcohol to the chloride was accomplished by the use of thionyl chloride in the presence of tri-*n*-butylamine (79% overall yield).

$$CH_3(CH_2)_4C\equiv C\text{-}H \;+\; n\text{-BuLi} \longrightarrow CH_3(CH_2)_4C\equiv C\text{-}Li$$

$$\xrightarrow{CH_2O)_n} CH_3(CH_2)_4C\equiv C\text{-}CH_2OH \xrightarrow[(n\text{-Bu})_3N]{SOCl_2}$$

$$CH_3(CH_2)_4C\equiv C\text{-}CH_2Cl$$

The reaction of 1-chloro-2-octyne with DIAH in methylene chloride, however, proved to be complex. Numerous products were detected by glc analysis, and only 32% of 1,2-octadiene was formed.

$$CH_3(CH_2)_4C\equiv C\text{-}CH_2Cl \xrightarrow{\text{DIAH}} CH_3(CH_2)_4CH{=}C{=}CH_2$$

Although the tetrahydropyranyloxy moiety (THP) is not generally considered to be a good leaving group[92], it was thought that the presence of the two oxygen atoms in the THP group might facilitate the coordination with DIAH. However, when the THP-derivative of 2-octyn-1-ol was reacted with DIAH, only 36% (glc) of the desired allene could be detected.

$$CH_3(CH_2)_4C{\equiv}C\text{-}CH_2OTHP \xrightarrow{\text{DIAH}} CH_3(CH_2)_4CH{=}C{=}CH_2$$

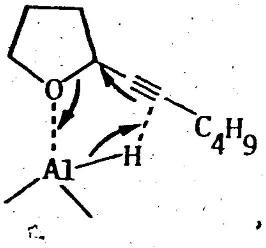
Finally, the mesylate of 2-octyn-1-ol (from reaction of the carbinol with CH_3SO_2Cl/Et_3N) was investigated.

$$CH_3(CH_2)_4C{\equiv}C\text{-}CH_2OH \xrightarrow[Et_3N]{CH_3SO_2Cl} CH_3(CH_2)_4C{\equiv}C\text{-}CH_2OSO_2CH_3$$

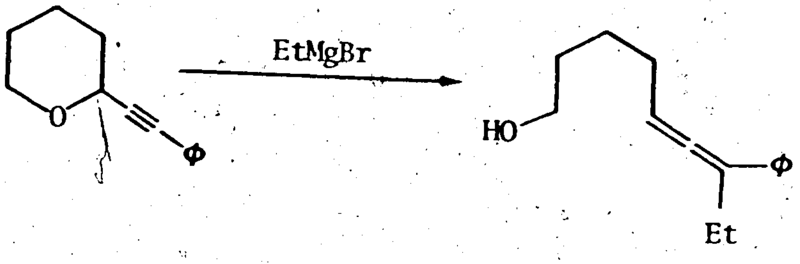
Upon treatment of this derivative with DIAH, at -20°, the reaction took an entirely different course and a quantitative yield (glc) of 2-octyne was produced.

$$CH_3(CH_2)_4C{\equiv}C\text{-}CH_2OSO_2CH_3 \xrightarrow{\text{DIAH}} CH_3(CH_2)_4C{\equiv}C\text{-}CH_3$$

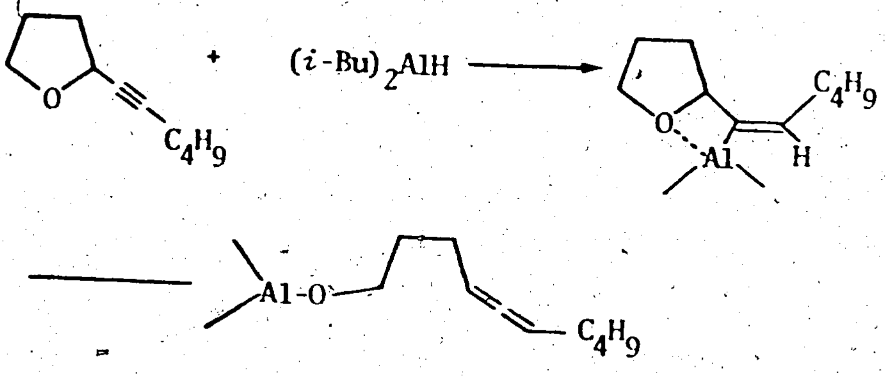
Although the precise mechanism of this reaction is unknown, there are two conceivable pathways by which the products can arise. One attractive possibility is initial Al-O coordination, followed by intramolecular delivery of hydride via a six-membered transition state (a formal S_N2' mechanism). The reaction is presumably facilitated for a cyclic propargylic ether due to the release of ring strain.



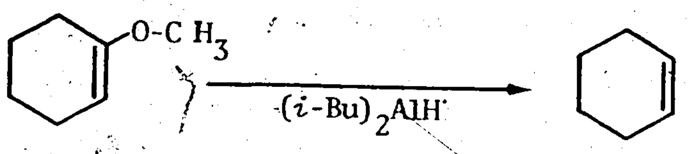
A similar reaction has been observed recently (once this research was completed) by Nelson and Miller[86] utilizing Grignard reagents.



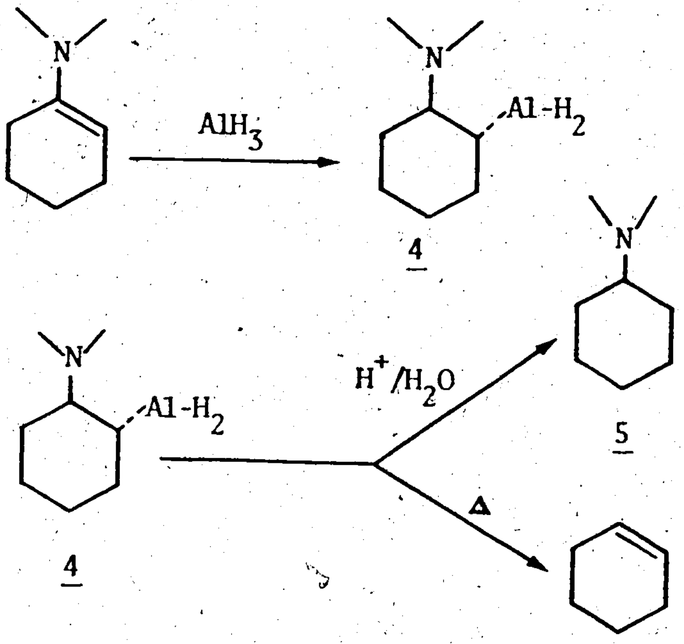
Another alternative for the mechanism may involve the initial hydroalumination of the alkyne followed by an elimination reaction. The orientation of addition of aluminum is to be expected in the sense indicated below (*i.e.*, next to the oxygen atom) since this should be assisted by coordination.



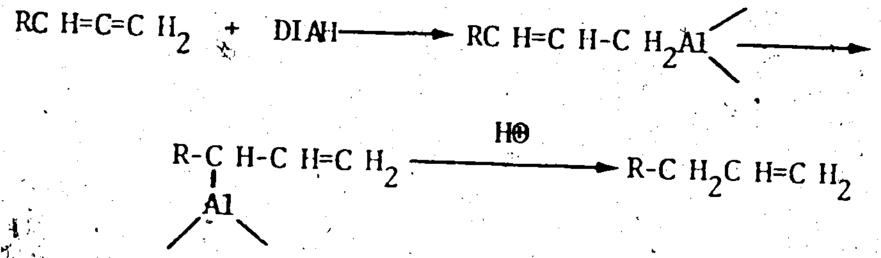
There is a precedent in the literature for addition - elimination reactions utilizing either DIAH or aluminum hydride. Prino and Lorenzi[93] reported the formation of cyclohexene upon treatment of 1-methoxy-1-cyclohexene with DIAH.



Similarly, enamines react with aluminum hydride[94] to afford adduct , 4, which either upon hydrolytic treatment form the amine , 5, or upon reflux undergo elimination to produce cyclohexene 6.



The treatment of linear propargyl ethers with DIAH affords the corresponding 1-olefin in addition to the desired allene. The presence of this by-product can be explained by the fact that allenes themselves undergo hydroalumination. Due to steric factors the aluminum is attached to the terminal carbon; however, the allylic alane formed undergoes allylic rearrangement to the thermodynamically more stable internal alane[89]. Hydrolysis of this intermediate gives rise to the 1-olefin.



$$RCH{=}C{=}CH_2 + DIAH \longrightarrow RCH{=}CH{-}CH_2Al\langle \longrightarrow R{-}\underset{\underset{\wedge}{Al}}{C}H{-}CH{=}CH_2 \xrightarrow{H^{\oplus}} R{-}CH_2CH{=}CH_2$$

In brief, the reaction between propargylic ethers and [illegible]isobutylaluminum hydride affords high yields of allenes when [illegible]lic propargylic ether is utilized. However, the formation of terminal allenes is limited by the necessity of finding optimum conditions for each specific substrate. Moreover the formation of the corresponding 1-olefin makes the isolation procedure laborious.

EXPERIMENTAL

General Considerations

Infrared (ir) spectra were recorded using a Unicam SP 1000 Infrared Spectrophotometer.

Nuclear magnetic resonance (nmr) spectra were recorded on a Varian A-60 or HR-100 spectrometer. Unless otherwise stated, carbon tetrachloride (CCl_4) was employed as the solvent with tetramethylsilane (TMS) as the internal standard, and chemical shifts are reported in δ values. The following abbreviations are used in the text: s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet. ^{13}C nmr spectra were determined using a BRUKER HFX-90 Spectrometer.

Mass spectra were recorded at 70 *ev*. on an AEI Model MS-2 or Model MS-9 Spectrometer. Spectra are recorded in the following manner: *m/e* : peak mass (relative intensity).

Gas chromatographic (glc) analyses were performed using an Aerograph A-90 - P-3 and a Varian Aerograph Series 1200 versus a reference solution of the authentic compounds, with the following columns: column A, 20% NPGSE on Chromosorb W; column B, 15% FFAP on Chromosorb W; column C, 15% Carbowax 20M on Chromosorb W; column D, 20% SE-30 on Chromosorb W; column E, 10% NPGSE on Fluoropak; column F, 10% DEGS on Chromosorb W. Refractive indices were measured on a Bausch and Lomb Abbe-3L Refractometer.

The aryl diazonium fluoroborates were prepared by well known established procedures[83]. These salts were crystallized from acetone-chloroform[84] and kept in the refrigerator, without apparent decomposition, for indefinite period of time.

All reactions were carried out using oxygen-free nitrogen[24].

General Procedure for the Preparation of Diisobutylalkynylalanes in Tetrahydrofuran

To a cooled (-20°) solution of the 1-alkyne (25 mmole) in tetrahydrofuran (50 ml), *n*-butyllithium (15.6 ml, 25 mmole, 1.6M) was added dropwise over a period of twenty minutes. The solution was stirred for 30 minutes at 0° and then diisobutylaluminum chloride (4.88 ml, 25 mmole) was added (10 minutes). The mixture was made up to 100 ml (0.25M solution) with dry THF and stirred overnight.

General Work-up Procedure for the Reactions Utilizing Organoaluminum Compounds

The reaction mixture was poured into ice-6M hydrochloric acid and extracted with ether or pentane. The combined organic extracts were washed successively with saturated sodium bicarbonate and finally again with saturated sodium chloride.

Reaction of Diisobutyl-1-hexynylalane with Phenyldiazonium Fluoroborate in Tetrahydrofuran.

To a cooled (0°) suspension of phenyldiazonium fluoroborate (3.836 g, 20 mmole) in 40 ml of tetrahydrofuran, was added dropwise a solution of diisobutyl-1-hexynylalane (80 ml, 20 mmole, 0.25M, prepared as described above) in tetrahydrofuran over a thirty minute period. A smooth evolution of nitrogen was produced (91%). When no more nitrogen was given off the dark mixture was worked up in accordance with the general procedure. Analysis by glc (column A, 150°) showed the formation of 63% of 2-(1-hexynyl)tetrahydrofuran. Removal of the solvent at atmospheric pressure and fractional distillation under reduced pressure afforded 1.67 g (55%) of 2-(1-hexynyl)tetrahydrofuran, bp 72-73°/3 mm. An analytical sample was obtained by bulb to bulb distillation (130°/ 23 mm), n_D^{20} 1.4639; ir (liquid film): 2230 (C≡C) and 1050 cm^{-1} (C-O-C); nmr: δ 4.45 (m, 1H) C≡C-C*H*O-, 3.75 (m, 2H) -CH_2O-, 1.65-2.22 (m, 6H) CH_2CH_2CH_2O and C≡C-CH_2, 1.15-1.65 (m, 4H) CH_2CH_2CH_3, 0.9 (m, 3H) CH_3; mass spectrum *m/e*: 152.1180, M^+-1, *m/e*: 151.1123 (*Calcd.* for $C_{10}H_{16}O$: 152.1201; *Calcd.* for $C_{10}H_{15}O$: 151.1123), 124(62), 110(57), 95(70), 81(70), 67(52), 53(52), 41(100), 39(90). *Anal Calcd.* for $C_{10}H_{16}O$: C, 78.90; H, 10.59. *Found:* C, 78.64; H, 10.81.

Reaction between Diisobutyl-1-butynylalane and Phenyldiazonium Fluoroborate in Tetrahydrofuran

To a cooled (0^{o}) suspension of phenyldiazonium fluoroborate (3.836 g, 20 mmole) in 40 ml of tetrahydrofuran, a solution of diisobutyl-1-butynylalane (80 ml, 20 mmole, 0.25M, prepared as described above) in tetrahydrofuran was added at a rate sufficient to produce a smooth evolution of nitrogen (96%). Then the mixture was allowed to warm to room temperature and worked up in the usual way. Glc analysis (column A, 140^{o}) revealed a 55% yield of 2-(1-butynyl)tetrahydrofuran. The solvent was removed at atmospheric pressure and a portion of the forerun was purified by bulb distillation (100^{o}/23 mm), n_D^{20} 1.4640; ir (liquid film): 2235 (C≡C), 1045 cm^{-1} (C-O-C); nmr: δ 4.45 (m, 1H) C≡C-C *H*-O, 3.75 (m, 2H) C H_2C H_2O-, 1.65-2.5 (m, 6H) C H_2C H_2 and C≡C-C H_2, 1.15 (t, J = 7 Hz, 3H) C H_3; mass spectrum *m/e*: 124.0892 (*Calcd.* for $C_8H_{12}O$: 124.0888), 124(10), 123(24), 109(15), 96(100), 95(44), 82(99), 81(73), 79(50), 77(30), 67(42), 66(23), 55(40), 54(30), 53(44), 51(19), 42(60), 41(54), 39(58). *Anal Calcd.* for $C_8H_{12}O$: C, 77.38; H, 9.74. *Found:* C, 77.37; H, 9.58.

Reaction of Diisobutylphenylethynylalane and Phenyldiazonium Fluoroborate in Tetrahydrofuran

A solution of diisobutylphenylethynylalane (80 ml, 20 mmole, 0.25M, prepared according with the general procedure) was added dropwise to a cooled (0^{o}) suspension of phenyldiazonium fluoroborate (3.836 g, 20 mmole) in 40 ml of tetrahydrofuran. A 91% yield of nitrogen was given off. After the solution was allowed to warm to room temperature the mixture was worked up in the usual way. Analysis by glc (column D, 245^{o}) showed the formation of 2-phenylethynyltetrahydrofuran in 67% yield. Removal of the solvent at reduced pressure and fractional distillation afforded 1.7 g (49%) of 2-phenylethynyltetrahydrofuran, bp 110^{o}/1.5 mm, n_D^{20} 1.5690; ir (liquid film): 2230 (C≡C), 1050 (C-O-C), 1600 (aromatic), 755 and 690 cm^{-1} (C_6H_5); nmr: δ 7.3 (m, 5H), 4.75 (m, 1H) C≡C-C *H*O-, 3.8 (m, 2H) C H_2O, 2.0 (m, 4H) C H_2C H_2C H_2O-; mass spectrum *m/e*: 172.0890 (*Calcd.* for $C_{12}H_{12}O$: 170.0893), 172(49), 171(59), 157(37), 144(61), 131(89), 16(100), 103(77), 102(67), 77(60), 70(62), 63(64), 51(63), 42(65), 39(61). *Anal Calcd.* for $C_{12}H_{12}O$: C, 83.69; H, 7.02. *Found:* C, 83.53; H, 7.30.

Reaction between Diisobutylphenylethynylalane with Phenyldiazonium Fluoroborate in Tetrahydrofuran at -20^{o}

The same procedure as described above was followed but the reaction was carried out at -20^{o}. At this temperature a smooth evolution of nitrogen was produced (85%). Glc analysis (column D, 245^{o}) showed the formation of 70% yield of 2-phenylethynyltetrahydrofuran.

Reaction between Diisobutylphenylethynylalane with Two Equivalents of Phenyldiazonium Fluoroborate in Tetrahydrofuran

To a cooled (0°) suspension of phenyldiazonium fluoroborate (7.672 g, 40 mmole) in 60 ml of THF, a solution of diisobutylphenylethynylalane (80 ml, 20 mmole, 0.25M, prepared as described above) was added dropwise. At the end of the addition 120% of nitrogen was given off. When the temperature was allowed to increase to 25° the rest of the nitrogen was evolved. Work-up in the usual way and analysis by glc (column D, 245°) showed the formation of 2-phenylethynyltetrahydrofuran in 72% yield.

Preparation of Diisobutylphenylethynylalane in *p*-Dioxane

To a cooled (10°) solution of phenylacetylene (2.74 ml, 2.55 g, 25 mmole) in 60 ml of *p*-dioxane was added 10.2 ml of a 2.45M solution of *n*-butyllithium (25 mmole). The mixture was stirred at 0° for thirty minutes and then diisobutylaluminum chloride (4.89 ml, 25 mmole) was added dropwise. Lithium chloride precipitated, the suspension was stirred overnight. Enough *p*-dioxane was added to obtain a volume of 100 ml (0.25M).

Reaction of Diisobutylphenylethynylalane with Phenyldiazonium Fluoroborate in *p*-Dioxane

A suspension of phenyldiazonium fluoroborate (3.836 g, 20 mmole) in 40 ml of *p*-dioxane was cooled to 10° and then 80 ml

(20 mmole, 0.25M) of the alane solution prepared above was added dropwise. The mixture became gradually darker upon addition of the alane and a smooth evolution of nitrogen was produced. After warming to room temperature the solution was worked up in the usual way. Analysis by glc demonstrated the formation of 2-phenylethynyl-β-dioxane in 33% yield. The solvent was removed in the rotatory evaporator (water aspirator pressure). A small sample was distilled bulb to bulb (190°/ 0.3 mm), n_D^{20} 1.5606; ir (liquid film) 2230 (C≡C), 1600 (C_6H_5), 1120, 1090 (C-O-C), 760 and 695 cm^{-1} (C_6H_5); nmr: δ 7.35 (m, 5H) C_6H_5, 4.4 (q, 1H) -OC *H*C≡C, 3.35-4.0 (m, 6H) 3(O-CH_2); mass spectrum *m/e*: 188.0837 (*Calcd.* for $C_{12}H_{12}O_2$: 188.0837), 188(100), 158(10), 130(30), 129(69), 114(39), 103(94), 102(96), 74(15), 63(15), 51(20), 39(10). No satisfactory analysis could be obtained for this sample.

Preparation of Diisobutylphenylethynylalane in Ethyl Ether

To a cooled (-20°) solution of phenylacetylene (2.74 ml, 2.55 g, 25 mmole) in 60 ml of ethyl ether was added dropwise *n*-butyllithium (10.2 ml, 25 mmole, 2.45M). The white suspension was stirred at 0° for 30 minutes and then diisobutylaluminum chloride (4.89 ml, 25 mmole) was added over ten minutes. Lithium chloride precipitated and the mixture was stirred overnight. Enough ether was added to make the total volume 100 ml (0.25M).

Reaction of Diisobutylphenylethynylalane with Phenyldiazonium Fluoroborate in Ethyl Ether

A solution of the alane prepared above (80 ml, 20 mmole, 0.25M) was added dropwise to a suspension of phenyldiazonium fluoroborate (3.836 g, 20 mmole) in ethyl ether (40 ml) at 16°. After no further nitrogen was evolved the solution was warmed to 25° and worked up according to the general procedure. Analysis by glc (column A, 230° and 150°) showed the formation of 2-phenylethynyl ethyl ether in 52% yield and the presence of 46% of phenylacetylene. The solvent was removed *in vacuo*, and from the residue an analytical sample was obtained by bulb to bulb distillation (84°/2 mm); n_D^{20} 1.5271; ir (liquid film) 2240 (C≡C), 1600 (C_6H_5), 1110 (C-O-C), 750 and 690 cm^{-1} (C_6H_5); nmr: δ 7.28 (m, 5H) C_6H_5, 4.25 (q, J = 7 Hz, 1H) C≡C-C *H*O-, 3.05 - 4.0 (m, 2H) C H_2O, 1.45 (d, J = 6 Hz, 3H) C H_3C *H*, 1.2 (t, J = 7 Hz, 3H) C H_2C H_3; mass spectrum *m/e*: 174.1040 (*Calcd.* for $C_{12}H_{14}O$: 174.1045), 174(25), 173(68), 159(41), 145(10), 131(87), 130(76), 129(100), 127(21), 115(49), 103(21), 91(7), 77(21), 63(7), 51(13), 43(61), 39(4). *Anal Calcd.* for $C_{12}H_{14}O$: C, 82.72; H, 8.10. *Found:* C, 82.70; H, 7.91.

Preparation of Diisobutylphenylethynylalane in Tetrahydropyran

To a cooled (-20°) solution of phenylacetylene (2.74 ml, 2.55 g, 25 mmole) in 40 ml of tetrahydropyran, *n*-butyllithium (10.2 ml, 25 mmole, 2.45M) was added over thirty minutes. The mixture was stirred at 0° for 15 minutes and then diisobutylaluminum chloride (4.88 ml, 25 mmole) was added. At 25° none of the lithium chloride precipitated. After stirring overnight a small amount separated from the solution. Tetrahydropyran was added to make up to 100 ml (0.25M).

Reaction between Diisobutylphenylethynylalane and Phenyldiazonium Fluoroborate in Tetrahydropyran

To a cooled (9°) suspension of phenyldiazonium fluoroborate (3.836 g, 20 mmole), 80 ml of the alane prepared above (20 mmole, 0.25M) was added dropwise. Nitrogen was given off in 72% yield. The mixture was allowed to warm to 25° and the work-up was carried out as usual. Glc analysis (column E, 230°) showed the formation of 2-phenylethynyltetrahydropyran in 28% yield. Evaporation of the solvent under reduced pressure and molecular distillation (100°/0.08 mm) of a small portion of the residue afforded a pure sample. n_D^{20} 1.5611 (lit.[85] n_D^{20} 1.5600); ir (liquid film) 2230 ($C\equiv C$), 1600 (C_6H_5), 1080, 1030 (C-O-C), 755 and 692 cm^{-1} (C_6H_5); nmr: δ 7.3 (m, 5H) $C_6\mathit{H}_5$, 4.5 (m, 1H) $C\equiv C\text{-}C\mathit{H}O\text{-}$, 3.5-3.9 (m, 2H) $CH_2C\mathit{H}_2O\text{-}$, 1.3-2.0 (m, 6H) $C\mathit{H}_2C\mathit{H}_2C\mathit{H}_2CH_2O\text{-}$. The ir and nmr spectra were in agreement with the ones reported in the literature[86].

Preparation of Diisobutylphenylethynylalane in Diisopropyl Ether

To a [illegible] (-20°) solution of phenylacetylene (2.74 ml, 2.55 g, 25 mmole) in diisopropyl ether (50 ml), *n*-butyllithium (10.2 ml, 25 mmole, 2.45M) was added dropwise over a thirty minute period of time. The white suspension was stirred at 0° for one hour. Diisobutylaluminum chloride (4.88 ml, 25 mmole) was added. Lithium chloride precipitated and the mixture was stirred overnight. The volume was adjusted to 100 ml (0.25M).

Reaction of Diisobutylphenylethynylalane with Phenyldiazonium Fluoroborate in Diisopropyl Ether

The alane solution (80 ml) prepared above (20 mmole, 0.25M) was added dropwise to a suspension of phenyldiazonium fluoroborate (3.836 g, 20 mmole) in diisopropyl ether (40 ml) at room temperature. A very slow evolution of nitrogen was produced upon addition of the alane, accompanied by a rapid darkening of the solution. After no more nitrogen was given off (70%), the resultant red mixture was worked up in the usual way. Analysis by glc on different columns failed to reveal the presence of the expected product.

Preparation of Diisobutylphenylethynylalane in 2,5-Dimethyltetrahydrofuran

To a cooled (-20°) solution of phenylacetylene (1.35 ml, 1.255 g, 12.5 mmole) in 30 ml of 2,5-dimethyltetrahydrofuran, *n*-butyllithium (5.1 ml, 12.5 mmole, 2.45M) was added dropwise and with stirring during fifteen minutes. The mixture was stirred at 0° for one hour and then diisobutylaluminum chloride (2.43 ml, 12.5 mmole) was added. The mixture, from which lithium chloride separated, was stirred overnight and the volume made up to 50 ml with 2,5-dimethyltetrahydrofuran (0.25M).

Reaction of Diisobutylphenylethynylalane with Phenyldiazonium Fluoroborate in 2,5-Dimethyltetrahydrofuran

Treatment of a cooled (0° to -5°) suspension of phenyldiazonium fluoroborate (1.918 g, 10 mmole) in 2,5-dimethyltetrahydrofuran (20 ml) with 40 ml of the alane solution prepared above (10 mmole, 0.25M) resulted in a smooth evolution of nitrogen (100%). Usual work-up and analysis by glc (column A, 150°) showed the presence of 62% phenylacetylene. The solvent was evaporated under reduced pressure. Fractional distillation afforded a 0.741 g of a yellow liquid, bp 77-78°/0.05 mm, which was purified by bulb to bulb distillation (130°/0.2 mm). The 0.53 g (26%) of 2,5-dimethyl-2-phenylethynyltetrahydrofuran was a mixture of diasteroisomers. n_D^{20} 1.5351; ir (liquid film) 2240 (C≡C), 1600 (C_6H_5), 750 and 695 cm^{-1} (C_6H_5); nmr: δ 7.25 (m, 5H), C_6H_5, 4.15 (m, 1H) CH_3CH, 1.58, 1.53 (s, s, 3H) isomeric CH_3C-(C≡C-Φ)-O-, 1.25, 1.28 (d, d, J = 6 Hz, J = 6.5 Hz, 3H) isomeric CH_3CH-; mass spectrum *m/e*: 200.1196 (*Calcd.* for

$C_{14}H_{16}O$: 200. 1201), 200(20), 185(27), 145(20), 129(100), 115(17), 77(5), 42(45), 41(7). *Anal. Calcd.* for $C_{14}H_{16}O$: C, 83.96; H, 8.05. *Found*: C, 83.69; H, 8.22.

Preparation of a Solution of Diisobutylphenylethynylalane in Methylene Chloride

To a cooled (-20°) solution of phenylacetylene (2.74 ml, 2.55 g, 25 mmole) in 48 ml of purified pentane and 2 ml of tetrahydrofuran, *n*-butyllithium (11.0 ml, 25 mmole, 2.30M) was added. The white suspension formed was stirred at 0° for one hour and then diisobutylaluminum chloride (4.88 ml, 25 mmole) was added dropwise. LiCl precipitated and the mixture after being stirred for 6 hours at room temperature was filtered under nitrogen. The clear solution was evaporated utilizing a slow stream of nitrogen and gentle warming at 30°. The residue was dissolved in enough methylene chloride to make a volume of 100 ml (0.25M).

Reaction of Diisobutylphenylethynylalane with Tetrahydrofuran and Phenyldiazonium Fluoroborate in Methylene Chloride

A suspension of phenyldiazonium fluoroborate (3.836 g, 20 mmole) in methylene chloride (40 ml) in the presence of 2 ml of tetrahydrofuran was cooled to 0°. The solution (80 ml) of alane prepared above (20 mmole, 0.25M) was added dropwise. An immediate darkening occurred and nitrogen was given off very slowly (54%). Analysis by glc showed that no 2-phenylethynyltetrahydrofuran was produced.

Reaction of Diethylphenylethynylalane with Phenyldiazonium Fluoroborate in Tetrahydrofuran

To a cooled (0°) suspension of phenyldiazonium fluoroborate (3.836 g, 20 mmole), a solution of diethylphenylethynylalane (80 ml, 20 mmole, 0.25M, prepared as described for the diisobutyl case, but utilizing 3.13 ml, 25 mmole of diethylaluminum chloride) was added dropwise. Nitrogen was given off in 75% yield. Usual work-up and analysis by glc (column A, 240° and 150°) revealed the formation of 47% yield of 2-phenylethynyltetrahydrofuran and the presence of phenylacetylene in 53%.

Preparation of *bis*(Phenylethynyl)isobutylalane in Tetrahydrofuran

To a cooled (-20°) solution of phenylacetylene (5.5 ml, 5.12 g, 50 mmole) in 80 ml of tetrahydrofuran, *n*-butyllithium (31.3 ml, 50 mmole, 1.6M) was added dropwise. The mixture was stirred for one hour at 0° and then treated with 3.45 ml (25 mmole) of isobutylaluminum dichloride. The solution was stirred overnight and then the volume made up to 150 ml (0.167M).

Reaction of *bis*(Phenylethynyl)isobutylalane with Phenyldiazonium Fluoroborate in Tetrahydrofuran

A suspension of phenyldiazonium fluoroborate (3.836 g, 20 mmole) in 75 ml of tetrahydrofuran was cooled to -30°. Then 120 ml of the alane solution prepared above (20 mmole, 0.167M) was added dropwise. A smooth evolution of nitrogen was produced (92%). Work-up and analysis by glc showed the formation of 2-phenylethynyltetrahydrofuran in 70% yield.

Reaction of *bis*(Phenylethynyl)isobutylalane with *p*-Methoxyphenyl diazonium Fluoroborate

To a cooled (-10°) suspension of *p*-methoxyphenyldiazonium fluoroborate (4.436 g, 20 mmole) in 75 ml of tetrahydrofuran, a solution of *bis*(phenylethynyl)isobutylalane (120 ml, 20 mmole, 0.167M, prepared as described above) was added at a rate to produce a smooth evolution of nitrogen (89%). Work-up in the usual way and glc analysis showed the presence of 82% yield of 2-phenylethynyltetrahydrofuran.

Reaction of *bis*(Phenylethynyl)isobutylalane with *m*-Chlorophenyldiazonium Fluoroborate

A suspension of *m*-chlorophenyldiazonium fluoroborate (4.526 g, 20 mmole) in 75 ml of tetrahydrofuran was cooled to 5°. Then a solution of *bis*(phenylethynyl)isobutylalane (120 ml, 20 mmole, 0.167M, prepared as described above) was added dropwise. Nitrogen was evolved in 75% yield. Work-up and analysis showed the presence of 27% of 2-phenylethynyltetrahydrofuran.

Reaction of *bis*(Phenylethynyl)isobutylalane with *m*-Tolyldiazonium Fluoroborate

A solution of *bis*(phenylethynyl)isobutylalane (120 ml, 20 mmole, 0.167M, prepared as described above) was added dropwise to a suspension of *m*-tolyldiazonium fluoroborate (4.116 g, 20 mmole) in 70 ml of tetrahydrofuran cooled at -25°. Nitrogen was given off in 90% yield and 2-phenylethynyltetrahydrofuran was formed in 73% yield.

Preparation of *tris*(Phenylethynyl)alane in Tetrahydrofuran

A solution of phenylacetylene (8.25 ml, 7.66 g, 75 mmole) in 80 ml of tetrahydrofuran was cooled to -20°. Then a solution of *n*-butyllithium (75 mmole, 47.5 ml, 1.58M) was added dropwise. The mixture was stirred at 0° for one hour and then cooled to -10°. A solution of aluminum chloride (3.33 g, 25 mmole) in 35 ml of tetrahydrofuran was added. The solution was stirred overnight and enough THF was added to bring the volume to 200 ml (0.08M).

Reaction of *tris*(Phenylethynyl)isobutylalane with *p*-Methoxyphenyldiazonium Fluoroborate in Tetrahydrofuran

To a cooled (-15°) suspension of *p*-methoxyphenyldiazonium fluoroborate (4.436 g, 20 mmole) in 70 ml of tetrahydrofuran, a solution of *tris*(phenylethynyl)isobutylalane (160 ml, 20 mmole, 0.08M, prepared as described above) was added dropwise. A smooth evolution of nitrogen was produced (100%). Analysis by glc showed the formation of 85% of 2-phenylethynyltetrahydrofuran.

Reaction of Diisobutylphenylethynylalane with *p*-Methoxyphenyldiazonium Fluoroborate

A suspension of *p*-methoxyphenyldiazonium fluoroborate (4.436 g, 20 mmole) in 50 ml of ethyl ether was cooled to 14^{0}. A solution of diisobutylphenylethynylalane in ethyl ether (80 ml, 20 mmole, 0.25M, prepared as described above) was added dropwise to produce a smooth evolution of nitrogen (100%). Work-up in the usual way and glc analysis showed the formation of 2- phenylethynyl ethyl ether in 64% yield. Also anisole was present in 84% and phenylacetylene in 22%.

Reaction of Diisobutylphenylethynylalane with *p*-Methoxyphenyldiazonium Fluoroborate in *p*-Dioxane

A mixture of *p*-methoxy-phenyldiazonium fluoroborate

(4.436 g, 20 mmole) and dioxane (50 ml) was cooled to 10°. A dioxane solution (80 ml) of diisobutylphenylethynylalane (20 mmole, 0.25M, prepared as described above) was added dropwise. A smooth evolution of nitrogen was produced (81%). Work-up utilizing the usual procedure and analysis by glc (column B, 240° and column A, 150°) revealed the formation of 2-phenylethynyl-*p*-dioxane in 43% yield. Anisole was produced in 58% yield and phenylacetylene present in 42%.

Reaction of Diisobutylphenylethynylalane with *p*-Methoxyphenyldiazonium Fluoroborate in Tetrahydropyran

To a cooled (15°) suspension of *p*-methoxyphenyldiazonium fluoroborate (4.436 g, 20 mmole) in tetrahydropyran (40 ml), a solution of diisobutylphenylethynylalane in tetrahydropyran (80 ml, 20 mmole, 0.25M, prepared as described above) was added dropwise such that a smooth evolution of nitrogen was produced (68%). Work-up and glc analysis (column E, 230° and column A, 150°), detected the formation of 36% yield of 2-phenylethynyltetrahydrofuran. Anisole was produced in 41% and phenylacetylene was present in 43%.

Reaction of Diisobutylphenylethynylalane with *p*-Methoxyphenyldiazonium Fluoroborate in 2,5-Dimethyltetrahydrofuran

A solution of diisobutylphenylethynylalane in 2,5-dimethyltetrahydrofuran (80 ml, 20 mmole, 0.25M, prepared as previously described) was added to a suspension of *p*-methoxyphenyldiazonium fluoroborate (4,436 g, 20 mmole) in 2,5-dimethyltetrahydrofuran (40 ml) at 15°. Nitrogen was evolved in 47% yield. Work-up in the usual way and glc analysis (column B, 240° and column A, 150°) showed the formation of 2,5-dimethyl-2-phenylethynyltetrahydrofuran in 35% yield. Also anisole was produced in 65% and phenylacetylene was present in 43%.

Reaction of Diisobutylphenylethynylalane with *p*-N,N-Dimethylaminophenyldiazonium Fluoroborate in Ethyl Ether

To a cooled (15°) suspension of *p*-N,N-dimethylaminophenyldiazonium fluoroborate (4.696 g, 20 mmole) in ethyl ether (40 ml), a solution of diisobutylphenylethynylalane in ethyl ether (80 ml, 20 mmole, 0.25M) was added dropwise. No nitrogen was evolved at this temperature. The mixture was brought up to reflux resulting in a smooth evolution of nitrogen. After 5 hours the reaction mixture was worked up in the usual way. The formation of 2-phenylethynyl ethyl ether in 11% yield was detected by glc.

Preparation of Diisobutyl-*trans*-1-hexenylalane

To a cooled (10°) solution of 1-hexyne (2.24 ml, 1.64 g, 20 mmole) in 30 ml of olefin-free ligroine, diisobutylaluminum hydride (3.57 ml, 20 mmole) was added dropwise maintaining the temperature below 20°. Then the mixture was refluxed for two hours. The solution was cooled to room temperature and the solvent removed *in vacuo* using the water aspirator. The residue was dissolved in 40 ml of tetrahydrofuran (c a. 0.5M).

Reaction of Diisobutyl-*trans*-1-hexenylalane with *p*-Methoxyphenyldiazonium Fluoroborate in Tetrahydrofuran

A suspension of *p*-methoxyphenyldiazonium fluoroborate (4.436 g, 20 mmole) in 60 ml of tetrahydrofuran was cooled to -10°. Then a solution of the alane prepared above (40 ml, 20 mmole, c.a. 0.5M) was added in such a way as to achieve a smooth evolution of nitrogen (70%). Work-up on the mixture and analysis by glc (column A, 180°) detected the formation of *trans*-2-(1-hexenyl)tetrahydrofuran in 38% yield and anisole in 63%. Elimination of the solvent at atmospheric pressure followed by preparative glc (12% NPGSE, 150°) and bulb to bulb distillation (60°/3 mm) resulted in a pure sample of the *trans*-allylic ether. n_D^{20} 1.4542; ir (liquid film) 1670 (C=C), 1055 (C-O-C), 965 (*trans* C H=C H); nmr: δ 5.1-5.8 (m, 2H) $\mathrm{C}\,H{=}\mathrm{C}\,H$, 3.9-4.3 (m, 1H) $\mathrm{O{-}C}\,H{-}(\mathrm{C\,H_2})(\mathrm{C\,H{=}C\,H})$, 3.4-3.9 (m, 2H $\mathrm{O{-}C}\,H_2$, 1.6-2.2 (m, 6H) $\mathrm{C}\,H_2\mathrm{C}\,H_2\mathrm{C\,H_2O}$ and $\mathrm{C\,H{=}C\,HC}\,H_2$, 1.1- 1.5 (m, 4H) $\mathrm{C}\,H_2\mathrm{C}H_2\mathrm{C\,H_3}$, 0.85 (m, 3H) $\mathrm{C}\,H_3$; mass spectrum *m/e*: 154.1366 (*Calcd.* for $C_{10}H_{18}O$: 154.1358), 111(22), 97(100), 84(18), 69(20), 55(70), 39(29). *Anal Calcd.* for $C_{10}H_{18}O$: C, 77.87; H, 11.76. *Found:* C, 78.15; H, 11.63.

Reaction between Triisobutylaluminum and *p*-Methoxyphenyldiazonium Fluoroborate in Tetrahydrofuran

A suspension of *p*-methoxyphenyldiazonium fluoroborate (4,436 g, 20 mmole) in tetrahydrofuran (50 ml) was treated with a solution of triisobutylaluminum (5.08 ml, 20 mmole) in 10 ml of tetrahydrofuran at room temperature. After no more nitrogen was given off (70%) the mixture was worked up. Glc analysis showed the presence of 48% yield of anisole. No other volatile product could be detected.

Reaction between Diisobutylphenylethynylalane and Phenyldiazonium Fluoroborate in Tetrahydrofuran in the Presence of Galvinoxyl

To a cooled (-20°) suspension of phenyldiazonium fluoroborate (3.836 g, 20 mmole) in 40 ml of tetrahydrofuran containing galvinoxyl (0.422 g, 1.0 mmole, 5%), 80 ml of a solution of diisobutylphenylethynylalane (20 mmole, 0.25M) was added dropwise. An immediate evolution of nitrogen was produced (82%). Work-up followed by glc analysis detected the formation of 2-phenylethynyltetrahydrofuran in 60%.

Synthesis of 4,5-Decadien-1-ol

To a stirred solution of 2-(1-hexynyl)tetrahydrofuran (1.52 g, 10 mmole) in 10 ml of ligroin, diisobutylaluminum hydride (DIAH) (1.87 ml, 10 mmole) was added dropwise keeping the temperature below 25° by means of a water bath. Stirring was continued overnight. Work-up of the reaction mixture was carried out in the usual way. Analysis by glc (column G, 150°) detected the formation of 4,5-decadien-1-ol (92%). A pure sample was obtained by elimination of the solvent at atmospheric pressure followed by evaporative distillation (50°/0.05 mm), n_D^{20} 1.4759, nmr: δ 4.8-5.2 (m, 2H) C *H*=C=C *H*, 3.55 (t, J = 6.2 Hz, 2H) C H_2OH, 3.43 (s, 1H) O*H*; ^{13}C nmr: ppm (relative to TMS) 204.1 (C=$\overset{*}{C}$=C), 91.53, 90.29, 62.41, 32.20, 31.50, 28.75, 25.40, 22.22, and 13.86; mass spectrum *m/e*: 154.1510 (*Calcd.* for $C_{10}H_{18}O$: 154.1514), 154(1), 138(15), 110(18), 82(80), 78(100), 77(92), 54(70), 39(38); ir (liquid film) 3320 (OH), 1950 (C=C=C), 1060 (C H_2OH).

Synthesis of 1-Methoxy-2-octyne

To a cooled (0°) solution of 1-heptyne (13.4 ml, 9.617 g, 0.1 mole) in ether (150 ml), a solution of *n*-butyllithium in hexane (55.3 ml, 0.1 mole, 1.81M) was added during one hour. The white suspension was cooled to -20° and chloromethyl methyl ether (7.58 ml, 8.05 g, 0.1 mole) was added dropwise over 20 minutes. The mixture was allowed to warm to room temperature and then poured into ice-water, saturated with NaCl, and extracted with ether. The organic layers were combined, washed with brine and dried over Na_2SO_4. The solvent was eliminated at reduced pressure and the residue was fractionally distilled. A fraction boiling at 66°/8 mm afforded 6.40 g (46%) of 1-methoxy-2-octyne, n_D^{20} 1.4391; ir (liquid film): 2220 and 2280 (C≡C), 1100 (C-O-C); nmr: δ 3.95 (t, J = 2 Hz, 2H), $\mathrm{C}H_2\mathrm{OCH}_3$, 3.26 (s, 3H) $\mathrm{OC}H_3$, 2.0-2.4 (m, 2H) $\mathrm{CH_2C}H_2\mathrm{C{\equiv}C}$, 1.1-1.65 (m, 6H) $\mathrm{CH_3(C}H_2)_3$, 0.7-1.1 (m, 3H) $\mathrm{C}H_2\mathrm{CH_2}$; mass spectrum M^+-1 (M^+ not large enough to measure) *m/e*: 139.1123 (*Calcd.* for $C_9H_{15}O$: 139.1115), 97(99), 84(70), 79(68), 67(97), 45(75), 41(100). *Anal Calcd:* C, 77.09; H, 11.50. *Found:* C, 77.10; H, 11.23.

Reaction between 1-Methoxy-2-octyne and Diisobutylaluminum Hydride (DIAH)

To a stirred solution of 1-methoxy-2-octyne (1.40 g, 10 mmole) in 3 ml of ligroin, DIAH (1.87 ml, 10 mmole) was added and the mixture maintained at 34° for 5.5 hours. The mixture was worked up in the usual way and analyzed by glc (column A, 110°), 1,2-octadiene was detected in 57% and 1-octene in 5%. The solvent was evaporated at atmospheric pressure and pure samples were isolated by preparative glc. When the reaction was repeated at 50°, the allene was produced in 55%, 1-octene in 5% and starting material present in 21%. 1,2-Octadiene, n_D^{20} 1.4401 (lit.[95a] n_D^{15} 1.4440); nmr: δ 4.75-5.3 (m, 1H) $\mathrm{C}H\mathrm{{=}C{=}CH_2}$, 4.4-4.75 (m, 2H) $\mathrm{CH{=}C{=}C}H_2$, 1.7-2.3 (m, 2H) $\mathrm{C}H_2\mathrm{CH{=}C{=}CH_2}$, 1.1-1.65 (m, 6H) $\mathrm{CH_3(C}H_2)_3\mathrm{CH_2}$, 0.7-1.1 (m, 3H) $\mathrm{C}H_3\mathrm{CH_2}$; ir (liquid film): 1950, 1695, 838 ($\mathrm{CH{=}C{=}CH_2}$). 1-Octene was shown to be identical (nmr or ir) with an authentic sample.

Reaction between 1-Methoxy-2-octyne and Diisobutylaluminum Hydride in Methylene Chloride

The same procedure described above was followed, but methylene chloride was used instead of ligroin. After six hours, 1,2-octadiene was present in 56%, starting material 20% and 1-octene in 8%. After 12 hours: allene, 67%; starting material, 15%; 1-octene, 10%.

Synthesis of 2-Octyn-1-ol

To a cooled (0^o) solution of 1-heptyne (26.8 ml, 19.23 g, 0.2 mole) in 500 ml of ether, *n*-butyllithium in hexane (110.6 ml, 0.2 mole, 1.81M) was added dropwise over 1.5 hours. The white suspension was allowed to warm to room temperature and then paraformaldehyde (6.6 g, 0.22 mole, dried over P_2O_5) was added. The mixture was stirred for two hours and then poured into ice water. The organic layer was separated and the aqueous layer extracted with ether. The combined layers were washed with water, brine and dried over Na_2SO_4. The solvent was eliminated at atmospheric pressure. Distillation of the residue afforded 19.34 g (78%) of 2-octyn-1-ol, bp $101-102^o/15$ mm (lit.[96] $98^o/15$ mm).

Synthesis of 1-Chloro-2-octyne

To a boiling mixture of thionyl chloride (3.65 ml, 5.65 g, 50 mmole), tri-*n*-butylamine (15 drops) and 15 ml of ether, 2-octyn-1-ol (6.3 g, 50 mmole) was added dropwise and then the mixture refluxed for 4 hours. Evaporation of the solvent and fractional distillation afforded 6.53 g (92%) of 1-chloro-2-octyne, bp 71-72°/9 mm (lit.[97] 40-41°/0.5 mm), n_D^{20} 1.4604, lit.[97] n_D^{26} 1.4590.

Reaction between 1-Chloro-2-octyne and Diisobutylaluminum Hydride (DIAH)

To a stirred solution of 1-chloro-2-octyne (2.89 g, 20 mmole) in methylene chloride (10 ml), DIAH (3.75 ml, 20 mmole) was added dropwise maintaining the temperature below 25°. After a reflux period, the reaction mixture was worked up and analyzed by glc. 1,2-octadiene was present in 32%. Furthermore, many unidentified compounds were detected by glc.

Synthesis of 1-Tetrahydropyran-2'-yloxy-2-octyne

A solution of 2-octyn-1-ol (12.6 g, 100 mmole) and dihydropyrane (9.22 g, 110 mmole, freshly distilled from sodium) in 150 ml of methylene chloride was treated with a few crystals of *p*-toluensulphonic acid. After a slight increase in temperature, the mixture was stirred for 30 minutes followed by addition of 0.1 g of anhydrous K_2CO_3. The stirred mixture (one hour) was filtered and concentrated in the rotatory evaporator. Fractional distillation afforded 20.91 g (c.a. 100% yield) of the title compound, bp 72-79°/0.1 mm (lit.[98] bp 91-96°/0.3 mm).

Reaction of 1-Tetrahydropyran-2'-yloxy-2-octyne with Dissobutyaluminum Hydride (DIAH)

To a stirred solution of the tetrahydropyranyl ether synthesized above (5.25 g, 25 mmole) in 20 ml of pentane, DIAH (4.7 ml, 26 mmole) was added over 30 minutes. After a reflux period of 9 hours, the reaction mixture was analyzed by glc. 36% of 1,2-octadiene was detected.

Reaction of 2-Octyn-1-ol methanesulphonate with Diisobutylaluminum Hydride (DIAH)

To a cooled (10°) solution of 2-octyn-1-ol (2.52 g, 20 mmole) and triethylamine (3.13 g, 30 mmole) in 80 ml of benzene was treated with methanesulphonyl chloride (2.52 g, 22 mmole). The mixture was stirred for 30 minutes at 10° and then poured into ice-cold 5% H_2SO_4. The organic layer was separated and washed twice with water, cold 10% K_2CO_3 solution and finally again with water. Concentration of the solution *in vacuo* afforded a residue (3.20 g) which was analyzed by nmr: δ 4.86 (t, J = 2.3 Hz, 2H) /CH_2OCH_3, 3.1 (s, 3H) OSO_2CH_3, 2.0-2.4 (m, 2H) $CH_2CH_2C{\equiv}C$, 1.1-1.7 (m, 6H) $CH_3(CH_2)_3CH_2$, 0.7-1.1 (m, 3H) CH_3CH_2. The residue obtained above was dissolved in 50 ml of methylene chloride, the solution was cooled to -20° and treated with DIAH (2.8 ml, 15 mmole). Slow warming to room temperature and stirring overnight afforded, after the usual work-up, a quantitative formation of 2-octyne (glc). A pure sample was isolated by evaporative distillation (140°/700 mm), n_D^{20} 1.4280 (lit.[26] n_D^{20} 1.4285); nmr: δ 1.9-2.3 (m, 2H) $CH_2C\equiv C$, 1.73 (t, J = 2.1 Hz, 3H) CH_3, 1.1-1.7 (m, 6H) $CH_3(CH_2)_3CH_2$, 0.7-1.1 (m, 3H) CH_3CH_2; ir (liquid film): absence of absorption between 2100-2300 cm^{-1}.

Synthesis of 1-Methoxy-2-undecyne

To a cooled (0°) solution of 1-decyne (36.2 ml, 27.65 g, 0.2 mole), a hexane solution of *n*-butyllithium (110.6 ml, 0.2 mole, 1.81M) was added during one hour. The mixture was cooled to -20° and chloromethyl methyl ether (15.16 ml, 16.10 g, 0.2 mole) was added dropwise. After slow warming to room temperature the mixture was poured into ice-water and extracted with ether. The layers combined, washed with brine and dried over Na_2SO_4. The solvent was removed under reduced pressure. Distillation at reduced pressure afforded 18.64 g (67%) of 1-methoxy-2-undecyne, bp 114-115°/9.5 mm, n_D^{20} 1.4596; ir (liquid film): 2220 and 2280 cm^{-1} ($C\equiv C$); nmr: δ 3.95 (m, 2H) $C-C\equiv CH_2OCH_3$, 3.26 (s, 3H) $O-CH_3$, 2.0-2.5 (m, 2H), $CH_2CH_2C\equiv C$, 1.3 (broad singlet, 12H) $CH_3(CH_2)_6CH_2$, 0.68-1.1 (m, 3H) CH_3; mass spectrum *m/e*: 182.1516 (*Calcd.* for $C_{12}H_{22}O$: 182.1671), 93(42), 81(62), 79(42), 70(61), 67(76), 55(100). *Anal Calcd.* for $C_{12}H_{22}O$: C, 79.06; H, 12.16. *Found:* C, 79.26; H, 12.04.

Reaction between 1-Methoxy-2-undecyne and Diisobutylaluminum Hydride (DIAH)

A solution of 1-methoxy-2-undecyne (1.82 g, 10 mmole) in pentane (2 ml) was treated with DIAH (1.78 ml, 10 mmole), and then refluxed for [illegible] hours. Work-up and analysis by glc detected the formation of 39% of 1,2-undecadiene, no starting material was present. A pure sample of the allene was isolated by preparative glc (column A, 150°) ir (liquid film) 1970 and 840 cm^{-1} ($H\text{-}C=C=C\,H_2$) (lit.[95b] 1975 cm^{-1}). nmr: δ 4.7-5.2 (m, 1H) $C\,\mathit{H}=C=C\,H_2$, 4.4-4.7 (m, 2H) $C\,H=C=C\,\mathit{H}_2$, 1.65-2.2 (m, 2H) $C\,\mathit{H}_2C\,H=C=C\,H_2$, 1.3 (broad singlet, 12H) $C\,H_3(C\,\mathit{H}_2)_6C\,H_2$, 0.68-1.0 (m, 3H) $C\,\mathit{H}_3$. When the aforementioned reaction was carried out utilizing 1.5 equivalents of DIAH (3.99 ml, 15 mmole), at room temperature, after 4.5 hours 1,2-undecadiene was present in 68%; starting material, 27%. After 24 hours: 1,2-undecadiene, 69%; 1-undecene, c a. 5-7% and starting material, c a. 10%. When this reaction was repeated using ethyl ether as the solvent, the reaction was very slow. After 18 hours, less than 40% of allene was produced.

CHAPTER IV

THE REDUCTIVE CYCLIZATION OF UNSATURATED KETONES

INTRODUCTION

The synthetic chemistry of radical ions is a relatively new area of study. Despite the fact that many reactions occur by an electron transfer mechanism, this was not recognized until more sophisticated physical methods were developed (*i.e.*, epr, CIDNP). Reactions which were once believed to be "purely" ionic have since been revised and more clearly understood in terms of a free radical mechanism involving an initial electron transfer process[99].

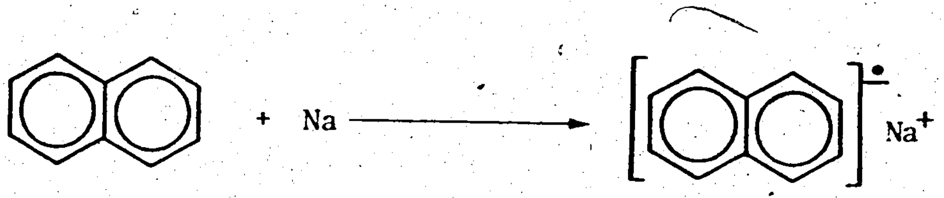
Several of these procedures have found wide application in organic synthesis, and now form part of standard methods used in the organic chemistry laboratory[100] (*i.e.*, Birch reduction, pinacol condensation, etc.). Unfortunately in many instances, determining the optimum conditions for these reactions has been carried out in a semi-empirical fashion. Only recently have such factors as the influence of the solvent, the nature of the electron transfer reagent, and the resulting changes in the state of aggregation of the electron transfer reagent been taken into consideration.

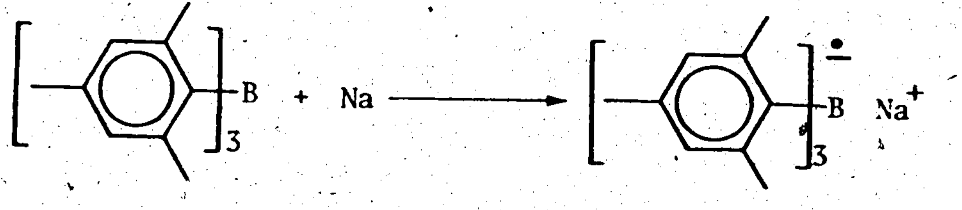
Some of the most frequently used electron transfer reagents are solutions of metals (Li, Na, Ca, etc.) in liquid ammonia.

These have found success especially in Birch reductions and the reductive hydrogenation of internal acetylenes[100]. A disadvantage of these electron transfer reagents, often referred to as solutions of "solvated electrons", is the poor selectivity observed with sensitive substrates.

Another class of electron transfer reagents are the ones generated by interaction of metals and neutral molecules in ethereal solvents. These neutral molecules are generally aromatic hydrocarbons or compounds capable of accommodating an "extra" electron. Some examples are naphthalene, biphenyl, anthracene, hexamethylphosphoramide (HMPA) and trimesitylboron (TMB)[102].

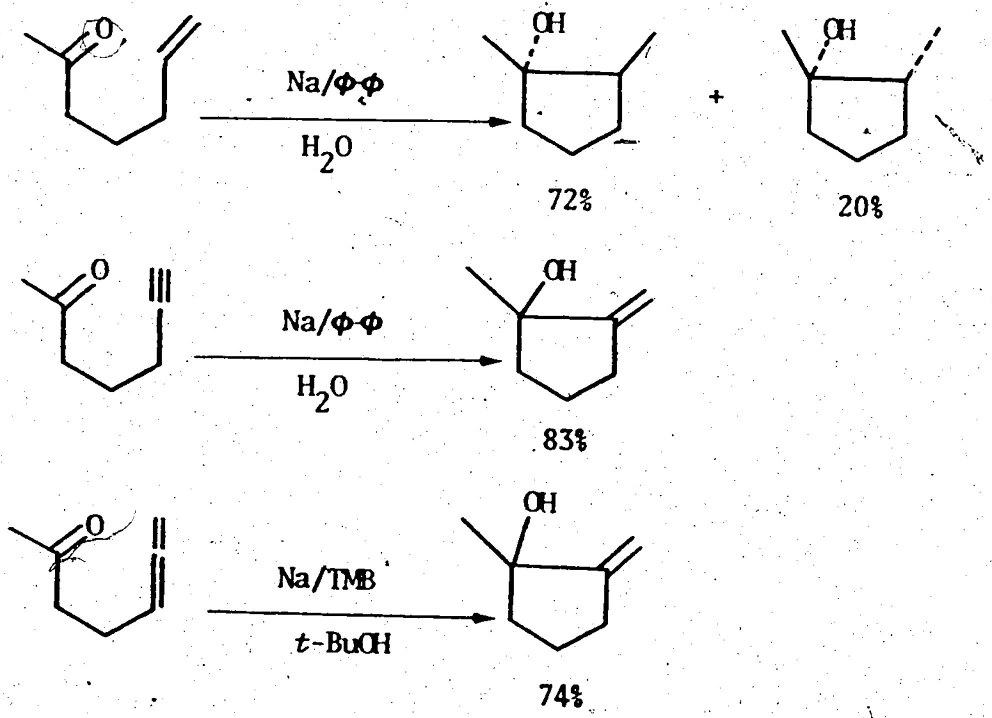
When ethereal solutions of these compounds (HMPA can act as a solvent by itself) are treated with alkali metals, strongly colored solutions (usually green-dark-blue) are produced due to the formation of the radical anion.

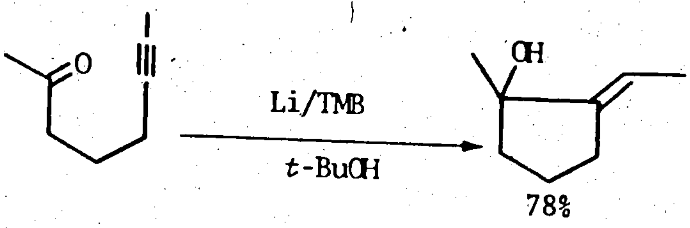


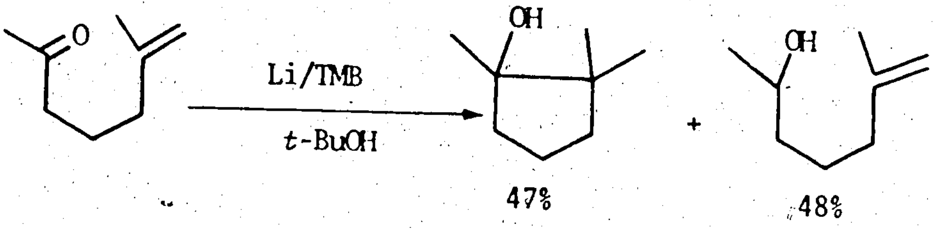


A possible advantage of using these electron transfer reagents over solutions of metals in liquid ammonia is that by the proper choice of the reagent, it may be possible to select the required electron potential necessary for a given chemical transformation. The versatility of such reagents as tools for organic synthesis is becoming more evident by the many transformations they are reported to accomplish[102]. Although at present some of these synthetic applications do not present any significant superiority over current classical methods, it is hoped that a better understanding of these reactions by means of more research in this area will provide an even wider source of applications to organic synthesis.

Recently in our laboratories, a new synthetic application utilizing electron transfer reagents has been developed. The reductive cyclization of several unsaturated ketones was successfully accomplished[103]. Some examples are depicted below.

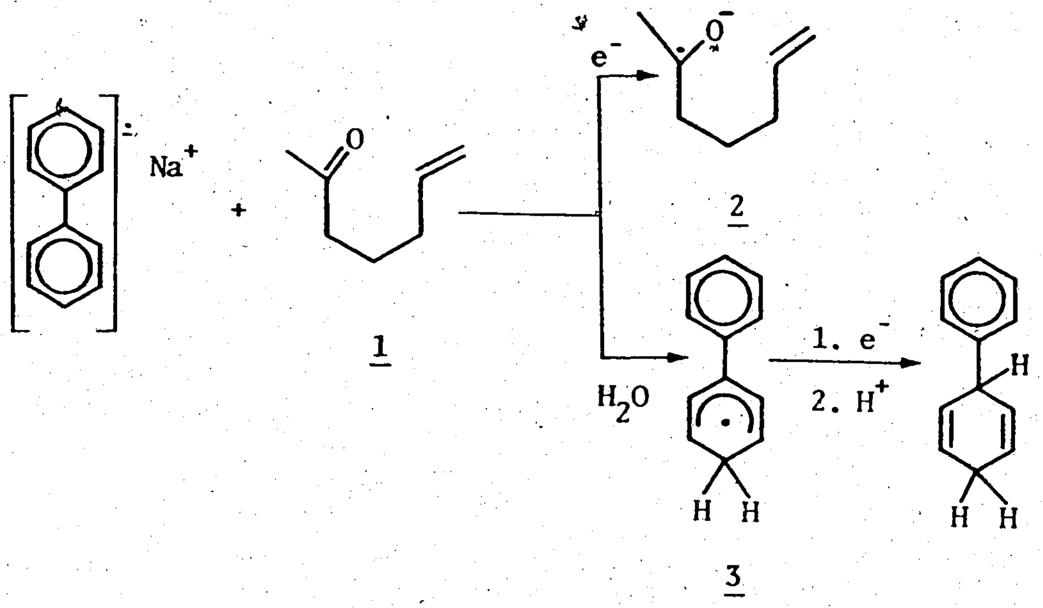




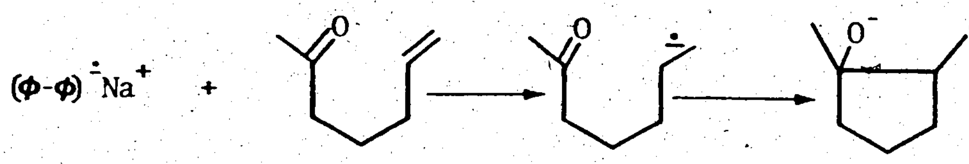


The success of this procedure is no doubt due to a delicate balance of many factors, and in the following discussion, some of the factors controlling this reaction will be described. As a model system the cyclization of 6-hepten-2-one using sodium biphenyl as the electron transfer reagent and water as the proton source will be considered.

Initially, two competing reactions appear possible. Sodium biphenyl (half-wave potential ($E_{\frac{1}{2}}$) of biphenyl = -2.65 V)^{112} can either transfer an electron to the carbonyl of the unsaturated ketone <u>1</u> ($E_{\frac{1}{2}}$ (C=O) = -2.0 to -2.5 V)^{112} to form ketyl <u>2</u>, or behave as a base and abstract a proton from water to produce the intermediate <u>3</u>. Intermediate <u>3</u> upon further electron transfer and proton absraction eventually gives rise to the Birch reduction product of biphenyl.

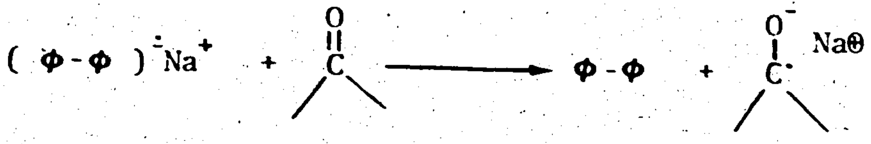


The feasibility of tranferring an electron to the olefin followed by intramolecular nucleophilic attack on the carbonyl is considered to be a less likely occurrence, since olefins (because of their high reduction potential) are stable in solutions of sodium in liquid ammonia in the presence of a proton source[104]. Only such powerful electron transfer reagents as Na-HMPA ($E_{\frac{1}{2}}$ of HMPA = -2.9) are reported to transfer an electron to an isolated double bond[105].



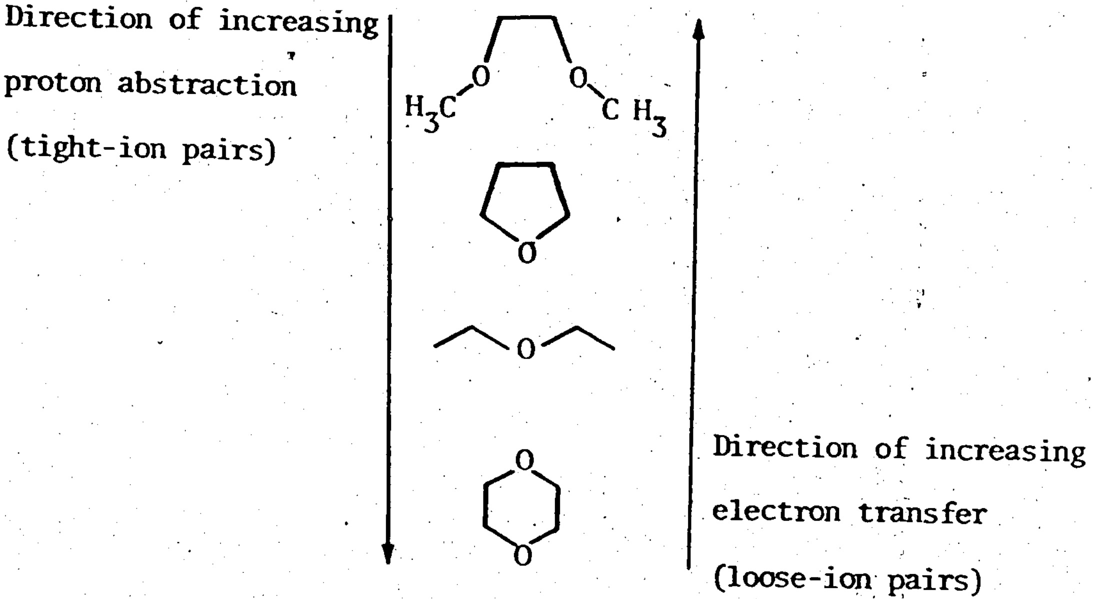
The dual behavior in reactivity of electron transfer reagents has been the subject of numerous studies[106-7]. It has been found that the extent of electron transfer and proton abstraction is a function of the state of aggregation (ion-pairing) and depends on the solvent system used. Solvents which provide efficient coordination, such as dimethoxyethane (DME), tend to favor the formation of "loose ion" pairs. The opposite is observed when solvents such as diethyl ether are employed (in which the formation of "tight-ion" pairs is enhanced).

Studies by Banks and coworkers[106] have indicated that the extent of electron transfer is favored by solvents favoring "loose-ion" pairs[106-7]. This phenomenon has been explained on the basis that an electron transfer also involves an ion transfer (generally described as atom transfer), *i.e.*,



On this basis it is reasonable to expect that less energy is required to transfer the counterion to the new carbanion if the pairs are solvent-separated. Thus, the transfer between free ions is formally a simple electron transfer, while the transfer between ion pairs is a formal atom transfer[108].

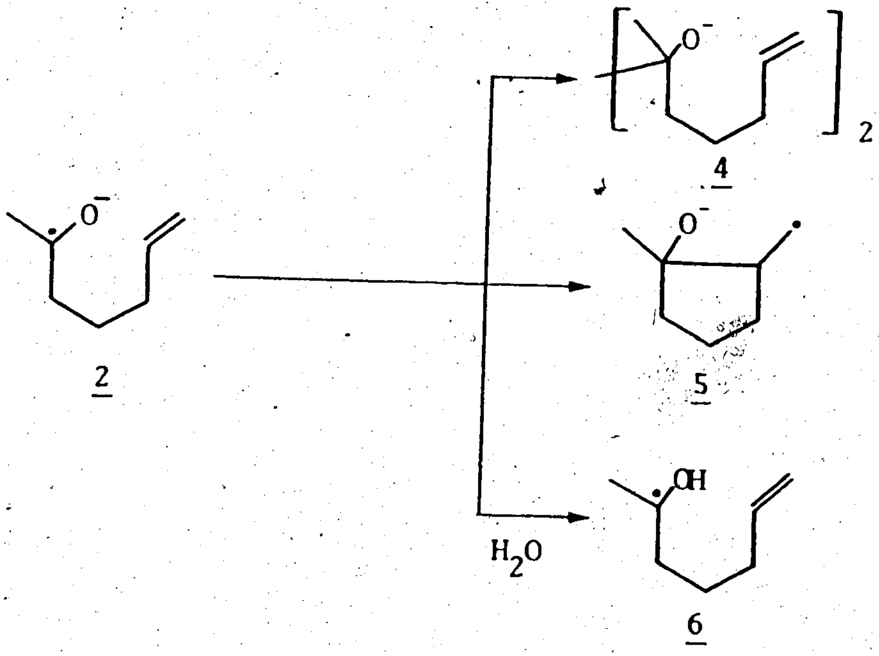
By carrying out a reaction between a radical anion and an electrophilic substrate in a solvent such as DME, it is possible to favor the electron transfer process. The rate of electron transfer has been found to be very fast, approaching the diffusion control limit (rate constant c a. 10^8 $M^{-1}sec^{-1}$), while the rate of proton abstraction, a formal atom transfer, is much smaller (rate constant c a. 10^4 $M^{-1}sec^{-1}$)[106,109].



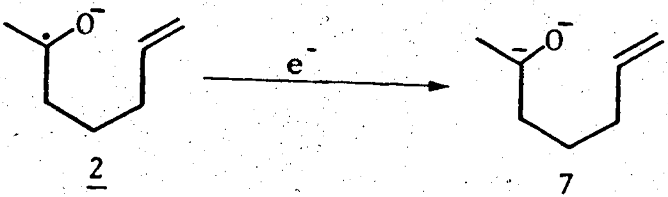
It is important to mention at this point that sodium-TMB displays a preference for electron transfer. This is due to the remarkable stability of this reagent towards proton sources[110].

Once ketyl 2 has been preferentially formed, it can conceivably undergo dimerization (pinacol type) to 4, intramolecular cyclization to produce 5, or abstraction of a proton from water to yield the hydroxy radical 6.

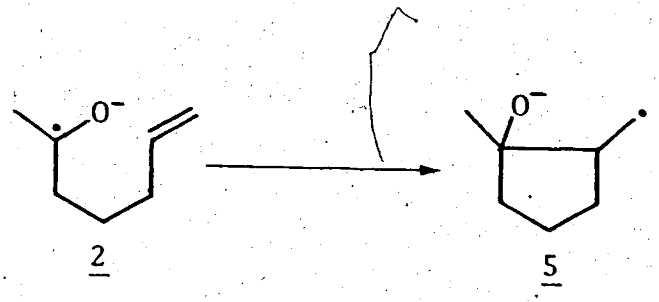
The dimerization of ketyl 2, which ultimately would produce a pinacol, has not been observed in any of our cyclization reactions. One of the reasons for this could be that dimerization of ketyls is generally favored by the presence of a di- or polyvalent counterion such as magnesium or aluminum. These ions presumably effectively compensate for the electrostatic repulsion of the approaching negative charges. Also, it has been observed that dimerization of ketyls is minimized by use of effective coordinating solvents[111].

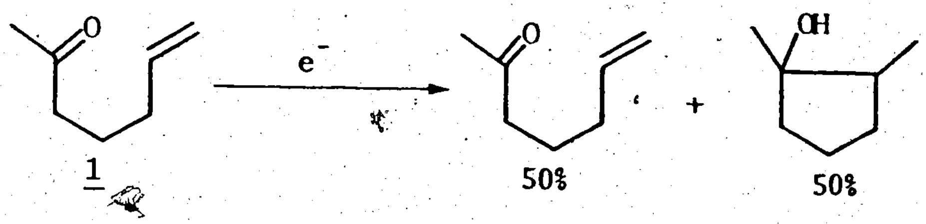


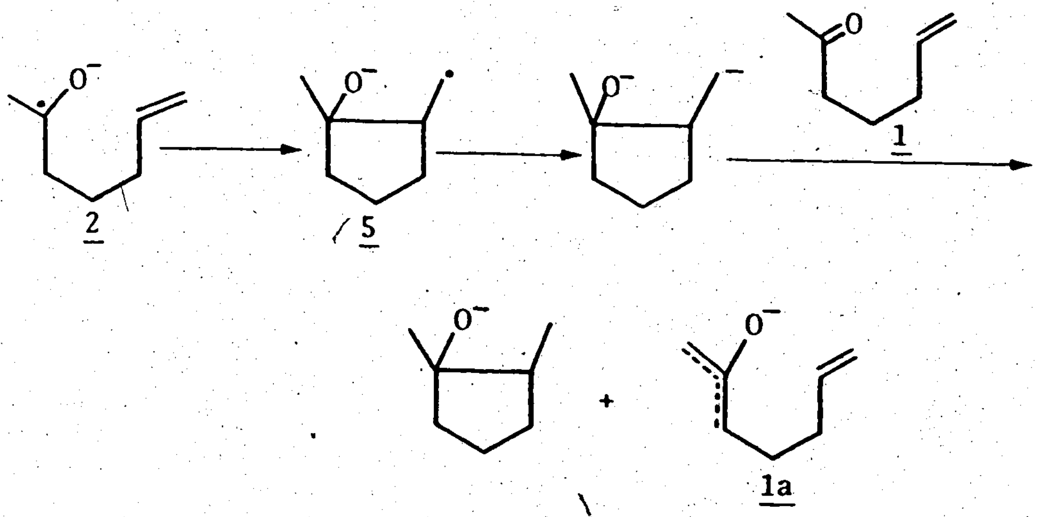
The possibility of transferring a second electron to give dianion 7 appears highly unlikely since the potential expected for addition of a second electron to a single ketyl is significantly more negative than -3V[112].



If the cyclization of ketyl 2 to form the cyclic intermediate 5 is indeed the path by which the desired cyclic alcohol arises, this would indicate that the presence of a proton source is not required. Experiments in our laboratories[103] have shown that when the cyclization was carried out in the absence of an external proton source, 50% of starting material together with 50% of cyclized product was obtained. This result may reflect the fact that the ketone 1 is itself serving as proton source with formation of the enolate 1a, which, upon hydrolytic work-up, affords the starting material.

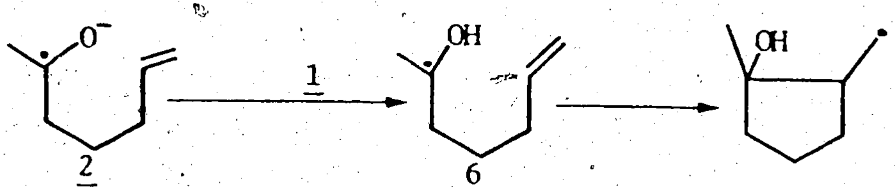






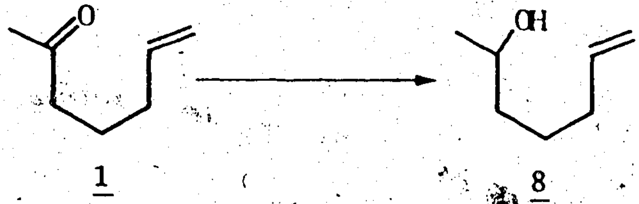
Thus, the presence of external proton source would be necessary to drive the reaction to completion by converting the unreactive enolate 1a, into the ketone 1 (and thence into cyclized product).

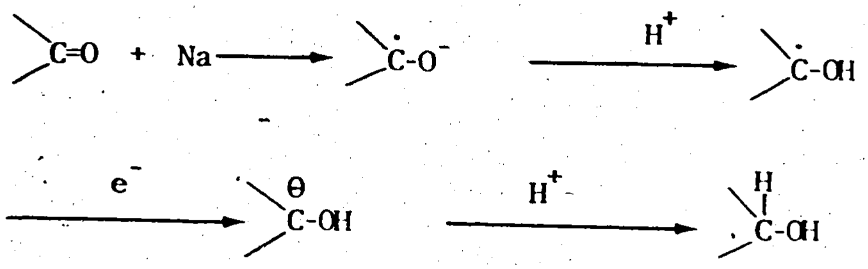
At the same time, a mechanism involving a hydroxy radical 6, resulting from abstraction of a proton from the ketone 1 (or other proton source) is also feasible.



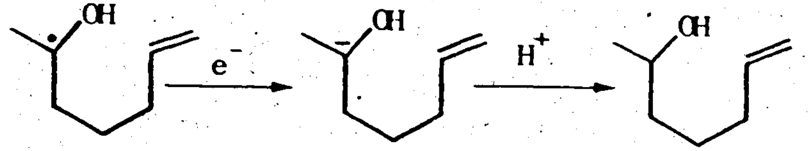
Thus, either ketone 2 or hydroxy radical 6 could be conceivable intermediates in the cyclization step.

One piece of chemical evidence for the possible existence of the hydroxy radical 6 is found in the formation, under certain circumstances, of small amounts of the reduced ketone 8. An analogy for a somewhat similar formation of hydroxy radicals is the reduction of ketones with sodium in hydroxylic solvents[111].





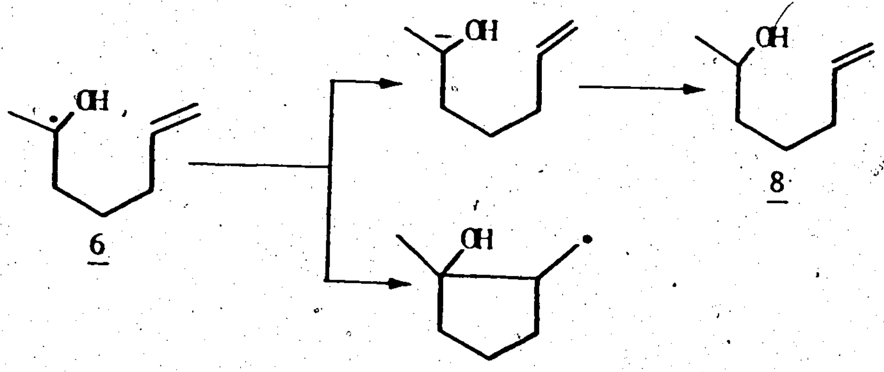
Thus, hydroxy radical 6 can undergo an electron transfer and subsequent proton abstraction to afford 8.



6

8

According to this line of argument, if 6 is an intermediate in the cyclization reaction, the ratio of reduction/cyclization product should depend on whether the cyclization is faster or slower than the second electron transfer step.

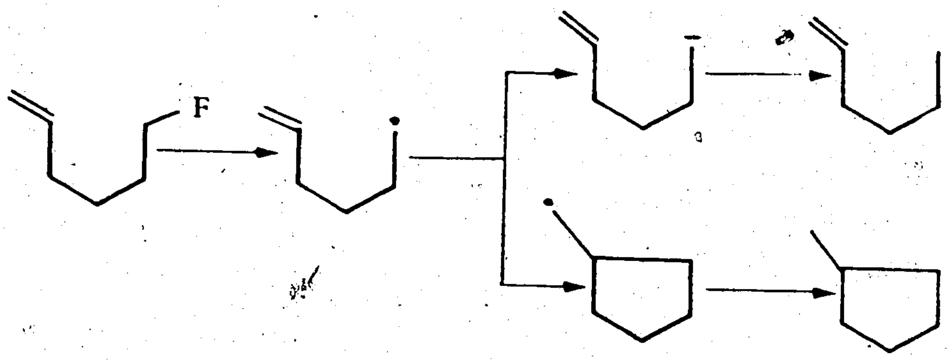


6

8

Independent studies carried out on the cyclization of 5-hexenyl radicals have shown that the reduction depends mainly on the concentration of the electron transfer reagent[113].

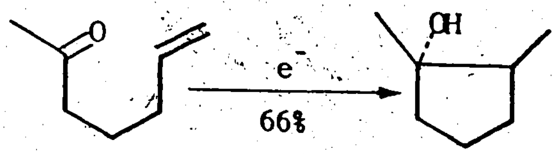
When 6-fluorohexene was treated with a 0.273 x 10^{-3}M solution of sodium-naphthalene the reduction/cyclization ratio was 2.0. However, when the initial radical anion concentration was increased approximately 17-fold(*i.e.*, 4.61 x 10^{-3}M) this ratio changed to 15.2.



On the basis of these results, it would be expected that if the hydroxy radical 6 is the intermediate of the reaction, cyclization should be favored by low concentrations of the electron transfer reagent. Experimentally, this can be performed by generating the sodium-biphenyl *in situ* . That is, as soon as the initial blue coloration starts to develop in the surface of the sodium, the enone and the proton source are added so that the radical-anion is consumed as quickly as it is formed.

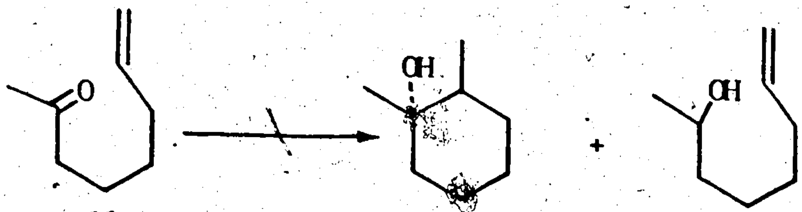
Factors such as the aforementioned ones were taken into consideration for the study of reduction cyclization of several unsaturated ketones undertaken here.

Several attempts to synthesize tertiary alcohols by intramolecular cyclization have been reported in the literature[103]. Among these, the most successful is the electrochemical method recently reported by Shono and Mitani[114]. One very interesting aspect of this method is the remarkable stereoselectivity observed. For example, enone 9 was shown to undergo cyclization to afford exclusively, 66% of the *cis* alcohol 10.



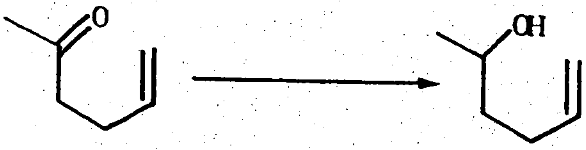
9 10

Furthermore, the *cis* six membered ring alcohol 12 was formed in 50%, accompanied by 10% of the uncyclized alcohol when the unsaturated ketone 11 was subjected to electrolysis.



11 12

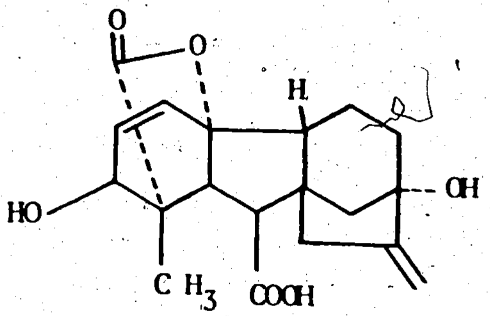
An attempt to cyclize the enone 13 proved to be unsuccessful and only reduced ketone 14 was produced.



13 14

The cyclic tertiary alcohols obtained above by reductive cyclization are rather simple molecules and can be readily synthesized by other routes. Nevertheless, when these tertiary alcohols of a similar structural type are present as a unit in complicated molecules (*i.e.*, some natural products), the synthesis of such systems poses a serious challenge. This is especially true when the hydroxyl group is at a bridgehead position.

Recently a great deal in interest has been devoted to the synthesis of gibberellic acid 15. One of the more interesting challenges in such a synthesis is the construction of the 1-hydroxy-7-methylenebicyclo(3.2.1)octane ring system (C-D rings). This unusual feature of an exocyclic methylene adjacent to a bridgehead hydroxyl group makes this system especially unstable, since it undergoes rearrangement to the isomeric ketone in the presence of acids[115].



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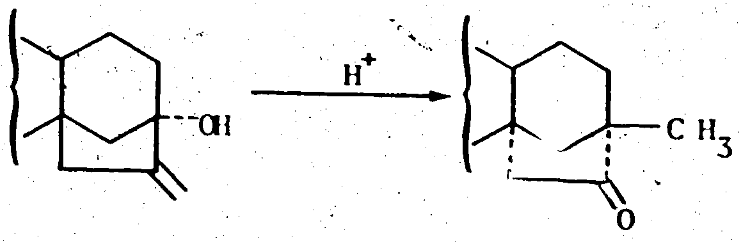
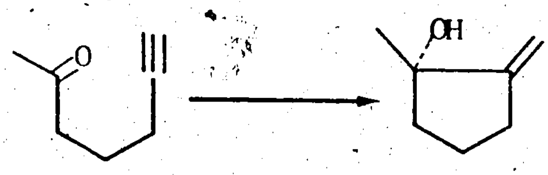


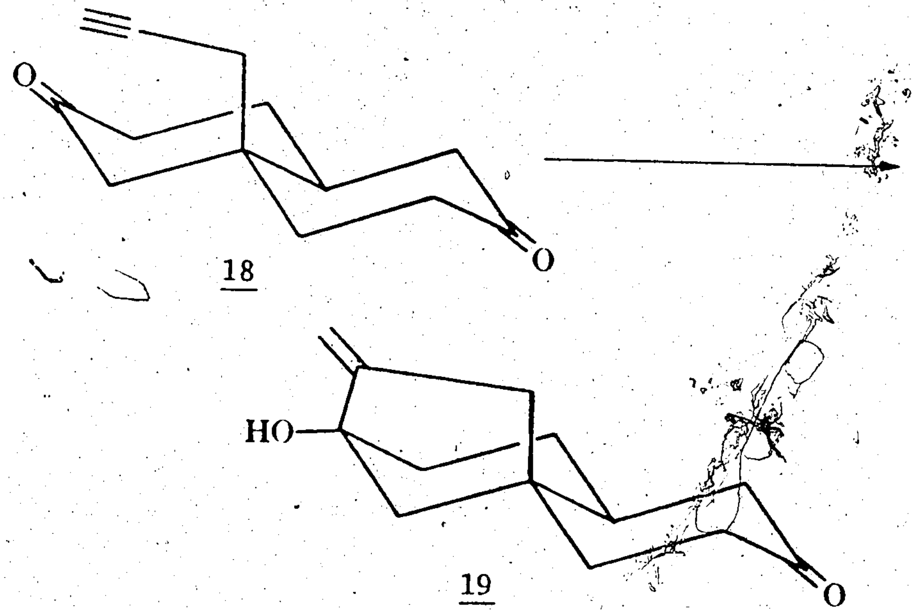
The first approach to the construction of a model of the C-D rings of gibberillic acid was reported by Stork and co-workers[116].

It was shown that the γ-ethynyl ketone 16, upon treatment with lithium in liquid ammonia afforded c a. 50% yield of the cyclic allylic alcohol 17. However, this compound could not be isolated in pure form due to the presence of reduction products.



16 17

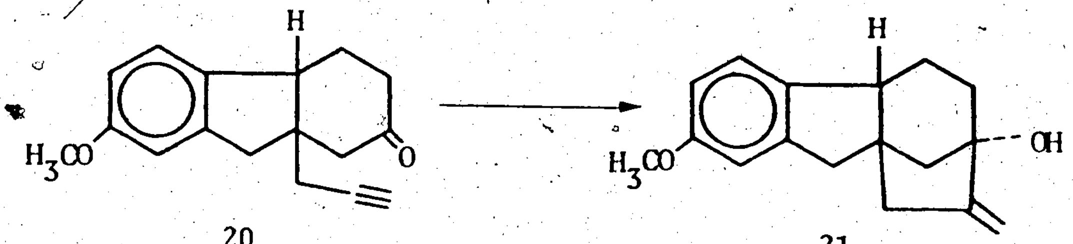
A more favorable case, 18, where the propargyl group was in a 1,3-axial position to the carbonyl group, produced c a. 50% yield of the tricyclic alcohol 19 upon reductive cyclization.



18

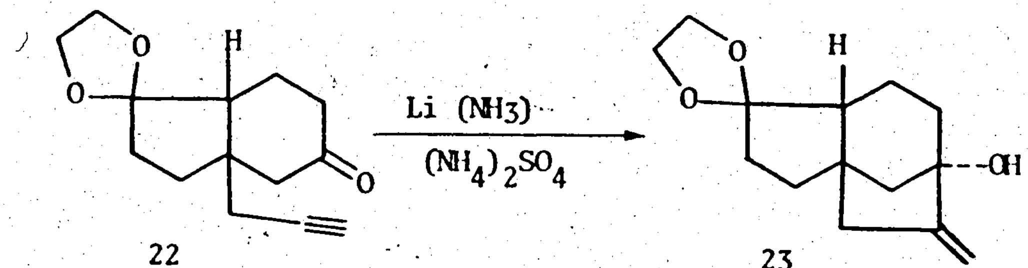
19

Although these results were encouraging, the system studied was not entirely representative because the ring junction was *trans*, thus making the approach to the two unsaturated centers more favorable. An attempt to cyclize 20, a more realistic model in connection with gibberellic acid synthesis, resulted in low yields of the cyclized product 21. This was probably due to the predominant equatorial conformation of the propargyl group.



20 21

Recently, the same approach has been utilized by Miller[117] for the synthesis of the tricyclic model 23 by reductive cyclization of 22 with lithium in liquid ammonia.



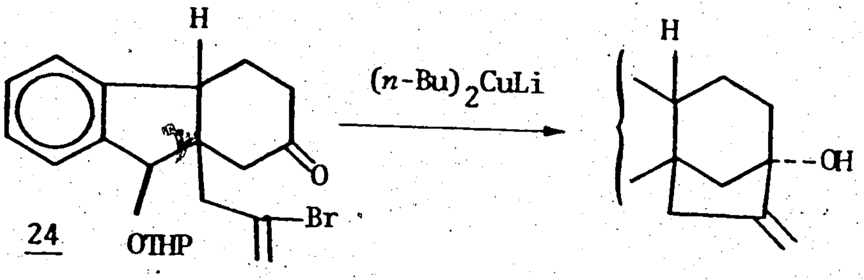
22 23

Compound 23 was produced in 50% yield accompanied by reduction products. However, the stereochemistry of the ring fusion of either

22 or 23 was not proven to be *cis*. This point has considerable importance in light of the results reported by Stork and coworkers[116], since a *trans* fusion in 22 would place the propargylic group in an axial position favoring cyclization.

Several new approaches to the synthesis of the bicyclo(3.2.1) system present in gibberellic acid have been reported recently.

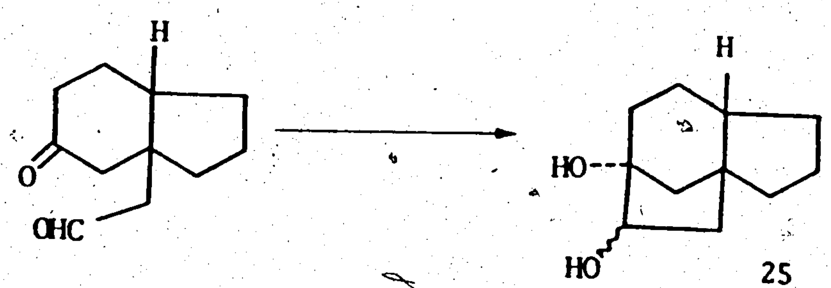
Especially interesting is the reductive cyclization of substrates such as 24 utilizing dibutylcopper lithium[118].



24

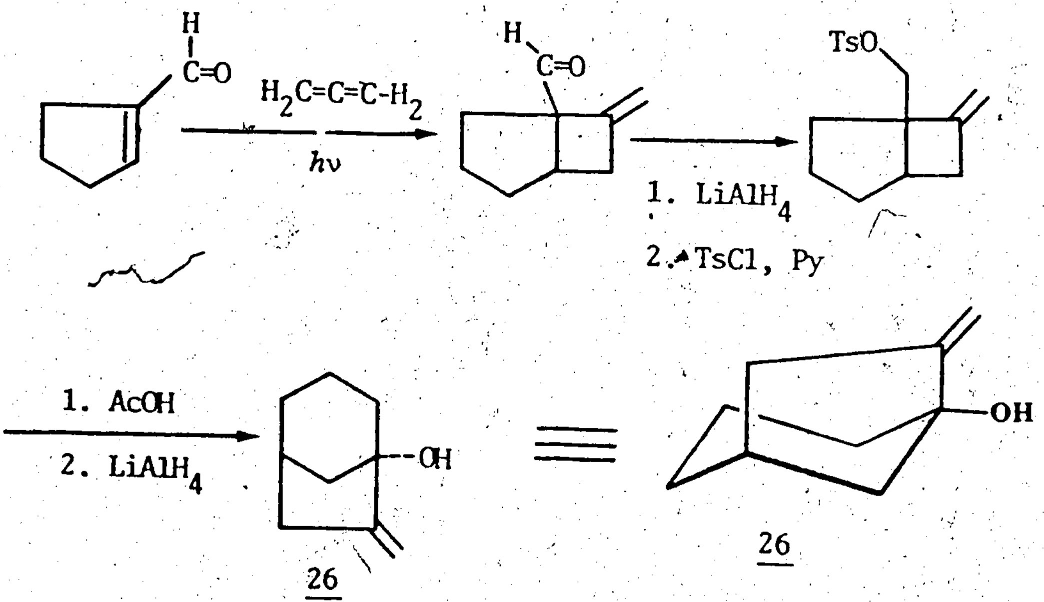
One of the drawbacks of this approach is the requirement of very carefully controlled conditions, since side reactions (such as the coupling of the cuprate with the vinyl bromide portion) are also possible.

Corey and coworkers reported the construction of the tricyclic compound 25 by means of the pinacol cyclization[119].



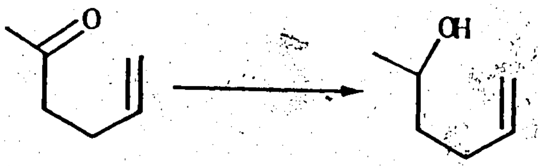
25

Another interesting sequence of reactions which led to the synthesis of the model 1-hydroxy-7-methylene-bicyclo(3.2.1)octane system 26 was described by Ziegler and Kloek[127]. The steps are depicted below.



Several other approaches to the bicyclooctane system have been developed by the groups of House[120] and Ireland[121]. However, these approaches all involve multi-step procedures.

Recently the successful reductive cyclization of several unsaturated ketones by electron transfer reagents has been accomplished in our laboratories. A variety of five membered ring tertiary alcohols were synthesized by this method; however, the possibility of forming six membered ring tertiary alcohols was not examined. Also, as in the electrolytic work of Shono and Mitani[114], attempted radical anion promoted cyclization of 5-hexen-2-one resulted in the exclusive formation of 5-hexen-2-ol.

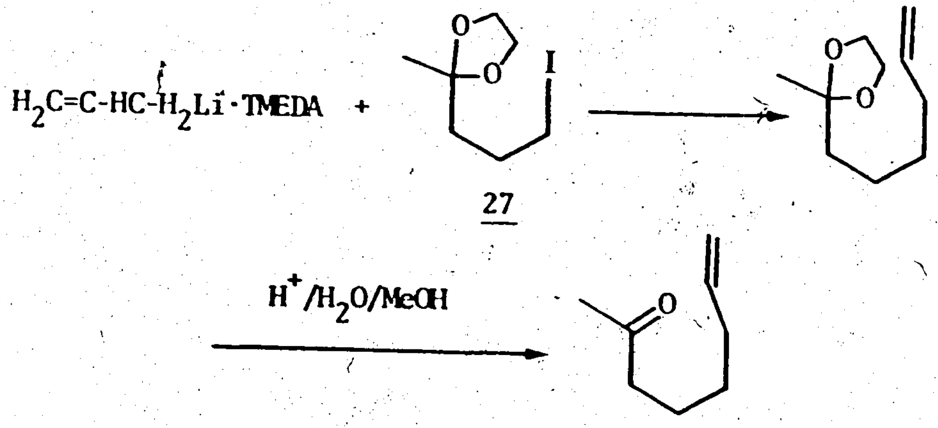


The purpose of the research undertaken here was to investigate the feasibility of extending the scope of the reactions to the synthesis of six membered ring alcohols. Also, a reinvestigation of the cyclization of β-vinyl ketones was undertaken. In addition, the possibility of forming a bicyclic system similar to the one present (C-D ring) in gibberellic acid utilizing reductive cyclization was investigated.

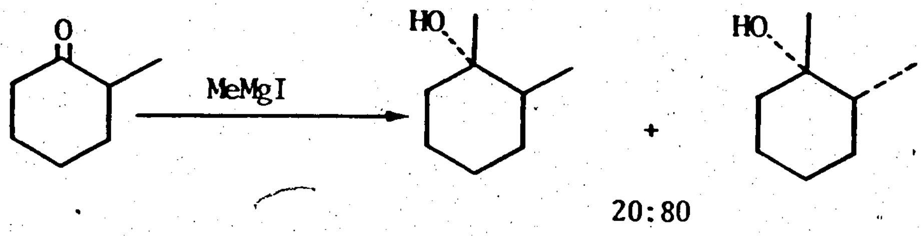
RESULTS AND DISCUSSION

The research was initiated with the study of the formation of six membered ring tertiary alcohols. The substrate chosen for this purpose was 7-octen-2-one. This compound was prepared by the coupling reaction between the iodoketal 27 with the allyllithium-TMEDA complex, followed by hydrolysis. The synthesis of the allyllithium-TMEDA complex was carried out by the direct metalation of propylene with *n*-butyllithium in the presence of TMEDA.[122]

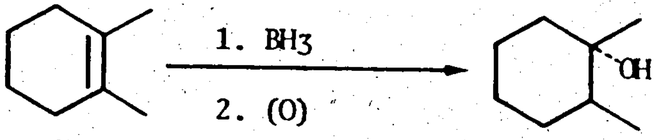
$$\mathrm{C\ H_3C\text{-}H{=}C\text{-}H_2} + n\text{-}\mathrm{BuLi} \xrightarrow{\mathrm{TMEDA}} \mathrm{C\text{-}H_2{=}C\ H\text{-}C\text{-}H_2Li\cdot TMEDA}$$



In order to compare the cyclization products with authentic samples, *cis* and *trans* 1,2-dimethylcyclohexanol were synthesized. The reaction between methylmagnesium iodide and 2-methylcyclohexanone afforded a mixture of the *cis* and *trans* alcohols in a ratio of c a. 20:80 respectively. The *trans* isomer was obtained as a pure compound by preparative glc. The mixture of *cis* and *trans* alcohol was dehydrated utilizing phosphoric acid; 1,2-dimethylcyclohexene was obtained as the major product (> 95% pure).



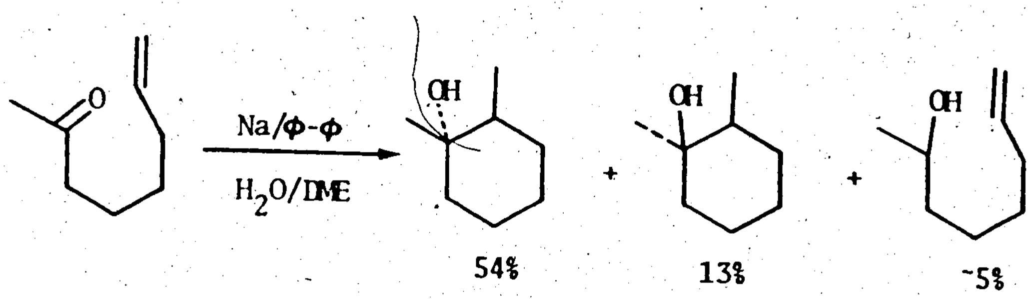
Hydroboration of the olefin mixture followed by an oxidative work-up resulted in the formation of the *cis* alcohol (> 97% pure by glc) An analytical sample was isolated by preparative glc.



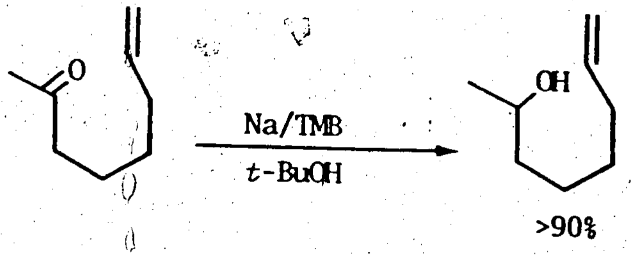
As an exploratory experiment, the cyclization of 7-octene-2-one was carried out under the same optimum conditions utilized for the cyclization of 6-heptene-2-one. These conditions involved using sodium-biphenyl (6 and 3 equivalents, respectively) as the electron transfer reagent and water (1.2 equivalents) as the proton source in dimethoxyethane as the solvent. The sodium-biphenyl radical anion was not preformed, but instead, was used in an *in situ* procedure. That is, a solution of biphenyl in DME at -35° to -40°

was treated with sodium shavings, and once the surface of sodium became blue a solution of the enone and water in DME was added at a rate to maintain the blue coloration on the surface of the sodium. This technique presumably assures the presence of radical anion in low concentration. It was observed that after 1.5 hours the mixture stayed permanently blue. After an additional 30 minutes the mixture was quenched and analyzed by glc. The *cis* and *trans*-1,2-dimethylcyclohexanols were formed in a ratio of 3:1 respectively; however more than 40% of starting material remained.

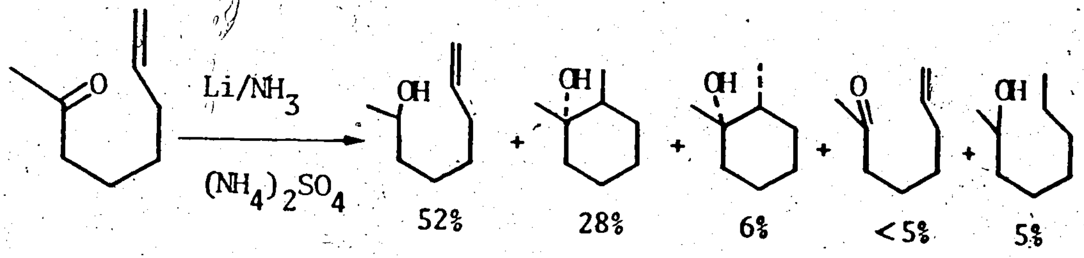
It was finally found that 3 equivalents of water were necessary to drive the reaction to completion. This resulted in the formation of 54% of *cis* alcohol and 13% of the *trans* carbinol. In addition, 5% of the reduced ketone, 7-hexen-2-ol, was produced.



The possibility of increasing the yields was examined utilizing sodium trimesitylboron (Na-TMB) instead of sodium-biphenyl as the electron transfer reagent. Also, water was replaced by *t*-butyl alcohol as the proton source. The reaction with 5-octen-2-one proved very slow and although small amounts of *cis* and *trans* cyclized alcohols were formed shortly after addition of the enone, the formation of 7-octen-2-ol was increasing steadily (as monitored by glc). At the end of the reaction, more than 90% of the uncyclized alcohol was produced, in marked contrast with the results obtained with sodium-biphenyl and water.

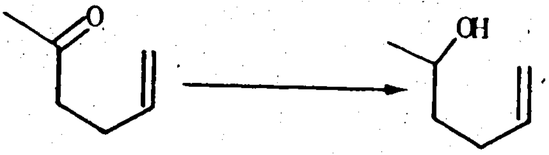


As a matter of comparison, Stork's method[116] for the cyclization of γ-alkynyl ketones utilizing lithium in liquid ammonia in the presence of ammonium sulphate, was utilized with 7-octen-2-one. After six hours, glc analysis of the mixture showed the following product distribution: 7-octen-2-ol (52%), *cis* and *trans*-1,2-dimethylcyclohexanol (28% and 6%, respectively), 7-octen-2-one (< 5%), and 2-octanol (ca. 5%).

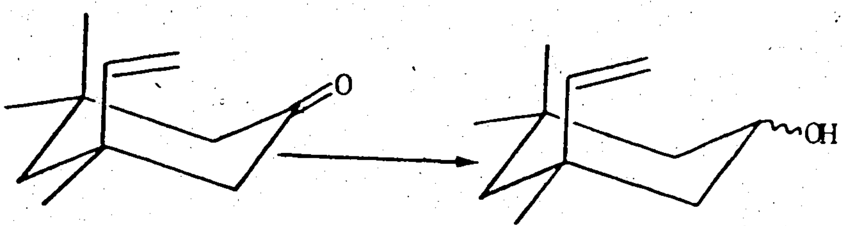


In light of these results it is clear that the sodium-biphenyl method offers a clear advantage over the lithium in ammonia procedure for reductive cyclizations to cyclohexanol derivatives.

It has been observed by Shono and Mitani[114], and also in our laboratories, that acyclic β-olefinic ketones, such as 5-hexen-2-one, undergo reduction upon electrolysis, or treatment with electron transfer reagents.



In an attempt to establish if a β-vinylcyclohexanone derivative could cyclize, attempted cyclization of enone 28 was examined in our laboratories[103]. However, this experiment resulted in the exclusive formation of the isomeric alcohols 29, and no bicyclic alcohol could be isolated.



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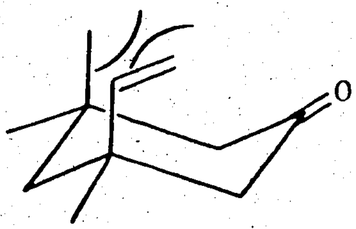
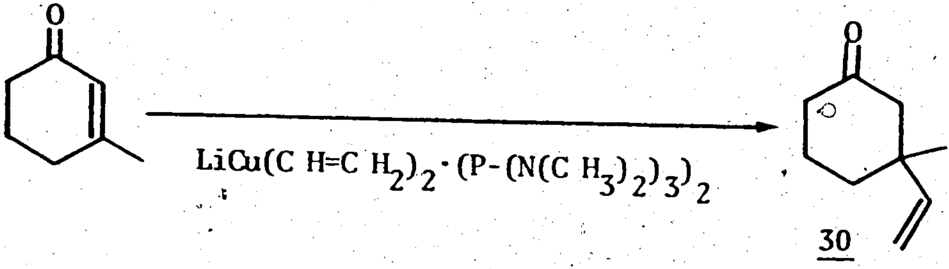
Nevertheless, it can be argued that the presence of the axial methyl group in ketone 28 produces a 1,3-axial interaction which hinders the approach of the vinyl group to the carbonyl.



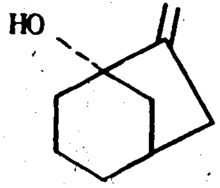
28

To test this possibility, the unfavorable 1,3-axial interaction was removed by the preparation of enone 30 (by 1,4-addition[123-4] of the divinylcopper lithium-hexamethylphosphorous triamide complex to 3-methyl-2-cyclohexenone.)



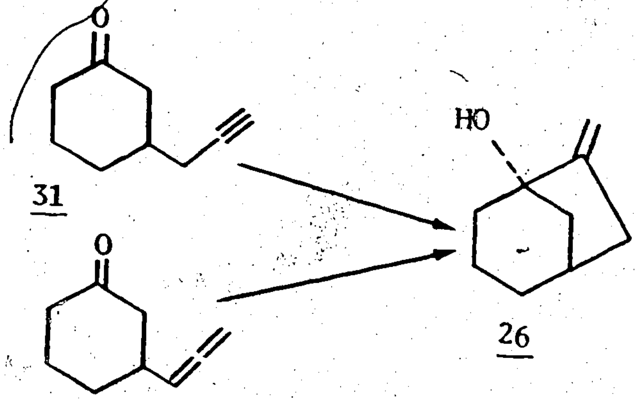
The ketone 30 was subjected to a variety of reaction conditions such as: sodium-biphenyl/water, sodium-biphenyl/*t*-butyl alcohol, sodium-TMB/*t*-butyl alcohol, etc.. In all cases complex mixtures were formed and no bicyclic alcohol could be isolated. In view of the complexity of this system this reaction was not further explored. The lack of success in the cyclization of such β-vinyl ketones may be a consequence of the unfavorable geometry of these systems. Although models of these systems indicate that the terminal carbon of the vinyl group and the carbonyl carbon can approach the range of bonding distances, nonetheless, the *p*-orbitals of these centers are non-parallel (which would be required for maximum favorable overlap).

Finally, in connection with gibberellic acid, the possibility of preparing a model of the C-D unit of this natural product, namely, 1-hydroxy-7-methylene-bicyclo(3.2.1) octane 26 was considered.



26

The finding that 5 and 6 membered rings can be readily prepared by reductive cyclization of γ-ethynylketones and β-allenylketones[103], suggested two potential precursors for the synthesis of 26.



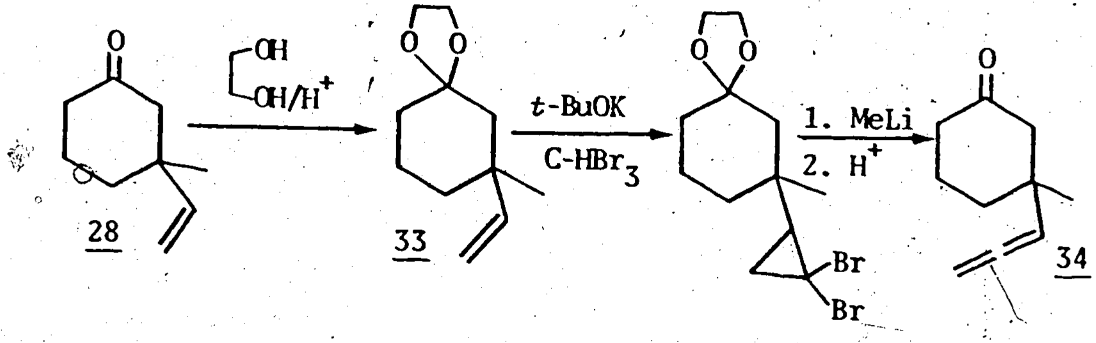
31

32

26

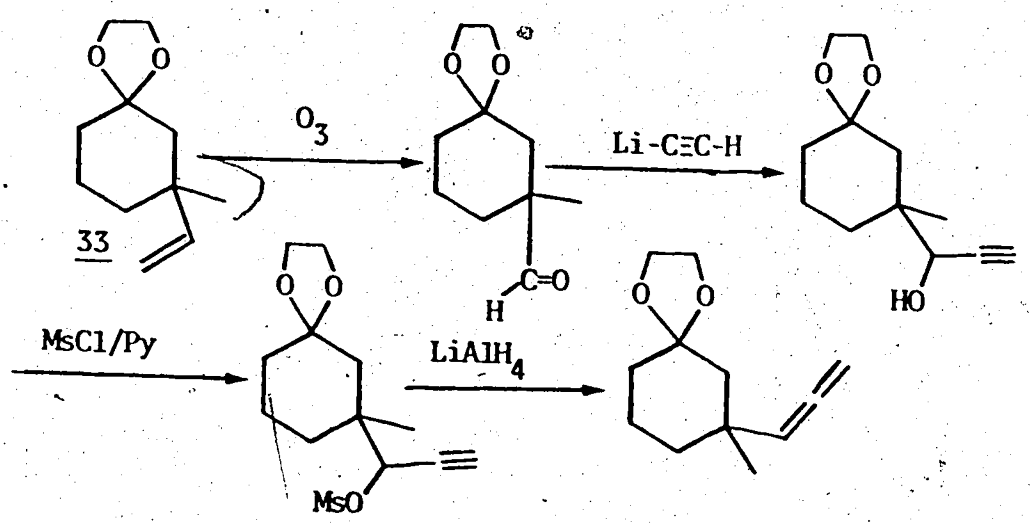
Attention was first focused on the synthesis of the allenylketone 32. Having already synthesized ketone 28, it was decided to first explore the possibility of preparing β-allenic ketone 34. By analogy with the synthesis of 5,6-heptadien-2-one[103], the preparation of compound 34 was approached as depicted in Scheme I.

Scheme I



Compound 28 was readily ketalized using ethylene glycol and *p*-toluensulphonic acid to produce the olefinic ketal 33 in high yield. However, attempts at preparing the dibromocyclopropane unit by treatment of 33 with bromoform and potassium *t*-butoxide in pentane resulted in > 90% recovery of starting material. In view of this result, the synthesis of allenic ketone was replanned by a procedure similar to the one reported by Thompson[125] to introduce an allenic group at the bridgehead. Scheme II indicates the steps.

Scheme II

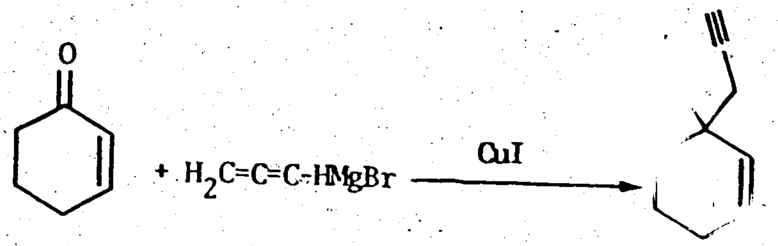


Disappointingly, ozonolysis of 33 was found to be complex. Utilizing solvents such as pentane, methanol, or methylene chloride and carrying out the decomposition of the ozonide with dimethylsulfide, these reactions invariably afforded mixtures of products resulting from transketalization.

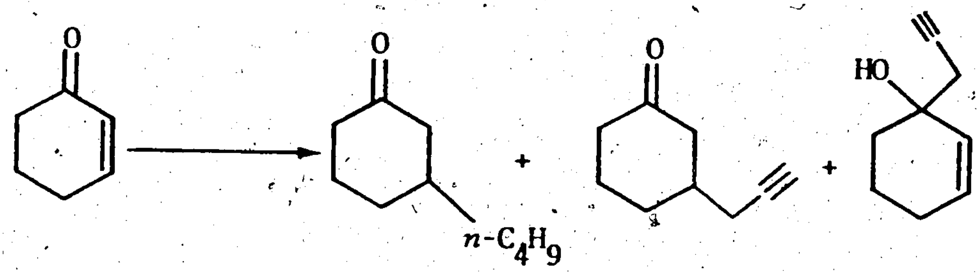
As a consequence, a reinvestigation of the 1,4-addition of a propargyl unit to cyclohexenone as described previously (Chapter I) was undertaken.

Organocuprates are selective reagents for the conjugate addition of alkyl, vinyl, allyl, and aryl groups to unsaturated ketones[126]. Nevertheless, despite several attempts, the conjugate addition of a propargyl group has not yet proven successful.

The reaction between cyclohexenone and the Grignard reagent derived from propargyl bromide in the presence of one equivalent of cuprous iodide resulted in the exclusive formation of the 1,2-addition product. A similar result was obtained when zinc instead of magnesium was used.



The observations described above (Chapter I) utilizing the "propargylating reagent" and cuprous iodide represent the first example of the successful 1,4-addition of a propargyl group to an unsaturated ketone. At the outset of the reinvestigation of this reaction, results were difficult to reproduce. For example, if the mixture of allene and *n*-butyllithium in ether:hexane (1:1) (after being warmed to -20°) was stirred for one hour, sequential treatment with cuprous iodide and cyclohexenone produced exclusively the 1,2-addition product. However, if the mixture was warmed to -20°, stirred for ca. 15 minutes, then treated with cuprous iodide followed by cyclohexenone, three products were obtained: 3-butylcyclohexanone as the major component, 3-(2-propynyl)cyclohexanone, the desired substrate, and 1-(2-propynyl)-2-cyclohexene-1-ol, the 1,2 addition product.



If it is assumed that the 1,4-addition product resulting from the migration of the propargyl group arises from the cuprate (from interaction of allenyllithium and cuprous iodide), these observations can be rationalized on the basis of the disproportionation of allenyllithium. Presumably, under the first set of conditions (*i.e.*, after stirring for one hour), the propargylating reagent undergoes disproportionation to the dilithium salt, $C_3H_2Li_2$, and in part also rearranges to propynyllithium.

$$CH_2{=}C{=}C\text{-}HLi \longrightarrow C_3H_2Li_2 + CH_3C{\equiv}C\text{-}Li$$

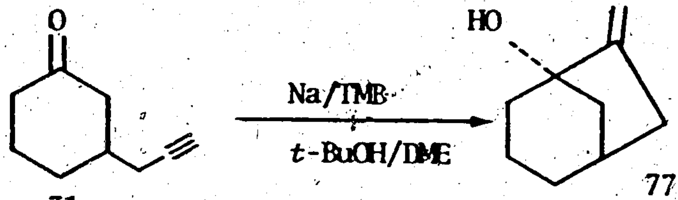
Thus, no migration of the propargyl group is observed. If the propargylating mixture is stirred for too short a period of time (*i.e.*, allene metalation is incomplete) the unreacted *n*-butyllithium can give rise to the formation of 3-butylcyclohexanone, (presumably via the *n*-butylcuprate complex).

By manipulating these conditions, it was ultimately found that the best yield of 3-(2-propynyl)cyclohexanone was c a. 30%. The pure γ-ethynyl ketone was separated by column chromatography over alumina.

To cyclize this ketone, the optimum conditions found in our laboratories for the cyclization of 6-heptyn-2-one were initially employed.

Reaction of 3-(2-propynyl)cyclohexanone with sodium-biphenyl generated *in situ* in the presence of water (2 equivalents) resulted in the formation of the desired cyclized product. However, c a. 40% of the starting ketone was also detected by glc. Attempts to purify the cyclized product were unfruitful due to the presence of by-products with very similar glc retention times. When the reaction was carried out in the presence of 3 or 4 equivalents of water, the proportion of by-products increased. When the proton source was changed to *t*-butyl alcohol, the main product was the simple reduction product, the uncyclized alcohol. In all the aforementioned experiments, the isolated cyclized product was contaminated by aromatic compounds (by nmr) probably arising from the reduction of biphenyl. Thus, it was decided to explore the use of sodium-TMB, since this electron transfer reagent is reasonably stable towards proton sources.

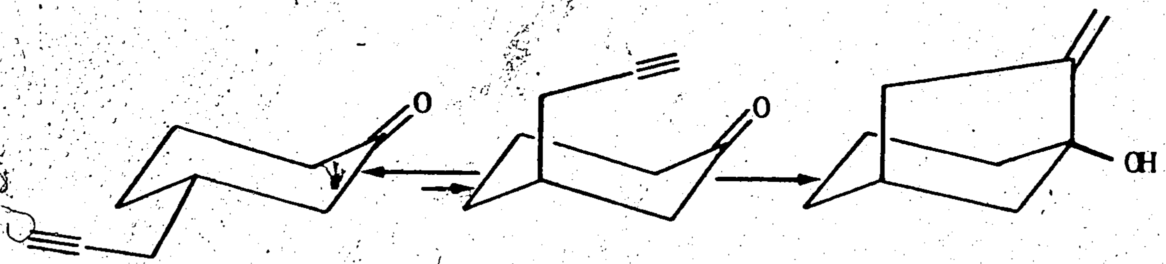
In an exploratory run utilizing Na-TMB at 0^{o} in the presence of *t*-butyl alcohol (2 equivalents), 40% of the cyclized alcohol was produced; nevertheless the reaction was incomplete. However, when a large excess of *t*-butyl alcohol was used (10 equivalents), after four hours, 55% of the cyclized product was present. Work-up of the reaction mixture after seven hours afforded 77% (glc) yield of 1-hydroxy-7-methylene-bicyclo(3.2.1)octane which was isolated in 65% (> 95% pure by glc).



31 26

77%, glc
65%, isolated

It is worthwhile mentioning that although only one of the conformers (presumably the less stable) of the γ-ethynyl ketone can undergo cyclization, high yields of cyclized product were obtained.



In conclusion, the scope of the reductive cyclization of unsaturated ketones utilizing electron-transfer reagents was extended to the synthesis of six membered ring tertiary alcohols. Also, the versatility of one of the cyclization reactions was demonstrated in the synthesis of a structurally complex molecule, namely, 1-hydroxy-7-methylene-bicyclo(3.2.1)octane, a model for gibberellic acid synthesis.

The use of the cyclization reaction, in concert with the novel 1,4-addition of a propargyl group to an unsaturated ketone allowed the preparation of the above mentioned bicyclo compound in two steps from 2-cyclohexenone.

EXPERIMENTAL

General Considerations

Mass spectra were recorded at 70 *ev.* on an AEI Model MS-9 Spectrometer. Spectral data are expressed in the following manner: *m/e*: peak mass (relative intensity).

Infrared spectra (ir) were recorded using a Unicam SP 1000 Infrared Spectrophotometer. Proton nuclear magnetic resonance (nmr) spectra were recorded on a Varian A-60 or HR-100 Spectrometer. Unless otherwise stated, carbon tetrachloride was employed as the solvent and chemical shifts are reported in δ values. The following abbreviations are used in the text: s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet.

The ^{13}C nmr spectra were determined using a Bruker HFX-90 spectrometer. Gas chromatographic (glc) analyses were performed using a Varian Aerograph Series 1200 versus a reference solution of the authentic compounds or utilizing an internal standard (*n*-butylbenzene).

All the reactions were carried out under an atmosphere of oxygen-free nitrogen[24].

Preparation of Radical Anion Solutions

Biphenyl was crystallized from methanol and dried over P_2O_5. Trimesitylboron was purified by passing a solution of this compound in benzene though a short column of alumina or silica gel and the solvent eliminated *in vacuo*. Dimethoxyethane (DME) was freshly distilled prior to use from sodium-benzophenone ketyl.

Sodium Trimesitylboron

A solution of trimesitylboron (one equivalent) in DME was treated with sodium shavings (two equivalents). The solution was stirred for three hours at ambient temperature (glass coated stirring bar).

Synthesis of 7-Octen-2-one

To a cooled (-50°) hexane solution of *n*-butyllithium (21.3 ml, 33 mmole, 1.55M) in 10 ml of ether, TMEDA (3.83 g, 4.9 ml, 33 mmole) in 10 ml of ether was added dropwise. The mixture was cooled to -78° and propylene (6.93 g, 11.55 ml, 165 mmole) was distilled into the flask. Then the bath was removed. The contents of Dry-Ice condenser were allowed to evaporate overnight after which a precipitate had formed. The mixture was cooled to -78° and a solution of the ethylene ketal of 5-iodo-2-pentanone (3.5 g, 13.7 mmole) in 20 ml of ether was added (30 minutes) followed by slow warming to room temperature and stirring for two hours. The mixture was poured into ice-water and saturated with NaCl. The aqueous layer was extracted with ether, the organic layers combined and washed with brine and dried over Na_2SO_4. The solvent was removed at atmospheric pressure and the residue was refluxed in a mixture of methanol (10 ml) and water (10 ml) in the presence of one drop of concentrated hydrochloric acid for one hour. The mixture was poured into water and extracted with pentane. The organic layer was washed three times with water and brine. Distillation of the dried (Na_2SO_4), concentrated residue afforded 1.0 g (64%) of 7-octen-2-one, bp 69-70°/15 mm (lit.[122] 70-71°/15 mm), identical in all respects (nmr and ir) with an authentic sample.

Reaction between Methylmagnesium Iodide and 2-Methylcyclohexanone

A solution of 2-methylcyclohexanone (22.4 g, 0.2 mole) in 100 ml of ether was added to a solution of methylmagnesium iodide in ether (0.25 mole, 500 ml, 0.5M, prepared by the interaction of 35.4 g/0.25 mole of methyl iodide and 16.5 g, (0.3 g-atom), of magnesium) keeping the temperature below -5°. The mixture was brought to room temperature and poured into a mixture of ice and 10% hydrochloric acid. The aqueous layer was extracted with ether, the organic layers were combined and washed successively with 5% hydrochloric acid, water and brine. The dried (Na_2SO_4) concentrated residue was distilled under vacuum to provide 22.82 g (89%) of an isomeric mixture of *cis* and *trans*-1,2-dimethylcyclohexanol (*cis:trans*, 20:80). Preparative glc (10% Carbowax 20M) afforded an analytical sample of the *trans* isomer, n_D^{20} 1.4611 (lit.[60] n_D^{20} 1.4590); nmr: δ 1.15 (s, 3H) CH_3C-OH

Dehydration of *cis* and *trans*-1,2-dimethylcyclohexanol

A mixture of *cis* and *trans*-1,2-dimethylcyclohexanols obtained above (10 g, 0.78 mole) and 2.5 ml of 85% H_3PO_4 was distilled and the fraction boiling below 145° was collected. The distillate was washed with water and dried over $CaCl_2$. Distillation of 130-131°/700 mm (lit.[60] bp 135-136°/760 mm) afforded 7.75 g (91%) of 1,2-dimethyl-1-cyclohexene containing c a. 5% of 1,2-dimethyl-2-cyclohexene; nmr: δ 1.55 (broad singlet) =C-CH_3, 0.98 (d, J = 6 Hz) C H-C H_3 (impurity).

Synthesis of *cis*-1,2-dimethylcyclohexanol

To a cooled (5°) solution of 5.5 g (50 mmole) of the olefinic mixture obtained above in 50 ml of THF was added a solution of diborane in THF (50 ml, 50 mmole, 1M). The temperature was allowed to rise to 25° and the solution was stirred overnight. Water (5 ml) was added (0°) to destroy the excess of diborane. Then 3 N NaOH (15 ml) was added, followed by the dropwise addition of 15 ml of 30% H_2O_2, keeping the temperature between 30 and 40°. After stirring the mixture at 45° for 30 minutes, it was poured into water and saturated with NaCl. Extraction with ether and elimination of solvent from the dried (Na_2SO_4) extract afforded a residue which was fractionally distilled to provide 4.88 g (76%) of a clear liquid, bp 99-100°/50 mm (lit.[60] bp 82.8°/25 mm), consisting of more than 97% of *cis*-1,2-dimethylcyclohexanol. An analytical sample was collected by preparative glc (10% Carbowax 20M); n_D^{20} 1.4647 (lit.[60] n_D^{20} 1.4625); nmr: δ 1.05 (s, 3H); CH_3C-OH.

Reaction between 7-octen-2-one and Sodium-Biphenyl (formed *in situ*)

To a cooled (-35° to -40°) solution of biphenyl (0.462 g, 3.0 mmole) in 15 ml of DME, sodium shavings (0.138 g, 6.0 mg-atoms) were added. Immediately after the blue color appeared on the surface of the sodium, a solution of 7-octen-2-one (0.126 g, 1 mmole) and water (0.054 g, 3.0 mmole) in 5 ml of DME was added dropwise during one hour. After stirring for 2.5 hours, the mixture turned blue. After 30 minutes of additional stirring the reaction was quenched by adding 3 ml of saturated NH_4Cl to destroy the excess of sodium. Brine (10 ml) was added and the layers separated. The aqueous layer was extracted with ether (3 times). The organic phases were combined, washed with brine and dried over Na_2SO_4. A weighed amount of internal standard was added to the solution and it was analyzed by glc (10% β,β-oxydipropionitrile). *cis*-1,2-Dimethylcyclohexanol and the *trans* isomer were produced in 54% and 13% yield, respectively. Also, the formation of 7-octen-2-ol was detected (compared with an authentic sample prepared by reduction of 7-octen-2-one with $NaBH_4$). The three alcohols were characterized by peak-enhancement and glc mass spectral analysis.

Reaction between 7-Octen-2-one with Sodium Trimesitylboron (TMB) in the Presence of *t*-Butyl Alcohol

To a cooled (0^o) solution of sodium-TMB in 15 ml of DME (prepared from 0.552 g (1.5 mmole) of TMB and 0.069 g (3 mg-atom) of sodium), *t*-butyl alcohol (0.111 g, 1.5 mmole) was added followed by the dropwise addition of 7-octen-2-one (63 mg, 0.5 mmole) in 3 ml of DME. The mixture was stirred for 4 hours at 0^o, then overnight at room temperature. Work-up as described above and analysis by glc revealed the formation of 90% of 7-octen-2-ol (characterized by peak enhancement and glc mass spectral analysis).

Reaction between 7-Octen-2-one and Lithium in Liquid Ammonia in the Presence of Ammonium Sulphate

To a stirred mixture of $(NH_4)_2SO_4$ (264 mg, 2 mmole) and liquid ammonia (20 ml, distilled twice from sodium), a solution of 7-octen-2-one in THF (20 ml) was added dropwise. The admixture of lithium shavings (35 mg, 5 mg-atom) resulted in the immediate formation of a blue solution. After six hours the mixture was quenched and worked up in the usual way. Analysis by glc (external standard) and characterization by glc mass spectral revealed the presence of *cis* and *trans*-1,2-dimethylcyclohexanol in 28% and 6% yields, respectively; 7-octen-2-one, less than 5%; 7-octen-2-ol, 52%; 2-octanol, 5% (base peak at *m/e* = 45).

Synthesis of 3-(2-propynyl)cyclohexanone

To a cooled (-60°) solution of allene (6.0 ml, c.a. 100 mmole) in ethyl ether (50 ml) was added 53 ml of a 1.52M hexane solution of *n*-butyllithium (80 mmole) during 30 minutes. The mixture was allowed to warm slowly. At -20° a white precipitate formed. Stirring was continued for 15 minutes and the mixture was cooled to -50°. Cuprous iodide (7.6 g, 40 mmole) was added and the temperature was slowly increased to -30°. After stirring for 10 minutes, the mixture was cooled to -78° and 2-cyclohexenone (2.0 g, 20.8 mmole) in 20 ml of ether was added over 45 minutes. The reaction mixture was poured into a stirred ice-cooled solution of 5% hydrochloric acid and filtered through celite. The aqueous phase was extracted with ether and the organic layers combined. Removal of the solvent from the dried (Na_2SO_4) extract afforded a residue which was chromatographed over alumina (200 g) using ether as eluent. The first fractions contained mixtures of 3-butylcyclohexanone and 3-(2-propynyl)-2-cyclohexen-1-ol. 3-(2-propynyl)cyclohexanone was isolated as a pure compound (280 mg, 10% yield) by bulb to bulb distillation at $120^\circ/5$ mm; n_D^{20} 1.4834; nmr: δ 1.0-2.6 (broad multiplet); ^{13}C nmr: ppm (relative to TMS): 210.71 ($\overset{*}{C}$=O), 81.36 ($\overset{*}{C}\equiv$C-H), 70.43 (C$\equiv\overset{*}{C}$-H), 47.01, 41.07, 37.79 ($\overset{*}{C}$-H), 30.33, 25.42, 24.81; ir (liquid film): 3280 ($\equiv$C-H), 2120 (C$\equiv$C), 1720 cm^{-1} (C=O); mass spectrum *m/e*: 136.0887 (*Calcd.* for $C_9H_{12}O$: 136.0888), 136(25), 121(7), 108(15), 97(100), 93(20), 79(25), 69(45), 55(55), 41(85), 39(37). *Anal Calcd:* C, 79.37; H, 8.88.

Found : C, 79.30; H, 9.03.

Reaction of 3-(2-Propynyl)cyclohexanone with Sodium Trimesitylboron in the presence of *t*-Butyl Alcohol. Synthesis of 1-Hydroxy-7-methylene Bicyclo(3.2.1)octane

To a cooled (0^{o}) solution of sodium-TMB (from 1.104 g, 3 mmole of TMB and 138 mg, 6 mg-atom of sodium) containing *t*-butyl alcohol (740 mg, 10 mmole) in DME (30 ml), a solution of 3-(2-propynyl)cyclohexanone (136 mg, 1 mmole) in DME (5 ml) was added over 30 minutes and stirred for 7 hours. Work-up as described above afforded a residue which was dissolved in the minimum amount of benzene and chromatographed over alumina (30 g, activity III). Elution with Skelly B afforded a quantitative recovery of TMB. Increasing the polarity by using Skelly B/ether (3:1) produced 95 mg (69%, 77% yield determined by glc from the original solution of the reaction mixture, utilizing 10% Carbowax 20M as the column). The compound was shown to be > 95% pure by glc, and identical (ir and nmr) with an authentic sample[127]. Nmr: δ 4.94 and 4.77 (m, m, 1H, 1H) C=C H_2, 2,38 (s, 1H) OH; ^{13}C nmr: ppm (relative to TMS) 115.07 ($\overset{*}{C}$=C H_2), 103.47 (C=C H_2), 79.68 ($\overset{*}{C}$-OH), 46.61, 40.62, 35.49, 31.72, 30.53, 20.23; ir (liquid film): 3360 (OH), 3080, 1668 and 892 (C=C H_2), 1130 (R_3COH).

Synthesis of 3-Methyl-3-vinylcyclohexanone

To a stirred suspension of cuprous iodide (22.85 g, 120 mmole) in 100 ml of tetrahydrofuran, hexamethylphosphorous triamide (44 ml, 39.19 g, 240 mmole) was added dropwise keeping the temperature below 25° by means of a water bath. The mixture was cooled to -78° (crystallization of cuprous iodine-phosphine complex occurred) and a solution of vinyllithium in THF (77.4 ml, 240 mmole, 3.1M) was added during one hour. At this temperature 3-methyl-2-cyclohexenone (6.6 g, 60 mmole) dissolved in 70 ml of THF was added dropwise over one hour. The mixture was poured into saturated NH_4Cl, filtered through celite and the solvent removed *in vacuo*. The residue was dissolved in ether and the solution washed with water, 5% H_2SO_4, and NaCl saturated solution. The dried extract (Na_2SO_4) was concentrated at atmospheric pressure. Fractional distillation afforded 4.98 g (60%), bp 77-78°/10 mm of 3-methyl-3-vinylcyclohexanone, n_D^{20} 1.4668; ir (liquid film) 1710 (C=O), 990, 910 ($\mathrm{CH{=}CH_2}$); nmr: δ 5.5-6.0 (m, 1H) $\mathrm{C}H{=}\mathrm{CH}_2$, 4.78-5.2 (m, 2H) $\mathrm{CH{=}C}H_2$, 2.1-2.5 (m, 4H) $\mathrm{C}H_2\mathrm{-C{=}O-C}H_2$, 1.5-2.1 (m, 4H) $\mathrm{C}H_2\mathrm{C}H_2$, 1.1 (s, 3H) $\mathrm{C}H_3$; mass spectrum *m/e*: 138.1045 (*Calcd.* for $C_9H_{14}O$: 138.1057), 138(72), 123(45), 95(75), 81(75), 45(55). *Anal Calcd.* for $C_9H_{14}O$: C, 77.87; H, 11.76. *Found*: C, 78.15; H, 11.63.

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