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Rhodium Trichloride Promoted Hydroboration of Alkenyl Nitriles and Alkenyl Chlorides

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Approved by:

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Thesis Advisor

Department Head

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I would like also to thank our research group for their active discussions of my research results.

Abstract

Previous studies of the rhodium trichloride ($RhCl_3$) catalyzed hydroboration mechanisms of alkenes showed rearrangements and unusual regiochemistry compared to simple uncatalyzed hydroboration, and complex mechanisms have been proposed to explain these results. Earlier studies suggested that isomerization of alkenes in the presence of $RhCl_3$ prior to hydroboration accounted for these results. Studies of alkene rearrangements in the presence of $RhCl_3$ also suggest that the results are due to a different mechanism. The elimination-addition promoted elimination of R-Rh-B structures was shown to be responsible for isomerization and formation of different alcohol isomers after hydroboration. These interesting results prompted us to study the hydroboration reactions of alkenes with functional groups in the presence of $RhCl_3$. Previous studies on the uncatalyzed hydroboration reactions of alkenes with fuctional groups showed that the presence of substituents can introduce marked directive influences on the hydroboration reaction. In the case of alkenyl chlorides this is followed by elimination reactions. Hydroboration reaction of alkenyl nitriles has been studied for the first time in this work in detail. The presence of $RhCl_3$ exerted a profound effect upon the hydroboration reactions of alkenyl nitriles and alkenyl chlorides. $RhCl_3$ mainly served to reduce this substituent effect and to isomerize the elimination products. An unexpected process-trimerization reaction of acetonitrile has also been observed from the result of carbon-carbon bond breaking in allyl cyanide. The mechanism of this process has been studied in detail. Alkenyl chlorides favored the formation of racemic mixtures of chiral compounds in the presence of rhodium trichloride. In addition to that the effect of temperature on the hydroboration of alkenyl nitriles and chloride has been studied for the first time.

Introduction

1.1. History

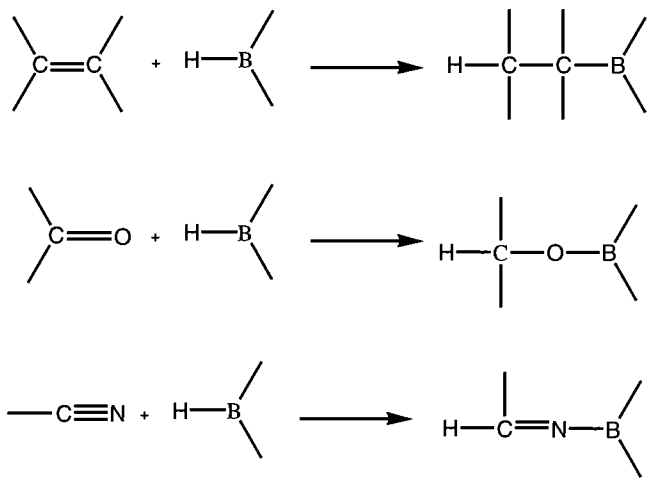
The discovery of hydroboration reaction by Prof. H.C. Brown of Purdue University in 1956 opened a very fascinating field of research in organic chemistry.[1,2] Prof. H.C. Brown was awarded with Nobel Prize for this dicovery in 1979. In this reaction alkenes can be easily and quantitatively converted into organoboranes under mild experimental conditions. The following stoichiometry applies if all B-H bonds add to alkene.

$$6\ RCH{=}CH_2 \ + \ B_2H_6 \longrightarrow 2(RCH_2CH_2)_3B$$

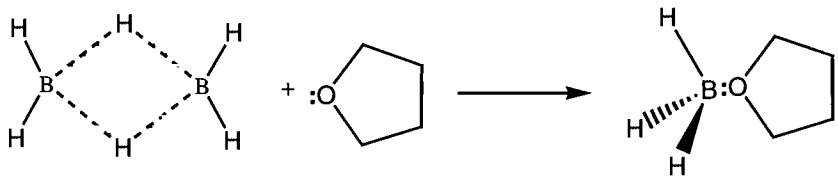
This involves the addition of boron-hydrogen bonds to the carbon-carbon double bond. Consequently, the hydroboration of such alkenes, followed by the oxidation *in situ* of the resulting organoborane, provides a very convenient procedure for the *anti*-Markovnikov hydration of double bonds.[3]

$$(RCH_2CH_2)_3B \xrightarrow{[O]} 3\ RCH_2CH_2OH \ + \ B(OH)_3$$

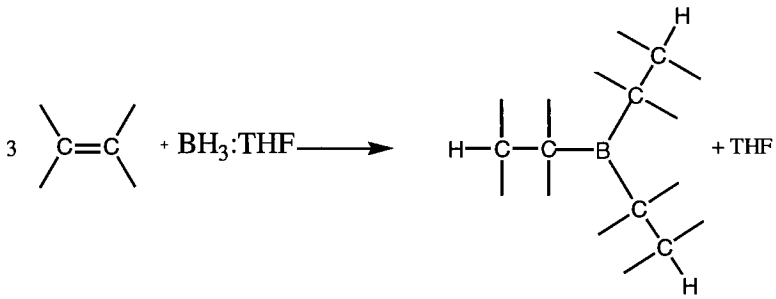
The boron-hydrogen bond has been observed to add with remarkable ease to carbon-oxygen double bonds and to carbon-nitrogen double and triple bonds.[1,2]



In tetrahydrofuran, diborane undergoes reaction with tetrahydrofuran to form a 1:1 complex:[4]

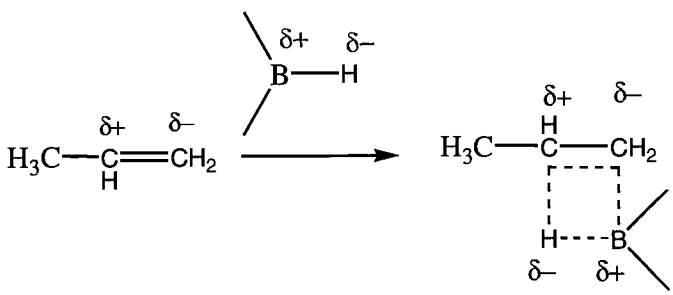


The hydroboration reaction involves the addition of the BH_3 of this complex to the olefin to give the corresponding trialkylborane in three steps. Overall:



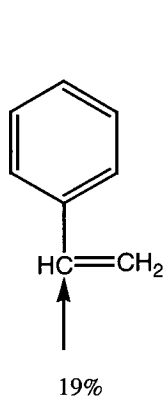
The reactions of diborane with single carbon-carbon double and triple bonds are fast (room temperature, a few hours), and much faster in fact than the reaction of diborane with many functional groups. An important consequence is that many functional groups can be tolerated and are left intact in the hydroboration, readily providing organoboranes containing such substituents.[5,6,7,8]

It was concluded by H.C.Brown that the hydroboration reaction involves a simple four-center transition state, with the direction of addition controlled partly by the polarization of the boron-hydrogen bond:



1.2. Hydroboration of alkenes containing functional groups

The presence of relatively inert substituents, such as halogen and ether groupings on benzene rings does not cause any difficulty in the hydroboration reaction. For example, the hydroboration of *p*-chlorostyrene and *p*-methoxystyrene proceeds normally.[9] However, the product isomers distribution is altered somewhat by substituents in the *para* position. The presence of a methoxy group decreases the Markovnikov proportion to 7%, whereas a *p*-chloro substituent raises it to 27%.



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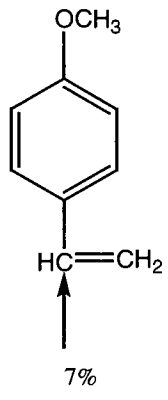

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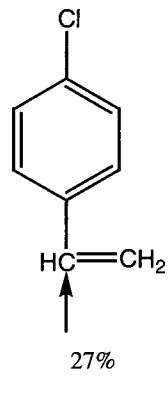
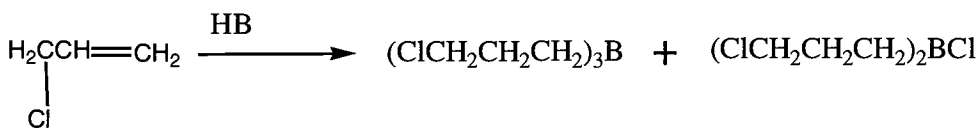


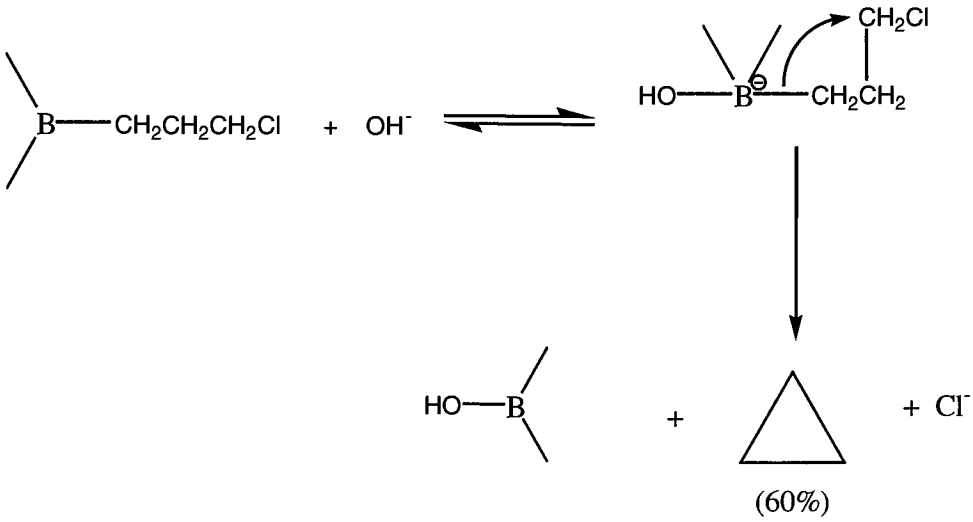
27%

Similarly, aliphatic derivatives such as allyl chloride[10] and vinyl ethyl ether[11] and a number of related derivatives have been hydroborated.[12,13]

An early article describing the hydroboration of allyl chloride appeared in 1958.[10] The hydroboration of allyl chloride leads to the related dertivatives, tri-(γ-chloropropyl)-borane and di-(γ-chloropropyl)-boron chloride. Under the influence of aqueous alkali,

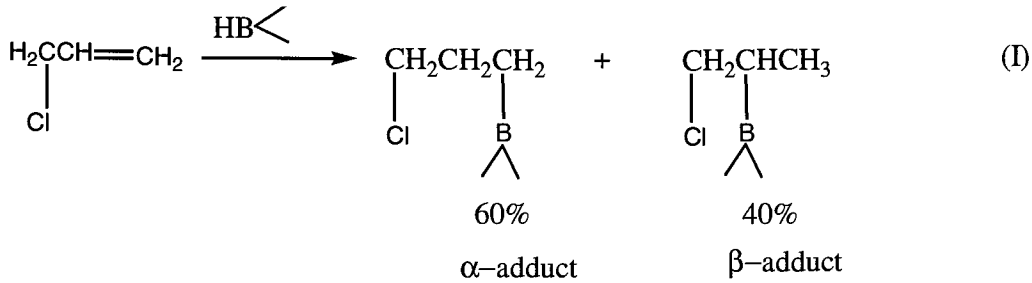


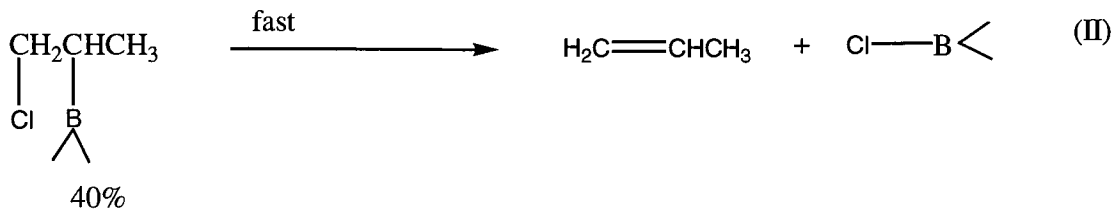
these derivatives undergo an almost quantitative conversion to cyclopropane 60% of total product.

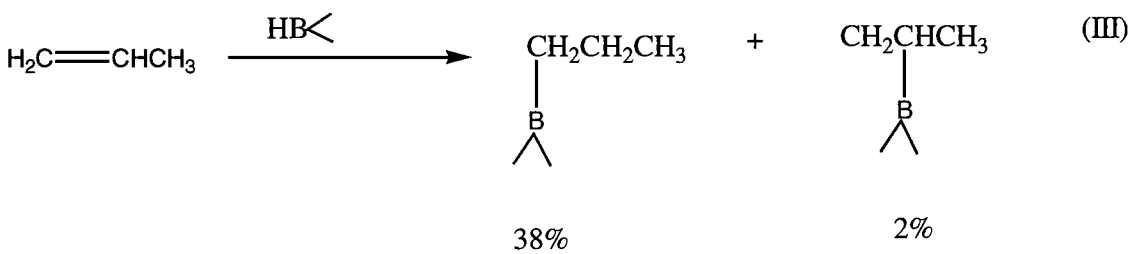


Oxidation of the residual alkaline reaction mixture yielded 38% 1-propanol and 2% 2-propanol.[12]

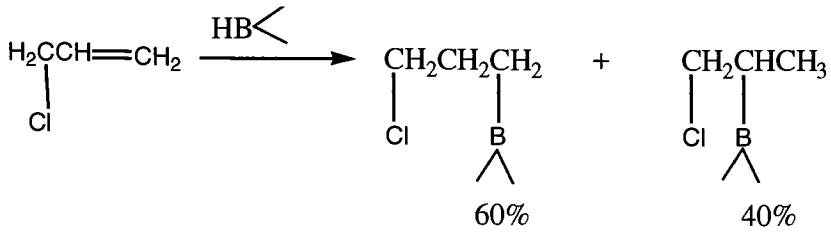
In terminal olefins, the addition of boron takes place predominantly on the terminal carbon atom of the double bond. This is partly explained in terms of polarization of the double bond by the alkyl substituent, increasing the electron density at the terminal carbon atom and thereby favoring the attachment of the electrophilic boron atom at that position. The introduction of electron-withdrawing functional groups at the allyl position brings about a marked increase in the addition of boron to the secondary carbon atom of the double bond. Thus, in the hydroboration of allyl chloride and allyl tosylate , 40 and 45%, respectively, of the boron addition occurs at the non-terminal position (I). It has also been observed in both allyl chloride and allyl tosylate that addition of boron to the non-terminal position was accompanied by a spontaneous elimination of boron and the substituent in the β-position (chlorine and tosylate group) which was quantitative even at 0° (II). The resulting olefin, in the presence of excess diborane, then underwent further hydroboration (III).[12]

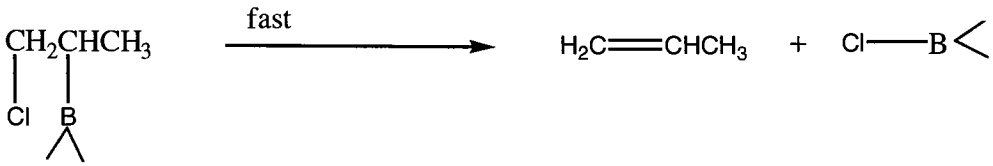


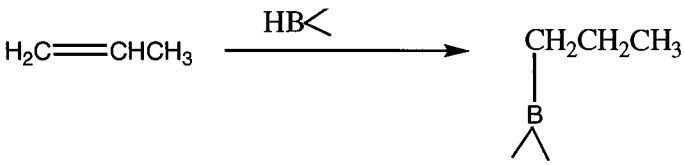




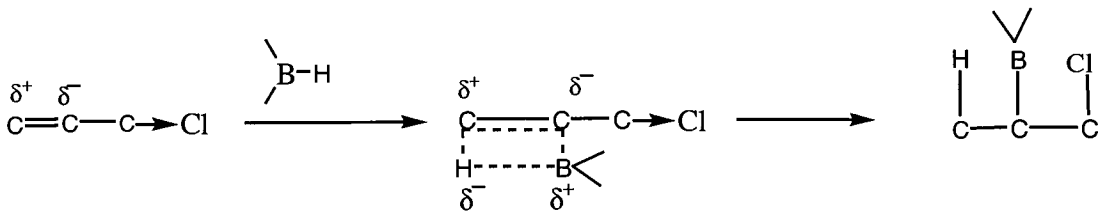
Further studies of the hydroboration of allyl chlorides do not reveal 2-propanol and therefore the reported formation[13] of 2-propanol was refuted.



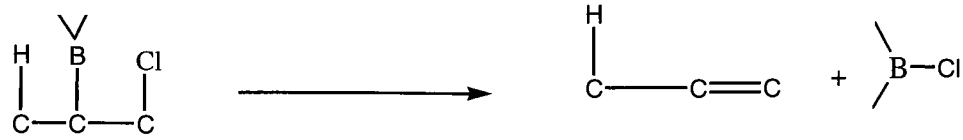




Hydroboration of symmetric, internal olefins places equal amounts of the boron on each carbon of the double bond, whereas, hydroboration of crotyl chloride produces only the β–adduct (Markovnikov).[6] The directive effect of the chloride operates through a polarization of the double bond by the electronegative chloride. This produces an electron enrichment of the β–carbon making this carbon more attractive to the electrophilic boron.[17]

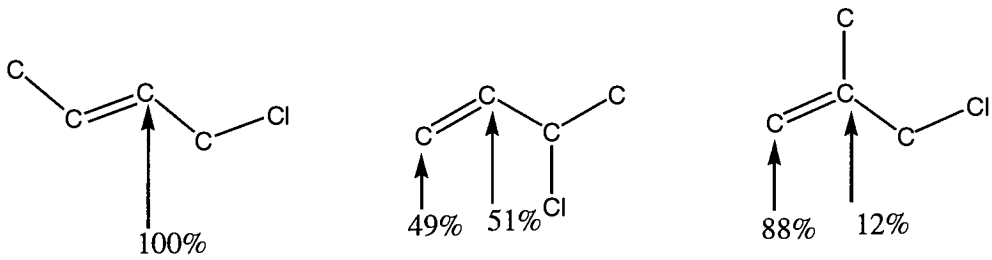


The production of β–adduct was followed by spontaneous elimination:



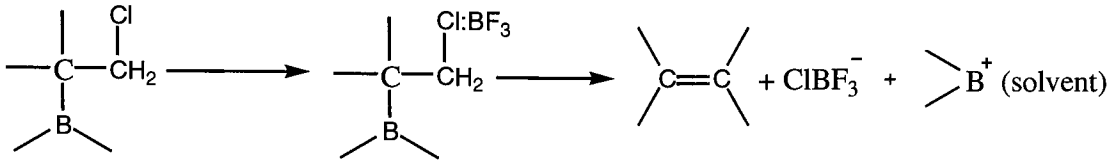
The use of disiamylborane as the hydroborating agent resulted in greater steric preference for addition to the less substituted carbon and only 6% β–addition and elimination have been observed. Likewise, 3-chloro-1-butene showed only 4% elimination with disiamylborane, compared to 51 % with diborane. In the case of 1-chloro-2-methyl-2-propene, the double bond is formed between a methylene and a quaternary carbon. There was no β–adduct and no elimination. With diborane only 12 % of boron is inserted on β–position.

In the case of crotyl chloride (1-chloro-2-butene) and 3-chlorocyclopentene, the double bond is formed by two secondary carbons. In this symmetric system, the directive effect of the chloride is felt full force and exclusive β–addition (Markovnikov) occurs even with disiamylborane. In summary the following regioselectivity was observed with diborane:



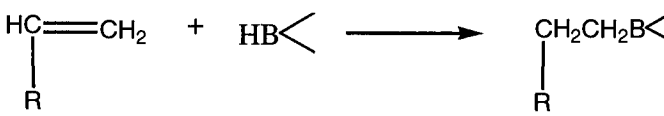
I II III

In compound III, the inductive and steric effects of the β–alkyl group largely overcomes the directive effect of the chloro substituent. No γ–addition occurs with symmetric olefins (I). Recent work on the hydroboration of 3-chlorocyclohexene suggests that the elimination occurs via a *trans* mechanism.[21] Evidently tetrahydrofuran has sufficient solvating power to act as a Lewis base in a base catalyzed elimination. Ethyl ether, with a less basic oxygen, does not catalyze the elimination and β–chloroorganoboranes are stable in ethyl ether.The elimination reaction was catalyzed by addition of the Lewis acids borane and boron trifluoride. Both of these Lewis acids may coordinate with the chlorine atoms and thereby facilitate the *trans* elimination:

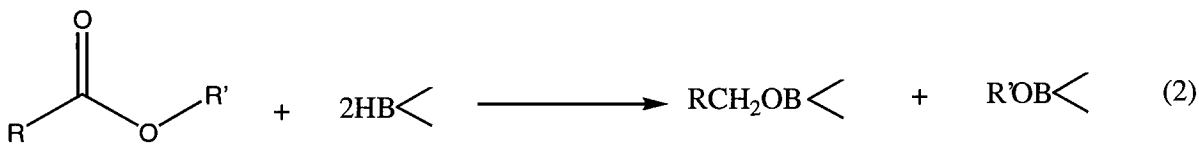


Even for cases in which the molecule contains reducible groups, it has been possible to achieve hydroboration. Thus a number of unsaturated esters have been hydroborated with diborane and disiamylborane. Even derivatives containing the double bond much closer to the ester group are readily converted into the corresponding organoboranes.[16]

Diborane reacts both with esters (1) and with olefins (2).

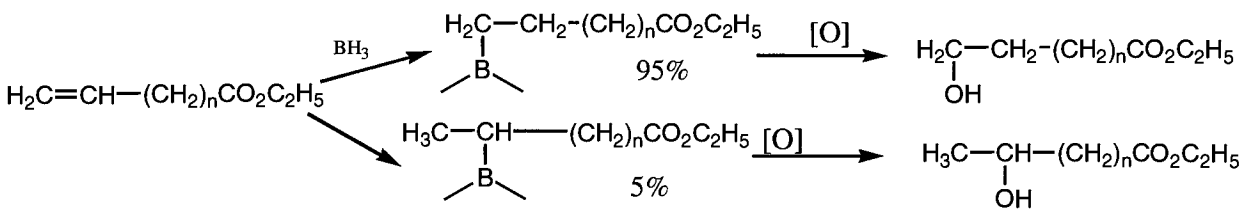


(1)



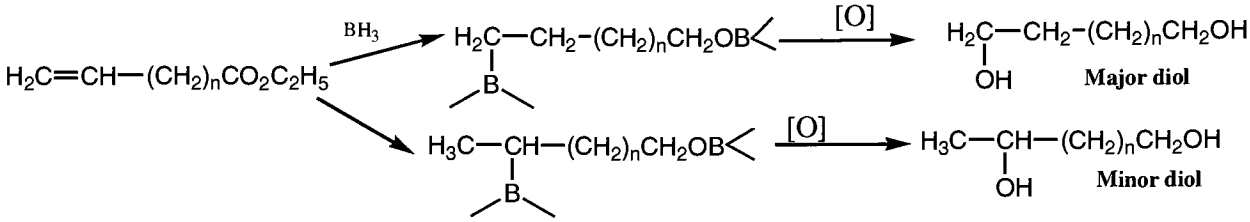
(2)

However, the reaction of diborane with esters is generally much slower than with olefins. It would be, therefore, be anticipated that in a system containing both the olefinic linkage and the ester group diborane could react preferentially with the olefinic linkage, even in the presence of excess reagent.



Where n=0,1,2 and so on

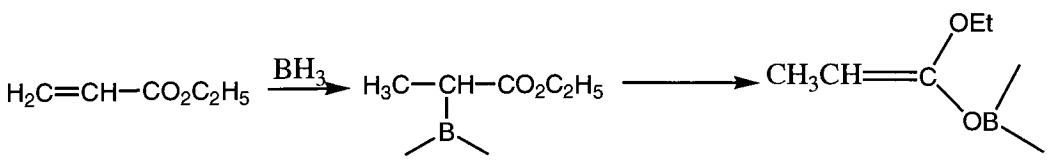
All of the unsaturated esters tested, with the exception ethyl acrylate (n = 0), gave the expected mixture of hydroxy esters and diols. Diols are formed in small amounts (10%).



Where n=0,1,2 and so on

Yield 10%

The ratios of diols to hydroxy esters were in reasonably good agreement with the extent of ester group reduction indicated by the data of the stoichiometry study. However, ethyl acrylate was exceptional in that no hydroxypropionates were detected. Instead, only the propanediols, 1-propanol, and 1-ethoxy-2-propanol were found in the reaction products. The unusual rectivity of ethyl acrylate, as well as the unexpected reaction products suggest that the hydroboration reduction of this ester must proceed by a very different path. The first step might involve a 1,2-addition in which the powerful directive influence of the carboethoxy group would favor placing the boron atom predominantly in the α–position, followed by a rapid transfer of boron from carbon to the neighboring oxygen. This rearrangement would lead to an intermediate, II, capable of forming ethyl propionate on hydrolysis, or of reacting further with the



II

hydroborating agents. All the products observed in the reaction can be explained by a series of addition -β-elimination steps. The tendency of the carboethoxy group to influence the direction of the hydroboration of the double bond appears to be greater than that of the phenyl group and approximately the same as that of the chloromethyl group. The available data on the directive influence of various substituents on the direction of hydroboration of a terminal double bond are summarized in Table 1.

Table 1

Directive Effects in Hydroboration Exhibited by Various Functional Substituents in the System Y-CH=CH_2 (1^0-*anti*-Markovnikov, 2^0- Markovnikov)[16]

Substituent Y	Diborane		Disiamylborane	
	1°	2°	1°	2°
CH_3CH_2-	94	6		
C_6H_5-	80	20	98	2
p-ClC_6H_4-	65	35		
p-$MeOC_6H_4$-	91	9	98	2
$C_6H_5CH_2$-	90	10		
EtO_2CCH_2-	83	17	98	2
$EtO_2CCH_2CH_2$-	91	9	99	1
$ClCH_2$-	60	40	97	3
$ClCH_2CH_2$-	82	18	99	1
p-$MeC_6H_4SO_3CH_2$-	55	45	95	5
Me_3Si-	67	33		
F_3C-	26	74		

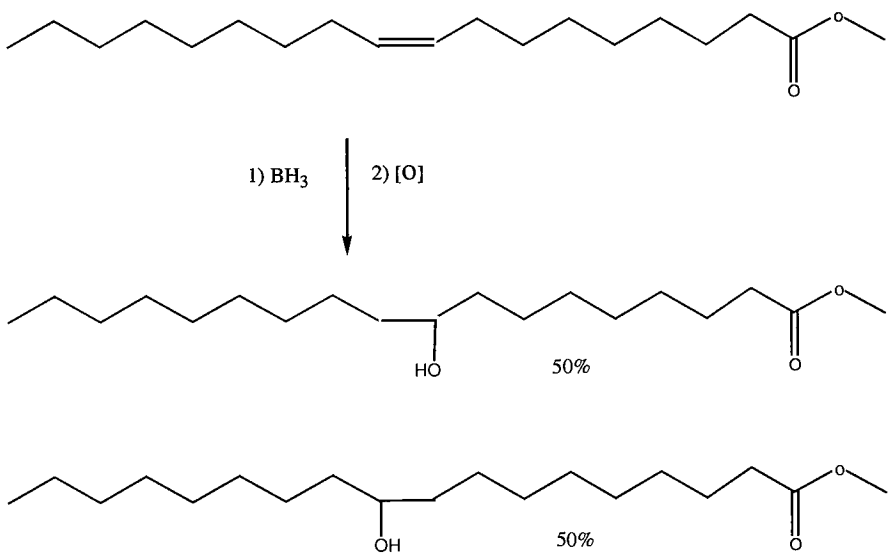
Electron withdrawing groups increases the formation of Markovnikov products. For example, chlorine in the parachlorophenyl substituent group (p-ClC_6H_4) increased Markovnikov product to 35%, chlorine in the substituent of chloromethyl group ($ClCH_2$-) increased the Markovnikov product to 40% and fluorine in the substituent of trifluoromethyl group (F_3C-) increased the Markovnikov product to 74%. However, regioselectivity in the hydroboration with the boronic reagent-disiamylborane completely favored *anti*-Markovnikov products.

Knowledge of the directive effect of representative substituents might make it possible to predict the approximate isomer distribution in the hydroboration of other unsaturated molecules containing functional substituents, and to utilize the directive effect to achieve useful results in planning a synthetic approach.[16]

The hydroboration of representative allyl derivatives was examined in order to observe the effect of the substituent on the direction of addition of diborane to the

double bond.[13] The amount of addition of the boron to the secondary carbon atom decreases with decreasing electronegativity of the substituent: allyl tosylate, 45%; chloride, 40%; acetate, 35%; benzoate, 25%; borate, 18%; phenyl ether, 32%; phenyl thioester, 22%; ethyl ether, 19%; alcohol, 24%. While the secondary boron derivatives derived from allyl tosylate, chloride, benzoate, and acetate undergo a spontaneous elimination to propylene during the hydrboration of the allyl derivative, the borate, phenoxide, and ethoxide derivatives survive the hydroboration reaction at 0°.However, at elevated temperatures the elimination reaction is essentially complete within 2 hr. for these derivatives. Methyl oleate has been converted to an equimolar mixture of 9- and 10- hydroxyoctanoic acids by the hydroboration-oxidation procedure[14] and methyl ester of 10-undecenoic acid has likewise been converted into the 11-hydroxy derivative. [15]

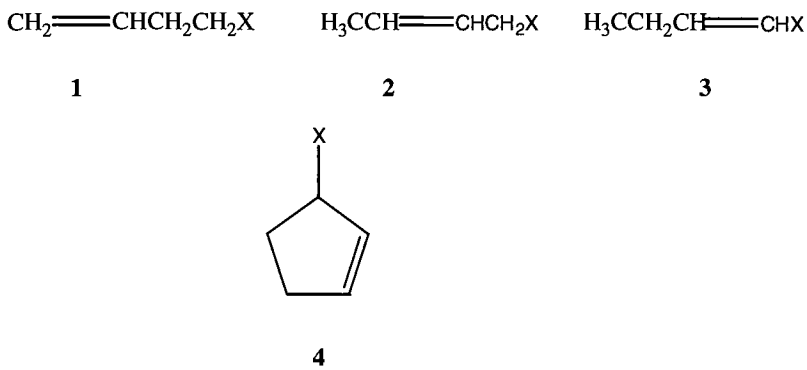
Hydroboration of Methyl Oleate (9-octadecenoic acid methyl ester)



The high reactivity of the aldehyde group and the free carboxylic acid group toward diborane would doubtless result in a competition for the diborane. However, simple conversion of these groups into the acetal and ester, respectively, circumvents this problem.

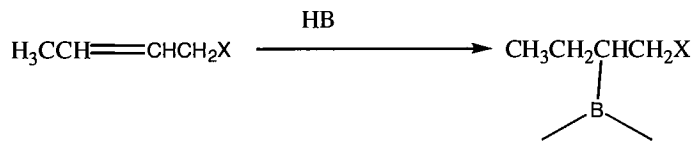
The foregoing results can be generalized as follows.

The presence of substituents can introduce marked directive influences on the hydroboration reaction.



1 **2** **3** **4**

In some cases this may complicate the sitiuation; in others, one can take advantage of it. A systematic study of the hydroboration of 3-butenyl dertivatives[5] (**1**), 2-butenyl (crotyl) derivatives[6] (**2**), 1-butenyl (vinyl) derivatives[7] (**3**), and related cyclopentenyl derivatives[17](**4**) provides the basis for an understanding of the directive effects. Hydroboration of many of the 3-butenyl derivatives proceeds to place as much as 20 percent of the boron in the secondary 3-position. This is an unacceptably high propotion of secondary product. The difficulty is readily overcome by using a suitable dialkylborane, such as disiamylborane, for the hydroboration. Otherwise, no difficulties were encountered for a wide variety of substituents (X = OCH_3, OC_6H_5, OH, O_2CCH_3,Cl, NH_2, SCH_3 and $CO_2C_2H_5$). In the crotyl derivatives the strong directive influence of the substituents places the boron predominantly (~90 percent) in the 2-position.

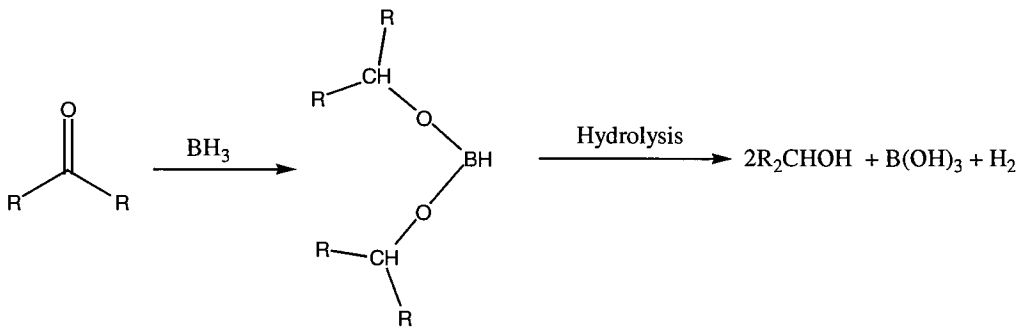


When X is a good leaving group, such as Cl, elimination occurs to give 1-butene, which then undergoes hydroboration. This side reaction can be avoided in ethyl ether. Apparently elimination is catalyzed by the donor properties of tetrahydrofuran.
In the case of the 1-butenyl derivatives, the presence of an alkoxy substituent directs the boron strongly to the 2-position. On the other hand, a chlorine substituent directs the boron to the 1-position. Acetoxy lies in between. With an appreciation of these

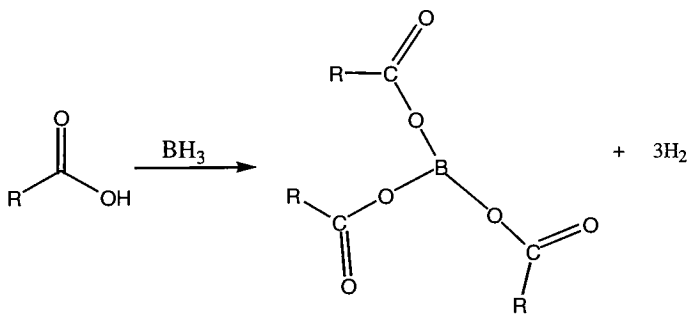
phenomena, it is possible to utilize directive effects to produce the desired organoboranes for transfer to carbon or other atoms as required in a specific synthesis.

1.3. Hydroboration of carbon-oxygen double bonds and carbon-nitrogen triple bonds

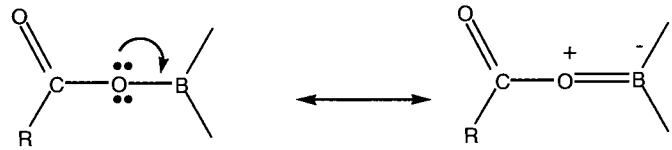
Both aliphatic and aromatic ketones are rapidly reduced in the hydroboration reactions with borane at room temperature. Such reductions generally involve the rapid reaction of two moles of carbonyl compound per mole of borane to form the dialkoxyborane. The third hydride reacts with difficulty. Hydrolysis yields the alcohol.[4]



The reduction of acid chlorides under these conditions is quite slow. The electron–withdrawing effect of the chlorine substituent greatly reduces the donor properties of the carbonyl oxygen atom. Consequently, borane does not readily coordinate with it. Esters and lactones are reduced relatively slowly. On the other hand, carboxylic acids are reduced rapidly. This was unexpected. Normally carboxylic acids are much more resistant to hydrogenation or reduction than the corresponding esters.

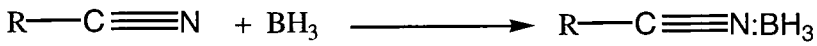


The precise explanation for the high reactivity of carboxylic acids has been studied.[18] The first step in the reaction is the formation of the triacyloxyborane. This product contains a highly reactive carbonyl group, as shown by its ready reduction to the alcohol stage by sodium borohydride as well as by diborane. It was proposed that the electron deficiency of the boron atom in the triacyloxyborane exerts a powerful demand on the electron-pairs of the acyloxy oxygen. Consequently, resonance will



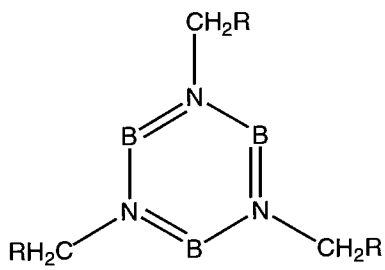
involve interaction of this oxygen atom with the boron atom, rather than the usual resonance with the carbonyl group.According to this interpretation, the carbonyl group in the triacyloxyboranes should resemble that in a simple aldehyde or ketone far more than the resonance-stabilized, less reactive carbonyl group in an ester. Indeed, the carbonyl groups in the triacyloxyborane react readily with sodium borohydride as well as with diborane. Typical aldehydes and ketones are likewise highly reactive towards both sodium borohydride and diborane.

Tertiary amides are rapidly reduced. The reaction of the reagent is somewhat slower, but the reduction to the amine is readily achieved. The nitrile group is highly inert to nucleophilic attack by sodium borohydride. However, diborane evidently



reacts through an electrophilic attack on the nitrile nitrogen.

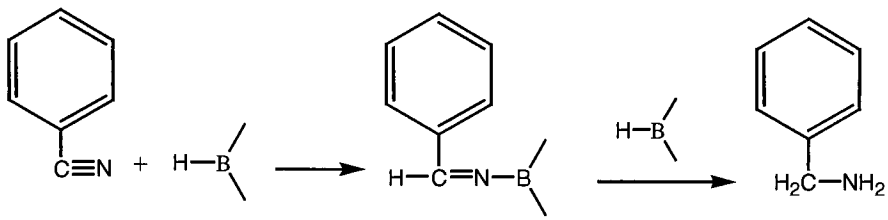
The reaction then proceeds to the formation of the corresponding N,N',N''-



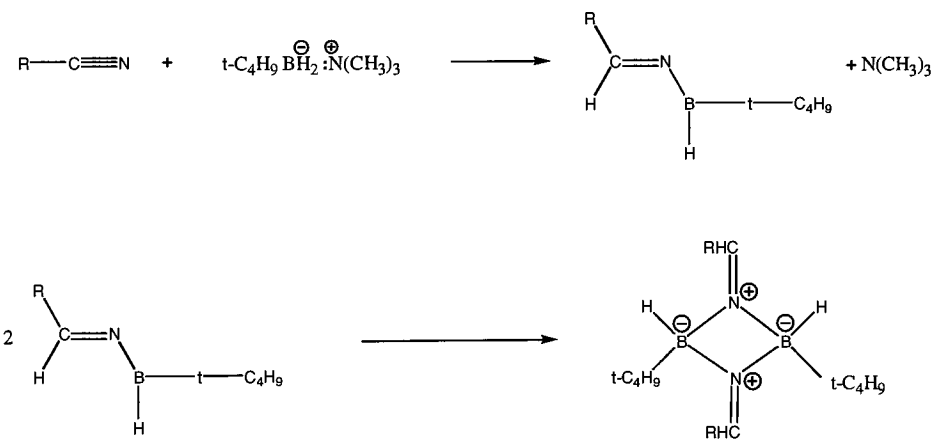
trialkylborazoles (5).[19] (5)

This intermediate is readily hydrolyzed by acid to the corresponding amine.[19] Further studies of the hydroboration reactions of acetonitrile, propionitrile, benzonitrile and acrylonitrile with diborane have reaffirmed the existence of such 1:1 borane-nitrile adducts which earlier were not well characterized .[19]

Brown and Subba Rao[18] have shown that diborane may function as a reagent for the reduction of nitriles to the corresponding primary amine.



The hydroboration reaction of representative nitriles were carried out with trimethylamine t-butyl borane.[22] Aliphatic nitriles such as acetonitrile, propionitrile, butyronitrile and isobutyronitrile were treated with equimolar quantity of trimethylamine completed to t-butylborane in dyglyme solution at 100^0. Analysis suggested the products to be 1:1 adducts of t-butylborane and starting nitrile.



Hydroboration reaction of aryl nitriles such as benzonitrile and its p-methoxy-, p-chloro-, p-fluoro, p-methyl and m-methyl derivatives with the trimethylamine t-butyl borane were carried out in the same condition as in the aliphatic nitriles. The products were similar to those of aliphatic nitriles. Again in this case, 1:1 adducts of the starting nitrile and t-butylborane were obtained.

Nitro compounds, as might be expected because of their very weakly basic properties, show no sign of reaction with borane-tetrahydrofuran under the mild test conditions over many hours. Sulfones, sulfonic acids, disulfides, and organic halides also are stable to the reagent. The reduction results with the standard substrates may be summarized as follows.

Aldehyde	→	alcohol
Ketone	→	alcohol
Acid chloride	→	very slow reaction
Lactone	→	glycol
Epoxide	→	alcohol (slow)
Ester	→	alcohol (slow)
Carboxylic acid	→	alcohol (fast)
Carboxylic acid salt	→	no reduction
Tertiary amide	→	amine
nitrile	→	amine
Nitro	→	no reduction
Olefin	→	organoborane (fast)

A study of the relative reactivity of a number of representative groups toward diborane in tetrahydrofuran indicated the following order of reactivity:[20]

carboxylic acids >olefins >ketones >nitriles >epoxides >esters >acid chlorides.

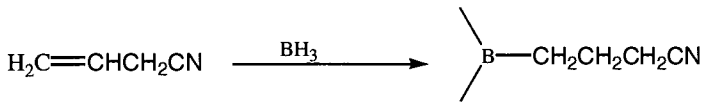
On the other hand , the order of reactivity toward alkali metal borohydride is:

acid chlorides >ketones >epoxides >esters >nitriles >carboxylic acids

With such markedly different reactivities, the judicious use of either diborane or alkali metal borohydrides permits the reduction of one group in the presence of a second, or the reverse. For example, in the half ester of a dicarboxylic acid it should be possible

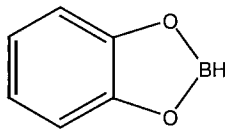
to use borane in tetrahydrofuran to reduce the free carboxylic acid group preferentially. Alternatively, by converting the free acid to the carboxylate salt, it should then be possible to reduce the ester group preferentially with lithium borohydride.

The hydroboration reaction of allyl cyanide has never been studied in detail. However there is a suggestion of the possible hydroboration of the double bond in allyl cyanide.[41]

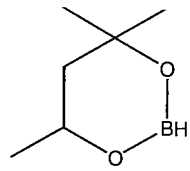


1.4. Hydroborations Using Catalysts

Usually a hydroboration needs no catalyst. However when the boron of the hydroborating agent is attached to heteroatoms that lower the electron deficiency at boron, then uncatalysed hydroboration requires elevated temperatures.[23,24,] Examples of such boranes are 1 and 2. Some fifteen years ago it was shown that hydroborations by catecholborane, 1 (catBH) could be catalyzed by some transition metal complexes so that reactions could be carried out at room temperature.[34]

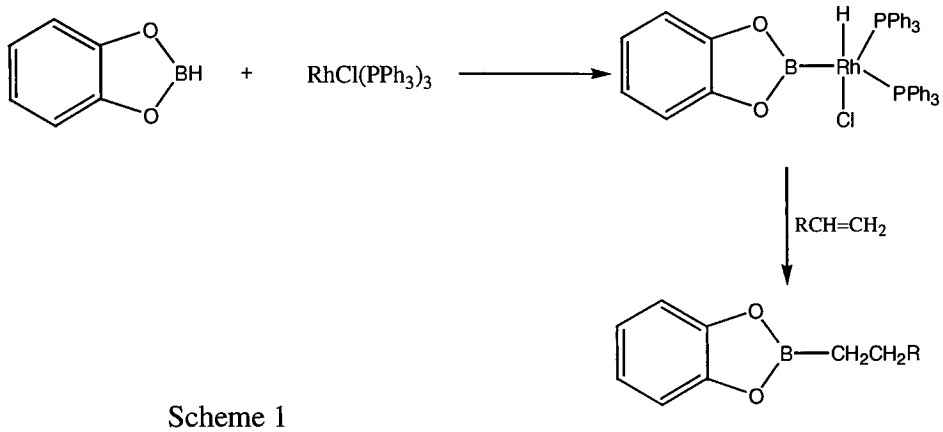


1



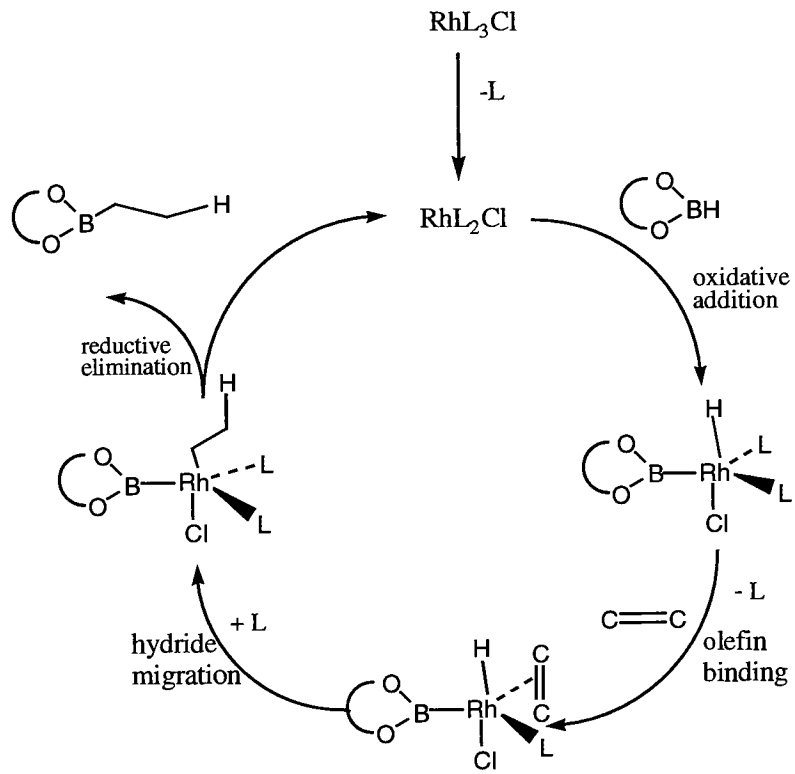
2

Catalyzed hydroborations are potentially valuable in organic syntheses when one is restricted by the chemo-, regio-, or stereoselectivity of conventional hydroborations. Consequently, many scientists[25-33] became interested in exploiting transition metal catalysis reactions in organic synthesis. It was clear from the beginning that the differences in products between the catalysed and uncatalysed reactions reflected different mechanisms of hydroboration. It was clear also that there was possibility of chiral hydroboration by the use of catalysts containing chiral ligands, which would allow for the introduction of chirality, depending on the turnover number. The most efficient catalysts for hydroboration appear to be rhodium complexes of the Wilkinson type.[34] These form H-Rh(III)-B, the most probable intermediates in the catalytic cycle, by addition of H-B. This intermediate can hydroborate alkenes (Scheme 1)



Scheme 1

The following catalytic cycle has been proposed by Mannig and Noth.[34]



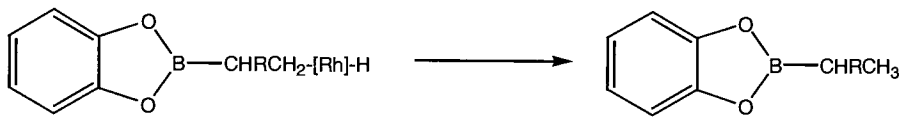
Scheme 2.

The first step is insertion between the B-H to give the intermedate which adds alkene. The third step, hydride migration leads to products followed by reductive elimination to give respectively the anti-Markovnikov and the Markovnikov products together with $RhCl(PPh_3)_2$ to complete the catalytic cycle.

Another possibility is the earlier insertion of the alkene into the Rh-B bond (boron migration) to give 3 and/or 4 which later undergo reductive elimination to give 5 and/or 6 (Scheme 3)

Scheme 3.

3 5



4 6

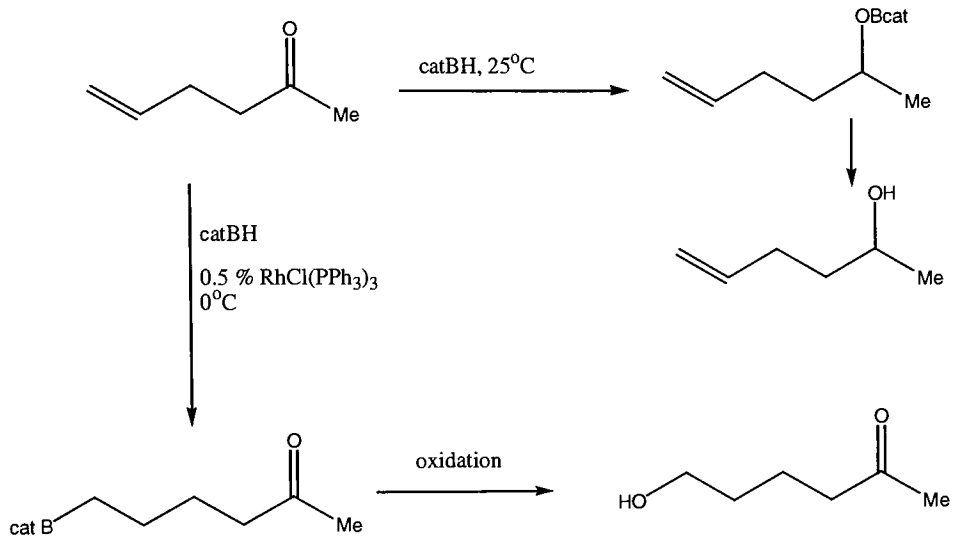
The insertion into a Rh-B bond has been proven by the diborylation of alkenes.The regioselectivity of hydroboration of simple terminal alkenes is almost the same for non-catalytic and catalytic hydroboration. [34,35,36] In both cases the *anti*-Markovnikov product is the major product (Table 1). The largest difference between the two processes is that catalytic hydroboration with catBH takes less than 5 min. at 20°C as compared with extended heating at 90°C for the non-catalytic reaction.[36]

Table 1 Regiochemistry of Hydroboration with catBH at 20°C (THF solvent)

		Anti-Markovnikov	Markovnikov
n	Catalyst	anti-Markovnikov	Markovnikov
7	None	98	2
3	$RhCl(PPh_3)_3Cl$	99	1
3	$Rh(nbd)(diphos)BF_4$	90*	10
3	$Ir(COD)(Pcy_3)Py)PF_6$	98	2

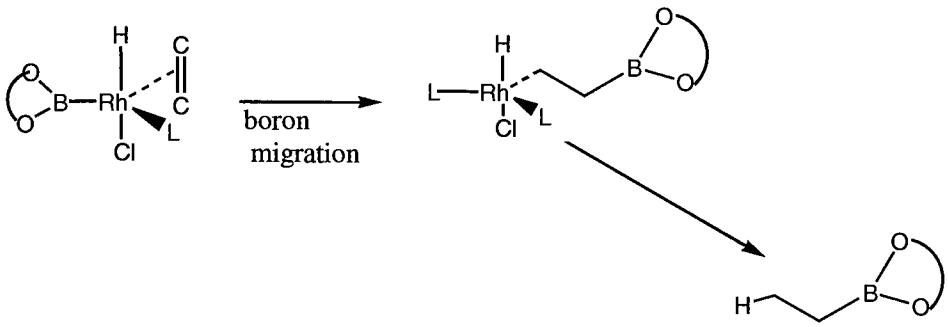
*Ratio becomes 97:3 at –40°C
nbd and diphos are ligands.

The nature of the solvent is unimportant when using Wilkinson and iridium complexes, but regioselectivity using a cationic rhodium complex improved upon changing solvent from THF to ether and then to 1,2-dichloroethane.[36]The catalytic reaction can be *chemoselective* in a different fashion from the uncatalyzed reaction[34] (Scheme 4), thus enhancing its value.



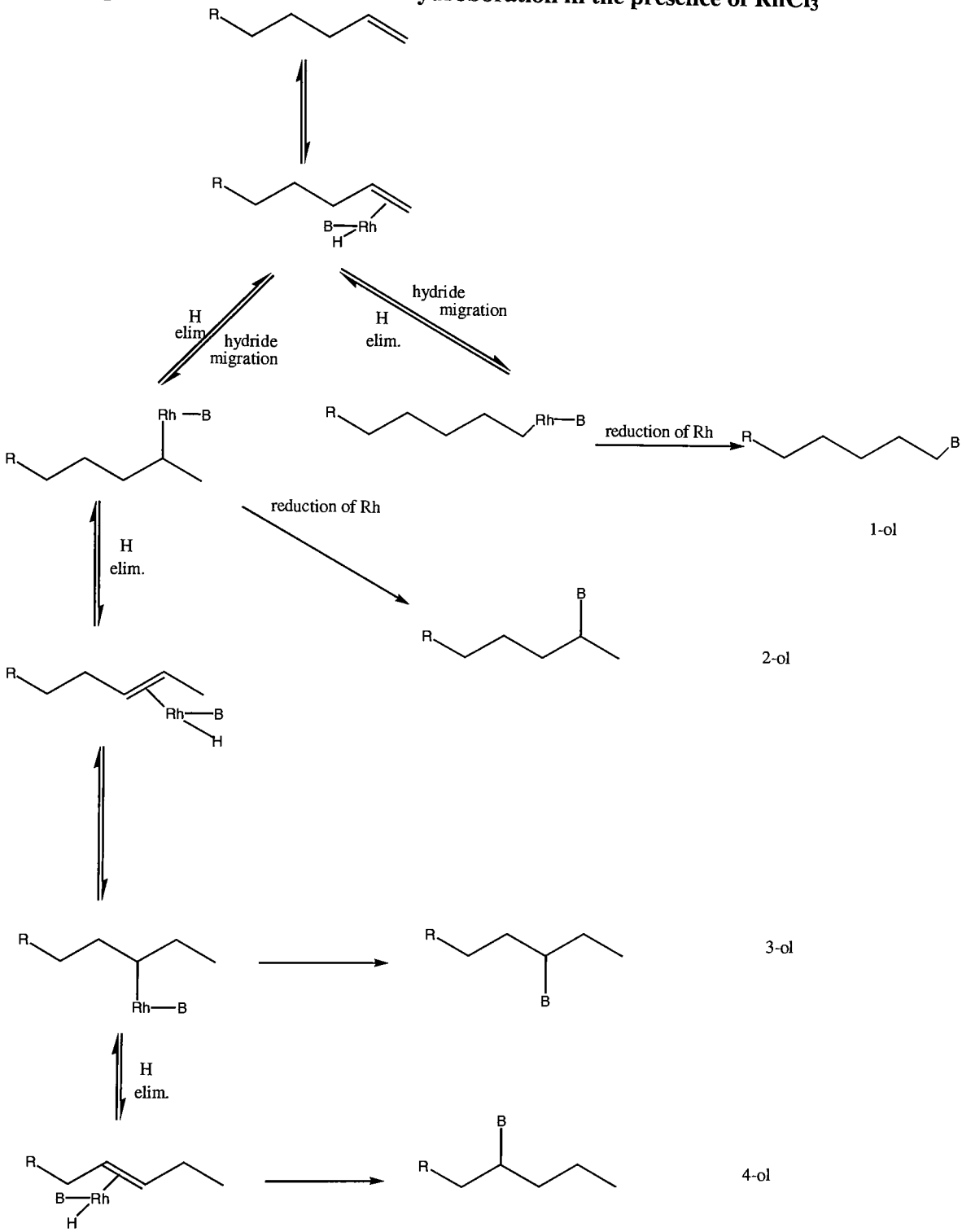
Scheme 4

Evans refined the Mannig-Noth mechanism by proposing 1) the possibility of boron migration rather than hydride and 2) the reversibility of elementary steps of the catalytic cycle.[37]



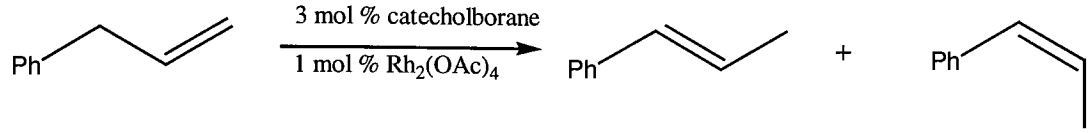
Formation of multiple alcohol isomers from alkenes after hydroboration reactions is easily explained by the reversibility of elementary steps of catalytic cycle:

Complete Mechanism of Alkene Hydroboration in the presence of $RhCl_3$

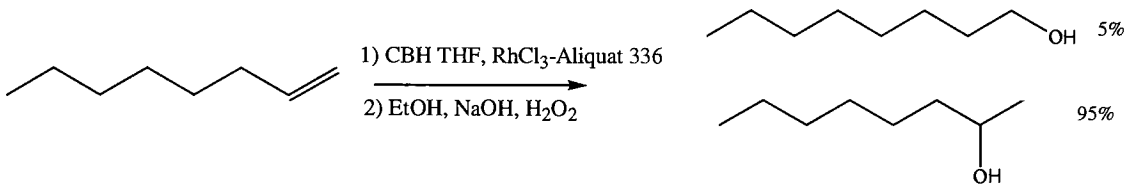


This is the work of Mr.Anvar Buranov, a member of the research group of Dr.Morrill from 1999-2001 at Rochester Institute of Technology, Rochester, NY.

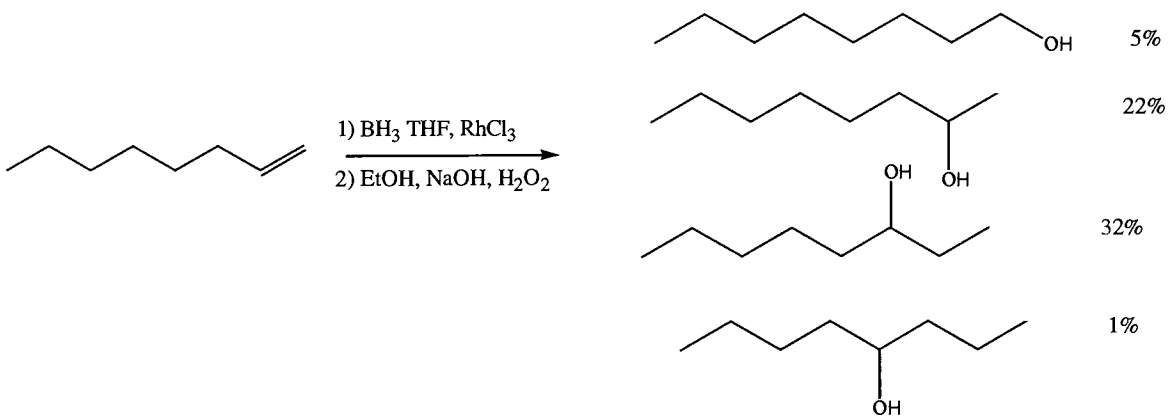
M. Doyle of Trinity University in Texas and M. Protopopova of Zelinsky Organic Chemistry Institute in Russia suggested that the olefin isomerization induced by Rh(II) might be caused by a Rh-H species after comparing their results of hydrosilylation reactions which causes alkene isomerization.[38]



$RhCl_3$ was used as a catalyst for the first time by a graduate student of RIT , Lu Yang, a member of Dr.Morrill's research group. She found that regioselectivity can be reversed in hydroboration reaction of alkenes with catecholborane in the presence of $RhCl_3$.[39]



A more recent graduate student, Anthony J. Sampognaro, from Dr. Morrill's research group, found that $RhCl_3$ not only does reverse the regioselectivity but it can induce alkene isomerization.[40] Sampognaro did show, however, that the Rh(III) induced alkene

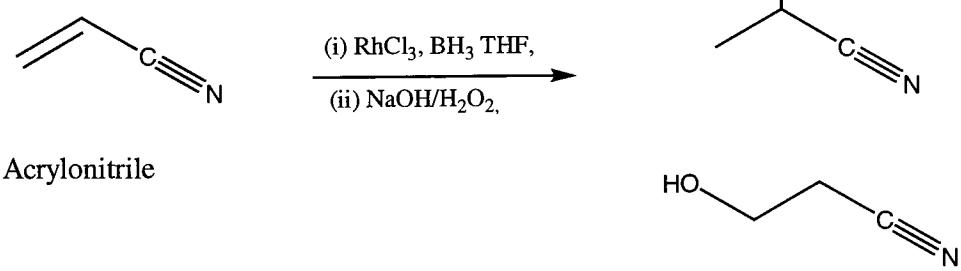


isomerization was too slow to account for the 95% product in Lu Yang's work. Sampognaro also showed that the 95% Lu Yang product was actually a mixture of 2-, 3-, and 4- octanols.

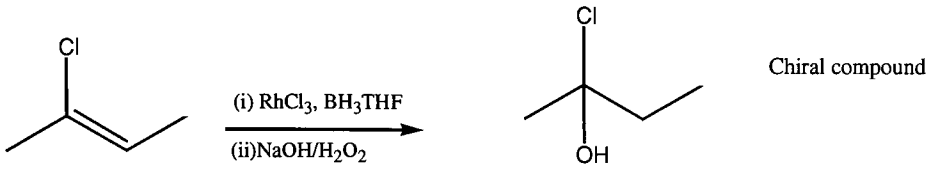
Objective

Recent studies on hydroboration of simple alkenes in the presence of $RhCl_3$ in our lab showed novel regioselectivity and as well as some isomerization. Hydroboration of unsaturated compounds containing functional groups lead to interesting results because of the substituent effect of the group and these results have been described in the preceding sections. Therefore we decided to study the catalytic effects of $RhCl_3$ upon hydroboration of alkenes containing functional groups and carbon-nitrogen triple bonds. Because carbon-triple bonds were not studied in detail, it seemed to be more interesting to examine the effect of $RhCl_3$ in the well-studied systems like alkenyl chlorides. We have chosen several representatives of alkenyl nitrile and alkenyl chloride molecular classes as alkenes containing fuctional groups.

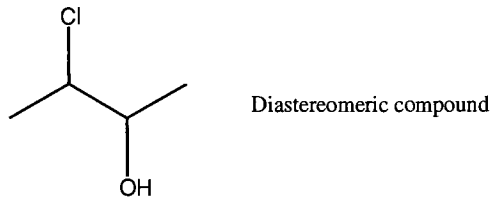
The main purpose of this research is to study the effect of the catalyst $RhCl_3$ in the hydroboration of alkenyl nitriles and alkenyl chlorides and as well to make chiral products. From the previous work similar to the systems chosen, I expected the following racemic mixtures of chiral products and diastereomeric products.



Acrylonitrile



2-chloro-2-butene



Yield and product ratio were of interest.

The following representative alkenyl nitriles and alkenyl chlorides have been subjected to hydroboration and the results are described in Sect.3.

- **Representative Nitriles**

Allyl Cyanide (3-butenenitrile)

Acrylonitrile

5-Hexenenitrile

Acetonitrile

Propionitrile

2-Chloropropionitrile

3-Chloropropionitrile

- **Alkenyl Chlorides**

Allyl Chloride (3-Chloro-1-propene)

3-Chloro-2-methylpropene

1-Chloro-2-methylpropene

Crotyl Chloride (1-Chloro-2-butene)

2-Chloro-2-butene

2.0. Experimental

2.1. Instrumentation

All chemicals were obtained from Aldrich Chemical Company. Gas Chromatography-Mass Spectrometer (GS/MS) analyses were performed on a Hewlett Packard model 5995c with the following capillary column and dimensions: HP-5 [poly(5%-diphenyl-95% dimethyl-siloxane)] 60m x 0.25mm x 0.25μm. Nitrogen carrier gas flow rate was 33.4 ml/min. The GC/MS temperature range for analyses of alkenyl nitriles was 60-250^{0}C and for alkenyl chlorides was 40-160 ^{0}C.

All of the reactions were carried out while flushed by ultra pure nitrogen gas. The reaction set-ups for hydroboration is displayed on the next page (Fig.1). This set up consisted of the following: reflux condenser, three-neck flask, nitrogen inlet, septum, stirring bar, stirrer. See Fig.1 on the next page.

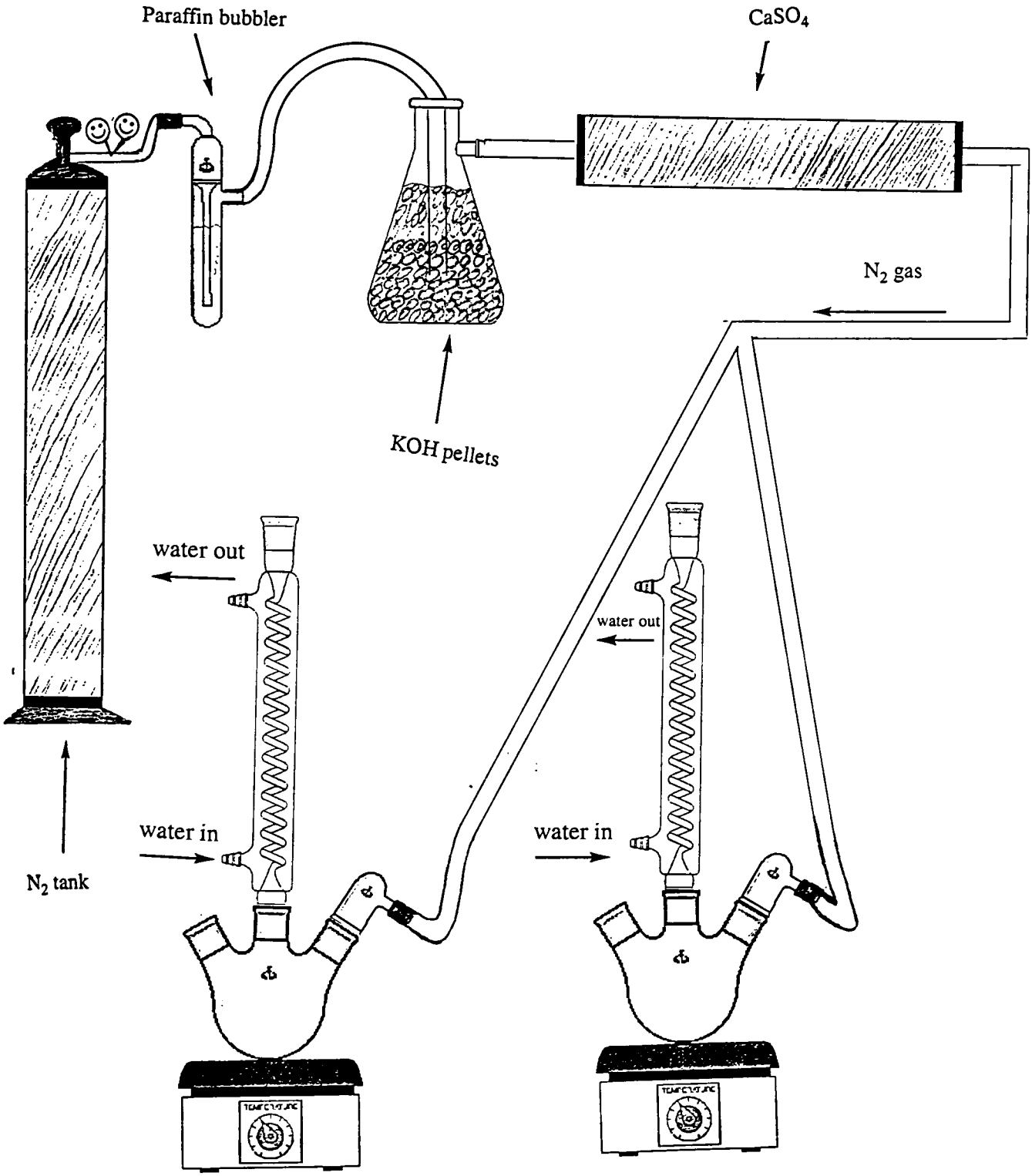
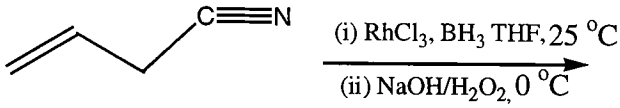


Figure 1. Reaction system for the hydroboration of alkenyl nitriles and alkenyl chlorides.

2.2. Typical Procedure for the Hydroboration of Alkenyl Nitriles

Example: Allyl Cyanide (3-Butene nitrile).



(See pages 36-40 for the products)

An oven dried, round bottom, three-neck flask was cooled down with the flush of ultrapure nitrogen for 5 min. Place 10 mg of $RhCl_3$ into the flask. Add 10 ml of freshly distilled THF to the flask. Stir the mixture until the $RhCl_3$ completely dissolves in the THF. Add 1.0 ml (0.0125 mol) of allyl cyanide to the solution. Let it stir for 10 min. Install a water-cooled condenser on the middle neck of the flask to prevent the solvent escape and on the neck on the left install septum. On the right neck, the adapter of nitrogen flow is attached. Add 3 ml (0.03 mol) of 0.1 M BH_3 in THF (0.03 mol of BH_3) to the flask slowly through septum using a syringe. The color of solution becomes yellow. Let the reaction mixture stir for 2 hours. Then add 10 ml of 30% H_2O_2 and 10 ml of 3 M NaOH into the reaction mixture. A weakly exorthermic reaction becomes more exorthermic (70°C) in 5 min. After 4 hours filter the solution and extract with 40 mL of diethyl ether at least three times. Remove the extra solvent with rotator evaporator and analyze on GC/MS. See the next page for the sample gas chromatograph and mass spectrum.

Conditions in GS/MS for the separation of products resulting from the hydroboration of alkenyl nitriles:

Initial temperature: 60 ^{0}C

Initial time (solvent delay): 4.00 min

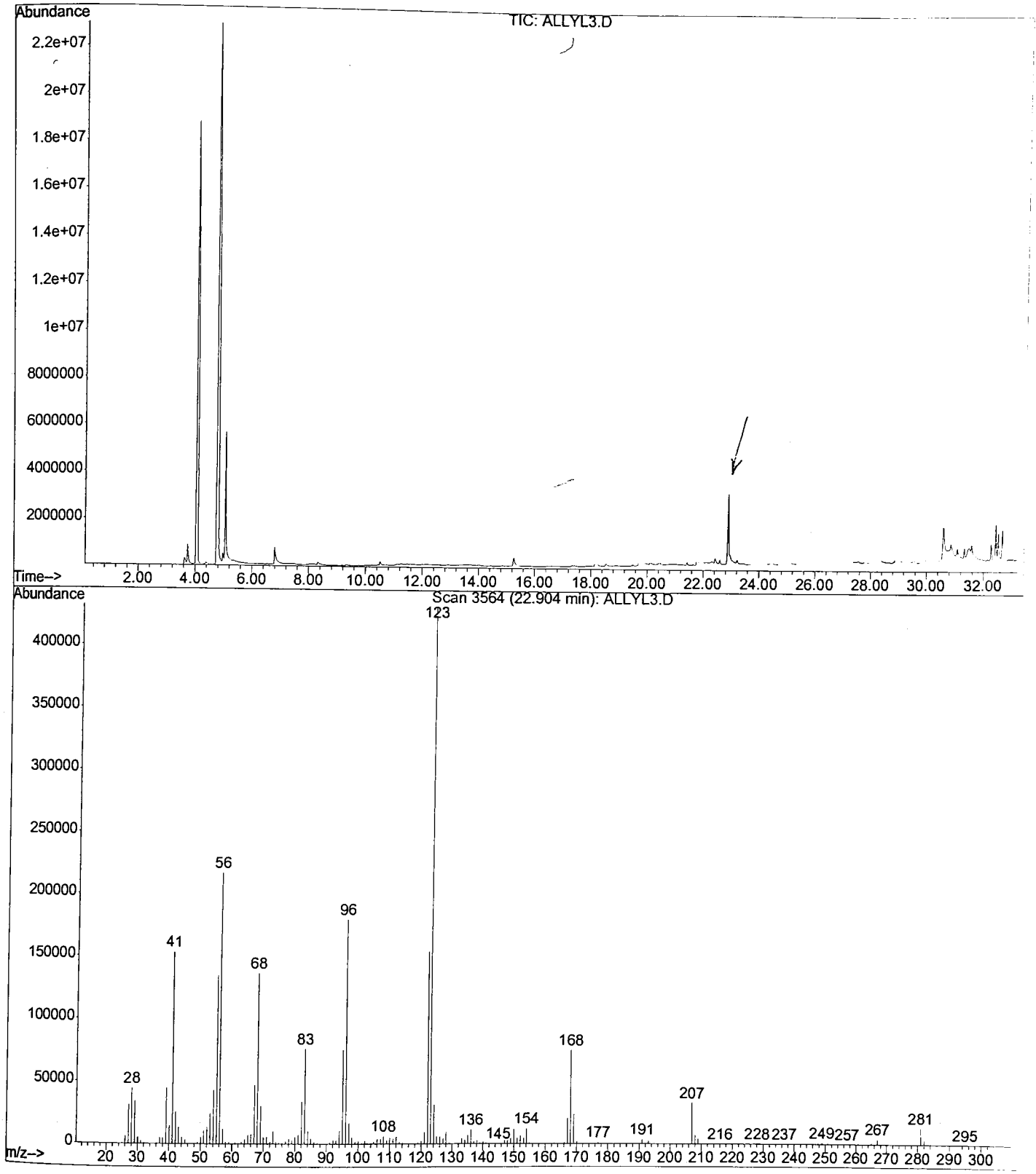
Rate: 5 ^{0}C/min

Final Temperature: 250 ^{0}C

Inlet Temperature: 260 ^{0}C

Splitless condition

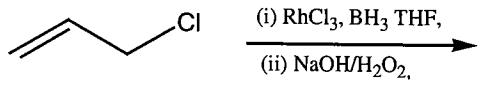
Total carrier gas flow rate (nitrogen): 33.4 ml/min



I. Sample Gas chromatogram and mass spectra of 2,6-dimethylpyrimidinamine, a product from the hydroboration of allyl cyanide.

2.3. Typical Procedure for the Hydroboration of Alkenyl Chlorides

Example: Allyl Chloride



(see pages 45-46 for products)

An oven dried, round bottom, three-neck flask (300 ml) is cooled down with a flush of ultra pure nitrogen for 5 min. Place 10 mg of $RhCl_3$ in the flask. Add 10 ml of THF (distilled) to the flask. Stir the mixture until the $RhCl_3$ completely dissolves in the THF. Add 1.0 ml (0.012 mol) of allyl chloride to the solution. Stir for 10 min. Install a water-cooled condenser on the middle neck of the flask to prevent the solvent escape, and on the neck on the left install a septum. On the right neck, a nitrogen adapter is attached. Add 3 ml (0.03 mol) of BH_3 in THF into the flask slowly through septum using a syringe. The color of solution becomes yellow. The reaction mixture is stirred for one hour. Then add 10 ml of 30% H_2O_2 and 10 ml of 3M NaOH to the reaction mixture. This is normally an exothermic reaction (80°C). After 2 hours filter the solution and extract with 40 ml. of diethyl ether. Remove the extra solvent with rotator evaporator and analyze on GC/MS. See the next page for the sample gas chromatogram and mass spectra.

Conditions in GC/MS for the separation of products resulting from the hydroboration of alkenyl nitriles:

Initial temperature: 40 ^{0}C

Initial time (solvent delay): 0.00 min

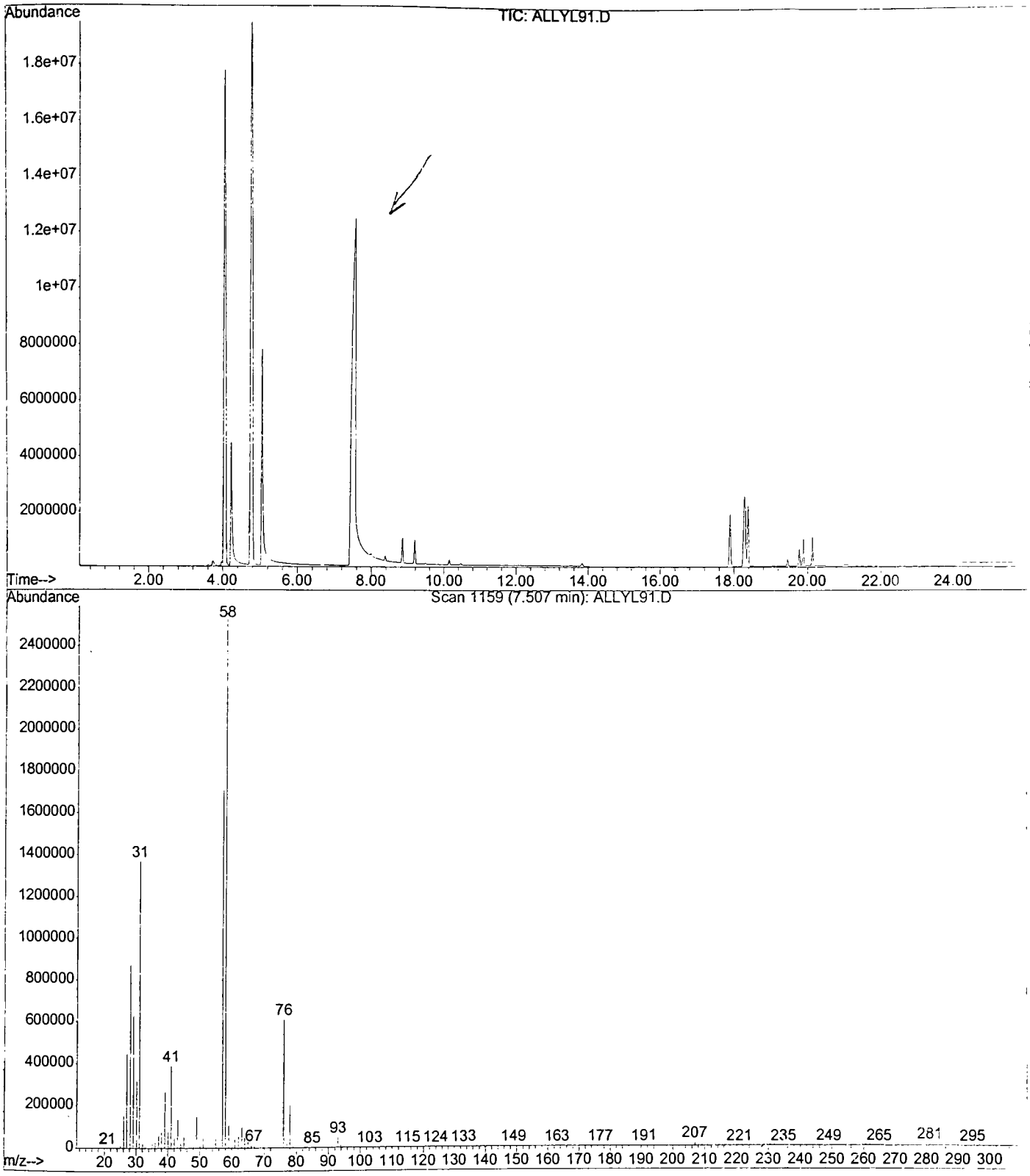
Rate: 5 ^{0}C/min

Final Temperature: 140 ^{0}C

Inlet Temperature: 250 ^{0}C

Splitless condition

Total carrier gas flow rate (nitrogen): 33.4 ml/min



II. Gas chromatogram and mass spectra of 3-chloro-1-propanol, a product from the hydroboration of allyl chloride.

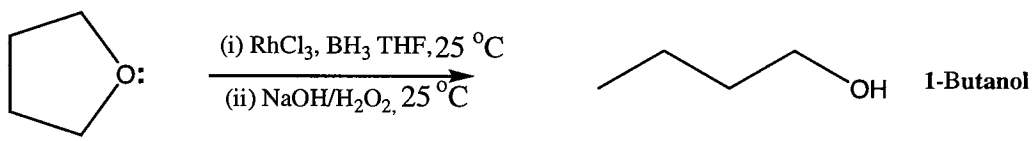
3.0. Results and Discussion

Solvent Effects in Hydroboration Reactions and the Assosiated Side Reactions

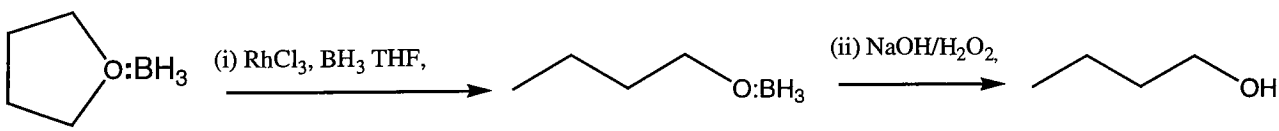
Changes in the solvent (tetrahydrofuran and dichloromethane) used for hydroboration did not affect the the main results of reactions. However, some side reactions apparently due to these solvents were observed. These side reactions interfered with the identification of the products.

1) BH_3:THF in THF

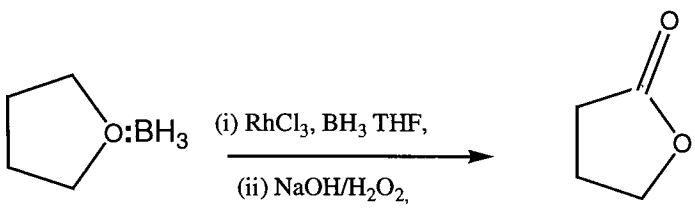
Tetrahydrofuran undergoes the following ring opening reaction:



Apparently this ring opening reaction occurs with the THF in the BH_3:THF complex. This conclusion is based on the results of many hydroboration reactions. When the amount of BH_3:THF complex was increased, the amount of 1-butanol increased. However, this likely does not affect the hydroboration of interest and can be ignored. The following transformation was suggested for the stepwise reaction.



During the hydroboration reaction of nitriles, this reaction can produce more highly oxidized products like butyrolactone.



2) BH_3:$S(CH_3)_2$ in dichloromethane

With dichloromethane such kinds of ring opening reactions did not occur and it served as good solvent for the comparison. The extremely bad smell of the borane-dimethylsulfide prevented its use.

Other solvents (diethyl ether and toluene) were not used because $RhCl_3$ did not dissolve very well in them.

3.1.0. Hydroboration of Representative Nitriles

3.1.1. Hydroboration of allyl cyanide (3-butenenitrile) in the presence of $RhCl_3$ lead to the following transformations.

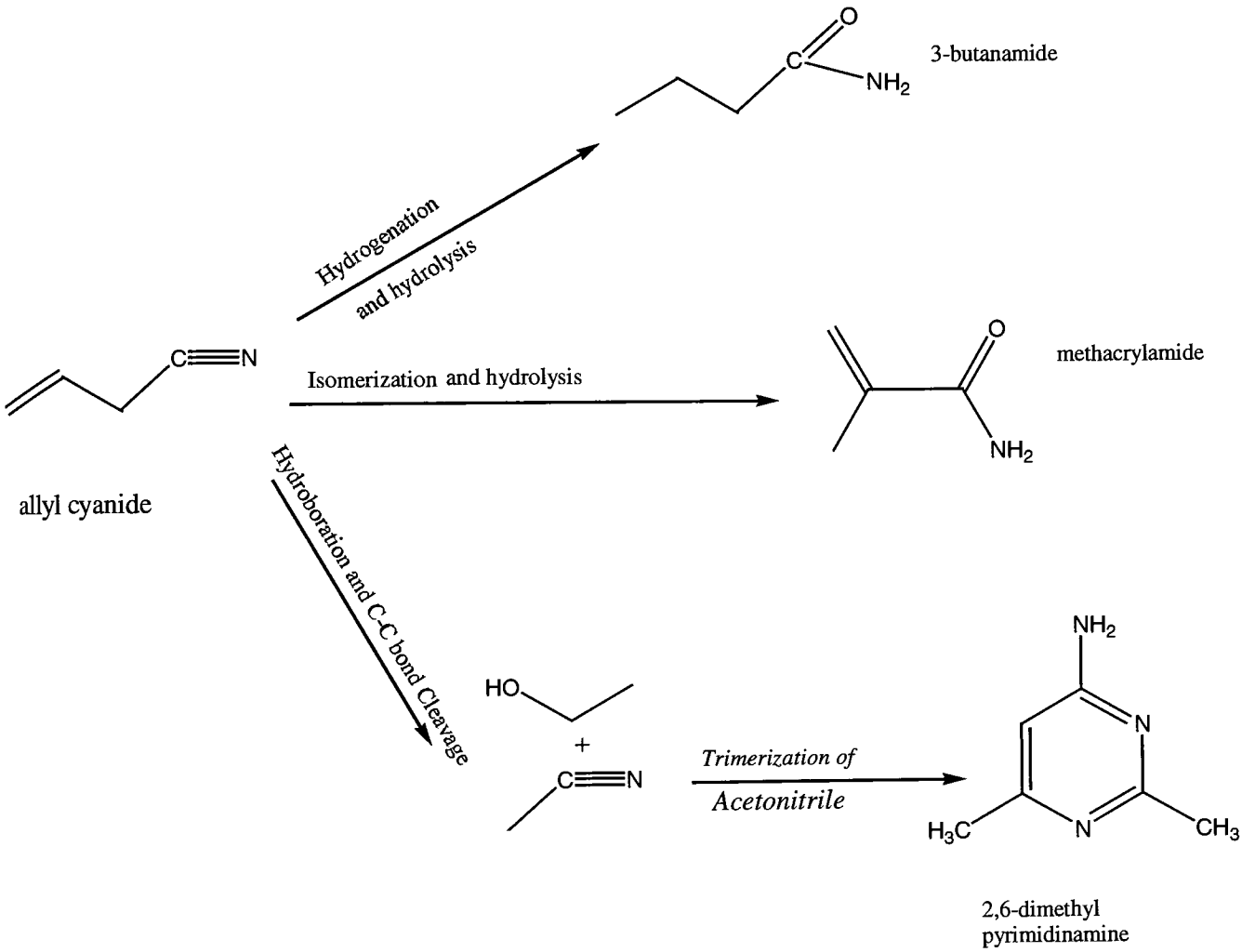


Table I. Hydroboration of Allyl Cyanide with Borane in the presence of $RhCl_3$

Selective synthesis by changing the ratio of reactants

Exp. #	Allyl Cyanide (ml)	Borane (ml)	Volume Ratio	Mole Ratio	Total Yield (%)	Yield of Ethanol (%)	Yield of Products *Hydro-n/Isomer-n/Trimeri-n* (%)
1	1.00	15.00	1:15	1:1.5	60	15.07	13.62/0.00/71.30
2	1.00	10.00	1:10	1:1	60	16.33	31.30/0.00/52.33
3	1.00	5.00	1:5	1:0.5	55	9.95	68.25/0.00/22.00
4	1.00	3.00	1:3	1:0.3	40	3.44	58.74/33.38/4.44
5	1.00	2.00	1:2	1:0.2	40	12.33	71.36/16.30/0.00
6	1.00	1.00	1:1	1:0.1	61	4.60	0.00/95.40/0.00
7	1.00	0.50	2:1	1:0.05	50	2.44	0.00/97.56/0.00
8	1.00	0.25	4:1	1:0.025	60	2.43	0.00/97.57/0.00
9	1.00	0.00	1:0	1:0.00	20	1.90	0.00/50.0/0.00

Hydroboration of allyl cyanide at elevated temperature resulted in the hydrogenation of only the C=C double bond.

Table II. Kinetic study of the Hydroboration reaction of Allyl Cyanide

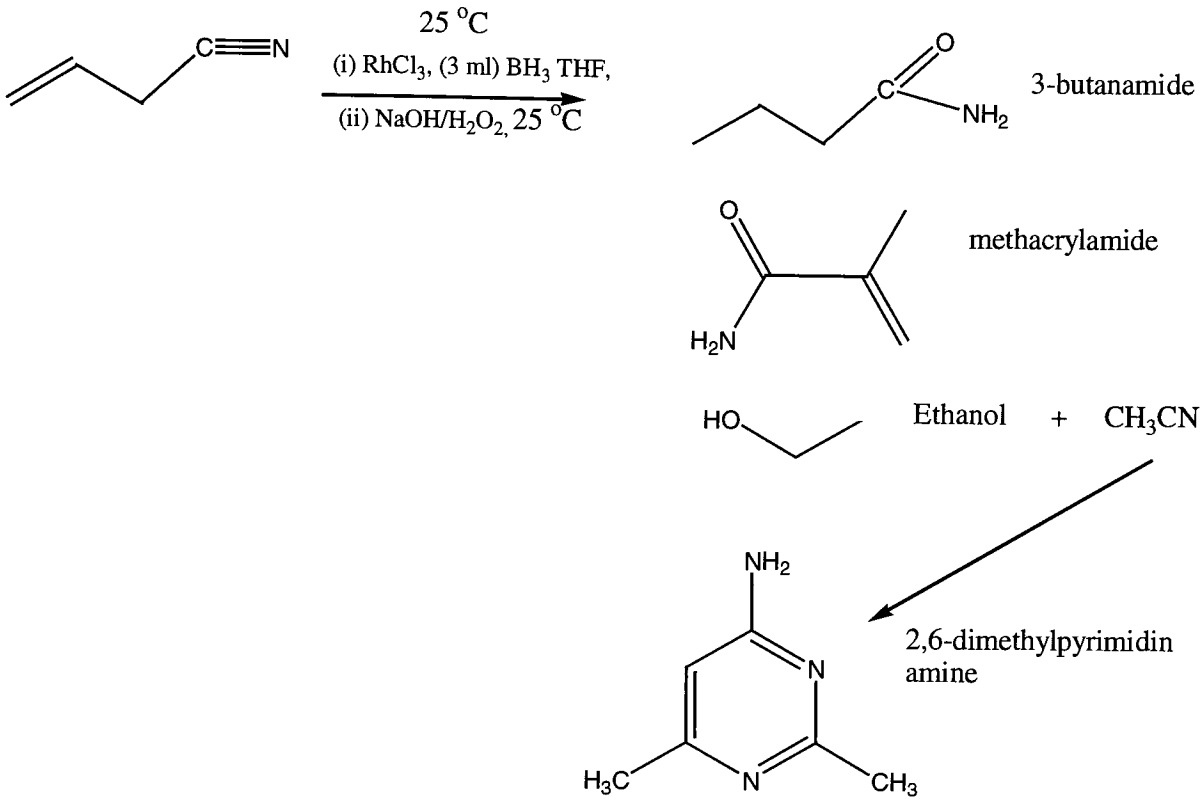
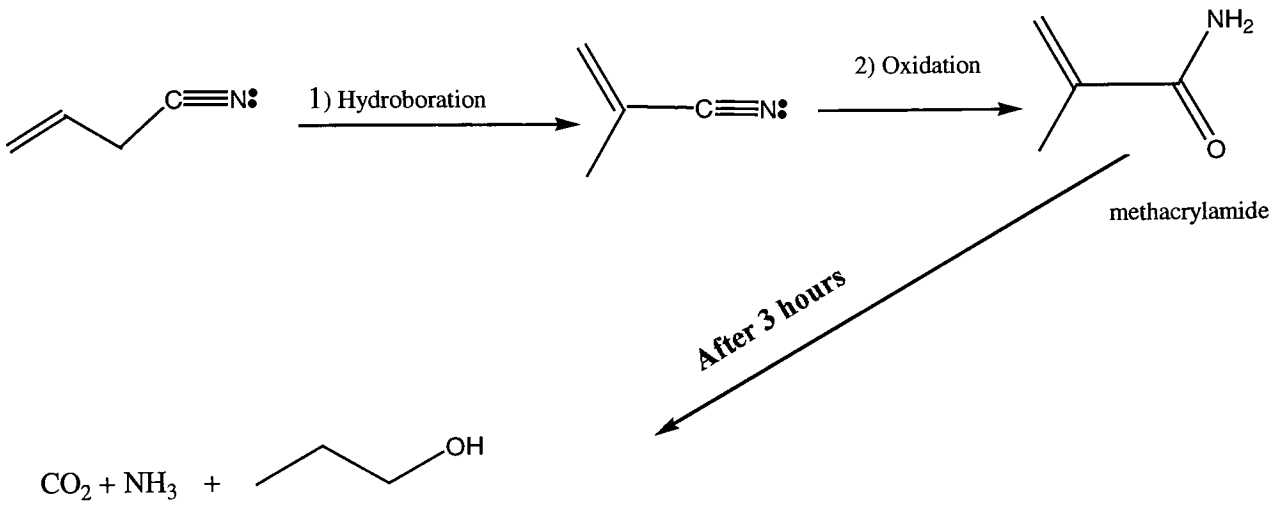


Table II. Kinetic Study of Hydroboration of Allyl cyanide (results are percentage of total product).

Exp. #	Time (hr)	Butanamide	Methacrylamide	Uncoupled Acetonitrile	Ethanol	2,5-dimethyl pyrimidinamine
1	0.25	68	32	0.00	0.00	0.00
2	0.5	54	15.75	2	21.5	6.5
3	1.0	51.2	17.3	2	22.6	6.8
4	1.50	33.34	13.34	5.7	37	10.5
5	2.0	45	25.5	8	18	3.34
6	3.0	68.4	10.3	10.6	10.6	2.54
7	5.0	80.6	14.5	2.5	2.5	3.00

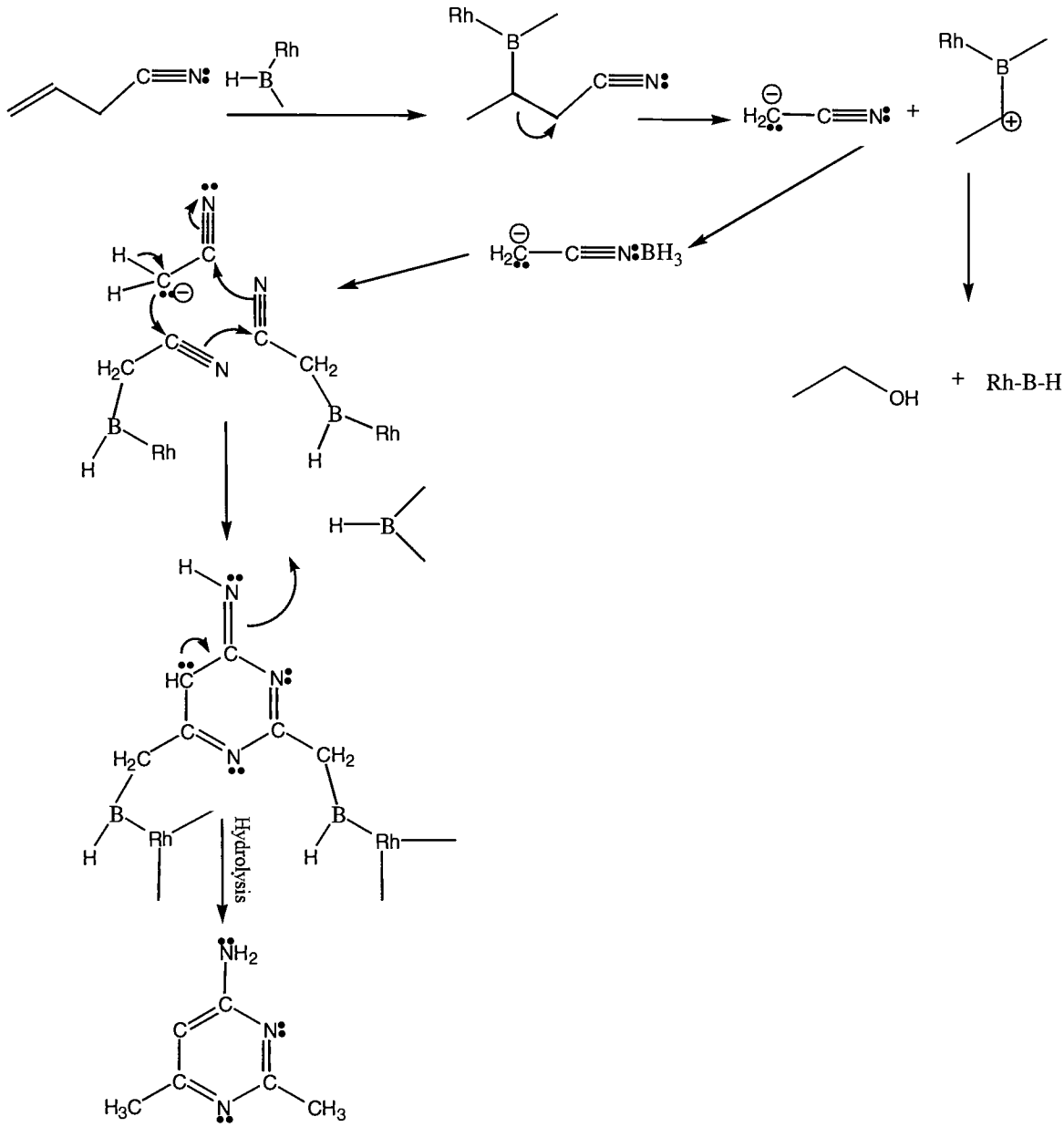
Trimerization gives rise to the results in the last column of Table II. The fact that the amount of acetonitrile and 2,6-dimethylpyrimidinamine [(6.5)(3)+2] is equal to the amount of ethanol (21.5) is an indication of trimerization as the same of the heterocycle. After 3 hours of hydroboration another side reaction, propanol formation began. Perhaps the source of propanol is methacrylamide.



1-Propanol

In addition to the above compounds

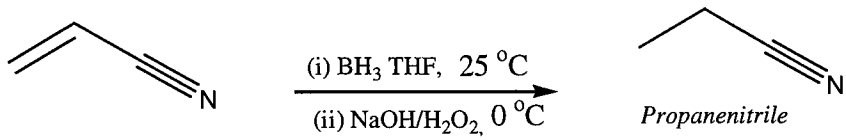
Mechanism for the formation of 2,6-dimethylpyrimidinamine



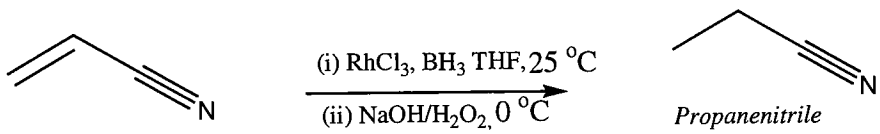
The structure of 2,6-dimethylpyrimidin has been established with Mass Spectrometer and NMR after the separation with HPLC.

3.1.2 Hydroboration of Acrylonitrile

Hydroboration of acrylonitrile yields propanenitrile which is the hydrogenation product of the carbon-carbon double bond reduction of acrylonitrile. Both room temperature and reflux conditions also afforded the same product.



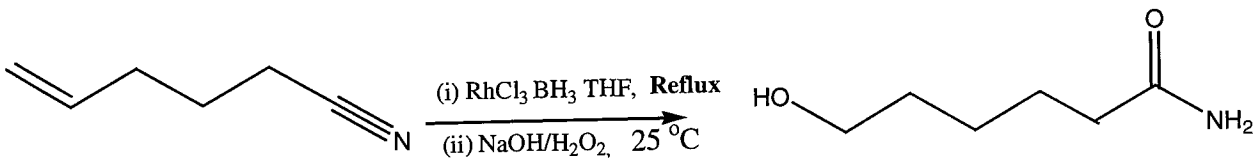
Acrylonitrile *Propanenitrile*



Acrylonitrile *Propanenitrile*

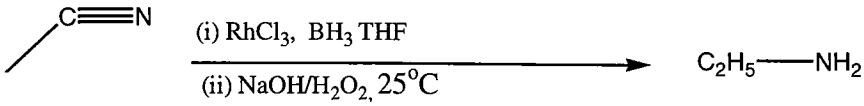
3.1.3. Hydroboration of 5-Hexenenitrile

Hydroboration of 5-hexenenitrile gave hydration product on the carbon-carbon double bond.



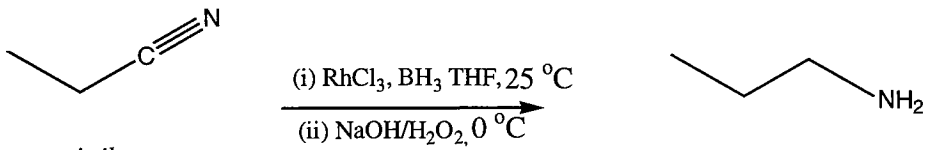
3.1.4. Hydroboration of Acetonitrile

Acetonitrile that forms complex compounds with borane can be easily reduced by BH_3-THF in the presence of $RhCl_3$ at room temperature



3.1.5. Hydroboration of Propionitrile

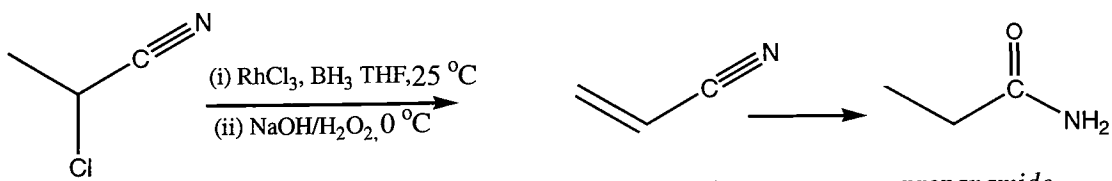
Propionitrile can be even more easily hydrogenated than acetonitrile at the nitrile group in the presence of $RhCl_3$. The only difference between uncatalyzed and catalyzed hydroboration of propionitrile is the speed. The latter is faster.



Propanenitrile *1-Propanamine*

3.1.6. Hydroboration of 2-Chloropropionitrile

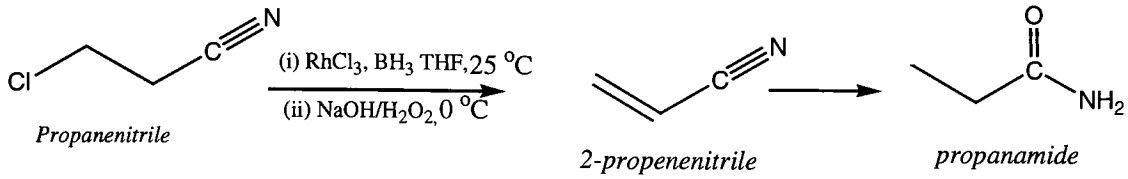
Hydroboration of 2-chloropropionitrile results in 2-propenamide, the elimination product which is hydrogenated to give propanamide



Propanenitrile *2-propenenitrile* *propanamide*

3.1.7. Hydroboration of 3-Chloropropionitrile

The hydroboration of 3-chloropropionitrile gave the same products with the 2-chloropropionitrile. However, the rate of the reaction was slower.



Propanenitrile *2-propenenitrile* *propanamide*

Table III. Relative Rates of Hydroboration of Nitriles with Borane and $RhCl_3$. See Fig.1.

Time, t	0	0.25	0.5	1	1.5	2	3	5
Propionitrile	0	23	25	26	27	28	29	29
Acteonitrile	0	20	21	22	22	23	23	23
3-ChPNitrile	0	15	16	16	17	17	22	23
2-ChPNitrile	0	13	14	14	15	15	20	21
Acrylonitrile	0	5	6	6.5	7	7	10	12
Allyl cyanide	0	10	11	11.5	12	13	13	14
Hexenenitrile	0	3	3.5	4	4.3	4.7	4.9	5

The numbers indicate the loss of original compound. The units are in mole/hour. Relative rates of nitriles vary whether it contains double bond. The presence of more reactive double bond makes nitrile group indifferent towards reduction until it is completely reduced.

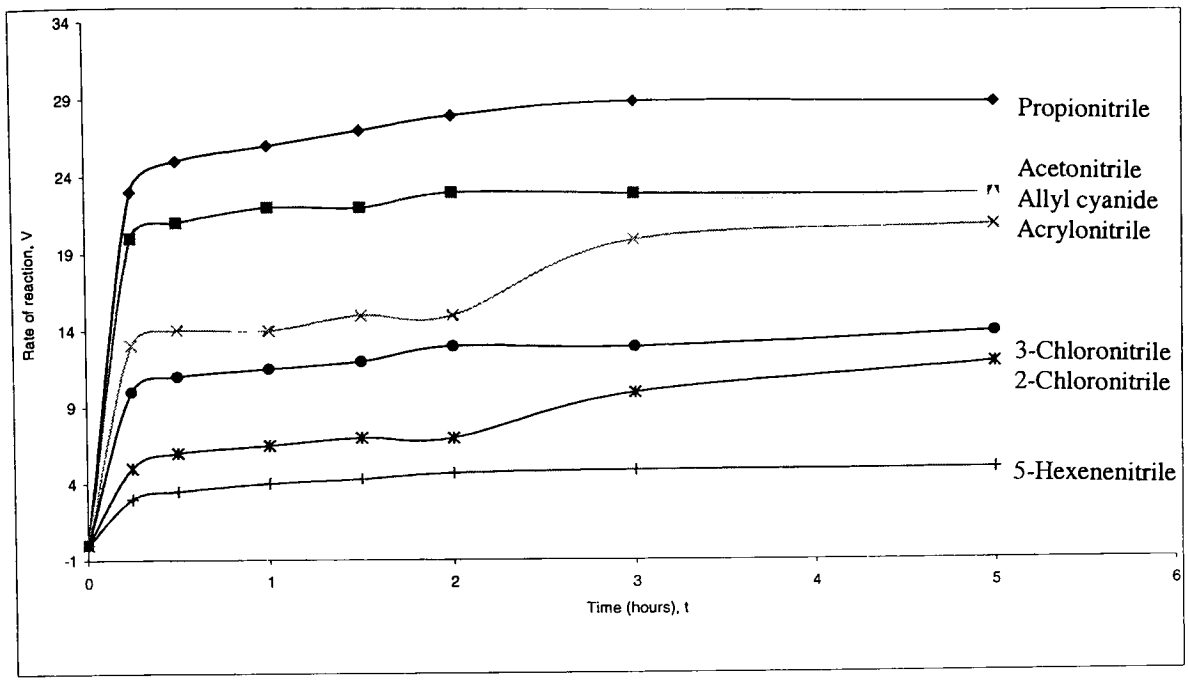


Fig. I. Relative Rates of Hydroboration of Nitriles with Borane and $RhCl_3$.

The tolerance of nitrile groups to hydroboration has been examined and the following sequence has been suggested:

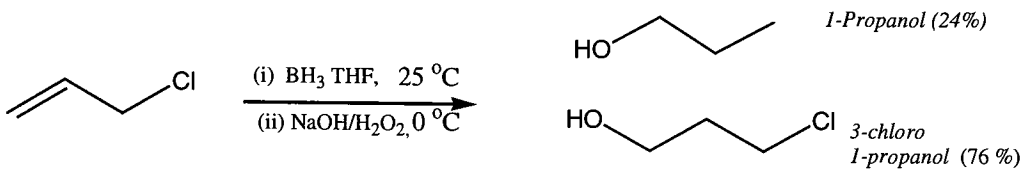
allyl cyanide>2-chloropropionitrile>3-chloropropionitrile>acetonitrile>propionitrile

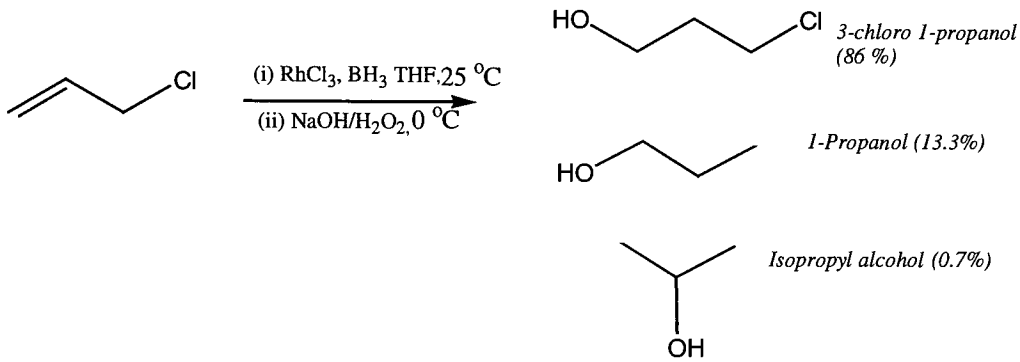
Nitriles containing electron withdrawing groups are less reactive towards hydroboration than nitriles with electron donating groups.

3.2.0. **Hydroboration of Alkenyl Chlorides**

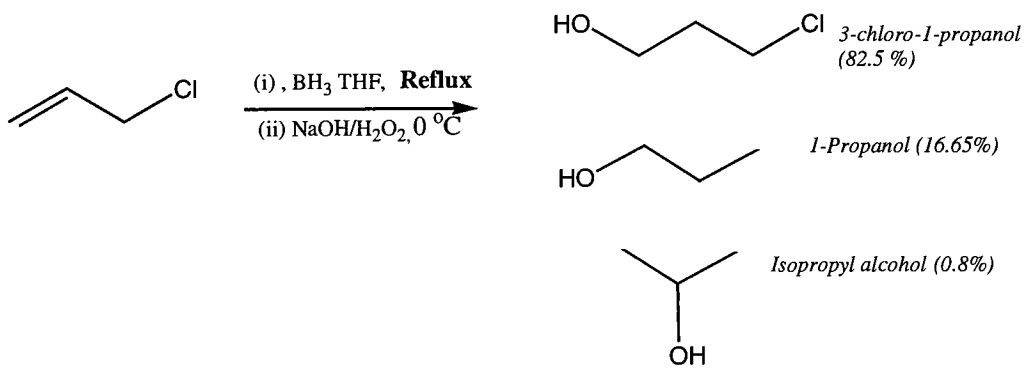
3.2.1. Hydroboration of Allyl Chloride (3-Chloro-1-propene)

Hydroboration of allyl chloride has been carried out according to the general procedure described in section 2.4. The yield of products is 72% .



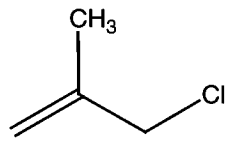


The use of $RhCl_3$ as a catalyst in the hydroboration reaction of allyl chloride increased the proportion of the main product (3-chloro-1-propanol) and it also made possible the formation of a new product isopropyl alcohol. The increase in temperature had the same influence as did $RhCl_3$ on the hydroboration reaction of allyl chloride. For example:



3.2.2. Hydroboration of 3-Chloro-2-methylpropene

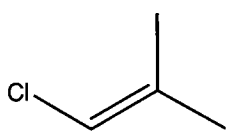
Hydroboration of this compound was unsuccessful. This compound can be viewed as the methylated derivative of allyl chloride. The insertion of methyl group on the second carbon atom prevented it from hydroboration. Neither catalyst nor temperature have an impact.



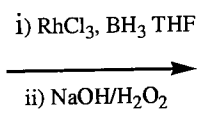
3-chloro-2-methylpropene

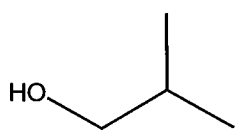
3.2.3. Hydroboration of 1-Chloro-2-methylpropene

The hydroboration of this compound without catalyst was unsuccessful. However, in the presence of $RhCl_3$ it gave 2-methyl-1-propanol. The yield is 45%



1-chloro-2-methylpropene



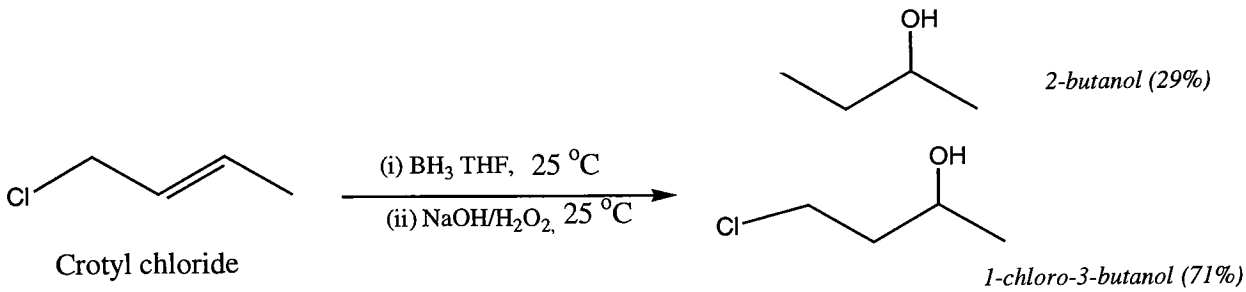


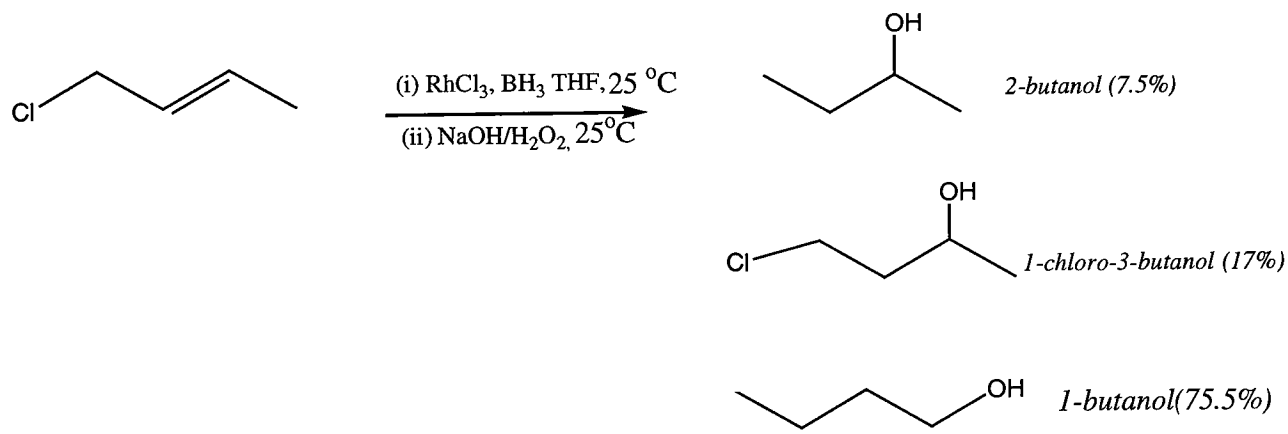
2-methylpropanol

Only product

3.2.4. Hydroboration of Crotyl Chloride (1-Chloro-2-butene)

Hydroboration of crotyl chloride has been carried out according to the general procedure for alkenyl chlorides in section 2.4. A volume of 1 ml of crotyl chloride has been used. In this reaction the formation of 1-butanol from BH_3:THF complex interfered with the determination of product identity and ratio. Thus this reaction was carried out as well in dichloromethane. The yield is 65%.

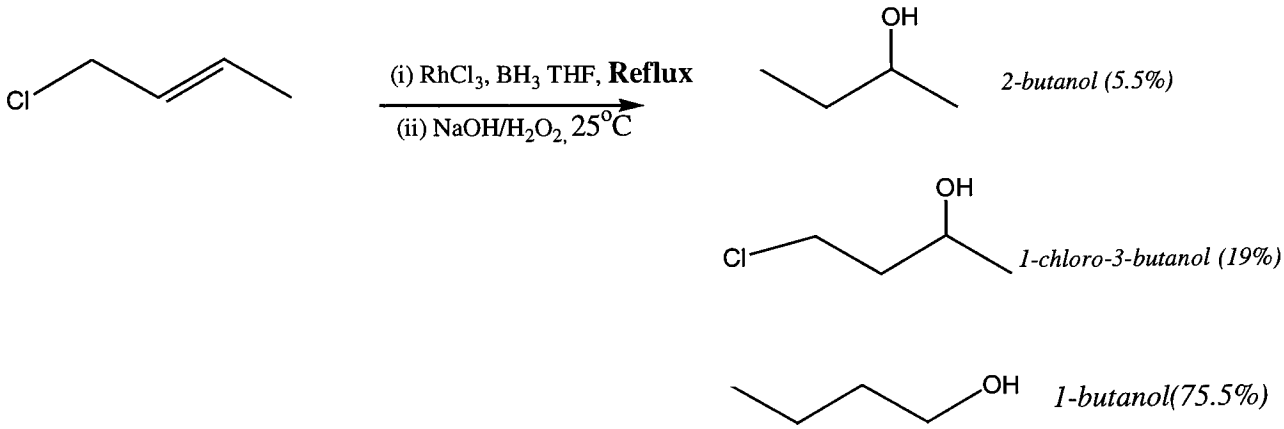




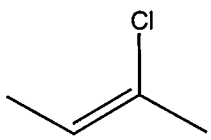
The GC/MS analysis of crotyl chloride starting material purchased from Aldrich and TCI indicated the presence of 80 % 3-chloro-2-methyl-1-propene. However the pure 98% 3-chloro-2-

methyl-1-propene did not give the same products that crotyl chloride gave. Thus, GC/MS analysis of the crotyl chloride reaction has been interpreted as misleading.

Reflux condition considerably affected the ratio of 3-chloro-2-butanol:2-butanol in the absence of catalyst. The 2.45:1 ratio is in normal and 3.7:1 is observed at reflux condition. Increase in temperature in the presence of $RhCl_3$ favored the formation of more 3-chloro-2-butanol.



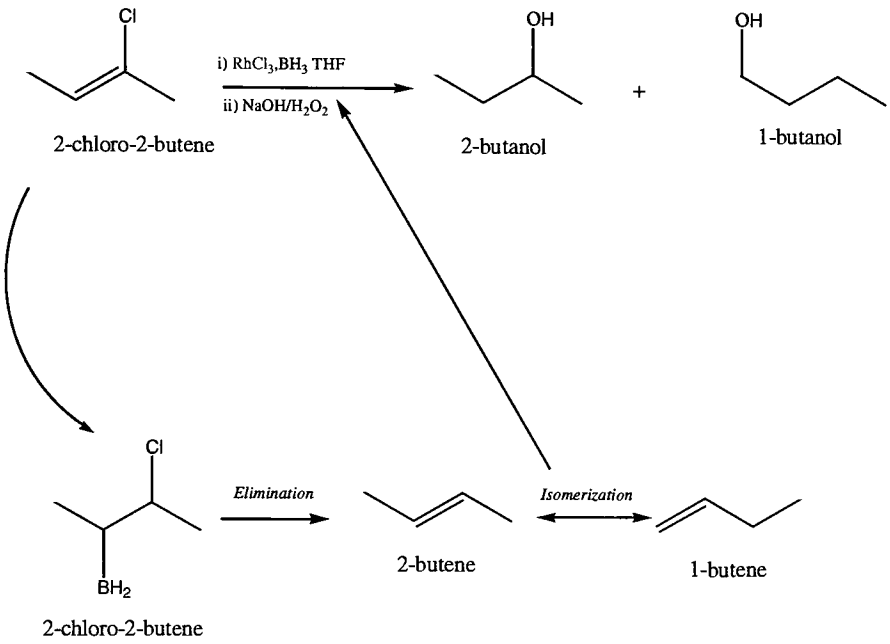
3.2.5. Hydroboration of 2-Chloro-2-butene



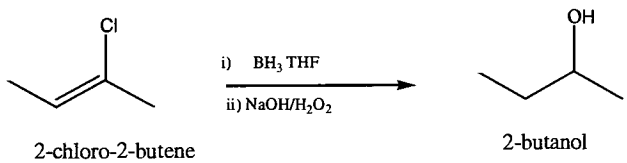
2-chloro-2-butene

Hydroboration of 2-chloro-2-butene has been carried out according to the general procedure for alkenyl chlorides in section 2.4. A sample of 1 ml of 2-chloro-2-butene was used. In this reaction also, the formation of 1-butanol from BH_3:THF complex in

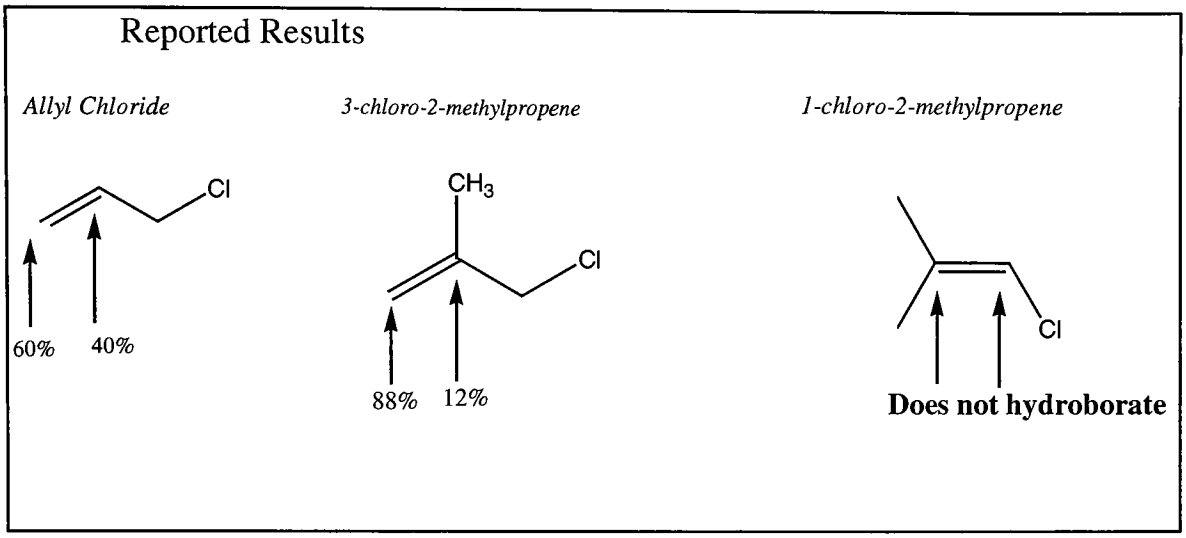
THF interfered with determination of product identity and ratio. That's why this reaction was then carried out in dichloromethane.



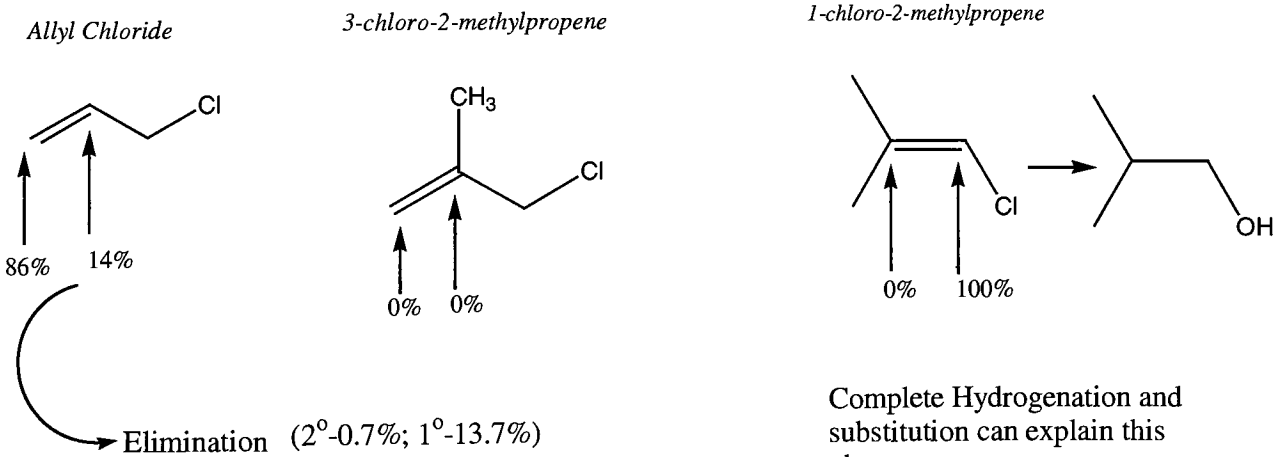
We find 2-butanol to be the major product (85%). This product ratio has been also confirmed with hydroboration in diclorometane. The hydroboration reaction of the same product without catalyst gave the following product.



The Hydroboration of Alkenyl chlorides can be summarized as follows:



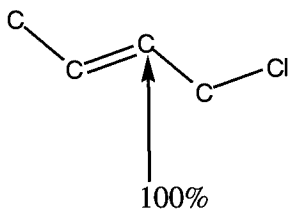
Influence of $RhCl_3$ and temperature



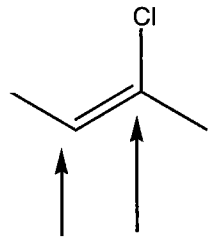
Complete Hydrogenation and substitution can explain this phenomenon.

Reported results

Crotyl Chloride



2-chloro-2-butene

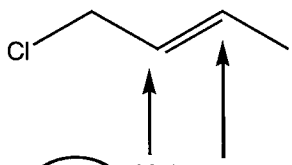


Not hydroborated

New results with BH_3 no $RhCl_3$

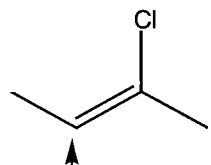
No isomerization

Crotyl Chloride



Elimination (2^o-29%)

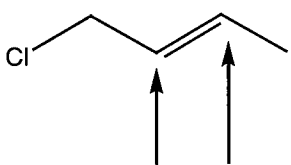
2-chloro-2-butene



Complete elimination (2^o-100%)

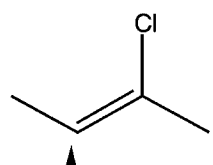
Effect of $RhCl_3$ and Temperature

Crotyl Chloride



Elimination (1^o-75.5%; 2^o-7.5%)

2-chloro-2-butene



Complete elimination (2^o- 85%; 1^o-15%)

Hydroboration of alkenyl chlorides in the presence of $RhCl_3$ resulted in two products: β–haloalkylborane and γ–haloalkylborane. However, β–haloalkylborane underwent complete elimination reaction forming alkenes. $RhCl_3$ caused the isomerization of this alkenes and subsequently they have been hydroborated with borane forming the isomers of corresponding alcohols. In the case of allyl chloride, 1-propanol and 2-propanol formed. 1-butanol and 2-butanol have been isolated in the case of crotyl chloride and 2-chloro-2-butene.

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