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LIST OF ABBREVIATIONS

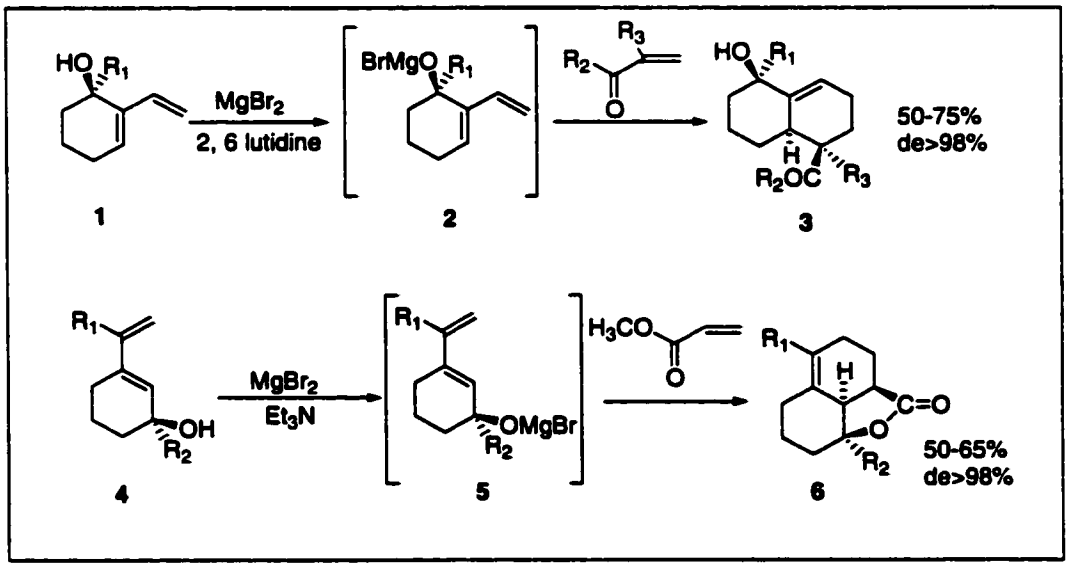
AIBN	2,2'-Azobisisobutyronitrile
Bn	benzyl
BuLi	butyl lithium
DCM	dichloromethane
E	electron withdrawing group
equiv	equivalents
Et	ethyl
EtOAc	ethylacetate
Et_2O	diethylether
Et_3N	triethylamine
HPLC	high pressure liquid chromatography
HRMS	high resolution mass spectrum
iPr	isopropyl
iPrOH	isopropanol
IR	infrared
Me	methyl
mp	melting point
$MgBr_2 \cdot OEt_2$	magnesium bromide diethyletherate
NMR	nuclear magnetic resonance
PG	protecting group
Ph	phenyl
PhMgBr	phenylmagnesium bromide
PMB	para-methoxy benzyl
Pyr	pyridine
ppm	parts per million
PTSA	para- toluene sulfonic acid
THF	tetrahydrofuran
TLC	thin layer chromatography
TS	transition state

ABSTRACT

The Diels-Alder reaction has proven to be an invaluable tool in the arsenal of the synthetic organic chemist for the relatively facile construction of cyclic cores. However, the utility of this reaction is not without its shortcomings. Lack of regio and stereoselectivity are two problems that are often encountered with asymmetric dienophiles.

Although Lewis acids have been successfully employed to control the selectivity of Diels-Alder reactions involving activated dienophiles, there is little precedent in the literature for their use with dienes containing a tertiary alcohol functionality, due to elimination complications.

To this end, a new method has been developed, and reported herein, for the control of both the regio and facial selectivity of the Diels-Alder reaction via a Lewis acid tether to the dienophile directed by the tertiary alcohol on the diene.



ACKNOWLEDGEMENTS

It is indeed true that "*No man is an Island*", so I must recognize the contribution of many others toward this accomplishment of attaining my Masters degree.

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The number of people to whom I am grateful far exceeds the limits of this page so I apologize for any omissions. To my wonderful parents, Julie and Ronald, and all the members of my extended family I thank you for your support and encouragement. This journey began many miles away in the tiny island of Trinidad and culminated in Ottawa, Canada. You all have stood with me throughout the way and for this I am humbled.

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I can't emphasize enough how important the friendships that I have made here in Ottawa have been to me. I must especially thank mon chum Frenchy for being a true

I can't emphasize enough how important the friendships that I have made here in Ottawa have been to me. I must especially thank mon chum Frenchy for being a true friend and an upstanding individual. Thanks for letting me chill at your place when I gave up my apartment before finishing my thesis (I must have been crazy thinking that I could write this in a month). I will certainly miss our hanging out days at "Griffin's", "Honest Lawyer" and dancing to "Family Affair" at "On Tap". You're a good sport Danny. Good luck with your seminar and upcoming interviews. We're going to rock Europe next summer (Amsterdam baby!).

Pat and Ross you guys rock! I'll miss our 4pm tart break and daily "Qualité intermission" (Oops, maybe I shouldn't have said that). Ross, I wouldn't worry too much if I were you. You're a very smart guy with a lot going for you. Relax, everything will be fine. Pasquale, thanks for putting me up when I gave up my apartment. Too bad you couldn't catch me snoring on tape. I'll miss our days as floor mates. Although I never did get those guitar lessons, your's is still the best rendition of "Splish, Splash" (Ok, "Lie in our graves").

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"To my beloved mother, for your continued support and eternal love"

CHAPTER 1

1.1 Introduction

The Diels-Alder reaction is inarguably one of the most effective tools in the arsenal of the synthetic organic chemist for the construction of cyclic compounds. A glance at the many total syntheses performed over the past four decades corroborates the popularity of this reaction. Monumental synthetic achievements such as Taxol[1], Cholesterol[2] and Dynemicin A[3] along with theoretical contributions from Fleming [4], Fallis[5] and many others have made the Diels-Alder reaction one of the most extensively studied and understood reactions in organic chemistry[6].

Although the Diels-Alder reaction is quite versatile, it is not without its shortcomings. Perhaps the most significant problem it faces is the lack of diastereoselectivity and regioselectivity that may occur with asymmetric dienophiles. Although Lewis acids have been used, with much success, to preclude this undesirable result there remains room for improvement.

The studies presented herein are aimed at developing a method to control the regio and diastereoselectivity of the Diels-Alder reaction involving dienes possessing an allylic tertiary alcohol functionality in the presence of a Lewis acid.

An understanding of the factors governing the chemoselectivity of the Diels-Alder reaction is required in order to address this problem. The following discussions on Frontier Molecular Orbital (FMO) theory, Stereoselectivity and the role of Lewis acids in Diels-Alder reactions are provided for this purpose.

1.2 Overview of the Diels-Alder reaction

The Diels-Alder reaction is a [π4s + π2s] cycloaddition between the π electrons of a diene and those of a dienophile (figure 1). In a "normal" Diels-Alder reaction, the dominant interaction involves the HOMO of the diene with the LUMO of an activated dienophile. In an inverse electron demand Diels-Alder reaction (in which the dienophile has an electron donating group), the dominant interaction is between the HOMO of the dienophile and the LUMO of the diene. The driving force of the reaction is the formation

of two new σ bonds in exchange for two π bonds, which is sufficient to overcome the large energy barrier between the HOMO and the LUMO[7].

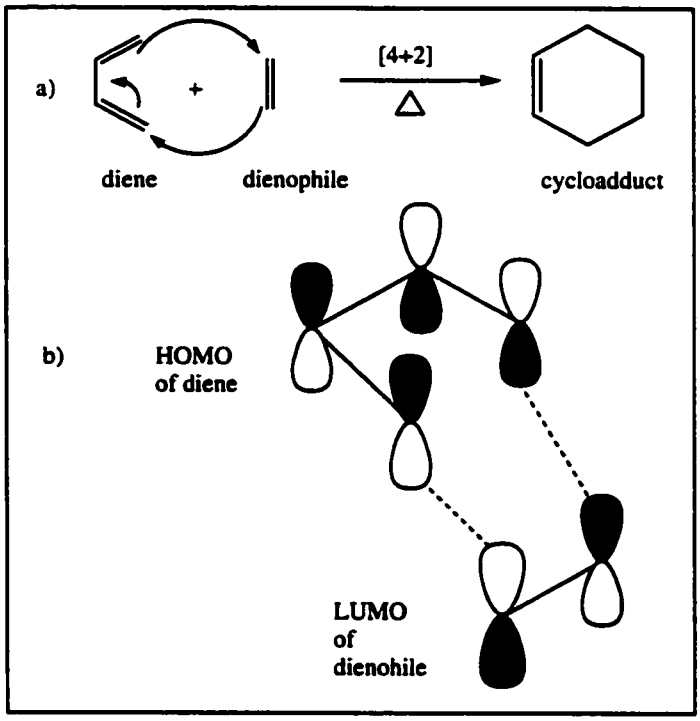


Figure 1: a) Diels-Alder reaction. b) Molecular orbital representation.

Like all concerted, thermal pericyclic reactions, the Diels-Alder reaction is governed by a set of selection rules which relates the number of π electrons involved; the method of activation and the stereochemistry. The Woodward-Hoffman rules is perhaps the cornerstone on which the selection rules are built. The feasibility of a cycloaddition, the regio and stereochemical outcome can all be predicted on the basis of this rule. In its simplified form, the Woodward-Hoffman rule states that: *A ground-state pericyclic change is symmetry allowed when the total number of* $(4q+2)_s$ *and* $(4r)_a$ *components is odd*[A]. This rule, in conjunction with FMO theory, accounts for the suprafacial tendency of the Diels-Alder reaction due to symmetry allowed orbital interactions. The diastereoselectivity and regioselectivity of the reaction can also be explained by these molecular orbital interactions.

1.3 Stereoselectivity

The two main factors influencing the chemoselectivity of the Diels-Alder reaction are steric and electronic interactions. In the case where either the diene or dienophile is sterically encumbered, reaction will occur from the less hindered face. However, for most intermolecular Diels-Alder reactions it is the electronic interactions that govern the stereoselectivity. In reactions involving activated dienophiles, approach can occur in one of two ways resulting in formation of either the endo **7** or exo cycloadduct **8** (figure 2).

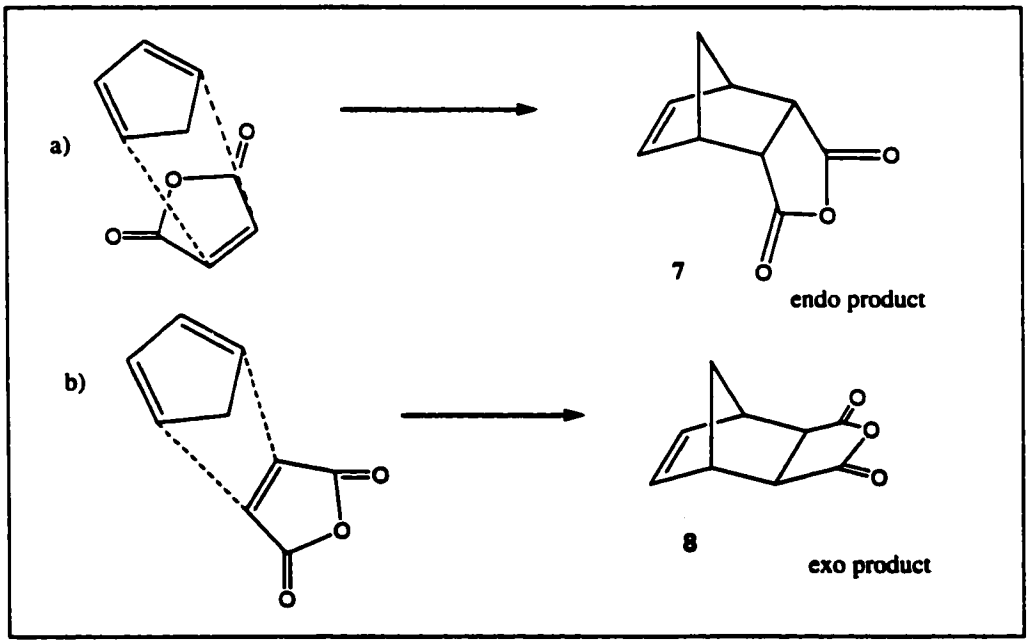


Figure 2: Formation of a) endo and b) exo products of Diels-Alder reaction between cyclopentadiene and maleic anhydride.

Although the formation of either product is possible, the reaction favours the endo product (Alder's endo rule). This is an interesting result because the endo adduct is the kinetic product whereas the exo adduct is the thermodynamic one. This result is common to the intermolecular reaction of dienes with activated dienophiles and can be attributed to interactions of the secondary orbitals.

1.3.1 Endo selectivity

The endo selectivity of the Diels-Alder reaction is attributed to secondary orbital interactions. Overlap between the π electrons of the carbonyl group on the activated dienophile and the π electrons of the diene stabilizes the transition state such that, under kinetically controlled conditions, the endo adduct is preferred (figure 3).

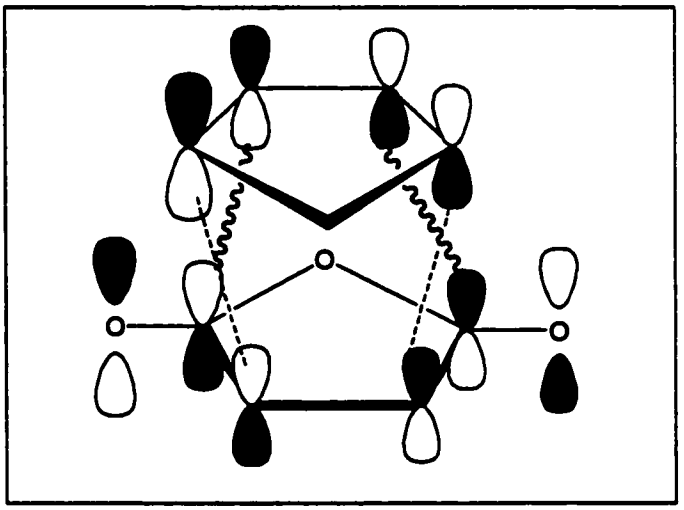


Figure 3: Endo selectivity of the Diels-Alder reaction between cyclopentadiene and maleic anhydride as a result of the secondary orbital interactions.

In the above figure, the dashed lines represent the primary interactions between the π electrons where the new bonds will be formed. The curly lines represent the secondary interactions between the π electrons that are not involved in bond formation. Since the orbital signs are the same there is a secondary (bonding) interaction. These secondary interactions stabilize the transition state of the endo adduct relative to that of the exo counterpart where these interactions are absent. Thus, the endo product is favoured under kinetically controlled conditions.

The ability to control both the stereochemical and regiochemical outcome of the Diels-Alder reaction is paramount to synthetic organic chemistry. As such, the lack of regioselectivity that is often encountered will be addressed in the scope of this thesis.

1.4 Regioselectivity

It is impossible to discuss [4+2] cycloadditions without mentioning regioselectivity, or the lack thereof. The ability to control this very important feature, though well studied, remains one of the most significant challenges in Diels-Alder chemistry. For example, the reaction depicted in figure 4 can result in the formation of two cycloadducts. The regioselectivity is improved if an electron-donating group is placed on C-1 of the diene **9**. Such a substitution favours the formation of the ortho product **11**.

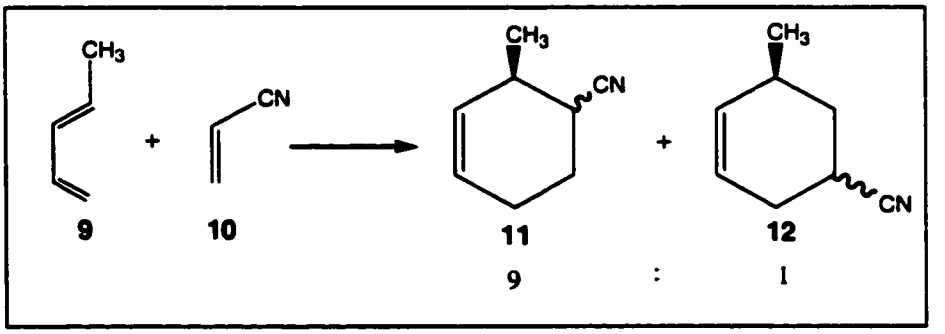


Figure 4: Regioselectivity of the Diels-Alder reaction of a 1-substituted diene.

The methyl substituent at C-1 of the diene (figure 4) is electron donating. Thus, the size of the coefficient of the atomic orbitals at C-4 of the diene is increased (figure 5). The electron withdrawing group (CN) at C-1 of the dienophile **10** alters the size of the coefficients of the atomic orbitals on C-1 and C-2 of the dienophile (figure 5). The large coefficient at C-4 of diene **9** interacts with the large coefficient of the dienophile **10** (C-2). Correspondingly, the small coefficient of the diene (C-1) interacts with that of the dienophile (C-1). These complementary interactions between the polarized coefficients favour the formation of the ortho product[4].

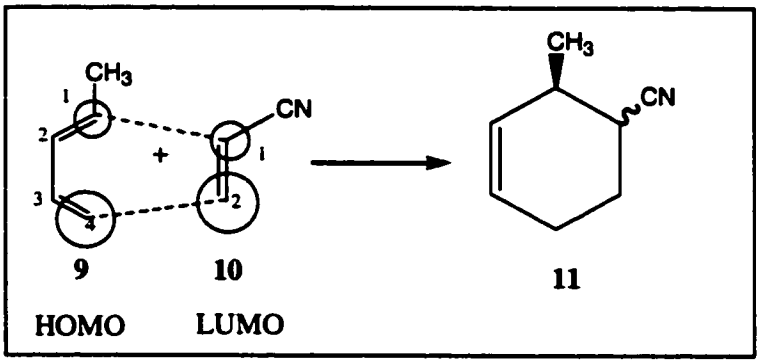
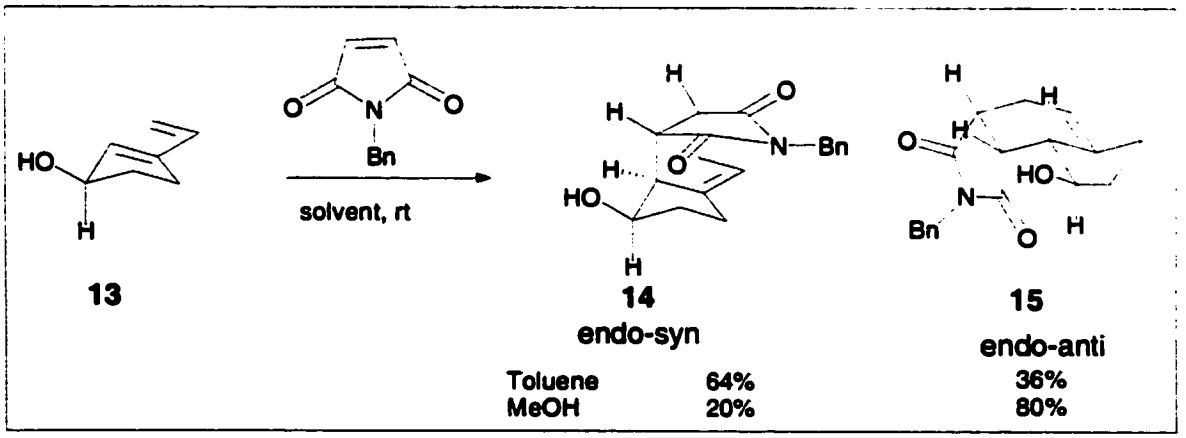


Figure 5: Effect of substituent groups on the regioselectivity as a result of polarization of the coefficients of the frontier orbitals.

1.5 Diastereoselectivity

Independent research from Overman[8] and Frank[9] reported that heteroatomic substitutions at the allylic position on semicyclic dienes can control the diastereoselectivity of [4+2] cycloadditions.

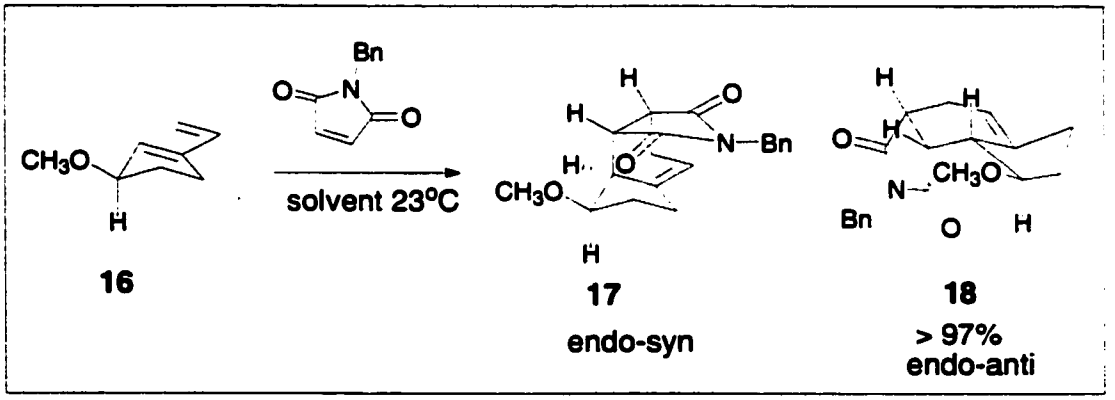


Scheme 1: Lack of diastereoselectivity of Diels-Alder reaction with an allylic heteroatom substituted diene.

In the above example, a 1.8:1 mixture of cycloadducts favouring the endo-syn product **14** is obtained when toluene is used as the solvent. However, the ratio becomes

4:1 in favour of the endo-anti product **15** when the reaction is performed in methanol. This lack of selectivity can be detrimental to synthetic efforts.

At first glance, it seems as if the use of a non-hydrogen bonding solvent (toluene) favours the formation of the endo-syn cycloadduct (scheme 1). However, when a methoxy group is placed on the alcohol **16**, the reaction favours the formation of the endo-anti product **18** almost exclusively, irrespective of the solvent (scheme 2). This result can be attributed to the steric effect of the methoxy group which hinders the approach of the dienophile from the top face (i.e. syn to methoxy).



Scheme 2: Diels-Alder reaction of a methoxy allylic substituted diene.

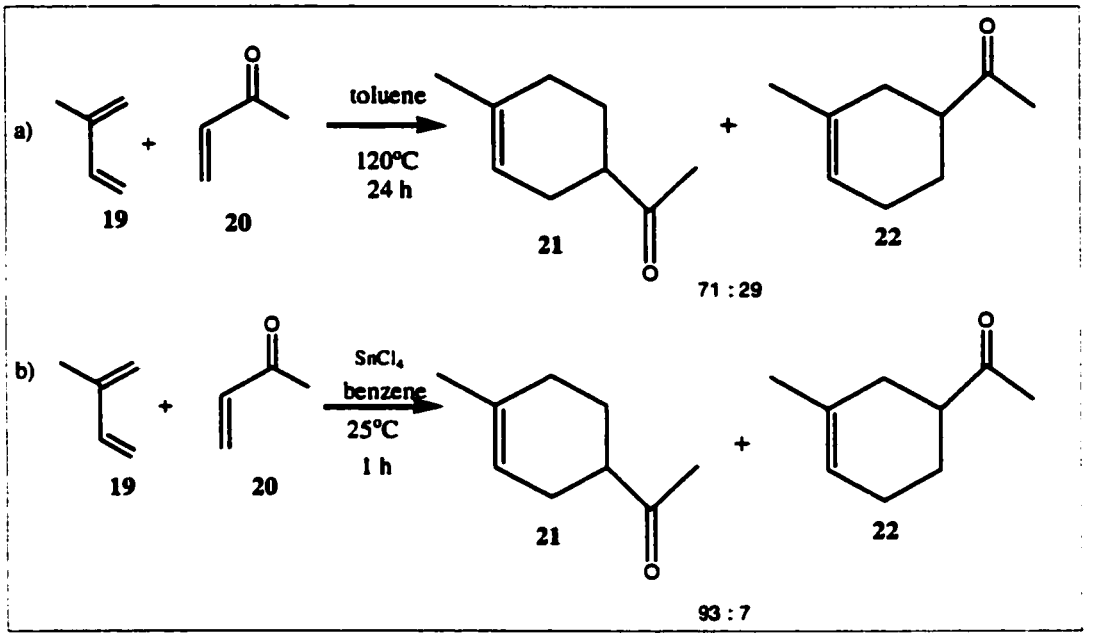
Solvents do not provide a reliable means of controlling the selectivity of Diels-Alder reactions. Lewis acids, however, are known to effectively control the regio and facial selectivity. This project will be directed toward the development of a method that incorporates the use of Lewis acids to control the Diels-Alder reaction of dienes with an allylic tertiary alcohol functionality, which is as of yet, unprecedented.

1.6 The role of Lewis acids in Diels-Alder reaction

The use of Lewis acids in the Diels-Alder reactions has been well studied[10]. They have been shown to have a great influence on the regioselectivity of the reaction. Their ability to control the regioselectivity is attributed to their tendancy to complex to heteroatoms on activated dienophiles thus further increasing their electron withdrawing ability. This increase in magnitude of the coefficient of the dienophile results in an

increase in the formation of the ortho cycloadduct in the case of electron donating, 1-substituted dienes (recall figure 5).

The effect of the Lewis acid on the Diels-Alder reaction is threefold. Firstly, it lowers the energy of the LUMO of the dienophile. Secondly, it increases the difference in magnitude of the coefficients of the dienophile and thirdly, it changes the coefficient at the dienophile substituent, hence increases the opportunity of secondary orbital interactions[7]. These effects combine to increase: the rate of the reaction; the regioselectivity and the endo diastereoselectivity of the reaction.



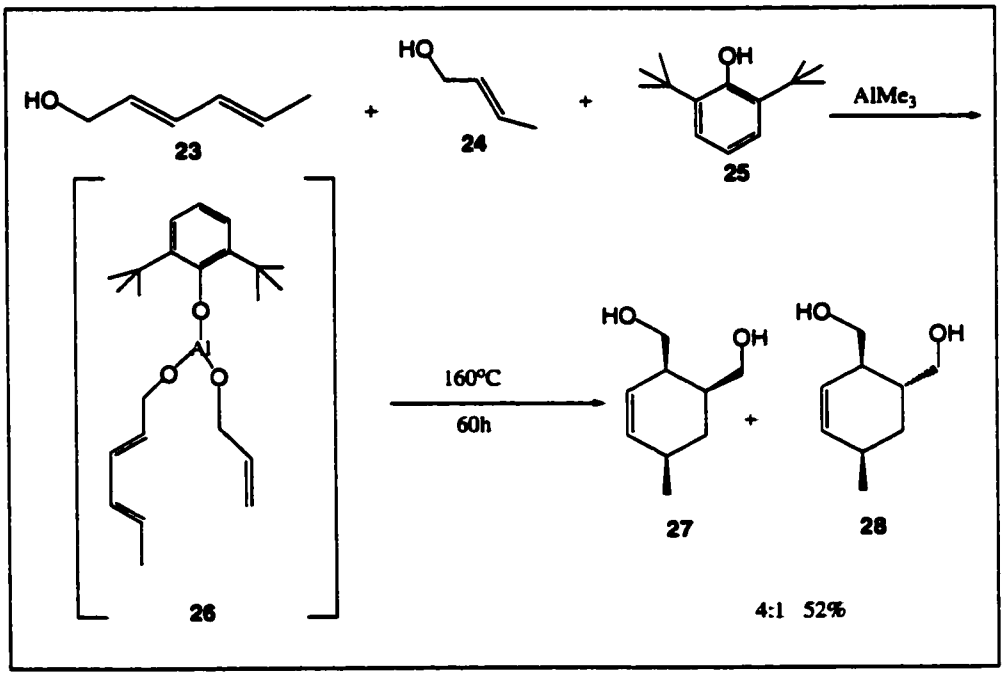
Scheme 3: Lewis acid controlled Diels-Alder reaction.

The regioselectivity obtained using dienes with electron donating substituents and activated dienophiles can be further improved with the use of Lewis acids. For example, Lutz et al.[11] demonstrated that the reaction between 2-methylbutadiene **19** and methylvinylketone **20** favours the para-cycloadduct **21** in 71% yield (scheme 3a). However, Yates[12] et al. have shown that the regioselectivity of the reaction is further improved with the use of $SnCl_4$ which increases the formation of **21** to 93% (scheme 3b).

The success of Lewis acids in Diels-Alder reactions has been well documented in the literature. Among the most commonly used Lewis acids are Aluminum, Silicon, Boron and Magnesium compounds. These Lewis acids all work by the same principle, which primarily involves complexation to a heteroatom (usually oxygen) on the dienophile.

1.6.1 Aluminum Lewis acid tethers

The most commonly used aluminum Lewis acids are $AlMe_3$, $AlMe_2Cl$ and $AlMeCl_2$. They are used to control the stereochemical outcome of Diels-Alder reactions by forming a temporary *in situ* tether between the diene and dienophile, thus converting an intermolecular reaction to an intramolecular one. An application of this strategy has been demonstrated in independent works by the research groups of Stork[13] and Olsson[14]. In Olsson's example, a mixture of the diene **23**, dienophile **24**, 2,6-di-tert-butylphenol **25** and $AlMe_3$ resulted in the formation of a temporary tether **26** between aluminum and



Scheme 4: Olsson's $AlMe_3$ stereocontrolled Diels-Alder reaction.

the hydroxy groups on the diene and dienophile accompanied by the evolution of methane (scheme 4). The tether is responsible for the observed regioselectivity of the reaction (cycloadducts **27** and **28**).

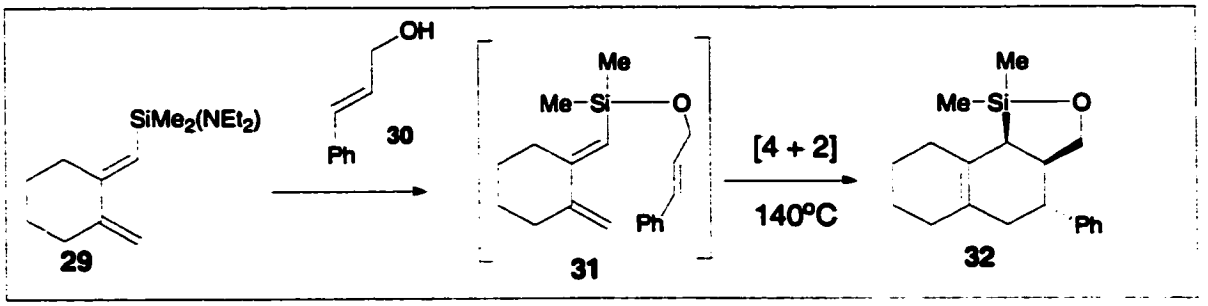
There are, however, a few points worth noting in this example. The tether is formed between the Lewis acid, a primary alcohol on the diene and the secondary alcohol on the dienophile. Many of the Lewis acid controlled Diels-Alder reactions presented in the literature are of this type. A more challenging scenario, one that will be addressed by this thesis, involves the use of dienes with an allylic tertiary alcohol moiety.

A second point of interest in the Olsson example is the high temperature and long reaction time required for the reaction. It was necessary to heat the reactants in a sealed tube for 60 h at 160°C. A method requiring less harsh conditions would be preferred. Also, there is room for improvement of the yield and diastereoselectivity of the reaction. These issues will be addressed in our developed methodology .

1.6.2 Silicon tethers

The use of silicon Lewis acids in stereocontrolled Diels-Alder reactions has been quite succesful. The principle is the same as the Al Lewis acids- the formation of a temporary tether between the diene and dienophile. The affinity of silicon for oxygen makes it a good choice for use in these reactions. The utility of silicon Lewis acids can be seen in the works of Stork[15], Craig[16] and Shea[17].

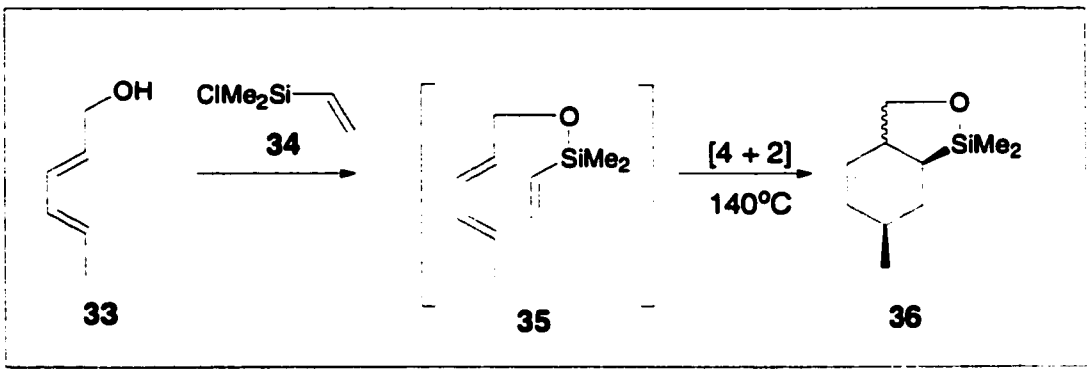
Pioneering work by Tamao et al.[18] demonstrated that the regioselectivity of the Diels-Alder reaction can be controlled by the formation of a temporary tether between Si incorporated on the diene **29** and a hydroxy group on the dienophile **30** (scheme 5).



Scheme 5: Tamao's Si controlled Diels-Alder reaction.

As a result of the tether, the intermolecular reaction is transformed to an intramolecular reaction via intermediate **31** to give cycloadduct **32.**

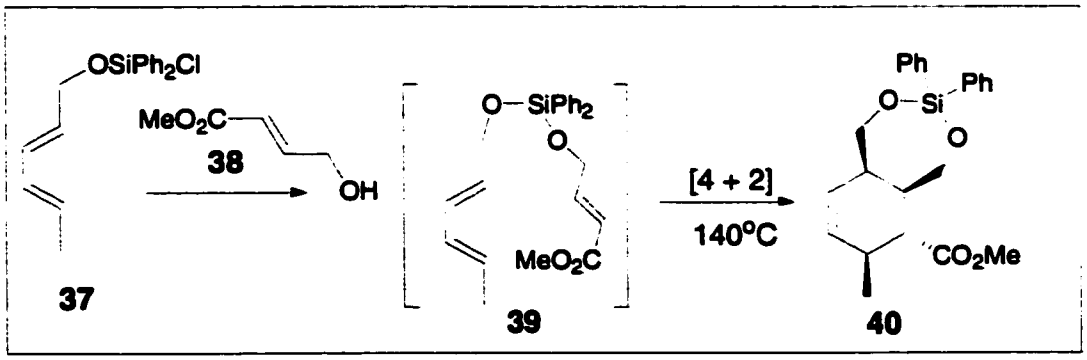
Silicon has since been used by many researchers in stereocontrolled Diels-Alder reactions. In an example by Stork et al.[15] a "temporary silicon connection" **35** is used to transform allyl alcohol diene **33** and dienophile **34** to cycloadduct **36** (scheme 6).



Scheme 6: Stork's silicon- tethered stereocontrolled Diels-Alder reaction.

In this case, the silicon is incorporated in the structure of the dienophile rather than being provided by an external source. Note the use of the primary alcohol functionality on the diene and the temperature of the reaction (140°C).

In the example by Craig[16] (scheme 7), a similar concept is employed. However, in this case, the primary alcohol on the diene is protected as the silyl ether **37** which forms a silylacetal **39** with the hydroxyl group on the dienophile **38.** This reaction also suffers from the temperature requirement drawback as the previous ones with Al.

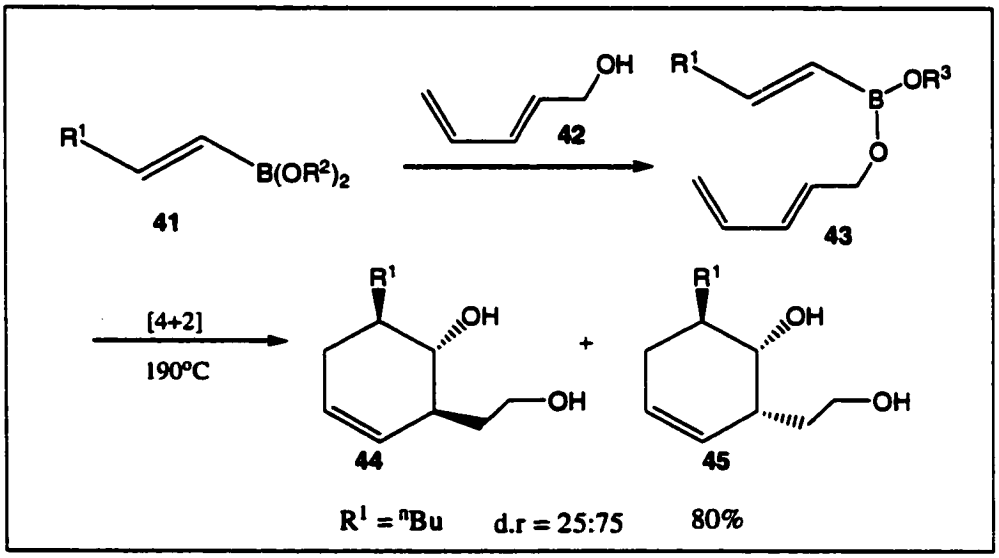


Scheme 7: Craig's Si stereocontrolled Diels-Alder reaction.

The additional transformations required to remove the silyl ether from the cycloadduct is also an undesirable feature of the Si tethered reactions.

1.6.3 Boron tethers

Boron Lewis acids have also been successfully applied to stereocontrolled Diels-Alder reactions. Batey et al.[19] have demonstrated that the regio and stereoselectivity can be controlled by the formation of a temporary boron tether which connects alkenyl boronic acids (or esters) **41** to a diene component **42** to give alkenyl boronic esters **43** (scheme 8).



Scheme 8: Batey's Stereocontrolled Diels-Alder reaction using boron.

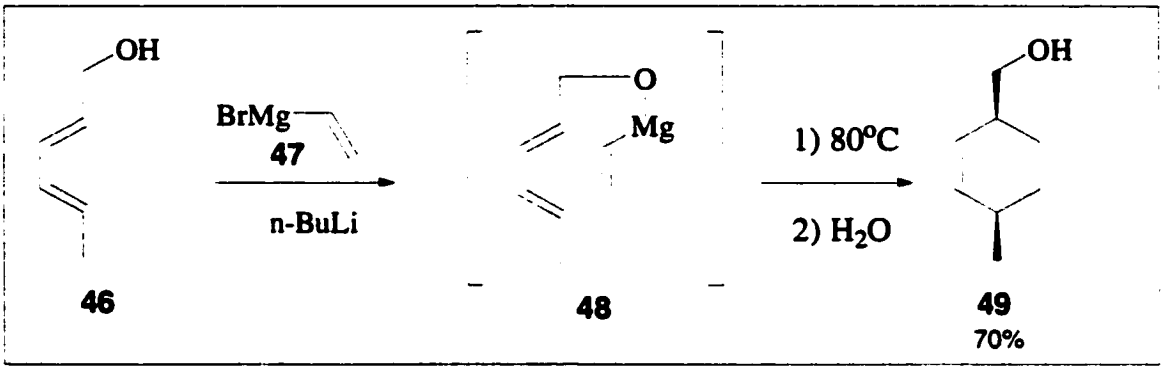
This reaction proceeds in good yield and acceptable diastereoselectivity. However, like the previous examples using Al and Si, it requires high temperatures and additional transformations to liberate the cycloadduct from the organoborane.

1.6.4 Magnesium tethers

Magnesium provides an attractive alternative to Al, Si and Boron. In some cases, the reaction temperature requirement is lower and the yields are better than that for

silicon. Independent research by the Stork and Ward groups have shown the successful application of Mg tethers in Diels-Alder reactions.

Stork has demonstrated that the temporary Mg tether **48** can be made *in situ* by treatment of the allylic alcohol **46** with n-BuLi at –78°C followed by transmetallation with vinylmagnesium bromide to give cycloadduct **49** [13](scheme 9).

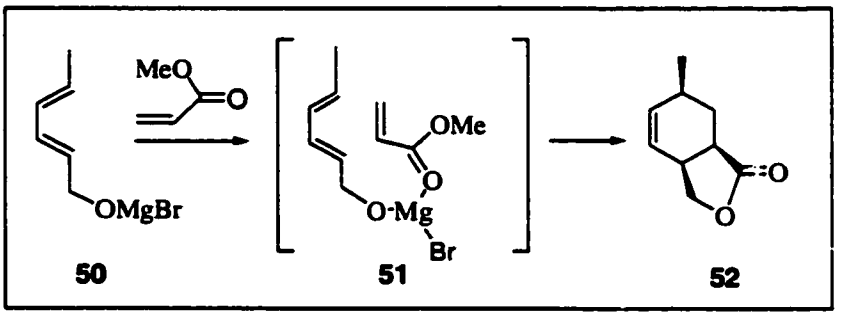


Scheme 9: Stork's magnesium tethered Diels-Alder reaction.

In this example, the magnesium used to form the tether is cleverly incorporated in the diene (as a Grignard reagent). This reaction is facilitated at 80°C for 1h compared to 3h at 160°C for the silicon tethered reaction and 10h at 160°C for the non-tethered reaction, i.e. with the allyl ether (CH_2 instead of Mg).

The successful application of Mg tethers has also been demonstrated by Ward et al.[20]. In this example, Lewis acids such as MeMgBr or $MgBr_2 \cdot OEt_2$ are used as the source of Mg in contrast to the Grignard reagents used by Stork (scheme 10). Treatment of allylic alcohol **50** with MeMgBr and methyl acrylate afforded cycloadduct **52** in 75% yield after stirring the reaction for 7 days when 0.5 equiv of a 3M solution of the Lewis acid was used.

Although Ward et al. were successful in controlling the regio and stereoselectivity of the reaction, they were limited to the use of dienes with a primary allylic alcohol functionality. To the best of our knowledge, there is no evidence for Lewis acid stereocontrolled Diels-Alder reactions with dienes possessing an allylic tertiary alcohol functionality.



Scheme 10: Ward's Mg tethered Diels-Alder reaction.

In addition to the Lewis acids mentioned, Zn[21], Sn[22] and S[23] have also been used. The typical requirements for a Lewis acid are: the linkage should be assembled by straightforward synthetic transformations from readily available components; if possible, the intermolecular reaction precursor should be stable to purification and the subsequent reaction conditions and finally, the temporary tether should be susceptible to easy and selective cleavage upon formation of the cycloadduct[17]. These criteria will serve as the basis of our method development.

1.7 Aim of this Project

In this thesis, the control of the facial and regioselectivity of the Diels-Alder reaction of semicyclic dienes with allylic tertiary hydroxy substitution will be addressed. The failure of the aforementioned examples to address this issue warrants a solution to this problem since allylic tertiary alcohol dienes are important synthetic components. These dienes are particularly attractive candidates because their use in Lewis acid controlled Diels-Alder reactions is complicated by their relative instability to such acidic conditions and high temperature. However, the successful incorporation of these dienes under such conditions will present rewarding benefits to synthetic chemistry in terms of the relative ease at which cyclic target compounds can be attained due to the controlled, contiguous quatenary centres created by this method.

CHAPTER 2

2.1. Introduction

The use of Lewis acids in controlling the regioselectivity and facial approach of Diels-Alder reactions has been well studied, yet there is little precedent in the literature for their use with dienes possessing a tertiary alcohol functionality. This is due, to a great deal, to the susceptibility of such dienes to elimination of water in the presence of Lewis acids. However, there are many natural and non natural biologically active bicyclic compounds which possess a tertiary alcohol functionality or derivative thereof (Vinigrol and Dysidiolide). The synthetic utility of the Diels-Alder reaction presents a means to these targets and thus the development of a method which can accomodate such sensitive dienes is necessary, hence the purpose of this project.

2.2. Our Approach

In order to address the issue of using a Lewis acid in the presence of a diene with an allylic tertiary alcohol functionality to control the facial approach of the dienophile and the regioselectivity, we propose the following : The Lewis acid will tether to the hydroxyl group on the diene **53** and the carbonyl group of the dienophile **54** thereby directing facial approach syn to the alcohol. The regioselectivity can be controlled by the inability of the dienophile to rotate as a result of the Lewis acid tethered intermediate **55** (figure 6).

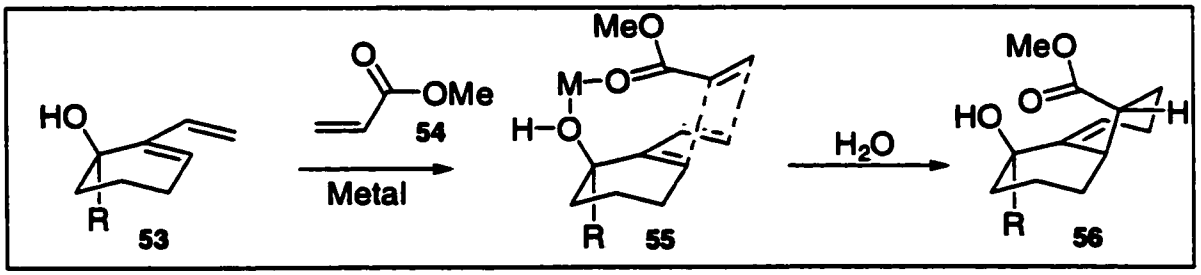
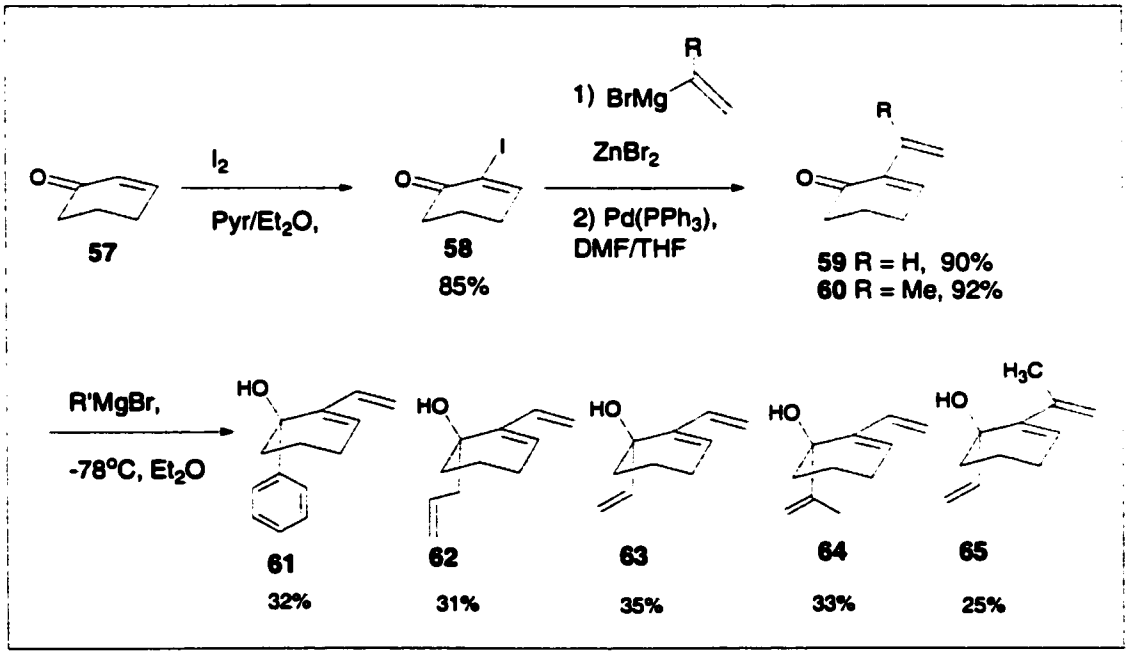


Figure 6: Proposed Lewis acid tethered Diels-Alder reaction with allylic, tertiary hydroxy substituted diene.

2.3. Results and Discussion

2.3.1 Preparation of dienes

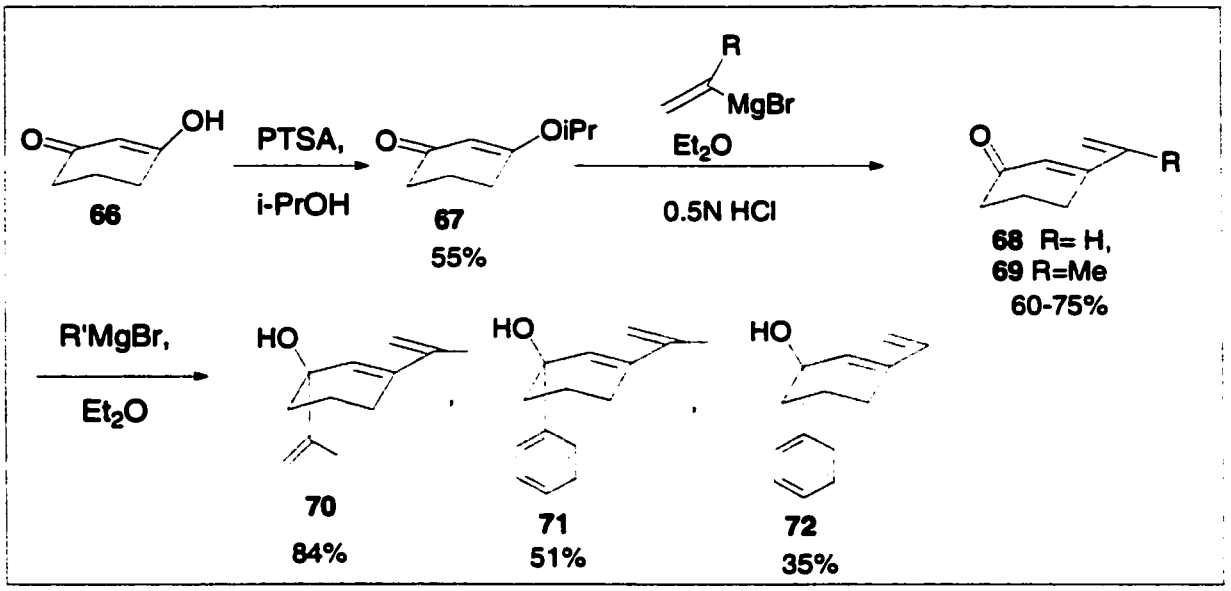
To investigate the feasibility of our tethered Diels-Alder reaction, four types of dienes were synthesized. The synthesis of the type I dienes began with α iodination of 2-cyclohexenone **57**[24] to give iodoenone **58** (scheme 11). Palladium catalyzed cross coupling under Negishi conditions[25-26] provided ketodienes (**59** and **60**). Subsequent Grignard addition with phenyl, allyl or vinylmagnesium bromide afforded dienes **61-65** with the required tertiary alcohol functionality.



Scheme 11: Synthesis of Type I dienes.

To further investigate the scope of the reaction, a second set of dienes (type II) were synthesized (scheme 12). In this case, the tertiary alcohol was placed in the β-position relative to the diene moiety. This synthetic sequence began with monoprotection of 1,3 cyclohexadione **66** as the isopropyl enol ether **67**, followed by Grignard addition and subsequent elimination of the resulting tertiary alcohol to afford ketones **68** and **69**.

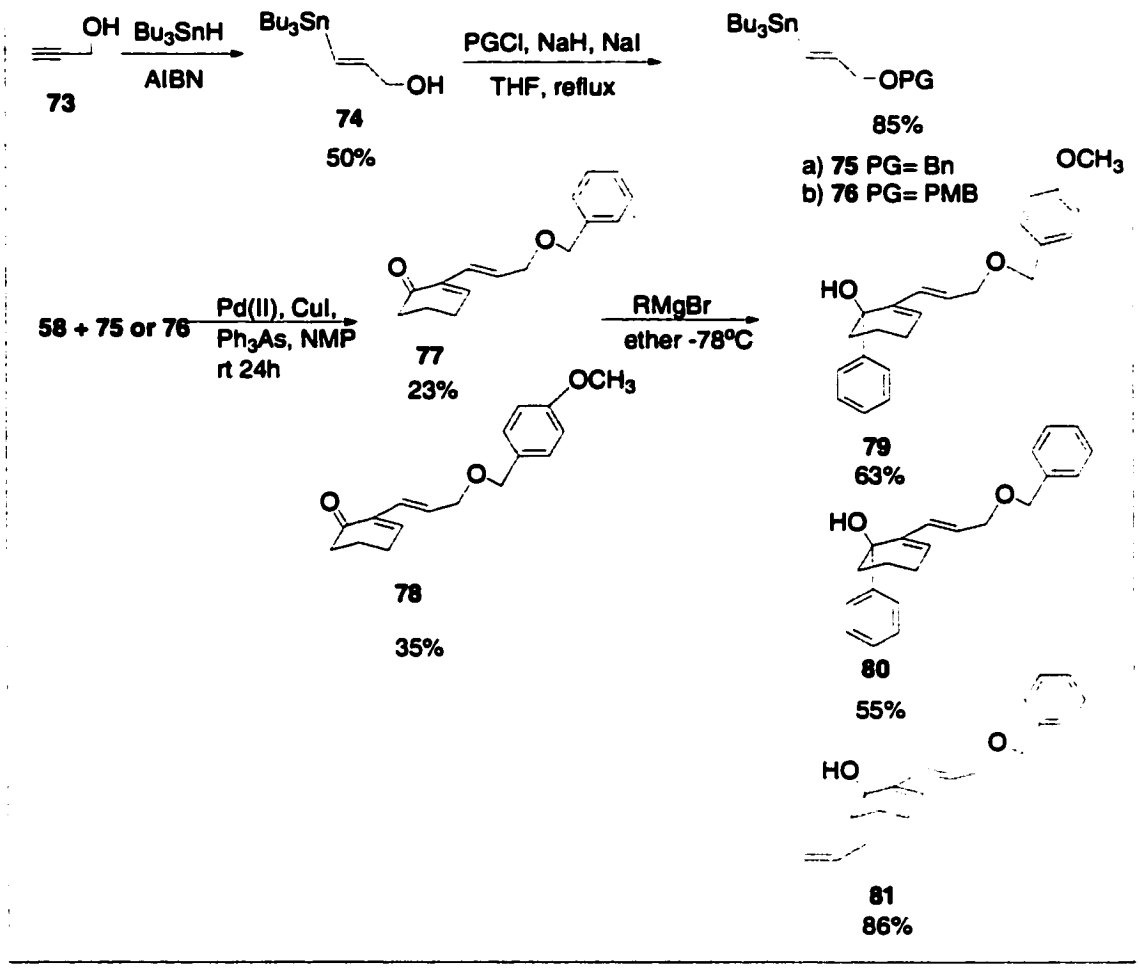
Grignard addition with isopropyl or phenylmagnesium bromide provided dienes **70-72** with the required tertiary alcohol functionality.



Scheme 12: Synthesis of Type II dienes (tertiary alcohol functionality in the β position).

The concept of our approach is based on the formation of a tether between the Lewis acid and the oxygen of the tertiary alcohol. The presence of a second oxygen on the diene might present an interesting scenario as it may provide an alternative tethering site for the Lewis acid. Should this be the case, the regio selectivity of the Diels-Alder reaction would be affected.

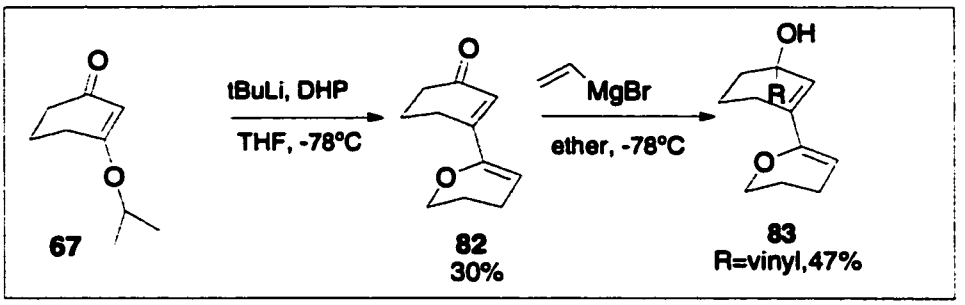
In order to investigate this scenario, type III dienes (**79-81**) were synthesized (scheme 13). This synthesis was accomplished by Stille coupling of iodide **58** with stannane **75** or **76** using a Pd(0) catalyst, CuI, and Ph_3As[27]. The latter was obtained from AIBN initiated stannylation of propargyl alcohols **75** or **76** (as the protected benzyl ether) with tributyltin hydride[28]. As in the previous cases, the tertiary alcohol functionality was installed by Grignard addition to the resultant ketone.



Scheme 13: Synthesis of Type III dienes.

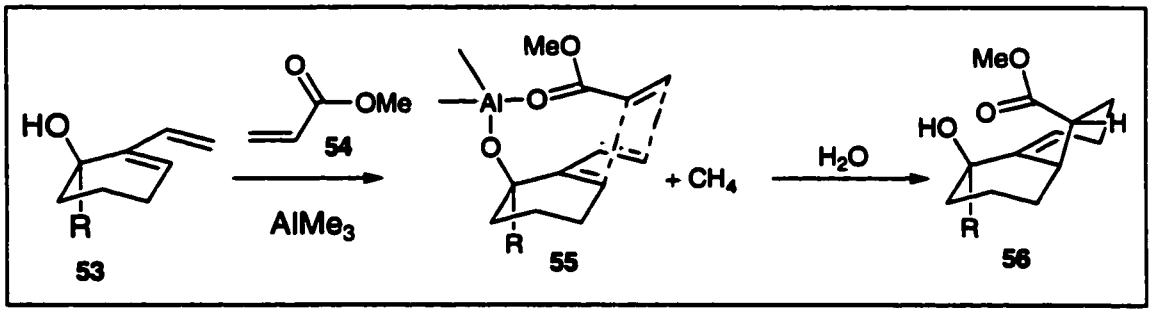
Finally, a fourth type of diene, having a dihydropyran incorporated in the diene moiety **83**, was synthesized (scheme 14). This synthesis began with C-alkylation of the monoprotected isopropyl enol ether **67** of 1,3 cyclohexadione by the organolithium dihydropyran species to give ketodiene **82**. Subsequent Grignard addition afforded diene **83** in 47% yield.

With these tertiary alcohol dienes in hand, the possibility of developing a Lewis acid tethered method for a regio and stereocontrolled Diels-Alder reaction was investigated.



Scheme 14: Synthesis of Type IV diene.

The choice of Lewis acid proved to be critical in the development of this methodology. The documented success of Al Lewis acids in the literature influenced our decision to use $AlMe_3$, $AlMeCl_2$ and $AlMe_2Cl$ in our initial attempts . We envisaged that an Al-alkoxide species **55** can be generated after mixing the Lewis acid with diene **53** and methylacryalte (scheme 15). The aluminum alcoholate **55** should then undergo [4+2] cycloaddition with complete stereocontrol to give cycloadduct **56**.



Scheme 15: Proposed Al stereocontrolled Diels-Alder reaction.

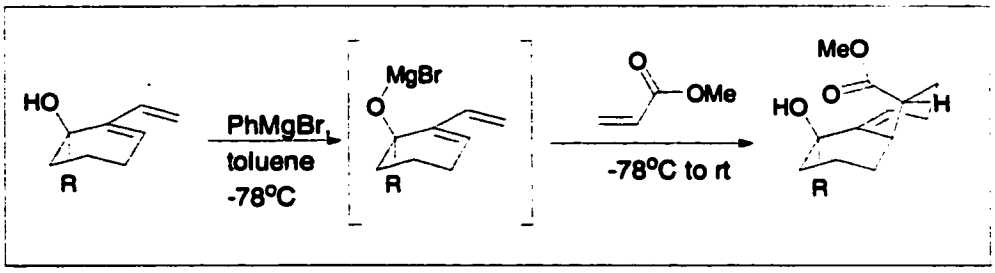
The success we anticipated was not achieved. The Al Lewis acids under investigation all failed. In each case, a black, viscous substance was produced throughout the flask upon the addition of the Lewis acid at –78°C or –90°C, which was highly UV active and showed no signs of product formation or starting material by ^1H NMR. A possible explanation for this phenomenon is that elimination of the tertiary alcohol may have occurred in the presence of such strong Lewis acids. Another possibility is that polymerization of the starting material may have occurred.

The futility of the Al Lewis acids meant that the tether would have to be made via another means. Silicon was not an option due to the high temperature necessary for reaction to occur and the additional transformations required to liberate the cycloadduct from the resulting silyl ether. One of the goals of this method development project is to create a procedure which is not energetically demanding while employing relatively inexpensive reagents that are easy to handle. This prompted the investigation of phenylmagnesium bromide.

2.4 Phenylmagnesium bromide

We decided to use a Grignard reagent rather than a typical Lewis acid because of the difference in reactivity of Grignard reagents with alcohols. The problems encountered with the Al Lewis acids might be due to the initial step which is complexation of the Lewis acid to the tertiary alcohol. In the case of $AlMe_3$, the loss of CH_3^- accompanied by deprotonation of the alcohol to generate methane occurs. However, the elimination of the hydroxyl group might supersede deprotonation. Whereas, the initial step upon addition of a Grignard reagent to an alcohol is deprotonation to generate an alkoxide, which then bonds to the metal (i.e. Mg). Perhaps the Mg alkoxide species thus generated is more labile than its Al counterpart. Thus, elimination of the tertiary alcohol should not occur with the Grignard reagent.

Phenylmagnesium bromide was chosen due to its stability and availability. Our developed method for its use in the Diels-Alder reaction is as follows: A solution of the diene in toluene was cooled to –78°C followed by addition of the Grignard reagent. After 20 min of stirring, the reaction was slowly warmed to 0°C. The reaction was stirred for 10 min then cooled again to –78°C. The dienophile (methylacrylate) was then added. The temperature was slowly raised to room temperature and the reaction was stirred and monitored by TLC. After three hours, the desired cycloadducts were formed as the only diastereomer (scheme 16).



Scheme 16: General procedure for PhMgBr controlled Diels-Alder reaction.

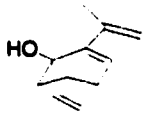
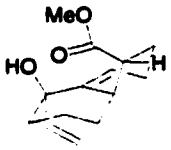
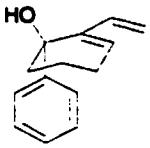
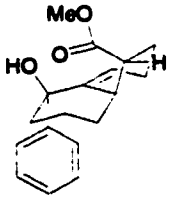
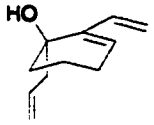
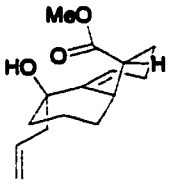
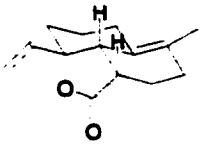
Entry	Diene	Cycloadduct	Yield (de>98%)
1	 **65**	 **84**	85%
2	 **61**	 **85**	64%
3	 **62**	 **86**	48-65%
4	 **70**	 **87**	30%

Table 1: Results for PhMgBr controlled Diels-Alder reaction.

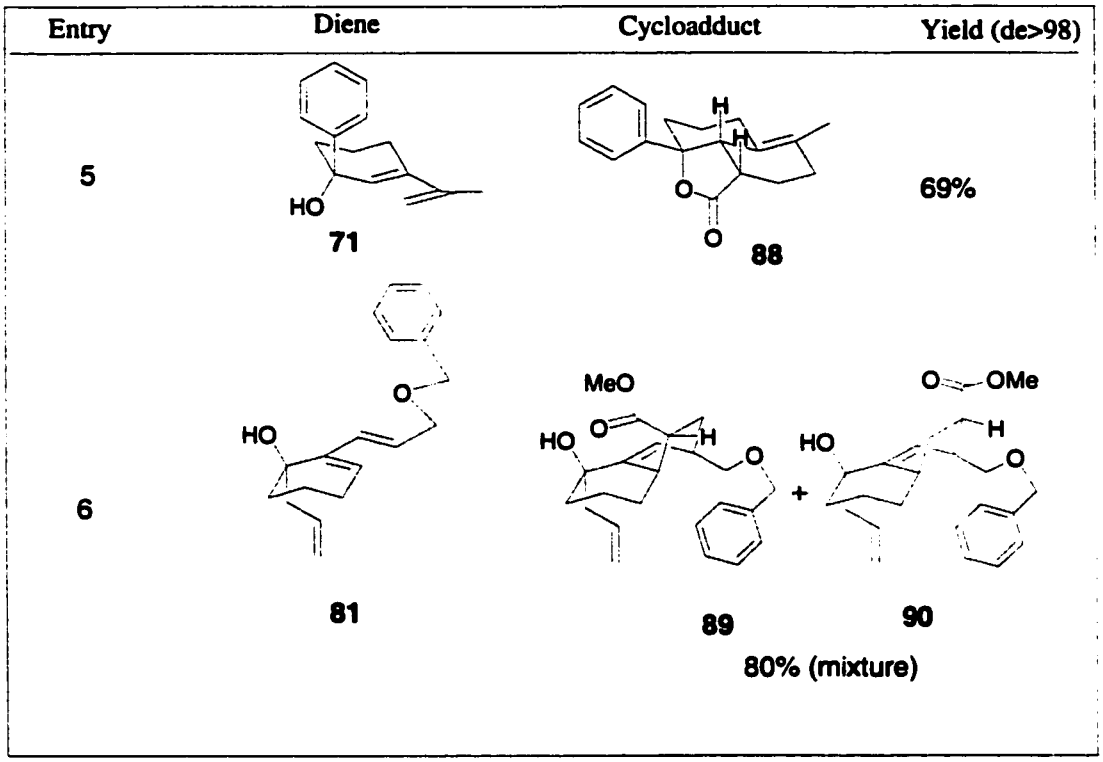


Table 1 (continued): Results of PhMgBr regio and stereocontrolled Diels-Alder reaction.

The results with PhMgBr were quite good. As shown in table 1, the reaction worked with yields as high as 85% (entry 1) and greater than 98% diastereoselectivity for both the type I (entries 1- 4) and type II (entry 5) dienes. In each case, the only observed product was that which was expected. Thus, the control of the regio and stereoselectivity via the Mg alkoxide tether was successful. The reaction was tolerant of vinyl (entry 1), isopropyl (entry 4), phenyl (entries 2 and 5) and allyl (entries 3 and 6) substitution on the tertiary alcohol moiety.

The high regio and stereoselectivity can be rationalized by the proposed transition state (figure 7). The facial approach of the dienophile is governed by the magnesium alkoxide, i.e. syn to the alcohol. Endo approach is favored, due to increased stability as a result of secondary orbital interactions between the π-electrons of the diene and dienophile.

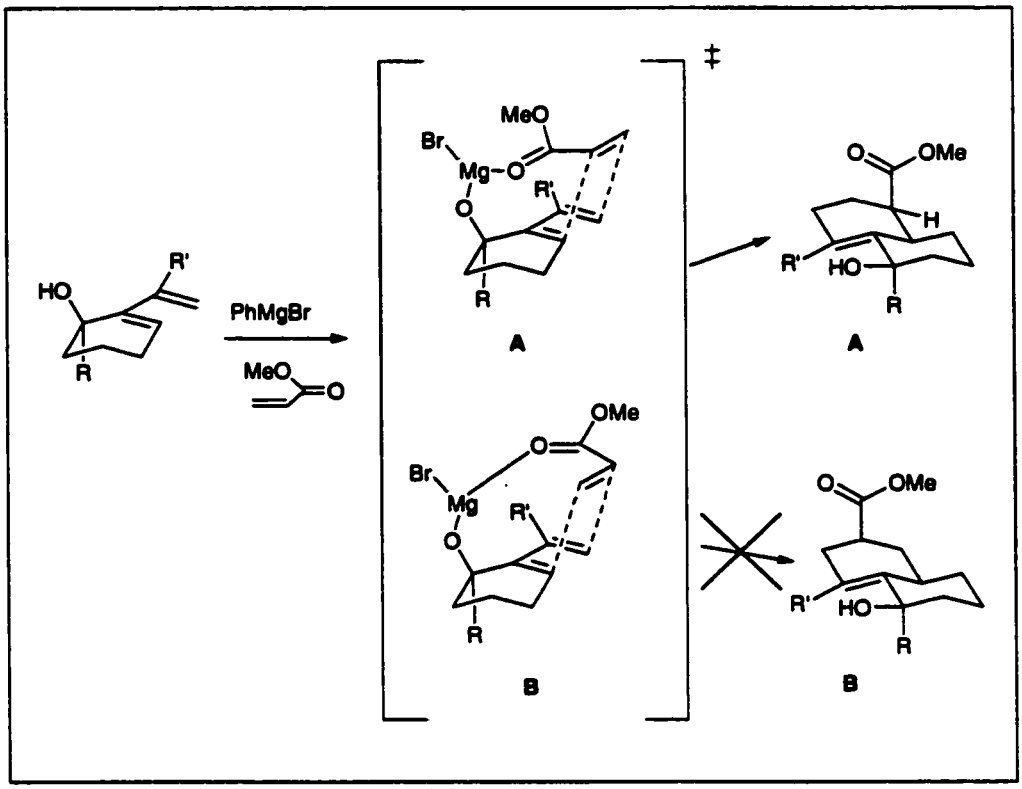


Figure 7: Proposed transition states of tethered Diels-Alder Reaction with type I diene

Endo approach of the dienophile can occur in two ways resulting in two possible transition states **A** or **B**. In transition state **A**, an eight member ring intermediate is formed whereas in transition state **B** a nine member ring intermediate is formed. Transition state **A** should be favored and cycloadduct **A** should be the observed product, as was indeed the case.

The absolute stereochemistry of the cycloadducts was proven by X-ray crystallography (figure 8). It is evident that the electron withdrawing group (of the dienophile) is syn to the hydroxyl group (of the diene) in the cycloadduct. This confirms our claim that the tertiary alcohol dictates the facial selectivity and that the formation of the tether controls the regioselectivity.

In the case of the type II dienes **70-72**, spontaneous lactonization occurred to give cycloadducts **87** and **88** which were crystalline solids.

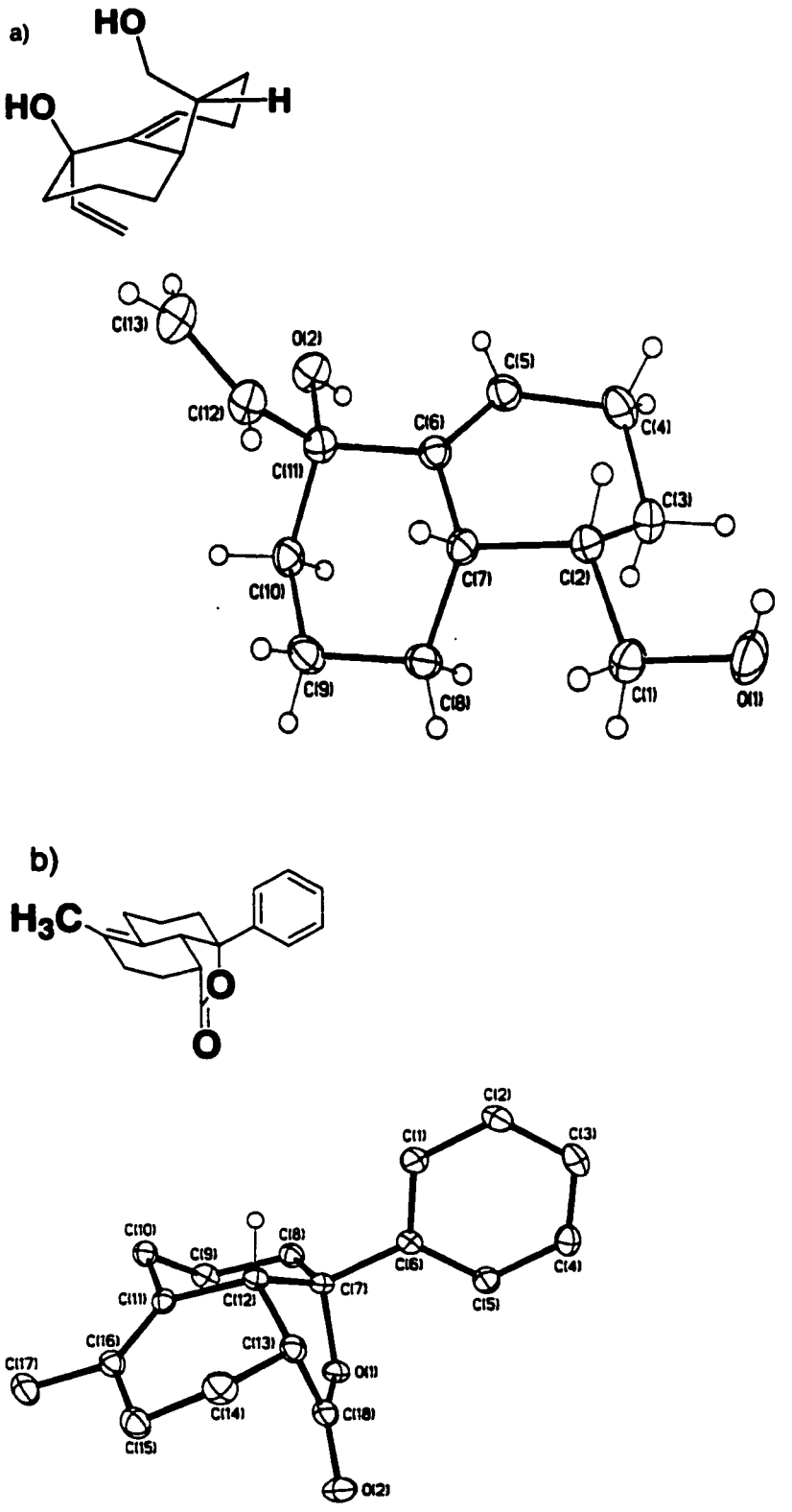


Figure 8: X-ray crystallographs of a) type I and b) type II cycloadducts.

In order for lactonization to occur, the methyl ester must be syn to the hydroxyl group of the tertiary alcohol and it must also be in the required proximity in the cycloadduct for the formation of a five-member lactone. This occurrence can be explained by the transition state diagram below (figure 9). As was the case with the type I dienes, the dienophile can approach in two ways to give transition state intermediates **A** or **B**. However, only the product arising from transition state **A** has the methyl ester group in the right position for formation of the lactone (cycloadduct **A**). Cycloadduct **A** is formed via a 7-member ring intermediate whereas cycloadduct **B** would result from an 8-member ring intermediate. Transition state **A** should be favoured and thus cycloadduct **A** is the only observed product.

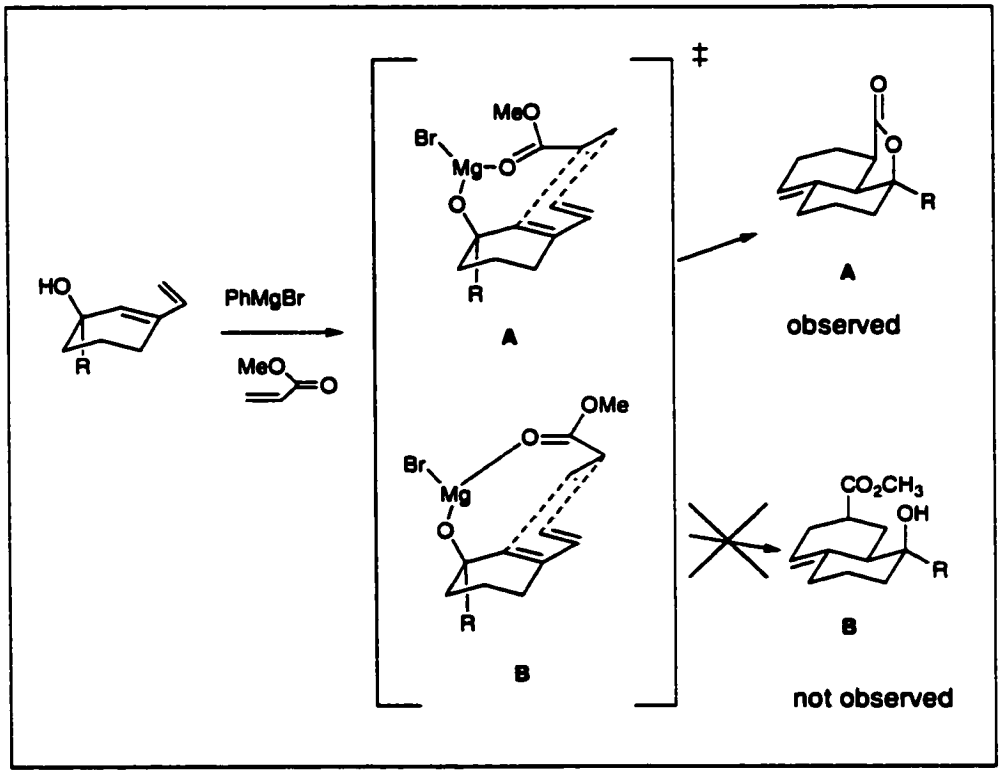
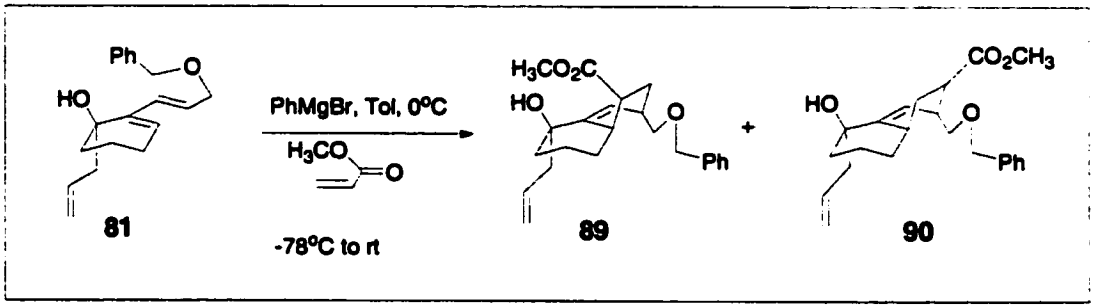


Figure 9: Proposed transition state for type II dienes.

The results with the type III dienes were particularly interesting. Treatment of diene **81** with PhMgBr and methylacrylate gave an inseparable mixture of cycloadducts (entry 6, table 1) believed to be the two regioisomers shown in figure 17.



Scheme 17: Possible cycloadducts from type III dienes.

The lack of regioselectivity obtained with these dienes may be the result of the Lewis acid complexing to the oxygen on the side chain. This will result in the formation of a nine member ring transition state **TS**, depicted in figure 10, which although not favoured, can result in the formation of regioisomer **90**. It is also possible that the $-CH_2OBn$ moiety acts as a withdrawing group thus changing the size of the coefficient of the atomic orbitals on the diene and consequently affecting the regioselectivity.

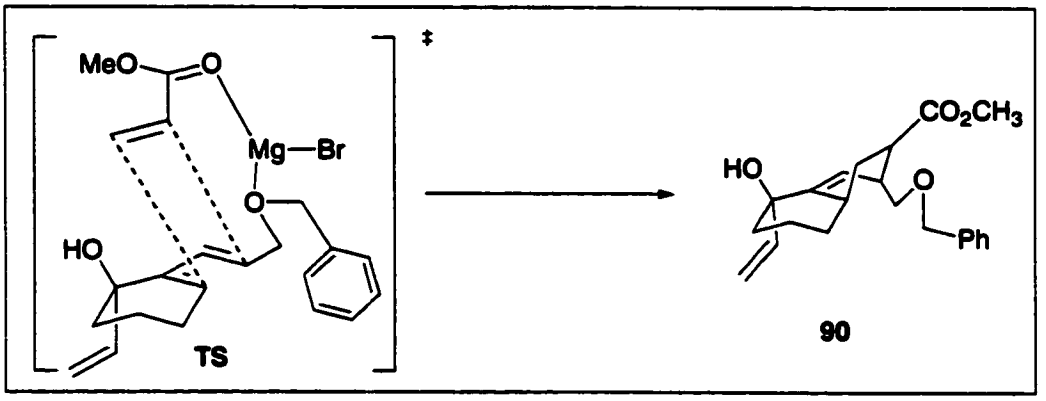


Figure 10: Transition state for alternative binding site of the Lewis acid.

The hypotheses of alternative tethering of the Lewis acid can be proven by subjecting a diene with an alkyl side-chain to the Diels-Alder reaction. In the absence of a second oxygen (alternative tethering site), we expect complete control of

regioselectivity. Another way of proving that the oxygen on the side chain serves as an alternative tethering site for the Lewis acid would be to use a longer chain, with the oxygen atom closer to the terminus. This would result in the formation of a transition state intermediate which is highly unlikely to form a cycloadduct. Investigation of these scenarios are currently in process.

Although the results with PhMgBr were successful, they were not entirely satisfactory because of the irreproducibility of the reaction yields, which ranged from 30-85% (entries 4 and 1 respectively, table 1). It was later discovered that the yield of the reaction was related to the quality and concentration of the PhMgBr being used. The PhMgBr was prepared in our lab and it was observed that the use of a freshly prepared bottle gave good yields. However, as the Grignard reagent aged, the yields diminished.

The inconsistency of the yields with PhMgBr necessitated an alternative means of forming the semicyclic diene magnesium alkoxide.

2.5 Formation of tether with Magnesium bromide Diethyletherate and Et_3N

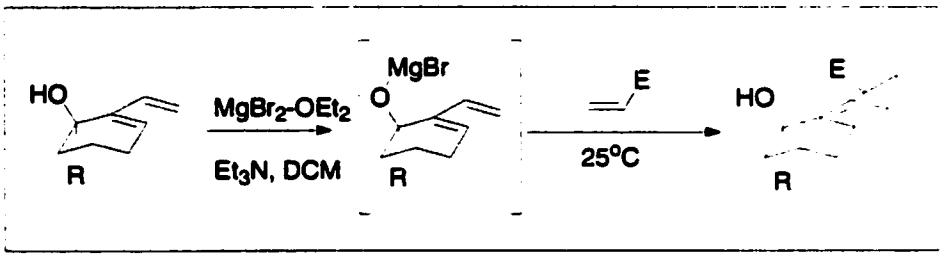
Magnesium bromide diethyletherate is a stable, yellow solid which was easily prepared by reaction of 1,2 dibromoethane and magnesium turnings, in diethylether as solvent (see experimental for procedure). The dried solid was stored under nitrogen in a glove box. Based on the initial success with magnesium alkoxide via PhMgBr we were optimistic about the success of $MgBr_2 \cdot Et_2O$ in the Diels-Alder reaction. However, success was not as easily achieved as we had hoped.

Initial attempts with $MgBr_2 \cdot Et_2O$ were unsuccessful. Addition of 0.5 or 1 equivalent of $MgBr_2 \cdot Et_2O$ to a solution of the diene in dicholoromethane (to generate the magnesium alkoxide prior to addition of the dienophile) resulted in complete degradation of the starting material (similar to the observation with the Al Lewis acids). The, addition of $MgBr_2 \cdot Et_2O$ to a solution of the dienophile, followed by addition of the diene, had the same undesirable result. It seemed as if $MgBr_2 \cdot Et_2O$ was an unlikely candidate for our investigation. However, its legitimacy was salvaged by a report from the Vedejs group on the formation of magnesium alkoxides (for acylation reactions) using

$MgBr_2 \cdot Et_2O$ and Et_3N[29]. This information brought renewed hope to employing $MgBr_2 \cdot Et_2O$ in our Diels-Alder reactions.

We discovered that the sequence of addition of the reagents is imperative to the success of the reaction. The successful method involves addition of 4 equiv of Et_3N to a solution of $MgBr_2 \cdot Et_2O$ (2 equiv) in dichloromethane at room temperature. This mixture must be stirred until a pink colour persists. The diene is then added and stirred for 20 min. Finally, the dienophile is added and the reaction is allowed to proceed with stirring (scheme 18).

The importance of 4 equiv of Et_3N and the generation of the pink colour are not fully understood. $MgBr_2 \cdot Et_2O$ is only partially soluble in DCM. The addition of Et_3N increases its solubility, which is a critical step in the reaction.



Scheme 18: General procedure for $MgBr_2 \cdot Et_2O$ Diels-Alder reaction.

The results of the $MgBr_2 \cdot Et_2O$ mediated reaction are shown in table 2. In each case, the desired cycloadduct was obtained as the only diastereomer. It is noteworthy that the reactions were carried out at room temperature with $MgBr_2 \cdot Et_2O$ as opposed to –78°C with PhMgBr. The reaction times were also faster with $MgBr_2 \cdot Et_2O$.

As was the case with PhMgBr, the reaction with $MgBr_2 \cdot Et_2O$ was highly diastereoselective. However, as we had hoped, the yields with $MgBr_2 \cdot Et_2O$ were much improved and reproducible. The reaction maintained its tolerance to a variety of substituents on the tertiary alcohol, such as vinyl (entries 3, 4 and 10), isopropyl (entries 5, 6 and 11) and phenyl (entries 1, 2 and 7, table 2) and was shown to be successful with dienes having allylic, secondary hydroxy substitution in simultaneous studies performed in our lab by colleague and labmate R. Clement[30].

To further demonstrate the scope of the reaction, acrolein (entry 2), methacrolein (entry 4) and N-phenylmaleimide (entry 11, table 2) were used as dienophiles in addition to methylacrylate. These dienophiles worked remarkably with yields as high as 80 %.

The reactions with acrolein gave an interesting result when Et_3N was used as the base. It was discovered that prolonged exposure to Et_3N resulted in epimerization of the cycloadduct. This observation was made by comparison of the crude ^1H NMR spectrum and that of the purified product. In the case where the reaction was stopped immediately upon completion, the crude ^1H NMR spectrum showed no sign of epimerization (single peak for aldehyde proton). However, upon purification in silica gel doped with Et_3N (to prevent elimination of the tertiary alcohol) the ^1H NMR spectrum showed two peaks at the aldehyde proton. Epimerization was also observed in the case where the reaction was left to stir overnight rather than stopping immediately upon completion.

To circumvent the epimerization problem encountered with Et_3N, 2,6-lutidine (a more hindered base) was used. This substitution was quite successful. The yield and selectivity of the Diels-Alder reaction were not affected and more importantly, epimerization was either minimized or prevented in some cases. Any epimerization that may have occurred is believed to be due to the Et_3N used in the flash column chromatography.

It was hoped that the use of $MgBr_2 \cdot Et_2O$ would solve the regioselectivity problem that was encountered with PhMgBr and the type III dienes. However, this was not the case.

The type IV diene was also successful in the Diels-Alder reaction (entry 10, table 2). This is an encouraging result and will be modified by colleague P. Ang in the development of a tandem Diels-Alder/Claisen reaction toward the total synthesis of Penostatin A.

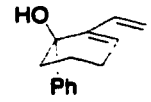
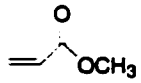
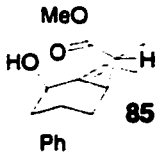
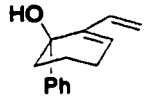
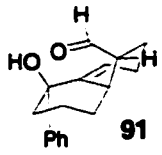
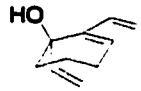
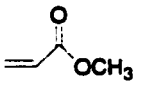
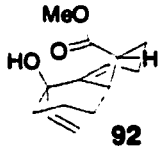
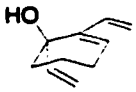
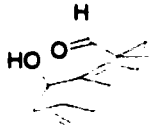
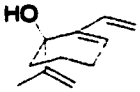
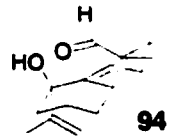
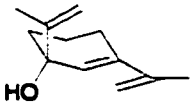
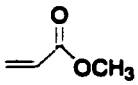
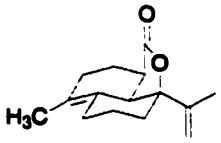
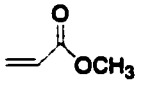
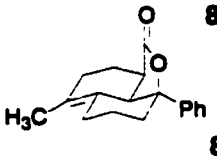
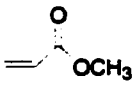
Entry	Diene	Lewis Acid	Dienophile	Base	Observed Product	Yield de>98%
1	 **61**	$MgBr_2$		Et_3N	 **85**	66%
2	 **61**	$MgBr_2$		2, 6- lutidine	 **91**	50%
3	 **63**	$MgBr_2$		2, 6 -lutidine	 **92**	73%
4	 **63**	$MgBr_2$		Et_3N	 **93**	74%
5	 **64**	$MgBr_2$		Et_3N	 **94**	71%
6	 **70**	$MgBr_2$		Et_3N	 **87**	58%
7	 **71**	$MgBr_2$		Et_3N	 **88**	57%
8	 **70**	$MgCl_2$		Et_3N	 **87**	65%

Table 2: Summary of Diels-Alder reaction with $MgBr_2 \cdot Et_2O$.

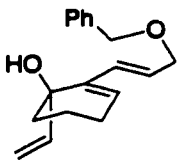
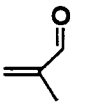
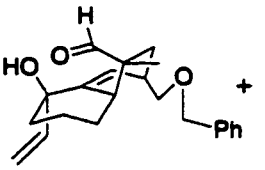
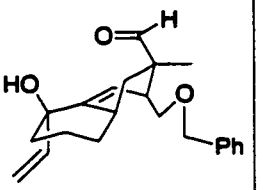
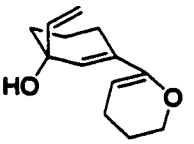
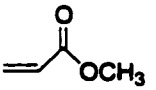
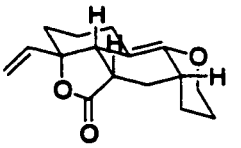
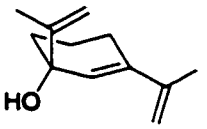
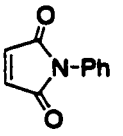
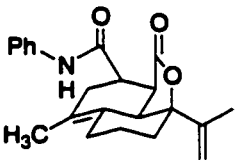
Entry	Diene	Lewis Acid	Dienophile	Base	Observed Product(s)	Yield (de>98%)
9	 **81**	$MgBr_2$		Et_3N	 **95** +  **96**	80% (mixture of of regiosomers)
10	 **83**	$MgBr_2$		Et_3N	 **97**	78%
11	 **70**	$MgBr_2$		Et_3N	 **98**	80%

Table 2 (continued): Summary of Diels-Alder reaction with $MgBr_2 \cdot Et_2O$.

2.6 CONCLUSION

The results presented in this study show the successful development of a method which controls the regio and stereoselectivity of the Diels-Alder reaction with PhMgBr or $MgBr_2 \cdot Et_2O$ and triethylamine of dienes possessing an allylic tertiary alcohol functionality and methylacrylate, methacrolein, acrolein and N-phenylmaleimide as dienophiles. The reaction is highly regioselective (de>98%) and efficient, with yields averaging 70%.

The reaction facilitates vinyl, phenyl, allyl and isopropyl substitution on the tertiary alcohol moiety of the diene, which can be in either the α or β position.

In the case of the PhMgBr controlled reactions, optimal results were obtained when a freshly prepared bottle of the Grignard reagent was used. These reactions required low temperatures and proceeded in moderate to good yields.

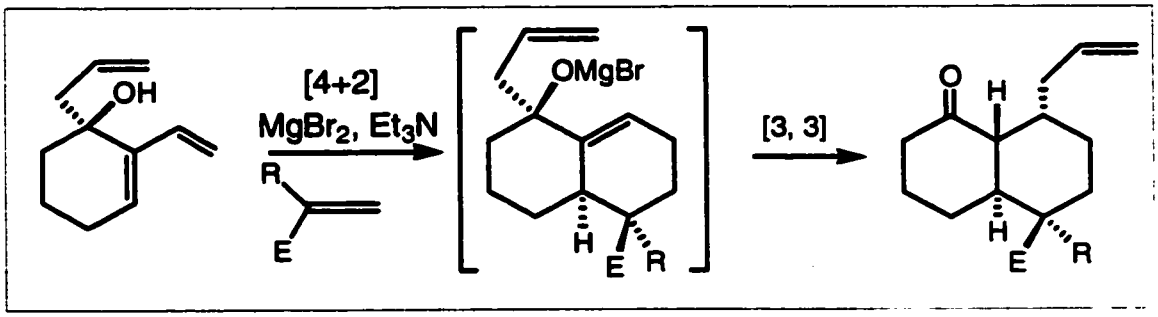
The reactions with magnesium bromide diethyletherate and triethylamine show an improvement in yields of the PhMgBr reactions. These reactions can be performed at room temperature and require less time for completion than the PhMgBr controlled reactions.

2.7 FUTURE PROSPECTS

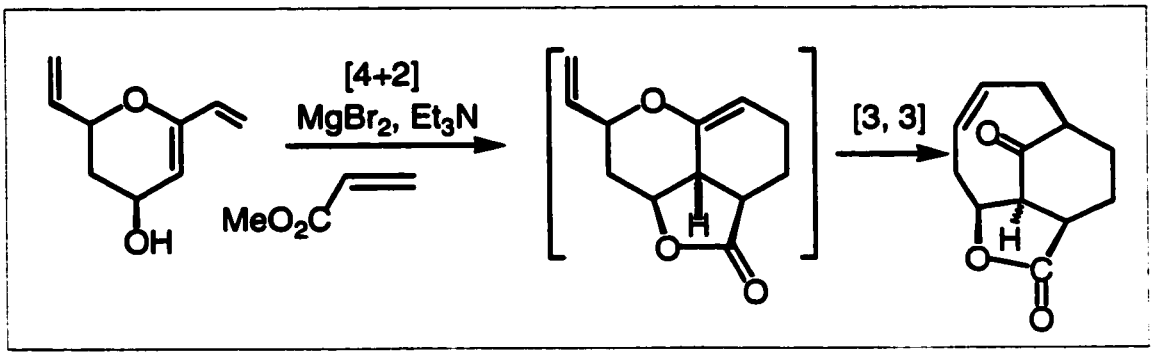
Future work in this study will involve proving the hypothesis of alternative tethering of the Lewis acid in the type III dienes and improvement of the regioselectivity of the ensuing Diels-Alder reaction.

The possibility of forming the Lewis acid tether to a heteroatom (other than oxygen) on the diene or dienophile is also an interesting prospect which will be investigated.

The ultimate goal of this project is the development a tandem Diels-Alder/Oxy-Cope (scheme 19) and a tandem Diels-Alder/Claisen rearrangement reaction (scheme 20) to be used in total synthesis. These two projects are currently under investigation in our laboratory.



Scheme 19: Tandem Diels-Alder/ Oxy-Cope reaction.



Scheme 20: Tandem Diels-Alder/ Claisen rearrangement reaction.

CHAPTER 3

3.1 Experimental

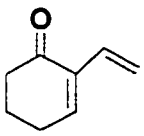
3.1.1 General

All reactions were carried out under dry N_2 atmosphere in flame-dried glassware equipped with a magnetic stir bar and a rubber septum, unless otherwise indicated. THF and Et_2O were freshly distilled from sodium/benzophenone. Dichloromethane, triethylamine and DMF were freshly distilled from CaH_2. $ZnBr_2$ was flame dried under vacuum (1 mmHg). $MgBr_2 \cdot OEt_2$ was prepared in-house and stored in the glove box. The other commercially available reagents were used directly, unless otherwise indicated.

Reactions were monitored by thin layer chromatography (TLC) analysis of aliquots using aluminum sheets pre-coated (0.2mm layer thickness) with silica gel 60 F_{254} (E. Merck). Flash chromatography was carried out on 230- 400 mesh silica gel 60. For purification of compounds containing tertiary alcohol functionality, the silica gel was doped with 2% Et_3N. TLC plates were viewed under UV light and stained with phosphomolybdic acid or p-anisaldehyde staining solutions. GC/MS was performed on a HP 6890 Gas Chromatograph using HP-5MS (cross linked 5% PH ME siloxane) column (30mx0.25mm, 0.25μm film). ^1H and ^{13}C NMR spectra were recorded on a Bruker 300 MHz or Bruker 500 MHz spectrometer. IR spectra were recorded on a Bomen Michaelson 100 FTIR spectrometer. Melting points were recorded on a Gallenkamp Melting Point Apparatus P 1106G. X-ray crystallographs were performed on a Bruker AX SMART 1k CCD diffractometer.

3.1.2 General Procedure for the preparation of dienes and precursors:

Type I dienes (Method A)

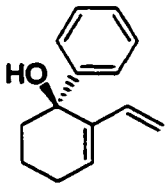


59

2-Vinyl-cyclohex-2-enone

The diene precursors were prepared by Negishi coupling[25, 26] of 2-iodo-cyclohex-2-enone and either vinylmagnesium bromide or isopropenylmagnesium bromide as follows: A 0.1 M solution of flame dried $ZnBr_2$ (2 equiv) in dry, degassed, THF was cooled to –78°C. Isopropenylmagnesium bromide or vinylmagnesium bromide (2 equiv) was then added and the reaction temperature was raised to room temperature over 1 h. In a separate flask, a mixture of 2-iodo-cyclohex-2-enone (1 equiv) and (tetrakis)triphenylphosphine palladium (0.03 mol%) was dissolved in a 1:1 mixture of dry, degassed DMF/THF and then added, via canula, to the flask containing the iodoenone, Grignard solution and $ZnBr_2$ mixture. Upon completion, saturated aqueous NH_4Cl was added. The reaction was extracted with a 1:1 mixture of ether/hexanes (3x) and the combined organic layers were dried over $MgSO_4$. The resulting solution was filtered and concentrated under vacuum. The product was then purified by flash column chromatography (20% EtOAc in Hexanes) to give the desired **59** in yields of 72-90%.

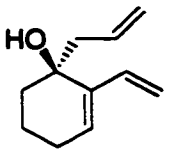
Subsequent alkenylation with either phenyl, vinyl, isopropyl, or allylmagnesium bromide afforded the corresponding dienes in 60-85% yield.



61

1-phenyl-2-vinyl-cyclohex-2-enol. To a solution of **59** (0.5372 g, 3.95 mmol) in ether (40 mL) was added a solution of phenylmagnesium bromide (2.0 M in ether, 2 mL, 4.0

mmol) at -78C. After stirring for 30 minutes, the reaction was quenched with a saturated aqueous solution of ammonium chloride (20 mL). The mixture was extracted with ether (3X). The combined organic phases were dried over magnesium sulfate, filtered and concentrated. The residue was purified by flash chromatography (20% EtOAc in hexanes) to provide **61** (0.26 g, 32%) as an unstable oil: IR (neat) 3453, 3091, 3059, 3023, 2937, 2865, 2828, 1634, 1601, 1491, 1447 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 7.56-7.52 (m, 2H), 7.10-7.04 (m, 1H), 7.23-7.16 (M, 2H), 5.95 (ddd, J=0.8 Hz, 11.2 Hz and 17.2 Hz, 1H), 5.85 (t, J=4.1 Hz, 1H), 5.01 (d, J=17.2 Hz, 1H), 4.75 (d, J=11.2 Hz, 1H), 2.00-1.70 (m, 5H), 1.45-1.20 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 148.0, 140.3, 136.4, 130.7, 128.0, 127.3, 126.4, 125.8, 115.0, 74.5, 42.7, 26.3, 19.0. HRMS (EI) m/z (M^+) calcd for $C_{14}H_{16}O$ 200.1258 found 200.1207.

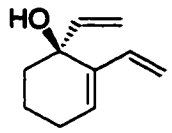


62

1-Allyl-2-vinyl-cyclohex-2-enol

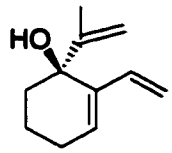
Use same procedure described in **61**. Reagents and quantities: **59** (62.2 mg, 0.510 mmol) in ether (5 mL), allylmagnesium chloride (0.31 mL, 0.612 mmol), to afford 35 mg of **62** as yellow oil in 42% yield.

IR (neat) cm^{-1}: 3429.3, 3071.3, 2936.0, 2865.1, ^1H NMR ($CDCl_3$, 300MHz) δ 6.37 (dd, J=11.2, and 5.5Hz), 5.93 (t, J=4.5Hz, 1H), 5.74-5.81 (m, 1H), 5.41 (d, J= 17.3 1H), 4.9-5.1 (m, 3H), 2.3-2.6 (m, 2H), 1.95-2.20 (m, 2H), 1.70-1.90 (m, 1H), 1.50-1.70 (m, 4H) ^{13}C NMR ($CDCl_3$, 75MHz) δ 141.1, 135.9, 134.2, 128.5, 118.8, 114.7, 71.9, 44.4, 36.4, 26.2, 19.3; HRMS (EI) *m/z* (M^+) calcd for $C_{11}H_{16}O$ 164.1201 found 164.1549.



63

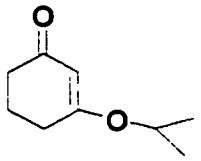
1,2-divinyl-cyclohex-2-enol. Use same procedure described in **61**. Reagents and quantities: **59** (0.666 g, 5.46 mmol), vinylmagnesium bromide (0.8 M in THF, 13.7 mL, 10.9 mmol), ether (55 mL) to afford **63** (0.286g, 35%) as an unstable oil. IR (neat) 3422, 3081, 2935, 1558 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 6.17 (dd, J=10.2 and 17.7 Hz, 1H), 5.99 (t, J=3.1 Hz, 1H), 5.92 (dd, J=10.6 and 17.3 Hz, 1H), 5.33 (d, J=17.7 Hz, 1H), 5.23 (dd, J=1.4 and 17.6 Hz, 1H), 5.13 (dd, J=1.4 and 10.7 Hz, 1H), 4.99 (d, J=10.2 Hz, 1H), 2.20-2.05 (m, 2H), 1.90 (large s, 1H), 1.80-1.55 (m, 4H) ^{13}C NMR ($CDCl_3$, 75 MHz) δ 143.4, 138.7, 135.7, 129.7, 73.2, 38.3, 25.9, 18.7. HRMS (EI) m/z (M^+) calcd for $C_{10}H_{14}O$ 150.1100 found 150.1019.



64

1-Isopropenyl-2-vinyl-cyclohex-2-enol (8). Use same procedure described in **61**. Reagents and quantities: **59** (0.423 g, 3.11 mmol), isopropylmagnesium bromide (0.4 M in THF, 9.4 mL, 3.75 mmol), ether (32 mL) to afford **64** (0.169g, 33%) as an unstable oil. IR (neat) 3470, 3082, 2938, 2865, 1643, 1451 cm^{-1}: , ^1H NMR (C_6H_6, 300 MHz) δ 6.15 (ddd, J=17.8 Hz, 11.3 Hz and 0.9 Hz, 1H), 5.75 (t, J=4.0 Hz, 1H), 5.43 (d, J=17.8 Hz, 1H), 5.32 (dd, J=2.1 Hz, 0.7 Hz, 1H), 4.96 (t, J=1.3 Hz, 1H), 4.92 (d, J=11.3 Hz, 1H),

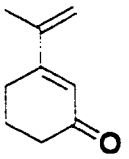
1.80-1.65 (m, 4H), (1.70 (dd, J=1.3 Hz, 0.7 Hz, 3H), 1.60-1.30 (m, 2H) ^{13}C NMR (C_6H_6, 75 MHz) δ 149.0, 136.7, 130.3, 113.7, 111.8, 75.0, 37, 1, 26.1, 19.2, 18.9. HRMS (EI) m/z (M^+) calcd for $C_{11}H_{16}O$ 164.1258 found 164.1173.



67

3-Isopropoxy-cyclohex-2-enone

To a solution of 1,3 cyclohexadione (89.2mmol, 10.0g) in isopropanol (200mL) was added 8.92mmol, 1.697g) of p-toluene solfunic acid (recrystallized from EtOAc). The reaction was stirred for 24 h then neutralized with an aqueous solution of $NaHCO_3$ (checked by litmus). The aqueous phase was extracted with ether (3x). The combined organic layers were dried over $MgSO_4$, filtered, concentrated and purified by flash chromatography (30% EtOAc in hexanes) to give 4.156g of **67** as a pale yellow oil in 45%. All spectroscopic data were in accordance with that reported in the literature[28].



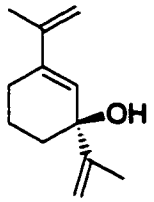
69

3-Isopropenyl-cyclohex-2-enone

To a solution of **67** in ether at -78°C was added either isopropenyl magnesium bromide (1.2 equiv, 1.6M). The reaction was monitored by TLC. Upon completion, the mixture was treated with 5 mL of an aqueous acidic solution. The aqueous phase was extracted with ether (3x). The combined organic phases were dried over $MgSO_4$, filtered, concentrated and purified by flash chromatography (20% EtOAc) to give **69** as a pale

yellow oil in 48%-65%. Subsequent Grignard addition (isopropyl or phenyl magnesium bromide) afforded the desired dienes in 60-80% yield.

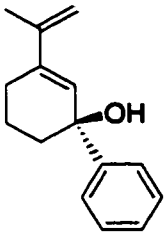
IR (neat) cm^{-1}: 2948, 1664, 1585, 1422, 1358, 1255, ^1H NMR ($CDCl_3$, 300MHz) δ 6.07 (s, 1H), 5.47 (s, 1H), 5.29 (s, 1H), 2.51 (t, J= 5.5Hz, 2H), 2.39 (t, J= 6.0, 2H), 1.98-2.06 (quintet, J= 6.0, 2H), 1.94 (s, 3H); ^{13}C ($CDCl_3$, 75MHz) δ 158.8, 142.8, 125.3, 119.4, 77.0, 37.8, 26.2, 22.9, 20.6. LRMS (EI) *m/z* (M^+) calcd for $C_9H_{12}O$ 136 obsd 136.



70

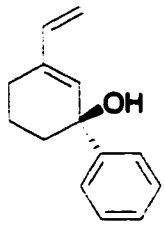
1,3-Diisopropenyl-cyclohex-2-enol

Use same procedure described in **61**. Reagents and quantities: **69** (0.155 g, 1.14 mmol) in ether (12 mL), isopropenylmagnesium bromide (0.5 M in THF, 4.56 mL, 2.28 mmol) to give **70** (0.17 g, 84%) yield as a yellow oil. IR (neat) cm^{-1}: 3412, 3083, 2932, 2855, 1640, 1413. ^1H NMR ($CDCl_3$, 300MHz) δ 5.69 (s, 1H), 5.05-5.10 (m, 1H), 4.9454-5.00 (m, 2H), 4.84- 4.89 (m, 1H), 2.25-2.32 (m, 1H),2.07-2.23 (m, 1H), 1.59-1.89 (m, 1H). ^{13}C NMR ($CDCl_3$, 75MHz) δ 150.3, 143.5, 139.8,128.7, 112.8, 111.6, 74.2, 34.8, 25.9, 21.0, 19.7, 18.6. LRMS (EI) m/z (M^+) calcd for $C_{12}H_{18}O$ 178 found 178.



71

3-Isopropenyl-1-phenylcyclohex-2-enol. Use same procedure described in **61**. Reagents and quantities: **69** (0.23 g, 1.68 mmol), phenylmagnesium bromide (1.56 M in THF, 2.16 mL, 3.36 mmol), ether (17 mL) to provide **71** (0.18 g, 51%). IR (neat) 3368, 3091, 3065, 3029, 2934, 2867, 1606 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 7.52 (d, J=8.4 Hz, 2H), 7.20-7.09 (m, 3H), 5.74 (s, 1H), 5.08 (dd, J=1.0 Hz and 0.6 Hz, 1H), 4.95 (s, 1H), 2.18-1.88 (m, 3H), 1.78 (d, J=0.6 Hz, 3H), 1.69 (dt, J=10.4 Hz and 3.1 Hz, 1H), 1.65-1.50 (m, 1H), 1.48-1.36 (m, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 148.8, 143.6, 139.2, 129.4, 127.7 (2C), 126.6, 125.7 (2C), 112.7, 72.8, 39.8, 25.7, 20.8, 19.6. HRMS (EI) m/z (M^+) calcd for C15H18O found 214.1345.



72

1-Phenyl-3-vinyl-cyclohex-2-enol

IR (neat) cm^{-1}: 3384.2, 3086.3, 3013.4, 29.4.3, 2855.2, 1608.5, 1438.1, 1170.6; ^1H NMR ($CDCl_3$, 300MHz) δ 7.21-7.46 (m, 5H), 6.43 (d, J=17.6 Hz, 1H), 5.77 (s, 1H), 5.29 (d, J=17.3, 1H), 5.11 (d, J=10.8Hz, 1H), 1.56-2.35 (m, 7H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 148.0, 139.6, 139.2, 133.2, 128.5 (2x CH), 127.3, 125.8 (2xCH), 114.0, 73.3, 39.9, 24.1, 19.4; HRMS (EI) *m/z* (M^+) calcd for $C_{14}H_{16}O$ 200.12012 found 200.12044.

74

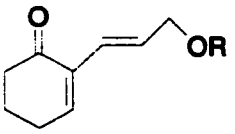
3-Tributylstannanyl-prop-2-en-1-ol

AIBN (2.75 mmol, 450.9 mg) was added to neat tributyltin hydride (71.6 mmol, 19.24 mL). Propargyl alcohol was then added and the mixture was heated overnight at 90°C. The mixture was then cooled to room temperature and directly purified by flash chromatography (5% EtOAc in hexanes) to give **74** as a volatile pale yellow oil.
All spectroscopic data were in accordance with that reported in the literature[28].

75 R= Bn; (3-Benzyloxy-propenyl)-tributyl-stannane

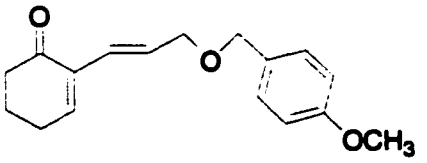
76 R= PMB; Tributyl-[3-(4-methoxy-benzyloxy)-propenyl]-stannane

Alcohol **74** was added (3.01 mmol, 1.045 g), via canula as a 0.1M solution in THF, to a mixture of NaH (3.31 mmol, 132.5mg) in THF (30mL). Benzylchloride (8.083 mmol, 0.93 mL) or p-Methoxybenzyl chloride (1.911 mmol, 0.26 mL) was then added, followed by NaI (0.734 mmol, 110.1 mg). Upon completion, an aqueous, saturated solution of NH_4Cl was added and the organic phase was extracted with ether (3x). The combined organic layers were dried over $MgSO_4$, filtered, concentrated and purified by flash chromatography (10% EtOAc in hexanes) to give **75** or **76** as a yellow oil 2.798 g – 3.041 (80-87%). All spectroscopic data were in accordance with that reported in the literature[28].



77 R= Bn; 2-(3-Benzyloxy-propenyl)-cyclohex-2-enone
78 R= PMB; 2-[3-(4-Methoxy-benzyloxy)-propenyl]-cyclohex-2-enone

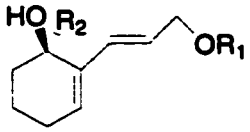
To an argon flushed flask was added **58** (5.341 mmol, 1.185 g) triphenylarsine (0.53 mmol, 165.7 mg), dichlorobis(benzonitrile) palladium (II) (0.267mmol, 102.4mg) and Copper (II) iodide (0.534 mmol, 165.7 mg). 1-methyl-2-pyrolidinone (5 mL) was added and the dark coloured mixture was stirred. A solution of **75** or **76** in NMP was then added to the mixture via canula. The mixture became a pale green colour then turned black upon continuous stirring. Upon completion, ethylacetate (100mL) was added. The organic phase was washed with aqueous KF solution (3 x 50mL) and H_2O (2 x 50mL). The resulting aqueous phase was back extracted with EtOAc (3x). The combined organic layers were dried over $MgSO_4$, filtered, concentrated and purified by flash column chromatography (10-30% EtOAc in Pet. Ether) to give 554.4 mg of **77** or 586.5 mg of **78** as a yellow oil in 43- 50% yield.



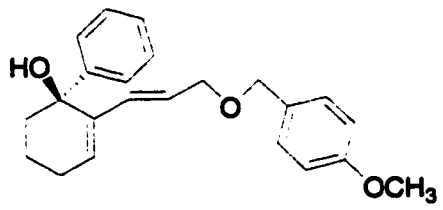
78

2-[3-(4-Methoxy-benzyloxy)-propenyl]-cyclohex-2-enone

IR (neat) cm^{-1}: 2926.2, 2853.5, 1734.9, 1638.9, 1511.3; ^1H NMR ($CDCl_3$, 300MHz) δ 7.24-7.26 (m, 2H), 6.82-6.88 (m, 3H), 6.17-6.22 (m, 1H), 6.02-6.12 (m, 1H), 4.40 (s, 2H), 3.77 (s, 3H), 3.43(t, J=6.5Hz, 2H), 2.35-2.44 (m, 4H), 2.14-2.21 (q, J= 14.1 and 7.0Hz, 2H), 1.91-2.00 (m, 2H), 1.63-1.74 (m, 2H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 159.4, 144.3, 136.7, 132.3, 131.1, 129.6 (2C), 124.7, 114.1(2C), 72.9, 69.8, 55.6, 39.2, 30.3, 29.7, 26.7, 23.1, 19.4; LRMS (EI) *m/z* (M^+) calcd for $C_{19}H_{24}O_3$ 316 obsd 316.



To a solution of **77** or **78** (0.29 mmol, 70.2 mg) in ether (3 mL) at –78°C was added either phenyl or allyl magnesium bromide (0.4 M, 0.58 mmol, 1.45 mL). The reaction was monitored to completion by TLC. An aqueous saturated solution of NH_4Cl was then added. The aqueous phase was extracted with ether (3x). The combined organic phases were dried over $MgSO_4$, filtered, concentrated and purified by flash chromatography (20% EtOAc in hexanes) to afford compounds **79** in 44 -55% yield.

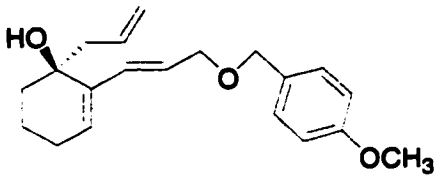


79

2-[3-(4-Methoxy-benzyloxy)-propenyl]-1-phenyl-cyclohex-2-enol

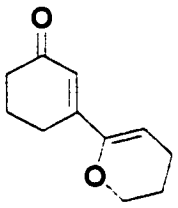
Prepared using Diels-Alder Method A.

IR (neat) cm^{-1}: 3458, 2942, 1612, 1513, 1248, 1036; ^1H NMR ($CDCl_3$, 300MHz) δ 7.12-7.43 (m,7H), 6.80-6.84 (m, 2H), 6.12-6.19 (t, J=4.1Hz, 1H), 5.93(d, J=16.1Hz, 1H), 5.49-5.58 (m, 1H), 4.22 (s, 2H), 3.79-3.84 (m,2H), 3.77 (s, 3H), 2.22-2.24 (m, 3H), 1.50-2.01 (m, 4H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 147.4, 139.0, 132.2, 132.0, 130.7, 129.8 (2C), 128.4 (2C), 127.4, 127.1, 127.0 (2C), 126.2, 114.1, 76.9, 74.9, 71.5, 70.9, 55.6, 42.5, 265, 19.2; LRMS (EI) *m/z* (M^+- H_2O) calcd for $C_{23}H_{24}O_2$ 332 found 332.



1-Allyl-2-[3-(4-methoxy-benzyloxy)-propenyl]-cyclohex-2-enol

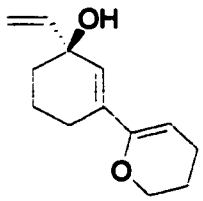
IR (neat) cm^{-1}: 3425.5, 3030.6, 2942.5, 2852.2, 1611.8. ^1H NMR ($CDCl_3$, 300MHz) δ 7.23-7.25 (m, 2H), 6.84-6.88(m, 2H), 6.04 (d, J=15.6, 2H), 6.01-6.07 (d, J=154.6Hz, 1H), 5.79-5.89 (m, 2H), 4.40 (s, 2H), 3.78 (s, 3H), 3.43 (t, 2H), 1.54-2.52 (m, 14H) ^{13}C NMR ($CDCl_3$, 75MHz) δ 159.5, 140.6, 134.4, 131.1, 130.9(2), 129.6 (2C), 118.6, 114.1, 77.8, 76.1, 72.9, 71.9, 69.8, 55.6, 44.6, 36.3, 30.1, 29.9, 26.2, 19.4. LRMS (EI) *m/z* (M^+-H_2O) calcd for $C_{22}H_{28}O_2$ 324 obsd 324.



82

3-(5,6-Dihydro-4H-pyran-2-yl)-cyclohex-2-enone

Tert-butyllithium (23.4 mmol, 15.63 mL) was added, via syringe, to a solution of dihydropyran (46.8 mmol, 4.28 mL) in THF at –78°C. The mixture was stirred for 40 min, then warmed to 0°C and stirred for 30 min. Isopropyl enol ether **67** (7.814 mmol, 1.020 g) was added and stirring was continued at 0°C. After 1 h, a few drops of acetic acid were added followed by treatment with an aqueous solution of $NaHCO_3$. The aqueous phase was then extracted with ether (3x). The combined organic layers were dried over $MgSO_4$, filtered, concentrated and purified by flash chromatography (20% EtOAc in hexanes) to afford 403.5 mg of **82** as a yellow oil in 29% yield.



83

3-(5,6-Dihydro-4H-pyran-2-yl)-1-vinyl-cyclohex-2-enol

To a solution of **82** (403.5 mg, 2.267 mmol) in ether (23 mL) at -78°C was added vinylmagnesium bromide (0.8 M, 2.72 mmol, 3.40 mL). The reaction was stirred and monitored by TLC until complete. The reaction was then quenched at -78°C with a saturated aqueous solution of NH_4Cl and extracted with ether (3x). The combined organic layers were dried with $MgSO_4$, concentrated under vacuum and purified by flash column chromatography (20% EtOAc in hexanes) to afford 200mg of **83** as a yellow oil in 43% yield.

IR (neat) cm^{-1}: 3414.8 cm^{-1}, 2938.4, 2865.1, 1713.0, 1447.7; ^1H NMR ($CDCl_3$ 300MHz), 5.92 (m, 2H), 5.21 (dd, J= 17.3 and 1.4 Hz, 1H), 5.05 (dd, J= 10.6 and 1.4Hz, 1H), 4.94 (t, J= 4.0Hz, 1H), 3.98-4.03 (m, 2H), 2.04, 2.14 (m, 4H), 1.62, 1.84 (m, 7H) ^{13}C NMR ($CDCl_3$, 75MHz) δ 151.9, 144.4, 134.7, 125.6, 113.4, 99.2, 71.6, 66.4, 36.3, 24.6, 22.7, 21.2, 19.5. LRMS (EI) *m/z* (M^+) calcd for $C_{13}H_{18}O_2$ 206 obsd 206.

3.1.3 General Procedure for Diels-Alder Reactions:

Method A

Phenylmagnesium bromide (1.2 equiv) was added, via syringe, to a 0.1M solution of the diene (1 equiv) in toluene at 0°C, with stirring. The reaction was stirred for 15 min then cooled to –78°C. After an additional 15 min of stirring, the dienophile (methylacrylate) (1 equiv) was added via syringe. The temperature was slowly raised to room temperature and the reaction was monitored by TLC until complete. A solution of saturated aqueous NH_4Cl was then added, followed by extraction with ether (3x). The combined organic layers were dried with $MgSO_4$, filtered and concentrated under vacuum. The crude

product was then purified by flash chromatography (10-20% EtOAc in hexanes) to provide the desired product as the only diastereomer (detected by GC and NMR).

Or

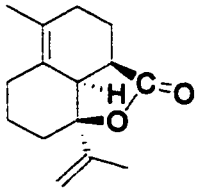
Method B

Triethylamine (4 equiv) was added to a mixture of $MgBr_2 \cdot OEt_2$ (2 equiv) in CH_2Cl_2 (2 M) and stirred until the initial pale yellow colour turned slightly pink. At this time, the diene (1 equiv) was added, via canula, as a solution in CH_2Cl_2 (1.5 mL). The reaction was stirred for 20 min, then the dienophile (2 equiv) was added, via syringe. The mixture was stirred and the reaction was monitored to completion by TLC. A solution of saturated aqueous NH_4Cl was then added, followed by extraction (3x) with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum. The crude product was purified by flash column chromatography (10%-20% EtOAc in hexanes) to provide the desired cycloadduct as the only diastereomer.

3.1.4 Preparation of Magnesium bromide diethyletherate

1,2-dibromoehtane (100 mmol, 8.62 mL) was added, very slowly via syringe, to a solution of Mg turnings (110 mmol, 24.31g) in ether in a round bottom flask adapted with an open-ended condenser (reflux set-up). Note: The reaction is very exothermic and thus was performed at 0°C. The reaction was stirred until most of the Mg was consumed. Upon completion, a bilayered solution was formed. The top phase was extracted via syringe and discarded. The bottom phase contained a 3M solution of $MgBr_2$ in ether as the diethyletherate. Vacuum induced crystallization yielded $MgBr_2 \cdot OEt_2$ as a pale yellow solid (15.0 g, 59%) which was stored under N_2 in the glove box.

3.1.5 Cylcoadducts



87

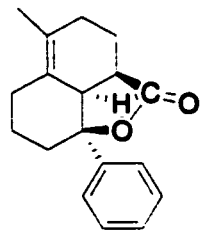
8a-Isopropenyl-5-methyl-2a,3,4,6,7,8,8a,8b-octahydro-naphtho[1,8-*bc*]furan-2-one

Prepared by Diels-Alder method A

Reagent (quantity): Phenyl magnesium bromide (0.39 mL, 0.607 mmol), **70** (90.1 mg, 0.506 mmol); toluene (5 mL). Methylacrylate (0.09 mL, 1.01 mmol) to afford 44.0 mg of **87** as a white solid in 30% yield. mp 126.1-128.2°C

IR (neat) cm^{-1}: 3001, 2919, 2864 , 1764 , 1640; ^1H NMR ($CDCl_3$, 300MHz) δ 5.08-5.13 (m, 1H), 4.93-4.95 (m, 1H), 2.86 (s, 1H), 2.64-2.69 (m, 1H), 2.04-2.101 (m, 2H), 1.78-1.91 (m, 6H), 1.50-1.75 (m, 8H); ^{13}C ($CDCl_3$, 75MHz) δ 179.0, 146.4, 129.7, 126.0, 112.4, 89.4, 42.5, 40.1, 33.2, 28.4, 28.0, 22.4, 20.0, 19.7, 19.3.

LRMS (EI) *m/z* calcd for $C_{15}H_{20}O_2$ 232 obsd 232.



88

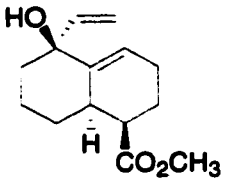
5-Methyl-8a-phenyl-2a,3,4,6,7,8,8a,8b-octahydro-naphtho[1,8,-*bc*]furan-2-one

Prepared using Diels-Alder method A.

Reagents and quantities: Phenylmagnesium bromide (0.29mL, 0.458mmol); **71** (81.6mg, 0.381mmol); toluene (4mL). Methylacrylate (0.07mL, 0.763mmol) to afford 70.6mg of **88** as a white solid in 69% yield. m.pt. 126.1-128.2°C.

IR (neat) cm^{-1}: 2983, 2921, 2856, 1773, 1597; ^1H NMR ($CDCl_3$ 300 MHz) δ 7.27-7.44 (m, 5H), 3.07 (s, 1H), 2.73-2.80 (m, 1H), 2.55-2.60 (m, 1H), 2.19-2.22 (m, 2H), 1.93-2.06 (m, 1H), 1.46-1.91 (m, 9H); ^{13}C ($CDCl_3$, 75MHz) δ 179.0, 144.8, 129.8, 128.9 (2C),

127.9, 126.2, 125.0 (2C), 88.5, 46.4, 40.4, 38.2, 28.7, 28.1, 23.1, 19.7, 19.2. LRMS (EI) calcd for $C_{18}H_{20}O_2$ 268 obsd 268.



92

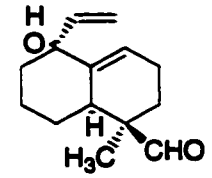
5-Hydroxy-5-vinyl-1,2,3,5,6,7,8,8a-octahydro-naphthalene-1-carboxylic acid methyl ester

Prepared using Diels-Alder method B:

Reagent (quantity): Triethylamine (0.13mL); $MgBr_2 \cdot OEt_2$ (0.621mmol, 160.5mg) in CH_2Cl_2 (1.5mL); **63** (0.311mmol, 55.3mg) in CH_2Cl_2 (1.5mL). Methylacrylate (0.684mmol, 0.06mL,) to provide 41.8mg of **92** as a colourless oil in 58% yield.

IR (neat) cm^{-1}: 3478.8, 2933.1, 1737.2, 1436.0, 1310.5.

^1H NMR ($CDCl_3$, 300MHz) δ 6.04 (dd, J=17.4 and 10.6, 1H), 5.85 (d, J=5.74, 1H), 5.25 (dd, J=17.4 and 1.2Hz, 1H), 5.18 (dd, J=10.5 and 1.2Hz, 1H), 3.65 (s, 3H), 2.62-2.66 (m, 1H), 2.46-2.50 (m, 1H), 2.12-2.18 (m, 1H), 1.96-2.05 (m, 2H), 1.61-1.81 (m, 4H), 1.41-1.45 (m, 2H), 1.34-1.37 (m, 1H), 1.23-1.28 (m, 1H); ^{13}C ($CDCl_3$, 75MHz) δ 175.0, 143.1, 142.4, 117.9, 115.7, 75.6, 51.3, 43.8, 41.7, 37.1, 29.6, 24.5, 23.1, 20.0. HRMS (EI) *m/z* (M^+) calcd for $C_{14}H_{20}O_3$ 236.1725 obsd 236.1411.



93

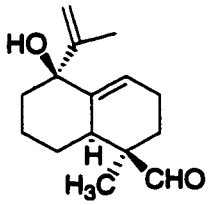
5-Hydroxy-1-methyl-5-vinyl-1,2,3,5,6,7,8,8a-octahydro-naphthalene-1-carbaldehyde

Prepared using Diels-Alder method B.

Reagents and quantities:

Triethylamine (1.164 mmol, 0.16 mL) $MgBr_2 \cdot OEt_2$ (0.581 mmol, 150.1 mg) in CH_2Cl_2 (1.5 mL); **63** (0.291 mmol, 43.6 mg) CH_2Cl_2 (1.5 mL); Methacrolein (0.873 mmol, 0.07 mL) to provide 47.5 mg of **93** as a colourless oil in 74% yield.

IR (neat) cm^{-1}: 3426.3, 3077.6, 2932.5, 2860.8, 1720.1, 1447.5, 1371.2, 990.6; ^1H NMR ($CDCl_3$, 300MHz) δ 9.62 (s, 1H), 5.98 (dd, J= 10.5 and 17.2Hz, 1H), 5.92-5.94 (m, 1H), 5.23 (dd, J= 17.2 and 1.2Hz, 1H), 5.19 (dd, J= 10.5 and 1.2Hz, 1H), 2.19-2.23 (m, 1H), 2.07-2.17 (m, 2H), 1.98- 2.06 (m, 1H), 1.70-1.76 (m, 2H), 1.64-1.69 (m, 2H), 1.43-1.52 (m, 3H), 1.14-1.22 (m, 1H), 1.05 (s, 3H); ^{13}C ($CDCl_3$, 75MHz) δ 206.9, 142.7, 141.4, 118.1, 116.1, 75.3, 47.2, 42.4, 41.3, 29.9, 25.8, 23.0, 21.4, 19.5. HRMS (EI) *m/z* (M^+) calcd for $C_{14}H_{20}O_2$ 220.1463 obsd 220.1418.



94

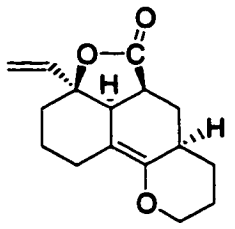
5-Hydroxy-5-isopropenyl-1-methyl-1,2,3,5,6,7,8,8a-octahydro-naphthalene-1-carbaldehyde

Prepared by Diels-Alder method B.

Reagents and quantities: Triethylamine (0.744mmol, 0.10mL) $MgBr_2 \cdot OEt_2$ (0.372mmol, 96.1mg) in CH_2Cl_2 (1mL); **64** (0.186mmol, 30.5mg,) in CH_2Cl_2 (1mL), methacrolein (0.558mmol, 0.05mL,) to provide 47.5mg of **94** as a colourless oil in 71% yield.

IR (neat) cm^{-1}: 3444.6, 2933.6, 1723.3, 1648.1, 1442.1, 1095.6.

^1H NMR (C_6D_6, 500MHz) δ 9.32 (s, 1H), 5.84-5.85 (m, 1H), 4.87 (d, J= 13.6Hz, 2H), 2.04-2.07 (m, 1H), 1.92-1.98 (m, 1H), 1.80-1.88 (m, 1H), 1.65-1.75 (m, 6H), 1.20-1.39 (m, 7H), 0.96-1.04 (m, 2H) ^{13}C NMR (C_6D_6, 125MHz) δ 205.5, 147.8, 142.1, 118.4, 113.9, 77.4, 47.4, 42.5, 39.5, 31.1, 24.6, 24.1, 21.8, 19.4, 19.1 LRMS (EI) *m/z* (M^+-H_2O) calcd for $C_{15}H_{20}O$ 216.1833 obsd 216.1537.



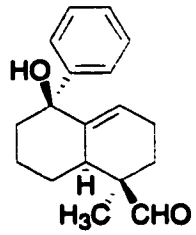
97

3a-Vinyl-2,3,3a,5a,6,6a,7,8,9,10c-decahydro-1*H*-4,10-dioxa-acephenanthylen-5-one

Prepared by Diels-Alder method B

Triethylamine (0.729 mmol, 0.10 mL); $MgBr_2 \cdot OEt_2$ (0.365 mmol, 94.1 mg) in CH_2Cl_2 (1 mL); **83** (0.182 mmol, 37.6 mg,) in CH_2Cl_2 (1 mL). Methylacrylate (0.365 mmol, 0.03 mL) to provide 37.2 mg of **97** as a white solid (mp 94.9-97.7°C) in 78% yield.

IR (neat) cm^{-1}: 3444.6, 2933.6, 2871.6, 1723.3, 1648.1, 1442.1, 1095.6, 888.2; ^1H NMR ($CDCl_3$), 300MHz) δ 5.83 (dd, J= 17.2, and 10.8Hz, 1H), 5.32 (dd, J=17.2 and 0.8Hz, 1H), 5.15 (dd, J=10.8 and 0.8Hz, 1H), 4.05-4.10 (m, 1H), 3.36-3.46 (td, J=10.8 and 2.4Hz, 1H), 2.98-3.07 (m, 1H), 2.83-2.90 (m, 1H), 2.70-2.76 (m, 1H), 2.15-2.20 (m, 1H), 1.95- 2.10 (m, 3H), 1.31-1.82 (m, 10H), ^{13}C NMR ($CDCl_3$, 75MHz) δ 179.5, 151.7, 140.9, 114.8, 113.3, 85.0, 71.1, 43.0, 38.8, 34.2, 32.5, 31.9, 27.1, 25.1, 23.8, 22.3. HRMS (EI) *m/z* (M^+) calcd for $C_{16}H_{22}O_3$ 262.1569 obsd 262.1476.



5-Hydroxy-1-methyl-5-phenyl-1,2,3,5,6,7,8,8a-octahydro-naphthalene-1-carbaldehyde

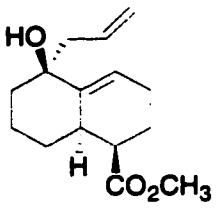
Prepared using Diels-Alder Method B.

Reagents and quantities: **61** (0.179 mmol, 35.8 mg), triethylamine (0.537 mmol, 0.07 mL), methacrolein (0.394 mmol, 0.04 mL) dichloromethane (2 ml).

IR (neat) cm^{-1}: 3424.4, 2932.5, 2862.2, 1721.4, 1447.3, 1260.7, 1050.2.

^1H NMR ($CDCl_3$, 300MHz) δ 9.49 (s, 1H), 7.26-7.44 (m, 5H), 6.12-6.13 (m, 1H), 2.72 (d, J=13Hz, 1H), 2.20-2.31 (m, 2H), 1.12-2.02 (m, 9H), 1.04 (s, 3H) ^{13}C NMR ($CDCl_3$,

75MHz) δ 206.6, 143.0, 142.2, 129.0, 127.8, 126.7, 118.1, 77.0, 47.2, 42.4, 39.2, 30.7, 23.7, 23.3, 21.3, 18.8; HRMS (EI) *m/z* (M^+) calcd for $C_{18}H_{22}O_2$ 270.1120 found 270.1071.



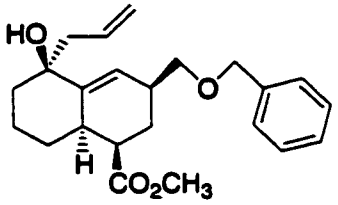
86

5 –Allyl- Hydroxy –1,2,3,5,6,7,8,8a-octahydro-naphthalene-1carboxylic acid methyl ester

Prepared using Diels-Alder method A.

Reagents and quantities: Phenylmagnesium bromide (0.144 mmol, 0.20 mL), **62** (0.144 mmol, 23.7 mg), toluene (2 mL) at 0°C, methylacrylate (0.288 mmol, 0.03 mL) to afford 24.7 mg of **86** as a colourless oil in 65% yield.

IR (neat) cm^{-1}: 3464, 2985, 2852, 1736 ^1H NMR ($CDCl_3$, 300MHz) δ 562-5.73 (m, 2H), 5.09-5.14 (m, 2H), 3.68 (s, 3H), 2.62-2.69 (m, 2H), 2.44-2.49 (m, 1H), 1.22-2.24 (m, 7H) ^{13}C NMR ($CDCl_3$, 75MHz) 175.5, 144.0, 133.9, 119.2, 118.3, 75.1, 51.8, 44.4, 43.0, 41.4, 37.1, 30.0, 24.9, 23.3, 20.2. LRMS (EI) *m/z* (M^+) calcd for $C_{15}H_{17}O_2$ 229 found 229.



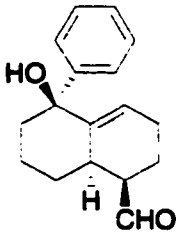
89 and **90** (mixture of regioisomers)

1-Allyl-2-(3-benzyloxy-propenyl)-cyclohex-2-enol

Prepared by both Diels-Alder methods A and B.

IR (neat) cm^{-1}: 3479.9, 3068.2, 3029.3, 2932.2, 2859.2, 1092.1. ^1H NMR ($CDCl_3$, 300MHz) 7.27-7.34 (m, 5H), 6.30-6.33 (m, 1H), 6.25-6.28 (m, 1H), 5.93-6.04 (m, 2H), 5.68-5.85 (m, 1H), 5.05-5.15 (m, 2H), 4.51 (s, 2H), 4.06 (dd, J=6.1 and 0.97Hz, 2H), 2.35-2.53 (m, 2H), 1.93-2.20 (m, 4H), 1.55-1.65 (m, 8H); ^{13}C NMR ($CDCl_3$, 75MHz)

140.0, 138.8, 134.2, 131.7, 128.9 (2xCH), 128.7, 128.2 (2xCH), 127.9, 126.7, 118.9, 76.5, 75.3, 72.3, 71.9, 71.5, 44.4, 39.2, 36.4, 26.2, 19.3. LRMS (EI) *m/z* (M^+) calcd for $C_{23}H_{30}O_4$ 354 obsd 354.

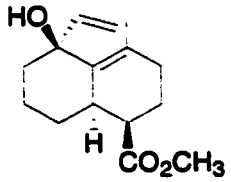


91

5-hydroxy-5-phenyl-1,2,3,5,6,7,8,8a-octahydro-naphthalene–1-carboxylicacid methyl ester

Prepared by Diels-Alder method B

IR (neat) cm^{-1}: 3483.6, 3045.4, 2936.4, 2858.8, 1734.8, 1492.3; ^1H NMR ($CDCl_3$), 500MHz) δ 7.24-7.47 (m, 5H), 6.08, (d, J= 0.02Hz, 1H), 3.58 (s, 3H), 2.62-2.71 (m, 2H), 2.01-2.71 (m, 3H), 1.59-1.88 (m, 5H), 1.21-1.51 (m, 3H); ^{13}C NMR ($CDCl_3$, 125MHz) δ 175.0, 143.7, 143.3, 128.9 (2xCH), 17.7, 16.7 (2xCH), 118.8, 77.3, 51.2, 43.7, 39.2, 37.3, 29.7, 24.6, 23.2, 20.0; HRMS (EI) *m/z* (M^+) calcd for $C_{18}H_{22}O_3$ 286.1569 found 286.1606.

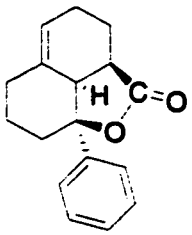


84

5-Hydroxy-4-methyl-5-vinyl-1,2,3,5,6,7,8,8a-octahydro-naphthalene-1-carboxylic acid methyl ester

Prepared by Diels-Alder method A.

IR (neat) cm^{-1}: 3515.5, 2940.7, 1735.0, 1435.7, 1157.8; ^1H NMR ($CDCl_3$, 300MHz) δ 5.91 (d, J=17.2Hz, 1H), 5.26 (dd, J=17.2 and 1.7Hz, 1H), 4.99 (dd, J= 10.5 and 1.7Hz, 1H), 3.41 (s, 3H), 2.43-2.56 (m, 2H), 1.35-1.86 (m, 14H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 175.5, 142.2, 134.4, 132.1, 128.7, 112.3, 51.8, 44.0, 39.0, 34.9, 33.7, 25.6, 20.8, 20.2, 18.5. LRMS (EI) *m/z* (M^+) calcd for $C_{15}H_{22}O_3$ 250.1 found 250.



8a-Phenyl-2,3,4,6,7,8,8a,8b-octahydro-naphtho-[1,8-*bc*]-furan-2-one

Prepared by Diels-Alder method A.

IR (neat) cm^{-1}: 2922.9, 2851.6, 1778.2, 1127.; ^1H NMR ($CDCl_3$, 500MHz) δ 7.26-7.45 (m, 5H), 5.66 (s, 1H), 3.09 (s, 1H), 2.60-2.62 (m, 1H), 1.05-2.20 (m, 10H); ^{13}C NMR ($CDCl_3$, 125MHz) δ 178.3, 144.0, 133.5, 128.6 (2xCH), 127.6, 124.8, 124.6, 87.7, 45.0, 39.8, 37.5, 34.5, 29.7, 23.5, 21.1, 18.6; HRMS (EI) m/z (M^+) calcd for $C_{17}H_{18}O_2$ 254.13068 found 254.13198.

CLAIMS TO ORIGINAL RESEARCH

1. Developed a highly regio and stereoselective method for the Diels-Alder reaction of dienes possessing a tertiary allylic alcohol functionality using $MgBr_2 \cdot OEt_2$ and Et_3N, evident by the synthesis of novel cycloadducts.

PRESENTATION OF ORIGINAL RESEARCH

1. Oral Presentations: "Highly regio and stereoselective hydroxy-directed Diels-Alder reaction" J.Thomas and L. Barriault. (i) November 9, 2001 Quebec-Ontario Minisymposium in Synthetic and Bio-organic Chemistry (QOMSBOC). University of Sherbrooke. Sherbrooke, Quebec. Canada. (ii) April 24, 2002. Torcan Chemicals. Aurora, Ontario. Cananda. (iii) April 29, 2002. Neokemia Inc. Sherbrooke, Quebec. Canada. (iv) May 9, 2002. Pfizer Global Research and Development. Ann Arbor, Michigan. USA. (v) May, 24 2002. Astra-Zeneca. Montreal, Quebec. Canada.

2. Poster Presentations: "Highly regio and stereoselective hydroxy-directed Diels-Alder reaction". J. Thomas and L. Barriault. (i) Symposium International en Synthèse Organique et Organométallique de l'Université de Montréal (SISOUM). Montreal, Quebec. Canada. (ii) The 85th Canadian Society of Chemistry (CSC) Conference and Exhibition. June 2002. Vancouver, British Columbia. Canada.

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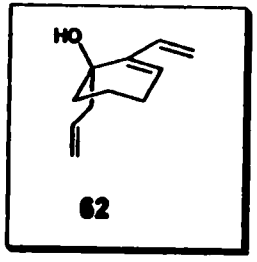
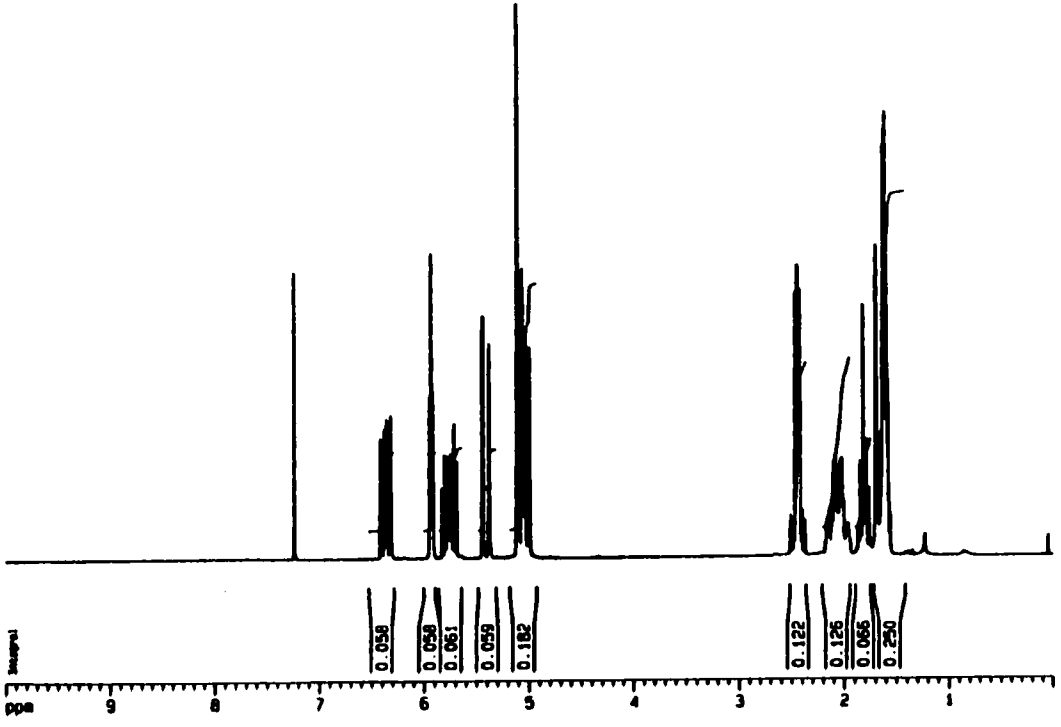
APPENDIX



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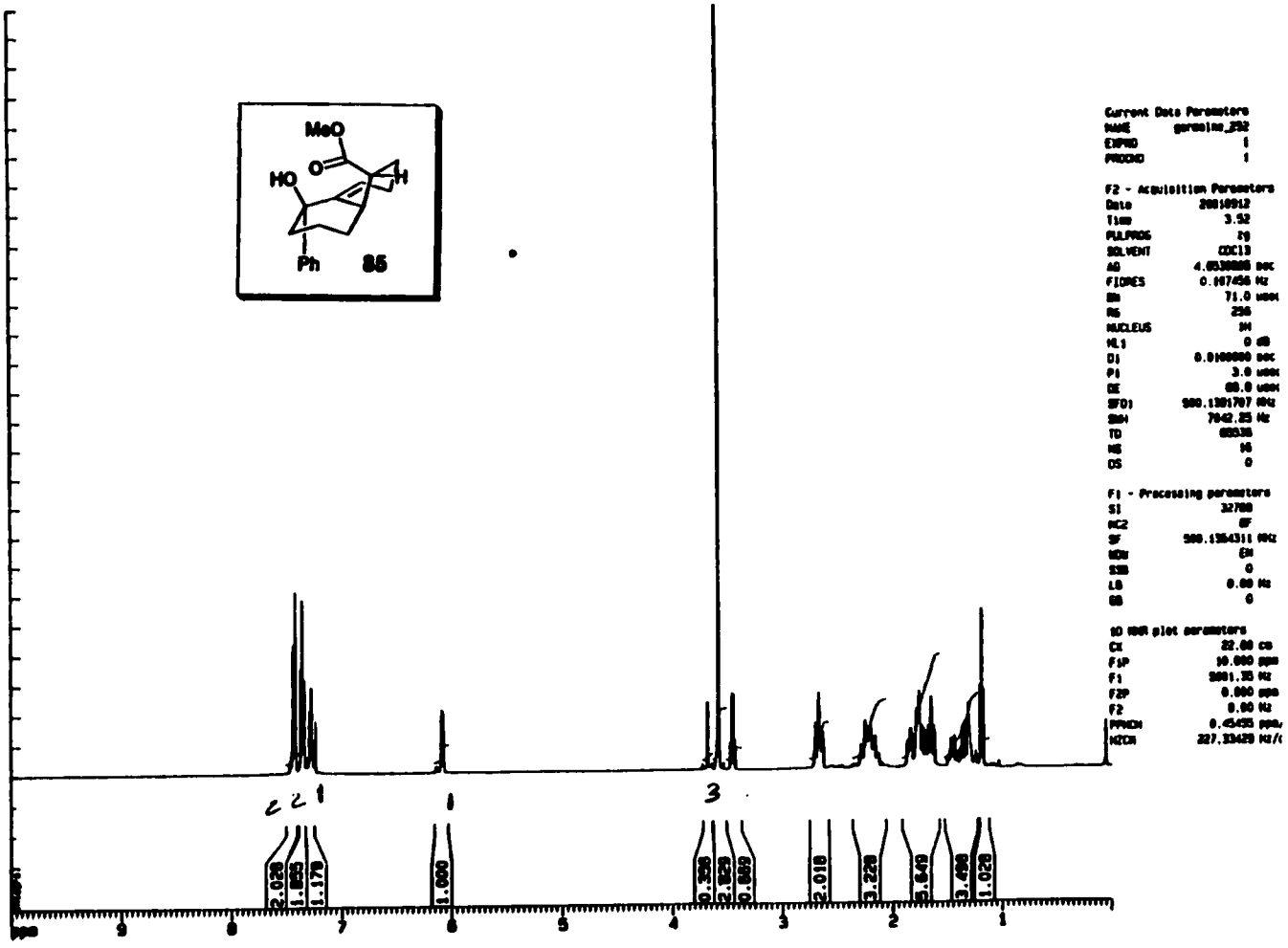
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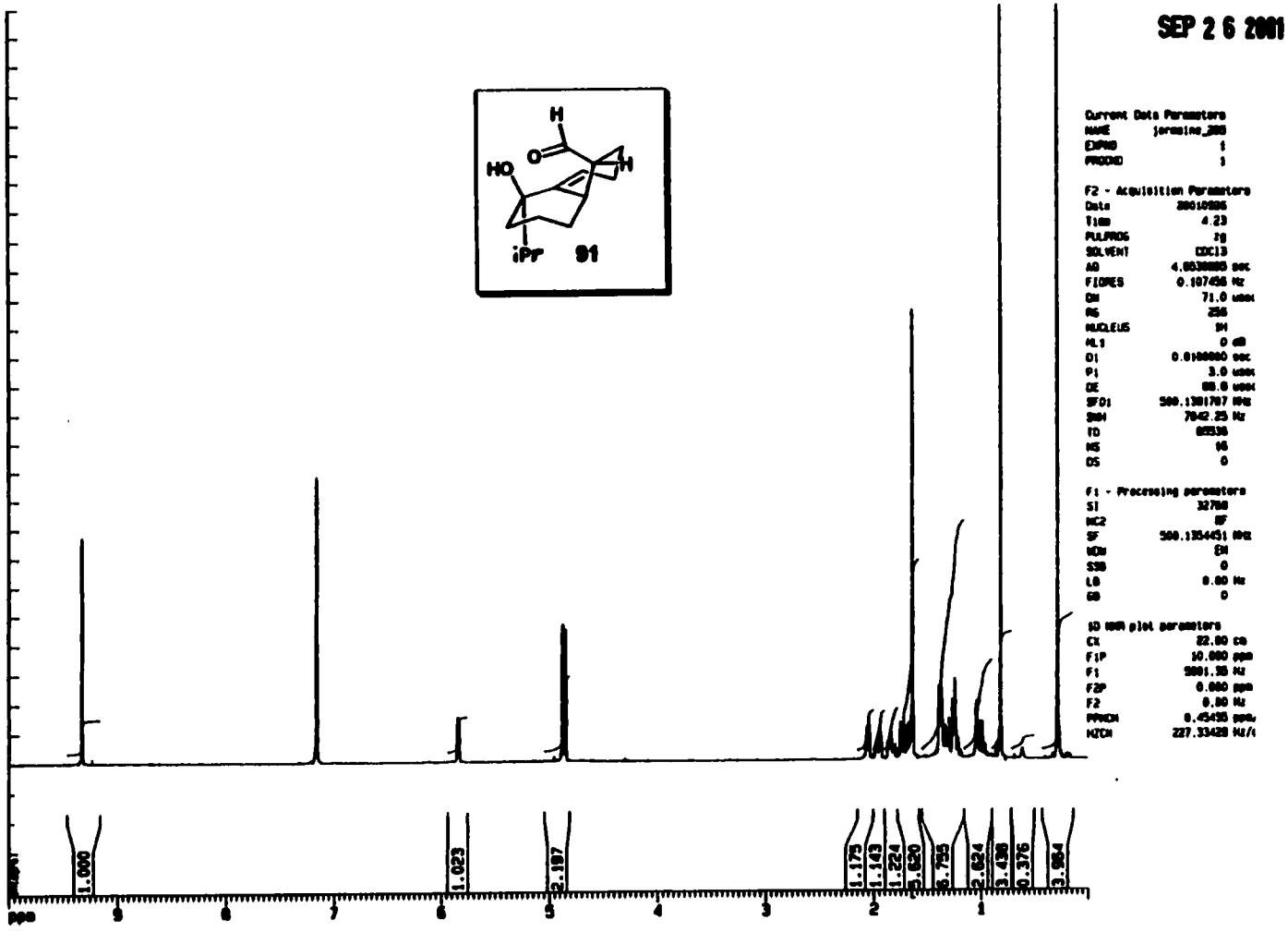
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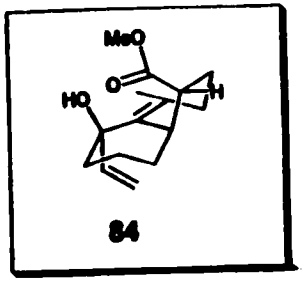

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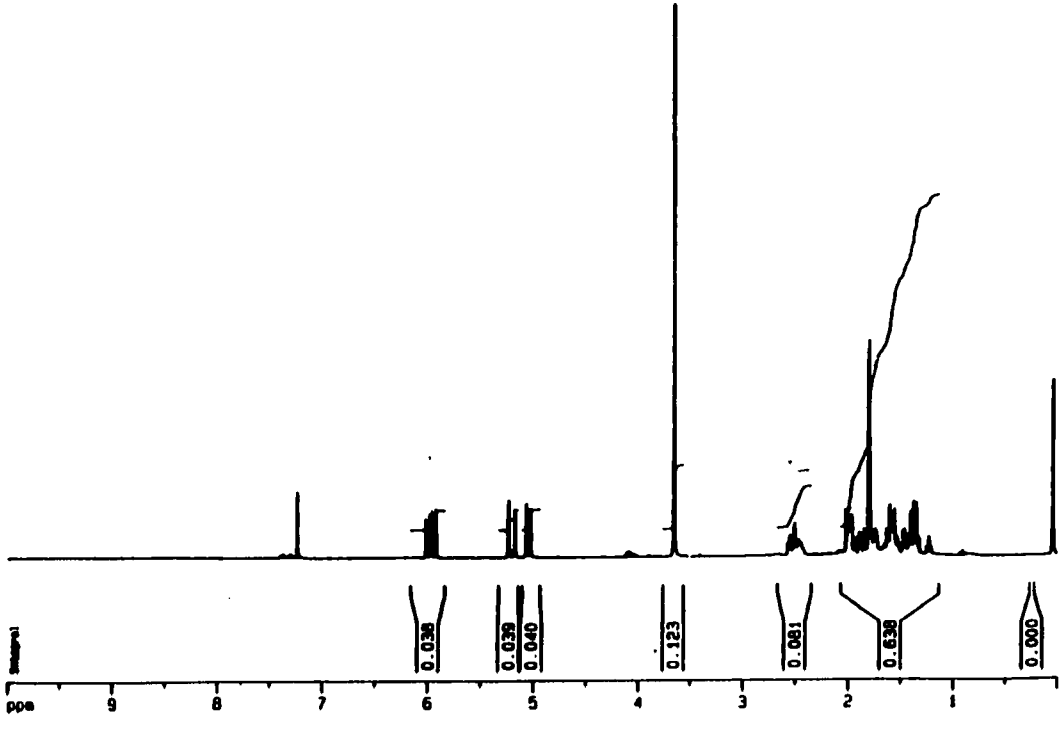


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PROCNO                 1

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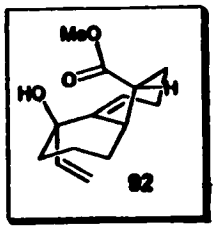
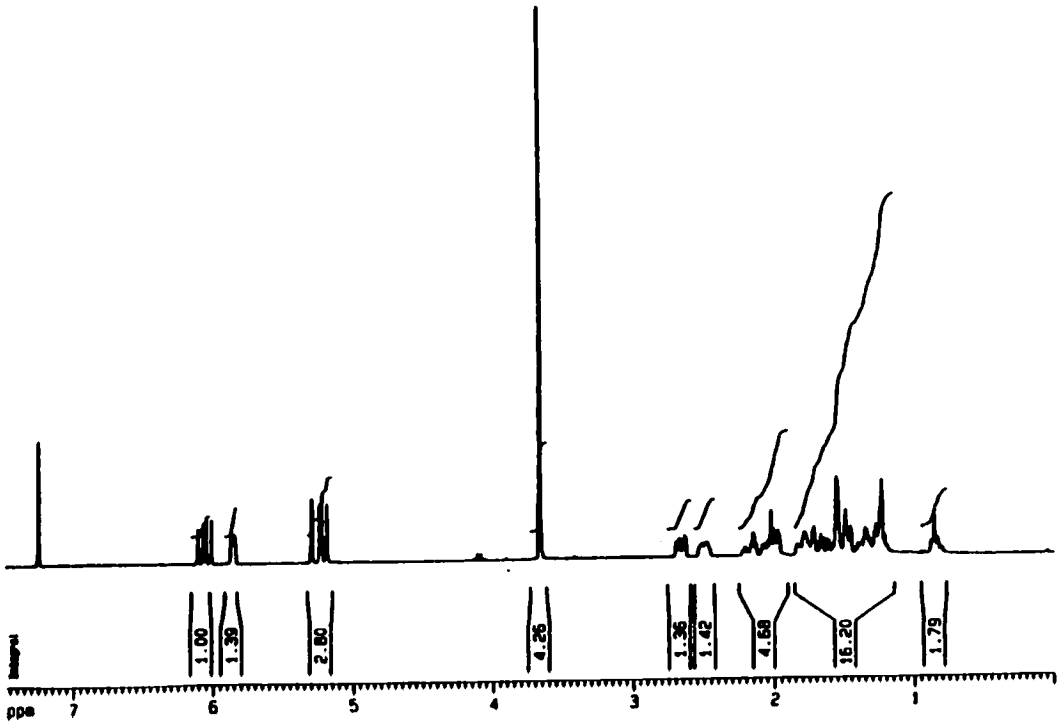
Date_           20010515
Time                17.13
INSTRUM             av300
PROBHD  5 mm BBF  1H/1
PULPROG             zg30
TD                 30720
SOLVENT             CDCl3
NS                     16
DS                      0
SWH              5081.301 Hz
FIDRES           0.165407 Hz
AQ               3.0228980 sec
RG                  228.1
DW                 98.400 usec
DE                  6.00 usec
TE                 300.0 K
D1              1.00000000 sec

------------ CHANNEL f1 -------------
NUC1                   1H
P1                  9.50 usec
PL1                -3.00 dB
SFO1          300.1319477 MHz

F2 - Processing parameters
SI                    65536
SF            300.1300000 MHz
WDW                    EM
SSB                     0
LB                   0.10 Hz
GB                      0
PC                   1.00

1D NMR plot parameters
CX                  20.00 cm
CY                  18.00 cm
F1P                 10.000 ppm
F1                3001.30 Hz
F2P                 0.000 ppm
F2                    0.00 Hz
PPMCM             0.50000 ppm/cm
HZCM            150.06580 Hz/cm
```





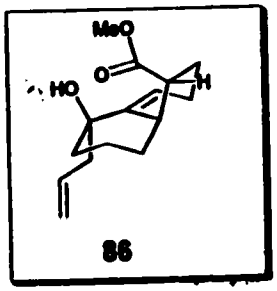

```
Current Data Parameters
NAME          jdet_262ara
EXPNO                   1
PROCNO                  1

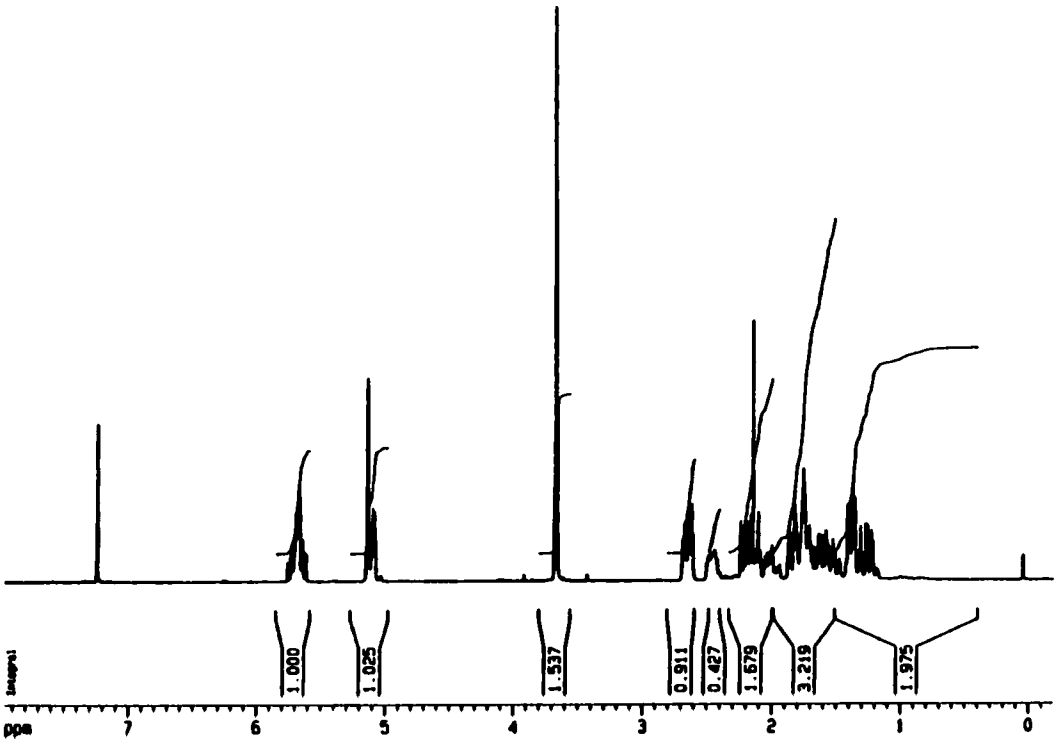
F2 - Acquisition Parameters
Date_            20020430
Time                11.57
INSTRUM             av300
PROBHD   5 mm BBF  1H/1
PULPROG             zg30
TD                 30720
SOLVENT             CDCl3
NS                     16
DS                      0
SWH              5081.301 Hz
FIDRES           0.165407 Hz
AQ               3.0220880 sec
RG                  645.1
DW                 98.400 usec
DE                  6.00 usec
TE                 300.0 K
D1               1.00000000 sec

------------ CHANNEL f1 -------------
NUC1                   1H
P1                 10.00 usec
PL1                -3.00 dB
SFO1          300.1318477 MHz

F2 - Processing parameters
SI                    65536
SF          300.1300000 MHz
WDW                    EM
SSB                     0
LB                   0.10 Hz
GB                      0
PC                   1.00

1D NMR plot parameters
CX                  20.00 cm
CY                  10.00 cm
F1P                 7.472 ppm
F1                 2242.64 Hz
F2P                -0.000 ppm
F2                 -0.00 Hz
PPMCM            0.37361 ppm/cm
HZCM            112.13207 Hz/cm
```





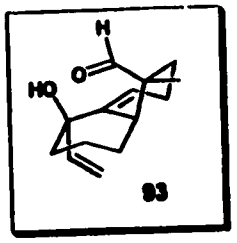

```
Current Data Parameters
NAME                 jeot_110
EXPNO                       1
PROCNO                      1

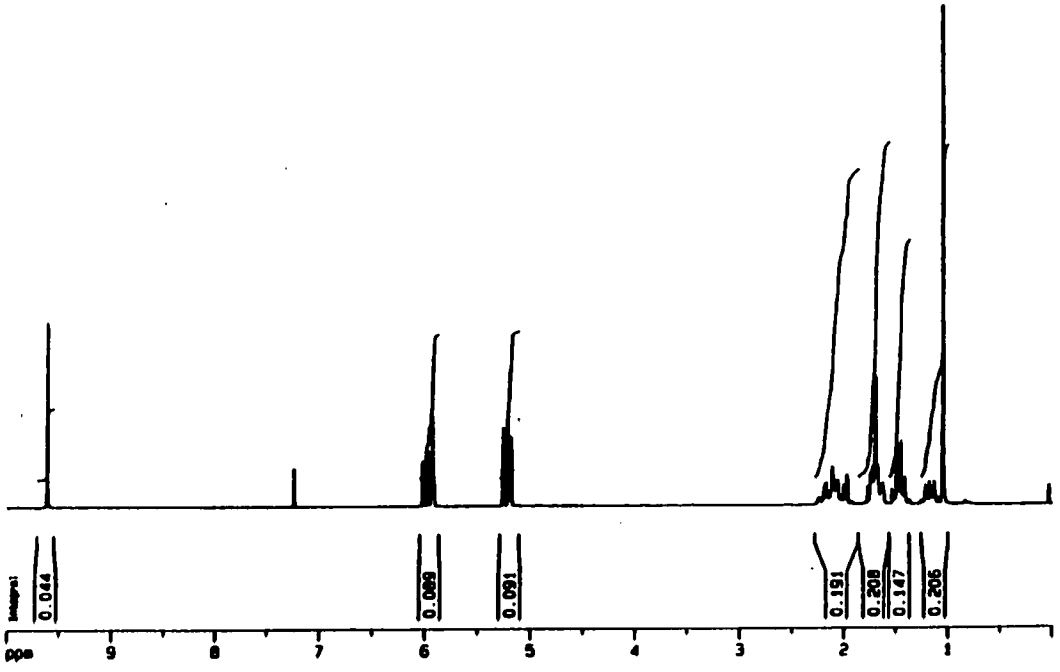
F2 - Acquisition Parameters
Date_               20010307
Time                   18.16
INSTRUM                av300
PROBHD   5 mm DUP  1H/1
PULPROG                zg30
TD                    30720
SOLVENT               CDCl3
NS                       16
DS                        0
SWH                5081.301 Hz
FIDRES             0.165407 Hz
AQ                 3.0220880 sec
RG                     203.2
DW                  98.400 usec
DE                    6.00 usec
TE                   300.0 K
D1                1.00000000 sec

============ CHANNEL f1 =============
NUC1                     1H
P1                    9.50 usec
PL1                  -3.00 dB
SFO1           300.1319477 MHz

F2 - Processing parameters
SI                      65536
SF             300.1300000 MHz
WDW                        EM
SSB                         0
LB                     0.10 Hz
GB                          0
PC                       1.00

1D NMR plot parameters
CX                     20.00 cm
CY                     25.00 cm
F1P                    7.959 ppm
F1                   2388.82 Hz
F2P                   -0.198 ppm
F2                    -58.58 Hz
PPMCM                0.40708 ppm/cm
HZCM               122.41626 Hz/cm
```





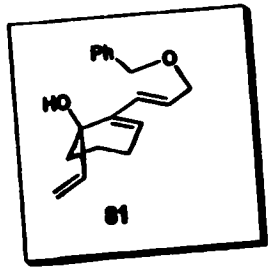

```
Current Data Parameters
NAME            jdet_263
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_          20010912
Time               11.59
INSTRUM            av300
PROBHD     5 mm BBO BB-
PULPROG            zg30
TD                30720
SOLVENT           CDCl3
NS                   16
DS                    0
SWH           5081.301 Hz
FIDRES        0.165407 Hz
AQ            3.0220800 sec
RG                143.7
DW               98.400 usec
DE                6.00 usec
TE               300.0 K
D1            1.00000000 sec

------------ CHANNEL f1 -------------
NUC1                 1H
P1                9.75 usec
PL1              -3.00 dB
SFO1        300.1318477 MHz

F2 - Processing parameters
SI                65536
SF          300.1300000 MHz
WDW                  EM
SSB                   0
LB                 0.10 Hz
GB                    0
PC                 1.00

1D NMR plot parameters
CX                20.00 cm
CY                18.00 cm
F1P               10.000 ppm
F1                3001.30 Hz
F2P               0.000 ppm
F2                0.00 Hz
PPMCM             0.50000 ppm/cm
HZCM            150.06500 Hz/cm
```



81

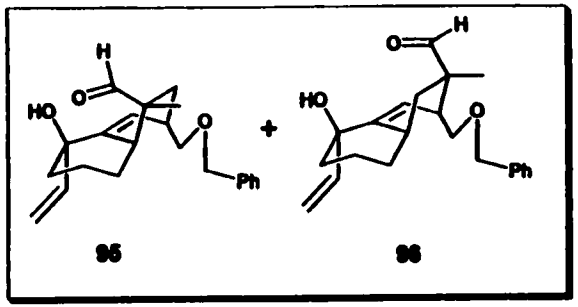

```
Current Data Parameters
NAME            jdet_207rr
EXPNO                    1
PROCNO                   1

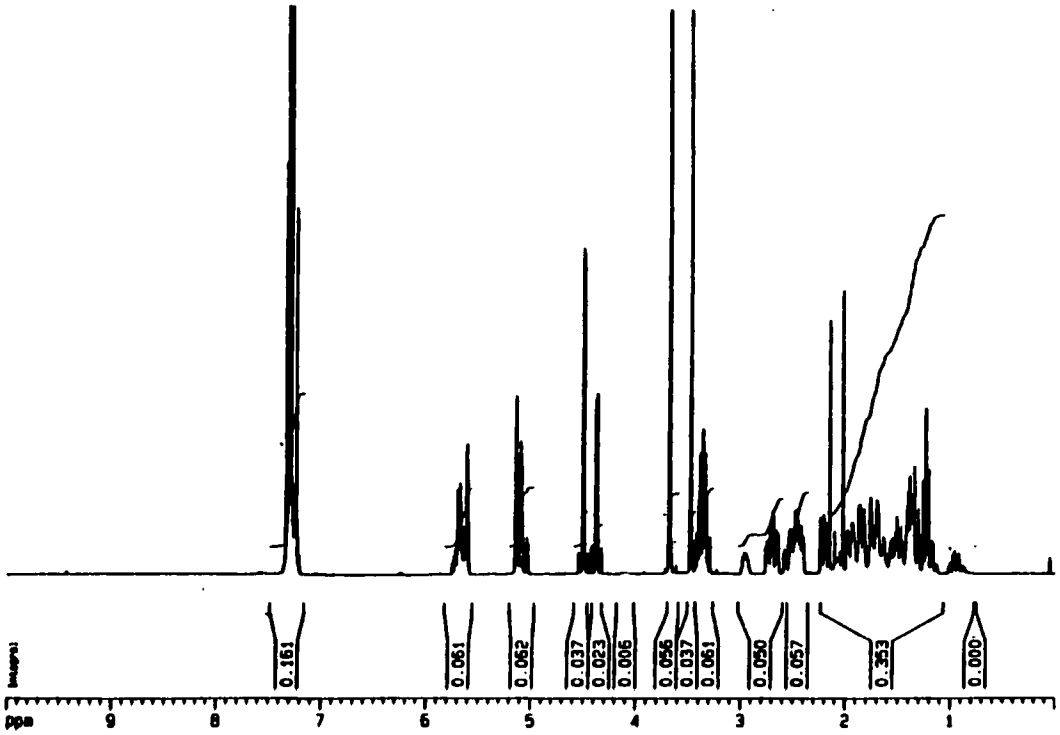
F2 - Acquisition Parameters
Date_              20011128
Time                  15.33
INSTRUM               av300
PROBHD  5 mm BBF  1H/1
PULPROG               zg30
TD                   30720
SOLVENT              CDCl3
NS                      16
DS                       0
SWH                5081.301 Hz
FIDRES             0.165407 Hz
AQ                 3.0228000 sec
RG                     203.2
DW                  98.400 usec
DE                   6.00 usec
TE                  300.0 K
D1                 1.00000000 sec

------------ CHANNEL f1 -------------
NUC1                     1H
P1                   11.00 usec
PL1                  -3.00 dB
SFO1              300.1319477 MHz

F2 - Processing parameters
SI                      65536
SF                300.1300000 MHz
WDW                        EM
SSB                         0
LB                       0.10 Hz
GB                          0
PC                       1.00

1D NMR plot parameters
CX                      20.00 cm
CY                      50.00 cm
F1P                    10.000 ppm
F1                    3001.30 Hz
F2P                    0.000 ppm
F2                       0.00 Hz
PPMCM                 0.50000 ppm/cm
HZCM                150.00300 Hz/cm
```





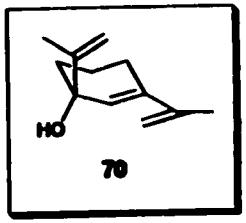
Data Parameters
jdot_109
1
1

Acquisition Parameters
20010307
19.19
dx300
5 mm QNP 1H/1
zg30
30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0220980 sec
RG 203.2
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

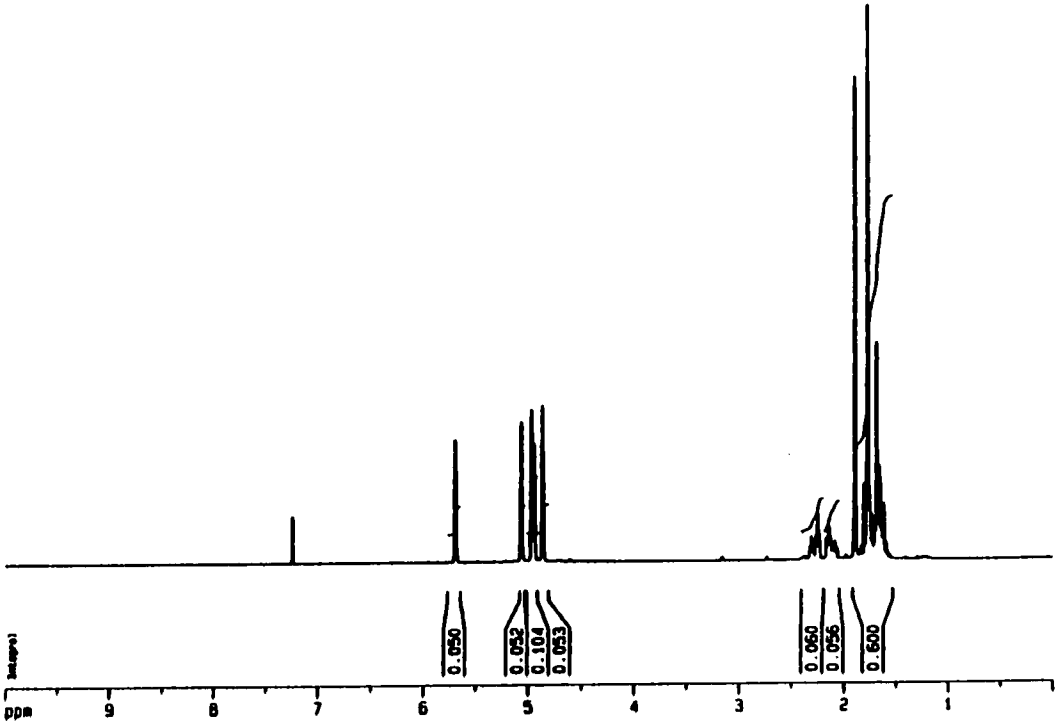
------------ CHANNEL f1 -------------
NUC1 1H
P1 9.50 usec
PL1 -3.00 dB
SFO1 300.1319477 MHz

F2 - Processing parameters
SI 65536
SF 300.1300000 MHz
WDW EM
SSB 0
LB 0.10 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 20.00 cm
CY 25.00 cm
F1P 10.000 ppm
F1 3001.30 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.50000 ppm/cm
HZCM 150.06500 Hz/cm



70



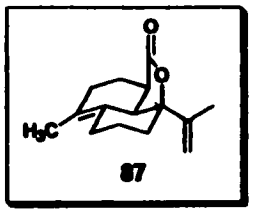

```
Current Data Parameters
NAME            jdot_183r
EXPNO                   1
PROCNO                  1

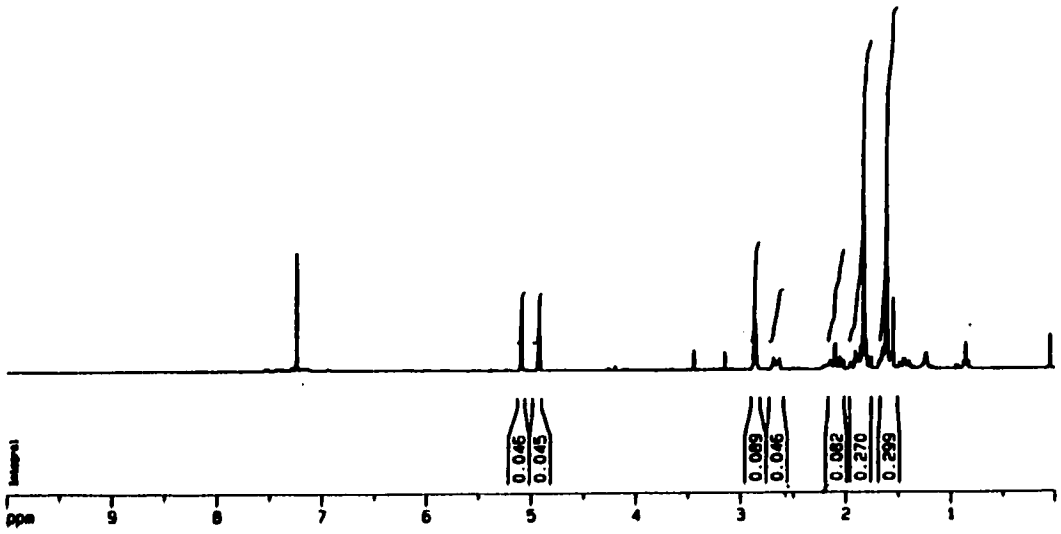
F2 - Acquisition Parameters
Date_         20010611
Time               13.46
INSTRUM            av300
PROBHD  5 mm QNP  1H/1
PULPROG            zg30
TD                32720
SOLVENT           CDCl3
NS                   16
DS                    0
SWH           5081.301 Hz
FIDRES        0.155407 Hz
AQ            3.0220000 sec
RG                 90.5
DW               98.400 usec
DE                6.00 usec
TE               300.0 K
D1           1.00000000 sec

------------ CHANNEL f1 -------------
NUC1                1H
P1                9.50 usec
PL1              -3.00 dB
SFO1        300.1319477 MHz

F2 - Processing parameters
SI                65536
SF          300.1300000 MHz
WDW                 EM
SSB                   0
LB                 0.10 Hz
GB                    0
PC                 1.00

1D NMR plot parameters
CX                20.00 cm
CY                10.00 cm
F1P               10.000 ppm
F1                3001.30 Hz
F2P               0.000 ppm
F2                0.00 Hz
PPMCM             0.50000 ppm/cm
HZCM            150.06500 Hz/cm
```





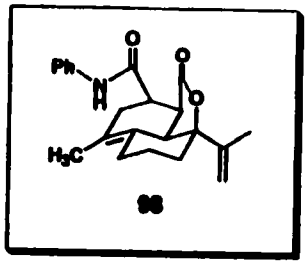

```
Current Data Parameters
NAME            jdot_172r
EXPNO                   1
PROCNO                  1

F2 - Acquisition Parameters
Date_         20010611
Time               15 00
INSTRUM            av300
PROBHD  5 mm QNP  1H/1
PULPROG             zg30
TD                 38720
SOLVENT            CDCl3
NS                    16
DS                     0
SWH           5081.301 Hz
FIDRES        0 165407 Hz
AQ            3.0220980 sec
RG                   512
DW              98.400 usec
DE               6.00 usec
TE              300.0 K
D1           1.00000000 sec

------------ CHANNEL f1 -------------
NUC1                1H
P1               9.50 usec
PL1             -3.00 dB
SFO1        300 1319477 MHz

F2 - Processing parameters
SI                 65536
SF          300.1300000 MHz
WDW                   EM
SSB                    0
LB               0.10 Hz
GB                     0
PC                  1.00

1D NMR plot parameters
CX                20.00 cm
CY                 3.00 cm
F1P               10.000 ppm
F1                3001.30 Hz
F2P                0.000 ppm
F2                   0.00 Hz
PPMCM             0.50000 ppm/cm
HZCM            150.06500 Hz/cm
```



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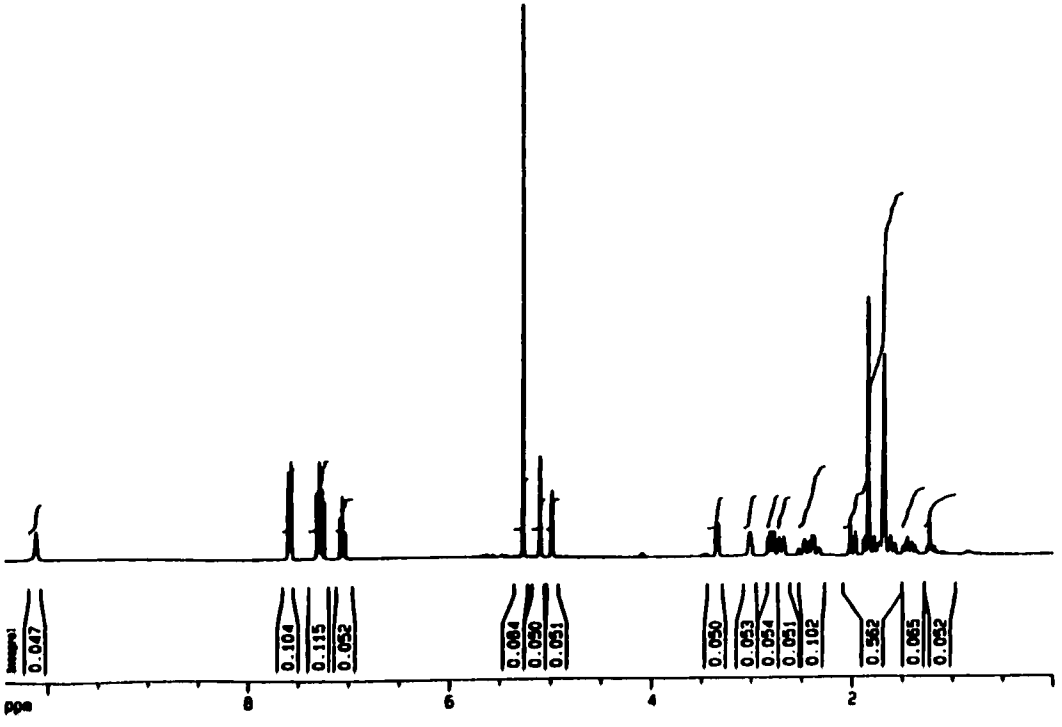


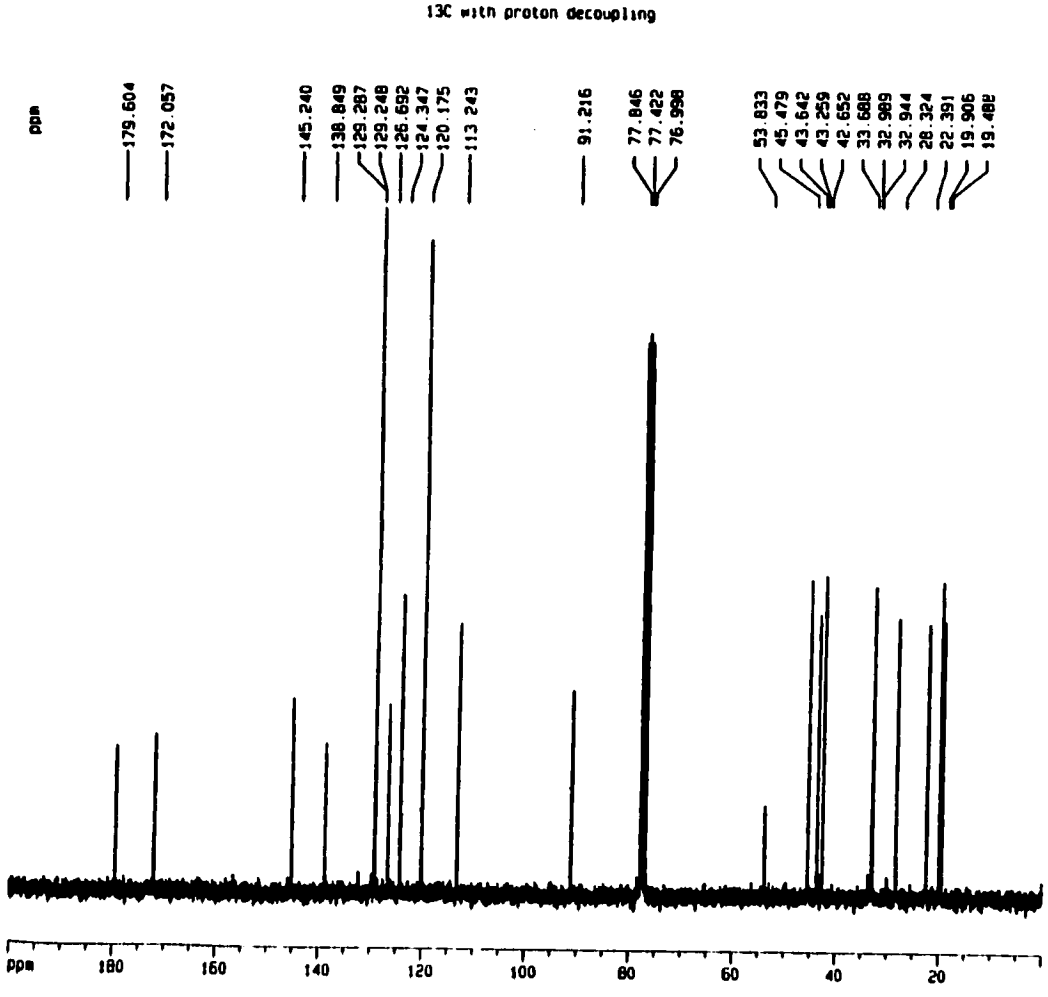

```
Current Data Parameters
NAME                jeat_363
EXPNO                      1
PROCNO                     1

F2 - Acquisition Parameters
Date_            20020530
Time                  9.57
INSTRUM                 av300
PROBHD   5 mm BBP  1H/1
PULPROG                 zg30
TD                     30720
SOLVENT                CDCl3
NS                        16
DS                         0
SWH                5081.301 Hz
FIDRES             0.165407 Hz
AQ                 3.0220800 sec
RG                       181
DW                  98.400 usec
DE                   6.00 usec
TE                  300.0 K
D1                 1.00000000 sec

------------ CHANNEL f1 -------------
NUC1                     1H
P1                   15.00 usec
PL1                  -3.00 dB
SFO1               300.1319477 MHz

F2 - Processing parameters
SI                      65536
SF                 300.1300000 MHz
WDW                        EM
SSB                         0
LB                       0.10 Hz
GB                          0
PC                       1.00

1D NMR plot parameters
CX                      20.00 cm
CY                      10.00 cm
F1P                    10.432 ppm
F1                    3130.98 Hz
F2P                    0.000 ppm
F2                       0.00 Hz
PPMCM                0.52160 ppm/cm
HZCM               156.54803 Hz/cm
```



Current Data Parameters
NAME 1dat_353
EXPNO 2
PROCNO 1

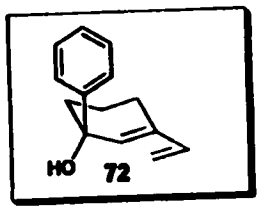
F2 - Acquisition Parameters
Date_ 20020530
Time 10.12
INSTRUM av300
PROBHD 5 mm BBF 1H/1
PULPROG zgpg30
TD 32768
SOLVENT CDCl3
NS 454
DS 0
SWH 17985.611 Hz
FIDRES 0.548877 Hz
AQ 0.9110004 sec
RG 3649.6
DW 27.800 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
d11 0.03000000 sec
d12 0.00002000 sec

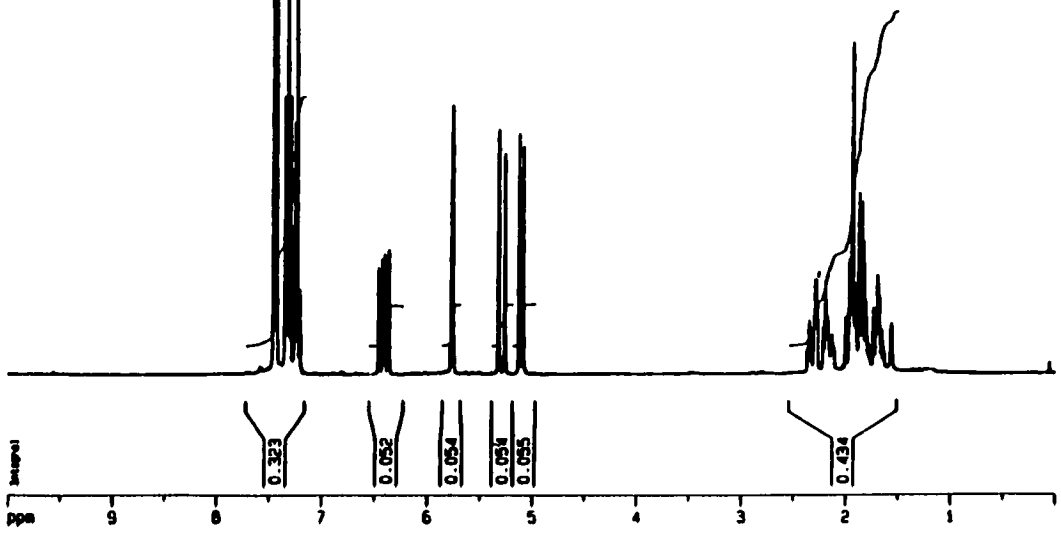
------------ CHANNEL f1 ------------
NUC1 13C
P1 5.10 usec
PL1 -6.00 dB
SF01 75.4752653 MHz

------------ CHANNEL f2 ------------
CPDPRG2 waltz16
NUC2 1H
PCPD2 70.00 usec
PL2 -3.00 dB
PL12 10.38 dB
PL13 13.90 dB
SF02 300.1314850 MHz

F2 - Processing parameters
SI 65536
SF 75.4677190 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

1D NMR plot parameters
CX 20.00 cm
CY 12.50 cm
F1P 200.000 ppm
F1 15093.54 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 10.00000 ppm/cm
HZCM 754.67719 Hz/cm





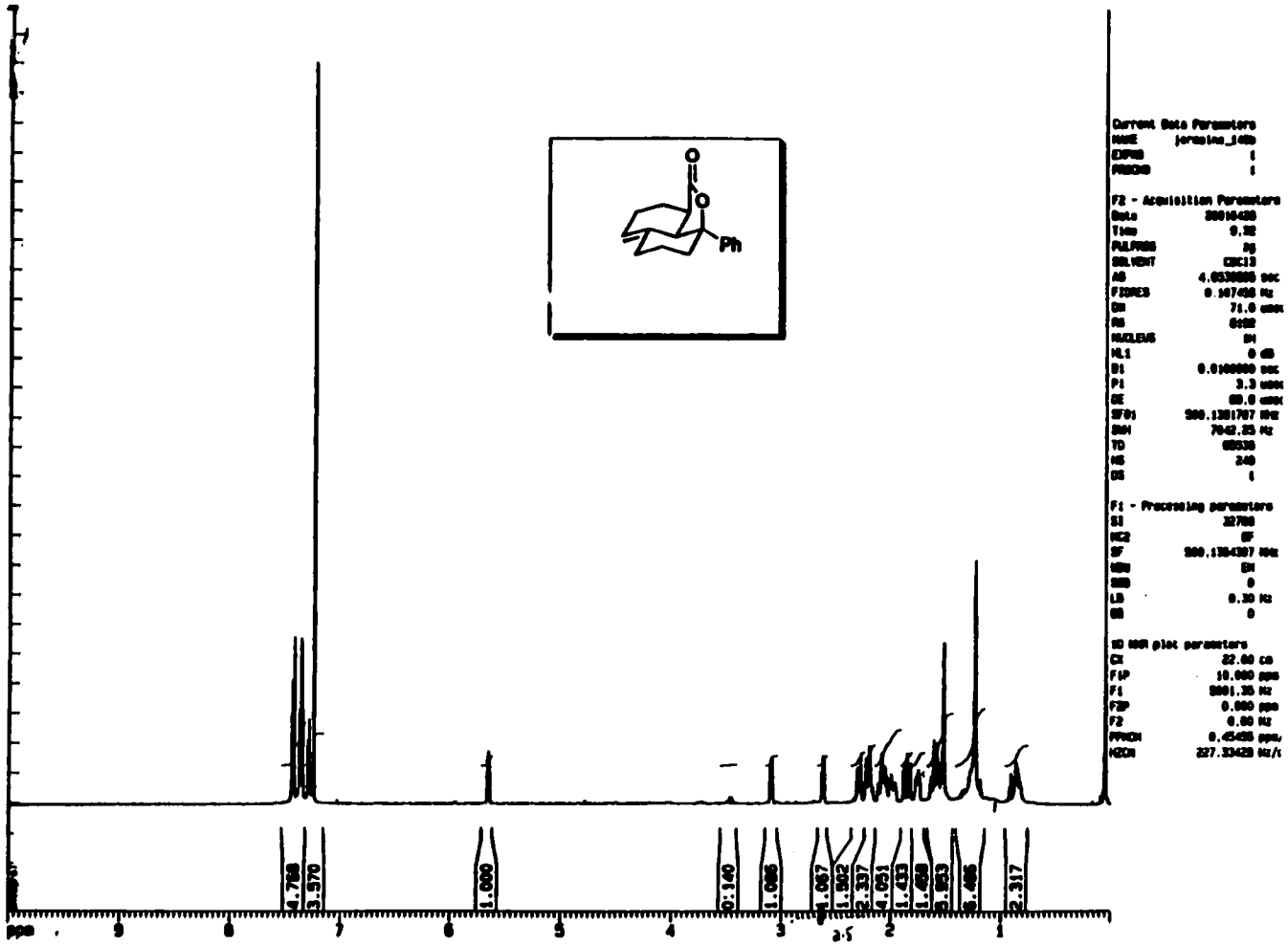

```
Current Data Parameters
NAME            jdot_130
EXPNO                  1
PROCNO                 1

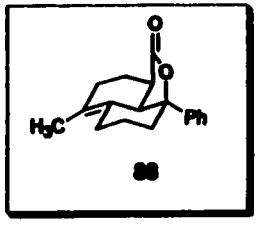
F2 - Acquisition Parameters
Date_          20010516
Time                16.21
INSTRUM           av300
PROBHD  5 mm BNP  1H/1
PULPROG             zg30
TD                 30720
SOLVENT            CDCl3
NS                    16
DS                     0
SWH              5081.301 Hz
FIDRES           0.165407 Hz
AQ               3.0228880 sec
RG                   362
DW                98.400 usec
DE                 6.00 usec
TE                300.0 K
D1           1.00000000 sec

------------ CHANNEL f1 -------------
NUC1                1H
P1                9.50 usec
PL1              -3.00 dB
SFO1        300.1319477 MHz

F2 - Processing parameters
SI                 65536
SF          300.1300000 MHz
WDW                   EM
SSB                    0
LB                  0.10 Hz
GB                     0
PC                  1.00

1D NMR plot parameters
CX                20.00 cm
CY                10.00 cm
F1P               10.000 ppm
F1                3001.30 Hz
F2P                0.000 ppm
F2                 0.00 Hz
PPMCM             0.50000 ppm/cm
HZCM            150.06500 Hz/cm
```


O
O
Ph
4.768
3.570
1.000
0.140
1.085
4.067
1.902
2.337
4.051
1.433
1.498
5.853
8.405
2.317
ppm
9
8
7
6
5
4
3
2.5
2
1



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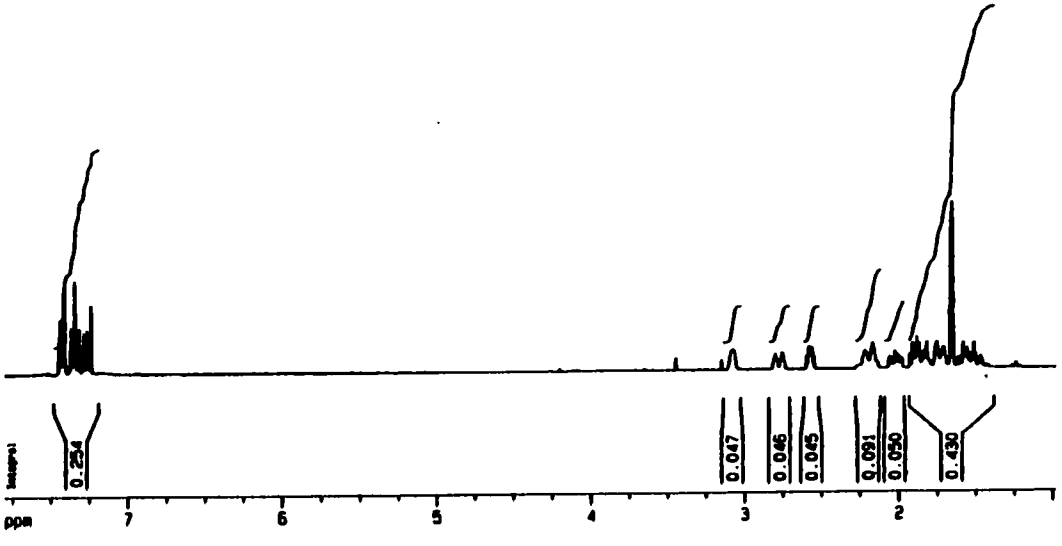


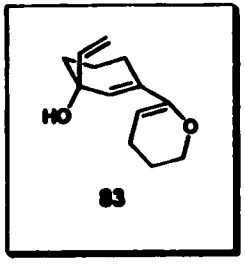

```
Current Data Parameters
NAME            jdot_177
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_          20010606
Time               18 42
INSTRUM            av300
PROBHD   5 mm GNP  IH/1
PULPROG            zg30
TD                 30720
SOLVENT            CDCl3
NS                    16
DS                     0
SWH             5081.301 Hz
FIDRES          0.165407 Hz
AQ              3.0228000 sec
RG                   256
DW                98.400 usec
DE                 6.00 usec
TE                300.0 K
D1              1.00000000 sec

------------ CHANNEL f1 -------------
NUC1                 1H
P1                 9.50 usec
PL1               -3.00 dB
SFO1          300.1319477 MHz

F2 - Processing parameters
SI                 65536
SF            300.1300000 MHz
WDW                   EM
SSB                    0
LB                  0.10 Hz
GB                     0
PC                  1.00

1D NMR plot parameters
CX                 20.00 cm
CY                  3.00 cm
F1P                 7.883 ppm
F1                2341.83 Hz
F2P                 0.979 ppm
F2                 293.83 Hz
PPMCM           0.34119 ppm/cm
HZCM            102.40818 Hz/cm
```



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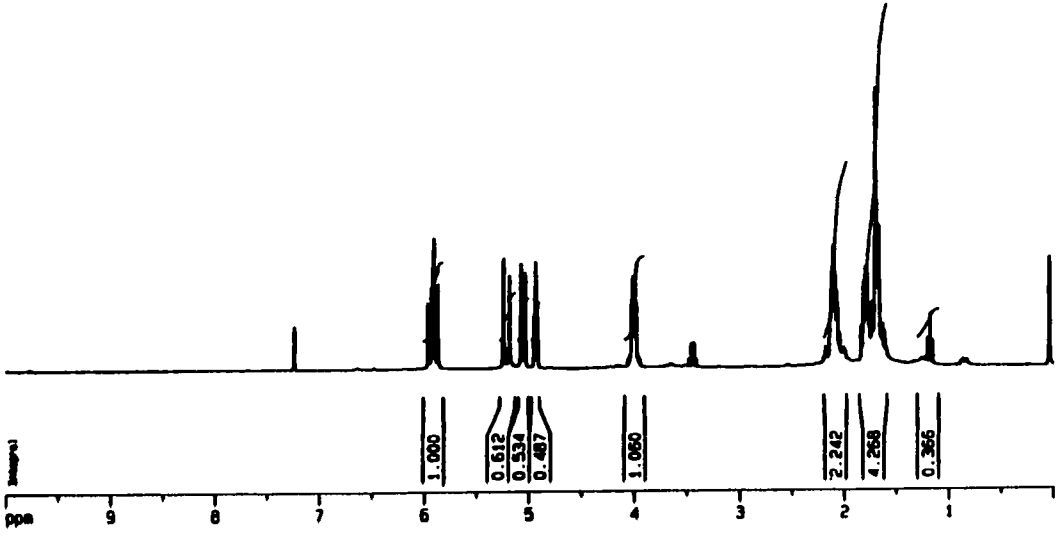


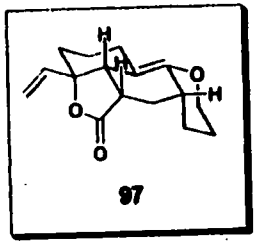

```
Current Data Parameters
NAME            jdot_305r
EXPNO                    1
PROCNO                   1

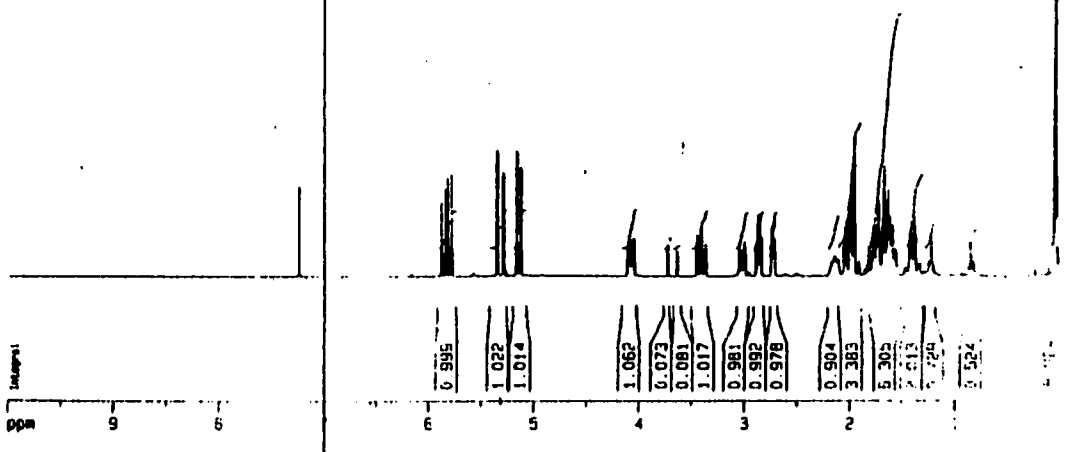
F2 - Acquisition Parameters
Date_          20011203
Time                16.02
INSTRUM             av300
PROBHD   5 mm BBP 1H/1
PULPROG             zg30
TD                 30720
SOLVENT             CDCl3
NS                     16
DS                      0
SWH              5081.301 Hz
FIDRES           0.165407 Hz
AQ               3.0220880 sec
RG                  143.7
DW                 98.400 usec
DE                  6.00 usec
TE                 300.0 K
D1               1.00000000 sec

------------ CHANNEL f1 -------------
NUC1                   1H
P1                  11.00 usec
PL1                 -3.00 dB
SFO1          300.1319477 MHz

F2 - Processing parameters
SI                     65536
SF            300.1300000 MHz
WDW                    EM
SSB                     0
LB                   0.10 Hz
GB                      0
PC                   1.00

1D NMR plot parameters
CX                  20.00 cm
CY                   5.00 cm
F1P                10.000 ppm
F1                 3001.30 Hz
F2P                 0.000 ppm
F2                  0.00 Hz
PPMCM             0.50000 ppm/cm
HZCM            150.00390 Hz/cm
```






```
Current Data Parameters
NAME                 root_306
EXPNO                       1
PROCNO                      1

F2 - Acquisition Parameters
Date_             20011204
Time                  13 39
INSTRUM                av300
PROBHD     5 mm QNP 1H/1
PULPROG                zg30
TD                    30720
SOLVENT               CDCl3
NS                       16
DS                        0
SWH                5081.301 Hz
FIDRES             0.165407 Hz
AQ                 3.0220880 sec
RG                      128
DW                  98.400 usec
DE                   6.00 usec
TE                  300.0 K
D1                  1.00000000 sec

====== CHANNEL f1 ============
NUC1                     1H
P1                  11.00 usec
PL1                 -3.00 dB
SFO1             300.1319477 MHz

F2 - Processing parameters
SI                      65536
SF                300.1300000 MHz
WDW                        EM
SSB                         0
LB                       0.10 Hz
GB                          0
PC                       1.00

1D NMR plot parameters
CX                      20.00 cm
CY                      50.00 cm
F1P                     10.000 ppm
F1                    3001.30 Hz
F2P                     0.000 ppm
F2                      0.00 Hz
PPMCM                0.50000 ppm/cm
HZCM               150.06500 Hz/cm
```