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Lewis acid catalyzed cycloadditions

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By

Roger A. Kennedy

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Author: Roger A. Kennedy (Mc Master University, Hamilton, Ont., Canada)

Supervisor: Professor R. F. Childs

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Scope and Contents:

This thesis describes an attempt to develop a potentially useful route to seven-membered carbocycles. α-Diketones and their enol ether derivatives were proposed to be suitable three-carbon cycloaddition dienophiles when complexed with a Lewis acid. Reaction with 1,3-dienes should then lead to the desired cycloheptyl system.

^{1}H-NMR and ^{13}C-NMR studies were used to determine the stoichiometry and charge delocalization of complexes formed between 2,3-butanedione, 1,2-cyclohexanedione, 2-methoxy-cyclohex-2-en-1-one and the Lewis acids $TiCl_4$ and $SnCl_4$. Observations from these studies suggested that 1,2-cyclohexanedione and 2-methoxy-cyclohex-2-en-1-one could behave as substituted allyl cations when complexed with $TiCl_4$ or $SnCl_4$.

Reaction of the 1,2-cyclohexanedione/$TiCl_4$ and 2-methoxy-cyclohex-2-en-1-one/$TiCl_4$ complexes with 1,3-butadiene gave rise to six-membered carbocycles from [4C+2C] cycloadditions. The reaction of 2,3-butanedione-mono-trimethylsilyl enol ether/$TiCl_4$ complex with 1,3-butadiene gave a mixture of the [4C+2C] and [4C+3C] cycloaddition products.

To Mr. and Mrs. Garven Kennedy

Acknowledgements

I wish to extend my sincere appreciation to Professor R. F. Childs for his continual guidance, encouragement and critical appraisal during the course of this work.

I would like to thank the many members of our research group for their friendship and helpful advice which made work on this project so enjoyable.

Finally, thanks are due to Mr. Brian Sayer and Mr. Ian Thompson for their assistance in the recording of NMR spectra.

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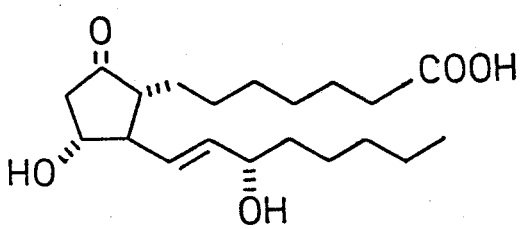
CHAPTER 1

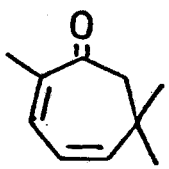
INTRODUCTION

The synthesis of odd-membered carbocyclic ring systems has received much attention during the past fifteen years. In particular, five and seven membered rings have been of special interest because of their ubiquitous nature among several classes of natural products. For example, the identification of prostaglandins such as PGE_1, 1 , and the recognition of their physiological importance, has stimulated new developments in the synthesis of five-membered carbocycles.[1,2]



1

Seven-membered carbocycles, such as eucarvone, 2 , can be found in a variety of plants[3] and their structural elucidation has renewed interest in the synthesis of cycloheptyl ring systems.



2

The work to be described in this thesis is concerned with developing a new synthesis of seven-membered carbocyclic rings. Before presenting this work, the current situation regarding the synthesis of seven-membered rings will be reviewed.

The methodology that has been developed for the synthesis of seven-membered rings can be divided into two different strategies. The first is basically a modification of cyclic homologues. Ring expansion and contraction reactions are the important examples of this approach. The second involves cyclization methods. These can be classified further as intermolecular or intramolecular reactions. Examples from the literature that illustrate these strategies are outlined below.

Synthesis of seven-membered rings

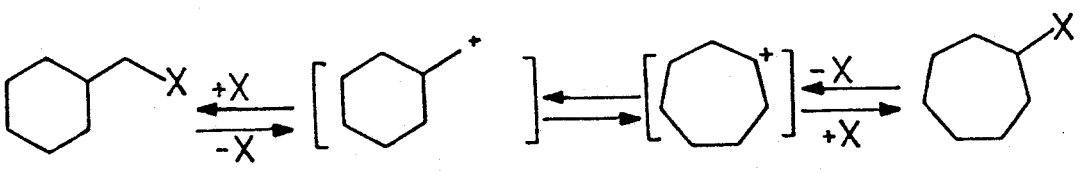
Part 1: Modification of Cyclic Homologues

A) Ring expansion

i) One-carbon expansions

a) Wagner-Meerwein Rearrangements[4]

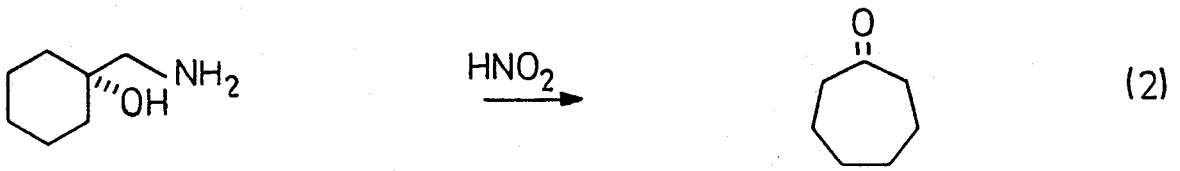
This type of rearrangement is characterized by the generation of a cationic intermediate. Subsequent migration of an alkyl group forms the rearranged intermediate which can be trapped by a nucleophile to form the ring expanded product. These rearrangements can be reversible and this can lead to complication in the formation of seven-membered rings. The general reaction scheme is shown below in equation 1.



(1)

The loss of molecular nitrogen acts as the driving force in the Demjanow-Tiffeneau synthesis of cycloheptanones from 1-hydroxycyclohexylcarbinylamines.[5] The increased strain that often accompanies the expansion of a six to seven-membered ring is offset in these cyclohexylcarbinyl systems by an electron-releasing group at C-1. Such systems can be induced to rearrange by the generation of a carbenium ion at the

carbon centre on the side-chain. An example of this reaction is given in equation 2.



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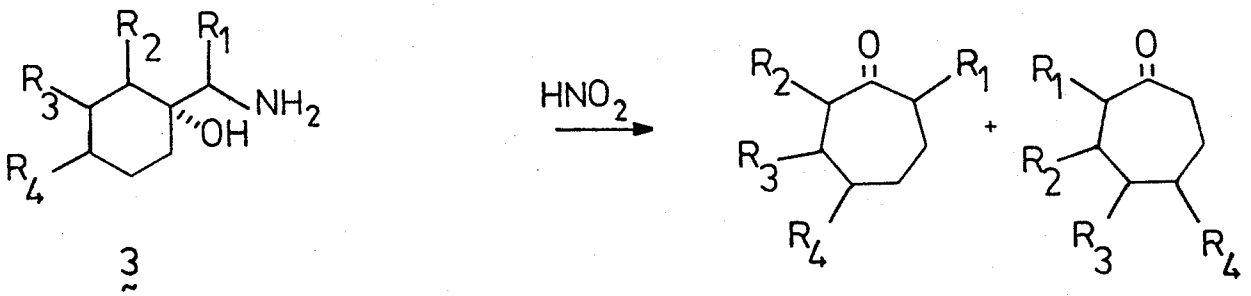
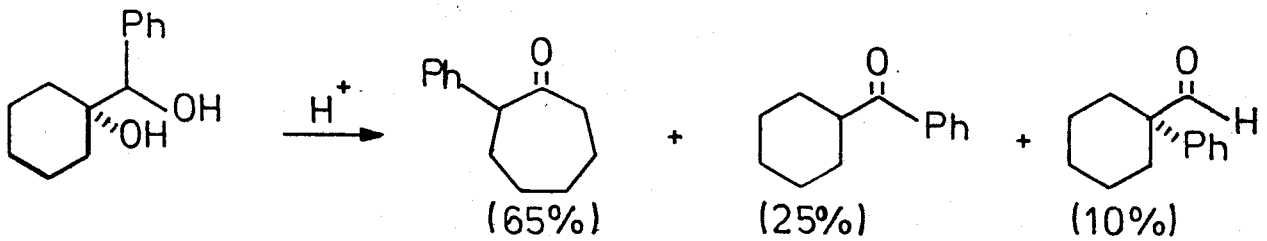
Unsymmetrically substituted cyclohexylcarbinyl amines, 3, often yield mixtures of isomers due to competition between migrating groups. These competing bond cleavages lead to reduced yields of the desired compound and necessitate separation.



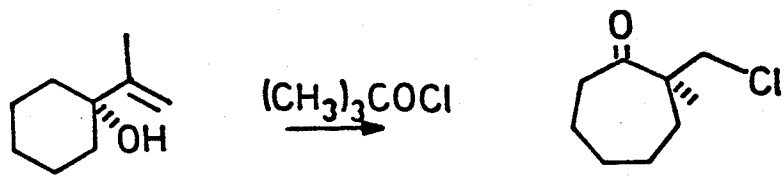
3

A further problem is encountered with a related approach based on the "pinacol" rearrangement of monocyclic diols. The preferred ring expansion of diol 4 for example produces the ketone 5 by initial ionization at the secondary alcohol site. Competing ionization of the tertiary alcohol can occur however and this leads to the cyclohexyl systems 6 and 7.[6]



4 5 6 7

Other methods for generating the carbenium ion centre have been developed. For example, treatment of the allylic alcohol 8 with t-butyl hypochlorite produces the substituted cycloheptanone 9.[7]

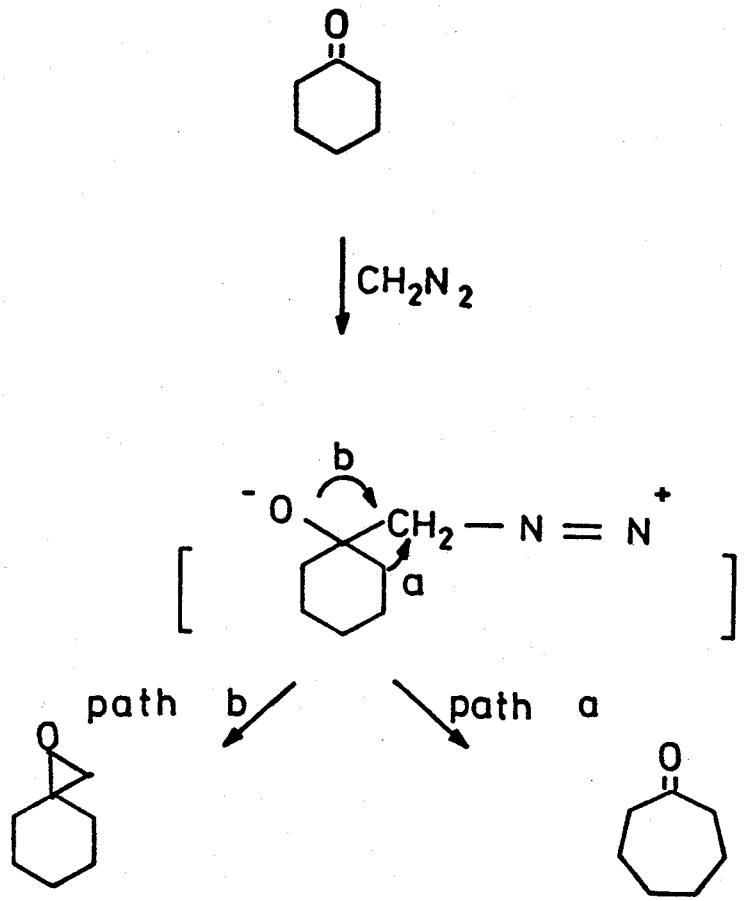


8 9

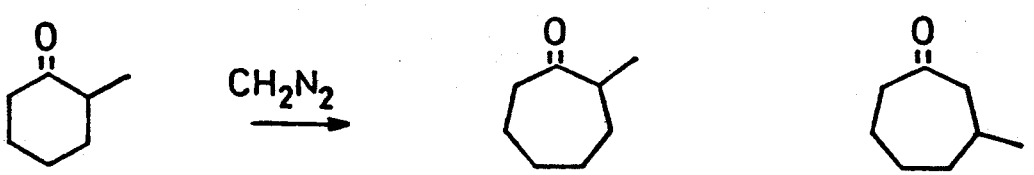
Generally, ring expansion reactions involving a cationic intermediate are of limited value. The starting materials are not easily synthesized and a strong driving force is needed to overcome the equilibrium problem. Competing sites of ionization and the difficulty associated with regiospecific migration of alkyl groups lead to complex product-mixtures.

b) Diazomethane Ring Enlargements

The reaction of cyclohexanones with diazomethane illustrates a further ring expansion route to cycloheptanones. The reaction proceeds through an alkoxide-type intermediate and the evolution of nitrogen acts as the driving force for the rearrangement. Competing epoxide formation can reduce the yield of the ring expanded product. This route is illustrated below using cyclohexanone as the precursor.

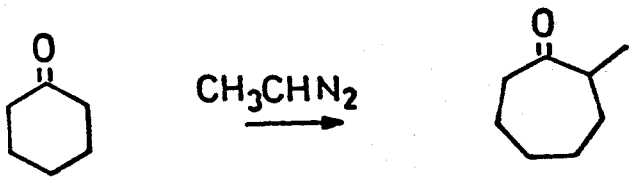


Isomeric product-mixtures are difficult to avoid when unsymmetrical cyclohexanones are used. The substituted cyclohexanone 10 for example reacts with diazomethane to yield a mixture of isomers 11 and 12.[8]



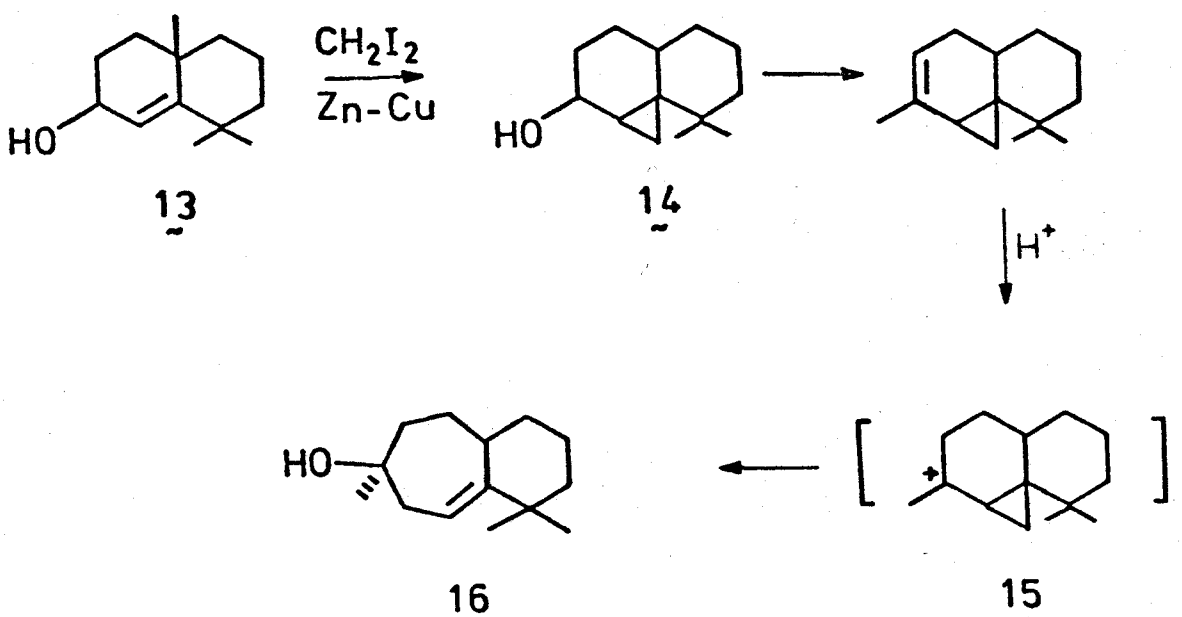
10 11 12

The versatility of this reaction can be increased by using substituted diazomethanes. Cyclohexanone for example reacts with diazoethane to yield 2-methylcycloheptanone.[8]

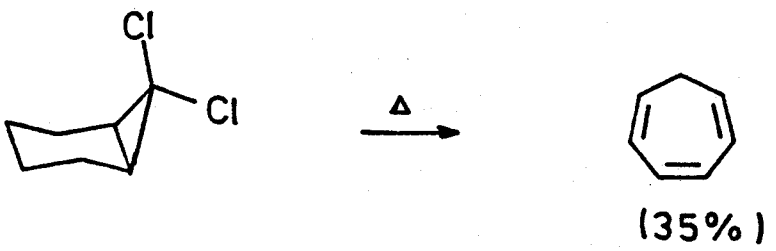


c) Ring Expansion via Bicyclo[4.1.0.] Intermediates

The expansion of a six-membered ring to a seven-membered ring can be carried out in a sequence beginning with cyclohexene derivatives. For example, the cyclohexenol derivative 13 has been converted to 16 via the bicyclo[4.1.0.]heptene 14.[9] This particular reaction is catalyzed by acid and is known to involve the substituted cyclopropylcarbinyl cation 15 as an intermediate.

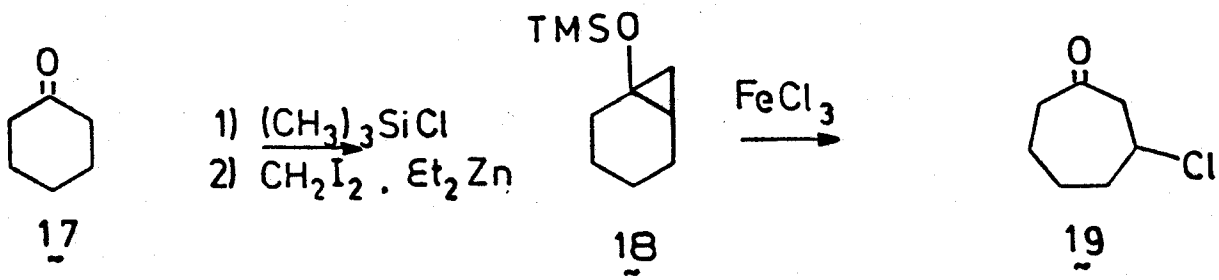


7,7-Dihalobicyclo[4.1.0.]heptanes can thermally rearrange to cycloheptatrienes as shown in equation 3.[10] Although the precursor is easy to prepare, the yield of cycloheptatriene is rather low.



(3)

Recently, the expansion of cyclohexanone 17 to 3-chlorocycloheptanone 19 was accomplished using the trimethylsilyl enol ether as a precursor to the bicyclo-[4.1.0.] heptene, 18.[11]



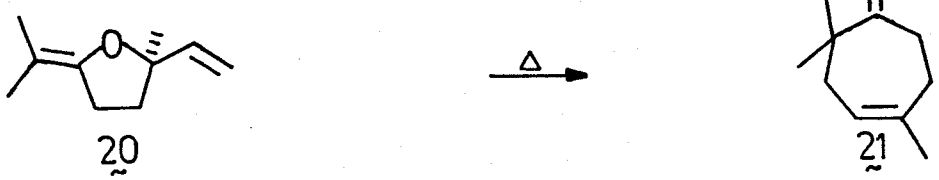
17 18 19

Although the mechanism of the reaction is not known with certainty, it is assumed that an alkoxy radical is involved and that this radical undergoes homolytic scission of the more highly substituted carbon-carbon bond of the cyclopropane ring. The resulting carbon radical could then abstract a chlorine atom from $FeCl_3$.

ii) Two-carbon ring expansion routes

Most of the ring expansion routes to seven-membered rings make use of six-membered ring precursors. There are a few examples of two-carbon expansion routes.

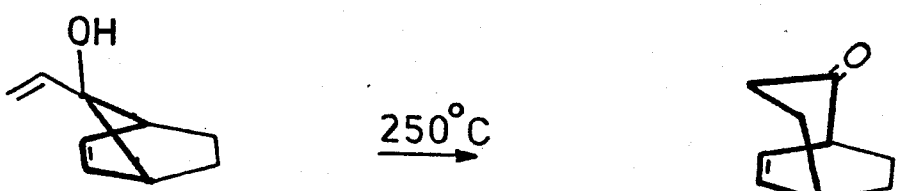
The substituted furan 20 for example, thermally rearranges to give the expanded cycloheptenone 21.[12]



20 21

This is an example of the Claisen rearrangement and the product, karahanaenone, is a known constituent of hop oil.

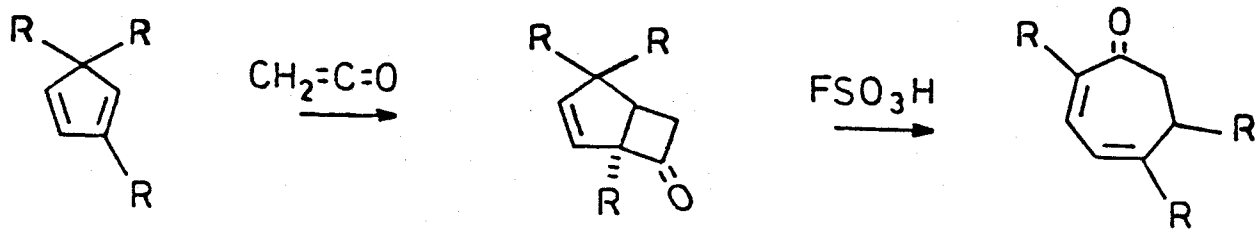
The allylic alcohol 22 reacts by a Cope rearrangement to give the bicyclo-[3.3.2.] system 23 when heated at 250°C.[13] This reaction again represents a two-carbon expansion of a five-membered ring.



22 23

Reactions such as the Claisen and Cope rearrangements are useful in specific circumstances because of the stereochemical control that accompanies them. As a general route to seven-membered rings however, these systems are not practical because of difficulties in preparing the desired precursors.

Finally, the acid catalyzed rearrangement of bicyclo[3.2.0.]heptenones 24 provides a route to cycloheptadienones.[14] The bicyclic precursors are prepared by the addition of ketene to substituted cyclopentadienes and rearrangement occurs upon protonation.



24

There are many examples of this type of reaction and they represent an efficient synthesis of tropones.

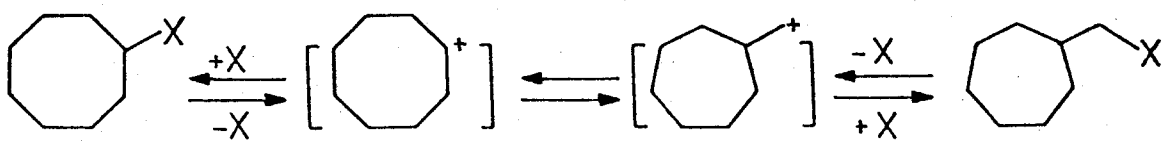
B) Ring Contraction Routes

Unlike the ring expansion methods, there have been only a few developments of ring contraction routes to seven-membered carbocyclic rings. Undoubtedly, this is due to the difference in availability of six and eight-membered carbocyclic precursors.

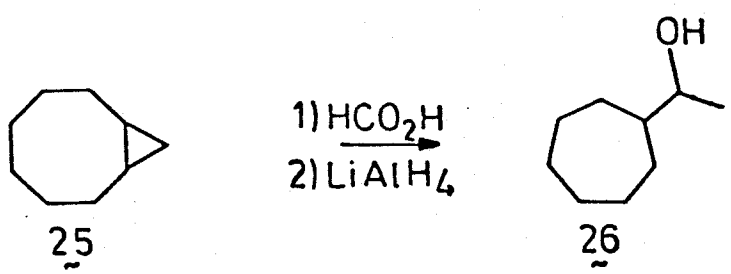
i) One-carbon contractions

a) Wagner-Meerwein Rearrangements

Ring contraction reactions of this type involve a cationic intermediate. In contrast to the analogous ring expansion method, the cationic centre must develop within the ring, rather than external to the ring, to cause ring contraction. Formally at least, the reaction must proceed as shown below.



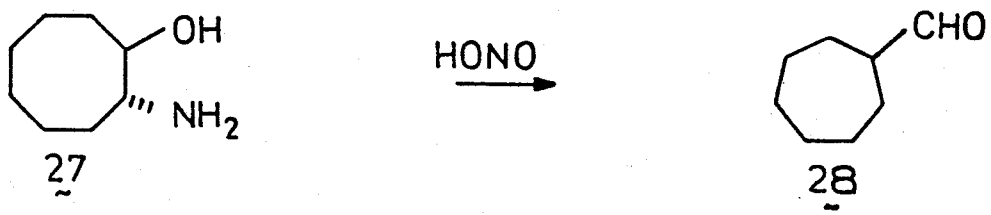
There are only a limited number of examples of this type of approach to seven-membered rings. The formolysis of trans-bicyclo[6.1.0.]nonane 25 followed by lithium aluminum hydride reduction generates a mixture of products containing cycloheptylmethylcarbinol 26 in rather low yield (29%).[15]



25 26

Initial protonation of the cyclopropyl group is followed by an alkyl group migration causing ring contraction. Many other products resulting from hydride shifts are also formed in this reaction and for this reason it is not a practical method for cycloheptyl ring formation.

Carbinolamines have been used for ring expansion reactions and they can be used also for ring contractions. The deamination of trans-2-aminocyclooctanol 27 for example yields cycloheptanecarboxaldehyde 28 in 60% yield.[16]

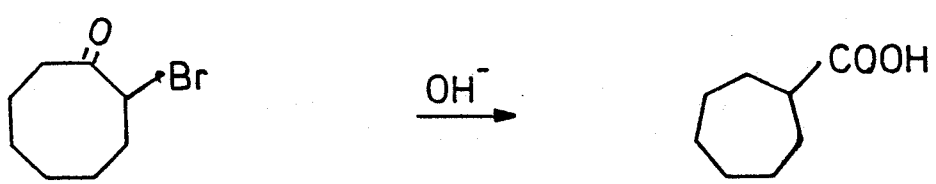


27 28

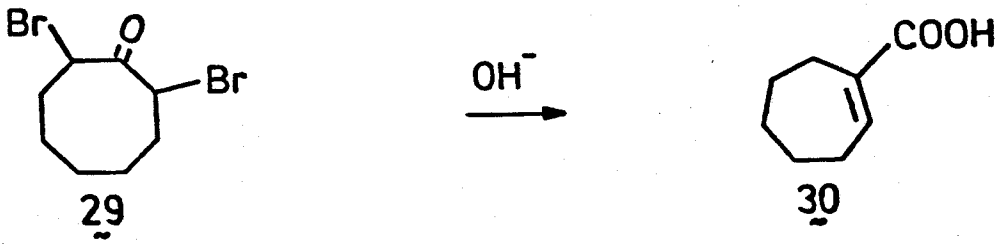
The problems of rearrangement and competing migration are present in these systems too. It is interesting that the cis isomer gives less than 10% ring contraction. The difficulty associated with preparing the trans isomer specifically limits the usefulness of these carbinolamines as general precursors to seven-membered rings.

b) Favorskii Rearrangement

In contrast to the Wagner-Meerwein rearrangement, the Favorskii-type ring contraction proceeds via an anionic reaction intermediate. As an example, 2-bromocyclooctanone can be converted in 70% yield to cycloheptanecarboxylic acid in the presence of aqueous base.[17]



Alternatively, the α,α-dihaloketone 29 can be converted to the unsaturated carboxylic acid 30.



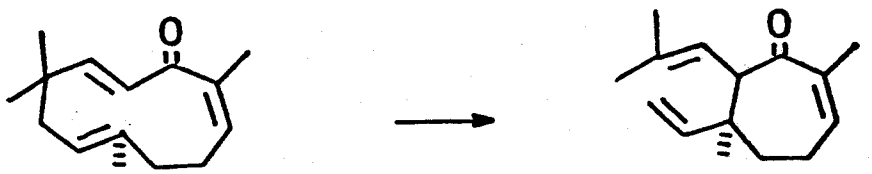
29 30

Side reactions leading to epoxyethers form the main limitation of this route. Further reaction of the epoxyether with the solvent produces a variety of unwanted side-products.

ii) Four-carbon contraction

a) Cope rearrangement

Ring contractions involving more than one carbon centre are rare. One example that has been reported however, is the thermal rearrangement of the cycloundecatriene 31 to the divinylcycloheptenone 32.[18]



31 32

As mentioned before, this type of rearrangement gives well defined stereochemistry and the yields are often high. The difficult synthesis of the precursor however, makes this route unattractive as a general scheme to seven-membered rings.

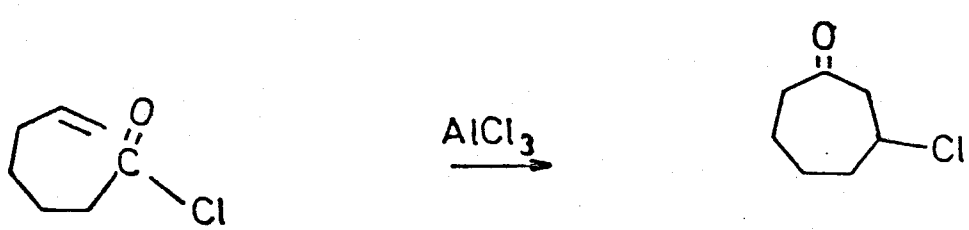
Part 2: Cyclization Methods

A) Intra-molecular cyclizations

Conceptually, perhaps the simplest method of forming a cyclic framework is to bring together two centres within a straight-chain precursor. Formally, this can be thought of as a reaction leading to the elimination of the elements X and Y from the acyclic precursor, 33.

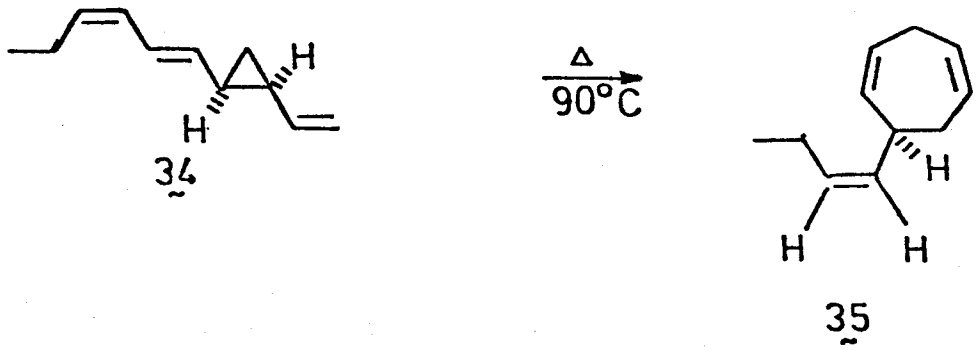
33

An example of this type of synthesis is shown in equation 4. The Lewis acid catalyzed condensation of an acid chloride with an alkene provides a route to cycloheptanones.[19]



(4)

A more elegant example is the Cope rearrangement of cis-divinylcyclopropanes into cyclohepta-1,4-dienes. Compound 35 for example can be obtained by heating compound 34 at 90°C for several hours.[20]



34 35

An empirical study has been done on these types of cyclization reactions to predict the relative facility of ring formation.[21] The physical basis of these so-called Baldwin rules lies in the stereochemical requirements of the transition states for the various tetrahedral, trigonal and digonal geometries involved in the ring closure processes. The linking chain restricts the relative motion of the terminal groups and so determines whether these groups can attain the required transition state geometry for ring closure. For closures to a carbon atom, the favoured paths to the transition states are represented by Figures 1-3 where X and Y are the terminal groups on the chain.

Cyclizations leading to seven-membered rings are favoured, in general, for each of the required trajectories in Figures 1-3. [22,23] For a particular synthesis though, it is important to consider the affect of the carbon chain upon the available geometries that lead to ring closure.

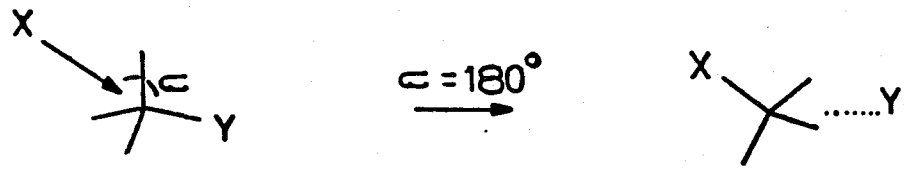


Figure 1: Tetrahedral geometry for intramolecular cyclizations

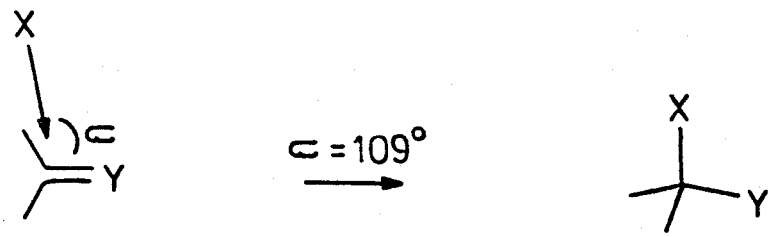


Figure 2: Trigonal geometry for intramolecular cyclizations

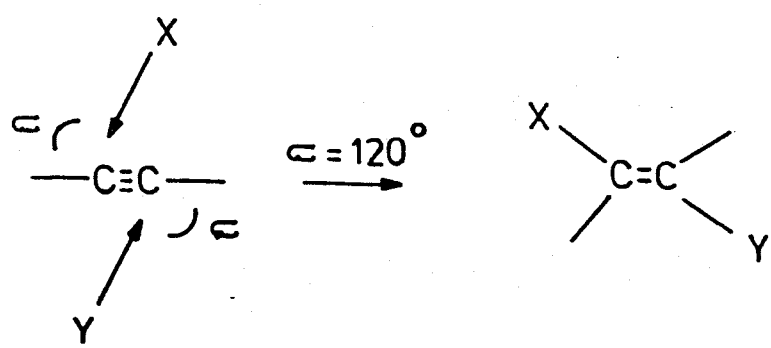
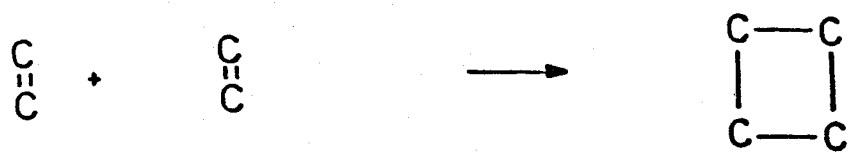


Figure 3: Digonal geometry for intramolecular cyclizations

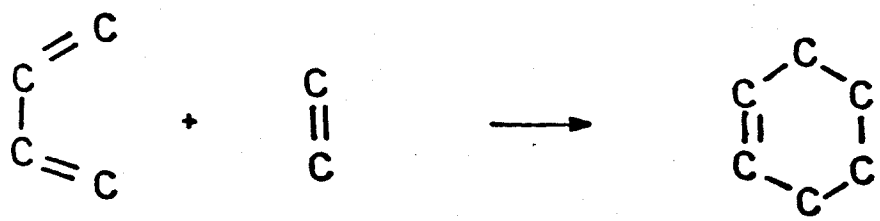
B) Intermolecular Cyclization Routes

These cyclo-coupling reactions can be defined[24] as ring formation by the combining of termini from two separate components. The ring formation can be formally classified according to the number of carbon units that participate in the coupling reaction. Thus, cyclobutane rings can be constructed by a [2C+2C] photocycloaddition of olefins,



"[2C+2C]" cycloaddition

and the [2C+4C] cycloaddition or Diels-Alder reaction is commonly used for the construction of six-membered carbocycles.



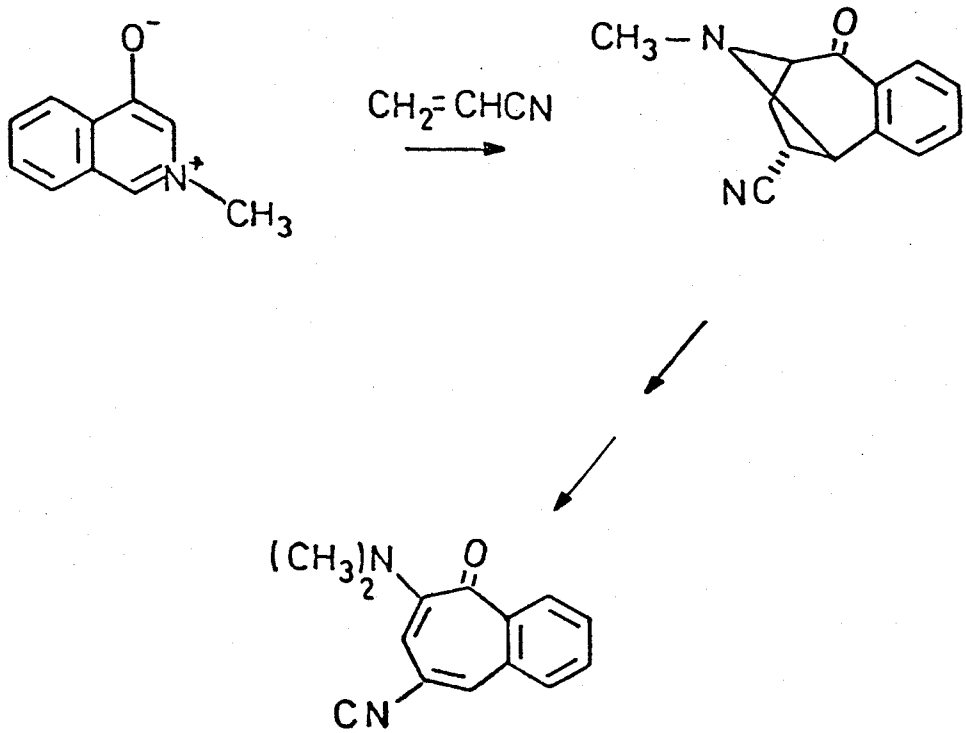
"[4C+2C]" cycloaddition

The coupling of two even-numbered carbon components to form even-numbered homocyclic systems can be achieved with ease and these reactions occupy an important position in organic synthesis.

In contrast, only recently has progress been made in the preparation of odd-membered carbocycles employing odd-numbered carbon moieties as one component. This can be ascribed to the difficulties that have been encountered in trying to prepare suitable odd-numbered carbon substrates. Nevertheless, the synthesis of seven-membered carbocyclic rings can be achieved by cyclo-coupling routes and these are discussed below.

i) [5C+2C] cycloadditions

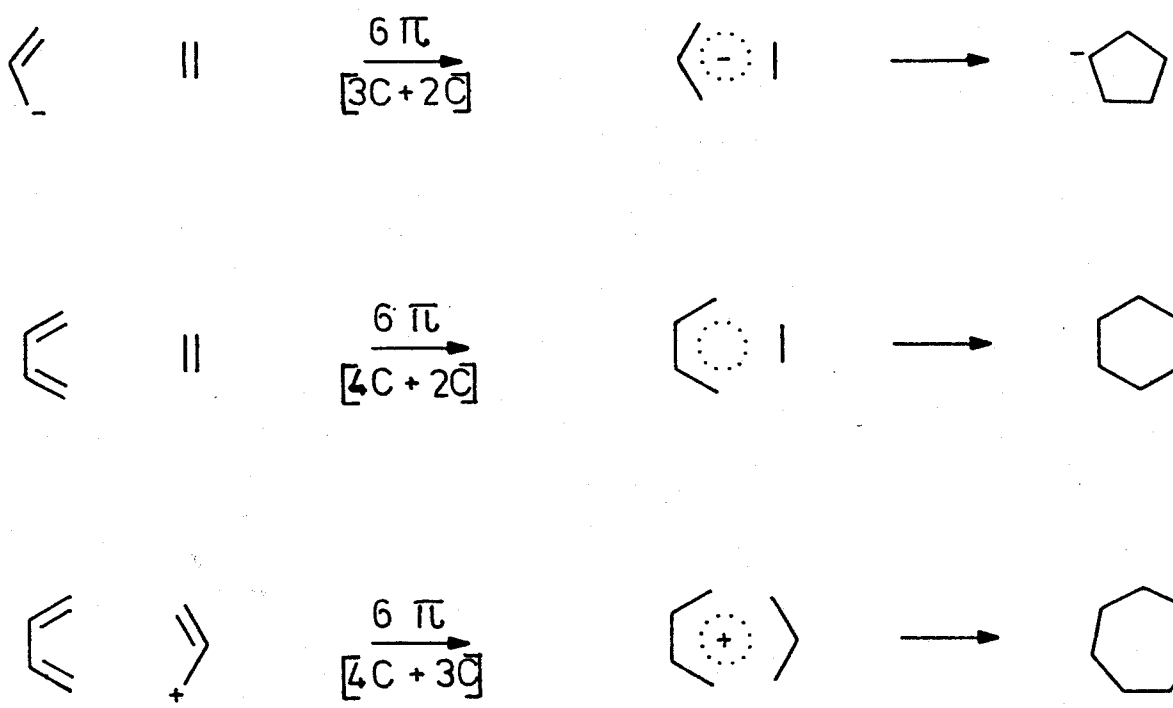
Betaines can be employed in a cycloaddition reaction with olefins to prepare substituted cycloheptadienones.[25] One such synthesis is illustrated in equation 5.



(5)

ii) [4C+3C] cycloadditions

The most general cyclocoupling method that has been developed for the synthesis of seven-membered carbocycles is the cycloaddition of an allyl cation to a conjugated diene. This cycloaddition involves six π-electrons and is therefore an extension of the [3C+2C] dipolar addition and the [4C+2C] Diels-Alder reaction leading to five and six-membered rings, respectively.



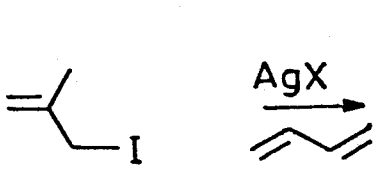
The initial studies of allyl cations investigated their solvolytic behaviour.[26] Subsequently they have been studied as long lived species in strongly acidic media.[27] The conditions used in these experiments to generate the cations were not suitable for synthetic purposes. Solvolysis studies generated cations with lifetimes too short to be trapped by dienes and thus they were impractical for synthetic work. Equilibrium studies generated cations with sufficiently long lifetimes, how-

ever, the highly acidic medium that is used precludes the coexistence of suitable trapping agents.

It was necessary to develop procedures for the preparation of reactive three-carbon units that were suitable for synthetic work and could be used as a general tool for the construction of seven-membered carbocycles. Several techniques have been developed recently, particularly by the groups of Hoffmann and Noyori and it has been shown that the [4C+3C] cyclocoupling of substituted allyl cations and conjugated dienes is an effective method for seven-membered carbocyclic ring formation. These techniques are outlined below and each is evaluated as a general synthetic route to seven-membered carbocycles.

a) Silver-salt Route

The initial strategy that was used involved preparation of the allyl cation from an allyl halide using silver ion to abstract the halide anion. 2-Methyl 36 and 2-methoxy 37 allyl halides were used as cation precursors and in the presence of silver ion were shown to add to conjugated dienes to form seven-membered carbocycles. The yields of these reactions however were very low.[28-31]



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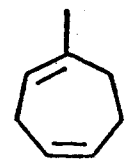
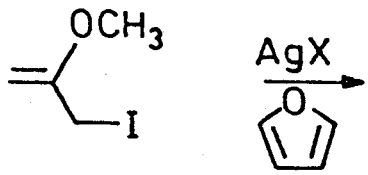


(6%)

$X = CF_3COO^-, CCl_3COO^-$



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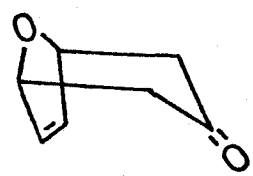
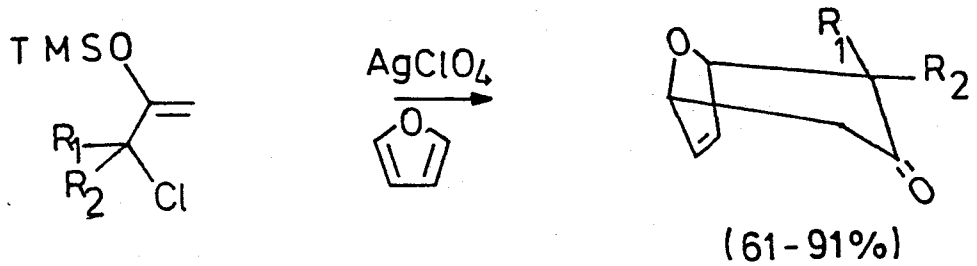


(15%)

Recently, the use of 2-(trimethylsiloxy)allyl chlorides as the allyl cation precursor has been shown to improve the yield markedly. In the presence of silver perchlorate, these allyl chlorides react with 1,3-dienes to produce cyclic seven-membered ketones,[32] as shown in equation 6.

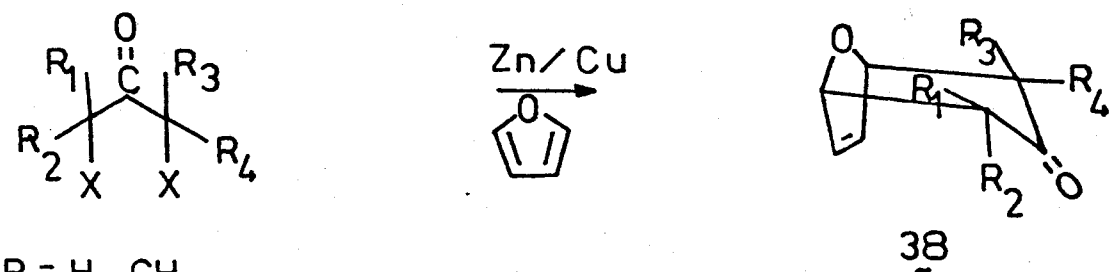


(6)

b) α,α-Dihaloketone Route

A second approach to allyl cation formation was designed to produce the 2-alkoxyallyl cation through a double elimination of a halide from an α,α-dihaloketone. Several procedures have been developed to accomplish this.

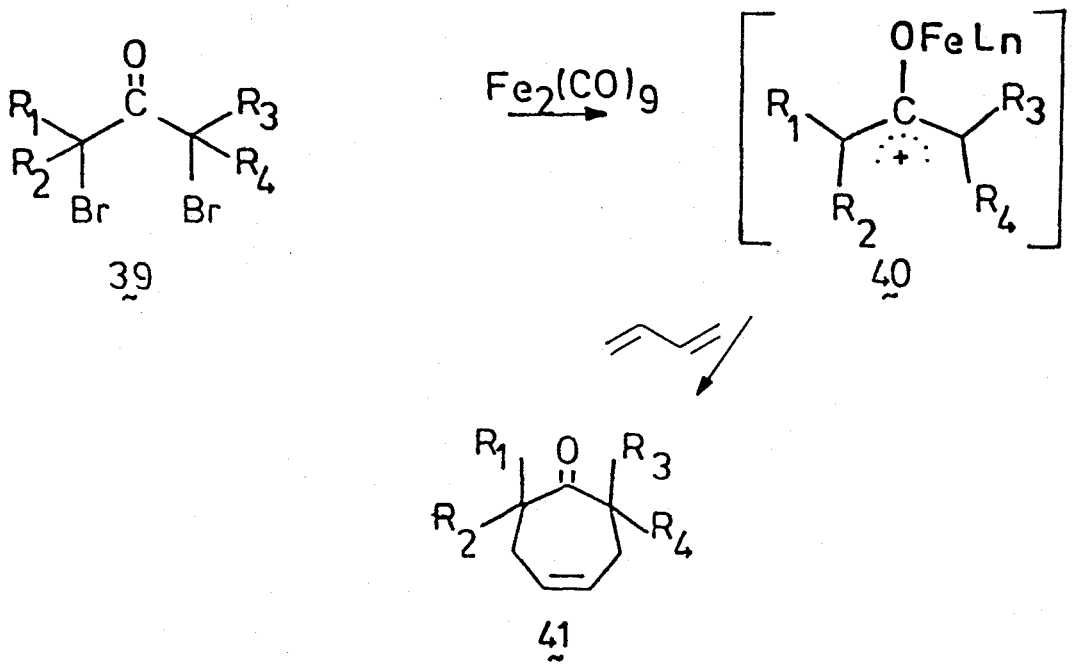
A zinc-copper couple has been used as a catalyst to promote halide elimination.[33] Under these conditions, a variety of α,α-dihaloketones on reaction with furan produced 8-oxabicyclo[3.2.1.]oct-6-en-3-ones 38.



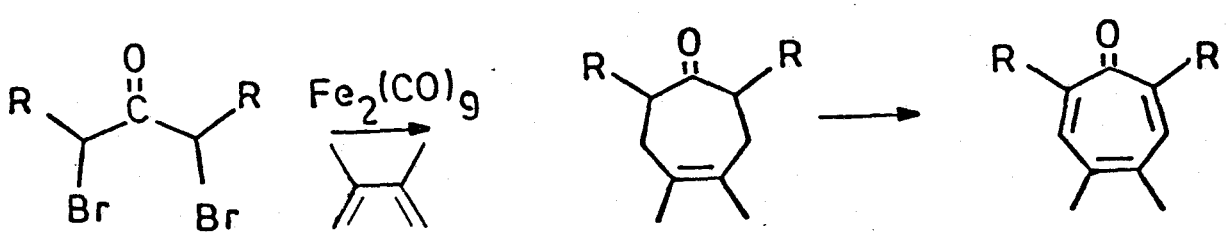
R = H, CH_3
X = Br, I

38

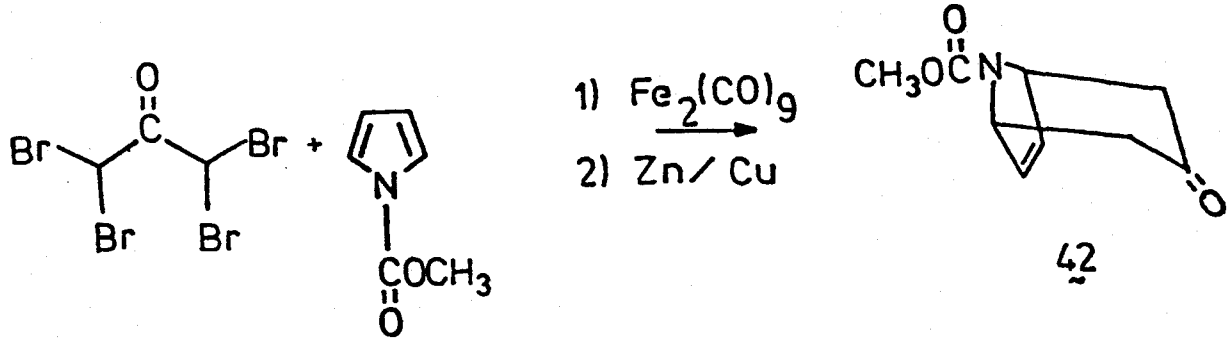
Similarly, iron carbonyls such as diironnonacarbonyl [$Fe_2(CO)_9$] have proved to be effective catalysts in promoting cycloaddition of dihaloketones. The dibromide 39 for example is a precursor for the allyl cation 40 which can react with conjugated dienes to produce cycloheptanone derivatives 41.[34-39]



The generation of substituted allyl cations via iron carbonyl catalysis has proved to be very useful in the synthesis of several different classes of natural products. For instance, the cycloadducts derived from secondary dibromoketones and open- chain 1,3-dienes serve as intermediates for troponoid synthesis.[40,41]

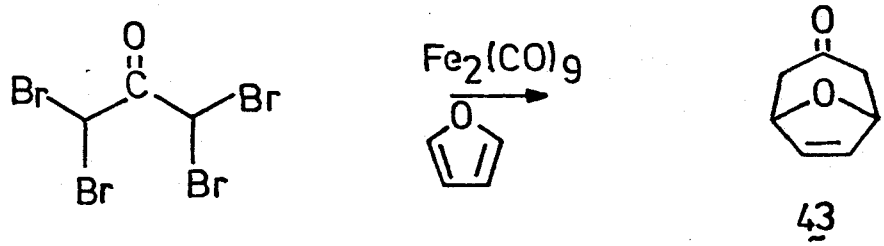


The reaction of polybromoketones with pyrrole derivatives leads to the tropane skeleton 42 and provides a general synthesis of many alkaloids.[42-44]



42

Finally, the oxabicycloketone 43 resulting from tetrabromoacetone and furan has provided a route to C-nucleosides.[45] Synthesis of such compounds is desirable since they possess important antibiotic, anticancer and antiviral properties.[46]

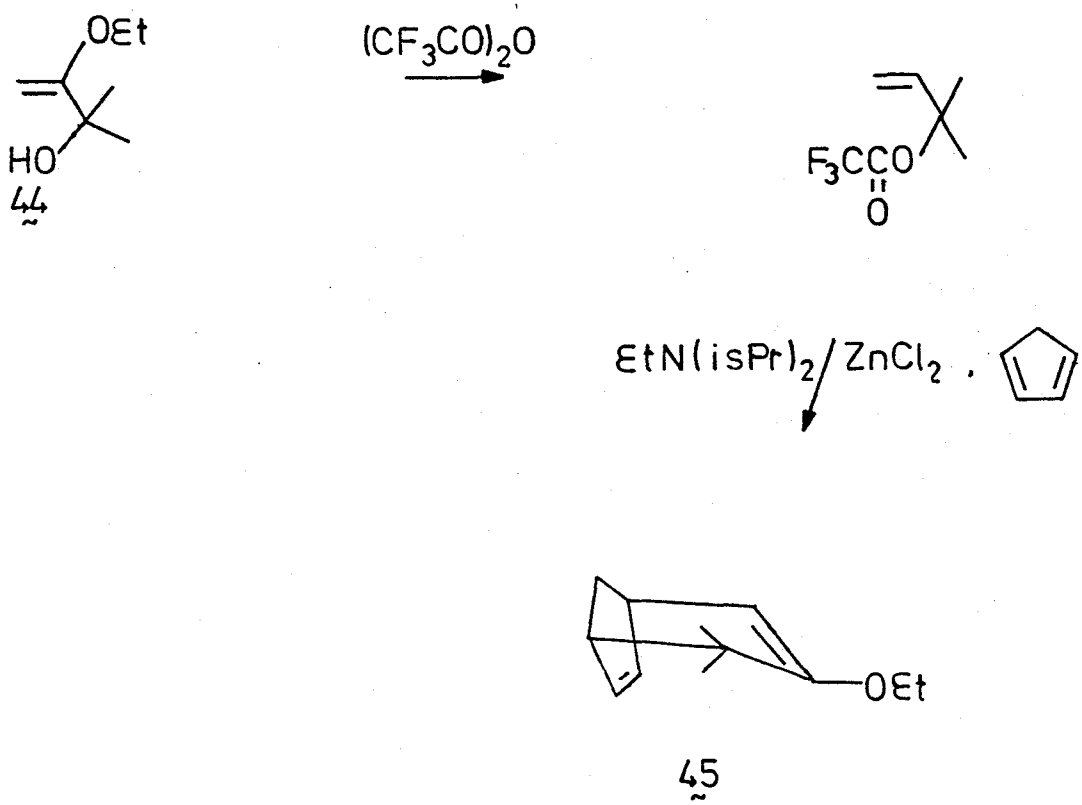


43

c) Allylic Alcohol Route

In some instances, the halides or dihaloketones that would be needed for the above routes are difficult to prepare. An alternative route has been developed using functionalized allylic alcohols. For example, trifluoroacetylation of the allylic alcohol 44 followed by zinc-halide induced heterolysis has proved to be satisfactory for generating the reactive three-carbon component.[47] The cation can be trapped by

conjugated dienes and in the presence of a hindered amine, the seven-membered cyclo-addition product 45 retains the enol-ether functionality.



44 45

These three routes that have been described represent the present scope of [4C+3C] cycloadditions. Although such routes have been successful in synthesizing seven-membered carbocyclic rings the yields have often been quite low and reaction conditions are restrictive.

The silver salt reaction for example must be kept in the dark since silver halides are sensitive to light, and the reaction mixture must be carefully buffered to prevent accumulation of acid. The use of 2-alkoxy allyl halides as allyl cation precursors is not desirable because of the low yields of these compounds during their synthesis. A further problem is that α,α-dihaloketones were found to be prone to bimolecular reductive coupling; a reaction that leads to 1,4-diketones.

In a more general sense though, the systems that have been developed generate three-carbon dienophiles of a transient nature only. Such species are susceptible to attack by nucleophiles and this reaction may compete effectively with the desired cycloaddition. Other side-reactions such as eliminations can also occur. Frequently, the more reactive cyclic dienes are used to minimize these side-reactions but when the less reactive acyclic dienes are used, the yields are very low.

This review of the literature then clearly illustrates the current interest in the synthesis of seven-membered carbocyclic ring systems. Despite the seemingly large number of synthetic routes available to such ring systems, improvement is needed in the development of a general synthetic scheme for constructing the cycloheptyl framework.

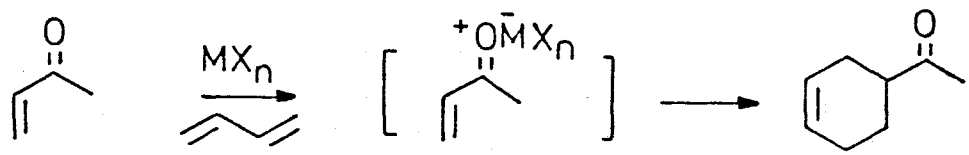
The [4C+3C] intermolecular cyclization seems to hold the most promise as a general route to seven-membered carbocycles. A variety of substituents can be used on the diene or on the allyl cation and rearrangements to give undesired products are scarce. Access to many natural products by this route is justification for exploring this method further.

Our initial strategy then was to develop a method for preparing substituted allyl cations that would circumvent the problems associated with a transient-type of reaction intermediate. The three-carbon intermediates could then be trapped by conjugated dienes to give seven-membered ring products. The work described in the remainder of this thesis examines one such potential route.

CHAPTER 2

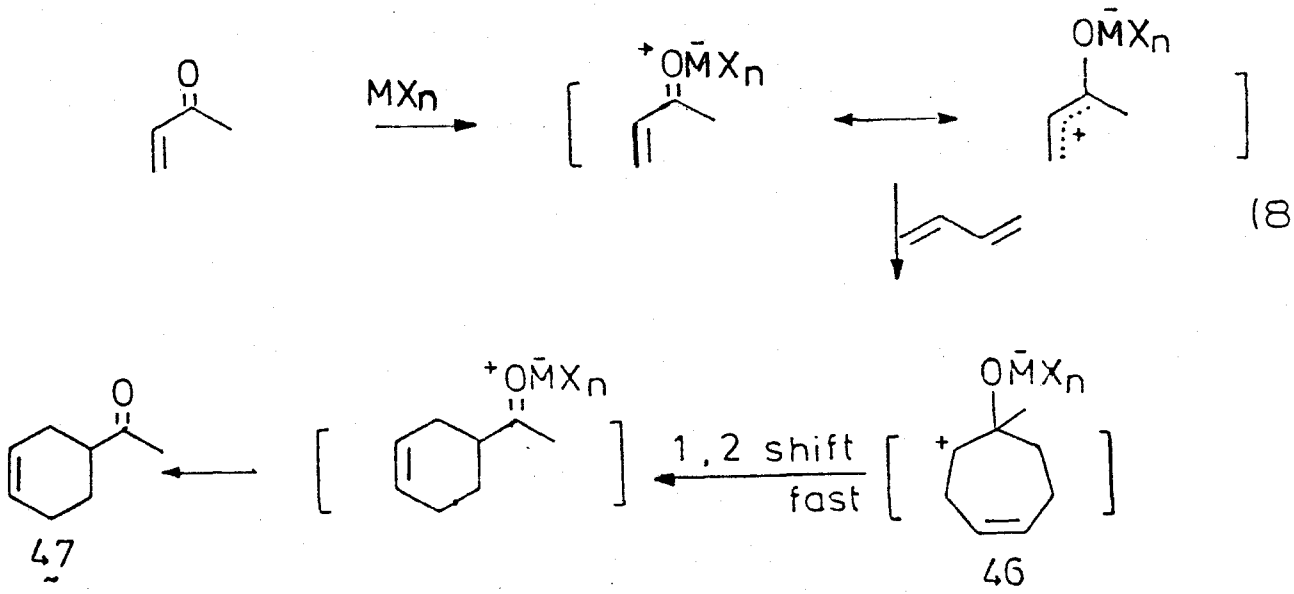
RESULTS AND DISCUSSION

A large number of reactions of α,β-unsaturated ketones can be catalyzed by Lewis acids. One example is the Diels-Alder reaction involving a diene and a dienophile. The complex formed between the enone and the Lewis acid (MX_n) serves as a dienophile toward 1,3-dienes in this cycloaddition reaction. The products formed are the familiar [4C+2C] cycloaddition adducts[48] as shown in equation 7.



(7)

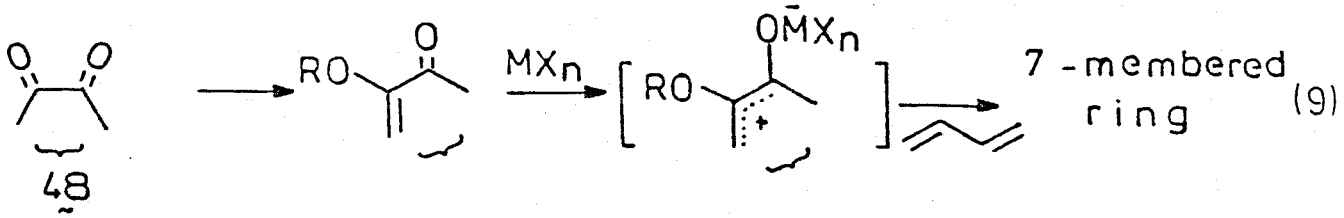
In principle, it should be possible for this reaction to proceed through a [4C+3C] cycloaddition intermediate. As shown in equation 8, the intermediate, 46, would be very unstable because of charge buildup on the carbon atom adjacent to the carbonyl group. If formed, this intermediate would probably rearrange to the [4C+2C] product, 47, via a 1,2-carbon shift.



(8)

47 46

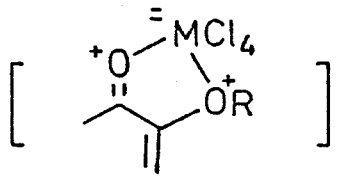
If a suitable charge-stabilizing functional group could be positioned adjacent to the carbonyl, the intermediate 46, would be stabilized and rearrangement to the six-membered ring would be less favourable. An oxygen-containing functional group was thought to possibly be a suitable substituent. In this regard, it was decided that the reactions of α, β -unsaturated ketones containing either an OH or an OR group at the α-position would be examined. To generate such unsaturated ketones, α-diketones, 48, were proposed as convenient starting materials. The reaction sequence is shown in equation 9.



48 (9)

In this reaction sequence a Lewis acid, MX_n, is used to generate the allyl cation by complexing with the carbonyl oxygen atom. It was thought that such complexes and other related bridged structures, vide infra, would be sufficiently stable to have a long lifetime in solution. This should enhance the utility of such "allyl" cations in cycloaddition reactions.

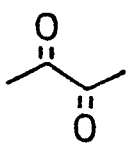
For a cyclic dione the s-cis conformation of the complex is established by the ring system. For an acyclic system however, the complex is more likely to favour the s-trans conformation in order to minimize dipolar interactions. If a Lewis acid was chosen that has two acceptor sites then interaction of both oxygen atoms with the Lewis acid may be enough to hold the complex in the desired s-cis conformation. $TiCl_4$ and $SnCl_4$ are examples of Lewis acids that have two empty d-orbitals and these could potentially bind with an acyclic precursor to form a complex such as 49.



M=Ti ,Sn

49

The compounds shown below are the systems that were studied. An attempt was made to define the nature of the Lewis acid/base complex for the acyclic compound 50 and the cyclic compounds 51 and 52 using NMR spectroscopy. Two Lewis acids, $TiCl_4$ and $SnCl_4$, were used in these studies.



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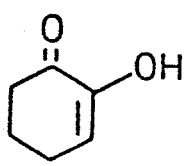
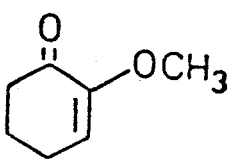


51



52

Part 1: NMR Studies

2,3-Butanedione

This acyclic α-diketone 50, was studied because of it's availability and it's simplicity in regards to it's ^{1}H-NMR spectrum. This dione is known to exist almost exclusively in the s-trans conformation with respect to the two carbonyl groups.[49]

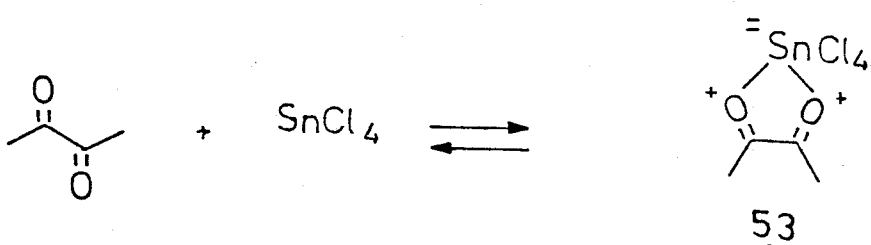
Initial studies made it quite clear that the complex would have to be formed at low temperatures to avoid side reactions that occur in the presence of the Lewis acid. For example, when biacetyl/$SnCl_4$ and biacetyl/$TiCl_4$ complexes (1:1) were prepared at room temperature the methyl signal from the complexed dione had all but disappeared after one hour and other unidentifiable signals began to appear through-

out the alkyl region of the ^{1}H-NMR spectrum. At lower temperatures these side reactions were retarded and it was possible to obtain reproducible data on the biacetyl/$SnCl_4$ complexes. Limited solubility of the biacetyl/$TiCl_4$ mixtures at low temperatures prevented these data from being collected.

The approach that was used to study the nature of the complexes formed between 50 and $SnCl_4$ was to record their ^{1}H-NMR spectra as the ratio of the two components was varied over a wide range. The data obtained are summarized in Table 1.

First, it should be noted that at 255K only one resonance was observed for the two methyl groups over the entire concentration range. The chemical shift of this resonance moved downfield as the Lewis acid concentration increased. This observation indicates that at 255K the system is in equilibrium with rapid interconversions between the various species present. The chemical shift that is observed is an average one.

The plot of the chemical shift of the methyl resonance vs. the molar ratio of Lewis acid is presented in Figure 4. It appears that the chemical shift is approaching a limiting value but it is occurring at a $SnCl_4$ to biacetyl concentration that exceeds 4:1. If the reaction proceeds to form a complex such as shown in equation 10, then the equilibrium constant must be small so that only when a large excess of $SnCl_4$ is present does all of the biacetyl become complexed.



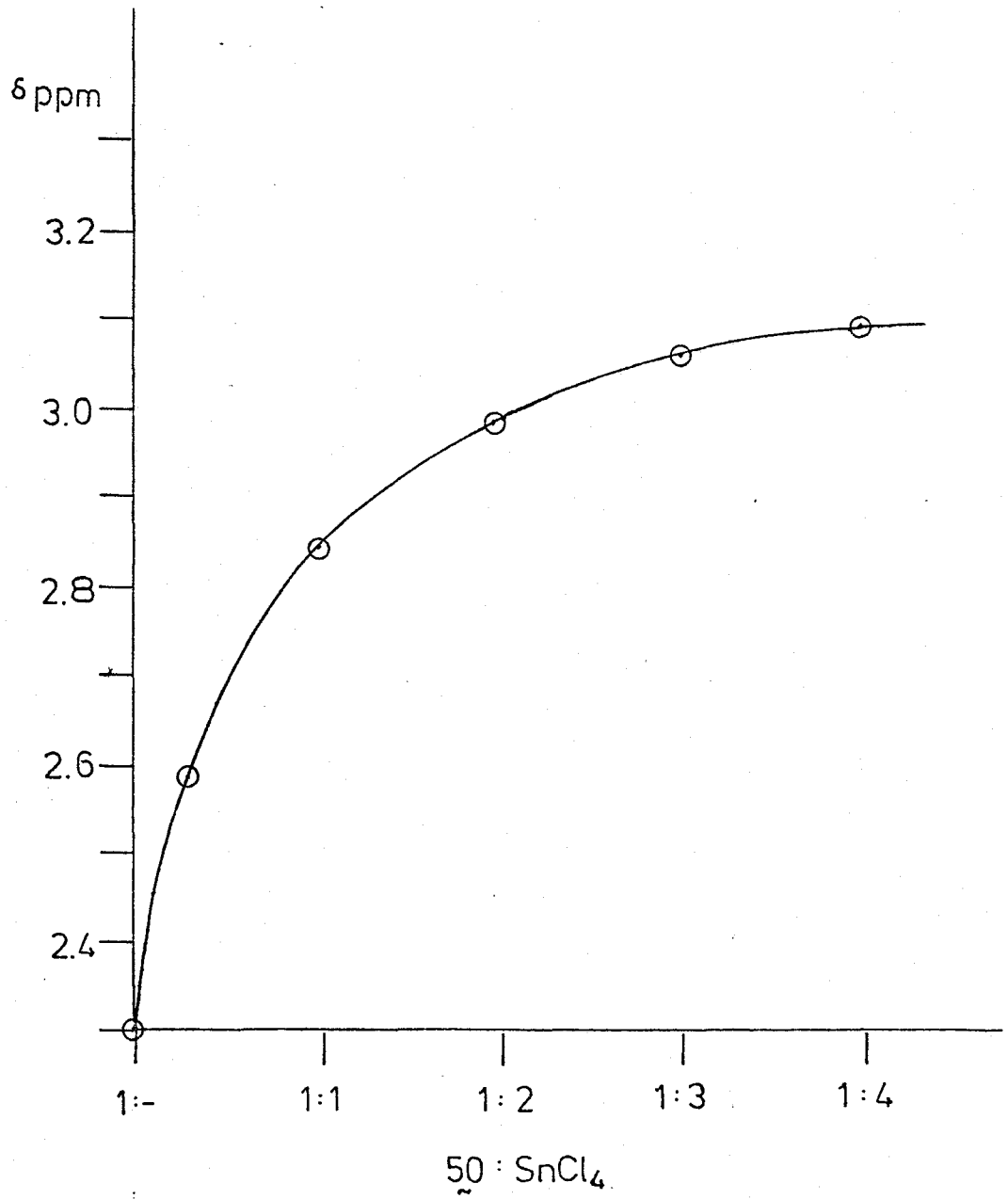
53 (10)

Table 1: ^{1}H-NMR spectral data for $\underset{\sim}{50}/SnCl_4$ complex

$\underset{\sim}{50}/SnCl_4$ ratio	Temp. (K)	Chemical Shifts (ppm)‡ CH_3
1: -	255	2.30
1:0.33	255	2.59
1:0.33	225	2.85
1:0.33	205	2.90
1:0.33	195	2.91
1:0.33	185	3.2, 2.4
1:0.33	175	3.31, 2.39
1:0.33	170	3.31, 2.39
1:0.5	255	2.72
1:0.5	195	3.29
1:0.5	185	3.29
1:1	255	2.84
1:1	205	3.28
1:1	185	3.29
1:2	255	2.98
1:2	205	3.28
1:3	255	3.05
1:3	205	3.28
1:4	255	3.08
1:4	205	3.28

‡ Reference: CD_2Cl_2 (5.33 ppm)

Figure 4: Chemical shift of CH_3 vs. $\underset{\sim}{50}/SnCl_4$ ratio[≠]



≠ Temp: 255K

The equilibrium constant for this reaction was estimated from a slightly modified Benesi-Hildebrand plot[50], Figure 5. The slope is given by $1/\ K$ and the intercept is given by $1/\Delta\delta$ (where $\Delta\delta$ is the chemical shift of the complex relative to the free base, and K is the equilibrium constant).

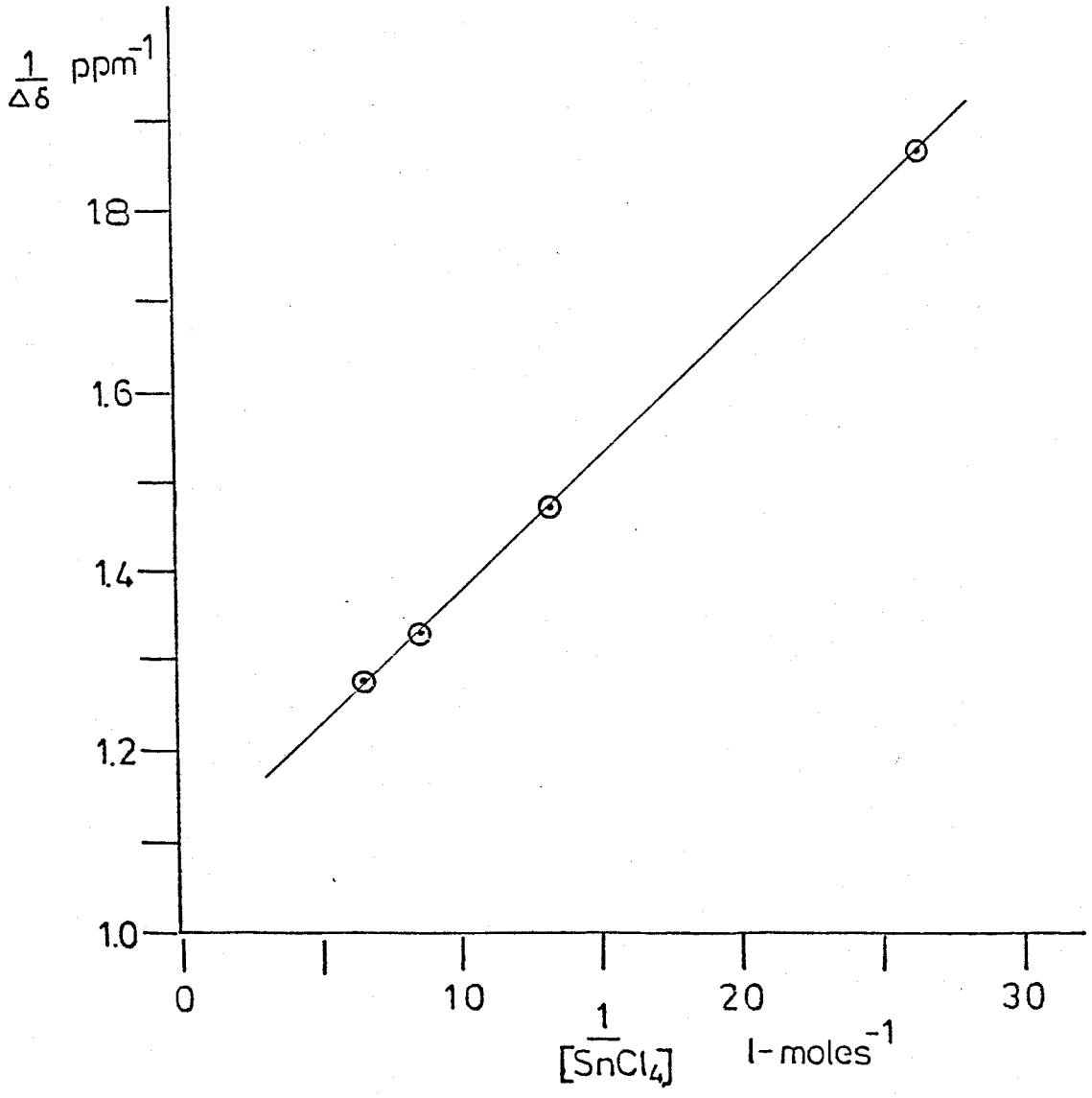
The fact that these data show a straight-line correlation indicates that at 255K there is only one equilibrium that is important. The equilibrium constant was calculated to be $K = 2.65 \times 10^{-2}$. As will be shown below these data are consistent with the idea that the complex formed is the one shown in equation 10.

Further support for this doubly-bound 1:1 complex, 53, was obtained by recording the spectra at lower temperatures. The advantage to this is that the rates of exchange can be reduced and the composition of equilibria can be changed. These data are also recorded in Table 1.

As can be seen from these data, considerable changes in chemical shift were observed as the temperature was lowered. All of these changes were reversed when the samples were warmed to 255K. It is interesting that in one case, more than one signal was observed for the methyl group. There are several points to be made from these observations.

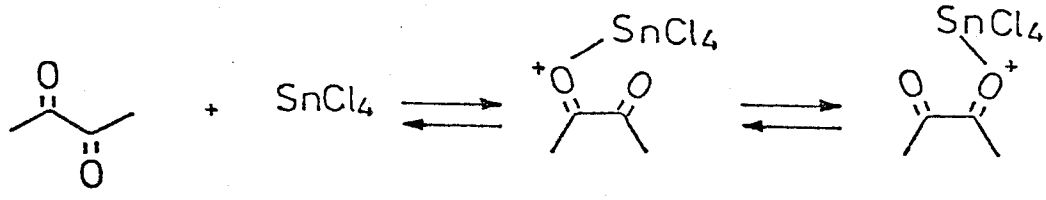
First, for all biacetyl/$SnCl_4$ ratios examined, the change in the averaged methyl resonance was toward lower field as the temperature was lowered. This suggests that the equilibrium was being shifted in favour of increased complexation; a result that is not suprising in terms of the overall free energy of the reaction. In cases where the Lewis acid is in a 1:1 or greater molar excess, at 205K all the spectra exhibited the same chemical shift for the single methyl resonance at 3.28 ppm. This observation strongly suggests that at lower temperatures the species present is the 1:1 complex as shown in equation 10.

Figure 5: $(CH_3$ chemical shift change$)^{-1}$ vs. $[SnCl_4]^{-1}$ ≠



≠ Temp: 255K

To confirm that both oxygens are bound in the complex at this temperature, the complex formed between 2-propanone and $SnCl_4$ was used as a model for the expected chemical shift changes. Data from the literature[51] indicate that on complexation with $SnCl_4$, the methyl resonance of acetone shifts downfield 0.57 ppm. If the complex formed between biacetyl and $SnCl_4$ was a rapidly equilibrating singly-bound complex as shown in equation 11, then the averaged chemical shift of the methyl groups would be expected to be intermediate between a non-complexed acetyl group and a complexed acetyl group. That is, the downfield shift of the methyl resonance for the equilibrating structure shown in equation 11 would be ~ 0.57/2 ppm.



(11)

The downfield shift of the methyl signal at 205K for complexes with an equimolar or excess of $SnCl_4$ amounts to 0.98 ppm. This large downfield shift cannot be accounted for by a singly-bound complex as shown in equation 11 but is better accounted for by a doubly-bound complex, 53, as shown in equation 10.

Where the 50/$SnCl_4$ ratio is less than 1:1, at very low temperatures two resonances were observed for the mixture. For example in the case of a ratio of 1:0.33, the two resonances were observed at 3.31 and 2.39 ppm in a ratio of 1:2.5 respectively. The resonance at 3.31 is very close to that observed above for those cases when the Lewis acid was in excess and where the species present was suggested to be 53. The other resonance at 2.39 corresponds closely to that of the original biacetyl. It should be noted too that the ratio of these two resonances corresponds to there being a 1:1 complex between biacetyl and $SnCl_4$ and free biacetyl remaining in solution. Obviously at 175K exchange between free and bound biacetyl has been

slowed sufficiently to see these two signals.

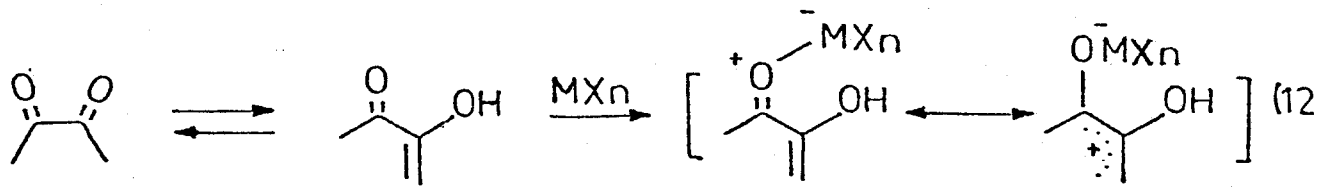
In summary then, it seems that the initially formed complex between biacetyl and $SnCl_4$ has both carbonyl groups bound to the Lewis acid but the equilibrium constant for this process is very small. Complete complexation can be obtained by using a large molar excess of the Lewis acid or by dropping the temperature in an effort to force the equilibrium in favour of the complex.

As a result of these complicating conditions and the need to remove HCl from the complex to form the allyl cation, it was decided that a simpler system would be studied.

1,2-Cyclohexanedione

α -Diketones exist in solution as a tautomeric pair. The acyclic diones exhibit di-carbonyl characteristics since dipolar interactions can be minimized by rotation about the C-C bond separating these two groups. Cyclic α -diketones on the other hand cannot undergo this rotation to the same extent but minimize dipolar interactions by tautomerizing to the mono-enol form. The extent to which the molecule is in either tautomeric form depends upon the size of the ring. Cyclopentane-1,2-dione for example exists almost entirely in the mono-enol form whereas the larger cyclooctane-1,2-dione favours the α -diketone structure.[52]

The mono-enol form of an α -diketone might serve as an immediate precursor to allyl cations as shown in equation 12.



(12)

Cyclohexane-1,2-dione exists primarily as the enol tautomer. By studying it's ^{1}H-NMR spectrum it was found to exist as the enol tautomer to the extent of 87% when dissolved in $CDCl_3$. By complexing this "diketone" with a Lewis acid and studying it's NMR spectra it was hoped that information regarding stoichiometry and charge delocalization could be obtained. Such information would be useful in deciding whether this system is suitable for a [4C+3C] cycloaddition reaction.

The ^{1}H-NMR and ^{13}C-NMR data for the reaction of 51 with $TiCl_4$ are shown in Tables 2 and 3. Table 4 shows the ^{1}H-NMR data for the complex formed with $SnCl_4$.

From these data there are several points to be made regarding the complex formed between 51 and $TiCl_4$. Referring to Figures 6 and 7, the change in chemical shift of the alkyl protons in the presence of the Lewis acid is evidence for complexation of the carbonyl group. Also, there is no further change in chemical shift when the stoichiometry is changed from 1:1 to 1:2 (dione:Lewis acid) suggesting that a 1:1 complex is formed between $TiCl_4$ and the α-diketone.

The prominent hydroxy proton signal that is present in the dione disappears when the dione is complexed with $TiCl_4$. A new peak does appear however at much higher field (1.2 ppm). The chemical shift of this signal proved to be sensitive to temperature. As the temperature was lowered, this signal moved downfield. The disappearance of the hydroxy signal and the appearance of this new signal suggests that HCl is evolved as the complex is formed. To confirm that this new peak was due to HCl, gaseous HCl was bubbled into the NMR tube. A very large signal appeared at the same chemical shift as the new signal suggesting that HCl is given off during complexation.

One further piece of evidence for the presence of HCl was obtained as the hindered base 2,6-di-tertiarybutyl pyridine was added to the NMR tube. This base does not react with a Lewis acid but will "mop-up" any protic acid that may be present.[53]

Table 2: ^{1}H-NMR spectral data for 5l/$TiCl_4$ complex

5l/$TiCl_4$ ratio	Temp. (K)	H_3	Chemical shifts (ppm)#		
			OH	H_4-H_6	HCl
1:-	255	6.21	6.10	2.65-1.8	
1:1	255	7.30 (+1.09)*	-	3.09-2.25 (+0.45)	1.35
1:2	255	7.30 (+1.09)	-	3.09-2.21 (+0.44)	1.35

Reference: $CDCl_3$ (7.25 ppm)

* ( ) is difference between chemical shift of 5l and 5l/$TiCl_4$.

+ve number indicates downfield shift

Table 3: ^{13}C-NMR spectral data for 5l/$TiCl_4$ complex

5l/$TiCl_4$ ratio	Temp. (K)	Chemical Shifts (ppm)≠					
		C_1	C_2	C_3	C_4	C_5	C_6
1:-	255	195.7	147.1	118.2	23.9	23.2	36.5
1:1.5	255	207.8 (+12.1)*	159.4 (+12.3)	132.5 (+14.3)	24.7 (+0.8)	21.9 (-1.3)	34.5 (-2.0)

≠ Reference: $CDCl_3$ (77.0 ppm)

* ( ) is difference between chemical shift of 5l and 5l/$TiCl_4$. +ve number indicates downfield shift.

Table 4: ^{1}H-NMR spectral data for $\underset{\sim}{5}$l/$SnCl_4$ complex

$\underset{\sim}{5}$l/$SnCl_4$ ratio	Temp. (K)	H_3	Chemical Shifts (ppm)≠ OH	H_4-H_6	HCl
1:-	255	6.21	6.10	2.65-1.8	-
1:2	255	7.19 (+0.98)*	8.00 (+1.90)	3.00-2.10 (+0.35)	1.23
1:3	255	7.20 (+0.99)	8.45 (+2.35)	3.00-2.10 (+0.35)	1.23
1:3	185	7.33 (+1.12)	-	3.06-2.10 (+0.41)	1.23

≠ Reference: $CDCl_3$ (7.25 ppm)

* ( ) is difference between chemical shift of $\underset{\sim}{5}$l and $\underset{\sim}{5}$l/$SnCl_4$.

+ve number indicates downfield shift.

Figure 6: ^{1}H-NMR spectrum of 51

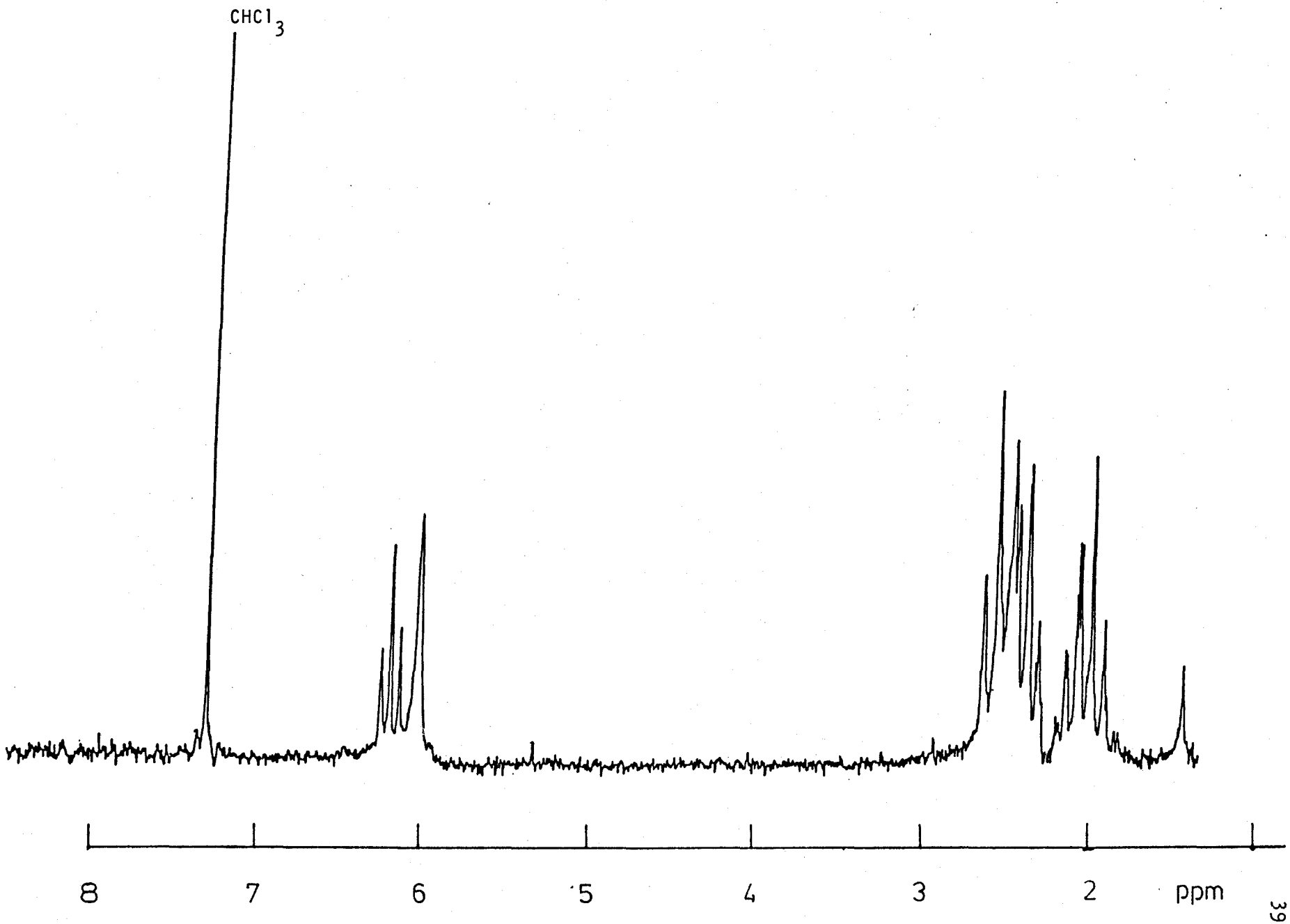
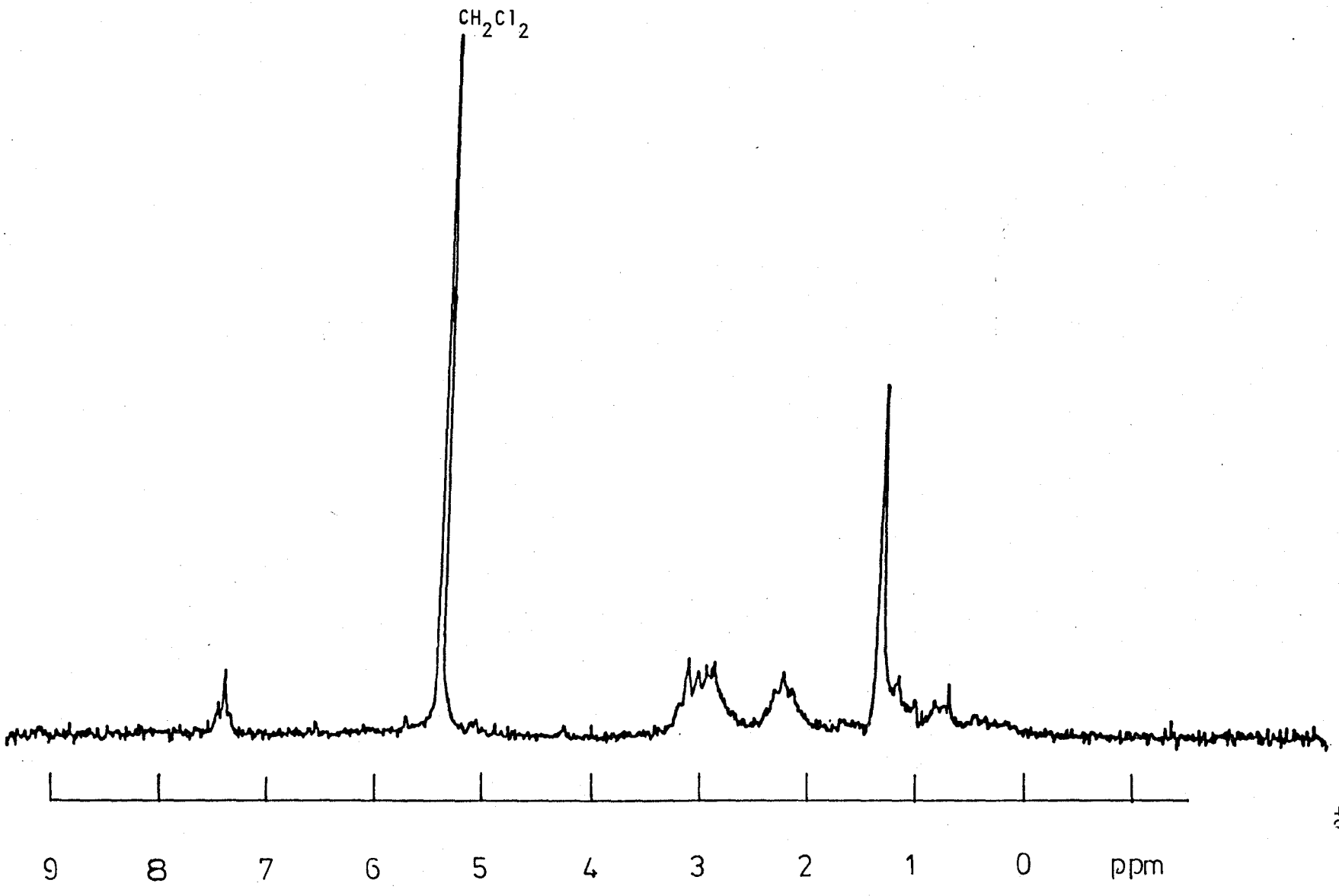
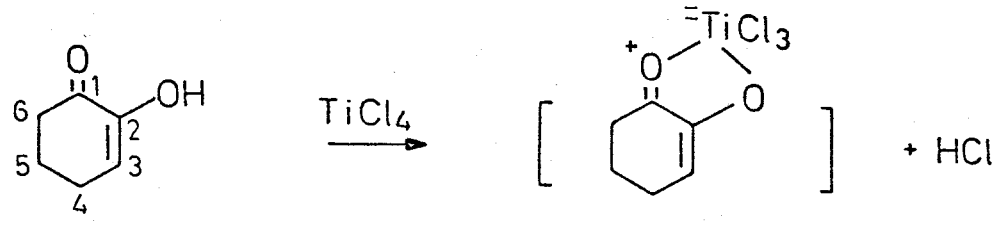


Figure 7: ^{1}H-NMR spectrum of $\underset{\sim}{5}$1/$TiCl_4$ complex



It is apparent from the ^{1}H-NMR spectrum shown in Figure 8 that the hindered base became protonated when added to the NMR tube since the signal from the tertiarybutyl group shifted downfield ($\Delta\delta$=0.3ppm).

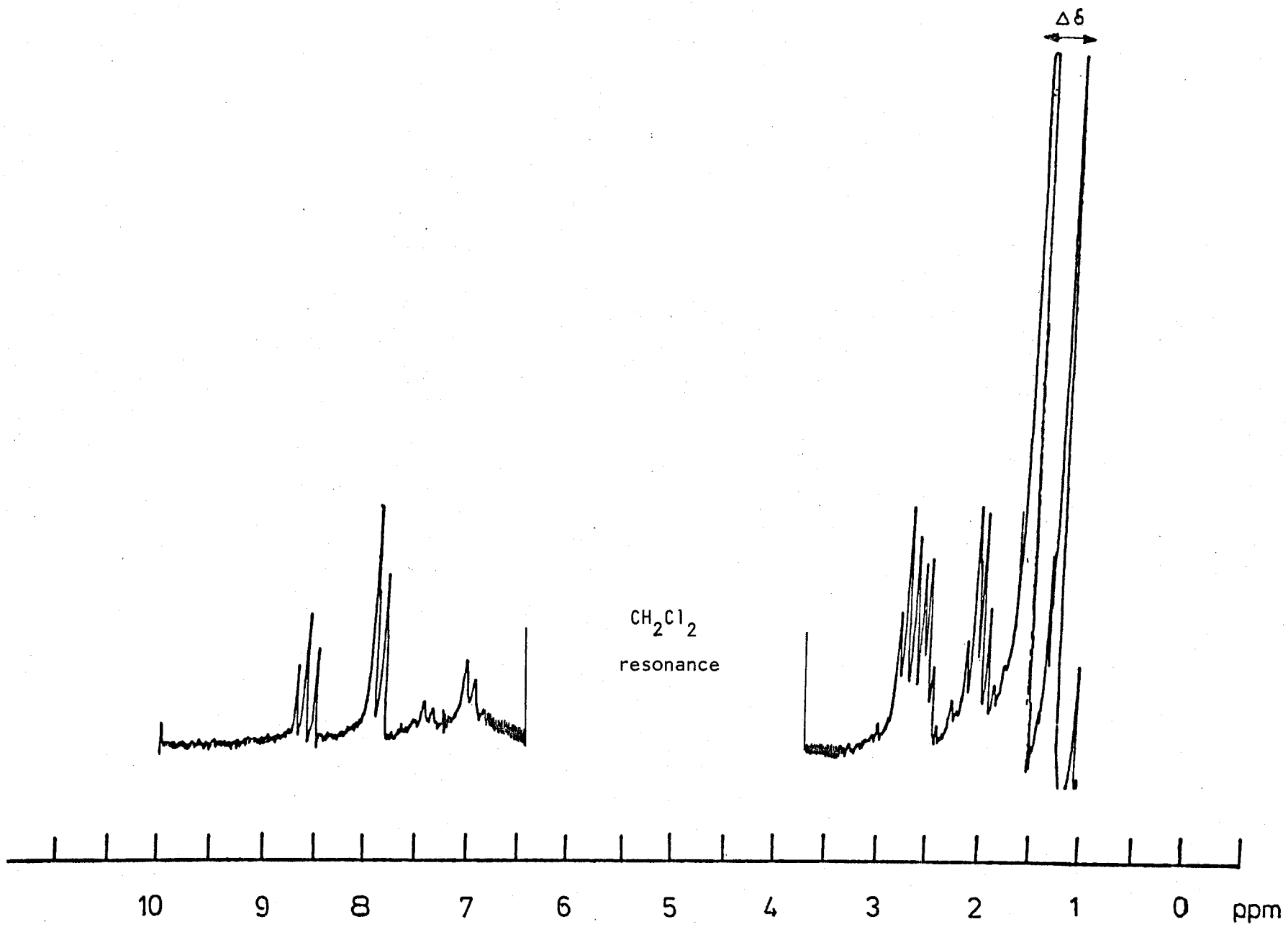
Evidence for the existence of a 1:1 complex and the evolution of HCl strongly suggests that both oxygen atoms of the dione are bound to the Ti atom and that the complex might appear as shown below.



When the complex is formed using $TiCl_4$ as the Lewis acid there is a significant downfield shift of the H_3 proton signal suggesting that there has been a decrease in electron charge density at C_3. The magnitude of this change in chemical shift is consistent with data reported for similar complexes,[54] and provides evidence for the reaction of the carbonyl oxygen with the Lewis acid.

Studies on ^{13}C-NMR chemical shifts of complexed unsaturated esters,[55] ketones,[56] ethers[57] and imines[58] have been reported and chemical shift differences have been taken to give an indication of the change in electron density.[59] The large shift downfield of the C_1 and C_3 signals upon complexation of 51 with $TiCl_4$ is typical again of that found for α, β -unsaturated carbonyl systems and suggests that there is an electron deficiency at these centres. The large downfield shift of the C_2 signal is rather surprising however, since reports from the literature on similar systems show a significant shift upfield for this signal. This complex is unique though, in that the substituent attached to C_2 is directly bound to the Lewis acid.

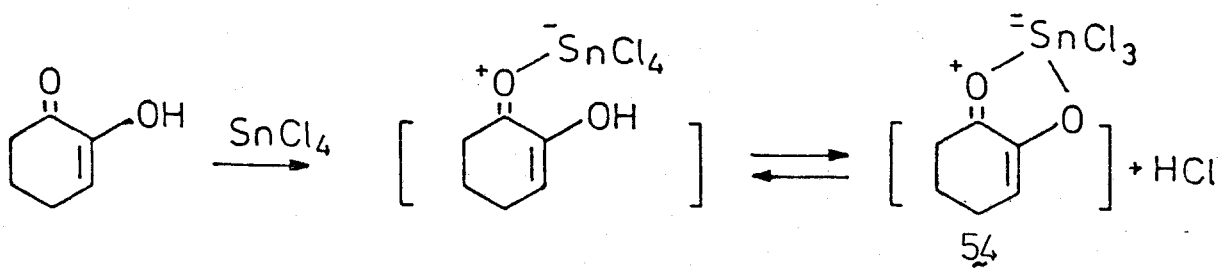
Figure 8: ^{1}H-NMR spectrum of $\underset{\sim}{5}$1/$TiCl_4$/2,6-ditertiarybutyl pyridine



Regardless of the origin of the downfield shift of the C_2 signal it is clear that there is a delocalization of positive charge over the carbon centres C_1 and C_3. Such delocalization should be favourable for a cycloaddition reaction leading to 7-membered rings.

The ^{1}H-NMR data of the dione : $SnCl_4$ complex is similar to that for the $TiCl_4$ complex, but there are a few important differences. For the (1:1) 51/$TiCl_4$ complex, the chemical shift of the H_3 proton resonance moves downfield by 1.09 ppm. On complexation, a smaller change (0.99 ppm) is observed for the 51/$SnCl_4$ complex, even when the ratio is as high as 1:3. Also, there is an additional very broad signal at 8.0 ppm for the (1:3) 51/$SnCl_4$ mixture that moves further downfield as more Lewis acid is added. It seems that this must be the hydroxy proton signal and the fact that it is very broad suggests that it is undergoing exchange. When the temperature is lowered to 185K, this very broad signal disappears but reappears when the sample is warmed to 255K again. Also, at this lower temperature the resonance due to the H_3 proton moves further downfield (7.33 ppm) to a chemical shift similar to that of the 51/$TiCl_4$ complex (7.30 ppm), to which a doubly-bound structure was assigned. It appears that there is some HCl being formed at both temperatures as indicated by the signal at 1.23 ppm.

It seems then that the weaker Lewis acid $SnCl_4$ does not bind both oxygen atoms completely and that there may be an equilibrium of the type shown in equation 13. As the temperature is lowered the equilibrium is pushed in favour of the cyclic bound complex 54.



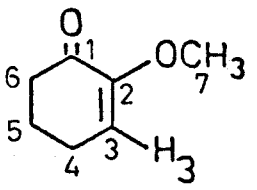
54 (13)

In summary then, the complex formed between 1,2-cyclohexanedione and $TiCl_4$ or $SnCl_4$ seems to have 1:1 stoichiometry and in both cases, the Lewis acid is bound to the carbonyl group. The complex formed with $TiCl_4$ shows characteristics indicative of both oxygen atoms being strongly bound to the Lewis acid. The complex formed with $SnCl_4$ seems to bind only weakly to the second oxygen atom unless a large excess of Lewis acid is used or the temperature is lowered. The delocalization of positive charge seems to be across the carbon centres C_1 and C_3 as well as the carbonyl oxygen.

2-Methoxy-cyclohex-2-en-1-one

The formation of HCl during complexation of 1,2-cyclohexanedione might catalyze a rearrangement of the desired [4C+3C] intermediate if it were formed in any cycloaddition reaction. Such a rearrangement would probably lead to the undesired six-membered ring.

Replacement of the enolic proton with a methyl group was chosen to overcome this difficulty. The methyl ether 52, was easily synthesized from 1,2-cyclohexanedione in the presence of base and dimethylsulphate. The data for the complexation experiments are recorded in Tables 5, 6 and 7.



52

Table 5: ^{1}H-NMR spectral data for $\underset{\sim}{52}/TiCl_4$ complex

$\underset{\sim}{52}/TiCl_4$ ratio	Temp. (K)	Chemical Shifts (ppm)≠		
		H_3	OCH_3	H_4-H_6
1:-	255	5.89	3.64	2.59-1.88
1:0.25	255	6.80 (+0.57)	4.21 (+0.57)	3.00-2.08 (+0.41)
1:0.5	255	6.92 (+1.03)	4.27 (+0.63)	3.05-2.10 (+0.46)
1:1	255	6.93 (+1.04)	4.27 (+0.63)	3.06-2.12 (+0.47)
1:1.5	255	6.93 (+1.04)	4.27 (+0.63)	3.06-2.12 (+0.47)
1:2	255	6.92 (+1.03)	4.27 (+0.63)	3.06-2.12 (+0.47)

≠ Reference: $CDCl_3$ (7.25 ppm)

* ( ) is difference between chemical shift of $\underset{\sim}{52}$ and $\underset{\sim}{52}/TiCl_4$.

+ve number indicates downfield shift.

Table 6: ^{13}C-NMR spectral data for $\underset{\sim}{52}/TiCl_4$ complex

$\underset{\sim}{52}/TiCl_4$ ratio	Temp. (K)	Chemical Shifts (ppm)≠						
		C_1	C_2	C_3	C_4	C_5	C_6	C_7
1:-	255	193.8	151.3	116.2	24.1	22.7	38.5	54.4
1:1.5	255	203.6 (+9.8)*	151.3 (0.0)	134.6 (+18.4)	25.1 (+1.0)	21.5 (-1.2)	35.9 (-2.6)	62.0 (+7.6)

≠ Reference: $CDCl_3$ (77.0 ppm)

* ( ) is difference between chemical shift of $\underset{\sim}{52}$ and $\underset{\sim}{52}/TiCl_4$.

+ve number indicates downfield shift.

Table 7: ^{1}H-NMR spectral data for $\underset{\sim}{52}/SnCl_4$ complex

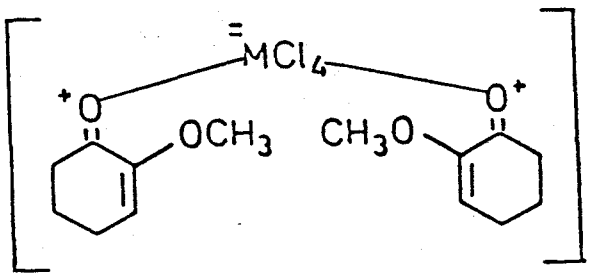
$\underset{\sim}{52}/SnCl_4$ ratio	Temp. (K)	Chemical Shifts (ppm)≠		
		H_3	OCH_3	H_4-H_6
1:-	255	5.89	3.64	2.59-1.88
1:0.25	255	6.88 (+0.99)*	4.26 (+0.62)	3.05-2.00 (+0.46)
1:0.5	255	6.94 (+1.05)	4.27 (+0.63)	3.05-2.00 (+0.46)
1:1	255	6.94 (+1.05)	4.27 (+0.63)	3.04-2.00 (+0.45)
1:2	255	6.94 (+1.05)	4.27 (+0.63)	3.05-2.00 (+0.46)

≠ Reference: $CDCl_3$ (7.25 ppm)

* ( ) indicates difference between chemical shift of $\underset{\sim}{52}$ and $\underset{\sim}{52}/SnCl_4$.

+ve number indicates downfield shift.

It is interesting that with both Lewis acids, no further change in the chemical shift occurs when the enol ether : Lewis acid ratio exceeds 1:0.5. This suggests that the Lewis acid may be bridging two carbonyl groups and so the complex may be best represented by structure 55.



55

If the Lewis acid is bridging in this way, then there could not be any direct interaction between the Lewis acid and the etheral oxygen since both empty sites on the metal would now be occupied. Yet there has been a downfield shift of the methyl resonance suggesting deshielding at this site. Through-space deshielding of nuclei by Lewis acids has been postulated to explain the shift to lower field of the H_2 proton of complexed cyclohexenone.[53] It may be that a similar affect is occurring here at the methyl group.

From the magnitude of the chemical shift change of the H_3 proton resonance it seems that the difference in Lewis acid strength between $TiCl_4$ and $SnCl_4$ has not affected the extent of charge delocalization. Also, the chemical shift change is of the same magnitude as was seen for the complexes of 1,2-cyclohexanedione. This is not surprising since the basicity of the carbonyl groups in each case should be similar.

In summary, the characteristics of the complexes formed between 2-methoxy-cyclohex-2-en-1-one and the acids $TiCl_4$ and $SnCl_4$ are different from the analogous 1,2-cyclohexanedione complexes. The stoichiometry is 1:0.5 suggesting intermolecular

bridging of the Lewis acid across two carbonyl groups. The second oxygen atom does not appear to be bound directly to the Lewis acid. The ^{1}H-NMR and ^{13}C-NMR spectra do indicate that there is a delocalization of charge over the carbon centres C_1 and C_3 in addition to the carbonyl oxygen.

Part 2: Reactions of Complexes

1) 1,2-Cyclohexanedione

1,2-Cyclohexanedione, 51, was reacted with 1,3-butadiene in the presence of $TiCl_4$ with the hope of observing the desired [4C+3C] cycloaddition product. Following neutralization, the crude reaction mixture was purified by distillation and analytical gas chromatographic analysis showed one major component (95%) with a retention time different from that of the starting material.

The spectral data for this component are tabulated in Table 8. The mass spectrum indicated a $M^+ = 166$, consistent with the addition of butadiene to 51. Elemental analysis supported this claim showing the empirical formula to be $C_{5.01}H_{7.07}O_{1.00}$.

Examination of the ^{1}H-NMR spectrum revealed three distinct types of resonances corresponding to 11 alkyl hydrogens, 2 vinyl hydrogens and 1 hydroxyl hydrogen. The I.R. spectrum showed a very broad OH vibration at 3490, an asymmetric stretching vibration of a CH=CH functional group at 3030 and a saturated C=O stretching band at 1710 cm^{-1}.

Table 8: Spectral data for product of Diels-Alder reaction from 51 and 1,3-butadiene

^{1}H-NMR (ppm)≠	Assignment
5.7 (m, 2H)	CH=CH
3.8 (s, 1H)	OH
2.7-1.5 (m, 11H)	CH_2-CH_2

I.R. (cm^{-1})	Assignment
3490	OH
3030	CH=C-H
1715	C=O

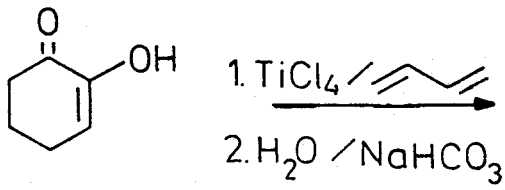
mass spec.
m^+ = 166 m/e

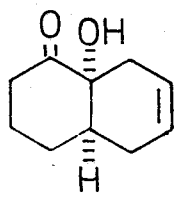
Anal. calcd for $C_{10}H_{14}O_2$; C, 72.26; H, 8.49

Found: C, 72.24; H, 8.55

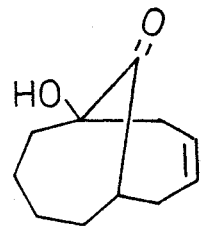
≠ Solvent CCl_4, TMS reference

These spectral data were not sufficient however for an unambiguous identification of the product. One can see from the reaction outlined below that each of the isomeric compounds 56 and 57 arising from a [4C+2C] and [4C+3C] cycloaddition has the appropriate mass and empirical formula consistent with the observed spectroscopic properties.



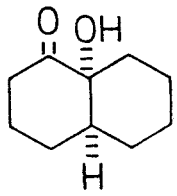


56



57

Neither of these compounds has been reported in the literature, but, if the reaction product is the simple Diels-Alder addition product, 56, then hydrogenation of this material would lead to 58, a compound that has been reported.[60]



58

The product obtained from the cycloaddition reaction was hydrogenated over Pd/C to give a single compound in 83% yield. The spectral data and physical properties of this reduced compound and the literature data on 1-hydroxy-bicyclo[4.4.0.]decan-2-one, are tabulated in Table 9. The spectral properties of authentic cis-1-hydroxy-bicyclo[4.4.0.]decan-2-one and the material obtained on reduction of the cycloadduct are similar. This suggested that the hydrogenated

Table 9: Spectral data for hydrogenated cycloaddition product and literature data of 1-hydroxy-bicyclo[4.4.0]decan-2-one

Experimental	Literature	
^{1}H-NMR (ppm)≠	^{1}H-NMR (ppm)≠	
3.7 (s, 1H)	cis	trans
2.4 (m, 2H)	3.67 (s, 1H)	3.03 (s, 1H)
		3.1-2.8 (m, 1H)
2.0-0.9 (m, 13H)	2.8-1.0 (m, 15H)	2.3-1.0 (m, 14H)
I.R. (cm^{-1})	I.R. (cm^{-1})	
3490	cis	trans
1710	3485	3610, 3490
	1708	1705
m.p.	m.p.	m.p.
56-60°C	cis	trans
	61-64°C	44-45°C

≠ Solvent CCl_4, TMS reference

material was in fact the structure shown above, 58. The melting point of the material obtained here is somewhat lower than reported in the literature. Tentatively, the product isolated from the catalyzed cycloaddition of 1,2-cyclohexanedione and butadiene would appear to be 56 suggesting that the reaction occurred via a [4C+2C] cycloaddition. Further support for this simple Diels-Alder addition product was found, vide infra, when the methoxy-ether of 1,2-cyclohexanedione gave products arising from [4C+2C] cycloadditions.

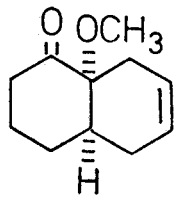
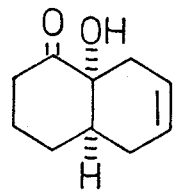
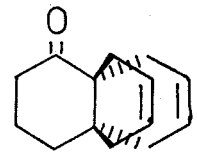
Despite the apparent delocalization of charge within the complex the [4C+2C] cycloadduct is the only identifiable product from this reaction. Loss of the enolic proton upon complexation of the dione to give HCl could possibly cause rearrangement of any [4C+3C] cycloadduct, 57, formed during the reaction. Replacement of this hydrogen atom by a methyl group should stop such a rearrangement from occurring. This idea led to the investigation of the reaction of 2-methoxy-cyclohex-2-en-1-one.

2) 2-Methoxy-cyclohex-2-en-1-one

2-Methoxy-cyclohex-2-en-1-one, 52, was prepared from 1,2-cyclohexanedione in 85% yield. It was reacted with butadiene in the presence of $TiCl_4$ in the same manner as 1,2-cyclohexanedione. Following neutralization, the crude reaction mixture was distilled to give a moderate yield of a product-mixture. Analytical gas chromatographic analysis of the distilled product showed that there were three major components, all of which had retention times different from that of the starting material. The three components were separated and purified by vapour phase chromatography. The spectral data of these compounds are shown in Table 10.

The data for component 1 of this mixture were consistent with the addition of butadiene to 52. The molecular ion in the mass spectrum and the elemental analysis

Table 10: Spectral data for products of Diels-Alder reaction from 52 and 1,3-butadiene

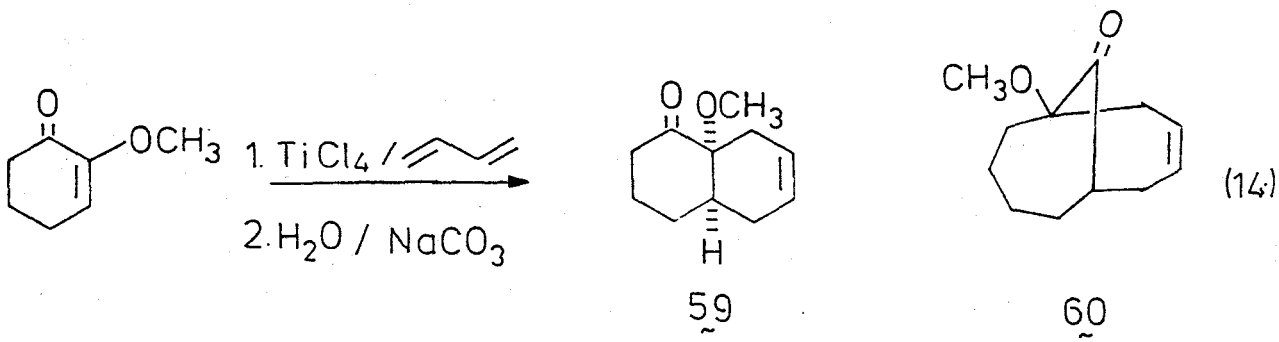
component 1	component 2	component 3
^{1}H-NMR (ppm)≠	^{1}H-NMR (ppm)	^{1}H-NMR (ppm)
5.8 (m, 2H) 3.4 (s, 3H) 2.6-1.6 (m, 11H)	5.7 (m, 2H) 3.0 (s, 1H) 2.8-1.5 (m, 11H)	5.3-6.0 (m, 4H) 1.5-2.8 (m, 14H)
mass spec.	mass spec.	mass spec.
m^+ = 180 m/e	m^+ = 148 (166-18)m/e	m^+ = 202 m/e
I.R. (cm^{-1})	I.R.* (cm^{-1})	I.R. (cm^{-1})
3020 1720 1080	3490 3030 1715	3025 1710
structure	structure	structure
		

≠ Solvent CCl_4, TMS reference

* Fingerprint region identical to 57

both supported a simple cycloaddition product. The ^{1}H-NMR data showed a vinyl resonance at 5.8 ppm, a methoxy resonance at 3.4 ppm and a complex alkyl region between 2.6-1.6 ppm.

These spectral data however were again not sufficient for a complete identification of this component. The products of both the [4C+2C], 59, and [4C+3C], 60, cycloadditions (equation 14) would be expected to have similar ^{1}H-NMR spectra; not readily differentiated when only one compound has been isolated.



59 60 (14)

To be completely certain about the identity of component 1 an independent synthetic route was needed to the methoxy decalones 61 and 62. Such a route has been described in the literature and is shown in Figure 9.[60]

61 62

α-Naphthol was purified by sublimation and then reduced with hydrogen over a 5% Rd/Al_2O_3 catalyst to give the hydrogenated product in 87% yield. The infra-red spectrum of the reduced product showed the presence of a hydroxyl group and a saturated carbonyl group suggesting that the product obtained was a mixture of the

Figure 9: Independent synthesis of methoxy-decalones 61 and 62

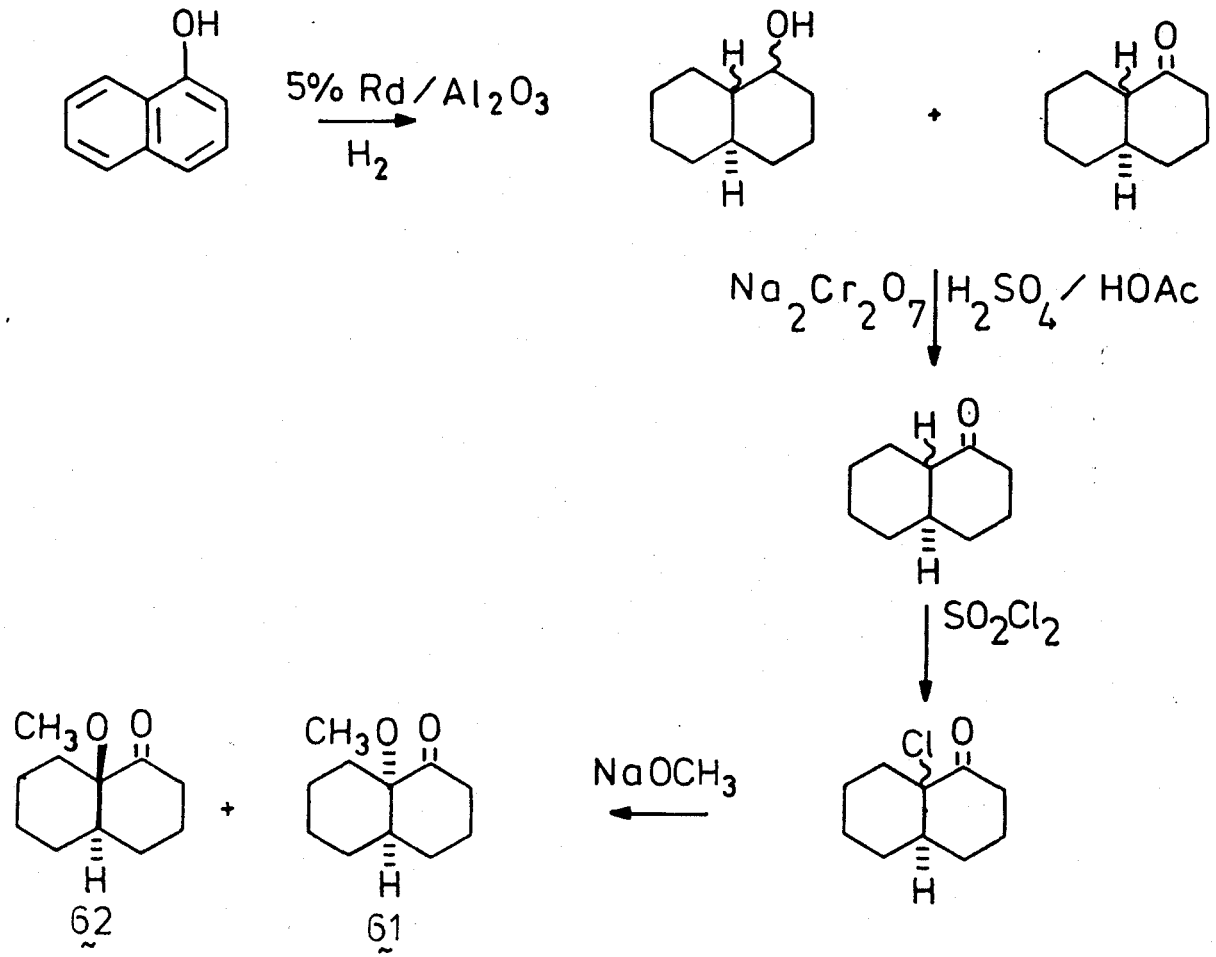


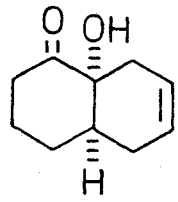
Table 11: Spectral data for methoxy-decalones 61 and 62

Cycloadduct	Independent Synthesis	
	trans	cis
^{1}H-NMR (ppm)	^{1}H-NMR (ppm)	
3.09 (s, 3H)	3.04 (s, 3H)	3.09 (s, 3H)
2.6-1.2 (m, 15H)	2.2-1.1 (m, 15H)	2.7-1.2 (m, 15H)
I.R. (cm^{-1})	I.R. (cm^{-1})	
1712	1712	1713
1083	1057	1084
Mass Spec.	Mass Spec.	
M^+ = 182 m/e	M^+ = 182 m/e	M^+ = 182 m/e

decalol(s) and decalone(s) shown in Figure 9. Oxidation of this mixture was accomplished using a modified Jones reagent and gave a 74% yield of cis decalone (30%) and trans decalone (60%). Sulfuryl chloride was used to introduce a chlorine atom at the position adjacent to the carbonyl group, a reaction proceeding in 79% yield. Finally, the chlorine was displaced by methoxide ion and gave in 64% yield a mixture of the cis decalone 61 (51%), and the trans decalone 62 (49%).

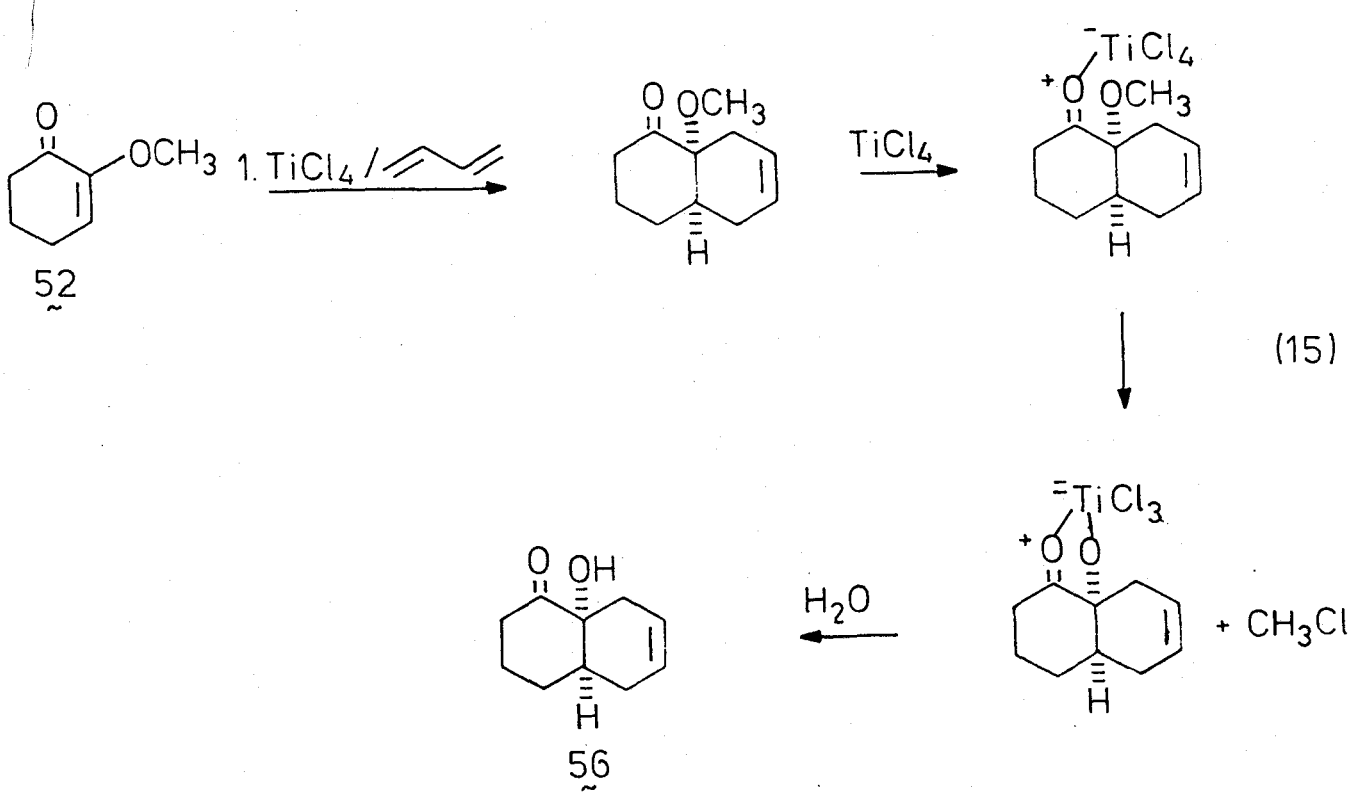
Table 11 shows the spectral data for these two compounds and the spectral data for the hydrogenation product of component 1 from the reaction of 52 with 1,3-butadiene. The very close similarity of these data shows conclusively that the reaction between 2-methoxy-cyclohex-2-en-1-one and 1,3-butadiene gave the cis [4C+2C] Diels-Alder product, 59, as one component.

The second component from the reaction of 52 with 1,3-butadiene showed a hydroxy band at 3490, a vinylic stretching vibration at 3030 and a saturated carbonyl band at 1715 cm^{-1} in the infra-red spectrum. The mass spectrum showed M^+ = 148 but with no significant peak at $M^+ - 18$ as expected for a compound containing an OH function. This suggested that the compound readily lost H_2O under the conditions used in obtaining the mass spectrum and that in fact the molecular weight of this compound is 166. The ^{1}H-NMR data is consistent with there being 2 vinyl hydrogens at 5.7, 1 hydroxyl hydrogen at 3.0 and 11 alkyl hydrogens between 2.8-1.5 ppm. These data are very similar to the data acquired for the compound derived from 1,2-cyclohexane-dione and butadiene, to which the structure 56 was assigned. The positions of the OH resonance in the ^{1}H-NMR spectra are different, however this could be due to differences in concentration of the samples.



56

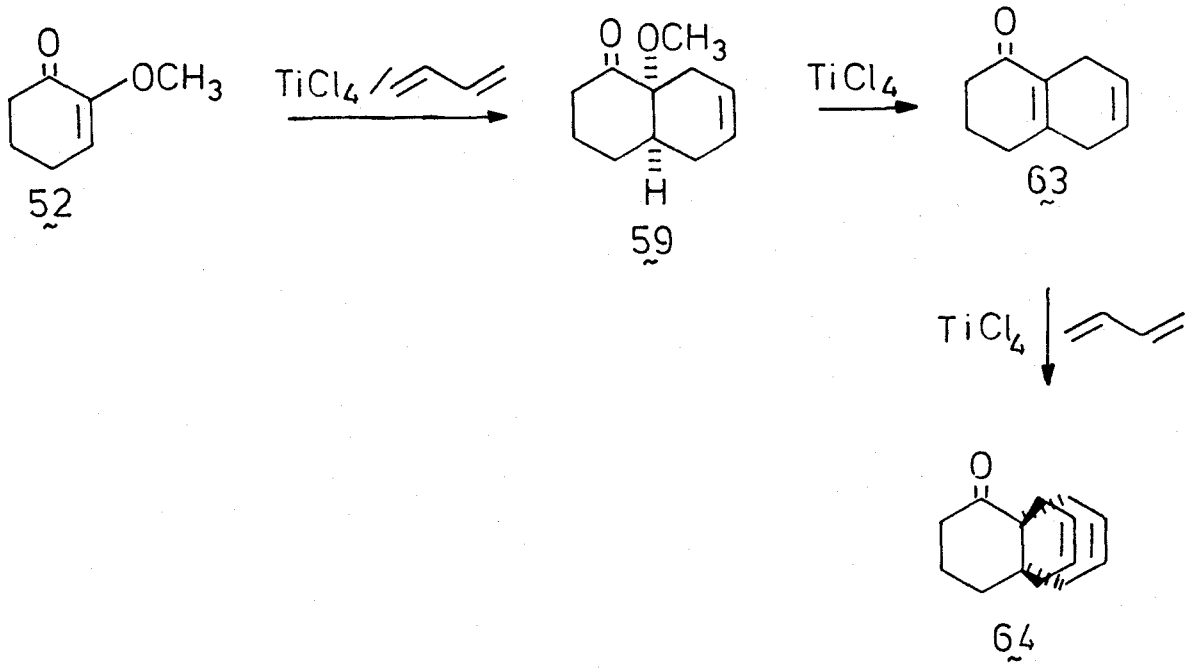
On closer examination of their spectral characteristics it was found that these two compounds gave indistinguishable I.R. spectra and that the mass spectra were very similar; the only difference being the M^+ peaks. It is clear then that these two compounds are identical. The most reasonable mechanism for the formation of 56 from 52 and butadiene, is shown in equation 15.



(15)

This $TiCl_4$ catalyzed displacement of the methyl group would not affect the stereochemistry at the α-position; consistent with the stereochemistry of the observed product 56.

The third component from the reaction of 52 with butadiene showed $M^+ = 202$ in the mass spectrum. The ^1H-NMR spectrum does not show any methoxy or OH signals and is consistent with there being only vinyl hydrogens and alkyl hydrogens in the ratio 3.5:1. A structure that is consistent with these limited data is shown below, 64. The $TiCl_4$ catalyzed elimination of CH_3OH from 59 would lead to structure 63 which when complexed by the Lewis acid should cycloadd to another molecule of butadiene.



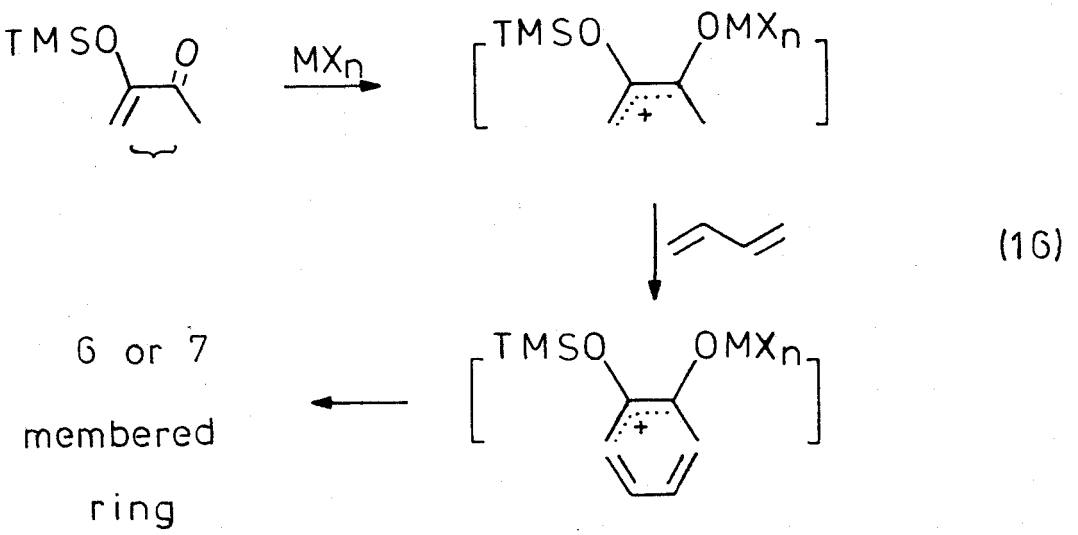
52 59 63 64

It seems then that the reaction between 52 and 1,3-butadiene gave only products derived from a [4C+2C] cycloaddition suggesting perhaps that cyclohexyl ring systems are not suited toward [4C+3C] cycloadditions.

3) 2,3-Butanedione-mono-trimethylsilyl enol ether

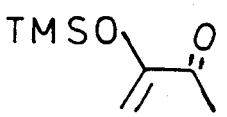
In recent years, silicon derivatives of aldehydes and ketones have been used to effect a large variety of transformations. Silyl enol ethers have offered tremendous potential as synthetic enol equivalents.[61] The Si-O bond in these enol ethers is weakened by the presence of the carbon-carbon double bond and this characteristic makes these compounds very reactive.

The synthesis of a mono-trimethylsilyl enol ether from a diketone could in principle serve as an effective route to substituted allyl cations. As shown in equation 16, the complex formed between such enol ethers and a Lewis acid may react with a conjugated diene to give seven-membered or six-membered ring adducts.



(16)

2,3-Butanedione-mono-trimethylsilyl enol ether 65, was prepared using a similar route to that described in the literature.[62] This compound was studied to determine its effectiveness as an allyl cation precursor.



65

1,3-Butadiene was reacted with 65 in the presence of $TiCl_4$ (-78°C). After 1 hour, the reaction mixture was neutralized and the crude mixture distilled in vacuo to give a product in moderate yield. The ^{1}H-NMR spectrum of the distilled material was quite complex suggesting that more than one compound was present. When analyzed by TLC, only one spot appeared and when recovered, the ^{1}H-NMR spectrum of this material suggested that only one compound had been eluted. Vapour phase chromatography (T > 90°C) allowed only one component to be isolated and the ^{1}H-NMR spectrum showed it to be the same component isolated by TLC. It was apparent that rearrangement was occurring under these conditions. Finally, the mixture was separated into two components by vapour phase chromatography when the temperature was kept at < 90°C.

The ease of interconversion of the one component into the other suggested that these two compounds were isomers. The spectral properties of these two compounds are recorded in Table 12. The infra-red spectrum showed in each case a hydroxyl group, a vinyl group and a saturated carbonyl group. The elemental analyses showed that these two compounds had the same empirical formula. The mass spectra however

Table 12: Spectral data for products from Diels-Alder reaction from 65 and 1,3-butadiene

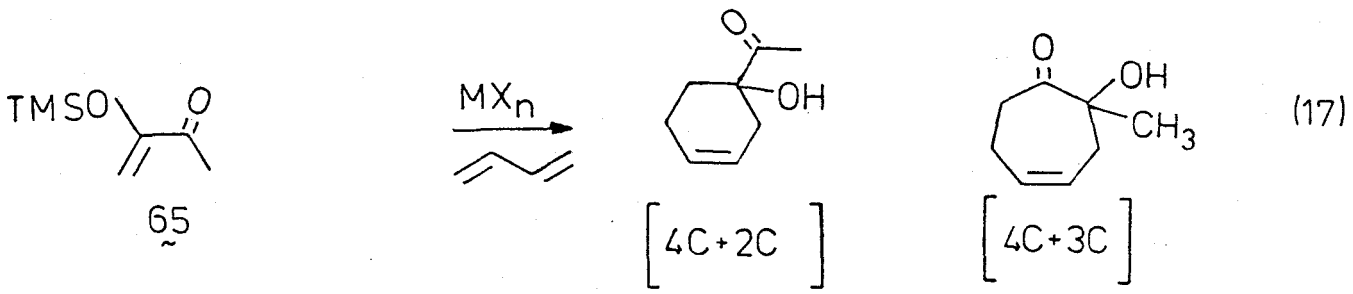
component 1	component 2
^{1}H-NMR (ppm)≠	^{1}H-NMR (ppm)
5.65 (m, 2H)	5.85 (m, 2H)
3.2 (s, 1H)	3.8 (s, 1H)
2.2 (s, 3H)	2.7-2.0 (m, 6H)
2.7-1.5 (m, 6H)	1.25 (s, 3H)
I.R. (cm^{-1})	I.R. (cm^{-1})
3480	3490
3035	3040
1710	1710
1090	1095
mass spec.	mass spec.
m^+ = 122 (140-18)m/e	m^+ = 140 m/e

≠ Solvent CCl_4, TMS reference

were different; the most noticeable difference was the $M^+ = 140$ for the one component and $M^+ = 122$ for the other component. In view of the above spectral data it appears that the one compound lost H_2O under the conditions used to obtain the mass spectrum.

It was concluded that these two compounds are isomers and that each corresponds to a 1:1 adduct formed between 65 and butadiene with subsequent loss of the TMS group. The TMS group is known to be easily removed by protic acid and in the workup procedure used for these reactions, HCl would be produced as the $TiCl_4$ was hydrolyzed.

The expected products resulting from a [4C+3C] and [4C+2C] cycloaddition of 65 with 1,3-butadiene are shown below, equation 17. The ^{1}H-NMR spectra of these cycloadducts could be used to distinguish one from the other. Both compounds would be expected to show a complex vinyl resonance, a complex alkyl region and a hydroxyl proton resonance. The uncoupled methyl signals would have quite different chemical shifts. The methyl group for the [4C+2C] adduct would be an acetyl-type function and as such would be expected to resonate at ~ 2.1 ppm. (Methyl group of acetone resonates at 2.09 ppm) The methyl group for the [4C+3C] adduct would be in a position β to the carbonyl group and β to the hydroxyl group. This group would be expected to resonate at ~1.4 ppm. (Methyl group of 3-hydroxy-2-butanone resonates at 1.36 ppm).



(17)

The ^{1}H-NMR spectra for the two components isolated from the reaction mixture are shown in Figures 10 and 11. The [4C+2C] reaction product in equation 17 is consistent with the spectrum shown in Figure 10. The methyl signal at 2.2 ppm is at the chemical shift predicted for an acetyl group and the vinyl signals at 5.65 ppm are quite complex because of the magnetic non-equivalence of the hydrogens to which they are coupled.

The [4C+3C] reaction product in Figure 10 is consistent with the spectrum shown in Figure 11. The methyl signal appears at 1.25 ppm and the vinyl region is again quite complex because of the magnetic non-equivalence of the hydrogens to which they are coupled.

Tentatively, it appears that 2,3-butanedione-mono-trimethylsilyl enol ether can be used in conjunction with $TiCl_4$ to produce a seven-membered ring when reacted with 1,3-butadiene. At present, the yield is very low, but the starting materials are readily available and the reaction time is quite short. This successful preparation of the [4C+3C] cycloadduct could lead to a general synthesis of seven-membered rings by varying the dione and the conjugated diene.

As this thesis was being written, a paper by T.Sasaki and workers entitled, " Catalyzed cycloaddition reactions of α-silyloxy-α,β-unsaturated ketone and aldehyde " appeared.[63] In this paper the $SnCl_4$ catalyzed cycloaddition of $\underset{\sim}{65}$ with 1,3-butadiene is described. They report the isolation of the six-membered ring adduct using these reageants but do not report the isolation of any seven-membered ring. The ^{1}H-NMR data reported for the six-membered ring are similar to those recorded in Table 12; the only difference being in the position of the hydroxy signal. It is not clear whether Sasaki and workers overlooked the presence of the 7-membered ring or whether

Figure 10: ^{1}H-NMR spectrum of [4C + 2C] reaction product from 65 and 1,3-butadiene

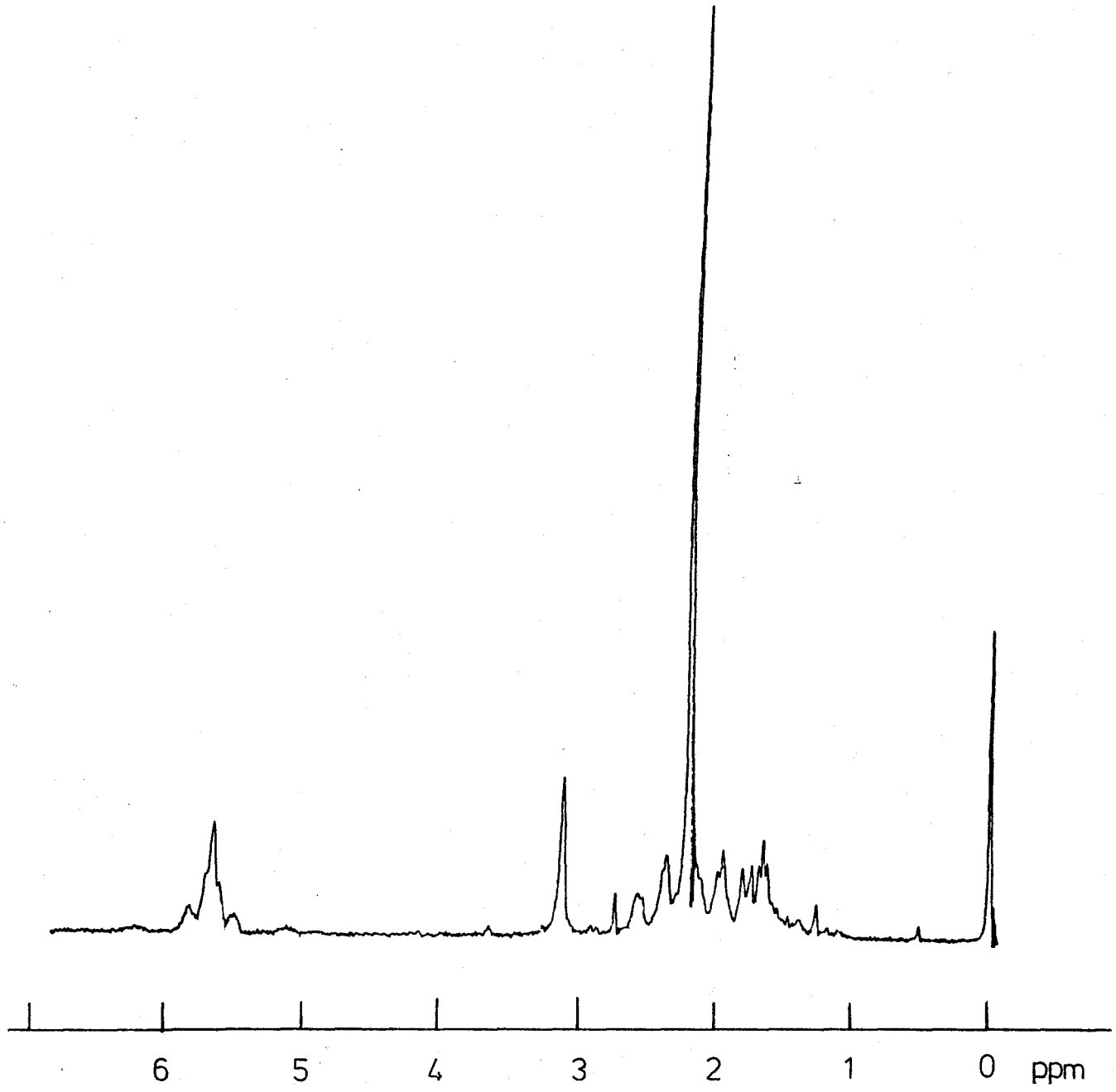
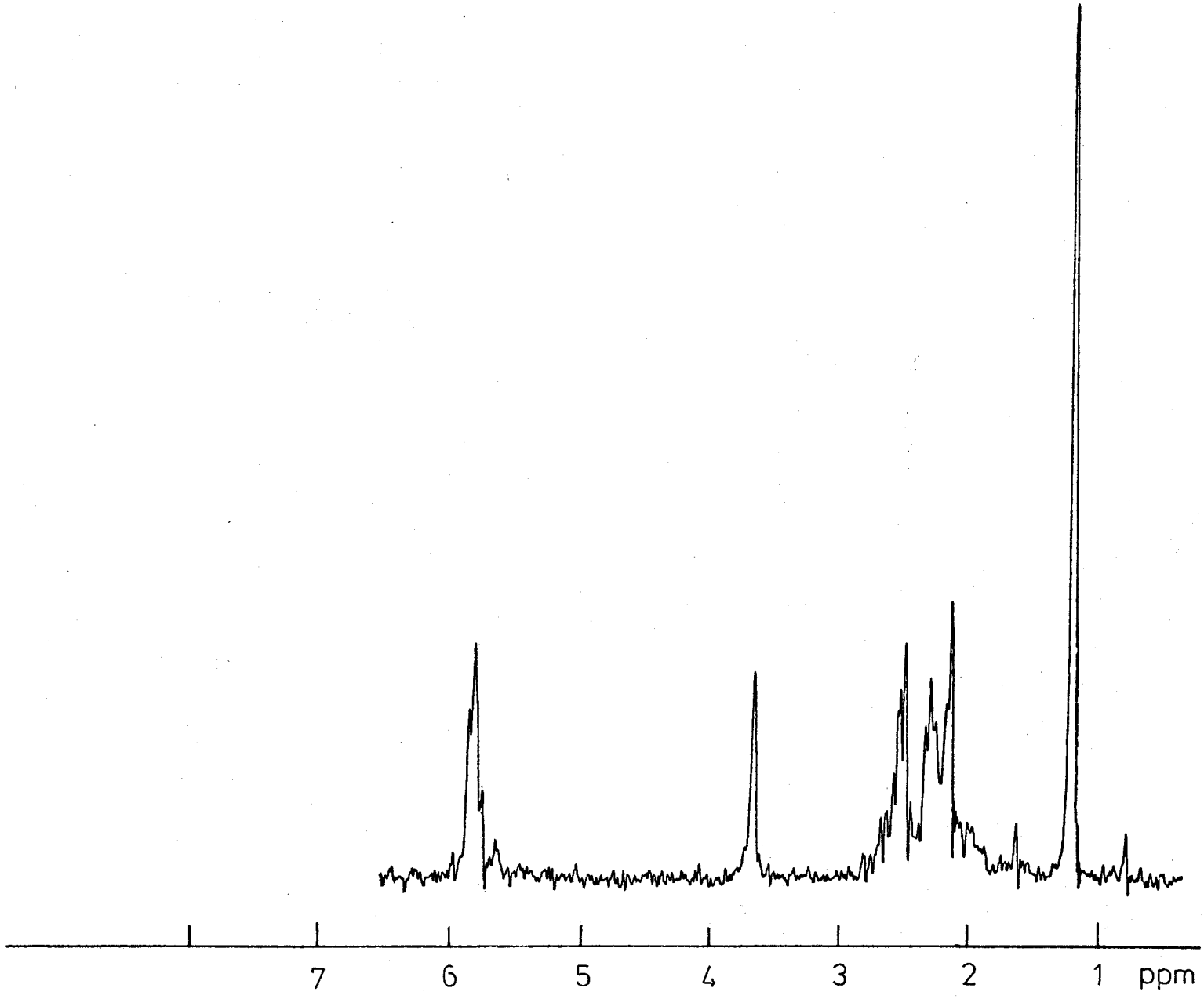


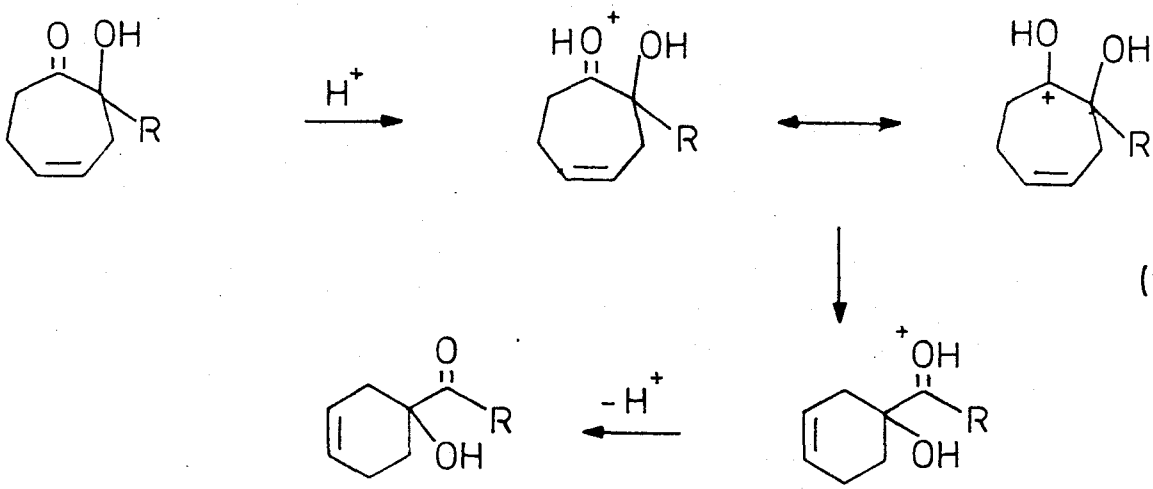
Figure 11: ^{1}H-NMR spectrum of [4C + 3C] reaction product from 65 and 1,3-butadiene



the 7-membered ring was formed initially but isomerized during the workup procedure. Their crude mixture was treated with MeOH/HCl and final purification was accomplished by passing the mixture through a silica gel column. In view of the rearrangement difficulties experienced by this author, it is quite possible that the 7-membered ring was formed but isomerized under the workup conditions used by Sasaki.

By changing the TMS-enol ether to pyruvaldehyde-2-TMS-enol ether, a seven-membered ring was isolated by Sasaki when butadiene was used as the conjugated diene. Figure 12 compares the results obtained by T. Sasaki with those obtained by this author.

Equation 18 shows a possible mechanism for the rearrangement of the isolated 7-membered ring from these reactions. The work by this author showed that when R= CH_3, rearrangement is facile. It may be however that when R =H, the migration of the ring does not occur easily and rearrangement is much less facile; thus allowing the seven-membered ring to be isolated under acidic workup conditions. Regardless of the exact mechanism, it is apparent that reaction and workup conditions are important to the isolation of the 7-membered ring.



(18)

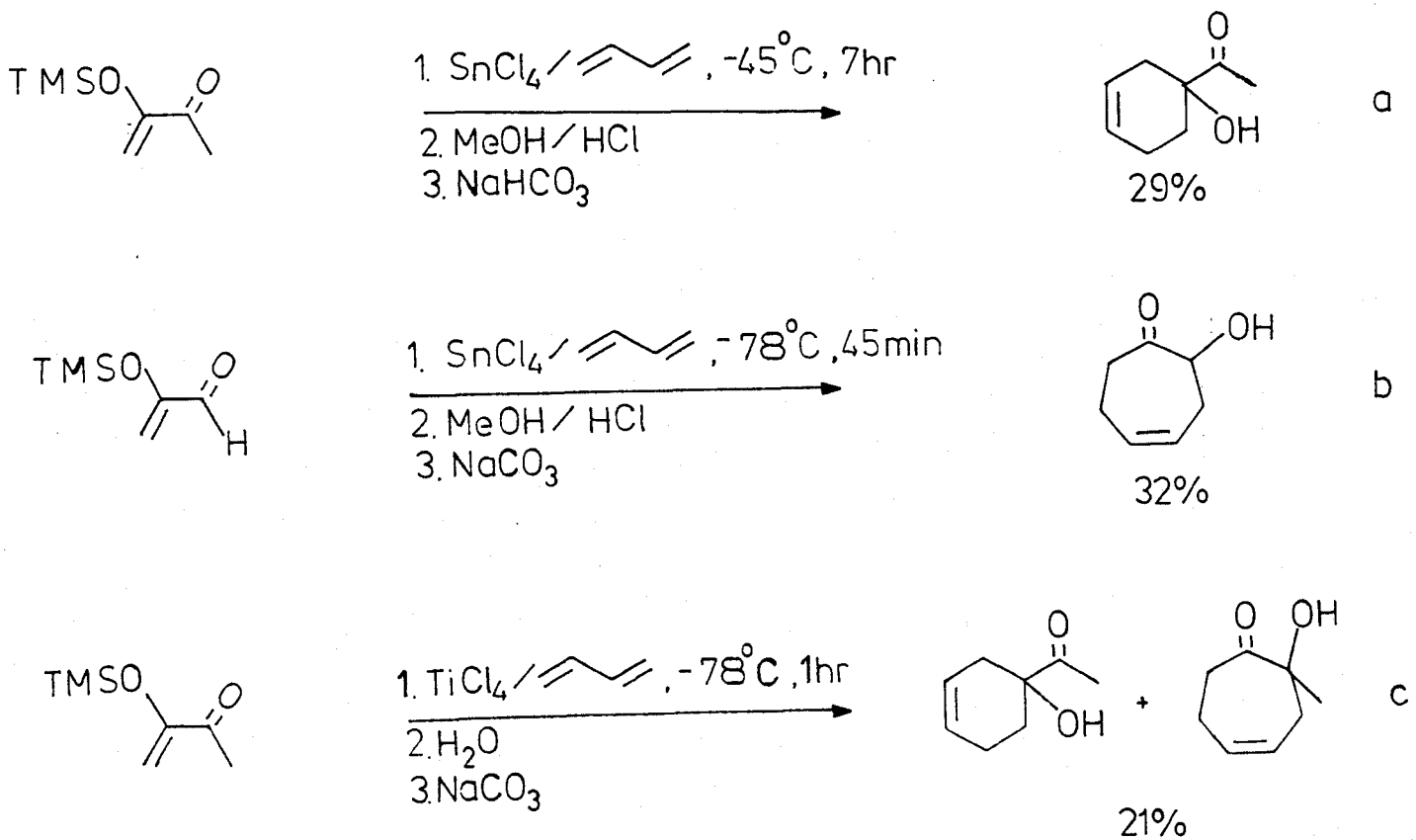


Figure 12: Sasaki's experiments (a, b) compared to the author's experiment (c)

It is not clear why the cyclic systems 51 and 52 did not undergo the expected three-centre cycloaddition. The cyclohexane systems were chosen because they represented systems of known conformation. It is possible however that the rigid nature of the ring prevents addition across the centres C_1 and C_3 or if such addition does occur, the system may be too strained and rearrangement to the bicyclo[4.4.0.] system the preferred route. Alternatively, the type of enol ether that is used (TMS vs. OR) may be important.

Two experiments need to be done to determine whether it is the TMS function that is important to the [4C+3C] cycloaddition or whether it is the flexibility of the acyclic precursor that is critical. The same cycloaddition reaction should be carried out using the TMS derivative of 1,2-cyclohexanedione, 66, and the methyl ether derivative of 2,3-butanedione, 67, as the allyl cation precursors. The results from these experiments could answer this question.

Overall it is clear that the use of compounds such as 65 in the presence of a Lewis acid provides a route to seven-membered rings. Much more work needs to be done to determine the generality, mechanism and best conditions of this reaction. It is clear however that this type of reaction offers a new method of preparing 7-membered rings.

CHAPTER 3

CONCLUSIONS

The initial aim of this work was to investigate a new general synthetic route to seven-membered rings via Lewis acid catalyzed [4C+3C] cycloadditions. It was proposed that NMR spectroscopy could be used to determine whether the complexes formed between α-alkoxy-α,β-unsaturated ketones and Lewis acids would serve as suitable precursors to substituted allyl cations.

The ^{1}H-NMR and ^{13}C-NMR results suggested that there was a delocalization of charge at C_1 and C_3 of 1,2-cyclohexanedione and 2-methoxy-cyclohex-2-en-1-one when complexed with $TiCl_4$ and $SnCl_4$. This delocalization was proposed to be the necessary requirement for the subsequent [4C+3C] cycloaddition. There was no indication however that a [4C+3C] cycloaddition product had formed from either of these starting materials; rather, only [4C+2C] adducts could be isolated. It may be that the formation of the seven-membered rings from 51, 52 and butadiene is thermodynamically less favourable then the six-membered rings because of the cyclic-nature of the precursors.

The formation of the [4C+3C] product in the reaction of 2,3-butanedione-mono-trimethylsilyl enol ether with butadiene is very encouraging. The ease with which the TMS derivative can be prepared and the short reaction time make this route to seven-membered carboycles an appealing one. More work is needed to improve the overall yield of this reaction and to discover the conditions that will favour the specific formation of the [4C+3C] adduct.

At this point, no work has been done to establish a viable mechanism for any of these reactions. Whether the reactions are best described by a concerted cycloaddition or a stepwise ionic mechanism is not known. Such information would be useful in deciding whether the TMS function is critical to the [4C+3C] reaction or

whether it is the flexibility of an acyclic system that is important.

The work described in this thesis has concentrated on the formation of seven-membered rings using a reactive three-carbon intermediate. In principle, this same allyl cation type of intermediate could be used to form five-membered rings if the conjugated diene was replaced by a simple alkene. Such [2C+3C] reactions are important for the synthesis of the cyclopentane systems found in many natural products. The possible extension of this [4C+3C] reaction of an α-siloxy-α,β-unsaturated ketone to the [2C+3C] analogue would be very useful.

CHAPTER 4

EXPERIMENTAL

Instrumental

Routine proton magnetic resonance spectra were recorded on a Varian EM 390 spectrometer. The chemical shifts are reported in ppm downfield from tetramethyl silane.

The proton spectra recorded for the complexation experiments and all ^{13}C magnetic resonance spectra were determined using a Bruker WP-80 Fourier-Transform spectrometer equipped with a variable temperature probe. The chemical shifts were recorded relative to the solvent signal ($CDCl_3$: ^{13}C- 77.0 ppm, ^{1}H- 7.25 ppm or CD_2Cl_2: ^{1}H- 5.33 ppm) but are reported in ppm downfield from tetramethylsilane.

Infra-red spectra were recorded on a Perkin-Elmer Model 283 spectrophotometer using NaCl discs or NaCl solution cells. The spectrophotometer was calibrated using the 1601.4 band of a polystyrene film and all absorption bands are reported in cm^{-1} units.

Vapour phase chromatography was performed on a Varian Aerograph A90-P3 (preparative) gas chromatograph and a Varian 3700 (analytical) gas chromatograph equipped with a Varian CDS 111 integrator unit.

The columns used for preparative separations were:

1) Column A: 5% OV-17 on Chromosorb W, 60-80 mesh, 6' x 1/4" stainless steel

2) Column B: 15% Carbowax on Chromosorb A, 20 mesh, 10' x 1/4" stainless steel

The columns used for analytical analyses were:

1) Column C: 5% OV-17 on Chromosorb W, 60-80 mesh, 7' x 1/8" stainless steel

2) Column D: 5% SE-30 on Chromosorb W, 60-80 mesh, 7' x 1/8" stainless steel

Mass-spectral data were recorded on a V.G. Micromass 7070F mass spectrometer at a source temperature of 200°C and ionization potential of 70 e.v.

Materials

Solvents

Deuterated methylene chloride and deuterated chloroform, used for preparation of the complexes, were dried over molecular sieves before use. Acetonitrile and methylene chloride were distilled and stored over molecular sieves.

Lewis Acids

$TiCl_4$ and $SnCl_4$ were distilled and stored in glass ampules.

2,3-Butanedione

Purchased from Fischer Scientic Chemical Co. and distilled before use.

^{1}H-NMR, $CHCl_3$: 2.29 ppm (s, 6H)

1,2-Cyclohexanedione

Purchased from Aldrich Chemical Co. and used as received.

^{1}H-NMR, $CHCl_3$: 6.25 ppm (t, 1H), 6.10 ppm (s, 1H), 2.65-2.25 ppm (m, 4H), 2.15-1.8 ppm (m, 2H)

1-Naphthol

5g samples of 1-naphthol were sublimed using a cold finger condenser under vacuum (4mm Hg). Heating to 120°C produced pale orange crystals.

^{1}H-NMR, CCl_4: 8.2-6.3 ppm (m, 7H), 5.0 ppm (s, 1H)

1,3-Butadiene

Instrument grade (99.5%) butadiene was purchased from Linde and was used directly.

Reactions and Syntheses

Complexations

The samples that were complexed with Lewis acids for NMR studies were weighed into an NMR tube and then dissolved in the solvent. A serum cap was used to seal the tube. The desired volume of Lewis acid was then injected into the NMR tube using a 10-microlitre syringe purchased from Scientific Glass Engineering Pty. Ltd. All samples were prepared under a nitrogen atmosphere.

Neutralizations

The work-up of reactions involving Lewis acids was done in the following manner. The reaction mixture was poured into a 1:1 ether-water mixture and solid $NaHCO_3$ was added until the evolution of CO_2 was complete. The solid precipitates were filtered and the filtrate was extracted with ether, dried over $MgSO_4$ and concentrated.

2-Methoxy-cyclohex-2-en-1-one, 52

Cyclohexanedione (1.1g) was dissolved in a NaOH solution (0.4g in 4 mls H_2O). The solution was vigorously stirred and 1 ml dimethyl sulphate was added dropwise over 1 hour while vessel was cooled with ice. Mixture was refluxed for 1 hour to complete methylation and hydrolyse excess dimethyl sulphate. Mixture was extracted with ether, concentrated and dried over $MgSO_4$. Crude mixture was distilled to give 1.05g (85%) of 52. Gas chromatographic analysis using Column C showed 98% purity.

^{1}H-NMR, CCl_4: 5.89 ppm (t, 1H), 3.64 ppm (s, 3H), 2.59-1.88 ppm (m, 6H)

I.R.: 3015 cm^{-1}(CH=CH), 1686 cm^{-1}(C=O)

1,2-Cyclohexanedione reaction with 1,3-butadiene

1,2-Cyclohexanedione (1.6g) was dissolved in dry acetonitrile (1ml) inside a Carius tube previously flushed with Argon and cooled to -78°C. $TiCl_4$ (1.8 mls) was added and the solution warmed and diluted with dry acetonitrile (6mls) then recooled to -78°C. Butadiene (4mls) was condensed into the solution and the tube sealed under argon. The mixture was warmed to room temperature and mechanically stirred for 14 hours. The mixture was neutralized and distilled to give 0.78g (35%) of the cyclo-addition product. Gas chromatographic analysis using Column C showed 95% purity.

^{1}H-NMR, CCl_4: 5.7 ppm (m, 2H), 3.8 ppm (s, 1H), 2.7-1.5 ppm (m, 11H)

I.R.: 3490 cm^{-1} (broad, OH), 3030 cm^{-1} (CH=CH), 1715 cm^{-1} (C=O)

Mass spec.: M^+= 166m/e

Anal. calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.24; H, 8.55.

2-Methoxy-cyclohex-2-en-1-one reaction with 1,3-butadiene

The same procedure used as for reaction of 1,2-cyclohexanedione. Distillation of the reaction mixture gave 38% yield of the cycloadducts. Gas chromatographic analysis using Column C showed three components. Separation of these components was done using vapour phase chromatography on Column B.

Component 1(58%):

^{1}H-NMR, CCl_4: 5.8 ppm (m, 2H), 3.4 ppm (s, 3H), 2.6-1.6 ppm (m, 1H)

Mass spec: M^+= 180 m/e

Component 2(12%):

^{1}H-NMR, CCl_4: 5.7 ppm (m, 2H), 3.0 ppm (s, 1H), 2.8-1.5 ppm (m, 11H)

I.R.: 3490 cm^{-1} (broad, OH), 3030 cm^{-1} (CH=CH), 1712 cm^{-1} (C=O)

Mass spec.: M^+= 148 (166-18)m/e

Component 3(12%):

^{1}H-NMR, CCl_4: 5.3-6.0 ppm (m, 4H), 1.5-2.8 ppm (m, 14H)

I.R.: 3025 cm^{-1} (CH=CH), 1710 cm^{-1} (C=O)

Mass spec.: M^+= 202m/e

Anal. calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.97. Found: C, 83.26; H, 9.03

Hydrogenation of cis-1-hydroxy-bicyclo[4.4.0.]deca-8-en-2-one, 56

The hydroxy-ketone 56, (44mg), was dissolved in ethanol (1.1mls) and hydrogenated on low pressure apparatus over Pd/C catalyst (4.3mg) at room temperature. The reaction was complete after 18 hours. Reaction mixture was concentrated and distilled to give 37mg (83%) of the hydrogenated product .

^{1}H-NMR, CCl_4: 3.6 ppm (s, 1H), 2.4 ppm (m, 2H), 2.0-0.9 ppm (m, 13H)

I.R.: 3490 cm^{-1} (broad, OH), 1710 cm^{-1} (C=O)

m.p. 56-60^{o}C

1-Naphthol hydrogenation

2.0g of purified 1-naphthol was dissolved in glacial acetic acid and hydrogenated at 40 psi over 1.0g of 5% rhodium on alumina. Hydrogenation was complete after 48 hours. Glacial acetic acid was evaporated and the crude material was distilled (4mm,100^{o}C) to give 1.84 g (87%) of the hydrogenated material. Gas chromatographic analysis using Column D showed 97% purity.

^{1}H-NMR, CCl_4: 3.7 ppm (m, 1H), 2.0-1.0 ppm (m, 17H)

I.R.: 3640 cm^{-1} (sharp, OH), 3500 cm^{-1} (broad, OH), 1715 cm^{-1} (C=O)

Oxidation of 1-decalol/1-decalone mixture

A modified Jones reagent was used to oxidize the mixture obtained from the hydrogenation of 1-naphthol.

Sodium dichromate (59mg) was dissolved in water (1.1mls) and mixed with H_2SO_4 (0.36 mls) and HOAc (0.2 mls). The solution was cooled to room temperature and added dropwise over several hours to a solution of 300 mg of the decalol/decalone mixture in 1.7 mls benzene. The mixture was stirred for 36 hours. The benzene layer was washed with sodium bicarbonate solution and dried with magnesium sulphate. Solvent was removed and the organic residue was distilled to give 219 mg (74%) of the oxidation product. Gas chromatographic analysis using Column D showed the cis (30%) and trans (66%) isomers.

^{1}H-NMR, CCl_4: 2.4-1.0 ppm (m, 15H)

I.R.: 1710 cm^{-1} (C=O)

Chlorination of 1-decalone

cis/trans 1-decalone mixture (0.098g) was dissolved in CCl_4 (0.5mls) and a solution of sulfuryl chloride (0.058mls) in CCl_4 (0.25 mls) was added dropwise and stirred for several hours. Reaction mixture was washed with $NaHCO_3$ solution, NaCl solution and dried with $MgSO_4$. The crude mixture was concentrated and distilled to give 95 mg (79%) of 9-chloro-1-decalone.

^{1}H-NMR, CCl_4: 3.1-1.0 ppm (m, 15H)

I.R.: 1725 cm^{-1} (C=O)

Reaction of 9-chloro-1-decalone with Sodium Methoxide

9-chloro-1-decalone mixture (10 mg) was reacted with a solution of sodium (20 mg) in methanol (0.5 mls). The mixture was allowed to stir for 10 hours and then diluted

with H_2O and extracted with ether. Organic residue was dried over $MgSO_4$, concentrated and distilled to give 6.2 mg (64%) mixture of cis/trans methoxy ketones 61 and 62. Gas chromatographic analysis using Column D showed 51% cis isomer, and 49% trans isomer. Separation was done using vapour phase chromatography on Column A.

Trans isomer:

^{1}H-NMR, CCl_4: 3.04 ppm (s, 3H), 2.2-1.1 ppm (m, 15H)

I.R.: 1712 cm^{-1} (C=O), 1057 cm^{-1} (C-O)

Mass spec.: M^+= 182 m/e

Cis isomer:

^{1}H-NMR, CCl_4: 3.09 ppm (s, 3H), 2.7-1.2 ppm (m, 15H)

I.R.: 1713 cm^{-1} (C=O), 1084 cm^{-1} (C-O)

Mass spec.: M^+= 182 m/e

2,3-Butanedione-mono-trimethylsilyl enol ether

To a mixture of biacetyl (0.5 mol) and trimethylsilyl chloride (0.5 mol) in pentane (200 ml) was added triethylamine (0.5 mol) at 0°C over a period of 1 hour. The mixture was stirred under a nitrogen atmosphere for 6 hours. The amine hydrochloride salt was removed by filtration through a bed of celite. The crude mixture was used directly in subsequent reactions. The spectral data was in agreement with the literature.[62]

^{1}H-NMR, CCl_4 0.2 ppm (s, 9H), 2.25 ppm (s, 3H), 4.8 ppm (s, 1H), 5.3 ppm (s, 1H)

I.R.: 1730 cm^{-1} (C=O), 1640 cm^{-1} (C=C)

2,3-Butanedione-mono-trimethylsilyl enol ether reaction with 1,3-butadiene

2,3-Butanedione-mono-trimethylsilyl enol ether (2.0g) was dissolved in dry CH_2Cl_2 and the mixture cooled to -78°C under a nitrogen atmosphere. An excess of

butadiene was bubbled into the mixture and $TiCl_4$ (1.4mls) was injected by a syringe into the reaction mixture. The mixture was stirred vigorously for 1 hour followed by neutralization. The crude material was distilled (4mm, 70°C) to remove the two most volatile components, 0.37g (21%). These were separated by vapour phase chromatography.(Column A: injector temp. 75°C, column temp. 75°C, detector/collector temp. 75°C)

First component:

^{1}H-NMR, CCl_4: 5.65 ppm (m, 2H), 3.2 ppm (s, 1H), 2.2 ppm (s, 3H), 2.7-1.5 ppm (m, 6H)

I.R.: 3480 cm^{-1} (broad, OH), 3035 cm^{-1} (CH_2=CH_2), 1710 cm^{-1} (C=O), 1090 cm^{-1} (C-O)

Mass spec.: M^+= 122 (140-18)m/e

Anal. calcd for $C_8H_{12}O_2$: C, 68.55; H, 8.63. Found: C, 68.63; H, 8.66.

Second component:

^{1}H-NMR, CCl_4: 5.85 ppm (m, 2H), 3.8 ppm (s, 1H) 2.0 ppm (m, 6H), 1.25 ppm (s, 3H)

Mass spec.: M^+= 140 m/e

Anal. calcd for $C_8H_{12}O_2$: C, 68.55; H, 8.63. Found: C, 68.56; H, 8.60.

A third component could be recovered during the distillation at higher temperatures (4mm, 90°C).

^{1}H-NMR, CCl_4: 2.4-2.1 ppm (m), 1.5-1.3 ppm (m), 0.3-0.1 ppm (m)

CHAPTER 5

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