Reaction of iridium with cyclopropanes contained in rigid ring systems
by William Henry Campbell Jr

A thesis submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Chemistry
Montana State University

Abstract:
The reaction of IrCl(CO)(Ph3P)2 (Vaska's catalyst) with cyclopropane moieties contained within rigid ring systems was investigated. A variety of substrates were investigated, and several were labeled with deuterium. The results show that exocyclic methylene products predominate in most cases, but a diversity of other products was also obtained. Analysis of products demonstrates a great deal of regioselectivity of reaction. Further, mechanistic pathways leading to products are varied and highly dependent on the electronic and steric environment provided by the substrate. Endo-cyclopropane compounds seem to be more reactive (when chloroform is used as the reaction solvent) than their exo-counterparts. Catalytic reaction is enhanced in the presence of oxygen and when chloroform is used as the reaction solvent, but regioselectivity of reaction is somewhat decreased. Olefin products and substrates are capable of reaction with Vaska's catalyst and have been shown to establish a dynamic equilibrium in some cases.

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APPROVAL

of a thesis submitted by

William Henry Campbell Jr.

This thesis has been read by each member of the thesis committee and has been found to be satisfactory regarding content, English usage, format, citations, bibliographic style, and consistency, and is ready for submission to the College of Graduate Studies.

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Date April 1, 1983

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ABSTRACT

The reaction of $IrCl(CO)(Ph_3P)_2$ (Vaska's catalyst) with cyclopropane moieties contained within rigid ring systems was investigated. A variety of substrates were investigated, and several were labeled with deuterium. The results show that exocyclic methylene products predominate in most cases, but a diversity of other products was also obtained. Analysis of products demonstrates a great deal of regioselectivity of reaction. Further, mechanistic pathways leading to products are varied and highly dependent on the electronic and steric environment provided by the substrate. Endo-cyclopropane compounds seem to be more reactive (when chloroform is used as the reaction solvent) than their exo-counterparts. Catalytic reaction is enhanced in the presence of oxygen and when chloroform is used as the reaction solvent, but regioselectivity of reaction is somewhat decreased. Olefin products and substrates are capable of reaction with Vaska's catalyst and have been shown to establish a dynamic equilibrium in some cases.

INTRODUCTION

The field of organometallics is a rapidly growing area of chemistry. Much theoretically and synthetically useful knowledge has come about by the extensive research in organometallics. However, the mechanistic transformations that occur upon reaction of transition metal complexes with organic molecules, as well as electronic effects, steriochemistry, regioselectivity, synthetic applications and more are still at a relatively young age of understanding. One area of organometallics that has created considerable interest is the reaction of cyclopropane containing compounds with transition metals. These reactions range from stoichiometric reactions, yielding isolatable organometallic complexes to catalytic processes. A variety of metal complexes have been isolated or implicated as intermediates in the reactions of cyclopropanes with low valent transition metals. The list includes metallocyclobutanes (1), π-allyl-metal hydrides (2), olefin-metallocarbenes (3) and others (Figure 1). As isolated products, any of these may have potential use for synthetic transformations, and all have been postulated as prominent intermediates in catalytic processes.

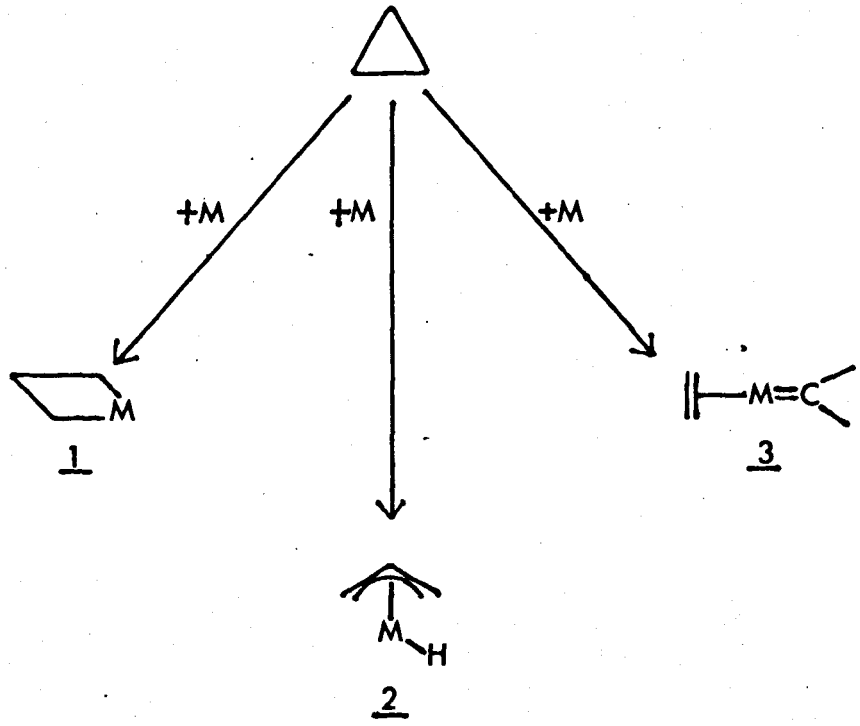


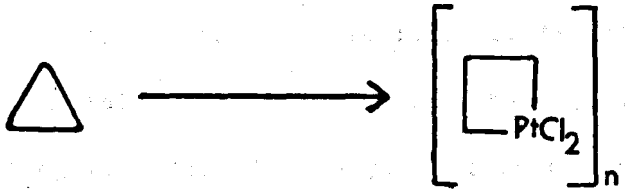
Figure 1. Postulated Intermediates and Isolated Product types from the Reaction of Cyclopropanes with Transition Metal Complexes.

The emphasis of this thesis is on the reaction of $IrCl(CO)(Ph_3P)_2$ (Vaska's catalyst) with cyclopropanes contained within rigid ring systems. The reactions studied involved catalytic isomerization of cyclopropanes to olefins and other cyclopropane products. As will be discussed shortly, Vaska's catalyst is somewhat novel with respect to its reaction with cyclopropane containing substrates, but the reactions of iridium have not been as extensively studied with the same detail as the reactions of other transition metal complexes. The intent of this research was to explore the reactions of Vaska's catalyst with a variety of substrates, which in some cases have been labeled with deuterium. Neither kinetic analysis nor charactarization of iridium intermediates was achieved, but consistent mechanistic schemes will be proposed by considering both literature and the data obtained in this research. The proposed mechanistic schemes and the results obtained are intended to provide insight for further investigation.

Before a discussion of the results of this research is presented, an overview of literature dealing with the reactions of cyclopropanes with transition metals will be given. This overview will include a discussion of relative bonding interactions, intermediates of possible importance in catalytic reactions and work that has direct relevance to this investigation. The majority of available references on the reactions of cyclopropanes with transition metals deal with platinum complexes. Platinum complexes do not give facile catalytic reactions with cyclopropanes, but do

give good stoichiometric reactions to yield stable organometallic complexes. Proper treatment of these cyclopropane derived platinum complexes give organic products that are analogous or identical to products obtained from catalytic processes. It therefore seems reasonable that similar structures are produced as intermediates in catalytic processes.

In 1955 the first organometallic complex derived from the reaction of a transition metal with cyclopropane was reported.[1] In this article, Tipper reported on the reaction of cyclopropane with hexachloroplatinic (IV) acid to give, what was later shown by Chatt[2] to be, platinacyclobutane 1 (equation 1).

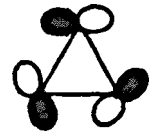


(1)

1

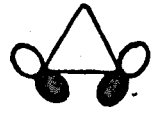
Before the structure of 1 was elucidated, it was postulated that cyclopropane-metal bonding was similar to olefin-metal bonding.[1] Analogous bonding interactions may still be of importance in transition states leading to metallocyclobutanes. In the Dewer-Chatt[3,4] model for metal-olefin bonding the π-HOMO of the olefin donates electron density into an unfilled d-orbital of the metal to form a σ bond, further bonding, called backbonding can arise through donation of electron density from a filled d-orbital of the metal to the π-LUMO of the olefin. Backbonding interactions generate olefin-

metal π-bonds. Analogous bonding for cyclopropanes is achieved with the σ-HOMO's (4 and 5) and σ* (6) of the cyclopropanes (Figure 2). These orbitals, according to the Walsh model[5], have a considerable amount of π character. Interaction of 4 with an unfilled d-orbital (7) and interaction of 6 with a filled d-orbital (8) are also illustrated in Figure 2. The interacton illustrated as structure 7 is considered more important for bonding in transition states leading to metal insertion into a cyclopropane, but does not describe the bonding in metallocyclobutanes.[6,7] Since the σ* orbital (6) is relatively inaccessible for backbonding, backbonding is deemed less important for initial bonding interactions. The bonding illustrated as structure 8, however, is more indicative of the bonding in metallocyclobutanes. Thus, the transition state interactions leading to formation of metallocyclobutanes should be most facile when electron donating substituents are present on the cyclopropane ring. McQuillin,[8,9] using cyclopropane substrates with para substituted phenyl substituents has shown that insertion of platinum into cyclopropane rings was more facile when the para substituents were electron donating. In some cases, strongly electron withdrawing substituents completely inhibited reaction. Electron donor ability of the cyclopropane is considered more important for primary interactions in or leading to the transition state, but backbonding from the metal to the cyclopropane σ* orbital is a prerequisite for metallocyclopropane formation. Insertion of the metal into a cyclopropane bond is an example of oxidative addition to



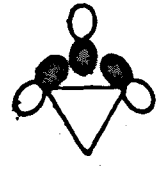
σ^*_{c-c}

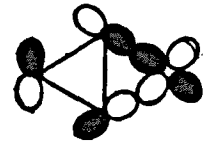
6



σ_{c-c} HOMO

4 5





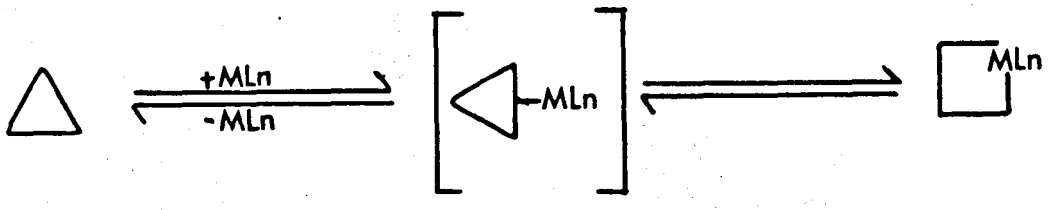
7 8

Olefin—Metal σ bond

Olefin—Metal π Bond Metal Backbonding

Figure 2. Molecular Orbitals for Cyclopropane and Cyclopropane-Metal Bonding.

the metal. Oxidative addition in these reactions results in a two electron oxidation of the metal.[10] The overall sequence is shown in equation 2.



(2)

9 10

Structures such as 7 and 9 are termed edge complexes and have been implicated as intermediates. Volger [11,12] reported that exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (11) and exo, exo-tetracyclo[3.3.1.$0^{2,4}0^{6,8}$]nonane (12) gave catalytic reaction upon treatment with Vaska's catalyst and other transition metal complexes, however endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (13), exo, endo-tetracyclo[3.3.1.$0^{2,4}0^{6,8}$]nonane (14) and 6-methylene-tricyclo[3.2.1.$0^{2,4}$]octane (15) were unreactive with the same metal complexes. From these results Volger suggested that endo-bidentate edge complexes such as 16 and 17 were required intermediates for reaction (Figure 3). Subsequent work with Vaska's catalyst has show facile reaction to occur with 13 and other substrates that are incapable of achieving an endo-bidentate configuration.[13] Waddington and Jennings[14,15] have further elucidated the structures of platina cyclobutanes 18, 19 and 20 (Figure 4) which are not necessarily obtained from endo-bidentate edge complexes. Several other examples

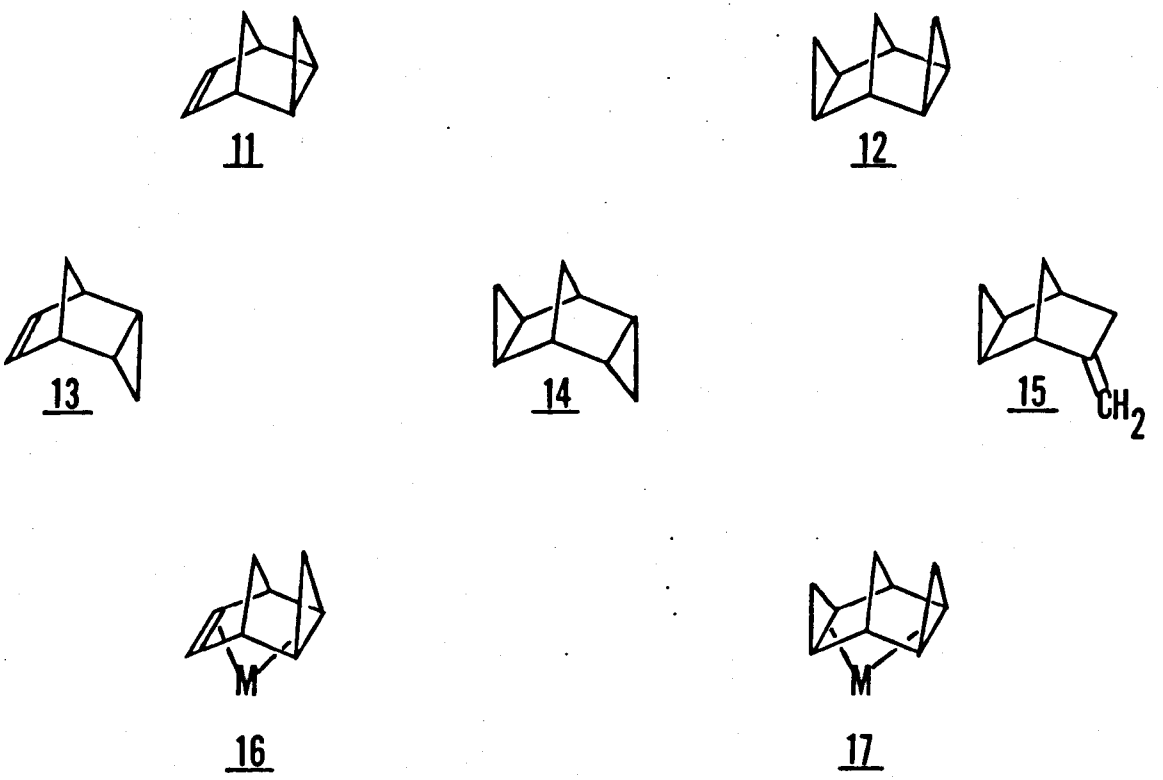
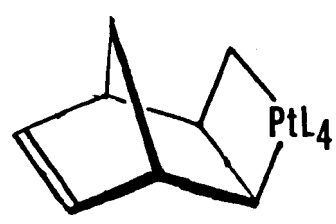


Figure 3. Substrates and Suggested Intermediates Investigated by Volger.



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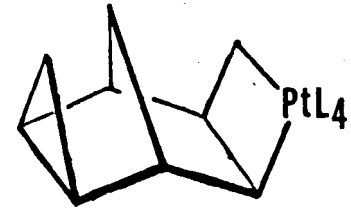

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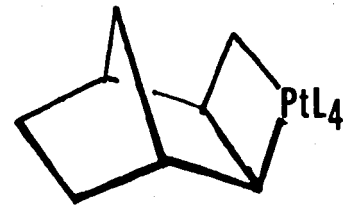
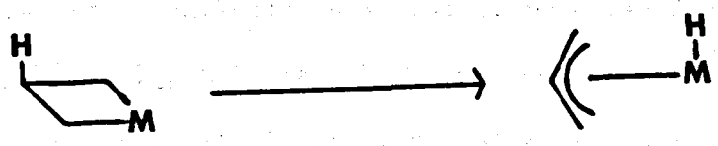


20

Figure 4. Platinum Complexes Characterized by Jennings and Waddington.

of platinacyclobutanes can be found in a review article by Puddephatt,[6] and Ibers[16] has published X-ray crystal data on some examples. No such intermediates have been isolated for iridium.

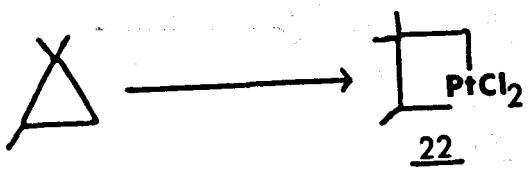
In both catalytic and stoichiometric reactions, metallocyclobutanes can go on to yield olefins as organic products. One major mechanistic pathway that has been implicated in the formation of olefins is β-hydride elimination. A hydrogen β to the metal in metallocyclobutane can be abstracted by the metal to give a π-allyl metal hydride (21) (equation 3).



(3)

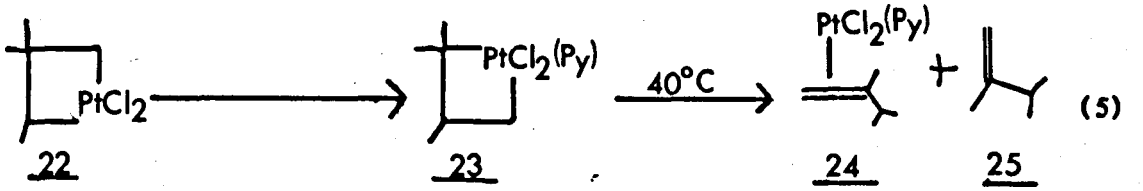
21

Cushman and Brown[17] obtained dichloro-2,3,3-trimethyl-1-platinacyclobutane (22) from the reaction between 1,1,2-trimethylcyclopropane and Zeise's dimer (equation 4). Treatment of 22 with pyridine gave the rearranged platinacyclobutane 23 which upon heating to 40°C gave a mixture of olefin-platinum complex 24 and olefin product 25 (equation 5).



(4)

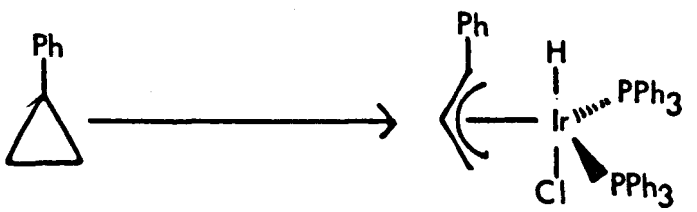
22



22 23 24 25 (5)

A more detailed investigation by Johnson and Cheng[18] resolved the mechanism of this reaction to be consistent with β-hydride elimination from 23 to yield presumably a π-allyl platinum hydride which subsequently undergoes a reductive elimination to give 25. This mechanistic conclusion was reached by observing the production of 25a, 25b and 25c (Figure 5). Some β-hydride elimination from the hydrogens on the α-methyl groups was also observed, but abstraction of the ring hydrogens was preferred.

Although π-allyl metal hydrides have been implicated by several researchers as catalytic intermediates,[7,10,19] no such intermediate had ever been characterized as a product from a β-hydride elimination reaction until 1979 when Ibers and Tulip[20] reported on the isolation of a π-allyl iridium hydride complex (27) from the reaction of phenyl cyclopropane (26) with $IrCl(N_2)(Ph_3P)_2$ (equation 6).



26 27 (6)

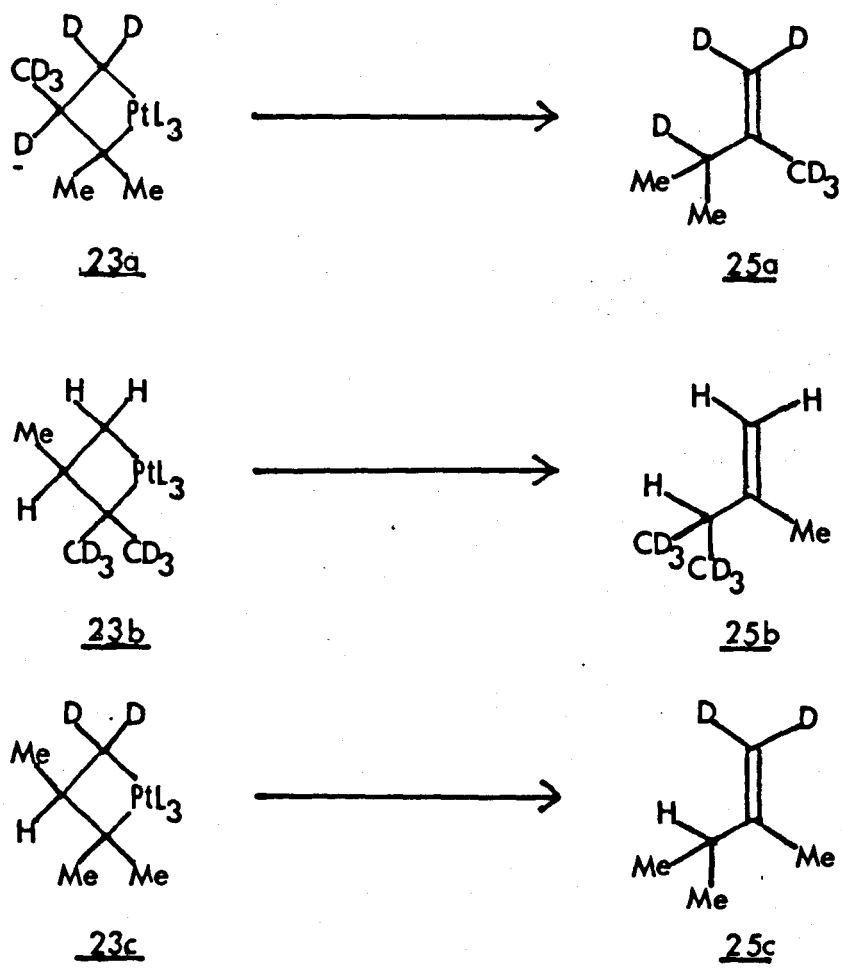


Figure 5. Production of Olefin Products from Deuterium Labeled 2,2,3-trimethyl-1-platinacyclobutane.

Product 27 was also obtained by the reaction of trans-β-methyl styrene and allyl benzene with the same iridium complex. The structure of 27 was confirmed by X-ray crystal data. Ibers attributes the isolation of 27 to its exceptional stability since attempts to obtain analogous complexes from cyclopropane and a number of simple olefins only gave organic products. Treatment of 27 with heat, CO or PF_3 gave β-methyl styrene as the only product.

The overall mechanism is depicted in Figure 6. Several points relative to the present research are demonstrated by this work of Ibers. First of course, β-hydride elimination is a viable decomposition pathway available to the iridacyclobutane 28. An equilibrium exists between the olefin product 30 and π-allyl hydride 27. In catalytic reactions the equilibrium lies furthest toward the free olefin, and in stoichiometric reactions the equilibrium favors metal complexes such as 27, 28 or 29. The position of equilibrium is suggested to be related to the thermodynamic stability of the iridium complex in question. Furthermore, the decomposition of 27 to 30 is regioselective. This regioselectivity is primarily due to the thermodynamic stability of the olefin. Starting materials are isomerized to the thermodynamically favored olefins, such as the isomerization of allyl benzene (31) to β-methyl styrene (30). One last point to consider in β-hydride eliminations is that the β-hydrogen and the metal must achieve a syn-periplanar configuration for β-hydride elimination to occur.[10,20]

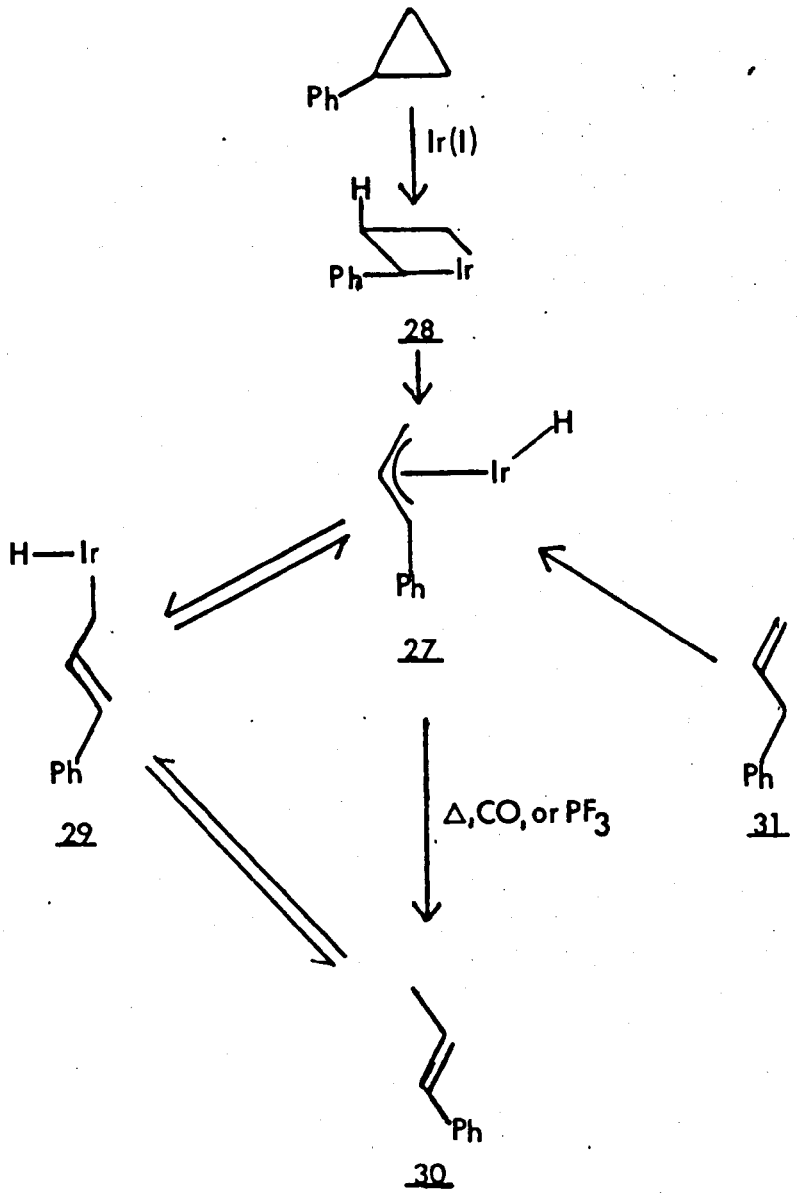
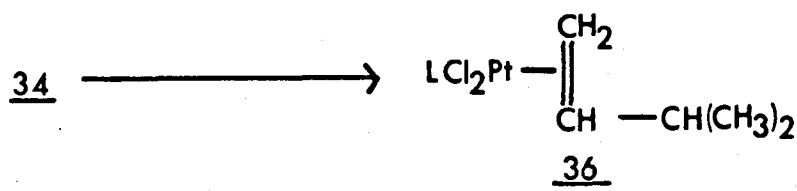


Figure 6. Reaction of Phenylcyclopropane with $IrCl(N_2)(Ph_3P)_2$.

Other modes of decomposition are also possible for metallocyclobutanes and are related to the present investigation. Small structural differences in substrates can cause effects that make β-hydride elimination unfavorable. Geometric or steric constraints in which the proper geometric conformation for β-hydride elimination cannot be adopted, and electronic restrictions may alter the mode of decomposition to α-elimination. Puddephatt[21] reported on a reaction involving a 1,3-hydride shift that was platinum mediated (Figure 7). In the mechanism proposed by Puddephatt, the platinacyclobutane 32 underwent loss of a ligand followed by abstraction of an α-hydride or deuterium to form 33 (note that depending on the position of platinum insertion, both possibilities result). The deuteride in 33 is then transferred to the next carbon via a reductive elimination resulting in platinum-carbon bond cleavage to give ylide 34. This ylide is then trapped by a ligand to give either 35 or 35a depending on the precursor platinacyclobutane. A similar mechanism in the same article explains the formation of olefin product 36. This product is obtained by a 1,2-hydride shift between 34 and 36 (equation 7).



(7)

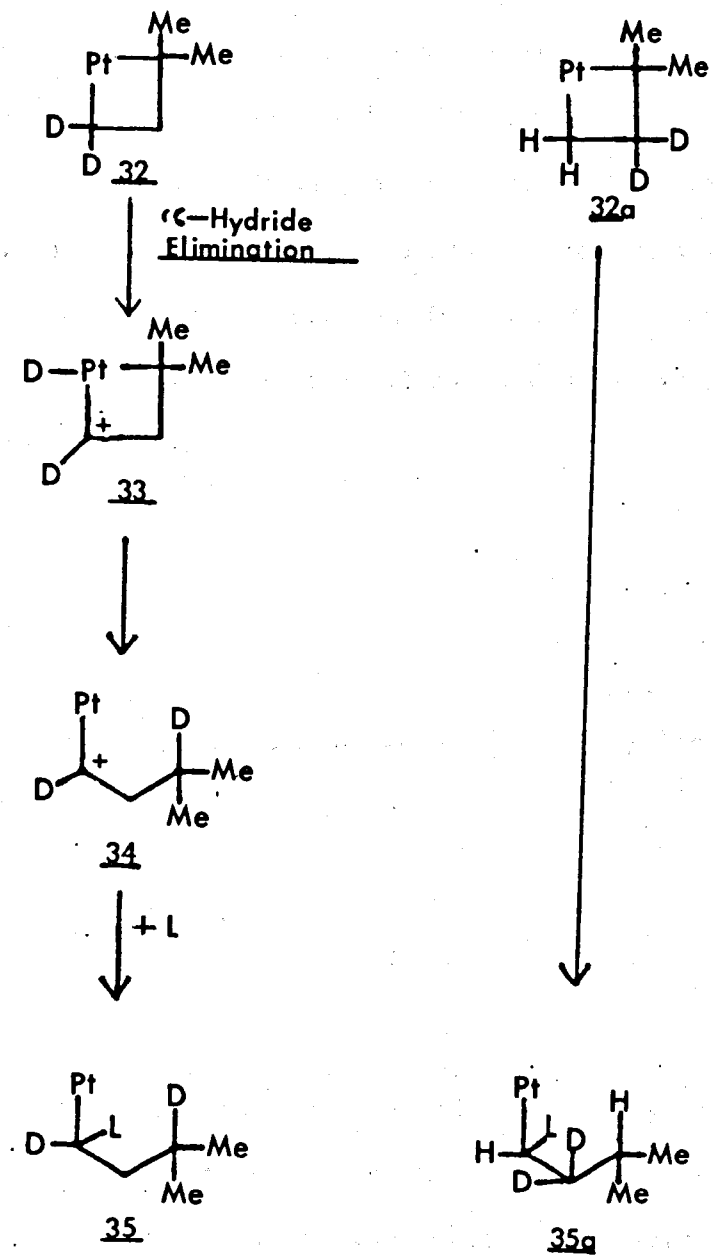
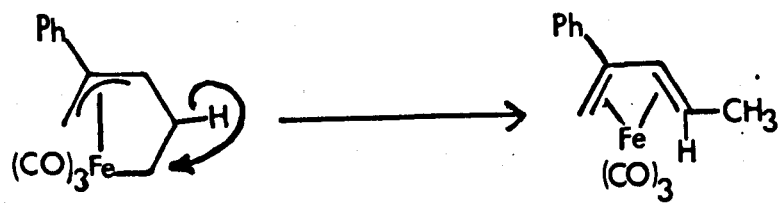


Figure 7. α-Hydride Elimination from a Platinacyclobutane.

A 1,2-hydride shift to displace a metal from a carbon in an Sn2 fashion is not commonly suggested as a mechanistic possibility. Katz[22] did consider such a possibility in the rhodium catalyzed isomerization of 11, but subsequently demonstrated another mechanistic scheme to be more likely. The work by Katz will be discussed shortly, but an Sn2 displacement of iridium by a 1,2-hydride shift is consistant with some results obtained in this investigation. A related example was demonstrated by Sarel[23] in which iron complex 37 underwent a 1,2-hydride shift to give the η^4-Fe complex 38 (equation 8.)

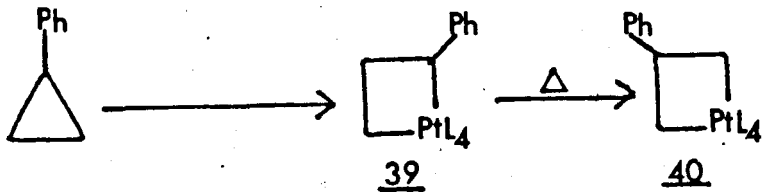


(8)

37 38

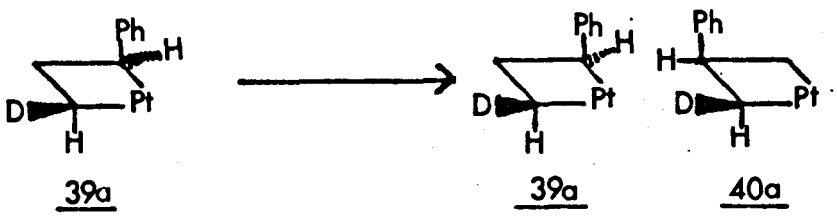
Metallocyclobutanes are known to yield starting cyclopropane as thermolysis products[6] (see equation 2). This shows that oxidative addition of a cyclopropane to a metal center is reversible. On a similar note, Puddephatt[24] found that the platinacyclobutane 39, obtained from the reaction of Ziese's dimer with phenylcyclopropane, isomerized to 40 upon heating at 50°C for 45 minutes in chloroform.

A 1:2.3 ratio of 39 to 40 was obtained (equation 9).



39 40 (9)

Crossover experiments done by Casey[25] with ρ-tolylcyclopropane showed this isomerization to be intramolecular since no (ρ-tolyl)-platinacyclobutanes were recovered as products. Further, deuterium labeling experiments showed retention of steriochemistry in the products (equation 10) indicating that disrotatory ring opening to a free olefin and a metal carbene is not likely since loss of stereochemistry would be expected.



39a 39a 40a (10)

Three mechanisms were postulated to explain these results and are illustrated in Figure 8. The Puddephatt[24] mechanism suggests a concerted process in which the dashed lines in structure 41 indicate bond reorganization. Casey[25] proposed the other two mechanisms. The

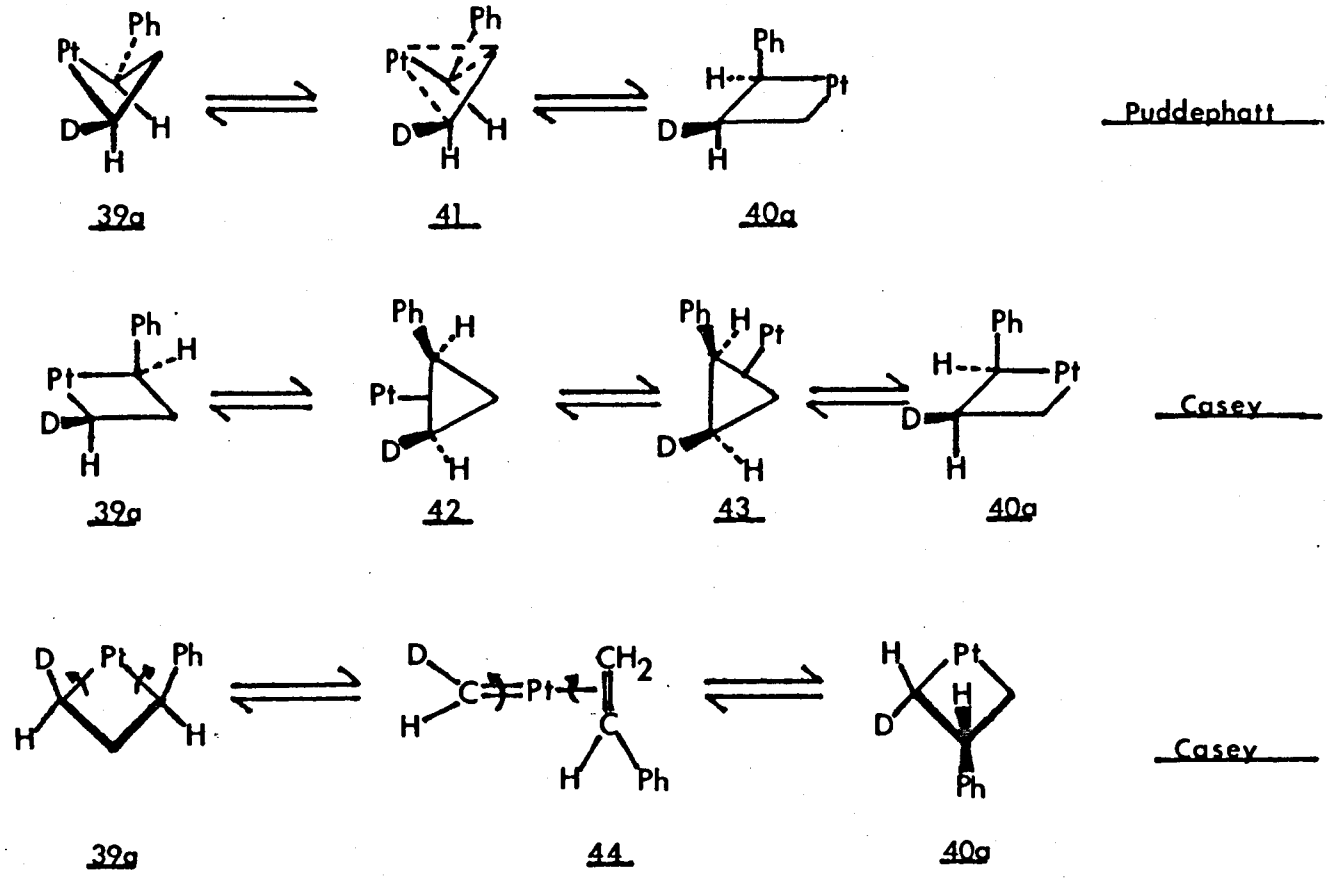
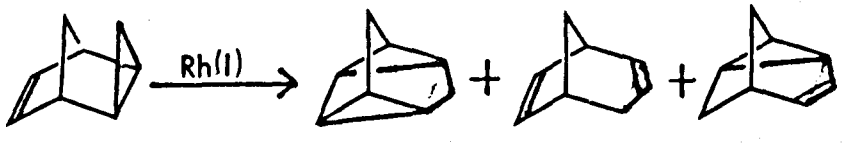


Figure 8. Postulated Mechanisms for the Isomerization of (Phenyl)-Platinacyclobutanes

first involves deinsertion of the metal to give the edge complex 42 which undergoes an edge to edge isomerization to 43 followed by reinsertion to give 40a. The second mechanism involves a disrotatory ring opening of 39a to give metalcarbene-olefin complex 44. The olefin and carbene are coplanar and perpendicular. A concerted rotation of the two ligands either gives 39a or 40a. As to which of these three mechanisms is most correct is not known. As will become clear later, isomerizations such as these may be implicated in the discussion of iridium catalysis. Future reference to this sort of isomerization will simply be referred to as a 1,2-metallo shift.

Cyclopropanes contained within rigid ring systems also undergo valence isomerization upon treatment with transition metal complexes; but reaction with these types of substrates have not been as heavily investigated. The only metal complexes that have been isolated and characterized from rigid ring cyclopropane substrates are those reported by Jennings and Waddington[14,15] illustrated in Figure 3. In addition to the work by Volger, which has already been mentioned, several other examples of these reactions appear in the literature.[7] Of particular interest to this research is the work reported by Katz[22,26,27,28] on the rhodium catalyzed isomerization of 11. Katz found that reaction of 11 with $RhCl(Ph_3P)_3$ gave three products as summarized in equation 11.



11 45 46 47 (11)

The mechanism of this reaction was pursued using deuterium labeled 11a and the overall mechanism shown in Figure 9 was postulated by Katz to account for the observed results.[28] No kinetic deuterium isotope effect was noted since in a mixture of 11 and 11a both substrates were consumed at an equal rate. However, the relative ratio of tetracyclo[3.2.1.$0^{2,7}0^{4,6}$]octane (45) in the product mixture increased when 11a was the starting substrate. Product 45 showed no deuterium migration, whereas bicyclo[3.2.1]octa-2,6-diene (46) and tricyclo[3.2.1.$0^{2,7}$]oct-3-ene (47) showed deuterium migration each into an endo position in the product. The rate determining step was deduced to be oxidative addition of the cyclopropane onto the rhodium, but the product determining steps ostensibly came after the metal insertion. The deuterium isotope effect was a result of a competition between β-hydride elimination and complexation of rhodium with the distill olefin bond in structure 48. Complexation of the olefin with rhodium in 48, followed by reductive elimination of the metal leads to 45, whereas when a similar pathway after β-hydride elimination occurs, 47 is obtained. Product 46 shows an overall 1,2-hydride shift which is mediated by a β-hydride elimination to form π-allyl hydride 49 from rhodacyclobutane 48. Intermediate 49 then rearranges to give the η^1-allyl complex 51 which upon reductive elimination yields 46.

The products obtained from the reaction of rhodium or platinum[29] with cyclopropanes in rigid ring matrices typically show a net cleavage of the cyclopropane ring juncture carbon-carbon bond.

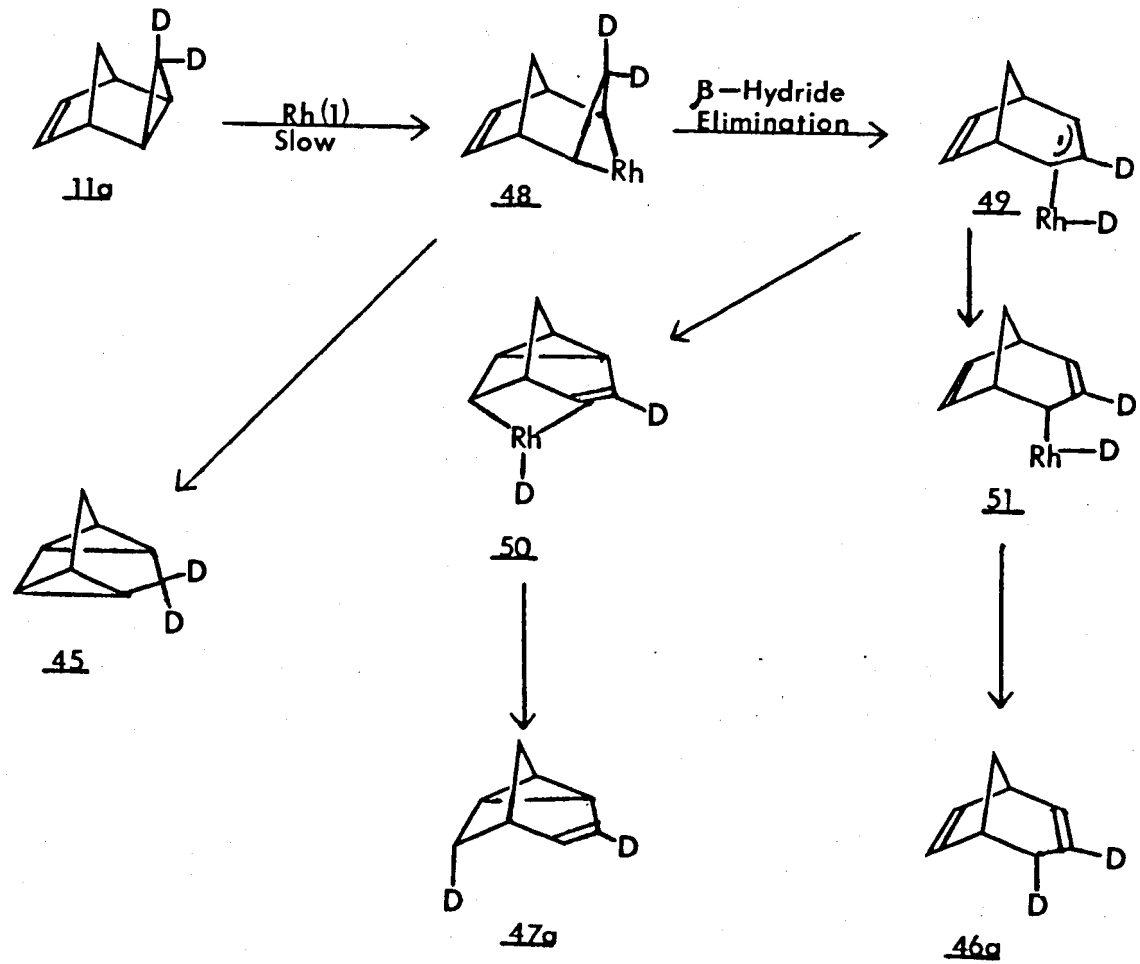


Figure 9. Mechanism for the Rhodium Catalyzed Valence Isomerization of 11.

Furthermore, platinum is stoichiometric rather than catalytic in these reactions.[14] Iridium, on the other hand, is catalytic and shows a preference for the formation of exocyclic methylene products which equate to the net cleavage of the cyclopropane bonds opposite to those cleaved in platinum and rhodium reactions. Other than the reactions reported by Volger, no research has been reported on the reactions of iridium catalysts with cyclopropanes contained in rigid polycyclic ring systems. The variety of tricyclic and tetracyclic cyclopropane containing compounds used as substrates for transition metal reactions is also limited, and much information may be gleaned from a greater variety of these sorts of substrates. As has been suggested by several researchers in this field, small structural changes in organic substrates can alter reaction pathways significantly. Finally, changes in reaction conditions could possibly yield reaction of substrates that were previously reported to be unreactive.

The work reported in this thesis was undertaken primarily as an exploratory investigation. By the use of deuterium labeling and various structural modifications of the substrates used, it was hoped to gain insight into the reaction of Vaska's catalyst with substrates containing cyclopropane moieties within a rigid polycyclic framework. Considering the available literature in combination with the results obtained in this research, consistent mechanistic schemes will be proposed. This work is considered to be a broad basis for further investigation rather than a detailed mechanistic investigation. A

more detailed investigation would require kinetic data, which was not obtained in the course of this research, as well as far greater insight into the nature of the active catalyst or catalysts. No serious attempts were made to investigate the inorganic aspects of these catalytic reactions, and the stucture of the actual catalytic species is still unknown. It is assumed that the active catalyst is a low valent, coordinately unsaturated complex. For purposes of discussion and schematic representation, it will simply be referred to as Ir(1).

DISCUSSION

Section I

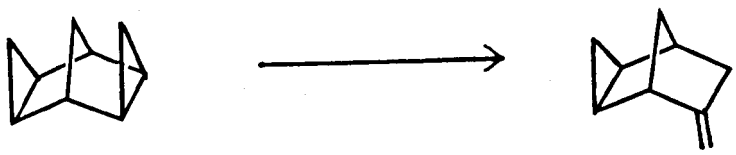
Reactions with Non-Deuterated Substrates

Preliminary Investigation

Volger,[11,12] in 1969, reported on the reactions of 11 and 12 with Vaska's catalyst. At 130°C and using benzene as the reaction solvent, substrates 11 and 12 were quantitatively converted to 5-methylenebicyclo[2.2.1]hept-2-ene (52) and 15 respectively (equations 12 and 13).

(12)

11 52



(13)

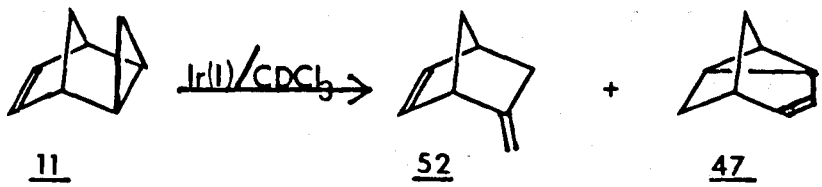
12 15

In attempting to reproduce Volger's work, reaction mixtures of 11 and 12 were placed in glass vessels, degassed by several successive freeze-thaw cycles under vacuum and finally sealed under vacuum. Analysis of the reaction mixtures showed that no reaction

had taken place after heating at 130°C for 2 hours. The experiments were repeated with heating for 32 hours, and still no observable reaction was obtained.

The reactions were then performed without N_2 purging or degassing prior to sealing the reaction vessels. Both reactions were successful upon heating for 2 hours, but the yields were not as high as expected. Reaction of 11 produced a 34% yield of 52 as the only product, and about 60% of 11 was recovered. Reaction of 12 gave a better yield of product, in that 15 was recovered, as the only product, in 60% yield. Repeated experiments gave consistent results. The results of these experiments demonstrated a definite need for oxygen as a reaction component, however the reason is not clear. The need for oxygen in these reactions will be addressed further in the conclusion of this thesis.

At this point it was decided to attempt the reaction of 11 in deuterochloroform ($CDCl_3$). This was done to facilitate the analysis of reaction mixtures by ^1H NMR spectroscopy while using a less expensive deuterated solvent. The reaction proceeded smoothly to afford two products in an overall higher yield than when benzene was used as the reaction solvent. Compound 52 was produced in 33% yield and 47 was produced in 28% yield. Equation 14 illustrates these results and gives relative product yields. Relative yields will henceforth be reported. Absolute yields, relative to an internal standard, will be found in the experimental portion of this thesis.



11 52 47 (14)

The use of $CDCl_3$ as the reaction solvent caused two effects. First, the reaction went further toward completion, and second, two products were obtained rather than one. The nature of the effect of chloroform remains unknown, but certain possible aspects of the reaction were investigated. A thermal process to yield 47 was considered since 47 had been reported as a thermal isomerization product of 11 at higher reaction temperatures.[30] Also the possibilities of a radical or an acid catalyzed process were considered. All three possibilities were ruled out by performing control experiments. Substrate 11 was subjected to identical reaction conditions, excluding catalyst, and only 11 was recovered after 2 hours. The possibility of acid catalysis was eliminated by an experiment in which Na_2CO_3 was added along with all of the other reaction components. A radical process was ruled out by running the reaction with all of the reaction components and 10% (V/V) cumene as a radical inhibitor. Both the Na_2CO_3 and the cumene reactions produced results similar to those obtained in the standard reaction. Thus, it appears that 47 is a product of iridium catalysis.

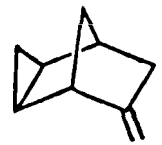
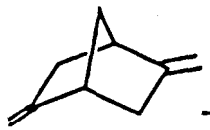
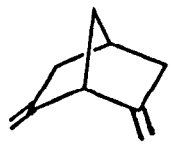
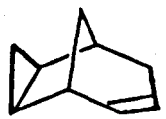
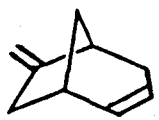
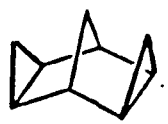
The reaction of 11 was also carried out using identical conditions except for the solvent used. Tetrahydrofuran, methanol and dichloromethane were independently used in place of chloroform. The catalyst failed to dissolve in any of these solvents, even at elevated temperatures, and no reaction ensued.

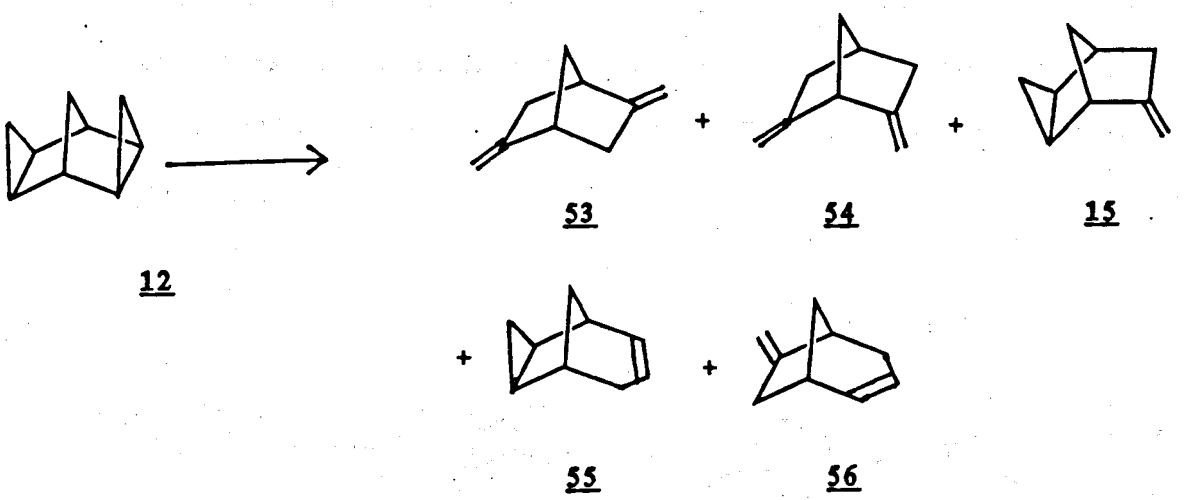
The role of chloroform in this reaction is obscure and has not been pursued. One possible explanation for the chloroform effect is that the polarity of this solvent may be stabilizing a polarized, if not charged, transition state or intermediate in or near the rate determining step. As will be seen later, carbocation intermediates are implicated in the reaction of some substrates. Transition state charge separation in all of these reactions is a reasonable hypothesis.

Reaction of 12 with Vaska's Catalyst in $CDCl_3$

When 12 was reacted with Vaska's catalyst in benzene, 15 was the only product obtained. The second cyclopropane ring did not undergo reaction. In light of the results obtained for the reaction of 11 in $CDCl_3$, it seemed reasonable that the reaction of 12 might also be made to go beyond the reaction of one cyclopropane ring. A three hour reaction with iridium in $CDCl_3$ at 130°C gave five products. The product structures are given in equation 15. The relative yields of the products in equation 15 are presented in Table 1 along with data obtained from product mixtures resulting from longer reaction times.

Table 1. Relative Product Yields from the Reaction of 12 with Vaska's Catalyst Relative to Time.

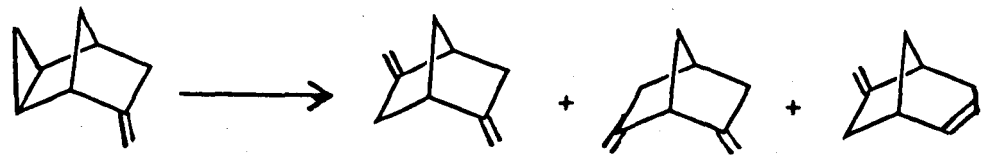
Product	% Yield Relative to Time		
	3 hours	6 hours	9 hours
 15	79	71	60
 53	9	17	23
 54	2	5	8
 55	2	—	—
 56	3	7	9
 12	5	—	—



12 → 53 + 54 + 15 + 55 + 56 (15)

The reaction of 12 was run for longer periods of time in an attempt to drive the reaction further toward completion. As can be seen from the data in Table 1, 15 was the predominant product even after 9 hours. Only 5% 12 was present after 3 hours and neither 12 nor exo-tricyclo[3.3.1.$0^{2,4}$]non-6-ene (55) were observable after 6 hours. It should be further noted that the percent change from 3 to 6 hours is similar to the change from 6 to 9 hours for products 15, 2,5-dimethylenebicyclo[2.2.1]heptane (53), 2,6-dimethylenebicyclo [2.2.1]heptane (54), and 6-methylenebicyclo[3.2.1]oct-2-ene (56). The indication is that the rate of formation of 53, 54 and 56 remain fairly constant between 3 and 9 hours and that the rate of reaction of 15 is also constant between 3 and 9 hours. It appears that 15 reacts at a much slower rate than 12 since 12 is virtually consumed after 3 hours. Product 15, on the other hand, is present in a relatively large amount even after 9 hours. Two possibilities exist

to explain this observation. First, catalytic activity of the iridium decreases with time, or second, 15 is less reactive than 12. As a test, 15 was isolated from a reaction mixture and subjected to identical reaction conditions for 3 hours. The results are presented in equation 16.

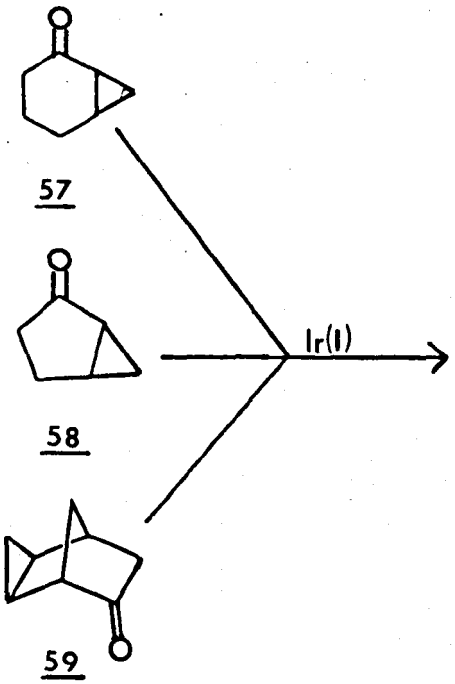


(16)

15 53(9%) 54(3%) 56(5%)

Production of 53, 54 and 56 paralleled the percent changes for 3 hour increments in the reactions using 12 as the starting substrate. Thus 15 reacts at a slower rate than does 12. Homoconjugation of the exocyclic methylene with the cyclopropane might cause electronic effects, in the cyclopropane, that retard iridium complexation or subsequent steps in the reaction mechanism. Using a frontier molecular orbital approach, one can envision electron donation from the HOMO of the cyclopropane to the LUMO of the olefin (see Figure 10). If it is assumed that in cyclopropane-iridium reactions the primary bonding interactions are between an empty d orbital of the metal and a HOMO of the cyclopropane, then this analysis might be at least partially valid.[3] Substrates with strongly electron with drawing groups in conjugation with a cyclopropane ring do not give catalytic reaction. Reaction was attempted with three substrates

containing a carbonyl functionality. They were bicyclo-[4.1.$0^{1,6}$]hept-2-one (57), bicyclo[3.1.$0^{1,5}$]hex-2-one (58) and exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-one (59). None of these three substrates afforded catalytic reaction (equation 17).



No Catalytic Reaction (17)

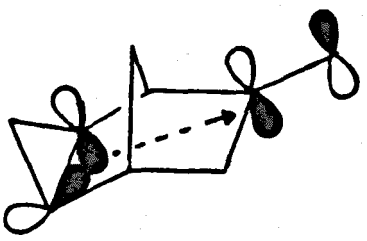


Figure 10. Through Space Electron Donation from a Cyclopropane HOMO to the Olefin LUMO in Compound 15.

Another possible explanation is that the exocyclic methylene might effectively compete with the cyclopropane for available bonding sites on the iridium. Kinetic analysis would be useful to discriminate such a competitive process from other effects, but reaction of 15 is inordinately slow to be attributed solely to product inhibition.

Reactions of substrates 11 and 12 with iridium demonstrates a fair amount of regioselectivity. Exocyclic methylenes are favored products from both substrates. Reaction of 15 also shows a great deal of regioselectivity in that 53 is preferred over 54 by about 4 to 1. More discussion of regioselectivity will be given after more examples are provided.

One topic that has not been mentioned is the identification of products. Product identification relied heavily on ^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectroscopy. Corroboration of structure was obtained, whenever possible, with elemental analysis or mass spectroscopy. Since ^{1}H NMR was very important to this work for both structure elucidation and specific proton assignment (for deuterium labeling studies), a fairly detailed discussion of ^{1}H and ^{13}C NMR data will be presented in Section II of this discussion. Suffice it to say for now that products 15 and 55 have been previously reported in the literature[12,29] and products 53, 54 and 56 have not been previously reported.

Preliminary Mechanisms

It might be helpful at this point, and useful for further discussion, to outline the mechanistic schemes that were being considered as working models early in this investigation. The mechanisms in Figure 11 show the initially proposed pathways to products. All steps have ample literature precedence. The initial step for both paths A and B is insertion of iridium into a carbon-carbon bond of the cyclopropane to give exo-iridacyclobutane 60 or endo-iridacyclobutane 64. Insertion is thought to be the slow step in similar reactions with other metals.[28] Once formed, the metallocyclobutanes could conceivably isomerize in a fashion as described by either Casey or Puddephatt.[24,25] Using this logic, insertion of the metal might be exclusive to give, for instance, only 64 which subsequently rearranges to 60. Such a rearrangement will, henceforth, be termed a 1,2-metallo shift. The next step would be β-hydride elimination to give the iridium hydride complexes 62 or 66. Evidence exists for the intermediacy of π-allyl iridium hydride complexes, such as 61 or 65, in the formation of 62 and 66.[16] Finally, reductive elimination of iridium from 62 and 66 gives products 63 and 67. For the sake of simplicity, products such as 63 will be termed exocyclic methylenes and products such as 67 will be termed ring expanded olefins.

Reaction of the Saturated Analogues of 11 and 13

One way to pursue this chemistry was to see the effects of substrate structural modifications on the products obtained by

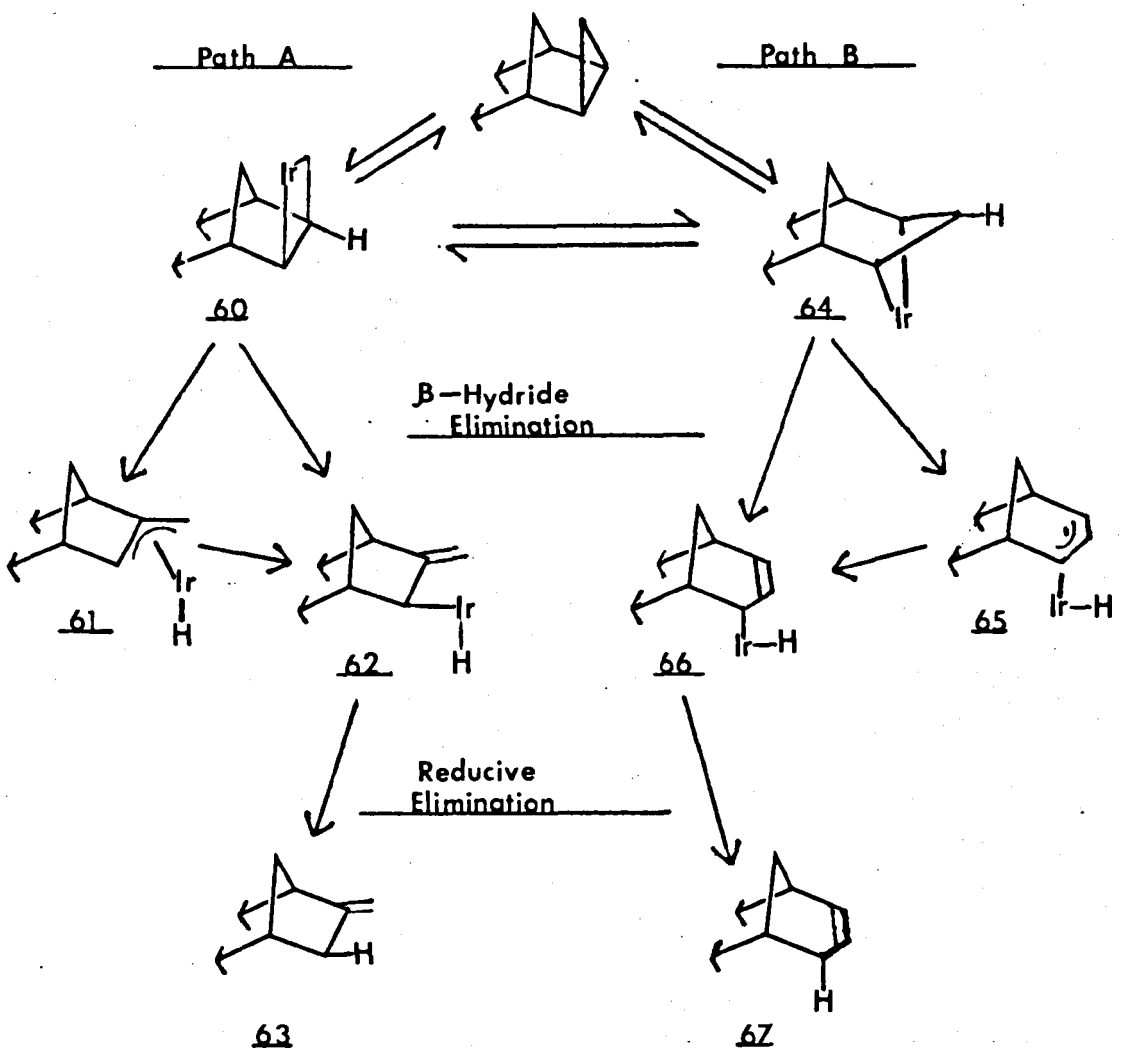
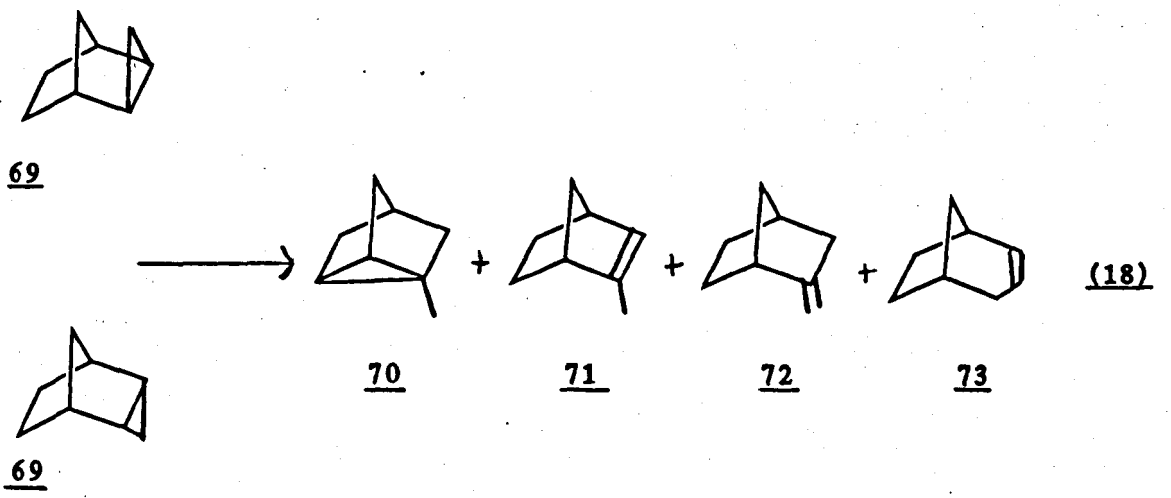


Figure 11. Preliminary Mechanistic Scheme for the Formation of Exocyclic Methylene and Ring Expanded Products.

iridium mediated reaction. To that end, and since reaction is more facile when $CDCl_3$ is used as the reaction solvent, it was decided to attempt reactions in $CDCl_3$ with substrates that were unreactive in benzene. The saturated analogues of 11 and 13, exo-tricyclo[3.2.1.$0^{2,4}$]octane (68) and endo-tricyclo[3.2.1.$0^{2,4}$]octane (69) respectively, gave no catalytic reaction when benzene was used as the reaction solvent. When reaction of 68 and 69 were run using $CDCl_3$ as the solvent, both gave good product yields. The results of these two reactions are summarized in equation 18 and in Table 2.

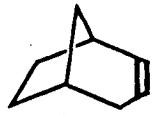
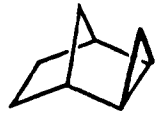


69 → 70 + 71 + 72 + 73 (18)

69

Both 68 and 69 gave 2-methylene bicyclo [2.2.1]heptane (72) as the major product. Compound 72, 2-methylbicyclo[2.2.1]hept-2-ene (71) and bicyclo[3.2.1]oct-2-ene (73) are known compounds (see experimental portion of this thesis). 2-methyltricyclo-[2.2.1.$0^{2,6}$]heptane (70) has no precedence in the literature and its structure has not been unambiguously proven in this research.

Table 2. Relative Product Yields from the Reaction of 68 and 69 with Vaska's Catalyst in $CDCl_3$ at 130°C.

Product	Relative percent from Substrate (Reaction Time)		
	68 (3 hours)	68 (4 hours)	69 (3 hours)
 70	—	3.5	—
 71	6	9.5	6
 72	47	78.5	61
 73	3	4.5	27
 68	43	4	—
 69	—	—	6

However, ^{1}H NMR data is consistent with the assigned structure (also see experimental portion of this thesis).

Products 72 and 73 are consistent with the mechanistic schemes in Figure 11. The isolation of 71 from these reaction mixtures adds another dimension to the proposed mechanism. Formation of 71, relative to the mechanism in Figure 11, can be explained as depicted in Figure 12. It is interesting to note that the ratio of 71 to 72 is fairly constant in all three product mixtures.

Path A (of Figure 12) is fundamentally identical to the mechanism proposed in Figure 11 up to the formation of the exocyclic methylene. Subsequent complexation of the iridium with the exocyclic methylene olefin followed by β-hydride elimination will yield the π-allyl complex 61. Complex 61 could also be formed directly from decomposition of the iridacyclobutane by β-hydride elimination (Path C). Once formed, 61 undergoes bond reorganization to yield iridium hydride 75 which, upon reductive elimination, gives the observed olefin methyl product 71. Path B describes another route for the decomposition of the iridacyclobutane yielding, again, intermediate 75. The formation of 71 from 69 can be perceived as occurring through analogous pathways.

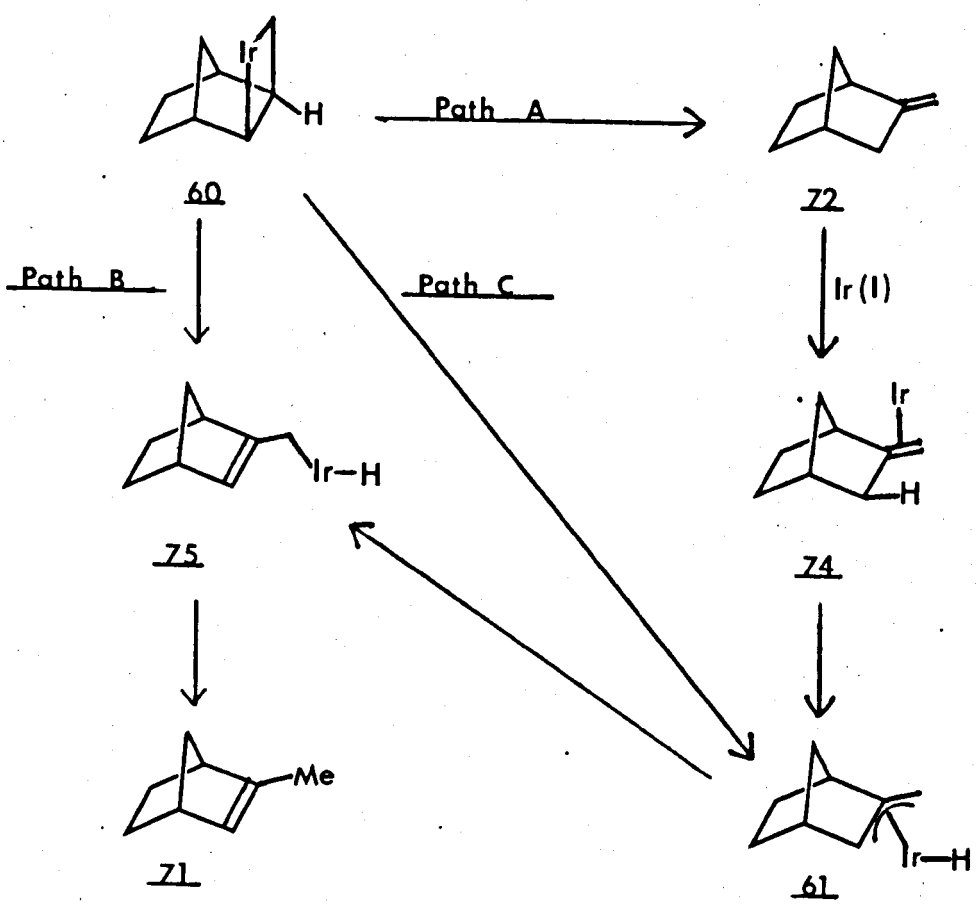
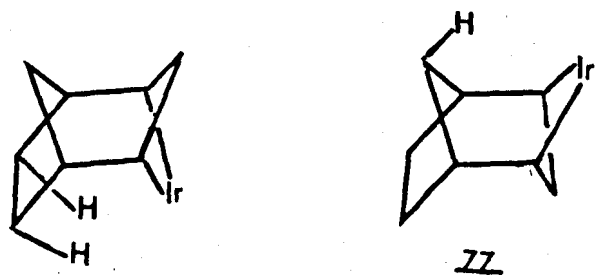


Figure 12. Possible Mechanistic Pathways to 71 from Substrates 68 or 69.

Product 70 is most likely formed in a fashion similar to 47 and will be discussed along with other similar products. Product 70 is not observable until late in the reaction and is most likely a product of the reaction of 71 with iridium.

It is also interesting to note the relative yields of 73 with respect to starting substrate. Product 73 represents a much larger proportion of the product mixture from the reaction of 69 than from 68. Considering the mechanism already proposed, the two intermediate iridacyclobutanes leading to 73 from 68 and 69 are 76 and 77 respectively (Figure 13).



76 77

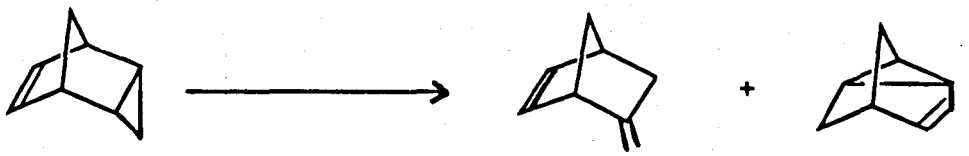
Figure 13. Iridacyclobutane Intermediates from Substrates 68 and 69.

The formation of 76 by direct attack of iridium from the endo side of the cyclopropane of 68 would be more sterically hindered than formation of 77 by direct attack of iridium from the exo side of the cyclopropane in 69. The endo protons on C_6 and C_7 shield the endo-cyclopropane bond of 68 to a greater extent than the bridge proton of 69 shields the exo-cyclopropane bond. The steric interactions between the ligands on iridium and the neighboring atoms on the carbocycle are difficult to assess. No analogous iridium

complex has ever been isolated, much less characterized.

The Reaction of Substrate 13 and 85

Substrate 13 was reported to be unreactive with Vaska's catalyst in a benzene solution.[11,12] In $CDCl_3$ the reaction of 13 goes virtually to completion in three hours to give 52 and surprisingly, 47. The results of this reaction are summarized in equation 19. The same control experiments that were run with 11 were also run with 13, and the results were analogous. The products, 52 and 47, are a result of iridium catalysis.



(19)

13 52(72%) 47(28%)

Product 52 can be rationalized as coming about via a scheme analogous to that proposed in Figure 11 (Path A). However, 47 does not fit the mechanistic scheme proposed as Path B in Figure 11. The equivalent of an inversion of configuration must take place at either C_2 or C_4 of 13 to form 47. Two different mechanistic schemes to account for the observed results are considered in Figures 14 and 15.

The Puddephatt rearrangements[24] nicely accommodate a 1,2-metallo shift equilibrium between 78 and 79, but 47 is not easily obtained from either of these intermediates. So, a 1,3-metalloshift was

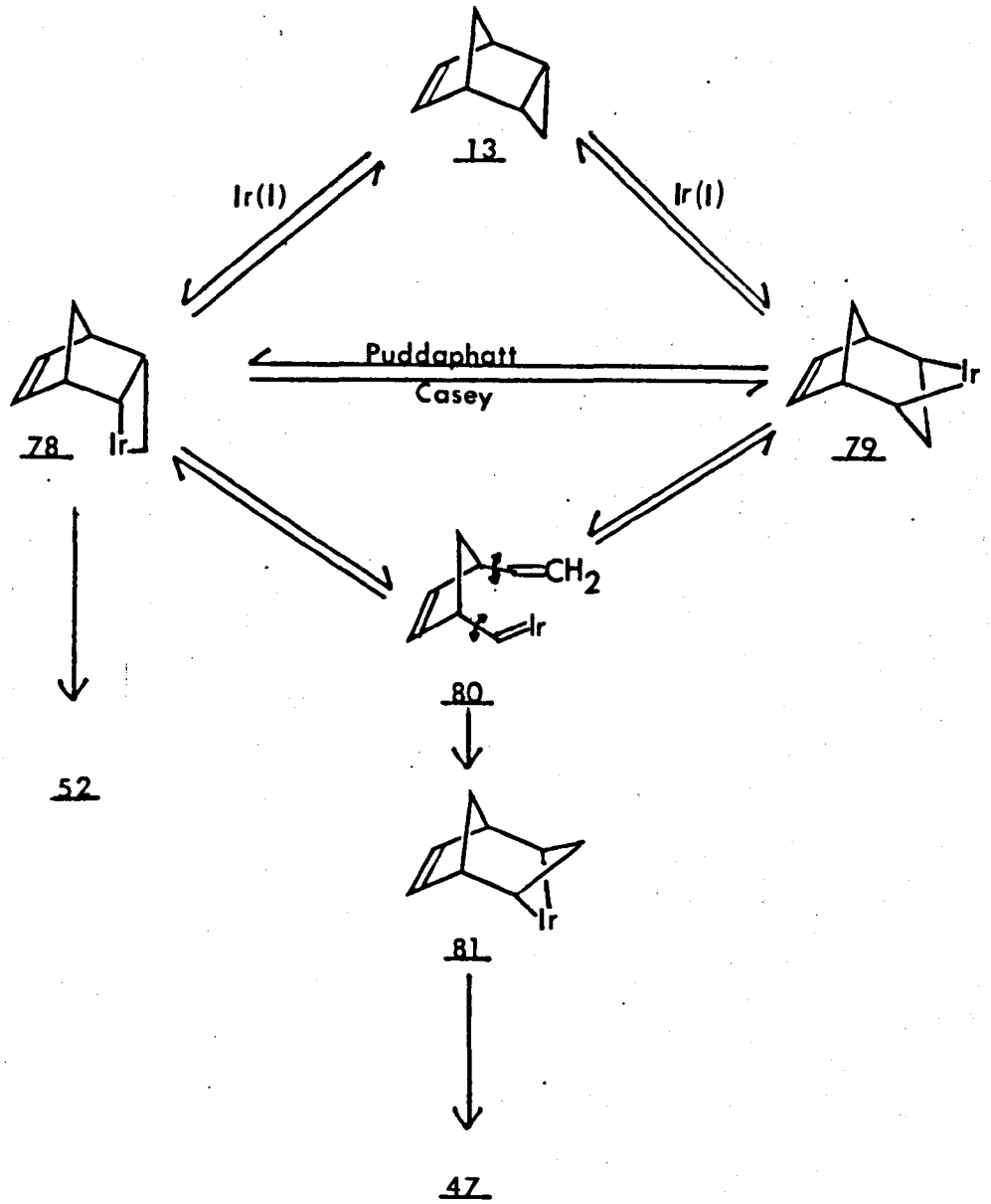


Figure 14. Production of 47 Through a 1,3-Metallo Shift Mechanism.

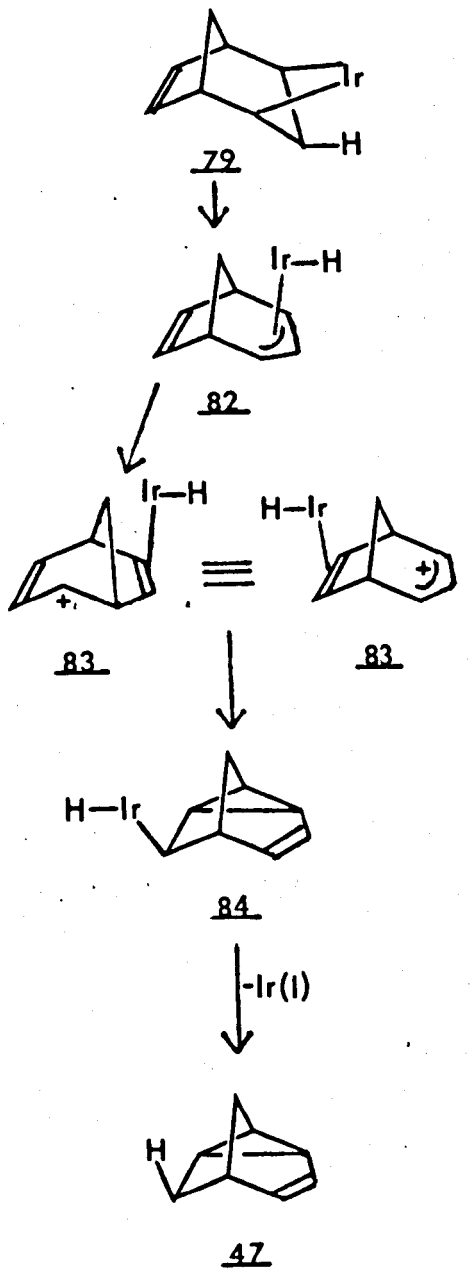


Figure 15. Production of 47 Through a 1,2-Bridgehead Shift Mechanism.

considered as a possible route to the product. A 1,3-metallo shift would yield an intermediate 81 identical to that proposed in Figure 11 (Path B). Subsequent mechanistic steps as described by Katz[28] (see Figure 9 on page 22) would yield the observed product. The alternative pathway to the Puddephatt rearrangement, is that which was proposed by Casey[25] for a platinacyclobutane system which rearranged at 52°C. Applying the Casey mechanism to this system, either intermediate 78 or 79 undergoes a 2 + 2 cycloreversion to form metallocarbene-olefin intermediate 80. Taking the Casey mechanism one step further, the reaction temperature of 130°C might be rigorous enough for dissociation of the iridium from olefin coordination to occur. This would allow the opportunity for free rotation of the sigma bonds of the carbene or olefin carbons. Thus, after proper rotation and recoordination, a 1,3-metallo shift could be envisioned to produce 80 from either 78 or 79. Although the intermediates used in Figure 14 have many precedents in the literature, a 1,3-metallo shift is a new idea.

Figure 15 depicts another pathway that was deemed feasible. In this mechanism, iridacyclobutane 79 decomposes to the π-allyl iridium hydride complex 82 upon β-hydride abstraction. Intermediate 82 then rearranges via a 1,2-bridge shift to give π-allyl carbocation/olefin-iridium hydride complex 83. Subsequent bond reoganization steps and, finally, reductive elimination of iridium provides product 47. The overall scheme in Figure 15 is unprecedented in the literature and was initially considered the less likely of the two proposed

possibilities. It should be easier to disprove the mechanism in Figure 15 than that in Figure 14 by labeling experiments since a skeletal rearrangement is implicit in this mechanism. Therefore, a labeling experiment was performed in which one of the bridgehead hydrogens of 13 was replaced by a methyl group.

Reaction of 1-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (85) could potentially give four ring expanded products: 4-methyltricyclo[3.2.1.$0^{2,7}$]oct-3-ene (86), 2-methyltricyclo [3.2.1.$0^{2,7}$]oct-3-ene (87), 1-methyltricyclo[3.2.1.$0^{2,7}$]oct-3-ene (88) and 5-methyltricyclo[3.2.1.$0^{2,7}$]oct-3-ene (89). All four products could be expected to result from a 1,2-bridge shift, whereas only 88 and 89 would be expected from the 1,3-metallo shift mechanism (Figure 16).

Upon reaction of 85 with iridium, only one product was obtained and that in 90% yield. ^{1}H and ^{13}C NMR spectral data as well as elemental analysis confirm the structure 86 to be that product. A discussion of the structure proof will be given in Section II. A check for thermal rearrangement was performed showing that 85 is thermally stable under the reaction conditions used.

Reaction of 85 shows remarkable regioselectivity of iridium insertion and regioselectivity of the subsequent rearrangement and cyclopropane formation. The presumed, rearranged intermediate (90) is illustrated in Figure 17. The carbocation is not only allylic but is also tertiary and thus regioselectivity is not surprising. More insight, however, was gained with a deuterium labeling experiment

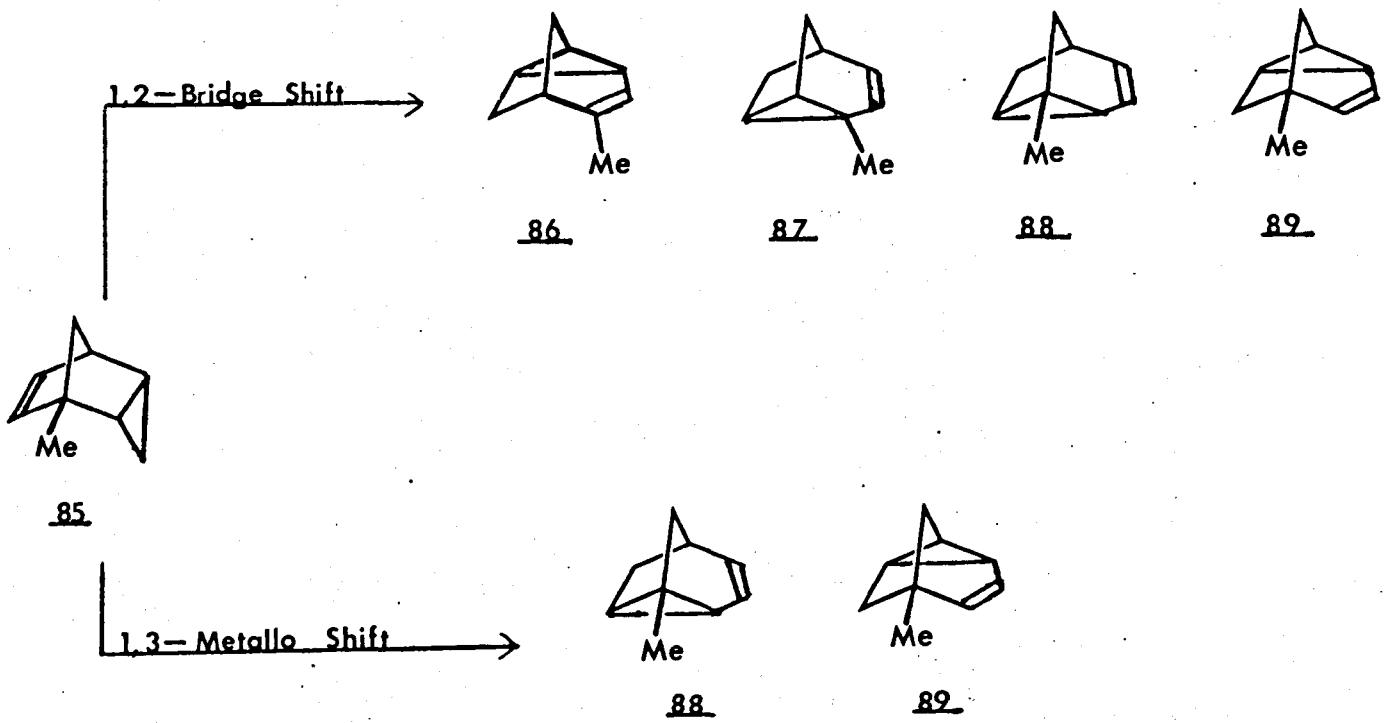
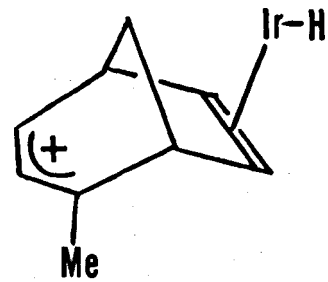


Figure 16. Possible Products from the Alternate Mechanisms of Reaction of 85 with Vaska's Catalyst.

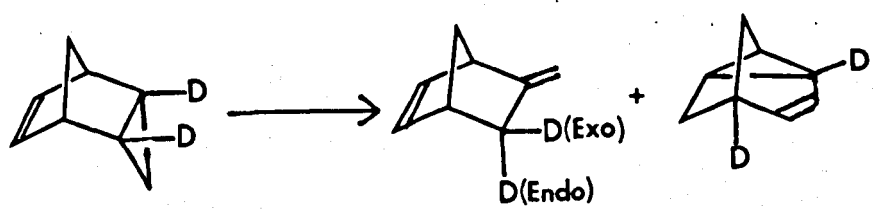
which will be discussed shortly.



90

Figure 17. Proposed Intermediate in the Reaction of 85 with IR(1).

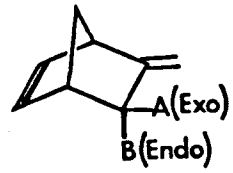
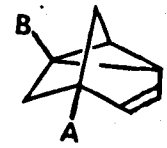
Even though 85 is thermally stable under the conditions used, the absolute regioselectivity of this reaction makes 85 suspicious as a good model for the reaction of 13 with iridium. Thus, it was decided to label 13 with deuterium to avoid the electronic or steric effects that might be active with the methyl label. Substrate 13a was synthesized and was found to contain 47% deuterium at each of the cyclopropane bridgehead carbons (this of course assumes equal distribution for the two positions). Reaction of 13a with iridium gave the results summarized in equation 20 and Table 3.



(20)

13a 52a(44%) 47a(56%)

Table 3. Deuterium Contents of Products from 13a.

Position	% Deuterium of Products[a]	
		
A	50%	43%
B	5%	52%

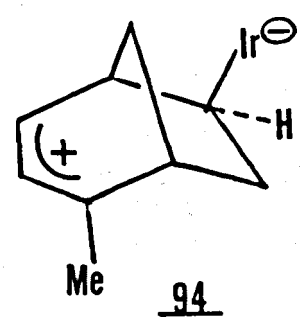
a) % Deuterium is expressed as percent reduction of the equivalent of a one proton integral in the ^1H NMR spectrum.

The proton assignments of the ^1H NMR spectrum will be discussed separately in Section II of this discussion. Suffice it for now to say that deuterium was found only in the positions indicated. Product 52a is also out of the realm of the present discussion and will be presented again in more detail in Section III along with the possible relationship between 47 and 52 which will be used to explain regioselectivity and product deuterium isotope effects.

Had the formation of 47 occurred via a 1,3-metallo shift, the deuteriums would have been found on C_4 and in the endo position of C_6 instead of being found on C_1 and C_5. However, an intermediate such as 90 in Figure 17 is not corroborated by the formation of 47a. A 1,2-bridge shift has occurred, but the product is derived from an

unsymmetrical intermediate. Consider Figure 18. An intermediate such as 91 would give both 47a and 47b as products. Also note that a deuterium isotope effect of 1.3 is present in favor of bridge migration to a non-deuterated carbon. A positive secondary isotope effect is consistent with a change in hybridization of the deuterium bearing carbon from sp^3 to sp^2 in the transition state. A revised mechanism that better explains the data is given in Figure 19.

The iridacyclobutane 79a is proposed, in this revised mechanism, to undergo carbon-iridium sigma bond cleavage rather than β-hydride elimination yielding carbocation 92. Bridge migration occurs, forming the more stable allylic carbocation 93. Loss of iridium with concomitant bond reorganization gives product 47a. An analogous mechanistic scheme can be envisioned for the reaction of 85 with iridium. The regioselectivity is greater with 85 due, most likely, to the additional driving force for the formation of an allylic-tertiary carbocation 94 (Figure 20).



94

Figure 20. Proposed Intermediate from Reaction of 85 with Vaska's Catalyst-Revised Mechanism.

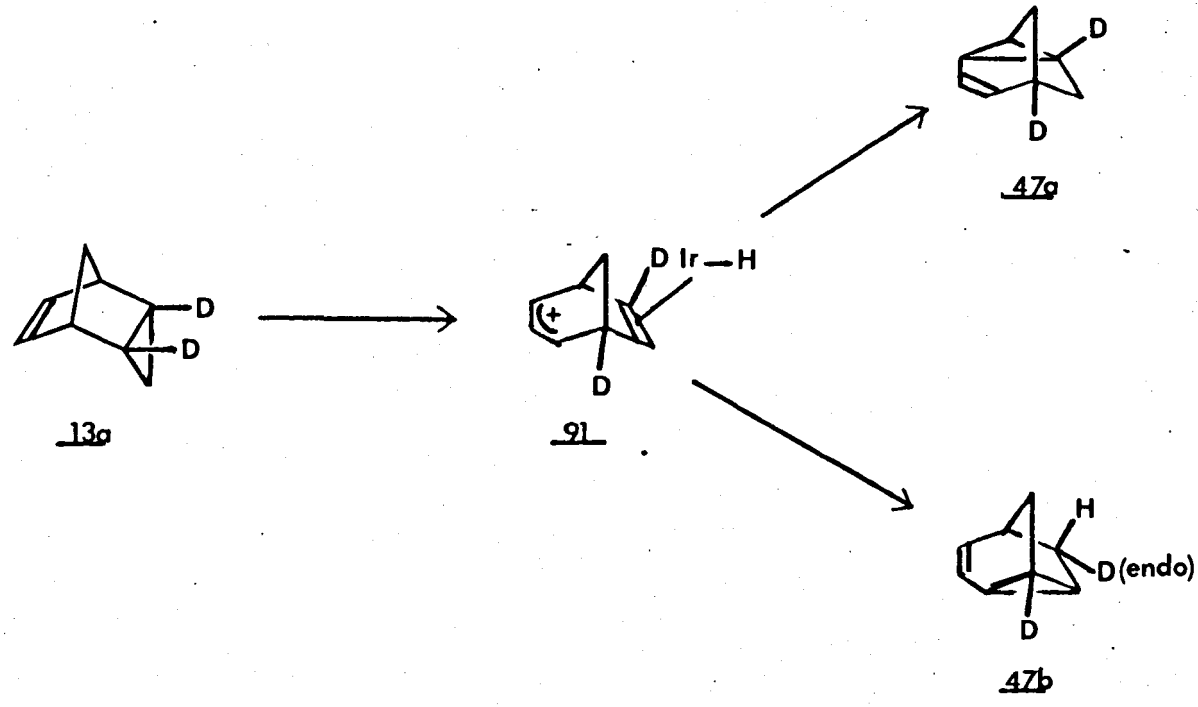


Figure 18. Scheme for the Expected Products from a Symmetrical Intermediate from 13a Via a 1,2-Bridge Shift.

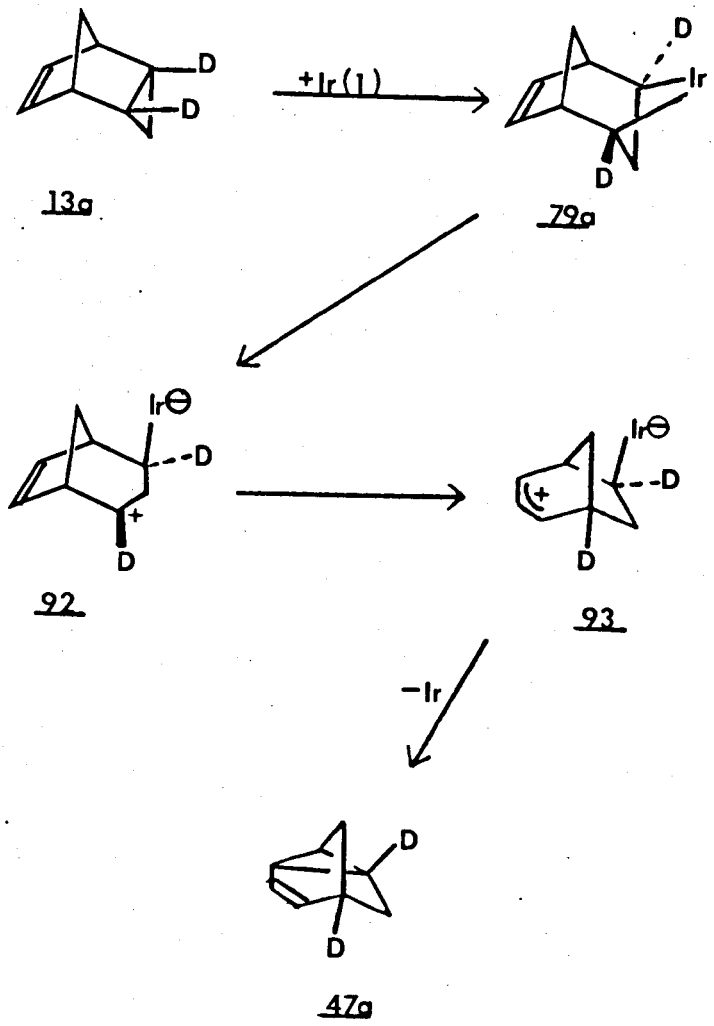
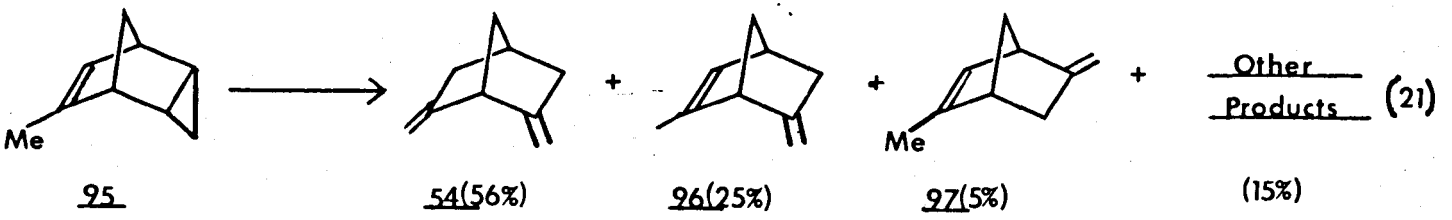


Figure 19. Revised Mechanism for the Production of 47a from 13a.

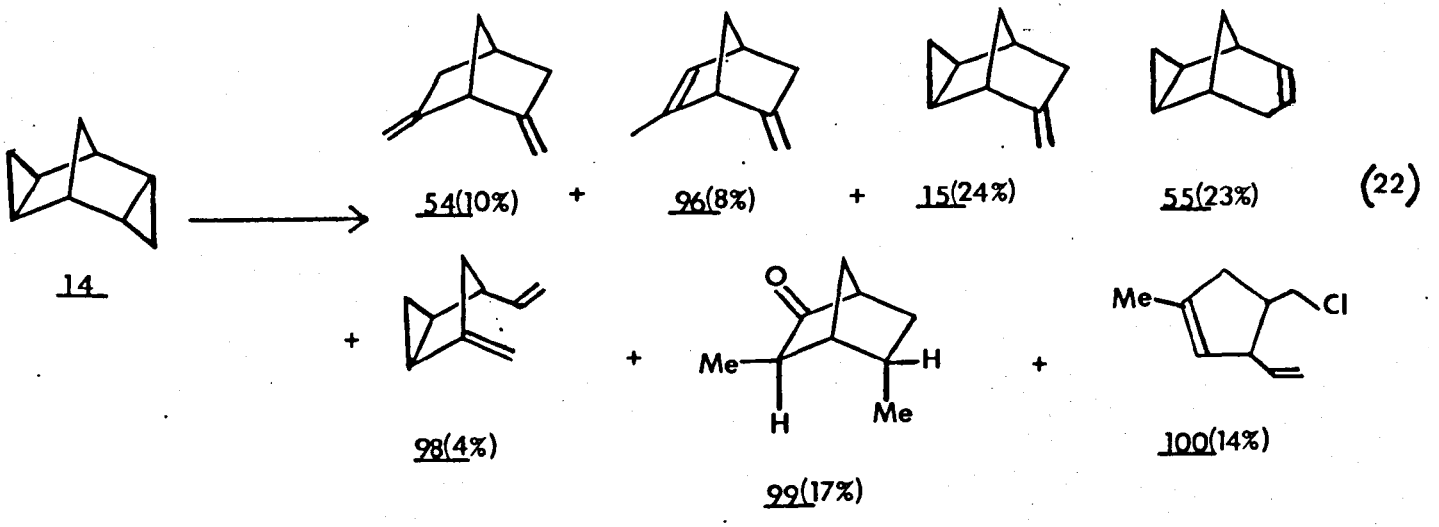
Reaction of Other Endo-Cyclopropane Compounds.

Two other substrates were used to investigate the 1,2-bridge shift of endo-cyclopropanes. These were 14 and 6-methyl-endo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (95). Neither of these substrates yielded isolatable quantities of rearranged products, but the resulting chemistry was interesting nonetheless.

The results of the reaction of 95 are given in equation 21 and the results of the reaction of 14 appear in equation 22. The results of these two experiments demonstrate some interesting points about the chemistry of endo-cyclopropane-iridium reactions. The reaction of 14 gives a rough comparison of the reactivity of the endo- versus the exo-cyclopropane toward iridium. Formation of 54 and 2-methyl-6-methylenebicyclo[2.2.1]hept-2-ene (96) show a great deal of regioselectivity. These same products also demonstrate the possibility of olefin isomerization which will be an important factor to consider in the discussion of deuterium labeling experiments. 4-Ethylidene-6-methylenebicyclo[3.1.$0^{1,3}$]hexane (98), exo-3-methyl-endo-5-methylbicyclo[2.2.1]hept-2-ene (99) and 4-chloromethyl-3-ethylidene-1-methylcyclopent-1-ene (100) also demonstrate some novel chemistry. The formation of 98 and 100 might very well have some mechanistic implications of interest.



95 54(56%) 96(25%) 97(5%) (15%)



14 54(10%) 96(8%) 15(24%) 55(23%) 98(4%) 99(17%) 100(14%)

Fifty one percent of the products from 14 still had an exo-cyclopropane intact. No products were found with an endo-cyclopropane still intact. Products 54, 96 and, possibly, 99 almost certainly resulted from reaction of iridium with the exo-cyclopropane prior to reaction of the endo-cyclopropane. The intermediate product enroute to 54 and 96 would either be 95 or 101 (see Figure 21), since 15 and possibly 102 would be expected to give the opposite regioselectivity.

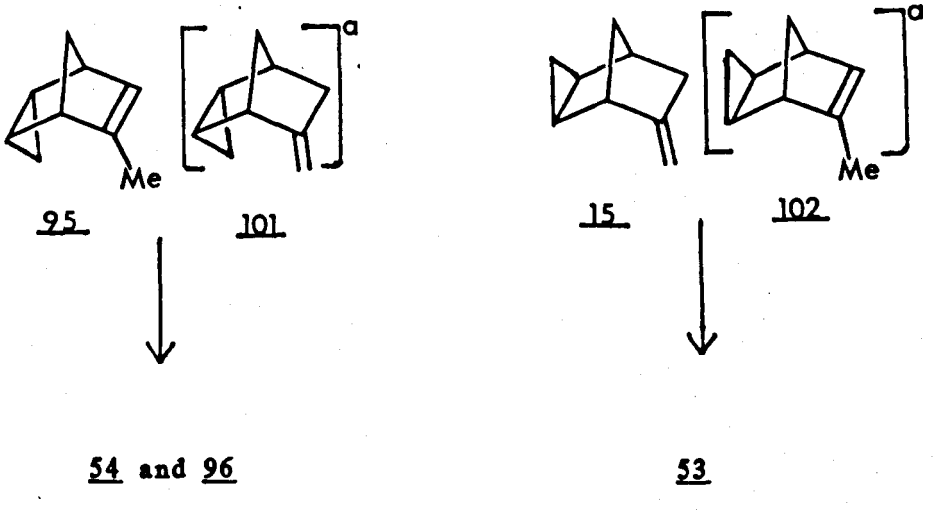


Figure 21. Intermediate Products from the Reaction of 14 with Iridium.

a) brackets indicate intermediates or products that were not observed.

Although further investigation is definitely needed, it is tempting to draw two general conclusions from these results. First, endo-cyclopropanes are kinetically more reactive than exo-cyclopropanes in $CDCl_3$. Second, the reaction rates of exo-

cyclopropanes are more seriously affected by electronic interactions from across the ring system. The first point is further supported by comparing the reactions of 11 versus 13 and 68 versus 69. In these cases, the reactions of the endo-cyclopropane substrates went to completion in less time than did the reactions of the exo-cyclopropane substrates. Support for the second conclusion, although more nebulous, comes from a comparison of the reactions of 95 and 15. Compound 95 completely reacted within 3 hours while 15 gave only a 10% conversion to products in the same time period. The endo-cyclopropane does not interact as well, in a through space manner, with functionality across the ring system as does the exo-cyclopropane. The molecular geometries of the endo-cyclopropane substrates are such that the cyclopropane orbitals that might interact with functionalities across the ring system are actually pointed away from those functionalities. On the other hand, the geometry of the exo-cyclopropane substrates is more suitable for homo-interactions. The apparently faster rates exhibited by endo-cyclopropanes in chloroform could very well be partially due to the lack of cross-ring homo-interactions, but other explanations are still elusive.

The high relative yield of 54 from 95 is certainly indicative of olefin isomerization. Isomerization between exocyclic methylenes and olefin methyl compounds has been shown, in this research, to be an iridium catalyzed process and will be discussed further in Section IV.

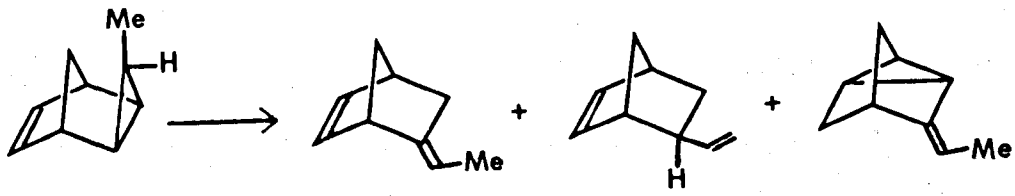
Products 98, 99 and 100 represent the only products of their types that have been observed during the course of this research. Absolute confirmation of the structures of 99 and 100 was not obtained as they proved inseparable by the several separation techniques employed.* The structures were deduced by ^{1}H and ^{13}C NMR spectroscopy (including homonuclear and heteronuclear decoupling experiments), mass spectroscopy and infrared spectroscopy. The available data for 98 and 99 can be found in the Experimental Section, but the structure elucidations will not be detailed. Compound 100 was also obtained as a product by Mark Waddington and spectral data is available in his Ph.D. Thesis.[31]

The Reaction of Syn- and Anti-3-Methyl-Exo-Tricyclo-[3.2.1.$0^{2,4}$]oct-6-ene.

The last pair of non-deuterated substrates that was investigated in this research was syn-3-methyl-exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (103) and anti-3-methyl-exo-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (104). All of the substrates used up until now have been cis-disubstituted cyclopropanes. The use of 103 and 104 provide an opportunity to preliminarily investigate trisubstituted cyclopropanes.

The reaction of 103 is summarized in equation 23. Substrate 104 failed to give a catalytic reaction under the conditions used.

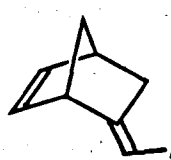
*Separation was attempted by column chromatography over silica gel, preparative gas chromatography and derivatization of the carbonyl of 99 with 2,4-dinitrophenylhydrazine.



(23)

103 105(57%) 106(33%) 107(10%)

The most noticeable aspects of the reaction of 103 are that all of the products are derived from cleavage of an exo-cyclopropane bond, and that anti-5-ethylidenebicyclo[2.2.1]hept-2-ene (105) shows sterioselectivity as well as regioselectivity of reaction (the geometric isomer of 105 was not obtained as a product of this reaction). Further, exo-5-vinylbicyclo[2.2.1]hept-2-ene (106) can conceivably be formed by β-hydride elimination of a methyl hydrogen. 105 to 106 isomerization however has also been shown to occur (equation 24). Isomerization of 105 does not occur in the absence of catalyst.



105 → 105 + 106 + 107 (24)

105 (37%) (25%) (38%)

The methyl group in 105 has a strong orienting effect relative to iridium insertion into the cyclopropane ring. A similar effect was noted with the reaction of 85. The methyl group might be envisioned as donating electron density into the cyclopropane ring rendering the exo-cyclopropane bonds more electron rich. This might occur by hyperconjugative electron donation into the HOMO of the

cyclopropane. Alternatively, the methyl group may aid in stabilizing a developing cationic charge on C_3 during a transition state or in an intermediate. Similar methyl group effects have been noted in reactions with rhodium catalysts.[32,33,34]

More investigation of trisubstituted cyclopropanes is needed before any firm conclusions about these results can be put forth.

Section II

^1H and ^{13}C Nuclear Magnetic Resonance (NMR) Data

The primary analytical tool in this research was NMR spectroscopy. NMR data was used in structure elucidation and in the determination of deuterium positions and content in starting materials and products. It is appropriate that a discussion of this all-important data be presented. It was deemed most facile to present this section prior to discussion of deuterium labeling experiments. The emphasis of this discussion will be on the general spectral features used in identification of products with particular attention paid to characterization of new products. Specific proton assignments of ^1H NMR data will also be detailed for positions which will become important for the deuterium labeling experiments. Several example spectra will be provided for discussion. This section is not, however, intended as a detailed discussion of all the spectral data that have been acquired. For details that are not presented in this discussion the reader is directed to the Experimental Section of this thesis. All compounds that have been

previously reported in the literature are referenced, but overall, the data presented in the Experimental Section of this thesis is more detailed than can be found in the literature.

Cyclopropane Compounds

The majority of substrates used in this investigation contained a cis-disubstituted cyclopropane moiety constrained to a rigid ring system. The cyclopropanes were either endo- or exo- in relation to the rest of the ring system and each of these has its own spectral characteristics. Figure 22 uses compound 11 to point out general structural features and further provides some of the terminology that will be useful in this and later discussion.

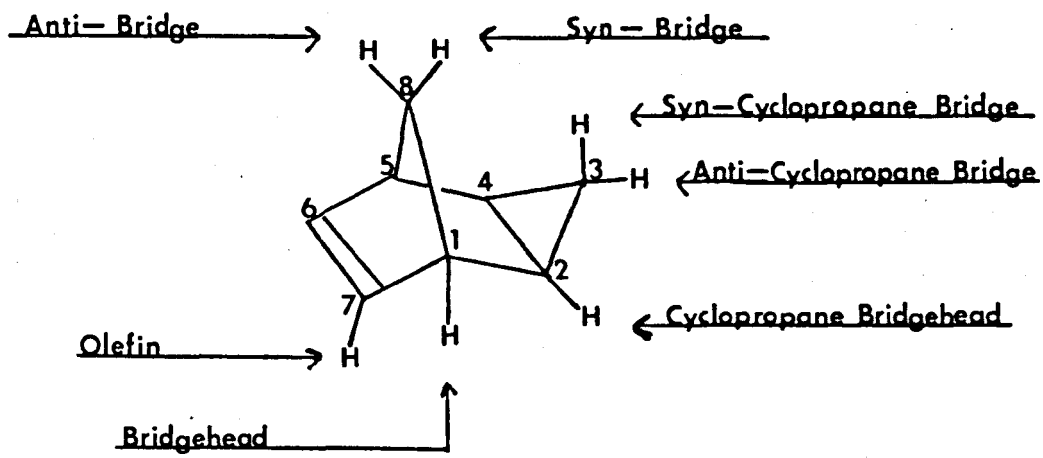


Figure 22. Structural Features of Cyclopropane Substrates.

The ^1H NMR spectrum of 11 is shown in Figure 23 and is used to illustrate some typical features. The spectrum of 13 is shown in Figure 24 for comparison. The substrates used in this investigation typically contain a plane of symmetry (with the exception of 85 and 95) which bisects the cyclopropane ring and the bridge carbon. Thus, (with the exception of 14, 85, 95, 103 and 104) three resonances for the cyclopropane protons are present in these spectra.* Two cyclopropane bridge resonances are present which show geminal coupling and coupling to the cyclopropane bridgehead protons. The geminal coupling is usually on the order of 6 to 7 Hz. The distinction between the syn and anti positions is made by examination of the coupling constants to the cyclopropane bridgehead protons. The syn cyclopropane bridge proton typically resonates at higher field than does the anti cyclopropane bridge proton. The syn position will typically show a 3 Hz coupling to the cyclopropane bridgehead protons, whereas the anti position will show a larger coupling on the order of 6 to 7 Hz. Thus the syn-cyclopropane bridge proton has the appearance of a doublet of triplets while the anti proton has the appearance of a simple quartet. It might be further pointed out that the couplings for all of the compounds discussed are consistent with the trend established by Karplus which relates the dihedral angle of adjacent protons to the magnitude of the

*Compounds 103 and 104 have two cyclopropane resonances, compound 14 has six and compounds 85 and 95 each have four cyclopropane resonances. The cyclopropane proton resonances, nonetheless, still fit the general patterns being discussed.

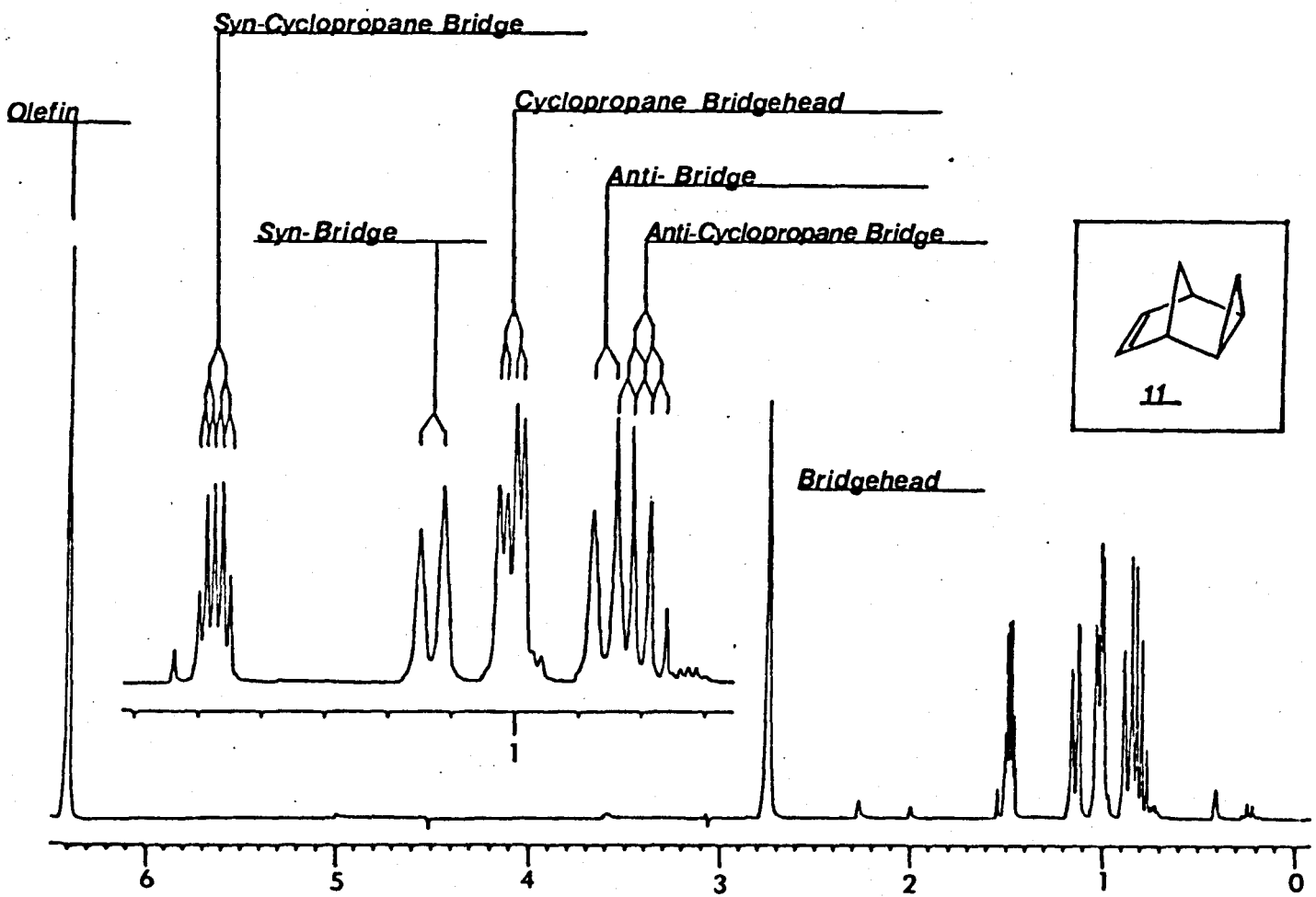


Figure 23. ^{1}H NMR Spectrum of 11.

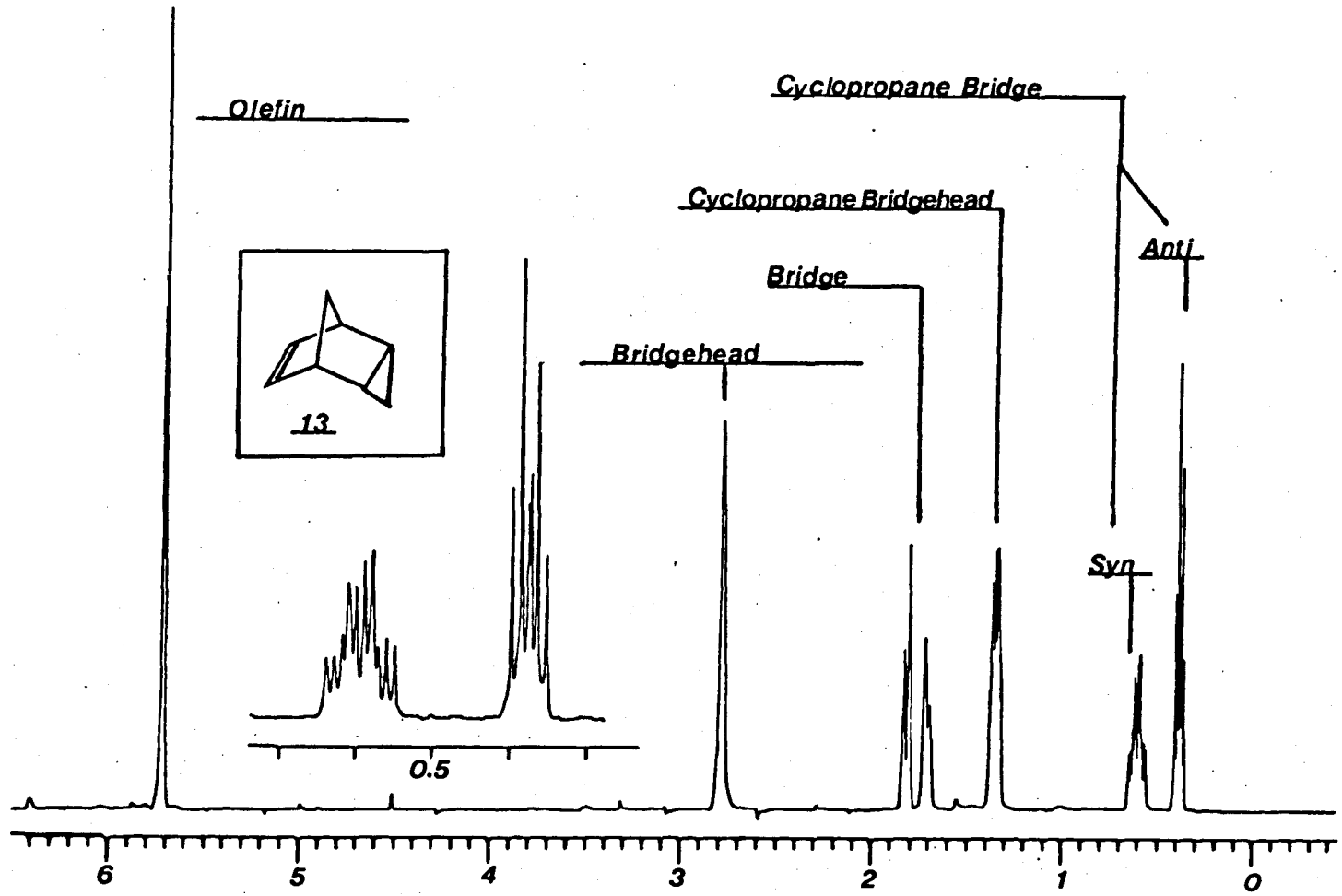


Figure 24. ^{1}H NMR Spectrum of 13.

coupling constant.[35] In addition to the cyclopropane bridge couplings, the cyclopropane bridgehead protons experience one other coupling depending on whether these protons are endo or exo. If they are endo, they will show a W-coupling to the anti bridge proton of between 1.5 to 2.5 Hz, and if they are exo they will show a 2 to 3 Hz coupling to the adjacent bridgehead protons. The bridge protons appear as broad doublets or doublets of multiplets depending on other structural features of the compound. Bridge protons will also show variability in chemical shift. The geminal coupling for bridge protons is typically 8 to 10 Hz.

Deuterium labeling of 11 gave 11a with deuterium at both of the cyclopropane bridge positions. Figure 25 shows the high field portion of the spectrum of 11a. Compare Figure 25 and Figure 23. The positions of deuterium in 11a were confirmed by the reduction of the associated integrals and by the loss of coupling to the cyclopropane bridgehead protons. Deuterium labeling of 13 gave 13a with deuterium at the cyclopropane bridgehead positions. This was confirmed by a decrease in the associated integral of the cyclopropane bridgehead resonance and loss of coupling to the cyclopropane bridge protons.

Figure 26 gives the ^{1}H NMR spectrum of 68a. Deuterium was incorporated into the syn and anti positions of the cyclopropane bridge. The cyclopropane resonances of the non-deuterated material are very similar to the analogous resonances in the spectrum of 11 (Figure 23). In Figure 26, note the almost complete loss of coupling

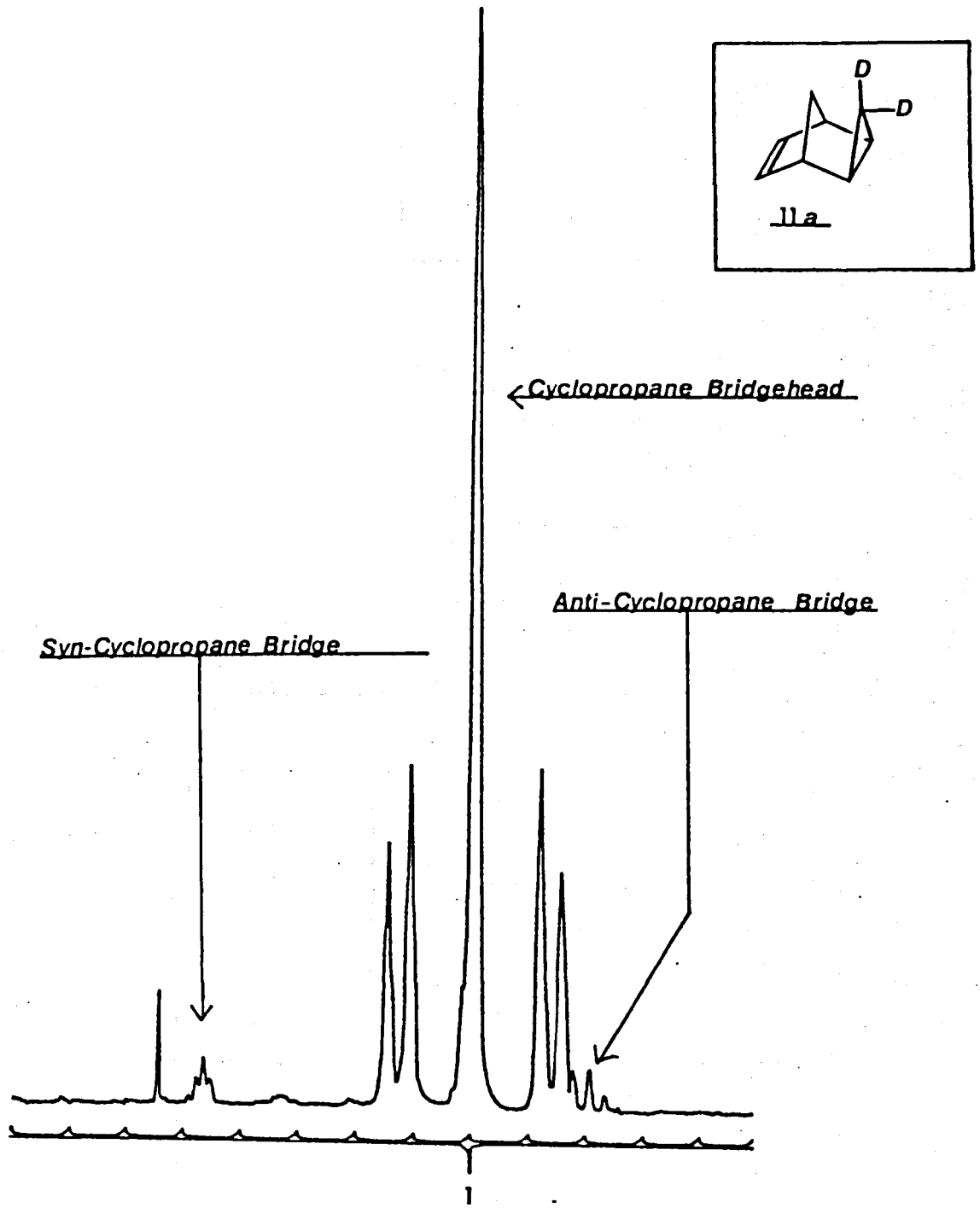


Figure 25. High Field Region of the Proton NMR Spectrum of 11a.

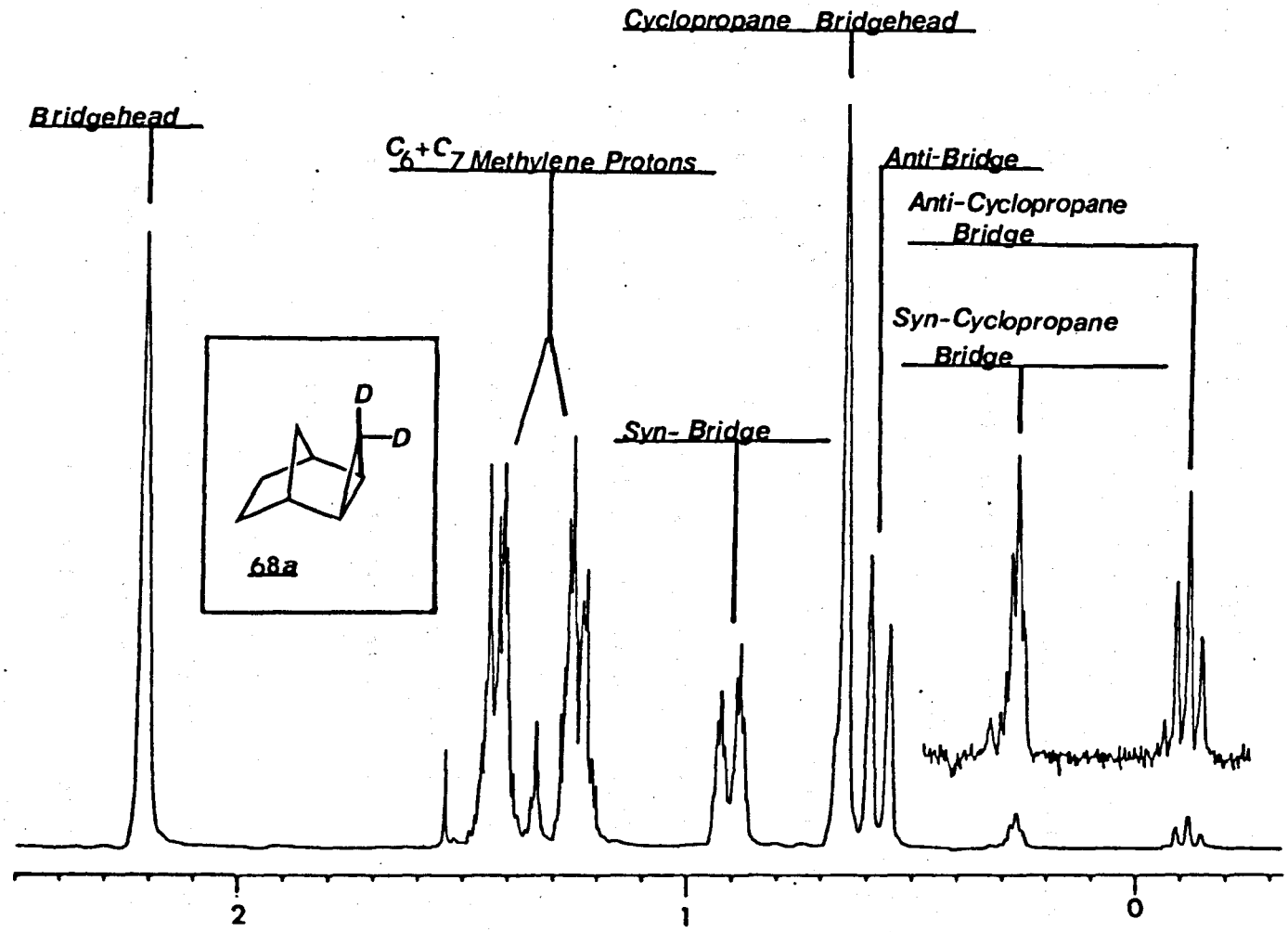


Figure 26. ^{1}H NMR Spectrum of Compound 68a.

to the cyclopropane bridgehead protons and the reduction in the intensity of the cyclopropane bridge proton resonances. It might be further noted that the cyclopropane bridge protons show a loss of geminal coupling. The percent deuterium for each position can be calculated by integration of the respective resonances and dividing that integral by the integral of a one proton resonance of a non-deuterated position. Of course, proper corrections must be made for resonances which are associated with more than one proton.

The stereochemistry of the bridge cyclopropane carbons for 103 and 104 was a simple matter to determine. First, in 103 the methyl group is in the syn position and thus, the anti proton of the cyclopropane is coupled to the cyclopropane bridgehead protons by 6.4 Hz. Alternatively, in 104, where the methyl group is anti, the syn-bridge cyclopropane proton shows smaller coupling to the cyclopropane bridgehead protons of 2.3 Hz. And of course, the methyl group is coupled to the cyclopropane bridge proton in each case. Considering other factors such as Van der Waals interactions and the fact that the rest of the spectrum in each case was similar to that of 11, these structures were easily assigned.

Assignment of structures for 85 and 95 were also straightforward. Since in both cases the cyclopropane bridgehead protons were not chemical shift equivalent, the asymmetry of these compounds was obvious. Further, 85 had distinct resonances for the two olefinic protons. The proton on C_7 appeared as a simple doublet due to the lack of coupling to a bridgehead proton, whereas the

olefin proton at C_6 demonstrated coupling to the C_7 proton and to the C_5 bridgehead proton. Product 95, of course, has only one olefinic proton which is allylicaly coupled to the methyl group on C_6. Coupling patterns of the cyclopropane protons for these two compounds were consistent with an endo cyclopropane ring.

Cyclopropane carbons are easily identified in the ^{13}C NMR spectrum. They typically appear at high field (above δ20 ppm) and show carbon-hydrogen coupling constants (J_{CH}) which are greater than 160 Hz. Usual J_{CH} values for sp^3 carbons are between 125 and 135 Hz.[36] ^{13}C NMR data for compounds 85, 95 and 104 corroborate the assigned structures. ^{13}C NMR data for 103 was, unfortunately, not obtained.

Exocyclic Methylene Compounds.

Exocyclic methylene containing compounds represent a major class of products obtained from the reactions studied in this research. The proton spectra show four very distinct resonances which are characteristic of this class of compounds. Figure 27 uses compound 52 as an example to illustrate the general features of exocyclic methylenes and to introduce useful terminology. The spectrum of 52 is given in Figure 28.

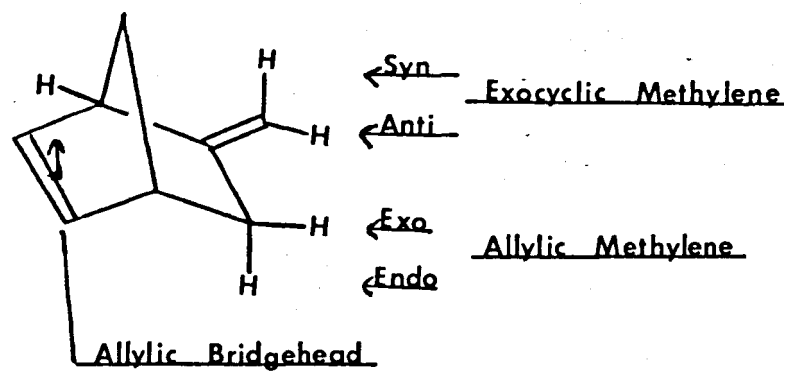


Figure 27. Structural Features of Exocyclic Methylene Products.

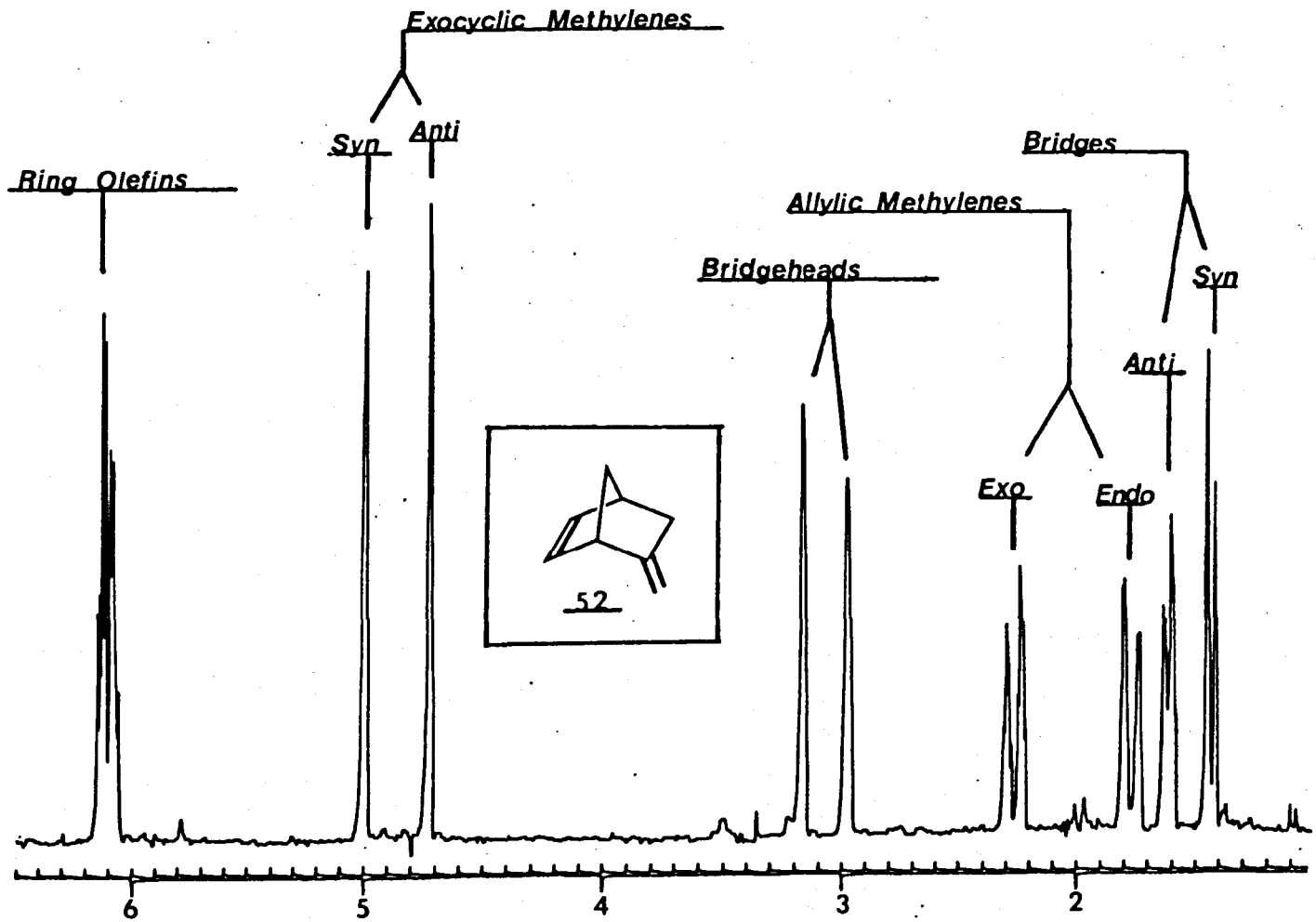


Figure 28. ^{1}H NMR Spectrum of Compound 52.

The key features in the proton spectra are the two resonances corresponding to the exocyclic methylene protons and the two resonances corresponding to the allylic methylene protons. The exocyclic methylene protons resonate between δ4.5 and 5.2 ppm. They both appear as broad singlets but are allylically coupled to the allylic methylenes and the allylic bridgehead proton. The syn-exocyclic methylene proton appears as the lower field resonance of the two. It has larger coupling to the allylic methylene protons, usually on the order of 2.5 Hz, and smaller coupling to the allylic bridgehead proton of roughly 1.5 Hz. The anti-exocyclic methylene resonates at higher field and shows coupling of 1.5 to 2 Hz to the allylic methylene protons and a typical coupling of 1.8 Hz to the allylic bridgehead proton. Allylic methylenes give patterns that range between a complex AB quartet to two distinct complex doublets. The endo position resonates at higher field, usually near δ1.7 ppm, and is W-coupled to the bridge proton oriented anti to it. The W-coupling may range between 2.5 and 3.5 Hz. The exo-allylic methylene proton resonance comes at lower field, typically between δ2.1 and 2.5 ppm, and shows coupling to the neighboring bridgehead proton of about 3 Hz. The geminal coupling between the endo- and exo-allylic methylene protons is on the order of 15 Hz.

Another interesting feature of the ^{1}H NMR spectra of exocyclic methylene compounds are the bridgehead proton resonances. The bridgehead proton that is allylic to the exocyclic methylene shows a sharper resonance which comes at lower field than the alternate

bridgehead proton.

The exocyclic methylene products from deuterated substrates had deuterium at both exocyclic methylene positions and on the exo-allylic methylene position (See Section III). The spectra of the deuterated and non-deuterated products of 72 are contrasted in Figure 29. Note the decreased intensities of the resonances corresponding to the deuterated positions (roughly 47% deuterium in each position) and the general broadening of associated resonances due to loss of proton-proton spin coupling and the addition of smaller, more complex proton-deuterium spin coupling. The most dramatic example of the loss of coupling can be seen in the resonance corresponding to the endo-allylic methylene proton at δ1.88 ppm. Here we see partial collapse of this complex doublet into a broad singlet with a concomitant upfield shift of the resonance.

Compounds 53, 54 and 96 are products that were obtained in this research but that are not previously reported in the literature. Compound 96 will be discussed later in this section. The proton spectra of compounds 54 and 53 can be found in Figures 30 and 31 respectively. Compound 54 was cleanly isolated, but compound 53 was obtained only as a mixture with 54. Therefore, the structure elucidation of 54 will be presented first.

The proton spectrum of 54 shows that all of the resonances have two proton integrals except the bridgehead resonances which have integrals equivalent to one proton. It can thus be assumed that a plane of symmetry bisects the bridge of this compound. The

bridgehead resonance at δ3.15 ppm is sharp and downfield relative to the other bridgehead resonance. The lack of coupling to the downfield resonance indicates that the corresponding proton is sandwiched between the two exocyclic methylenes. The remaining two proton resonances correspond quite nicely to the general spectral features of exocyclic methylene compounds. The allylic methylene protons appear as two complex doublets. The endo-proton resonates at δ2.0 ppm and shows a geminal coupling of 15.6 Hz to the exo-proton which resonates at δ2.27 ppm. The exocyclic methylene protons resonate as broad singlets at δ4.67 and δ4.92 ppm. Both bridge protons are equivalent and resonate at δ1.48 ppm. Elemental analysis and ^{13}C NMR data further support the assigned structure. Discussion of the ^{13}C data will follow discussion of the proton data for compound 53.

The proton spectrum of 53 is virtually identical to the spectrum of 54 with the exception of the bridgehead protons. Product 53 has only one bridgehead resonance in its spectrum. The geminal coupling constant for the allylic methylene protons was determined to be 15.4 Hz. The bridge protons are again equivalent, and two exocyclic methylene resonances are present. Overall, six resonances are present, each equivalent to two protons, and the spectrum has the general features of an exocyclic methylene compound. Elemental analysis and ^{13}C NMR data further support the assigned structure.

The ^{13}C NMR spectra of exocyclic methylene compounds have only two resonances that are unique to this compound type. The olefin

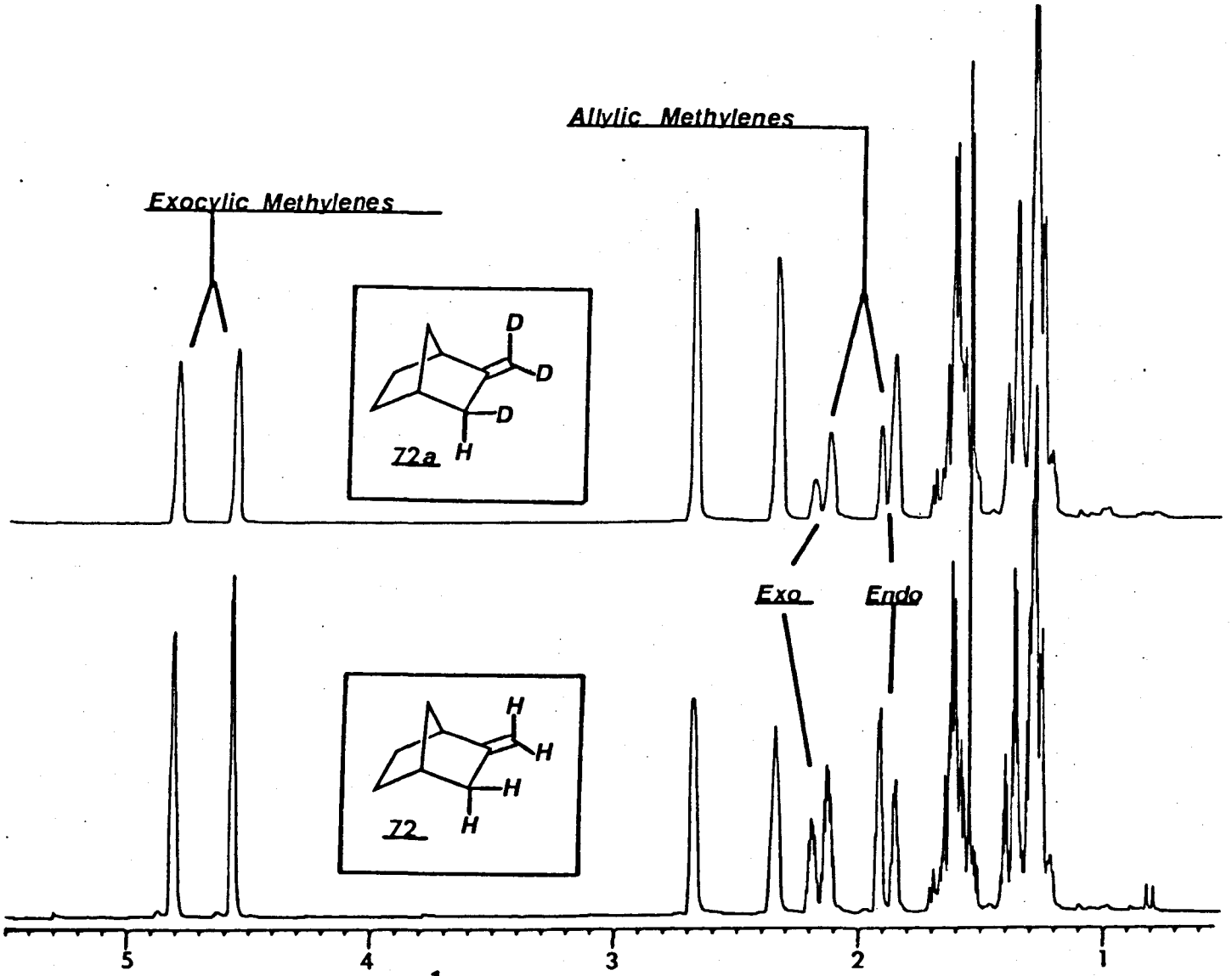


Figure 29. ^{1}H NMR Spectrum of Compounds 72 and 72a.

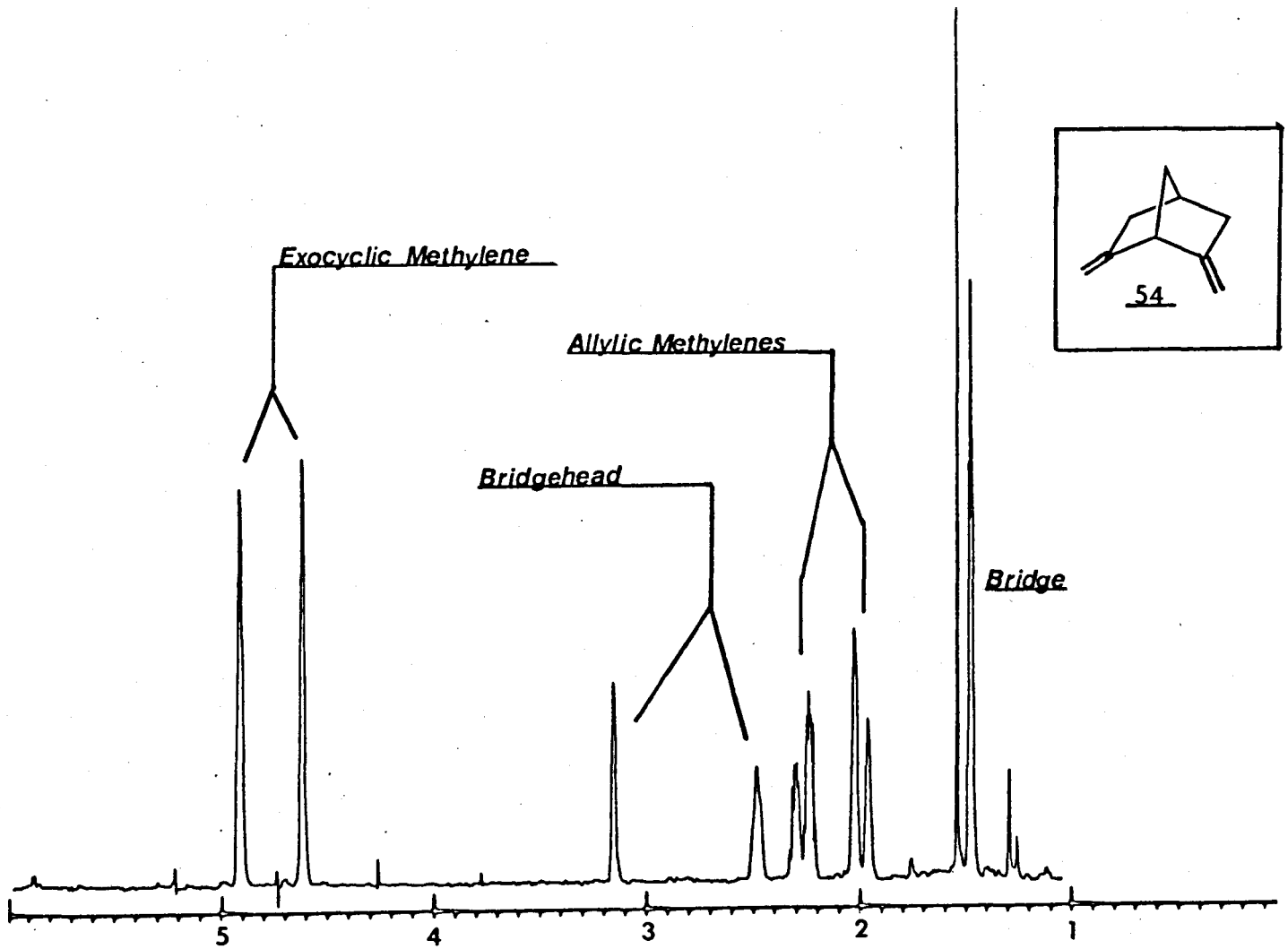


Figure 30. ^{1}H NMR Spectrum of Compound 54.

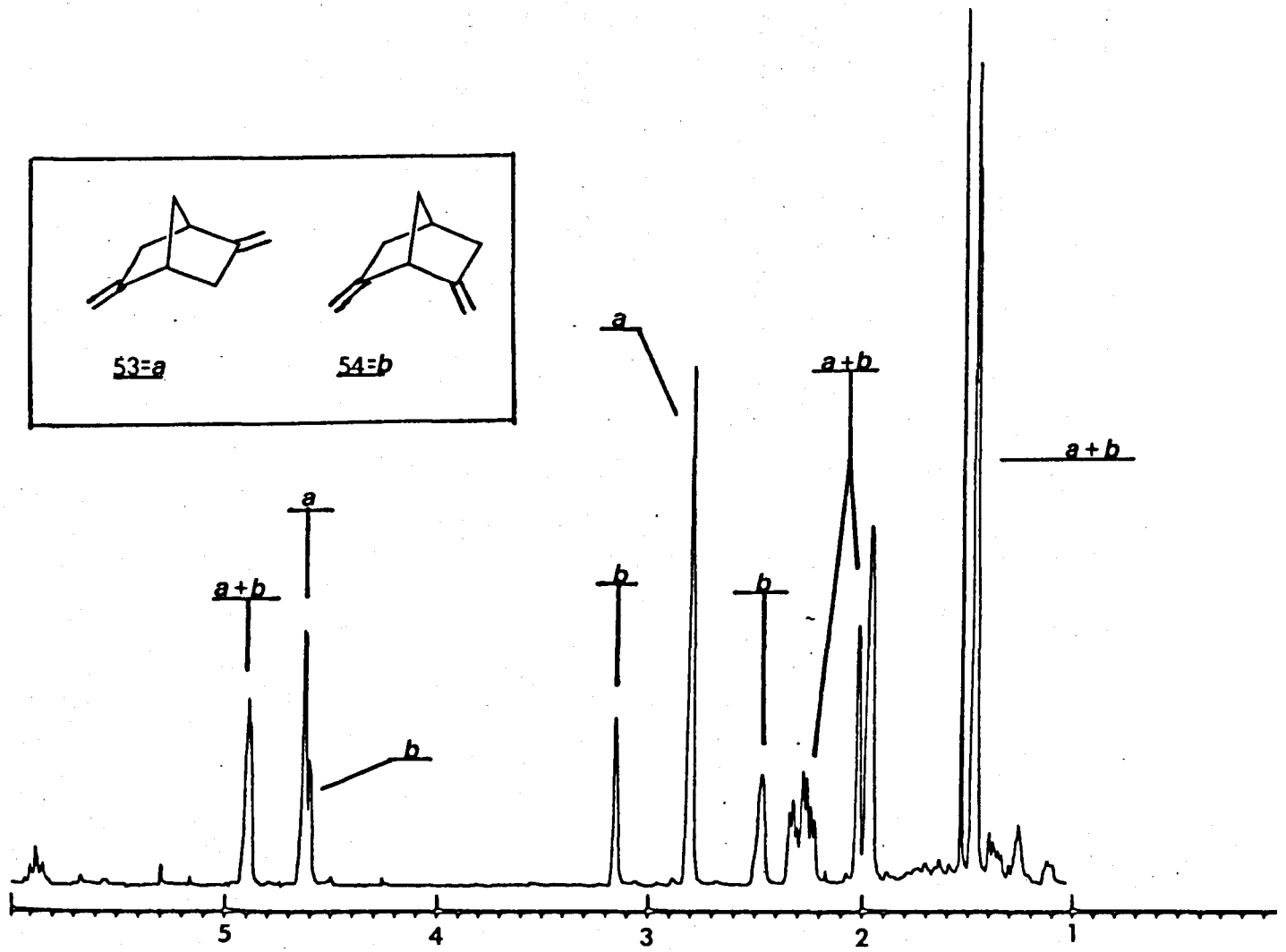


Figure 31. ^{1}H NMR Spectrum of a Mixture of Compounds 53 and 54.

carbon in the ring resonates near δ150 ppm and appears as a singlet in the gated decoupled spectrum. The terminal exocyclic methylene olefin carbon resonates near δ100 ppm and appears as a triplet in the gated decoupled spectrum with $J_{CH} \cong 155$ Hz.

Compound 53 shows two olefin carbon resonances, a triplet at δ102.4 ppm (J_{CH} = 155 Hz) and a singlet at δ153.4 ppm. The analogous resonances of 54 come at δ102.8 ppm (triplet with J_{CH} = 156 Hz) and δ152.4 ppm (singlet). Furthermore, the symmetry of 53 demands that the carbon spectrum show a total of five carbon resonances. In addition to the olefin resonances, one doublet and two triplets are expected. The doublet resonates at δ45.6 ppm (J_{CH} = 133 Hz) and the two triplets resonate at δ37.9 and 39.4 ppm (J_{CH} = 138 Hz and 127 Hz respectively). For 54, the symmetry dictates six carbon resonances. In addition to the olefin resonances, two doublets and two triplets are expected. Indeed the ^{13}C NMR spectrum agrees. The doublets resonate at δ55.3 and 36.4 ppm (J_{CH} = 152 Hz and 134 Hz respectively) and the two triplets resonate at δ36.8 and 39.9 ppm (J_{CH} = 127.6 Hz and 135 Hz respectively).

Olefin Methyl Compounds

Another less frequently encountered product type is the olefin methyl which is simply an isomer of an exocyclic methylene. The major distinguishing spectral features are a methyl doublet near δ1.7 ppm and a one proton olefin resonance near δ5.5 ppm. The methyl and olefin resonances are allylically coupled to one another by about 1.5 Hz. The bridgehead protons appear as two distinct resonances as do

the bridge protons.

Products from deuterium labeling show deuterium primarily in the methyl position. The spectra of deuterated and non-deuterated 71 are contrasted in Figure 32. Note that the intensity of the methyl resonance in the deuterated compound is reduced, but integration of this resonance could not be accurately achieved. The methyl resonance of the deuterated compound also demonstrates greater complexity due to geminal proton-deuterium coupling which was measured to be 2.1 Hz.

Compound 96, as has been stated, has not been reported in the literature. Its ^{1}H NMR spectrum is shown in Figure 33. A minor product, which is believed to be the isomer 97, is also noted in this spectrum. The olefin methyl and the exocyclic methylene functionalities are obvious in this spectrum. The endo-allylic methylene proton resonance, at δ1.82 ppm, is obscured by the methyl resonance, but irradiation of the exo-resonance at δ2.25 ppm collapses the obscured resonance to a visible singlet. The geminal coupling for these protons is 14.6 Hz. The methyl group is allylically coupled to the olefin resonance at δ5.64 ppm by 1.6 Hz. The exocyclic methylene protons are present as broad singlets at δ4.7 and 4.98 ppm. The syn nature of the exocyclic methylene relative to the methyl group was determined by considering the bridgehead proton resonances. Although both bridgehead resonances have similar chemical shifts (δ2.85 and 2.9 ppm), the δ2.9 ppm resonance is obviously sharper due to lack of coupling to neighboring hydrogens.

The broad bridgehead resonance at δ2.85 ppm is, furthermore, coupled to the olefin resonance at δ5.64 and to the exo-allylic methylene proton. These couplings are small and have not been accurately determined.

The ^{13}C NMR spectrum demonstrates nine resonances including a triplet at δ102.6 ppm (J_{CH} = 155 Hz) and a singlet at δ151.8 ppm. The olefin methyl functionality demonstrates two olefin carbon resonances which are a doublet at δ129.7 ppm (J_{CH} = 166 Hz) and a singlet at δ144.9 ppm. The methyl carbon shows a quartet at δ14.5 ppm (J_{CH} = 126 Hz). The bridgehead carbons appear as doublets and resonate at δ55.9 and 42.1 ppm (J_{CH} = 152 Hz and 146 Hz respectively). The large difference in chemical shift of the bridgehead carbon resonances is further support for the syn orientation of the methyl group relative to the exocyclic methylene.[36] The remaining two resonances are triplets and correspond to the bridge and allylic methylene carbons. They appear at δ34.8 and 49.7 ppm (J_{CH} = 135 Hz and 133 Hz respectively). Enough pure 96 was not obtained for elemental analysis but the mass spectrum demonstrates the expected molecular ion of m/e = 120.

Ring Expanded Compounds

The ring expanded compounds comprise two general classes of products that were encountered during the course of this investigation. The ring expanded tricyclo compounds will be discussed shortly in this section. The simple ring expanded

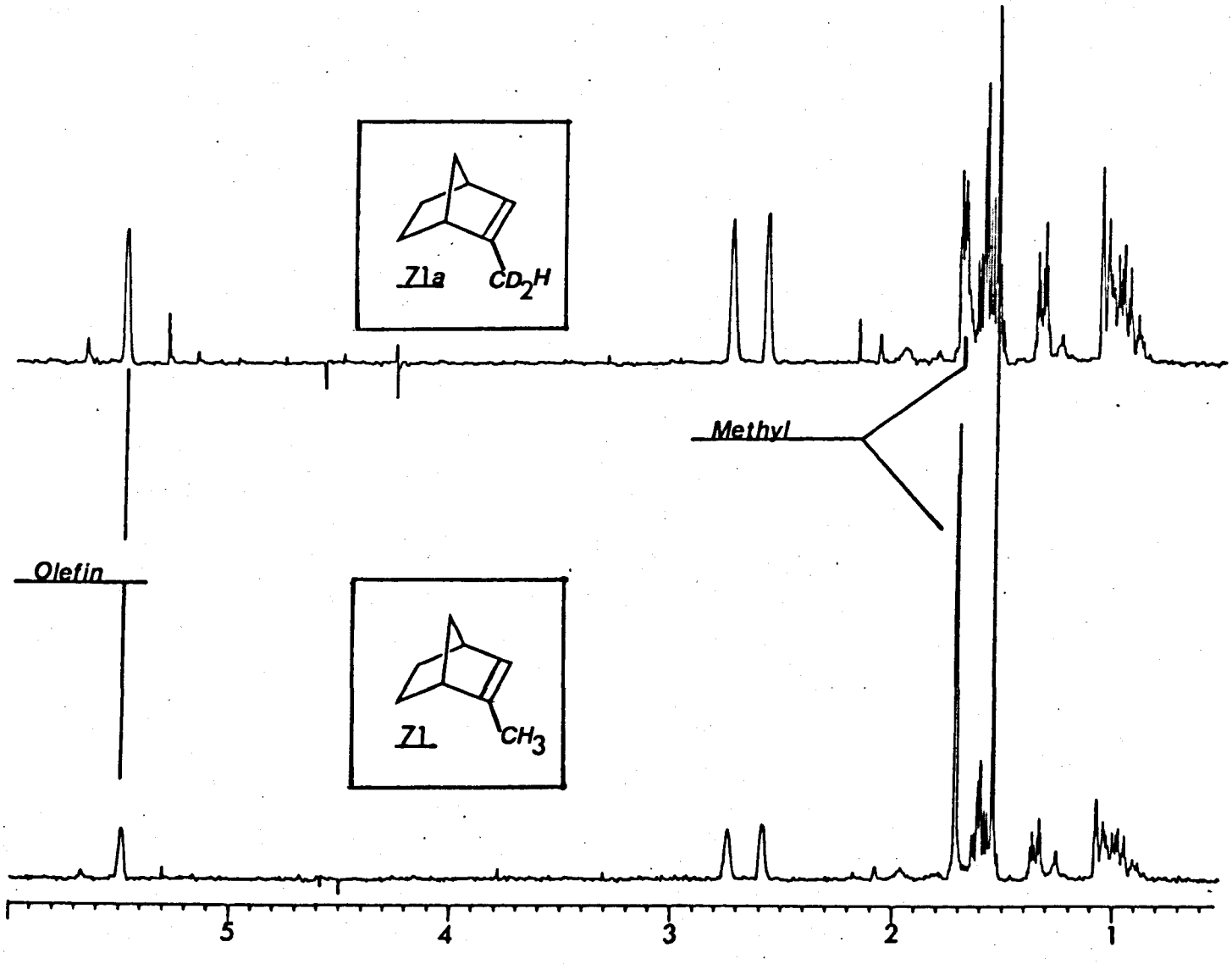


Figure 32. ^1H NMR Spectra of Compounds 71 and 71a.

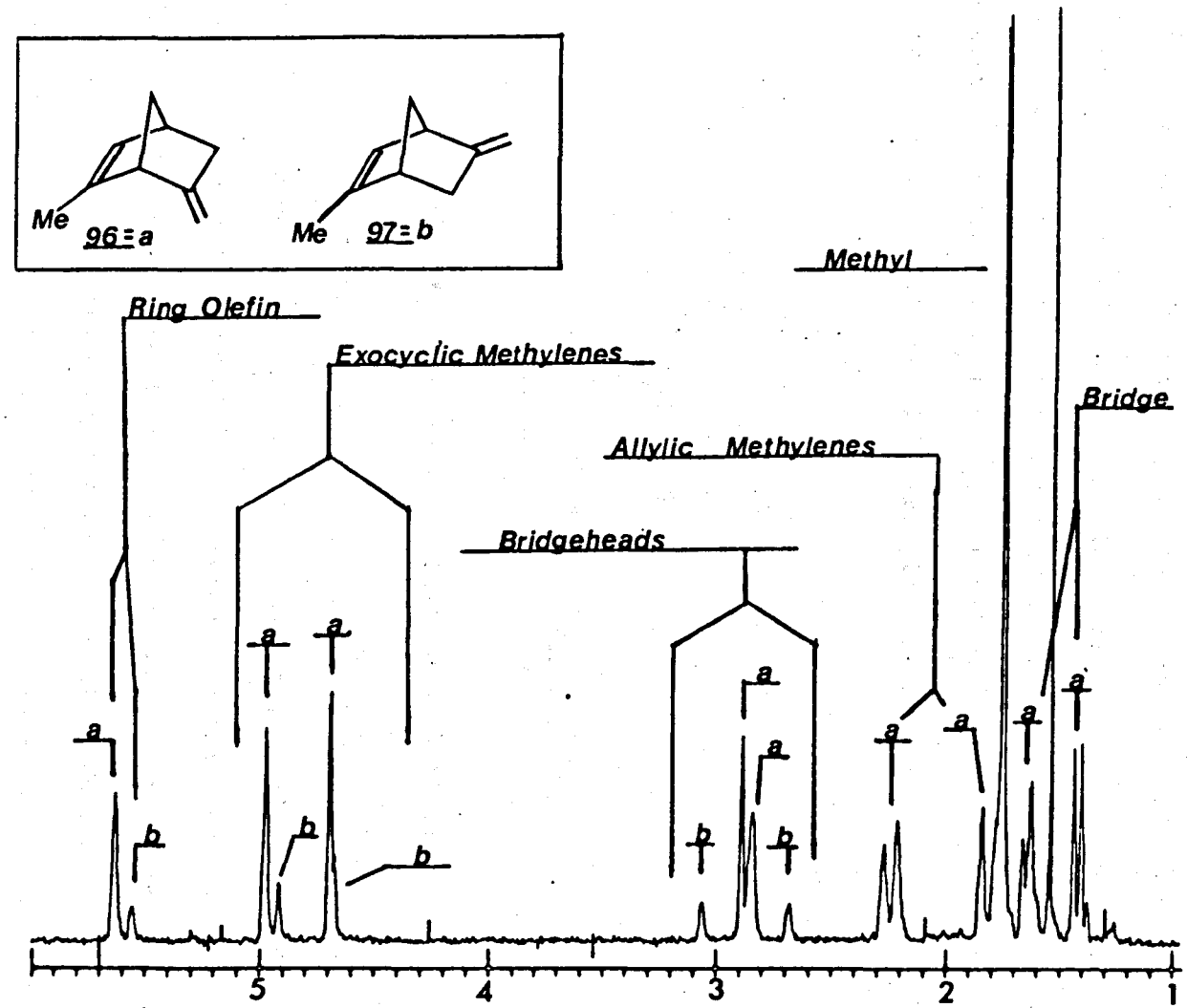


Figure 33. ^{1}H NMR Spectrum of a Mixture of Compounds 96 and 97.

compounds will be presented here.

The characteristic features in the ^1H NMR spectrum of ring expanded olefin compounds are the olefin protons themselves. Other identifiable features may or may not be present depending on other structural features of the compound in question. Figure 34 gives a representative example of a ring expanded olefin, 73, to illustrate the characteristic features and give terminology. The spectra of deuterated and non-deuterated 73 are given in Figure 35.

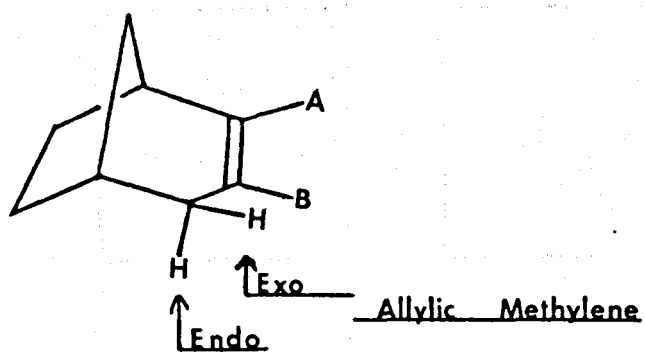


Figure 34. Structural Features of Ring Expanded Olefins.

Olefin proton A resonates at lower field than does B. These resonances appear near δ6 ppm and δ5.5 ppm respectively. Proton A shows coupling to B of about 9 Hz. Proton A is also coupled to the allylic bridgehead proton by about 6 Hz and shows various other small couplings. Thus, proton A appears as a doublet of doublets of multiplets. Proton B, in addition to the coupling to A, has a 2.5 to 3 Hz coupling to the endo-allylic methylene proton and other small couplings. The exo-allylic methylene proton is typically buried in a multiplet near δ2.5 ppm and, depending on the complexity of the

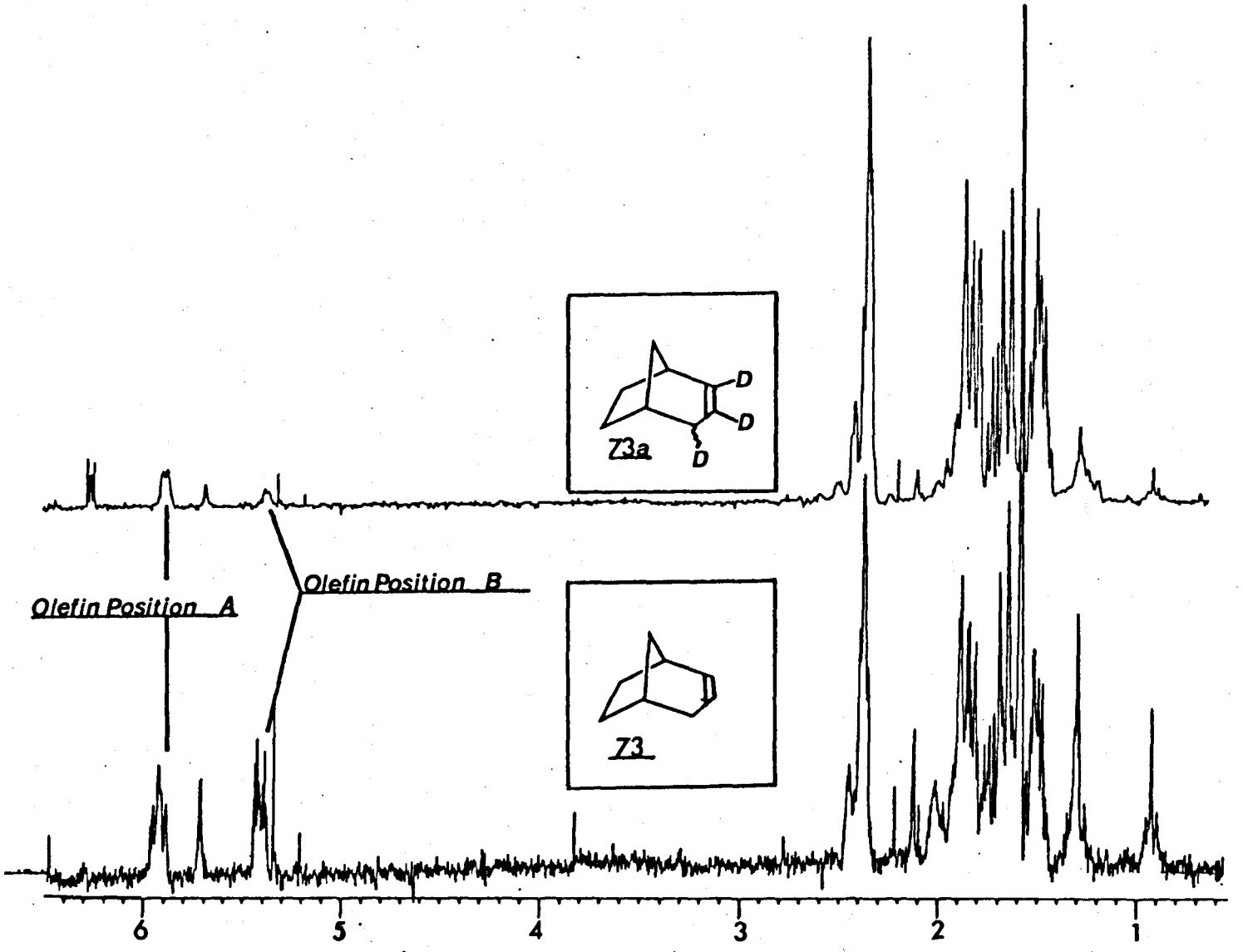


Figure 35. ^{1}H NMR Spectra of Cmpounds 73 and 73a.

spectrum, the endo-allylic methylene proton can be observed near δ2.0 ppm.[27] The geminal coupling for the allylic methylene protons is on the order of 17 Hz.

Deuterium, in these products, has been shown to be present in both olefinic positions and in the exo-allylic methylene position. Comparison of the two spectra in Figure 35 demonstrates the net effect on the NMR spectrum. Note again the general loss of coupling and reduced intensity of the resonances of the deuterated positions. The allylic methylene protons are not obvious in these spectra.

Compound 56 is also a product that has not been reported in the literature. Its ^1H NMR spectrum is shown in Figure 36. The general characteristics of the spectrum are the same as those of an exocyclic methylene and a ring expanded olefin. The carbons are numbered in the drawing in Figure 36 and the corresponding protons are indicated below the assigned resonances. The resonances and ultimately the assigned structure were determined primarily by employing proton-proton decoupling experiments. The bridgehead resonance at δ2.84 ppm is allylically coupled to the exocyclic methylene protons at δ4.93 and 5.03 ppm. This bridgehead proton does not show coupling to the ring expanded olefin proton A. Further, if this bridgehead proton were between both olefins, it would be expected to show a much sharper resonance than it does. The δ1.98 ppm doublet is geminally coupled by 17.7 Hz into the 4 hydrogen multiplet at δ2.35 to 2.55 ppm. Further coupling to the C_3 olefin hydrogen by 3.4 Hz was noted. Thus, this proton is endo on C_4. The ring olefins on C_2 and C_3 were

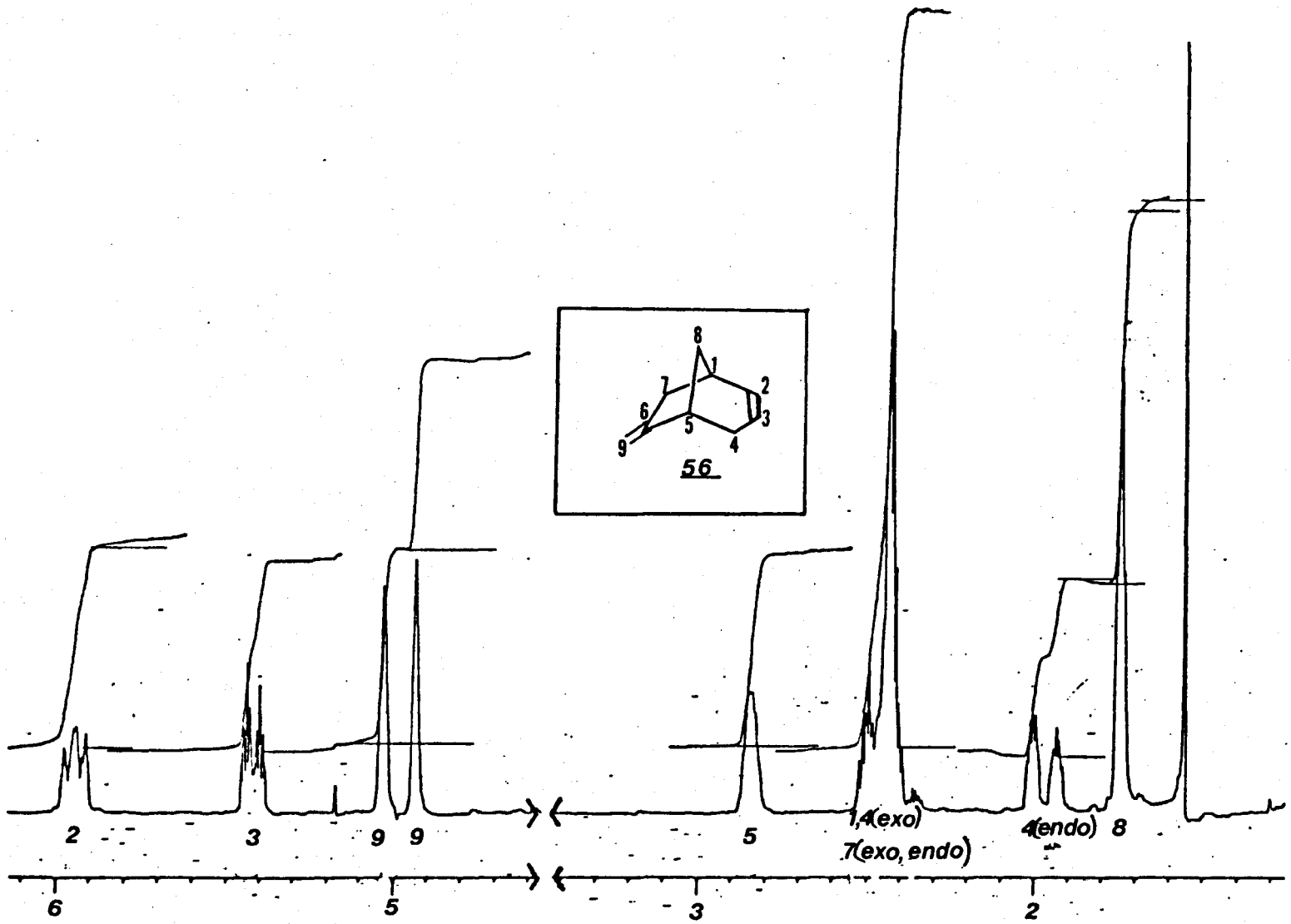


Figure 36. ^{1}H NMR Spectrum of Compound 56.

collapsed into a doublet and a doublet of doublets respectively upon irradiation of the four proton multiplet. These couplings were 9.4 Hz between the two olefin protons and 3.4 Hz between the C_3 olefin and the endo-C_4 methylene proton. The presence of the C_7 methylene protons in the large multiplet was also confirmed by the sharpening of the exocyclic methylene proton resonances upon irradiation of the multiplet. Elemental analysis corroborated the structure.

Tricyclic Ring Expanded Products

The last product type that will be presented is the tricyclic ring expanded products. Compounds 47 and 86 are the only compounds of this type that were cleanly isolated and characterized in this investigation. Compound 86 is not reported in the litrature. Compound 47 is known, but discussion of the proton NMR is necessary relative to deuterium labeling experiments. The ^1H NMR spectrum of 47 is shown in Figure 37 with the resonances labeled relative to the corresponding carbon number.

The doublet at δ0.7 ppm corresponds to the endo-protons on C_6 and C_8. This assignment is based on the large geminal coupling of 11 Hz exhibited by this two proton resonance. The two proton resonance at δ1.53 ppm is a doublet of doublets with couplings of 11 Hz and 4.3 Hz and corresponds to the exo-protons on C_6 and C_8. The 4.3 Hz coupling is to the bridgehead proton on C_5. The one proton resonance at δ1.59 ppm is a multiplet with coupling to the olefin, the C_5 bridgehead and 7.7 Hz to the two proton doublet at δ1.39 ppm. The

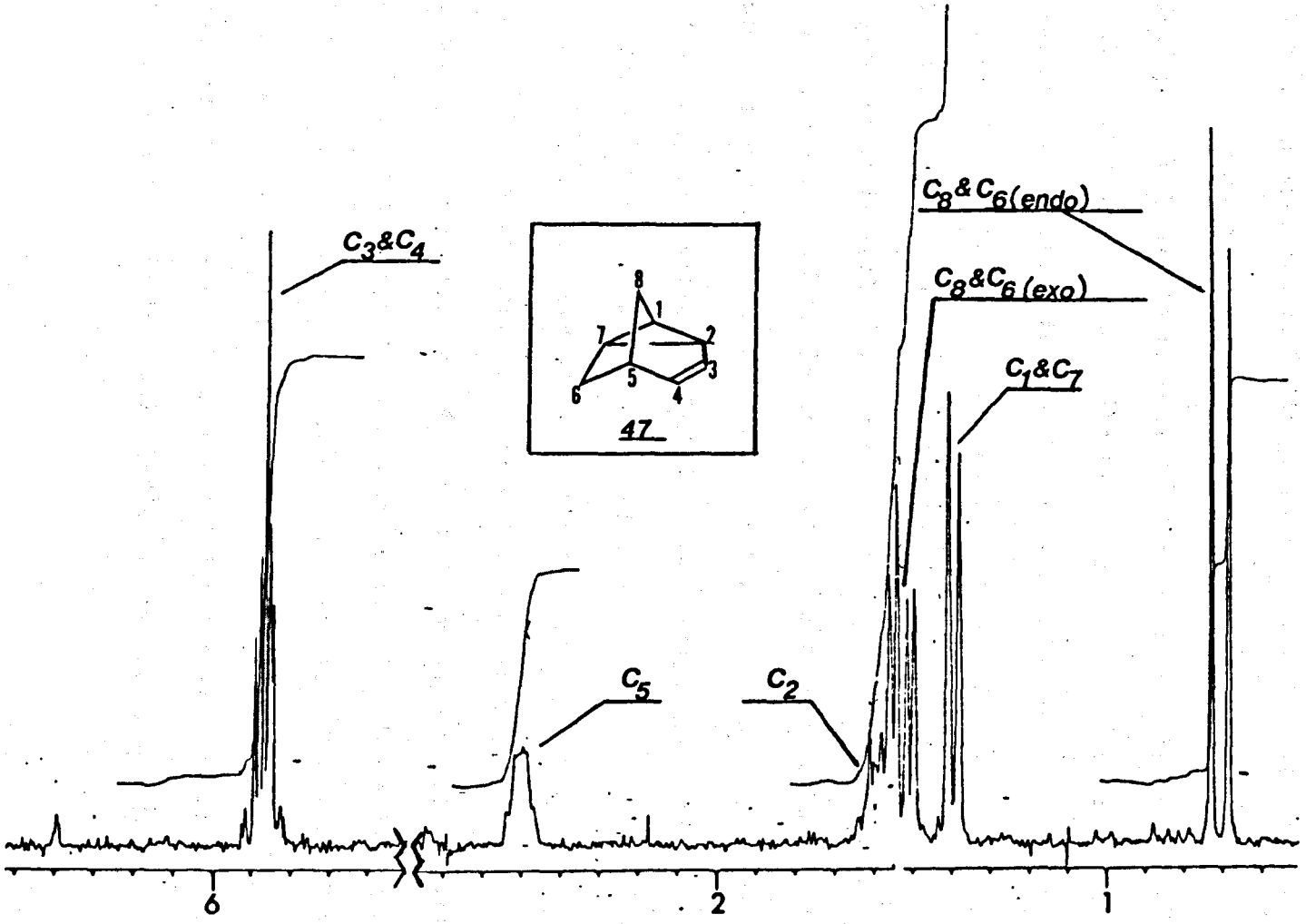


Figure 37. ^{1}H NMR Spectrum of Compound 47.

resonances at δ1.39 and δ1.59 ppm are assigned to the cyclopropane protons on C_2 and on C_1 and C_7 respectively.

The ^1H NMR spectrum of 86 is given in Figure 38. Comparison of this spectrum with that of 47 demonstrates a great deal of similarity. The C_6 and C_8 protons and the C_1 and C_7 protons show virtually identical patterns. The C_2 proton resonates at lower field than the analogous proton in 47 but does show similar coupling to the C_1/C_7 protons (7.3 Hz). The position of the methyl group on the olefin is logical not only due to the position of the resonance (at δ1.73 ppm) which is typical for olefin methyls, but also by virtue of the allylic coupling of 1.6 Hz to the olefin resonance at δ5.5 ppm. The olefin proton also shows 4.0 Hz coupling to the C_2 cyclopropane and 1.1 Hz allylic coupling to C_5. Thus the methyl group is one carbon removed from the cyclopropane ring.

^{13}C NMR data and elemental analysis further support this structure. The cyclopropane ring is evidenced, in the carbon spectrum, by two doublets at δ14.0 and 14.2 ppm (J_{CH} = 172 Hz each). The methyl resonance appears as a quartet at δ20.2 (J_{CH} = 125 Hz). The C_6/C_8 resonance comes at δ27.8 ppm as a triplet (J_{CH} = 130 Hz), the bridgehead carbon is a doublet at δ37.4 ppm (J_{CH} = 139 Hz) and the two olefin carbons appear as a doublet and a singlet at δ114.8 and 138.2 ppm respectively. The olefin doublet had J_{CH} = 161 Hz.

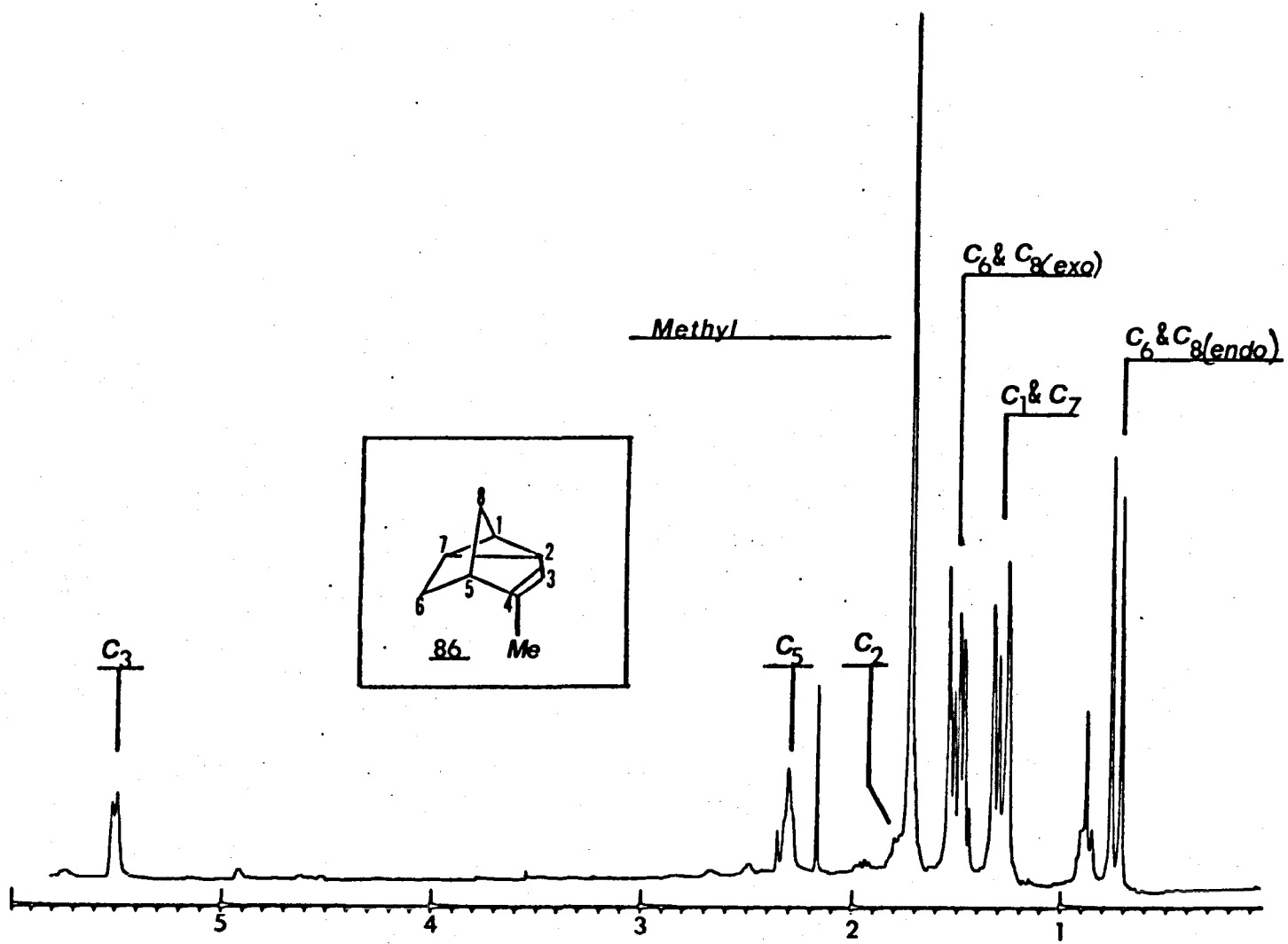


Figure 38. ^{1}H NMR Spectrum of Compound 86.

Section III

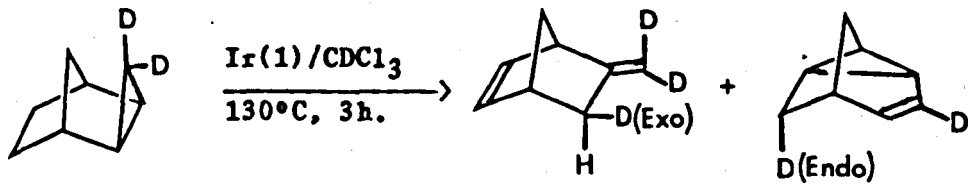
Reaction of Deuterated Substrates

In order that we might gain a better insight into the mechanistic transformations of the reactions of cyclopropanes with iridium, substrates 11a, 12a, 13a and 68a were synthesized with deuterium label as shown in Figure 39.

The deuterium position and content in the starting material and products was determined using ^1H NMR spectroscopy. The deuterium content of each position was calculated from the NMR data by comparing the integral of the corresponding resonance of a deuterated position with the integral of a non-deuterated position. Deuterium content calculated in this way is subject to error. Deviation as high as $\pm 3\%$ has been observed in repetitive NMR analyses in certain cases.

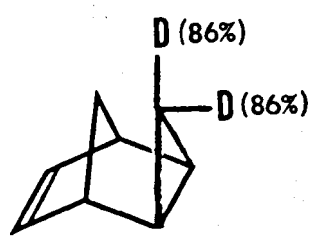
Reaction with Substrate 11a

Reaction of substrate 11a gave the results summarized in equation 25 and Table 4.

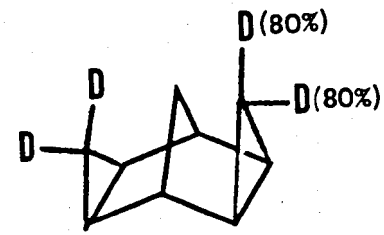


(25)

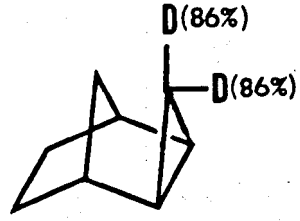
11a 52b 47c



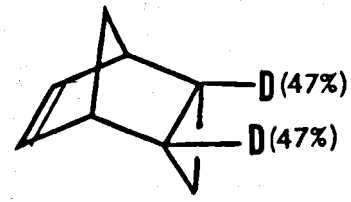
11a



12a



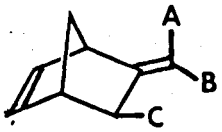
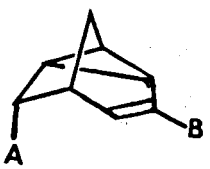
68a



13a

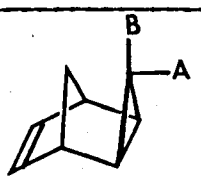
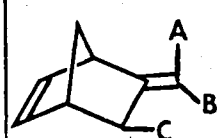
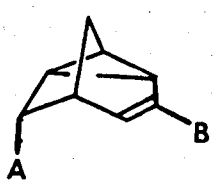
Figure 39. Deuterium Labeled Substrates.

Table 4. Results from the Reaction of 11a with Ir(1)

Product	Relative Yield	% Deuterium found for Position		
		A	B	C
	35%	75	75	5
	63%	83	44	–

Substrate 11a was also diluted with substrate 11 to afford a mixture that contained 50% deuterium for both the syn and anti positions of the cyclopropane bridge. This mixture was subjected to the usual reaction conditions for 1 hour. Analysis of the products and remaining substrate gave the results summarized in Table 5.

Table 5. Results from Reaction of 11/11a Mixture

Compound	Relative Yield	Relative Yield of Products	% Deuterium Found for Position		
			A	B	C
	76%	--	57%	57%	--
	11%	46%	47%	47%	0%
	13%	54%	28%	56%	--

The results from these two experiments demonstrate several points. The deuterium positions in 52b are consistent with the mechanism proposed in Figure 11 (Path A) on page 35. According to this mechanism, deuterium in the cyclopropane bridge positions should be in the exocyclic methylene positions of the product. Overall, the results for product 47c are consistent with the general mechanism proposed in Figure 11 (Path B) and with the mechanism for the analogous rhodium catalyzed process proposed by Katz (See Figure 9 on page 24).[28] However, the endo position on C_6 of 47c (labeled A in Tables 4 and 5) shows substantially lower deuterium content than expected. Since this deuterium is proposed to be transferred from the anti cyclopropane position of 11a via an iridium hydride intermediate, it seems reasonable that deuterium is being lost by exchange with other proton sources in the reaction mixture. This phenomenon has been noted in another reaction yet to be presented, and is discussed in an article by Parshall.[37]

Further points to be considered follow. In both reactions, a product isotope effect is noted. As would be expected, the effect is greatest when the substrate has the highest deuterium content. Reaction of 11 gave 55% 52 and 45% 47. When 50% of the two cyclopropane bridge positions were deuterated the product ratio was reversed. When 86% of these positions were deuterated, 47c predominated over 52b by almost a 2 to 1 ratio. A kinetic deuterium isotope effect is also noted. Substrate that was recovered from the mixed reaction shows a higher deuterium content than does the

starting mixture. The calculated kinetic isotope effect is k_H/k_D = 1.3 which appears to be borderline between a primary and secondary effect. At lower reaction temperatures the effect may indeed be greater, but reaction at lower temperatures is not facile and gives inconsistent results. Therefore, this avenue of pursuit was abandoned.

From the results obtained, it may be deduced that a kinetic isotope effect is present for the formation of 52b but not for 47c (at least to a much lesser extent for 47c). In addition to the product isotope effect, product 47c has very nearly the same deuterium content for the B olefin position as does either position in the starting material.

So, the assumption here is that the rate of formation of 47 is not altered by the presence of deuterium in the starting material. The rhodium catalyzed isomerization of 11a demonstrated a product deuterium isotope effect but did not show a kinetic isotope effect.[28] Conversely, product 52b does show reduced deuterium content relative to the starting material. Validation of this assumption requires kinetic data, but the general trend is present. Following this line of logic, the kinetic deuterium isotope effect may be greater than estimated for the formation of 52b but is being masked by the formation of 47c. Further, assuming insertion of iridium into the cyclopropane ring is rate determining, the product isotope effect argues against an equilibrium between intermediates leading to 52 and 47 as shown in Figure 11 on page 36.[38,39] However, if the rate

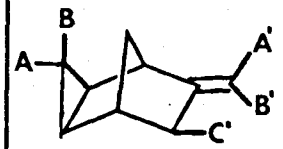
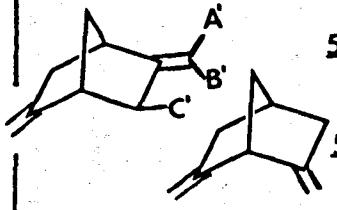
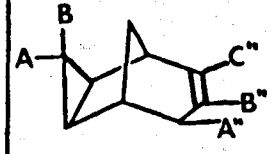
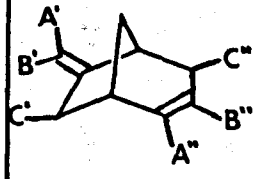
determining step is subsequent to iridium insertion, then a Puddephatt or Casey type of rearrangement might be responsible for the observed product isotope effect. Further discussion of the mechanistic implications of these results will follow the presentation and discussion of the results from the reactions of substrates 12a, 13a and 68a.

Reaction of Substrate 12a

Table 6 summarizes the results of the reaction of 12a with iridium. The starting material had 80% deuterium in each of the cyclopropane bridge positions. No startng material was recovered after a 3 hour reaction with iridium and the relative yields of products are very similar to those obtained with the non-deuterated substrate. The deuterium positions and content are interesting and suggestive, although no product deuterium isotope effect is obvious, a kinetic effect seems evident. Notice that the cyclopropane rings that are still intact show higher deuterium content than did the starting material. More deuterium scattering occurred than with substrate 11a, unequal distribution of deuterium in the various positions is noted, and in particular the A' position shows consistently higher deuterium content than does B'.

This data is not consistent with the mechanistic schemes shown in Figure 11 on page 35, but further discussion of these results will be deferred for the present time.

Table 6. Results from the Reaction of 12a with Ir(1)

Product	Relative Yield	% Deuterium Found for Position							
		A	B	A'	B'	C'exo	A''exo	B''	C''
 15a	63%	90	89	70	63	36	—	—	—
 53a 54a	25%	—	—	70	54	48	—	—	—
 55a	5%	90	89	—	—	—	42	86	31
 56a	7%	—	—	55	40	68		87	31

Reaction of 68a with Iridium

Reaction of 68a with iridium was carried out for 0.5, 2.5 and 4 hour time periods. Only the major product, 72a, and unreacted substrate were obtainable in high enough yield for ^{1}H NMR analysis. Only 72a was analyzed from all three reactions. It should be pointed out that the intent of these experiments was to follow the scattering of deuterium in the exocyclic methylene product with time. All products of the 4 hour reaction were analyzed by ^{1}H NMR and the results will be discussed.

Table 7 summarizes the GC yield data for all three reactions. Table 8 summarizes the deuterium positions and content for product 72a with respect to time. The starting material had 86% deuterium in each of the bridge cyclopropane positions.

Product 71a, isolated from the 4 hour reaction, has deuterium primarily in the methyl position. Although accurate integration data from the ^{1}H NMR spectrum could not be obtained, the methyl resonance definitely has a reduced intensity (See Figure 32 on page 77). Deuterium (13%) is also found in the olefinic position. Product 70a shows deuterium only in the methyl position. The deuterium content is 61% which is roughly equivalent to two deuteriums per methyl group. Product 73a, from the 4 hour reaction, shows the presence of deuterium on both olefinic positions. The position labeled A in Figure 34 (page 80) has 67% deuterium, and the position labeled B has 87% deuterium. The presence of deuterium in other positions of 73a is not discernable.

Table 7. Substrate and Product Yields from the Reaction of 68a with Ir(1) Relative to Time

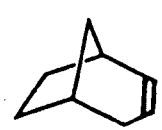
Compound	Relative Yield with Time		
	0.5h	2.5h	4.0h
 68a	81%	43%	14%
 72a	15%	47%	67%
 71a	1.6%	5%	8%
 70a	—	1%	4%
 73a	1.6%	5%	7%

Table 8. Deuterium Content for Product 72a Relative to Time

Reaction Time (hours)	Percent Deuterium for Position				Total Deuterium[a]
	A	B	C	E	
.5	51	38	59	0	74%
2.5	48	41	66	0	78%
4.5	49	51	50	15	82.5%

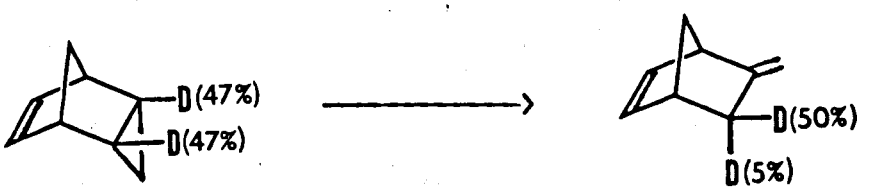
[a]Expressed as the total percent reduction relative to a two proton integral on the ^{1}H NMR spectrum.

It was previously assumed that deuterium scattering was entirely due to an iridium mediated equilibrium between exocyclic methylene and methyl olefin products. The farther the equilibria lie toward the methyl olefin, the faster the deuterium scattering should occur. Since product 71 was obtained from the reaction of 68 and no analogous product was obtained from 11, it was thought that a more dynamic equilibrium between 72 and 68 exists. An iridium mediated equilibrium between 71 and 72 has been shown to exist (See Section IV on olefin isomerization), but an equilibrium process does not completely explain the results from the reactions of 12a and 68a. An olefin isomerization equilibrium, as it was envisioned, should give products with equal deuterium content for both exocyclic methylene positions of these products. Examination of the data in Table 6 and Table 8 shows that deuterium is consistently higher in the syn-exocyclic methylene position. The data in Table 8 further reveals that, for shorter reaction times, the exo-allylic methylene position has higher deuterium content than do either of the exocyclic methylene positions. Thus the mechanistic schemes previously presented do not adequately explain the iridium mediated valence isomerization of cyclopropanes to exocyclic methylenes in these ring systems.

Reaction of 13a with Iridium

The results from the reaction of 13a are presented in equation 20 (page 47) and Table 3 (page 48). The results for the exocyclic methylene

(52a) are reproduced here for convenience in equation 26.



(26)

13a 52a (44%)

Deuterium is found only in the allylic methylene positions. A substantial product deuterium isotope is noted, and again deuterium seems to have been lost to the reaction medium. In the reaction of 13, 52 predominated over 47 by almost a 3 to 1 ratio (equation 19 on page 41). The reaction of 13a produced an inversion of yields with 47a now slightly predominating.

The loss of deuterium to the reaction medium is a mixed blessing. Due to this loss, it cannot be stated whether or not deuterium would have been found in the exocyclic methylene positions. But, assuming deuterium loss occurs only for deuteriums that are being tranferred from one carbon to another, this data suggests that the endo proton, in this case, was transferred rather than the exo proton. A better understanding of the deuterium exchange process would certainly facilitate interpretation of these results.[37]

Discussion of the Reaction of Deuterated Substrates with Iridium - Mechanistic Implications

Ignoring for the present time deuterium scrambling due to an olefin isomerization equilibrium process, some mechanistic

possibilities can be suggested to explain the observed results. The following observations must be considered in proposing any mechanistic schemes: 1) Deuterium shows an inconsistent trend depending on the substrate used. 2) Product 72a shows variable deuterium content for the deuterated positions relative to time - a trend does appear to be present here. 3) The various positions in question, in particular the exocyclic methylene positions, show an unequal distribution of deuterium at shorter reaction times. 4) Deuterium isotope effects are active, but again, are variable relative to substrate and deuterium positions. 5) The deuterium in the olefin methyl product (71a) resides almost exclusively on the methyl group.

The possible ramifications of both the product isotope effect and/or the kinetic isotope effect for the reaction of 11a are several. The rate determining step and the product determining step are not necessarily related. If however the rate determining step precedes the product determining step in the reaction pathway, then all products would experience the same kinetic effect. This is contrary to the observed results. So, it may be safely assumed that the exocyclic methylene products do not have a common intermediate with the ring expanded products. Thus, the product determining step must precede or be coincident with the rate determining step. Whether a primary or secondary isotope effect is active is not clear. The calculated isotope effect for the reaction of 11a is high in the range for secondary effects but may also be low in the range for

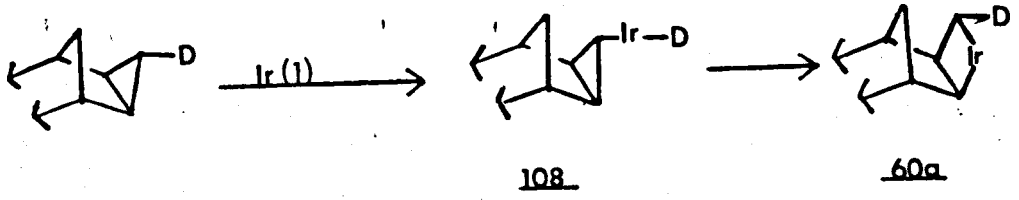
primary effects. The range for secondary isotope effects for deuterium is between k_H/k_D = 0.7-1.5 and the range for primary effects is usually 1.5 to 7.0, but these values are for reactions run at ambient temperatures.[38]

Secondary deuterium isotope effects indicate that the deuterium bearing carbon is undergoing a change in hybridization in or near the transition state of the rate determining step. A secondary effect greater than 1 is consistent with a change in hybridization from sp^3 in the ground state to sp^2 in the excited state. A primary effect is indicative of carbon-deuterium bond cleavage in the transition state. The point of the above discussion is to suggest (or evaluate) possible mechanistic options, and taking into account the available data, both a secondary and a primary kinetic isotope effect must be considered.

Previous researchers have suggested that metal insertion into a carbon-carbon bond of a cyclopropane ring is rate determining. From the standpoint of a primary kinetic isotope effect, this suggestion is inconsistent. A secondary isotope effect might be more reasonable for rate determining metal insertion into a carbon-carbon bond although, rate determining decomposition of an iridacyclobutane to give either an iridium olefin complex such as 62 or a π-allyl iridium hydride such as 61 (Figure 11 on page 35) would be more consistent with a secondary effect.

Two possibilities for a primary isotope effect seem reasonable. The first possibility is that the iridium inserts into a carbon-

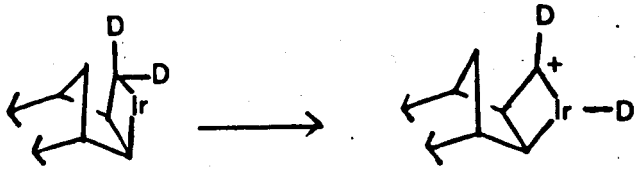
hydrogen bond instead of a carbon-carbon bond. Consider the lack of reaction of substrate 104. Figure 40 illustrates this possibility.



108 60a

Figure 40. Iridium Insertion into a Carbon-Hydrogen Bond

A second possibility is shown in Figure 41.



60a 109

Figure 41. α-Hydride Elimination of an Iridacyclobutane

Figure 41 illustrates the possibility of a rate limiting α-hydride elimination from an iridacyclobutane.

Having considered the above possibilities, results other than isotope effects must be entered into the argument. The results listed in Table 4 and Table 5 (page 91) compared to those in Table 8 (page 98) clearly demonstrate that the respective exocyclic methylene products are being formed by different pathways.

Most likely, 72a is being produced by competitive pathways. Consider the scheme shown in Figure 42. Regardless of any isotope effects, Path A adequately describes the production of 52b from 11a considering the available data. Path A may also be active in the production of 72a from 68a, but the data suggests that a competitive pathway is also present. Path B differs from Path A in that intermediates 61 and 62 are arrived at through an α-elimination followed by a 1,2-hydride shift. The net effect on the final product is that deuterium is transferred from one carbon to another through a metal mediated 1,3-deuteride shift without invoking symmetrical distribution of deuterium on the exocyclic methylene. This mechanism assumes that rotation during the formation of 61b or 62b from 110 is specific. The product should show highest deuterium content at the syn-exocyclic methylene position since both of the competitive pathways imply deuterium conservation at this position. However, averaging of the exocyclic methylene positions can occur through an olefin isomerization process as will be discussed in section IV. But before approaching the topic of olefin isomerization, discussion of the ring expanded products and overall product regioselectivity will be presented.

The ring expanded products also demonstrate some interesting results. Figure 11 (Path B) on page 35 gives a general mechanism for the formation of ring expanded products. Product 47b can be rationalized by this mechanism, and more specifically, by the mechanism proposed by Katz.[28] Products 55a, 56a and 73a do not fit

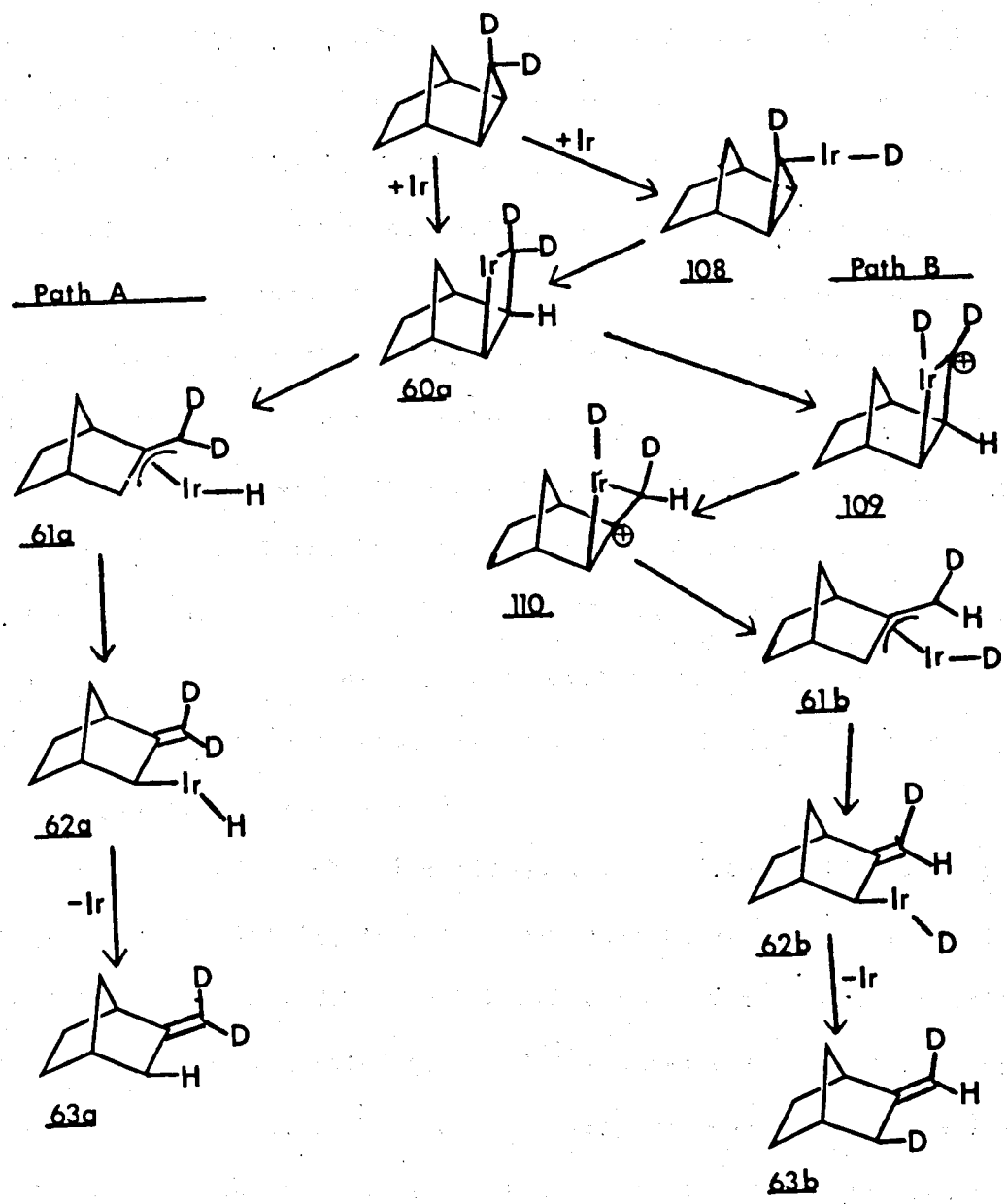


Figure 42. Competitive Pathways for the Production of Exocyclic Methylenes.

this general scheme because the deuterium in these products appear on both olefinic positions and in the exo-position of the allylic-methylene carbon. The scheme in Figure 11 demands that deuterium appear only on one olefin carbon and on the endo-position of the allylic-methylene carbon. As has already been noted, the ring expanded products do not exhibit a deuterium isotope effect. Further, their formation is affected by steric interactions from nearby atoms. Note that the relative percent composition of these products is much lower for product mixtures from 12, 68 and the exo-cyclopropane ring of 14 than for other substrates. Products 55a and 56a show identical results with respect to deuterium position and content of those positions. Product 73a also shows very similar results, although the exo-allylic position is not discernable by ^{1}H NMR analysis. A more consistent mechanism for production of 55a, 56a and 73a is shown in Figure 43.

In place of a β-hydride elimination, a 1,2-hydride shift can take place to give 111 from endo-iridacyclobutane 64a. This is certainly not a new idea. A 1,2-hydride shift to a metal bearing carbon has been suggested by Sarel[23] and has also been considered as a possibility by Katz.[27] Katz, however, demonstrated that a 1,2-hydride shift was not active in the system he was investigating. Thus, the apparent deuterium scrambling can be explained by the iridium mediated equilibrium between 67a and 67b. In this equilibrium, both 111 and 111a are olefin-iridium complexes which undergo β-hydride elimination to give the π-allyl hydride 65a. The

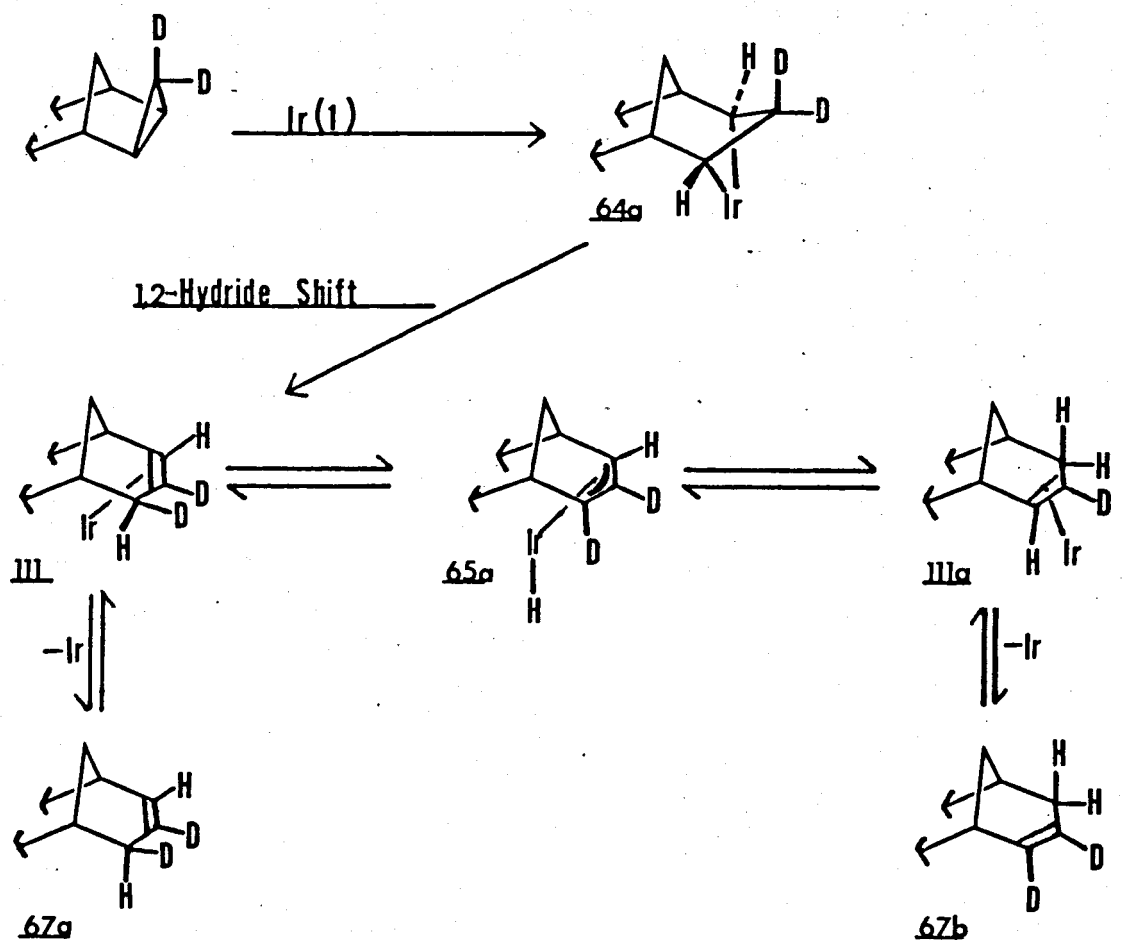


Figure 43. Mechanism for the Formation of Ring Expanded Products From Exo-cyclopropanes.

deuterium positions are fixed by the 1,2-hydride shift. The iridium in 65a, 111 and 111a is always endo and thus does not alter the observed steriochemistry of the deuteriums.

Regioselectivity and Product Deuterium Isotope Effects

The relationship between ring expanded and exocyclic methylene products, as well as the regioselectivity exhibited for products such as 53 and 54 is a consequence of either a rate determining insertion of iridium into one of the cyclopropane bonds or a 1,2-iridium shift equilibrium for the iridacyclobutanes. The latter possibility would suggest that decomposition of the iridacyclobutane is rate limiting.

As a general example consider the reaction of 13a (equation 20 on page 47). Note that the synthetic scheme used in the production of 13a would yield a product that, for the most part, would have a maximum of one deuterium per molecule of substrate. A product deuterium isotope effect was noted for the production of 47a. If iridium insertion into the cyclopropane were rate determining, no obvious rationale for selectivity of insertion into any of the three cyclopropane bonds exists (See Figure 44). If any selectivity would exist, iridacyclobutane 78b should be unique among the three possibilities. Furthermore, a secondary effect would not be expected to be very large.

Rate determining decomposition of the iridacyclobutanes is more consistent with the experimental results. A β-Hydride elimination in 78b to yield 112a would then show a primary deuterium isotope effect,

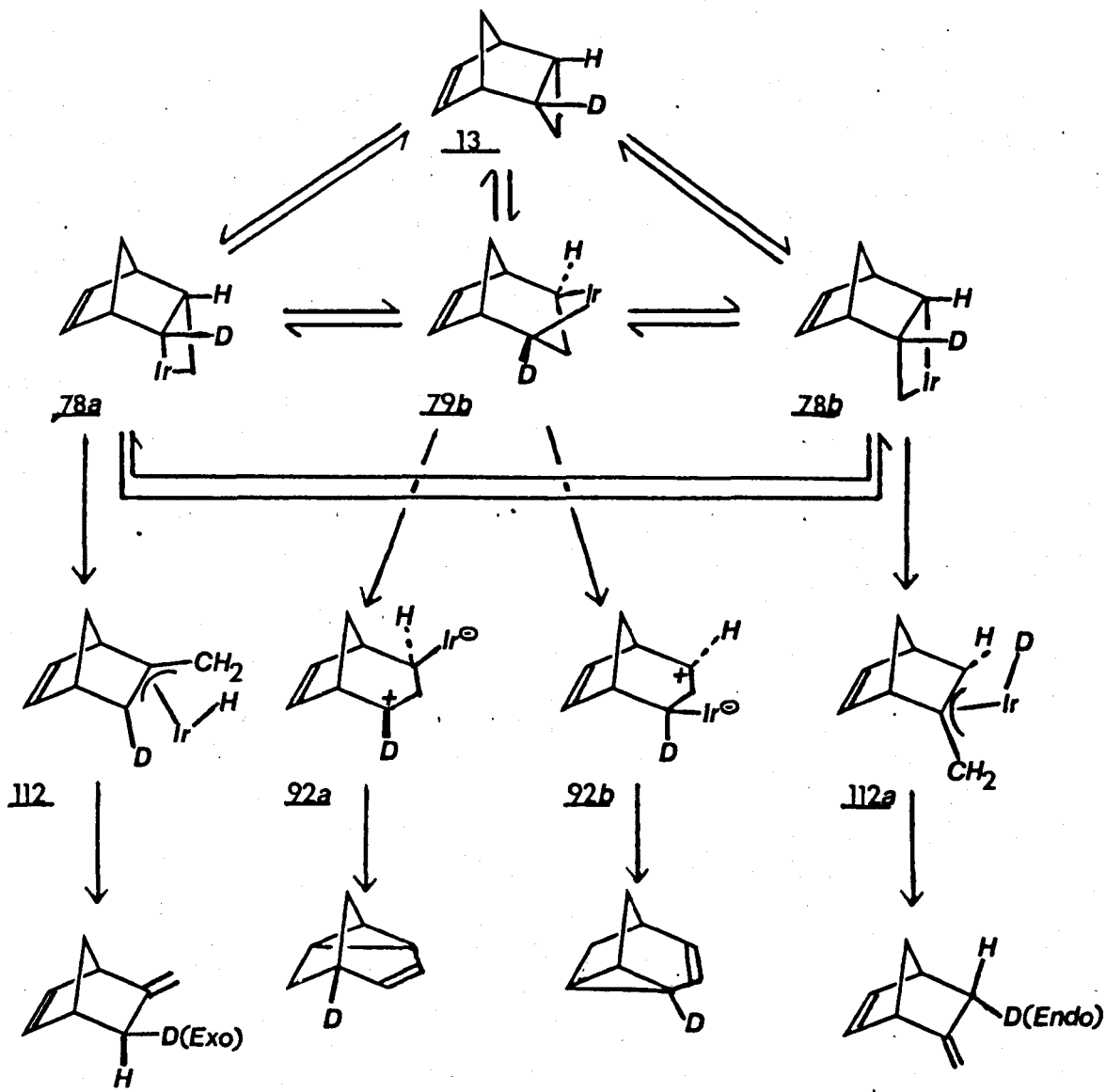


Figure 44. Product Regioselectivity from Substrate 13.

and decomposition of 78a could conceivably yield only a secondary effect. Decomposition of 79b would show a secondary effect for the formation 92a but not for 92b using this suggestion, the product distribution is a result of the position of equilibrium between the possible iridacyclobutanes, and factors affecting that equilibrium are more important for product determination than factors that affect iridium insertion into the cyclopropane. Steric or electronic interactions may favor one iridacyclobutane over another and similar effects may raise the activation barriers for 1,2-metallo shifts. Thus, an iridacyclobutane may decompose to go on to products rather than rearrange to an alternate iridacyclobutane. One possible example is the reaction of 85 in which no exocyclic methylene products were obtained and only one of the four possible ring expanded products was obtained (See Figure 16 on page 46). In this case, formation of intermediate 94 (Figure 20 page 51) from its precursor iridacyclobutane is so facile that isomerization to alternate iridacyclobutanes is not competitive. In other words, the activation barrier for isomerization is much higher than the activation barrier for decomposition of the exo-iridacyclobutane similar to 79b in Figure 44. If indeed an equilibrium exists, the reaction of 85 is resemblant of Le Chatelier's principle in which the equilibrium is virtually monodirectional due to the rapid removal of one of the products.

Similar arguments may be proposed for most of the reactions investigated in this research. The factors affecting the proposed

equilibrium are nebulous and probably range between extremes of steric and electronic affects. This aspect of iridium catalysis is certainly worth further investigation. If the reaction could be monitored by NMR spectroscopy, the above argument could be corroborated by observing a steady state concentration of iridacyclobutanes.

Section IV

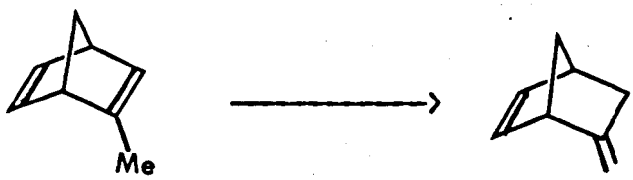
Iridium Mediated Olefin Isomerization

Olefins, like cyclopropanes, undergo reaction with transition metals and the associated chemistry can be equally intriguing. Since olefins are, for the most part, the products of cyclopropane reactions with iridium, a certain level of understanding of olefin-iridium interactions is necessary for the interpretation of data obtained in this investigation. The most important facet, relative to this research, is the iridium mediated isomerization of exocyclic methylenes and methyl olefins. Many conclusions in this research and in the literature are based on the positions of double bonds and deuteriums in the products of metal mediated organic transformations.

We were first alerted to the possible importance of olefin migration by the production of 54 from 95 (equation 21 on page 53) in which a methyl olefin functionality was converted to an exocyclic methylene. Several olefin substrates were used to investigate olefin isomerizations which, for the most part, addressed the relationships

between olefin methyl compounds and exocyclic methylenes.

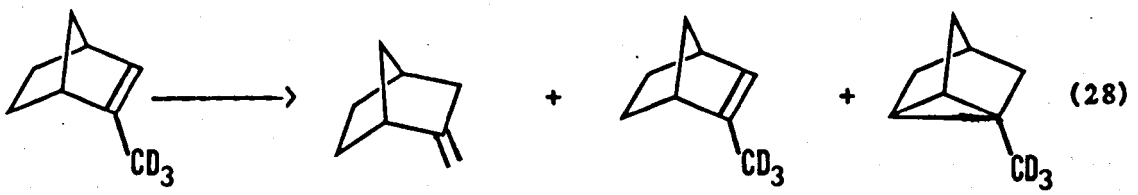
2-Methyl[2.2.1]hept-2,5-diene (113) was synthesized and subjected to reaction with iridium and gave the results shown in equation 27.



113 → 52 (32%) + 113 (68%) (27)

Reaction of commercial 105 has already been shown to yield 106 (page 57). Reactions with 105 and 113 were performed merely to further demonstrate the possibility of olefin isomerization. Compound 113 however is relatively unimportant as little evidence exists for its production or potential intermediacy in the reaction of either 11 or 13. Compound 71 however is an observed product and does have potential importance as an intermediate in deuterium scrambling. The remainder of this section will be devoted to demonstrating the relationship between 71 and 72.

Substrate 71b was synthesized as described in the experimental section with deuterium incorporated only into the methyl group. Reaction of 71b for 1.5 hours gave the results summarized in equation 28 and Figure 45.



71b 72b (74%) 71b (13.5%) 70b (12%) (28)

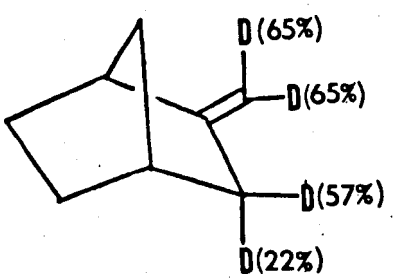


Figure 45. Position and Content of Deuterium for Product 72b.

The reaction of 71b to give 72b demonstrates that facile isomerization does occur. It also demonstrates that this isomerization gives equal deuterium content in both exocyclic methylene positions which are higher than the deuterium content in the exo-position of the allylic methylene. It might be further noted that deuterium was found in the endo allylic methylene position. Figure 46 illustrates a viable mechanism to explain these results.

The difference between the formation of 72c and 72d is in the

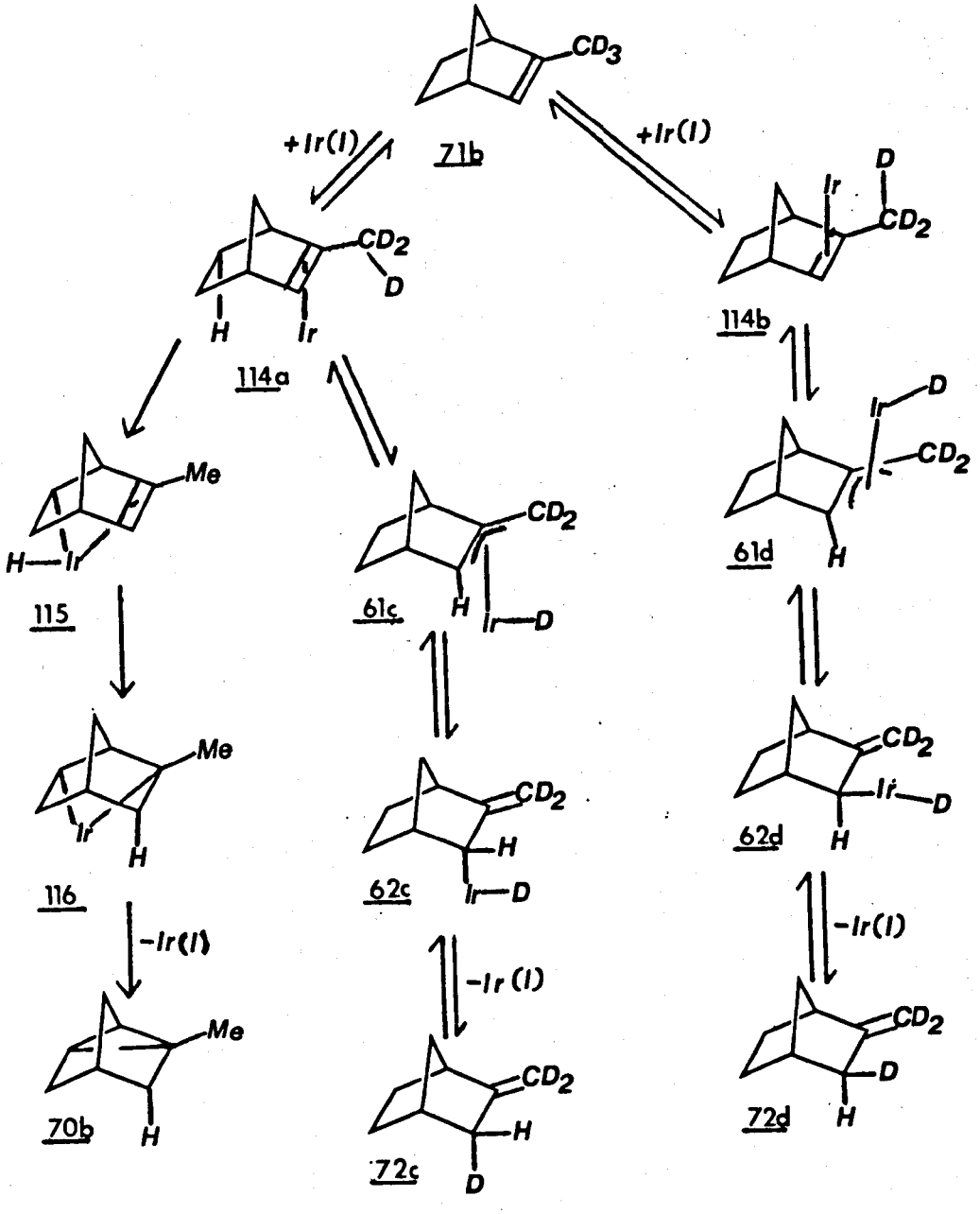


Figure 46. Mechanism of Olefin Isomerization.

direction from which iridium complexes with the double bond. If iridium complexation occurs in an exo orientation (114b), then 72d is the presumed product of reaction. Conversely, if complexation occurs in an endo orientation (114a), 72c would be the product. As implied in Figure 46, formation of 70b provides a possible alternate reaction pathway for 114a. From the results in equation 28 and Figure 45 it can be assumed that exo complexation is more facile, by almost 2 to 1 over endo complexation.

Triphenyl phosphine (Ph_3P) is a potential base in the reaction mixtures employing Vaska's catalyst. Bicyclic methyl olefins are known to isomerize to exocyclic methylenes in basic conditions[40], so a control reaction was performed in which a mixture of 71, Ph_3P and solvent were treated under reaction conditions identical to those of a standard reaction. A check for thermal isomerization was also performed. The results of these experiments are summarized in Table 9.

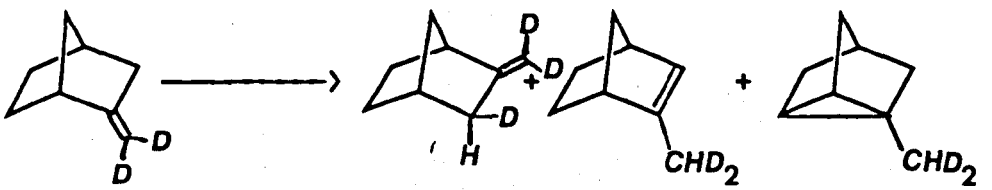
Both a Ph_3P catalyzed and a thermal process can participate in the observed isomerization, but these processes are far less facile than in the iridium catalyzed process.

It was of further interest to investigate the isomerization of 72 to 71. Assuming that the equilibrium would favor 72, it was deemed most efficient to use a deuterated substrate. Compound 72e was obtained as a major by-product in the synthesis of 71b. Compound 72e contained 80% deuterium in each of the exocyclic methylene positions with no deuterium in any other position. The reaction was

Table 9. Ph_3P Catalyzed and Thermal Isomerization of 71

Product	Relative Composition of Products	
	Ph_3P Catalyzed Reaction	Thermal Reaction
 72	18%	7%
 Me 71	82%	93%

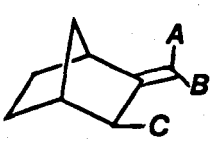
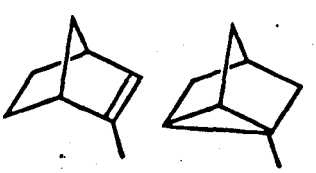
performed under the usual reaction conditions for 1 and 2 hours. The reaction is illustrated in equation 29 and the results are summarized in Table 10.



(29)

72e 72f 71c 70c

Table 10. Reaction of 72e with Vaska's Catalyst

Reaction Time (h)	Product					
						
	Rel. Yield	% D in Position			Yield (Rel. %)	Yield (Rel. %)
		A	B	C		
1	86%	73%	73%	7%	12.5%	1.4%
2	84.5%	59%	59%	29%	13.5%	2.0%

Control experiments, identical to those described for substrate 71, were performed with deuterated 72. No 72 was produced and no deuterium scrambling was noted. Thus, the results in Table 10 definitely show an iridium mediated dynamic equilibrium between 71

and 72. Review of the data from product mixtures in which 71 and 72 are present shows a consistent equilibrium ratio of about 1 to 7 respectively. The data, furthermore, indicates that equilibrium is reached rapidly.

Section V

Summary and Conclusions

This research was undertaken as an exploratory investigation to gain a better understanding of the reactions of Vaska's catalyst with polycyclic hydrocarbons containing cyclopropane moieties. Catalytic reaction with a large variety of substrates was achieved when the reactions were run in an oxygen containing atmosphere with $CDCl_3$ as the reaction solvent. The use of $CDCl_3$ potentiated the catalytic reactions such that a greater variety of substrates could be investigated and also diversified the products obtained from iridium catalysis. Overall, exocyclic methylenes predominated as reaction products. Several interesting and new products were identified in the course of this research and through the use of deuterium labeling and substrate structural modifications some unexpected reaction pathways were brought to light.

The effect of oxygen on the catalytic reaction of Vaska's catalyst is quite pronounced. Similar work by Barnett[32,33,34] with $Rh(Ph_3P)_2(CO)Cl$ and $Rh(Ph_3P)_3Cl$ has shown that a substantial increase in catalytic reaction rates occur when rhodium catalyzed reactions were carried out in an oxygen environment as compared to an argon

environment. Barnett further found that $[(Ph_3P)_2RhCl(O_2)]_2$ had similar catalytic activity in an oxygen free environment as did the other catalysts in an oxygen containing environment. The irreversible loss of Ph_3PO was discounted by Barnett because $[(Ph_3P)_2RhCl]_2$ was found to be unreactive in an oxygen free atmosphere. In the present research however Ph_3PO was found as a constituent of fresh product mixtures.

Volger[11,12] proposed that an endo-bidentate iridium complex was required in the reaction of iridium with cyclopropanes. By using $CDCl_3$ as the reaction solvent, we found that facile reactions occurred even with substrates that were reported to be unreactive. Substrates such as 14, 68, 69 and others are incapable of endo-bidentate coordination, but they do react catalytically with iridium. Thus, Volgers hypothesis was discounted (at least in a $CDCl_3$ medium), and insertion of iridium into a cyclopropane ring to give an iridacyclobutane better explains the observed results.

The results of this research indicate that decomposition of the iridacyclobutanes is most likely rate limiting. $CDCl_3$ can act to facilitate these decompositions by lowering transition state barriers through stabilization of polar activated complexes. Polar intermediates would also gain stability through solvation in $CDCl_3$. If iridacyclobutane decomposition is rate determining, then equilibrium between possible iridacyclobutanes can be established. Due to this equilibrium and stabilization of transition states that are not obtainable in a benzene medium, a greater diversity of

products are obtainable in a $CDCl_3$ medium. Also, using this rationale, product ratios are determined, in part, by the thermodynamic stability of products or intermediate iridacyclobutanes leading to those products. Figure 44 (page 108) illustrates an example of product determination from an iridacyclobutane equilibrium process, and Figure 46 (page 113) illustrates an example of an equilibrium between reaction products.

The mode of decomposition of iridacyclobutanes is probably determined kinetically. The most facile pathway available to an iridacyclobutane, be it isomerization or decomposition, will ultimately determine the product. Steric and electronic effects seem important in determining the pathway. Structural modifications, on the substrates, can alter the mode of decomposition from β-hydride elimination to a myriad of other possibilities. An unprecedented 1,2-bridge shift was noted in the reactions of 13 and 85, α-hydride elimination is consistent with the formation of exocyclic methylenes from 12a and 68a and nucleophilic displacement of iridium via a 1,2-hydride shift is consistent with the formation of ring expanded products from 12a and 68a. All in all, there seems to be a fine balance of the factors affecting the fate of iridacyclobutanes.

Although endo-cyclopropanes do not give catalytic reaction in a benzene medium, they appear to be kinetically more reactive than their exo counterparts in a $CDCl_3$ medium. For example, contrast the reactions of the two cyclopropane moieties in substrate 14. Further, contrast the reactions of substrates 11 and 13 and substrates 68 and

69. In all of these cases, less endo-cyclopropane moieties were left unreacted than were exo-cyclopropane moieties. A variety of factors are possibly active and have been discussed earlier, but the reversal of reactivity is certainly worth noting. The reason for the lack of reactivity of these substrates in benzene is elusive, but two explanations can be put forth to account for these results. In a benzene medium, endo-cyclopropane moieties may react in a non-catalytic fashion to yield iridium-hydrocarbon complexes, possibly iridacyclobutanes. For energetic reasons, these complexes are incapable of further reaction and may even decompose to give back the starting substrates. Conversely, a different iridium species may be generated in benzene than in chloroform, and this alternate complex is simply not reactive toward endo-cyclopropane moieties.

By observing the products obtained by deuterium labeling and structural modifications of substrates, and by altering reaction conditions, it was found that Vaska's catalyst is capable of producing a variety of transformations of cyclopropanes through a variety of possible mechanistic pathways. Product regioselectivity is pronounced, and reactions are quite facile in chloroform. Olefins have also been shown to be reactive with iridium. Further research on the reaction of iridium with both cyclopropanes and olefin containing substrates will undoubtedly yield interesting results from a theoretical as well as a pragmatic standpoint. The results contained within this thesis have hopefully provided insight and a basis for further investigation into reactions of this relatively

ignored transition metal. The latin meaning of iridium is rainbow.[41] Indeed a wide spectrum of chemistry is possibly available with iridium if only pursued. Who knows what waits at the end of the rainbow.

Experimental

Section I

Equipment and Chemicals

General Remarks

All ^{1}H and ^{13}C NMR spectra were obtained using a Bruker WM 250 spectrophotometer. $CDCl_3$ and C_6D_6 were used as NMR solvents, and Me_4Si was used as the internal standard. All NMR data reported herein will be reported as δ ppm relative to Me_4Si. Mass spectra were recorded on a Varian Mat CH5 or on a VG/MM16F (Vacuum Gas/Micro Mass) spectrometer. IR data were obtained using a Beckman-IR5A spectrometer. Analytical GLC data were measured with a Varian series 1400 chromatograph using a 10 ft. x 1/4 in. column packed with 5% SE 30 on Chromsorb W. Retention times and peak integrals were determined with a Spectra-Physics autolab minigrator. Preparative GLC collections were performed with an Aerograph Autoprep chromatograph series 2700 using a 10 ft. x 3/8 in. column packed with 10% SE 30 on chromsorb W or a 10 ft. x 1/2 in. column packed with 20% SE 30 on chromsorb W.

Methods and Chemicals

Chloroform-d_1, benzene-d_6 and water-d_2 were purchased from Stohler Isotope Chemicals and used for data aquisition and chemical reactions without further purification. Allyl chloride, cyclopentadiene, methylcyclopentadiene, norbornadiene and methyl

iodide were purchased from Aldrich and distilled prior to use. The following list of chemicals was purchased from Aldrich and used without further purification: sodium amide, diazald, palladium (II) acetate, sodium hydride, 2-cyclohexen-1-one, 2-cyclopenten-1-one, N-ethyl-N-nitro-N^1-nitrotsoquanadine, iodobenzene, norcamphor, 2-(ethoxy-ethoxy)ethanol, cuprous oxide, quinoline, dimethyl sulfoxide-d_6, triphenylmethylphosphonium bromide (Ph_3PCH_3Br), Ph_3PCD_3Br, methyl iodide-d_3, carbitol-d_1, pyridine, phosphoryl chloride, 30% sodium deuteroxide in D_2O and n-butyllithium in hexane. Phenyl lithium was purchased from Alfa Chemicals and Vaska's catalyst was purchased from Strem Chemicals and used without further purification.

All substrates for reaction with Vaska's catalyst were purified by preparative GC prior to use. Diethyl ether, dimethyl sulfoxide and benzene were all distilled from CaH_2 prior to use.

Section II

Synthesis of Substrates

Synthesis of 11, 12, 14, 59 and 68

All of these substrates were prepared by the method of Kottwitz[42] in which diazomethane was added to an olefinic substrate in the presence of a catalytic amount of Pd(II)OAc. Compounds 11 and 12 were prepared from norbornadiene, compound 14 was prepared from 13, compound 59 was prepared from bicyclo[2.2.1]hep-2-ene-5-one and compound 68 was prepared from norbornene. ^1H NMR data of all substrates agreed with literature values and are presented below with

references.

Compound 11:[41] ^{1}H NMR ($CDCl_3$), C_1,C_5, 2.72 (br s, 2H); C_2,C_4, 1.0 (dd, 2H, J= 6.8 and 3Hz); C_3 (syn), 1.45 (dt, 1H, J= 6.0 and 3Hz); C_3(anti), 0.80 (dt, 1H, J= 6.8 and 6.0Hz); C_6,C_7, 6.38 (m, 2H); C_8, 0.85 (d, 1H, J= 9.0Hz); C_8, 1.1 (d, 1H, J= .0Hz); ^{13}C NMR ($CDCl_3$) C_1,C_5, 41.6 (d, J_{CH}= 148Hz); C_2,C_4, 22.0 (d, J_{CH}= 173Hz); C_3, 19.3 (t, J_{CH}= 157Hz); C_6,C_7, 141.2 (d, J_{CH}= 168Hz); C_7, 37.5 (t, J_{CH}= 133Hz); MS, m/e (relative intensity); 106 (M^+,44), 105 (50), 92 (11), 91 (100), 79 (39), 78 (64), 77 (30), 66 (9), 65 (15), 64 (6), 63 (8), 51 (20).

Compound 12:[41] ^{1}H NMR ($CDCl_3$), C_1,C_5, 2.24 (br s, 2H); C_2,C_4,C_6,C_8, 0.96 (dd, 4H, J= 7.0 and 3.2Hz); C_3,C_7(syn), 0.7 (dt, 2H, J= 6.4 and 3.2Hz); C_3,C_7(anti), 0.20 (dt, 2h, J= 7.0 and 6.4Hz); C_9, 0.38 (br s, 2H), ^{13}C NMR ($CDCl_3$); C_1,C_5, 35.3 (d, J_{CH}= 144Hz); C_2,C_4,C_6,C_8, 18.4 (d, J_{CH}= 168Hz); C_3,C_7, 5.8 (t, J_{CH}= 157Hz); C_9, 13.7 (t, J_{CH}= 129Hz).

Compound 68:[43] ^{1}H NMR ($CDCl_3$) C_1,C_5, 2.20 (br s, 2H); C_2,C_4, 0.65 (dd, 2H, J=6.5 and 3.2); C_3(syn), 0.27 (dt, 1H, J= 6.5 and 3.2Hz); C_3(anti), -0.12 (dt, 1H, J= 6.5 and 6.5Hz); C_6,C_7, 1.15 to 1.45 (m, 4H), C_8, 0.55 (br d, 1H, J= 11Hz); C_8, 0.90 (dm, 1H, J= 11Hz); ^{13}C NMR ($CDCl_3$) C_1,C_5, 35.7 (d, J_{CH}= 139Hz); C_2,C_4, 14.5 (d, J_{CH}= 173.2Hz); C_3, 0.8 (t, J_{CH}= 160Hz); C_6,C_7, 29.7 (t, J_{CH}= 130Hz); C_8, 26.6 (t, J_{CH}= 133Hz); MS, m/e (relative intensity), 108 (M^+, 15), 107 (6), 93 (64), 91 (27), 81 (8), 80 (97), 79 (94), 77 (50), 67 (99), 66 (100), 54 (97).

Compound 14:[12] ^{1}H NMR ($CDCl_3$), C_1,C_5, 2.21 (br s, 2H); C_2,C_4, 0.49 (ddd, 2H, J= 7.0 and 3.0Hz); C_3(syn), 0.35 (dt, 1H, J= 5.5 and 3.0 Hz); C_3(anti), -0.05 (td, 1H, J= 7.0 and 5.5Hz); C_6,C_8, 1.2 to 1.3 (m, 2H); C_7(syn), 1.59 (dt, 1h, J= 5.5 and 3.3Hz); C_7(anti), 0.61 (dtm, 1H, J= 7.0 and 5.5Hz); C_9, 1.2 to 1.3 (m, 2H), ^{13}C NMR ($CDCl_3$), C_1,C_5, 35.1 (d, J_{CH}= 139.8Hz); C_2,C_4, 21,1 (d, J_{CH}= 169.3Hz); C_3, 1.63 (t, J_{CH}= 158Hz); C_6,C_8, 12.2 (d, J_{CH}= 169Hz); C_7, 14.8 (t, J_{CH}= 157Hz); C_9, 41.1 (t, J_{CH}= 135Hz).

Synthesis of 13, 69, 85 and 95

Compound 13 was prepared by using the method of Closs.[44] The dihydro derivative (69) was prepared from 13 by catalytic hydrogenation with 10% Pd on Carbon. Substrates 85 and 95 were prepared by the same method as for 13 except methylcyclopentadiene was used as the dienophile. The total yield of 85 and 95 was 10% in a ratio of 4:6 respectively.

Compound 13; ^{1}H NMR ($CDCl_3$), C_1,C_5, 2.77 (br s, 2H); C_2,C_4, 1.33 (ddm, 2H, J= 6.8 and 3.0Hz); C_3(syn), 0.36 (dt, 1H, J= 5.1 and 3.0Hz); C_3(anti), 0.58 (tdd, 1H, J= 6.8, 5.1 and 2.6Hz); C_6,C_7, 5.7 (br t, 2H); C_8, 1.62 (ddt, 1H, J= 6.8, 2.6 and 1.3Hz); C_8, 1.86 (dt, 1H, J= 6.8 and 1.7); ^{13}C NMR ($CDCl_3$), C_1,C_5, 42.5 (d, J_{CH}= 151Hz); C_2,C_4, 12.2 (d, J_{CH}= 171Jz); C_3, 17.2 (t, J_{CH}= 158.7Hz); C_6,C_7, 130.7 (d, J_{CH}= 168.5Hz); C_8, 63.9 (t, J_{CH}= 131Hz); MS, m/e (relative intensity), 106(M^+, 9), 105(28), 91(100), 79(32.5), 78(70), 77(22), 51(12).

Compound 69:[45] ^{1}H NMR ($CDCl_3$), C_1,C_5, 2.20 (br s, 2H); C_2,C_4, 1.35 (ddm, 2H, J= 7.3 and 3.0Hz); C_3(syn), 0.87 (dt, 1H, J= 5.9 and 3.0Hz); C_3(anti), 0.71(tdd, 1H, J= 7.3, 5.9 and 2.4Hz); C_6,C_7, 1.2 to 1.4(m, 4H); C_8, 1.43 (ddt, 1H, J= 8.2, 2.4 and 1.2Hz); C_8, 1.87 (dtt, 1H, J= 8.2, 2.1 and 1.9Hz); ^{13}C NMR ($CDCl_3$), C_1,C_5, 36.3 (d, J_{CH}= 139Hz); C_2,C_4, 23.27 (d, J_{CH}= 168.5Hz); C_3, 17.83 (dd, J_{CH}= 154 and 161Hz); C_6,C_7, 26.96 (t, J_{CH}= 131.8Hz); C_8, 53.7 (t, J_{CH}= 132Hz).

Compound 85:[31] ^{1}H NMR ($CDCl_3$), C_2, 1.42 (dddd, 1H, J= 7.3, 7.3, 4.4 and 3.1Hz); C_3(syn), 0.39 (ddd, 1H, J= 5.1, 3.1 and 3.1Hz); C_3(anti), 0.55 (dddd, 1H, J= 7.3, 7.3, 5.1 and 2.6Hz); C_4, 1.05 (ddd, 1H, J= 7.3, 7.3 and 3.1Hz); C_5, 2.66 (dddm, 1H, J= 4.4, 3.3 and 1.8); C_6, 5.64 (dd, 1H, J= 5.3 and 3.3Hz); C_7, 5.55 (d, 1H, J= 5.3Hz); C_8, 1.54 (ddm, 1H, J= 6.6 and 2.6Hz); C_8, 1.80 (dd, 1H, J= 6.6 and 1.8Hz); CH_3, 1.33 (s, 3H); ^{13}C NMR ($CDCl_3$), C_1, 50.7 (s)μ C_2, 17.6 (d, J_{CH}= 165Hz); C_3, 17.4 (t, J_{CH}= 161Hz); C_4, 14.8 (d, J_{CH}= 172Hz); C_5, 42.9 (d), C_6, 136.2 (d); C_7, 130.4 (d); C_8, 69.6 (t); CH_3, 18.8 (q, J_{CH}= 126Hz); Anal. Calcd. for C_9H_{12}: C, 89.94; H, 10.06. Found: C, 89.92; H, 10.04.

Compound 95:[31] ^{1}H NMR ($CDCl_3$), C_1, 2.53 (br s, 1H); C_2, C_4, 1.35 to 1.45 (m, 2H); C_3(syn), 0.21 (ddd, 1H, J= 5.1, 3.1 and 3.1Hz); C_3(anti), 0.57 (dddd, 1H, J= 7.0, 7.0, 5.1 and 2.6Hz); C_5, 2.64 (br s, 1H), C_7, 5.3 (br m, 1H); C_8, 1.72 (ddm, 1H, J= 6.6 and 2.6Hz); C_8, 1.77 (ddd, 1H, J= 6.6, 1.6 and 1.3Hz); CH_3, 1.67 (d, 3H, J= 1.7Hz); ^{13}C NMR ($CDCl_3$), C_1, 42.3 (d, J_{CH}= 144Hz); C_2, 12.0 (d, J_{CH}= 172Hz); C_3, 16.9 (t, J_{CH}= 162Hz); C_4, 15.8 (d, J_{CH}= 170Hz); C_5, 47.3 (d, J_{CH}=

144Hz); C_6, 140.9 (s), C_7, 124.7 (d, J_{CH}= 166Hz); C_8, 62.8 (t, J_{CH}= 133Hz); CH_3, 15.4 (q, J_{CH}= 127Hz); Anal. Calcd. for C_9H_{12}: C, 89.94; H, 10.06. Found: C, 89.74; H, 10.17.

Synthesis of 103 and 104.

KOH (6.9g) was dissolved in 7mL of water and placed in an erlenmyer flask containing 80ml ether. The mixture was stirred at 0°C while 3g of N-ethyl-N'-nitro-N-nitrosoguanidine was added in small portions. A white precipitate developed at the aqueous-etherial interface concomitantly with a yellow-orange color development in the ether layer. After addition was complete, the ether layer was decanted into a second flask containing 5g of norbornadiene and 61mg Pd(II)acetate in 100mL ether which was also stirred at 0°C. The KOH reaction flask was washed and decanted with 3-20mL portions of ether. The diazoethane reaction mixture was allowed to warm to room temperature while stirring for an additional 3 hours then checked for remaining diazoethane with a 25% acetic acid/ether solution. No N_2 gas evolution was noted upon addition of a drop of the reaction mixture to the acetic acid solution so the reaction mixture was filtered, to remove inorganic precipitates, and concentrated to half the original volume by rotoevaporation at 0°C and then distilled. The products were collected from 120° to 160°C. A total of 0.53g of the distillate was collected which was composed of 62% of 104, 19% of 103 and 5% of other products to give a combined yield of 103 and 104 of 19%. Final purification was achieved by preparative GC.

Compound 103: ^{1}H NMR ($CDCl_3$), C_1,C_5, 2.93 (br s, 2H); C_2,C_4, 1.12 (dd, 2H, J= 7.7 and 1.5Hz); C_3, 1.79 (dq, 1H, J= 7.7 and 6.4Hz); C_6, C_7, 6.55 (br s, 2H); C_8(anti); 1.08 (ddm, 1H, J= 9.5 and 1.5Hz); C_8(syn), 1.48 (br d, 1H, J= 9.5Hz); CH_3, 1.51 (d, 3H, J= 6.4Hz).
Compound 104: ^{1}H NMR ($CDCl_3$), C_1,C_5, 2.86 (br s, 2H); C_2,C_4, 0.87 (d, 2H, J= 2.56Hz); C_3, 1.97 (qt, 1H, J= 5.98 and 2.56Hz); C_6,C_7, 6.36 (br s, 2H); C_8(anti), 0.97 (dm, 1H, J= 8.96Hz); C_8(syn), 1.29 (br d, 1H, J= 8.96Hz); CH_3, 1.10 (d, 3H, J= 5.98Hz); ^{13}C NMR ($CDCL_3$), C_1,C_5, 41.62 (d, J_{CH}= 152Hz); C_2,C_4, 30.42 (d, J_{CH}= 170Hz); C_3, 26.7 (d, J_{CH}= 161Hz); C_6,C_7, 140.8 (d, J_{CH}= 170Hz); C_8, 38.6 (t, J_{CH}= 135Hz); CH_3, 17.4 (q, J_{CH}= 126Hz); MS, parent ion, m/e= 120.

Synthesis of 57 and 58.

Compounds 57 and 58 were synthesized by using the method of Lander and Punja.[46] Compound 57 was synthesized from 2-cyclohexen-1-one in 54% yield and 58 was synthesized from 2-cyclopenten-1-one in 20% yield. Both products were purified by column chromatography over silica gel and eluted with 10% (v/v) ethyl acetate in hexane. Final purification was achieved by preparative GC.
Compound 57:[46] ^{1}H NMR ($CDCl_3$), C_1,C_2,C_3,C_4 and C_5, 1.7 to 2.25 (m, 6H); C_3(anti), 2.41 (ddd, 1H, J= 16.5, 5.6 and 3.3Hz); C_7(syn), 1.24 (ddd, 1H, J= 9.4, 7.7 and 5.1Hz); C_7(anti), 1.38 (ddd, 1H, J= 9.4, 5.3 and 5.3Hz); ^{13}C NMR ($CDCl_3$), C_1, 25.74 (d, J_{CH}= 166Hz); C_2, 209.5 (s), C_3, 36.6 (t, J_{CH}= 125.8Hz); C_4, 21.1 (t, J_{CH}= 128Hz); C_5, 17.7 (t, J_{CH}= 125.8Hz); C_6, 17.4 (d, J_{CH}= 166.5Hz); C_7, 10.2 (t, J_{CH}=

162.8Hz); MS, m/e (relative intensity); 110(M^+,78), 95(11), 82(52), 81(41), 68(46), 67(74), 55(97), 54(100).

Compound 58:[46] ^{1}H NMR ($CDCl_3$), C_1,C_3 and C_4, 1.9 to 2.2 (m, 5H); C_5, 1.18 (ddd, 1H, J= 7.0, 4.6 and 4.0Hz); C_6(syn), 1.73 (ddd, 1H, J= 7.85, 4.5 and 4.0Hz); C_6(anti), 0.90 (ddd, 1H, J= 7.85, 4.6 and 4.6Hz); ^{13}C NMR ($CDCl_3$), C_1, 27.2 (d, J_{CH}= 176Hz); C_2, 215.0 (s); C_3, 31.2 (t, J_{CH}= 131Hz); C_4, 22.5 (t, J_{CH}= 135Hz); C_5, 21.4 (d, J_{CH}= 172Hz); C_6, 13.3 (t, J_{CH}= 163Hz).

Synthesis of 113.

Substrate 113 and the side product 1-methylbicyclo[2.2.1]hepta-2.5-diene (117) were synthesized by the method of Russell, Schmitt and Mattox.[47] Poor yields were realized in both of two attempts (less than 1%), but enough 113 was obtained for one reaction with iridium. ^{1}H NMR data agreed with literature values and are presented below.

Compound 113:[47] ^{1}H NMR ($CDCl_3$), C_1, 3.2 (br s, 1H); 6.12 (qd, 1H, J= 1.89 and 0.9Hz); C_4, 3.5 (br s, 1H); C_5,C_6, 6.7 to 6.85 (m, 2H); C_7, 1.94 (ddd, 1H, J= 6.0, 1.65 and 1.60Hz); C_7, 2.0 (ddd, 1H, J= 6.0, 1.8 and 1.8Hz); CH_3, 1.86 (d, 3H, J= 1.89Hz).

Compound 117:[47] ^{1}H NMR ($CDCl_3$), C_2,C_6, 6.46 (d, 2H, J= 5.0Hz); C_3,C_5, 6.7 (dd, 2H, J= 5.0 and 3.0Hz); C_4, 3.45 (dd, 1H, J= 3.0 and 1.74Hz); C_7, 1.9 (d, 2H, J= 1.74Hz); CH_3, 1.47 (s, 3H).

Synthesis of 72 using a Wittig Reaction.

A 3-neck round bottom flask, equipped with a reflux condenser

and a pressure equalizing dropping funnel, was charged with 1.46×10^{-2} mole NaH and 7mL dimethylsulfoxide. The mixture was heated at 75°C with stirring under a N_2 atmosphere until evolution of H_2 gas ceased. The resultant solution was cooled to 0°C with an ice bath and 5g (1.4×10^{-2} mole) Ph_3PCH_3Br in 14mL dimethylsulfoxide is added dropwise and then stirred for ten minutes. Then 1.7g (1.55×10^{-2} mole) norcamphor in 5mL dimethylsulfoxide was added dropwise and then stirred for an additional 30 min. at room temperature. The product was immediately distilled under vacuum and collected in a liquid N_2 trap. A total of 1.4g of a colorless liquid was collected. GC analysis showed the product was 80% pure. Further purification was achieved by preparative GC. ^1H NMR data agreed with literature values and are presented below.

Compound 72:[48] ^1H NMR ($CDCl_3$) C_1, 2.68 (br s, 1H), C_3(endo), 1.89 (dddd, 1H, J= 15.9, 2.6, 2.0 and 2.0), C_3(exo), 2.16 (dddd, 1H, J= 15.9, 3.2, 1.5 and 1.0), C_4, 2.33 (br s, 1H), C_7(syn), 1.38 (dm, 1H, J= 9Hz), exocyclic methylene (anti), 4.58 (br s, 1H), and (syn) 4.81 (br s, 1H), all other protons are contained in multiplets 1.2 to 1.32 (3H), and 1.5 to 1.72 (2H), MS, m/e (relative intensity), 108(M^+,38), 107(5), 93(66), 91(16), 81(6), 80(35), 79(100), 78(18), 77(25), 67(28), 66(75), 65(15).

Synthesis of Exo-2-Methyl-endo-2-Hydroxybicyclo[2.2.1]hexane (118).

To 12.9g (9.1×10^{-2} mole) methyl iodide in 50mL dry ether was added dropwise to 2.21g (9.1×10^{-2} mole) Mg with stirring under an N2 atmosphere. Stirring was continued for an additional 30 min.

followed by addition of 10g (9.0×10^{-2} mole) norcamphor in 30mL dry ether. Stirring was continued for an additional 3h. The reaction solution was slowly poured into a cold solution of 5g NH_4Cl in 15mL water and the ether layer was decanted. The magnesium salts were washed with 3-50mL portions of clean ether. The combined etherial solution was washed twice with 50mL water then once with 50mL saturated brine, dried ($MgSO_4$) and rotoevaporated to yield a thick yellow oil which was distilled under reduced pressure to give 9.47g (82% yield) of a white crystalline material distilling at 71°C and 13mm Hg. IR (NaCl) showed an OH stretch at 3300 cm^{-1} and the lack of any carbonyl stretching bands.

Compound 118: ^1H NMR ($CDCl_3$), CH_3, 1.3 (s, 3H), D_1, 2.2 (br s, 1H), All other protons resonate in two multiplets at 1.05 to 1.65 (m, 8H), and 1.9 to 2.03 (m, 2H), ^{13}C NMR (C_6D_6), C_1, 48.95 (d, J_{CH}= 140.6Hz), C_2, 76.8 (s), C_3,C_5,C_6 and C_7, 39.0 (t, J_{CH}= 133Hz), 22.5 (t, J_{CH}= 126Hz), 28.8 (t, J_{CH}= 130Hz), and 47.5 (t, J_{CH}= 132Hz), C_4, 37.1 (d, J_{CH}= 140.6Hz), CH_3, 30.7 (q, J_{CH}= 124Hz), MS, m/e (relative intensity), 126(M^+,12), 111(21), 108(14), 97(19), 93(30), 84(8), 83(29), 80(8), 79(18), 77(10), 71(71), 69(8), 68(21), 67(49), 66(34), 59(97), 58(71), 55(21), 53(12), 43(100).

Synthesis of 71 and 72.

Compounds 71 and 72 were synthesized by dehydration of 118 with $POCl_3$ in pyridine as described by Brown[49] and were produced in 43% yield in a 3:7 ratio, respectively. ^1H NMR data agreed with

literature values.

Compound 71:[48] ^{1}H NMR ($CDCl_3$), C_1, 2.87 (br s, 1H); C_3, 5.54 (q, 1H, J= 1.7Hz); C_5,C_6,C_7, 1.0 to 1.8 (m, 6H); C_4, 2.72 (br s, 1H); CH_3, 1.8 (d, 3H, J= 1.7Hz); MS, m/e (relative intensity); 108(M^+,42), 93(34), 91(24), 81(53), 78(100), 67(8), 66(10), 65(18), 53(16).

Section II

Synthesis of Deuterated Substrates

Synthesis of 11a, 12a and 68a.

Substrates 11a, 12a and 68a were synthesized and purified using the same procedure as for the non-deuterated substrates with the following exceptions: carbitol-d_1 was used in place of 2-(ethoxy-ethoxy) ethanol and 30% NaOD in D_2O was used in place of KOH in H_2O. A total yield of 84% of products was obtained in the synthesis of 11a and 12a with 11a representing 69% of the product mixture. Substrate 68a was obtained in 50% yield. Deuterium content and specific deuterium positions were determined by integration of the ^{1}H NMR spectra.

Compound 11a: ^{1}H NMR ($CDCl_3$) showed that both the syn and anti positions on C_3 were deuterated. The respective proton resonances at δ 1.45 and δ 0.85 ppm both showed an 86% reduction in integrals. Mass spectral data gave the following molecular ion pattern: m/e (relative intensity), 108(87), 107(89), 106(39), and 105(15).

Compound 12a: ^{1}H NMR ($CDCl_3$) showed that the syn and anti positions on C_3 and C_7 were deuterated. The proton resonances at δ 0.72 and

0.20 ppm demonstrated an 80% reduction in integrals.

Compound 68a: ^1H NMR ($CDCl_3$) showed that the syn and anti positions on C_3 were deuterated. The proton resonances at δ 0.27 and 0.12 ppm demonstrated an 86% reduction in integrals. Mass spectra gave the following molecular ion pattern: m/e (relative intensity), 110(8), 109(4), 108(1), and 107(1).

Synthesis of 13a.

Compound 13a was prepared by using the method of Magid and Welch.[50] The phenyl lithium used in the generation of cyclopropene-d_1 was either purchased from Alfa Chemicals as a 1.8M solution in hexane/benzene or prepared and purified by using the method of Schlosser and Ladenberger.[51] When the commercial phenyl lithium was used, 1% product was obtained showing a 47% reduction in the integral of the two proton resonance for the protons on C_2 and C_4 at δ 1.33. This equates to a 94% incorporation of deuterium into the cyclopropene dienophile. When the reaction was carried out using freshly prepared phenyl lithium, a 9% product yield was obtained. The proton resonance at δ 1.33 showed a 78% reduction in the integral indicating that a 2,4-dideutero product had been synthesized. This seems feasible since a threefold excess of phenyl lithium was used relative to allyl chloride. Mass spectral data further substantiated a di-deutero product. Mass spectral data gave the following molecular ion pattern: m/e, (relative intensity), 108(11.7), 107(32), and 106(26). Comparison with mass spectral data of the non-deuterated product showed that 67% of the product was di-deuterated,

30% was mono-deuterated, and 3% was non-deuterated.

Synthesis of 72f by the Wittig Method.

This synthesis was carried out as described for the synthesis of 72 (pg. 130). Two attempts at this synthesis were carried out. In the first, methyl-(d_3)-triphenylphosphonium bromide was used in place of the non-deuterated reactant. Deuterium exchange with the solvent occurred and thus the product, although obtained in high yield, had little or no deuterium incorporation. The second attempt employed DMSO-d_6 (99% d) as the solvent. Deuterium incorporation was high, but again, solvent deuterium exchange proved adventitious as deuterium was incorporated in the exo position of the allylic methylene carbon (C_3) as well as on both positions of the exocyclic methylene. ^{1}H NMR ($CDCl_3$) showed a 70% reduction in the integrals of both exocyclic methylene protons and a 43% reduction in the integral of theC_3(exo) proton at 2.16.

Synthesis of 118a.

Compound 118a was prepared in the same manner as the non-deuterated compound 118 (pg. 131) using methyl iodide-d_3 (99.6%-d). The ^{1}H NMR spectrum of the deuterated product was lacking the methyl resonance at δ 1.3, and the mass spectrum showed a molecular ion at m/e = 129(9) and 128(1), and no ions at m/e = 127 or 126. Yield of the purified product was 88%.

Synthesis of 71b and 72e.

These products were prepared as described for the synthesis of

the non-deuterated products (pg. 132). A 30% yield of these products was obtained in a ratio of 7:3, respectively.

Compound 72e: ^1H NMR ($CDCl_3$) showed that only the exocyclic metylene positions were deuterated with an 80% reduction of the integrals at δ 4.58 and 4.81 ppm.

Compound 71b: ^1H NMR ($CDCl_3$) showed that only the methyl group was deuterated. The methyl resonance at δ 1.8 was absent in the NMR spectrum. Integration of this resonance is tenuous since it appears within a complex multiplet.

Section III

Reaction of Non-Deuterated Substrates with Vaska's Catalyst

Attempted Reaction of 11 and 12 in an Oxygen Free Environment.

Two glass tubes for each substrate were charged with 0.45M substrate in benzene, 7 mole% catalyst and 20μL of cyclooctane (for substrate 11) or 20μL n-octane (for substrate 12) as GC standard. These samples were then subjected to several freeze-thaw cycles under vacuum with N_2 used as purging gas. After being sealed under vacuum, the reaction vessels were heated in an oven at 130°C. One tube for each substrate was opened after 2h, and the remaining two tubes were heated for 32h prior to opening. Analysis of the reaction mixtures by GC and ^1H NMR spectroscopy confirmed that >90% of the starting materials remained in all four tubes, and none of the expected products could be observed.

General Procedure for Reaction of Substrates with Vaska's Catalyst in $CDCl_3$ or Benzene with an Atmospheric Oxygen Environment.

The reactions were carried out in sealed glass tubes of about 18mm x 120mm which were heated at 130°C for specified periods of time. Each reaction mixture contained 0.4M substrate with 8-10 mole% Vaska's catalyst and each reaction mixture contained either n-octane or cyclooctane as an internal GC standard. The product mixtures were analyzed by GC and ^1H NMR spectroscopy immediately after opening the liquid N_2 cooled tubes. The product mixtures were subsequently distilled under vacuum at 25-60°C and the volatile components were collected in a liquid N_2 cold trap. Individual products were isolated for spectroscopic and elemental analysis by preparative GC. Percent and relative yields were determined from the analytical GC data of the whole reaciton mixtures and confirmed, when possible, by integration of the ^1H NMR spectra.

Reaction of Substrates 11, 12 and 68 Using Benzene as the Reaction Solvent.

For substrate 11, 52 was obtained as the only product in 34% yield. The remaining hydrocarbon was unreacted substrate. Substrate 12 also gave only one product, 15, in 60% yield. The remaining hydrocarbon was unreacted substrate. For substrate 68 only starting material was recovered in >90%. ^1H NMR data for products 52 and 15 agreed with literature values.[12]

Compound 52: ^1H NMR ($CDCl_3$), C_1, 2.98 (br s, 1H), C_2, 5.12 (dd, 1H, J= 5.5 and 3.0Hz), C_3, 5.08 (dd, 1H, J= 5.5 and 3.0Hz), C_4, 3.17 (br

s, 1H); C_6(exo), 2.28 (dddd, 1H, J= 14.6, 3.1, 2.45 and 1.8Hz); C_6(endo), 1.76 (dddd, 1H, J= 14.6, 2.7, 2.4 and 1.83Hz); C_7, 1.41 (d, 1H, J= 8.2Hz); C_7, 1.60 (dddd, 1H, J= 8.2, 2.7, 1.5 and 1.5Hz); exocyclicmethylenes, (anti), 4.73 (ddd, 1H, J= 1.83, 1.83 and 1.8Hz); and (syn), 5.0 (ddd, 1H, J= 2.45, 2.44 and 1.5Hz); MS, m/e (relative intensity); 106(M^+,26), 105(13), 91(66), 86(13.6), 84(22), 79(11), 78(38), 77(12), 66(100), 65(10.6), 51(10.7).

Compound 15: ^{1}H NMR ($CDCl_3$), D_1, 2.76 (d, 1H, J= 1.3Hz); C_2,C_4, 0.9 to 1.05 (m, 2H); C_3(syn), 0.68 (ddd, 1H, J= 6.8, 3.0 and 2.5Hz); C_3(anti), 0.26 (ddd, 1H, J= 6.8, 6.4 and 6.4Hz); C_5, 2.45 (br s, 1H); C_7(exo); 2.24 (ddd, 1H, J= 14.9, 3.4 and 2.5Hz); C_7(endo), 2.1 (ddd, 1H, J= 14.9, 2.6 and 2.1Hz); C_8, 1.19 (dm, 1H, J= 9.0Hz); C_8, 0.93 (br d, 1H, J= 9.0Hz); exocyclic methylene, (anti) 4.66 (br s, 1H) and (syn) 4.89 (br s, 1H); ^{13}C NMR ($CDCl_3$), C_1, 35.5 (d, J_{CH}= 138Hz); C_2 (C_4), 13.7 (d, J_{CH}= 169.6Hz); C_4 (C_2), 14.6 (d, J_{CH}= 166.5Hz); C_3, 2.2 (t, J_{CH}= 154Hz); C_5, 43.9 (d, J_{CH}= 141Hz); C_6, 154.9 (s); C_7, 37.5 (t, J_{CH}= 126Hz); C_8, 26.3 (t, J_{CH}= 138Hz); exocyclic methylene, 101.3 (t, J_{CH}= 155Hz); MS, m/e (relative intensity); 120(M^+,60), 106(15.5), 105(83), 104(13), 93(20), 92(78), 91(76), 86(8.5), 84(11), 80(25), 79(100), 78(46), 77(44), 66(15), 65(13), 53(12), 52(9), 51(15.5).

Reaction of 11 and 13 in $CDCl_3$.

Both reactions were run for 3h. Substrate 11 gave a 61% yield of products 52 and 47 in 33% and 28% yield respectively. Substrate

13 gave a total yield of 83% of the same products in 60% and 23% respectively. Remaining hydrocarbon in both reactions was starting material (25% of 11 and 2% of 13). Three control experiments were performed with each substrate using identical reaction conditions as above relative to reaction time, temperature, solvent, and substrate concentration. Thermal rearrangement was checked by running the reaction without the presence of catalyst. No reaction was observed with either substrate. Acid catalysis was checked by adding, in addition to the usual contents, 0.5 mole% Na_2CO_3. Reaction in both cases proceeded with very similar results as the standard reaction. Radical pathways were checked for by adding, in addition to the usual contents, 10% (v/v) cumene. Reaction with both substrates produced similar results as with the standard reaction. ^1H NMR data for compound 47 agreed with literature values. Our data is presented below along with ^{13}C NMR and mass spectral data.

Compound 47:[52,53] ^1H NMR ($CDCl_3$), C_1,C_7, 1.39 (br d, 2H, J= 7.7Hz); C_2, 1.59 (dm, 1H, J= 7.7Hz); C_3,C_4, 5.82 to 5.9 (m, 2H); C_5, 2.50 (br s, 1H); C_6,C_8, 0.70 (d, 2H, J= 11.1Hz); C_6,C_8, 1.53 (dd, 2H, J= 11.1 and 4.3Hz); ^{13}C NMR ($CDCl_3$), C_1,C_7, 13.6 (d, J_{CH}= 171Hz); C_2, 15.5 (d, J_{CH}= 161Hz); C_3, 129.1 (d, J_{CH}= 168.5Hz); C_4, 121.9 (d, J_{CH}= 165Hz); C_5, 32.0 (d, J_{CH}= 155Hz); C_6,C_8, 27.7 (t, J_{CH}= 132Hz); MS, m/e (relative intensity); 106(M^+,55.8), 105(20), 91(100), 84(6), 79(34), 78(74.8), 77(25.7), 51(11.7).

Reaction of 68 and 69 in $CDCl_3$

When reaction was continued for 3h, substrate 68 gave a total

yield of 51% of products 72, 71 and 73 in 42.5%, 5.5% and 3% respectively. A substantial amount of 68 (39%) was left in the product mixture. When 68 was heated for 4h, only 4% of 68 remained and products 72, 71, 73 and 70 constituted an 80% yield in 66%, 7%, 4.2% and 3% respectively. Product 70 was not isolated in high enough yield for elemental analysis, but mass spectral and ^{1}H NMR data have been obtained. Reaction of compound 69 was continued for 3h. A total yield of 79% products was obtained and only 5% 69 remained in the reaction mixture. The products and their yields were 72 (50%), 71 (5%) and 73 (22%).

Compound 73:[54] ^{1}H NMr ($CDCl_3$), C_1,C_5, 2.3 (m, 2H); C_2, 5.35 (m, 1H); C_3, 5.8 (m, 1H); C_4,C_6,C_7,C_8, 1.2 to 1.9 (m, 8H), MS, m/e (relative intensity); 108(M^+,27), 93(20), 91(10), 81(4), 80(39), 79(100), 78(18), 77(21), 67(37), 66(57), 65(6), 54(17).

Compound 70; ^{1}H NMR ($CDCl_3$), C_1,C_6, 0.79 (dd, 2H, J= 1.8 and 1.5Hz); C_3, 1.12 (d, 2H, J= 1.5Hz); C_4, 1.91 (m, 1H); C_5,C_7, 1.20 (dd, 2H, J= 10.4 and 1.2Hz); C_5,C_7, 1.34 (ddd, 2H, J= 10.4, 1.5 and 1.5 Hz); CH_3, 1.22 (s, 3H); MS, m/e (relative intensity); 108(M^+,42), 107(9), 94(13), 93(100), 92(10), 91(32), 89(3), 81(7), 80(26), 79(42), 78(10), 77(40), 67(8), 66(16), 65(12), 54(4), 53(12).

Reaction of 103 and 104 in $CDCl_3$

Reactions were continued for 4h. Substrate 103 gave an overall yield of products of 70%. The products obtained were 105, 106 and 107 in 40%, 23% and 7% respectively. No starting material was

observable in this product mixture. Substrate 104 did not give any catalytic reaction that could be detected by GC or ^{1}H NMR. Starting material was recovered in >85%. Structure assignment of 105 and 106 were confirmed by comparison of spectral data with commercial samples and literature data. Compound 107 was deduced solely by use of ^{1}H and ^{13}C NMR data, no literature data is available and enough material was not obtained for elemental analysis.

Compound 105:[55] ^{1}H NMR ($CDCl_3$), C_1, 3.19 (br s, 1H); C_6(endo), 1.82 (dm, 1H, J= 13.3Hz); C_6(exo), 2.27 (dm, 1H, J= 13.3Hz); C_4, 3.08 (br s, 1H); C_3, 6.11 (dd, 1H, J= 5.55 and 2.56Hz); C_2, 6.05 (dd, 1H, J= 5.55 and 2.99Hz); C_7, 1.51 (dm, 1H, J= 6.4Hz); C_7, 1.70 (obs, 1H); C_8, 5.44 (qd, 1H, J= 6.4 and 1.5Hz); CH_3, 1.70 (d, 3H, J= 6.4Hz); ^{13}C NMR ($CDCl_3$), $C_1(C_4)$, 50.7, C_2, 141.1, C_3 41.7, $C_4(C_1)$, 50.2, $C_5(C_6)$, 134.5, $C_6(C_5)$, 136.1, C_7, 41.7, C_8, 112.7, CH_3, 14.8.

Compound 106: ^{1}H Nmr ($CDCl_3$), C_1, 2.97 (br s, 1H); C_2, 6.07 (dd, 1H, J= 5.0 and 3.0Hz); C_3, 6.13 (dd, 1H, J= 5.4 and 2.56Hz); C_4, 2.72 (br s, 1H); C_5(endo), 2.27 (dddd, 1H, J= 8.24, 7.9, 2.1 and 1.3Hz); C_6, C_7, 1.35 to 1.58 (m, 4H); C_8, 5.87 (ddd, 1H, J= 16.6, 10.2 and 8.24Hz); C_9 (trans), 4.96 (ddd, 1H, J= 10.2, 2.0 and 1.3Hz); C_9 (cis), 5.05 (ddd, 1H, J= 16.6, 2.1 and 2.0Hz).

Compound 107: ^{1}H NMr ($CDCl_3$), C_1,C_6, 1.34 (d, 2H, J= 5.2Hz); C_2, 1.55 (td, 1H, J= 5.2 and 0.98Hz); C_4, 2.06 (br s, 1H); C_5,C_7, 1.27 (dd, 2H, J= 9.5 and 0.98Hz); C_5,C_7, 1.87 (dm, 2H, J= 9.5Hz); C_8, 5.28 (q, 1H, J= 6.2Hz); CH_3, 1.71 (d, 3H, J= 6.2Hz); ^{13}C NMR ($CDCl_3$), C_1,C_6, 14.5 (d, J_{CH}= 182Hz); C_2, 12.7 (d, J_{CH}= 180Hz); C_3, 147.0 (s);

C_4, 36.0 (d, J_{CH}= 148Hz), C_5,C_7, 33.7 (t, J_{CH}= 131Hz), C_8, 107.8 (d, J_{CH}= 151Hz), CH_3, 13.6 (q, J_{CH}= 126Hz).

Reaction of 85 in $CDCl_3$.

Reaction for 3h lead to production of only one product (86) in 90% yield. The reaction was run again under identical conditions excluding catalyst. Only starting material was recovered in >90%. Compound 86: ^1H NMR ($CDCl_3$), C_1,C_7, 1.3 (d, 2H, J= 7.3Hz), C_2, 1.7 to 1.75 (obs, 1H), C_3, 5.5 (dqd, 1H, J= 4.0, 1.62 and 1.1Hz), C_5, 2.30 (td, 1H, J= 4.0 and 1.1Hz), C_6,C_8, 0.74 (d, 2H, J= 11.2Hz), C_6,C_8, 1.51 (ddd, 2H, J= 11.2, 4.0 and 0.78Hz), CH_3, 1.73 (d, 3H, J= 1.62Hz), ^{13}C NMR ($CDCl_3$), C_1, C_7, 14.0 (d, J_{CH}= 172Hz), C_2, 14.18 (d, J_{CH}= 172Hz), C_3, 114.8 (d, J_{CH}= 161Hz), C_4, 138.2 (s), C_5, 37.4 (d, J_{CH}= 139Hz), C_6, C_8, 27.8 (t, J_{CH}= 130Hz), CH_3, 20.2 (q, J_{CH}= 125.8Hz), MS, m/e (relative intensity), 120(M^+,85), 119(12), 117(4), 115(4), 106(17), 105(100), 103(11), 92(61), 91(68), 79(35), 78(20), 77(34), 65(15), 63(7), 51(16), Anal. Calcd. for C_9H_{12}: C, 89.94, H, 10.06. Found: C, 90.04, H, 10.09.

Reaction of 95 in $CDCl_3$.

Reaction for 3h gave seven products in an 83% yield. Four of the products, comprising 12%, remain unidentified. The major products were 54 in 47% and 96/97 (5:1 ratio) in 24% yield. Attempts at obtaining enough pure 96/97 for elemental analysis were unsuccessful, but ^1H and ^{13}C NMR and mass spectral data all corroborate the assigned structure. Reaction of 95 with Vaska's

catalyst for only 2h gave the same results except the ratios of 54 and 96 were nearly reversed with 96 present in 41% yield and 54 present in 31%. Further, this substrate was subjected to identical reaction conditions, excluding catalyst, and was recovered unreacted in >90% yield.

Compound 96: H NMR ($CDCl_3$), C_1, 2.85 (br s, 1H), C_2, 5.64 (q, 1H, J= 1.6Hz), C_4, 2.9 (s, 1H), C_6(endo), 1.82 (dm, 1H, J= 14.6Hz), C_6(exo), 2.25 (dm, 1H, J= 14.6Hz), C_7, 1.4 (d, 1H, J= 8.2Hz), C_7, 1.67 (dm, 1H, J= 8.2Hz), CH_3, 1.78 (d, 3H, J= 1.6Hz), exocyclic methylene, 4.70 (br s, 1H) and 4.98 (br s, 1H), ^{13}C NMR ($CDCl_3$), C_1, 55.9 (d, J_{CH}= 151.7Hz), C_2, 144.9 (s), C_3, 129.7 (d, J_{CH}= 166Hz), C_4, 42.1 (d, J_{CH}= 146Hz), C_5, 49.7 (t, J_{CH}= 133Hz), C_6, 151.8 (s), C_7, 34.8 (t, J_{CH}= 135Hz), CH_3, 14.5 (q, J_{CH}= 126Hz), exocyclic methylene, 102.6 (t, J_{CH}= 155Hz), MS, m/e (relative intensity), 120(M^+, 52), 119(8), 117(4), 106(12), 105(100), 91(29), 80(78), 79(55), 78(18), 77(22), 65(12), 63(5), 51(17).

Compound 97:* ^1H NMr ($CDCl_3$), C_1, 2.68 (br s, 1H), C_3, 5.55 (q, 1H, J= 1.5Hz), C_4, 3.08 (br s, 1H), C_6,C_7 and CH_3, (obscured), exocyclic methylene, 4.67 (br s, 1H) and 4.92 (br s, 1H), ^{13}C NMR ($CDCl_3$), C_1, 46.8, C_2, 145, C_3, 127.1, C_4, 51.7, C_5 (not observed), C_6, 49.8, C_7, 34.1, CH_3, 13.9, exocyclic methylene, 102.0.

Compound 54: ^1H NMR ($CDCl_3$), C_1, 3.15 (br s, 1H), C_3 and C_5(endo), 1.99 (br d, 2H, J= 15.6Hz), C_3 and C_5(exo), 2.27 (dm, 2H, J= 15.6Hz),

*Compound 97 could not be cleanly isolated. ^1H and ^{13}C NMR data were obtained as a mixture of 96 and 97, and therefore the data for 97 are incomplete.

C_4, 2.49 (m, 1H); C_7, 1.48 (td, 2H, J= 1.6 and 1.0Hz); exocyclic methylene, 4.62 (br s, 2H) and 4.91 (br s, 2H); ^{13}C NMR ($CDCl_3$), C_1, 55.3 (d, J_{CH}= 152Hz); C_2,C_6, 152.4 (s); C_3,C_5, 36.8 (t, J_{CH}= 127.6Hz); C_4, 36.4 (d, J_{CH}= 134Hz); C_7, 39.9 (t, J_{CH}= 135Hz); exocyclic methylene, 102.8 (t, J_{CH}= 156Hz); MS, m/e (relative intensity); 120(M^+,85), 106(15), 105(100), 92(40), 91(70), 80(14), 79(56), 78(20), 77(43), 65(10), 63(7), 53(18), 51(19), Anal. Calcd. for C_9H_{12}: C, 89.94, H, 10.06. Found: C, 90.11, H, 10.01.

Reaction of 12 and 15 in $CDCl_3$.

Reaction of 12 was carried out for 3h, 6h and 9h. After 3h, 83% yield of products was obtained with 15 comprising 65%, 53 and 54 comprising 9.6% (in a 4:1 ratio), 56 in 3% and 55 in 2%. Two other unidentified products were present in 3%. Starting material (5%) was also present. Overall yields for the 6h and 9h reactions are not known, but the relative yields are 15 (71%), 53/54 (22%) and 56 (7%) for the 6h reaction and 15 (60%), 53/54 (31%), and 56 (9%) for the 9h reaction. No 12 or 55 was found in either the 6h or 9h experiments. Reaction of 15 for 3h gave 10% conversion to 53/54 and 4% conversion to 56.

Compound 53: ^1H NMR ($CDCl_3$), C_1,C_4, 2.80 (br s, 2H); C_3 and C_6(endo); 1.99 (dd, 2H, J= 15.4 and 1.7Hz); C_3 and C_6(exo), 2.30 (ddd, 2H, J= 15.4, 3.0 and 1.6Hz); C_7, 1.49 (tt, 2H, J= 1.7 and 1.6Hz); exocyclic methylene, 4.64 (br s, 2H) and 4.91 (br s, 2H); ^{13}C NMR ($CDCl_3$), C_1,C_4, 45.6 (d, J_{CH}= 133Hz); C_2,C_5, 153.4 (s); C_3,C_6,

37.9 (t, J_{CH}= 138Hz); C_7, 39.4 (t, J_{CH}= 127Hz); exocyclic methylene, 102.4 (t, J_{CH}= 155Hz); Anal. Calcd. for C_9H_{12}: C, 89.94; H, 10.06. Found: C, 90.11; H, 10.01.

Compound 56: ^{1}H NMR ($CDCl_3$), C_1,C_4(exo), C_7(exo), and C_7(endo), 2.37 to 3.55 (m, 4H); C_2, 5.95 (dddd, 1H, J= 9.1, 5.0, 2.3 and 1.0Hz); C_3, 5.42 (ddd, 1H, J= 9.1, 3.4 and 2.3Hz); C_4(endo), 1.98 (dddd, 1H, J= 17.7, 4.6, 3.4 and 1.0Hz); C_5, 2.84 (br s, 1H); C_8, 1.70 to 1.78 (br s, 2H); exocyclic methylene, (anti) 4.93 (br s, 1H) and (syn) 5.03 (br s, 1H); Anal. Calcd. for C_9H_{12}: C, 89.94; H, 10.06. Found: C, 89.76; H, 10.07.

Compound 55:[29] ^{1}H NMR ($CDCl_3$), C_1, 2.24 (dm, 1H, J= 4.7Hz); C_2, 0.98 (ddd, 1H, J= 7.3, 7.3 and 3.4Hz); C_3(syn), 0.38 (ddd, 1H, J= 5.6, 3.4 and 3.4Hz); C_3(anti), 0.12 (ddd, 1H, J= 7.3, 7.3 and 5.6Hz); C_4, 1.44 (dddm, 1H, J= 7.3, 7.3 and 3.4Hz); C_5, 2.20 (obscured); C_6, 6.07 (ddm, 1H, 9.4 and 6.0Hz); C_7, 5.24 (dm, 1H, J= 9.4Hz); C_8(endo), 2.00 (ddd, 1H, J= 17.1, 3.4 and 1.7Hz); C_8(exo), 2.30 (dddd, 1H, J= 17.1, 4.7, 2.6 and 2.6Hz); C_9, 1.25 to 1.30 (m, 2H).

Reaction of 14 in $CDCl_3$.

Seven products were obtained in a combined yield of 87%: 96 (7%), 54 (8.5%), 98 (3.5%), 15 (20%), 55 (21%), 99 (15%), and 100 (12%). No starting material was found in the product mixture. Products 99 and 100 co-eluted on preparative GC, so elemental analysis could not be obtained for either compound, but adequate separation was obtained for mass spectral and ^{1}H NMR data

acquisition. Elemental analysis and ^{13}C NMR data are available for compound 98.[31]

Compound 98:[31] ^1H NMR ($CDCl_3$), C_1, 1.83 (ddd, 1H, Jz, 7.5, 5.2 and 4.3Hz); C_3(exo), 1.90 (d, 1H, J= 15.8Hz); C_3(endo), 2.20 (dddd, 1H, J= 15.8, 7.7, 2.6 and 2.6Hz); C_4, 2.66 (ddd, 1H, J= 7.7, 7.7 and 0.85Hz); C_5, 1.51 (dddd, 1H, J= 6.7, 5.2, 4.3 and 0.85Hz); C_6(syn), 0.72 (ddd, 1H, J= 7.5, 6.7 and 4.3Hz); C_6(anti), 0.56 (ddd, 1H, J= 4.3, 4.3 and 4.3 Hz); C_7, 5.79 (ddd, 1H, J= 17.5, 10.2 and 7.7 Hz); C_8(cis), 5.02 (ddd, 1H, J= 17.5, 1.7 and 0.85Hz); C_8(trans), 4.91 (ddd, 1H, J= 10.2, 1.7 and 0.85Hz); exocyclic methylene, 4.69 (br s, 1H) and 4.93 (br s, 1H).

Compound 99: IR ($CDCl_3$), 1739 cm^{-1} (C=O), ^1H NMR ($CDCl_3$), C_1, 2.40 (br s, 1H); C_3(endo), 1.73 (dq, 1H, J= 7.6 and 3.4Hz); C_4, 2.24 (br s, 1H); C_5(exo), 2.21 (dqdd, 1H, J= 9.6, 7.0, 4.1 and 3.4Hz); C_6(endo), 0.93 (ddd, 1H, J= 11.1, 3.4 and 1.52Hz); C_6(exo), 2.15 (ddd, 1H, J= 11.1, 9.6 and 4.3Hz); C_7, 1.58 (dddd, 1H, J= 10.5, 3.4, 1.23 and 0.6Hz); C_7, 1.88 (ddd, 1H, J= 10.5, 1.52 and 1.5Hz); C_3-methyl, 1.06 (d, 3H, J= 7.6Hz); C_5-methyl, 0.94 (d, 3H, J= 7.0Hz); ^{13}C NMR ($CDCl_3$); C_1, 55.8 (d, J_{CH}= 152Hz); C_2, 209 (s); $C_3(C_4)$, 41.9 (d, J_{CH}= 144Hz); $C_4(C_3)$, 49.1 (d, J_{CH}= 144Hz); C_5, 31.95 (d, J_{CH}= 133Hz); C_6, 35.6 (t, J_{CH}= 133Hz); C_7, 36.8 (t, J_{CH}= 127.6Hz); C_3-methyl, 18.5 (q, J_{CH}= 124Hz); C_5-methyl, 14.0 (q, J_{CH}= 125.8Hz); MS, m/e (relative intensity); 138(M^+, 32), 123(18), 95(49), 82(37), 81(100), 69(10), 68(19), 56(25), 55(52).

Reaction of 57, 58 and 59 in $CDCl_3$.

All three substrates were subjected to reaction for 3h. GC and ^1H NMR analysis showed no catalytic reaction had occurred with any of these substrates, indeed each of these was recovered in >85%.

Reaction of 113 in $CDCl_3$.

This reaction was carried out in a sealed NMR tube and was continued for 1.5h. ^1H NMR analysis demonstrated that only reactant and product 52 were present at the end of the experiment in 68% and 32% yield, respectively.

Reaction of 105 in $CDCl_3$.

The reaction was run with commercial 105 for 3h. No internal standard was used in this reaction. The product yields, therefore, are reported as relative percentages. After reaction for 3h, GC and ^1H NMR analysis confirmed that olefin isomerization had occurred to give 106 in 25% and 107 in 38% with 105 remaining in 37%. An identical reaction was performed, excluding catalyst, and no thermal rearrangement took place.

Section IV

Reaction of Deuterated Substrates with Vaska's Catalyst in $CDCl_3$

General Procedure for Reaction and Analysis of Data Obtained from the Reaction of Deuterated Substrates.

The reactions of deuterated substrates were carried out in the same manner as the reactions with the non-deuterated substrates. Deuterium content and position in the products was determined

primarily by integration of the ^1H NMR spectra of these products. In some instances, deuterium positions were determined by loss of coupling to geminal protons. The ^1H NMR parameters used to acquire the spectral data for deuterium content were standard parameters except for the receiver delay, which was set at 30 seconds. The deuterium content for each product will be reported as the percent reduction of the normal integral. For a one proton integral, the percent reduction of the integral will equal the percent deuterium content within experimental uncertainty.

Reaction of 11a.

Reaction for 3.5h gave an 83% yield of products, and 5% of the substrate remained unreacted. A 31% yield of 52b was obtained along with 52% 47c. Position and deuterium content for each product is given below.

Compound 52b: ^1H NMR ($CDCl_3$) showed deuterium to be present in equal amounts on both exocyclic methylene positions. The resonances at 4.73 and 5.0 both demonstrated a reduction of 75% of their respective integrals. The resonance at δ 2.28, corresponding to the exo proton on C_6, demonstrated a 5% reduction of its integral. The mass spectrum gave the following pattern for the molecular ion region: m/e (relative intensity), 108(31.2), 107(29.3), 106(10.5), and 105(3.9).

Compound 47c: ^1H NMR ($CDCl_3$) showed deuterium to be present in C_3 and in the endo position of C_6. Respective reduction of integrals are 83% and 44%. No other deuterium was found by ^1H NMR. The mass

spectrum gave the following molecular ion region: m/e (relative intensity), 108(100), 107(46.4), 106(21.4) and 105(7.1).

Reaction of an Equamolar Mixture of 11 and 11a.

An equamolar mixture of 11 and 11a was subjected to standard reaction conditions with Vaska's catalyst for 1h. ^{1}H NMR analysis of the starting mixture demonstrated that both the syn and anti positions of the cyclopropane carbon, C_3, were 50% deuterated. The substrate isolated after reaction demonstrated 57% deuterium in the same positions. Relative yields for the products are 11% for 52b and 13% for 47c. ^{1}H NMR analysis of the products is given below.

Compound 52b: ^{1}H NMR demonstrated that both exocyclic methylene positions were deuterated equally. Deuterium was not observed in any other position. The reduction of the integrals for the exocyclic methylene positions was 47% each.

Compound 47c: ^{1}H NMR showed deuterium to be present on C_3 and on the endo position of C_6. Respective reductions of integrals were 56% and 28%.

Reaction of 12a.

Reaction for 3h gave a product yield and distribution similar to that obtained from reaction with 12. No starting material was present in the product mixture. Individual product yields were: 15a (50%), 53a/54a (20%), 56a (5.5%) and 55a (3.5%). Mass spectral data was not obtained for this set of products, but ^{1}H NMR data are given below including deuterium position and content.

Compound 15a: ^{1}H NMR ($CDCl_3$) established the presence of deuterium in five positions. Both resonances corresponding to the cyclopropane protons on C_3 showed an 89% reduction of their integrals. The exocyclic methylene protons had an unequal distribution of deuterium with the syn position, at δ 4.89, having a 70% reduction of its integral, and the anti position, at δ 4.66, showing a 63% reduction of its integral. The exo-allylic methylene position, resonating at δ 2.24, showed a 36% reduction of its integral.

Compound 53a/54a: ^{1}H NMR ($CDCl_3$) demonstrated the presence of deuterium in three positions. Again, the exocyclic methylenes had unequal distribution of deuterium. The syn position, at δ 4.91, showed a 70% reduction of its integral and the anti position, at δ 4.64, showed a 54% reduction of its integral. The exo-allylic methylene positions on C_3 and C_6, at δ 2.30, exhibited a 48% reduction of their integral.

Compound 56a: ^{1}H NMR ($CDCl_3$) established the presence of deuterium in six positions. Unequal distribution of deuterium is again noted for the exocyclic positions. The syn position at δ 5.03, had a 55% reduction of the associated integral, and the integral for the anti position, at δ 4.93, was reduced by 40%. The other two olefin positions also had deuterium present. Position C_2, at δ 5.95, had a 31% reduction of its integral and position C_3, at δ 5.42, had a 86.5% reduction of its integral. Protons on C_4(exo) and C_7(exo) both resonate in the same multiplet and therefore, specific deuterium content for these two positions cannot be determined. However, the 4

proton multiplet containing these two resonances showed a 34% reduction of the total integral which corresponds to 68% reduction of a 2 proton integral. The presence of deuterium on the exo position of C_4 was determined by the loss of geminal coupling to the endo proton at δ 1.98. The presence of deuterium in the exo position of C_7 is interpolated from compounds 15a and 53a.

Componnd 55a: ^1H NMR ($CDCl_3$) showed five positions to be deuterated. Both of the cyclopropane positions on C_3, at δ 0.38 and δ 0.12, demonstrated a 90% reduction of the respective integrals. The olefins were also deuterated. The position on C_7, at δ 5.24, had an 86% reduction of its integral, and the position on C_6, at δ 6.07, had a 31% reduction of its integral. The exo-allylic methylene position, at δ 2.3, showed a 42% reduction of its integral.

Reaction of 13a.

Substrate 13a, prepared from commercial phenyl lithium, was used for this reaction, and thus, 47% of the C_2 and C_4 cyclopropane positions were deuterated in the starting material (see page 158). The reaction was continued for 2h and resulted in an 82% yield of products. Starting material (8%) remained at the end of the reaction. Product 52a was obtained in 34% yield and 47a was obtained in 43.5% yield. Mass spectral data were not obtained for these reaction products, but adequate ^1H NMR data are given below.

Compound 52a: ^1H NMR ($CDCl_3$) demonstrated that deuterium was only present in the exo and endo positions of C_6. The exo position exhibited a 50% reduction of the integral, and the endo position had

a 5% reduction of its integral.

Compound 47a: ^{1}H NMR ($CDCl_3$) demonstrated deuterium to be present in two positions. The resonance for position C_5, at δ 2.50, showed a 43% reduction of its integral, and the resonance for position $C_1(C_7)$, at δ 1.39, showed a 52% reduction of its integral.

Reaction of 68a.

The reaction was carried out for 0.5h, 2h and 4h. Product ratios, as well as deuterium cotent and position were compared for these three rections. After 0.5h, 68a comprised 81% of the reaction mixture, 73a was obtained in 1.6%, 72a in 15% and 71a in 1.6%. After a 2h reaction period, 68a comprised 43%, 73a - 5%, 72a - 47%, 71a - 5% and 70a - 1%. After a 4h reaction period, 68a comprised 14%, 73a - 7%, 72a - 67%, 71a - 8% and 70a - 4%. ^{1}H NMR analysis was performed on compound 72a for all three reactions, and on all of the products of the 4h reaction. Mass spectral data were obtained for all products of the 4h reaction.

Compound 72a: ^{1}H NMR ($CDCl_3$) of the product isolated from the 0.5h reaction showed deuterium on both exocyclic methylene positions, but the deuterium content was not equivalent. The syn position, at δ 4.81, had a 51% reduction of its integral, and the anti position, at δ 4.58, had a 38% reduction of its integral. Deuterium was also found on the exo-allylic methylene position, at δ 2.16, which had a reduction of its integral of 59%. The mass spectrum of this sample gave the following molecular ion region: m/e (relative intensity),

111(6), 110(38), 109(26), 108(6), 107(3) and 106(1).

^{1}H NMR analysis on the product of the 2h reaction showed deuterium in the same positions but in different relative ratios. The syn-exocyclic methylene position had a 48% reduction of its integral, the anti position had a 41% reduction of its integral and the exo-allylic methylene position had a 66% reduction of its integral. The mass spectrum gave the following molecular ion region: m/e (relative intensity), 111(8), 110(38), 109(18), 108(8), 107(2) and 106(1).

^{1}H NMR analysis of compound 72a, which was isolated from the 4h reaction, exhibited deuterium in the same positions, but in this sample the deuterium was equally distributed in all three positions. The syn and anti exocyclic methyene positions showed 49% and 52% integral reductions, and the exo-allylic position showed a 50% reduction in its integral. Further, the endo-allylic position had a 15% reduction of its integral. The mass spectrum gave the following molecular ion region: m/e (relative intensity), 111(11), 110(24), 109(23), 108(9), 107(1) and 106(1).

Compound 71a: The product of the 2h reaction gave the following molecular ion region of the mass spectrum: 111(5), 110(15), 109(18), 108(2) and 107(2).

^{1}H NMR analysis of the 4h reaction product showed a definite decrease in the intensity of the methyl resonance at δ 1.8, but accurate integration was not obtained. Further, the methyl resonance exhibited deuterium coupling of 2.1Hz. The C3 olefinic resonance

also demonstrated a 13% reduction of its integral. The mass spectrum gave the following molecular ion region: m/e (relative intensity), 111(7), 110(14), 109(14) and 108(5).

Compound 70a: This product was not evident by ^{1}H NMR or GC analysis in either the 0.5h or the 2h reactions. The product from the 4h reaction showed a 61% reduction of the integral of the methyl resonance at δ 1.22 upon ^{1}H NMR analysis. The mass spectrum gave the following molecular ion region: m/e (relative intensity), 111(41), 110(60), 109(34) and 108(13).

Compound 73a: ^{1}H NMR analysis of the product of the 4h reaction showed deuterium on both of the olefinic positions, but deuterium was not discernable in any other position of the molecule. The olefin resonance at δ 5.35 had an 87% reduction of its integral and the olefinic resonance at δ 5.8 had a 67% reduction of its integral. The mass spectrum gave the following molecular ion region: m/e (relative intensity), 111(6), 110(41), 109(23) and 108(5).

Reaction of 71b.

The reaction was continued for 1.5 hours. Relative product yields were: 72b in 74%, 71b in 13.5% and 70b in 12.5%. Product 72b was isolated for NMR analysis and gave the results presented below. Control experiments were also performed on compound 71 in which compound 71 was subjected to Ph_3P induced and thermal induced isomerization. Two reaction mixtures were prepared, one containing Ph_3P (20 mole %) and 0.4M 71 in $CDCl_3$ and the other containing only 0.4M 71 in CDC13. Each was heated for 2 hours at 130°C. The Ph3P

containing mixture gave 17.5% conversion to 72, and the thermal process gave 6.5% conversion to 72.

Compound 72b: ^{1}H NMR ($CDCl_3$) demonstrated the presence of deuterium in 4 positions. The exocyclic methylene positions had equal deuterium content with integrals showing 65% reduction each. The exo-allylic methylene position showed a 57% reduction of its integral and the endo-allylic methylene position showed a 23% reduction of its integral.

Reaction of 72e.

Reaction of 72e, prepared by using the method of Brown was carried out for 1h and 2h. Both reactions gave very similar relative product yields: 86% and 84% 72f, 12.5% and 13.5% of 72c and 1.4% and 2% of 70c. Product 72f was isolated from both reaction mixtures and analyzed by ^{1}H NMR spectroscopy. Control experiments with Ph_3P and thermal conditions were also performed with compound 72e, but after 2 hours at 130°C, no reaction had occurred.

Compound 72f: ^{1}H NMR ($CDCl_3$) analysis of the product from the 1h reaction demonstrated equal deuterium content for both exocyclic methylene positions, both showed a 73% reduction in integrals. The exo-allylic methylene position demonstrated a 7% reduction of its integral.

The product from the 2h reaction also demonstrated equal deuterium content for both the exocyclic methylene positions. Integral reductions for this reaction were 59% for each of the exocyclic methylenes and 29% for the exo-allylic methylene position.

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