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# Formation of cycloheptyne-dicobalt hexacarbonyl complexes via Nicholas allylation reactions and ring closing metathesis: Intramolecular 2+2+2 and Pauson-Khand reactions on cycloheptyne complexes.

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# Formation of Cycloheptyne-$Co_2(CO)_6$ Complexes via Nicholas Allylation Reactions & Ring Closing Metathesis: Intramolecular 2+2+2 And Pauson-Khand Reactions On Cycloheptyne Complexes

by

Ahmed Bashir Mohamed

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## ABSTRACT

One of the objectives of this thesis was to reduce the formation of vinyl silane side **140a,b,c** & **145** products formed in the 4+3 cycloaddition reactions. By employing allyltrimetal nucleophile **149**, virtually eliminated or reduced to trace amounts these vinyl silane side products observed earlier. DIBAL reduction and *in situ* acetylation, followed by exposuere to $BF_3$ afforded cycloheptenyne dicobalt complex **156a,b** & **163a**, bearing a allyl trimethyl silane functional group and a silyl group at β-position.

The second and major objective of my thesis was to prepare tethered alkenes or alkynes of cycloheptyne dicobalt complexes. Cyloheptyne dicobalt complexes of **187**, **188**, **215**, and **220** bearing an acetoxy group was prepared by ring closing metathesis. These complexes were functionalized easily via Nicholas reactions in high yields. Tethered alkenes did undergo Pauson-Khand reactions with good to excellent yields furnishing 7,5,5 fused ring systems. While the tethered alkynes did undergo 2+2+2 cycloaddition reactions, giving fused 7,6,5 ring systems, with respectable yield.

## DEDICATION

I dedicate this thesis to all my family, particularly my brother Hussein and his wife Ayan for their support and generosity throughout my studies.

## ACKNOWLEDGEMENTS

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## List of Abbreviations

| | |
|---|---|
| ABq | AB quartet |
| $AC_2O$ | acetic anhydride |
| Bn | benzyl |
| Br | broad |
| BuLi | butyl lihium |
| $Bu_2BOTf$ | dibutyl{[(trifluoromethyl)sulfonyl]oxy}borane |
| CAN | ceric ammonium nitrate |
| $CyNH_2$ | cyclohexylamine |
| $CDCl_3$ | deutrated chloform |
| $\delta$ | chemical shift in ppm |
| $Me_2S$ | dimethyl sulfide |
| dq | doublet of quartet |
| dt | doublet of triplet |
| Et | ethyl |
| $Et_2O$ | dirthyl ether |
| Equiv | equivalent |
| h | hour |
| HRMS | high resolution MS |
| $^iPr$ | isopropyl |

| | |
|---|---|
| IR | infrared |
| M | multiplet |
| Me | methyl |
| m/e | mass/charge ratio |
| MS | mass spectrometry |
| NMO | N-methylmorpholine N-oxide monohydrate |
| NMR | nuclear magnetic resonance |
| NOE | nuclear Overhauser effect |
| NOESY | nuclear Overhauser and exchange spectroscopy |
| PKR | Pauson Khand Reaction |
| ppm | parts per million |
| q | quartet |
| RT | room temperature |
| s | singlet |
| sept | septet |
| THF | tetrahydrofuran |
| TLC | thin layer chromatography |
| TMEDA | N,N,N',N'-tetramethylethylenediamine |
| TMS | trimethylsilyl |
| $Bu_3SnCl$ | tributyltin chloride |
| $TS_2O$ | p-Toluenesulfonic anhydride |

## 1.0 Introduction

### 1.1 Strained Cycloalkynes

In order to have unstrained alkyne[1] or cycloalkyne, the bond angles at the sp hybridized carbons (i.e., between the carbon-carbon triple bond and the propargylic carbons) have to be near-linear. Cyclooctyne has been isolated, but it is a strained cycloalkyne. It is unstable and easily rearranges and polymerizes. Cycloheptyne, cyclohexyne and cyclopentyne[2] exist as a transient species. Cyclobutyne and cyclopropyne and their derivatives remain elusive.

Mainly three techniques have been employed to stabilize these highly reactive strained compound classes. Placing bulky substituents adjacent to the triple bond diminishes the accessibility of the π electrons. Replacing one or more carbon atom by a heteroatom with a longer carbon-heteroatom bond (for example C-S bond) also decreases the reactivity of the triple bond. Finally, complexation of the triple bond with transition metals brings about a dramatic relief of strain. There are many potential alkyne metal complexes, but those of dinuclear cobalt complexes are the most synthetically useful ones.

Since Reppe's[3] first report, various transition metal complexes have been discovered to form alkyne metal complexes. Basically, there are three modes of coordination of metals to the alkyne: mononuclear, dinuclear and trinuclear (Fig.1).

Dicobalt hexacarbonyl complexes are known to exist as dinuclear structures such as **a**. In this thesis structure **b** will be used to represent structure **a**.

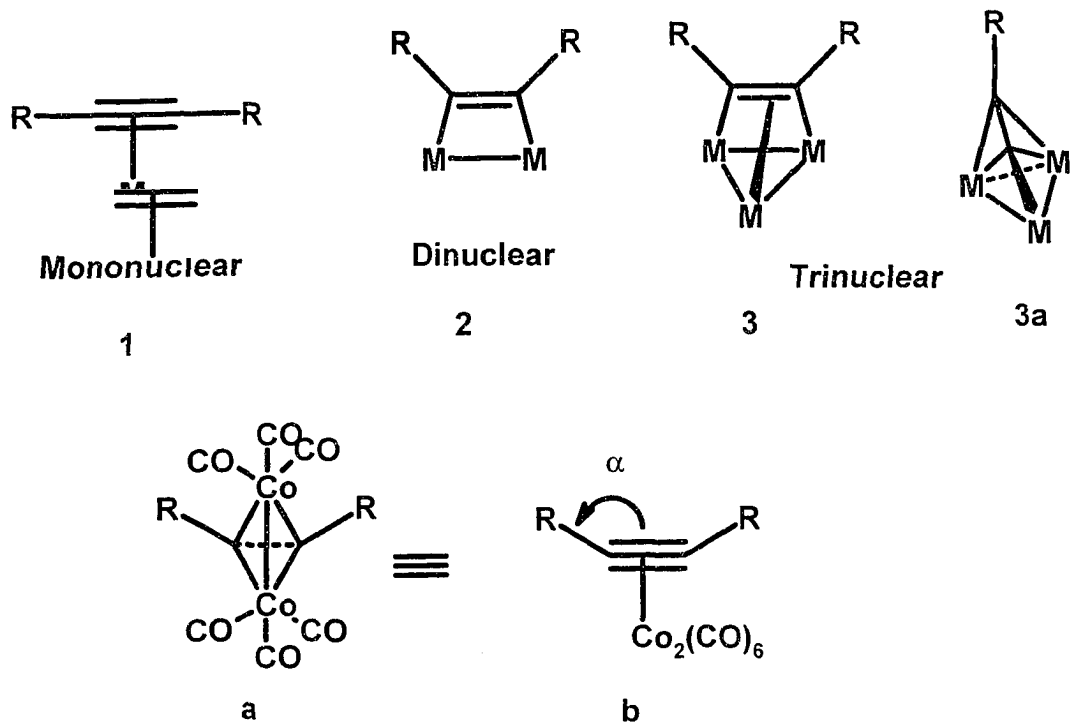



**Figure 1. Metal-Alkyne Coordination Modes**

The structures of dicobalt-alkyne complexes are pseudo tetrahedral geometry at carbon, with a change in the bond angle at the formally sp hybridized carbons of the alkyne [(α) Fig.1, for example] from 180° to 140° in cycloalkynedicobalt complex.

The last three decades have seen extensive research and rapid development of alkyne-$Co_2(CO)_6$ dinuclear cluster chemistry.[4] These clusters can be easily prepared, in excellent yields, just by mixing the alkyne and the commercially available dicobalt octacarbonyl in organic solvents at room

temperature. The alkyne cobalt complexes are stable dark red solids or liquids that can be chromatographed easily.

The complexation imparts three fundamental changes to the chemistry of the triple bond: 1) a change in bond angles, 2) protection of the triple bond, and 3) propargyl cation stabilization. The first of these features has been discussed above. Secondly, the dicobalt hexacarbonyl unit dramatically reduces the reactivity of the triple bond to the typical alkyne reactions such as hydrogenation, electrophilic attack and alkyne metathesis. Thus it is often used as a protecting group for alkynes, since it is equally easy to deprotect.[5]

There are several methods to decomplex with or without the reduction of the triple bond. Strong oxidants that are commonly used to oxidize the cobalt metal include: ceric ammonium nitrate, ferric nitrate, trimethylamine N-oxide and N-methylmorpholine N-oxide. Sensitive substrates are decomplexed with milder oxidants such as iodine or a weak competitive ligand such as pyridine. Lithium in ammonia or tributyltin hydride can be used to decomplex dicobalt carbonyl with concomitant reduction of the triple bond to a Z-alkene.[6]

## 1.2 Nicholas Reaction

Perhaps the most synthetically useful change associated with complexation is the tremendous stabilization of propargylic carbocations by the dicobalt hexacarbonyl unit as compared to uncomplexed propargyl cation. In 1972, Nicholas and Petit[7] discovered that the dicobalt hexacarbonyl unit can effectively stabilize propargylic carbocations. When dicobalt complexed propagylic alcohols were treated with tetrafluoroboric acid, propargyl cation complexes could be isolated as a stable tetrafluoroborates. These propargyl carbocations[8] are as stable thermodynamically as triphenylmethyl cation (commonly known as trityl cation), as indicated by its $pK_R^+$[ca -7 compared to -6.6 for trityl]. Experimental evidence supports a highly delocalized carbocation species. IR spectra show a shift in the carbonyl absorption to higher frequencies by the order of 40-60 $cm^{-1}$, while the carbonyl resonance in the $^{13}C$-NMR spectrum shows a small deshielding relative to the parent alcohol.

Schreiber[9] studied the variable temperature NMR spectra of dicobalt propargyl cations and proposed that they exist as highly fluxional structures with various species in equilibrium [Fig. 2]. Schreiber proposed a model that stated that the propargylic carbon bends towards one of the cobalt atoms. An antarafacial migration leading to enantiomerization (A to B and D to C) is the lower energy fluxional process. The energy barrier depends on substitution at the propargylic position. It is undetected for primary cations, 11.5 kcal/mol for secondary cations and 10.1 kcal/mol for tertiary cations. At higher temperatures a second process can

be detected. It is attributed to a suprafacial migration leading to syn/anti isomerization (A to C and B to D). Again, this higher isomerization energy barrier depends on the degree of substitution at the propargylic carbon, decreasing in the order $1^0 > 2^0 > 3^0$.

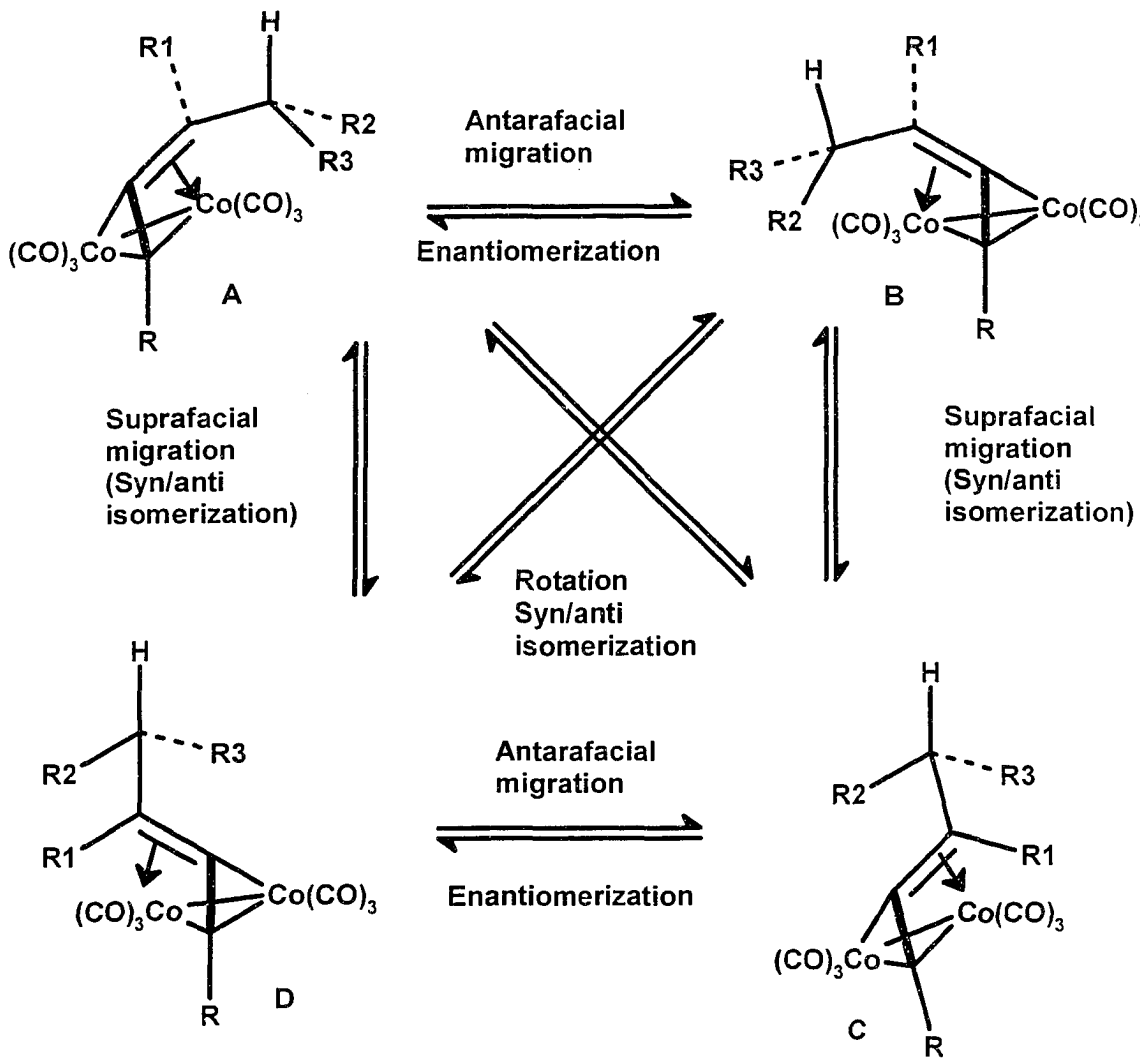
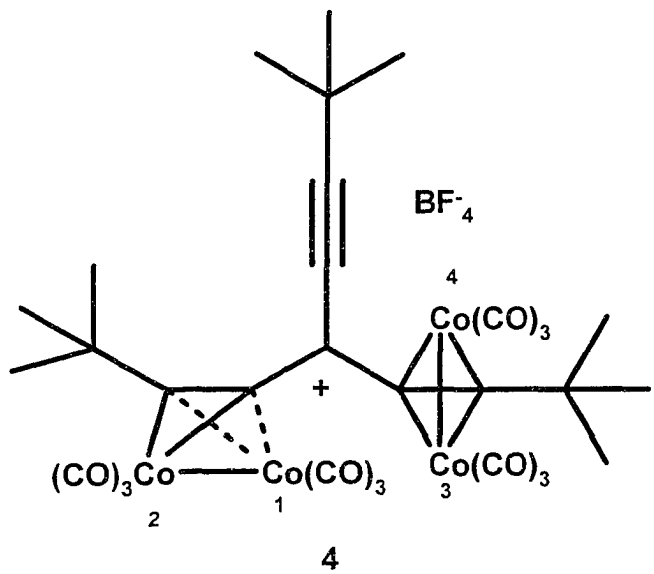



**Figure 2. Fluxional Behavior of the Propargyldicobalt Cation**

Melikyan's group[10] was able to isolate and perform successfully x-ray crystallography on cation **4**, which supports Schreiber's model. The distances from the propargylic carbon to the two sets of cobalt atoms vary distinctly and the formal cation carbon is $sp^2$ hybridized trigonal planar.




4

**$C^+$-$Co_1$ 3.07A⁰** **$C^+$-$Co_3$ 3.27 A⁰**
**$C^+$-$Co_2$ 2.81A⁰** **$C^+$-$Co_4$ 2.89 A⁰**

**Figure 3. Tetracobalt Cation Used by Melikyan for X-ray Crystallography**

There are several ways to generate these carbocations, as shown in (Fig. 4). Protonation of propargylic alcohols, epoxides or alkenes can provide the carbocation complex. The addition of Lewis acids to alkoxides, acetates, or acetals is also known to provide dicobalt hexacarbonyl cations. It is also possible to generate the complexed cation from the action of $AgBF_4$ on propargyl chlorides.[11]

An alternative method of generating the carbocation is the electrophilic addition to an enyne (**7** to **6**), usually followed by either elimination to an alkene or trapping with a nucleophile.

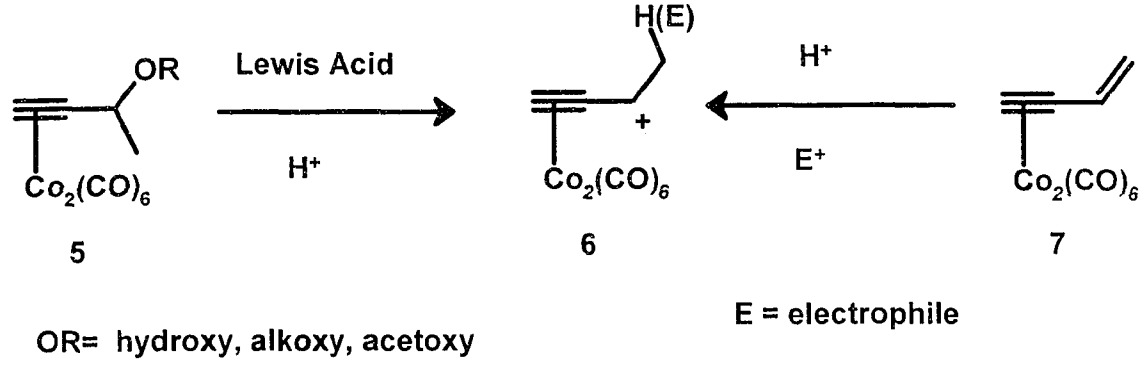



**Figure 4. Propargylic Carbocation Formation**

### 1.2a Intermolecular Nicholas Reactions

The range of nucleophilies that can add to propargyldicobalt carbocations is extensive. The addition usually gives excellent yields and always occurs exclusively at the propargylic position unless the cation is conjugated to an alkene. By contrast, ionization of uncomplexed alkyne at the propargylic position forms a cation with ambident propargylium-allenylium resonance forms, upon which nucleophilic attack can occur at either end, yielding a mixture of acetylenic and allenic products. However, in the dicobalt complex alkynes, formation of allenes, without prior decomplexation of the complex, has never been reported.[12]

Based on the work by Nicholas and others, the substitution effect at the α–carbon or the remote γ-propargylic carbon has only a marginal effect on the reactivity of the dicobalt propargylium cation ( i.e., **8**, **9**) (Fig. 5). However, replacing one carbon monoxide with an electron donating ligand further stabilizes the propargylium cation and therefore drastically reduces its reactivity. Thus, mono-(triphenylphosphine) substituted cluster **11** is less reactive towards addition of π-nucleophies (by ca. $10^5$ fold)[13] than dicobalt hexacarbonyl propargylium cation **10**.

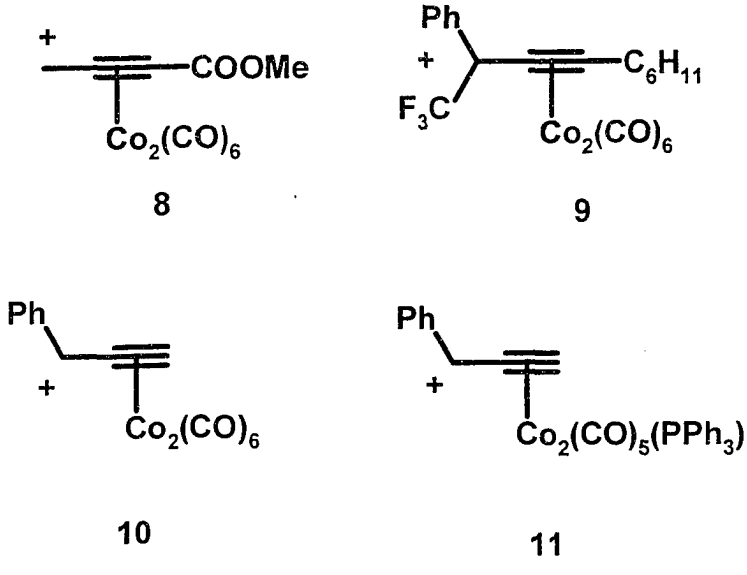
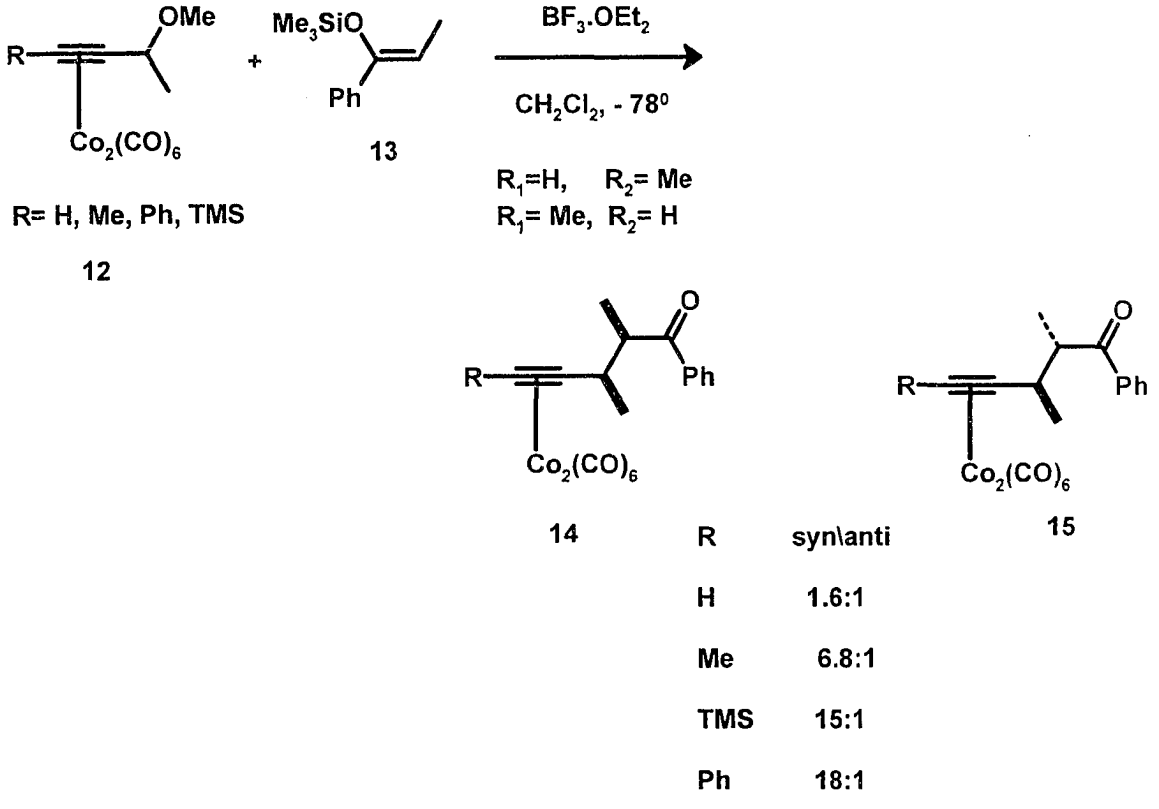



**Figure 5. α-, and γ-Substituted Propargylium Cation Complexes**

Mayr's empirical scale[14] gives a quantitative prediction of the types of nucleophiles that can add to the propargylium cation complexes. The scale confirms the suitability of electron rich aromatics and heteroaromatics as

nucleophilic partners to these dicobalt cation complexes, while benzene and toluene are inefficient, unless used as a solvent. Heteroatom centered nucleophiles such as alcohols, carboxylic acids, water, thiols, amines, nitriles, and hydrides are known to add well to these dicobalt cationic complexes. Carbon-atom centered nucleophiles such as enols, enol ethers, enamines, silyl ketene acetals, β-dicarbonyl compounds, and alkenes also add to the propargyl dicobalt cation. Allylsilanes and allylstannanes efficiently add to these carbocations, even forming quaternary carbons.

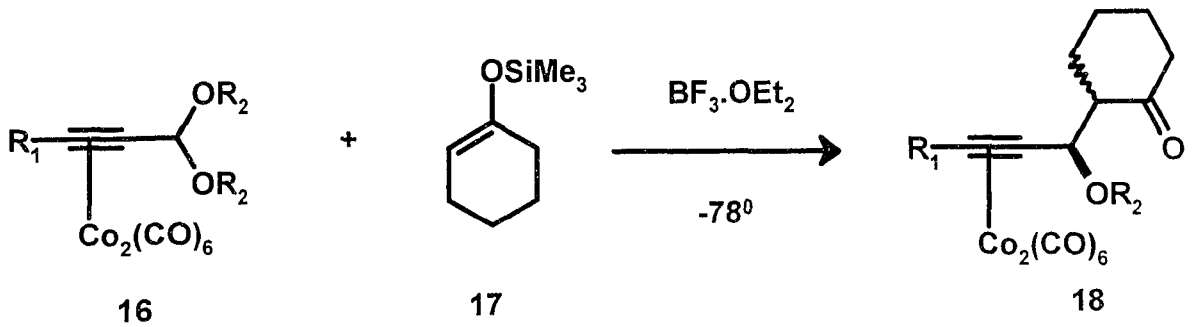
Schreiber[15] has demonstrated that acyclic silyl enol ethers and particularly Evans-type boron enolates couple with the propargylium cation (such as that derived from **12**) to furnish products with good to excellent diastereoselectivity about the newly formed bond. The level of *syn* diastereoiselection was found to be slightly higher in the Z-enol silyl ether than the E-enol silyl ether (i.e. **13**). However, a substituent at the remote alkynyl carbon of the complexes (**12**) was shown to have a substantial influence on the streochemical outcome. For example, *syn:anti* ratios (**14:15**) were found to increase significantly as the steric bulkiness of the R group increased from 1.6:1 when R=H to 18:1 when R=Ph (Fig. 6).




| R | syn\anti |
|---|---|
| H | 1.6:1 |
| Me | 6.8:1 |
| TMS | 15:1 |
| Ph | 18:1 |

**Figure 6. The *syn* Selectivity of Propargyl Alkylation**

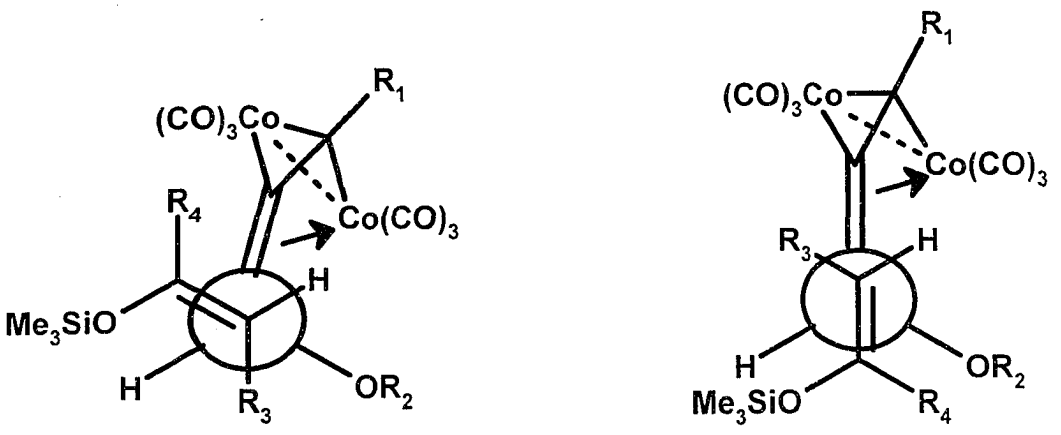
When alkynyl acetals (**16**) were added to acyclic silyl enol ether (**17**) in the presence of a Lewis acid, aldol complexes (**18**) with the s*yn* diastereomer as the major isomer were generated. However, it was noticed that by changing the remote propargylic substituent, there was only a small difference in diastereoisomeric ratio compared to those reported by Schreiber. Nicholas[16] pointed out that the diastereoisomeric ratio of the β-alkoxy ketone complexes was far more dependent on the bulkiness of the acetal group rather than the remote alkynyl group..




| $R_1$ | $R_2$ | syn\anti |
|---|---|---|
| Me | Et | 8:1 |
| Ph | Et | 6:1 |
| Me | Me | 1.5:1 |
| Ph | Me | 3:1 |

**Figure 7. Alkylation of Acetal Dicobalt Complexes**

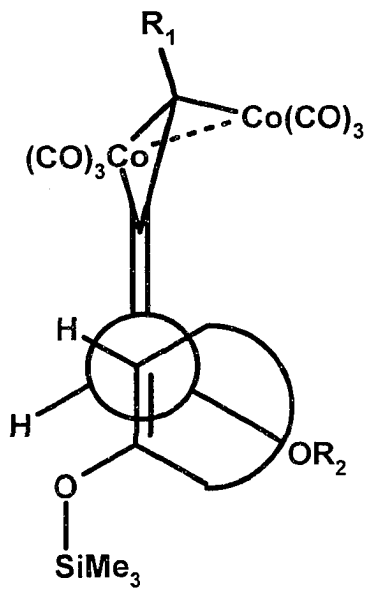
The high *syn* diastreoisomeric induction observed in these reactions was rationalized according to the Seebach[17] transition state system. Schreiber suggested a synclinal orientation of the CC double bond of the enolate and the alkynyl propargyl carbon as the preferred conformation in the transition state for reaction carried out under kinetic conditions (Fig. 8).



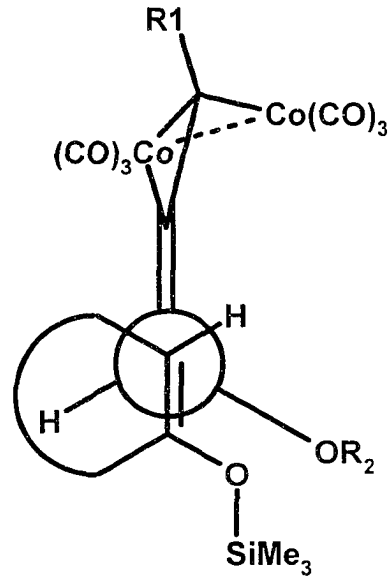

**Synclinal**
**gives syn-isomer**

**Antiperiplanar**
**anti-isomer**

**Figure 8. Synclinal and Antiperiplanar Transition States of Acyclic Enolates**




**Antiperiplanar gives syn isomer**




**Antiperiplanar gives anti-isomer**

**Figure 9. Synclinal and Antiperiplanar Transition States of Cyclic Enolates**

In the cyclic model shown above (Fig. 9), the antiperiplanar transition states are favored, because synclinical transition states suffer a severe steric interaction between the bulky dicobalt unit and either the ring or the TMS group. Of the two antiperiplanar transition states, the one leading to the *anti* isomer seems to be the less hindered one; nevertheless, it may suffer from dipolar repulsion between the trimethylsiloxy and the alkoxy groups thus favoring the other antiperiplanar transition state. Although cyclic enol ethers still yield predominantly the *syn*-isomer, the diastereoselectivity varies from as high as >99:1 to as low as 1.3:1.

Such striking differences cannot be completely explained by one model for cyclic enol ethers.

Though the antarafacial migration of the dicobalt cation is fast, chiral enols should be able to distinguish the enantiomeric faces and should provide diastereomerically and enantiomerically enriched products. Indeed, Schreiber showed that chiral boron enolates react with propargyl dicobalt complexes to afford chiral products with good levels of enantiofacial selectivity[9] (Fig. 10).

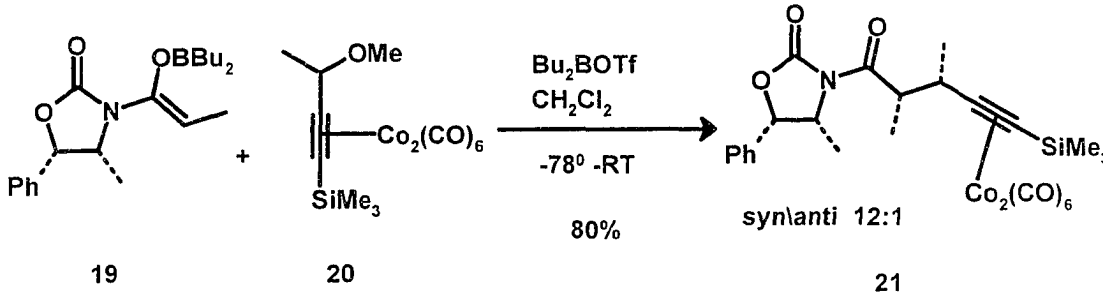



**Figure 10. Condensation with Chiral Boron Enolates**

Schreiber contended, based on the synclinical model, that a double stereo-differentiation takes place and that the rapid enantiomerization of the propargyl dicobalt cation is faster than the alkylation. The synclincal transition state (**A**) (Fig. 11), which gives rise to the anti isomer, suffers from a steric interaction between the methyl on the propargylic carbon and the pendant butyl group on the boron enolate, and is therefore considered to be inferior to the alternative synclinal transition state (**B**).

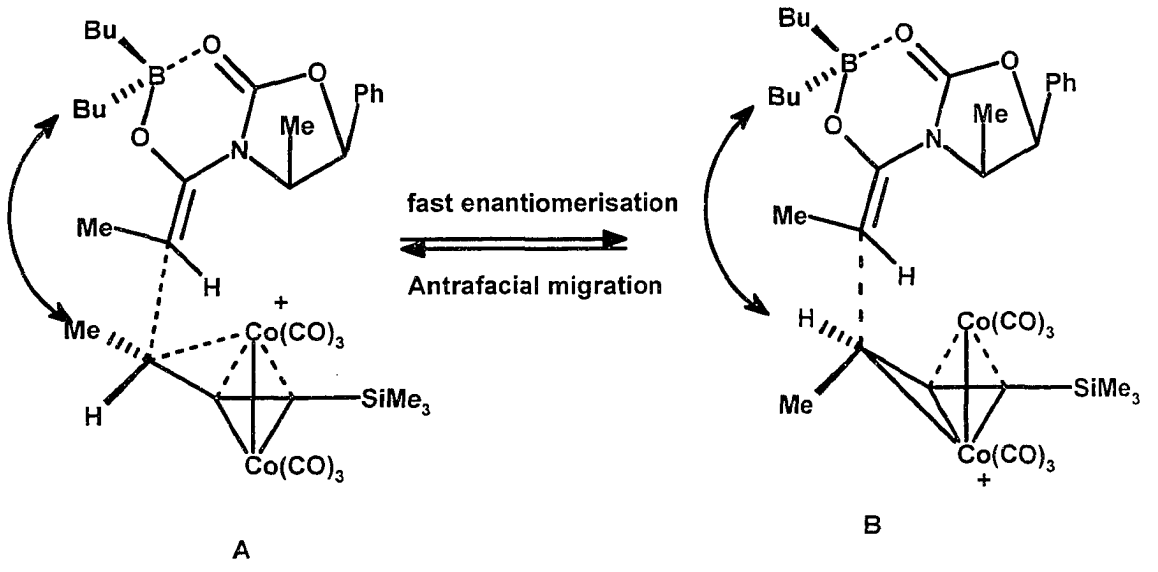
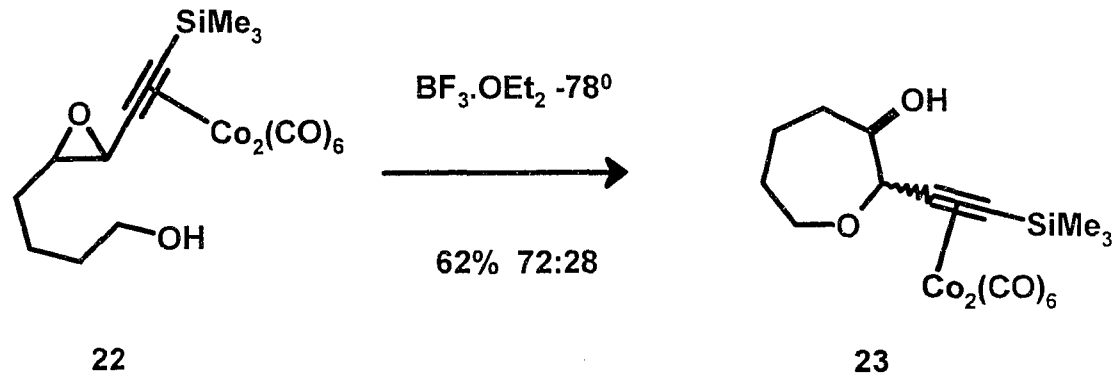



**Figure 11. Transition States for the N-Acyl Oxazolidinone Boron Enolates**

### 1.2b Intramolecular Nicholas Reaction

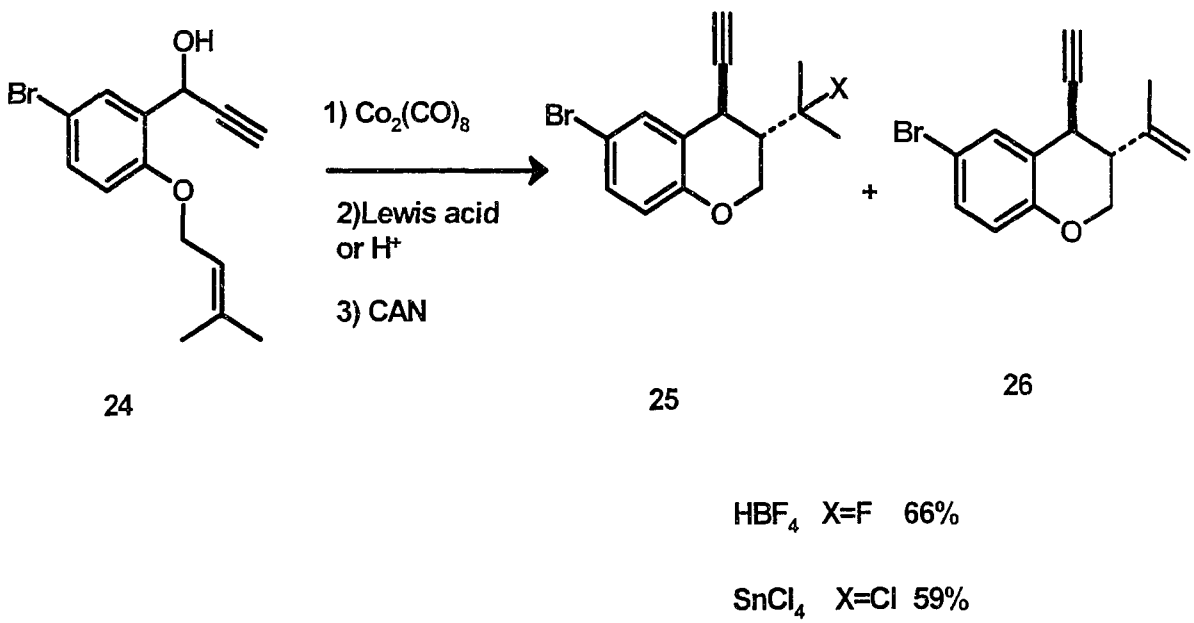
The last two decades have seen a considerable amount of work reported on intramolecular Nicholas reactions. The intramolecular Nicholas cyclization can provide either the dicobalt hexacarbonyl moiety as a part of the ring or placed as a substituent on the ring. Mukai[18] studied the formation of 5, 6, and 7 membered cyclic ethers from the reaction of a pendant alcohol to an epoxy alkyne-dicobalt complex (i.e. **22-23**). It is interesting to note the ready formation of a seven membered ring over six membered ring. Formation of the most stable carbocation overrides the normal tendency to form a six membered ring.




22 23

**Figure 12. Oxepane Formation**

Tyrrell[19] was able to cyclize a suitably disposed propargyl cation complex on to non-activated alkenes (Fig. 13). The tertiary cation intermediate was either trapped with a halide ion or lost a proton by β-elimination to provide (**25**) and (**26**) as their *trans* diastereomers.




24 25 26

**Figure 13. Alkene as the Trapping Nucleophile**

While not strictly an intramolecular Nicholas reaction, the work of Krafft's group is clearly related. Krafft[20] was able to generate the propargyl cation with a terminally disubstituted alkene and capture the resultant tertiary carbocation intramolecularly with a carboxylic acid or an ester to form a lactone (Fig. 14). The analogous chemistry can be used to form a cyclic carbonate with alkenyl carbonates or carbamates.

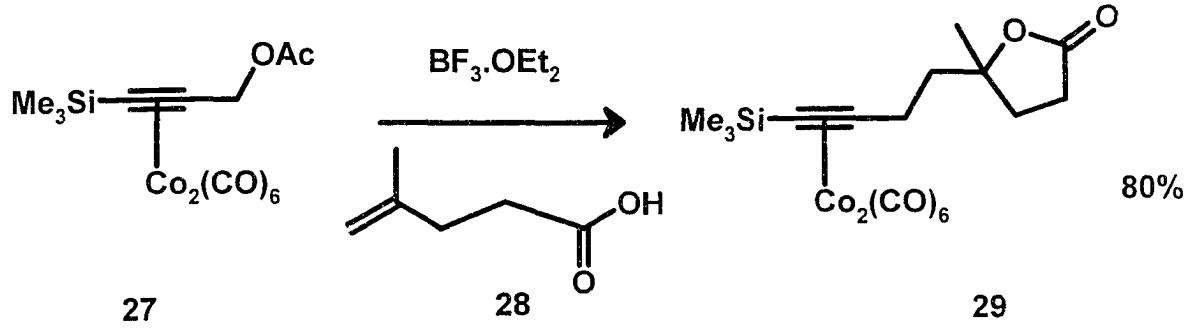



**Figure 14. Krafft's Lactone Formation**

Tyrrell[21] prepared several acyclic alkynes bearing a dicobalt complex and with a trimethylsilyl enol ether at the opposing end as the cation quencher. It was possible to form 5, 6 and 7 membered rings in Lewis acid mediated Nicholas reactions of these substrates (Fig. 15).

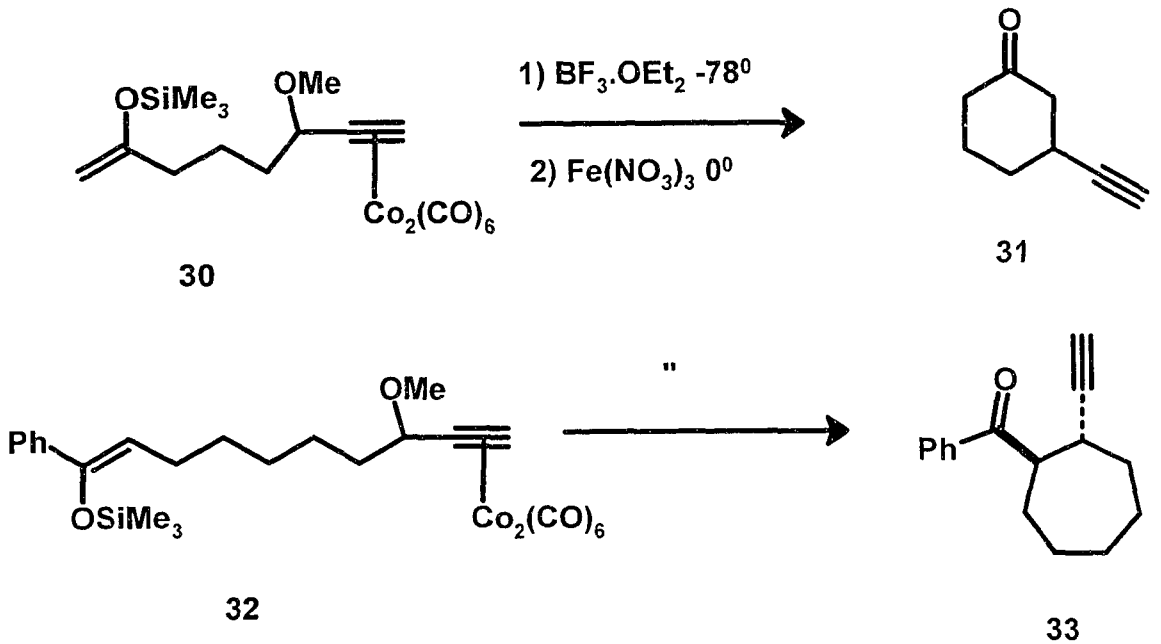



**Figure 15. Intramolecular Enolsilane Trapping**

Tyrrell[22] also elegantly exploited the difference in reactivities between enol ethers and alkenes towards a propargylic cation. When the silyl enol ether (**34**) was mixed with acetal complex (**35**) in the presence of boron trifluoride etherate, complex (**36**) was formed, exclusively as the *cis* diastereoisomer (Fig.16). Further treatment with tetrafluoroboric acid and subsequent decomplexation with CAN did not afford the expected bicyclic enyne (**37**), but instead furnished a tricyclic product (**38**) with a *cis, anti, trans* relative configuration. The formation of this unusual tricyclic product and possible intermediates is under investigation by the authors.

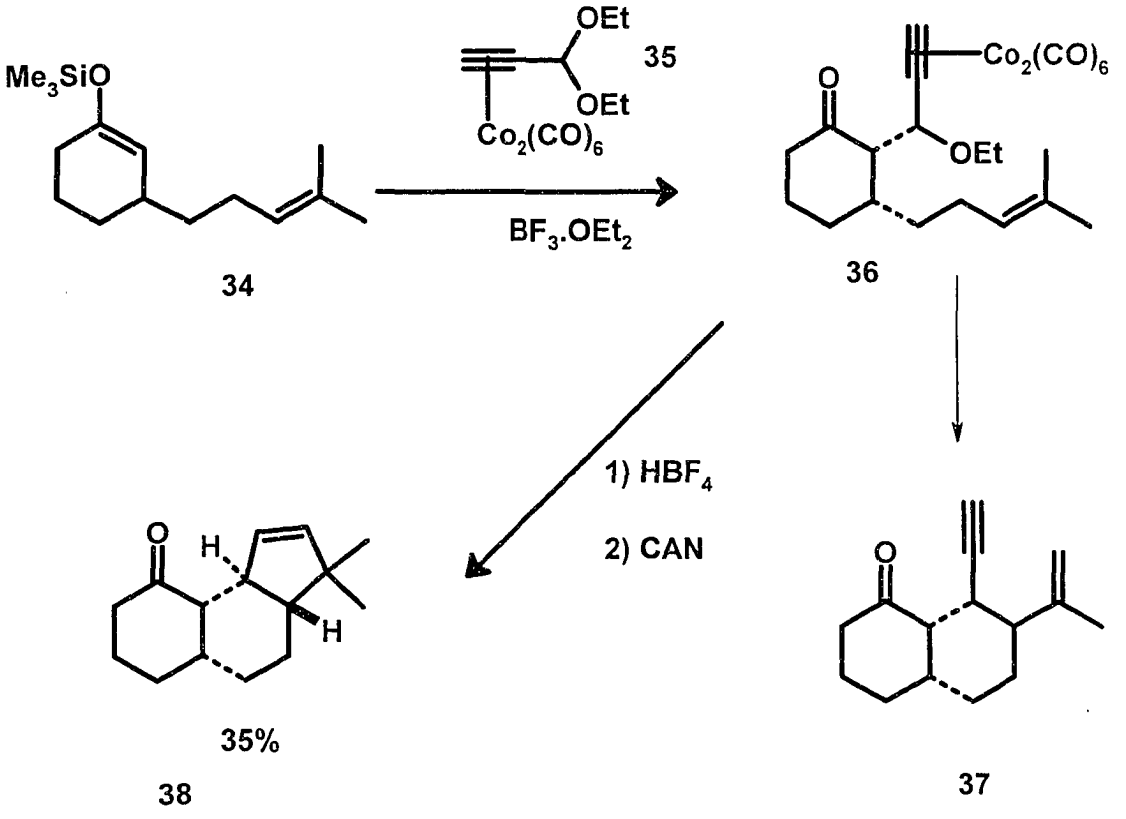
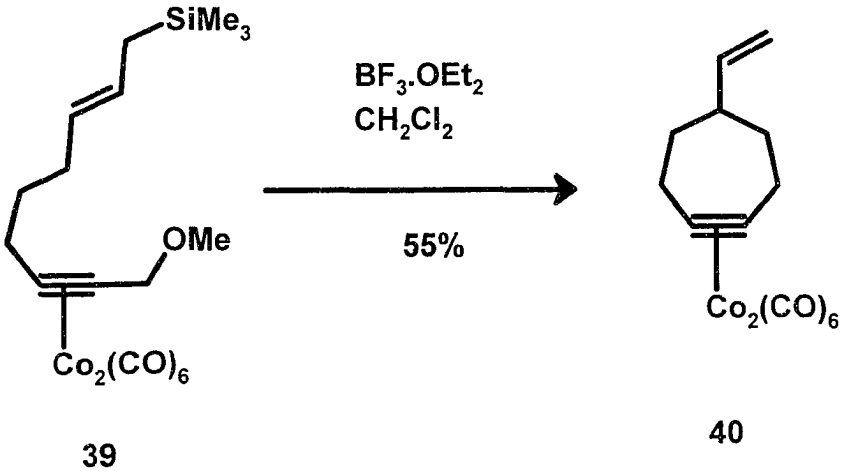



**Figure 16. Sequential Nicholas Reactions of Enolsilane/ Alkene**

Conceptually, it is possible to form cycloalkynes containing the complexed triple bond. The Schreiber group has reported the exo-trig cyclization of various alkyne complexes containing an allylsilane moiety. Formation of six, seven, and eight membered cyclic products are possible in good yields (Fig. 17). The formation of a cyclohexyne dicobalt hexacarbonyl complex is quite remarkable. However, to date, it remains one of only two examples in the literature.[15,23]




39 40

**Figure 17. Intramolecular Nicholas Alkylation**

Magnus[24] has extensively used Nicholas chemistry for the synthesis of endiyne antibiotics. The use of a tandem Micheal addition-Lewis mediated cyclization allowed the formation of a 10-membered ring containing a dicobalt hexacarbonyl complexed alkyne (**43**). The bicylic thus obtained is a core unit of the endiyne antibiotic calicheamicinone (**44**) (Fig. 18).

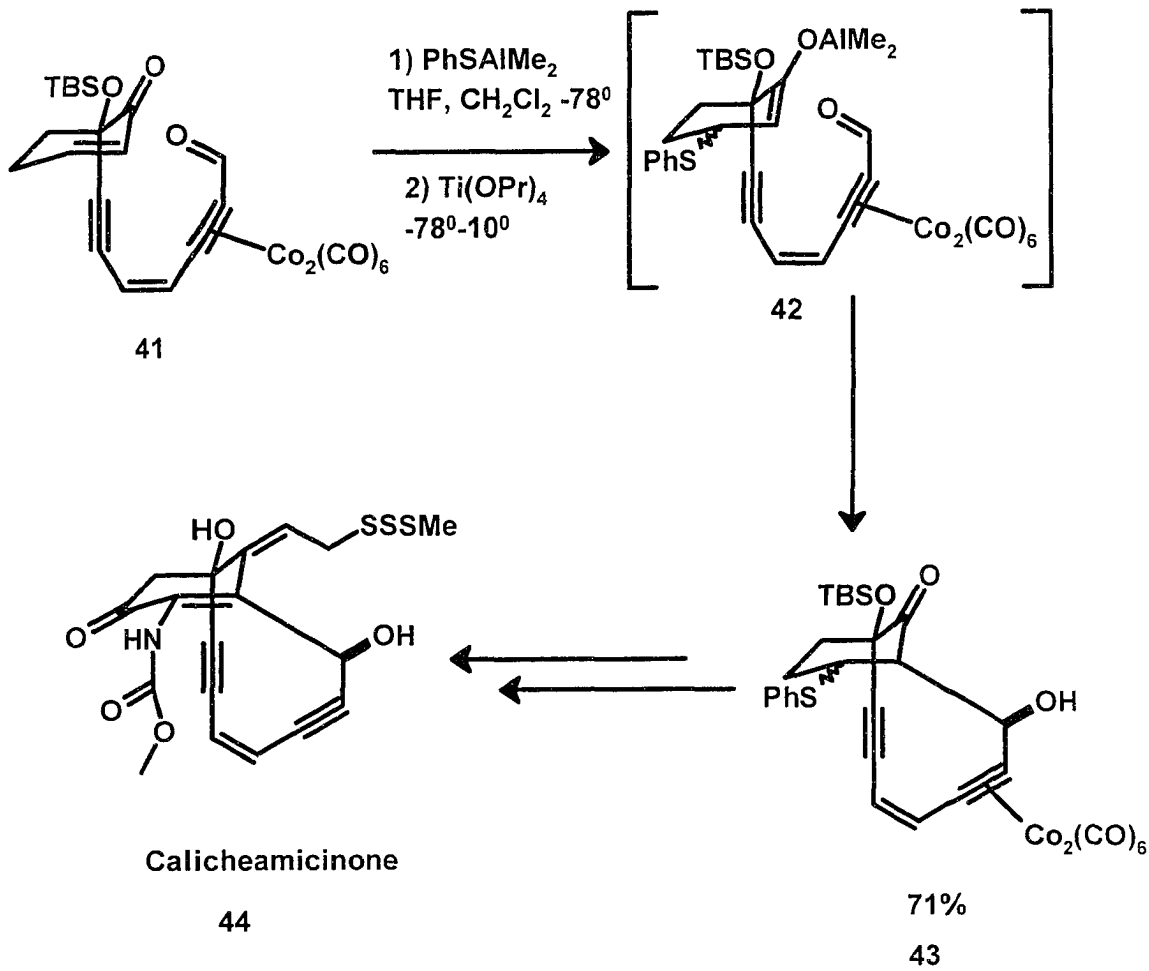



**Figure 18. Magnus' Synthetic Approach Towards Calicheamicinone**

Isobe[25] has taken full advantage of the facile formation of cyclic ethers possessing the complexed alkyne in the ring. These cyclic ether formation reactions have been used elegantly in the synthesis of several portions of the natural products ciguatoxin **45** and the related gambiertoxin **46** (Fig. 19).

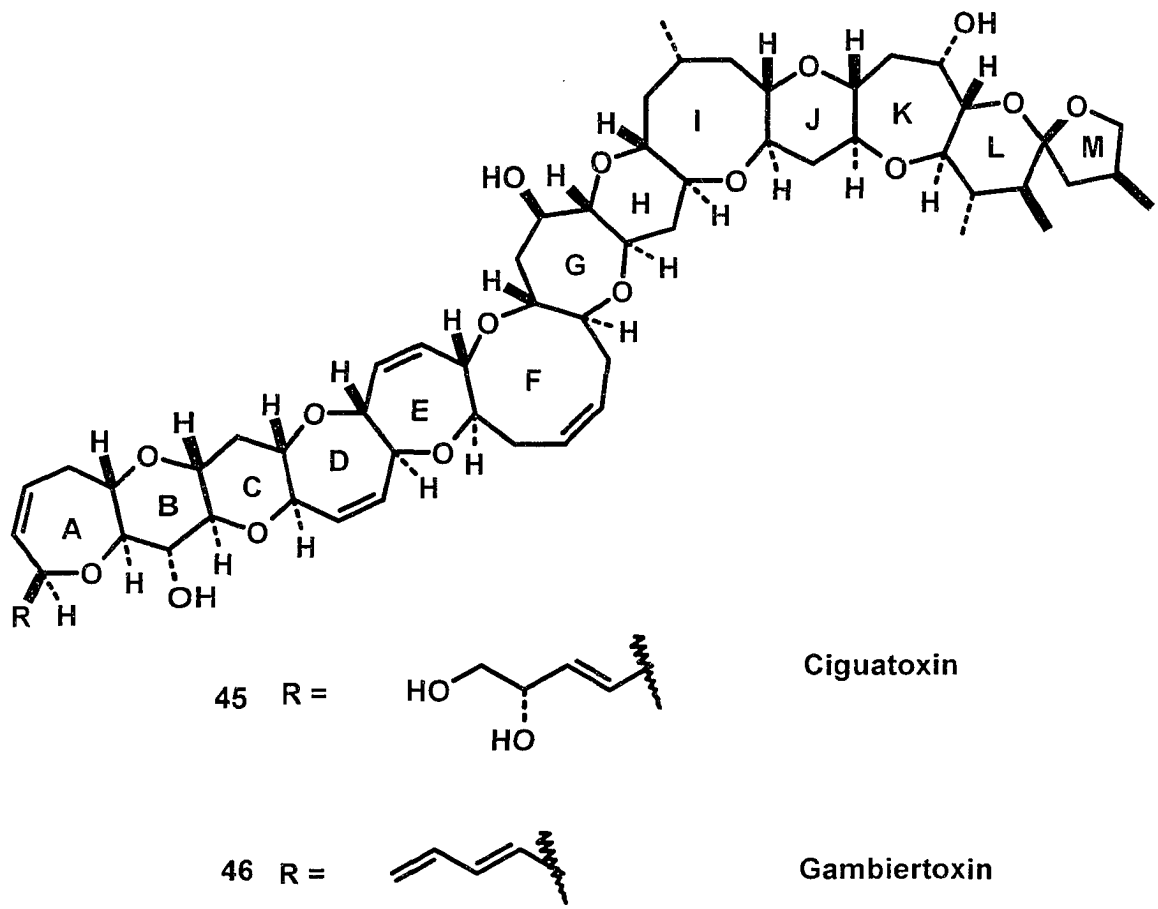
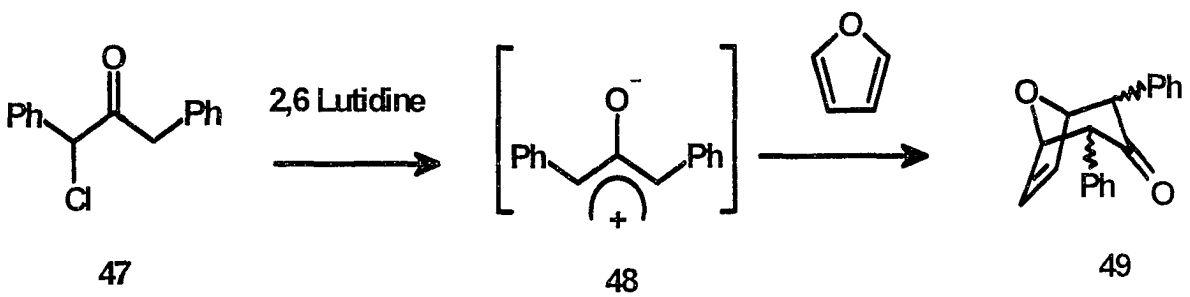



**Figure 19. Ciguatoxin and Gambiertoxin**

### 1.2c The Double Nicholas [4+3] Cycloaddition Reactions

Cycloheptane frameworks are usually obtained either from acyclic precursors, from ring modification or from cycloaddition reactions.[26] Cycloaddition reactions are by far the best choice in terms of synthesis due to the simplicity of the starting material and thecomplexity of the products. Conceptually, of all the

cycloaddition reactions, the most powerful and attractive way of making a cycloheptane ring is the 4 + 3 cycloaddition reaction. In 1962, Fort[27] first reported the 4 + 3 cycloaddition reaction, between an allylic cation and a diene to form a cycloheptane ring (Fig. 20). This reaction which involves an oxyallyl (2πC) cation and a diene (4πC) can be viewed as a variant of Diels-Alder reaction.




47 48 49

**Figure 20. Fort's 4+3 Cycloaddition**

Since there are numerous readily available dienes, much of the effort in this field has always been concentrated on the preparation of the allylic moiety. There are several known methodologies[28] to generate the oxyallyl cation (i.e., **48**). The most useful methods employ α,α-dihaloketones with a reducing agents such as $Fe_2(CO)_9$. Hoffman[29] has proposed three plausible mechanisms to explain the products observed in the reactions. The concerted mechanism is type (**A**) via transition state **50** (Fig. 21). Type (**B**) mechanism involves the stepwise formation of the bonds via **51**. Finally, type (**C**) leads to the formation of a five membered ring or acyclic products (**52a**, **52b**) rather than the cycloheptane ring. Consequently, a

successful 4+3 cycloaddition reaction depends on factors such as the substrates used, the oxyallyl formation and its conformation[30] as well as the reaction conditions employed.[31]

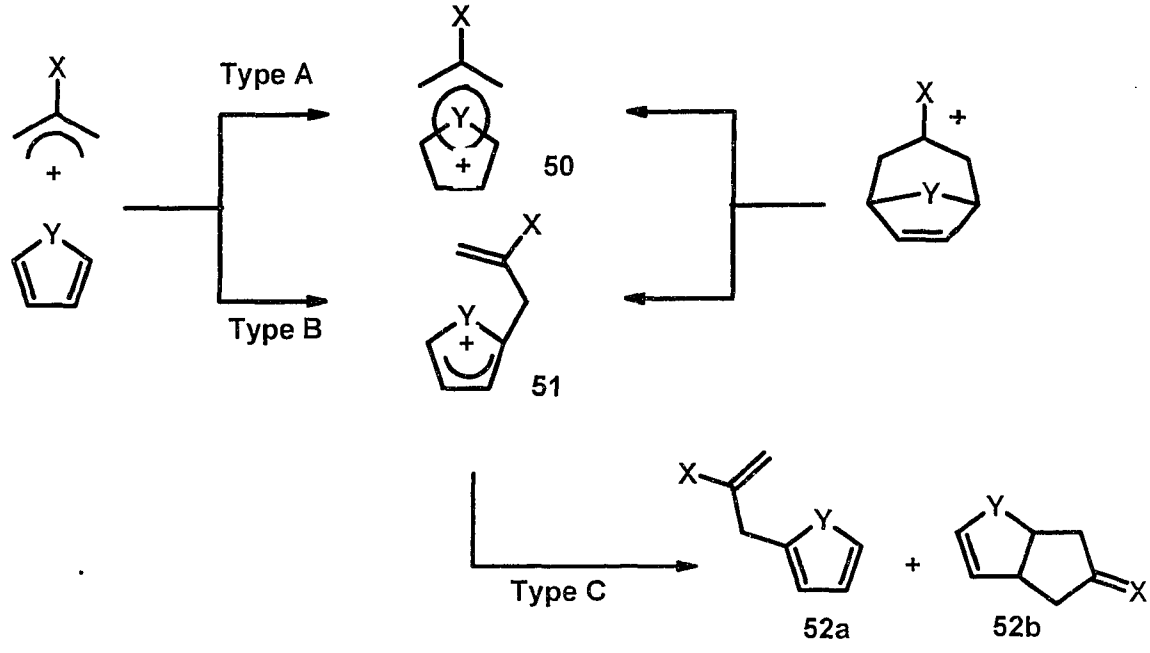



**Figure 21. Plausible Mechanisms for the Oxyallyl 4+3 Cycloaddition**

Takano[32] first conceived the idea of synthesizing the cycloheptyne dicobalt complex by tandem double Nicholas reaction. He attempted to form the cycloheptyne dicobalt complex by a [4+3] cycloaddition reaction employing 1,4-dibenzyloxybut-2-yne dicobalt hexacarbonyl complex (**53**) and 1,3-bis(trimethylsilyl)propene (**54**) in the presence of boron triflouride (Fig. 22). Unfortunately, only acyclic products were observed.

Subsequently, the Green group[33] successfully demonstrated that with a wise choice of the allyldimetal equivalent, such as the vinysilyl stannane **56**, it was possible to obtain the cycloheptyne dicobalt complex **55** in one pot reaction in good yield (Fig. 22). The choice of the dimetallic nucleophile proved to be crucial in the 4+3 tandem double Nicholas cyclization.

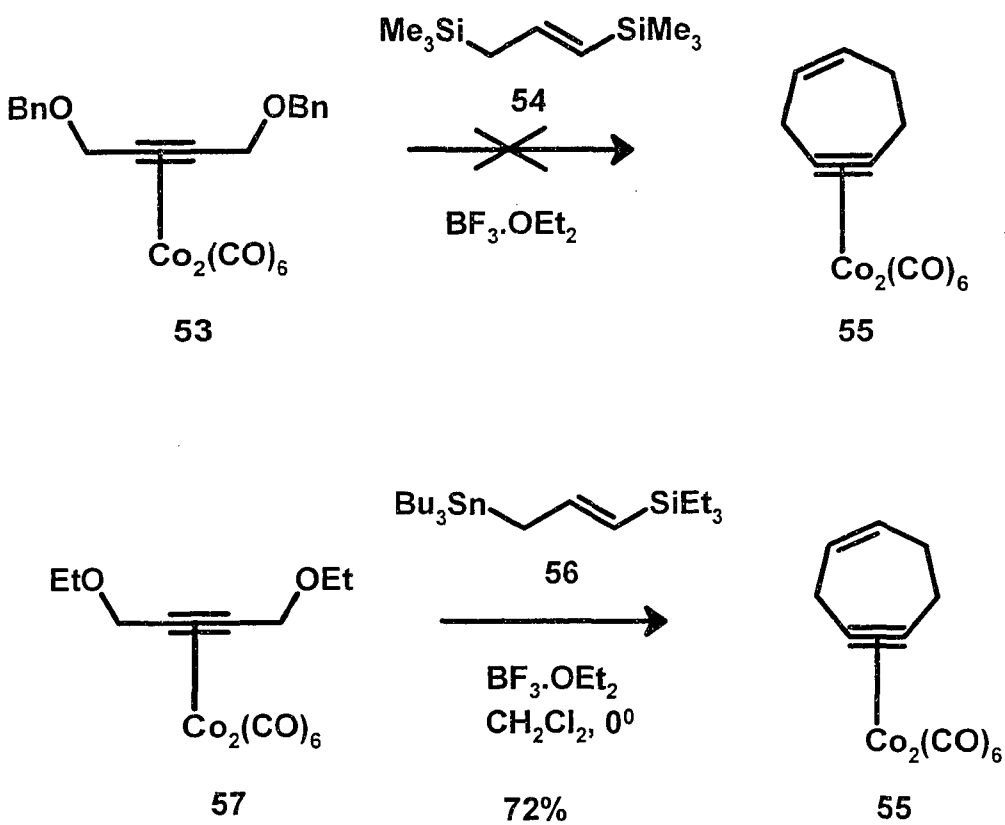



**Figure 22. The 4+3 Tandem Double Nicholas Cycloaddition**

The proposed mechanism for the cycloaddition involves a stepwise process (Fig. 23). Initial formation of **59** is followed by the nucleophilic attack of the

silylstannane, resulting in the formation of the first Nicholas adduct **60**. The second carbocation **61** forms when a second molecule of Lewis acid is attacked by the propargyl ether complex. Intramolecular trapping with the allylsilane moiety forms the cation **62,** which then loses the formal trimethylsilyl cation to form the cycloheptenyne dicobalt complex **63**.

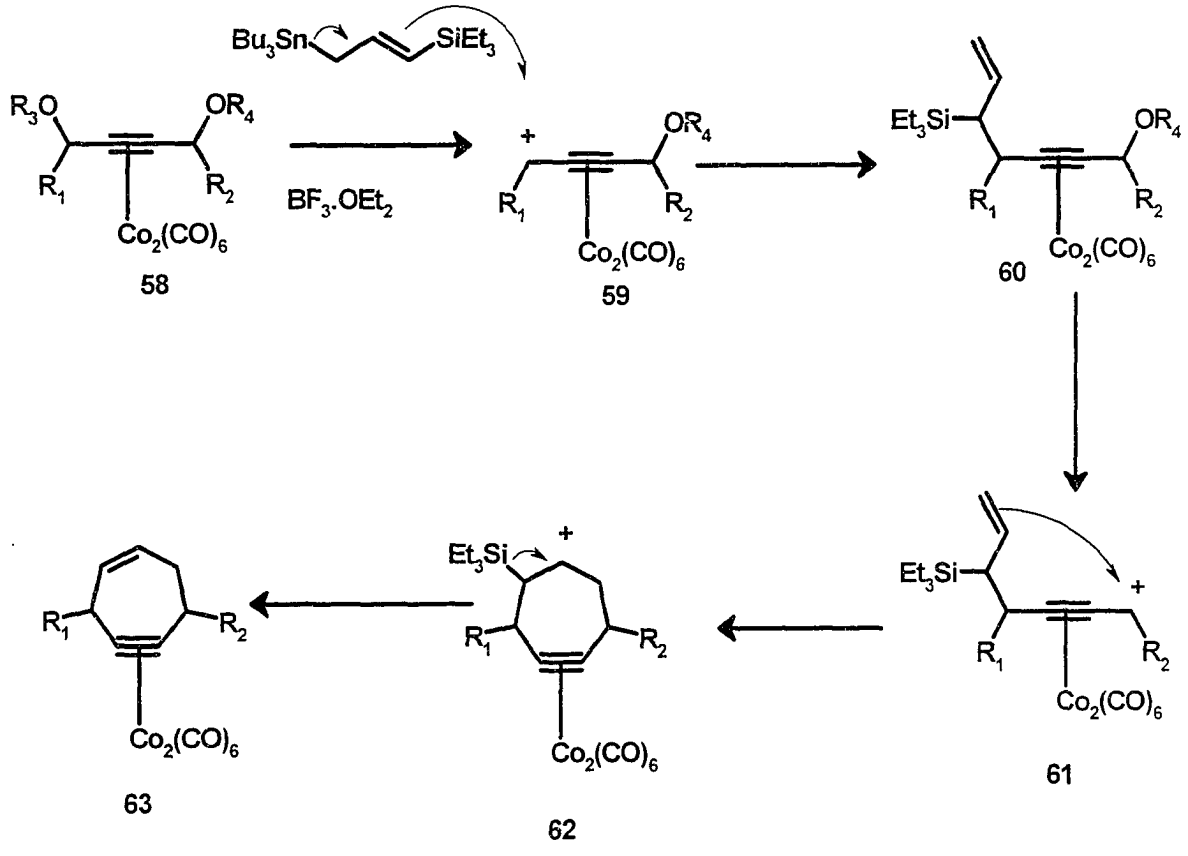



**Figure 23. Mechanism of the Tandem Nicholas Cycloaddition**

The substituent effects on the regioisomeric ratio of the reaction have been studied by this group. Apparently a kinetic factor plays an important role in

determining the formation of the regioisomeric products. This kinetic discrimination stems from the interaction between the Lewis acid and the leaving alkoxy functional group. Bulkier alkoxide groups (i.e. isopropoxy vs methoxy) encumber the approach of the Lewis acid, thus reducing the rate of formation of the propargyl cation complex. Indeed Schreiber[34] was able to ionize selectively the less hindered side of the cylic acetal in complex **64** in route towards the synthesis intermediate **65**, a precursor of epoxydictymene (Fig. 24).

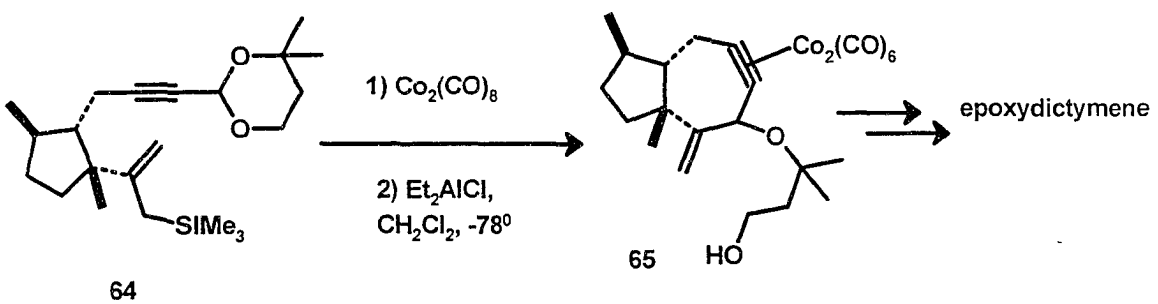



**Figure 24. Selective Ionization of Cyclic Acetals**

A second type of double Nicholas cycloaddition on **57** was found to occur in the presence of allyltrimethylsilane and boron trifluoride. The reaction afforded exclusively γ-fluorocycloheptane dicobalt complex in 75% yield.[35] When a dichloromethane solution of unsusbtituted 1,4-diethoxy complex **57** and allyltrimethyl silane were mixed with $SnCl_4$, γ–chloro cycloheptyne dicobalt complex was obtained in 78% yield. When $SnBr_4$ was used as the Lewis acid, γ-bromide trapping was achieved in only 26% yield. When benzene was used as the solvent and $B(C_6F_5)_3$ as the Lewis acid, γ-phenylcycloheptyne complex were obtained in

70% yield. Toluene and chlorobenzene trapping gave a mixture of ortho, meta, and para substituted γ-cycloheptyne complexes in 58% and 51% yields, respectively.

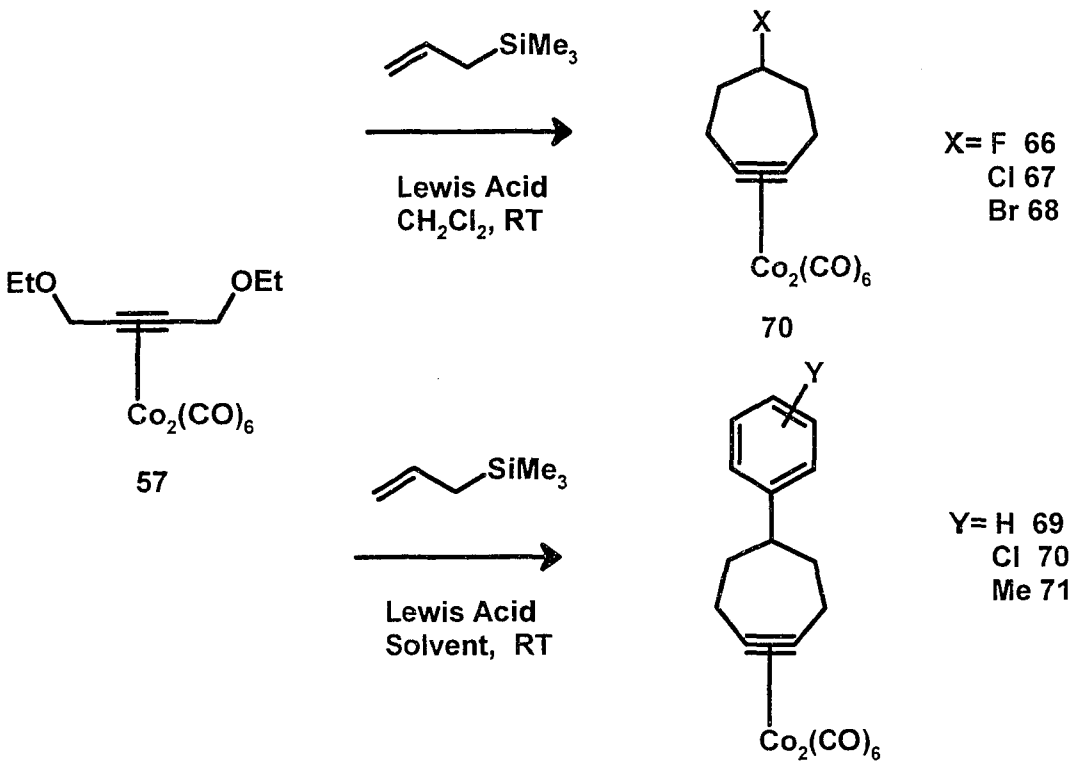
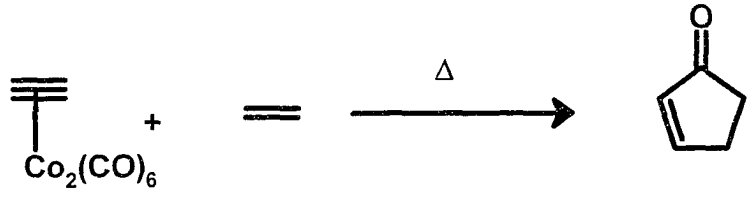



**Figure 25. Intermolecular Trapping Using Allyltrimethylsilane**

## 1.3 Pauson-Khand Reaction

Another synthetically useful and perhaps equally valuable change associated with complexation of the triple bond is the Pauson-Khand reaction (PKR). When dicobalt hexacarbonyl alkyne complexes are heated in the presence of an alkene, it forms a cyclopentenone in a [2+2+1] cycloadditon reaction (Fig. 26). First reported by Pauson and Khand in 1971, the alkene and the alkyl portions of the cyclopentenone clearly stem from the alkyne and alkene, respectively, while the carbonyl's source is one of the CO ligands.[36] Compound containing various transition metals such as titanium, ruthenium, rhodium, and iridium are also known to catalyze the PKR reaction. However, cobalt, as a dicobalt hexcarbonyl alkyne complex, remains the dominant metal of choice for the Pauson-Khand reaction.[37]




72 73 74

**Figure 26. Typical Pauson-Khand Reaction**

### 1.3a PKR Mechanism

In 1985 Magnus[38] proposed the widely accepted mechanism of the Pauson-Khand reaction (Fig. 27). The stable dicobalt hexcarbonyl complex first suffers a loss

of a CO ligand from one of the cobalt atoms, followed by complexation of the alkene. The steps are invariably a reversible processes the first of which is thought to be the rate determining step of the reaction. Amine oxide promoted Pauson–Khand reactions accelerate the reaction by oxidizing the CO produced to carbon dioxide, thus making the first step irreversible. This is followed by insertion of the alkene from the less hindered π-face into the less substituted alkyne carbon-cobalt bond, to form the first carbon-carbon bond. The regioselectivity with respect to both the alkyne and the alkene is determined at this step. This is followed by addition of CO to give the cobaltacycle, and then reductive elimination and decomplexation of the metal furnishes the cyclopentenone.

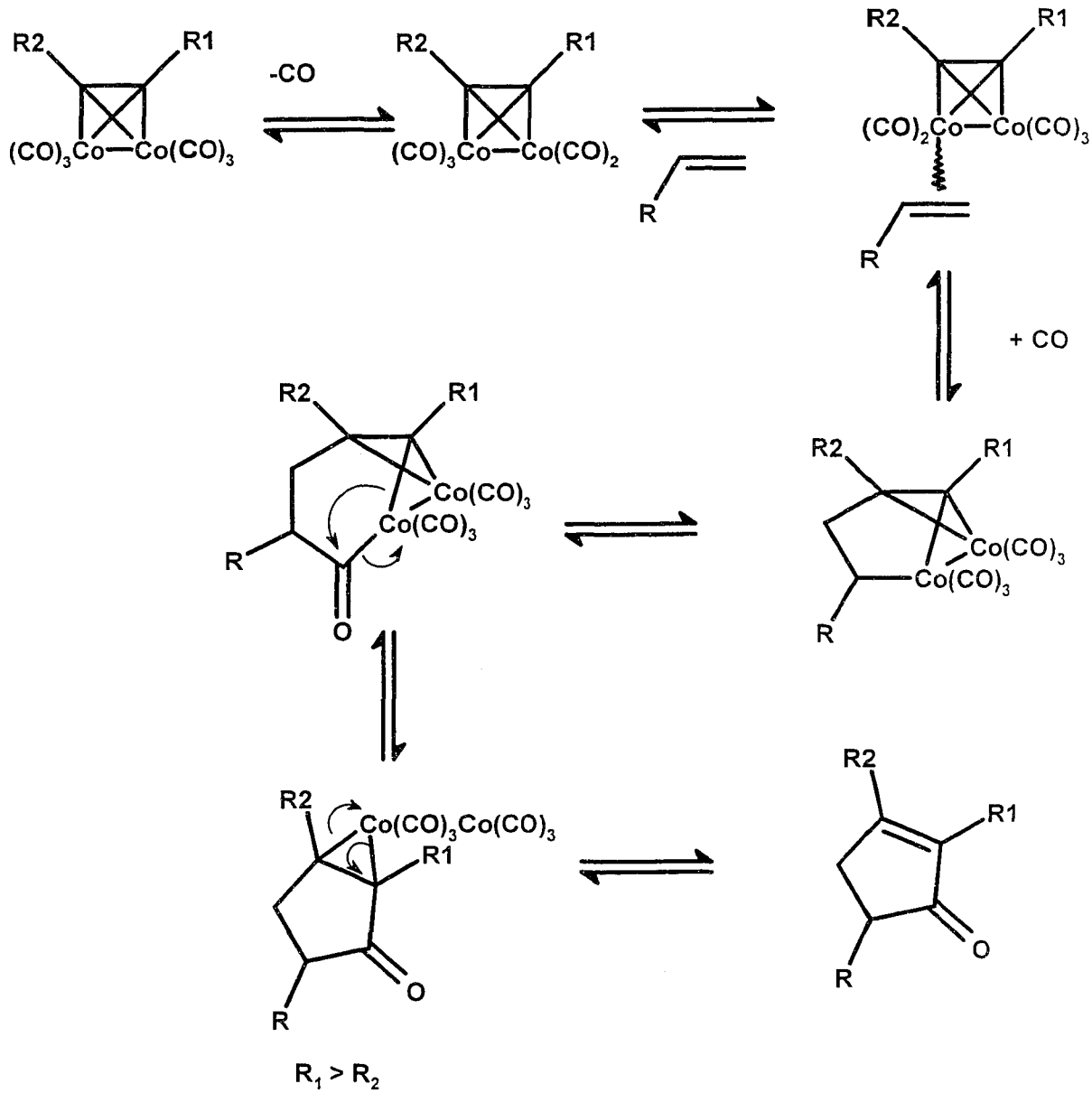
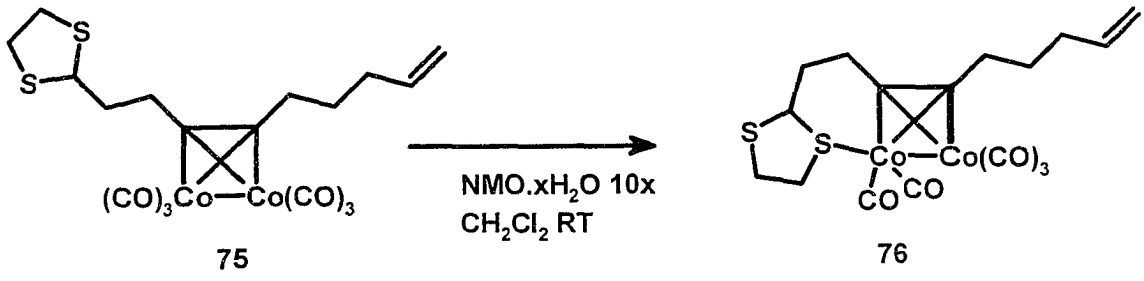



**Figure 27. Accepted PKR Mechanism**

Pauson proved unambiguously the intermediacy of dicobalt alkyne complex in Pauson-Khand reaction. Though alkene cobalt complexes are known, they do not form cyclopentenones when heated with alkynes.[39] Besides the initial alkyne cobalt complexes and the cyclopentenone products, no intermediates have ever been

trapped or isolated along the reaction pathway. The only exception to this is Krafft's observation and isolation of a 2:1 mixture of diastereoisomers **76** (Fig. 28).[40] However, the intermediate complex **76** lies off the direct reaction pathway to cycloaddition. Nevertheless, it supports an initial dissociative pathway.




75 76

**Figure 28. Krafft's Intermediate Complex**

### 1.3b PKR the Early Years: Intermolecular and Intramolecular PKR

The Pauson group focused on the scope and limitations of intermolecular reactions. The reaction tolerates a wide range of common organic functional groups. All terminal or internal alkynes participated efficiently with the exception of propynoic acid dicobalt complex. Strained cyclic olefins efficiently afforded the cyclopentenones in high yields, whereas ordinary alkenes gave modest yields.

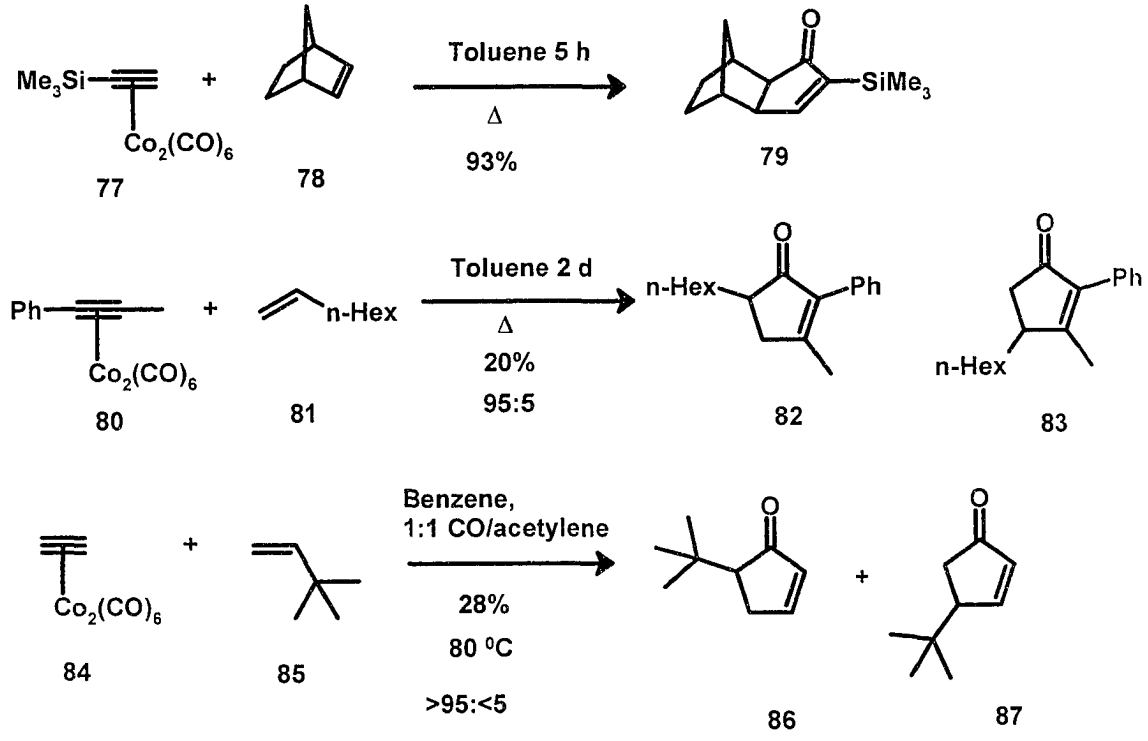



**Figure 29. Regioselectivity in Pauson-Khand Reactions**

The regiochemical outcome of the reaction is highly dependent on the nature of substituents on both the alkenes and the alkynes. Steric effects are the dominant factors that determine the regioselectivity of the PKR. Most intermolecular Pauson-Khand reactions give a mixture of regioisomers; bulkier substituents on terminal alkynes are always placed $\alpha$-to the carbonyl group in the products. On the other hand, the regioselectivity of terminal alkenes is not as readily predictable. In general, reactions of terminal alkenes with ethyne or terminal alkynes give minimal regioselectivities, while internal alkynes give better regioselectivity. Nevertheless, terminal alkenes with a bulky substituent, i.e., tert-butyl group, are more regioselective and the bulky group is preferentially placed $\alpha$-to the carbonyl group.[41]

Electron deficient alkynes gave both high yields and high regioselectivity. Electron deficient alkenes however, generally are poor substrates for PKR reaction and they tend to yield dienes (Fig. 30).[42]

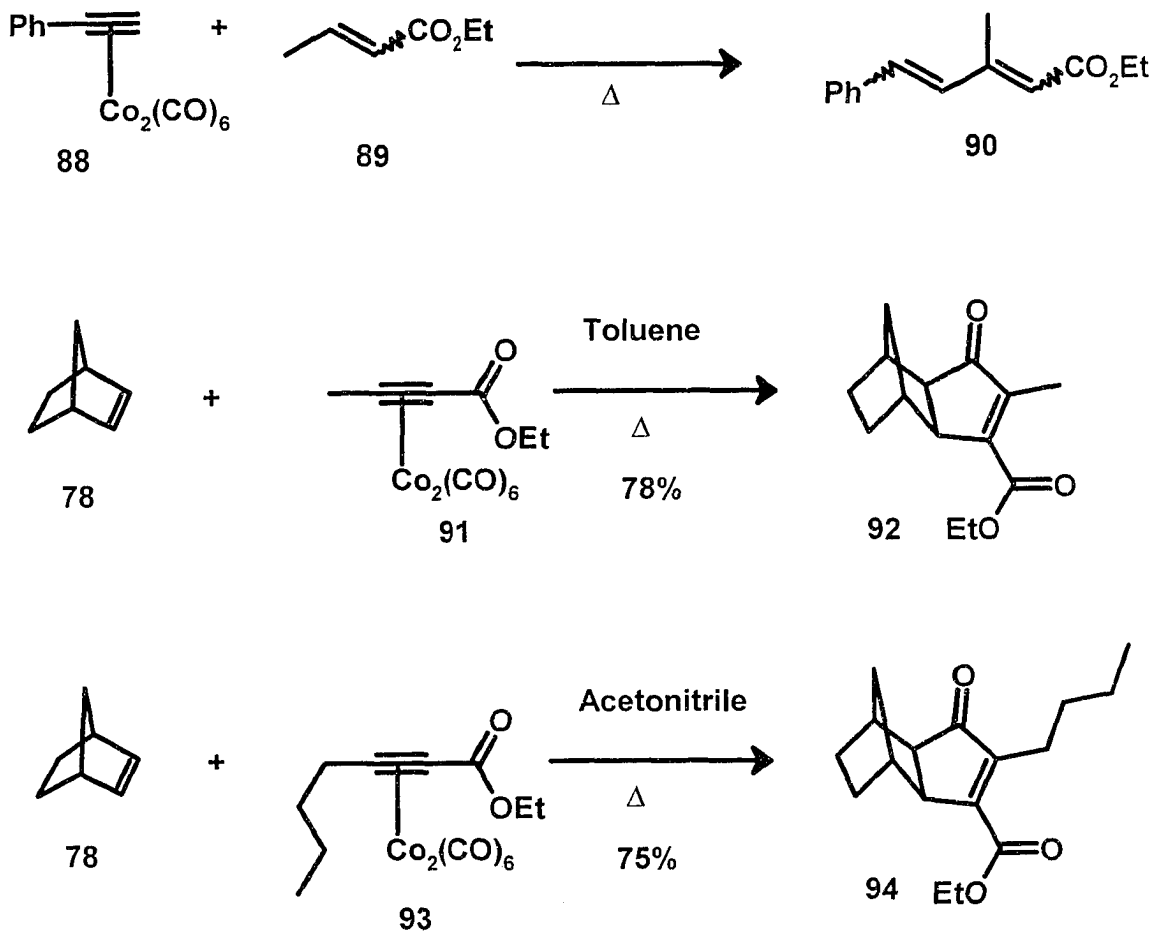



**Figure 30. PKR of Electron Deficient Alkynes and Alkenes**

A weak electronic effect has been shown to have an impact on the regioselectivty of the product.[43] In fact, when substrate **95** was subjected to thermal conditions it afforded **96a** and **96b** in a ratio of 76:24 (Fig. 31). Apparently, the insertion of the alkyne occurs at the electron deficient carbon. On the other hand,

substrate **97**, where the electronic effect was removed, when subjected to the same conditions gave almost 1:1 mixture of products **98a** and **98b**.

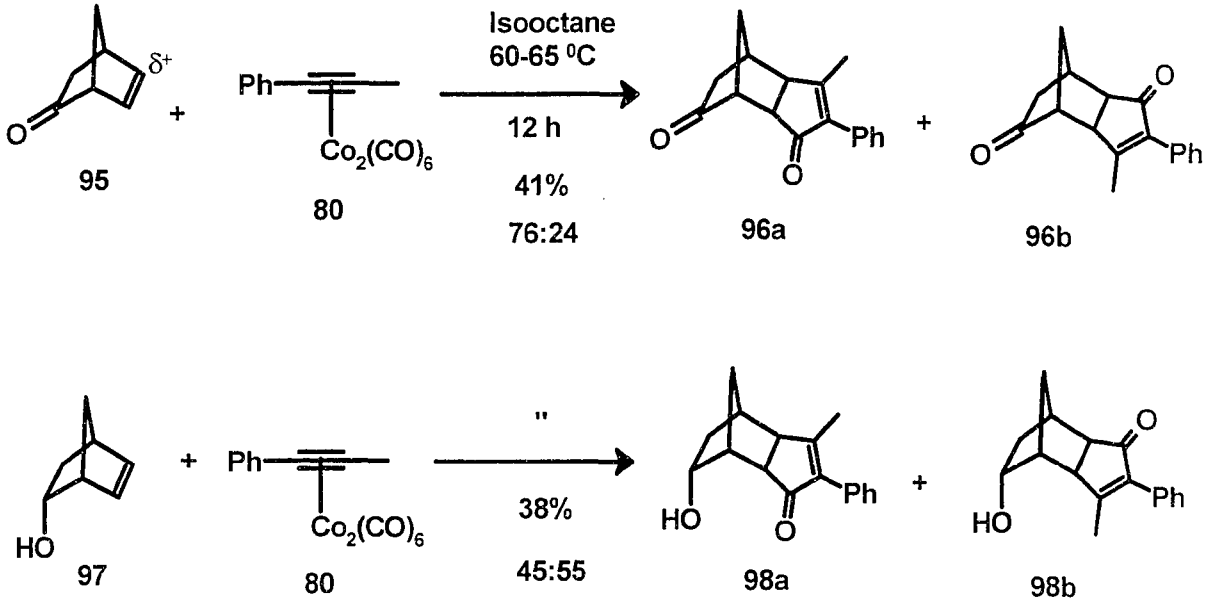



**Figure 31. Electronic Effect on the Regioselectivity on PKR**

The drawbacks of the intermolecular PKR include the harsh reaction conditions, (i.e., high temperature), and the long time required to form the cycloaddition adduct. This may not be appropriate for sensitive substrates. In addition, the chemical yields obtained from unstrained alkenes in intermolecular Pauson-Khand reactions are normally poor, though strained alkenes and those possessing a heteroatom at the homoallylic position gave excellent yields. The reaction is susceptible to steric and electronic effects on the alkene.

In 1981, Schore[45] expanded the scope of the reaction when he published the first example of an intramolecular Pauson-Khand. In general, intramolecular PKR gives both high yields and complete regioselectivity.

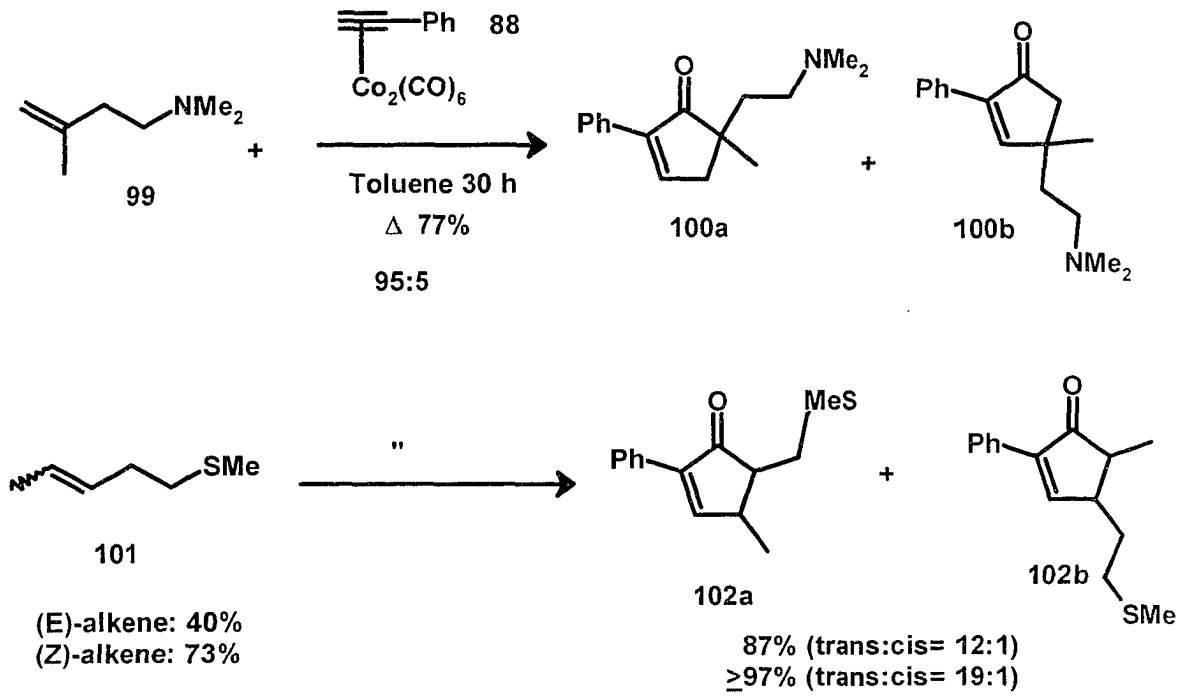


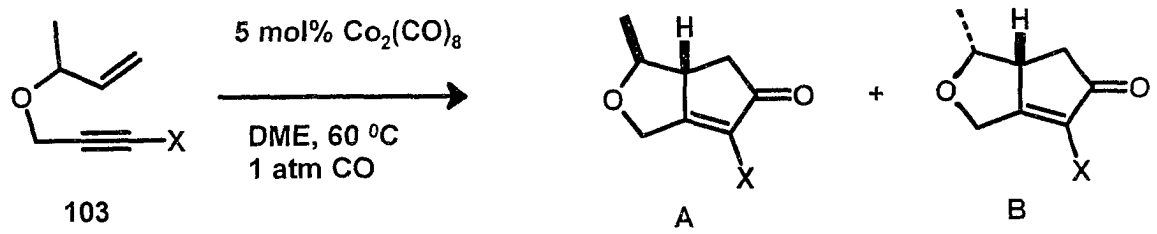

**Figure 32. Heteroatom Acceleration Effect**

### 1.3c PKR Recent Progress

The Pauson-Khand reaction has become popular and widely exploited in synthesis with the advent of additives that accelerated the reaction. Smit and Caple[46] first introduced the Dry State Absorption Conditions (DSAC) absorption technique with silica gel or alumina. This allowed that the PKR to be run in shorter reaction times and lower temperatures. Krafft[39] has added the observation that a

hetero-atom attached at the homoallylic position of an unstrained olefin has an accelerating effect on the PKR (Fig. 32). It was realized that the use of polar solvents, especially DMSO and acetonitrile, has a beneficial effect in promoting PKR compared to non-polar solvents.[47] In the early 1990's, Schreiber and Jeong[48] independently described the promotion of the intramolecular Pauson-Khand reaction at room temperature using N-methylmorpholine N-oxide and trimethylamine N-oxide, respectively. Finally Sugihara[49] group showed that addition of amines or sulfides dramatically accelerated the intramolecular Pauson-Khand reaction. Both intermolecular and intramolecular PKR have enormously benefited from these additives.

The further development of the PKR has been accomplished with the recognition that the reaction could be carried out catalytically. Indeed the last few years have seen an increase in the reports of the catalytic Pauson-Khand reaction [CPKR]. Livinghouse and Pagenkopf reported a photolytic promotion of PKR in 1 atm of CO pressure. The same authors demonstrated that with a careful control of temperature, it is possible to avoid the need for the photoactivation of dicobalt octacarbonyl catalyst.[50] Presence of a thioether in the substrates gave not only better yield, but also improved diastereoselectivities of the cyclized product (Fig. 33). Additives were also shown to accelerate the CPKR.




| X | Yield | Ratio |
|---|---|---|
| H | <23% | 5:1 |
| SMe | 81% | 12:1 |
| S$^t$Bu | 78% | 42:1 |

**Figure 33. Use of Thioalkynes in CPKR**

Almost all successful CPKR are intramolecular PKR, and the substrate tolerance varies from metal to metal. Several groups have succeeded in utilizing different transition metals [Zr, Ti, Fe, Mo, W, Ni, Ru, Rh, and Ir] in PKR and mostly in a catalytic fashion.[51] In general, late transition metals tolerate the presence of polar groups in the enyne, while titanium tolerates substituents around the alkynes and alkenes in the enyne systems.

Another area of Pauson-Khand reactions that has seen a great deal of activity is the asymmetric Pauson-Khand reactions. Pauson first reported the use of a chiral phosphine ligand in the complex and was able to separate and obtain a pure diastereoisomer. Thus, from the pure distereoisomer it should be possible to obtain a pure enantiomer of cyclopentenone. However, low yields and low ee's were observed, due to the epimerization of the complex at high temperature. The use of a chiral auxiliary in the organic fragment, with a chelating capability, did give an

efficient transfer of chirality to the complex. Several groups have reported high asymmetric induction in both stoichiometric and catalytic PKR (i.e. Fig. 34).[52]

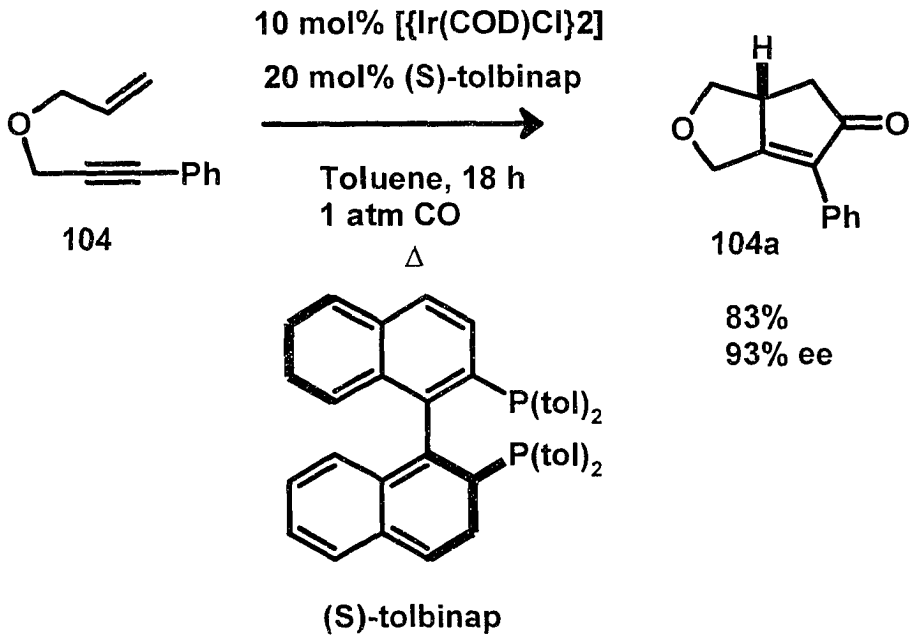



**Figure 34. Asymmetric Catalytic Pauson-Khand Reaction**

Despite the advances in Pauson-Khand reactions, the use of intermolecular PKR has been limited to only strained alkenes. This limitation was not imposed to the intramolecular versions. Therefore, the use of traceless tether has appeared lately to reap the benefits of the intramolecular PKR, and solve most of the limitations on the intermolecular PKR (i.e. low yields and low regioselectivities). [53] The Austin group[53a] has successfully used an N-O as tether link in **105** (Fig. 35). Cleavage of the tether was achieved by $SmI_2$. Pericãs[53b] *et al* reported the use of sulfur as the tether in **108**. The PKR adduct **109** can be desulfurized by Raney

Nickel®. Pagenkopf[53c] reported that vinylsilyl ethers of propargylic alcohols did undergo the PKR with concomitant extrusion of a siloxy group (Fig.35).

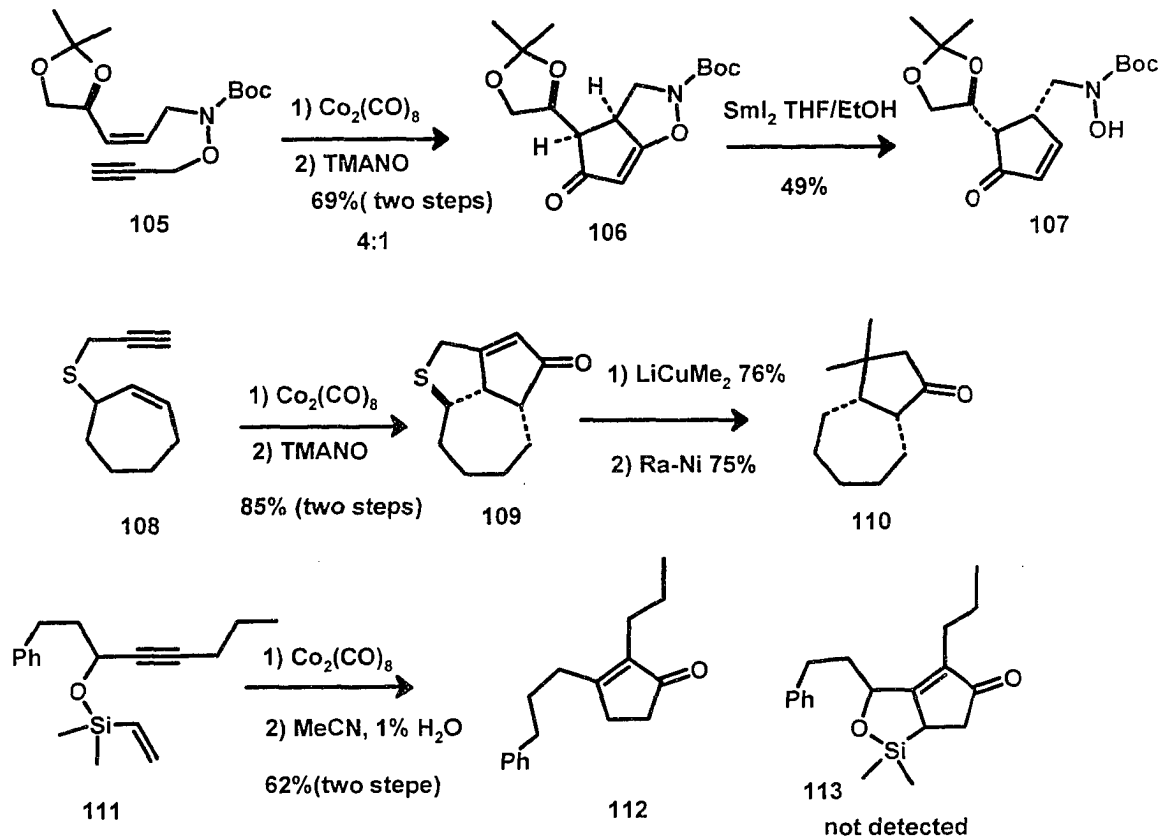



**Figure 35. Use of Traceless Tethers in PKR**

The Pauson-Khand reaction has been extensively exploited in total synthesis of natural and unnatural products. Some recent examples[54] are shown below (Fig. 36). Mukai[54a] used intramolecular PKR as the key step towards the total synthesis of 8-hydroxystreptazolone **116**. Keese[54b] reported a fascinating sequential intramolecular PKR for the synthesis of fenestrane via **119**. Finally, Takano[54c]

employed the intramolecular P-K to establish the carbocyclic framework of the densely functionalized dendrobine**122** in one step.

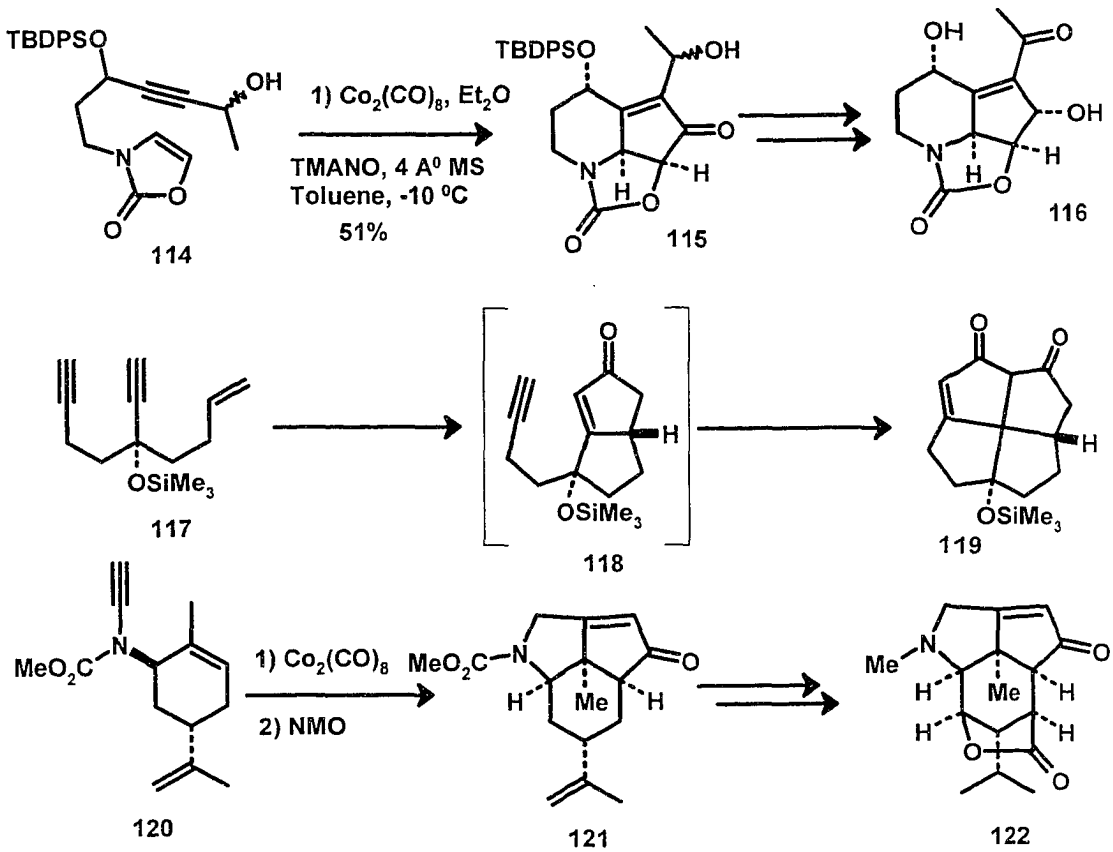



**Figure 36. Examples of PKR Application Towards Total Synthesis**

## 1.4 2+2+2 Cycloaddition Reactions

The trimerization of acetylene to form benzene has been known since 1866. However, the reaction required high temperatures (~400 $^{0}$C) and afforded mixtures of products.[55] In 1949 Reppe first described the use of nickel in the cyclotrimerization of alkynes to form substituted benzene ring.[56]

### 1.4a Mechanism of 2+2+2

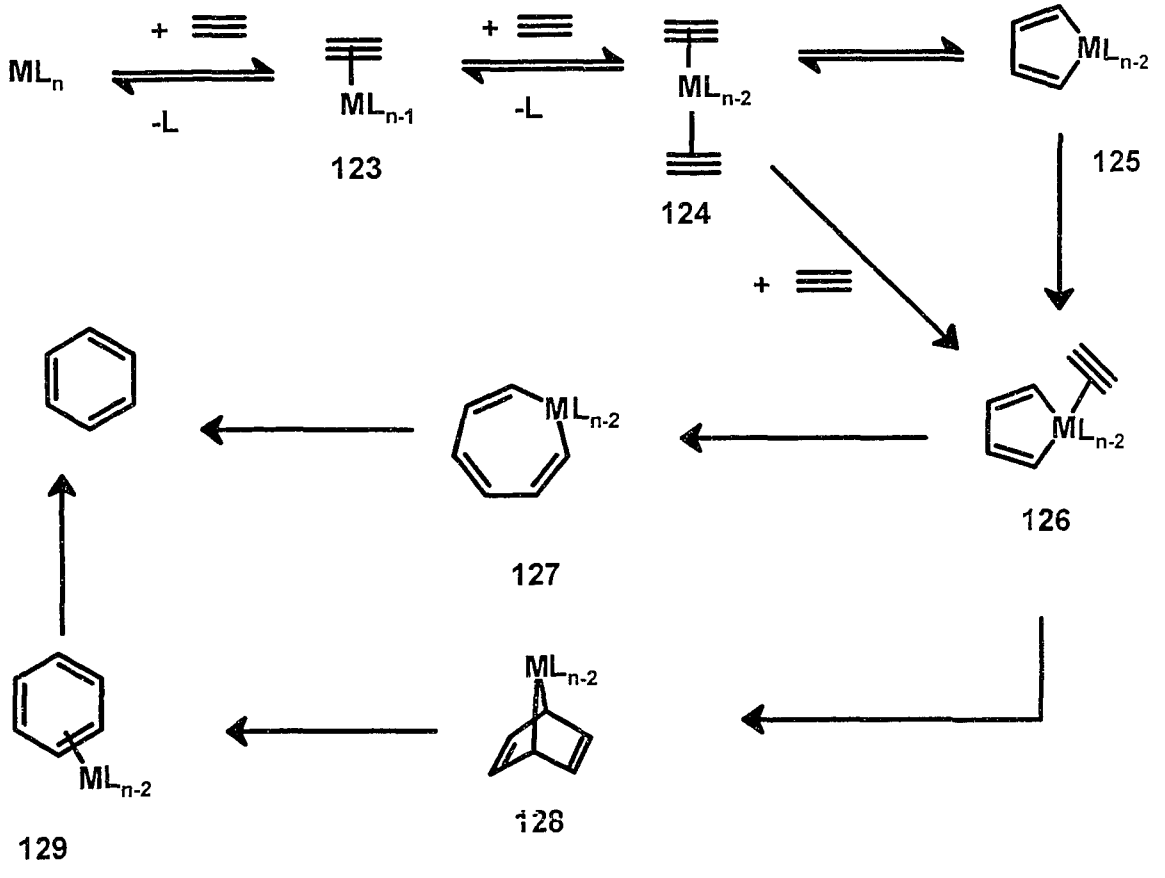



**Figure 37. Mechanism of 2+2+2**

The mechanism of the reaction involves the formation of metallacycle **125** or **126** through oxidative cyclization, followed by either insertion of the third alkyne or a 4+2 Diels-Alder type reaction to furnish complexes **127** and **128**, respectively (Fig. 37). All possible intermediates have been characterized.[57]

Cyclotrimerization of terminal alkynes yields a mixture of 1, 2, 4- and 1, 3, 5-trisubstituted benzenes. The use of two or three different alkynes should be expected to provide an intractable mixture of substituted benzene rings. Tethering two alkynes to undergo an intramolecular 2+2+2 reaction with a third alkyne does provide a partial or completely regioselective formation of benzene ring.

The third alkyne can be substituted by an alkene to obtain a cyclohexadiene or two alkenes and an alkyne can be submitted to 2+2+2 cycloaddition reaction to afford cyclohexenes. The third coupling partner can be a nitrile or isonitrile to furnish pyridines and pyridones.[57]

The 2+2+2 cycloaddition reaction has been used in synthesis. Vollhardt used the cycloaddition as the key step in an elegant synthesis of estrone.[58] The same author used the 2+2+2 cycloaddition reaction in the synthesis of lysergine and strychnine (Fig. 38).[59]

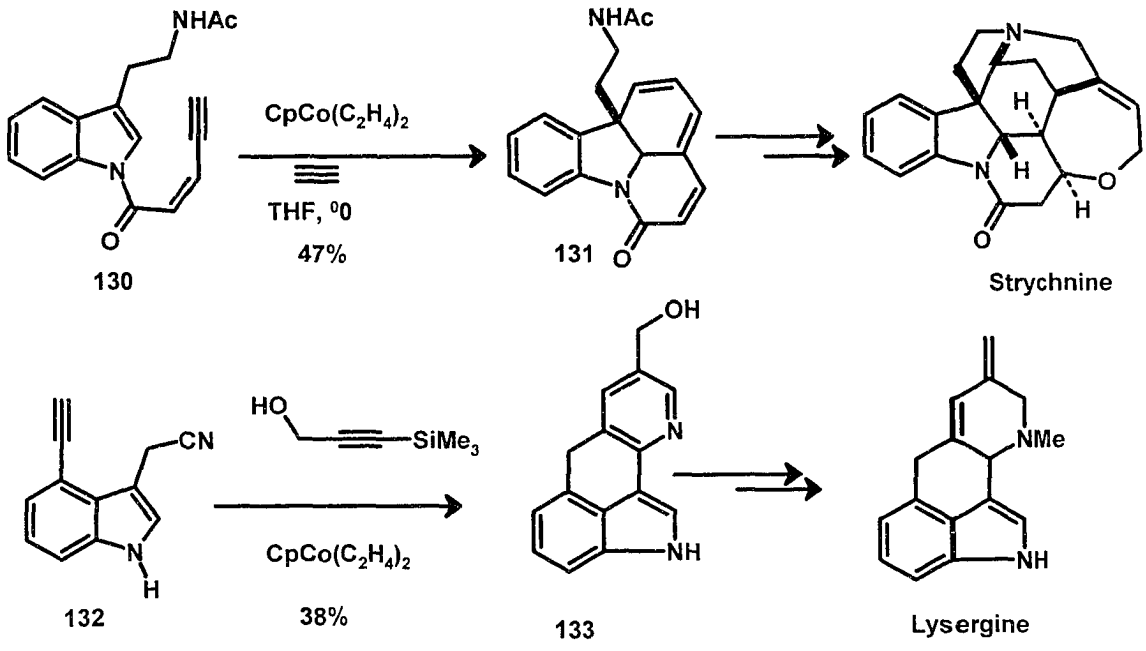
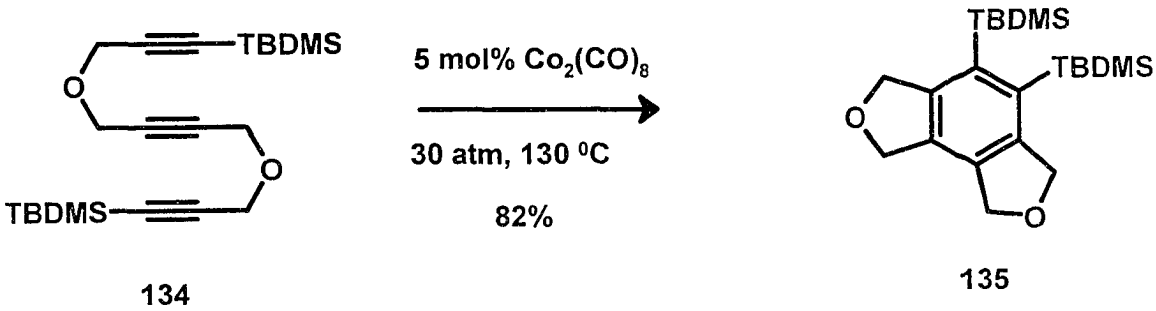



**Figure 38. Use of 2+2+2 Chemistry in Total Synthesis**

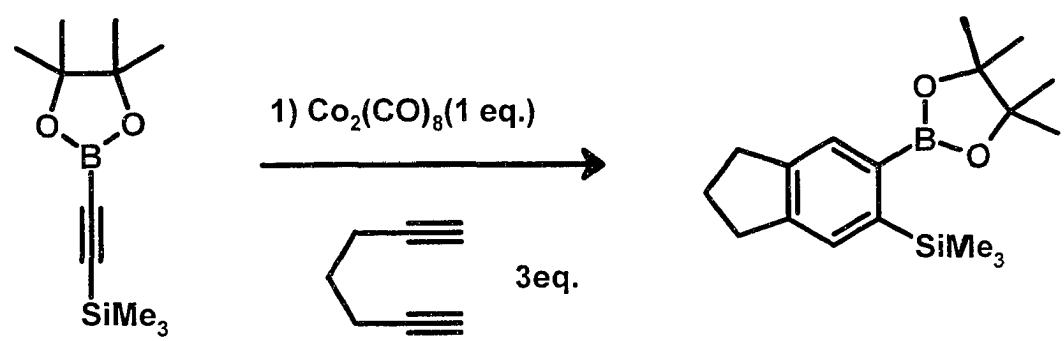
Though cobalt(I), in the form of $CpCo(CO)_2$ or $CpCo(C_2H_4)_2$, dominates this field, several transition metal complexes centered on Pd, Rh. and Ni are known to catalyze the cyclotrimerization of alkynes.[60] Cobalt (0), in the form of dicobalt hexacarbonyl unit, on occasion has been used as the transition metal to accomplish a 2+2+2 cycloaddition reaction.[61] Sappa[61d] reported that asymmetrically substituted alkyne dicobalt hexacarbonyl complexes do undergo cyclotrimerization reactions to furnish a regioisomeric mixture of substituted benzenes. Chung group[61a] also used catalytic $Co_2(CO)_8$ to prepare tricyclic **133** in high yield (Fig.39). The group proposed that the mechanism of the 2+2+2 as similar to the one proposed for Co(I).




134 135

**Figure 39. Chung's 2+2+2 Cyloaddition Reaction**

Recently, Vollhardt group prepared various arylboronic esters, for example **137** from dicobalt hexacarbonyl alkynyl boronate complexes via 2+2+2 cycloadditon reaction with α,ω-diynes (Fig. 40).[62]




136 54% 137

**Figure 40. Preparation of Aryl Boronate Esters**

## 2.0 Use of Allyltrimetal Equivalent in Nicholas Reactions

### 2.1 4+3 Cycloaddition Reactions: Formation and Elimination of Vinylsilane Side Products

The Green group has successfully developed a formal 4+3 cycloaddition by employing a double Nicholas reaction of hexacarbonyldicobalt complexes of propargyl diethers in good yields. It also has been shown[63] that it is possible to form cycloheptynedicobalt complexes sequentially, by employing an allyldimetal equivalent **56** and a γ-alkoxyalkynone or alkynoate complex **138** (Fig. 41). The use of (triethylsilylallyl)stannane **56** allowed the formation of the tethered allylsilane complexes **139a,b,c** as the major product in the Nicholas reaction of **138a,b,c**. Subsequent DIBAL-H reduction of the ester or the ketone function and *in situ* acetylation afforded the acetate complexes **141a,b,c**. These complexes, when exposed to boron trifluoride, gave cycloheptenyne complexes **142a,b,c** in excellent yields.

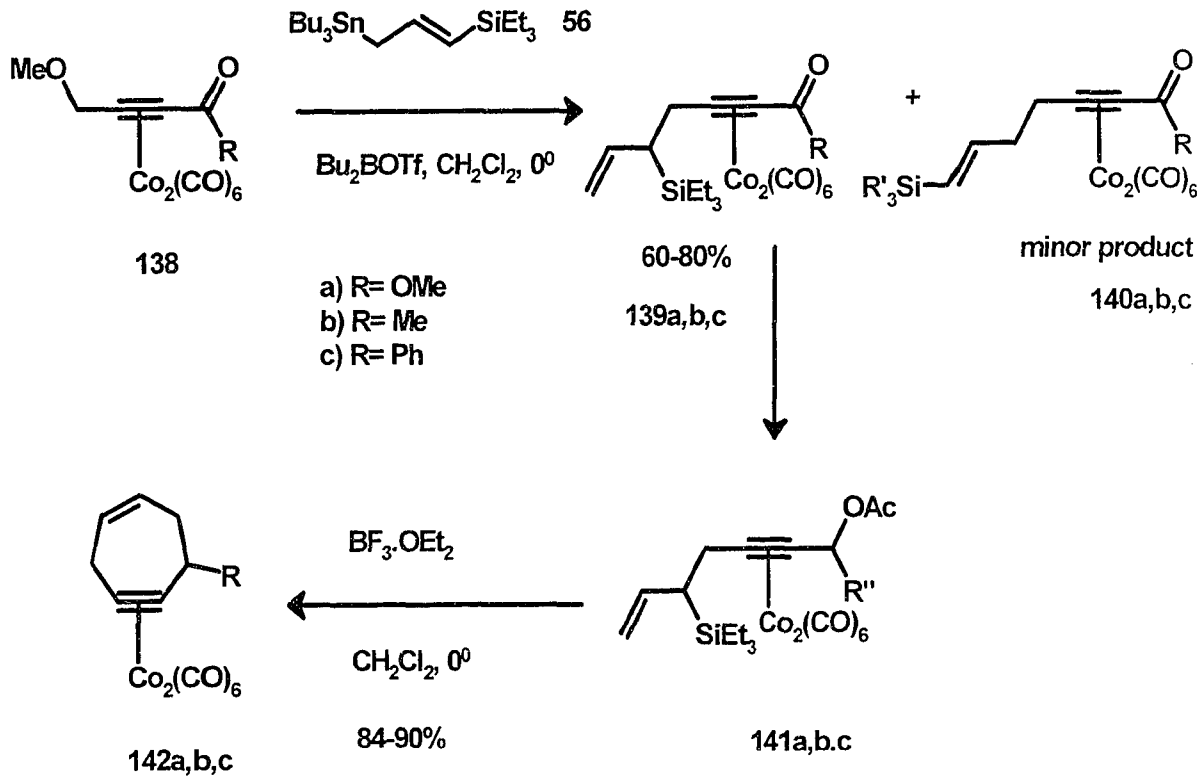



**Figure 41. Stepwise Formation of Cycloheptenynes by Sequential Nicholas Reactions**

The most significant side product of the initial Nicholas condensation step was vinylsilane **140 a,b,c**. The source of the vinylsilane byproduct is believed to originate from an allylic rearrangement of the tin moiety in the Lewis acid media prior to the formation of the Nicholas adduct (Fig. 42).[64]

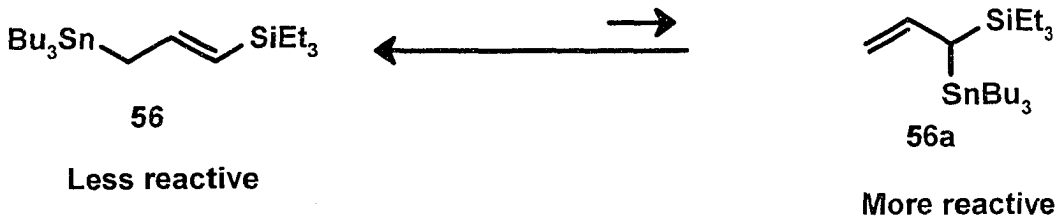



**Figure 42. Lewis Acid Mediated Allyltin Rearrangement**

Recovered **56**, however, did not show evidence supporting the presence of noticeable **56a** in the reaction mixture.[65] Formation of vinylsilane side product increases with decreasing the bulkiness of the silyl moiety in **56**. Indeed, use of allyltrimethylsilylstannane **142** as nucleophile provided the lowest ratio of allylsilane to vinylsilane side product (Fig. 43), when a bulkier triisopropylsilyl group was used, a better regioisomeric ratio in favor of the allylsilane product was obtained at the expense of the chemical yield. As a compromise, a triethylsilyl group, as in **56**, was chosen in the double Nicholas cycloaddition studies.[66]

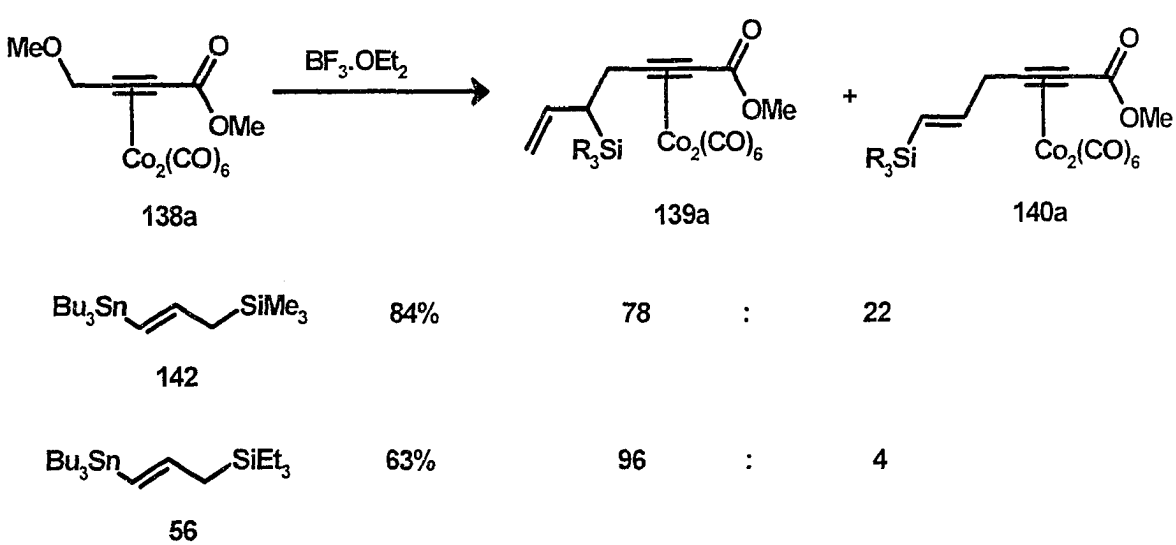



**Figure 43. Regioisomeric Improvement of Silylstannanes**

When substituents reside on the propargylic carbon, the vinylsilane byproduct also becomes more competitive. Indeed, **143** gave 55:45 ratio of allylsilane and vinylsilane products **144** and **145** (Fig. 44). In addition, when substrate **146** was subjected to the double Nicholas 4+3 cycloaddition conditions, only a modest yield of the cycloheptenyne complex (42%) was obtained. The low yield was attributed to extensive formation of vinylsilane **148**. The vinylsilane thus formed does not cyclize to cycloheptyne complex.

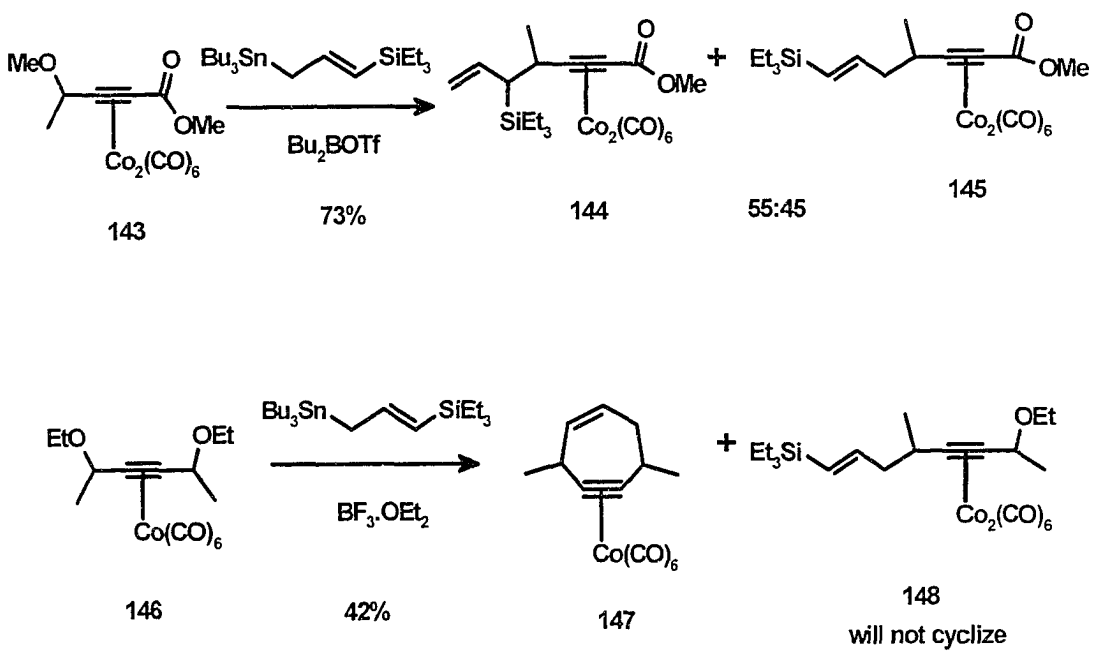
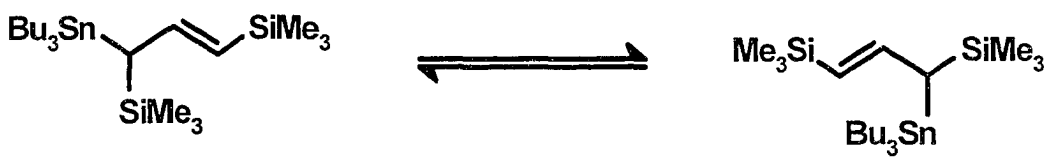



**Figure 44. Propargylic Substitution and Vinylsilane Formation**

## 2.2 Preparation and Nicholas condensation of Nucleophile 149

One of the objectives of this thesis is to solve the problem associated with the formation of vinylsilane side products. Therefore, we proposed to prepare and employ nucleophile **149**, since an allyltin rearrangement of **149** gives the same species (Fig. 45).




**149**

**Figure 45. Lewis Acid Mediated Rearrangement of Allyltrimetal Equivalent**

Allyltrimetal **149** was prepared by deprotonation of the known compound[32] **54** with butyllithium in dry hexane and trapping the resulting allyl anion with $Bu_3SnCl$. After conventional workup and distillation, compound **149** could be isolated in 80% yield (Fig. 46).

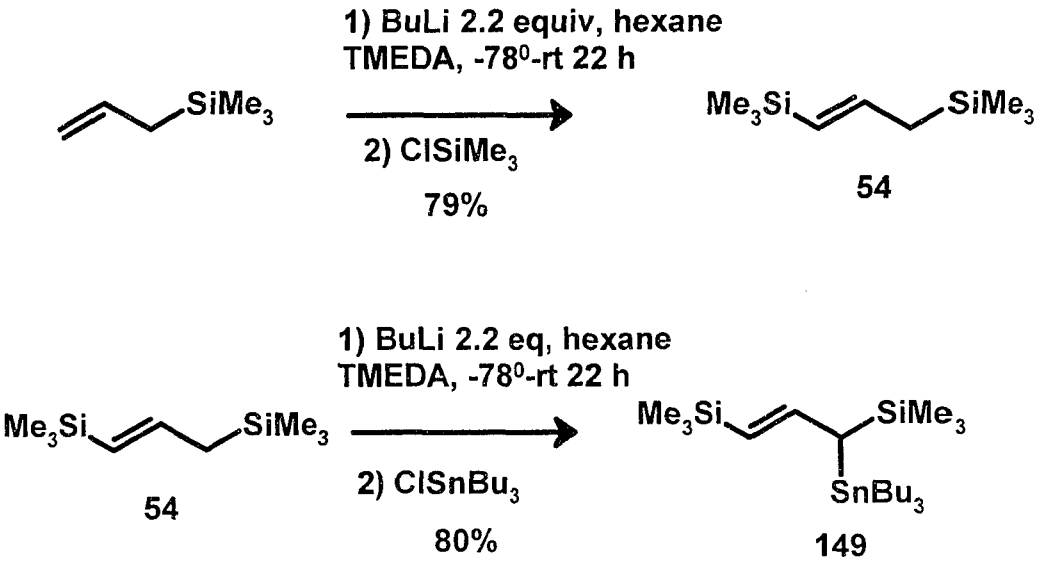



**Figure 46. Preparation of Allyltrimetal Nucleophile 149**

Substrates **138c** and **143**, which gave substantial amount of vinylsilane side products with allyldimetal equivalent **56**, were chosen to test the ability of nucleophile **149** to reduce or eliminate completely the undesired vinylsilane products.

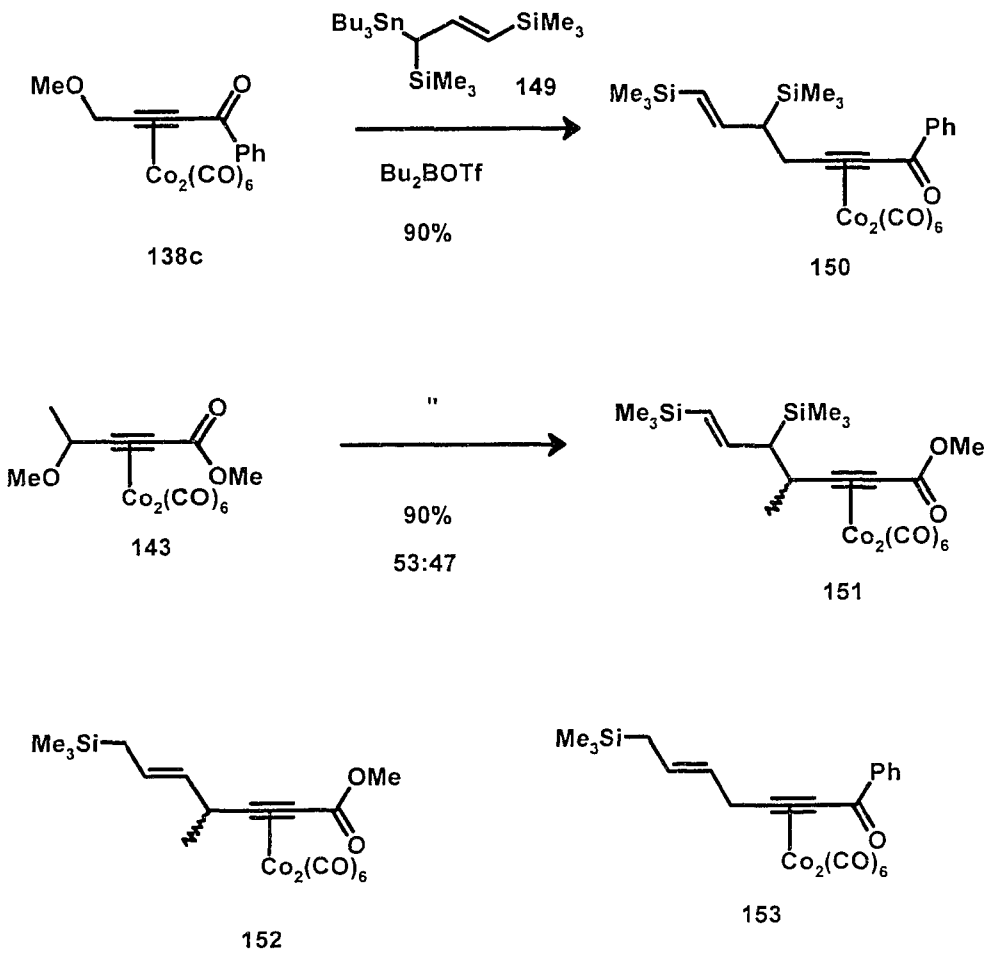



**Figure 47. Reactivity of Allyltrimetal Tin as the Nucleophile**

When dibutylboron triflate in dry $CH_2Cl_2$ was slowly added at room temperature to a mixture of substrate **138c** and nucleophile **149** in dry $CH_2Cl_2$ and after conventional workup and purification, **150** was isolated in 90% yield (Fig. 47). Similarly when **143** and **149** were mixed in dry $CH_2Cl_2$ and treated with dibutyl boron triflate, the reaction gave **151** as an inseparable *syn:anti* diastereoisomeric (53:47 dr) mixture in 90% yield. Only trace amounts (<5%) of the allylsilane side products **152** and **153** were observed. Formation of the trace side products **152** and **153** likely are due to loss of the tin moiety prior to the Nicholas condensation.

This destannylation was first observed and its mechanism elucidated in reactions of allylstannane **56** by Green and Lu (Fig. 48).[35]

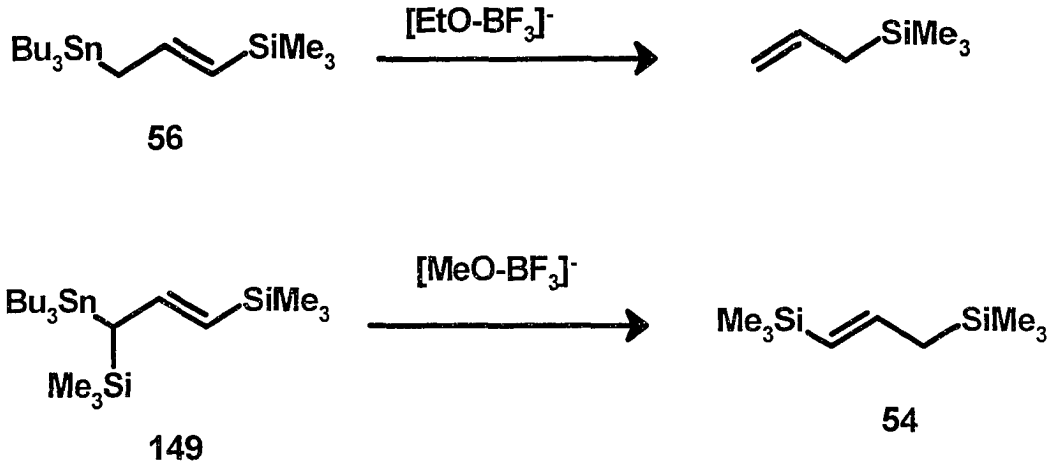



**Figure 48. Destannylation of Allyltrimetal and Allyldimetal Nucleophiles**

Consequently, a similar destannylation is probably taking place as well with the allyltrimetal nucleophile **149**. Destannylation of **149** would afford nucleophile **54**, which incidentally was the nucleophile first used by the Takano group in their unsuccessful attempts at a 4+3 double Nicholas reaction. It is our belief that this failure was due to preferential loss of the internal TMS group over the terminal TMS group (Figure 49). This indicates that there is a strong steric interaction between the internal TMS group with the bulky dicobalt hexacarbonyl unit. Therefore, a nucleophilic attack of **54** on **143** would provide an intermediate (Fig. 49), which loses the internal TMS moiety to afford **152**. The operation of a similar mechanism would explain the formation of **153**.

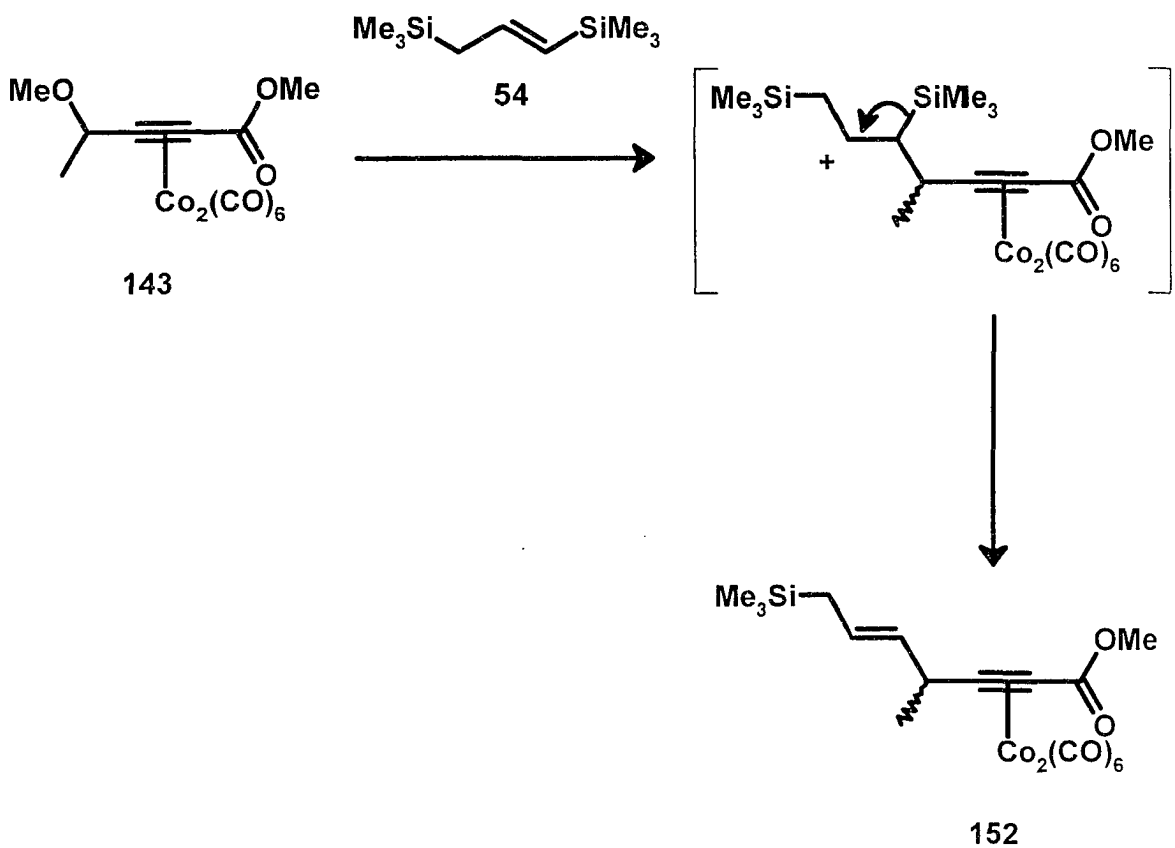



**Figure 49. Mechanism of Formation of 152**

## 2.3 Formation of Silylated Cycloheptenyne Cobalt Complexes

With the ability of allyltrimetal equivalent **149** to participate in Nicholas reactions demonstrated, we wished to explore the possibilities of its use for formation of cycloheptenyne dicobalt complex. Indeed, DIBAL reduction and *in situ* acetylation of phenyl ketone **150** afforded acetate **154** in 90% yield (54:46 dr). Similarly, methyl ester **151** gave acetate **155** as a mixture of *syn:anti* (64:36 dr)

diastereoisomers in 77% yield. The identities of the major and minor diastereomer were not assigned.

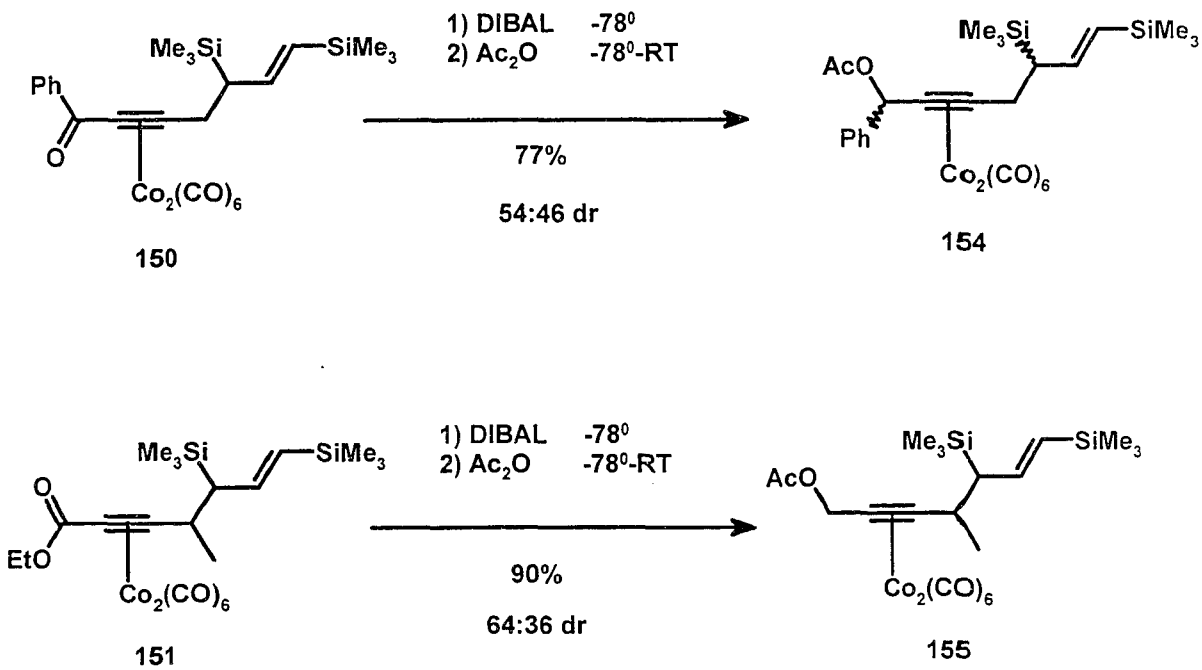



**Figure 50. Reduction and Acetylation of Complexes 150 & 151**

When acetate **154** was exposed to boron trifluoride etherate, cyclization to cycloheptenyne complex occurred, giving a 67:33 mixture of *trans: cis* **156** isomers in 59% overall yield. Conversely, exposure of boron trifluoride to a dichloromethane solution of acetate **155** gave *cis*-**157**: *trans*-**157**: **157a** (70:11:19) as the major product in 90% yield.

The stereochemical assignment for silylated cyloheptenyne dicobalt complexes were based on molecular modeling and calculation of vicinal coupling constants of the methine protons indicated in (Fig. 51). The major diastereomer **156** exhibited a coupling constant of 10.8 Hz, while the minor isomer possesses a

corresponding coupling constant of 4.5 Hz. MM3 calculations {CACHE®} predict two sets of coupling constants for the *trans*, 11.1-12.3 Hz for the pseudo axial-axial and 0.8-1.0 Hz for the pseudo equatorial-equatorial.[67] Conversely, the calculations for the *cis*-isomer do not include such a large couplings ( 5.7-6.5 & 3.7-4.0 Hz for the two pseudo axial-equatorial couplings). Thus, the major isomer of **156** was assigned as the *trans* isomer.

Analogously, the major diastereomer **157** which exhibited a coupling constant of 2.7 Hz was assignment as having *cis* configuration. MM3 calculations {CACHE®} predicted 8.2-9.0 and 7.7-8.7 Hz for the pseudo equatorial-equatorial and pseudo axial-axial coupling, while 4.9-5.6 and 3.1-3.7 Hz for the two pseudo axial-equatorial couplings.

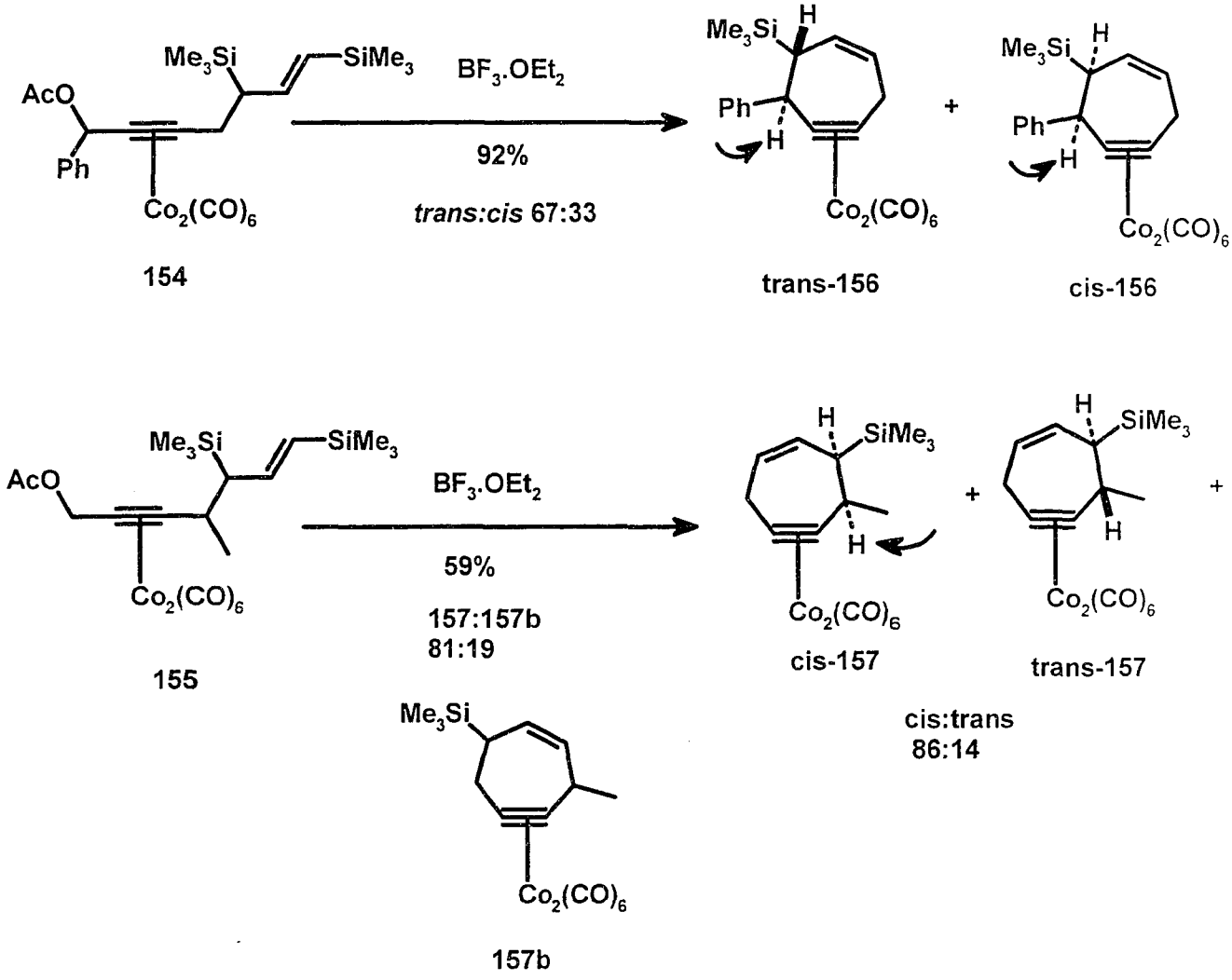



**Figure 51. Formation of Silylated Cycloheptenyne Complexes**

It is interesting to note which silyl group was removed from the starting acetate in the production of cycloheptenyne dicobalt complexes. For product **156** the internal silyl group in **154** was eliminated, while product **157**, it is the terminal silyl group in **155** that was preferentially eliminated during the formation of **157**. A plausible mechanism for the formation of silylated cycloheptenyne dicobalt complexes **156** and **157** is shown below. Formation of **158** is followed by intramolecular attack of the allylsilane to form intermediate **159a**. The reaction could

exist in equilibrium between the Nicholas adduct **159a** and retro-Nicholas[68] **158**. Second retro-Nicholas equilibrium could also exist between **159a** and **159b** (Fig. 52). Similarly, Nicholas adduct **161a** and retro-Nicholas species **160** and **161b** equilibrium could be established upon exposure of the Lewis acid to complex **155**. While attempts at MM3 modeling of the β–silyl cations were inconclusive, it is possible that the silyl group adjacent to the substituent only readily assumes a pseudo-equatorial position, whereas a pseudo-axial orientation for proper overlap with the cation is required for its ultimate loss. Analogous equilibrium can exist for the **155-157** transformation (Fig. 53). Therefore, elimination in **159a** and **161a** preferentially occurs from the least substituted side of the molecule.

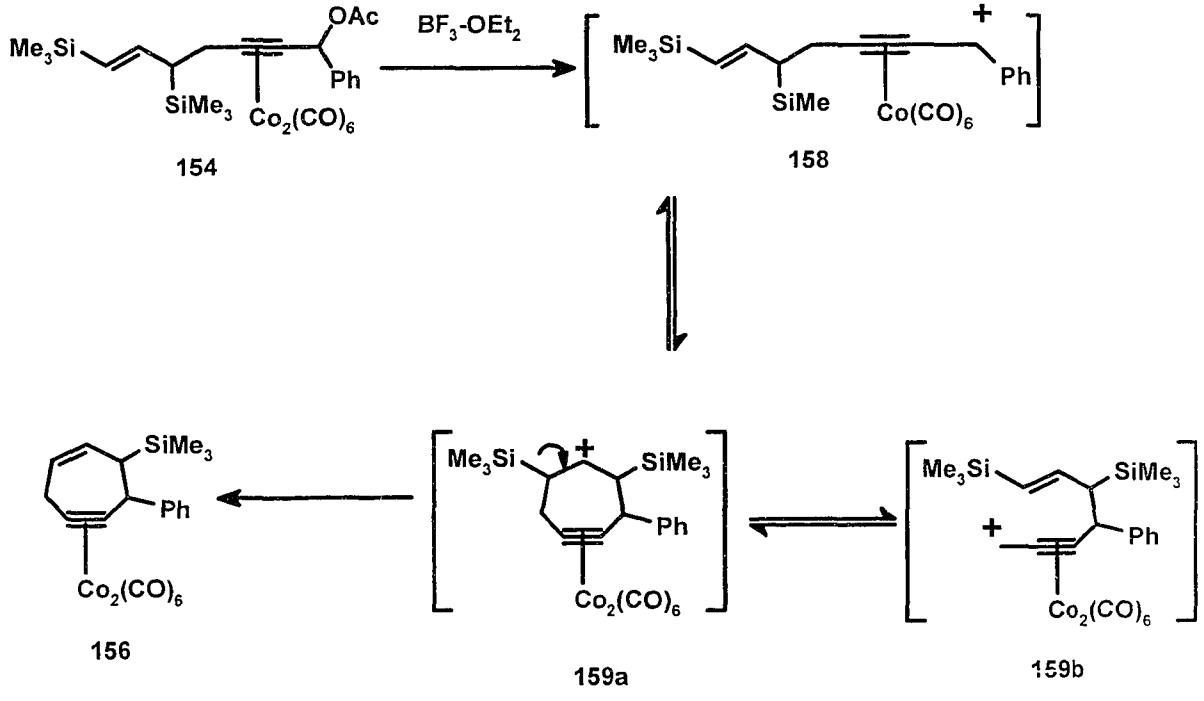



**Figure 52. Proposed Mechanism for Formation of 156**

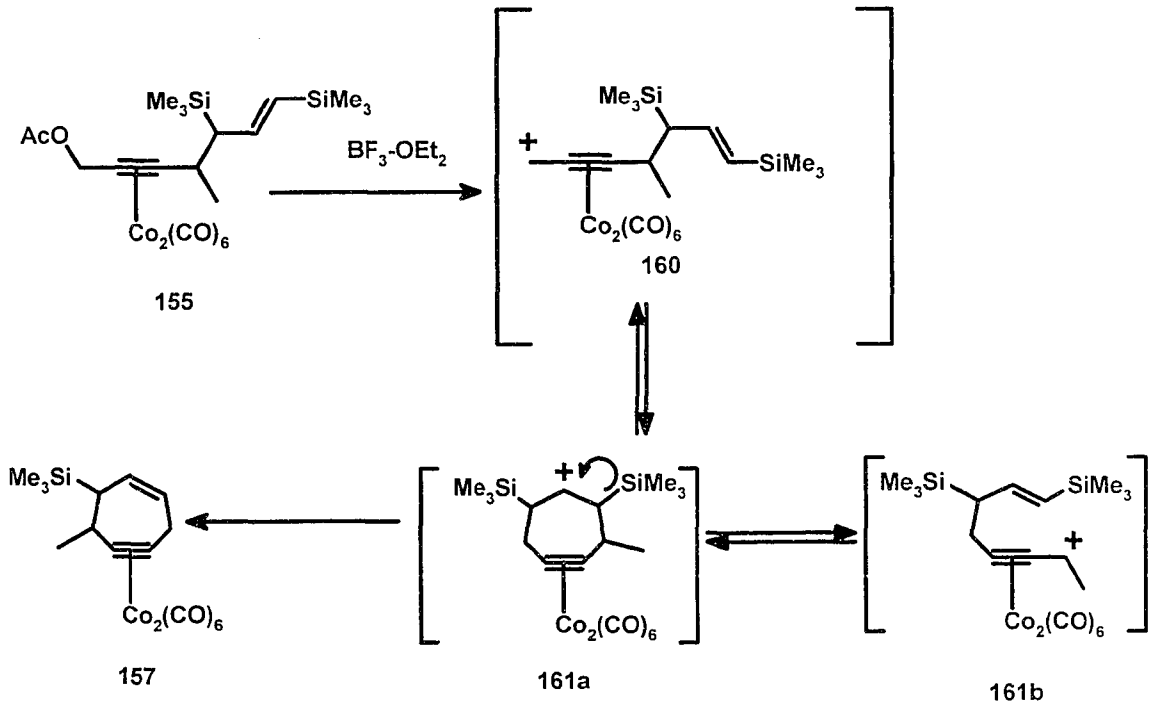



**Figure 53. Proposed Mechanism for Formation of 157**

A tandem Nicholas 4+3 cycloadditions employing substrate **162** and allyltrimetal **149**, in the presence of $BF_3.OEt_2$ as the Lewis acid, were also investigated. In the event, formation of silyl cycloheptenyne dicobalt complex **163a** was observed in 48% yield. Several other side products were also observed in various amounts depending on the reaction conditions. Shorter reaction times and fast addition of the Lewis acid gave predominantly **163b** as the side product, while longer reaction times and slow addition of the Lewis acid gave predominantly **163c** and **163d**, with substantial decrease in the yield of the silylcycloheptenyne complex. The susceptibility to rapid loss of tin moiety is clearly confirmed in the formation of

**163c**. The formation of complex **163d** could arise from the degradation of the trimetal equivalent nucleophile **149** to allyltrimethylsilane.

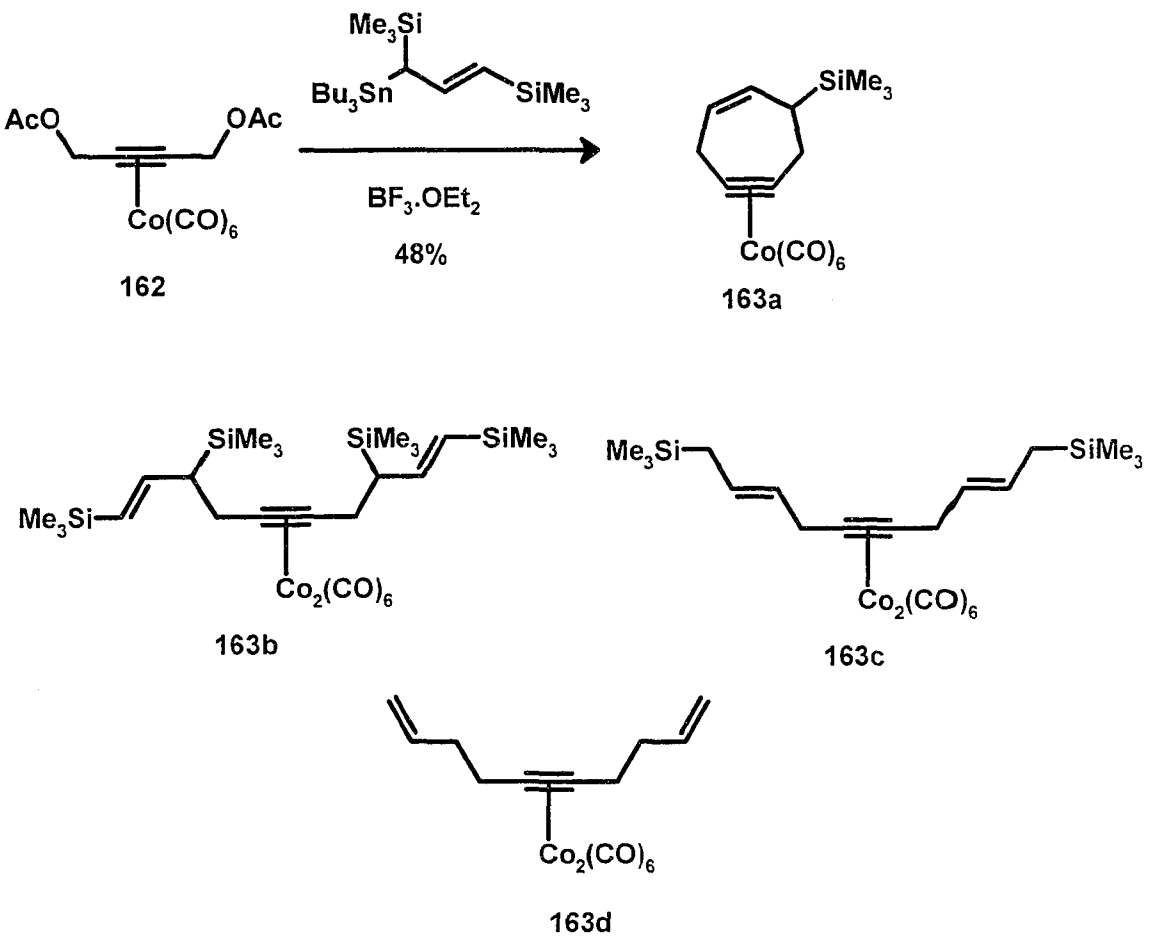



**Figure 54. Tandem Nicholas Reaction Using Nucleophile 149**

## 2.4 Summary

One of the objectives of this thesis was to eliminate or limit to trace amounts, the formation of vinylsilane side products formed in the 4+3 cycloadditions developed by in our lab. By employing allyltrimetal nucleophile **149**, virtually eliminated or reduced to trace amounts the vinylsilane side products **140a,b,c** & **145** observed earlier. The possibility for the step wise formation of cycloheptyne dicobalt complexes of complexes **154** and **155** were studied. DIBAL reduction and *in situ* acetylation of these complexes followed by exposure to $BF_3$ afforded cycloheptenyne dicobalt complex **156a,b** & **163a**, having a 1,2 disubstituted pattern as the major product. These cycloheptenyne complexes possess an allylsilane functionality and a silyl group at β-position, therefore, they could be used to further functionalize the cycloheptyne ring.

Attempted tandem Nicholas 4+3 cycloadditions of allyltrimetal **149** with substrate **162** were tried but afforded a low yield of silyl cycloheptenyne dicobalt complex **163a** mainly to due to the formation of **163b**.

## 2.5 Experimental Section

### General Methods

All dry solvents were distilled from the appropriate drying agent prior to use. Diethyl ether tetrahydrofuran and benzene were distilled from sodium-benzophenone ketyl, while dichloromethane was dried from calcium hydride. Most of the reactions were performed under a nitrogen atmosphere. The term "-78°C" refers to a bath containing solid $CO_2$ and acetone. The term 0°C refers to an ice bath.

A typical work-up was to quench the reaction with either a saturated ammonium chloride or saturated sodium bicarbonate solution, followed by extraction of the organic product from the aqueous phase with diethyl ether or dichloromethane. The organic solution was then dried over anhydrous magnesium sulphate. Filtration and evaporation of the solvent under reduced pressure yielded the crude product.

All column chromatography was performed using 230-400 Mesh silica gel from SiliCycle Chemical Division. Merck precoated silica gel 60 $F_{254}$ sheets were used for analytical thin layer chromatography (TLC), while preparative thin layer chromatography was carried out using Analtech silica gel GF-254 plates. Flash chromatography refers to Still's method.[69]

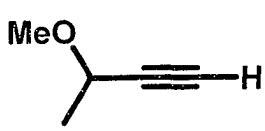
$^1$H-NMR spectra were recorded on either a Brüker Avance 300 or 500MHz spectrometer at room temperature in $CDCl_3$ solution, unless otherwise stated. Proton decoupled $^{13}$C-NMR spectra were obtained on a Brüker Avance 300 spectrometer at

75MHz in $CDCl_3$ at room temperature. IR spectra were recorded as neat on KBr plates using a Brüker Vector 22 FT–IR spectrophotometer. Maxima are reported as wavenumber ($cm^{-1}$). Mass spectra were run on a Varian Saturn 2000 GC/MS direct probe using the electron impact mode; high mass accuracy mass spectra were obtained from the McMaster Regional Centre for Mass Spectroscopy.

**3-Methoxy-1-propyne(164)**


Prepared by the method of Brandsma[70] in 57% yield, bp 60-62°C; Lit. bp 61°C

**3-Methoxy-1-butyne(165)**




Prepared by similar method to **164** from 3-butyne-2-ol in 57% yield bp 60-6°C; Lit. bp 61° C.

**Methyl 4-Methoxy-2-pentynoate (166)**


To a stirred solution of **165** (1.50g, 17.86 mmol) in dry THF (20 mL) at –78 $^{0}$C was added methyllithium (1.20 equiv) dropwise. After stirring the solution for 5 minutes, 2 equivalents of methyl chloroformate dissolved in THF were added. The reaction was then allowed to warm to room temperature. Conventional workup and bulb to bulb distillation of the crude material afforded **166** (1.92 g, 76% yield): bp 95-100 $^{0}$C/ 33-34 torr; IR (cm $^{-1}$) 2928, 2854, 1721, 1256; $^{1}$H-NMR: 4.17 (q 6.7 Hz 1H), 3.77 (s 3H), 3.41 (s 3H), 1.46 (d 6.7 Hz 3H); $^{13}$C-NMR: 153.7, 109.6, 86.9, 66.5, 56.8, 52.7, 21.0; Ms m/e 142 ($M^{+}$), 127 ($M^{+}$-$CH_3$), 111 ($M^{+}$-OMe): HRMS m/e for $C_7H_{10}O_3$ calculated ($M^{+}$-$CH_3$) 127.0395, found 127.0397

**4-Methoxy-1-phenyl-3-butyn-1-one (167)**

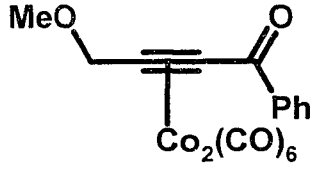

To a stirred solution of **164** (0.83 g, 11.84 mmol) in dry THF (20 mL) at -78 $^0$C was added methyllithium (7.5 mL, 1.00 equiv.) followed by addition of anhydrous $ZnCl_2$ (1.36 g, 1.00 equiv) in 10 mL of dry THF dropwise. The dry ice/ acetone bath was removed and the solution was allowed to warm to room temperature. The white suspension solution was cooled to around 5-10 $^0$C in an ice/water bath. Freshly distilled benzoyl chloride (1.41 g, 0.01 mmol) in THF (10 mL) was added dropwise. The reaction was then allowed to warm to room temperature. Conventional workup and bulb to bulb distillation of the crude material afforded **167** (1.00 g, 58% yield) [71]: bp 85-90°C/4torr; IR (cm $^{-1}$)1789, 1726, 1279, 1213: $^1$H-NMR: 8.15 (m 2H), 7.64 (m 1H), 7.51 (m 2H), 4.41 (s 2H), 3.51(s 3H); $^{13}$C-NMR: 177.2, 136.3, 134.3, 129.6, 128.6, 89.9, 84.2, 59.8, 58.2; MS m/e 174 ($M^+$), 159 ($M^+$ -$CH_3$), 144 ($M^+$ -OMe); HRMS m/e for $C_{11}H_{10}O_2$ calculated ($M^+$) 174.0681, found 174.0678.

**5-Methoxy-3-pentyn-2-one (167a)**

To a stirred solution of **164** (0.83 g, 11.8 mmol) in dry THF (20 mL) at –78 $^{0}$C was added methyllithium (8 mL, 1.10 equiv) dropwise. After stirring the solution for 5 minutes, freshly distilled acetic anhydride (1.5 mL, 1.3 equiv.) in THF (5mL) was added dropwise by syringe pump over 0.5 h. The reaction was then allowed to warm to room temperature. Conventional workup and bulb to bulb distillation of the crude material afforded **168** (0.57 g, 48% yield)[72]: bp 85-87°C/32 torr; IR (cm $^{-1}$); 2934, 2852, 2211, 1678, 1241; $^{1}$H-NMR: 4.22 (s 2H), 3.37 (s 3H), 2.32 (s 3H); $^{13}$C-NMR: 183.8, 87.1, 85.6, 59.3, 57.9, 32.4; Ms m/e; HRMS m/e for $C_6H_8O_2$ calculated ($M^+$) 389.8985, found 389.8984.

**Procedure A: Typical complexation reaction**

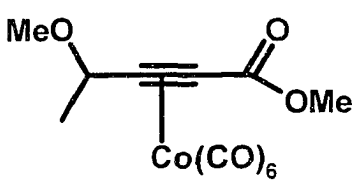
**Hexacarbonyl [μ-η$^4$ -(4-methoxy-1-phenyl-but-3yn-1one )]dicobalt (138c)**




Compound **167** (0.500 g, 2.87 mmol) was dissolved in anhydrous diethyl ether (6mL) and cooled to 0°C. Excess dicobalt octacarbonyl was added in one portion and stirred for 1 h. The reaction was then allowed to warm to room

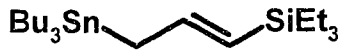
temperature. The resulting solution was filtered through Celite® and concentrated *in vacuo*. Flash chromatography using 50:1 petroleum ether:diethyl ether yielded **138c** (1.09 g 83%): IR (cm $^{-1}$) 2824, 2101, 2064, 2033, 1639,1600, 1029; $^{1}$H-NMR : 8.01 (d 7.7 Hz 2H), 7.58 (t 7.3 Hz 1H), 7.48 (dd 7.7 Hz, 7.3 Hz 2H), 4.79 (s 2H), 3.58 (s 3H); $^{13}$C-NMR: 198.4, 193.0, 137.3, 133.1, 128.5, 128.4, 93.0, 84.2, 73.0, 59.2; MS m/e 404 ($M^+$-2CO), 376 ($M^+$-3CO), 348 ($M^+$-4CO), 320 ($M^+$-5CO); HRMS m/e for $C_{15}H_{10}Co_2O_6$ calculated ($M^+$-2CO) 403.9141 found 403.9156.

**Hexacarbonyl [μ-η$^4$ -(ethyl 4-methoxy-2-pentynoate)] dicobalt (143)**



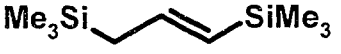

Compound **166** (1.64 g 11.55 mmol) was complexed via procedure A. Flash chromatography using 50:1 petroleum ether:diethyl ether gave (2.91g 59%): IR (cm $^{-1}$) 2986, 2953, 2828, 2102, 2073, 2015, 1711, 1222; $^{1}$H-NMR : 4.50 (q 6.3Hz 1H), 3.87 (s 3H), 3.46 (s 3H), 1.50 (t 6.3Hz 3H); $^{13}$C-NMR: 198.2, 170.4, 100.0, 94.1, 76.8, 57.2, 53.0, 22.4; MS m/e 400 ($M^+$-CO), 372 ($M^+$-2CO), 344 ($M^+$-3CO), 316 ($M^+$-4CO), 288 ($M^+$-5CO), 260 ($M^+$-6CO); HRMS m/e for $C_{13}H_{120}Co_2O_9$ calculated ($M^+$) 427.8989, found 427.9008.

**(E)-Triethyl-(3-tributylstannanyl-1-propenyl)silane(56)**



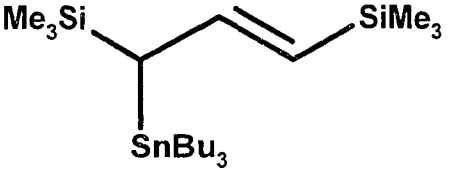
Compound **56** was prepared by the method of Green and Patel[64] in 93% yield: b.p 80-110 $^0$C/1 mmHg.

**(E)-1,3-Bis(trimethylsilyl) propene(54)**



Compound **54** was prepared in 79% by the method of Takano[32]: b.p 100-120 $^0$C/ 4 mmHg.

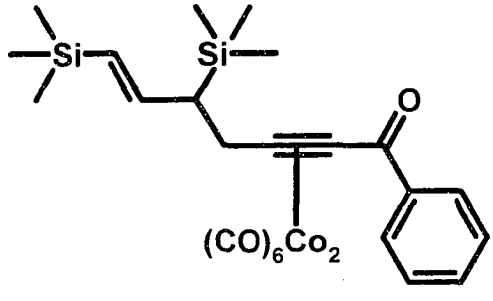
**3-Tributylstannyl-1,3-bis(trimethylsilyl) propene (149)**



Compound **54** (6.00 g, 32.18 mmol) and TMEDA (4.1 mL, 1.1 equiv) in dry hexane (60 mL) was stirred at room temperature. Butyllithium (14 mL, 1,1 equiv) was added dropwise and the solution was left to stir for 22h. The orange solution was then cooled to -78 $^0$C and freshly distilled $Bu_3SnCl$ (9.6 mL,1.1 equiv) in 5 mL dry hexane was added dropwise. The solution was then allowed to warm to room temperature and stirred for 1h. After conventional workup and bulb to bulb distillation (100-120 $^0$C/1 mmHg), gave **149** as clear oil (14.52 g, 93%): IR (cm $^{-1}$) 2959, 2922; $^1$H-NMR : 6.04 (dd 18 Hz, 11.7 Hz 1H), 5.25 (d 18 Hz 1H), 1.64 (d 11.7 Hz 1H), 1.48 (m 6H), 1.34 (m 9H), 0.89 (m 12H), 0.02 (s 9H), 0.01 (s 9H); $^{13}$C-NMR: 147.5, 124.0, 29.2, 27.3, 13.7, 10.1, -0.4, -0.8; MS m/e 475.5, 418 (M $^+$-$C_4H_9$), 290, 234, 177; HRMS m/e for $C_{21}H_{458}Si_2Sn$ calculated ($M^+$-15) 461.2082 found 461.2082

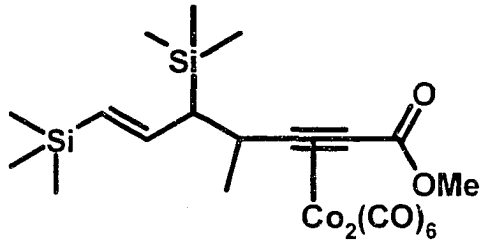
**Procedure B: Typical Nicholas condensation reactions**

**Hexacarbonyl [μ-η$^4$-{(E)-1-phenyl-5,7-bis(trimethylsilyl)-6-hepten-2-yn-1-one}] dicobalt (150)**



Compound **138c** (0.20 g, 0.44 mmol) and nucleophile **149** (0.62 g, 3 equiv) were dissolved in anhydrous dichloromethane (10.5 mL) and cooled to 0°C. $Bu_2BOTf$ (1.30 mL, 3equiv) in dry dichloromethane (3 mL) was slowly added. The reaction was monitored by TLC. Upon completion (16 h), a saturated solution of $NaHCO_3$ was added. After a conventional workup, flash chromatography (50:1 petroleum ether:diethyl ether) afforded complex **150** (0.24 g 90%) : IR ($cm^{-1}$) 2957, 2095, 2059, 2029, 1642,1600. $^1$H-NMR : 7.94 (d 7.2 Hz 2H), 7.59 (t 7.4 Hz 1H), 7.49 (m 2H), 5.85 (dd 8.8 Hz 18.6 Hz 1H), 5.48 ( d 18.6 Hz 1H), 3.27 ( m 2H), 1.94 (m 1H), 0.07 ( s 9H), -0.13 (s 9H); $^{13}$C-NMR: 198.9, 192.7, 146.0, 137.2, 133.0, 129.4, 128.54, 128.46, 100.6, 87.2, 41.5, 34.1, -1.6, -3.4; MS m/e 614 ($M^+$), 586 ($M^+$-CO), 558 ($M^+$-2CO), 530 ($M^+$-3CO), 502($M^+$-4CO); HRMS m/e for $C_{25}H_{28}Co_2O_7Si_2Na^+$ calculated 636.9930, found 636.9922.

**Hexacarbonyl [μ-η$^4$-(4-methyl-5,7-bis(trimethylsilanyl)hept-6-en-2-ynoic acid methyl ester] dicobalt (151)**

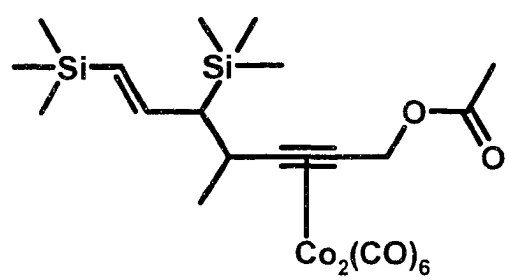



Compound **143** (233.9 mg, 0.55 mmol), nucleophile **149** (0.79 g, 3 equiv) and $Bu_2BOTf$ (1.65 mL, 3equiv) were mixed via procedure B. After a conventional

workup, flash chromatography (50:1 petroleum ether:diethyl ether) afforded complex **151** (0.29 g, 90%): IR (cm $^{-1}$) 2959, 2929, 2099, 2064, 2030, 1711, 1217; $^{1}$H-NMR: 6.10 ( dd 18.5 Hz, 10.1 Hz 1H), 5.96 (dd 18.9 Hz, 9.1 Hz 1H), 3.85 (s 3H), 3.83 (s 3H), 3.3 (m 2H), 2.13 (d 10.0 Hz 1H), 1.77 (t 9.5Hz 1H), 1.44 (d 2.9 Hz 3H), 1.43 (d 2.7Hz 3H), 0.01 (s 9H), 0.06 (s 9H), 0.05 (s 9H), 0.04 (s 9Hz); $^{13}$C-NMR: 198.9, 170.5, 170.0, 146.6, 142.0, 132.4, 131.0, 129.0, 127.3, 108.3, 108.1, 79.3, 77.9, 52.9, 47.1, 46.2, 41.1, 38.2, 37.6, 24.1, 22.8, 22.4, 19.7, -0.7, -1.3, -2.0; MS m/e 582 (M $^{+}$), 554 (M $^{+}$-1CO), 526 (M $^{+}$-2CO), 498 (M $^{+}$-3CO), 470 (M $^{+}$-4CO), 442 (M $^{+}$-5CO); HRMS m/e for $C_{21}H_{28}Co_2O_8Si_2Na^{+}$ calculated 604.9879, found 604.9981.

**Procedure C: DIBAL-H Reduction and *in-situ* Acetylation**

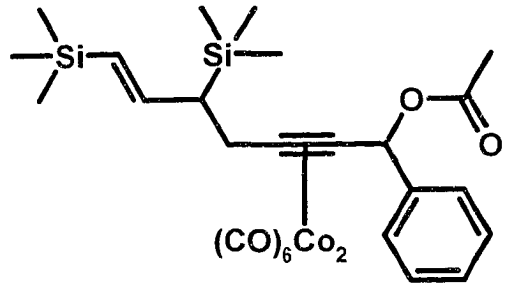
**Hexacarbonyl [μ-η$^4$-acetic acid (E)-4-methyl-5,7-bis(trimethylsilyl)6-hepten-2-ynyl ester] dicobalt (155)**




Complex **151** (96 mg, 0.17 mmol) was dissolved in dry diethyl ether (10 mL) and cooled to -78 $^{0}$C. DIBAL (1.7 mL, 10 equiv) in dry diethyl ether (3 mL) was

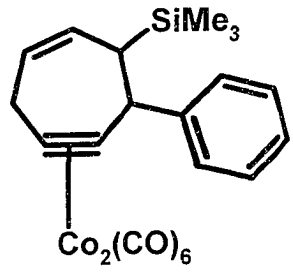
added dropwise to the cooled solution. The reaction was kept at -78 $^{0}$C and monitored by TLC until the reduction was complete. A large excess of freshly distilled acetic anhydride (1 mL, 62 equiv) in dry diethyl ether (3 mL) was added to the mixture and the reaction was allowed to warm to room temperature. The acetylation progress was monitored by TLC. Upon completion of the reaction, a conventional workup and flash chromatography (50:1 petroleum ether:diethyl ether) afforded the diastereoisomeric products **155** (76 mg 77% 54:46 dr): IR (cm $^{-1}$) 2958, 2091, 2052, 2023, 1745; $^{1}$H-NMR: 6.13 (dd 18.5 Hz, 10.2 Hz 1H), 6.01 (dd 18.9 Hz, 9.1 Hz 1H), 5.58 (d 18.5 Hz 1H), 5.53 (d 19 Hz 1H), 5.58 (d 14.2 Hz 1H), 5.26 (½ABq, 14.1Hz, 1H ), 5.23 (½ABq, 14.1 Hz, 1H), 5.11 (½ABq, 14.1 1H), 3.24 (m 2H), 2.13 (s 3H), 2.12 (s 3H), 2.09 (d 8.9Hz 1H), 1.77 (t 9.9 Hz 1H), 1.42 (d 2.2 Hz 3H), 1.40 (d 2.6 Hz 3H), 0.11 (s 9H), 0.10 (s 9H), 0.07 (s 18H); $^{13}$C-NMR: 199.9, 170.6, 170.6, 147.4, 142.2, 131.2, 129.0, 108.6, 106.6, 92.4, 92.4, 66.3, 64.9, 47.5, 47.1, 38.5, 38.3, 23.7, 20.5, 20.3, 20.2, -0.8, -1.3, -1.4; MS m/e 596 ($M^{+}$), 568 ($M^{+}$-1CO), 540 ($M^{+}$-2CO), 512 ($M^{+}$-3CO), 484 ($M^{+}$-4CO), 456 ($M^{+}$-5CO), 428 ($M^{+}$-6CO); HRMS m/e for $C_{17}H_{30}Co_2O_3Si_2Na^{+}$ ($M^{+}$ -5CO) calculated 479.0290, found 479.0232.

**Hexacarbonyl [μ-η$^{4}$- (acetic acid (E)-1-phenyl-5,7-bis(trimethylsilyl)6-hepten--2-ynyl ester)] dicobalt (154)**



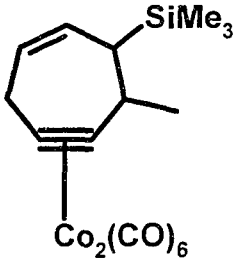

DIBAL reduction and acetylation of complex **150** (168 mg, 0.274 mmol) via procedure C afforded **154** (163 mg, 90% 54:46 dr): IR ($cm^{-1}$) 2958, 2090, 2052, 2023, 1748; $^1$H-NMR: 7.51-7.33 (m 10H), 7.01 (s 1H), 7.00 (s 1H), 5.96 (dd 18.8 Hz, 8.5 Hz 1H), (5.88 (dd 18.8 Hz, 8.4 Hz 1H), 5.53 (dd 18.8 Hz, 0.8 Hz 1H), 5.50 (dd 18.8 Hz, 1Hz), 2.94 (½ABq 15.8 Hz, 10.6 Hz 1H), 2.81 (m 3H), 2.19 (s 3H), 218 (s 3H), 1.91 (m 1H), 1.79 (m 1H), 0.06(s 9H), 0.04 (s 18H), 0.03 ( s 9H), ; $^{13}$C-NMR: 199.4,169.7,169.6, 147.1, 147.1, 140.8, 140.6, 128.6, 128.5, 128.4, 128.2, 128.1, 125.8, 125.7, 100.0, 99.6, 97.3, 75.5, 40.5, 40.2, 32.3. 32.2, 22.6, 20.7, 14.1, -1.0, -1.3, -3.4, -3.5; MS m/e 574 ($M^+$-3CO), 546 ($M^+$-4CO), 518 ($M^+$-5CO), 490 ($M^+$-6CO):

**Hexacarbonyl [μ-η$^4$-(trimethyl-(7-phenyl-cyclohept-2en-5-ynyl)-silane] dicobalt (cis/trans156)**



The diastereoisomeric mixtures (67:33) of **154** (225.5 mg, 0.34 mmol) dissolved in dry benzene (17 mL) at room temperature and $BF_3.OEt_2$ (200 µL, 5 equiv) were mixed via procedure B. A conventional workup and flash chromatography (100% petroleum ether) gave trans-**156** and cis-**156** (67:33) as an inseparable mixture (164 mg, 92%): IR ($cm^{-1}$) 3029, 2955, 2090, 2048, 1583, 1055, 840; $^1$H-NMR ($CD_2Cl_2$): 7.32 (m 5H), 5.90 (m 1H), 5.81 (m 1H), 4.18 (d 10.8 Hz 1H), 3.66 (m 2H), 2.38 (m 1H) , 0.17 (s 9H); (minor isomer) 7.24 (m 5H), 6.10 (m 2H), 4.47 (d 4.5 Hz 1H), 3.78 (d 18.7 Hz 1H), 3.71 (m 1H), 2.29 (m 1H) , -0.16 (s 9H); $^{13}$C-NMR: 200.5, 145.3, 145.0, 133.5, 133.2, 131.4, 129.6, 129.1, 128.7, 128.7, 127.4, 110.2, 109.1, 97.2, 93.8, 52.5, 50.9, 35.1, 34.5, 34.1, 33.3, -1.8, -2.4; MS m/e 526 ($M^+$), 470 ($M^+$-2CO), 442 ($M^+$-3CO), 414 ($M^+$-4CO), 386 ($M^+$-5CO), 358 ($M^+$-6CO) ; HRMS m/e for $C_{22}H_{19}Co_2O_6Si$ ($M^+$ -1) calculated 524.9615, found 524.9589.

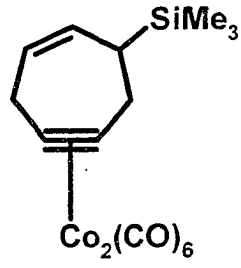
**Hexacarbonyl [µ-η$^4$-(6- methyl -7- trimethylsilyl -cyclohept-1-en-4-yne)] dicobalt (157)**




The diastereoisomeric mixtures (64:36) of **155** (61.2 mg, 0.10 mmol) was dissolved in dry benzene (5 mL) at room temperature and $BF_3.OEt_2$ (70.5 mg, 5

equiv.) were mixed via procedure B. After conventional workup and flash chromatography (100% petroleum ether) **156a,b,c** (70:19:11) were obtained (28.9 mg, 59% yield): IR (cm $^{-1}$); $^{1}$H-NMR: (**156a**) 60.5 (m 1H), 5.85 (m 1H), 3.72 (d 18.8 Hz 1H), 3.62 (dd 18.8 Hz, 7.2 Hz 1H), 3.43 (dq 7.2 Hz, 2.7 Hz 1H), 1.91 (d 7.7 Hz 1H), 1.21 (d 7.2Hz 3H), 0.12(s 9H); (**156b**) 5.8 (hidden 1H), 5.76 (m 1H), 3.84 (br 1H), 3.22 (d 17.0 Hz, 1H), 2.80 (dd 17.0 Hz, 13.3 Hz 1H); $^{13}$C-NMR:200.5, 132.5, 132.1, 110.6, 94.1, 40.5, 34.4, 33.4, 20.8, -2.1; MS m/e 464 ($M^+$), 436 ($M^+$-CO), 408 ($M^+$-2CO), 380 ($M^+$-3CO), 352 ($M^+$-4CO), 324 ($M^+$-5CO), 296 ($M^+$-6CO) ; HRMS m/e for $C_{16}H_{18}Co_2O_5Si$ ($M^+$ -CO) calculated 435.9587 found 435.9587.

**Hexacarbonyl [μ-η$^4$ – (7-trimethylsilylcyclohept-1-en-4-yne)]dicobalt (163a)**




Compound **162** (156 mg, 0.34 mmol) and **149** (162 mg, 0.34) were dissolved in dry benzene (2 mL) at room temperature and $BF_3.OEt_2$ (241 mg, 5 equiv) in of dry benzene (5 mL) were mixed via procedure B. A conventional workup and flash chromatography (100% petroleum ether) **163a** was obtained (73.9 mg, 48%): IR (cm $^{-1}$) 2956, 2089, 2055, 2012; $^{1}$H-NMR: 5.93 (m 1H), 5.83 (m 1H), 3.73 (d 18.8 Hz 1H), 3.62 (dd 18.8 Hz, 6.2 Hz 1H), 3.20 (dd 16.7 Hz, 2.4 Hz 1H), 2.83 (dd 16.7 Hz, 12.9 Hz 1H), 1.73 (m 1H), 0.08 (s 9H); $^{13}$C-NMR: 200.5, 133.6, 130.4, 102.9, 95.8, 35.4,

33.3, 28.8, -5.0; MS m/e 450 ($M^+$), 422 ($M^+$-CO), 394 ($M^+$-2CO), 366 ($M^+$-3CO), 338 ($M^+$-4CO), 310 ($M^+$-5CO), 282 ($M^+$-6CO) ; HRMS m/e for $C_{15}H_{16}Co_2O_5Si$ ($M^+$-CO) calculated 421.9431, found 421.9424.

## 3.0 Intramolecular Pauson-Khand Reactions

### 3.1 Intermolecular Pauson-Khand Reaction on Cycloheptyne-$Co_2(CO)_6$ Complexes

Cycloheptanes fused to five or six membered ring systems are widely encountered in nature particularly among the terpenoid classes of compounds[73]. Examples of classes of compounds having fused 7,5 ring system are shown in figure 55. There is a general paucity for direct synthetic methods[74] to access them. Therefore, it would be a highly valuable method to first synthesize an appropriate cycloheptyne dicobalt complex and then capitalize on the hidden triple bond to fuse it into a cyclopentane ring through a Pauson-Khand reaction. Heating the cycloheptyne complex in the presence of an alkene should furnish a fused 7, 5- ring system.

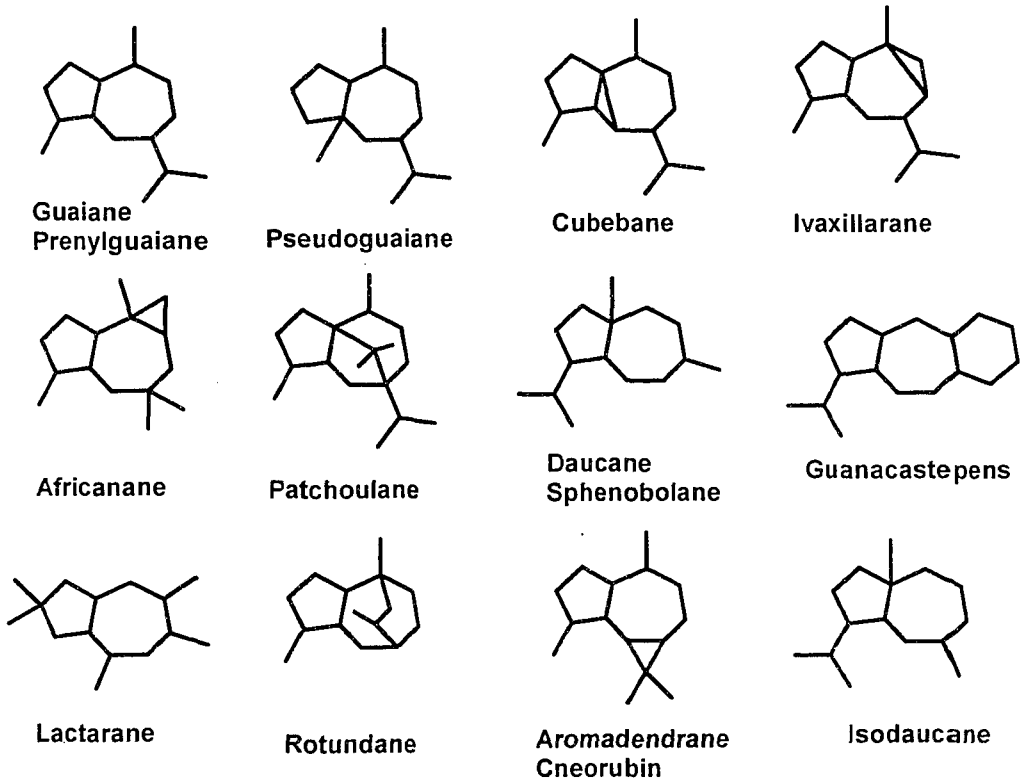



**Figure 55. Examples of Fused 7,5 Ring Systems Found in Nature**

### 3.2 Attempted Formation of Cycloheptyne-$Co_2(CO)_6$ Bearing an Oxygen Function Via 4+3 cycloaddition Reactions

An early study of the Pauson-Khand reactions of cycloheptenyne complexes was undertaken in our laboratories.[66] Given that not all of the currently available additives or conditions were available at that time, the results suggest that the cycloheptenyne-$Co_2(CO)_6$ complex behaves as a standard alkyne for Pauson-Khand purposes; bridged bicyclic alkenes participate well in the cycloaddition (**168a/168b**), whereas ordinary alkenes give little or no yields of 2+2+1 adduct. Attempts to employ thiomethyl substituted alkenes (**169a/169b**) or silylated allenes (**170a/170b**),

in the fashion of Krafft[39] and Cazes,[75] respectively, produced some amount of Pauson-Khand products but were at best marginal in yield. High regioselectivity in these cycloadditions was neither expected nor observed, given the very limited steric differences between $CH_2$-$CH_2$-$CH_2$ and $CH_2$-CH=CH functions. Our conclusion based on these results was that the Pauson-Khand reactions on cycloheptynedicobalt complexes should be rendered intramolecular in order to have a greater likelihood of high chemical yields, as well as high regioselectivity.

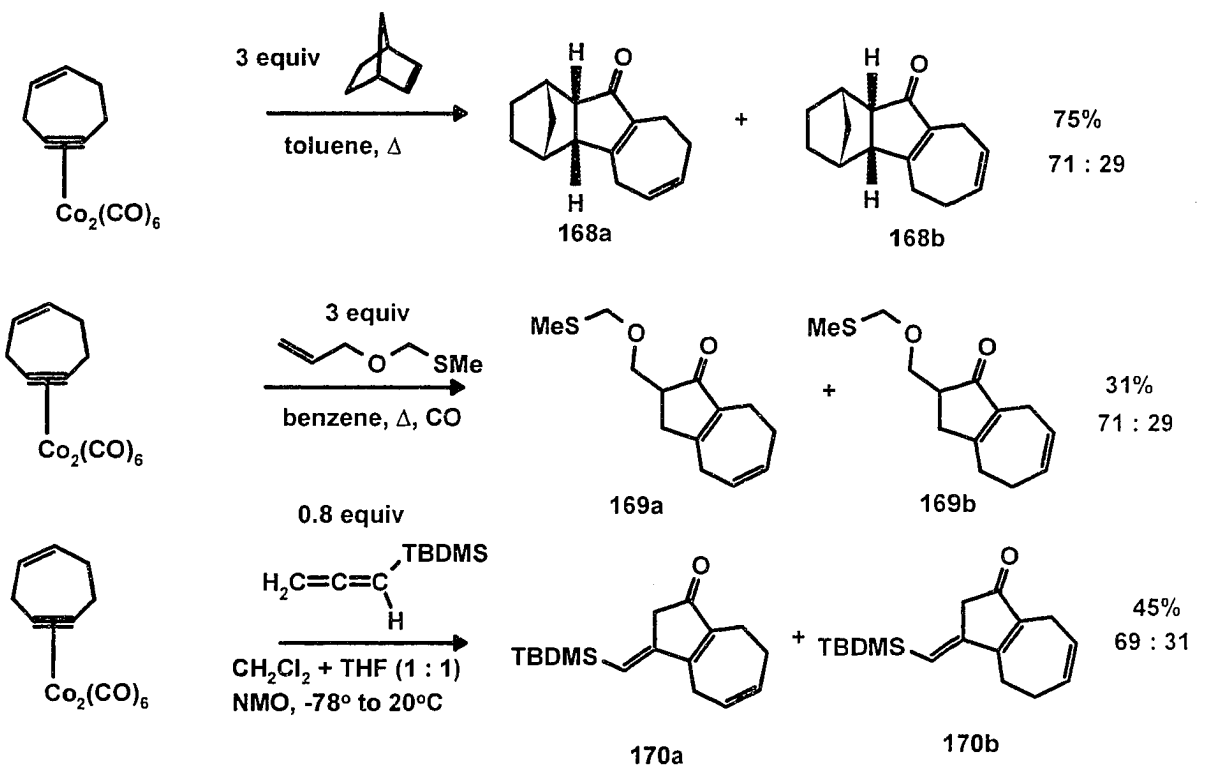



**Figure 56. Intermolecular Pauson-Khand on Cycloheptenyne Dicobalt Complex[66]**

Our initial efforts to form cycloheptynedicobalt complexes containing propargylic oxygen based functions centered on the 4+3 reaction of allyldimetal equivalent **56** and γ–alkoxyalkynone complexes (**138b,c,172**), reasoning that these reactions would be able to give complexes **178** in one synthetic operation. Compounds **138b** and **138c** have been synthesized previously in our laboratory; compound **172** could be easily prepared by deprotonation of methyl propargyl ether with methyllithium and trapping the resulting alkynyllithium with isobutyryl chloride, followed by conventional workup and distillation to afford a colorless oil in 56% yield. Complexation of **171** by $Co_2(CO)_8$ under conventional conditions furnished **172** in 63% yield.[71]

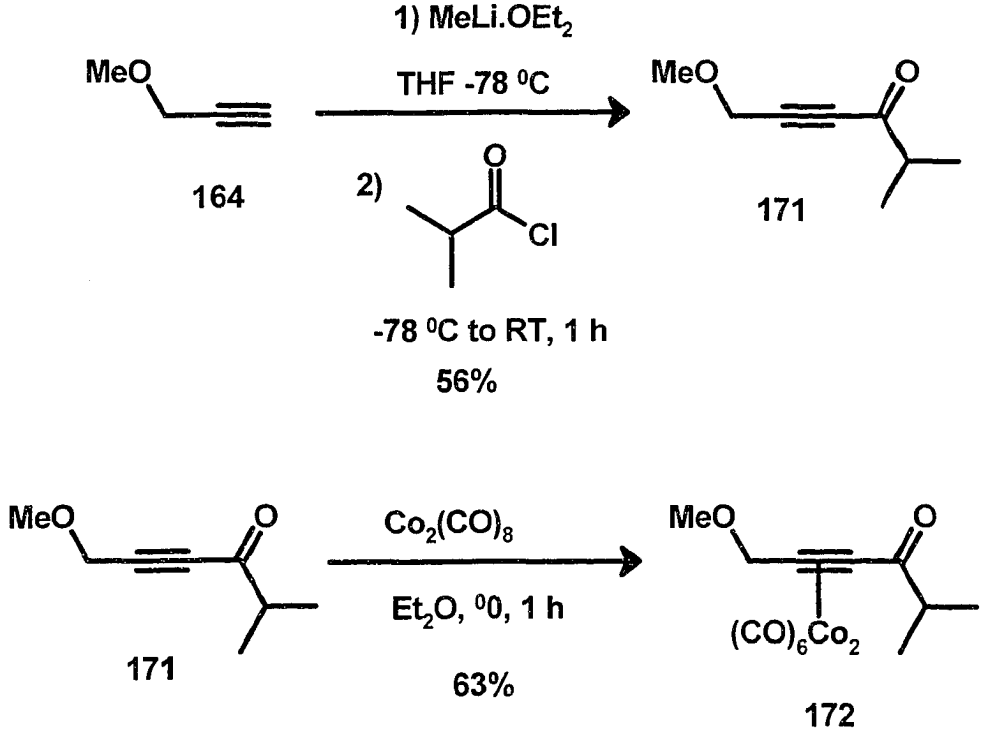



**Figure 57. Preparation of Complex 172**

The synthesis of complex **175** began with deprotonation of 3,3-diethoxypropyne with methyllithium in dry diethyl ether, followed by addition of paraformaldehyde and after conventional workup to give alcohol **173** in 51% yield.[76] Deprotonation of **173** with potassium hydride in diethyl ether at room temperature and quenching of resulting alkoxide with iodomethane afforded methyl ether **174** in 86% yield.[77] Subsequent complexation with $Co_2(CO)_8$ afforded complex **175** in 79% yield.

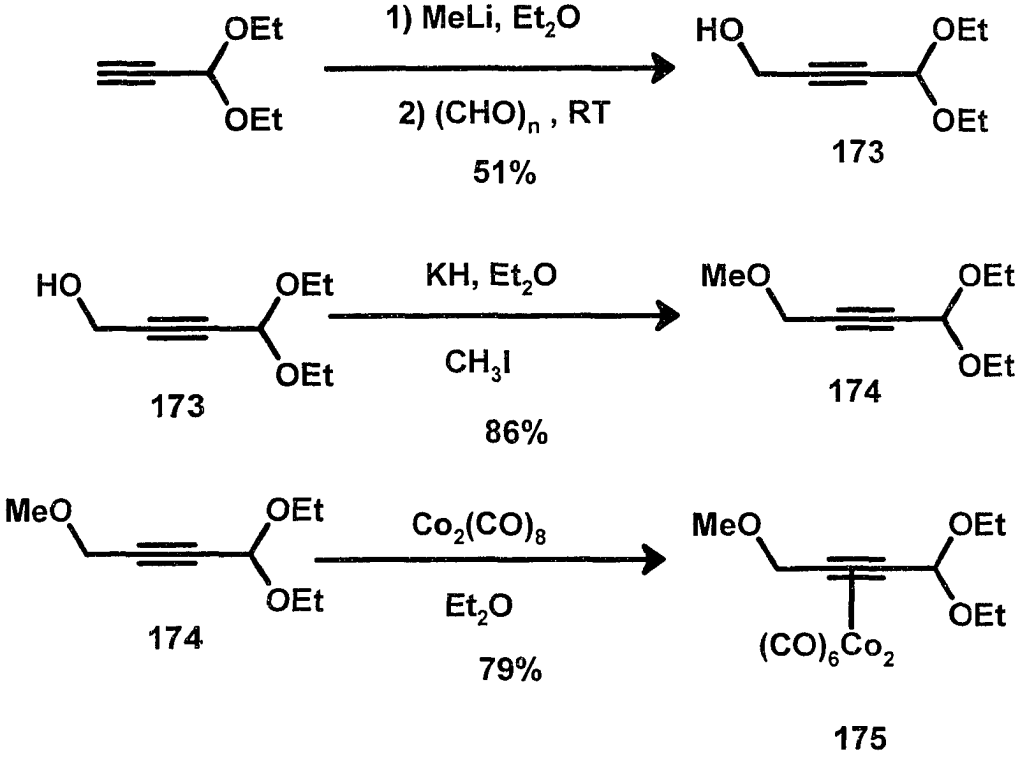



**Figure 58. Preparation of Complex 175**

With the starting materials available, the possibility of forming cycloheptenyne dicobalt complex bearing an alcohol or an alkoxy group by Lewis acid mediated

reaction with **56** was investigated. After several attempts and using various reaction conditions, however, there was not a trace of the desired product **178** obtained. On the other hand, the reactions provided the elimination products **176 a,b,c** and **177** together with acyclic byproducts **136** and **137**; optimization of **176-177** gave these compounds in synthetically useful yield. The transient formation of the desired products **178** could be inferred from the elimination byproducts **176 a,b,c**. Apparently **178** could not survive the acidic media. Therefore, any attempts to synthesize cycloheptyne-$Co_2(CO)_6$ under acidic conditions were abandoned.

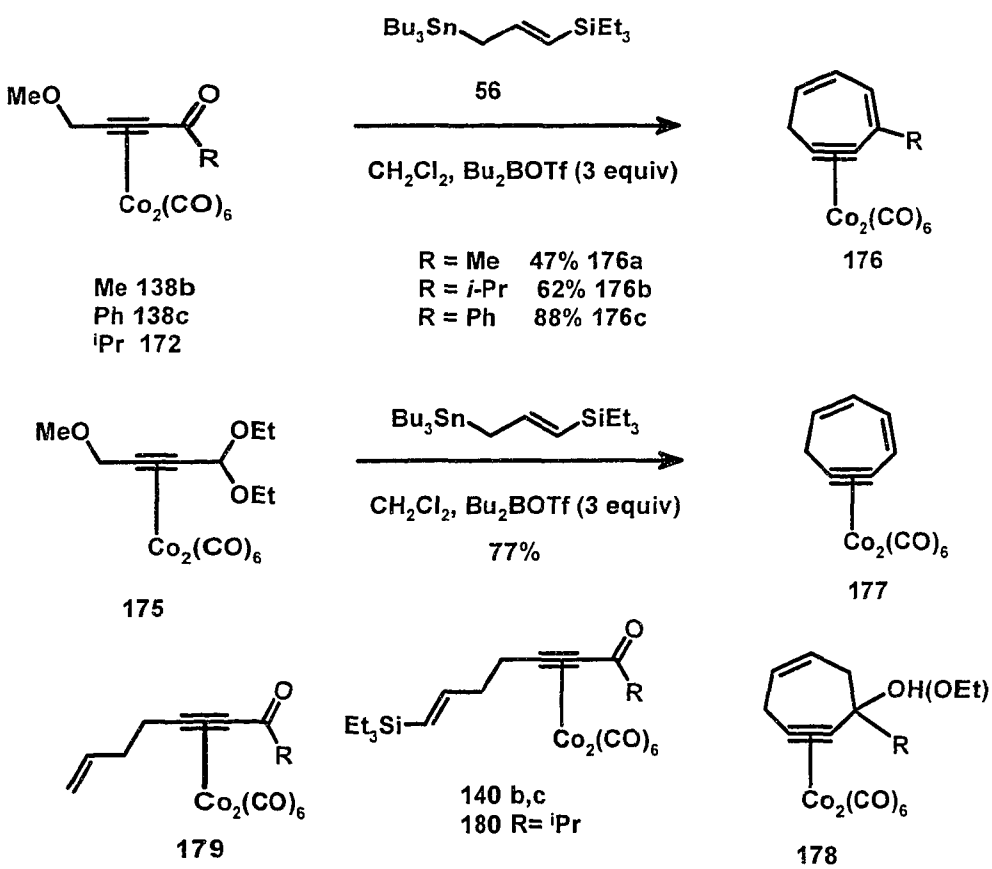



**Figure 59. Formation of Cycloheptadienyne Complexes**

The cyclic diene formation was confirmed by NMR ($^1$H and $^{13}$C) spectroscopy. The resonances for three distinct olefenic protons, between 6.4 and 5.6 ppm for **176 a,b,c** and four olefenic protons between 5.7 and 6.7 ppm in **177** could be observed in the $^1$H-NMR spectra. The $^{13}$C-NMR spectrum of **177** showed four $sp^2$ carbons ranging between 120-146 ppm and a single $sp^3$ carbon at 36 ppm. The facile elimination to form cycloheptadienyne complex was later confirmed [*vide infra*] in the Nicholas reactions of cycloheptenyne dicobalt complexes bearing an acetoxy group. These cycloheptadienyne-$Co_2(CO)_6$ complexes are thermally stable and can be chromatographed easily. Compound **177** was found to be volatile under high vaccum. The vinylsilane side products **180a,b,c** arose from the allylic rearrangement of the tin moiety in nucleophile **56**, while acyclic product **179** arose from the addition of allyltriethylsilane to substrates **140 b,c.** Apparently complete destannylation of **56** to allyltriethylsilane occurred prior to the addition reaction.

### 3.3 Formation of Cycloheptyne-$Co_2(CO)_6$ by Ring Closing Metathesis

It became apparent that an alternative, non Lewis acidic route was required for the preparation of cycloheptyne complexes bearing an oxygen function. Green[78] has reported the preparation of cyloheptyne dicobalt complexes bearing an acetoxy group at the propargylic position by ring closing metathesis in excellent yields.[79]

Using this synthetic method, we prepared the appropriate acyclic diene complex by the route illustrated in (Fig. 60).

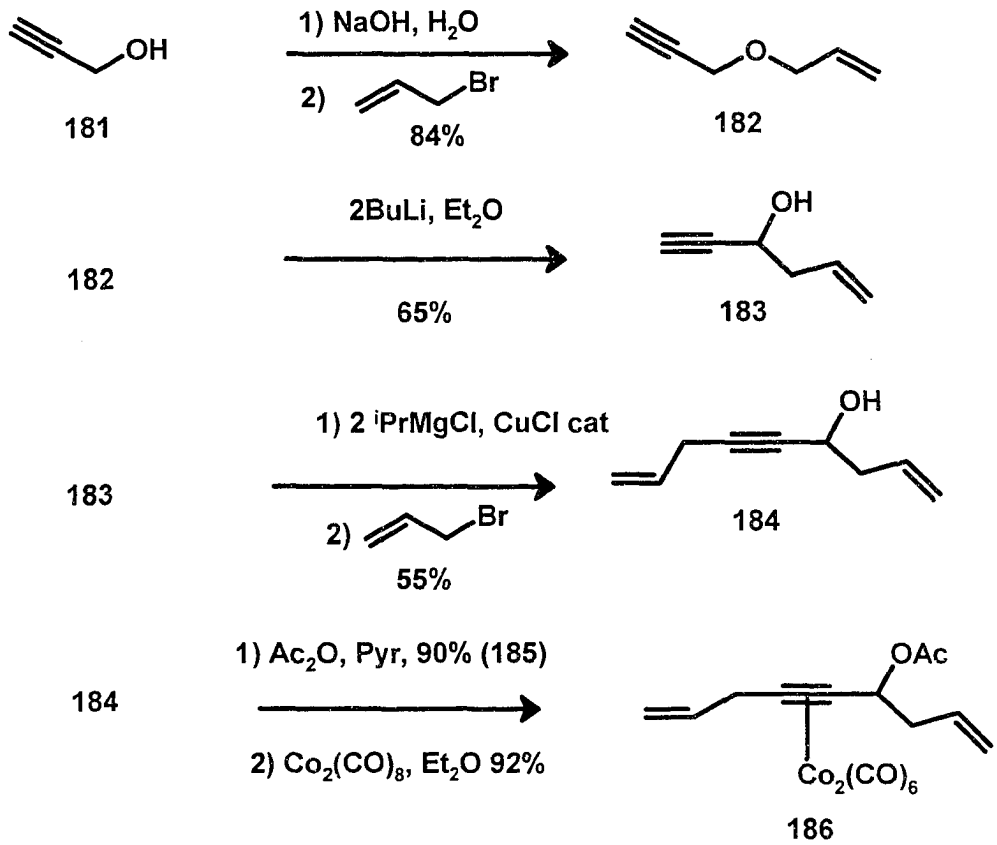
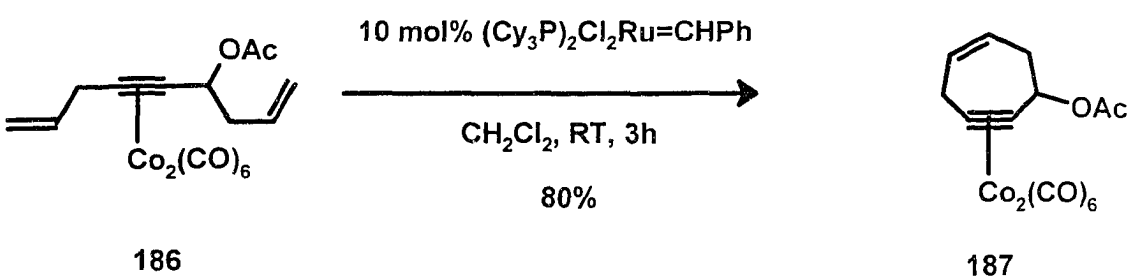



**Figure 60. Preparation of Acyclic Dienol Acetate Complex 179**

Propargyl allyl ether was prepared by using a modification of the known procedure.[80] Starting from the commercially available propargyl alcohol, deprotonation by aqueous KOH and alkylation with allyl bromide, followed by distillation and drying over anhydrous sodium sulfate, afforded propargyl allyl ether in 84% yield. Treatment of the propargyl allyl ether with 2 equivalents of butyllithium

in diethyl ether converted it to the known alcohol[81] **182** through a [2,3]- Wittig rearrangement[82]. Normally [1,2] Wittig rearrangement competes with the [2,3] rearrangement, but in this case both rearrangements would deliver the desired alcohol (**182**). Deprotonation of alcohol **182** with the 2 equivalents of isopropylmagnesium chloride, followed by the slow addition of allyl bromide in the presence of a catalytic amount of Cu(I)Cl afforded alcohol **184** in 55% yield[83]. Acetylation of the dienyl alcohol under conventional conditions furnished dienyl acetate **185**. Complexation of the dienyl acetate **184** then afforded the desired diene dicobalt complex **186**. The cycloheptenyne dicobalt complex **187** bearing an acetoxy group at the propargyl carbon was prepared in 82% yield by treating **186** in $CH_2Cl_2$ with the first generation Grubbs' catalyst.

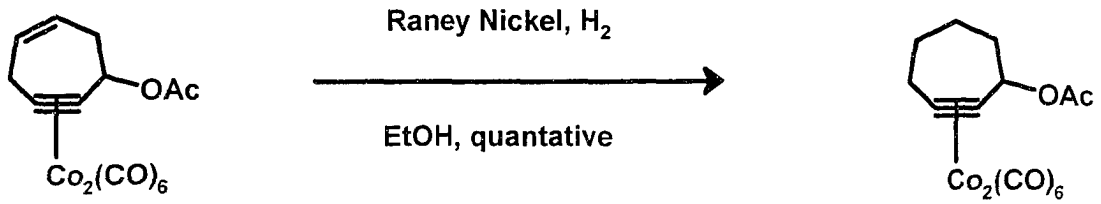



**186** **187**

**Figure 61. Preparation of Cycloheptenyne Complex 187 Bearing an Acetoxy Group**

The $^1$H-NMR, $^{13}$C-NMR and IR spectra of **187** were identical to those published earlier. Although complex **187** is stable for long periods under nitrogen and low temperature, its handling in air for long period of time brought significant

amount of decomposition of the complex. The fickleness of complex **187** was addressed by reducing the double bond with Raney Nickel® to complex **188**, which has greater air stability and is more easily handled.




**187** **188**

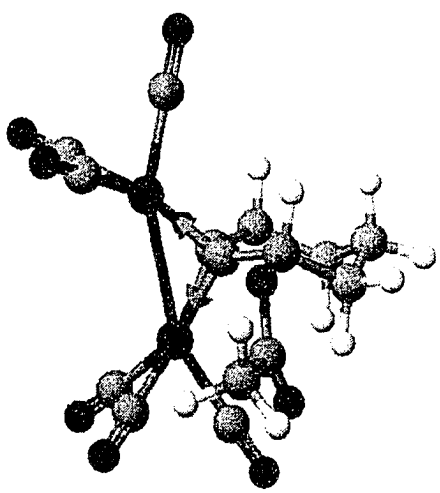


**Figure 62. Raney Nickel Reduction of Complex 187 and PCMODEL MMX Minimization of Cycloheptyne-OAc Complex**

### 3.4 Nicholas Chemistry on Cycloheptenyne/Cycloheptyne Cobalt Complexes

Substrates **187** and **188** were used to study Lewis acid mediated Nicholas reactions with nucleophiles containing an alkene function. Various allyl alcohols, allyl thiol, and homoallyl alcohol were employed in the presence of $BF_3.OEt_2$. The condensations were straightforward; reaction at room temperature for substrate **187** (Fig. 62) and 0 $^0$C for substrate **188** (Fig.63) gave the corresponding propargyl allyl ethers, propargyl allyl thioethers, and propargyl homoallyl ether **189-194** in good to excellent yields. At the beginning of these studies, using room temperature reaction, 10 equivalents of the nucleophile and 5 equivalents of $BF_3.OEt_2$ conditions were used for substrate **187** and trace amount of diene **177** was formed along with the desired **189** and **190**. However, use of lower temperature (0 $^0$C) and slower addition of the Lewis acid was found to completely suppress the competitive elimination process. Therefore, the latter reaction condition was adopted as the standard procedure, unless it failed to form the Nicholas adduct.

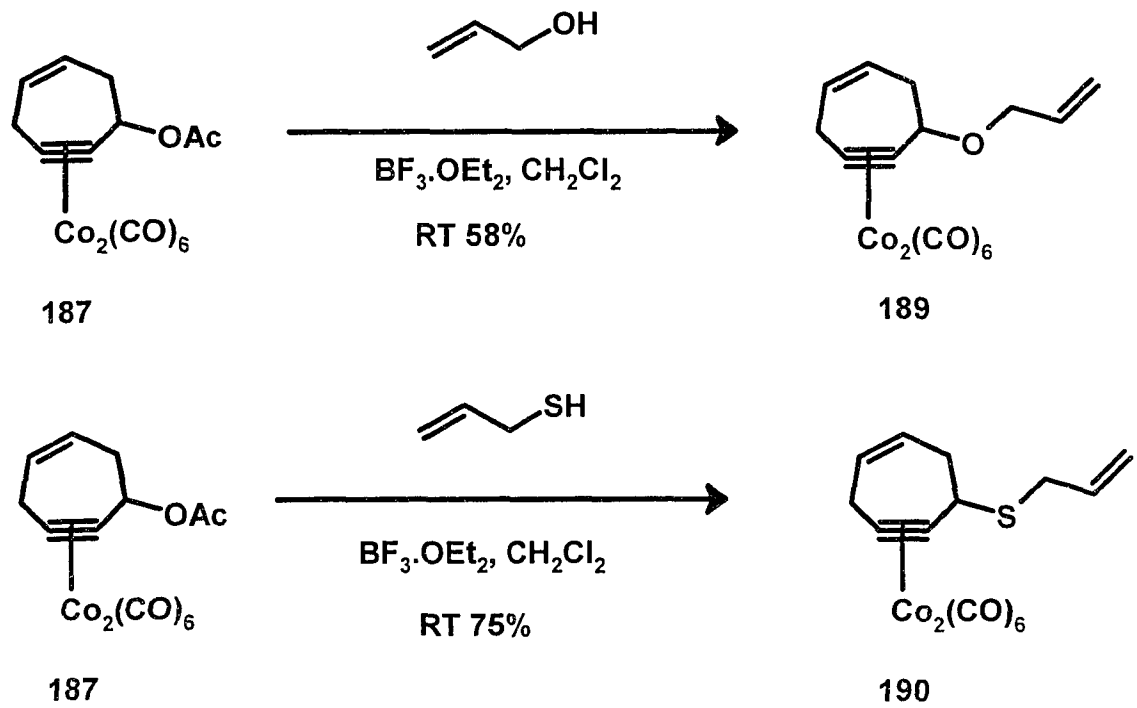



**Figure 63. Tethered Alkene Incorporation on Cycloheptenyne Dicobalt Complexes 187**

It is our belief based on molecular mechanics calculations (MM3, CACHE® MM2, PC Model) that cycloheptyne dicobalt complexes are in chair-like conformations (Fig 62). From the coupling constants (10.0-10.7 Hz and 4.2-4.5 Hz) of the substituted propargylic methine proton in each of the cyloheptyne dicobalt complexes (for example **188,191,192,193,** and **194**), it is clear that there are axial-axial and axial-equatorial couplings of the protons, suggesting strongly that the proton is axial, and therefore that the allyloxy and thioallyl functions are equatorially disposed.

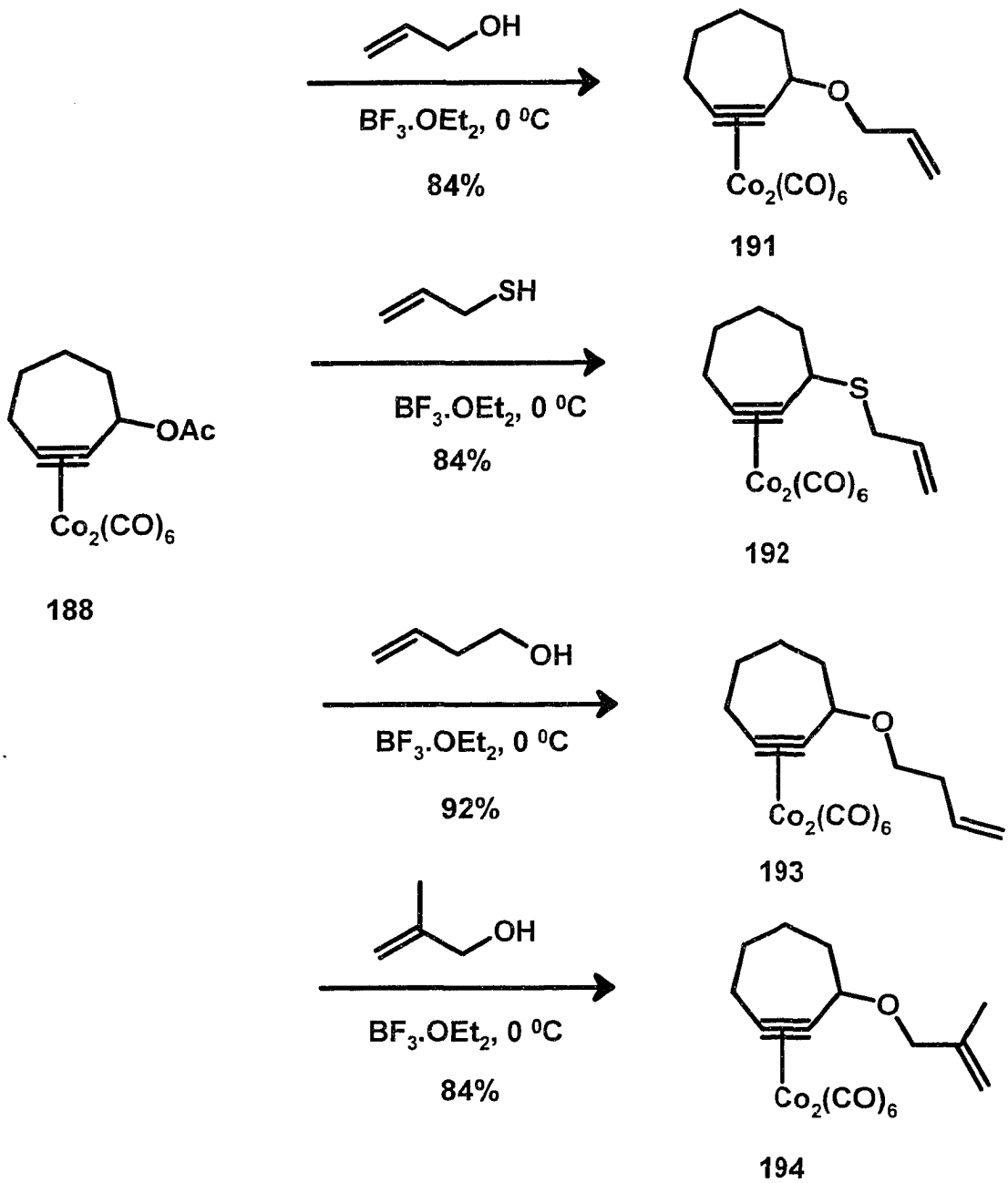



**Figure 64. Tethered Alkene Incorporation on Cycloheptyne Dicobalt Complexes 188**

Attempts to incorporate a nitrogen function at the propargylic position met with considerable difficulty. The Lewis acid mediated reaction of allylamine with

**188** did not progress, likely due to the Lewis basicity of the amine function. A nitrogen function could be incorporated at the propargylic position by Ritter reaction[84] of complex **188** with acetonitrile in the presence of $H_2SO_4$, giving **195** in excellent yield (91% yield). However, attempts to reduce the amide functional group in **195** to the desired amine **196** without concomitant destruction of the alkynedicobalt hexcarbonyl unit were futile.[85]

Faced with this difficulty, resort was made to the tactic of Amouri and Gruselle[86], which involves generation of a discrete sulfonium ion as a propargyl cation equivalent, and subsequent addition of the nucleophile. In the event, the addition of $HBF_4$ to complex **188** in $Et_2O$, in the presence of dimethyl sulfide generated sulfonium ion **197** in quantative yield. Addition of 1 equivalent of allylamine and 2 equivalents of diisopropylethylamine as a proton scavenger in dichloromethane to a solution of the sulfonium complex in dichloromethane, and subsequent treatment of the crude material with acetic anhydride or p-toluenesulfonic anhydride afforded the propargylic allyl amine complex **198** (73% yield from **188**) or propargyl allyl sulfonamide **199** (62% yield from **188**), respectively, in reasonable synthetic yields (Fig. 65).

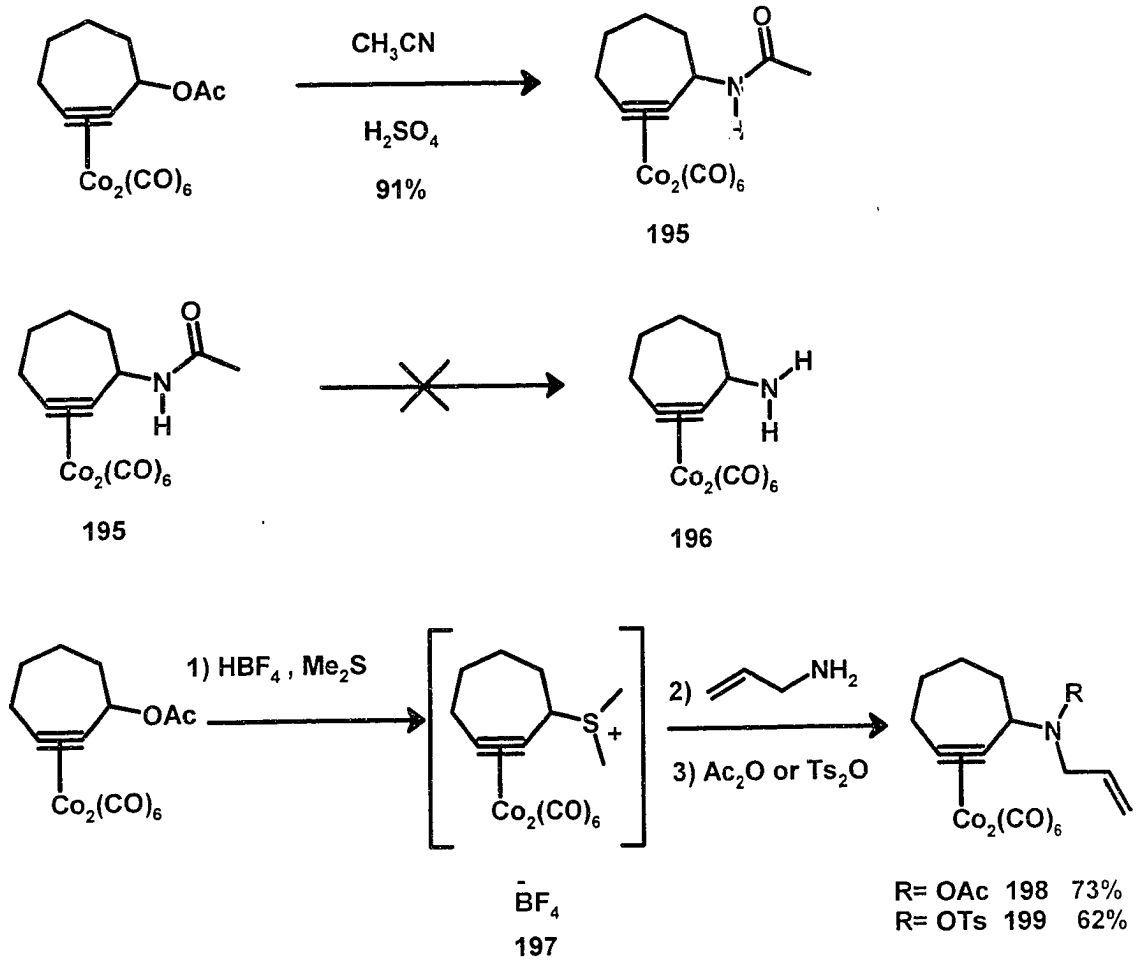



**Figure 65. Formation of Nitrogen Linked Enyne Complex**

### 3.5 Intramolecular Pauson-Khand Reactions of Tethered Enyne Complexes

With the appropriate cycloheptyne tethered alkene complexes available, we focused our attention on the study of the PKR of these complexes. We chose **199** for the investigation under several sets of conditions for the Pauson-Khand reaction (Fig. 66). The Sugihara amine[49a] conditions ($CyNH_2$, $ClCH_2CH_2Cl$, reflux) indeed gave Pauson-Khand product **200** in 65% yield, as a 84:16 mixture of diastereoisomers favoring the *cis* isomer, along with a smaller amount of Pauson-Khand/allylic reduction product **201** (12.5%). Attempted use of the Sugihara sulfide[49b] conditions (BuSMe, $ClCH_2CH_2Cl$, reflux) eliminated completely the byproduct **201**, but at the expense of **200** (51%, 67:33 *cis:trans*). In addition, $Me_3NO$ (49% yield of **200**, 55:45 *cis:trans*) and refluxing toluene (20% **200**, 54:46 *cis:trans*) were judged inferior to the Sugihara amine conditions. Consequently, the Sugihara amine conditions were chosen for all substrates, and only in the case of failure of these conditions were other protocols adopted.

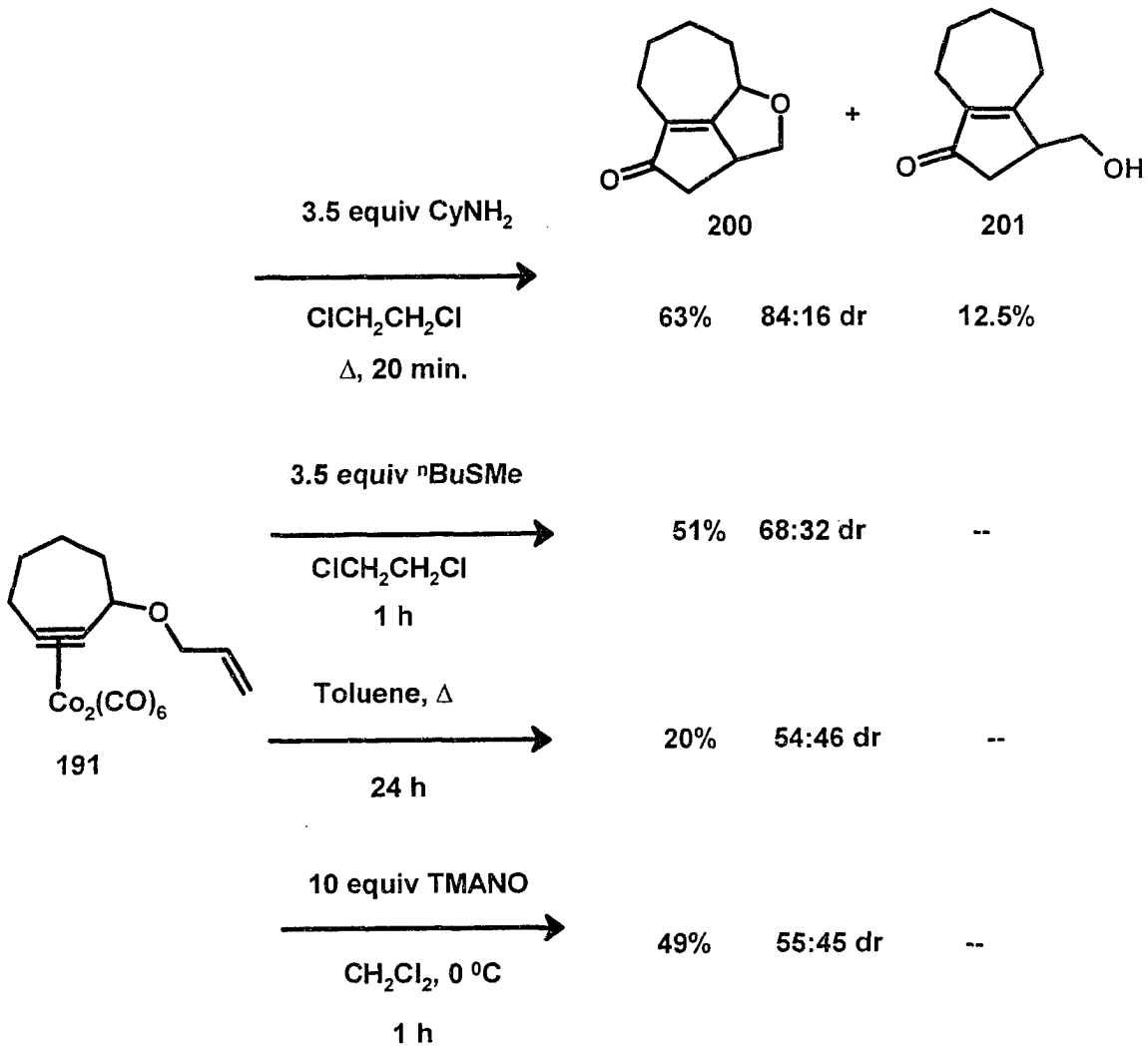



**Figure 66. PKR of Cycloheptyne Complex 190 Under Different Protocols**

Substrate **189** under went a PKR, using the Sugihara amine conditions to afford a 91:9 diastereoisomeric mixture of tricyclic ethers **202** in 89% yield. Under analogous conditions, thioethers **203** (57%, 67:33 dr) and **204** (73%, 77:23 dr) were also obtained in good yields from compounds **190** and **192**, respectively (Fig. 67). Homoallylic tethered cycloheptyne dicobalt complex **193** also cleanly provided tricyclic ether **205** (60:40 dr) in 73% yield.

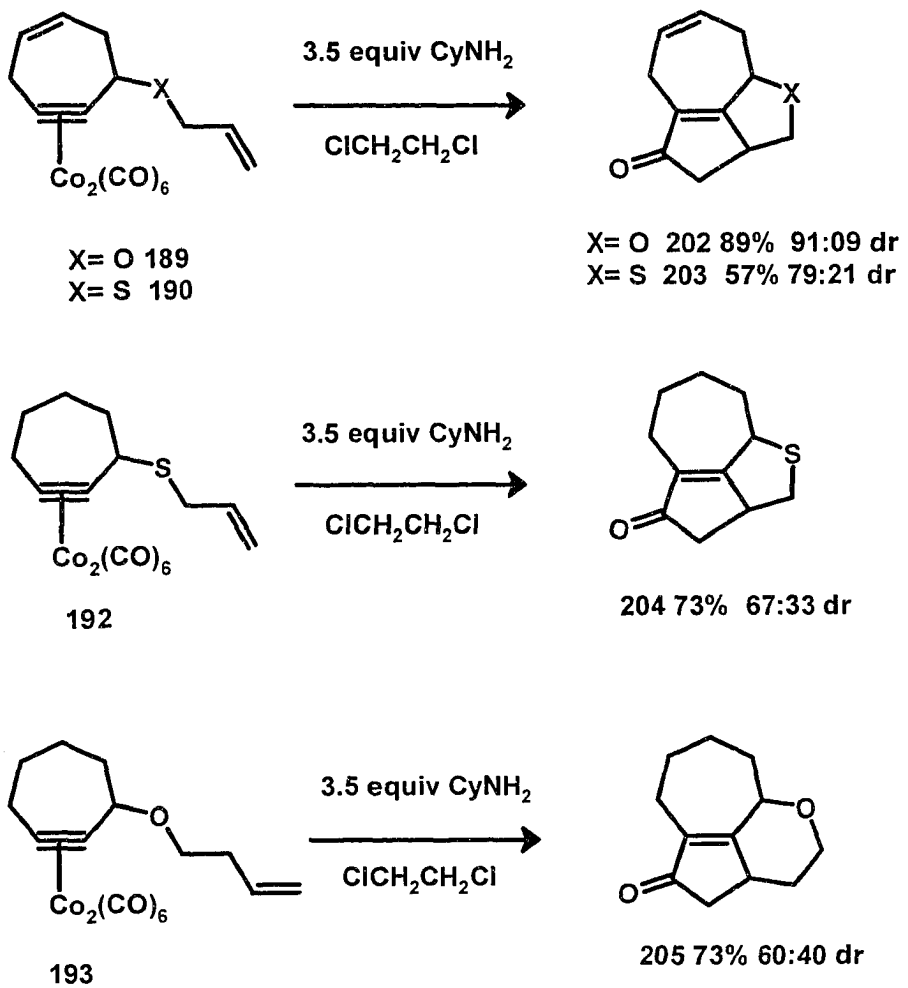



**Figure 67. PKR of Allyl and Homoallyl Ether and Allyl Thioethers Cycloheptyne Complexes**

The Sugihara cyclohexylamine conditions were judged as failures in two cases. When substrate **194**, which bears a 2,2-disubstitution on the alkene, was subjected to the Sugihara amine conditions, no tricyclic products could be isolated, but only bicyclic alcohol **206** in 14% yield. However, by using trimethylamine N-oxide (TMANO) and low reaction temperature, the desired tricyclic material **207** was obtained as a single diastereoisomer in 59% yield (65% based on recovered

material) (Fig. 68). Similarly, substrate **199** failed to provide the tricyclic amide **208** when the Sugihara amine conditions were employed. Nevertheless, by using Sugihara n-butyl methyl sulfide method, the intended product **208** was obtained in 51% yield.

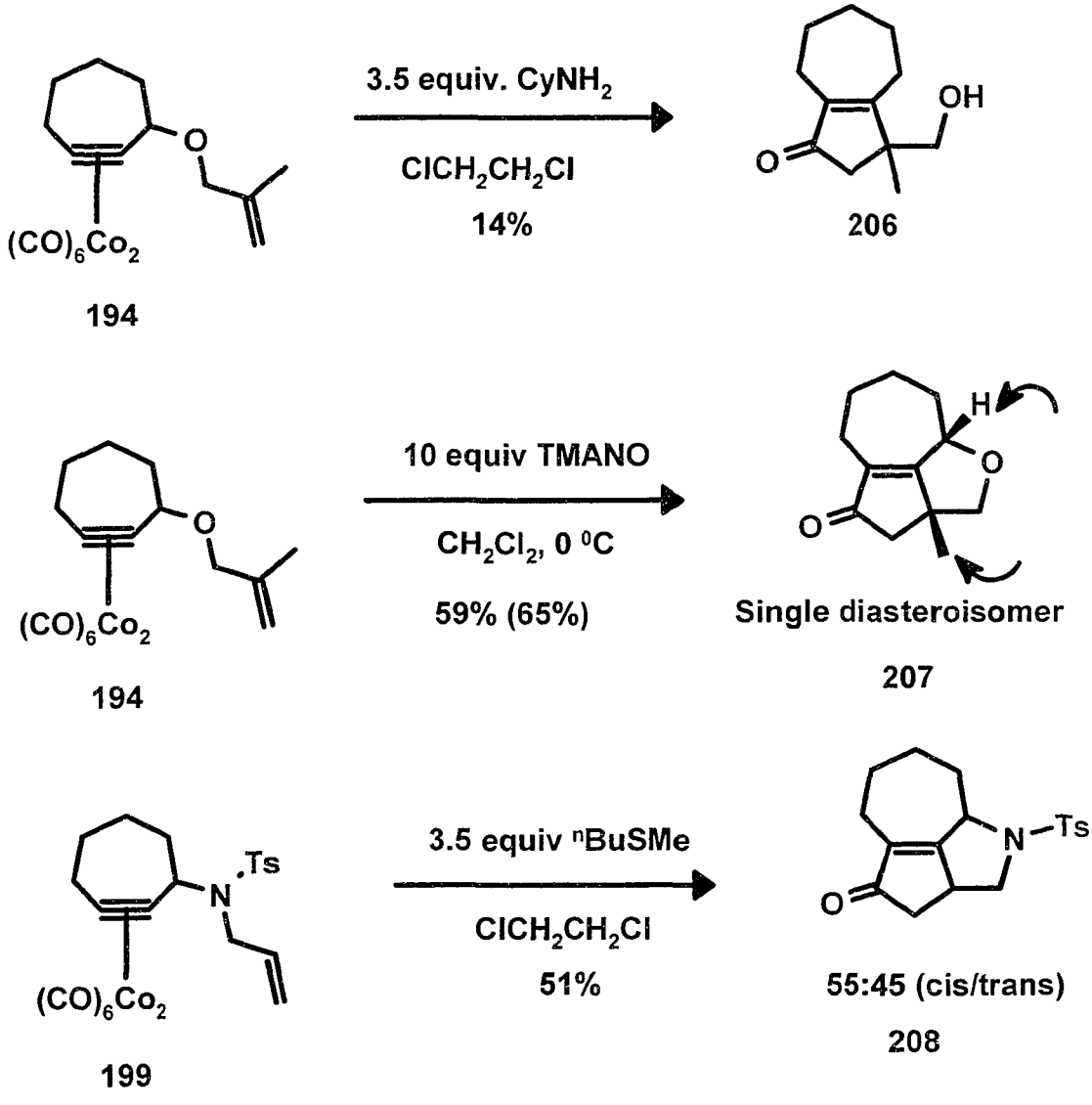



**Figure 68. PKR of Substituted 1,1-Alkene and Nitrogen Linked Alkene Cycloheptyne Complexes**

### 3.6 The Stereochemical Assignments of the PKR Products

Prior to this study, a related tricyclic product **210** (8,5,5 instead of 7,5,5 ring system) was published by the Schreiber's group.[15] A thermal PKR of complex **209** afforded a single tricyclic diasteroisomer **210** in high yield. The *cis* relationship of the two methine protons indicated in **210** was established by $^1$H-NMR (Fig. 69). Recently, another related PKR product, tricyclic **212** (9,5,5 ring system) was synthesized by the Young group.[87] An intramolecular PKR of complex **211** under Sugihara sulfide conditions afforded tricyclic **212** in 54% yield. The authors assigned the stereochemistry of the two indicated methine protons as the *cis* configuration.

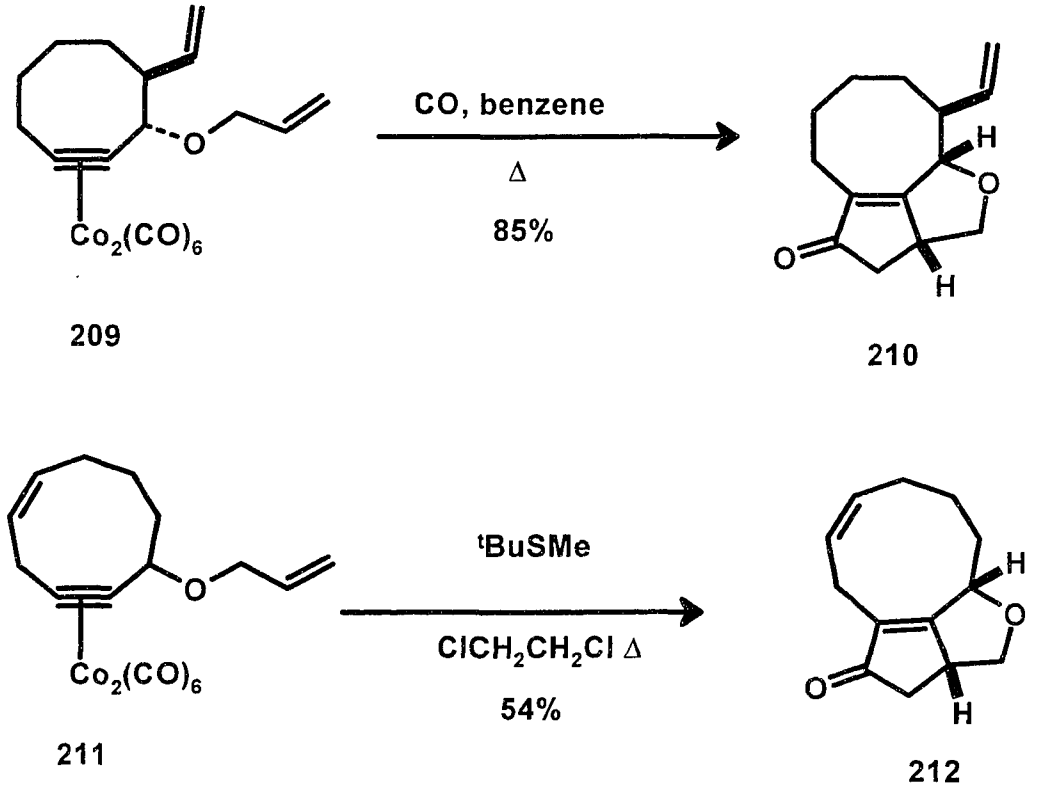



**Figure 69. Formation of Tricyclic Products 210 & 212 by Intramolecular PKR**

To our surprise, the $^1$H NMR spectra of majority of the PKR adduct did not give nOe enhancements between the methine hydrogen atoms for either diastereomer indicated (Fig. 67). Conversely, the 2D-NOESY spectrum of methyl substituted **207** displayed a positive nOe between the methine hydrogen and the methyl hydrogens, establishing their relationship as *cis*. The methine H atoms α- to the heteroatoms of **207** and the major diastereomers of the cycloheptane products **200**, **2005**, and **208** also displayed very similar $^1$H NMR vicinal coupling constants (dd, 9.9-10.9 Hz, 4.2-5.7 Hz). This pattern was not repeated in the minor diastereomers. However, an X-ray diffraction study performed on the *minor* isomer of **204** indicated a *trans* relationship between the two methines. The stereochemical assignment of **202** & **203** were based on analogy as well as the extensive calculations done on the proposed alkene coordination intermediate, the alkene insertion transition state (MMX, PCMODEL; MM3, CACHE®) and on **202** & **203** themselves (PM3, CACHE®).

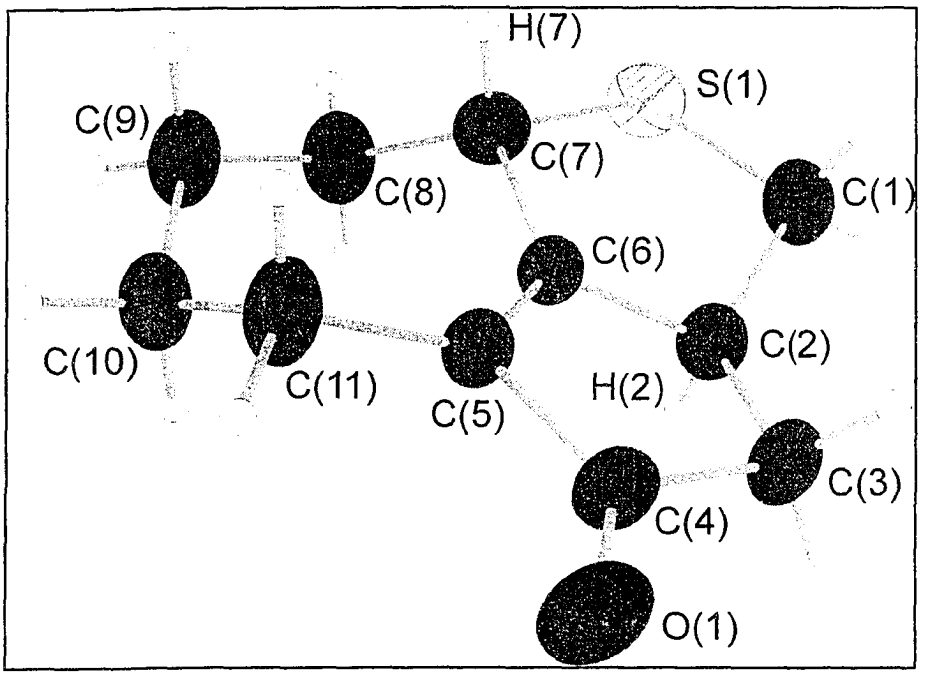



**Figure 70. Single Crystal Structure of the *trans*-Isomer 204**

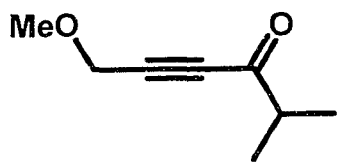
### 3.7 Summary

We have tried to synthesize cycloheptyne-$Co_2(CO)_6$ bearing a hydroxyl or ethoxy group (i.e. **178**) at the propargylic carbon through 4+3 cycloaddition. Unfortunately, the desired complexes were not stable enough in the reaction medium to be isolated. However, we did isolate the hydrolyzed cycloheptadienyne complexes in good yields. Nevertheless, we were able to develop a rapid and facile method to prepare cycloheptenyne and cycloheptyne dicobalt complexes bearing an acetoxy functional group at the propargylic carbon and through ring closing metathesis (**187**) in excellent yield and Raney Nickel® reduction (**188**).

These complexes could be functionalized easily via Nicholas reactions in excellent yield. We were able to prepare oxygen, sulphur, and nitrogen tethered alkenes that participated Pauson-Khand reactions affording tricyclic compound **200**, **201**, **202**, **204**, **205**, **207,** and **208** in good to excellent yield.

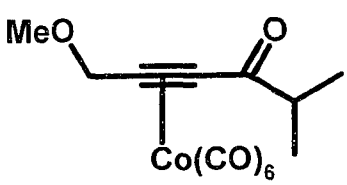
## 3.8 Experimental Section

### 6-Methoxy-2-methyl-hex-4-yn-3-one (171)



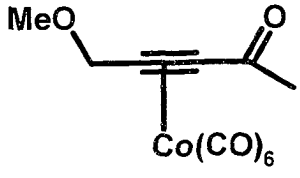

To a stirred solution of **164** (0.83 g, 11.84 mmol) in dry THF (20 mL) at -78 $^{0}$C was added methyllitium (7.5 mL, 1.00 equiv.). Freshly distilled isobutyryl chloride (1.5 mL, 1.5 equiv.) was added dropwise and the solution was allowed to warm to room temperature. A conventional workup and bulb to bulb distillation of the crude material afforded **167** (0.78 g, 56% yield): bp 108-110°C/32 torr; IR; (cm $^{-1}$) 2938, 2827, 2209, 1681, 1226; $^{1}$H-NMR: 4.29 (s 2H), 3.43 (s 3H), 2.67 (septet. 7.0 Hz, 1H), 1.21 (d 7.0 Hz 6H); $^{13}$C-NMR: 191.5, 88.3, 84.4, 59.6, 58.0, 42.9, 17.8

### Hexacarbonyl [$\mu$-$\eta^4$ -(6-methoxy-2-methylhex-4-yn-3-one)] dicobalt (172)



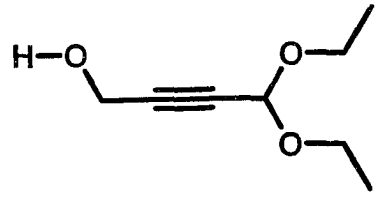
Compound **171** (400 mg 2.85 mmol) was complexed via procedure A. Flash chromatography using 50:1 petroleum ether:diethyl ether gave **172** (770 mg, 63% yield): IR ($cm^{-1}$) 2976, 2935, 2824, 2101, 2064, 2033, 1671, 1098; $^1$H-NMR : 4.62 (s 2H), 3.52 (s 3H); 2.99 (septet 6.8Hz 1H), 1.23 (d 6.8 Hz 6H); $^{13}$C-NMR: 207.2, 198.3, 93.9, 85.3, 72.6, 59.1, 41.8, 19.2; MS m/e 398 ($M^+$-CO), 370 ($M^+$-2CO), 342 ($M^+$-3CO), 314 ($M^+$-4CO), 286 ($M^+$-5CO), 258 ($M^+$-6CO); HRMS m/e for $C_{14}H_{12}Co_2O_8$ calculated ($M^+$) 425.91961, found. 425.919067.

**(Hexacarbonyl) [μ-η$^4$ –(5-methoxy pent-3-yn-2-one)] dicobalt (138b)**



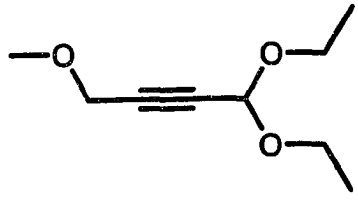

Compound **140b** (122 mg, 1.09 mmol) was complexed via procedure A. Flash chromatography using 50:1 petroleum ether:diethyl ether gave **138b** (400 mg 63% yield): IR ( $cm^{-1}$) 2927, 2102, 2063, 2031,1673, 1053; $^1$H-NMR: δ 4.61 (s 2H), 3.50 (s 3H); 3.0 (septet 3H); $^{13}$C-NMR: ; MS m/e 398 ($M^+$-CO), 370 ($M^+$-2CO), 342 ($M^+$-3CO), 314 ($M^+$-4CO), 286 ($M^+$-5CO), 258 ($M^+$-6CO); HRMS m/e for $C_{13}H_{12}Co_2O_7$ calculated($M^+$-CO) 369.8934 found 369.8925.

**4,4-Diethoxybut-2-yn-1-ol (173)**



To a stirred solution of the commercially available 3,3-diethoxy-propyne (0.63 g, 4.92 mmol) in dry $Et_2O$ (20 mL) at -78 $^0$C was added methyllithium (4 mL, 1.2 equiv) dropwise over 30 minutes. The solution was allowed to warm to room temperature and paraformaldehyde (0.18 g, 1.2 equiv) was added. A conventional workup and bulb to bulb distillation of the crude material afforded **173** (0.40 g, 51% yield): bp 110-120°C/3 torr; IR (cm $^{-1}$) 3430, 2978, 2895, 1052; $^1$H-NMR: 5.13 (s 1H), 4.13 (s 2H), 3.75 (br 1H), 3.58 (m 2H), 3.42 (m 2H), 1.06 (m 6H); $^{13}$C-NMR: 90.8, 83.7, 79.8, 60.5, 49.8, 14.5.

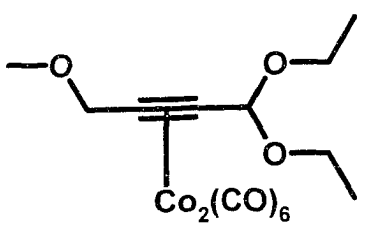
**1,1-Diethoxy-4-methoxybut-2-yne (174)**



To a solution of potassium hydride (675 mg of 30% oil dispersion, 5.06 mmol), washed free of mineral oil by dry diethyl ether, in THF (25 mL) at room temperature was added **173** (400 mg, 2.53 mmol) and the white suspension was left

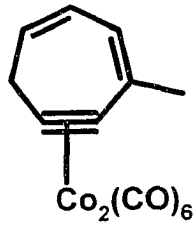
to stir for 1 hr. Iodomethane (0.3 mL, 2 equiv.) in THF (5mL) was added dropwise and left to stir for additional hour. The color of the solution gradually changed to dark brown. A conventional workup and bulb to bulb distillation of the crude material afforded **174** (0.37 g, 86% yield): bp 90-100°C/11 torr; IR ( $cm^{-1}$) 2978, 2932, 2887, 1054; $^{1}$H-NMR: 5.26 (s 1H), 4.11 (s 2H), 3.67 (m 2H), 3.54 (m 2H), 3.33 (s 3H), 1.18 (m 6H); $^{13}$C-NMR: 91.1, 81.6, 81.0, 60.7, 59.5, 57.4, 14.8.

**Hexacarbonyl [μ-$\eta^4$ –(1,1-Diethoxy-4-methoxy-but-2-yne)] dicobalt (175)**



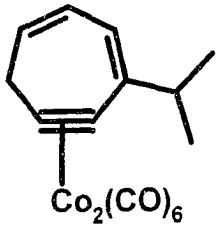

Compound **174** (350 mg, 2.03 mmol) was complexed via procedure A. Chromatography employing neutral alumina and using 50:1 petroleum ether:diethyl ether gave **175** (725mg, 79% yield): IR ( $cm^{-1}$) 2981, 2933, 2822, 2096, 2055, 2026, 1098, 1061; $^{1}$H-NMR: 5.5 (s 1H), 4.60 (s 2H), 3.80 (m 2H), 3.67 (m 2H), 3.52 (s 3H), 1.24 (m 6H); $^{13}$C-NMR: 199.7, 102.0, 92.5, 91.3, 72.8, 63.3, 58.9, 15.0; MS m/e 458 ($M^+$), 430 ($M^+$-CO), 402 ($M^+$-2CO), 374 ($M^+$-3CO), 346 ($M^+$-4CO), 318 ($M^+$-5CO), 290 ($M^+$-6CO), HRMS m/e for $C_{15}H_{16}Co_2O_9$ calculated ($M^+$) 457.9458 found 457.9456.

**Hexacarbonyl [ μ-η$^4$-(4-methylcyclohepta-1,3-dien-5-yne)] dicobalt (176a)**




Complex **140b** (196 mg, 0.49 mmol), nucleophile **56** (656 mg, 3 equiv) in dry benzene (2 mL) and $Bu_2BOTf$ (1.50 mL, 3 equiv.) in dry benzene (5 mL) were mixed at room temperature via procedure B. After conventional workup and flash chromatography (100% petroleum ether), **176a** was obtained (90 mg, 47%) IR: (cm$^{-1}$) 2957, 2090, 2053, 2022; $^1$H-NMR: 5.91 (d 7.7 Hz 1H), 5.82 (m 1H), 5.70 (dt 12.0 Hz, 4.5 Hz 1H), 3.79 (d 4.0 Hz 2H), 2.16 (s 3H); $^{13}$C-NMR: 200.5, 137.5, 128.0, 123.6, 117.6, 94.1, 35.1, 23.1; MS m/e 390 ($M^+$), 362 ($M^+$-CO), 334 ($M^+$-2CO), 306 ($M^+$-3CO), 278 ($M^+$-4CO), 250 ($M^+$-5CO), 222 ($M^+$-6CO), 389 ($M^+$-1), 361 ($M^+$-1-CO), 333 ($M^+$-1-2CO), 305 ($M^+$-1-3CO), 277 ($M^+$-1-4CO), 249 ($M^+$-1-5CO), 221 ($M^+$-1-6CO), HRMS m/e for $C_{14}H_8Co_2O_6$ calculated ($M^+$) 389.8985 found 389.8984.

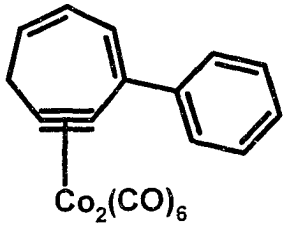
**Hexacarbonyl [ μ-η$^4$-(4-isopropylcyclohepta-1,3-dien-5-yne)] dicobalt (176b)**



Complex **171** (190 mg, 0.45 mmol), nucleophile **56** (602 mg, 3 equiv.) in dry benzene (4.5 mL) and $Bu_2BOTf$ (1.35 mL, 3 equiv) in dry benzene (2 mL) were mixed at room temperature via procedure B. After conventional workup and flash chromatography (100% petroleum ether), **176b** was obtained (259.2 mg, 62%) IR: (cm $^{-1}$) 2958, 2876,2095, 2059, 2031; $^1$H-NMR: 6.00 (d 7.7 Hz 1H), 5.91 (m 1H), 5.73 (dt 11.9 Hz, 4.6 Hz 1H), 3.79 (d 4.6 Hz 2H), 2.68 (sept 6.9 Hz 1H), 1.23 (d 6.9Hz 6H); $^{13}$C-NMR: 200.0, 147.8, 128.5, 128.2, 99.8, 88.4, 35.5, 35.2, 31.9, 23.0; MS m/e 418 ($M^+$), 362 ($M^+$-2CO), 334 ($M^+$-3CO), 306 ($M^+$-4CO), 278 ($M^+$-5CO), 250 ($M^+$-6CO), HRMS m/e for $C_{14}H_{12}Co_2O_4$ calculated ($M^+$-2CO) 361.9400, found 361.9394.

**Hexacarbonyl [ μ-η$^4$-(4-phenylcyclohepta-1,3-dien-5-yne)] dicobalt (176c)**

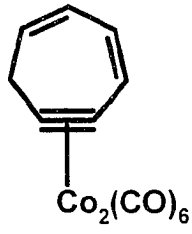
1




Complex **140c** (300 mg, 0.65 mmol), nucleophile **56** (870 mg, 3 equiv) in dry dichloromethane (6.5 mL) and $Bu_2BOTf$ (1.95 mL, 3 equiv.) in dry dichloromethane (2 mL) were mixed at -15 $^0$C via procedure B. After conventional workup and flash chromatography (100% petroleum ether), **176c** was obtained (575 mg, 88%) IR: (cm $^{-1}$) 2925, 2091, 2054, 2022, 1596; $^1$H-NMR: 7.62 (d 7.2 Hz 2H), 7.39 ( t 7.2 Hz 2H),

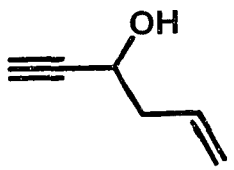
7.31 (t 7.2 Hz 1H), 6.43 (d 7.7 Hz 1H), 6.08 (m 1H), 5.88 (dt 11.9 Hz, 4.7 Hz 1H), 3.88 (dd 4.7 Hz, 1.3 Hz 2H); $^{13}$C-NMR: 199.5, 141.4, 141.2, 129.6, 128.8, 12.8.2, 127.9, 126.5, 124.6, 101.1, 86.7, 35.5; MS m/e 452 ($M^+$), 424 ($M^+$-CO), 396 ($M^+$-2CO), 368 ($M^+$-3CO), 340 ($M^+$-4CO), 312 ($M^+$-5CO), 284 ($M^+$-6CO), HRMS m/e for $C_{19}H_{10}Co_2O_6$ calculated ($M^+$) 451.9141 found 451.9132.

**Hexacarbonyl [ μ-η$^4$-(cyclohepta-1,3-dien-5-yne)] dicobalt (177)**



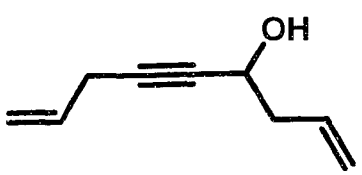

Complex **175** (380 mg, 0.86 mmol), nucleophile **56** (3 equiv) in dry dichloromethane (8.6 mL) and $Bu_2BOTf$ (2.6 mL, 3 equiv) in dry dichloromethane (2 mL) were mixed at 0 $^0$C via procedure B. After conventional workup and flash chromatography (100% petroleum ether), **177** was obtained (249 mg, 77%): IR (cm$^{-1}$) 3025, 2958, 2095, 2046; $^1$H-NMR: 6.68 (d 9.7 Hz 1H), 6.07 (dd 7.5 Hz, 9.7 Hz 1H), 5.92 (m 1H), 5.80 (m 1H), 3.86 (m 2H), $^{13}$C-NMR: 200.0, 130.7, 129.4, 128.0,126.9, 117.6, 98.3, 35.6; MS m/e 376 ($M^+$), 348 ($M^+$-CO), 320 ($M^+$-2CO), 292 ($M^+$-3CO), 264($M^+$-4CO), 375 ($M^+$-1), 347 ($M^+$-1-CO), 319 ($M^+$-1-2CO), 291 ($M^+$-1-3CO), 263 ($M^+$-1-4CO) HRMS m/e for $C_{13}H_6Co_2O_6$ calculated ($M^+$) 375.8828 found 375.8809.

**Hex-5-en-1-yn-3-ol (183)**




A stirred solution of allyl propargyl ether (5.30 g, 55 mmol) in dry diethyl ether (20 mL) was cooled to –78 $^{0}$C. Butyllithium (44 mL, 2.0 equiv) was added dropwise and the solution was allowed to warm to room temperature and was left to stir overnight. A conventional workup and bulb to bulb distillation of the crude material afforded **183** (3.18 g, 60% yield): bp 140-150 $^{0}$C; The above product was spectroscopically identical to literature.[89]

**Nona-1,8-dien-5-yn-4-ol (184)**

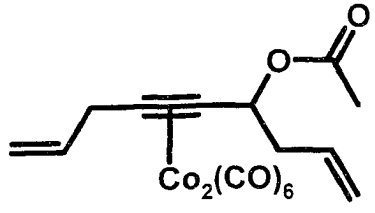



To a stirred solution of **183** (2.00g, 20.83 mmol) in dry THF (20 mL) at –78 $^{0}$C was added isopropylmagnesium chloride (21 mL, 2 equiv.) dropwise and the solution was then allowed to warm to 0 $^{0}$C. A catalytic amount of Cu(I)Cl (30-50 mg) was

added and after stirring the solution for 30 minutes, allyl bromide ( 1.8 mL, 1 equiv) dissolved in THF (5 mL) was added and the reaction was then allowed to warm to room temperature. A conventional workup and bulb to bulb distillation of the crude material afforded **184** (1.56 g, 55%): bp 50-70 $^0$C/ 1.5 mmHg. The above compound was spectroscopically identical to literature[90].

**Procedure D: Standard Acetylation & Complexation**

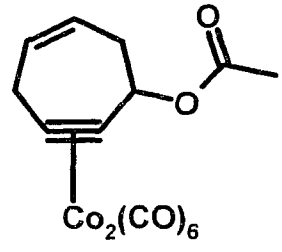
**Hexacarbonyl [μ-η$^4$-(6-acetoxynona-1,8- dien-4-yne)] dicobalt (185)**




Compound **184** was subjected to standard acetylation conditions. Alcohol **184** (1.55 g. 8.7 mmol) was dissolved in acetic anhydride (5 mL) and pyridine (1mL) at 0 $^0$C, the reaction was allowed to warm to room temperature and was left to stir for overnight. A solution of 3M HCl acid (10 mL) was added to the reaction mixture and after conventional workup and removal of the excess acetic anhydride through high vaccum, the crude material was complexed via procedure A. Flash chromatography using 50:1 petroleum ether:diethyl ether gave (3.71g, 91%): IR (cm $^{-1}$) 2925, 2093, 2052, 2022, 1744, 1229; $^1$H-NMR: 6.13 (dd 7.5 Hz, 6.0 Hz 1H), 5.93 (m 1H), 5.84 (m 1H), 5.20 (m 4H), 3.53 (d 7.1 Hz 2H), 2.59 ( apparent triplet 6.6 Hz 2H), 2.10 (s 3H);

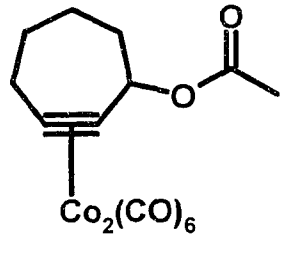
$^{13}$C-NMR: 199.4, 170.2, 135.5, 132.9, 118.5, 117.6, 96.5, 95.0, 73.2, 41.3, 38.1, 20.6; MS m/e; HRMS m/e for $C_{15}H_{14}Co_2O_6$ calculated ($M^+$-2CO) 407.9454, found 407.9455.

**Hexacarbonyl [μ-η$^4$ –(6-acetoxycyclohept-1en-4-yne)]dicobalt (187)**




Complex **187** was prepared according to Green's method[80]. The above compound was spectroscopically identical to literature (82% yield).

**Hexacarbonyl [μ-η$^4$ – (3-acetoxycycloheptyne)] dicobalt (188)**

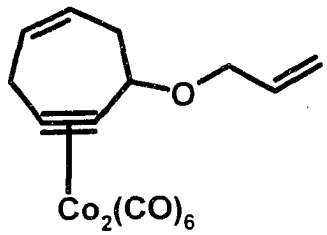



Complex **186** (394 mg, 0.85 mmol) was dissolved in dichloromethane (43 mL) at room temperature. A solution of $(Cy_3P)_2Cl_2Ru$=CHPh (70 mg, 10 mol%) in dichloromethane (10mL) was added dropwise. The reaction progress was

monitored by TLC and upon completion of the reaction, the solution was filtered through a pad of Celite® and concentrated. Thoroughly washed Raney nickel® catalyst (200 mg) and 95% ethanol (200 mL) were added to the flask. The solution was purged with hydrogen gas and the heterogeneous mixture was left to stir for 3 hours under hydrogen atmosphere. The reaction progress was monitored by TLC (petroleum ether:diethyl ether 10:1). After completion of the reaction, the solution was filtered and the solvent was concentrated under reduced pressure. (Caution must be exercised in handling Raney Nickel catalyst as it is pyrophoric when dry). Flash chromatography (petroleum ether: diethyl ether 50:1) gave complex **188** (298.1 mg, 80% overall yield): IR (cm $^{-1}$) 2933, 2859, 2093, 2049, 2020, 1742; $^{1}$H-NMR: 5.93 (dd 10.7 Hz, 4.5 Hz 1H), 3.18 (d 16.4 Hz 1H), 2.77 (m 1H), 2.15 (m 1H), 2.08 (s 3H), 2.03 (m 2H), 1.66 (m 2H), 1.56 (m 1H), 1.47 (m 1H); $^{13}$C-NMR: 199.5, 170.4, 98.0, 97.6, 75.8, 35.6, 35.1, 29.2, 25.6, 20.7; Ms m/e 438 ($M^+$), 410 ($M^+$-CO), 382 ($M^+$-2CO), 354 ($M^+$-3CO), 326 ($M^+$-4CO), 298 ($M^+$-5CO), 270 ($M^+$-6CO); HRMS m/e for $C_{15}H_{12}Co_2O_8$ calculated ($M^+$) 437.9196, found 437.91907.

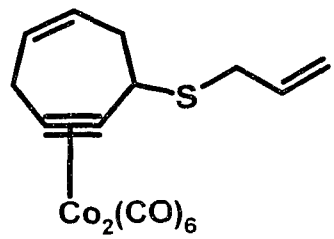
**Procedure E: Nicholas Reactions on Cycloheptyne Complexes**

**Hexacarbonyl [μ-η$^4$ – (6-allyloxycyclohept-1-en-4-yne)] dicobalt (189)**



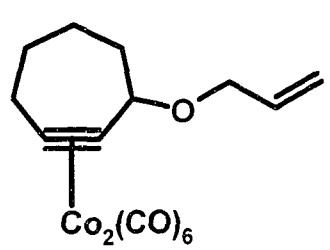

Complex **187** (59 mg, 0.13 mmol) and propargyl alcohol (87 μL, 10 equiv) were dissolved in dry dichloromethane (6.5 mL) at room temperature. $BF_3.OEt_2$ (92 mg, 5 equiv) in dry dichloromethane (2 mL) was added slowly over 0.5 h and the reaction was followed by TLC. Upon completion, conventional workup followed by flash chromatography afforded complex **222** ( 40.1 mg, 73%): IR ($cm^{-1}$) 2932, 2090, 2047, 2020 $cm^{-1}$; $^1$ H NMR 5.98 (m, 1H), 5.34 (dd, J = 17.1, 1.5, 1H), 5.21 (dd, J = 10.4, 1.5, 1H), 4.48 (dd, J = 10.4, 4.2, 1H), 4.35 (dd, J = 12.5, 5.1, 1H), 4.19 (dd, J = 12.5, 5.7, 1H), 3.19 (apparent dt, J = 16.7, 3.4, 1H), 2.76 (m, 1H), 2.19 (m, 1H), 2.05 (m, 1H), 1.97 (m, 1H), 1.48-1.65 (m, 2H), 1.39 (m, 1H); $^{13}$C NMR 203.9, 138.7, 121.0, 103.6, 102.5, 84.4, 74.2, 40.9, 39.4, 33.1, 29.7 ; MS m/e 380 ($M^+$-2CO); HRMS m/e for $C_{16}H_{14}Co_2O_7$ calculated. ($M^+$-2CO) 379.9500, found 379.9466.

**Hexacarbonyl [μ-η$^4$ – (6-Allylsulfanylcyclohept-1-en-4-yne)] dicobalt (190)**




Complex **187** (78.5 mg, 0.18 mmol), allyl mercaptan ( 150 µL, 10 equiv) and $BF_3.OEt_2$ (128 mg, 5 equiv) in dry dichloromethane (2 mL) were mixed via procedure D. A conventional workup followed by flash chromatography afforded complex **190** (61 mg, 75%): IR ($cm^{-1}$) 2924, 2091, 2052, 2021; $^1$H NMR 5.92 (m, 3H), 5.19 (d 17.5 Hz, 1H), 5.15 (d 10.1 1H), 4.04 (dd 10.4 Hz, 2.9 Hz 1H), 3.68 (s 2H), 3.33 (m 2H), 2.62 (m 1H), 2.36 (m 1H); $^{13}$C NMR 199.7, 134.5, 130.9, 129.8, 117.1, 102.1, 94.4, 46.9, 35.4, 34.7, 33.4 ; MS m/e 450 ($M^+$), 422 ($M^+$-CO), 394 ($M^+$-2CO), 366 ($M^+$-3CO), 338 ($M^+$-4CO), 310 ($M^+$-5CO); HRMS m/e for $C_{16}H_{12}Co_2O_6S$

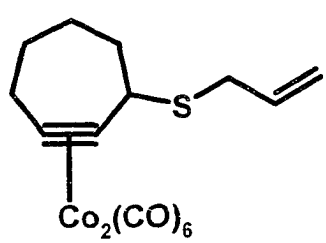
**Hexacarbonyl [µ-η$^4$ - 3-allyloxy-cyclohept-1-yne] (Co-Co) (191)**




Complex **188** (75 mg, 0.17 mmol) was condensed with allyl alcohol (115 µL, 10 equiv) via procedure D. A conventional workup followed by flash chromatography

afforded complex **191** (62 mg, 84%): IR (cm $^{-1}$) 2931, 2857, 2091, 2047, 2020, 1092; $^{1}$H NMR: 5.98 (m 1H), 5.34 (dd 15.0 Hz, 1.5 Hz, 1H), 5.21 (dd 10 Hz, 1.2 Hz 1H), 4.48 (dd 10.3 Hz, 4.3 Hz, 1H), 4.34 (dd 12.6 Hz, 5.3 Hz 1H), 4.19 (dd 12.6 Hz, 6.0 Hz 1H), 3.19 (dt 16.3 Hz, 3.3 Hz, 1H), 2.77 (ddd 16.3 Hz, 12.0 Hz, 4.3 Hz, 1H), 2.19 (ddd 13.2 Hz, 7.9 Hz, 4.3 Hz, 1H), 2.05 ( q 7.3 Hz, 1H), 1.96 (m 1H), 1.6 ( m 2H), 1.38 (m 1H); $^{13}$C-NMR: 203.9, 138.7, 121.0, 103.6, 102.5, 84.4, 74.2, 40.9, 39.4, 33.1, 29.7 ; MS m/e 436 ($M^+$), 406, 380 ($M^+$-2CO), 352 ($M^+$-3CO), 324 ($M^+$-4CO), 296 ($M^+$-5CO), 268 ($M^+$-6CO) MS m/e 380 ($M^+$-2CO); HRMS m/e for $C_{16}H_{14}Co_2O_7$ calculated. ($M^+$-2CO) 379.9500, found 379.9466.

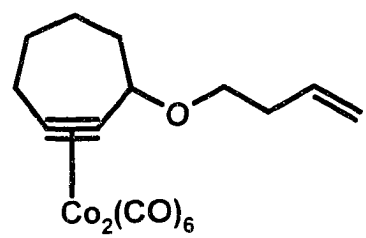
**Hexacarbonyl [μ-η$^4$ – (3-allylsulfanyl-cycloheptyne)] dicobalt (192)**




Complex **188** (111.4 mg, 0.25 mmol) and allyl mercaptan (210 μL, 10 equiv) were mixed via procedure D. A conventional workup followed by flash chromatography afforded complex **190** (94.9 mg, 84%): IR (cm $^{-1}$) 2927, 2089, 2049, 2020 cm$^{-1}$; H NMR 5.88 (m, 1H), 5.15 (d 17.7 Hz 1H), 5.12 (d 12.0 Hz 1H), 3.89 (dd 14.2Hz, 4.2 Hz 1H), 3.29 (d 7.5 Hz 2H), 3.12 (dt, 16.3 Hz, 3.6 Hz 1H), 2.82 (m 1H), 2.27 (m 1H), 2.11 (m 1H), 1.95 (m 1H),1.68 (m 1H), 1.59 (m 1H), 1.45 (m 1H); $^{13}$C-NMR: 200.0, 134.7, 116.9, 102.0, 99.9. 48.5, 38.0, 35.5, 35.0, 29.8, 28.8; MS m/e ,

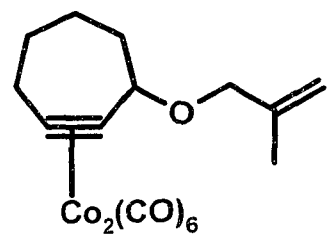
424 ($M^+$-CO), 396 ($M^+$-2CO); HRMS m/e for $C_{16}H_{14}Co_2O_6S$ calculated. ($M^+$-2CO) 395.9271, found 395.9295.

**Hexacarbonyl [$\mu$-$\eta^4$ – (3-but-3-enyloxycyclohept-1-yne)] dicobalt 193**



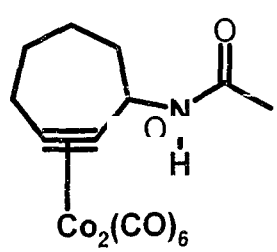

Complex **188** (115.9mg, 0.26 mmol) was condensed with homoallyl alcohol (224 µL, 10 equiv) via procedure D. A conventional workup followed by flash chromatography afforded complex **191** (109.1 mg, 92%): IR (cm $^{-1}$) 2930, 2856, 2091, 2050, 2020, 1099; $^1$ H-NMR: 5.86 (m 1H), 5.11 (dd 17.1 Hz 1H), 5.04 (d 10.1 Hz 1H), 4.42 (dd 10.2 Hz, 4.2 Hz 1H), 3.87 (m 1H), 3.64 (m 1H), 3,18 (d 16.3 Hz 1H), 2.77 (m 1H), 2.41 (m 2H), 2.17 (m 1H), 2.04 (m 1H), 1.95 (m 1H), 1.62 (m 2H), 1.40 (m 1H); $^1$ C-NMR: 200.2, 135.1, 116.4, 99.9, 98.3, 81.5, 69.0, 36.7, 35.4, 34.4, 29.2, 25.7; Ms m/e 394 ($M^+$-3CO), 366 ($M^+$-4CO), 310 ($M^+$-5CO), 282 ($M^+$-6CO), HRMS m/e for $C_{17}H_{16}Co_2O_7$ calculated ($M^+$) 449.9555 found 449.9572.

**Hexacarbonyl [μ-η$^4$ –{3-(2-methylallyloxy)cycloheptyne}] dicobalt 194**



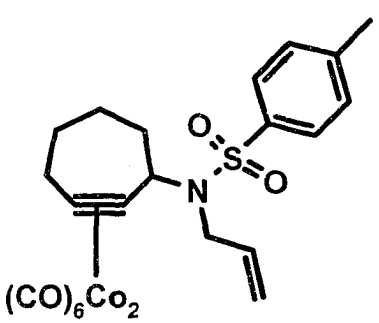

Complex **188** (140 mg, 0.32 mmol) was condensed with 2-methyl-2-propenol (275 μL, 10 equiv) via procedure D. A conventional workup followed by flash chromatography afforded complex **194** (121.2 mg, 84%): IR (cm $^{-1}$) 2931, 2090, 2052, 2021; $^1$H-NMR 5.03 (s, 1H), 4.93 (s, 1H), 4.46 (dd, 10.5 Hz, 4.5 Hz 1H), 4.21 (1/2 ABq, 12.5 Hz, 1H), 4.13 (1/2 ABq, 12.5 Hz, 1H), 3.19 (dt, 16.5 Hz, 3.4 Hz 1H), 2.76 (m 1H), 2.20 (m 1H), 2.05 (m 1H), 1.97 (m 1H), 1.80 (s 3H), 1.49-1.65 (m 2H), 1.38 (m 1H); $^{13}$C-NMR 200.2, 142.3, 112.2, 99.7, 98.4, 80.1, 73.0, 36.7, 35.4, 29.2, 25.7, 19.5; MS m/e 394 ($M^+$-2CO); HRMS m/e for $C_{17}H_{16}Co_2O_7$ calculated. ($M^+$) 449.9555, found 449.9515.

**Hexacarbonyl [μ-η$^4$ –(N-cyclohept-2-ynylacetamide)] dicobalt (195)**



Complex **188** (303.5 mg, 0.69 mmol) was dissolved in acetonitrile (35 mL) at room temperature in an open flask. Concentrated sulfuric acid (3 drops) was added to the solution and the mixture was left to stir for 5 minutes. After conventional workup followed by flash chromatography afforded complex, **195** (273.7 mg, 91%) was obtained: IR (cm $^{-1}$) 3326, 2929, 2856, 2087, 2016, 1649; $^{1}$H-NMR 5.51 (d 6.6 Hz 1H), 5.11 (m 1H), 3.17 (d 16.1 Hz 1H), 2.77 (m 1H), 2.33 (m 1H), 2.09 (m 2H), 2.02 (s 3H), 1.48 (m 3H); $^{13}$C-NMR: 199.1, 169.3, 101.5, 98.8, 53.5, 37.2, 35.1, 29.5, 27.4, 23.0; MS m/e 381 ($M^+$-2CO), 353 ($M^+$-3CO), 325 ($M^+$-4CO), 297 ($M^+$-5CO), 269 ($M^+$-6CO); HRMS m/e for $C_{12}H_{13}Co_2NO_4$ calculated. ($M^+$-3CO) 352.9509 found 352.9536.

**Hexacarbonyl[μ-η$^4$-(N-allyl-N-cyclohept-2-ynyl- methylbenzenesulfonamide] dicobalt (199)**

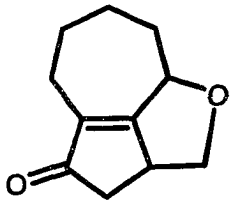



A solution of $HBF_4$ (174 μL, 2 equiv) in dry diethyl ether (2 mL) was slowly added to a stirred solution of complex **186** (117.9 mg, 0.27 mmol) and dimethyl

sulfide (20 μL, 5 equiv) in dry diethyl ether (5 mL) at room temperature. The solution was left to stir until the precipitation of the red sulfonium complex **197** was complete (1h) or the TLC of the solution showed that the absence of the starting material. After completion of the reaction, the supernatant ether solution was discarded through a syringe and the red solids were washed with dry ether (5X10 mL). The red solids were dried under high vaccum for 1h and then dissolved in dry dichloromethane (13.5 mL) and stirred at room temperature. Allylamine (21 μL, 1equiv) and diisopropylethyl amine (99 μL, 2 equiv) in dry dichloromethane (5 mL) was slowly added to the sulfonium solution. The reaction was followed by TLC and after the completion of the reaction and conventional workup, *p*-toluenesulfonic anhydride (441 mg, 5 equiv) in dry $CH_2Cl_2$ (5 mL) was added to the crude material. The sulfonamide formation reaction was followed by TLC. Upon completion of the reaction, a conventional workup and flash chromatography (20:1 petroleum ether : diethyl ether) gave complex **199** (98 mg, 62% yield): IR ($cm^{-1}$) 3082, 2928, 2093, 2051, 2025 $cm^{-1}$; 1H NMR δ 7.72 (d, J = 8.3, 2H), 7.28 (d, J = 8.3, 2H), 5.76 (m, 1H), 5.20 (dd, J = 17.2, 1.3, 1H), 5.07 (dd, J = 10.2, 1.3, 1H), 4.96 (dd, J = 11.7, 3.2, 1H), 4.14-4.26 (m, 2H), 3.23 (br d, J = 13.5, 1H), 2.73 (m, 1H), 2.43 (s, 3H), 2.11 (m, 1H), 1.92-2.04 (m, 2H), 1.73 (m, 1H), 1.35-1.60 (m, 2H); $^{13}C$-NMR: 200.0, 143.1, 138.6, 135.9, 129.6, 127.3, 117.3, 102.2, 96.9, 63.5, 46.2, 37.0, 35.6, 29.0, 21.5; MS m/e , 533 ($M-2CO^+$), 505 ($M-3CO^+$), 421 ($M-6CO^+$) ; HRMS m/e for $C_{23}H_{21}Co_2NO_8S$ calculated ($M-3CO^+$) 504.9804, found 504.9828.

**Procedure F: Typical Sugihara Conditions for the PKR**

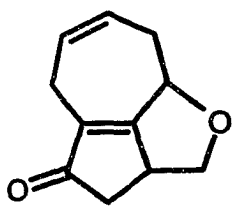
**2a,5,6,7,8,8a-Hexahydro-2H,3H-1-oxa-cyclohepta[cd]azulen-4-one (200)**



A solution of **191** (41.5 mg, 0.10 mmol) and cyclohexylamine (40 µL, 3.5 equiv) in 1,2-dichloroethane (5 mL ) was heated to reflux for 20 minutes. The solution was cooled to room temperature, diethyl ether (20 mL) was added, and the crude mixture was filtered through a pad of silica gel. Preparative TLC (4:1 petroleum ether:diethyl ether) of the crude material afforded **200** (10.6 mg, 63% yield 84:16 *cis*:*trans*): IR (cm $^{-1}$) 2927, 1714, 1680; $^{1}$H-NMR 4.74 (dd, 10.9 Hz, 5.7 Hz 1H), 4.27 (apparent t, 7.7 Hz, 1H), 3.36 (dd, 11.3 Hz, 7.7 Hz 1H), 3.27 (m 1H), 2.64 (dd, 17.7 Hz, 6.3 Hz 1H), 2.58 (m 1H), 2.21 (m 1H), 2.14 (dd 17.6 Hz, 3.1 Hz 1H), 2.09 (m 1H), 1.99 (m 1H), 1.93 (m 1H), 1.56 (m 1H), 1.30-1.49 (m 2H); resonances for the minor diastereomer were observed at 4.35 (obscured m 1H), 4.32 (apparent t 7.8 Hz 1H), 3.35 (dd 11.4 Hz, 8.3 Hz 1H), 2.26 (dd 16.6 Hz, 4.7 Hz 1H), 2.55 (obscured m 1H); $^{13}$C NMR 208.4, 186.0, 137.7, 79.6, 71.9, 44.8, 41.0, 34.0, 27.6, 26.5, 23.5; resonances for the minor diastereomer were observed at 206.8, 182.2, 135.4, 77.1,

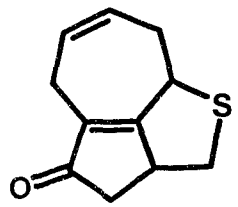
71.4, 43.6, 39.0, 29.5, 27.5, 24.6, 23.4 MS m/e 178 ($M^+$), 150 ($M^+$-CO) ; HRMS m/e for $C_{11}H_{14}O_2$ calculated. ($M^+$-CO) 150.1045, found 150.1038.

**2a,5,8,8a-Tetrahydro-2H,3H-1-oxa-cyclohepta[cd]azulen-4-one (202)**



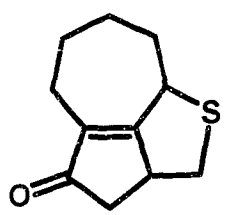
A solution of **189** (85mg, 0.20 mmol) and cyclohexylamine (80 µL, 3.5 equiv) in 1,2-dichloroethane (10 mL) was reacted according to procedure F. Preparative TLC (4:1 petroleum ether:diethyl ether) of the crude material afforded **202** (: IR (cm $^{-1}$) 3079, 2957, 1737, 1715 $cm^{-1}$; $^1$H NMR 5.84 (m, 1H), 5.80 (m, 1H), 4.69 (br d, J = 10.9, 1H), 4.28 (apparent t, J = 7.1, 1H), 3.31 (m, 1H), 3.29 (d, J = 7.1, 1H), 2.95-3.08 (m, 2H), 2.63-2.71 (m, 2H), 2.23 (m, 1H), 2.16 (dd, J = 18.5, 2.7, 1H); resonances for the minor diastereomer were observed at 4.72 (apparent t, J = 6.0, 1H), 4.38 (apparent t, J = 7.4, 1H), 3.46 (dd, J = 10.9, 8.7, 1H), 2.11 (J = 18.0, 2.7, 1H); $^{13}$C NMR 208.1 179.9, 128.7, 125.3, 72.9, 70.5, 43.2, 38.8, 33.3, 29.7, 25.1; MS m/e 176 ($M^+$); HRMS m/e for $C_{11}H_{12}O_2$ calculated. ($M^+$) 176.0837, found 176.0842.

**2a,5,8,8a-Tetrahydro-2H,3H-1-thia-cyclohept[cd]azulen-4-one (203)**



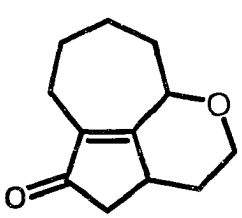

A solution of **190** (47 mg, 0.10 mmol) and cyclohexylamine (40 µL, 3.5 equiv) in 1,2-dichloroethane (5 mL) was reacted according to procedure F. Preparative TLC (4:1 petroleum ether:diethyl ether) of the crude material afforded **203** (11 mg, 57% yield, 79:21 *cis:trans*): IR ($cm^{-1}$) 3012, 2922, 1709, 1678; $^{1}$H-NMR 5.59, (ddd 12.4 Hz, 7.2 Hz, 2.1 Hz 1H), 5.61 (m 1H), 4.48 (br d, 12.0 Hz 1H), 3.37 (m 1H), 3.13 (dd 10.9 Hz, 6.7 Hz 1H), 3.07 (m 1H), 2.95 (m 1H), 2.73 (1/2 ABq, 6.3 Hz 1H), 2.70 (1/2 ABq, 6.3 Hz 1H), 2.57 (m 1H), 2.43 (m 1H), 2.22 (dd, 17.1 Hz, 4.1 Hz 1H); resonances for the minor diastereomer were observed at 4.20 (br d 4.2 Hz, 1H), 2.66 (d 6.5 Hz 1H), 2.18 (obscured dd 1H); $^{13}$C-NMR 207.0, 183.4, 135.2, 126.6, 126.1, 47.9, 44.9, 42.6, 37.1, 32.3, 23.8; resonances for the minor diastereomer were observed at 129.2, 47.0, 43.2, 40.3 ; MS m/e 192 ($M^{+}$); HRMS m/e for $C_{11}H_{12}O$. S calculated. ($M^{+}$) 192.0603, found 192.0580.

**2a,5,6,7,8,8a-Hexahydro-2H,3H-1-thia-cyclohept[cd]azulen-4-one (204)**



A solution of **192** (73.0 mg, 0.16mmol) and cyclohexylamine (64 µL, 3.5 equiv) in 1,2-dichloroethane (8 mL) was reacted according to procedure F. Preparative TLC (4:1 petroleum ether:diethyl ether) of the crude material afforded **204** (20.2 mg, 65% yield, 67:33 *cis*:*trans*): IR (cm $^{-1}$) 2928, 1703, 1665 cm$^{-1}$; $^{1}$ H-NMR 4.14 (br d 11.6 Hz 1H), 3.31 (m 1H), 3.04 (dd 10.6 Hz, 6.7 Hz 1H), 2.69 (dd 17.0 Hz, 6.0 Hz 1H), 2.65 (m 1H), 2.60 (apparent t 11.3 Hz 1H), 2.18 (dd 16.8 Hz, 4.3 Hz 1H), 2.04 (m 1H), 1.85-1.97 (m 2H), 1.53 (m 2H), 1.47 (m 1H), 1.14 (m 1H); resonances for the minor diastereomer were observed at 4.19 (br d 11.3 Hz 1H), 2.65 (dd 18.5 Hz, 6.2 Hz 1H), 2.58 (m 1H), 2.23 (m 1H), 1.41 (m 1H); $^{13}$C-NMR 207.4, 184.9, 139.0, 48.5, 42.6, 36.1, 31.2, 30.9, 27.0, 23.0; resonances for the minor diastereomer were observed at 208.1, 181.0, 139.5, 48.2, 46.8, 41.2, 37.4, 35.3, 28.5, 23.5 MS m/e 194 ($M^+$); HRMS m/e for $C_{11}H_{14}OS$ calculated. ($M+Na^+$) 217.0658, found 217.0650.

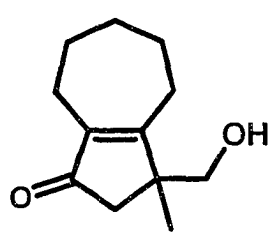
**2a,3,4,5a,6,7,8,9-Octahydro-2H-5-oxa-benzo[cd]azulen-1-one (205)**




A solution of **193** (74 mg, 0.16mmol) and cyclohexylamine (64 µL, 3.5 equiv) in 1,2-dichloroethane (8 mL) was refluxed as procedure F. Preparative TLC (4:1 petroleum ether:diethyl ether) of the crude material afforded **205** (22.8 mg, 73% yield, 60:40 *cis*:*trans*): IR (cm $^{-1}$) 2928, 1702, 1648 cm$^{-1}$; $^{1}$ H-NMR 4.23 (dd 9.9 Hz,

4.2 Hz 1H), 4.06 (m 1H), 3.66 (apparent dt 2.1 Hz, 11.9 Hz 1H), 2.77 (m 1H), 2.62 (dd 18.7 Hz, 6.3 Hz 1H), 2.26-2.28 (2H), 1.97-2.15 (m 3H), 1.81-1.91 (m 2H), 1.28-1.75 (m 4H); resonances for the minor diastereomer were observed at 4.26 (br d obscured 1H), 4.09 (m 1H), 3.74 (ddd 11.4 Hz, 9.3 Hz, 4.6 Hz 1H), 3.01 (m 1H), 2.70 (m 1H), 2.67 (dd 18.2 Hz, 6.3 Hz 1H), 2.70 (m 1H), 1.41 (m 1H), 1.14 (m 1H); $^{13}$C-NMR 207.5, 170.4, 139.2, 78.6, 66.8, 41.0, 37.8, 34.0, 32.2, 25.9, 22.3, 21.3; resonances for the minor diastereomer were observed at 206.5, 179.3, 137.5, 63.6, 41.1, 32.3, 31.9, 28.2, 27.5, 26.6; MS m/e 192 ($M^+$); HRMS m/e for $C_{12}H_{16}O_2$ calculated. ($M+Na^+$) 215.1048, found 215.1050.

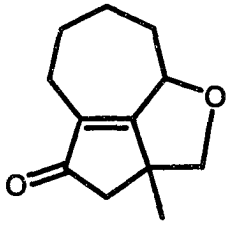
**3-Hydroxymethyl-3-methyl-3,4,5,6,7,8-hexahydro-2H-azulen-1-one (206)**




A solution of **194** (91.6 mg, 0.20 mmol) and cyclohexylamine (80 µL, 3.5 equiv) in 1,2-dichloroethane (10 mL) was reacted according to procedure F. Preparative TLC (4:1 petroleum ether:diethyl ether) of the crude material afforded **206** (5.4 mg, 14% yield): IR (cm $^{-1}$) 2924, 1683, 1636 cm$^{-1}$; $^1$ H NMR 3.60 (1/2 ABq 10.9 Hz 1H), 3.53 (1/2 ABq10.9 Hz 1H), 2.56 (d 18.1 Hz 1H), 2.42 (m 1H), 2.33 (m 1H), 2.14 (d 18.1 Hz 1H), 1.78-1.87 (m 2H), 1.49-1.72 (m 4H), 1.48-1.57 (m 2H), 1.15 (s, 3H); $^{13}$C NMR 206.8, 179.2, 143.9, 67.3, 46.6, 45.5, 31.7, 28.0, 26.4, 23.1,

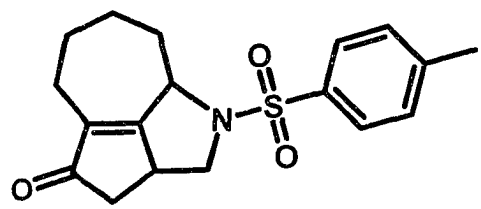
21.1 ; MS m/e 194 ($M^+$); HRMS m/e for $C_{12}H_{18}O_2$ calculated. ($M^+$) 194.1301, found 194.1295.

**2a-Methyl-2a,5,6,7,8,8a-hexahydro-2H,3H-1-oxa-cyclohepta[cd]azulen-4-one (207)**



A solution of **194** (89.3 mg, 0.20 mmol) in dichloromethane (10 mL) was stirred at 0 $^0$C. TMANO (132 mg, 10 equiv) was added portionwise over an hour and the solution was then allowed to warm to room temperature for 1 hour. The crude mixture was filtered through a pad of silica gel and concentrated under reduced pressure. Preparative TLC (4:1 petroleum ether:diethyl ether) of the crude material afforded **207** (22.5 mg, 59% yield) 65% based on the recovered starting material **194** (7.2 mg): IR (cm $^{-1}$) 2928, 1713, 1677; $^1$H NMR 4.79 (ddd, 10.9 Hz, 5.7 Hz, 1.6 Hz 1H), 3.93 (d 8.0 Hz 1H), 3.54 (d 8.0 Hz 1H), 2.55 (apparent dt 16.1 Hz, 4.2 Hz 1H), 2.39 (1/2 ABq 17.1 Hz 1H), 2.35 (1/2 ABq 17.1 Hz 1H), 2.21 (m 1H), 2.05 (m 1H), 1.98 (m 1H), 1.90 (m 1H), 1.55 (m 1H), 1.40 (m 1H), 1.33 (m, 1H),1.31 (s 3H); $^{13}$C-NMR 208.1, 185.7, 136.2, 76.1, 48.6, 47.4, 33.8, 27.5, 24.9, 24.5, 23.4; MS m/e 192 ($M^+$); HRMS m/e for $C_{12}H_{16}O_2$ calculated. ($M^+$) 192.1150, found 192.1143.

**1-(Toluene-4-sulfonyl)-1-2a,3,5,6,7,8,8a-octahydro-2H-azuleno[8,1-bc]pyrrol-4-one (208)**



A solution of **199** (45.4 mg, 0.08 mmol) and n-butyl methyl sulfide (35 µL, 3.5 equiv) in 1,2-dichloroethane (4 mL) was reacted according to procedure F. Preparative TLC (4:1 petroleum ether:diethyl ether) of the crude material afforded **208** (14 mg, 55% yield, 55:45 *cis*:*trans*): IR (cm $^{-1}$) 2923, 1714, 1680 cm$^{-1}$; $^{1}$ H-NMR 7.78 (d 8.2 Hz 2H) and 7.72 (d 8.2 Hz 2H), 7.34 (d 8.2 Hz 2H) and 7.38 (d 8.2 Hz 2H), 4.46 (ddd 10.9 Hz, 5.4 Hz, 1.5 1H), 4.00 (dd 12.0 Hz, 7.8 Hz 1H), 3.96 (apparent t 7.8 Hz 1H), 3.57 (br d 9.8 Hz 1H), 3.12 (m 1H), 2.94 (apparent t 11.5 Hz 1H), 2.73 (m 1H), 2.62 (dd 16.9 Hz, 6.0 Hz 1H), 2.50-2.54 (m 3H), 2.43 (s 3H) and 2.45 (s 3H), 2.39-2.50 (m 3H), 2.18 (m 1H), 1.96-2.10 (m 4H), 1.79-1.93 (m 2H), 1.43-1.64 (m 4H), 1.24-1.39 (m 2H), 1.13 (m 1H); $^{13}$C-NMR 207.2, 205.4, 180.9, 178.5, 144.3, 143.8, 139.2, 137.7, 136.0, 130.0, 129.9, 128.0, 127.1, 131.7, 62.6, 61.4, 54.2, 52.7, 41.6, 40.9, 40.4, 39.3, 35.7, 30.9, 30.3, 28.1, 27.1, 27.0, 25.9, 23.5, 22.8, 21.6; MS m/e 331 ($M^+$); HRMS m/e for $C_{18}H_{21}NO_3S$ calculated. ($M^+$) 331.1242, found 331.1237.

## 4.0 Intramolecular 2+2+2 Reactions

### 4.1 2+2+2 Cycloaddition Reactions on Cycloheptyne-$Co_2(CO)_6$

A wide variety of natural products possessing 7,6 fused ring systems are found in nature, particularly in the terpene classes of compounds. Some examples of classes of compounds are shown in (Fig. 71). Alkyne dicobalt complexes are known to participate in 2+2+2 cycloaddition reactions in the presence of other alkynes to form six-membered ring systems (see 1.4). Therefore, having developed synthetic methods to prepare cycloheptyne-$Co_2(CO)_6$ complexes, a 2+2+2 ring fusion reaction would provide a valuable addition to the synthesis of these ring systems.

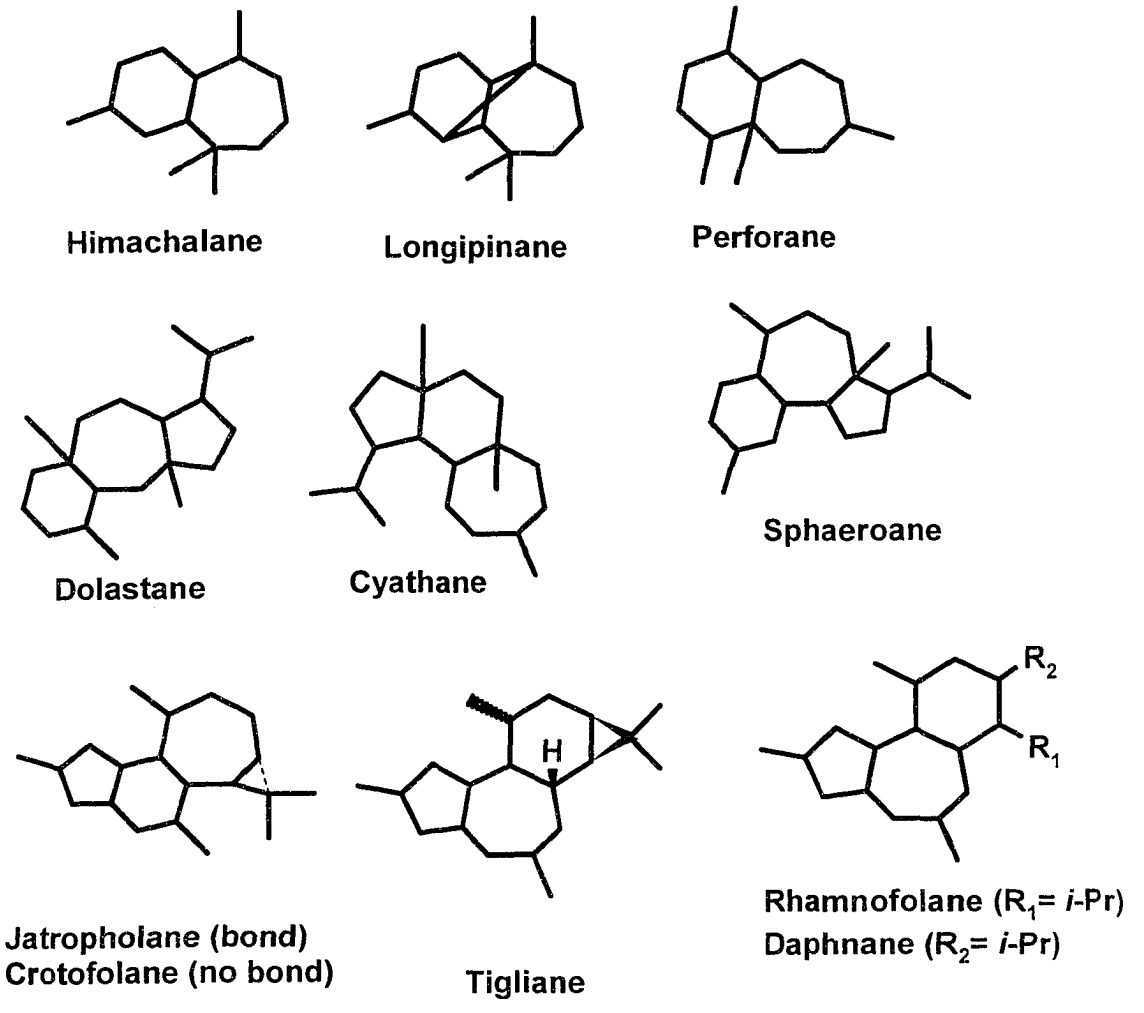



**Figure 71. Examples of Fused 7,6 ring Systems Found in Nature**

An approach analogous to that of the Pauson-Khand chemistry was adopted. Cycloheptyne complexes bearing a propargylic acetate were chosen to be substituted by Nicholas reactions with propargylic alcohols. The resulting ethers, now containing a tethered diyne bearing one $Co_2(CO)_6$ moiety, would be subjected to a reaction with a third alkyne in order to study the feasibility of the 2+2+2 process.

In addition to **187** and **188**, two other propargyl actetates were employed as starting points. Deprotonation of allyl propargyl ether with two equivalents of butyllithium, followed by addition of acrolein in diethyl ether and furnished **213** in 68% yield after conventional workup (Fig. 72). Acetylation and complexation of diols **213** provided diacetate complexes **214** in excellent yields (85% and 87%, respectively). Ring closing metathesis, followed by immediate hydrogenation of the crude material in the presence of Raney Nickel® catalyst provided a separable 1:1 mixture of *cis* and *trans* diastereoisomers of **215** in 82% overall yield. The stereochemical assignments were based on $^1$H-NMR coupling constants (10.4 Hz and 4.5 Hz) for the *cis* isomer and (7.1 Hz and 3.7 Hz) for the *trans* isomer of the propargylic protons in each complex.

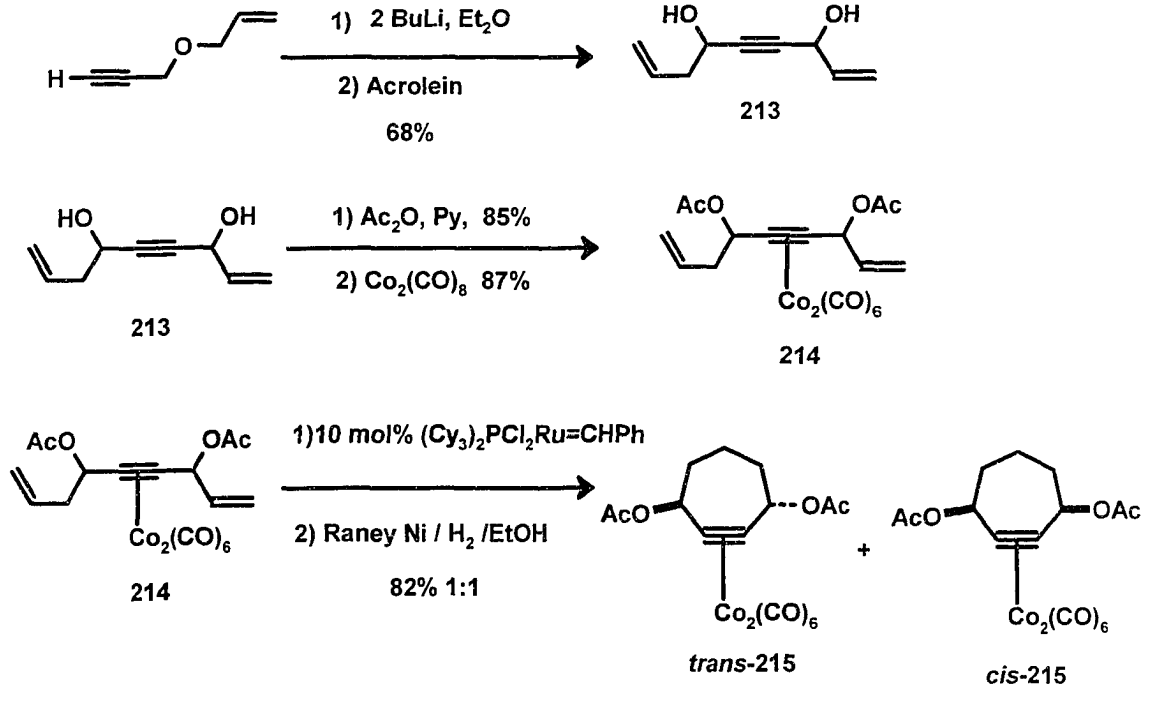



**Figure 72. Preparation of Diacetate Complexes 215**

Deprotonation of 1-hexyne with two equivalents of butyllithium, followed by sequential addition of one equivalent of allyl bromide and one equivalent of acrolein and hydrolysis of the mixture afforded alcohol **216** in 64% yield (Fig. 73). Standard acetylation (**217**, 80% yield) and complexation of acetate **217** gave complex **218** (89% yield). Ring closing metathesis of diene complexes **218** using Grubbs' first generation catalyst gave cycloheptenyne cis/trans complexes **219** in 80% yields (50:50 ratio) (Fig. 73). Reduction of this mixture with a large excess of diimide gave *cis/trans* complexes **220** (72%, 50:50 ratio). It seems that cycloheptenyne-$Co_2CO)_6$ complexes bearing homoallylic acetates are easily hydrogenated using Raney Nickel® catalysis, while cycloheptenyne–$Co_2$ $(CO)_6$ complexes bearing an allylic acetate but no homoallyl acetate, do not reduce with Raney Nickel. Allylic acetate complexes, however, are reduced by the diimide reduction method.

Although complexes **220** could be separated by chromatography, the *trans*-**220** has a very similar $R_f$ by TLC to the unreduced cycloheptenyne *cis*-**220**. Therefore only the cis-**220** was isolated and fully characterized and used in this study. It is also possible to enrich the *cis* isomer of **220** with respect to the *trans* isomer. When a 50:50 mixture of **220** and a large excess of acetic acid (>10 equiv) were dissolved in dry dichloromethane and treated with $BF_3$ etherate (3 equiv) for 4 hours, the diastereoisomeric ratio of the product obtained was 9:91 in favor of the *cis* isomer.

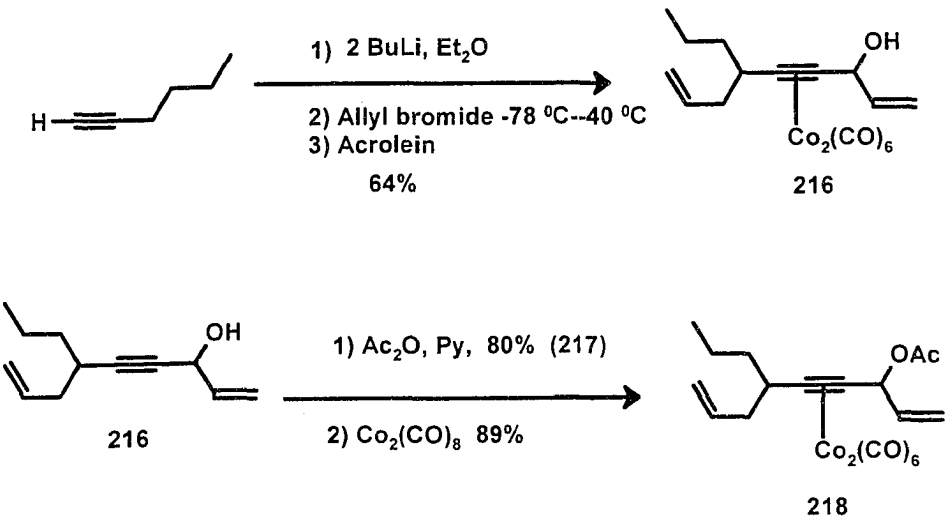



**Figure 73. Synthesis of Diene Complexes 218**

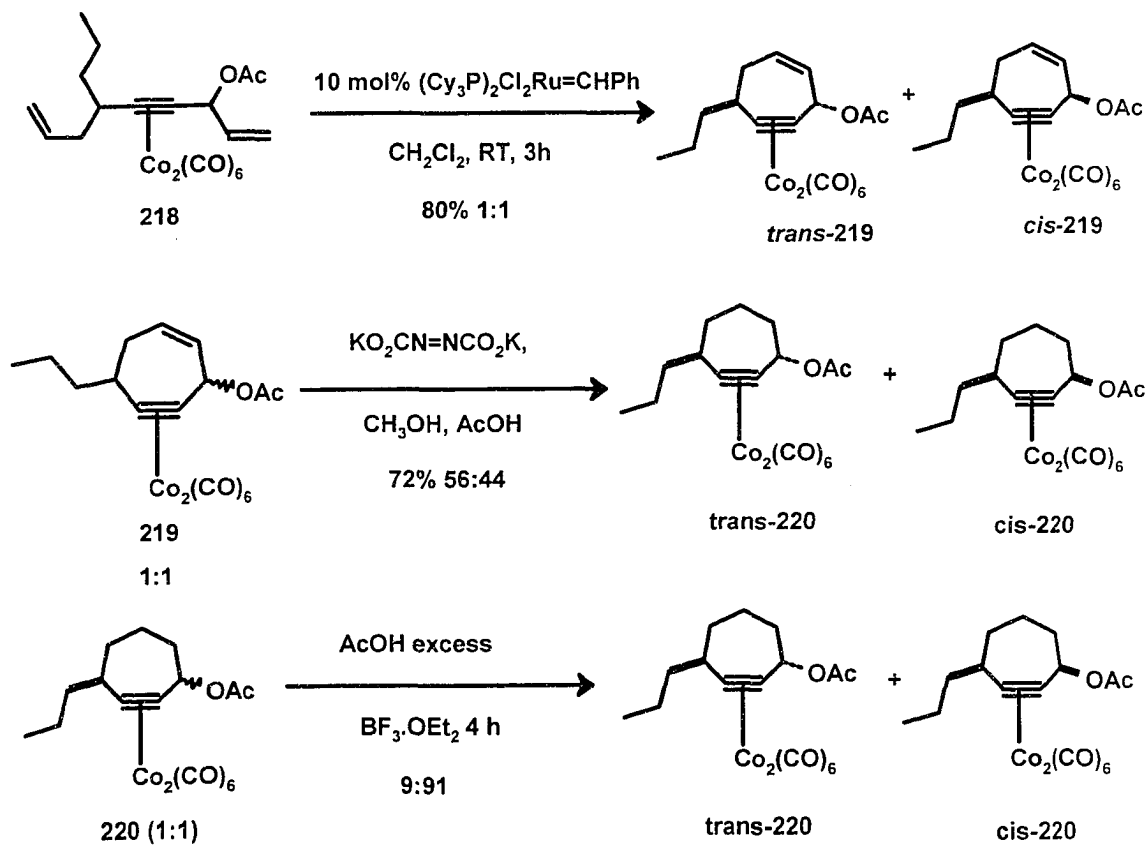



**Figure 74. Synthesis of Dicobalt Hexacarbonyl Complexes 220**

## 4.2 Nicholas Chemistry on Cycloheptenyne/Cycloheptyne Cobalt Complex

The reactions for formation of the tethered diynes complexes were straightforward Lewis acid mediated Nicholas reactions which were analogous to the formation of the tethered enyne complexes. A solution of $BF_3.OEt_2$ in dichloromethane was slowly added to a cooled mixture of the dicobalt complex and propargyl alcohol to give, after conventional workup, the Nicholas condensation products in high yields. Under these conditions, **187** and **188** gave compounds **221** and **222** in 73% and 85% yields respectively, Similarly, 2-butyn-1-ol afforded **223** (76% yield) from **188** (Fig. 75).

Diacetates *cis*-**215** and *trans*-**215** readily underwent substitution to give diastereomeric mixtures of **224** in 84% and 88% yields, respectively (Fig. 76). Disubstituted cycloheptyne complex *cis*-**220** also underwent analogous Nicholas reactions with propargyl alcohol to afford mixtures of **225** in 75% yield. Contrary, to the majority of Nicholas reactions[88] were complete racemization occurs at the propargylic site, products **224** and **225** reflect partial retention of configuration of the starting acetate complexes **215** and *cis*-**220**.

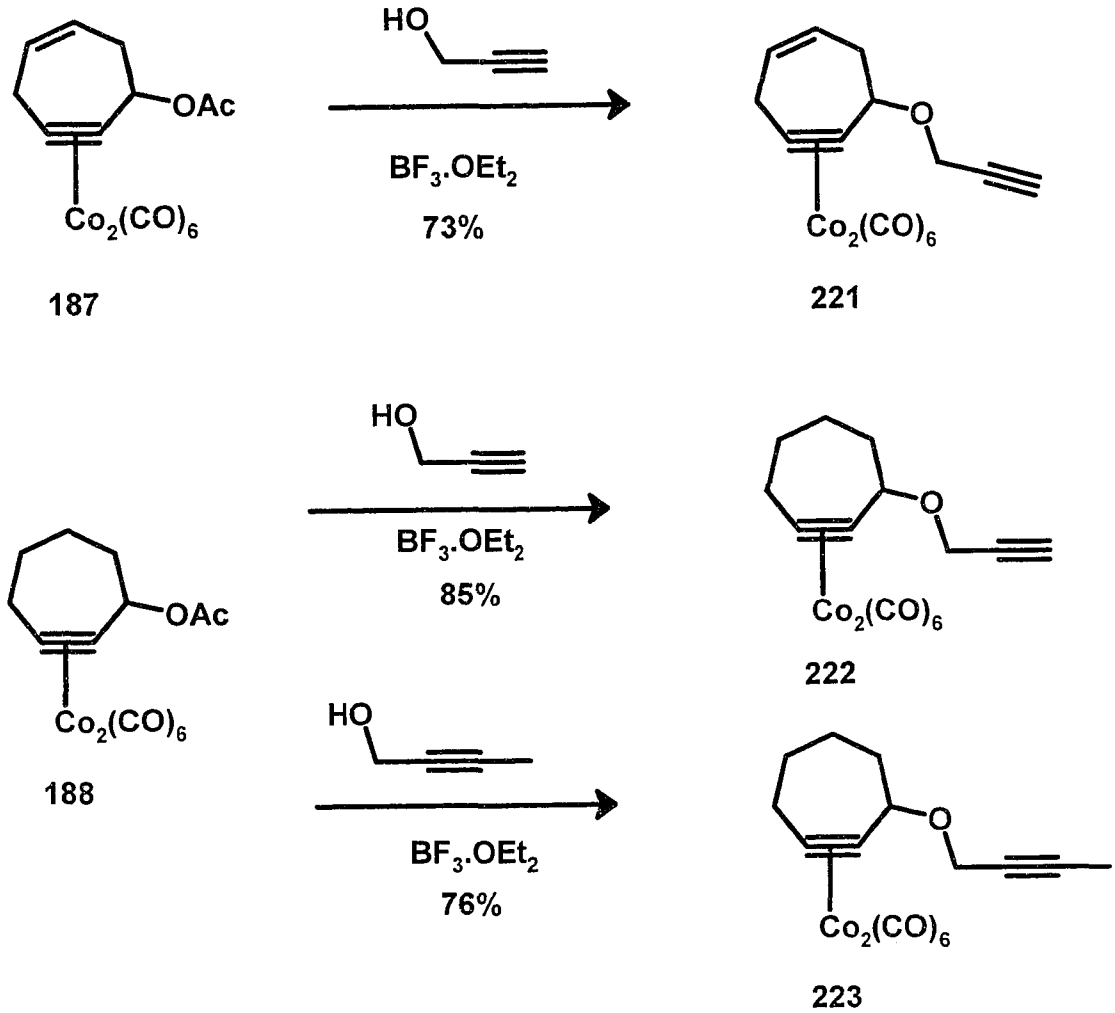



**Figure 75. Tethering of Alkynes on Cycloheptenyne and Cycloheptyne Dicobalt Complexes**

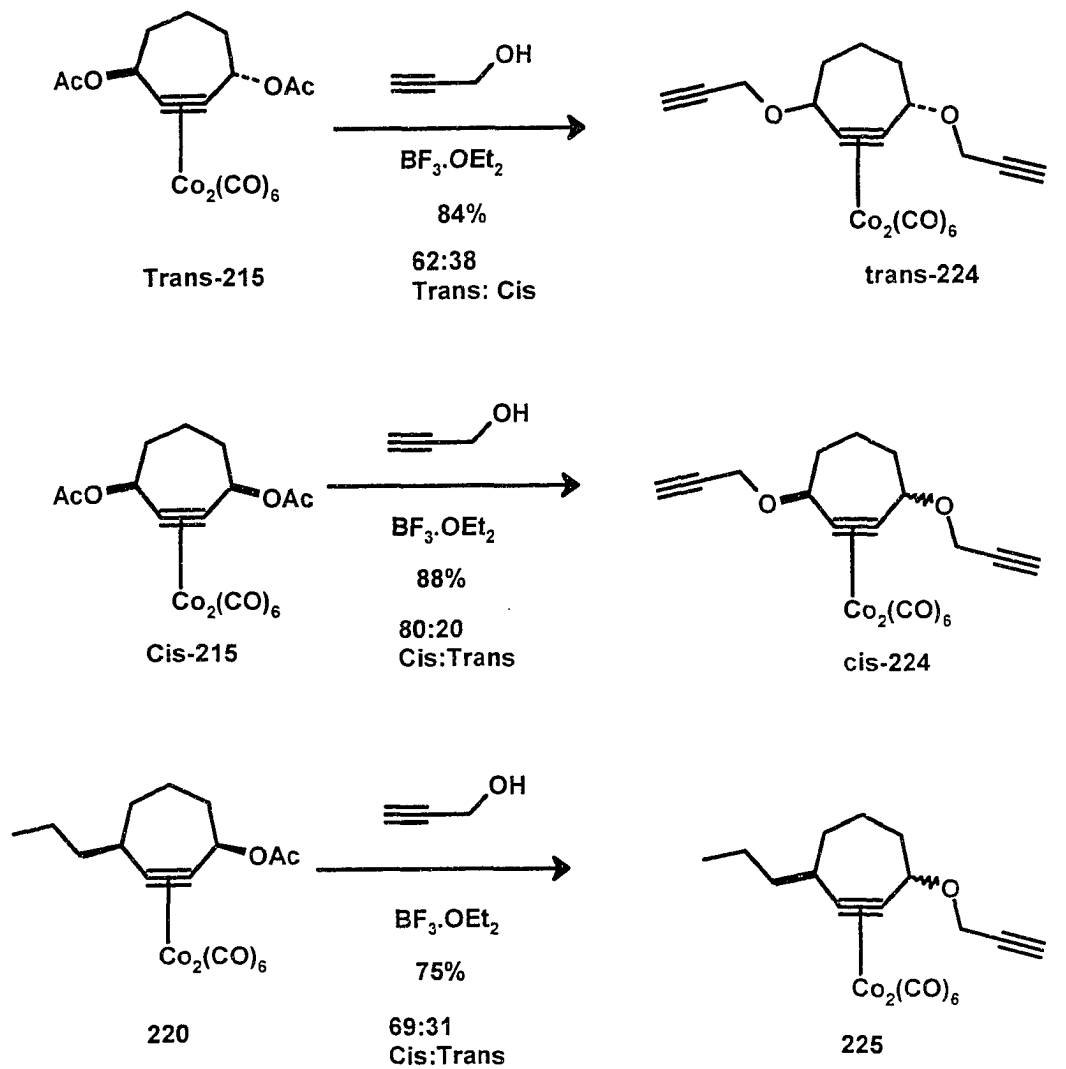


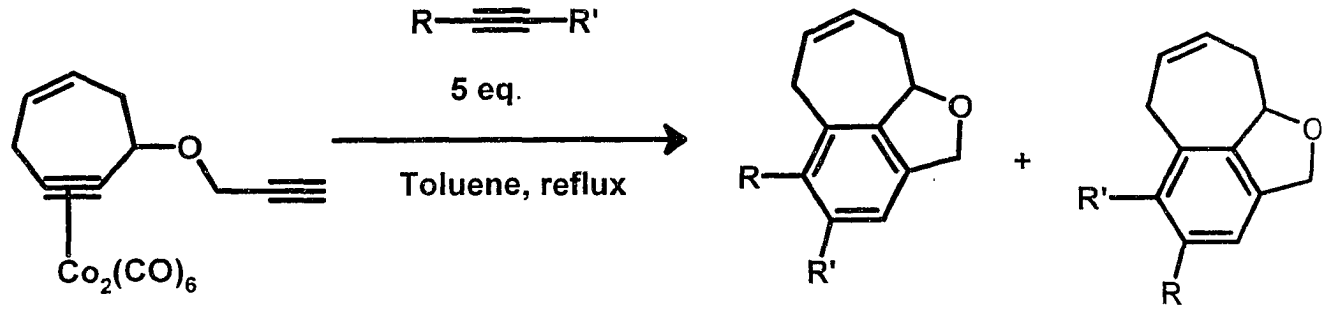

**Figure 76. Nicholas Reaction on Disubstituted Cycloheptenyne Complexes**

$^1$H-NMR spectroscopy of the Nicholas adducts confirmed the equatorial disposition of the tethered alkynes in most cases. The configurational assignments of **224** were made on the basis of the coupling constants of the methine hydrogens. For the *cis*-**224** $J_{ax\text{-}ax}$ of 9.8 Hz and $J_{ax\text{-}eq}$ of 4.6 Hz indicated axial methine hydrogens. By contrast, *trans*-**224** had J= 6.6 Hz and 3.8 Hz for the corresponding

methine hydrogens. The *cis* isomer of **225** ($J_{ax\text{-}ax}$ 10.6 Hz, $J_{ax\text{-}eq}$ 4.6 Hz), was assigned analogously.

### 4.3 2 2+2+2 Cycloadditions of Tethered Alkyne dicobalt complexes

With access to several tethered diyne-$Co_2(CO)_6$ complexes secured, our attention was turned to the 2+2+2 cycloaddition reactions. The diyne complexes were exposed to a series of alkynes (5 equiv) at reflux in toluene over three hours and the resulting crude material was filtered through a pad of silica gel to furnish tricyclic products. Bis(trimethylsilyl)acetylene performed well as the third alkyne partner by virtue of giving cleaner reaction mixtures, even when the ultimate product yields were not higher for substrates **221** and **222**, giving arenes **226** and **230** in 60% and 63% yields, respectively (Fig. 77 & 78). The 2+2+2 cycloaddition reactions of complex diyne **222** with symmetrical 2-butyne-1,4-diacetate gave 58% of arene **227**. While unsymmetrically substituted 1-octyne and ethyl 2-butynoate as the third alkyne partner for substrate **222** afforded regioisomeric mixtures of arenes **228a** and **228b** (50:50) and **229a/229b** (43:57) in 59% yield, there was little or no regioselectivity in the process. Arene **228a** and **228b** can be easily distinguished by the doublets for the aromatic protons in **228a** (J=7.5 Hz) versus the singlets for **228b**.The regiochemical assignment of the major arene product in **229a** was based on the lower chemical shift of the aromatic proton (7.46 ppm) for **229a**, due to its close proximity to the ester function, relative to isomer **229b** (6.94 ppm).




| | | |
|---|---|---|
| R=R' $SiMe_3$ | 60% | 226 |
| R=R' $CH_2OAc$ | 58% | 227 |
| R=n-$C_6H_{13}$, R'=H | 59% | 228a : 228b 50:50 |
| R= Me, R'= COOEt | 59% | 229a: 229b 57:43 |

**Figure 77. 2+2+2 Cycloaddition Reactions on Cycloheptenyne Complex 222**

When diyne complex **223** was refluxed with propargyl alcohol, arenes **231a** and **231b** (70% yield) were formed in a 75:25 regioisomeric mixture respectively. The regiochemical assignment of **231** was based on 2D $^1H$-$^1H$ NOESY experiments, which displayed an nOe coupling of the aromatic proton (Fig. 78) to both the methylene protons of the benzyl alcohol and the methyl protons in the major isomer. Conversely, nOe coupling of the methylene protons of the benzylic alcohol to the methyl protons was observed in the minor product, thus indicating that **231a** is the major product. However, when diyne *cis*-**225** was refluxed in the presence of 5 equivalents of propargyl alcohol in toluene, a more modest regioisomeric mixture (43:57) of benzocycloheptane *cis*-**232a** and *cis*-**232b** in 52% yield was obtained (Fig. 78).

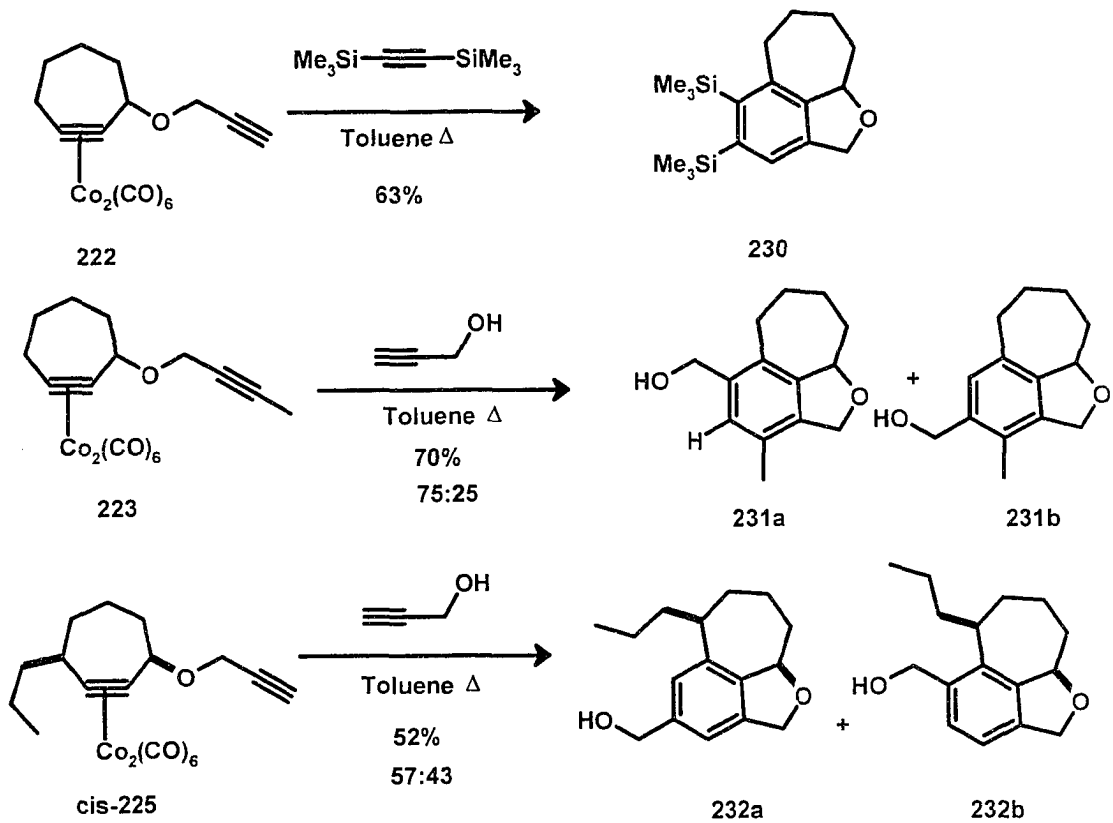



**Figure 78. Formation of Benzocycloheptanes**

The capability of an all intramolecular 2+2+2 variant was also investigated. As discussed previously, both diyne complexes *cis*-**224** and *trans*-**224** were available in diastereomerically pure form. When subjected to the standard refluxing toluene conditions, *trans*-**224** underwent 2+2+2 cycloaddition reaction to give *trans*-**233**, while *cis*-**224** gave *cis*-**233**, in 60% yield in both cases.

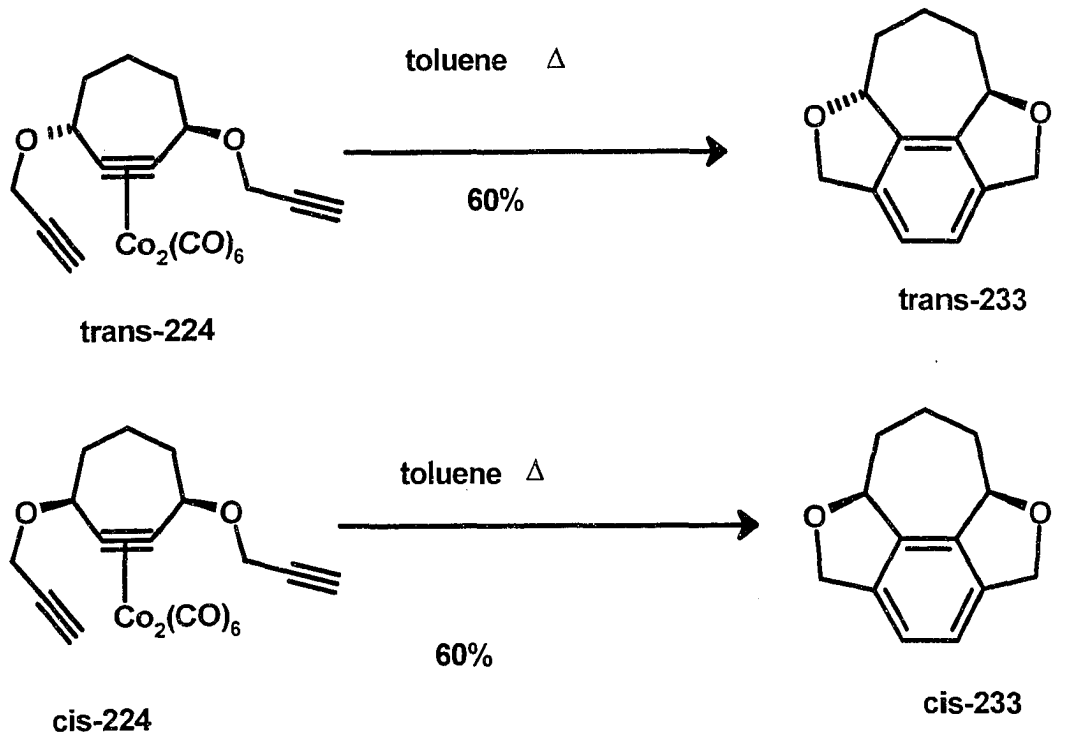



**Figure 79. All intramolecular and N-Linked Diyne 2+2+2 Cycloadditions**

Preliminary attempts were made to probe the possibility of alkene participation in the 2+2+2 cycloaddition reaction. When diyne complex **222** and 5 equivalents of cyclohexene in toluene were heated to reflux for 3 hours, only intractable mixtures resulted. When 5 equivalents bis(trimethylsilyl)acetylene and enyne complex **191** were refluxed in toluene, the presence of the PKR product **200** was observed from $^1$H-NMR spectrum of the crude mixtures. There was, however, no indication of 2+2+2 cycloaddition product.

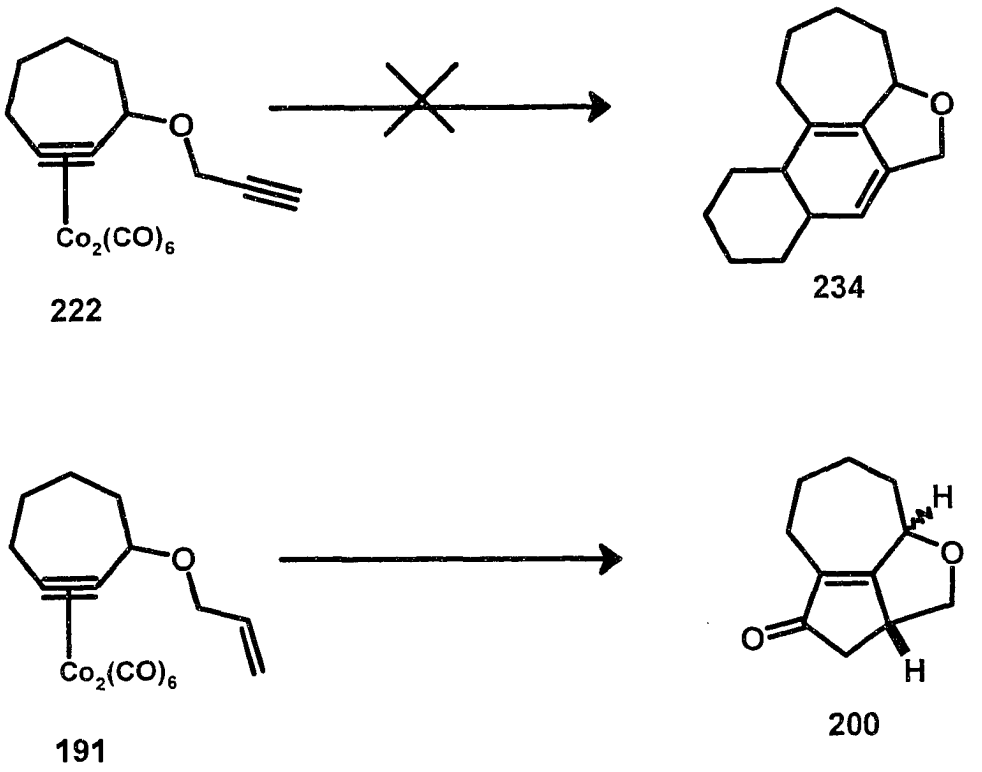



**Figure 80. Attempt on Alkene Participation in 2+2+2 Cycloaddition Reaction**

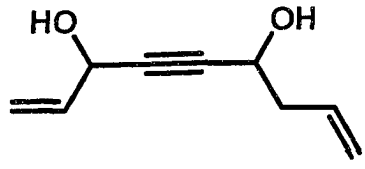
## 4.4 Summary

Cyloheptyne complexes **215** and **220** were prepared by ring closing metathesis, followed by reduction using Raney Nickel® or diimide. Theses complexes along with **187** & **188** react with propargylic alcohols to provide tethered diyne complexes **222**, **223**, and ***cis*-225** and tethered triyne complexes ***cis*-224**, ***trans*-224** in excellent yields. The latter complexes could be separated by chromatography.

These cycloheptyne-$Co_2(CO)_6$ complexes, in the presence of a third alkyne did undergo 2+2+2 cycloaddition reactions, giving fused 7,6,5 ring systems, with respectable yield. Complexes ***trans*-224** & ***cis*-224** did undergo all-intramolecular 2+2+2 cycloaddition reaction.

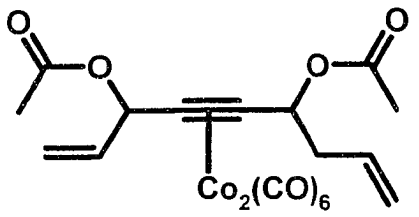
## 4.5 Experimental Section

**Nona-1,8-dien-4-yne-3,6-diol (213)**



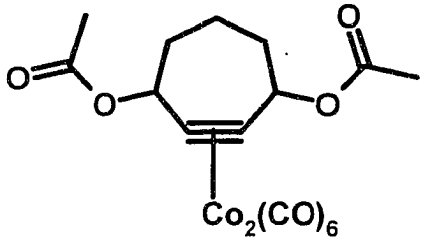

A stirred solution of allyl propargyl ether (3.00 g, 31.3 mmol) in dry diethyl ether (50 mL) was cooled to –78 $^{0}$C. Butyllithium (35 mL, 2.2 equiv.) was added dropwise and the solution was allowed to warm to room temperature and left to stir overnight. The reddish solution was cooled to –78 $^{0}$C, acrolein (2.3 mL, 1.0 equiv.) in dry diethyl ether (5 mL) was added dropwise to the solution and then allowed to warm to room temperature. Conventional workup and bulb to bulb distillation of the crude material afforded **213** (3.57 g, 75% yield): bp 110-120 $^{0}$C/ 0.75 torr; IR (cm $^{-1}$) 3332, 3082, 2982, 2859, 1034; $^{1}$H-NMR: 5.91 (m 2H), 5.45 (d 17.0 Hz, 1H), 5.22 (m 3H), 4.93 (m 1H), 4.48 (t 5.9 Hz, 1H), 3.05 (br 1H), 2.95 (br 1H), 2.48 (t 6.6 Hz, 2H); $^{13}$C-NMR: 136.6, 132.9, 118.9, 116.6, 86.6, 84.0, 62.9, 61.5, 41.9; MS m/e

**Hexacarbonyl [μ-η$^{4}$ –(3,6-diacetoxynona-1,8-dien-4-yne)] dicobalt (214)**



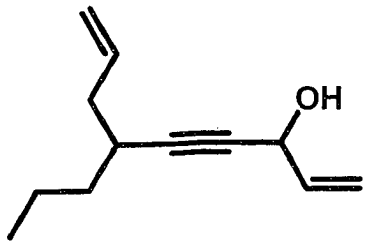

Compound **213** (411 mg, 2.70 mmol) was subjected to the standard acetylation and complexation via procedure D. Flash chromatography (20:1 petroleum ether:diethyl ether) gave a 50:50 mixture of diasteroisomers (1.21g, 86%): IR (cm $^{-1}$) 2935, 2096, 2029, 1745, 1227; $^{1}$H-NMR: 6.46 (d 6.5 Hz, 1H), 6.40 (6.5 Hz, 1H), 6.01 (m 2H), 5.95 (m 2H), 5.82 (m 2H), 5.43 (dd 18,3 Hz, 1.0 Hz 2H), 5.29 (dd 10.3 Hz, 0.8 Hz 2 H), 5.18 (m 4H), 2.60 (m 1H), 2.53 (m 3H), 2.12 (s 3H), 2.10 (s 3H), 2.08 (s 6H); $^{13}$C-NMR: 198.9, 170.1, 170.1, 169.6, 169.6, 135.3, 135.1, 133.0, 132.7, 118.8, 118.4, 117.7, 94.2, 93.4, 74.3, 74.0, 72.9, 72.7, 41.5, 41.4, 20.6, 20.6, 20.5, 20.5; MS m/e; HRMS m/e for $C_{17}H_{16}Co_2O_8$ ([$M^+$-2CO]) calculated 465.9509, found 465.9508

**Hexacarbonyl [μ-η$^4$ –(3,7-diacetoxycycloheptyne)] dicobalt (215)**



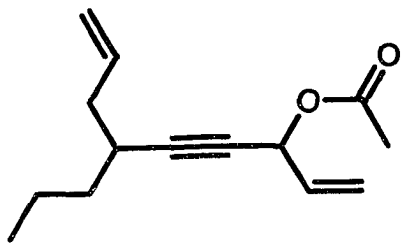
Compound **214** (*cis:trans* mixture, 183.7 mg, 0.35 mmol) was dissolved in dichloromethane (17.5 mL) at room temperature. $(Cy_3P)_2Cl_2Ru{=}CHPh$ (14.5 mg, 5 mol%) in dichloromethane (10mL) was added dropwise to the dichloromethane solution. After 3 hours, the solution was filtered through a pad of Celite® and the solution was concentrated under reduced pressure. The residue was dissolved in dry dichloromethane (17.5 mL) and additional $(Cy_3P)_2Cl_2Ru{=}CHPh$ (14.5 mg, 5 mol%) as solution in dichloromethane (10 mL) was added dropwise. The solution was then left to stir for another 3 hours. The solution was again filtered through a pad of Celite® and concentrated in *vacuo*. The reaction progress was monitored by TLC. The crude material was dissolved in ethanol 95% (200 mL) and the flask was purged with hydrogen gas. A thoroughly washed Raney nickel catalyst (100 mg) was added and the heterogeneous mixture was stirred for 4 hours. After completion of the reaction, the solution was filtered and the solvent was concentrated under reduced pressure. Flash chromatography (petroleum ether: diethyl ether 50:1) as cis:*trans* **215** (1:1) mixtures (142.4 mg, 82% overall yield). Careful repeated chromatography allowed separation of the isomers: (*cis* isomer) IR: ($cm^{-1}$) 2926, 2851, 2097, 2057, 2028, 1741; $^1$H-NMR: 5.98 (dd 10.4 Hz, 4.5 Hz 2H ), 2.14 (m 2H), 2.12 (s 6H), 2.11 (m 2H), 1.57 (m 2H); $^{13}$C-NMR: 198.0, 170.4, 94.5, 75.7, 34.6, 22.3, 20.7; MS m/e 468, 440, 412, 384, 356, 328; (*trans* isomer) IR: 2932, 2861, 2098, 2056, 2029, 1739, 1231; $^1$H NMR: 6.04 (dd 7.1 Hz, 3.7 Hz 2H), 2.11 (s 6H), 1.99 (m 2H), 1.94 (m 2H), 1.85 (m 2H); $^{13}$C-NMR: 199.0, 170.0, 93.9, 73.3, 34.2, 20.8, 19.4; MS m/e 468 ($M^+$-CO), 440 ($M^+$-2CO), 412($M^+$-3CO), 384 ($M^+$-4CO), 356 ($M^+$-5CO), 328 ($M^+$-6CO).

**6-Propylnona-1,8-dien-4-yn-3-ol (216)**



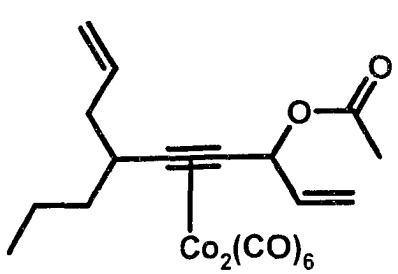

Butyllithium (10 mL, 2 equiv) was slowly added to a solution of 1-hexyne (1.027 g 12.5 mmol) in dry diethyl ether (36 mL) cooled to -78 $^{0}$C. The solution was then allowed to warm to room temperature and was left to stir overnight. The solution was then cooled to -78 $^{0}$C and allyl bromide (1.1 mL, 1 equiv) in dry diethyl ether (5 mL) was slowly added via syringe pump. After completion of addition the solution was kept below -40 $^{0}$C for 4 hrs, acrolein (0.9 mL, 1 equiv) in dry diethyl ether (5 mL) was added; the solution was then allowed to warm to room temperature. After conventional workup, the pale yellow residue was distilled by bulb to bulb distillation under vacuum to afford a clear oil (1.314 mg, 64%): b.p. 130-150 $^{0}$C; IR (cm $^{-1}$) 3312, 3078, 2959, 2933, 2873, 1642, 1022; $^{1}$H-NMR: 5.94 (m 1H), 5.85 (m 1H), 5.44 (d 17.0 Hz 1H), 5.18 (d 10.0 Hz 1H), 5.07 (d 17.6 Hz 1H), 5.04 (d 9.3 Hz, 1H), 4.87 (s 1H), 2.46 (m 1H), 2.22 ( t 6.9 Hz 2H), 2.11 (d 4.6 Hz 1H), 1.51 (m 1H), 1.42 (m 3H), 0.91 (t 7.1 Hz 3H); $^{13}$C-NMR: 137.6, 136.0, 116.5, 115.9, 89.8, 80.4, 63.2, 39.2, 36.4, 31.3, 20.4, 13.8.

**2-Acetoxynona-1,8-dien-6-propyl-4-yn (216a)**



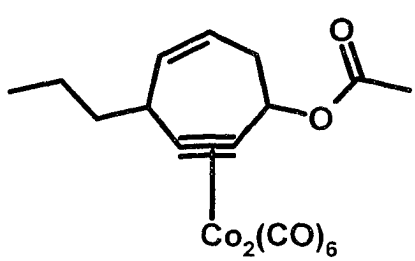
Compound **216** (1.06 g, 6.4 mmol) was subjected to the standard acetylation condition and flash chromatography (50:1 petroleum ether:diethyl ether) gave (1.13 g, 80%): IR (cm $^{-1}$) 3079, 2959, 2933, 2874, 1747, 1643, 1229; $^{1}$H-NMR: 5.89 (m 3H), 5.55 (d 15.5 Hz 1H), 5.29 (d 9.6 Hz 1H), 5.08 (d 16.2 Hz 1H), 5.06 (d 9.4 Hz, 1H), 2.48 9 (m 1H), 2.35 (t 6.9 Hz, 2H), 2.10 (s 3H), 1.52 ( m 1H), 1.43 (m 3H), 0.92 (t 7.1 Hz, 3H); $^{13}$C-NMR: 169.7, 135.8, 135.6, 118.5, 116.6, 90.8 (two), 64.8, 39.1, 36.3, 31.4, 21.1, 20.4, 13.9; MS m/e 220 ($M^+$) HRMS m/e for $C_{11}H_{15}O_2$ calculated ($M^+$-$CH_2CHCH_2$) 178.1072, found 179.1110.

**Hexacarbonyl [μ-η$^4$ -(3-acetoxy-6-propyl-1,8- nonadien- -4-yn )] dicobalt (217)**



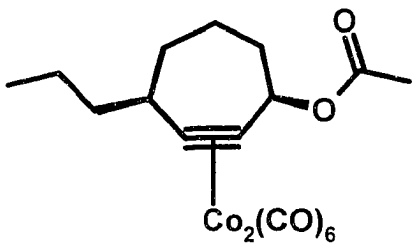
Compound **216a** (308.3 mg. 1.4 mmol) was complexed via procedure A. Flash chromatography using 50:1 petroleum ether:diethyl ether gave (630 mg, 89%): IR (cm $^{-1}$) 3082, 2963, 2935, 2878, 2091, 2022, 1747, 1641, 1226; $^{1}$H-NMR: 6.53 (t 5.6 Hz 1H), 5.88 (m 2H), 5.43 (dd 17.2 Hz, 3.4 Hz 1H), 5.28 (d 10.4 Hz 1H), 5.15 (m 2H), 2.77 (m 1H), 2.31 (m 2H), 2.14 (s 3H), 1.50 (m 4 H),0.95 (7.2 Hz 3H); $^{13}$C-NMR: 199.6, 169.8, 136.5, 136.4, 135.2, 135.1, 117.4, 117.3, 117.0, 104.3, 95.9, 74.9, 74.7, 41.6, 41.5, 41.4, 41.4, 39.3, 39.0, 21.2, 20.7, 20.6, 14.0; MS m/e 422 ($M^{+}$-3CO), HRMS m/e for $C_{17}H_{20}Co_2O_5$ calculated ($M^{+}$-3CO) 421.9975, found 421.9970.

**Hexacarbonyl [μ-η$^4$–(6-acetoxy-3-propyl-cyclohept-1-en-3-yne] dicobalt (218)**



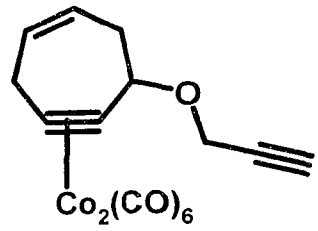

Complexes **218a** and **218b** were prepared in 80% yield according to Green's method.[78]

**Hexacarbonyl [μ-η$^4$ –(3-acetoxy-7-propylcycloheptyne] dicobalt (*cis*-220)**



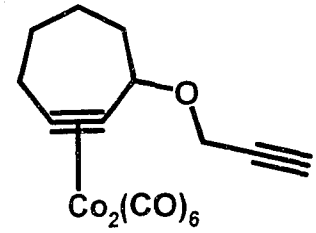

Complexes **218** (94 mg, 0.20 mmol) and freshly made dipotassium azodicarboxylate (136 mg, 3.5 equiv) were dissolved in methanol (20 mL) at room temperature. Excess amount of acetic acid dissolved in methanol was added portion-wise to the dicobalt hexacarbonyl complex solution. The reaction was monitored by TLC and upon completion of the reaction, the solvent was evaporated and a conventional workup followed by flash chromatography afforded a 56:44 mixture of *trans*:*cis* **220** (68.3 mg 72%). Careful repeated chromatography allowed the isolation of pure *cis*-**220**: IR (cm $^{-1}$) 2932, 2852, 2092, 2049, 2023, 1742, 1231; $^{1}$H-NMR: 5.94 (dd 11.0 Hz, 4.7 Hz 1H), 2.64 (m 1H), 2.16 (m 1H), 2.10 (s 3H), 2.00 (m 3H), 1.58-1.40 (m 6H), 0.98 (t 7.2 Hz 3H); $^{13}$C-NMR: 200.3, 170.6, 103.3, 97.7, 76.1, 43.6, 40.0, 35.3, 35.2, 29.7, 25.1, 20.6, 14.1; MS m/e 424 ($M^+$-2CO), 396 ($M^+$-3CO), 368 ($M^+$-4CO), 340 ($M^+$-5CO), 312 ($M^+$-6CO); HRMS m/e for $C_{16}H_{18}Co_2O_6$ calculated. ($M^+$-2CO) 423.9767, found 423.9753.

**Hexacarbonyl [μ-η$^4$ –(6-prop-2-ynyloxy)cyclohepten-4-yne] dicobalt (221)**



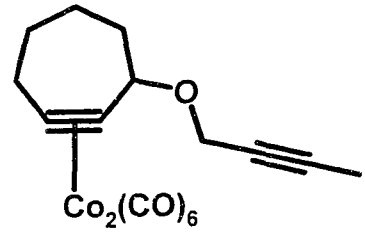

Complex **187** (59 mg, 0.13 mmol) and propargyl alcohol (76 µL, 10 equiv) were dissolved in dry dichloromethane (4 mL) at room temperature. $BF_3.OEt_2$ (92 mg, 5 equiv) in dry dichloromethane (2 mL) was added slowly over 0.5 h and the reaction was followed by TLC. A conventional workup and flash chromatography (50:1 petroleum ether: diethyl ether) afforded complex **221** ( 40.1 mg, 73%): IR ($cm^{-1}$) 3309, 3024, 2929, 2861, 2089, 2051, 2019, 1082; $^1H$ NMR: 5.90 (m 2H), 4.84 (dd 10.7 Hz, 3.5 Hz 1H), 4.45 (m 2H), 3.69 (m 2H), 2.59 (m 1H), 2.46 (t 2.4 Hz 1H), 2.28 (m 1H); $^{13}C$-NMR: 199.5, 130.1, 127.1, 97.5, 79.5, 77.5, 74.5, 56.1, 34.4, 33.7; MS m/e 432 ($M^+$-CO), 404 ($M^+$-1CO), 376 ($M^+$-2CO), 348 ($M^+$-3CO), 320 ($M^+$-4CO), 292 ($M^+$-5CO), 264 ($M^+$-6CO) ; HRMS m/e for $C_{14}H_{10}Co_2O_5$ ($M^+$-2CO) calculated 375.9192 found 375.9194.

**Hexacarbonyl [µ-$\eta^4$ –(3-prop-2-ynyloxycycloheptyne)] dicobalt (222)**



Complex **188** (38.6 mg, 0.09 mmol), propargyl alcohol (53 µL, 10 equiv) and $BF_3.OEt_2$ (64 mg, 5 equiv) were reacted according to procedure E. A conventional workup followed by flash chromatography (50:1 petroleum ether: diethyl ether) afforded complex **222** ( 32.5 mg, 85%): IR ($cm^{-1}$) 3312, 2927, 2855, 2091, 2051, 2020, 1090; $^1H$ NMR: 4.76 ( dd 10.4 Hz, 4.3 Hz 1H), 4.45 (d½ABq, 15.9 Hz, 2.4 Hz, 1H), 4.42 (d½ABq, 15.9Hz, 2.4 Hz, 1H), 3.21 (dt 16.3 Hz, 1.9 Hz 1H), 2.27 (m 1H), 2.44 (t 2.4 Hz 1H), 2.20 (m 1H), 2.05 (m 1H), 1.98 (m 1H), 1.60 (m 2H), 1.40 (m 1H); $^{13}C$-NMR: 199.6, 98.7, 98.0, 79.7, 79.4, 74.4, 56.0, 36.7, 35.4, 29.1, 25.7; MS m/e 434 ($M^+$-CO), 406 ($M^+$-1CO), 378 ($M^+$-2CO), 350 ($M^+$-3CO), 322 ($M^+$-4CO), 294 ($M^+$-5CO), 266 ($M^+$-6CO) ; HRMS m/e for $C_{14}H_{12}Co_2O_5$ ($M^+$-2CO) calculated 377.9349 found 377.9349.

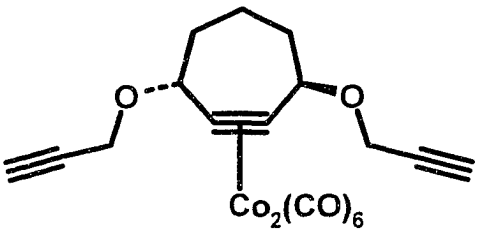
**Hexacarbonyl [µ-$\eta^4$ –(3-but-2-ynyloxy-cycloheptyne)] dicobalt (223)**




Complex **188** (96 mg, 0.22 mmol), but-2-yn-1-ol (168 µL, 10 equiv) and $BF_3.OEt_2$ (156 mg, 5 equiv) was combined according to procedure E. A conventional workup followed by flash chromatography (50:1 petroleum ether: diethyl ether) afforded complex **223** (74.6 mg, 85%): IR ($cm^{-1}$) 2928, 2855, 2091, 2048, 2017, 1070; $^1H$-

NMR: 4.75 (dd 10.4 Hz, 4.2 Hz 1H), 4.40 (½ABq 15.5 Hz 1H), 4.37 (½ABq 15,5 Hz 1H), 2.76 (m 1H), 2.18 (m 1H), 2.05 (m 1H), 1.98 (m 1H), 1.86 (t 2.3 Hz 3H), 1.59 (m 2H), 1.42 (m 1H); $^{13}$C-NMR: 199.6, 98.8, 98.5, 82.6, 79.1, 75.0, 56.6, 36.8, 35.5, 29.1, 3.5; Ms m/e 448 ($M^+$), 420 ($M^+$-1CO), 392 ($M^+$-2CO), 364 ($M^+$-3CO), 336 ($M^+$-4CO), 308 ($M^+$-5CO), 280 ($M^+$-6CO) ; HRMS m/e for $C_{17}H_{14}Co_2O_7$ ($M^+$) calculated 447.9403, found 447.9403.

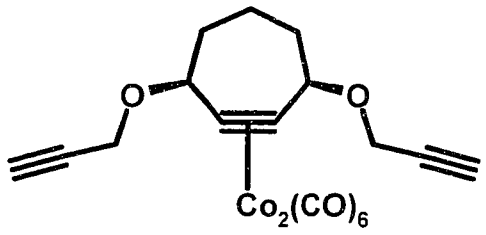
**<u>*trans*-Hexacarbonyl [μ-η$^4$-( 3,7-bis(prop-2-ynyloxy)cycloheptyne)] dicobalt (224)</u>**




Diacetate complex *trans*-**215** (63 mg, 0.12 mmol), propargyl alcohol (70 μL, 10 equiv) and $BF_3.OEt_2$ (85 mg, 5 equiv) were reacted according to procedure E. A conventional workup followed by flash chromatography (50:1 petroleum ether: diethyl ether) afforded a mixture complexes **226** (*trans*:*cis* 62:38) in 82% yield. Careful repeated chromatography resulted in isolation of *trans* isomer. *trans*-**226**: IR (cm $^{-1}$) 3311, 2926, 2856, 2054, 2023, 1446, 1072; $^1$H-NMR: 4..81 (dd 6.6 Hz, 3.8 Hz

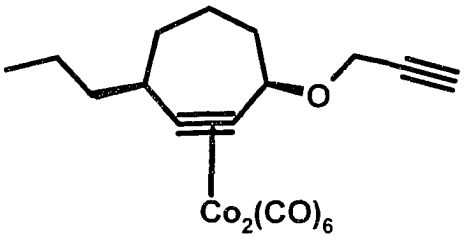
2H), 4.40 (dd 15.9 Hz, 2.3 Hz 2H), 4.34 (dd 15.9 Hz, 2.3 Hz 2H), 2.44 (t 2.3 Hz 2H), 1.91 (m 4H), 1.82 (m 2H); $^1$C-NMR: 199.5, 95.9, 79.7, 74.7, 56.4, 34.5, 18.8.

**<u>*cis*-Hexacarbonyl [μ-η$^4$-(3,7-bis(prop-2-ynyloxy)cyclohept-1-yne)] dicobalt (224)</u>**




Complex *cis*-**215** (83 mg, 0.16 mmol), propargyl alcohol (94 μL, 10 equiv) and $BF_3.OEt_2$ (114 mg, 5 equiv) were reacted according to procedure E. A conventional workup followed by flash chromatography (50:1 petroleum ether: diethyl ether) afforded complexes **226** as a mixture of *trans*:*cis* (20:80) isomers (63.4 mg, 88%). Careful repeated chromatography resulted in isolation of *cis* isomer. *cis*-**226**: IR 3310, 2929, 2855, 2095, 2053, 1079; $^1$H-NMR: 4..68 (dd 9.8 Hz, 4.6 Hz 2H), 4.48 (dd 16.0 Hz, 2.4 Hz 2H), 4.41 (dd 16.0 Hz, 2.4 Hz 2H), 2.46 (t 2.4 Hz 2H), 2.20 (m 4H), 1.44 (m 2H); $^1$C-NMR: 199.5, 96.1, 79.8, 79.6, 74.6, 56.1, 35.2, 22.3; MS m/e 488 ($M^+$), HRMS m/e for $C_{14}H_{14}Co_2O_3$ ($M^+$-5CO) calculated 347.9601 found 347.9581.

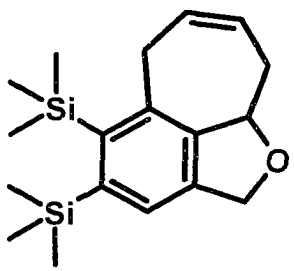
***cis*-Hexacarbonyl [μ-η$^4$ –{(3-prop-2-ynyloxy)-7-propylcycloheptyne] dicobalt (225)**




Complex *cis*-**220** (132.5 mg, 0.28 mmol), propargyl alcohol (166 μL, 10 equiv) and $BF_3.OEt_2$ (199 mg, 5 equiv) were reacted according to procedure E. A conventional workup followed by flash chromatography (50:1 petroleum ether: diethyl ether) afforded complex **227** (98.1 mg, 75%) as a mixture of 69:31 (*cis*:*trans*) isomer. Careful repeated chromatography resulted in isolation of pure *cis* isomer. *cis*-**227**: IR 2963, 2932, 2875, 2087, 2049, 2016; $^1$H NMR: 4.73 (dd 10.6 Hz, 4.5 Hz 1H), 4.68 ( dd 15.9 Hz, 2.4 Hz 1H), 4.41 ( dd 15.9 Hz, 2.4 Hz 1H), 2.60 (m 1H), 2.45 (t 2.4 Hz 1H), 2.23 (m 1H), 2.05 (m 2H), 1.73 (m 1H), 1.53 (m 1H), 1.45 (m 5H), 0.98 (t 7.1 Hz 3H); $^{13}$C-NMR: 199.9, 104.5, 98.3, 79.9, 79.7, 74.5, 56.2, 43.9, 39.8, 36.2, 34.7, 25.2, 20.5, 14.1; Ms m/e 476 ($M^+$), 420 ($M^+$-2CO), 392 ($M^+$-3CO), 364 ($M^+$-4CO), 336 ($M^+$-5CO), 308 ($M^+$-6CO).

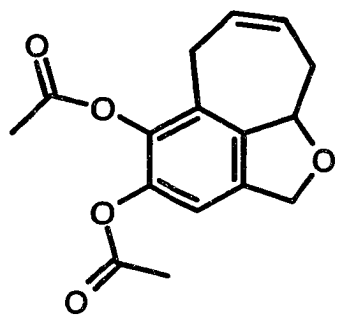
**Procedure G: Typical 2+2+2 Cycloaddition Reactions**

**4,5-[Bis-(trimethylsilanyl)-2,6,9,9a-tetrahydro-1-oxa-benzo[cd]azulene] (226)**



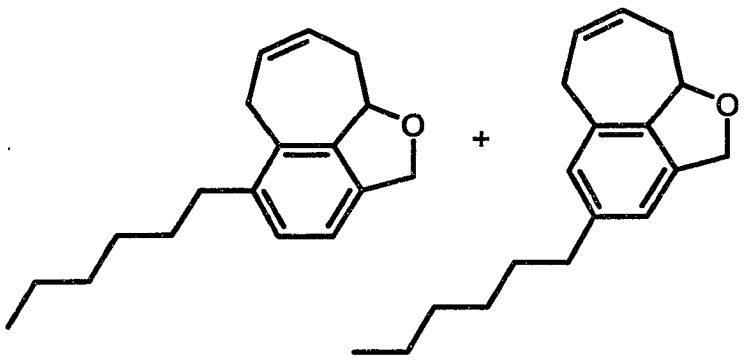

Complex **222** (89.6 mg, 0.20 mmol) and bis(trimethylsily)acetylene (34 mg, 5 equiv) were dissolved in toluene (10 mL) and stirred under $N_2$; the mixture was then heated at reflux for 3 h. The resulting solution was cooled to room temperature, diluted with $Et_2O$ (20 mL) and then filtered through a pad of silica gel. Evaporation of the solvent under reduced pressure and preparative TLC (4 :1 petroleum ether : Et$_2$O) furnished **228** (37.9 mg, 60%) as viscous oil: IR (cm $^{-1}$) 3016, 1595 cm$^{-1}$; $^1$H-NMR 7.44 (s, 1H), 5.77 (m, 1H), 5.71 (m, 1H), 5.60 (m, 1H), 5.23 (d ½ABq, 2.8, 12.3, 1H), 5.15 (½ABq, 12.3, 1H), 3.61 (apparent t of ½ABq, J = 3.3, 17.0, 1H), 3.48 (d of ½ABq, J = 8.3, 17.0, 1H), 2.73 (m, 1H), 2.35 (m, 1H), 0.44 (s, 9H), 0.38 (s, 9H); $^{13}$C 147.3, 143.2, 142.9, 142.1, 137.4, 126.4, 126.1, 125.7, 82.2, 73.4, 35.6, 33.6, 4.0, 3.1; MS (EI) m/e 316; HRMS m/e for $C_{18}H_{28}OSi_2$ calculated 316.1679, found 316.1674.

**4,5-Diacetoxy-2,6,9,9a-tetrahydro-1-oxa-benzo[cd]azulen-4-yl ester (227)**



Complex **222** (63.4 mg, 0.15 mmol) and 2-butyne-1,4-diacetate (128mg, 5 equiv.) were refluxed in toluene (7.5 mL) according to procedure G. After preparative TLC (4 :1 petroleum ether : $Et_2O$) furnished **229** ( 24.5 mg, 58%) as a yellowish oil: IR ($cm^{-1}$) 3019, 2925, 1739; $^1$H-NMR: 7.16 (s 1H), 5.71 (m 1H), 5.64 (m 1H), 5.61 (br d 10.9 Hz 1H), 5.24 (s 4H), 5.22 (d of ½ABq 2.7 Hz, 12.6 Hz 1H), 5.11 (½ABq 12.6 Hz 1H), 3.58 (br 2H), 2.71 (m 1H), 2.47 (m 1H), 2.08 (s 3H), 2.06 (s 3H); $^{13}$C-NMR: 170.6, 170.6, 143.4, 139.1, 135.5, 135.1, 130.4, 125.4, 125.4, 120.8, 82.0, 72.8, 64.7, 59.3, 35.2, 29.2, 20.8, 20.8; MS 256 $(M\text{-}CH_3CO_2H)^+$; HRMS m/e ($C_{18}H_{20}O_5$ + $Na^+$) calculated 339.1208, found 339.1207.

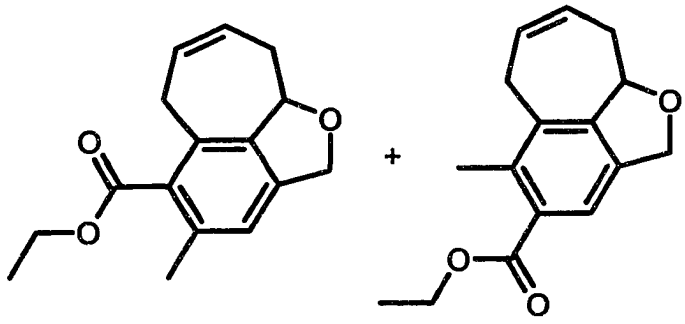
**5-Hexyl-2,6,7,8,9,9a-hexahydro-1-oxabenzo[cd]azulene and 4- Hexyl-2,6,7,8,9,9a-hexahydro-1-oxabenzo[cd]azulene(228a /228b)**



Complex **222** (66.3 mg, 0.15 mmol) and 1-octyne (111 µL, 5 equiv) were refluxed in toluene (7.5 mL) according to procedure G. After preparative TLC (4 :1 petroleum ether : $Et_2O$) furnished **230a:230b** (50:50) (22.6 mg, 59%) as a viscous oil: IR ($cm^{-1}$); $^1H$ NMR 7.07 (d 7.5 Hz 1H), 6.99 (d 7.5 Hz 1H), 6.89 (s 1H), 6.84 (s 1H), 5.72 (m 2H), 5.65 (m 2H), 5.58 (d 10.7 Hz 1H) and 5.51 (d 9.8 Hz 1H), 5.18 (d of ½ABq 2.7 Hz, 12.0 Hz 1H), 5.16 (d½ABq 2.8 Hz, 12.0 Hz 1H), 5.10 (½ABq, 12.0 Hz 1H), 5.08 (½ABq 12.0 Hz 1H), 3.67 (br d 19.6 Hz 1H), 3.51 (m 2H), 3.31 (dd 6.0 Hz, 19.6 Hz 1H), 2.71 (m 2H), 2.61 (m 4H), 2.41 (m 2H), 1.65 (m 2H), 1.50 (m 2H), 1.10-1.40 (m 12H), 0.91 (t 7.0 Hz, 3H) and 0.90 (t 7.1 Hz 3H) ; $^{13}C$-NMR: 142.8, 142.6, 139.2, 138.8, 138.5, 135.7, 133.2, 131.8, 129.1, 127.3, 126.5, 126.1, 125.4, 124.5, 118.5, 118.4, 82.1, 81.9, 73.1, 73.0, 35.8, 35.7, 34.1, 33.0,

31.8, 31.7, 31.3, 29.3, 29.1, 22.6, 14.1; MS m/e 256 ($M^+$); HRMS m/e calculated for $C_{18}H_{24}O$ 256.1827, found 256.1826.

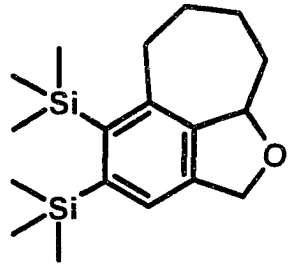
**4-Methyl-2,6,9,9a-tetrahydrobenzo[cd]azulene-5carboxylic acid ethyl ester and 5-Methyl-2,6,9,9a-tetrahydrobenzo[cd]azulene-4-carboxylic acid ethyl ester (229a/229b)**



Complex **222** (80.5 mg, 0.19 mmol) and ethyl 2-butynoate (114 µL, 5 equiv) were refluxed in toluene (9,5 mL) according to procedure G. Preparative TLC (4 :1 petroleum ether : $Et_2O$) furnished **231a/231b** (57:43) (27,9 mg, 58%) as a pinkish oil: IR ($cm^{-1}$) 3019, 2980, 1722; $^1$H-NMR: Major isomer 7.46 (s 1H), 5.72 (m 1H), 5.67 (m 1H), 5.51(d 10.0 Hz 1H), 5.17 (1/2 ABq 12.0 Hz 1H), 5.08 (1/2 ABq 12.0 Hz 1H), 4.37 (q 7.4 Hz 2H), 3.59 (d of ½ ABq 4.8 Hz, 19.6 Hz 1H), 3.48 (1/2 ABq 19.6 Hz 1H), 2.69 (m 1H), 2.47 (s 3H), 2.38 (m 1H), 1.39 (t 7.4 Hz 3H); Minor isomer 6.94 (s 1H), 5.65 (m 2H), 5.50 (obscured m 1H) 5.15 (d of ½ ABq 2.8 Hz, 12.6 Hz 1H), 5.07 (1/2 ABq 12.6 Hz 1H), 4.41 (q 7.2 Hz 2H), 3.65 (d of ½ ABq 4.4 Hz, 19.0 Hz 1H),

3.29 (dd of ½ ABq 1.7 Hz, 6.0 Hz, 19.0 Hz 1H), 2.70 (m 1H), 2.38 (m 1H), 2.33 (s 3H), 1.40 (t 7.2 Hz 3H); $^{13}$C-NMR: Major isomer 168.9, 145.4, 135.5, 134.7, 133.4, 131.8, 126.1, 125.1, 120.0, 82.1, 72.5, 61.0, 35.2, 30.0, 16.2, 14.3; minor isomer 168.9, 140.0, 139.5, 134.6, 132.3, 130.5, 125.6, 125.0, 120.4, 82.0, 72.9, 61.2, 35.4, 30.9, 19.7, 14.3 (obscured); HRMS m/e for $C_{16}H_{18}O_3$ calculated 258.1256, found 258.1262.

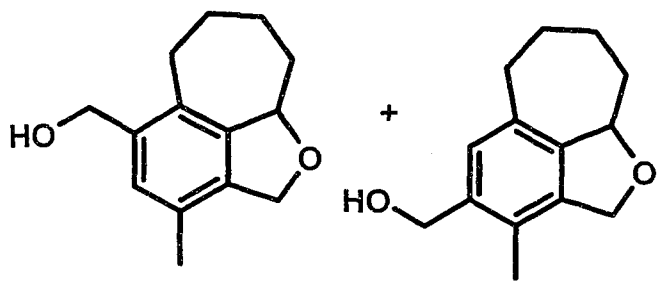
**4,5-[Bis-(trimethylsilanyl)-2,6,7,8,9,9a-hexahydro-1-oxa-benzo[cd]azulene] 230**




Complex **223** (65.0 mg, 0.150 mmol) and bis(trimethylsilyl)acetylene (170 mL, 0.75 mmol) in toluene (6 mL) were refluxed according to procedure G. Preparative TLC (4 :1 petroleum ether : $Et_2O$) furnished **230** (75:25) (30.2 mg, 63%) as a viscous oil: IR (cm $^{-1}$) 3054, 2927, 1450; $^1$H- NMR 7.40 (s 1H), 5.21 (obscured m 1H), 5.19 (½ABq J = 11.9 Hz 1H) , 5.08 (½ABq 11.9 Hz 1H), 3.27 (dd 5.7Hz, 14.7 Hz 1H), 2.55 (dd 11.7Hz, 14.7 Hz 1H), 2.20 (d 11.5 Hz 1H), 2.04 (m 2H), 2.20-2.90 (m 3H) , 0.41 (s 9H), 0.38 (s 9H) $^{13}$C-NMR: 147.0, 144.6, 143.5, 143.3, 138.3, 126.0, 86.5,

73.2, 36.5, 35.5, 28.2, 27.9, 4.2, 3.3; MS (EI) 318 $(M)^+$; HRMS m/e for $C_{18}H_{30}OSi_2$ calculated 318.1835, found 318.1853.

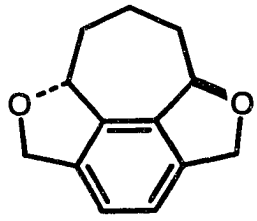
**(3-Methyl-2,6,7,8,9,9a-Hexahydro-1-oxa-benzo[cd]azulen-5yl)-methanol and (3-Methyl-2,6,7,8,9,9a-Hexahydro-1-oxa-benzo[cd]azulen-4-yl)-methanol 232a/232b**




Complex **225** (60 mg, 0.13) and propargyl alcohol (39 µL, 5 equiv.) were refluxed in toluene (6.5 mL) according to procedure F. After preparative TLC (2 :1 petroleum ether : $Et_2O$) furnished **232a:232b** (20.5mg, 70%): IR ($cm^{-1}$) 3379, 3034; $^1$H-NMR 7.01 (s 1H), 5.24 (d 9.1 Hz 1H), 5.18 (d of ½ABq 2.7 Hz, 12.3 Hz 1H) 5.02 (½ABq 12.3 Hz 1H), 4.69 (br 2H), 3.19 (dd 6.4 Hz, 15.1 Hz 1H), 2.43 (dd 11.9 Hz, 15.1 Hz 1H), 2.21 (s 3H), 1.95-2.10 (m 2H), 1.45-1.75 (m 3H), 1.20-1.40 (m 2H);

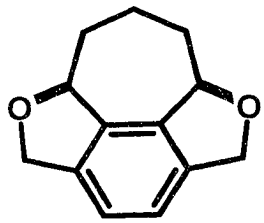
absorptions for the minor regioisomer were observed at 7.03 (s 1H), 5.19 (obscured 1H), 5.03 (obscured 1H), 2.79 (d of ½ABq 5.2 Hz, 15.7 Hz 1H), 2.69 (d of ½ABq 11.7 Hz, 15.7 Hz 1H) $^{13}$C-NMR: 143.5, 137.7, 136.8, 133.4, 129.3, 127.9, 86.57, 72.5, 63.5, 35.7, 30.5, 27.9, 27.8, 18.2; absorptions for the minor regioisomer were observed at 141.7, 138.8, 134.6, 128.5, 127.0, 86.65, 72.8, 63.2, 35.9, 35.8, 28.4, 27.7, 14.6; MS (EI) m/e: 218 ($M^+$); HRMS m/e for $C_{14}H_{18}O_2$ calculated 218.1307, found 218.1305.

**(*trans*)-5,6a,7,8,9,9a-Hexahydro-2H-1,6-dioxa-cyclohepta[jkl]-as-indacene 233**



Complex *trans*-**220** (36.4 mg, 0.08 mmol) was refluxed in toluene (4 mL) according to procedure G. Preparative TLC (4 :1 petroleum ether : $Et_2O$) furnished *trans*-**235** (9.7 mg, 60%): IR (cm $^{-1}$) 3038, 2928; $^1$H-NMR: 7.12 (s 2H), 5.09 (d of ½ABq 1.9 Hz, 12.2 Hz 2H), 5.02 (½ABq 12.2 Hz 2H), 4.94 (d 12.2 Hz 2H), 2.34 (m 2H), 1.99 (m 2H), 1.83 (m 2H); $^{13}$C-NMR: 139.1, 137.1, 119.6, 79.5, 72.9, 31.0, 20.7; MS (EI) 202 ($M^+$); HRMS m/e calculated for $C_{13}H_{14}O_2$ 202.0994, found 202.0995.

**(*cis*)-5,6a,7,8,9,9a-Hexahydro-2H-1,6-dioxa-cyclohepta[jkl]-as-indacene 233**



Complex *cis*-**220** (110.4 mg, 0.25 mmol) was refluxed in toluene (12.5 mL) according to procedure G. Preparative TLC (4 :1 petroleum ether : $Et_2O$) furnished *cis*-**235** (30.1 mg, 60%) as a viscous oil: IR ($cm^{-1}$) 3379, 3034; $^1$H-NMR: 7.11 (s 2H), 5.13 (br m 6H), 2.30 (m 2H), 2.07 (m 1H), 1.72 (dt 14.2 Hz, 13.0 Hz, 1H), 1.48 (apparent dt 12.1 Hz, 11.8 Hz 2H); $^{13}$C-NMR: 138.2, 136.5, 119.9, 84.2, 73.4, 35.6, 21.2. MS (EI) 202 ($M^+$); HRMS m/e calculated for $C_{13}H_{14}O_2$ 202.0994, found 202.0992.

## Future Work

Tricyclics that possess the fused 7,5,5 framework in such compounds as **200** are rare in nature.[89] Therefore, it is advantageous to reduce the tricyclic compound to a fused bicyclic 7,5 ring system. For that reason, sulfur and oxygen tethered alkenes complexes such as **189**, **190**, **191**, **192**, **193**, and **194** are useful substrates to form the desired bicyclic systems. By changing the Pauson-Khand reaction conditions, it should be possible to reductively cleave the furan ring as was observed in **201** and **206** [Fig. 66 and Fig. 68]. It also should be possible to reduce tricyclics **203** and **204** by Raney nickel® hydrogenation, to bicyclic **235**, analogous to Pericãs's work[53b]. Since most classes of compounds shown in Fig. 55 contain a methyl (e.g. Guaianes and Aromadendranes) or an isopropyl substituent (e.g. Daucanes and Isodaucanes) on the five membered ring, the thioether as a tether to prepare these natural products would be a valuable tool.

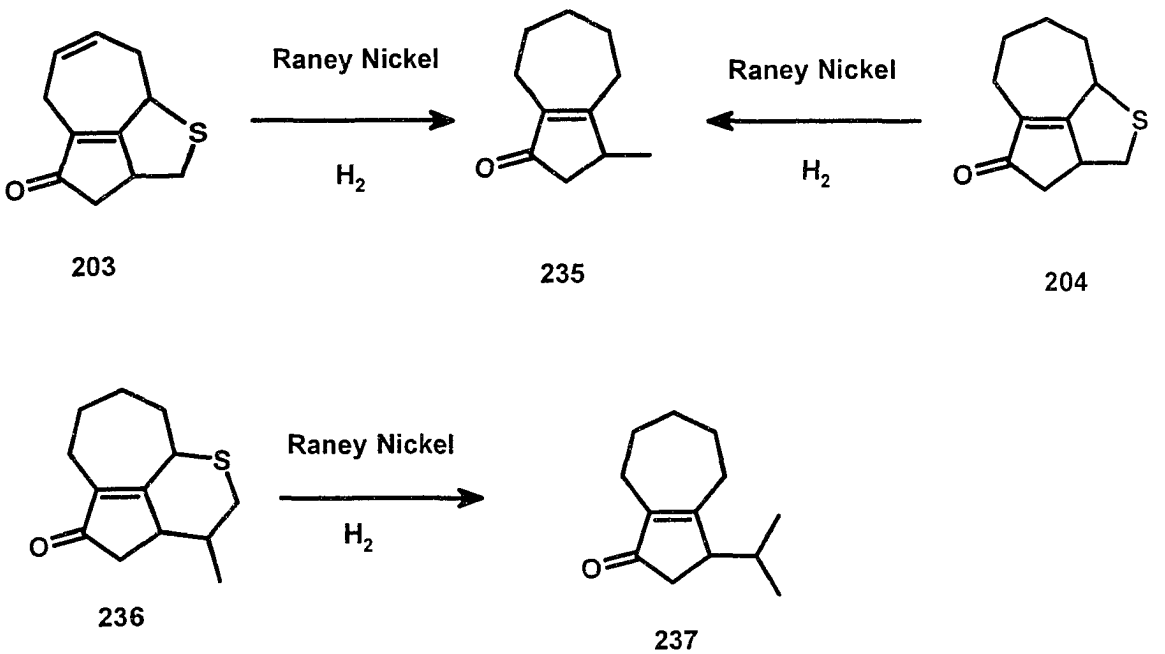



**Figure 81. Desulfuration of Complexes 203 and 204**

A traceless silyl tether route to Pauson-Khand reactions would be of value. It should be facile to synthesize complex **238** (similar to complex **214**), by ring closing metathesis and careful hydrolysis should afford complex **239**. Tethering the vinyl silane to the cycloheptyne ring is likely to afford complex **240**, which can be used as the so called traceless method to prepare 7,5 fused compounds **241**.[53] The latter compound could be used as a model to study the general functionalization of the 7,5 fused ring system. For example, DIBAL reduction of **241** and oxidation should furnish α,β unsaturated compound **242** which could undergo Diels-Alder reaction to provide fused 7,6,5 ring systems (i.e. **243**) found in the Dolastane and Guanacastepene frameworks.

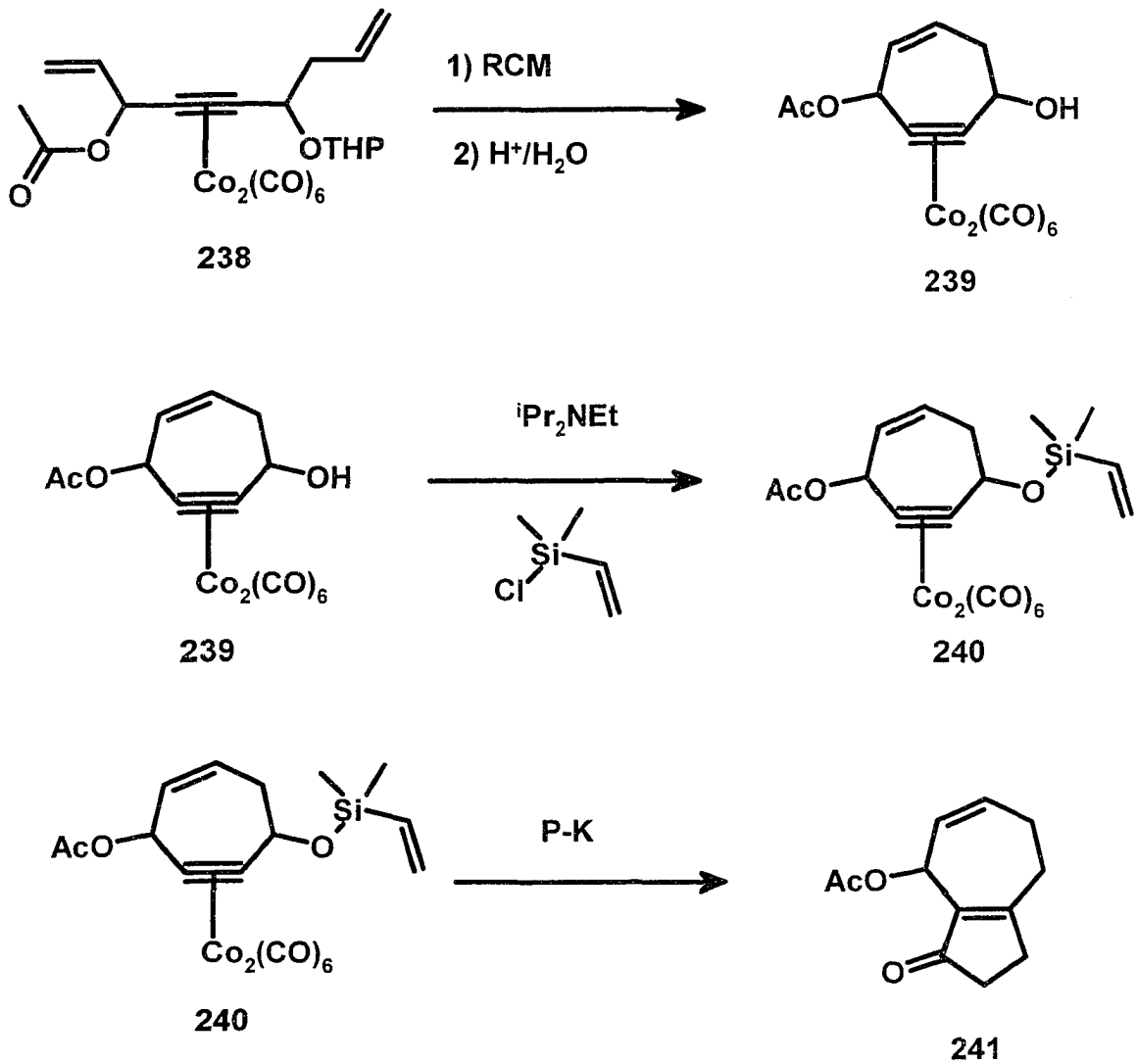



**Figure 82. Use of Traceless Tether to Prepare 241**

Analogously, complex **214** is known to isomerize under acid conditions[90] to complex **244**. DIBAL reduction and $MnO_2$ oxidation of this compound is also known to afford complex **245**.[91] Complex **245** may tested for participation in Diels-Alder reactions, to provide **246**. Tethering vinyl silanes as silyl ether, followed by Pauson-Khand reaction should provide **247.** The latter compounds posses Sphaeroane, Rhamnofolane, Daphnane and Tigliane type fused 7,6,5 ring systems.

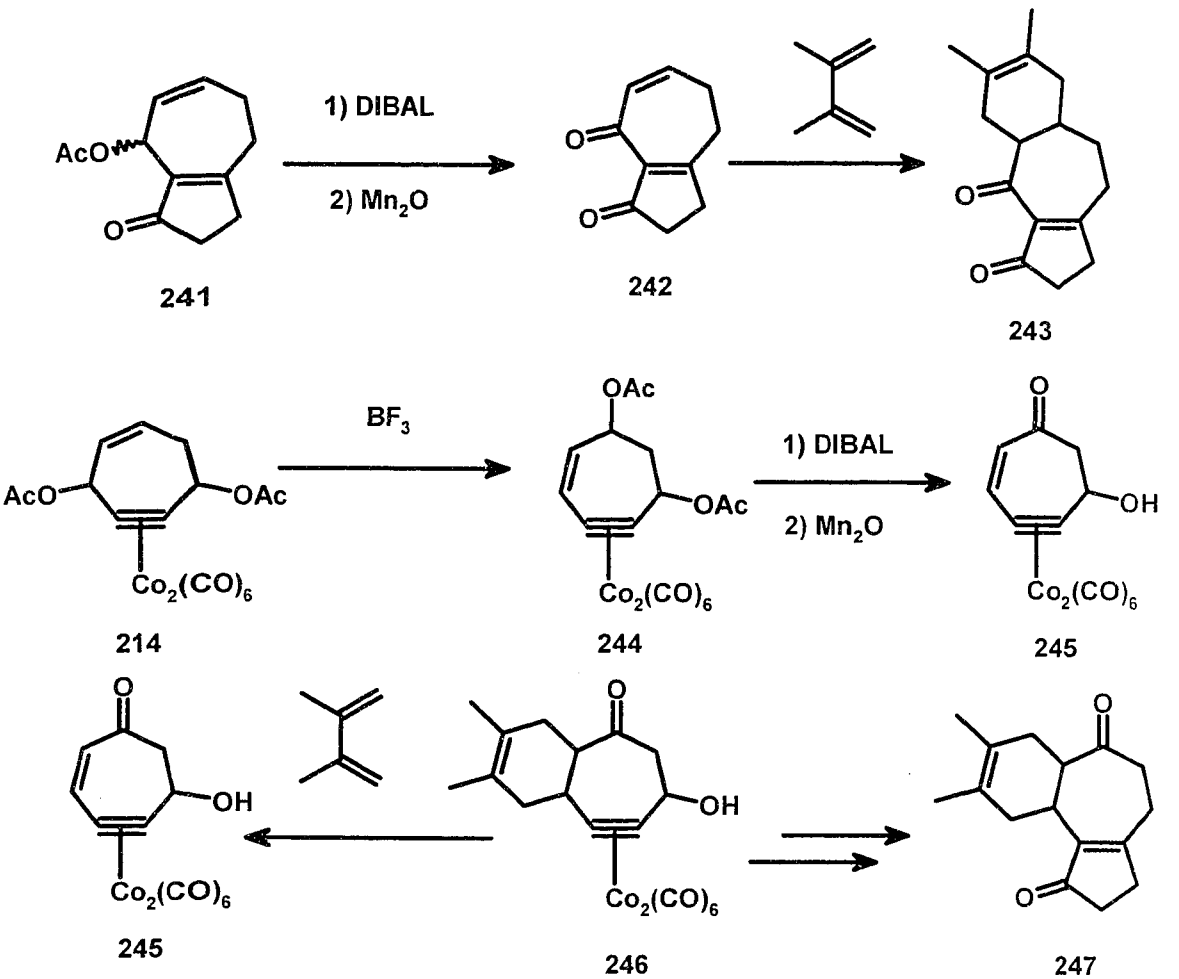



**Figure 83. Possible Diels-Alder Adducts of 242 and 245**

## References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