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Generation and reactivity studies of dehydrotropylium -cobalt hexa(carbon monoxide)complex: Aromaticity of tropyne-cobalt hexa(carbon monoxide) complexes

Sheida Amiralaei
University of Windsor

GENERATION AND REACTIVITY STUDIES OF DEHYDRO-TROPYLIUM -$Co_2(CO)_6$ COMPLEX: AROMATICITY OF TROPYNE-$Co_2(CO)_6$ COMPLEXES

by

Sheida Amiralaei

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I hereby declare that this thesis incorporates material that is result of joint research, as follows:

The thesis also incorporates the outcomes of a joint research undertaken under supervision of professors James Green and James Gauld. The collaboration is covered in Chapter 2 of the thesis. In all cases, the key ideas, primary contributions, experimental designs, data analysis and interpretation, were performed by the author, and the contribution of co-authors was primarily through the provision of advice when needed.

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Thesis Chapter	Publication title	Publication status
Chapter 2	Dehydrotropylium-$Co_2(CO)_6$ Ion. Generation, Reactivity and Evaluation of Cation Stability.	Submitted
Chapter 2	Generation and Reactivity of Dehydrotropylium – $Co_2(CO)_6$ Ion, Chem.Commun. 2008, 4971.	Published

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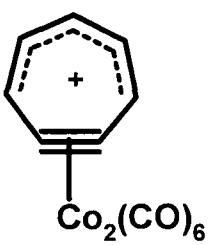
ABSTRACT

Despite a large amount of information on the application of Nicholas reactions in organic syntheses, little attention has been paid to the structural variation of cationic intermediates and the factors that may influence reactivities and stabilities of these species.

The primary focus of this project was to design and generate a new type of Nicholas carbocation that possesses multiple sources of stabilization. For this matter, nominally aromatic cation **99** was chosen as the target compound. The effects of resonance stabilization on the stability and reactivity of the cation **99** were investigated both experimentally and by means of computational calculations. From reactivity studies of cation **99**, a sharp switching of reaction pathway from electrophilic addition to dimerization was observed for the nucleophiles with N <1. Non-aromatic, highly conjugated acyclic cation **127**, was prepared as structural model and its reactivities in Nicholas reactions were investigated for comparison purposes. From experimental and computational studies cation **99** was found to be weakly aromatic with its NICS (1) value approximately 28% of tropylium ion.



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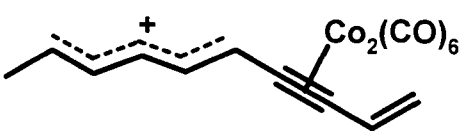

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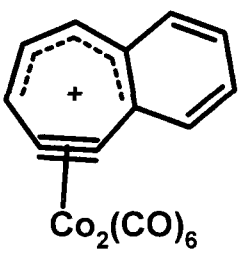
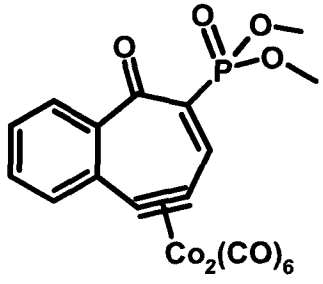


100

Preliminary attempts were made to prepare the precursor to the benzo-fused derivative of dehydrotropylium cation (**100**). This has led to the formation of phosphonate substituted benzo-fused dehydrotropone (**151**). The scope and limitations of the method for synthesis of other $Co_2(CO)_6$- complexes of substituted benzo-fused dehydrotropone (**152** and **153**) were further investigated.



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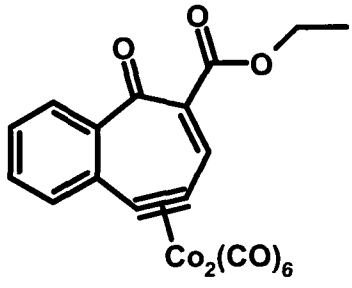

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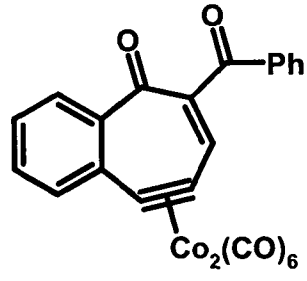

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DEDICATION

I dedicate this thesis to my parents and my sister, for their love, endless support and encouragement.

ACKNOWLEDGMENTS

First and foremost I would like to thank my supervisor, Prof. James Green for his constant guidance, good teaching, patience and support throughout my graduate years.

I would like to thank Dr. James Gauld for his great contribution to the computational part of this thesis. I also would like to thank Mike Fuerth for his help in NMR spectroscopy.

I thank all the present and past members of Green group, especially Dr. Ahmed Mohamed, for their kindness and support.

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LIST OF ABBREVIATIONS

Å	angstrom
Ac	acetate
Ad	1-adamantyl
App	apparent
ASE	aromatic stabilization energy
Bn	benzyl
Boc	tert-butoxycarbonyl
Br	broad
Bu	butyl
BuLi	butyl lithium
Bu_2BOTf	dibutyl{[(trifluoromethyl)sulfonyl]oxy}borane
CAN	ceric ammonium nitrate
$CDCl_2$	deutrated dichloromethane
$CDCl_3$	deutrated chloroform
δ	chemical shift in parts per million downfield shift from a standard
d	doublet
de	diastereomeric excess
DFT	density functional theory
DIBAL-H	diisobutylaluminum hydride
dppm	1,1-bis(diphenylphosphino)methane
dt	doublet of triplet

Et	ethyl
Et_2O	diethyl ether
Eqn	equation
Equiv	equivalent
EHMO	extended Hückel molecular orbital
E_h	energy in hartrees
etc.	and so forth
eV	electron volt
GIAO	gauge-independent atomic orbital
h	hour
HF	Hartree-Fock
HIA	hydride ion affinity
HOMA	harmonic oscillator model of aromaticity
HOMO	highest occupied molecular orbital
HRMS	high-resolution mass spectrometry
Hz	hertz
^{i}Pr	isopropyl
INR	intramolecular Nicholas reaction
IR	infrared
ISE	isomeric stabilization energy
LUMO	lowest unoccupied molecular orbital
m	multiplet
Me	methyl

m/e	ratio of mass to electron charge
MPM	4-methoxybenzyl
MS	mass spectroscopy
NAP	naphthylmethyl
NICS	nucleus independent chemical shift
NMR	nuclear magnetic resonance
PET	petroleum ether
PKR	Pauson-Khand reaction
ppm	parts per million
Py	pyridine
q	quartet
RCM	ring closing metathesis
RT	room temperature
s	singlet
SET	single electron transfer
S_N2	second-order nucleophilic substitution
t	triplet
$t_{1/2}$	half-life
TBAF	tetrabutylammonium fluoride
TBDS	*tert*-butyldimethylsilyl
TBDPS	*tert*-butyldiphenylsilyl
TCNE	tetracyanoethylene
tert	tertiary

THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl
Ts	tosyl(4-toluenesulfonyl)
w/w	weight per weight

1. INTRODUCTION

1.1 CARBOCATION CHEMISTRY

Carbocations have been known for more than 100 years, but the modern concept of a carbocationic intermediate was not recognized until 1922, when Meerwein proposed a cationic intermediate in the Wagner rearrangement of camphene hydrochloride.[1] Since then the intervention of cationic intermediates has been implicated in numerous reactions, isomerizations, rearrangements and other transformations. With the isolation of long-lived carbocations and their characterization by modern spectroscopic techniques, the chemistry of carbocations has now become one of the most exciting research areas for chemists.

Generally speaking, two types of carbocations are known; trivalent (classical) carbenium ions, which contain an sp^2-hybridized carbon, and penta- (or higher) coordinate (non-classical) carbonium ions. Classical carbocations, such as CH_3^+, with six valence electrons, are highly electron deficient. They can be described by two-electron two-center bonds (Lewis valence bond structures). Non-classical carbocations, on the other hand, with 8 electron carbocationic centers, are electron deficient due to sharing of two electrons between three atoms. They can be described by two-electron three(or multi) center bonds. CH_5^+ can be considered the parent for carbonium ions (non-classical carbocations).[2]

While this classification is useful to emphasize the significant difference between these two ions, there exists a broad range of charge delocalization (incorporating both

inter- and intramolecular interactions) in which these two are the ends of the spectrum of possibilities (Figure 1.1).

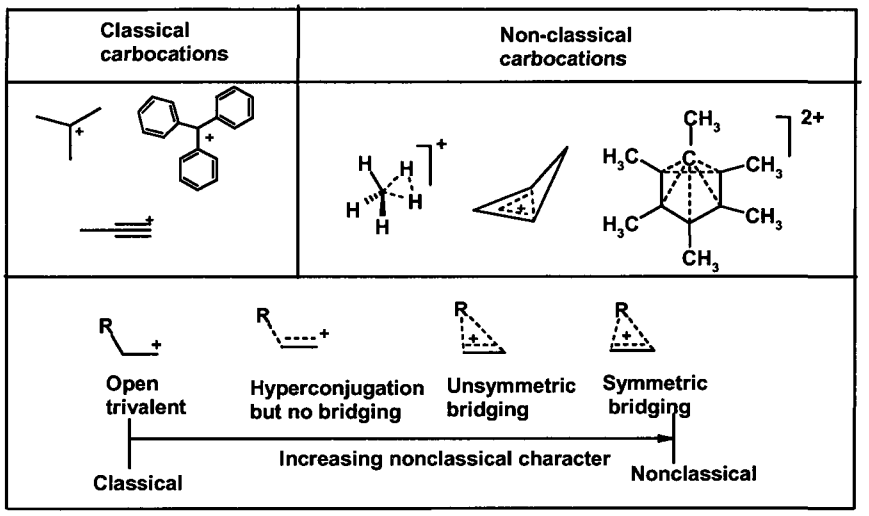


Figure 1.1. Classical vs. non-classical carbocations[2]

Carbocations are known as relatively high energy intermediates and their formation is usually the rate determining step. These highly electron deficient species, once formed have only insignificant stability and limited lifetime under normal conditions. Several factors are known to influence the carbocations' stabilities; neighboring group participation is amongst the most important stabilization factors. This can be done by participation of electron pairs from neighbouring atoms (n donors), π-electron systems (direct conjugation or allylic stabilization), bent sigma bonds, C-H and C-C sigma bonds (hyperconjugation).[2] In a similar manner, various organometallic groups have been found to stabilize adjacent carbocations.[3a-f] The higher stability of these carbocations relative to their metal free counterparts is in general attributed to an ideal overlap of the occupied d orbital on the metal and the vacant p orbital at the carbenium center at the alpha-position. Thereby, based on the kind and amount of stabilization, a

wide range of carbocations with different reactivities are found to exist in numerous situations.

The desire to understand the relationships between the structures, stabilities and reactivities of the carbocations has led to the development of several carbocation stability scales.[4a-d] In these scales, stabilities of carbocations are ranked based on different sets of data derived from either thermodynamic investigations (hydride affinity, heat of ionization, equilibrium constant in solution (pK_{R+})) or kinetic studies (rate of the reaction with Nu, solvolysis, etc).[4a-f]

1.1.1 Thermodynamic stability

With the help of modern mass spectrometry and ion cyclotron resonance techniques, as well as computational methods, the intrinsic stabilities (the carbocations' stabilities in the absence of any solvents), based on the thermodynamic functions, can be determined for various types of carbocations. Hydride ion affinity (HIA) is one of the most common and valuable methods of measurement and comparison for absolute stabilities of structurally diverse carbocations in the gas phase. Hydride ion affinity, defined as ΔH^{o} for the equation 1, is inversely proportional to stability of carbocation. That is, the higher HIA is associated with the less stable carbocation. Table 1.1 shows some of the reported HIA values for selected carbocations.

Eqn. 1 $\quad RH \longrightarrow R^{+} + H^{-} \qquad \Delta H^{o} = HIA$

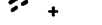
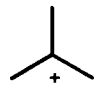
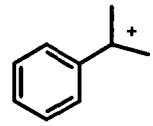
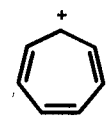
Carbocations						
HIA (kcal/ mol)	**312**	**258**	**256**	**231**	**220**	**201**

Table 1.1. Reported hydride ion affinity for selected carbocations [4g]

There also exists a large amount of information on the thermodynamic stability of carbocations in solution. These data have been collected as a result of a great discovery of Olah and coworkers [4a] on the formation of carbocations in superacidic media with very low nucleophilicity. Following Olah's method, Arnett and coworkers[4b] were able to find the heat of ionization for several alkyl chlorides and alcohols in the presence of the very strong acid SbF_5, using inert solvents such as SO_2, SO_2ClF, etc. Relative stabilities of different carbocations measured based on the heat of ionization in superacidic media were in good agreement with gas phase studies, but generalization of the method to compounds with smaller structural differences can be problematic due to low accuracy of the calorimetric method.[5]

The pK_{R+} series,[6a-c] where K is equilibrium constant for carbinol-cation equlibrium in acidic solutions (Eqn. 2), is another well known and widely used measure of thermodynamic stability of carbocations in solutions.

Eqn. 2 $R^+ + H_2O \rightleftharpoons R{-}OH + H^+$ $\quad K_{R+} = a_{ROH}\, a_{H+} / a_{R+}\, a_{H2O}$

a = activity

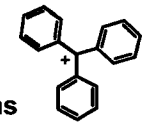
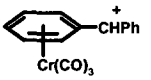
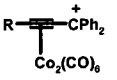
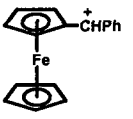
Carbocations							
pK_{R+}	- 6.6 [6a]	-10.4 [6e]	-7.4 [6c]	-6.63 [6a]	2.34 [6b]	0.75 [6e]	4.75 [6d]

Table 1.2. Reported pK_{R+} for selected carbocations.

As it can be seen from Table 1.2, the larger negative number for pK_{R+} corresponds to the less stable carbocation. Reported pK_{R+} values are usually compared with other stability parameters (thermodynamic or kinetic related parameters) to establish the relative stability of carbocations.

1.1.2 Kinetic stability of carbocations

Electrophiles and nucleophiles participate in a large number of chemical reactions. The concept of **electrophiles (electron seeking species)** and **nucleophiles (nucleus seeking species)** were introduced by Ingold in 1930s.[7] The first quantification of these terms and placing them into the scales of electro- and nucleophilicity is believed to be reported by Swain and Scott in 1953.[8] Since then, much work has been done to build a general scale of electro-nucleophilicity. From these studies[7-9] it has been well established that in a wide range of reactions, the relative reactivities (selectivity) of electrophiles and nucleophiles are independent of the nature (strength) of the other reactant partners. As a result, electrophilicity and nucleophilicity parameters along with the corresponding indexes have been introduced and defined by means of experimental and theoretical (computational) methods.

Perhaps one of the most comprehensive and widely used electrophilicity/ nucleophilicity scale has been proposed by Mayr et al. From several hundred rate constants

that his group obtained experimentally for reactions of different carbocations with π, σ and n-nucleophiles, the following equation (Eqn. 3) was obtained through correlation analysis.[9a]

$$\log k\ (20\ ^{\circ}C) = s\ (E + N) \qquad \textbf{Eqn. 3}$$

For this relationship, k is the rate constant, E (electrophilicty) is the electrophile dependent parameter, N (nucleophilicty) is the nucleophile dependent parameter and s, a nucleophile-specific constant, is also related to the nucleophile property. This equation has found widespread application due to the fact that the kinetics of many reactions were found to obey the free energy linear relationship as described by Mayr (Eqn. 3). Thereby, Eqn. 3 has been used as a reliable source to predict the rate constants for a wide range of reactions and also to determine E and N values for new compounds (by reacting them with reference elctrophiles/nucleophiles with known E and N values).[9b-c] Table 1.3 shows E values for some selected carbocations and metal stabilized carbocations. In the scale of electrophilicty, the higher value of E corresponds to the more reactive carbocations (less stable).

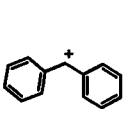
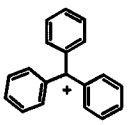
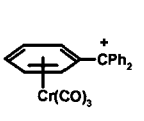
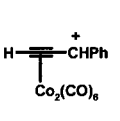
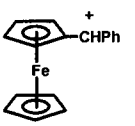
Carbocations						
Electrophilicity (E)	**5.90[9d]**	**-3.72[9e]**	**0.51[9f]**	**- 0.25[9e]**	**-0.97[9e]**	**-2.64[9d]**

Table 1.3. Electrophilicity values for selected carbocations.

1.1.3 Metal stabilized carbocations

The influence of metal fragments on carbocations' stabilities was initially recognized by the great rate enhancement observed in solvolysis of the corresponding halides.[10] Subsequent studies on pK_{R+} and E values of numerous metal stabilized carbocation further confirmed the great influence of metals on carbocation stabilities.[11a] Indeed, the presence of a metal-centered fragment has given some interesting features to the chemistry of organometallic carbocations. These include the isolation of highly reactive or otherwise unstable species, the changing of the reaction pathways, rate enhancement, and stereocontrol of the reactions.[11b] Many examples of metal stabilized carbocations exist in the literature; Figure 1.2 shows two of the systems in which a C-CR_2^+ is bound to and stabilized by mono- metallic centers.[12,10]

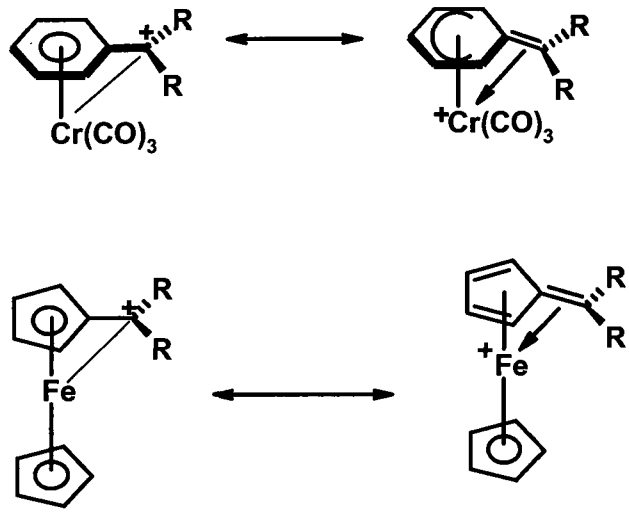
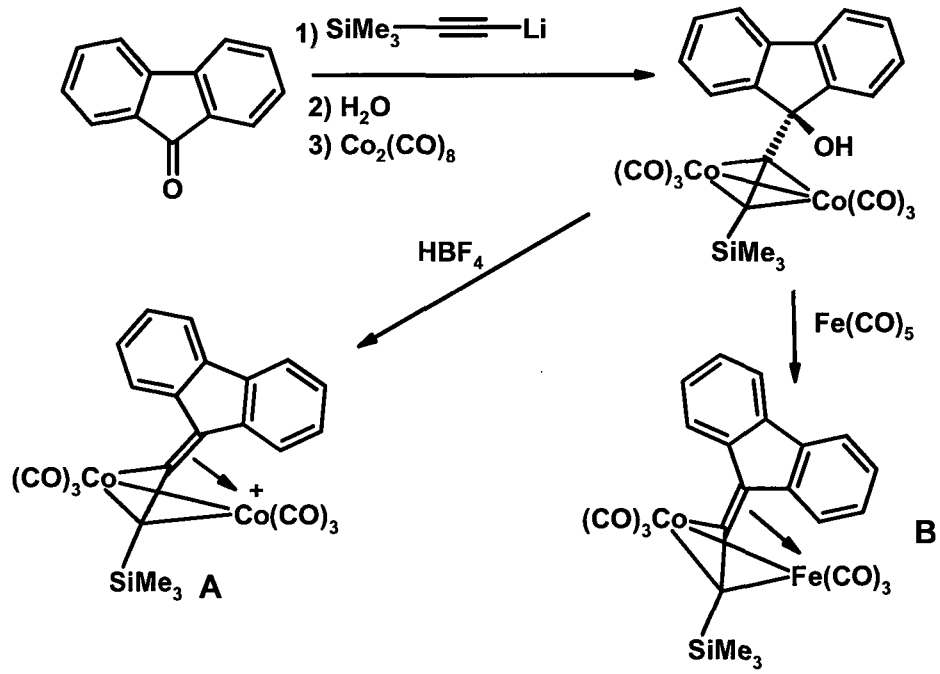


Figure 1.2. Selected metal stabilized carbocations.

McGlinchey's group has synthesized a variety of organometallic species of this type and investigated a wide range of fluxional processes in them.[11b,13] Among them are cluster stabilized cations of otherwise unavailable species such as the anti-aromatic

fluorenyl, indenyl, and cyclopentadienyl cations, substituted by alkynyl-$Co_2(CO)_6$ complexes (Scheme 1.1). These cations were generated by protonation of the corresponding alcohols and their structures were identified by NMR studies. According to variable-temperature NMR studies, charge delocalization on the metal center was more pronounced in cations with greater anti-aromatic character (i.e., in the 8π indenyl cation vs the 12π fluorenyl cation). Furthermore, isolable crystals (**B**) were prepared for X-ray structural analysis by replacing $Co(CO)_3^+$ unit in (**A**) with the isolobal $Fe(CO)_3$ moiety . Based on molecular orbital calculations these mixed metal species are known to serve as excellent structural models for cobalt cluster cations. From these structural studies, bending of fluorenyl unit toward the iron atom was detected. Also, a smaller distance between the iron and the cationic center in the indenyl system versus fluorenyl system was observed, which again reflects the greater need for the metal assistance in more unstable cationic systems.[13]



Scheme 1.1. Cobalt and iron stabilized anti-aromatic fluorenyl cations.

Moreover, the same group was able to compare different organometallic fragments in their ability to stabilize carbocationic centers by incorporating different groups in the same cluster (Figure 1.3).[11b] Isolation and characterization of these mixed-metal clusters suggested (from NMR analysis and X-ray crystallography data) the relative order of $Ru(CO)_3$ > $Fe(CO)_3$ > $CpW(CO)_2$> $Co(CO)_2PPh_3$ > $Co(CO)_3$ for stabilization of cationic center.[11b]

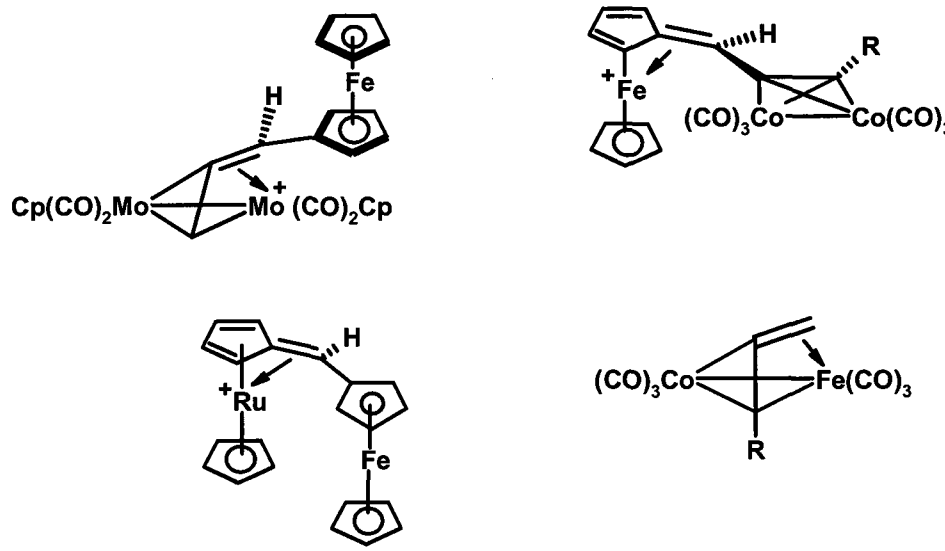
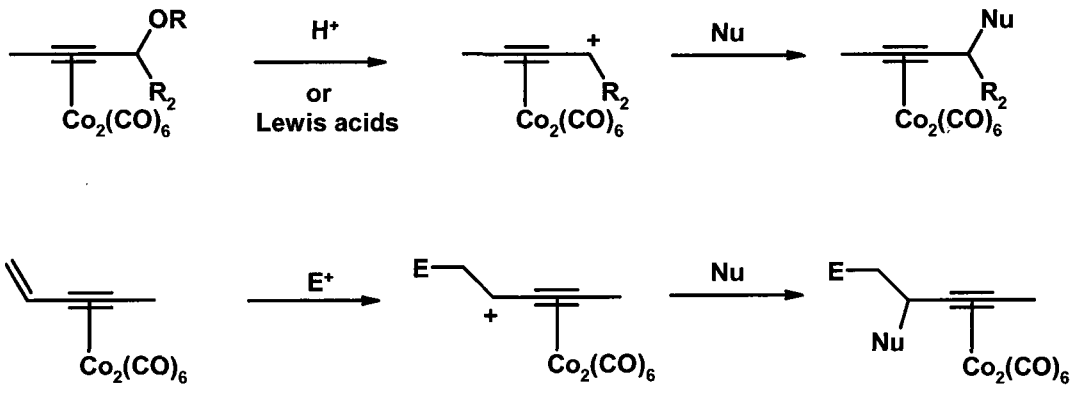


Figure 1.3. Selected mixed-metal cluster stabilized carbocations.

Most frequently, the structures of these carbocations are elucidated from detailed NMR studies, along with X-ray crystallographic characterizations (when available). Rotational and migrational barrier energies derived from variable-temperature NMR studies can be used to estimate the strength of interactions between the carbocationic center and the metal clusters.[14,15]

1.2 DICOBALT STABILIZED CATION

In 1972, Nicholas and Petit discovered that dicobalt hexacarbonyl can effectively stabilize a propargylic carbocation.[16] Isolation, characterization and evaluation of the stability of this type of carbocation have been under continued investigation since then.[17] A major advantage of these carbocations is their straightforward generation. Dicobalt hexacarbonyl complexes of propargyl alcohols, ethers, or acetates can be prepared under mild conditions, which upon the addition of protic or Lewis acids, will generate the corresponding carbocations. Alternatively, enyne hexacarbonyldicobalt complexes can also generate these cations in the presence of suitable electrophiles (Scheme 1.2).[18] The propargyldicobalt carbocation after generation can be trapped with different nucleophiles in the so called Nicholas reaction.



Scheme 1.2. Dicobalt stabilized propargylic carbocation generation and Nicholas reaction

Early studies of these carbocations suggested extensive charge delocalization on to the $Co_2(CO)_6$ of the cations. An increase in the carbonyl stretching frequencies (40-60 cm^{-1}) in the IR spectrum and very small downfield shift observed (at the propargylic site) in both ^1H and ^{13}C NMR spectra of cations relative to the precursor alcohol complexes support the assertion that these are highly delocalized carbocations.[19a,b] A non-

symmetrical bent structure (Figure 1.4, compound **f**) has been proposed for the propargyl dicobalt cations based on the experimental data (NMR studies) and on analogy with similar isolobal cluster compounds (compounds **a-e**), (Figure 1.2).[20] Hoffman predicted that in the closely related alkylidynetricobalt nonacarbonyls (d), bending of the cationic carbon towards the metal center would result in hyperconjugative stabilization.[21] His prediction was later confirmed experimentally by Mislow and Norton through ^{13}C NMR analysis of compound **e**.[22]

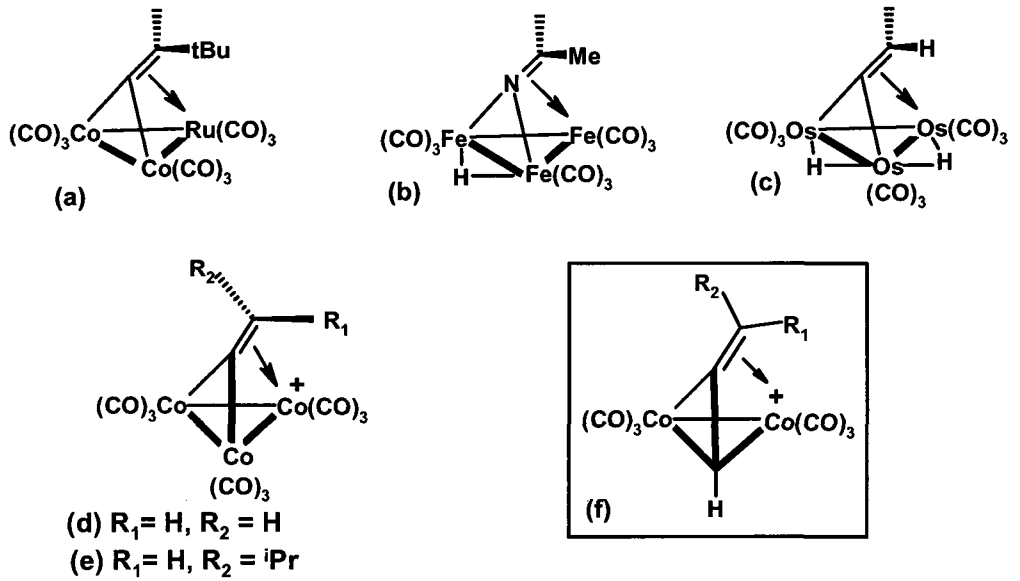
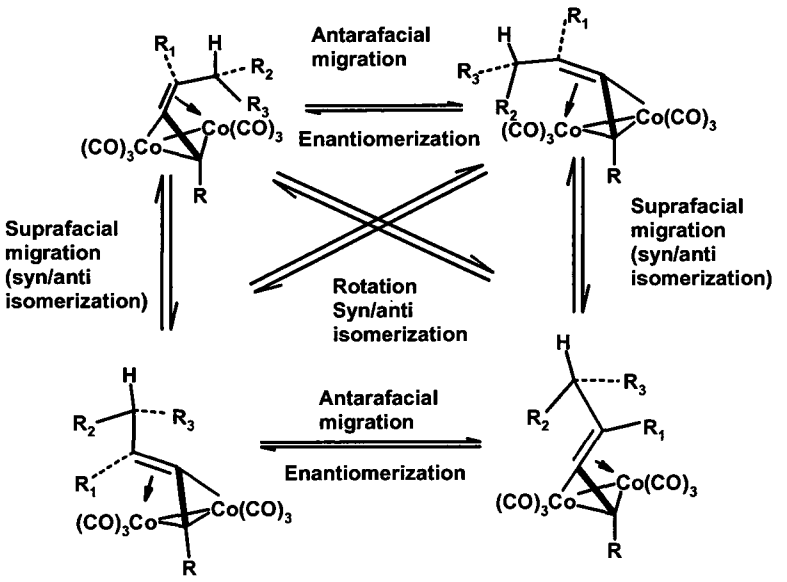


Figure 1.4. Dicobalt propargyl cations and selected isolobal compounds with bent structures.

Variable temperature NMR studies by Schreiber revealed two modes of fluxionality for these dicobalt hexacarbonyl cations; a lower energy antarafacial migration of the cationic center between metal atoms and a higher energy syn/anti interconversion.[20] Antarafacial migration results in enantiomerization of each cobalt cation isomer while suprafacial migration results in *syn/anti* isomerisation (Scheme 1.5).



Scheme 1.3. Fluxional behaviour of the propargyldicobalt cation.*

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The stereochemical fate of the propargylic substitution reaction depends on the relative rate of alkylation and enantiomerization of the cation. In most cases, racemization of the cation is fast relative to alkylation; in the case of a chiral nucleophile, the relative rate of addition (kinetic resolution) therefore dominates the stereochemical outcome of the reaction. It has been shown that substituent changes can affect the kinetics of the isomerization process of the cation, and therefore structural modification of the cation, as well as rendering the combination reaction intramolecular, might result in enhanced stereospecificity (see Section 1.4).[20]

1.2.1 Structural analysis, stability and reactivity of propargyldicobalt cation

Understanding the electronic structure and nature of chemical bonding in alkynedicobalt complexes has been a matter of interest for both theoretical and experimental chemists. Primary spectroscopic studies for alkynedicobalt hexacarbonyls indicate a C_{2v} geometry with the alkyne being in a perpendicular position to the Co-Co direction, in a pseudo-tetrahedral core (Figure 1.5).[23a] Recently the Overgaard group has used a series of *ab initio* calculations using complete active space method (CAS (6,6)) and DFT/B3LYP to solve the electronic structure of a dicobalt alkyne complex. Based on their calcuations, small but still significant bonding (covalent) exists between the two metal centers, and a bond order of 1.45 to 2 for the C-C of the alkyne was found. [23b]

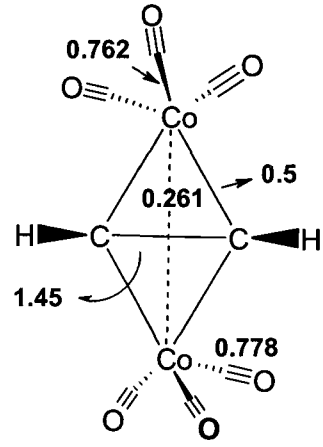
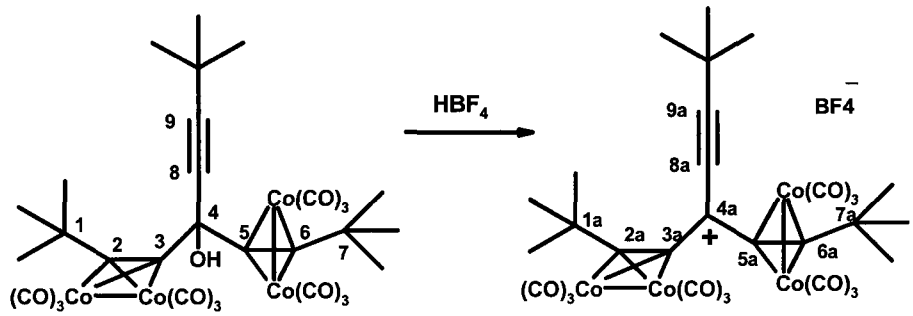


Figure 1.5. Alkynedicobalt complex geometry and bond orders.

Good agreement between previously reported experimental results (X-ray, and spectroscopic data) and recent computational studies validate computational techniques as suitable methods for structural analysis of alkynedicobalt complexes.

Unlike alkynyl cobalt complexes with high thermal and air stability, the related propargyldicobalt cation has limited stability under normal conditions. Structural analysis

of these cations has been mostly based on spectroscopic data, with the first X-ray crystallography of doubly stabilized cation **1** appearing in 1998.[24] To date, the crystal structure of cation **1** is still the only example for a dicobalt hexacarbonyl stabilized propargyl cation, yet there are several examples of mixed-metal stabilized species or dicobalt complexed cations with various phosphine ligands. [25,13a]



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Scheme 1.4. X-ray analysis of dicobalt stabilized cation 1.

From the X-ray analysis of cation **1**, rehybridization of carbon 4 from sp^3 in the alcohol to sp^2 in the cation, and nearly planar arrangement around the cation was confirmed. Moreover, no change was observed in bond angles of C_2-C_3-C_4 and C_6-C_5-C_4 and those of C_{2a}-C_{3a}-C_{4a} and C_{6a}-C_{5a}-C_{4a} indicating no geometrical change at that point. On the other hand, a substantial change was observed in dihedral angels C_{1a}-C_{2a}-C_{3a}-C_{4a} and C_{7a}-C_{6a}-C_{5a}-C_{4a}, changing from 4.8° and 4.4° in neutral compound to 55 ° and 43 ° in cation **1.** More importantly, the orientation of Co-Co bond relative to alkyne bond has shown a twist of 7.7° from almost perpendicular (89.2°) towards a skew geometry (82.3°). This observation supported previous assumptions on bending of the cationic center toward the metal center.[24]

The thermodynamic stability of cobalt coordinated propargylium cations have

been investigated by Nicholas and Connor. These propargyl carbocations pK_{R+} values vary between -6.8[19a] (-5.5[19b]) to -7.40, meaning that they have been found to be approximately as stable as triphenylmethyl cations (Table 1.2).[19a]

Kinetic investigation by Mayr's group on the electrophilic reactivities of cobalt stabilized propargylium cations towards different π-nucleophiles and hydride donors has revealed second order kinetics for these reactions which follows the free enthalpy relationship (see Eqn. 3).[9a] Consequently, electrophilicity pararmeters for these cations could be calculated by measuring the rate constant of the reactions with different nucleophiles with known nucleophilicity values. The $Co_2(CO)_6$ stabilized propargyl cations could then be ranked in terms of their reactivities along with other electrophiles and were found to behave like xanthyium and ferrocenylmethylium ions. According to Mayr's electrophilicity scale, these cobalt stabilized propargylium ions have electrophilicity values E = -1 to -2. Therefore they are expected to react with electron rich nucleophiles (N > -3) such as anisole but expected not to be so reactive toward simple benzene or toluene (N = -4.47) .[26]

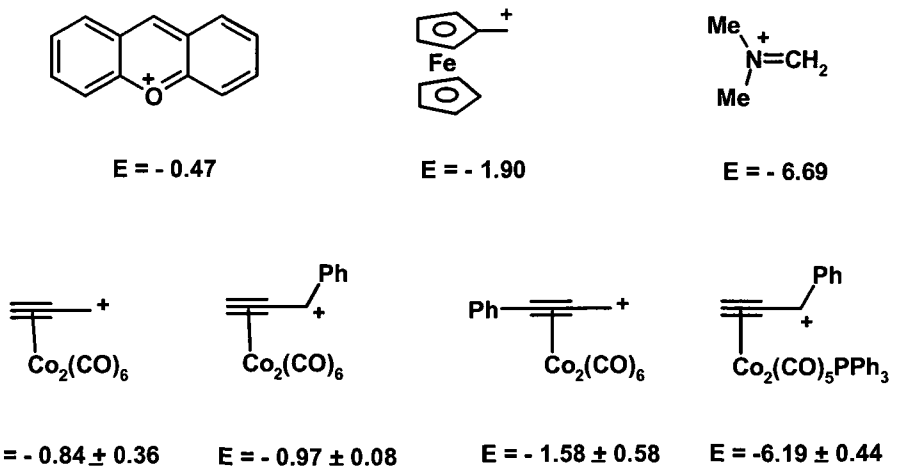


Figure 1.6. Electrophilicity values for selected propargyl dicobalt cations, xanthylium, ferrocenylmethylium and iminium ions.

The reactivity of these carbocations has shown to be almost independent of the nature of substituents at the propargylic site (Figure 1. 6). It has been found that addition of a phenyl group, to render the cation benzylic, decreases its reactivity by only a very modest amount (i.e., by about 25%). In contrast, replacing one carbonyl ligand by PPh_3 ligand improves the cation's stability and reduces the electrophilic reactivity of these species by factor of 10^5, which makes it comparable to iminium ions in its reactivity.[26] Similarly, the substituent changes at the propargylic site are shown to have minimal effect on the pK_{R+} values (thermodynamic stabilities) of the cation (Figure 1.7).[19a]

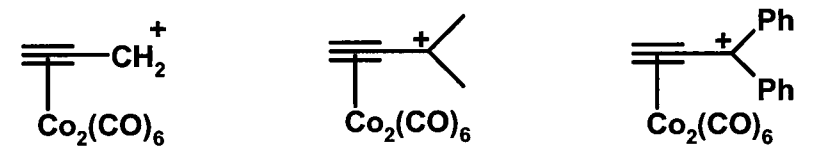
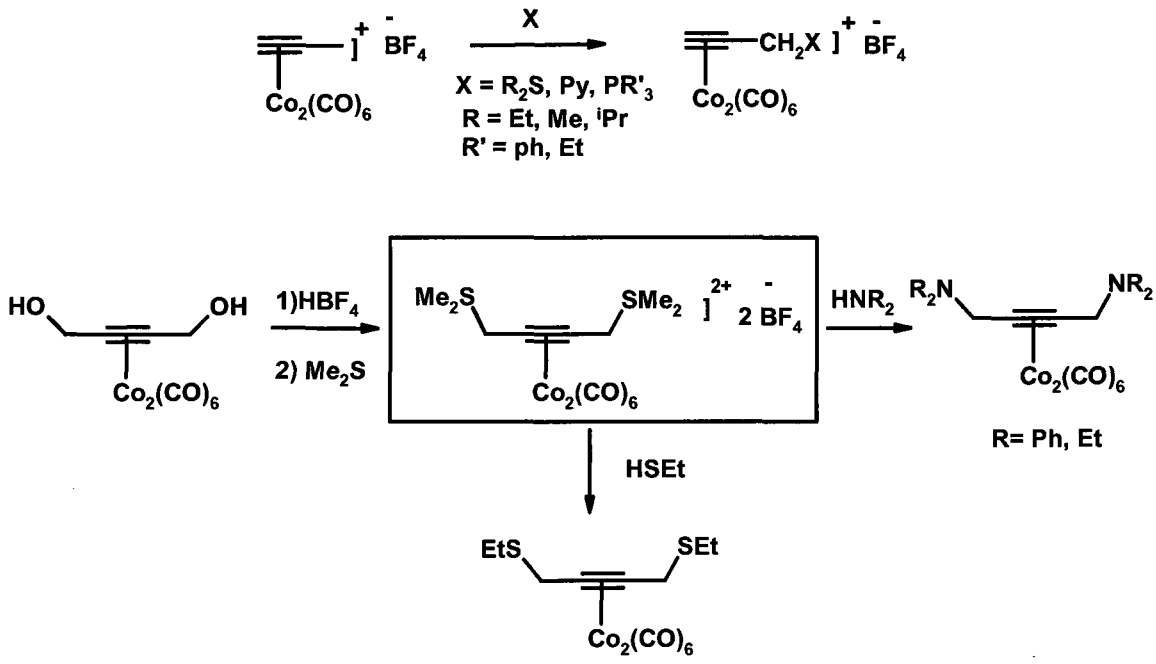


Figure 1.7. pK_{R+} values for selected propargyl dicobalt cations.

Reaction of propargylic dicobalt cations with different sulfides, phosphines and pyridine, and isolation of the corresponding salts has been suggested by Jaouen and coworkers as an alternative way to improve the stability and modify the reactivity of these species.[27] This study has shown greater stability for these complexes relative to common propargylic dicobalt cations, with positive charge localized more on the heteroatom versus the metal center as compared to normal propargyl cobalt complexes. Moreover, a reactivity study of the sulfonium cobalt complex has determined the reactive species as sulfonium complex rather than propargylic cobalt cation, as the former reacts with nucleophiles in S_N2 manner.



Scheme 1.5. Heteroatom stabilized cobalt propargyl cations and use of sulfide stabilized cations in Nicholas reactions.

Went and coworkers[28] used sulfide-stabilized cationic cobalt cluster in the synthesis of cobalt and molybdenum complexes of dithiaalkynes.[28b] Later, this group applied the same approach in synthesis of alkylamine complexes, which due to basicity of amine were not easily accessible under normal Nicholas reaction conditions. In this work, the thermally stable and storable disulfonium salt was isolated in high yield (Scheme 1.5).[29]

1.3 PROPARGYLDICOBALT CATIONS IN ORGANIC SYNTHESIS

The Nicholas reaction is one the most important transformations in organic synthesis and has been applied in the synthesis of a wide range of cyclic and acyclic compounds.[17a-d]

Propargyldicobalt carbocations (Nicholas carbocations) can react inter- or intra-molecularly in both solution and solid phases [30] with a wide range of nucleophiles, such as electron rich arenes, heteroatom nucleophiles (O, S, P, N) carbon nucleophiles (enols, enol ethers, alkenes, allysilanes, allylstannanes) and hydride donors, to form a new bond. The reaction selectively happens at the propargylic site without any allene by-product formation. The Nicholas reaction is especially well recognized for its application in construction of highly strained cycloalkynes, synthetically important medium-sized rings (natural product synthesis) and macrocyclic compounds of a variety of ring sizes. Furthermore, using suitable unsaturated nucleophiles in tandem Nicholas and Pauson-Khand reactions allows construction of more complex structures.

1.3.1 Strained cycloalkynes

Strained cycloalkynes, due to the considerable angle strain that exists at the alkynyl carbons, are generally known as transient species with limited lifetime. In this category, cyclooctyne is known as the smallest isolable cycloalkyne. Cycloheptynes, on the other hand, are generally known as transient species. Yet, it was found to be isolable if it exists in the form of tetramethylsubsitututed cycloheptyne, wherein tetramethyl substitution prevents the oligomerization of strained cycloalkyne and permits its isolation ($t < 1$ h).

It is worth mentioning that the relative stabilities of cycloalkynes have shown to be highly dependent on the ring size and the amount of conjugation. The effect of former is evidenced by isolability of cyclooctyne and cyclononyne and transiency of cycloheptyne and cyclohexyne and no intermediacy for cyclopropyne or butyne. [31]

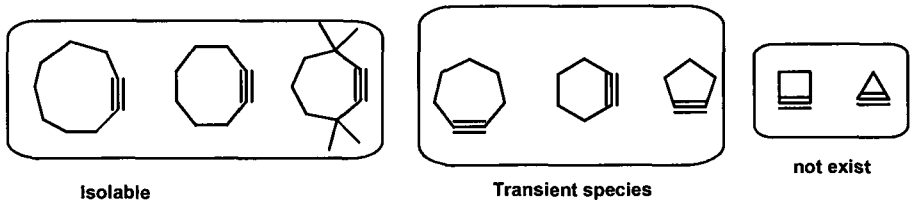
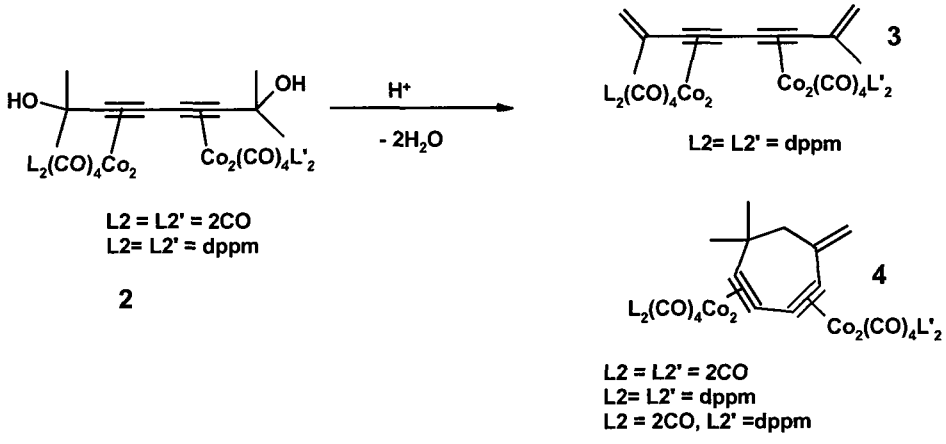


Figure 1.8. Structural effects on the isolability of strained cycloalkynes.

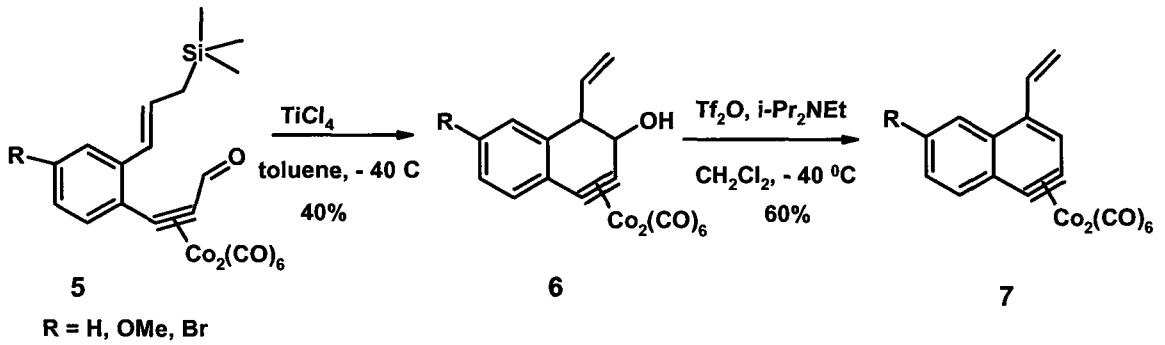
The presence of the cobalt cluster not only enhances the stability of the propargylium cation but also brings a significant change in the geometry of the triple bond by decreasing the bond angle from 180° in the free alkyne to 140° in the alkynedicobalt complexe. As a result, complexation of alkynes with cobalt carbonyl and its subsequent Nicholas reaction has been used in the synthesis of otherwise synthetically challenging (strained) cycloalkynes.

Woods and his coworkers have been able to synthesize the smallest known conjugated cyclodiyne complexes (**4**) from conjugated dialkyne complexes; surprisingly, compound **4** was the sole product of the reaction even in the presence of large amounts of external nucleophiles (Nu: PhOH, PhSH, PhOMe, 1,4- $C_6H_4(OH)_2$, HSC_3H_6SH) (Scheme 1.6).[32]



Scheme 1.6. Acid catalyzed reaction of tetracobalt coordinated bis-propargylic complexes.

Iwasawa's group[33] was able to synthesize naphthalyne-$Co_2(CO)_6$ complexes (**7**) for the first time utilizing intramolecular Nicholas reactions on benzene derivatives having allyltrimethylsilanes and alkyne-cobalt functions at the ortho position (**5**), Scheme 1.7. Cyclohexyne is the absolute limit for $Co_2(CO)_6$- cycloalkyne complexes and only two other examples of these systems have been reported so far .[34]



Scheme 1.7. Synthesis of naphthalyne dicobalthexacarbonyl complexe.

Perhaps the most common ring size encountered in cycloalkyne cobalt complexes is the 7-membered ring.[35] The straightforward formation and high stability of cyclo-heptynedicobalt complexes are due to reduced angle strain in these complexes as compared to their metal free counterparts. Nicholas reactions have been used widely as an efficient method for synthesis of this class of compounds. We and other groups, in the course of the past few years, have been able to synthesize and isolate a wide range of cycloheptynes, cycloheptenyes, cycloheptadienyne and aryl-fused cycloheptynes in the form of their dicobalt complexes (Figure 1.9).[35]

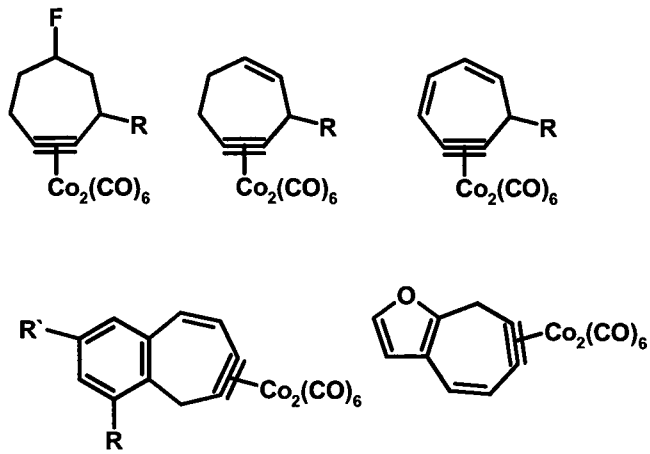
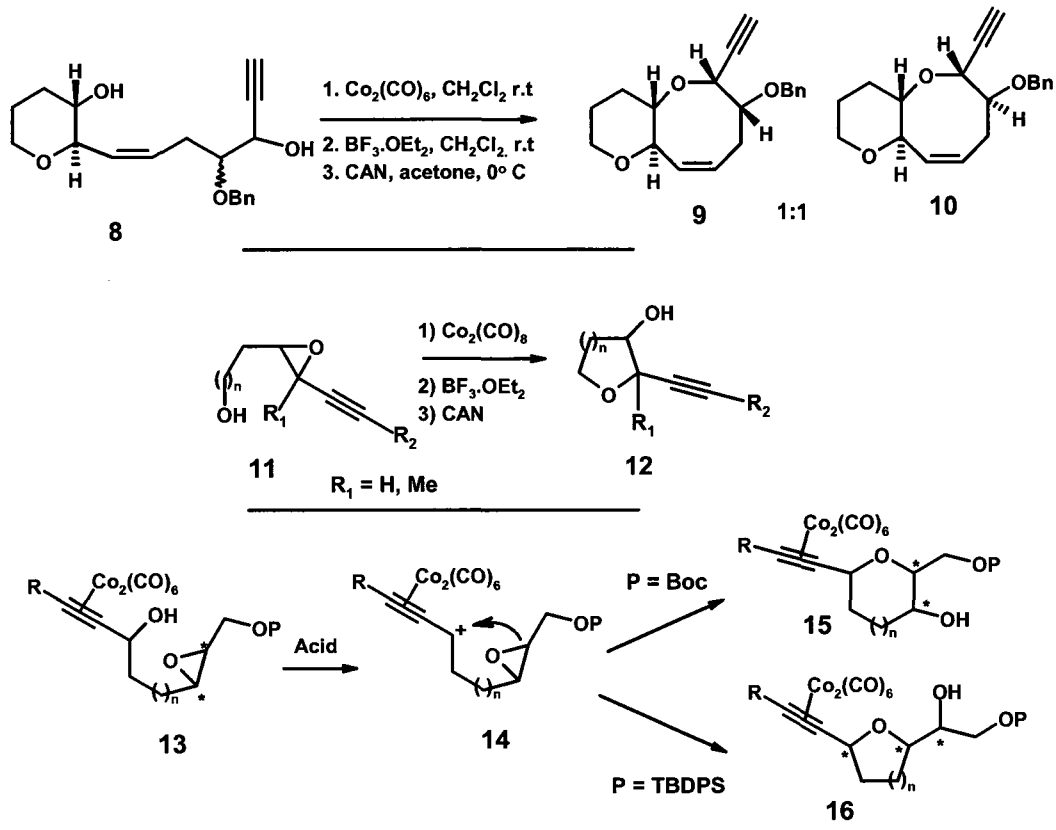


Figure 1.9. Selected examples of known dicobalt hexacarbonyl complexes of cycloalkynes.

1.3.2 Medium sized rings via intramolecular Nicholas reaction

Intramolecular Nicholas reactions (INR) have been used in synthesis of a wide range of carbo- and heterocyclic compounds, both in cases where the alkyne moiety is part of the ring (endo- cyclization), or it resides as a pending substituent (exo-cyclization). Medium sized cyclic ethers are of great importance in organic synthesis due to their existence as common structural motifs in different classes of natural products such as brevetoxin A and B, ciguatoxin, and maitotoxin. Martin's group has developed an elegant method for the synthesis of six-to-nine membered cyclic ethers based on INRs, using primary or secondary alcohols as nucleophiles located at proper distance from propargyl alcohol complexes.[36] Applying the same strategy in carefully designed systems, substituted oxocenes and bicyclic 6,8- systems were synthesized (**9, 10**). The presence of both a fused ring and Z-double bond in the linear chain was necessary to overcome the unfavourable entropic effect for cyclization to obtain the 8-membered ring in the 6,8-systems (Scheme 1.8).[37]

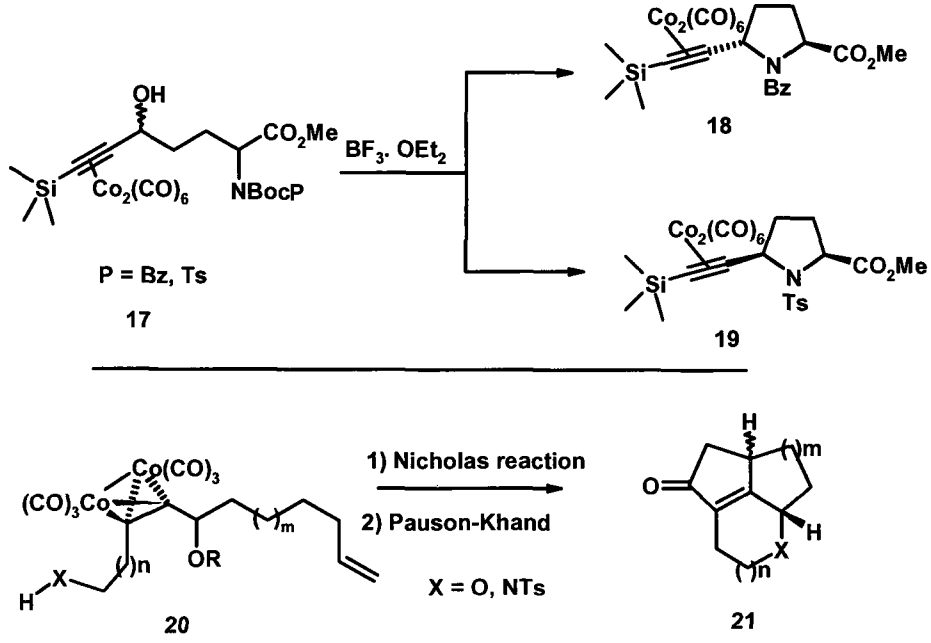


Scheme 1.8. Intramolecular Nicholas reaction in the synthesis of cyclic ethers.

Mukai and Hanoaka have performed the same type of cyclization to obtain 5-, 6-, or 7- membered cycic ethers using an alkynyl epoxide complex (**11**) to generate the propargylic carbocation.[38] These ring closing reactions occur with complete regioselectivity and in case of R_1 = H with high stereoselectivity (**12**, Scheme 1.8). Martin's group, on the other hand, used an epoxide (**13**) as the nucleophile in an intramolecular Nicholas reaction to trap propargylic cations for the formation of 5-, 6- , and 7- membered polysubstituted cyclic ethers. Cyclization proceeded in a regio- and stereoselective manner, in which the distance between epoxide and propargylic center, nature of protecting group, the reaction temperature and time play significant roles (Scheme 1.8). Under kinetic conditions (4 h and – 20 °C) with Boc as protecting group and n=1, a single isomer of compound **15** was isolated (70%), while nearly same starting

material with TBDPS as protecting group, under thermodynamic conditions gave **16** as single isomer, albeit with low yield (25 %).[39]

Other heteroatom nucleophiles[40,41] have also been used in INRs, but to a lesser extent than carbon and oxygen nucleophiles. Martin's group was able to synthesize substituted 5-alkynylproline derivatives in highly stereo-selective manner by using protected amines. The stereoselectivity of the product has shown to be highly dependent on the nature of N-protective group (Scheme 1.9).

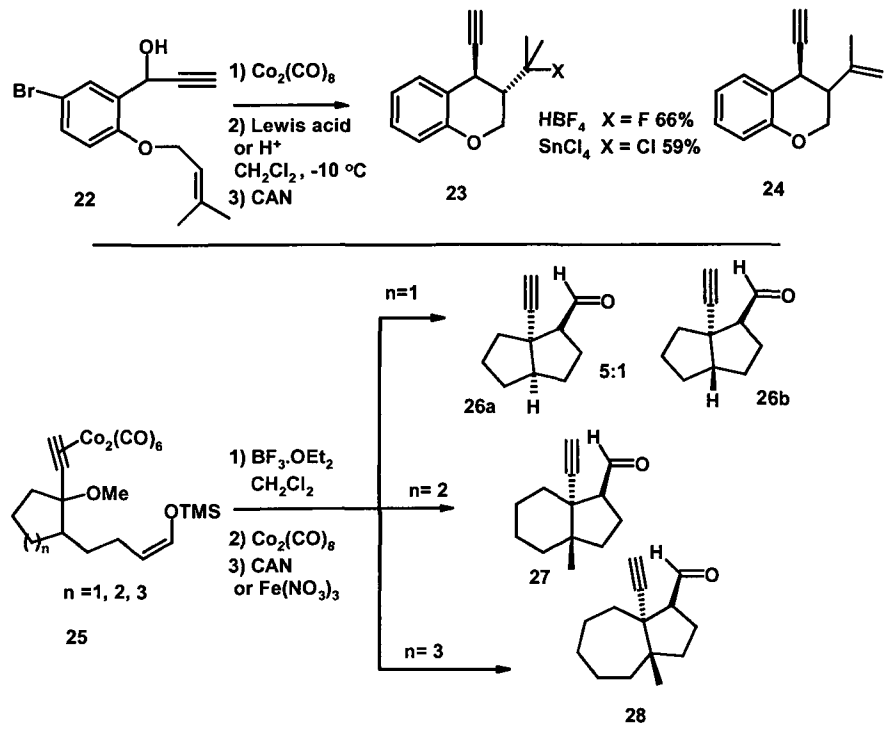


Scheme 1.9. Intramolecular Nicholas reaction in the synthesis of N-heterocylic compounds.

The scope and limitations of endocyclic intramolecular Nicholas reactions in the synthesis of heteroatoms (N and O) containing tricyclic systems have been examined by Shea and coworker. According to their study, the tandem Nicholas / Pauson-Khand reaction of **20** can be properly used in syntheses of [5,8,5 and 5,7,5]- heterocyclic systems (**21**), but not for [5,6,5 or 5,9,5]- tricyclic systems. Nicholas reactions to obtain 6-

membered ring cycloalkynes failed due to the angle strain, and in case of 9-membered rings the subsequent Pauson-Khand reaction to give a 5-membered ring was not successful (Scheme 1.9).[41]

Analogously, a variety of carbon nucleophiles such as alkenes, allyltrimethyl-silane, allylstannanes, or silyl enol ethers have also been used in intramolecular Nicholas reactions to trap propargylic carbocations. Tyrrell et al have used a tethered trisubstituted alkene **22** as a nucleophile in intramolecular Nicholas cyclization reactions to form benzopyrans (Scheme 1.10). The tertiary carbocation intermediate may either be trapped with the different halide ions present in the Lewis acid (**23**), or may lose a proton by β-elimination to form an alkene unit (**24**).[42a,b]Attempts to do an analogous cyclization with a disubstituted alkene have failed. In accord with the previous results of Krafft[43] on this type of cyclization, it has been concluded that for the best results the intermediate carbocation should be tertiary.



Scheme 1.10. Intramolecular Nicholas reaction with carbon nucleophiles.

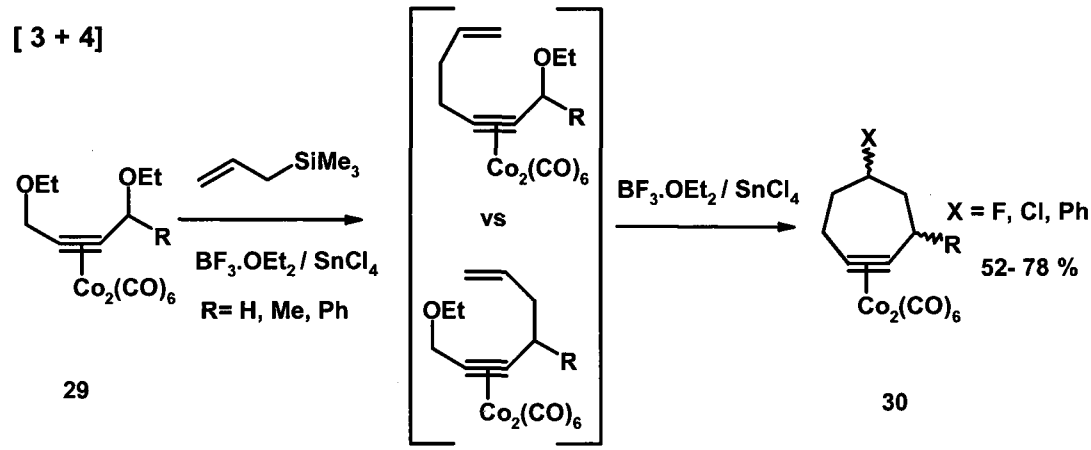
The same group has applied enol ethers (**25**) as nucleophiles in the synthesis of bicyclic systems (Scheme 1.10).[42c] In cases where n =2 and n=3, only the isomer which alkynyl and aldehyde were trans to each other were formed (**27** and **28**), in full agreement with Schreiber model (see Section 1.4).[34b]

1.3.3 Nicholas reactions in cycloadditions

Intermolecular Nicholas reactions, in a similar process to intramolecular Nicholas reactions, have been used in the synthesis of numerous cyclic and acyclic compounds. In this regard, Nicholas carbocations participating in numerous cyclization reactions such as [3+4], [3+2], [3+3] and [5+2] cycloadditions are worth mentioning.

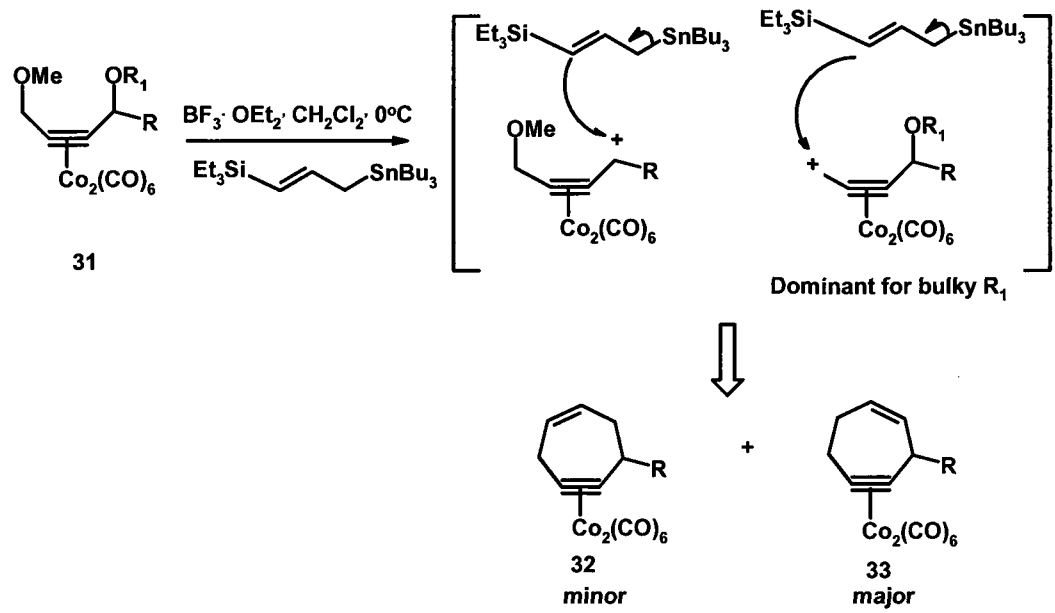
[3+4] and [5+2] cycloadditions are most commonly used in synthesis of 7–membered rings. Nucleophilic addition of allyltrimethylsilane to bis-propargylic ethers

29 has been shown in Scheme 1.11 as an example of [3+4] cycloadditon. Initial nucleophilic addition of allyltrimethylsilane on the less substituted propargylic site is followed by a second alkene attack on the more substituted propargylic site to give cycloheptyne cobalt complexes in a selective manner. The reaction generally gives halo-cycloheptyne cobalt complexes but when benzene was used as solvent, arylated products were formed.[44]



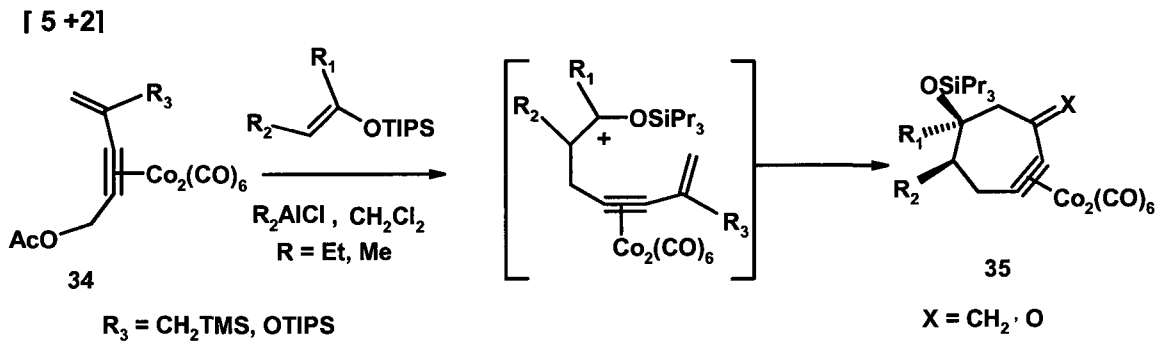
Scheme 1.11. Intermolecular Nicholas reaction in [3+4] cycloaddition.

The observed selectivity could be further enhanced by putting larger ether group on the more subsitututed propargylic site. This effect has been well illustrated by the Green group in synthesis of cycloheptenyne cobalt complexes (**32**, **33**). In this work Green has used a doubly nucleophilic allylmetals which contain both Si and Sn metalloids in the proper position. The first nucleophilic addition occured from the more strongly nucleophilic end (allylstannane) of the alkene to the less substituted propargylic side of the alkyne dicobalt complex, and by having an isopropyl ether at the substituted propargylic site, the reaction went with almost full selectivity (Scheme 1.12).



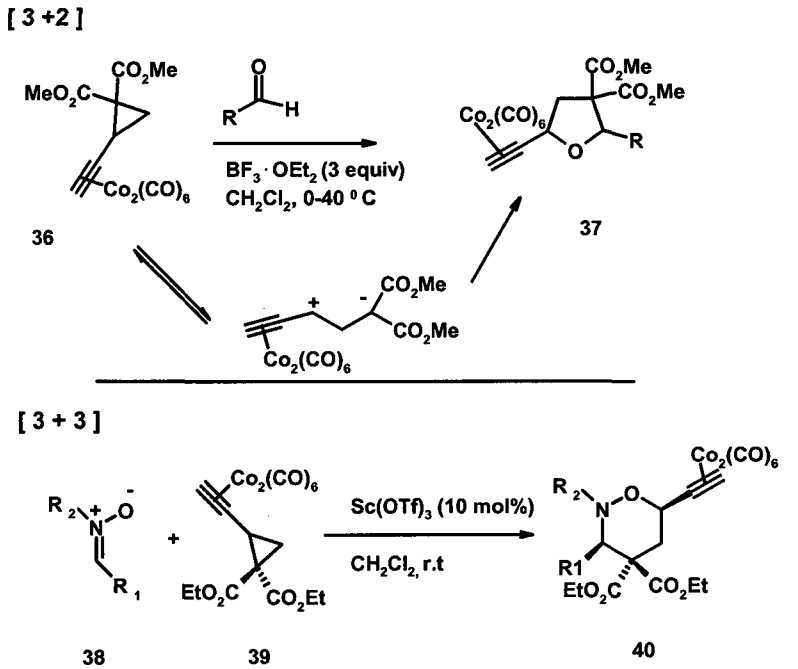
Scheme 1.12. Site selectivity in intermolecular Nicholas reactions.

A novel method for the synthesis of cycloheptyne cobalt complexes, through [5+2] cycloadditions, has been provided by the Tanino group.[45] In their elegant design, two C-C bonds were made sequentially from intermolecular Nicholas and intramolecular Nicholas reactions. In this process, initial attack of enolsilane to the propargylic carbocation forms the first C-C new bond, which then is followed by second attack of allyl TMS to the newly generated siloxyalkyl carbocation. The second attack of a nucleophile finalizes the cycloheptyne ring formation with an exo-methylene group at the propargylic site. This method, with slight changes on the propargyl substrates (R = OTIPS), has been used in the synthesis of conjugated keto-cycloheptynes, **35** (Scheme 1. 13).



Scheme 1.13. [5+2] cycloaddition via intermolecular Nicholas reactions.

Other types of cycloadditions (exocyclic) through intermolecular reactions of Nicholas carbocations are also known. Among them, the [3 +2] cycloaddition by the Christie group and [3+3] dipolar cycloaddition by the Kerr group are especially remarkable. Christie's group has generated a Nicholas- type carbocation from the cleavage of C-C bond for the first time and has used it in the synthesis of highly substituted tetrahydrofurans (**37**), as shown in (Scheme 1.14).[46] Later, Kerr and coworkers, in an analogous fashion, used activated cyclopropanes in reactions with nitrones to prepare tetrahydro-1,2-oxazines (**40**) through [3+3]- dipolar cycloadditions.[47]



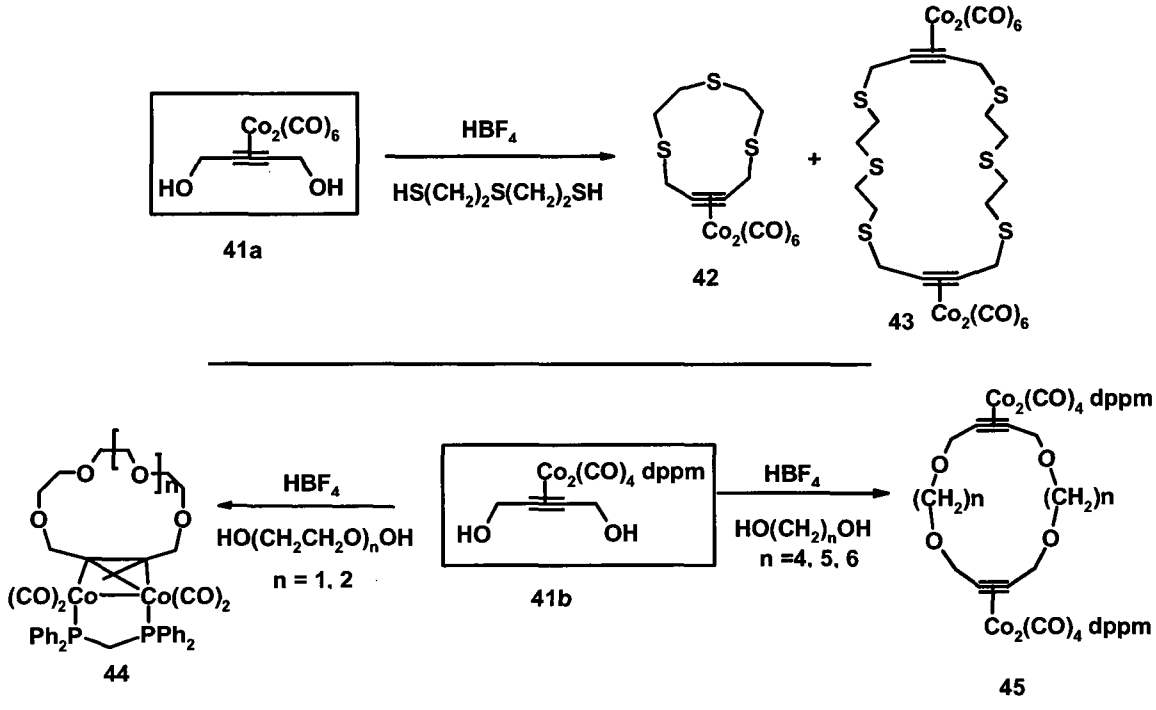
Scheme 1.14. [3+2] and [3 +3] cycloadditions via intermolecular Nicholas reactions

1.3.4 Macrocyclic formation from propargylic cations

Application of the Nicholas reaction in construction of small and medium sized alkyne rings has been extended to larger ring systems with special attention towards both rigid and flexible (crown type) macrocycles. The importance of these systems is reflected in their widespread application as binding ligands for metals or cations, in nanoscience, natural products and more.[48-50]

Sequential bispropargylic carbocations, such as those derived from **41a** and **41b**, have been used in intra and intermolecular Nicholas reactions with a variety of bifunctional nucleophiles, such as alkanedithiols and alkanediols to give access to linear bispropargylic ethers and crown-like macrocyclic ethers/thioethers of various ring sizes. Went and coworkers have thoroughly investigated this area and were able to synthesize

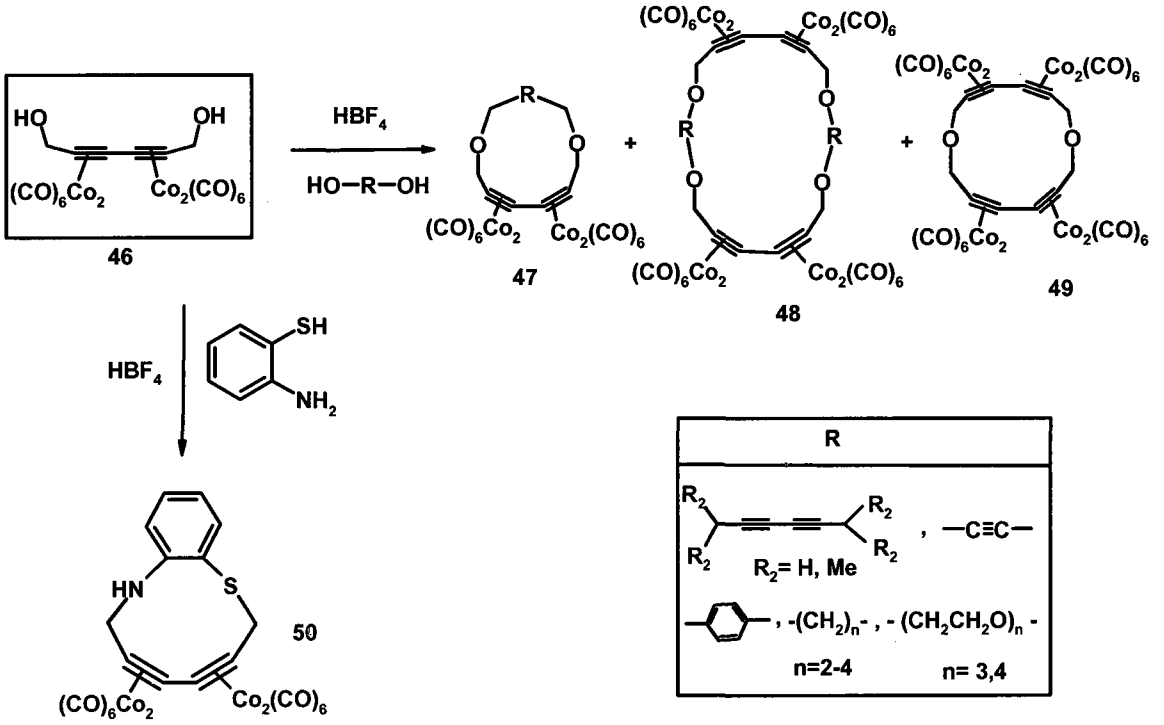
numerous macrocyclic alkynes containing oxygen and sulfur with a potential application for use as bidentate or crown type ligands (compounds **42-45**).[48a,b]



Scheme 1.15. Nicholas reaction in synthesis of macrocyclic compounds containing oxygen and sulphur atoms.

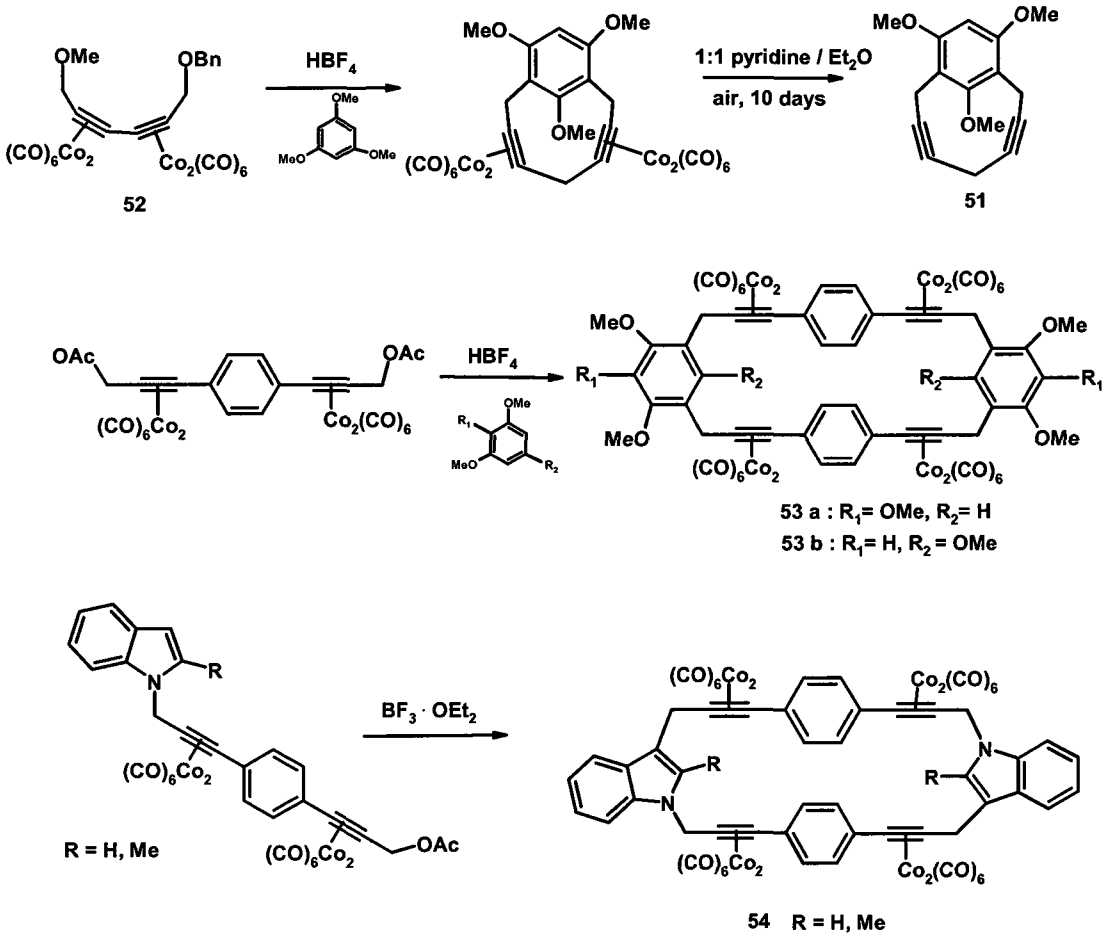
The Mays group has used bispropargylic dialkyne cations in a similar manner to obtain large (up to 28 membered) crown type macrocycles with diyne units in them. When diol **46** was treated with different diols, in the presence of acid, a mixture of monomeric **47**, dimeric **48** as well as self-condensation products **49**, were obtained. The ratio of these products has been shown to be highly dependent on the concentration of the diols and the nature of the linkers in the diols. It seems that with the more bulky and rigid R groups (linkers) such as alkynyls and p-phenylene, the dimeric compound forms favourably, with monomeric product being favoured with glycols as linkers, and a mixture of both products forming with alkyls or 1,3-diynes as linkers.[49] In related work,

the Mays group have explored the synthesis of 1,3-diyne- macrocycles with mixed S, N donor atoms in them. They have found, only in case of 2-aminothiophenol, that double nucleophilic addition could furnish 10-membered macrocyclic **50,** while other substitution patterns and the use of 2-mercaptopyridine gave linear chain products (Scheme 1.16).[50]



Scheme 1.16. Nicholas reaction in synthesis of macrocyclic compounds with diyne units in them.

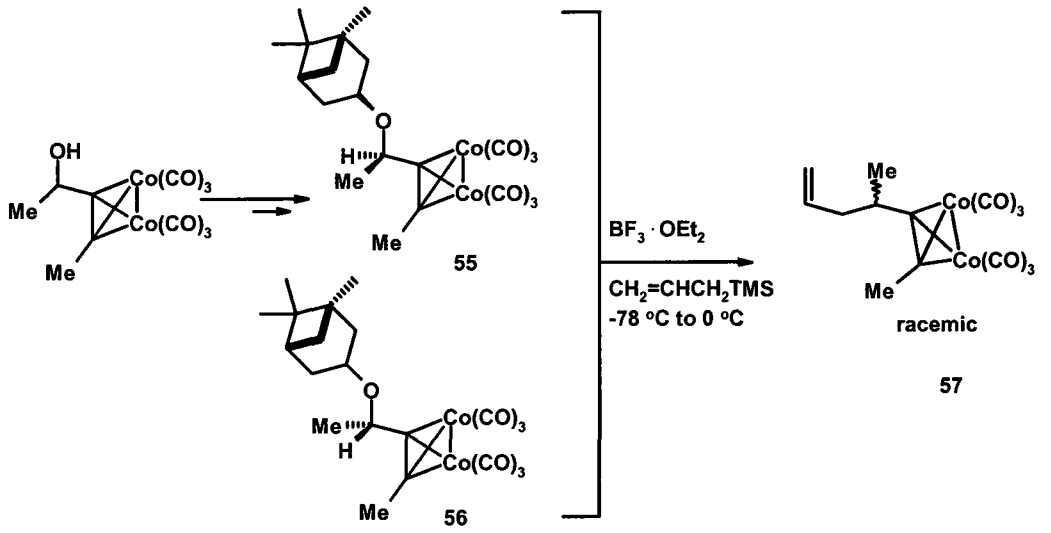
Green and coworkers have reported the synthesis of various cyclophanes through Nicholas reactions. They have found a rapid access to highly strained metacyclophanediynes such as **51** by addition of electron rich arenes to propargylic ether **52.** In a similar manner, cyclophanetetraynes **53** and indolophanetetrayne **54** were obtained under high dilution conditions with an excess amount of Lewis acid and a stoi-chiometric amount of nucleophile (in case of **53a** and **53b**).[51]



Scheme 1.17. Nicholas reaction in synthesis of cyclophanes of different sizes.

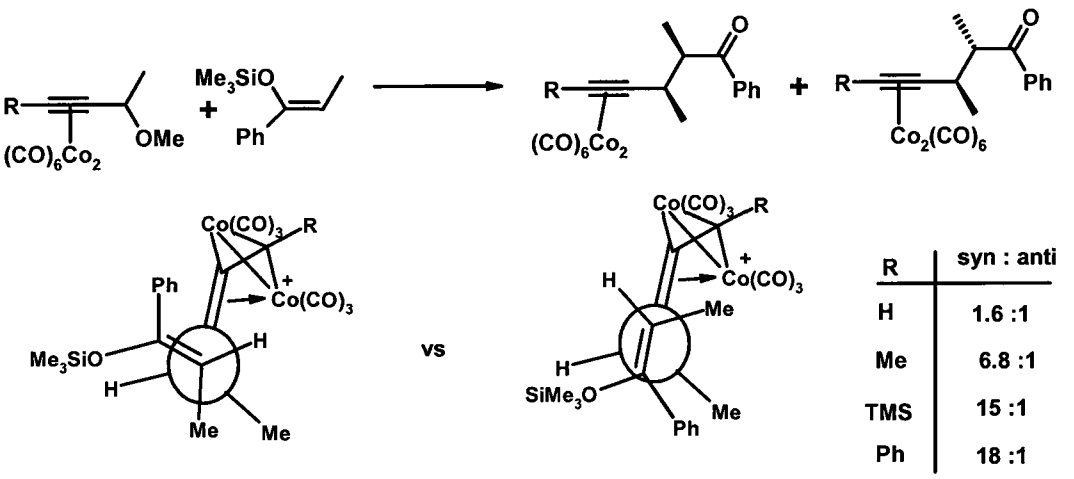
1.4 STEREOCHEMISTRY OF THE NICHOLAS REACTION

The complex fluxional processes possessed by cobalt carbonyl propargyl cations have several implications in stereochemical properties of the Nicholas reaction. Since the rapid antarafacial migration results in the loss of pre- existing chirality at that site (see Scheme 1.5), it is not surprising that when chiral cobalt complex **55** and **56** were separately subjected to a Nicholas reaction with allyltrimethylsilane, racemic product **57** was obtained in each case (Scheme 1.18).[20]



Scheme 1.18. Nicholas reaction with chiral cobalt complexes

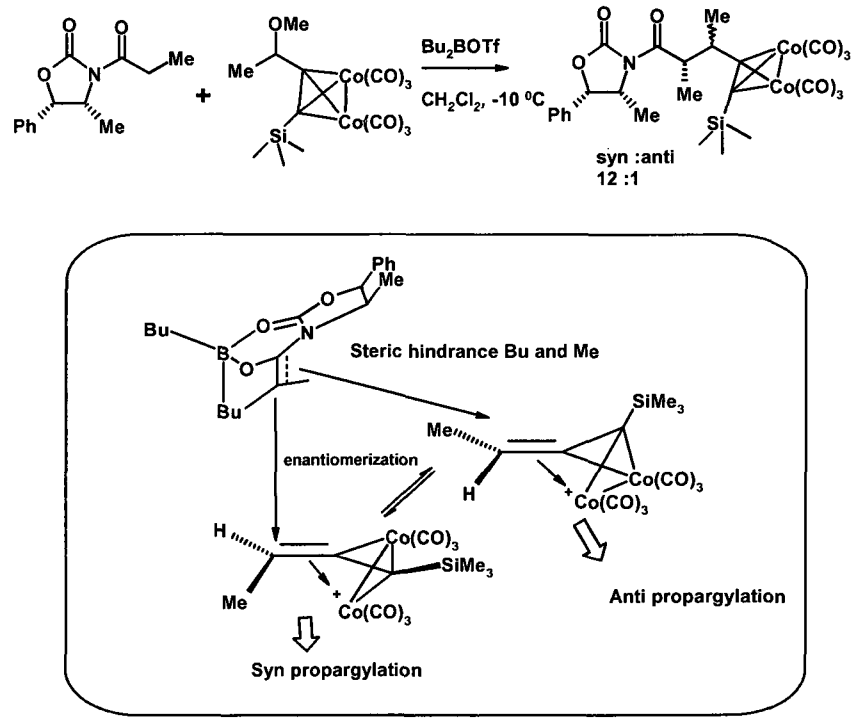
On the other hand, it has been shown that the presence of the bulky cobalt cluster can affect stereochemical orientation of the cations towards some nucleophiles and results in stereoslective propargylation of prochiral nucleophiles, such as silyl enol ethers. Schreiber has proposed a synclinal orientation of the C-C double bond of the enol ether and the alkynyl-propargyl bond in order to explain the observed diastereoselectivity and its dependency on the size of the remote alkynyl group (Scheme 1.19).[34b]



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

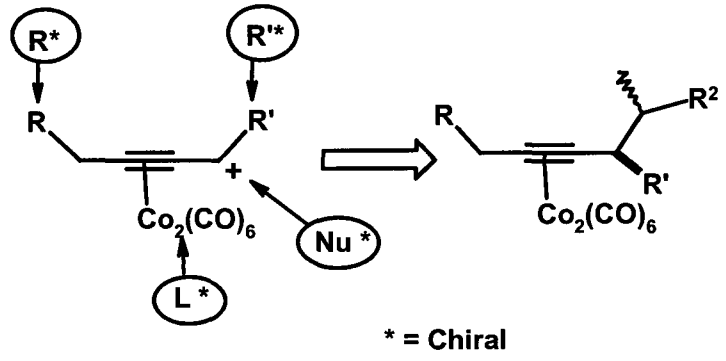
Scheme 1.19. Stereoselective propargylation of a prochiral nucleophile.

In other words, if enantiomerization of a cobalt cation combines with a relative face-selectivity of the reaction, kinetic resolution of chiral cations with chiral/prochiral nucleophile might be possible. Therefore, high stereoselectivity might be achievable in Nicholas reaction by careful selection of nucleophiles and propargyl cations through kinetic resolution. In this regard, Schreiber has investigated the reaction of propargyl cations with chiral nucleophiles such as the boron enolates derived from chiral propionimides (Evans' enolates). In accord with the previous assumptions on possible double stereodifferentation, these reactions occurred with a good level of enantiofacial selectivity, suggesting rapid enantiomerization of the propargyl cation relative to alkylation (Scheme 1.20). The proposed transition state for this reaction shows favourable interaction (less steric hindrance) between one of the two *syn* enantiomers and the boron enolate, which results in more *syn* propargylation (Scheme 1.20).[20]



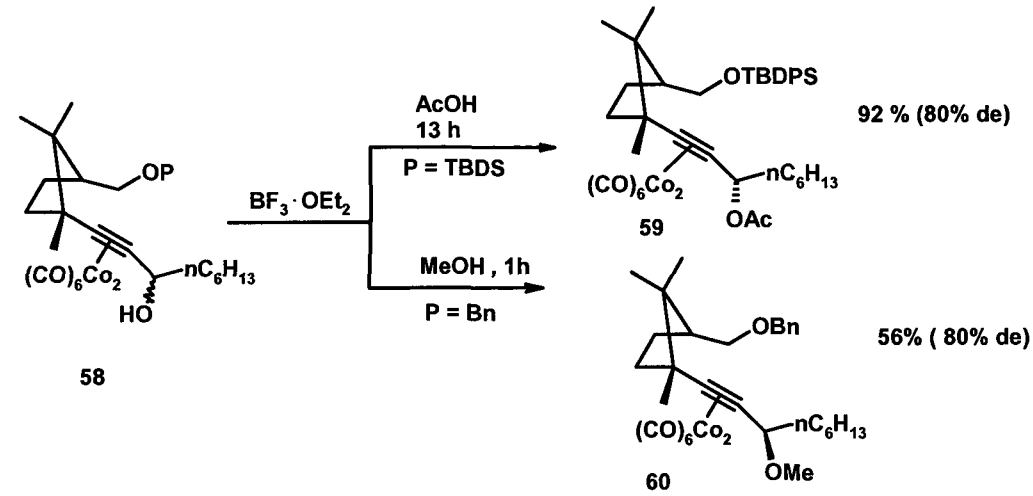
Scheme 1.20. Stereoselective Nicholas reaction with a chiral nucleophile.

In addition to the usage of chiral nucleophiles (such as Evans' boron enolates) and bulky substitutents, several other approaches have been taken to perform asymmetric Nicholas reactions. The two other alternative methods include: (1) introduction of chiral substituents on the propargylic chain; either proximal (R') or distal (R) to the cationic site; (2) asymmetric induction from the metal cluster by desymmetrization of the ligands on metal (Scheme 1. 21).



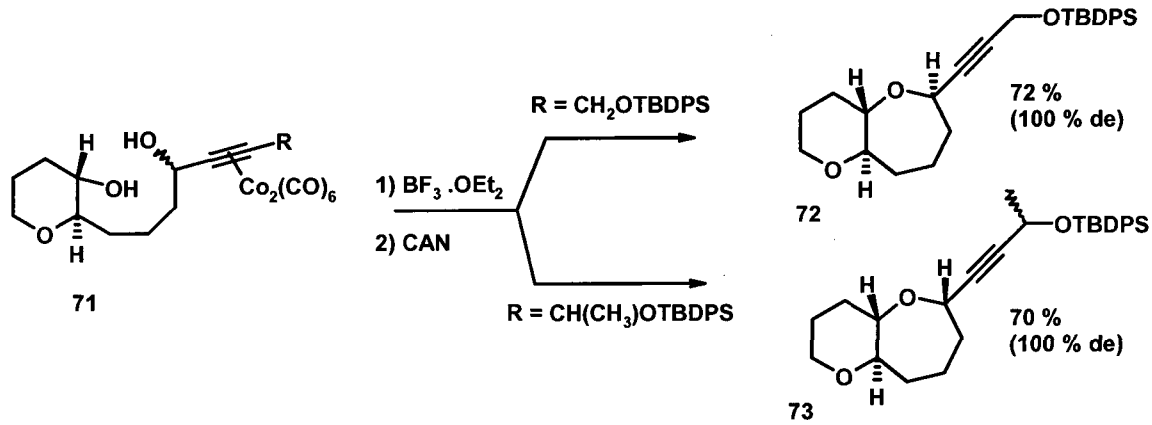
Scheme 1.21. Asymmetric induction in Nicholas reactions.

The Martin group has shown successful chirality transfer from a chiral substituent on the alkyl chain to the newly formed bond in both inter- and intramolecular Nicholas reactions. A diastereomeric mixture of propargyl dicobalt complexes **58** is readily accessible from camphoric acid. Upon acid treatment and under controlled reaction conditions, **58** can give access to both diastereomers of solvolysis products (**59** and **60**). It has been shown in the absence of any nucleophile or when MeOH was used as nucleophile, the kinetic product **60** was obtained in high yield, but when acetate was used as the nucleophile over a long reaction time, the thermodynamically more stable product was obtained (**59**). This can be explained by the acetate's ability to act as both nucleophile and as a leaving group, which results in an equilibrium situation to reach the thermodynamically stable product (Scheme 1.22).[52a]



Scheme 1.22. Chirality transfer in intermolecular Nicholas reactions.

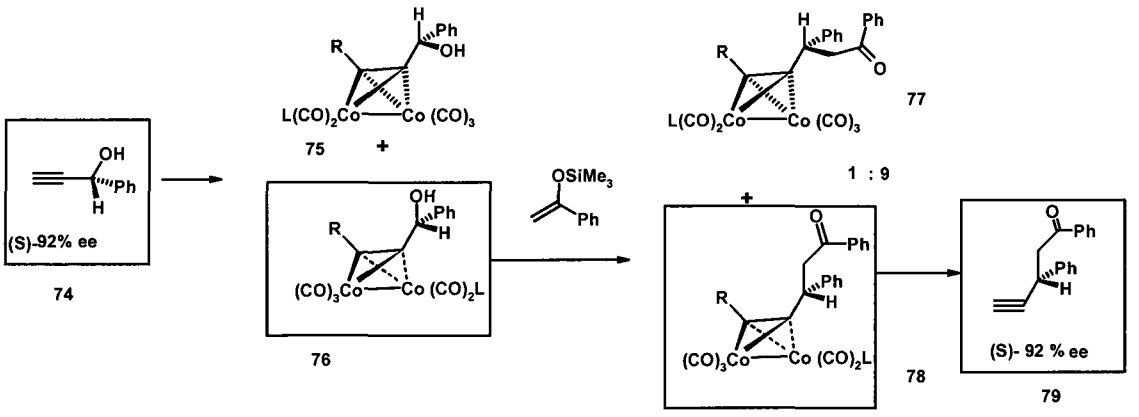
The same group has examined the feasibility of chirality transfer from an additional stereocenter in intramolecular Nicholas reactions. This work has been demonstrated in the synthesis of 6,7 and 6,8 membered bicyclic ethers (Scheme 1.23).[52b]



Scheme 1.23. Chirality transfer in intramolecular Nicholas reactions.

Asymmetric induction through chiral clusters has been investigated by the Nicholas group. In their initial investigations, diastereomeric cobalt complexes of chiral propargyl alcohols were prepared by using the unsymmetrical $Co_2(CO)_5PPh_3$ fragment

instead of the commonly used $Co_2(CO)_6$. These complexes have shown greater configurational rigidity in their cationic forms (due to higher energy barriers for isomerisation) and improved diastereoselectivity in reactions with oxygen based nucleophiles. On the other hand, their reactivity towards milder nucleophiles was significantly decreased due to the electron rich character of the phosphine ligand.[53a,b] To overcome the low reactivity associated with phosphine based ligands, the same group has incorporated a bulky and strongly π-accepting ligand $P[OCH(CF_3)_2]_3$, into the cobalt cluster and investigated its potential for asymmetric induction in Nicholas reactions . Moderate to high diastereoselectivity with absolute retention of stereochemistry (when an enantiomerically enriched propargyl alcohol was used) has been achieved for Nicholas reaction of alkynyl-$Co_2(CO)_5L$ clusters (L= $P[OCH(CF_3)_2]_3$ **74** with mild carbon nucleophiles. The diastereoselectivity of the reaction was found to be dependent on both the nature of nucleophilic partner and the substituents on the propargylic site Scheme 1. 24.[53c]

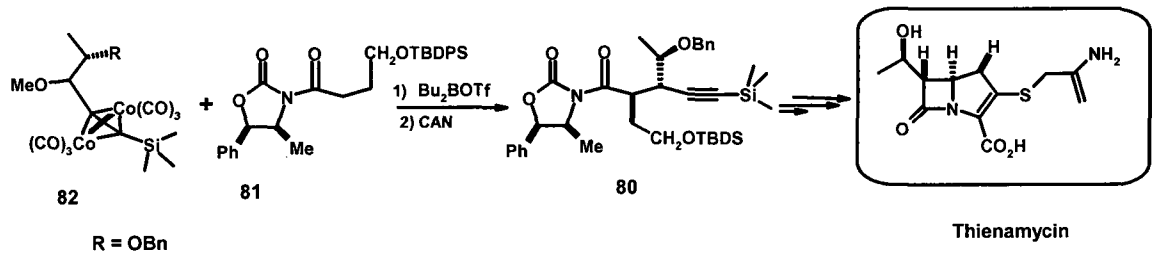


Scheme 1. 24. Assymetric induction through chiral cluster.

1.5 HIGHLIGHTS IN THE APPLICATION OF NICHOLAS REACTION IN NATURAL PRODUCTS SYNTHESIS

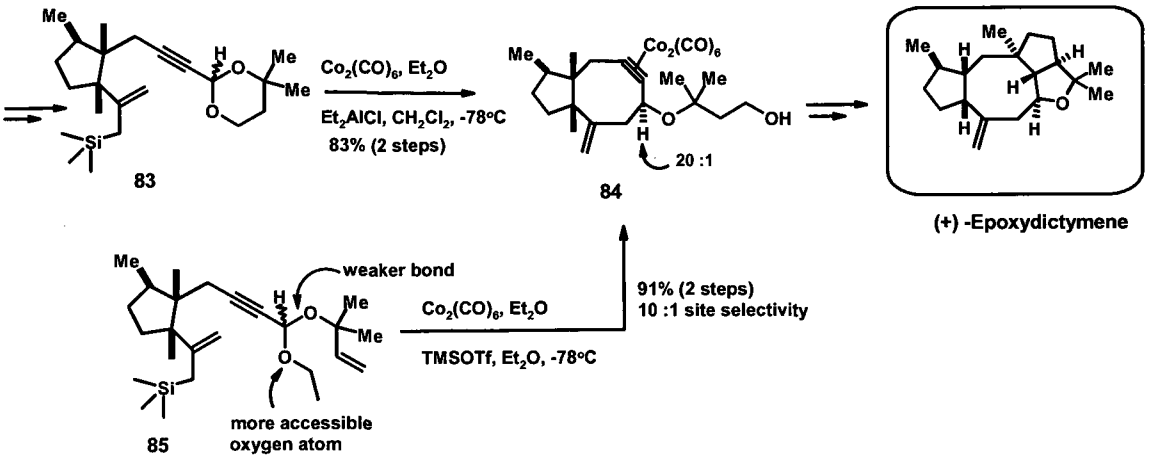
While some research groups have their attention focused on the scope and limitations of the Nicholas reaction itself, other research groups have applied the Nicholas reaction in the multi-step synthesis of biologically or structurally important compounds. Among many interesting examples of the Nicholas reaction in synthesis, its application in total synthesis of thienamycin by Jacobi, (+)-epoxydictymene by Schreiber, ciguatoxin 1B by Isobe, N-acetylcolchinol-O-methyl ether (NSC 51046) by Green, and the core of dynemicin by Magnus, are worth of note .[54a-e]

In the formal total synthesis of thienamycin[54a] reported by Jacobi, the Schreiber modified Nicholas reaction was used as a key feature to control both relative and absolute stereochemistry at the stereocenters (Scheme 1.25). In the model studies towards the total synthesis, they observed excellent diastereo- and enantioselectivity (*syn:anti* ratio of > 98:2) in the condensation of a chiral enolate with chiral propargyl ether in case of matched substrates. Additionally, the great influence of the chiral substituent of the alkyne complex on the stereochemical outcome of the Nicholas reaction has been illustrated; when the same reaction was repeated with a model chiral propargyl ether and achiral boron enolate, gave the same diastereoselectivity ratio (*syn:anti* = 98:2). Eventually, the desired stereochemistry of thienamycin was obtained in precursor **80** by a mismatched condensation of oxazolidinone **81** with cobalt complex **82**. This condensation reaction afforded the precursor to thienamycin (**80**) in 79 % yield with ~ 17 :1 *anti*-selectivity (Scheme 1. 25).



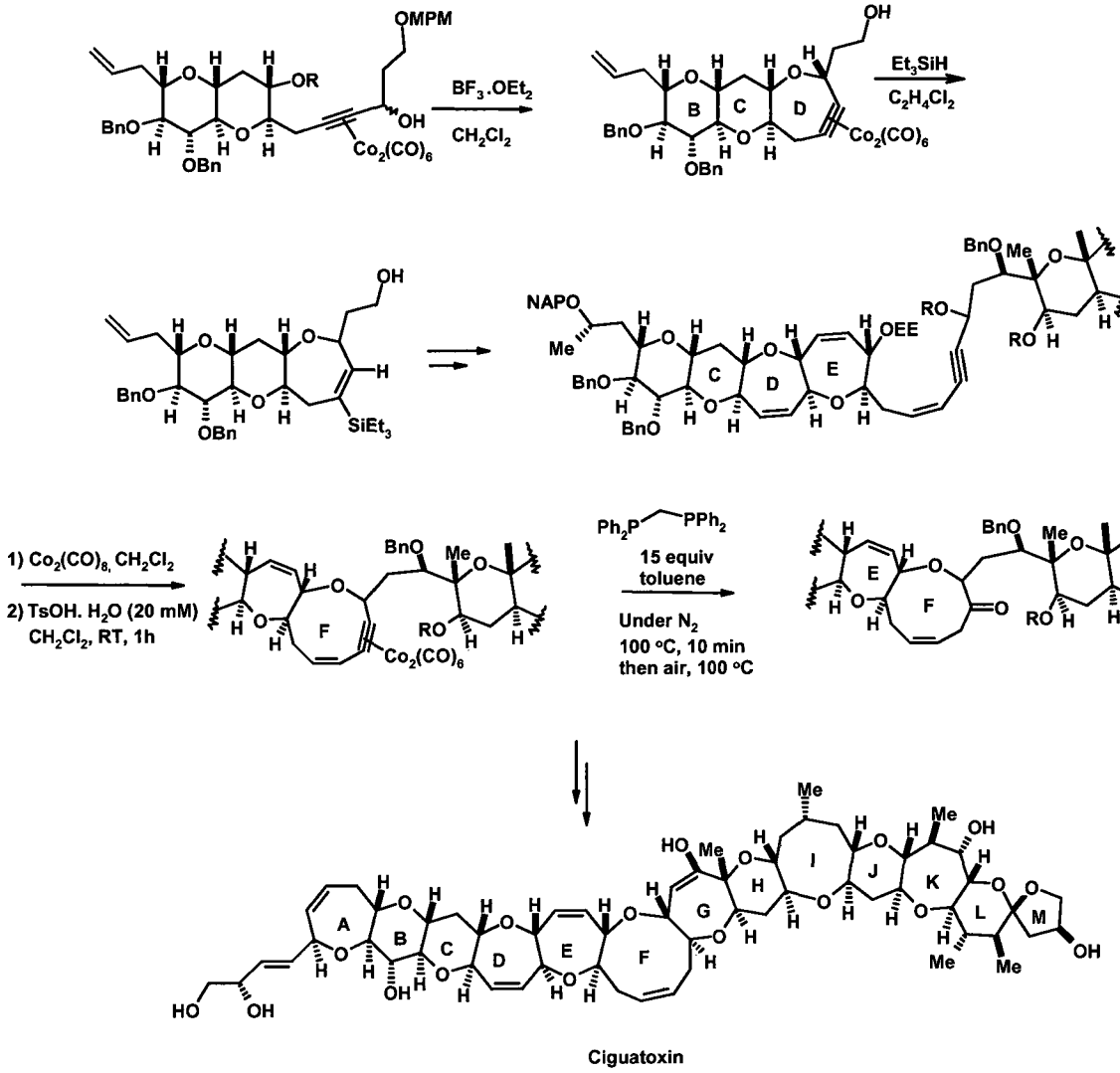
Scheme 1.25. Nicholas reaction in total synthesis of thienamycin.

In the reported total synthesis of (+)-epoxydictymene by Schreiber[54b], the rather difficult cyclization to an 8-membered ring was achieved by treating **83** with a stoichiometric amount of Et_2AlCl at low temperature. The cyclization occurred with complete regioselectivity and high diastereoselectivity to afford **84**. Furthermore, the authors explored the efficiency of the simillar procedure for acyclic acetal **85**, with the intent to find a more direct route to the Pauson-Khand educt. The cobalt complex of acyclic acetal **85** was found more resistent towards cyclization and a range of site selectvitity was obtained depending on the reaction conditions; the best result was obtained with TMSOTf and diethyl ether as solvent. According to this study, it seems between two competing factors affecting the removal of the alkoxy group by the Lewis acid, the accesibility of the oxygen atom outweighs the weaker C-O bond of tertiary alkoxy substituents (Scheme 1. 26).



Scheme 1.26. Nicholas reaction in total synthesis of (+)-epoxydictymene

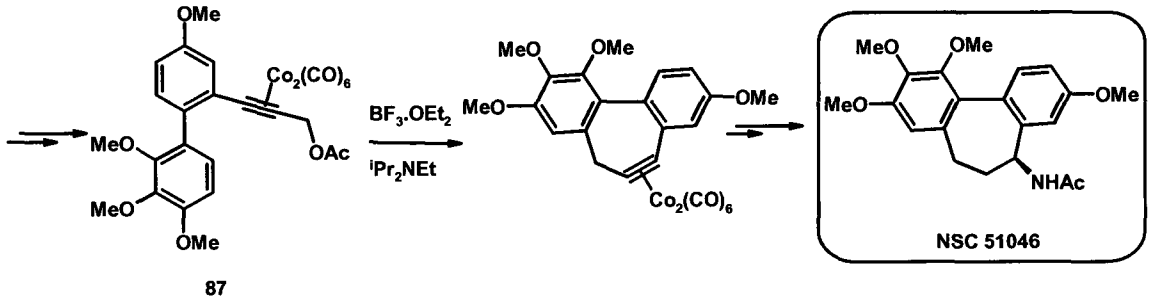
The reported total synthesis of ciguatoxin by Isobe[54c] featured the great ability of acid induced Nicholas reactions in the construction of 7-,8- and 9- membered cyclic ethers with all syn/trans stereochemistry at ring junctions (D, E, F, I) . Furthermore, reductive decomplexation of endocyclic acetylene cobalt complexes to either olefins or vinylsilanes and an oxidative decomplexation to a ketone were also used at different steps of synthesis (Scheme 1.27).



Scheme 1.27. Construction of the 7, 8 and 9 membered rings of ciguatoxin by Nicholas reactions.

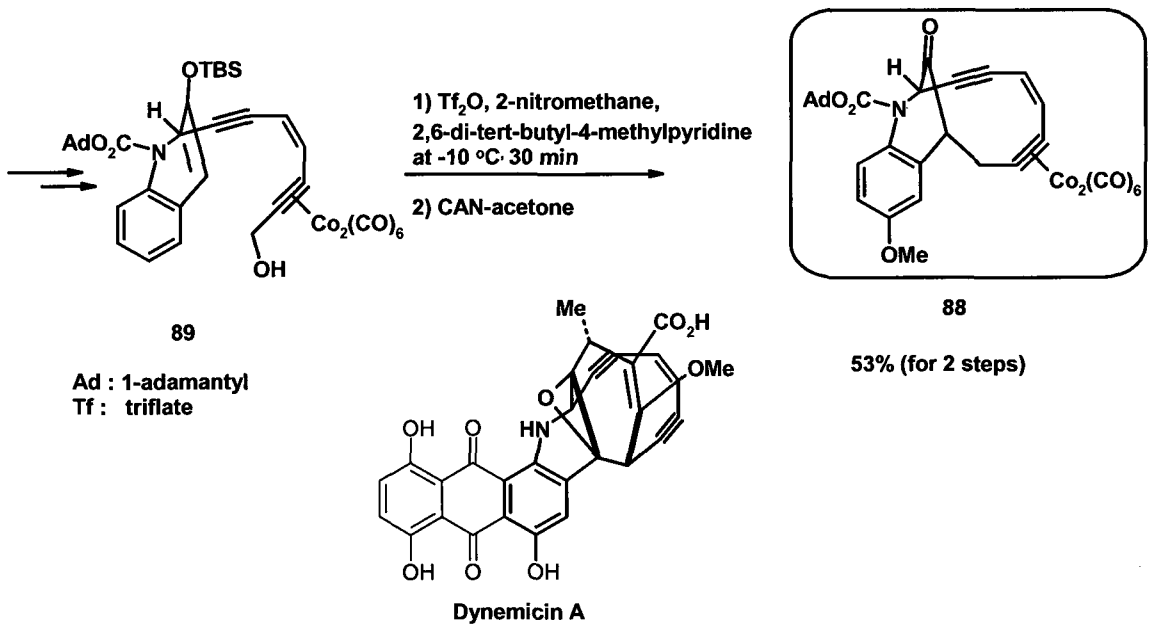
Green[54d] has reported the first total synthesis of allocolchicine NSC 51046, wherein, a suitably positioned dicobalt propargyl cation was generated upon the addition of the Lewis acid and captured by a remote electron-rich aryl group in an intramolecular manner. The presence of diisopropylethylamine was found to be beneficial for the reaction yield but caused lengthening of the reaction time. This intramolecular Nicholas

cyclization led to the straightforward formation of 7-membered ring in tricyclic core of the allocolchicines (Scheme 1.28).



Scheme 1.28. Nicholas reaction in total synthesis of allocolchicine NSC 51046.

In another novel strategy, Mangus[54e] was able to extend the intramolecular Nicholas cyclization into the synthesis of the 10-membered ring of the core of dynamicin A (**88**). Treating **89** with triflic anhydride at -30 °C in 2-nitropropane containing of 2,6-di-*tert*-butyl-4-methylpyridine generated the propargyl cation in situ; its reaction with the enol silane afforded the desired 10-membered ring rapidly (Scheme 1.29).



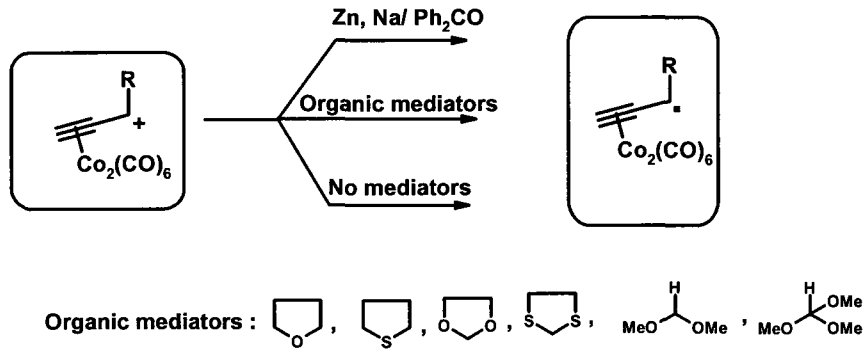
Scheme 1.29. Nicholas reaction in synthesis of the 10-membered ring core of dynamicin A.

1.6 PROPARGYLDICOBALT RADICAL FORMATION

There has been a growing interest in the chemistry of organometallic radicals, mainly due to their application in catalytic processes and syntheses. Although many reports exist on the formation of organometallic radicals and their subsequent reactions, the exact nature of the metal interaction with the radical center is not fully understood. To date, radical couplings of this kind with high stereo-, chemo- and regioselectivity are known as valuable methods for C-C bond formation. Furthermore, with the help of the metal fragment, new methods of radical generation are now available which can give access to otherwise inaccessible organic radicals.

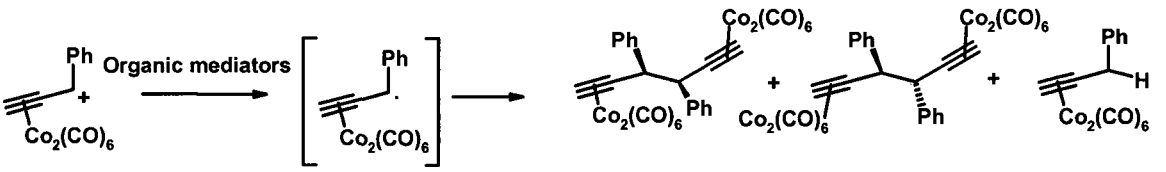
Propargyl radical- $Co_2(CO)_6$ complexes belong in this category. They can be generated from the corresponding cations and undergo inter- or intramolecular coupling

reactions. The radical formation is possible either in the presence of organic mediators such as THF, various reducing reagents (such as Zn, Na/Ph_2CO), or even in the absence of any external mediator when propargyl cations have suitable substituents (Scheme 1.30).[55]



Scheme 1.30. Propargyl dicobalt radical generation.

The Melikyan group has investigated the chemistry of cobalt propargyl radicals in detail. In their preliminary studies, they reported the highly diastereoselective (98 % de) synthesis of cyclooctadiynes, from intramolecular coupling of propargylic diradicals, which themselves were generated by the addition of hetero- or homogeneous reducing agents such as Zn or Na/Ph_2CO to the corresponding dications.[55a] Later, they reported the intermolecular dimerization of compound **90** under homogeneous conditions by using organic molecules such as tetrahydrofuran and tetrahydrothiophene as radical mediators (Scheme 1. 31).[55b]



90

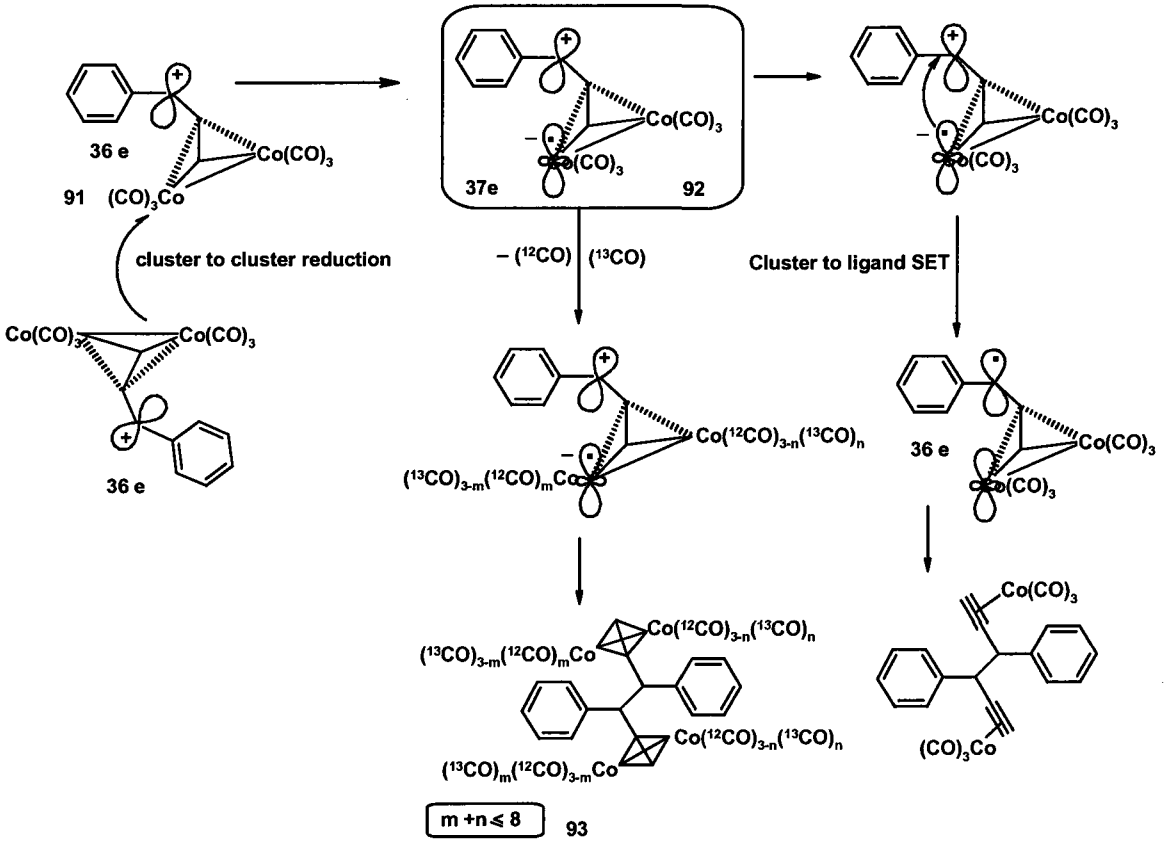
Scheme 1.31. Propargyl dicobalt radical coupling reaction under homogeneous conditions.

The first spontaneous generation (in the absence of any radical mediator) of aryl-substituted $Co_2(CO)_6$-propargyl radicals followed by an intermolecular coupling was reported by the Melikyan group in the synthesis of (d,l)-3,4-diaryl-1,5-alkadiynes.[55c] More recently, the effect of high temperature on the spontaneous dimerization reaction of propargyl radicals such as **92** has been investigated. It has been shown that the reaction time can be reduced from 660 min at 20 °C to 1 min at 147 °C without a dramatic change in diastereoslectivity or the yield of the reaction. Furthermore, the rate of the reaction was also found to be dependent on electronic nature of the substituents and their position on the phenyl ring.[55d]

Among different methods that exist for $Co_2(CO)_6$-propargyl radical coupling reactions, spontaneous and THF- mediated radical couplings were found to be the most efficient ones. The proposed mechanisms for these reactions are depicted in Scheme. 1.32 and 1.33.

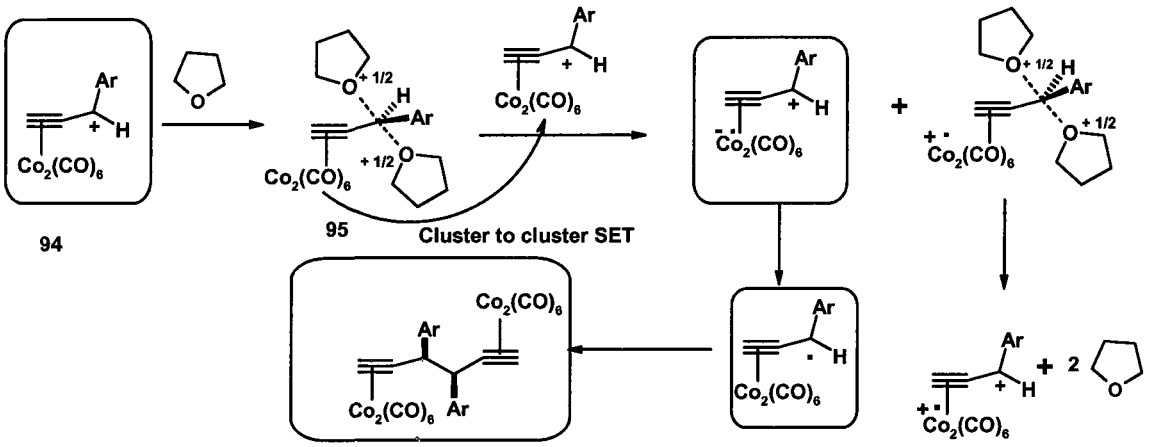
In the proposed mechanism for spontaneous reaction (Scheme 1.32), cluster to cluster reduction and formation of a reduced metal cluster (**92**) was confirmed by isotopic enrichment experiments in which an incorporation of up to eight ^{13}CO ligands in to the metal cores of the dimer was detected (**93**). Accelerated ligand substitution (replacement) of this kind is generally observed in the reduced metal clusters. An alternative mechanism

that includes intramolecular reduction (cluster to ligand) prior to cluster to cluster electron transfer, was ruled out according to the calculational data and experimental results.[55d]



Scheme 1.32. Proposed mechanism for spontaneous propargyl dicobalt radical generation and its dimerization reaction.

In proposed mechanism for THF- mediated radical coupling (Scheme 1. 33), THF, although used in 2-fold excess, is believed to act as a catalyst. It can coordinate to the electrophilic center and accelerate cluster to cluster single electron transfer (SET) by changing the cobalt complexed propargyl cations (**94**) to a source of electrons (**95**), and ultimately separates from the organometallic molecule without any change.[55e]



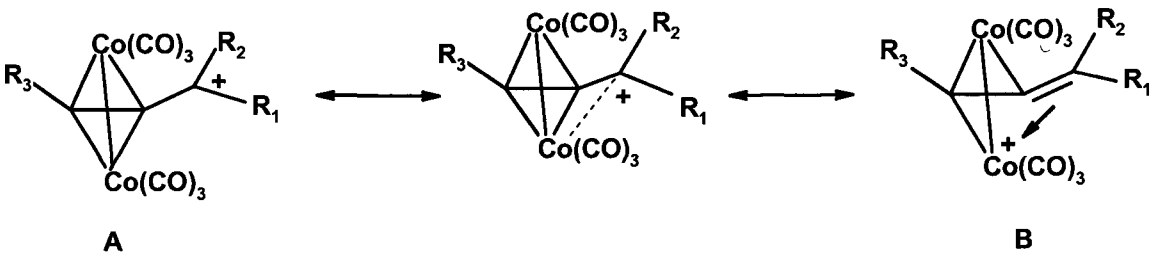
Scheme 1.33. Proposed mechanism for THF mediated propargyl dicobalt radical dimerization.

1.7 STRUCTURAL EFFECTS OF PROPARGYL CATIONS IN THE NICHOLAS REACTION

Despite a large amount of information on the application of Nicholas carbocations in organic synthesis, the structural variation of cation itself and its influence on the outcome of Nicholas reactions has not been fully explored.

In the same manner, the precise distribution of a positive charge in these cationic systems is not well understood, even though they are widely accepted as highly delocalized cationic systems. Nicholas realized that while spectroscopic data (^{1}HNMR, ^{13}CNMR and IR) for a $Co_2(CO)_6$-propargyl cation complex was suggestive of positive charge being more localized on the metal, the influence of different substituents on the ^{13}C NMR signals of the cation was indicative of contribution of other substituents on the charge localization as well.[6c]

Later, Schreiber and coworkers, in their studies on the fluxional behaviour of a cobalt stabilized cation, demonstrated the unsymmetrical nature of cation and confirmed its view as alkylidene complexed cobalt cation (Scheme 1.34 structure B).[20] In their study, a comparison was made between primary, secondary and tertiary propargylic cations based on the activation barrier for enantiomerization (antarafacial migration) and syn/anti diastereomrization of each cation (see Scheme 1.5 for fluxional behaviour of Nicholas carbocations). The highest activation barrier for antarafacial migration, was found to be that of primary cation, which had the greatest demand for electron donation from the cobalt center (18 kcal/mol for primary vs 11 kcal/mol for tertiary cation).



Scheme 1. 34. Schematic representation of a Nicholas carbocation.

Similarly, McGlinchey's group in their study on several cobalt stabilized anti-aromatic cations, realized the extent of cobalt participation in charge stabilization would be inversely related to the stability of Nicholas carbocations. This also was justified based on variable temperature NMR studies of cations and X-ray crystallography data of structural models.[13a]

In summary therefore, it is now well established that amount of cobalt participation in stabilization of Nicholas carbocations varies depending on the stability of cationic center. Yet, to what extent the cation can be considered as metal stabilized if

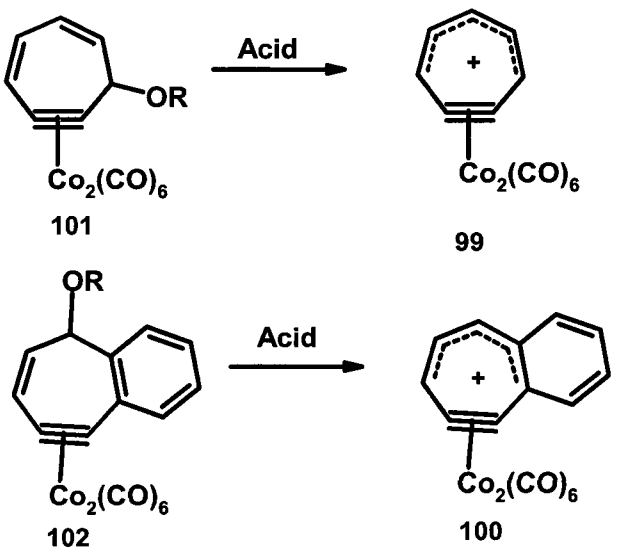
other sources of stabilization exist, and when the effect of metal in charge stabilization would disappear, has not been fully examined in these cations. Also, considering the significant structural changes that occur upon participation of cobalt in charge stabilization, adjusting such effects may bring some new insights into the chemistry of Nicholas carbocations as well as offering potential new applications. Hence in here, as primary focus of the project, we sought to design a new type of Nicholas carbocation that has multiple-stabilizing factors and perhaps expose a different stability than other common cations of this type.

On the other hand, similar to thermodynamic stability, detailed mechanistic investigation on reactivity of the Nicholas carbocations has not been reported yet. This lack of attention might be due to the narrow range of reactivity and stability that has been found for these cations based on substitutional changes. Nevertheless, there are a few reports in the literature on the effect of pre-existing factors such as substituents, leaving groups and metallic ligands on the reactivity and stability of propargyl dicobalt carbocations (substituents and ligand effects have been discussed in Section 1.2).

Here, as a contribution to the on-going interest in mechanistic aspects of Nicholas reaction, the secondary focus of the project was to investigate the relationship between the stability of a cationic species and its reactivity in Nicholas reactions.

To cover both aspects of thermodynamic stability and kinetic reactivity of Nicholas carbocations as described above, we envisioned a system with the possibility of aromatization upon the formation of the cation. For that, the structurally interesting dehydrotropylium dicobalt cation and its derivatives (Scheme 1. 35) were chosen. These systems, not only are among the rare examples of highly strained 7-membered

cycloalkynes, but also they can offer a great opportunity to compare or combine two possible sources of stabilization in Nicholas cations: "π interactions or resonance stabilization in a nominally aromatic system" versus localized "metal stabilization" (Scheme 1. 35).



Scheme 1. 35. Generation of dicobalt hexacarbonyl stabilized dehydrotropylium and benzo-fused dehydrotropylium cations.

Also, it is worth mentioning that in other cases where highly stable carbocations (such as tropylium and pryrylium rings) were attached to the organometallic fragments, minimal delocalizations of positive charge on metal centers were observed. In other words, X-ray crystallographic data, in accord with EHMO calculations, revealed no tendency for these cationic rings to lean towards metal moieties (Figure 1.10).[56a,b]

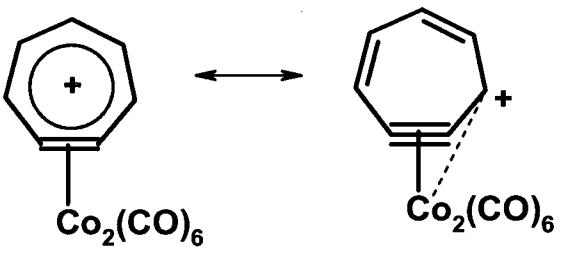
Figure 1.10. Pyrylium and tropylium salts bearing $(C_6H_5)Cr(CO)_3$ and ferrocenyl substituents respectively.

Based on these results, if a great amount of resonance stabilization exists in cations **99** and **100**, it would be expected to be the major factor in charge stabilization. That is, with structural analysis of the proposed cations we might be able to indirectly estimate the amount of resonance stabilization in the dehydrotropylium rings. This would answer the question on the possibility and the amount of aromaticity in dehydrotropylium dicobalt cation, which itself is interesting, based on the limited examples of small aromatic cyclynes.

With these in mind, we decided to synthesize the structures of type **101** and **102** as precursors to the desired aromatic cations and generate corresponding cations afterwards. This was followed by further investigation on the reactivity of the cations towards various nucleophiles.

2. GENERATION AND REACTIVITY STUDIES OF DEHYDRO-TROPYLIUM-$Co_2(CO)_6$ COMPLEX

2.1 AROMATICITY OF TROPYNE-$Co_2(CO)_6$ COMPLEXES



Knowing the limited stability of cycloheptyne, it is expected for highly conjugated cycloheptynes to be even less stable and more reactive than normal cycloheptynes.[57] Therefore, it is not surprising that there is no report on the isolation of dehydro-cycloheptatriene or any of its derivatives; nor is there any report for dehydrotropylium cation in the free form.

Figure 2.1. Dehydrocycloheptatriene and dehydrotropylium cation

The first example on the preparation and isolation of platinum complex of tropyne was reported by Jones group in 1992. Since then, the same group has prepared several transition metal complexes (Pd, Zr, Pd-Mo) of tropyne and studied the characteristic properties of these complexes (Figure 2.2). While these complexes have been fully characterized and in some cases their crystal structures were determined, aromaticity and stability of these cations were not the focus of these studies.[58]

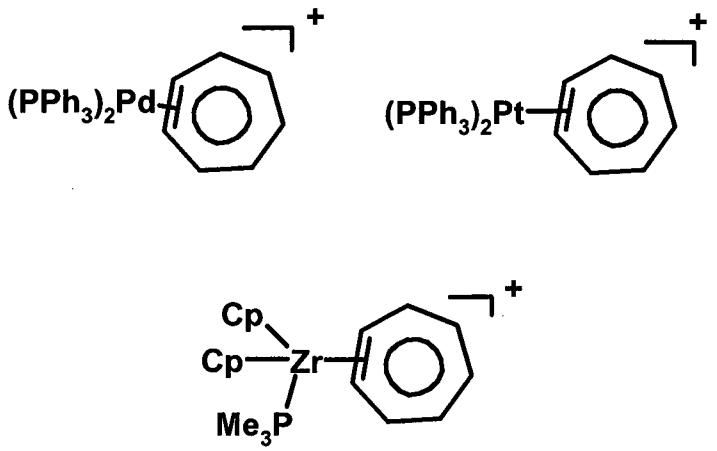


Figure 2.2. Selected transition metal complexes of tropyne.

Herein, we have focused on the dicobalt hexacarbonyl stabilized complexes of dehydrotropylium cations, for the reasons explained in Section 1.7 and most of all to explore the presence of aromaticity in such systems for the first time.

The question of what makes a compound aromatic has been a matter of debate for a long time. Despite the amount of confusion and controversy exist on precise meaning and definition of term aromaticity, it has long been employed as an accepted scientific term to describe a class of compounds with special characteristic properties. A wide range of criteria have been proposed for characterization of aromaticity. The most important ones can be summarized as: (1) geometrical criterion: bond length equalization; (2) chemical behaviour: electrophilic aromatic substitution; (3) enhanced stability: large resonance energy; (4) magnetic properties: ring current, magnetic susceptibility, ^{1}H NMR chemical shift, nucleus independent chemical shift (NICS). Based on these criteria, numerous methods have been developed to measure/quantify the amount of aromaticty in a wide range of chemically and structurally diverse compounds from planar aromatic hydrocarbons to inorganic analogues, all-metal clusters and many more.[59]

Benzene and its derivatives, historically established as aromatic compounds, are sometimes considered as the smallest stable member of a larger family of cyclic compounds called annulenes. Annulenes, are monocyclic compounds with alternating single and double bonds, where the number in bracket indicates the number of continuous sp^2 carbons. Annulenes with smaller/larger ring-sizes than benzene can range from non-aromatic ([8] annulene) to aromatic ([14]- or [18]-annulene) and anti-aromatic ([4] annulene) depending on the number of π electrons, size of the rings, strain and planarity of the system. When planar, annulenes have shown to obey Huckel's 4n+2 (aromaticity) /4n π (antiaromaticity) rule. For example, neutral [8]annulene exists as non-planar tub shaped and hence is non-aromatic, but if by suitable annelation forced into planarity, it would reinforce a paratropic ring current as expected for 4nπ electron (anti-aromatic) systems (Figure 2.3).[60]

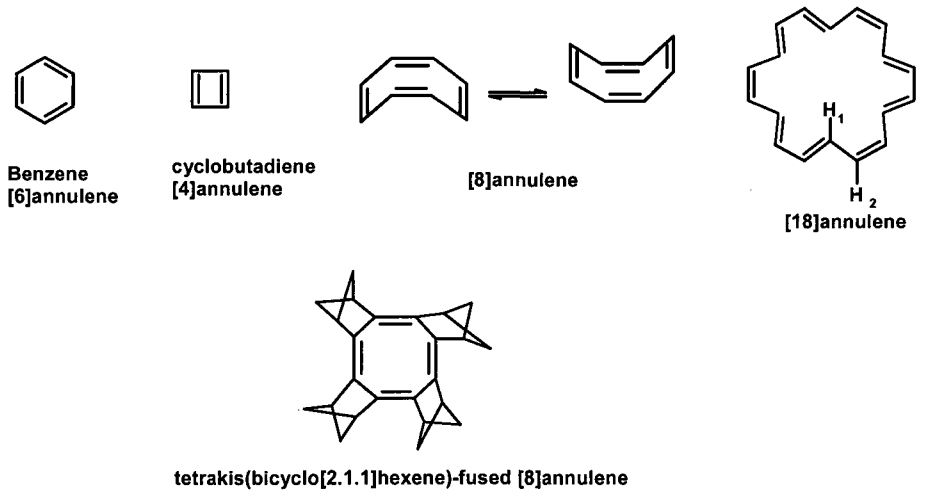
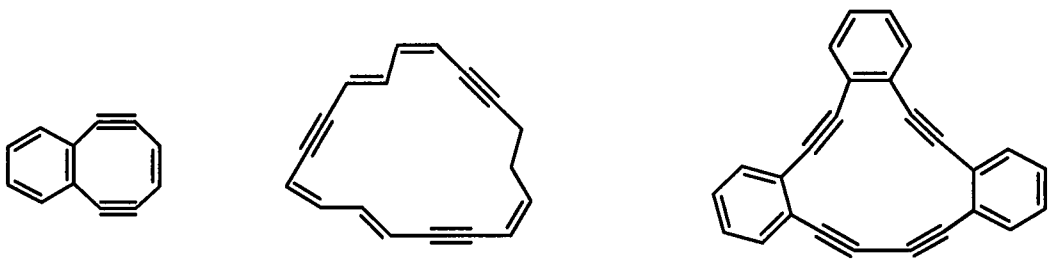


Figure 2.3. Annulenes of different sizes.

Dehydroannulenes, structurally related to annulenes, have regained attention in recent years. This is mainly due to the significant progress that has been made in synthesis of their complex structures and also for the discovery of their fascinating

chemical reactivities.The most spectacular finding in this area, might be Vollhardt's discovery[61] on explosive decomposition of large dehydroannulenes to carbon nano-materials, which stimulated considerable attention in the chemistry of such alkynes.

The original interest in these systems, however, was in connection with the aromaticity/antiaromaticity of annulenes and to see if the same type of π-bond delocalization could exist in dehydroannulenes in spite of the existing bond alternation.[62a] Indeed, numerous theoretical calculations and spectroscopic studies of isolated dehydroannulenes have proved dehydroannulenes (such as **103-105**) can be aromatic/antiaromatic in accord with 4n+2 /4n electron counts of Huckel's rule.[62b,c]

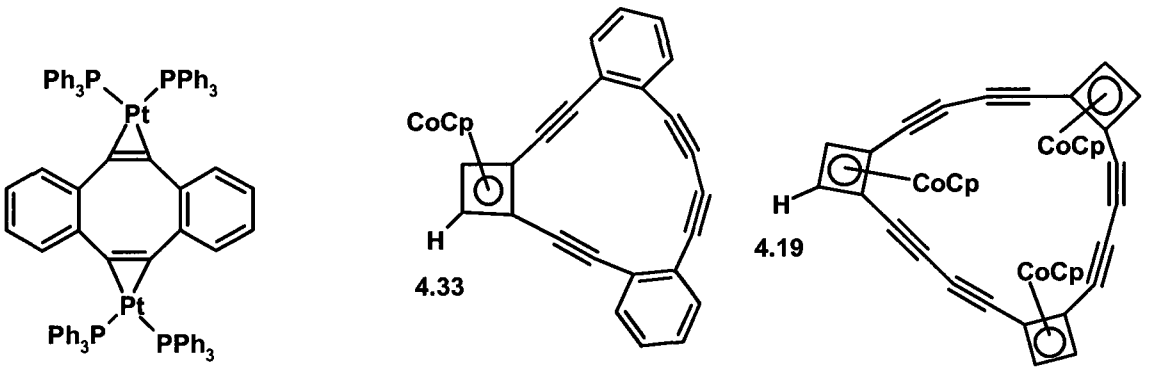


103 **104** **105**

Figure 2.3. Dehydroannulenes of different sizes.

Although dehydroannulenes are often considered less stable than their annulene counterparts, incorporation of the triple bond in some cases was found to be beneficial regarding to geometrical fixation of otherwise flexible non-planar annulenes. Benz-annulation is another factor commonly encountered in the chemistry of annulenes/ annulynes to improve the kinetic stability of these systems. Regarding to the tropicity of the system, benzannulation, incorporation of triple bonds as well as increasing the ring-size, have shown to weaken the overall diatropicity or paratropicity of a system.[62a]

Metal complexes of dehydroannulenes, are also known (**106 -108**, Figure 2.4).[63] Yet, in comparison to the large amount of data existing for metal free annulenes and dehydroannulenes, the chemistry of their metal complexes is less developed. This may be partly due to the lack of suitable organometallic modules and unavailability of conventional methods for construction of these systems. Nevertheless, the interest in this area is growing rapidly and a wide range of potential applications have either been found or predicted for these systems. Among them, their potential applications as precursors for carbon nanotube synthesis and as candidates for nonlinear optically (NLO) active materials are especially attractive.[64]



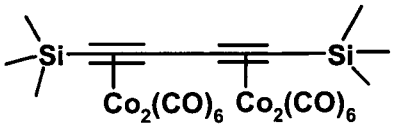
106 **107** **108**

Figure 2.4. Some known examples of organometallic dehydroannulenes.

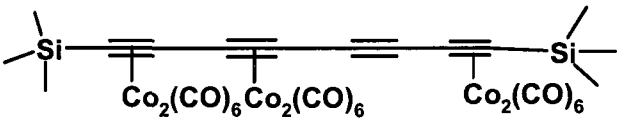
Bunz and coworkers, in their novel report on synthesis of compounds **107** and **108**, were able to detect weak diatropicity in these organometallic dehydroannulenes. Based on that, it was concluded the Huckel's rule is also in effect for organometallic dehydroannulenes. In this study, the ^{1}H NMR chemical shift of the protons on the cyclobutadiene was used as an aromaticity probe, which exhibited small downfield shift

upon the incorporation of cyclobutadiene in the dehydroannulene rings (**107** and **108**). Also, it was noticed as the ring size increased from **107** to **108** the amount of diatropicity decreased.[63b]

In summary, even though the study on aromaticity of organometallic dehydroannulenes is limited to a few available examples, the presence of such an effect has been confirmed. Also, it has been shown that the 4n +2/4n Hückel rule can be extended to planar annulenes/dehydroannulenes and their organometallic derivatives, albeit with consideration of the attenuating effect of increasing the ring size. Based on these and the fact that calculations[65] suggested, in complexed carbon chains such as **109** and **110,** a significant amount of conjugation can survive, we predicted dehydrotropylium dicobalt cation and its benzo-fused derivatives (**99, 100**) should exhibit aromatic character.

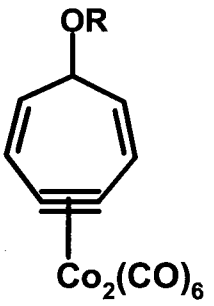


109

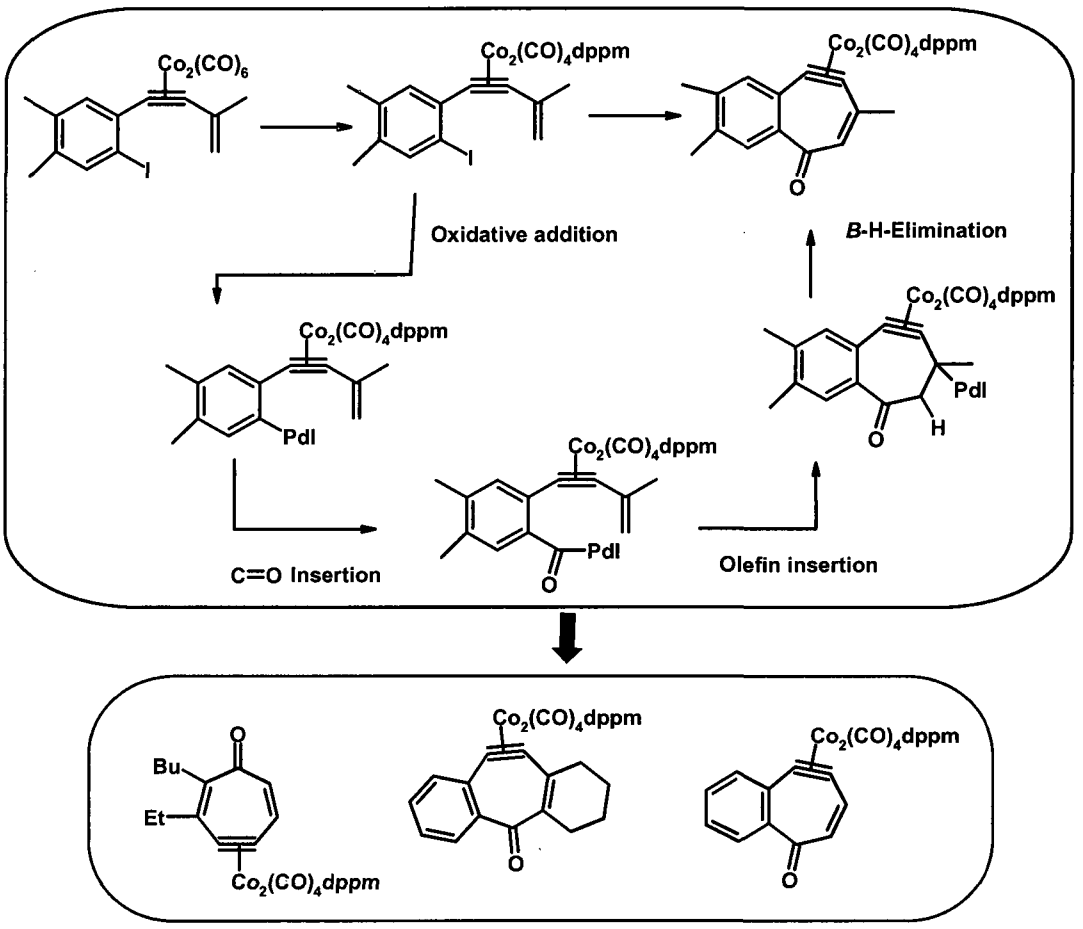


110

2.2 SYNTHESIS OF DEHYDROTROPYLIUM- $Co_2(CO)_6$ COMPLEX PRECURSORS



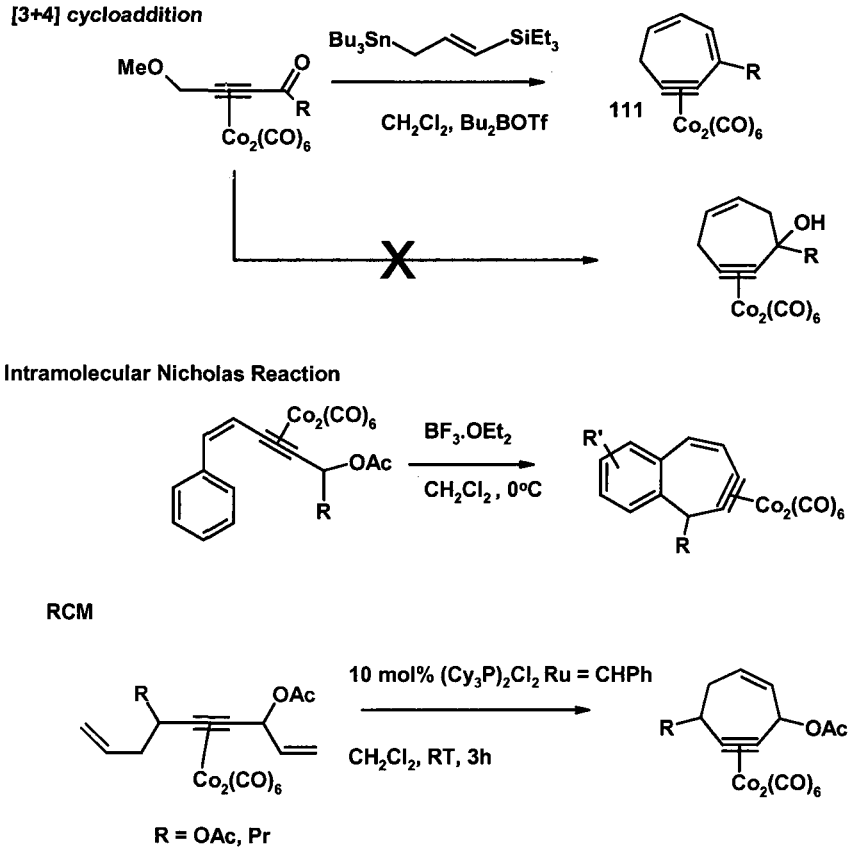
To the best of our knowledge, there is only one report on the syntheses of disubstituted dehydrotropone and benzo-fused dehydrotropones in the form of $Co_2(CO)_4$dppm stabilized complexes. In this elegant synthesis, Iwasawa and Satoh, were able to apply palladium-catalyzed Heck-type carbonylative cyclization in to the synthesis of highly conjugated $Co_2(CO)_4$dppm- 4,5-didehydrotropones.[66] The reaction failed when common $Co_2(CO)_6$-alkyne complexes were used, presumably due to low thermal stability of these complexes. Also, this method was not successful in the synthesis of the parent dehydrotropone, as only disubstituted and benzo-fused systems could be synthesized (Scheme 2.1).



Scheme 2.1. Palladium-catalyzed Heck-type carbonylative cyclization.

This method, even though attractive due to the straightforward accessibility it offers for this class of compounds (with the limitation regarding the unsubstituted dehydrotropone), suffers from limited reactivity of the final products. It is a known fact that phosphine substituted cobalt complexes of alkynes have considerably lower reactivity in Nicholas reactions. Furthermore, cobalt alkyne phosphine complexes (such as dppm substituted ones) are found not to be good substrates for Pauson-Khand reactions.[67] Therefore, these limitations render these complexes inappropriate for two of the most common reactions of cobalt alkyne complexes.

Several approaches have been taken by our group and others in the synthesis of 7-membered ring $Co_2(CO)_6$-cycloalkynes.[35] Among them, [3+4] intermolecular cycloadditions, intramolecular acid induced Nicholas cyclizations, and ring closing metathesis (RCM) are the most frequently applied methods. Scheme 2.2 shows several examples of cycloheptyne cobalt complexes which have been synthesized in our group employing the aforementioned methods.

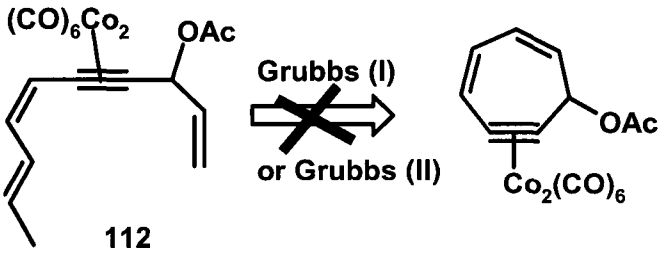


Scheme 2.2. Selected methods for the synthesis of seven membered $Co_2(CO)_6$-cycloalkynes.

Previous experience in our lab has shown acid mediated [3+4] cyclization reactions would not be a suitable method for the synthesis of cycloheptynes bearing oxygen function (Scheme 2.2). In most of the cases, the alkynal complex derivative did

undergo [3 +4] cycloaddition with allyldimetal equivalent reaction but loss of hydroxyl group resulted in elimination product (**111**). Therefore, in our case, for the synthesis and isolation of a cycloheptadienynol complex, a non-acidic route was required.

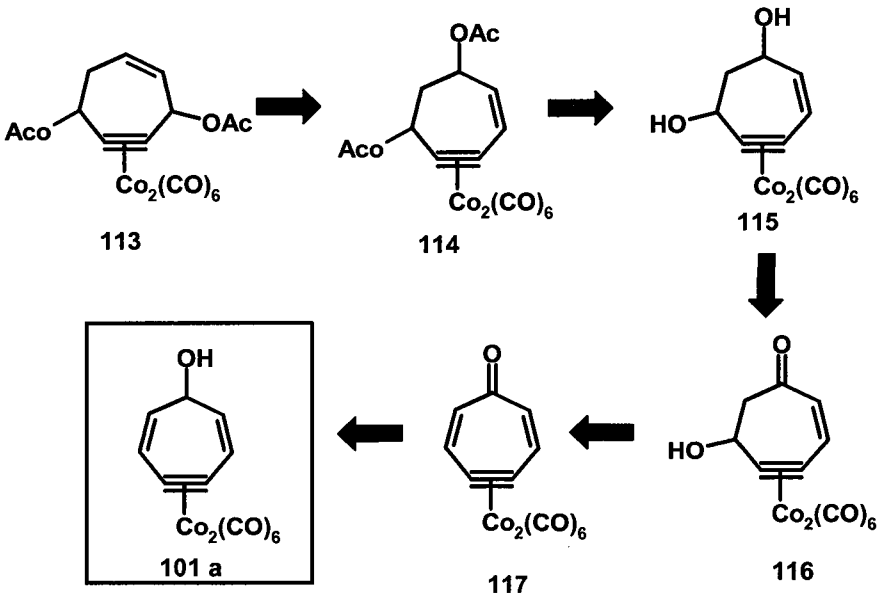
Green[68a] and others[68b] have demonstrated that formation of medium sized cycloalkynes (7-9 membered rings) is feasible via a ring closing metathesis (RCM) approach in several cases. Consequently, we decided to test the efficiency of the RCM method for the target compound (**101**). For that, RCMs on suitably positioned tetraenynes were attempted, hoping it would furnish fully conjugated system in one step. The initial trial in this area was on substrate **112**, constructed by way of Sonogashira on the (Z) 1-bromodiene. Unfortunately, subjecting this compound to attempted ring closing metathesis chemistry, using either Grubbs 1st or 2nd generation catalyst, failed to give any cyclization product and predominantly returned **112** unchanged (Scheme 2.3).[69]



Scheme 2.3. Selected substrates for ring closing metathesis.

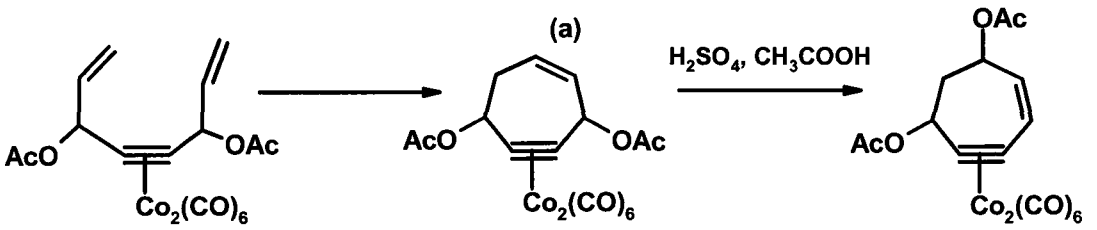
Since RCM failed to afford directly the highly conjugated 7-membered rings of interest, a new synthetic approach was designed so that the second double bond of cycloheptadienyne complex was formed after the ring closure had occurred. Fortunately, cycloheptenyne complex **113**,[68a] previously prepared in our group, possessed all the functions necessary for the synthesis of **101a**, and was therefore selected as the starting

point (Scheme 2.4). From the experience in our lab, we predicted that acid catalyzed rearrangement of **113** should provide **114**, which upon deprotection of acetates would give dialcohol **115**. Selective oxidation of allylic alcohol to give **116** and further acid catalyzed condensation reaction of ketoalcohol **116** should furnish the ketone **117**. Based on the well-established methods for reduction of organic carbonyl groups in the presence of cobalt complexes, conversion of ketone **117** to alcohol **101** should be feasible.



Scheme 2.4. Retrosynthetic analysis of **101a**.

Compound **113** was synthesized in four steps from propargyl alcohol following the reported procedure.[68] RCM catalyzed by Grubbs 1st generation catalyst to convert compound **118** to **113** was successful in this case (80 % yield).

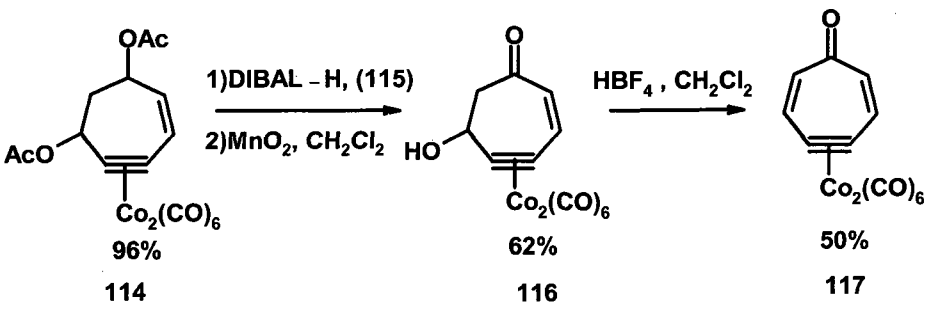


118 **113** **114**

Scheme 2.5. Synthesis of compound **113** and its acid rearrangement.

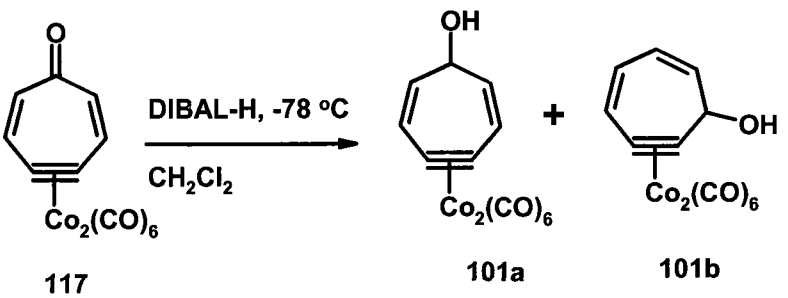
The C-5 oxygen function was incorporated by acid catalyzed rearrangement of diastereomeric mixture of **113**, which gave compound **114** as a single isomer in high yield (94%). This type of rearrangement had previously been observed in our group in selective nucleophilic addition to γ carbon in α-acetoxy cyloheptenyne cobalt complexes.[71] In this case, perhaps the ability of acetate group to act as both nucleophile and leaving group reversibly resulted in the formation of the most stable isomer.

Following the isolation of **114**, the next step was the deprotection of acetate groups in **114**. Experience in our lab has shown that typical base-induced ester hydrolysis conditions on dicobalt alkyne complexes give low yields due to a competitive decomplexation reaction. Therefore, reductive removal of acetate with DIBAL-H was selected as the method of choice. Removing acetate groups in **114** with DIBAL-H provided dialcohol **115**, which as a crude reaction mixture was subjected to oxidation by MnO_2. Selective oxidation of allylic alcohol by the mild oxidizing agent occurred providing keto-alcohol **116** in 62% overall yield (2 steps).



Scheme 2.6. Stepwise formation of compound **117** from **114**.

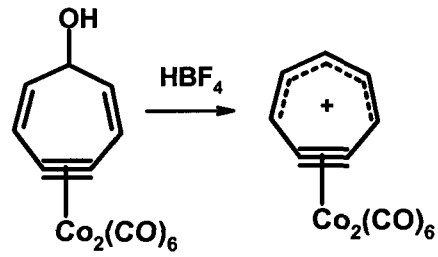
At this point, the elimination of water from **116** to give ketone **117** was attempted. Careful selection of conditions and monitoring of the reaction was required. p-Toluenesulfonic acid gradually afforded **117** in variable yields. However the best results (50 % yield) was obtained when a large amount of excess acid (HBF_4) was added to the keto-alcohol at 0°C and when the reaction was stopped shortly after the addition of acid. A longer reaction time resulted in gross decomposition of the product and a reduced yield. Reduction of ketone **117** with DIBAL-H gave the desired alcohol (**101a**, 70%) with small amount of rearranged alcohol (**101b**, 5%). The two isomers were separated by column chromatography and their structures were confirmed from spectroscopic data.



Scheme 2.7. Reduction of ketone **117** to alcohol **101a** and **101b.**

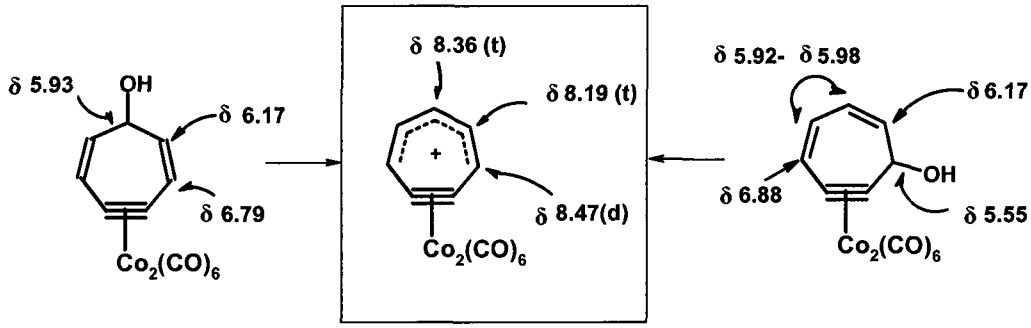
In summary, the precursor to dehydrotropylium-$Co_2(CO)_6$ cation, compound **101** were successfully synthesized in 9 steps, albeit with low overall yield.

2.3. GENERATION OF DEHYDROTROPYLIUM -$Co_2(CO)_6$



101 99

Dehydrotropylium-$Co_2(CO)_6$ cation **99** was generated at -75 °C by addition of HBF_4 to the solution of alcohol **101a** in Et_2O or CH_2Cl_2 . The carbocation, as dark solid particles, was precipitated from CH_2Cl_2 solution upon the addition of Et_2O. Solvents were removed under a reduced pressure and the residue was dissolved in CD_2Cl_2 for NMR spectral analysis. Its ^1H NMR spectral studies at low temperature (-80 °C to -20 °C) revealed three new characteristic signals which we assigned to the cation **99**. These resonances appeared at 8.47 (d, J= 9.5, 2H), 8.36 (t, J= 9.4, 1H) and 8.19 (apparent t, J =9.5, 2H) (Scheme 2.8). Unfortunately, due to the presence of impurities and the low concentration of cation, we were not able to obtain a reasonable ^{13}C NMR spectrum of the cation.



Scheme 2.8. Comparison between ^1H NMR chemical shifts of cation **99** and those of the precursor alcohols.

The chemical shifts of the protons in cation **99** are all shifted downfield relative to both precursor alcohols. From the reported ^{1}H NMR results on 1-methyl/phenyl/ hydrogen substituted dicobalt propargyl cations, relatively small chemical shifts have been observed at propargylic site on going from alcohol complexes to the corresponding cations ($\Delta\delta$ = 0.2- 0.7 for methyl and phenyl substituents and $\Delta\delta$ = 0.7-1.6 for hydrogens directly attached to the cationic site).[6c] Unfortunately, due to the lack of literature information on the chemical shifts of the dicobalt cations with conjugated double bonds, no direct comparison can be made between our system and analogous cobalt stabilized cations. However, the proton chemical shifts of cation **99** are comparable to the reported values for bis(triphenylphosphine)palladium and -platinum dehydrotropylium complexes (**118** and **119**). In both of these complexes, all the remote hydrogens on the tropyne ring are shifted siginificantly upfield from the tropylium ion (which shows a singlet at δ 9.28). It is worth mentioning, while both Pd and Pt tropyne complexes exhibit the proton chemical shifts that are very smillar, a dramatic stability difference exists between them; the former is very thermally unstable even at temperature as low as -35 °C and the latter is stable even up to 70 °C.[58a,e]

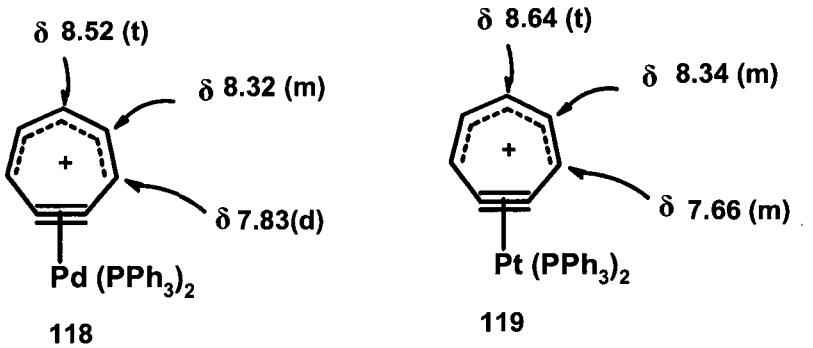


Figure 2.5. ^{1}H NMR chemical shifts of palladium and platinum complexes of tropyne.

Moreover, in our experiment, along with the desired cation (**99**) some unreacted alcohol and a trace amount of dimer (see section 2.3, **120**) were also detected in the ^1H NMR spectrum. The low solubility of HBF_4 at - 75°C might be responsible for the presence of unreacted alcohol. However, the formation of dimer at this temperature was unexpected and needs more detailed investigation before it can be explained confidently.

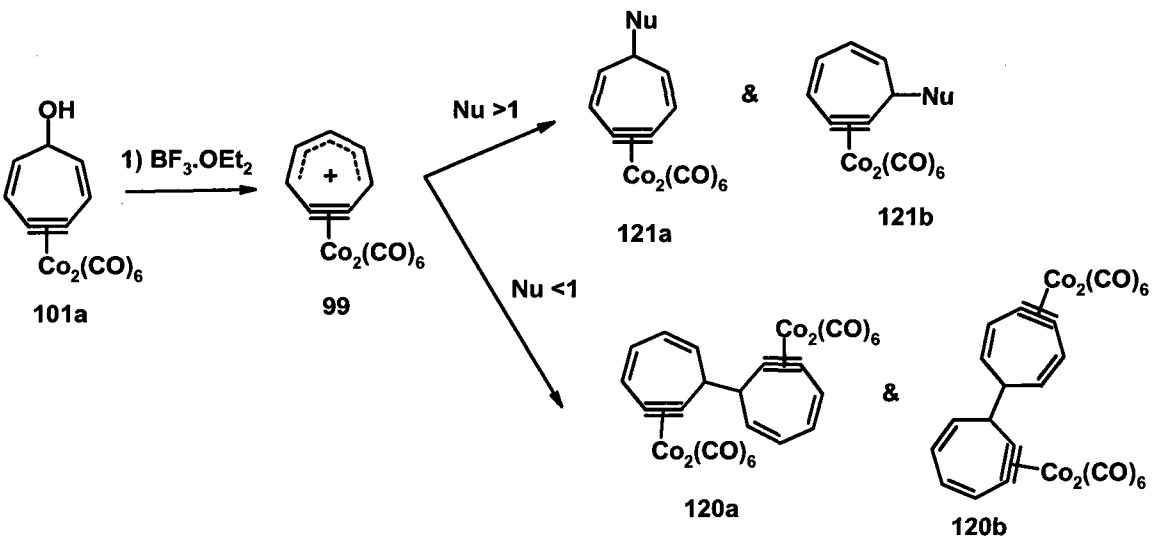
Gradual degradation of the cation by increasing the temperature prevented us from a more detailed structural analysis of isolated cation. Therefore, to get better insight into the characteristic properties of the cation we decided to explore the reactivity of the cation with various nucleophiles by generating the cation in situ.

2.4 REACTIVITY STUDIES OF CATION 99 WITH VARIOUS NUCLEOPHILES

It has been shown that the reaction of the Nicholas cation with different nucleophiles roughly obeys Mayr's linear free enthalpy equation: log k (20 °C) = s (E +N). In this model nucleophile/electrophile combinations with E +N $\geq$- 5 are expected to proceed with a reasonable rate at room temperature. Accordingly, propargyl cations with electrophilicity values ranging between -1.2 to -2.2 are expected to react with nucleophiles with N > -4.

Herein, by addition of $BF_3.OEt_2$ to the solution of alcohol **101a**, cation **99** was generated in situ and its reactions with various nucleophiles were investigated. The nucleophiles were selected based on their nucleophilic strength (N value) from Mayr's nucleophilicity scale. From these studies, it was intended that the limit for reactivity of

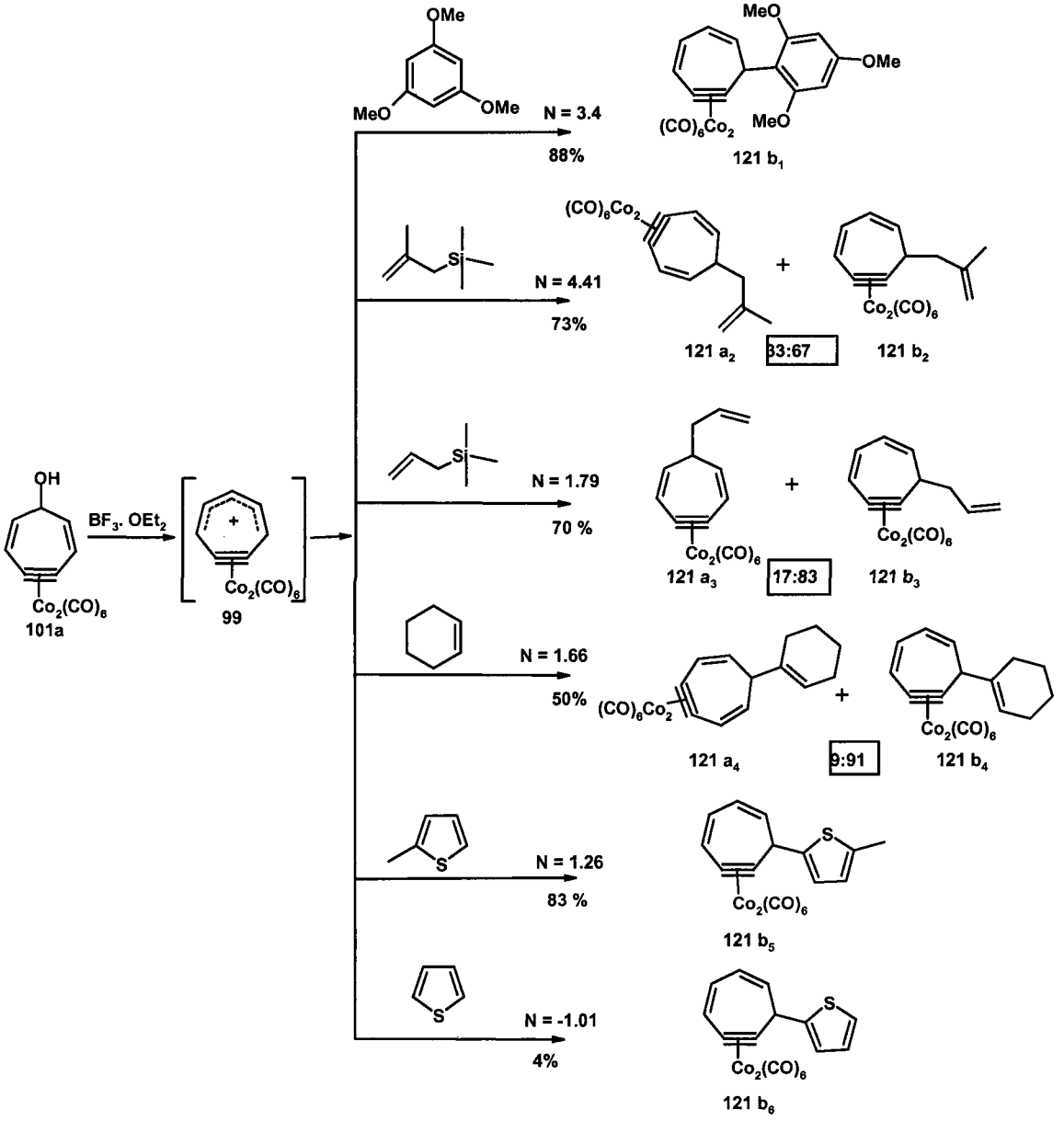
cation **99** could be determined experimentally and it could be compared to reactivity of common cobalt stabilized propargyl cations. It was found cation **99** reacts with relatively strong nucleophiles (N>1) to give condensation products (**121**) and undergoes dimerization (**120**) in the presence of weaker nucelophiles (N<1) (Scheme 2.9).



Scheme 2.9. Reaction of alcohol **101a** with relatively strong and weak nucleophiles.

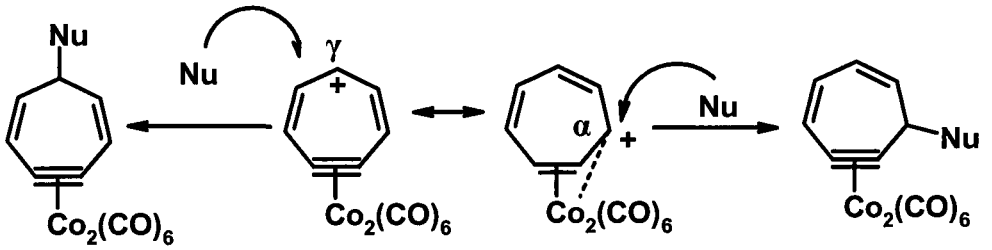
Scheme 2.10 summarizes the results from reaction of cation **99** with relatively strong nucleophiles N >1. Starting from 2-methylallyltrimethyl silane (N = 4.41), an isomeric mixture of condensation products was obtained with 67:33 (**$121b_2$:$121a_2$**) ratio in favour of addition to the carbon α- to the alkyne complex. Moving to weaker nucleophiles such as allyltrimethylsilane (N = 1.79) and cyclohexene (N = 1.66), the ratio of α:γ addition was increased to 83:17 and 91:9 respectively, and reached complete selectivity (**$121b_5$**) with 2-methylthiophene (N = 1.26). With weaker nucleophiles (N <1) such as thiophene, only 4 % condensation product was obtained, yet as a single isomer (**$121b_6$**). The seemingly inconsistent result that was observed for trimethoxybenzene (N =

3.4) (**121b$_1$** as the sole product) might be due to its known ability to go under reversible Nicholas reaction.



Scheme 2.10. Reaction of alcohol **101a** with relatively strong nucleophiles.

In summary, in all cases compound **121b** was formed in favour of the other isomer **121a**, with the ratio of α to γ attack being increased when weaker nucleophiles were added.

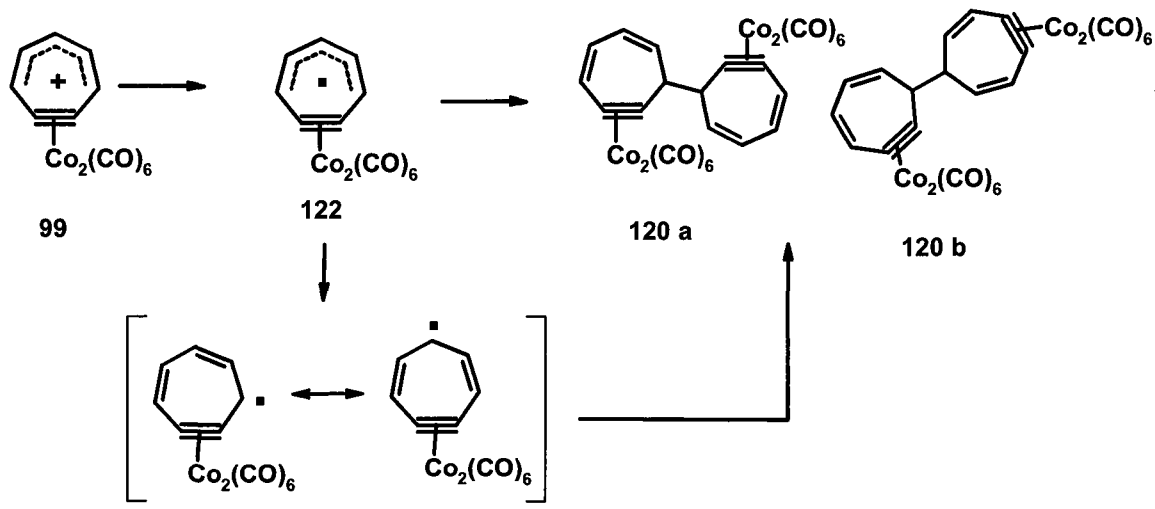


121 a **121 b**

Scheme 2.11. α versus γ attack and corresponding condensation products.

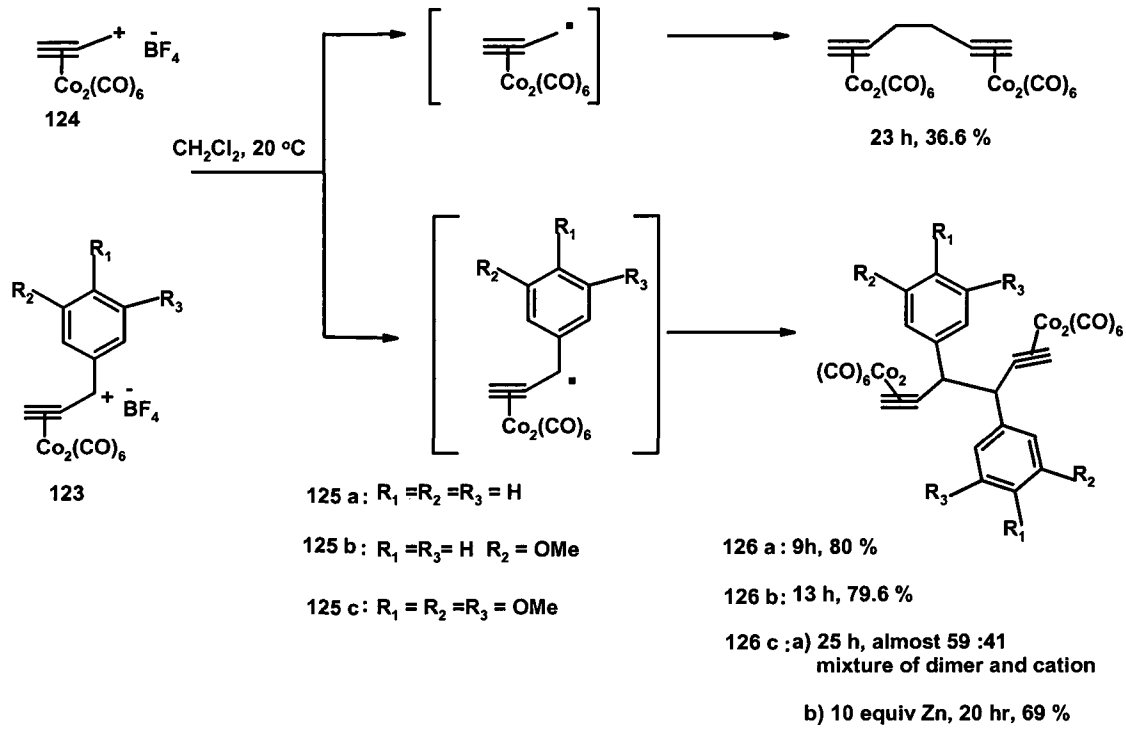
The products of these reactions were identified spectroscopically, and the relative isomeric ratio was determined from ^{1}H NMR spectra based on the relative intensities of characteristic signals of each isomer. Olefinic protons that were in conjugation with complexed alkyne appeared downfield in comparison to the other olefinic protons. In cases where the mixture of isomers was obtained, the corresponding signal(s) appeared as two sets of peaks each belonging to one of the isomers; in these cases the vinyl proton nearest to the alkynedicobalt complex in **121b** was shifted further downfield ($\delta \sim 6.8$ than in **121a** ($\delta \sim 6.5$-6.7).

Reaction of cation **99** with thiophene and weaker nuleophiles (N <1) resulted in dramatic decrease in the amount of condensation product and a concomitant increase in dimer (**120**) formation. Dimer **120** was obtained as a mixture of both α,α and α,γ coupling products with the latter being less stable and gradually decomposing (Scheme 2.12). Given the extensive work on propargyl dicobalt radicals and their ease of formation from propargyldicobalt cations, it is highly likely that single electron reduction of the propargyl dicobalt cation (**99**) resulted in the formation of a propargyl cobalt radical (**122**), which is known to be responsible for the dimerization reactions (Scheme 2.12).[55]



Scheme 2.12. Dehydrotropylium dicobalt hexacarbonyl radical formation and its dimerization reaction.

The chemistry of propargyldicobalt radicals has been thoroughly studied by Melikiyan and coworkers. They have been able to generate propargyl dicobalt radical from its corresponding cations under different reaction conditions. Among these conditions, are spontaneous radical generation (at ambient temperature/ high temperature) and organic solvent mediated radical formation (Section 1.5). In the case of spontaneous radical dimerization, the rate of the dimerization reaction was found to be substituent-dependent. While highly stabilized propargyl cations proved inefficient for spontaneous radical generation, the presence of phenyl group on propargylic site was found crucial for radical stabilization and subsequent dimerization (Scheme 2.13). This was evidenced from the improved yield and rate acceleration which was observed in the dimerization reaction of **123** comparing to **124**. On the other hand, increasing the number of OMe group on phenyl ring resulted in the rapid formation of cations but reduced the rate of radical formation.[55c]



Scheme 2.13. Substituents effects on spontaneous propargyl dicobalt radical dimerization reaction.

In our case, thiophene was the weakest nucleophile with which we could detect the condensation product (only 4 %), along with 34% of dimer products **120**. Applying the same condition, various aryl nucleophiles with N <1 were tested (Table 2.1). In each case, the dimers were the dominant reaction products but were formed with different yields, suggesting the amount of dimerization (radical formation) was dependent on the nature of the arene. Dimer formation was observed even in the absence of any nucleophile, but only in 9 % yield. Looking at the nucleophiles that we have tried, the highest yield of dimerization was obtained for mesitylene. Curiously, in the cases studied here, by reducing the number of methyl group on the phenyl ring and addition of OMe on the

arene ring , the yield of dimer formation was decreased (the same trend was observed by Melikyan for phenyl-substituted propargyl cations). Even though it might very well be a superficial trend, it seems that the presence of an aryl group (not too electron rich) either at propargylic site or as a potential electron donor would enhance the rate of dimer formation.

Also, it should be noted that oxygen or sulphur containing organic compounds such as tetrahydrofuran and tetrahydrothiophene are known as organic mediators for radicalization processes.[55b] Therefore, the presence of a small amount of ether in our reaction mixture might have contributed in the formation of propargyl radical **122** and its dimerization as well.

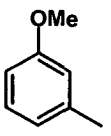
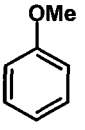
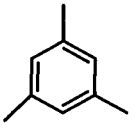
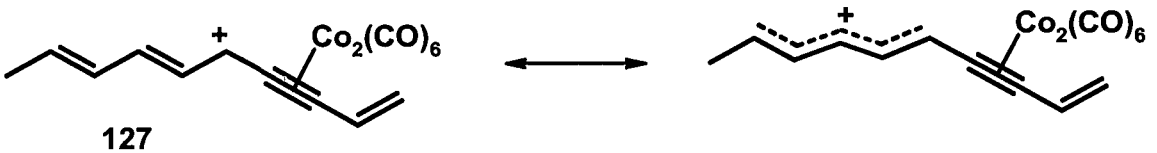
Nucleophiles					none
	N = 0.13	N= -1.01	N= -1.18	N = -2.5	
120 a : 120 b	33: 67	33 :67	33 :67	33: 67	33 :67
Yield	26 %	34 %	18 %	50%	9 %

Table 2.1. Dimerization reactions in the presence of nucleophiles with N < 1.

Aside from the factors that resulted in the formation of dimer **120**, radical formation is usually considered as indicative of lower stability of the corresponding cation.[55c] In our case, while the reduced reactivity of cation **99** towards different nucleophiles may suggest higher stability of these cations relative to common propargyl dicobalt cations, the ease of formation of dimers at relatively low temperature more likely indicated lack of extensive stabilization for cation **99**.

At this point, since the experimental results from reactivity studies of **99** towards different nucleopiles was disrupted by dimerization pathway, we were not able to make a certain statement on the stability/ reactivity of the nominally aromatic cation. Consequently, we decided to prepare an acyclic analogue of cation **99** and study its reactivity for comparison purposes.

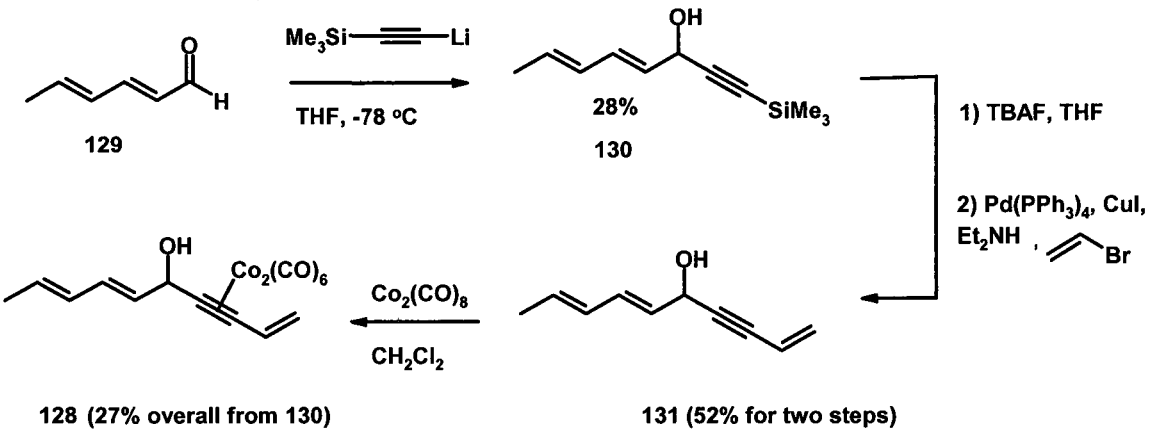
2.5. ACYCLIC DIENYNYL CATION



127

In search for a model compound that can be used as a probe to estimate the amount of resonance stabilization in the dehydrotropylium dicobalt cationic systems, we decided to prepare acyclic dienyl propargyl alcohol cobalt complex **127**. Compound **127** was chosen as an appropriate model based on the fact that it has a dienyl cation just like the dehydrotropylium ion complex, with an additional remote π system to the cation, in order to have an sp^2 carbon on the remote side of the alkyne complex.

For this purpose, compound **128**, as precursor for the cation **127**, was synthesized based on the synthetic method described in Scheme 2.14.

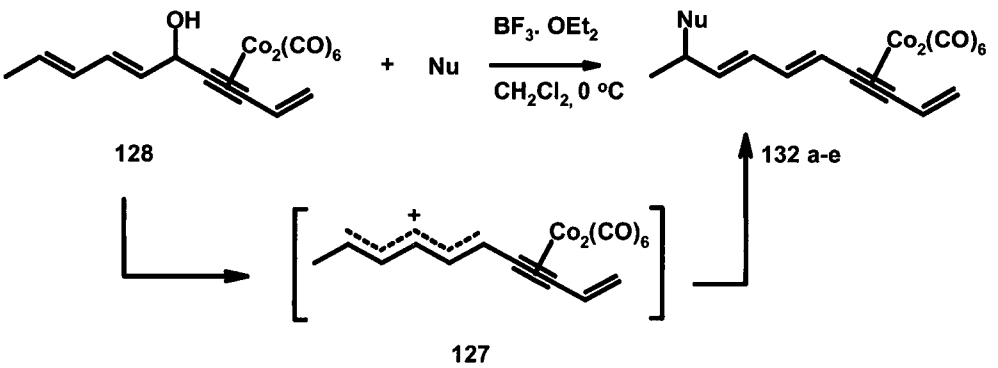


Scheme 2.14. Synthesis of dienyl propargyl alcohol complex **128.**

Reaction of sorbaldehye (**129**) with lithiated trimethylsilylacetylene, after purification, provided alcohol **130** in 28 % yield. Alcohol **130** was found to be sensitive to silica gel and could only be purified on triethylamine-neutralized silica. From several attempts to optimize the reaction overall yield, and based on the fact that crude material was pure enough for subsequent use, it was concluded it would be more efficient if no purification was done at this step. Quantitative removal of TMS-protecting group by TBAF (tetrabutylammonium fluoride), followed by Sonogashira coupling with vinyl bromide afforded dienyl propargyl alcohol **131**. A one- time purification of **131** (52 %) was accompanied by substantial decomposition and loss of the product. Therefore for the next step, the alcohol **131** was not purified but subjected to immediate complexation with dicobalt octacarbonyl. After purification, the three-step process afforded the desired dienyl propargyl complex **128** in 27 % (for three steps from **130**). The best overall yield was obtained from sorbaldehyde (14 %) when purification was done only after the last step.

2.6 REACTIVITY STUDIES OF ACYCLIC DIENYL PROPARGYL ALCOHOL DICOBALT COMPLEX (128) WITH VARIOUS NUCLEOPHILES

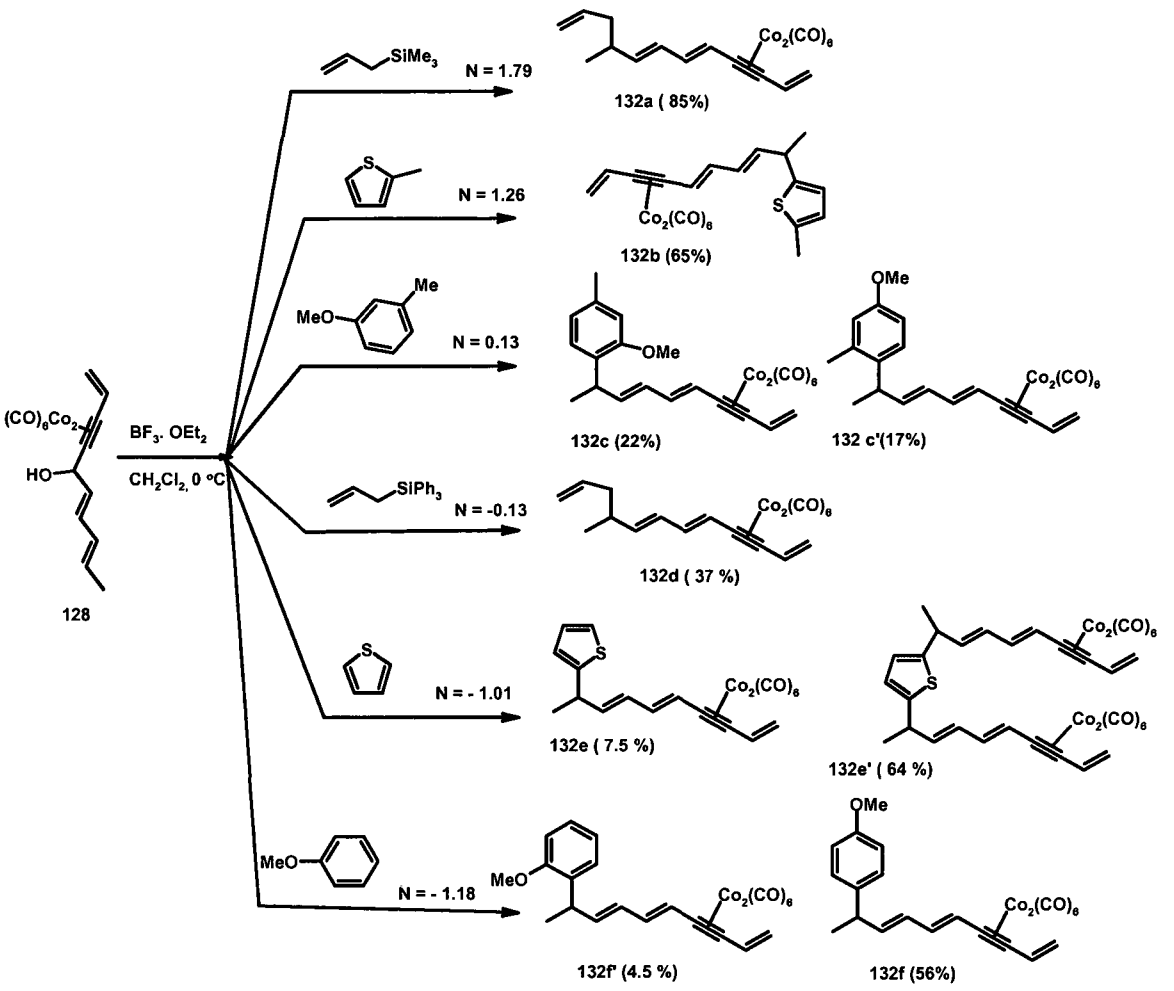
Acyclic dienes bearing a $Co_2(CO)_6$-complexed triple bond are well known as potential substrates for Pauson-Khand reactions, but their application in Nicholas reactions are less developed. Here, the $BF_3 \cdot OEt_2$ mediated reactions of **128** with a variety of nucleophiles were undertaken in order to establish a basic reactivity pattern, and so that a reactivity comparison can be made between the cyclic dehydrotropylium ion cobalt complex (**99**) and its acyclic analogue **127**.



Scheme 2.15. Reactivity studies of complex **128**.

As for dehydrotropylium cation **99**, a range of π-nucleophiles were selected from Mayr's table, with nucleophilicity values in a range between $-2 < N < 2$ (Scheme 2.15). Under normal Nicholas reaction conditions, alcohol **128** reacted with an excess amount of allyltrimethylsilane (N= 1.79) to give the addition product (**132a**) as dominant

isomer in high yield (85%). From subsequent subjection of the alcohol **128** to Lewis acid mediated reactions with less reactive nucleophiles such as 2-methylthiophene (N = 1.26), 3-methylanisole (N = 0.13), allyltriphenylsilane (N = -0.13), thiophene (N = - 1.01) and anisole (N = -1.18), a gradual decrease in reaction yield was observed, but not in uniform way (Scheme 2.16). It is worth noting that between three possible reactive sites (α, γ, ϵ) only one site (ϵ) reacted with significant selectivity. This was concluded from the ^{1}H NMR spectra of the product, the upfield shift that was observed for protons of Me group (by 0.6-0.2 ppm) and the downfield shift observed for olefinic protons suggested nucleophilic attack ocurred at ϵ site and that the double bonds were in conjugation with complexed alkyne. Only in one case (compound **132a)**, additional methyl group resonances at δ 1.7-1.8 was observed in the spectra, ca.10 % of the other isomers, whereas in case of other nucleophiles (**132b-132f**) the addition was exclusively at ϵ site.



Scheme 2.16. Reaction of dienyl propargyl alcohol complex **128** with π-nucleophiles.

In cases of 3-methylanisole and anisole, the reaction was rather slow and an excess amount of these nucleophiles was added subsequently to give complete conversion. The steric hindrance might have contributed to the reduced reactivity/yield that was observed for 3-methylanisole. On the other hand, in the reaction of the alcohol with thiophene, the mono-addition product was captured by the second nucleophile to give mainly dicondensation product **132e`**, suggesting these (anisole (N=-1.18) and thiophene (N= -1.01)) are right at the limit of reactivity possible for **127** (Scheme 2.16).

In summary, it was concluded that the nucleophilic addition to **127** occurred with nucleophiles as weak as anisole and predominantly at the end of dienyl remote from the

alkyne dicobalt function. Reactions with weaker nucleophiles such as cyclopentene (N = -1.55), mesitylene (N < -2.5) and 1-methylnapthalene (N_{cal} = -2.4)[9e] resulted mainly in decomposition of alcohol or recovery of small amount of starting material with no isolable condensation product or dimerization product. The fact that cation **127** was found to be efficiently reactive towards nucleophiles with N > -1, is consistent with (but not conclusive of) an approximate E value of -4 for the cation. This value would be approximately 100 times less electrophilic than simple propargyl dicobalt cation.

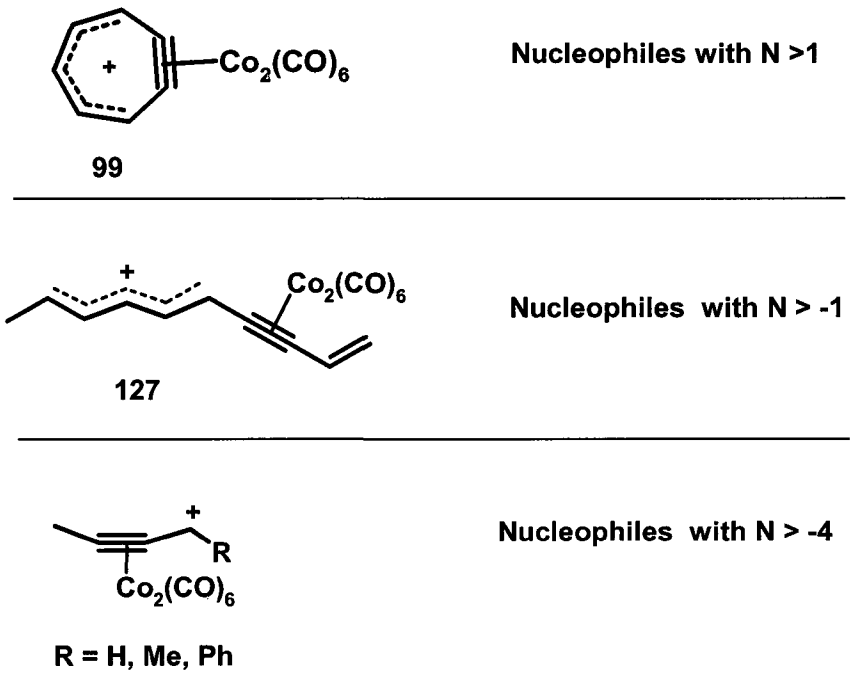


Figure 2.6 Comparison on relative reactivity of dehydrotropylium cobalt cation (**99**) dienyl propargyl cobalt cation complex (**127**), and common propargylic cobalt cation.

On the other hand, ***if*** these indirectly determined E values are accurate, resonance stabilization could be counted on for a difference of 10^2 in the reactivity of nominally aromatic cation **99** and acyclic analogues **127** (Figure 2.6). Nevertheless, rapid conversion of cyclic propargyl cation to its corresponding radical and formation of dimers

in case of cyclic cation (**99**) makes indirect estimation of E values for this cation rather unreliable.

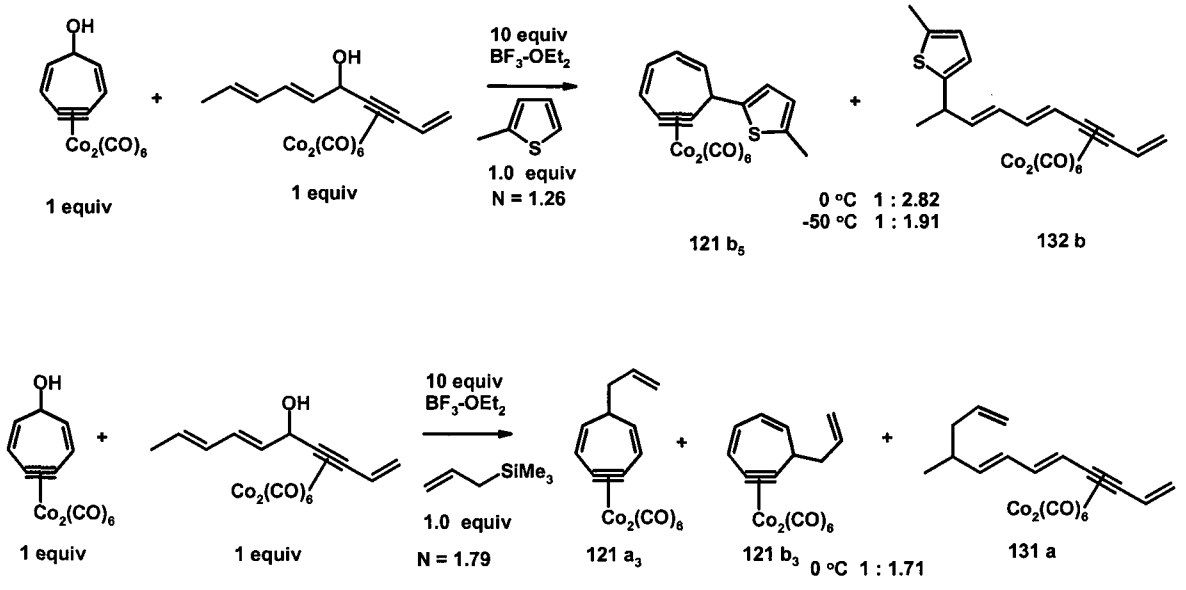
Therefore, for direct comparsion of the reactivity of cation **99** and that of **127** we chose to perform competitive reaction of the two with mild nucleophiles that perfomed well with each substrate. Also, for better estimation on the stability of the cation **99** and on the amount of aromaticity it possesses, we decided to rely on computational calculations.

2.7 COMPETITIVE REACTIVITY STUDIES OF ACYCLIC DIENYL-PROPARGYL COBALT CATIONS (99) WITH CYCLIC DEHYDROTROPYLIUM COBALT CATION (127)

Here, recognizing the shortcoming in estimating E values the way it has been done, a better way to compare the dienyl and dehydrotropylium cases is to study the competitive reactivity of the two. Assuming that the 1st step of these S_N1 reactions are rate determining (and that could be an issue), the more stable cation would be generated and react preferentially. Based on these considerations, the relative reactivity of two cations was investigated in a series of competitive reaction conditions.

When an equimolar mixture of both alcohols (**101** and **127**) was subjected to a Lewis acid treatment in the presence of one equivalent of nucleophile (allyltrimethylsilane or 2-methylthiophene) a mixture of condensation products of each was obtained. In both cases the ratio was found to be in favour of addition to acyclic cation (**127**), (Scheme 2.17). In case of 2-methylthiophene running the reaction at lower

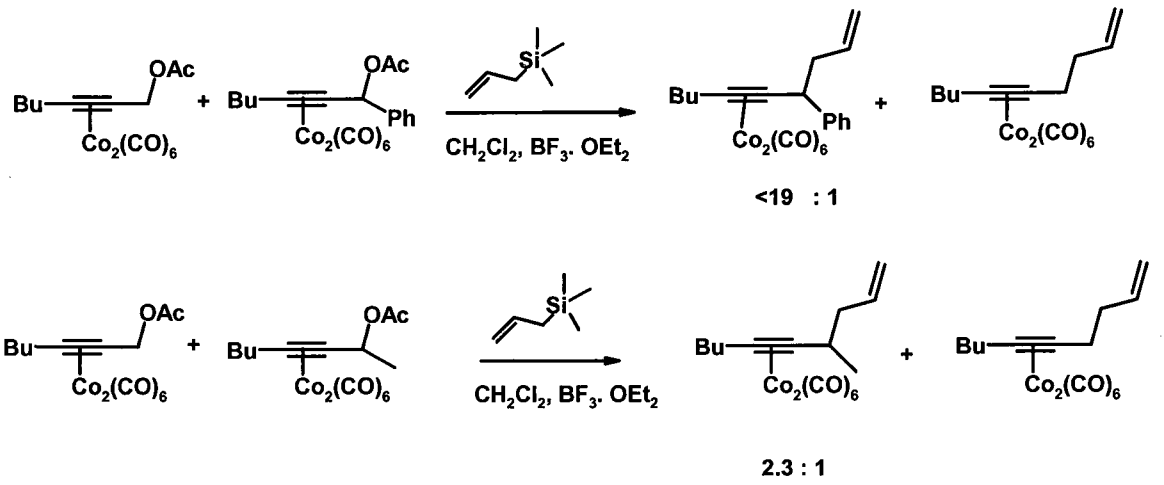
temperature resulted in less selective reaction (**121b$_5$:132b** ratio as 1:1.9 at -50 °C and 1:2.8 at 0 °C). The relatively close products ratios for allyltrimethylsilane (1:1.7) and 2-methylthiophene (1:1.91, at low temperature) may be considered as relative kinetic product ratios. The discrepancy in the **121b$_5$:132b** ratio at higher temperature might be due to 2-methylthiophene showing some signs of reversibility in its reaction.



Scheme 2.17. Competitive reactions of cyclic and acyclic cations with two mild nucleophiles.

Along with our study on the possibility of resonance stabilization in cation **99**, very recent work in our group has focused on the electronic effects of substituents in selectivity of Nicholas reaction.[72] In case of substitution at propargylic site, additional resonance stabilization was quite in evidence and greater reactivity was observed for phenyl substituted alcohol versus alkyl substituted or unsubstituted one (Scheme 2.18). Thus, for the cases studied, the acetate precursor to the more stable cation reacts faster in

the competitive Nicholas reactions, suggesting the first step of generation of the cation to be the rate determining step.



Scheme 2.18. Competitive reactions between different substituted propargyl cations.

Therefore in our case, the higher reactivity of acyclic dienyl propargyl alcohol **127** towards nucleophiles (relative to **101a**) can be interpreted as a slightly lower activation energy for formation of the acyclic cation, which indicates the higher stability of it (**127**) relative to the cyclic cation (**99**).

To check if this assumption was correct we did calculations on the total energies of both reactants and their cations using DFT calculation (B88-PW91 functional) with smaller (dzvp) basis set. To our surprise, we found the formation of acyclic cation was indeed more favourable than formation of cyclic one according to the following equation.

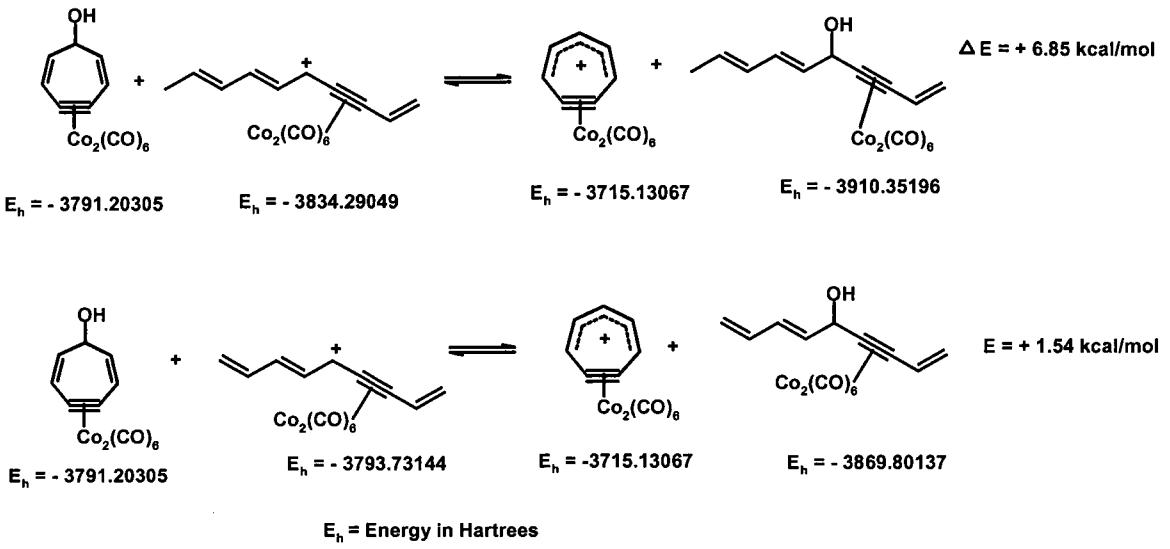


Figure 2.7. Relative stabilities of cations **99** and **127** based on their calculated total energies (DFT/ B88-PW91).

The higher stability of our acyclic model could partly be due to the inductive effect of the methyl group as it was evidenced from the lower Δ E that we obtained for the same equation with analogous acyclic alcohol with no methyl group at the terminal double bonds. Ring strain might be another factor that is contributing to the relative instability of the cyclic cation versus acyclic one. Nevertheless, the trends of these calculations were in accord with the experimental observation, although the exact value of Δ E hardly corresponds to the observed ratios.

At this point, rather contradictory and inconclusive results obtained experimentally on the stability and reactivity of cyclic cation, in addition to the lack of an appropriate model for comparison, made it impossible for us to make a definite statement on the stability of cation **99**. These factors, in addition to the lack of crystallographic data due to instability of the cation, prompted us to investigate more deeply on the aromaticity and thermodynamic stability of the system by means of calculational techniques.

2.8. DFT CALCULATIONS

In the last few decades, quantum chemical calculations methods based on density functional theory (DFT) have gained immense popularity for study of molecular structure and properties. This is due to the computational efficiency and high accuracy that these methods offer relative to other more computational demanding methods. DFT-based methods are generally capable of computing molecular properties such as IR frequencies, magnetic properties (NMR), dipole moments, ionization energies, hardness, geometries and more.[70]

The contents of this section are arranged in the sequence described below:

First, the optimized structure, geometrical parameters and total energy of nominally aromatic cation **99,** acyclic cation **127** and their corresponding alchols were calculated by using DFT calculation at B88-PW91/ dzvp level of theory (CAChe® Scigress Explorer). Then the relative theromodynamic stability of the cation was calculated from an appropriate isodesmic equation with an attempt to estimate E (electrophilicity of the cation) value by combining the theoretical data obtained here with the experimental results in previous section. Finally, a detailed investigation on the aromaticity of the cation was undertaken by means of known indexes of aromaticity.

2.8.1 Structural optimization and total energy

The dehydrotropylium dicobalt hexacarbonyl structure was optimized to the structure shown on the right. Near planarity and a relatively small bond alternation (between 0.001- 0.019 Å) were found for the minimum energy structure (Figure 2.8). The triple bond was found to have bond length of ~1.4 Å, which is within the typical range for alkyne dicobalt complexes.[24]

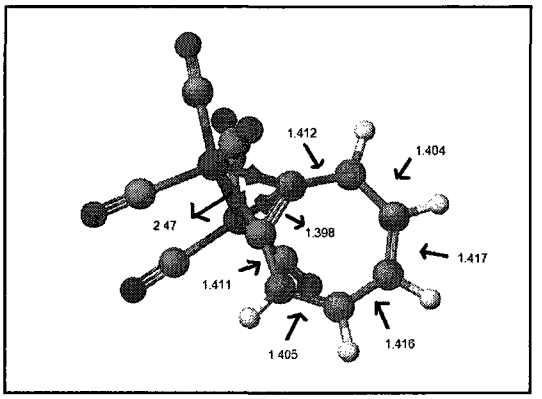
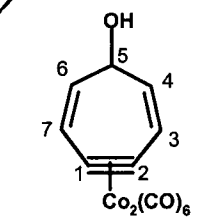


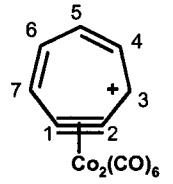
Figure 2.8. Optimized geometry for cation **99**.

Structures of the acyclic cation **126** and alcohols **101** and **127** were optimized using the same program and their selected bond lengths, bond angles, and total energies were determined for comparison (Table 2. 2).



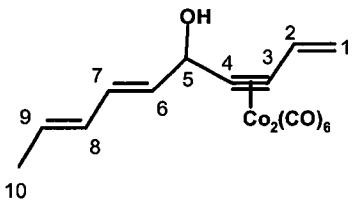
101

C_1-C_2 1.36	< (C_7-C_1-C_2) 132.94	E = -3791.20305
C_2-C_3 1.44	< (C_1-C_2-C_3) 133.10	
C_3-C_4 1.35	< (C_2-C_3-C_4) 122.65	
C_4-C_5 1.51	< (C_3-C_4-C_5) 131.48	
C_5-C_6 1.52	<(C_4-C_5-C_6) 123.38	
C_6-C_7 1.35	< (C_5-C_6-C_7) 131.88	
C_7-C_1 1.44		<C_7-C_1-C_2-C_3 = 1.35



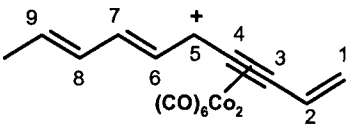
99

C_1-C_2 1.39	< (C_1-C_2-C_3) 132.38	E = -3715. 13084
C_2-C_3 1.41	< (C_2-C_3-C_4) 122.38	
C_3-C_4 1.40	< (C_3-C_4-C_5) 128.40	
C_4-C_5 1.41	< (C_4-C_5-C_6) 132.46	
C_5-C_6 1.41	<(C_5-C_6-C_7) 128.33	
C_6-C_7 1.40	<(C_6-C_7-C_1) 122.33	
C_7-C_1 1.41	<(C_7-C_1-C_2) 132.67	<C_7-C_1-C_2-C_3 = -0.84



128

C_1-C_2 1.34	< (C_1-C_2-C_3) 126.85	E = -3791.20305
C_2-C_3 1.46	< (C_2-C_3-C_4) 138.26	
C_3-C_4 1.36	< (C_3-C_4-C_5) 136.71	
C_4-C_5 1.51	< (C_4-C_5-C_6) 114.32	
C_5-C_6 1.51	< (C_5-C_6-C_7) 122.63	
C_6-C_7 1.35	<(C_6-C_7-C_8) 124.81	
C_7-C_8 1.45	< (C_7-C_8-C_9) 123.48	
C_8-C_9 1.35	< (C_8-C_9-C_{10}) 125.50	< C_2-C_3-C_4-C_5 = -2.44
C_9-C_{10} 1.50		



127

C_1-C_2 1.35	< (C_1-C_2-C_3) 125.97	E = -3791.20305
C_2-C_3 1.45	< (C_2-C_3-C_4) 136.73	
C_3-C_4 1.38	< (C_3-C_4-C_5) 143.25	
C_4-C_5 1.40	< (C_4-C_5-C_6) 124.13	
C_5-C_6 1.40	< (C_5-C_6-C_7) 123.35	
C_6-C_7 1.39	<(C_6-C_7-C_8) 123.09	
C_7-C_8 1.42	< (C_7-C_8-C_9) 122.64	
C_8-C_9 1.37	< (C_8-C_9-C_{10}) 125.04	< C_2-C_3-C_4-C_5 = -33.93
C_9-C_{10} 1.48		

The bond lengths in Å

Table 2.2

From alcohol **101** to the cation **99**, the dihedral angle at <C_7-C_1-C_2-C_3 changed from 1.35 to -0.84, which is a very small change in comparison to the 55° and 43° changes that were observed in X-ray analysis of the crystal obtained by the Melikyan group in a similar type of cation (**1**). Also, the difference between the distance of each cobalt to the propargylic centers, changed from 0.014 Å (i.e., near equal distance from both cobalt

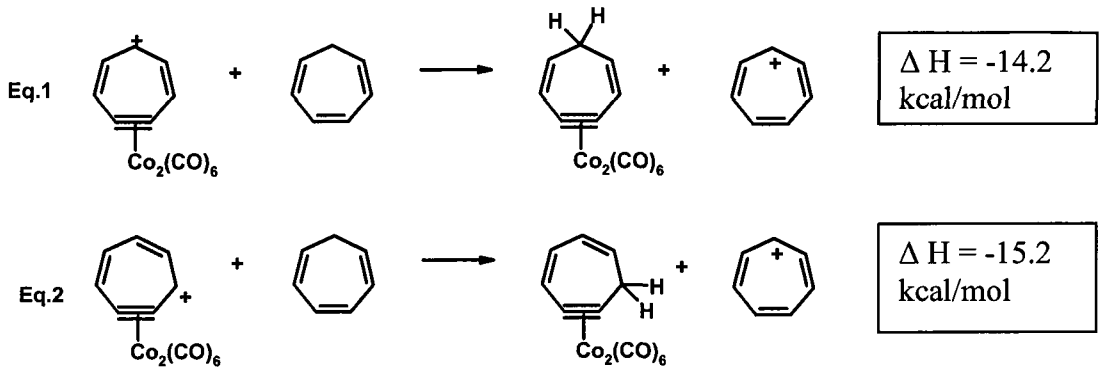
atoms to these centers) in alcohol **101** to 0.195 Å in cation **99**. The analogous difference was found to be in the range of 0.26-0.38 Å in the model cationic compound studied by the Melikyan group. Thus, based on the structural parameters obtained from calculation, near planarity of the system and the fact the positive charge is significantly delocalized inside the ring with a reduced level of bending towards the metal center was confirmed.

On the other hand, more structural changes were found between the acyclic cation and its corresponding alcohol. The most significant ones were the changes in the bond angles around the triple bond; < C_5-C_4-C_3 changed from 136° to 143° and the dihedral angle < C_2-C_3-C_4-C_5 from – 2.44° to -33.93°. These changes were in accord with the previous results obtained from other common cobalt stabilized cations indicating pronounced effect of metal in stabilization of positive charge for the acyclic cation **127**.

It is also worthy of mention that in both the cyclic alcohol and its derived cation there is a significant amount of angle strain at carbon 5 where the (C_4-C_5-C_6) bond angle around the sp^3 (in alcohol) and sp^2 (in cation) carbons came to 123.38° and 132.46°, respectively.

2.8.2 Isodesmic reactions

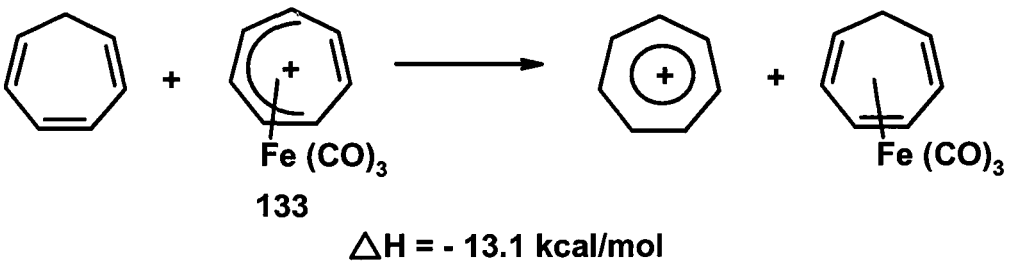
Isodesmic reactions, in which the number and type of bonds are conserved, are frequently used to estimate the aromatic stabilization energy. Here, the isodesmic equations 1 and 2 in Scheme 2.19 were used to compare the relative stability of cobalt cations **99** to the known aromatic tropylium cation.



Scheme 2.19. Isodesmatic equations to compare HIA of dehydrotropylium cation **99** with tropylium cation.

The greater hydride affinity (HIA) of cobalt cation to the free tropylium reflects the higher aromatic character of tropylium cation and greater thermodynamic driving force for the reaction of cobalt cations with nucleophiles.

In a novel study by Mayr[73] a comparison was made on the relative electrophilicity of various metal complexes of tropylium ion and free tropylium cations. In this study it has been shown the relative reactivity of these species is governed by several factors, such as thermodynamic driving force, the amount of interaction between HOMO (of the nucleophile) and LUMO (of the electrophile), and steric factors. For example, in the case of iron tricarbonyl tropylium complex **133**, the higher thermodynamic driving force for the reaction of the metal complex (calculated based on the following equation) has been shown to be compensated by its higher LUMO energy (less favourable orbital interaction) and by steric reasons. The net effect of these factors was the close similarity in the electrophilicity (reactivity) of free tropylium and its iron complex.



133

$\triangle H = -13.1$ kcal/mol

Scheme 2.20. Hydride ion affinity for iron tricarbonyl tropylium Complex **133**.

In a similar attempt to shed light on the reactivity of cation **99**, we calculated the LUMO energies of cation **99** and tropylium cation by using DFT/B88-PW91. The computed LUMO energy for cobalt cation **99** was found to be – 8.29 eV, whereas for tropylium it was -8.19 eV. So in this case as opposed to the iron complex, very close LUMO energies were found for the cobalt cation and tropylium cation indicating comparable orbital interactions. Hence, it may be that other factors such as steric hindrance and the tendency of the cation to undergo radical formation that are responsible for the low apparent reactivity that was observed for cation **99** (based on its reactivity with nucleophiles N >1).

A comparison between our calculated data for the dehydrotropylium dicobalt cation with similar information that has been reported for iron tricarbonyl tropylium complex **133** reveals great similarity between the two systems. From HIA calculations one can assume that only a small difference exist in thermodynamic stability of iron tropylium cation complex and our cation (**99**). Interestingly, Mayr has found E =- 3.81 for iron tricarbonyl tropylium cation and suggested it reacts with nucleophiles having N > -1. With a very rough estimation based on the calculations here and experimental results we may suggest the reactivity of cation **99** to be in a range between dehydrotropylium cation and its iron complex (Table 2.3).

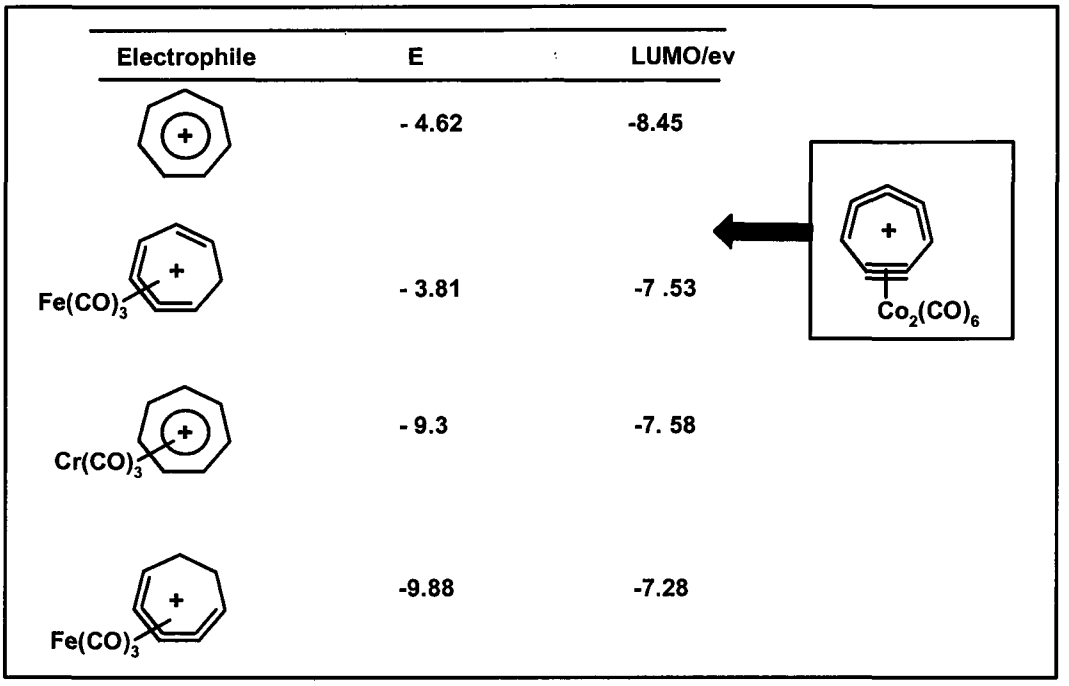


Table 2.3. Comparison of the electrophilicity *E* and the LUMO Energies (from DFT calculations) for the free tropylium cation and some of its metal complexes.[70]

Nevertheless, the main question on the stability/amount of aromaticity of cation **99** still remained to be investigated. For that, in next step we set to run the calculations which are specifically designed for measuring the amount of aromaticity of a system.

2.8.3 Aromaticity in dehydrotropylium cobalt cation

Despite the large number of methods existing, there is no unique criterion which one can rely on to assess the aromatic property of a system and a combination of several factors are needed to make an appropriate conclusion.[59]

In this work, the aromaticity of cation **99** was evaluated by some of the well established indexes of aromaticity : (1) based on the nucleus independent chemical shift (NICS) as a measure for magnetic properties; (2) from harmonic oscillator model of aromaticity (HOMA) an index for geometrical analysis; (3) by measuring the absolute hardness as an index of stability, and (4) by using the homodesmotic and isomerization reactions to measure the aromatic stabilization energy (ASE) and isomeric stabilization energy (ISE).

2.8.3-1 Nucleus independent chemical shift (NICS)

NICS measurement is based on a chemical shift of a probe which is placed at the center or 1Å above the center of a conjugated ring, NICS (0) and NICS (1), respectively. Basically, the computed NICS index corresponds to the negative of the magnetic shielding at the chosen point. Thereby, significantly negative NICS values are expected for aromatic compounds as a result of ring current while positive NICS values are expected for antiaromatic compound due to a paratropic ring current.[59]

Using HF/6-311+G(d,p) // B3LYP/6-311+G (d,p) optimized structures, the NICS value for the aromatic cation **99** was calculated by using the GIAO (gauge-independent atomic orbital) method. Calculations were carried out with Gaussian 03 program by Prof. J. Gauld.

Due to the fact that cycloheptadienyl portion and $Co_2(CO)_6$ portion of the molecule are not perfectly perpendicular, two locations at 1 Å above and below the ring center were considered (Figure 2.9). Their NICS (1) values are very close, with an average of -2.92. Also, the NICS (0) = + 1.58 was found for the center of the ring. Since the NICS values at the center (NICS(0)) are known to be less reliable (due to the possible contribution of σ-orbitals in addition to the π system in to the value of NICS), here we focus on NICS (1) as the more reliable measure of the ring current estimation. Thus, based on small value of -2.92 for NICS (1) cation **99** is expected to be very slightly aromatic.

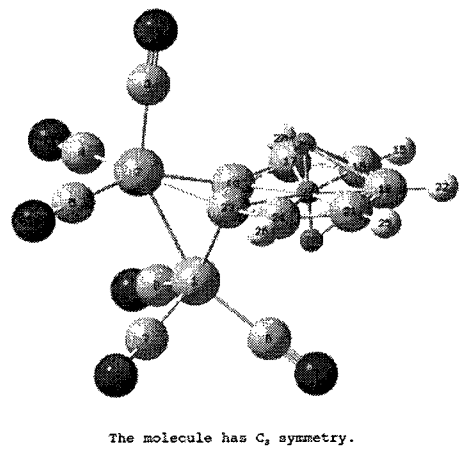
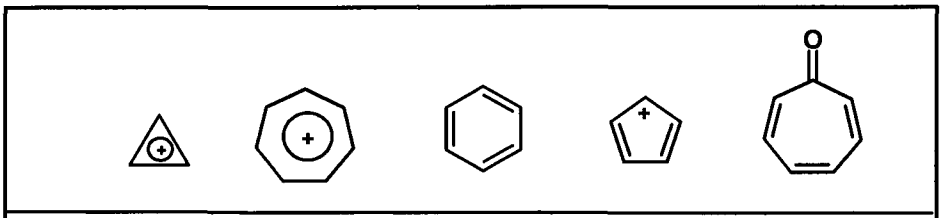


Figure 2.9. HF/6-311+G(d,p) // B3LYP/6-311+G (d,p) optimized structure and NICS values of **99.**

Table 2.4 shows reported NICS values for some of the known aromatic compounds. From the caluculated NICS (1) value in this work, the aromaticity of cation **99** is thus predicted to be comparable to that of tropone and about 28% of that of tropylium ion.



NICS (1)	-7.5	- 10.5*	-10.2	+ 47	-2.9

* calculated by us. The literature range is between -9.2 to -11.2

Table 2.4 Calculated NICS for some aromatic and anti-aromatic compounds.

2.8.3-2 Harmonic oscillator model of aromaticity (HOMA)

The HOMA index of aromaticity was first defined by Kruszewski and Krygowski as a structure-based measure of aromaticty in 1972.[74] Since then, it has been used as one of the most effective structural indexes of aromaticity.

$$\mathbf{HOMA = 1 - 257.7/n\ {}^{n}\Sigma_i (d_{opt} - d_i)^2} \qquad \textbf{Eqn. 2.1}$$

$\mathbf{d_{opt}}$ = 1.388 Å , $\mathbf{d_i}$ = calculated (experimental) bond length , **n**=number of bonds

Based on the harmonic oscillator model, an ideal aromatic compound has equivalent C-C bond lengths at 1.388 Å (as in benzene). The constant 257.7 was set to give HOMA = 0 for a model non-aromatic compound and HOMA =1 for an ideal aromatic compound (when d_i = 1.388). Furthermore, Kruszewski has found deviation from aromaticity in HOMA model can be described by contribution of two independent factors: (1) geometrical (**GOE**), which is due to increased bond alternation; (2) energetic (**EN**), which is due to an extended mean bond length (bond elongation).

$$\mathbf{HOMA = 1 - EN - GEO} \qquad \textbf{Eqn. 2.3}$$

Therefore, by calculating GEO and EN along with HOMA it is possible to determine which factor contributes more to the decreased aromaticity of a system. Based on the calculations with B3LYP/6-311 G(d, p) +zvpe by Prof. Gauld, the following results for HOMA, EN and GEO of dehydrotropylium cation **99** were obtained.

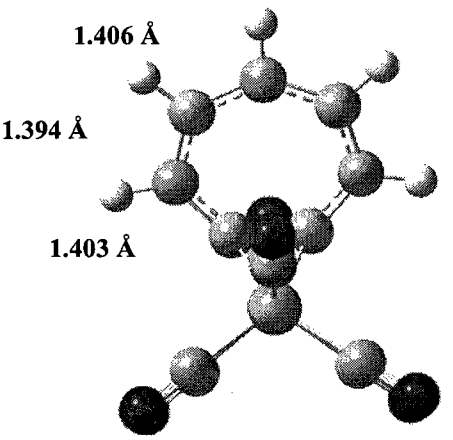


Figure 2.10. B3LYP/6-311 G(d, p) +dzvp optimized structure and HOMA vaue of **99**.

The HOMA value of 0.954 for cation **99**, suggests only a small deviation from an ideal aromatic system (HOMA = 1). The smaller value obtained for the term GEO term than the EN term indicated a dominant contribution of bond elongation in the decrease of aromaticity of cation **99**.

As a note, since the alkyne Cs are not technically sp^2-hybridized, it was assumed that might not be totally accurate to include the C_2-C_3 bond length in the calculations. It is excluding these bonds that give HOMA at 0.954; if they are included one gets HOMA = 0.950, EN = 0.044 and GEO = 0.007, which are essentially the same values.

2.8.3-3 Absolute and relative hardness

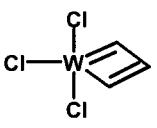
The term absolute hardness (η), first introduced by Pearson in 1987, is associated with the stability and reactivity of a given molecule. In his report, Pearson was able to explain the underlying causes of HSAB principles and gave new insight in to the old definition of hardness and softness, this time based on molecular orbital theory. Accordingly, absolute hardness was defined as half of the energy gap between LUMO and HOMO orbitals (Eq 2.4). It was found the larger the gap between occupied and empty orbital, the more stable/less reactive the compounds is. The principle of maximum hardness: "it seems to be the rule of nature that compounds arrange themselves so that to be as hard as possible" was also proposed by Pearson for the first time. [75]

$$\eta = (\epsilon_{LUMO} - \epsilon_{HOMO})/2 \qquad \textbf{Eqn. 2.4}$$

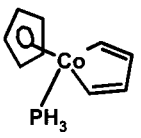
Considering the stability as one of the characteristic properties of aromatic compound, it is not surprising that absolute hardness as one of the indexes of stability/reactivity has been known as a measure of aromaticity for a long time. Zhou and Parr[76] in their studies over wide range of conjugated cyclic hydrocarbons, have tried to quantify hardenss as a measure of aromaticicty. They have found the borderline for aromaticity based on absolute hardness on 0.2 η_β, wherein η_β equals to the hardness of benzene. Compounds having η around 0.2 η_β would expected to be non-aromatic while those with very small η would probably be antiaromatic and those with very large η would be more aromatic.

More recently, Chamizo, Morgado, and Sosa have applied the absolute hardness as a measure of aromaticity for organometallic compounds. In their studies they calculated η

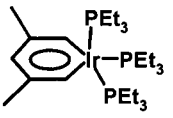
values for a series of metallacycles containing W, Co, Ti, Fe and Ir along with several heterobenzenes and heterocyclopentadienes. They have proposed η (EHMO) = 1.28 eV as dividing line between aromatic and non-aromatic compounds in their series.[77] In another study by Yang and coworkers[78] five diverse indexes of aromaticity including absolute hardness were applied and they all confirmed the selected organometallics (**134-137**) as aromatic. However due to multi-dimensional character of aromaticity, a good correlation on relative aromaticity of these compounds was not found. The calculated HF absolute hardness of some typical transition metal heterocyclic compounds from the Yang report and those of Hückel absolute hardness reported by Chamizo are summarized in Table. 2. 5.



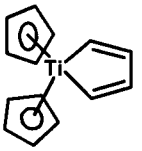
134



135



136



137

η (EHMO) = 1.57 eV	1.25 eV	0.6 eV	1.00 eV	2.27 eV
[a]η (Hartree) = 4.78 eV	4.62 eV	4.22 eV	-	6.47 eV
Our values	1.25[b] eV	0.42[b] eV	0.87[b] eV	2.57[b] eV
				3.30[c] eV

(a) B3LYP-6-31G** (b) B88-PW91/ dzvp (c) B3LYP/6-311G(d, p)

Table 2.5. Absolute hardness for selected organometallic compound.

In this work, we calculated the absolute hardness for cation **99** by using the HOMO and LUMO energies obtained from DFT/ B88-PW91/ dzvp optimized structures.

ϵ LUMO = - 0.305 au
ϵ HOMO = -0.357 au
} η = (-0.305 au + 0.357 au)/2 = 0.026 au = 0.72 eV

Applying the same basis set (DFT/ B88-PW91/ dzvp), η values for compound **135**, **136** and **137** were calculated for comparison. Also, the absolute hardness for cation **99** and benzene were calculated by B3LYP/6-311G (d, p) and found as 1.30 eV and 3.30 eV respectively.

ϵ LUMO = - 0.282 au
ϵ HOMO = -0.378 au
} η = (-0.282 au + 0.378 au)/2 = 0.048 au = 1.30 eV for **99**

From η value calculated above and considering Parr's estimation (0.2 x 2.57eV[a] or 0.2 x 3.30[b] eV) cation **99** would be aromatic. Yet, the small HOMO-LUMO gap found for it is close to the reported values for weakly aromatic organometallic comounds (such as Ir and Ti complexes **136** and **137**), suggesting small amount of aromaticity for cation **99**.

It is worth of mention that in a recent study on the comparison of DFT methods for measuring the LUMO-HOMO, the non-hybrid functionals are found to be better than hybrid functionals and among hybrid functional those with less percentage of HF exchange give less error. In other words, PW91 was found as accurate as B3LYP.[79]

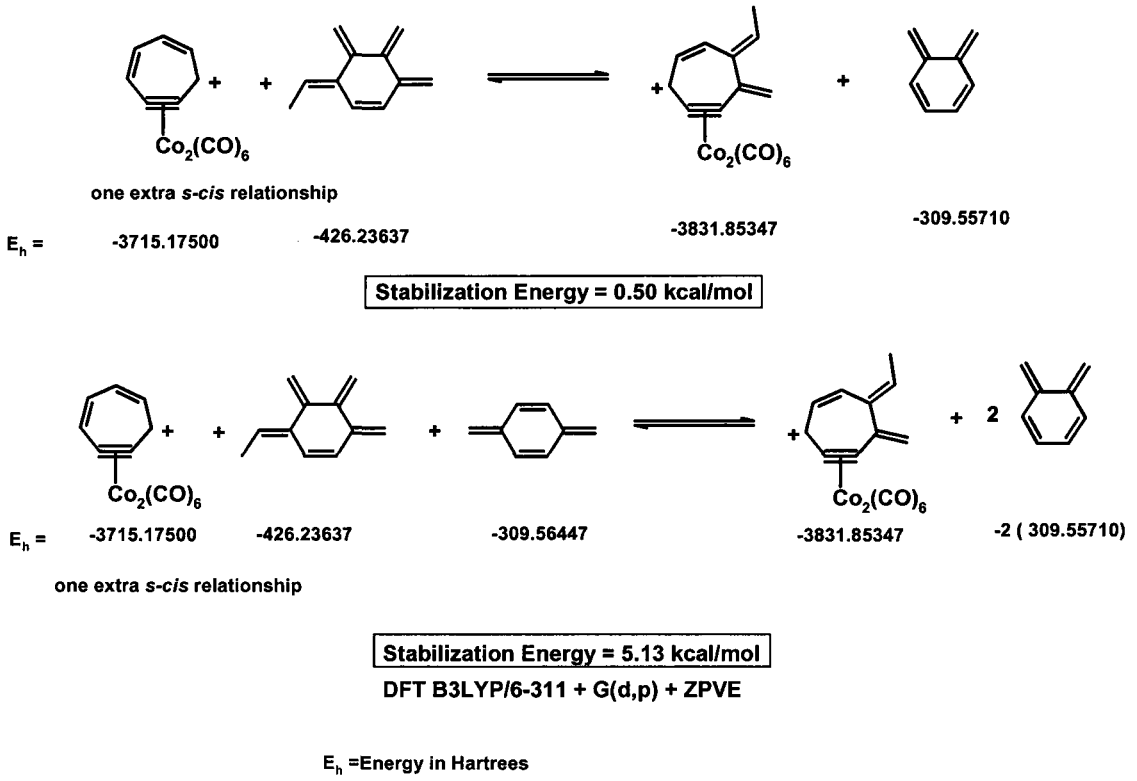
2.8.3-4 Homodesmotic reactions

Based on energetic criterion, most of the time the amount of aromaticity in a molecule is measured from the extra stability of the compound due to its cyclic conjugation relative to a well chosen reference compound due to cyclic conjugation in it. However the aromatic stabilization is just one of the components that contribute to the total energy of a system and to verify that correctly, one has to carefully balance all other components when choosing the reference compound. For this matter homodesomtic, isodesmic and hyperhomodesmotic reactions have been established to cancel the possible

sources of errors. Yet, it is very hard (impossible) to completely balance the strain, hyperconjugatvive effects, difference of types of bonds and atom hybridization all together in energetic schemes. This results in the significant discrepancies that often are observed in the reported aromatic stabilizations of different systems. Indeed, estimated stabilization energies depend largely on the kind of equation and the choice of the reference compounds.

Homodesmotic reactions as a subgroup of isodesmic reactions are defined as equations in which the number of carbon atoms in the corresponding hybridization states is balanced; with a matching of the type of carbon hydrogen bonds in terms of the number of hydrogen atoms attached to each individual carbon. While imperfections exist, homodesmotic reactions based on cyclic reference compounds, which can cancel the strain effects, are commonly used for estimation of aromatic stabilization energy.

Herein, we applied the following equations, designed by Prof. Green and carried out by Prof. Gauld, for measuring the amount of stabilization in cation **99** (Scheme 2.21).



Scheme 2. 21. Homodesmotic reactions for cation **99**.

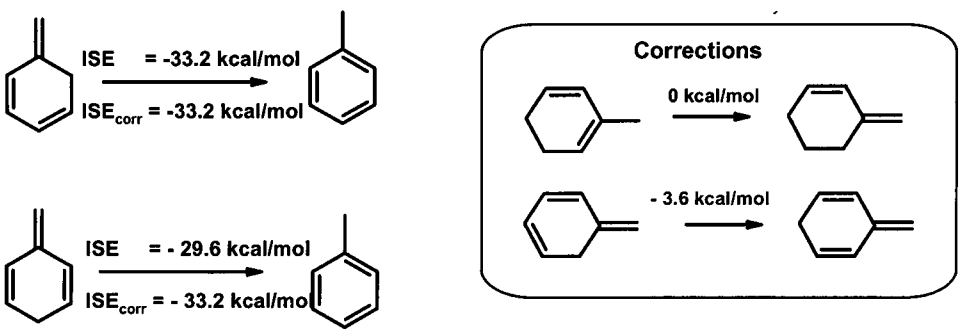
In the first reaction there was one extra *s-cis* relationship on the left side of the equation while in the second reaction the extra *s-cis* relation was put in the right side in order to cancel the error as much as possible. Based on the obtained stabilization energy for both equations, the amount of aromatic stabilization of cation **99** from equation 1 considering an extra *s-cis* diene, which costs about 3 kcal/mole [80] would be 3.5 kcal/mole. From the second equation, after correction for extra *s-cis* was applied, the aromatic stabilization would be 2.13 kcal/mol. Delightfully, these values were close enough and we could estimate aromatic stabilization of cation **99** as mean of these two values which came to 2.8 kcal/mol.

Applying the same equations for the tropylium cation, based on the average ΔG of two equations the aromatic stabilization energy of tropylium ion was calculated to be 11.6

kcal/mol. That is, the calculated amount of aromatic stabilization for cation **99** (2.81 kcal/mol) is approximately 24 % of that of tropylium cation. This result is very consistent with the NICS calculations (28 % of tropylium).

2.8.3-5 Isomeric stabilization energy (ISE)

Homodesmotic reactions like the ones shown above, even if balanced adequately, have the drawback of requiring computation of several reference compounds. Schleyer and Pühlhofer[81] have proposed an alternative way based on a single reference molecule, a non-aromatic isomer of the methyl derivative of an aromatic system (Scheme 2.22). In their proposed reaction the isomeric stabilization energy was calculated directly from the difference between the energy of the two isomers (Scheme 2.22).



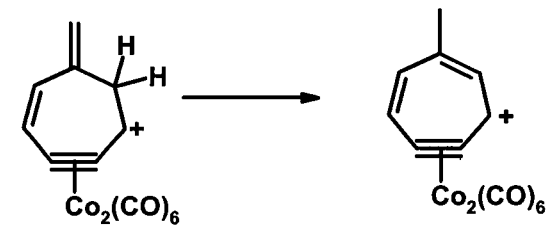
Scheme 2.22. Estimation of aromatic stabilization energy based on ISE.

The results obtained for ISEs, after the corrections were applied for the of *s-cis-s-trans* diene mismatches, were in good agreement with the reference Eqn. 2.6. In particular, ISE was found to be effective for the evaluation of aromatic stabilization energies in several highly strained systems.[81]

Eqn. 2.6

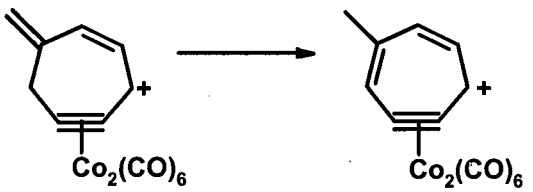
- 30.35 kcal/mol (calculated based on ΔHf)

Therefore, as the last index of aromaticity in our studies, we set out to calculate the ISE of the methyl derivative of our nominally aromatic cation **99** by using DFT/ B88-PW91/ dzvp (Scheme 2.23).



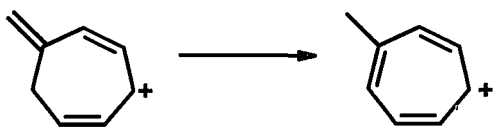
138 **139**

ISE = -19 .94 kcal/mol Eqn. 2.7



140

ISE = -14.7 kcal/mol Eqn. 2.8



ISE = -33.4187 kcal/mol

Scheme 2.23. Estimated aromatic stabilization of **99** and tropylium based on ISE.

Our first estimation of ISE based on Eqn. 2.7 indicated an appreciable amount of stabilization in the system (20 kcal/mol). However, more speculation on the optimized structures of two isomers (**138** and **139**) showed a difference in the amount of cobalt contribution in stabilization of positive charge between two isomers (judging from the

distance of metal center to cationic site in each case). Therefore, the calculation was repeated by changing the position of methyl group on the ring (**140**, Eqn. 2.8). In this new equation the environment around positive charge was kept as similar as possible in both sides of reaction. With that, we aimed to cancel the other factors that might influence the charge stabilization in the reference molecule from our estimation of aromatic stabilization of the system. Now the ISE of the system was calculated as -14.7 kcal/mol. Applying the same equation the amount of ISE for methyl substituted tropylium cation gave a calculated value of -33.4 kcal/mol. This number is close to the amount of ISE calculated for benzene and other known aromatic systems. Thus, based on the calculated ISE, we propose moderate amount of delocalization and the loss of 18.7 kcal/mol of aromatic stabilization in cation **99** in comparison to tropylium cation.

In summary, the aromaticity of cation **99** has been investigated by the use of 4 different indexes. (1) Structural analysis based on HOMA = 0.9 shows very little deviation from aromaticity. (2) From magnetic studies, a NICS value was found -2.92, which confirms the electron delocalization but indicates a little aromaticity in comparison with – 10.5 for tropylium ion. (3) Absolute hardness as stability index was calculated to be 0.77, which is more than 20 % of benzene value and based on Parr's approximation can be considered aromatic but weakly aromatic. (4) Aromatic stabilization energy of the system was calculated from homodesmotic reactions and found to be 2.82 kcal/mol. Moreover, a simpler index, ISE, was also calculated as 14.7 kcal/mol, which was almost half (41%) of the ISE of methyl-substituted tropylium ion that was obtained by applying the same method.

Therefore, while all the indexes suggest the presence of aromaticity, 3 out of 4 suggest the cation **99** as weakly aromatic. We believe the amount of stabilization energy obtained from homodesmotic to be the most reliable one for estimating the amount of aromaticity of cation **99,** because of the high level of theory applied and attempts to account for structural discrepencies.

Summary

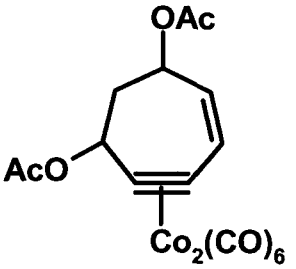
In summary, we were able to synthesize alcohol **101** and generate the desired dehydrotropylium dicobalt hexacarbonyl cation **99** in situ. The ^{1}H NMR spectrum of dehydrotropuliym cation was obtained at low temperature (-80 to -20 °C). The reactivity of cation **99** with a range of nucleophile was investigated. Interestingly, with the nucleophiles weaker than thiophene (N <1) a sharp switching of the reaction pathway from electrophilic addition to the radical dimerization was observed. The presence of the dimerized product in the ^{1}H NMR spectrum of cation **99**, and its formation in the absence of any nucleophile or in presence of relatively weak nucleophiles confirms a rapid and easy formation of propargyl radical from the dehydrotropylium dicobalt cation. Based on 4 indexes of aromaticity that were applied, cation **99** was found to be weakly aromatic; with its NICS (1) value approximately 28 % of tropylium ion.

2.9 EXPERIMENTAL SECTION

All the reactions containing cobalt carbonyl were carried out under dry condition under an N_2 atmosphere. The solvents used for the reactions obtained directly from solvent purification system (Innovative Technologies) prior to the application. Silica gel (Merck 230-400) obtained from Silicycle chemical division was used for column chromatography. Analytical thin layer chromatography (TLC) was performed over silica gel 60 F_{254} sheets, while Analtech silica gel GF-254 plates were used for preparative thin layer chromatography.

^{1}H NMR and ^{13}C NMR spectra were recorded on either Bruker Avance 300 or 500 MHz spectrometers. IR spectra were recorded on a Bruker Vector 22 FT-IR spectrophotometer. The samples were coated on NaCl or KBr plates as a thin layer. Mass spectra were initially recorded on a Varian Saturn 2000 GS /MS, in direct probe mode, using electron impact (20 eV) for structural confirmation. High resolution mass spectra were acquired from McMaster Regional Center for Mass Spectrometry (EI).

Hexacarbonyl [μ-η^4-(5,7-diacetoxycyclohept-1-en-3-yne)] dicobalt

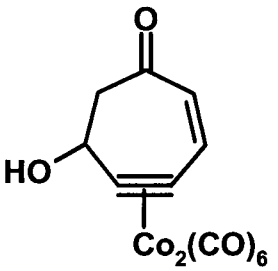


114

To a solution of **113** (1.41 g, 2.84 mmol) in CH_3CO_2H (20 mL) was added H_2SO_4 (10 drops). After stirring for 1.5 h, water was added and the mixture was subjected to a conventional extractive workup with hexane. The organic layers were dried over $MgSO_4$, and concentrated under reduced pressure. Flash chromatography (10:1 PET:Et_2O) afforded **114** (1.35 g, 95 % yield) as a single diastereomer.

(114), IR (neat, NaCl) ν_{max}= 3030, 2928, 2095, 2056, 2029, 1741 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 6.77 (d, J = 10.0, 1H), 6.27 (dd, J = 10.3, 3.7, 1H), 6.14 (dd, J = 10.0, 6.3, 1H), 5.57 (app t, J = 6.8, 1H), 2.40 (m, 1H), 2.16 (s, 3H), 2.05 (m, 1H), 2.03 (s, 3H); ^{13}C NMR ($CDCl_3$) 198.9 (br), 170.2, 170.0, 130.6, 130.3, 93.9, 81.4, 71.0, 67.3, 35.0, 21.0, 20.8; MS (EI, 20 eV) m/e 466 (M^+-CO), 438 (M^+ -2CO), 354 (M^+-5CO), 326 (M^+-6CO) ; HRMS (TOF) m/e for $C_{17}H_{12}Co_2O_{10}$ calcd. 465.9145 (M^+-CO), found 465.9159.

Hexacarbonyl[μ-η^4-(6-hydroxycyclohept-2-en-4-ynone)]dicobalt (116)

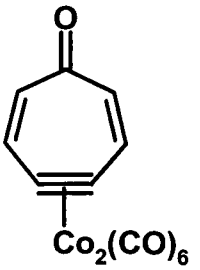


116

Compound **114** (1.00 g, 2 mmol) was dissolved in Et_2O (10 mL) and the solution was cooled to -75 °C. DIBAL-H (8.0 mL of a 1 M solution in Et_2O, 4 equiv) was added to the solution. After stirring for 1.5 h at -75 °C, saturated NH_4Cl (aq) was added and the organic product was extracted with Et_2O. Drying the combined organic layers with $MgSO_4$ and evaporating the solvent and other volatile compounds in vacuo, provided dialcohol **115** as a crude material. This crude containing **115** was dissolved in CH_2Cl_2 and excess amount of MnO_2 was added. After stirring for 8 h at 0°C, the solution was filtered through silica gel. The filtrate was concentrated under reduced pressure to gave a residue, which was subjected to flash chromatography (4:1 PET: Et_2O) to afford **116** (0.41 g, 50%).

(116), IR (neat, NaCl) ν_{max} = 3417, 3027, 2925, 2099, 2059, 2030, 1651 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 7.36 (d, J = 10.4, 1H), 6.26 (d, J = 10.4, 1H), 5.17 (m, 1H), 3.02 (m, 2H), 2.20 (d, J = 5.0, 1H); ^{13}C NMR ($CDCl_3$) 198.3 (br, obscured), 139.5, 132.2, 98.1, 78.4, 68.7, 52.3; MS (EI, 20 eV) m/e 408 (M^+), 380 (M^+-CO), 352 (M^+-2CO), 324 (M^+-3CO), 296 (M^+-4CO); HRMS (TOF) m/e for $C_{13}H_6Co_2O_8$ calcd. (M^+) 407.8727, found 407.8705.

Hexacarbonyl[μ-η^4-(cyclohepta-2,6-dien-4-ynone)]dicobalt (117)

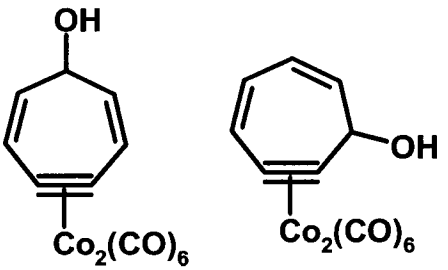


117

To a solution of **116** (0.200 g, 0.490 mmol) in CH_2Cl_2 (10 mL), HBF_4 (0.5 mL, 54 wt. % in Et_2O, excess) was added dropwise. The reaction was monitored with TLC and was quenched with saturated $NaHCO_3$ upon the disappearance of starting material (within a few minutes). (Note: using milder acids such as TsOH or BF_3. Et_2O slowed down the reaction with no improvement in the yield of the reaction). After conventional extractive workup (CH_2Cl_2) and evaporation of the solvent compound **117** was obtained as a crude material. Flash chromatographic purification (5:1 PET: Et_2O) afforded **117** (0.095 g, 50% yield).

(**117**), IR (neat, NaCl) ν_{max}= 3031, 2927, 2102, 2064, 2032, 1699 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 7.61 (d, J = 10.0, 2H), 6.59 (d, J = 10.0, 2H); ^{13}C NMR ($CDCl_3$) 198.0 (br), 191.1, 140.5, 135.3, 80.5; MS (EI, 20 eV) m/e 390 (M^+), 362 (M^+-CO), 334 (M^+ -2CO), 306 (M^+-3CO), 278 (M^+-4CO), 250 (M^+-5CO), 222 (M^+-6CO); HRMS (TOF) m/e for $C_{13}H_4Co_2O_7$ calcd. (M^+) 389.8621, found 389.8625.

Hexacarbonyl[μ-η^4-(cyclohepta-2,6-dien-4-ynol)]dicobalt (101a) and Hexacarbonyl μ-η^4-(cyclohepta-2,4-dien-6-ynol)]dicobalt (101b)



101a **101b**

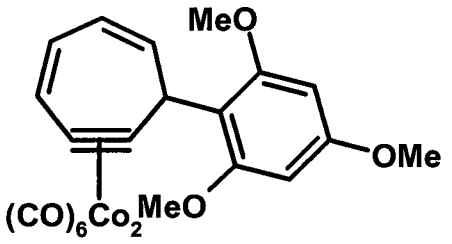
To a solution of **117** (0.170 g, 0.435 mmol) in Et_2O (10 mL) at -78 °C was added DIBAL-H (0.900 mL of 1M solution, 0.915 mmol). After stirring for 1.5 h at -78 °C, the reaction was quenched with saturated $NH_4Cl_{(aq)}$. Subsequent conventional extractive workup with Et_2O and evaporation of the solvent provided crude alcohol **101**. Flash chromatographic purification (100% PET – 5:1 PET: Et_2O gave the sequential elution of recovered **117** (0.008 g, 5%), alcohol **101b** (0.008 g, 5% yield), and **101a** (0.120 g, 70%). (**101 a**), IR (neat, NaCl) ν_{max} = 3324, 3021, 2923, 2099, 2053, 2053, 2028, 2009 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 6.79 (dd, J = 10.0, 1.8, 1H), 5.93 (dd, J = 10.0, 3.8, 1H), 4.94 (br, 1H,), 2.21 (br, 1H); ^{13}C NMR ($CDCl_3$) 199.1, 133.0, 127.5, 84.8, 70.3; MS (EI, 20 eV) m/e 392 (M^+); HRMS (TOF) m/e for $C_{13}H_6Co_2O_7$ calcd. 391.8763 (M^+), found 391.8764. (**101b**), IR (neat, NaCl): ν_{max} = 3400 (br), 3022, 2095, 2054, 2022 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 6.88 (d, J = 9.8, 1H), 6.17 (m, 1H), 5.92-5.98 (m, 2H), 5.55 (d, J = 6.2, 1H), 2.18 (br, 1H); ^{13}C NMR (CD_2Cl_2) 199.8 (br), 135.7, 131.4, 127.2, 126.4, 102.5, 83.1, 72.5; MS (EI,

20 eV) m/e 364 (M^+-CO), 336 (M^+-2CO), 308 (M^+-3CO), 280 (M^+-4CO), 252 (M^+ - 5CO), 224 (M^+-6CO).

Procedure A : Standard conditions for reaction of 101a with different nucleophiles

To a solution of alcohol **101a** (0.0180 -0.0280 g, 0.0459-0.0714 mmoles) and a nucleophile (4-5 equivalents) in CH_2Cl_2 (5 mL), at 0 °C was added 3 equivalents of $BF_3.OEt_2$. The reaction was monitored by TLC and quenched with saturated $NaHCO_{3(aq)}$ upon complete disappearance of starting material (mostly after 30 min of stirring). After conventional workup with CH_2Cl_2, drying the organic layer with $MgSO_4$ and evaporating the solvent, the crude residue was subjected to flash chromatography to afford the product in pure form.

Hexacarbonyl[μ-η^4-(7-(2,4,6-trimethoxyphenyl)cyclohepta-1,3-dien-5-yne)]dicobalt ($121b_1$)

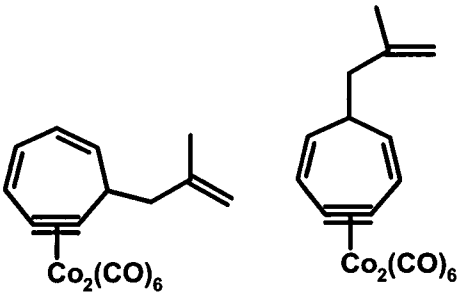


$121b_1$

Reaction of compound **101a** (0.023 g, 0.059 mmol) with 1,3,5-trimethoxybenzene (0.050 g, 0.29 mmol) under standard conditions (procedure A), after flash chromatography (10:1 PET: Et_2O), provided **$121b_1$** (0.028 g, 88% yield).

(**$121b_1$**), IR (neat, NaCl) ν_{max} = 3019, 2924, 2090, 2050, 2020 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 6.74 (d, J = 9.6, 1H), 6.17 (s, 2H), 6.12 (dd, J = 9.6, 7.5, 1H), 5.95 (dd, J = 11.9, 1.9, 1H), 5.83 (m, 1H), 5.59 (br s, 1H), 3.86 (s, 3H), 3.80 (s, 3H), 3.78 (s, 3H); ^{13}C NMR ($CDCl_3$) 199.8 (br), 160.3, 159.7, 158.2, 137.7, 129.3, 127.4, 124.7, 110.8, 106.4, 90.7, 90.1, 85.6, 55.3, 55.2, 54.5, 40.0; MS (EI, 20 eV) m/e 514 (M^+-CO), 486 (M^+-2CO), 458 (M^+-3CO), 430 (M^+-4CO), 402(M^+-5CO), 374 (M^+-6CO); HRMS (TOF) m/e for $C_{22}H_{16}Co_2O_9$ calcd. (M^+-2CO) 485.9560, found 485.9538.

Hexacarbonyl[μ-η^4-(7-(2-methylallyl)cyclohepta-1,3-dien-5-yne)]dicobalt(121a$_2$) and Hexacarbonyl[μ-η^4-(7-(2-methylallyl)cyclohepta-1,5-dien-3-yne)] dicobalt (121b$_2$):

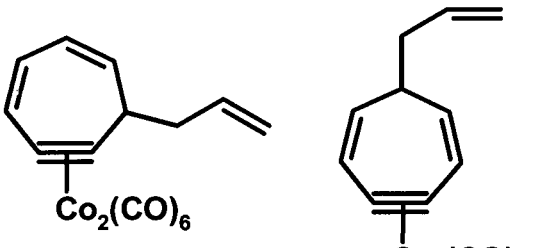


121b$_2$ **121a$_2$**

Reaction of **101a** (0.020 g, 0.051 mmol) with methallyltrimethylsilane (35 μL, 0.20 mmol) under the standard conditions afforded **121a$_2$ +121b$_2$** (0.016 g, 73%) as a 67:33 mixture of **121b$_2$: 121a$_2$** following purification by flash chromatography (100% hexanes).

(121a$_2$ +121b$_2$), IR (neat, NaCl): ν_{max} = 2091, 2050, 2021 cm^{-1}; ^{1}H NMR ($CDCl_3$) (major isomer) δ = 6.79 (d, J = 9.6, 1H), 6.12 (dd, J = 9.6, 7.2, 1H), 5.90 (ddd, J = 11.9, 7.2, 2.4, 1H), 5.73 (ddd, J = 11.9, 3.0, 0.9, 1H), 4.93 (s, 1H), 4.87 (s, 1H), 3.83 (m, 1H), 2.59 (dd, J = 14.1, 5.1, 1H), 2.44 (dd, J = 14.1, 10.2, 1H), 1.80 (s, 3H); (minor isomer) 6.71 (br d, J = 9.7, 2.2, 2H), 5.65 (dd, J = 9.7, 4.2, 2H), 4.87 (s, 1H), 4.76 (s, 1H), 3.15 (m, 1H), 2.33 (d, 7.7, 2H), 1.70 (s, 3H); ^{13}C NMR ($CDCl_3$) (major isomer) 199.7 (br), 142.6, 134.0, 127.61, 127.2, 113.2, 105.7, 85.8, 45.5, 41.1, 22.2; resonances from the minor isomer could be detected at 142.2, 135.0, 127.58, 113.4, 87.3, 44.8, 39.8, 22.0; MS (EI, 20 eV) m/e 402 (M^+-CO), 374 (M^+-2CO), 346 (M^+-3CO), 318 (M^+-4CO), 290 M^+-5CO), 262 (M^+-6CO); HRMS (TOF) m/e for $C_{17}H_{12}Co_2O_6$ calcd. (M^+-CO) 401.9349, found 401.9334.

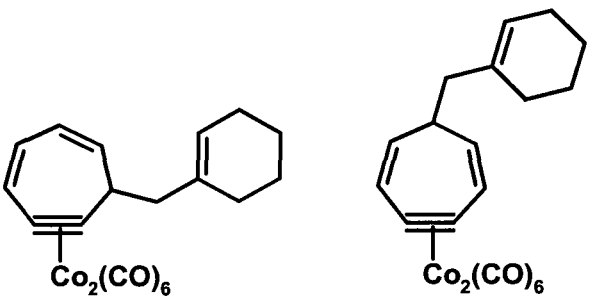
Hexacarbonyl[μ-η^4-(7-allylcyclohepta-1,3-dien-5-yne)]dicobalt(121b$_3$)and Hexacarbonyl [μ-η^4-(7-allylcyclohepta-1,5-dien-3-yne)]dicobalt (121a$_3$)



121 b$_3$ **121 a$_3$**

Reaction of **101a** (0.028 g, 0.071 mmol) with allyltrimethylsilane (56 μL, 0.36 mmol) under the standard conditions afforded **121a$_3$ +121b$_3$** (0.021 g, 70%) as a 83:17 mixture of **121b$_3$:121a$_3$** following purification by flash chromatography (100% hexanes). (**121a$_3$ +121b$_3$**), IR (neat, NaCl) ν_{max} = 2923, 2853, 2090, 2053, 2023 cm^{-1}; ^{1}H NMR ($CDCl_3$), δ (major isomer) = 6.79 (d, J = 10.0, 1H), 6.11 (dd, J = 10.0, 7.5, 1H), 5.96 (m, 1H), 5.90 (m, 1H), 5.74 (ddd, J = 12.0, 3.0, 1.0, 1H), 5.22 (dd, J = 17.0, 1.5, 1H), 5.17 (dd, J = 10.5, 1.5, 1H), 3.74 (m, 1H), 2.67 (m, 1H), 2.51 (m, 1H); (minor isomer) 6.69 (dd, J = 9.5, 2.0, 2H), 5.79 (m, 1H), 5.64 (dd, J = 9.5, 4.3, 2H), 5.10 (d, J = 9.4, 1H), 5.09 (d, J = 17.7, 1H), 3.16 (m, 1H), 2.37 (app t, J = 6.8, 2H); ^{13}C NMR ($CDCl_3$) (major isomer) 199.6 (br), 136.0, 135.0, 130.2, 127.7, 127.1, 117.4, 104.9, 85.8, 43.5, 41.3; resonances from the minor isomer could be detected at 135.5, 133.8, 127.4, 42.5, 41.1; MS (EI, 20 eV) m/e 418 (M^+), 388 (M^+-CO), 360 (M^+-2CO), 332 (M^+-3CO), 304 (M^+-4CO), 276 (M^+--5CO), 248 (M^+-6CO); HRMS (TOF) m/e for $C_{16}H_{10}Co_2O_6$ calcd. (M^+-CO) 387.9192, found 387.9166.

Hexacarbonyl[μ-η^4-(7-(cyclohexenylmethyl)cyclohepta-1,3-dien-5-yne)]dicobalt ($121b_4$) and Hexacarbonyl[μ-η^4-(7-(cyclohexenylmethyl)cyclohepta-1,5-dien-3-yne)]dicobalt ($121a_4$)



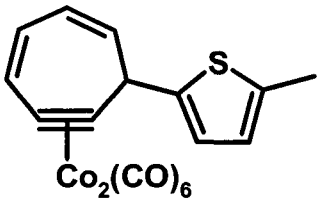
121 b_4 **121 a_4**

Reaction of **101a** (0.027 g, 0.068 mmol) with methylenecyclohexane (33 μL, 0.28 mmol) under the standard conditions afforded **$121a_4$ + $121b_4$** (0.016 g, 50%) as a 90:10 mixture of **$121b_4$:$121a_4$** following purification by flash chromatography (10:1 PET: Et_2O).

(**$121a_4$ + $121b_4$**), IR (neat, NaCl) ν_{max}= 3018, 2929, 2090, 2050, 2020 cm^{-1}; ^1H NMR ($CDCl_3$) (major isomer) δ = 6.77 (d, J = 9.5, 1H), 6.11 (dd, J = 9.5, 7.0, 1H), 5.88 (m, 1H), 5.73 (dd, J = 12.0, 1.0, 1H), 5.58 (br s, 1H), 3.82 (m, 1H), 2.53 (m, 1H), 2.34 (m, 1H), 2.00-2.10 (m, 4H), 1.55-1.75 (m, 4H); resonances from the minor isomer could be detected at 6.49 (dd, J = 9.5, 2.2, 1H), 5.64 (dd, J = 9.5, 4.5, 1H), 5.49 (br s, 1H), 3.16 (m, 1H), 2.24 (d, J = 7.5, 2H); ^{13}C NMR ($CDCl_3$) (major isomer) 199.7 (br), 135.4, 134.8, 130.0, 127.3, 127.2, 124.2, 106.1, 85.9, 46.0, 41.0, 28.2, 25.3, 22.9, 22.4; peaks from the minor isomer could be observed at 134.4, 124.5, 45.3, 40.0, 20.0; MS (EI, 20 eV) m/e 470

(M^+), 442 (M^+- CO), 414 (M^+-2CO), 386 (M^+-3CO), 358 (M^+-4CO), 330 (M^+-5CO), 302 (M^+-6CO); HRMS (TOF) m/e for $C_{20}H_{16}Co_2O_6$ calcd. (M^+) 469.9611, found 469.9626.

Hexacarbonyl[μ-η^4-(7-(5-methyl-2-thienyl)cyclohepta-1,3-dien-5-yne)]dicobalt (121b$_5$)

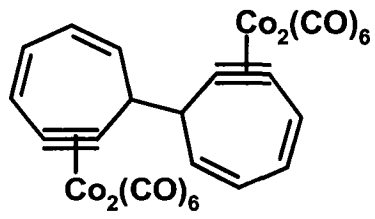


121 b$_5$

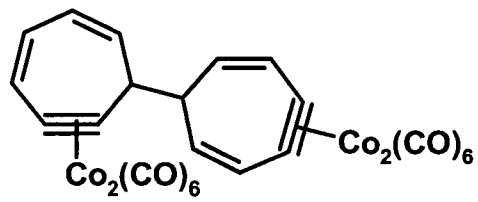
Reaction of **101a** (0.018 g, 0.046 mmol) with 2-methylthiophene (23 μL, 0.23 mmol) under the standard conditions afforded **121b$_5$** (0.018 g, 83% yield) following purification by flash chromatography (100% hexanes).

(**121b$_5$**), IR (neat, NaCl) ν_{max} = 3020, 2923, 2091, 2052, 2022 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 6.84 (d, J = 9.0, 1H), 6.76 (d, J = 3.0, 1H), 6.61 (d, J = 3.0, 1H), 6.18 (m, 1H), 6.00-6.08 (m, 2H), 5.16 (s, 1H), 2.46 (s, 3H); ^{13}C NMR ($CDCl_3$) 199.0 (br), 145.0, 139.0, 134.3, 131.0, 127.9, 126.6, 124.7, 124.4, 105.9, 84.5, 45.7, 15.4; MS (EI, 20 eV) m/e 472 (M^+), 444 (M^+-CO), 416 (M^+-2CO), 388 (M^+- 3CO), 360 (M^+-4CO), 332 (M^+-5CO), 304 (M^+-6CO); HRMS (TOF) m/e for $C_{18}H_{10}Co_2O_6S$ calcd. (M^+) 471.8862, found 471.8851.

Hexacarbonyl[μ^4-η^2,η^2,η^2,η^2-(1,1'-bi(cyclohepta-2,4-dien-6-yne)]tetracobalt (120a) and Hexacarbonyl[μ^4-η^2,η^2,η^2,η^2-(7-(cyclohepta-2,6-dien-4-ynyl)cyclohepta-1,3-dien-5-yne)]- tetracobalt (120b)



120a



120b

To a solution of **101a** (0.028 g, 0.071 mmol) and mesitylene (49 μL, 0.36 mmol) in CH_2Cl_2 (5 mL) at 0 °C was added BF_3-OEt_2 (26 μL, 0.21 mmol). After 15 min, saturated $NaHCO_{3(aq)}$ was added and the mixture subjected to a conventional extractive workup (CH_2Cl_2). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Flash chromatography (100% hexanes) afforded **120a+120b** (0.0133 g, 50%) as a 33:67 mixture of **120a:120b**. Compound **120b** slowly decomposed in solution in $CDCl_3$.

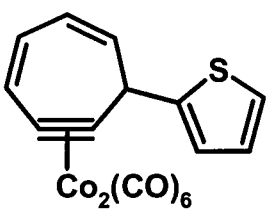
(**120a+120b**), IR (neat, NaCl) ν_{max} = 3020, 2923, 2091, 2053, 2023 cm-1; ^{1}H NMR ($CDCl_3$) (major isomer) δ = 6.96 (dd, J = 9.8, 2.6, 1H), 6.94 (dd, J = 9.3, 2.6, 1H), 6.87 (d, J = 9.6, 1H), 6.17 (dd, J = 9.6, 7.3, 1H). 6.0-6.08 (m, 2H), 5.96 (dd, J = 9.3, 3.6, 1H), 5.77 (ddd, J = 11.9, 3.1, 1.0, 1H), 3.96 (m, 1H), 3.38 (m, 1H); resonances from the minor isomer could be detected at 6.89 (d, J = 9.7, 2H), 6.25 (dd, J = 9.7, 7.3, 2H), 6.13 (m, 2H), 6.00 (ddd, J = 12.0, 2.5, 1.0, 2H), 4.16 (br s, 2H); ^{13}C NMR ($CDCl_3$) 199.3 (br), 133.4 (major), 132.8 (major), 132.3 (major), 131.6 (minor), 130.8 (major), 130.5 (major), 130.2

(minor), 129.8 (minor), 129.6 (major), 127.7 (minor), 126.9 (major), 104.2, 86.4, 48.5 (minor), 46.7 (major); MS (EI, 20 eV) m/e 638 (M^+-4CO), 610 (M^+-5CO), 582 (M^+-6CO), 554 (M^+-7CO), 526 (M^+-8CO), 498 (M^+-9CO), 470 (M^+-10CO), 442 (M^+-11CO), 414 (M^+-12CO); HRMS (TOF) m/e for $C_{26}H_{10}Co_4O_{12}$ calcd. (M^+) 749.7500, found 749.7515.

Reaction of 3-methylanisole (35 μL, 0.284 mmol) with (0.028 g, 0.071 mmol) of alcohol **101a**, anisole (25 μL, 0.229mmol) and thiophene (18 μL, 0.229mmol) with (0.018 gr, 4.59 x 10^{-5}moles) of alcohol **101a**, following procedure A, in each case gave dimer with the same isomeric ratio (33:67) and 26 %, 18 % and 34% (along with 4% condensation product) yields respectively.

Note: Subjection of alcohol **101a** to a large excess amount of anisole did not give any isolable condensation product, however, in case of thiophene as solvent; condensation product (**121 b_6**) was obtained as the sole product.

Hexacarbonyl[μ-η^4-(7-(2-thienyl)cyclohepta-1,3-dien-5-yne)]dicobalt (121b_6)

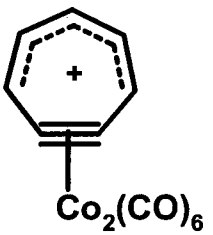


121 b_6

(**121 b_6**), IR (neat, NaCl) ν_{max} = 3020, 2092, 2053, 2024 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 7.23 (dd, J = 5, 1, 1H), 7.00-6.98 (m, 2H), 6.85 (d, J = 9.5, 1H), 6.20-6.17 (m, 1H), 6.07 (m, 1H), 5.25 (br s, 1H); ^{13}C NMR ($CDCl_3$) 198.8, 147.5, 134.1, 131.1, 128.2, 126.8, 126.67,

124.63, 124.34, 105.78, 84.40, 45.46; MS m/e : (M^+-1CO) : 430 , (M^+-2CO): 402. HRMS (TOF) m/e for $C_{17}H_8Co_2O_6S$, calc. (M^+) 457.8706 found 457.8713.

Cation generation :



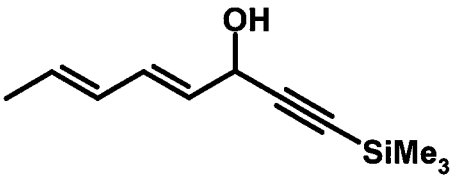
99

To a solution of alcohol **101a** (0.020 g, 0.051 mmol) in Et_2O (4 mL) was added HBF_4 (0.10 mL, 54 wt. % in Et_2O, excess) at -75 °C. The colour of solution has changed immediately and dark solid carbocation precipitated out of solution. After stirring the mixture for 15 min, the solvent was decanted, the solid was washed twice of times with Et_2O, and then dried under reduced pressure. The isolated solid was dissolved in CD_2Cl_2 and subjected to ^1H NMR analysis at -80 °C. The temperature was gradually increased from -80 °C to -50°C and then up to -20 °C while the spectrum was recorded.

In another attempt, a solution of alcohol **101a** (0.028 g, 0.071 mmol) in CH_2Cl_2 was subjected to the Lewis acid (BF_3. OEt_2, 26 μL, 3 equiv) and cation was precipitated by addition of Et_2O. Decanting the solvents and drying the solid provided similar results.

Note : Addition of an excess (0.20 mL) of allyl-TMS to the NMR tube and bringing the temperature to room temperature did not result in formation of condensation product, presumably due to gradual decomposition of carbocation. From this reaction after filtration and evaporation of solvents dimer was obtained in almost pure form.

(4E, 6E)-1-(Trimethylsilyl)octa-4,6-dien-1yn-3ol (130)

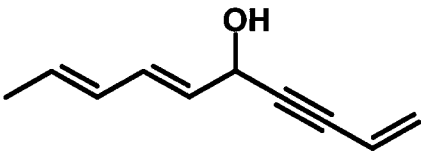


130

A solution of trimethylsilylacetylene (0.71 mL, 5.0 mmol) in diethyl ether (11 mL) was cooled to -75 °C and to that was added MeLi (3.12 mL, 1.6 M solution in Et_2O, 5.0 mmol). After stirring for an hour, sorbaldehyde (0.50 mL, 4.5 mmol) was added and the reaction stirred at -75° C for another one hour. The reaction was quenched by slowly adding saturated solution of $NH_4Cl_{(aq)}$, and the mixture was allowed to warm up to room temperature. Following an extractive work up with diethyl ether, the combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The crude residue was subjected to flash column chromatography on neutralized silica (for that, first a slurry of silica in PET: Et_2O: Et_3N 100:1:20 drops was prepared and after injection of the sample a mixture of PET: Et_2N: Et_2O with the ratio of 100: 20 drops :10 was used as eluent). Compound **130** (0.27 g, 1.3 mmol) was isolated (28% yield).

(130), IR (neat, KBr) ν_{max} = 3383, 3022, 2961, 2173, 1624, 1251, 1071, 1025, 844, 761cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 6.35 (dd, J= 10.5, 15.0, 1H), 6.07 (m, 1H), 5.8 (m, 1H), 5.64 (dd, J =15.0, 6.0, 1H), 4.88 (m, 1H), 1.78 (d, J = 6.50, 3H), 0.192 (s, 9H); ^{13}C NMR ($CDCl_3$) 132.7, 131.9, 130.4, 128.7, 104.7, 91.0, 63.3, 18.3, 0.05; HRMS (TOF) m/e for $C_{11}H_8OSi$ calc. 194.1127 found 194.1117.

(6E, 8E)-Deca-1, 6, 8-trien-3-yn-5-ol (131)



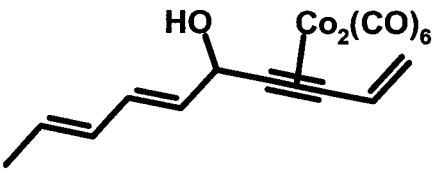
131

To a solution of **130** (0.50 g, 2.5 mmol) in THF (15mL) was added 3 equivalents of TBAF (7.5 mL, 1M solution in THF, 7.5 mmol); the mixture was stirred at room temperature for an hour. Water was added and the organic compounds were extracted with diethyl ether, the organic layer washed several times with water, dried over $MgSO_4$ and solvents were removed under reduced pressure. The crude residue was dissolved in diethylamine (5 mL), vinyl bromide (3.9 mL, 1M), $Pd(PPh_3)_4$ and CuI (1 mol %, 3mol %, 0.030 g) each were added to the solution and the mixture was stirred for 18 h at room temperature. Saturated NH_4Cl was added, the organic compounds were extracted with CH_2Cl_2, the aqueous layer was washed couple of times with Et_2O and the organic extracts were. Drying the solution with $MgSO_4$ and evaporation of solvents gave the crude product as a brown oil. Subjecting the crude residue to flash column chromatography on nuetrilized silica was accompanied with the formation of several new bands and loss of product at this step. Thus, even though the pure alcohol (**131**) was collected from column (PET: Et_2O: Et_3N, 100 mL: 10 mL: 20 drops) and characterized spectroscopically, for the practical purpose, the crude alcohol **130** was subjected to the cobalt carbonyl complexation in the subsequent step.

(**131**), IR (neat, KBr) ν_{max}= 3355, 3020, 2962, 2915, 2854, 1660, 1610, 1377, 1290 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 6.36 (dd, J =15.0, 11.0, 1H), 6.07 (dd, J =14.0, 10.0, 1H), 5.80-5.83

(m, 2H), 5.67 (app d, J =18.0, 2 H), 5.50 (d, J =11.0, 1H), 5.01 (d, J = 6.0, 1H), 1.77 (d, J = 6.5, 3H);^{13}C NMR ($CDCl_3$) 132.8, 132.2, 130.4, 128.7, 128.0, 116.8, 89.0, 85.0, 63.5, 18.5; MS (TOF) 148 (M^+).

Hexacarbonyl[μ-η4-((6E, 8E)-deca-1, 6, 8-trien-3-yn-5-ol) dicobalt (128)



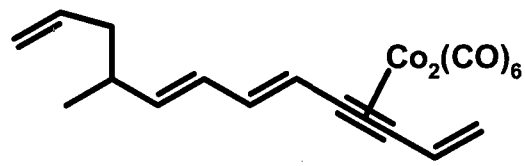
128

The crude mixture of compound **131** (which was obtained from alcohol **130** (0.200 g, 1 mmol, following the synthetic method described above), was dissolved in dichloromethane and an excess amount of $Co_2(CO)_8$ was added to the solution. The mixture was stirred for an hour, concentrated in vacuo and subjected to flash column chromatography (PET: Et_2O 5:1) for purification. Compound **128** (0.117 g, 27% from alcohol **130**) was obtained in pure form.

(**128**), IR (neat, KBr) ν_{max} = 3449, 2928, 2856, 2092, 2053, 2023, 1856, 987 cm^{-1};

^{1}H NMR ($CDCl_3$), δ = 6.83 (dd, J =16.5, 10.0, 1 H), 6.34 (dd, J =15.0, 10.5, 1H), 6.04 (app dt, J =10.5, 1.5, 1H), 5.79 (m, 1H), 5.65 (dd, J=15.0, 10.5, 1H), 5.60 (dd, J =16.5, 1.5, 1H), 5.50 (dd, J =10.5, 1.5, 1 H), 5.35 (app t, J =5.5, 1H), 1.94 (d, J =4.5, 1 H), 1.77 (dd, J=6.5, 1.3, 3H); ^{13}C NMR ($CDCl_3$) 199.1, 133.4, 131.6, 131.5, 131.2, 130.1, 120.2, 101.1, 89.5, 73.1, 18.1; HRMS (TOF) m/e for $C_{16}H_{12}Co_2O_7$ calcd. (M^+-CO) 405.9298, found 405.9279.

Hexacarbonyl[μ-η4-((5E, 7E)-9-methyldodeca-1, 5, 7, 11-tetraen-3-yne) dicobalt (132a)



132a (85%)

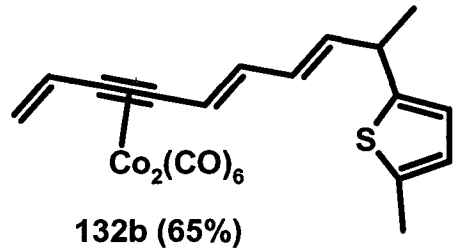
To a solution of alcohol **128** (0.033 g, 0.076 mmol) and allyltrimethylsilane (40 μL, 0.25 mmol) in CH_2Cl_2 (5 mL) was added $BF_3{\cdot}OEt_2$ (31 μL, 0.25 mmol) at 0 °C. The mixture was stirred for 0.5 h before it was quenched by addition of saturated solution of $NaHCO_{3(aq)}$. Extraction with dichloromethane, drying the organic layer with $MgSO_4$ and evaporation of the solvent provided the product **132a** as a crude mixture. Purification by flash column chromatography (100% hexanes) gave **132a** (0.030 g, 85 %).

(132a), IR (neat, KBr) ν_{max}= 2966, 2927, 2089, 2051, 2020, 1638, 982, 913, 515 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 6.91 (dd, J =16.0, 10.5, 1 H), 6.56-6.63 (m 2H), 6.16 (dd, J =15.5, 9.0, 1H), 5.73-5.83 (m, 2H), 5.62 (dd, J =16.5, 1.50, 1 H), 5.49 (dd, J =10.0, 1.50, 1H), 5.00-5.07 (m, 2 H), 2.31 (m, J=9.0, 1H), 2.14 (m, 1H), 2.08 (m, 1H), 1.04 (d, J=6.50, 3H). ^{13}C NMR ($CDCl_3$) 199.6, 142.5, 137.0, 136.5, 134.4, 128.7, 127.3, 120.0, 116.4, 41.3, 37.1, 19.8; HRMS (TOF) m/e for $C_{19}H_{16}Co_2O_6$ calcd. (M^+) 457.9611 found 457.9612.

To a solution of alcohol **128** (0.037 g, 0.085 mmol) and allyltriphenylsilane (0.090 g, 0.30 mmol) in CH_2Cl_2 (5 mL) was added $BF_3.OEt_2$ (31 μL, 0.25 mmol) at 0 °C. The mixture was stirred for 0.5 h before it was quenched by addition of saturated solution of $NaHCO_{3\,(aq)}$. Extraction with dichloromethane, drying the organic layer with $MgSO_4$ and

evaporation of the solvent provided the product **132a** as a crude mixture. Purification by flash column chromatography (100% hexanes) gave **132a** (15 mg, 38 %).

Hexacarbonyl[μ-η^4-(2-(3E, 5E)-deca-3, 5, 9-trien-7-yn-2-yl)-5-methylthiophene)]dicobalt (132b)



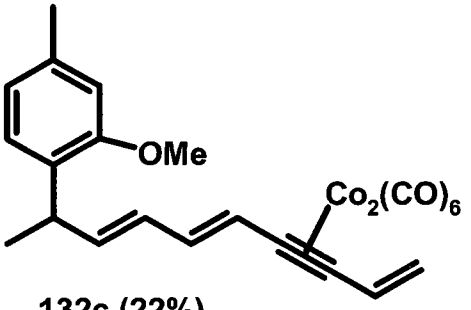
132b (65%)

To a solution of alcohol **128** (0.027 g, 0.062 mmol) and 2-methylthiophene (18 μL, 0.25 mmol) in CH_2Cl_2 (5 mL) was added $BF_3{\cdot}OEt_2$ (26 μL, 0.18 mmol) at 0 °C. The mixture was stirred for half an hour before it was quenched by addition of saturated solution of $NaHCO_{3\,(aq)}$. Extraction with dichloromethane, drying the organic layer with $MgSO_4$ and evaporation of the solvent provided the product **132b** as a crude mixture. Purification by flash column chromatography (100% hexanes) gave **132b** (0.020 g, 65 %).

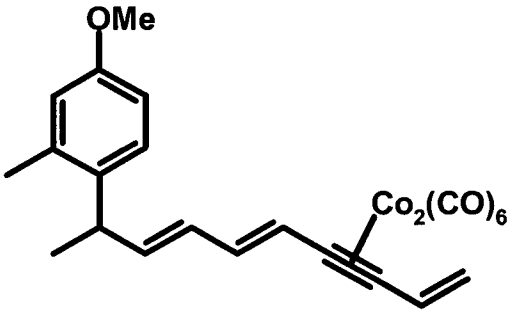
(132b), IR (neat, KBr) ν_{max} = 2996, 2924, 2870, 2089, 2050, 2019, 1631, 980, 514 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 6.91 (dd, J =17.0, 10.0, 1H), 6.58-6.68 (m, 4H), 6.22 (dd, J= 15.5, 10.0, 1H), 5.98 (dd, J =15.0, 7.0, 1H), 5.63 (dd, J =17.0, 1.50, 1H), 5.50 (dd, J =10.0, 1.0, 1 H), 3.72 (m, 1H), 2.44 (s, 3H), 1.45 (d, J =7.0, 3H); ^{13}C NMR ($CDCl_3$) 199.2, 146.5,

140.3, 137.8, 135.6, 134.0, 128.7, 128.1, 124.6, 122.8, 119.7, 91.6, 90.5, 38.2, 21.7, 15.3; HRMS (TOF) m/e for $C_{21}H_{16}Co_2O_6S$ calcd. (M^+) calculated, 513.9332 found 513.9328.

Hexacarbonyl[μ-η^4-(1-(3E, 5E)-deca-3, 5, 9-trien-7-yn-2-yl)-2-methoxy-4-methyl benzene)dicobalt (132c) and Hexacarbonyl[μ-η^4-(1-(3E, 5E)-deca-3, 5, 9-trien-7-yn-2-yl)-4-methoxy-2-methylbenzene)dicobalt (132c')



132c (22%)



132 c'(17%)

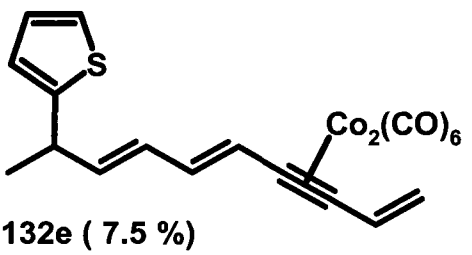
To a solution of alcohol **130** (0.044 g, 0.10 mmol) and 3-methylanisole (50 μL, 0.40 mmol) in CH_2Cl_2 (5 mL) was added $BF_3.OEt_2$ (37 μL, 0.30 mmol) at 0 °C. The mixture was stirred and the reaction progress was monitored by TLC. After 30 min, only a trace amount of product was formed (based on TLC); however, subsequent additions of 3-methylanisole (another 50 μL, and 200 μL) showed an increased in the rate of the reaction and ultimately the reaction was forced towards the the completion by adding more 3-methylanisole (until no carbocation was left; by TLC, approxiamtely 1 h). Quenching the reaction with saturated solution of $NaHCO_{3(aq)}$ was followed by conventional extractive work up with dichloromethane. The combined organic layers

were dried over $MgSO_4$, evaporation of the volatiles provided the product **132c** as a crude mixture. Purification on a preparative TLC plate (10:1 PET: Et_2O) gave, in order of elution **132c** (0.0120 g, 22 %) and **132 c`** (0.0092 g, 17 %).

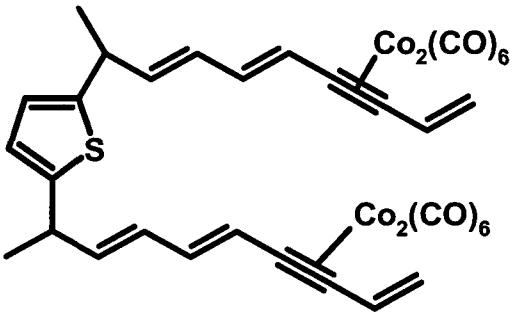
(132c), IR (neat, KBr) ν_{max}= 2961, 2928, 2855, 2089, 2051, 2020, 1501, 1455, 1290, 1250, 515 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 7.04 (d, J =7.50, 1 H), 6.89 (dd, J =16.5, 10.5, 1H), 6.75 (d, J =7.50, 1H), 6.69 (s, 1H), 6.59-6.67 (m, 2 H), 6.16 (m , 1H), 6.05 (dd, J =15.5, 6.0, 1H), 5.60 (d, J=16.5, 1H), 5.48 (d, J=10.5, 1H), 3.95 (m, 1H), 3.84 (s, 3H), 2.33 (s, 3H), 1.34 (d, J=7.00, 3H);^{13}C NMR ($CDCl_3$) 194.3, 156.5, 141.4, 137.2, 136.6, 134.1, 130.3, 128.2, 127.2, 126.9, 121.2, 119.6, 111.6, 91.6, 91.0, 55.4, 34.9, 21.4, 19.7; HRMS (TOF) m/e for $C_{24}H_{20}Co_2O_7$ calcd. (M^+) 537.9873, found 537.9891.

(132c`), IR (neat, KBr) ν_{max} = 2962, 2930, 2871, 2088, 2050, 2020, 1611, 1580, 1505, 1464, 1286, 1260, 811, 514 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 7.12 (d, J=8.50, 1H), 6.90 (dd, J =10.0, 17.0, 1H), 6.72-6.78 (m, 2H), 6.56-6.63 (m, 2H), 6.09 (m, 1H), 5.99 (dd, J =15.5, 6.00, 1H), 5.62 (d, J=16.5, 1H), 5.50 (d, J=10.0, 1H), 3.79 (s, 3H), 3.70 (m, 1H), 2.33(s, 3H), 1.38 (d, J=7.0, 3H). ^{13}C NMR ($CDCl_3$) 199.3, 157.8, 141.3, 136.9, 136.2, 135.2, 134.1, 128.3, 127.3, 119.7, 116.0, 111.4, 91.7, 90.9, 55.2, 37.4, 29.7, 20.3, 19.8.; HRMS (TOF) m/e for $C_{24}H_{20}Co_2O_7$ calcd. (M^+) 537.9873, found 537.9868.

Dodecacarbonyl[μ,μ,η^4,η^4-(2,5-di((3E, 5E)-deca-3, 5, 9-trien-7-yn-2-yl)thiophene)tetracobalt (132d) and Hexacarbonyl[μ,η^4-(1-2-((3E, 5E)-deca-3, 5, 9-trien-7-yn-2-yl)thiophene)]dicobalt (132e)



132e (7.5 %)



132d (65 %)

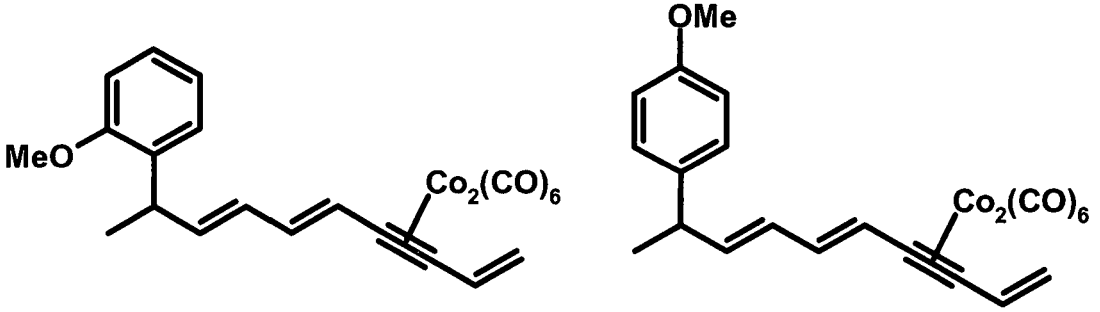
To a solution of alcohol **128** (0.036 g, 0.082 mmol) and thiophene (19 μL, 0.24 mmol) in CH_2Cl_2 (5 mL) was added $BF_3.OEt_2$ (30 μL, 0.241 mmol) at 0 °C. The reaction was completed within a few minutues after the addition of acid (ca. 10 min). A saturated solution of $NaHCO_{3(aq)}$ was added, followed by an extractive work up with dichloromethane. The combined organic layers were dried over $MgSO_4$ and the solvents were evaporated under reduced pressure to provide the product **132d** and **132e** as a crude mixture. Purification by flash column chromatography (100% hexanes) gave in order of elution **132d** (0.017 g, 45%) and **132e** (0.0029 mg, 6.9 %) in pure forms.

(**132d**) IR (neat, KBr) ν_{max}= 2923, 2851, 2089, 2051 2020, 1456, 514 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 6.91 (dd, J=16.5, 10.1, 2H), 6.59-6.70 (m, 6H), 6.24 (dd, J=15.9, 10.2, 2H), 5.98 (dd, J=15.0, 7.3, 2H), 5.63 (dd, J=16.5, 1.00, 2H), 5.51 (dd, J=10.1, 1.00, 2H), 3.74 (m, 2H), 1.46 (d, J = 6.9, 6H); ^{13}C NMR ($CDCl_3$) 199.3, 147.0, 140.2, 135.6, 134.1,

128.9, 128.3, 122.8, 119.8, 91.7, 90.5, 38.52, 21.8. HRMS (TOF) m/e for $C_{36}H_{24}Co_4O_{12}S$ calculated (M^++Ag) 1022, found 1022.

(**132e**), IR (neat, KBr): ν_{max} =2970, 2089, 2053, 2020, 1632 cm^{-1}; ^1H NMR ($CDCl_3$), δ = 7.18 (d, J=5.0, 1H), 6.88-6.97 (m, 2H), 6.85 (d, J=3.5, 1H), 6.61-6.69 (m, 2H), 6.23 (dd, J= 15.0, 10.0, 1H), 6.00 (dd, J =15.0, 7.5, 1H), 5.63 (d, J = 16.5, 1H), 5.51 (d, J =10.0, 1H), 3.02 (m, 1H), 1.49 (d, J =7, 3H); ^{13}C NMR ($CDCl_3$) 199.3, 149.0, 140.1, 135.5, 134.0, 129.0, 128.3, 126.8, 123.4, 123.2, 119.8, 90.5, 38.2, 21.9; HRMS (TOF) m/e for $C_{20}H_{14}Co_2O_6S$ calcd. (M^+) 443.9277, found 443.9285.

Hexacarbonyl[μ,η^4-(1-((3E, 5E)-deca-3,5,9-trien-7-yn-2-yl)-2-methoxybenzene)] dicobalt (132f') and Hexacarbonyl[μ,η^4-(1-((3E, 5E)-deca-3,5,9-trien-7-yn-2-yl)-4-methoxybenzene)]dicobalt (132f)



132f' (4.5 %) **132f (56%)**

To a solution of alcohol **128** (0.052 g, 0.12 mmol) and anisole (250 μL, 2.30 mmol) in CH_2Cl_2 (5 mL) was added $BF_3{\cdot}OEt_2$ (26 μL, 0.18 mmol) at 0 °C. After 0.5 h stirring only a small amount of product was formed based on TLC observations. Thus

another 250 μL of anisole was added to the mixture and within a few minutues (ca.10 min) only the spots related to the products were detectable on TLC. The reaction was quenched by addition of $NaHCO_{3(aq)}$, followed by an extractive work up with dichloromethane. The combined organic layers were dried over $MgSO_4$ and the solvents were removed under reduced pressure to give **132f** and **132f'** as a crude mixture. Purification on a preparative TLC plate (10:1 PET:Et_2O) gave, in order of elution **132f** (0.034 g, 56%) as the major product, and **132f'** (0.0027 g, 4.5 %) as the minor product.

(**132f**), IR (neat, KBr) ν_{max} = 2964, 2931, 2089, 2050, 2019, 1510, 1301, 1246, 1038, 514 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 7.16 (d, J=7.8, 2H), 6.91 (m, 1H), 6.87 (d, J=7.8, 2H), 6.59-6.67 (m, 2H), 6.16 (dd, J=15.2 , 8.2, 1H), 6.01 (dd, J = 15.2, 6.7, 1H), 5.62 (dd, J = 16.5, 1, 1H), 5.50 (dd, J = 10.0, 1.0, 1H), 3.8 (s, 3H), 3.50 (m, 1H), 1.40 (d, J= 6.9, 3H); ^{13}C NMR: 199.4, 158.1, 141.6, 137.1, 136.1, 134.1, 128.3, 128.2, 127.5, 119.7, 113.9, 91.6, 90.7, 55.3, 41.8, 21.0; HRMS (TOF) m/e for $C_{23}H_{18}Co_2O_7$ calcd. (M^+) 523.9716, found 523.9722.

(**132 f'**), IR (neat, KBr): ν_{max}= 2961, 2924, 2851, 2088, 2051, 2021, 1491, 1241, 801, 752, 515 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 7.20 (m, 2H), 6.96-6.87 (m, 3H), 6.62-6.68 (m, 2H), 6.20 (dd, J = 15.5, 7.5, 1H), 6.08 (dd, J = 15.5, 6.5, 1H), 5.62 (d, J =16.5, 1H), 5.49 (d, J=10.5, 1H), 4.01 (m, 1H0, 3.85 (s, 3H), 1.38 (d, J=7, 3H); HRMS (TOF) m/e for $C_{23}H_{18}Co_2O_7$ calcd. (M^+) 523.9716, found 523.9734.

Competetive Reactions of acyclic alcohol and cyclic alcohol

General condition for competitive reactions: To a solution of an equimolar amount of cyclic alcohol **(101)**, acyclic alcohol **(128)** and the nucleophile, was added 10 equivalents of $BF_3.OEt_2$ at 0°C/ -50°C. The reaction mixture was stirred for half an hour before it was quenched by saturated solution of $NaHCO_{3(aq)}$. Extarctive work up with dichloromethane, drying the combined organic layers over $MgSO_4$ and evaporation of the solvents provided the crude mixture of the products. The crude mixture was dissolved in $CDCl_3$ and subjected to ^1H NMR analysis in order to find the ratio of condensation products. Subsequent purification of the crude material was done by flash column chromatography (100% hexanes).

(A) Nucleophile : Allyltrimethylsilane

Compound **101** (0.022 g, 0.051 mmol) and **128** (0.020 g, 0.050 mmol) were reacted with allyltrimethylsilane (8.5 μL, 0.050 mmol) following the general condition described above. The ratio of the two condensation products was assigned based on ^1H NMR analysis of the crude mixture and its comparison with the ^1H NMR spectrum of each condensation product (**132a**, **121a$_3$** and **121b$_3$**). Four distinctive signals at 6.91 ppm, 6.83 ppm (corresponding to **132a**), 6.79 ppm and 3.74 ppm (corresponding to **121a$_3$** and **121b$_3$** respectively) were detected and their related integrations were used to find the ratio of **132a** to the mixture of **121a$_3$** and **121b$_3$** (1.7:1). It was not possible to separate the two condensation products by chromatographic technique and after subjecting the crude to column chromatography purification (100% hexanes) a mixture of both products (0.017

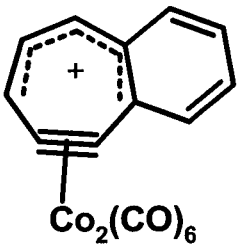
g) was obtained. The calculated yields based on the ^{1}H NMR spectrum of this mixture were 46 % for compound **132a** and 26 % for **121a$_3$** and **121b$_3$** together.

(B) ***Nucleophile : 2-methylthiophene***

Compound **128** (0.028 g, 0.067 mmol) and **101** (0.027 g, 0.069 mmol) were reacted with 2-methylthiophene (6.0 μL, 0.062 mmol) following the general conditions. Here, two characterestic signals at 5.16 ppm (for **121b$_5$**) and 3.73 ppm (for **132b**) in ^{1}H NMR spectrum of the crude reaction product were used to find the ratio of the two products, as 2.82:1. By subjecting the crude mixture to column chromatography (100% hexanes), compound **121b$_5$** (0.010 g, 30 %) and **132b** (0.021 g, 61 %) were isolated separately in pure form.

Repeating the same reaction with **128** (0.030 g, 0.069 mmol) and **101** (0.028 g, 0.071 mmol) and 2-methyltiophene (6.0 μL, 0.062 mmol) at -50 °C, resulted in a less selective reaction as evidenced by ^{1}H NMR analysis of the crude material. This time, the relative ratio of the products was found as 1.91:1 in favour of **132b.**

3. BENZO-FUSED DEHYDROTROPYLIUM $Co_2(CO)_6$-COMPLEXED CATIONS



100

The effect of additional 4n+2 π systems on the properties of conjugated cyclic systems has long been a matter of interest from both theoretical and experimental points of view. Consequently, hundreds of examples are now available on the syntheses and properties of a wide range of polycyclic compounds with extended π systems. In this series, the effect of single benzo-annulation on the properties of a system has shown to vary case by case. For example, while benzo-annulation is known to destabilize tropylium cation,[82a] it brings a significant kinetic stability to dehydro[8]annulene.[82b]

Regarding the aromaticity of the system, the calculated NICS values[83] (at DFT/ B3LYP/ 6-311 +G* level) for a series of benzo-fused derivatives of benzene and tropylium ion, suggests a significant diatropic character for each individual rings (Figure 3.1).

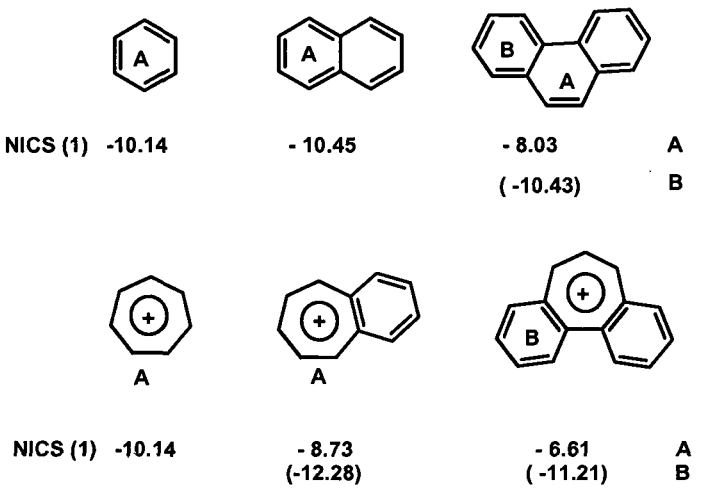
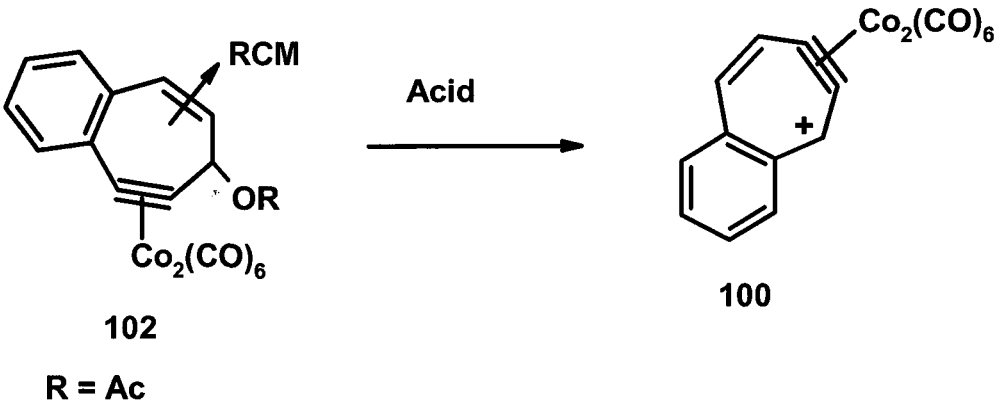


Figure 3.1. Selected benzo-fused derivatives of benzene and tropylium ion.

Here, as an extension to our study on $Co_2(CO)_6$-dehdrotropylium cation **99**, a second system of this type was desired and a benzo-fused derivative was a logical choice.

3.1 TOWARDS SYNTHESIS OF BENZO-FUSED DEHYDRO TROPYLIUM-$Co_2(CO)_6$ COMPLEXES

Compound **102** was initially selected as the precursor to benzo-fused dehydrotropylium cation, which upon the addition of acid would generate the desired cation **100**.

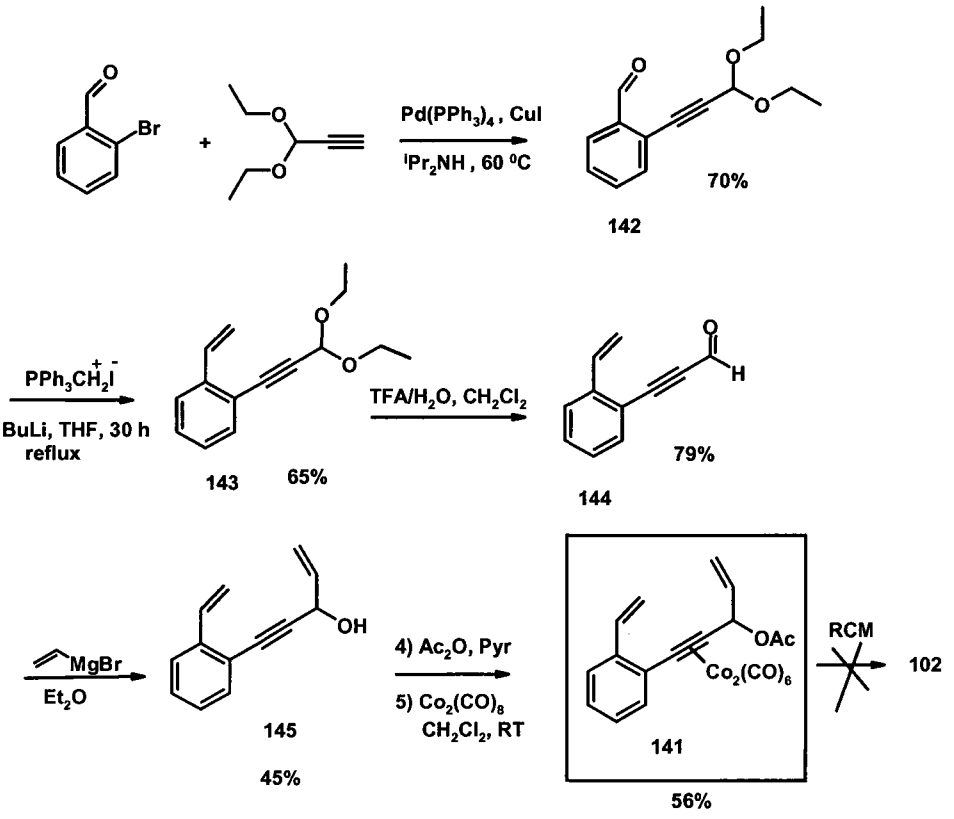


102

R = Ac

100

The initial attempt was based on olefin ring closing metathesis (RCM) [68] of suitably positioned double bonds for construction of highly conjugated 7-memebered ring of **102**. We anticipated that in this case the introduction of a benzene ring might impose a conformational constraint and hence would promote the formation of the ring via RCM. With that in mind, precursor **141** was selected as a suitable substrate for RCM (Scheme 3.1).

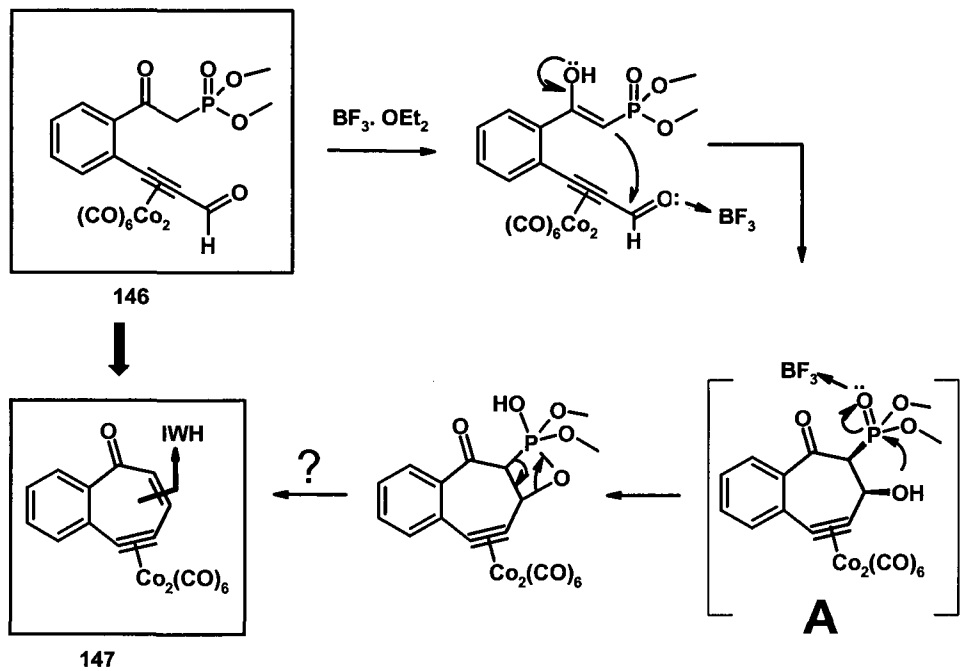


Scheme 3.1. Preparation and attempted RCM of **141**.

Synthesis of compound **141** began with Sonogashira coupling of propargyl aldehyde diethyl acetal with 2-bromobenzaldehyde, which gave **142** in 70 % yield. Subsequent conversion of the carbonyl to the alkene by means of Wittig reaction gave **143** in fair yield (65%). This was followed by hydrolysis of the propargyl acetal to aldehyde **144** (79%). A Grignard reaction of the aldehyde with vinylmagnesium bromide

gave compound **145** (45%). Finally, acetylation and complexation of **145** furnished **142** in 56% yield. Unfortunately, RCM of **142** by using Grubbs' 1st and 2nd generation catalyst each failed to give any of the cyclized product (**102**).

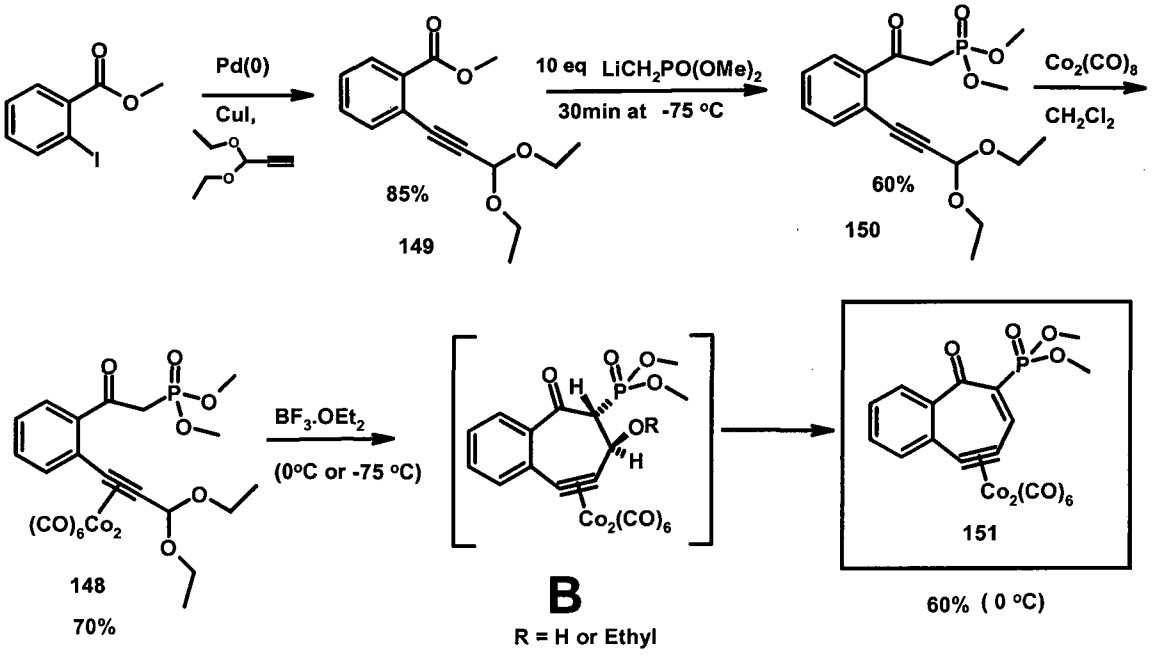
Since the RCMs failed to give the desired precursor to $Co_2(CO)_6$-benzo-fused dehydrotropylium cation, a new approach was required. This time we envisioned intramolecular Wittig-Horner (IWH) type reaction of compound **146** as a possible route for the synthesis of compound **147**, (Scheme 3.2). If successful, compound **147**, after the reduction of carbonyl group, would give the precursor to benzo-fused dehydrotropylium cation **100** (Scheme 3.2). Intramolecular Wittig-Horner cyclizations of this type are routinely employed in preparation of cyclic alkenes of different sizes.[84] Their application is especially well recognized in the synthesis of cyclopentenones.



Scheme 3.2. Proposed mechanism for IWH reaction of **146** in the presence of $BF_3.OEt_2$.

After screening several potential routes, **148**, the precursor to compound **146,** was efficiently synthesized following the method described in Scheme 3.3. Starting from

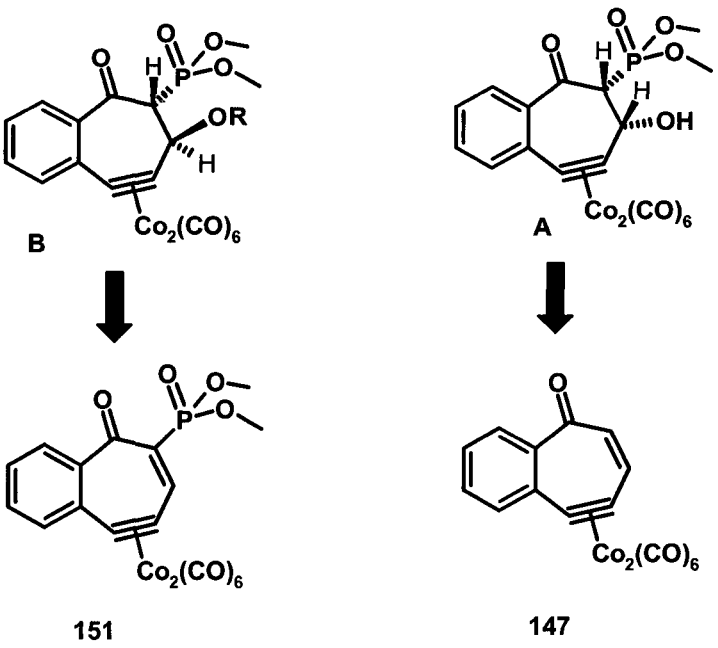
methyl-2-iodobenzoate, its reaction with propargyl aldehyde diethyl acetal under common Sonogashira reaction conditions gave **149** in high yield (85%). Next, the ester **149** was reacted with a large excess (10 equivalents) of lithiated dimethyl methanephosphonate at low temperature (-75 °C) to afford **150** in moderate yield (60%). Finally complexation of **150** with $Co_2(CO)_6$ gave access to **148** (70%). Due to the sensitivity of dicobalt carbonyl complexes to the strong bases, an acidic set of conditions was chosen for the one-pot synthesis of the aldehyde and its subsequent IWH reaction.



Scheme 3.3. Synthesis of phosphonate substituted benzo-fused dehydrotropone complexes

Subjecting **148** to acid treatment under various conditions did not give **147** as was expected, but in all the cases the phosphonate substituted tropone derivative (**151**) was obtained, presumably via intermediate **B** (Scheme 3.3). Reducing the reaction temperature to -75 °C and using an alternative acid such as $TsOH_{(aq)}$ were among the conditions applied, and in both cases compound **151** was obtained as the sole product.

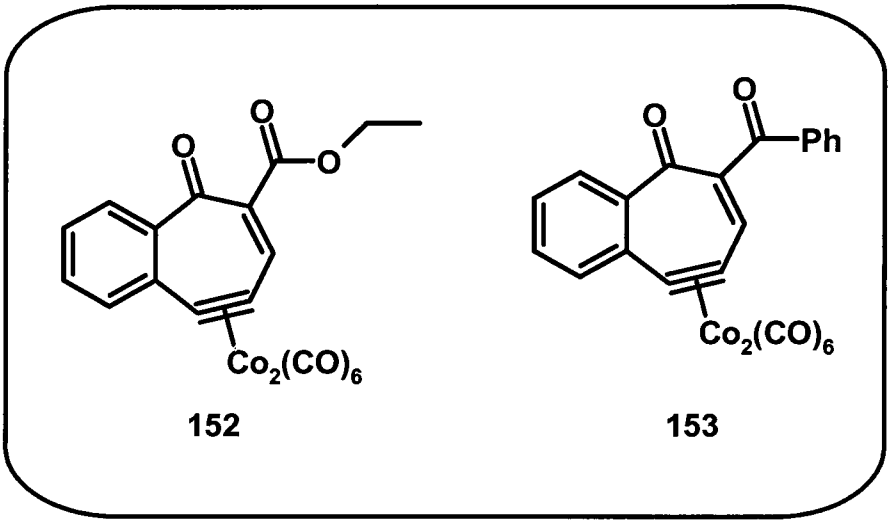
The formation of this type of compound which can be considered as product of Knoevenagel reaction has been observed before in similar situations and might be explained by more favourable orientation of the substituents in **B** than in **A** which results in the formation of **151** instead of **147** (Scheme 3.4).[84c]



Scheme 3.4 Formation of **151** versus **147**

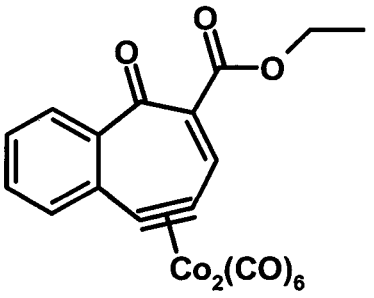
Tropone has been known as a structural motif in a wide range of natural products, many of which possess interesting biological activities.[85] The synthesis of substituted tropones still remains as a synthetic challenge. Here, with the easy and straightforward formation of compound **151**, we decided to explore the feasibility of this novel method in construction of a new class of benzo-fused substituted dehydrotropones. These compounds have the potential to be used either in cobalt related reactions such as Nicholas and Pauson-Khand reactions, or undergo reductive/ oxidative decomplexation of

cobalt to give substituted benzo-fused tropones. For this matter, ester and phenyl ketone substituted derivatives of benzo-fused dehydrotropone were selected as the next targets.



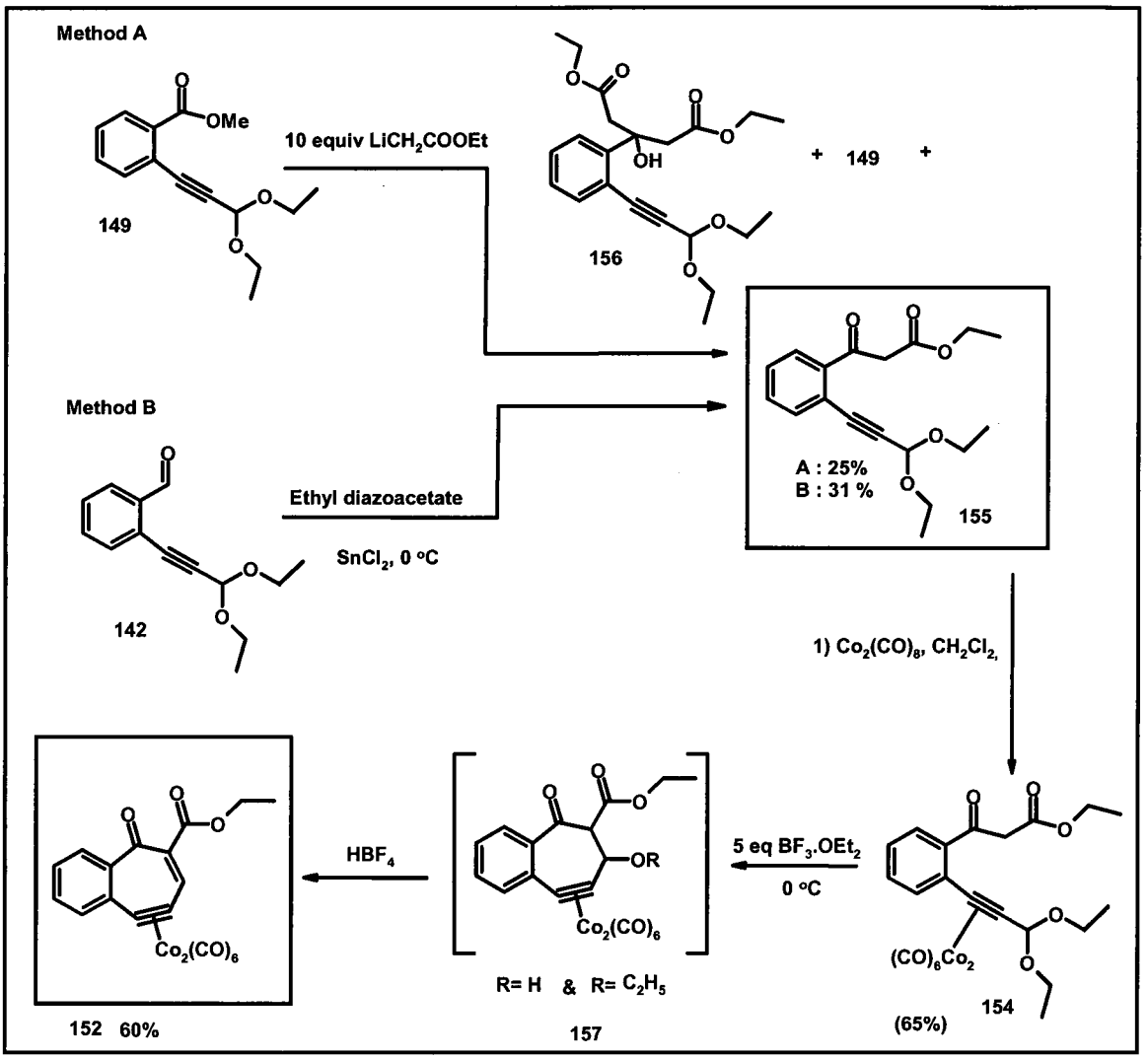
152 153

3.2 SYNTHESIS OF THE ESTER DERIVATIVE OF BENZO-FUSED DEHYDROTROPONE COMPLEXES



152

Based on the method that resulted in the formation of phosphonate derivative **151**, compound **154** was selected as precursor to **152**. The obvious precursor to **154**, compound **155**, was to be synthesized. The initial attempt (method **A**) on the synthesize of intermediate **155**, started by the addition of an excess amount of $LiCH_2COC_2H_5$ to the ester **149**. This aldol type addition, gave a mixture of **149**, double addition product **156**, and desired product **155** (25%) along with some unidentified side products. Changing the reaction conditions to an equimolar or less excessive amount of $LiCH_2COC_2H_5$ did not improve the yield of formation of compound **155**. Eventually, due to the low reproducibility and tedious product purification of method **A**, an alternative method **B**,[86] was chosen to access the intermediate **155**. In path **B**, compound **142** was reacted with ethyl diazoacetate following the literature method to give compound **155** as a mixture of keto and enol tautomers (1:1.17) in low yield (31%), but with an easier purification step (Scheme 3.5).

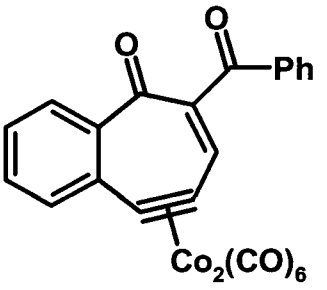


Scheme 3.5. Synthesis of the carboethoxy substitued benzo-fused dehydrotropone complexe (**152**).

Complexation of compound **155** with dicobalt octacarbonyl provided **154** as a mixture of keto and enol tautomers (3:1), in a good yield (65%). Interestingly, upon complexation with cobalt, the amount of enol form was reduced in the mixture as compared with the metal free form (**155**). Also, it is worthy of mention that even though the hydrogens on the aromatic ring were little affected by complexation of alkyne unit,

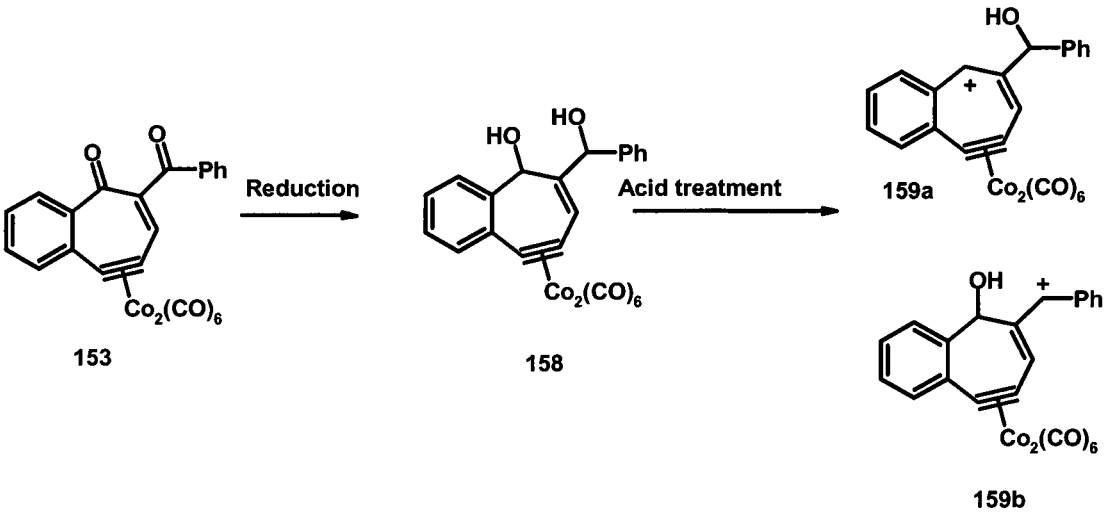
there was a significant upfield shift for the hydrogens between two carbonyl units in the ^{1}H NMR spectrum, and an analogous upfield shift for the olefinic hydrogen of the enol form. Subjecting **154** to Lewis acid treatment ($BF_3{\cdot}OEt_2$) gave the intermediates **157a/157b**, which were identified by ^{1}H NMR spectral analysis. Subsequent addition of HBF_4 to the reaction mixture resulted in the formation **152** in moderate yield (60%) from **154**. HBF_4 was added to the reaction mixture based on the previous observation on an enhanced rate of an elimination step by using HBF_4 instead of $BF_3.OEt_2$ in the formation of **117**. In summary, applying the same methodology as for phosphonate **151**, compound **152** was successfully synthesized (albeit in low overall yield (3.7%)), with the synthesis of keto ester **155** as the most challenging step.

3.3 ATTEMPTED SYNTHESIS OF THE PHENYL KETONE DERIVATIVE OF THE BENZO-FUSED DEHYDROTROPONE COMPLEX



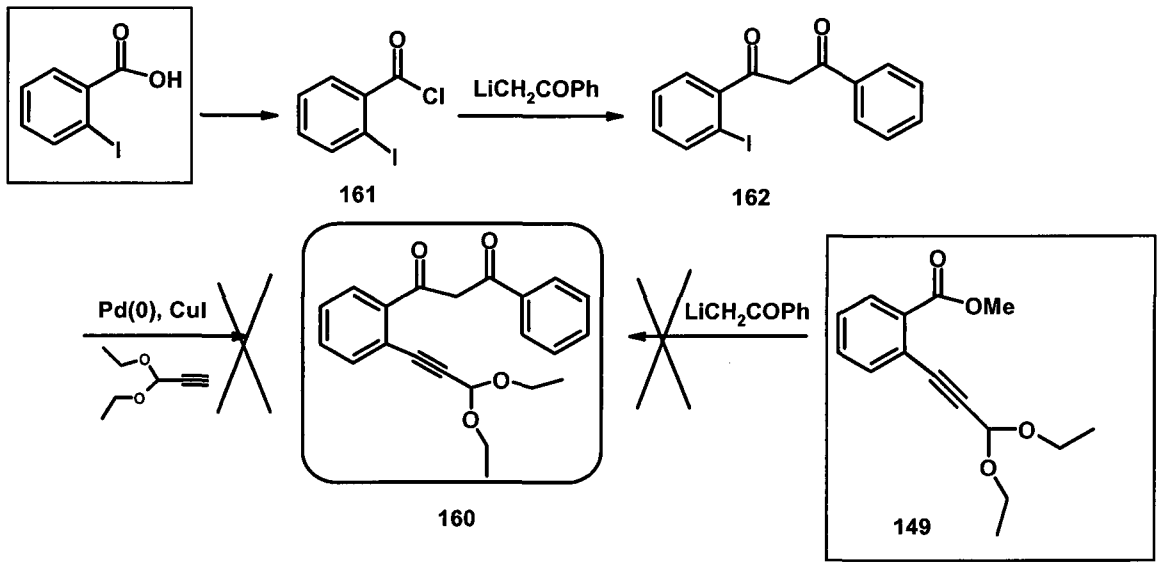
153

With the successful cyclization of diketone **151** to **152**, we turned our attention to the synthesis of phenyl ketone substituted derivative **153**. This compound was of interest not only as another example of benzo-fused dehydrotropylium cobalt complex, but also as the precursor to diol **158** (Scheme 3.6). Diol **158**, which possesses two sites for possible ionization to cations, was considered as the most appropriate structural model for competitive cation formation. In this model compound, both sites for the cation generation are benzylic and the difference between them is expected to arise from one of them being generated in a dehydrotropylium ring with additional resonance stabilization (**159a**) while the other one does not have that extra source of stabilization (**159b**). In other words, if compound **158** was synthesized, it could be used as structural probe to compare the relative stability/ reactivity of the two cationic sites (Scheme 3.6).



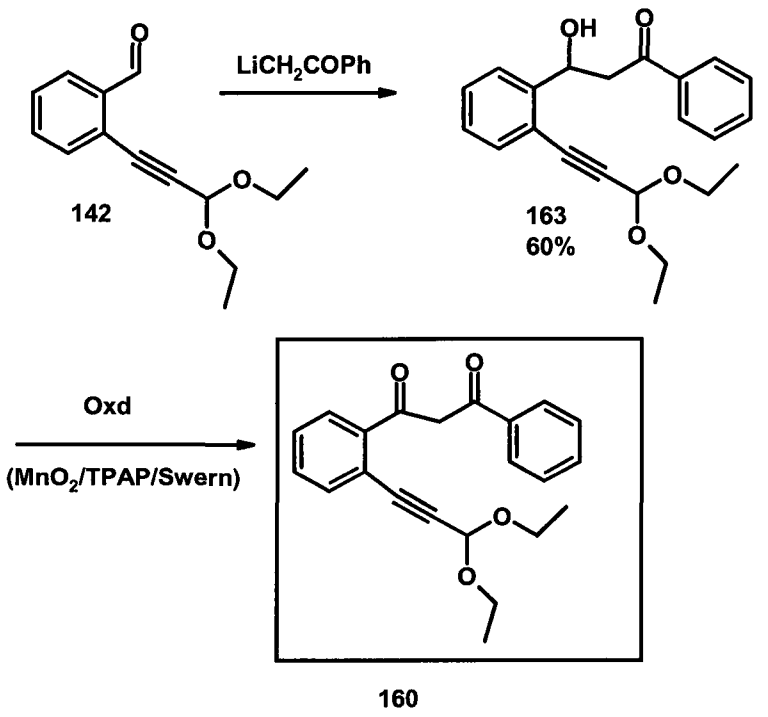
Scheme 3.6. Phenyl ketone substitued benzo-fused dehydrotropone cobalt complex and its diol.

Following the previous method, we envisoned the synthesis of benzo ketone derivative (**153**) to originate from the cobalt complex of precursor **160** (Scheme 3.7). Starting from 2-iodobenzoic acid, acid chloride **161** was prepared and reacted with $LiCH_2COPh$ to give compound **162**. However, an attempted palladium catalyzed Sonogashira coupling of **162** with propargyl aldehyde diethyl acetal failed to afford compound **160.** By switching to our previously used method in the synthesis of the phosphonate derivative, compound **149** was reacted with $LiCH_2COPh$ in another reaction. This led to a self condensation of acetophenone with most of the starting material (**149**) being recovered (Scheme 3.7).



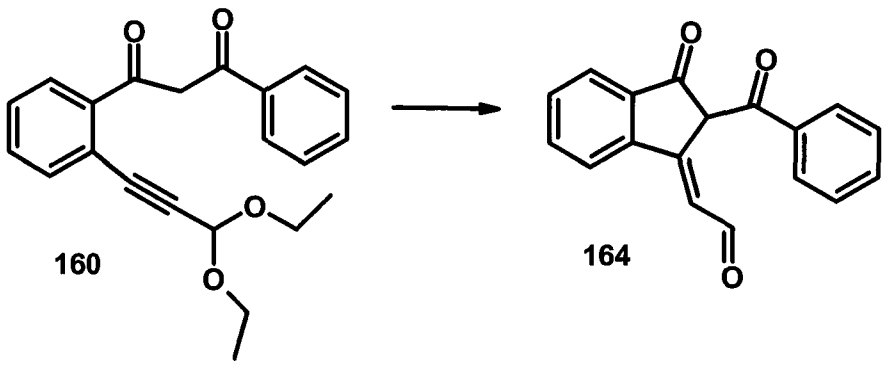
Scheme 3.7. Failed attempts of the efficient synthesis of compound **160**.

To overcome the low reactivity observed for **149** towards lithiated acetophenone, it was replaced by aldehyde **142** in an analogous aldol type reaction, with the intent that further oxidation of alcohol **163** would provide the desired alkynyl diketone **160** (Scheme 3.8). Indeed, the aldol addition of lithio-acetophenone to aldehyde **142** at -75 °C provided keto-alcohol **163** in fair yield (60%). Unfortunately, attempts at further oxidation of **163** with a variety of oxidizing agents gave only a trace amount of compound **160,** which was identified by ^{1}H NMR spectroscopy.



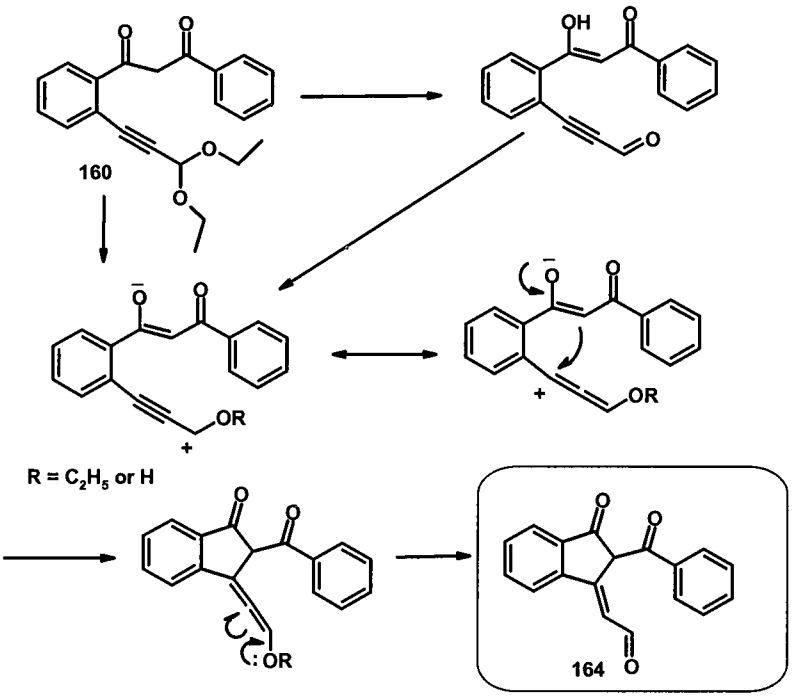
Scheme 3.8. Towards the synthesis of compound **160**

From the ^{1}H NMR spectral analysis of the small amount of isolated **160**, a gradual decomposition of **160** to what was assigned as **164** was observed. Compound **164** exists only in the keto form; based on the highly downfield chemical shift (10.25 ppm) observed for the aldehyde proton in the ^{1}H NMR spectrum, the presence of an enol form is highly unlikely.



Scheme 3.9. Decomposition of **160** to **164**.

The reactivity of analogous triple bonds in cycloaddition reactions has been observed in numerous cases; for example, the intramolecular ionic Diels-Alder reaction of α-acetylenic acetals has led to the formation of aldehyde or keto-substituted cyclic products.[87] Here, we may propose a similar type of mechanism for the formation of **164** (Scheme 3.9).

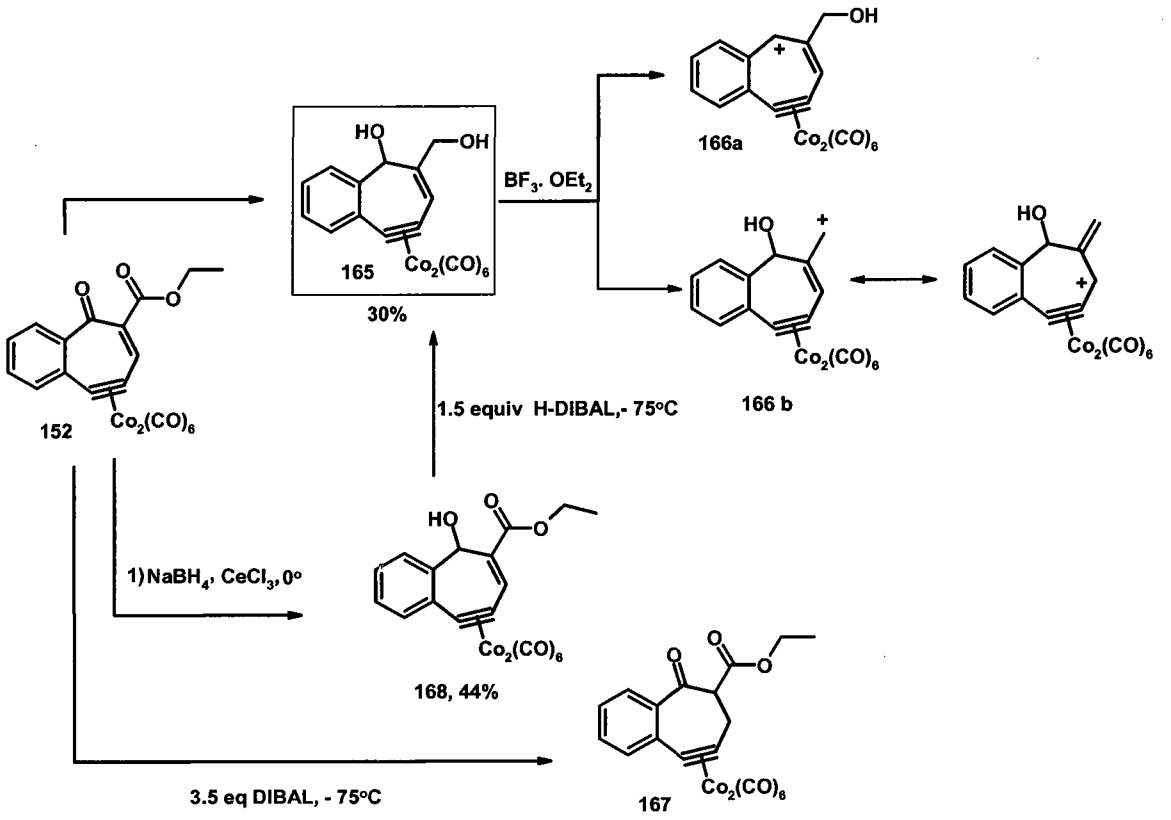


Scheme 3.10. Proposed mechanism for the formation of **164**.

The acetal group in **160** under slightly acidic conditions can be converted to an aldehyde or lose one ethoxy group to form an electron deficient intermediate. This species is then captured by an enolate in an intramolecular fashion to form an allene substituted cyclic pentenone that ultimately rearranges to **164**. The difference of the instability of **160** versus the stability of **148** and **154** must come from the slightly greater acidity of **160**.

This limited stability of **160** prevented us from perfoming further complexation and acid catalyzed cyclization reactions. Thus, with the many failed attempts to efficiently synthesize compound **160**, we decided to rely on computational studies for more structural information on the cation derived from **158**.

On the other hand, with the availability of compound **152**, the feasibility of its reduction to the corresponding diol **165** was explored (Scheme 3.11). Even though diol **165,** possessing two potential cationic sites, was not the best structural model to estimate the amount of resonance stabilization in the dehydrotropylium ring (as it has an extra benzylic stabilization effect for **166a** but not for **166b**), it was the closest structural model that could be synthesized in the lab. This model compound was then used to compare the relative stability of dehydrotropylium cation **166a** with its isomeric, conjugated but non-aromatic cation of the same kind, **166b.**



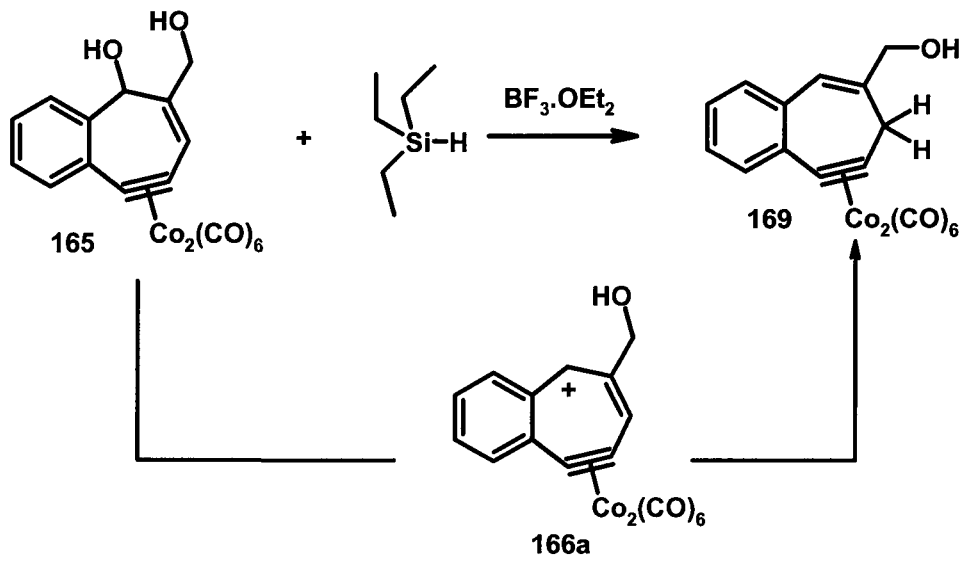
Scheme 3.11. Reduction of **152** to diol **165** with subsequent cation generation.

Initial attempts to reduce both carbonyls with DIBAL-H (excess) at low temperature,resulted in the reduction of conjugated double bond instead (Scheme 3.11, compound **167**). This was addressed by inducing a primary reduction of the ketone by $NaBH_4$ in the presence of $CeCl_3$, to give **168** (44 %), followed by subsequent reduction of the ester group with DIBAL-H, providing **165** in 30 % yield (Scheme 3.11).

Here it is worthy of mention that the reduction of the carbonyl group with $NaBH_4$, and to a greater extent when DIBAL-H was used, was a tedious process with a very low yield. Several attempts on the optimization of the reaction conditions failed to improve the yields of these steps. While $NaBH_4$ reduction was prone to undergo alkene reduction, in the case of the DIBAL–H reduction, decomposition was a competitive pathway. Low

reactivity of the carbonyl group and conjugate reduction of this type are commonly observed in similar type of systems, such as tropone and its derivatives.[88]

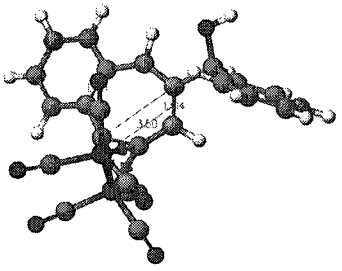
Having a very small amount of diol **165** in hand, the reactivity of its corresponding cation towards a nucleophile (a hydride source) was investigated with the intent to determine the most reactive site. By using the equimolar amount of each reactant, compound **169** was obtained as the sole reaction product. This indicates the rapid formation and reaction of **166a** relative to **166b,** and thus suggesting a higher stability of **166a** than **166b** (Scheme 3.12).



Scheme 3.12. Lewis acid mediated hydride substitution of **165.**

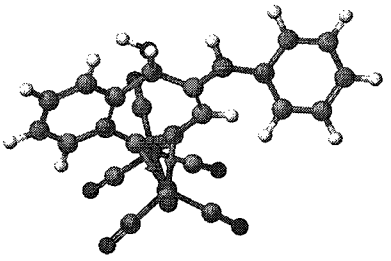
3.4 DFT CALCULATIONS

Given the difficulties in preparing **160** and the small amount of **165** prepared, we turned to calculations to evaluate the stability of benzo-fused dehydrotropylium ion. For this matter, benzo -fused dehydrotropylium dicobalt hexacarbonyl structures **159a** and **159b** were optimized based on DFT calculations with a B88-PW91 functional and dzvp basis set, to give the structures shown below. A planar structure and relatively small bond alternation (from 0.005 to 0.015 Å) was predicted for cation **159a.**



159a

E = -2499562.0832808 kcal



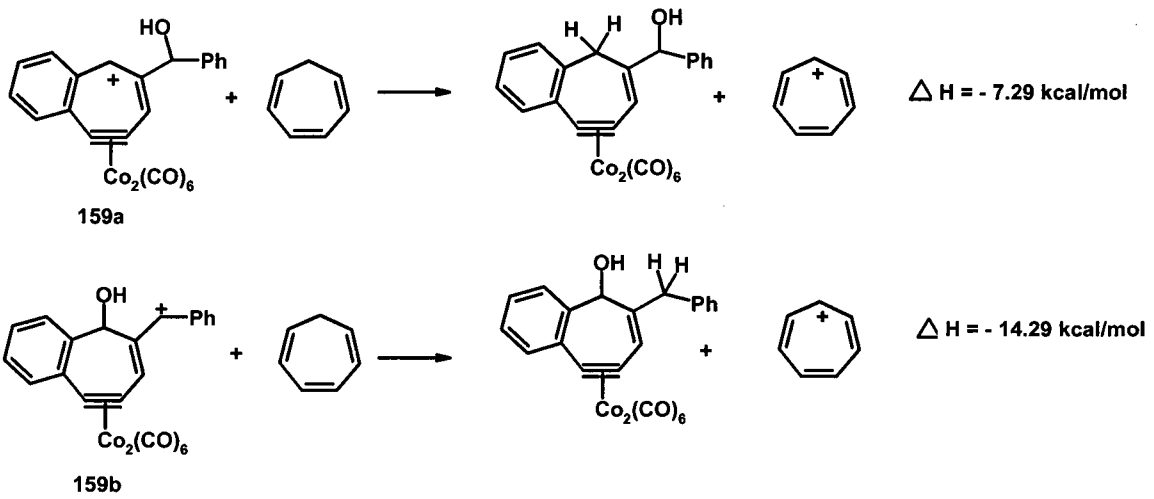
159b

E = -2499577.5592536 kcal

According to these DFT calculations, the aromatic cation **159a** is 15.47 kcal/mol more stable than its isomeric but non-aromatic cation **159b**. The relatively high amount of stabilization predicted here for **159a** versus dehydrotropylium ion itself could be due to the lower level of DFT calculation applied here.

Also, the relative thermodynamic stabilities of the benzo-fused dehydrotropylium cation **159a** and **159b** versus tropylium cation were assessed from the isodesmic reaction shown in Scheme 3.13, by using DFT calculations with B88-PW91 functional and dzvp basis set.

The greater hydride affinity of cobalt cation **159b** relative to **159a** reflects the higher stability of latter (**159a**) and the 7.0 kcal/mol difference in the stability of the two isomer, is perhaps due to the presence of resonance stabilization in **159a**.



Scheme 3.13. Isodesmic equations to compare HIA of cation **159a** and **159b**.

Based on these calculations, while a greater amount of stablization is predicted for benzo-fused tropylium cation **(159a)** relative to dehdydrotropylium cation- $Co_2(CO)_6$ **(99)**, both of these ions are found considerably less stabilized than tropylium ion itself.

Summary

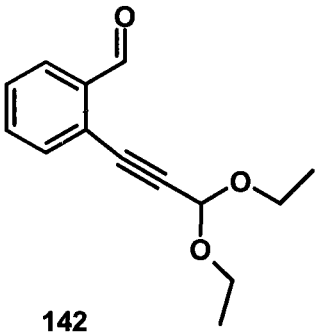
In our attempts to the synthesis benzo-fuzed dehydrotopone, the precursor to cation **100**, we have developed a new strategy for synthesis of substituted benzo-fused cyloheptadienyne derivatives. The scope and limitations of the method were explored; it was found the success of the method was highly dependent on the stability of reactive intermediates. For example, the β- diketone derivative bearing an alkynal

acetal is not stable and therefore can not be used to obtain benzofused cycloheptadienyne complex.

In the case of competitive cation generation investigated (**166a** and **166b**), the nominally aromatic cation was generated preferentially (**166a**) and reacted with a hydride source; however, it should be noted that this was based on experimentally biased model. DFT calculations on an unbiased structural model (**159**) were carried out in order to estimate the relative thermodynamic stability of aromatic vs non-aromatic cation when they both could exist in a molecule; the nominally aromatic cation (**159a**) was more stable by 7 kcal/mol.

3.5 EXPERIMENTAL SECTION

1-(2-Formylphenyl)-3,3-diethoxyprop-1-yne (142)

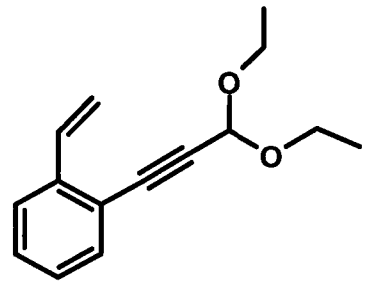


142

2-Bromobenzaldehyde (1.0 mL, 13 mmol) was subjected to typical Sonogashira coupling conditions ($Pd(PPh_3)_4$/CuI 1/3 mol%, 0.15 g) with propargyl aldehyde diethyl acetal (2.3 mL, 16 mmol) in diisopropylamine (5 mL). After stirring for 24 h at room temperature, a saturated solution of $NH_4Cl_{(aq)}$ was added, organic compounds were extracted with CH_2Cl_2 and dried over $MgSO_4$. Evaporation of the solvents provided the crude mixture. Subsequent purification of the mixture by flash column chromatography (10:1 PET: Et_2O) provided pure **142** (2.1 g, 70 %).

(**142**), IR (neat, KBr): ν_{max}= 2977, 2884, 1699, 1594, 1114, 1053, 1009, 825, 764 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 10.53 (s, 1H), 7.93 (d, J=11.5, 1H), 7.57-7.62 (m, 2H), 7.48-7.5 (m, 1H), 5.55 (s, 1H), 3.83 (m, 2H), 3.7 (m, 2H), 1.29 (t, J=10, 6H); ^{13} C NMR ($CDCl_3$) 190.9, 136.2, 133.6, 129.1, 127.1, 125.2, 91.6, 91.6, 80.5, 61.1, 15.0; HRMS (TOF) m/e for ($C_{14}H_{16}O_3$) M^+ calculated 232.1099 found 232.1102.

Synthesis of compound 143

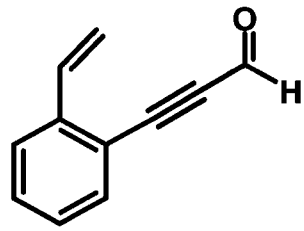


143

To a solution of methyl(triphenyl)phosphonium bromide (0.78 g, 2.2 mmol) in THF (10 mL) at 0 °C was added a solution of n-BuLi (0.75 mL, 2.5 M in hexane, 1.9 mmol), and the mixture stirred for 1 h. To this solution was added **142** (0.30 g, 1.3 mmol), and the mixture stirred at 50 °C overnight (14 h). The reaction mixture was then quenched by addition of water. This was followed by a conventional extractive workup (diethyl ether) and drying the organic layers over $MgSO_4$. Evaporation of the solvents under reduced pressure and subsequent purification of the crude residue by flash column chromatography (hexane: diethyl ether 10:1) afforded the olefination product **143** (0.19 g, 65%).[90]

(143), IR (neat, KBr): ν_{max} = 3063, 2977, 2930, 2884, 2234, 1478, 1448, 1112, 1053, 1008 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 7.58 (d, J=8.0, 1H), 7.48 (d, J =7.5, 1H), 7.32 (t, J=7.5, 1H), 7.27-7.16 (m, 2H), 5.81 (d, J=18.0, 1H), 5.55 (s, 1H), 5.36 (d, J=11.5, 1H), 3.86-3.83 (m, 2H), 3.70-3.67 (m, 2H), 1.29 (t, J=7.5, 6H); ^{13}C NMR: 139.3, 134.6, 132.9, 128.9, 127.4, 124.5, 120.6, 115.8, 91.9, 88.9, 83.4, 61.0, 15.1; MS (TOF) 230 (M^+).

Synthesis of compound 144

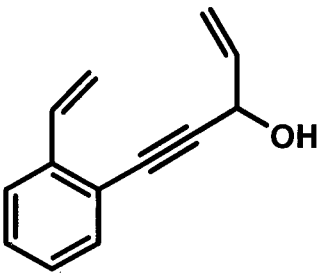


144

To a solution of **143** (0.14 g, 0.60 mmol) in CH_2Cl_2 (3 mL) was added a 50% mixture of TFA/H_2O (2.5 mL/2.5 mL) at 0°C. The reaction mixture stirred for 1h before it was quenched by addition of water. The organic compounds were extracted with dichloromethane, dried over $Mg(SO_4)$ and concentrated under reduced pressure. Further removal of volatiles under high vacuum provide **144** as a crude mixture. Final purification of the crude material by means of preparative TLC (PET:Et_2O 10:1 as eluent) afforded **144** in pure form (0.075 g, 79%).

(143), IR (neat, KBr): ν_{max}= 3063, 2855, 1658, 1476, 981 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 9.50 (s, 1H), 7.67 (d, J=8.0, 1H), 7.61 (d, J=7.5, 1H), 7.49 (t, J=7.5, 1H), 7.32 (t, J =7.5, 1H), 7.22 (dd, J=17.5,11.0, 1H), 5.91 (d, J=17.5, 1H), 5.49 (d, J=11.0, 1H); ^{13}C NMR ($CDCl_3$) 176.5, 141.1, 134.1, 133.7, 131.3, 127.6, 124.9, 117.8, 117.3, 93.3, 92.5; MS (TOF) 156 (M^+).

Synthesis of compound 145

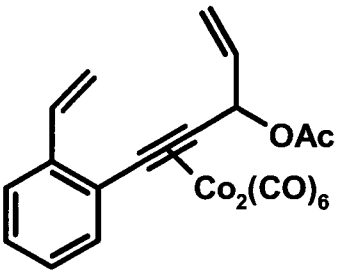


145

To a solution of **144** (0.058 g, 0.37 mmol) in Et_2O (3 mL) was slowly added vinylmagnesium bromide (1.2 mL, 1M in THF) at room temperature. The reaction mixture stirred for 3 h and saturated solution of NH_4Cl (aq) was added. A conventional extractive work up with Et_2O, drying the organic layers over $MgSO_4$ and evaporation of solvents under reduced pressure provided compound **145** as a crude mixture. Further purification of the crude by means of preparative TLC (PET:Et_2O 7:1) afforded **145** (0.031 g, 45%) in pure form.

(**145**), IR (neat, KBr) ν_{max} = 3331, 3087, 3062, 2926, 2855, 1658, 1017, 988 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 7.58 (d, J=8.0, 1H), 7.45 (d, J=8.0, 1H), 7.31 (d, J=8.0, 1H), 7.24-7.16 (m, 2H), 6.12-6.06 (m, 1H), 5.81 (d, J=17.5, 1H), 5.57 (dd, J=17.0, 1.0, 1H), 5.36 (d, J=10.0, 1H), 5.29 (dd, J=10.0, 1.0, 1H), 5.16 (m, 1H); ^{13}C NMR($CDCl_3$) 139.2, 137.0, 134.8, 132.8, 128.8, 127.5, 124.6, 116.7, 115.8, 92.3, 84.6, 63.8; MS (TOF) 184 (M^+).

Synthesis of compound 141

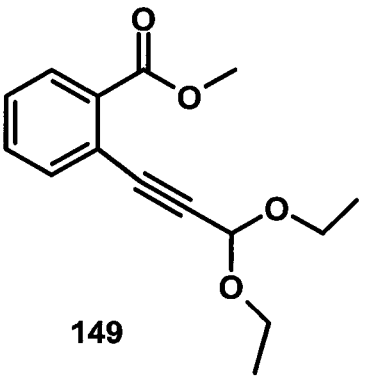


141

To a solution of compound **145** (0.020 g, 0.11 mmol) in acetic anhydride (4 mL) was added pyridine (1 mL) and the mixture stirred at room temperature for 16 h. The excess reactants were removed under reduced pressure to provide the acetylation product as a crude mixture. This mixture was dissolved in dichloromethane (5 mL) and $Co_2(CO)_8$ (excess) was added to it. The mixture stirred for 2 h under N_2 gas flow. The solution was then concentrated under reduced pressure and filtered through a short path of silica. Further evaporation of the solvents provided the crude residue which was purified by flash column chromatography on silica gel (PET: Et_2O 10:1) to afford compound **141** in pure form (0.031 g, 56 % from **145**).

(**141**), IR (neat, KBr): ν_{max}= 2926, 2855, 2092, 2054, 2024, 1746, 1227 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 7.53 (d, J=7.5, 1H), 7.49 (d, J=7.5, 1H), 7.35 (t, J=7.0, 1H), 7.28 (t, J=7.5 1H), 7.10 (dd, J=17.0, 10.5, 1H), 6.84 (dd, J=5.5, 1.0, 1H), 5.91-5.85 (m, 1H), 5.74 (d, J=17.5, 1H), 5.46 (d, J=10.5, 1H), 5.40 (d, J=17.5, 1H), 5.16 (dd, J=10.5, 1.0, 1H), 2.19 (s, 3H); ^{13}C NMR ($CDCl_3$) 199.3, 170.0, 137.1, 135.5, 135.4, 134.7, 132.5, 128.5, 128.4, 126.7, 116.9, 116.8, 97.5, 88.3, 74.9, 20.8 ; HRMS (TOF) m/e for ($C_{21}H_{14}Co_2O_8$) (M^+-CO) calculated 483.9403 found 483.9372.

1-(2-Methoxycarbonylphenyl)-3,3-diethoxyprop-1-yne (149)

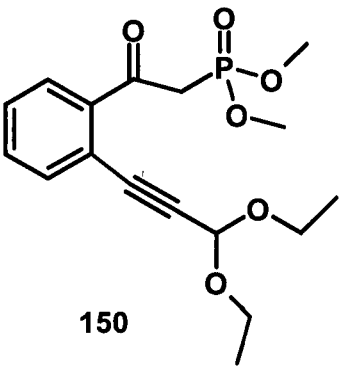


149

Methyl-2-iodobenzoate (1 mL, 6 mmol) was subjected to typical Sonogashira coupling conditions ($Pd(PPh_3)_4$/CuI , 1 /3 mol %, 0.07 g) with propargyl aldehyde diethyl diethyl acetal (1.2 mL , 7.2 mmol) in diisopropylamine (5 mL). The reaction mixture was stirred for 3h, saturated $NH_4Cl_{(aq)}$ was added and organic compounds were extracted with CH_2Cl_2. Drying the organic layers over $MgSO_4$ and evaporation of the solvents provided a crude residue. Subsequent purification by means of flash column chromatography (5:1 PET:Et_2O) on silica afforded **149** (1.25 g, 80%) in pure form.

(**149**), IR (neat, KBr) ν_{max}= 2977, 2885, 2360, 1732, 1596, 1569, 1485, 1447, 1328, 1297, 1276, 758, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 7.92 (dd, J=7.5, 1.0, 1H), 7.58 (dd, J= 7.5, 1.0, 1H), 7.46 (dt, J= 8.0, 2.0, 1H), 7.38 (dt, J= 7.5, 1.0, 1H), 5.53 (s, 1H), 3.92 (s, 3H), 3.85 (m, 2H), 3.69 (m, 2H), 1.27 (t, J= 7.0, 6H). ^{13}C NMR ($CDCl_3$) 166.2, 134.3, 132.3, 131.5, 130.2, 128.4, 122.3, 91.8, 89.4, 83.5, 61.0, 52.0; HRMS (TOF) m/e for ($C_{15}H_{18}O_4$) (M^+) calculated 262.1205 found 262.1186.

Synthesis of Compound 150

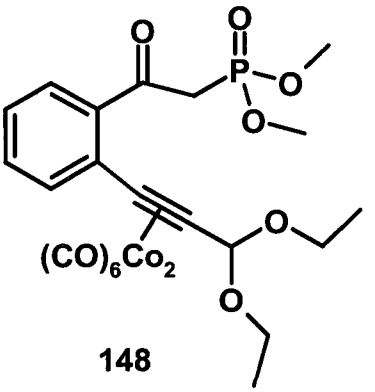


150

To a solution of dimethyl methylphosphonate (6.0 mL, 56 mmol) in THF (20 mL) was added BuLi (21.6 mL, 2.50 M in hexane) at -75 °C. After stirring for 1 h, a cooled solution of compound **149** (1.5 g, 5.7 mmol) in THF (19 mL) was added gradually to the mixture.[89] The reaction mixture was stirred for 30 min at -75 °C, then was quenched by addition of saturated $NH_4Cl_{(aq)}$. Extraction of aqueous layer with ethyl acetate, washing the combined organic layers with brine, drying over $MgSO_4$ and evaporating the solvents under reduced pressure gave the crude product. Subjecting the crude residue to flash column chromatography (3:1 ethyl acetate:hexane) afforded compound **151** (1.2 g, 60%) in pure form.

(**151**), IR (neat, KBr) ν_{max} = 3476, 2977, 2360, 1690, 1481, 1444, 1258, 1094, 1052, 883, 842, 811, 766 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 7.74 (dd, J=8.0, 1.0, 1H), 7.58 (dd, J=8.0, 1.5, 1H), 7.47 (ddd, J=7.5, 7.8, 1.0, 1H), 7.43 (ddd, J=7.5, 7.8, 1.0, 1H), 5.51 (s, 1H), 3.84 (d, J= 25.5, 2H), 3.80-3.83 (m, 2H), 3.76 (d, J=11.0, 6H), 3.66-3.69 (m, 2H), 1.27 (t, J=7, 6H); ^{13}C NMR ($CDCl_3$) 194.2 (d, J=6.5), 141, 134.7, 132.1, 129.5, 129.4, 120.6, 92.2, 91.1, 83.7, 61.6, 53.5(d, J=1.5), 40.7(d, J=129.4), 15.5; HRMS (TOF) m/e for ($C_{17}H_{23}O_6P$) (M^+) calculated 354.1232 found 354.1227.

Synthesis of Compound 148

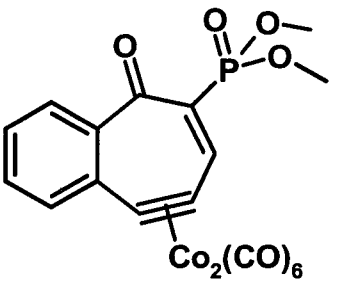


148

Compound **150** (0.50 g 1.4 mmol) was dissolved in anhydrous CH_2Cl_2 (10 mL) and cooled to 0 °C. Dicobalt octacarbonyl was added in excess and the solution was stirred for 1 h under N_2 gas flow. Filtration through Celite® and concentration in vacuo, followed by purification by flash column chromatography afforded compound **148** (0.60 g, 70%) in pure form.

(**148**), IR (neat, KBr) ν_{max} = 2978, 2091, 2054, 2025, 1688, 1259, 1060, 764, 514 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 7.96 (dd, J=7.5, 1.0, 1H), 7.78 (dd, J=8.0, 0.50, 1H), 7.50 (ddd, J=7.5, 8.0, 1, 1H), 7.42 (ddd, J=8.0, 8.0, 1.0, 1H), 5.76 (s, 1H), 3.82 (d, J=11.0, 6H), 3.77-3.80 (m, 1H), 3.62-3.65 (m, 2H), 3.59 (d, J= 26.5, 2H), 3.49 (d, J= 5.50, 1H), 1.19 (t, J=7.0, 6H). ^{13}C NMR ($CDCl_3$) 199.6, 193.3, 137.5, 136.1, 135.8, 132.4, 129.7, 127.4, 101.9, 98.9, 86.8, 63.3, 53.2 (d, J=6), 40.5 (d, J=130.6), 15.1; HRMS (TOF) m/e for $C_{23}H_{23}O_{12}Co_2P$ (M^+-3CO) calculated 555.9744 found 555.971.

Synthesis of Compound 151



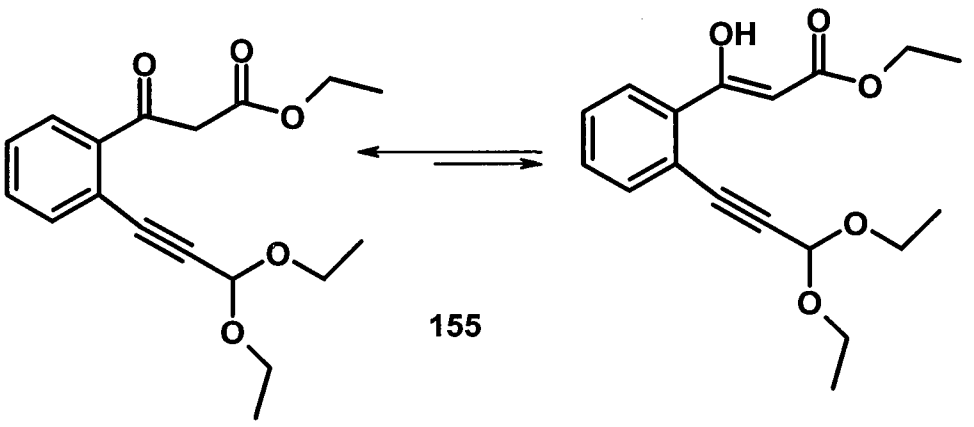
151

To a solution of **148** (0.10 g, 1.5 mmol) in CH_2Cl_2 (7 mL) at 0 °C was added $BF_3.OEt_2$ (0.55 μL, 4.5 mmol, 3 equiv) in a dropwise fashion. After stirring for 20 min, the reaction was quenched by addition of $NaHCO_{3(sat.aq)}$. Conventional extractive work up with CH_2Cl_2, evaporation of solvents in vacuo, and purification of the crude residue by flash column chromatography (PET: Et_2O 5:1) afforded **151** (0.49 g, 60 %) in pure form.

(**151**), IR (neat, KBr) ν_{max}= 2956, 2100, 2064, 1631, 1584, 1463, 1343, 1249, 1032, 834, 511 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 8.63 (d, J=18.0, 1H), 8.07 (d, J=8.0, 1H), 7.83 (d, J=7.5, 1H), 7.69 (appt, J=8.0, 1H), 7.55 (appt, J=8.0, 1H), 3.89 (d, J=11.5, 6H); ^{13}C NMR ($CDCl_3$) 197.7, 191.5, 151.9 (d, J=8.2), 137.7(d, J=125.2), 133.9, 132.8, 131.8, 129.6, 53.41(d, J=6).

*This reaction was repeated once at -75 °C with the same condition and another time at 0 °C by using TsOH instead of $BF_3.OEt_2$. In both cases only compound **151** was observed based on the ^1H NMR spectrum of the crude product mixture.

Synthesis of compound 155



155

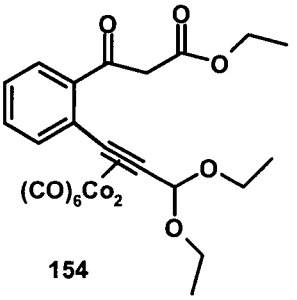
Method A: To a solution of diisopropylamine (1.60 mL, 11.2 mmol) in THF (15.0 mL) was added BuLi (4.50 mL, 2.50 M solution in hexane) at -75 °C. The mixture was stirred for 30 min at 0 °C and cooled again to -75 °C before dry ethyl acetate (1.11 mL, 11.3 mmol, distilled over CaH_2) was added to it. The mixture was stirred at -75 °C for an hour, then a cooled solution of compound **149** (0.30 g, 1.1 mmol, in 5 mL THF) was added to it in a dropwise fashion. The reaction was stirred for another 45 min at -75 °C before it was slowly quenched with saturated solution of NH_4Cl. After an extractive work up and evaporation of the solvents, the crude product was subjected to flash column chromatography purification (PET: Et_2O 7:1) to afford **155** (0.075 g, 25 %) in pure form.

Method B: To a solution of aldehyde **142** (1.0 g, 4.3 mmol) and ethyl diazoacetate (0.73 g, 6.4 mmol) in dichloromethane (5 mL) at 0 °C was added tin (II) chloride (0.050 g). The mixture was stirred at room temperature for 2 h, additional (0.050 g) of tin(II) chloride was added, and the mixture was stirred for another 2 h. Filtration through Celite® and evaporation of volatiles under reduced pressure provided a crude product

mixture. Subsequent purification by fash column chromatography (PET:Et_2O 7:1) provided **155** (0.46 g, 33%) as mixture of enol and keto tautomers (1:1.17).

(**155**), IR (neat, KBr) ν_{max} = 2978, 2932, 2886, 1742, 1695, 1626, 1480, 1195, 1053, 768 cm^{-1}; ^1H NMR ($CDCl_3$) **(keto)** δ = 7.77 (d, J=7.5 , 1H), 7.57 (t, J=9.0, 1H), 7.42-7.50 (m, 2H), 5.52 (s, 1H), 4.2 (q, J=7.0, 2H), 4.16 (s, 2H), 3.67- 3.71 (m, 4H), 1.25-1.33 (m, 9 H). **enol**: 7.71 (d, J=8.5, 1H), 7.57 (t, J=9.0, 1H), 7.37-7.42 (m, 2H), 5.94 (s, 1H), 5.52 (s, 1H), 4.26 (q, J=7.0, 2H), 3.80-3.84 (m, 4H), 1.25-1.33 (m, 9H); ^{13}C NMR ($CDCl_3$) 194.2, 173.0, 167.2, 139.7, 135.9, 134.4, 134.2, 131.7, 129.8, 129.0, 128.9, 128.8, 128.0, 120.4, 119.8, 92.1, 91.8, 90.8, 89.9, 83.5, 83.3, 61.2, 61.2, 61.0, 60.3, 48.4, 15.0, 14.2, 14.0. HRMS (TOF) m/e for $C_{18}H_{22}O_5$ (M^+-ethyl) calculated: 289.1076, found 289.1082.

Synthesis of Compound 154

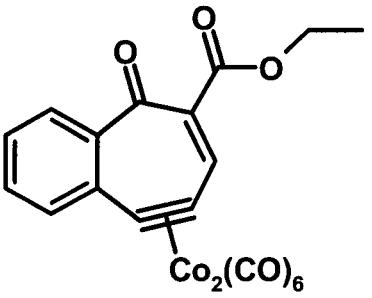


154

Compound **155** (0.50 g, 1.5 mmol) was dissolved in anhydrous CH_2Cl_2 (10 mL) and cooled to 0 °C. Dicobalt octacarbonyl was added in excess and the solution was stirred for 1h, under N_2 gas. Filtration through Celite® and concentrarion under reduced pressure, followed by purification by flash column chromatography (PET:ethylacetate 10:1) afforded compound **155** (0.61 g, 65 %) as a mixture of enol and keto tautomers (1: 3).

(**154**), IR (neat, KBr) ν_{max} = 2980, 2933, 2091, 2053, 1746, 1694, 1626, 1191 cm^{-1}; ^1H NMR ($CDCl_3$) **(keto)** δ = 7.81 (d, J=7.5, 1H), 7.68 (d, J=8.0, 1H), 7.51(app t, J=8.0, 1H), 7.39 (app t, J=7.5, 1 H), 5.76 (s, 1H), 4.23 (q, J=7.0, 2H), 3.95 (s, 2H), 3.81 (m, 2H), 3.65 (m , 2H), 1.26 (t, J=7.0, 3H), 1.20 (t, J=6.5, 6H) **enol:** 12.55 (s, 1H), 7.78 (d, J=8.0, 1H), 7.39 (app t, J=7.5, 1 H), 7.33 (m, 2H), 5.59 (s, 1H), 5.35 (s, 1H), 4.28 (q, J=7.0, 2H), 3.81 (m, 2H), 3.65 (m, 2H), 1.33 (t, J=7.0, 3H), 1.20 (t, J=6.5, 6H);^{13}C NMR ($CDCl_3$) 199.5, 194.3, 175.1, 173.0, 167.3, 137.9, 136.2, 135.9, 134.5, 134.14, 134.08, 132.4, 130.2, 129.7, 129.1, 127.5, 127.2, 102.2, 102.0, 99.5, 97.4, 92.4, 86.8, 64.0, 63.6, 61.5, 60.4, 48.3, 15.1, 15.1, 14.3, 14.1; HRMS (TOF) m/e for $C_{24}H_{22}O_{11}Co_2$ (M^+-2CO) calculated 575.9877, found 575.9885.

Synthesis of Compound 152

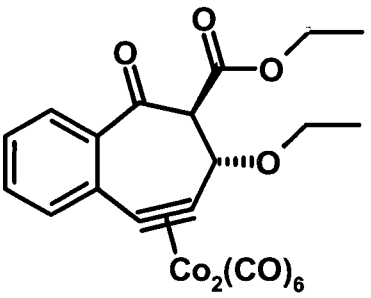


152

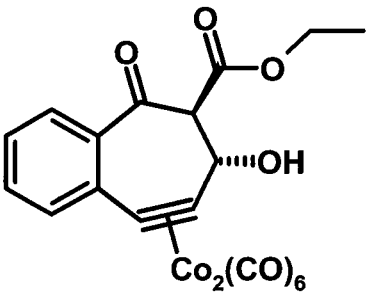
To a solution of **154** (0.28 g, 0.46 mmol) in dichloromethane (20 mL) was added $BF_3{\cdot}OEt_2$ (0.30 g, 2.1 mmol, 5 equiv), and the solution was stirred at room temperature for 1 h. At this point, monitoring the reaction progress by analytical TLC showed disappearance of starting material and formation of two major sopts, which in the initial attempt were separated and identified by ^1H NMR spectroscopy as intermediates **157a**

and **157b**. Then, to this mixture was added an excess amount of HBF_4 (one full pipet, 54% w/w ether solution) and the reaction stirred for 30 min. Quenching the reaction with $NaHCO_{3(aq)}$, a conventional extractive work up with dichloromethane, evaporation of the solvents, and purification with column chromatography (PET:ethyl acetate 15:1) afforded compound **152** (0.14 g, 60 % yield) in pure form.

(**152**), IR (neat, KBr) ν_{max}= 2099, 2062, 2032, 1724, 1645, 1587, 1367, 1238, 1208, 1114, 1084, 1029, 924, 771, 710 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 8.29 (s, 1H), 7.91 (dd, J=7.8, 1.0 1H), 7.80 (dd, J=7.5, 1.0, 1H), 7.66 (ddd, J=7.5, 7.5, 1.2, 1H), 7.56 (ddd, J=7.5, 7.5, 1.2, 1H), 4.35 (q, J= 7.2, 2H), 1.39 (t, J= 7.2, 3H). ^{13}C NMR ($CDCl_3$) 197.7, 191.9, 165.7, 142.8, 139.6, 136.4, 135.8, 133.4, 132.5, 131.0, 129.5, 85.6, 61.8, 14.1. HRMS (TOF) m/e for $C_{20}H_{10}O_9Co_2$ (M^+-2CO) calculated 455.9107, found 455.909.



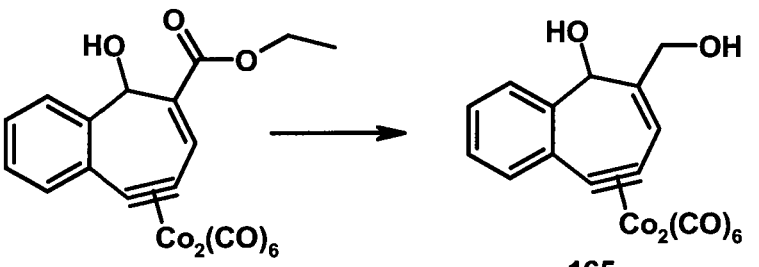
157a



157b

(**157a**), ^1H NMR ($CDCl_3$) δ =7.69 (d, J=8.0 Hz, 1H), 7.60 (d, J=7.5, 1H), 7.56 (app t, J= 7.5, 1H), 7.42 (app t, J=7.5, 1H), 5.08 (d, J=10.5, 1H), 4.32 (m, 2H), 4.19 (d, J=10.5, 1H), 4.01 (m, 1H), 3.84 (m, 1H), 1.25-1.33 (m, 6H). **157b:** ^1H NMR ($CDCl_3$) δ = 7.70 (t, J=7.0, 1H), 7.57 (t, J=7.5, 2H), 7.44 (m, 1H), 5.46 (dd, J=11.0, 4.0, 1H), 4.28 (m, 2H), 4.17 (d, J=10.5, 1H), 3.60 (d, J=4.5, 1H), 1.30 (m, 3H).

Synthesis of 168 and 166



168 **165**

To a solution of **152** (0.055 g, 0.10 mmol) in methanol (5 mL) was added $CeCl_3 \cdot 7H_2O$ (0.12 g, 0.30 mmol) at 0°C and the mixture was stirred for 5 min. $NaBH_4$ (0.012 g, 0.31 mmol) was added and the mixture was stirred at the same temperature for 30 min. Quenching the reaction with aqueous NH_4Cl(sat) was followed by conventional extraction with Et_2O. The extracts were combined, dried over $MgSO_4$, and concentrated under reduced pressure. The crude residue was then subjected to flash column chromatographyl on silica (PET: Et_2O 4:1) to isolate **168** (0.023 g, 44%).

Reduction of 168 with DIBAL-H:

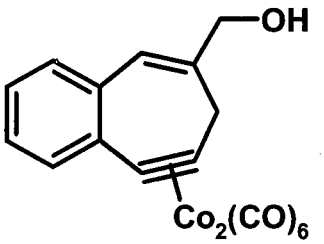
A solution of **168** (0.040 g, 0.07 mmol) in Et_2O (7 mL) was cooled to -75°C and 1 M solution of DIBAL-H (0.11 mL, 0.11 mmol) was added to it in dropwise fashion. The mixture stirred for 45 min, water was added slowly and solution warmd up to room temperature. After conventional extractive work up with Et_2O and evaporation of solvents, the residue was purified by preparative thin layer chromatography (TLC) using (PET:Et_2O 2:1) as mobile phase. Compound **165** was obtained in (0.008 g, 21%).

(**168**), IR (neat, KBr) ν_{max}=3468, 2983, 2093, 2058, 2026, 1701, 1561, 1367, 1244 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 8.20 (s, 1H), 7.82 (dd, J=9.5, 1.5, 1H), 7.45 (m, 3H), 5.88 (d, J=4.0,

1H), 4.34 (q, J=3.0, 2H) 2.38 (d, J=4.0, 1H), 1.41 (t, J=3.0, 3H); ^{13}C NMR ($CDCl_3$) 198.7, 166.6, 141.6, 138.1, 136.7, 133.9, 132.7, 130.2, 129.4, 129.2, 72.3, 61.6, 14.3.

(**165**), IR (neat, KBr) ν_{max} = 3354, 2926, 2091, 2053, 2023 cm^{-1}; ^1H NMR ($CDCl_3$) δ =7.73 (dd, J=7.5, 1.0, 1H), 7.54 (d, J=7.0, 1H), 7.41- 7.46 (m, 2H), 6.95 (s, 1H), 5.23 (d, J=3.0, 1H), 4.50 (d, J=5.0, 2H), 2.78 (d, J=3.5, 1H), 2.21(m, 1H); ^{13}C NMR: 199.0, 143.9, 138.5, 136.0, 133.2, 128.9, 128.7, 126.5, 126.3, 85.0, 74.0, 66.2. MS m/e, (M^+-CO): 444, (M^+-2CO): 416, (M^+-3CO): 388, (M^+-4CO): 360. HRMS (TOF) m/e for $C_{18}H_{12}O_8Co_2$ calculated (M^+) 471.904 found 471.9074.

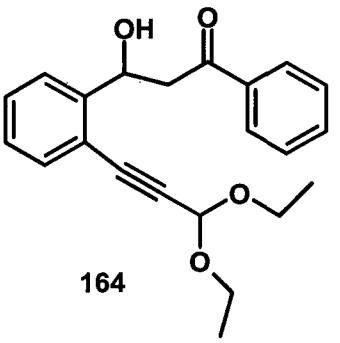
To an equimolar solution of **165** (0.008 g, 0.017 mmol) and triethylsilane (2.7 μL, 0.017 mmol) in dichloromethane (2 mL) was added $BF_3.OEt_2$ and the mixture was stirred for 0.5 h. The reaction was quenched by addition of saturated solution of $NaHCO_{3\,(aq)}$, and was followed by conventional extractive work up with dichloromethane to give the crude **170**.



170

(**170**) ^1H NMR ($CDCl_3$) δ = 7.65 (m, 1H), 7.28 (m, 2H), 7.14 (m, 1H), 6.54 (s, 1H), 4.26 (brs, 2H), 4.14(s, 1H), 3.93(s, 1H), 3.91 (s, 2H).

Synthesis of 164

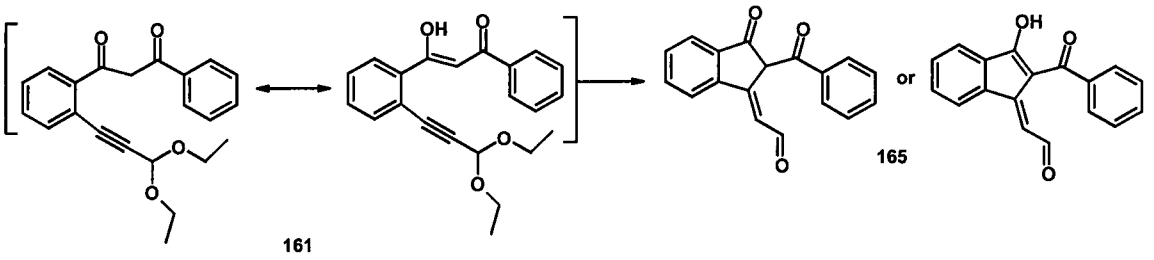


164

To a solution of diisopropylamine (1.2 mL, 8.5 mmol) in THF (10 mL) was added BuLi (3.4 mL, 2.5 M solution) at -75 °C. The solution was stirred for 30 min at 0 °C, and cooled again to -75 °C before dry acetophenone (1.0 mL, 8.6 mmol) was added to it. The mixture was stirred at -75 °C for an hour, then a cooled solution of compound **145** (0.20 g in 5 mL THF, 0.80 mmol) was added to it in a dropwise fashion. The reaction was stirred for another 45 min at -75 °C before it was slowly quenched with saturated solution of $NH_4Cl_{(aq)}$. After extractive work up and evaporation of the solvents, the crude product was subjected to purification by flash column chromatography (7:1 PET: ether) to afford **164** (0.18 g, 60 %).

(164), IR (neat, KBr) ν_{max}= 3476, 2977, 2890, 1681, 1481, 1448, 1094, 1053, 760, 692 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 7.97 (d, J=7.5, 1H), 7.70 (d, J=7.5, 1H), 7.59(t, J=7.0, 1H), 7.48 (appt dd, J=8.0, 7.5, 3H), 7.45 (t, J=7.5, 1H), 7.27(m, 1H), 5.73 (appt d, J=10.0, 1H), 5.43 (s, 1H), 3.82 (d, J=3.0, 1H), 3.55-3.72 (m , 5 H), 3.18 (dd, J=10.0, 9.0, 1H) 1.13 (m, 6H); ^{13}C NMR ($CDCl_3$) 200.0, 145.5, 136.6, 133.5, 132.5, 129.4, 128.6, 128.3, 128.2, 127.1, 125.5, 125.4, 118.7, 91.7, 90.3, 82.8, 68.0, 61.0, 60.9, 46.3, 15.0. HRMS (TOF) m/e for $C_{22}H_{24}O_4$ (M^+) calculated 352.1675 found 352.1674.

Attempted synthesis of 161



A solution of oxalyl choride (12 μL, 0.15 mmol) in CH_2Cl_2 (3.0 mL) was cooled to -75 °C and to that was added DMSO (21 μL, 0.29 mmol). The mixture stirred for 10 min and alcohol **164** (0.048 g 0.13 mmol, dissolved in 1.5 mL CH_2Cl_2) was added gradually. After stirring the mixture for another 15 min, triethylamine (94 μL, 0.68 mmol) was added to the mixture, stirred for 5 min and then allowed to warm to room temperature. Water was added and the aqueous layer was extracted several times with dichoromethane. The combined organic layers was dried over $MgSO_4$ and the solvents were removed under reduced pressure. The crude residue was purified on prepared TLC plates (by using PET: Et_2O 5:1, as eluent). A trace amount of product **161** in the enol form was isolated and identified solely based on ^1H NMR spectral analysis and low resolution mass spectroscopy, and which gradually decomposed to **165**.

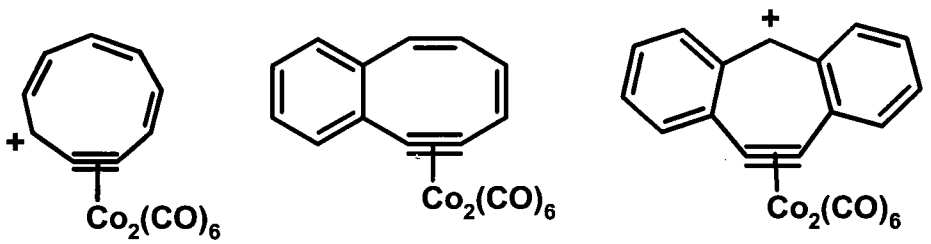
(**161**), ^1H NMR ($CDCl_3$): δ = 8.03 (d, J=7.5, 1H), 7.86 (dd, J= 3.0, 2.5, 1H), 7.63 (dd, J=3.0, 2.5, 1H), 7.55 (app t, J=7.0, 1H), 7.45-7.50 (m, 4H), 7.18 (s, 1H), 3.75-3.78 (m, 2H), 3.60-3.64 (m, 2H), 1.18 (dd, J=7.0, 4.0, 6H). MS m/e, (M^+) found 350.

(**165**), ^1H NMR ($CDCl_3$): δ =10.25 (d, J=8.0, 1H), 8.01 (d, J=8.5, 2H), 7.87 (d, J=7.5, 1H), 7.78 (d, J=7.5, 1H), 7.70 (app t, J=8.5, 2H), 7.6 (t, J=7.0, 2H), 7.5(app t, J=8.0, 4H), 6.79 (s, 1H), 5.97 (d, J=8.0, 1H).

4. FUTURE WORK

Aromaticity in transition metal complexes of annulenes/dehydroannulenes is of interest not only because of the ongoing curiosity on the concept of aromaticity but also to investigate more deeply on the nature of metal alkyne bonds. For this matter, as an extention to our study on the $Co_2(CO)_6$-tropylium ion complexes, it would be interesting to prepare anti-aromatic analogues (**171, 172**) of these systems (**99,100**). Comparison between the aromatic and anti-aromatic systems should give a better picture on the amount of π-electron delocalization in these systems. In addition, anti-aromatic models can be used to validate the reliability of DFT calculations (at the level we have applied) for estimation of aromatic properties (NICS values, ASE, and HOMA) of these systems (Figure 4.1).

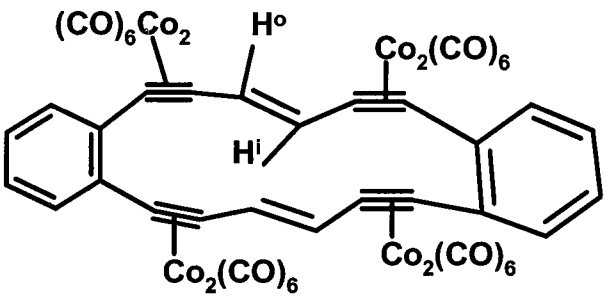
Dibenzo-substituted dehydrotropylium cation (**173**) would be another interesting member of this class of compounds which can be added to this series. Preliminary structural evaluation of this compound by using DFT calculations (B88-PW91/dzvp basis set) predicts a planar structure for this compound (Figure 4.1).



171 172 173

Figure 4.1. Structural models for anti-aromatic and aromatic dicobalt hexacarbonyl complexes of dehydroannulenes.

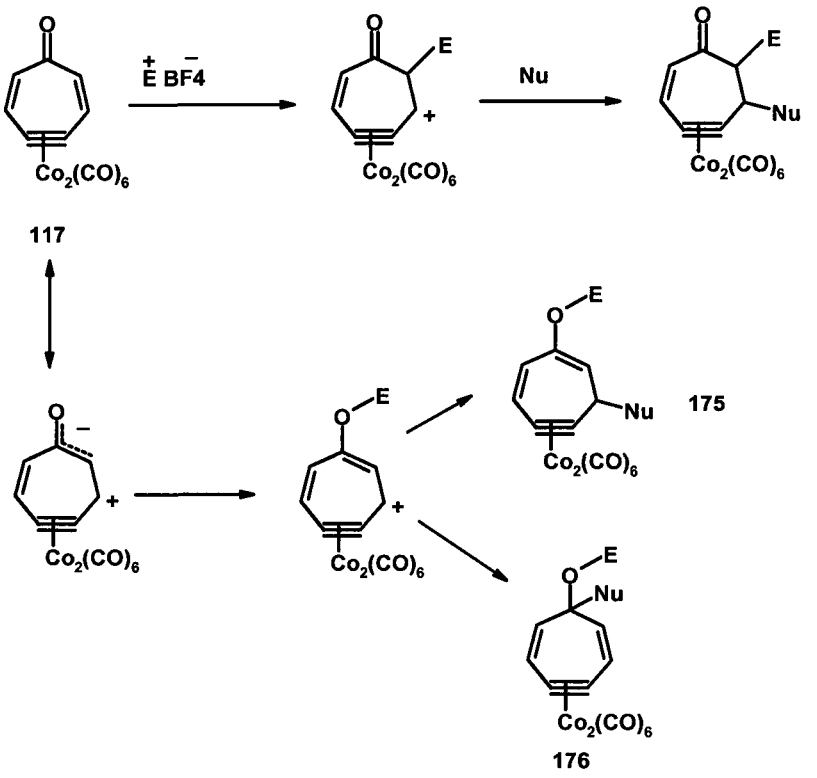
Furthermore, one can envision a larger (and perhaps strain free/less strained) dehydro -annulene molecule such as **174**, in which the incorporation of a trans-alkene, as suggested by Haley and coworkers [90] would allow one to perform aromaticity studies by ^{1}H NMR analysis of inner H^i and outer H^o protons of the ring (Figure 4.2).



174

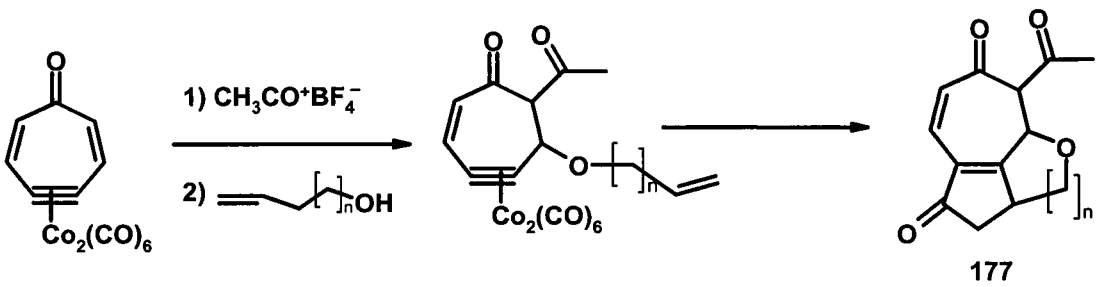
Figure 4.2. Expanded $Co_2(CO)_6$-dehydroannulene containing two isolated alkene units.

Another path worthy of consideration would be the reactivity studies on dehydrotropone dicobalt complex (**117**) and to determine if it can react with strong electrophiles (such as carbenium, acylium, nitronium ions, or arylsulfenium tetrafluoro-borates) and thus can be used in a stepwise electrophilic-nucleophilic addition as described by Smoliakova and coworkers for the other conjugated enyne-dicobalt complexes.[18] However, one may consider the possibility of the activation of carbonyl group by Lewis acid, formation of the enol, and nucleophilic attack from oxygen site as a competitive pathway. This, if it happens would give side product(s) **175** or/and **176** (Scheme 4.1).



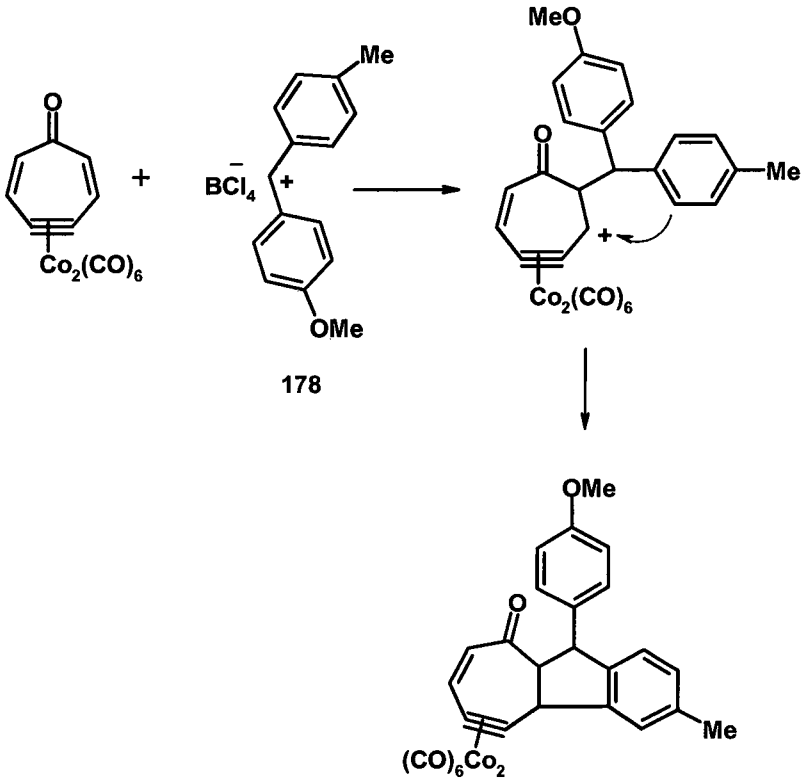
Scheme 4.1 Reactivity of compound **117** towards strong electrophile.

Nevertheless, if the reaction of dehydrotropyne cobalt compex (**117**) with strong electrophiles occurs efficiently (at the corresponding double bond), a wide range of electrophiles and nucleophiles can be examined to establish the scope and limitation of stepwise electrophilic-nucleophilic addition for highly conjugated enyne systems of this type. Moreover, by careful selection of the reactants (electrophiles or nucloephiles) in this sequentional electrophilic-nucleophilic addition, it would be possible to obtain a suitable substrate for the subsequent Pauson-Khand reaction and prepare polycyclic compounds such as **177**.



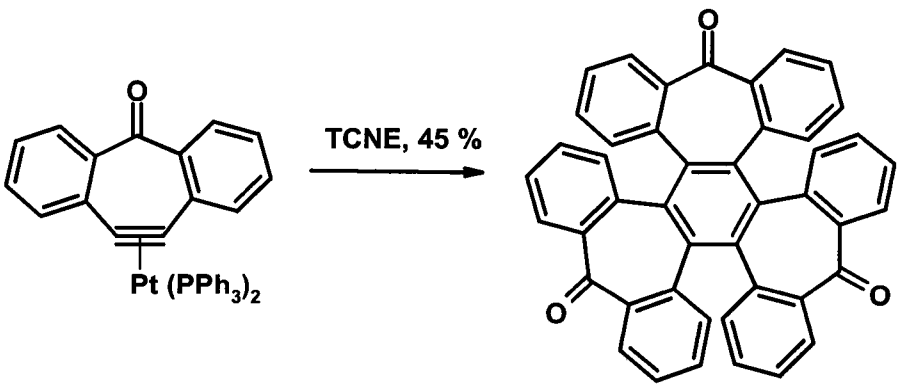
Scheme 4.2 Stepwise electrophilic-nucleophilic addition to **117** and formation of polycyclic compounds.

Among the possible range of electrophiles, benzhydryl cation **178** would be an interesting choice based on the previous observation of the ability of methyl-substituted ring to capture the intermediate cation in an intramolecular fashion.[91]



Finally, one might think of these highly conjugated molecules as benzyne analogues and study their reactivities in benzyne related reactions by generating the free

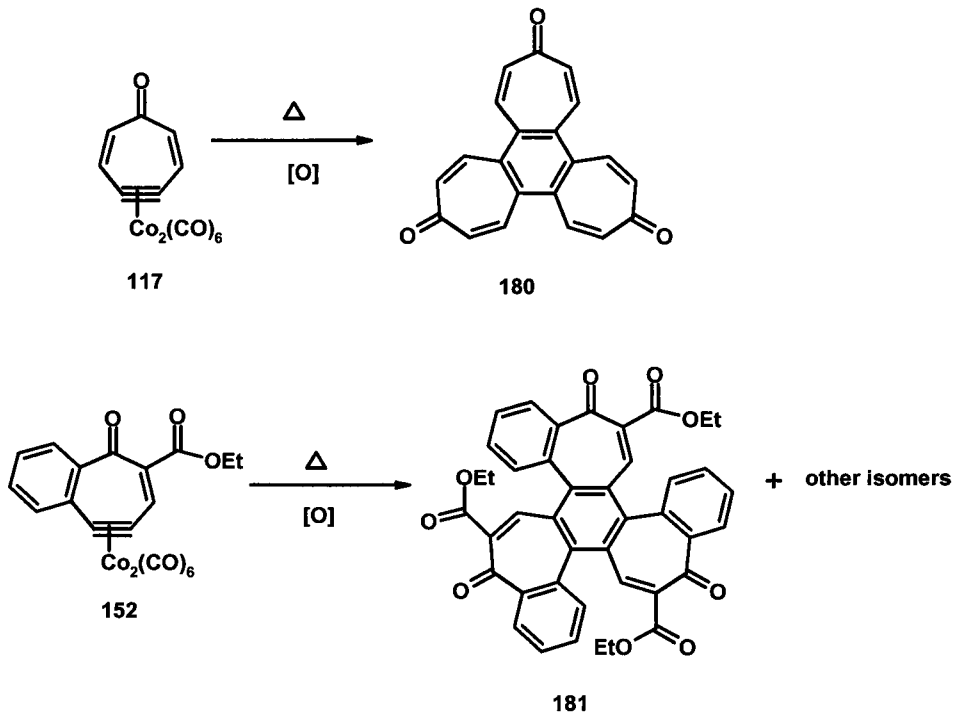
cyclic alkyne in situ. The dehydrotropones, after generation in situ, may be captured by a nucleophile or in the absence of any nucleophile and upon heating may undergo alkyne trimerization to give an access to new types of macrocyclic compounds. This kind of transformation (alkyne trimerization) has been observed for Pt-complexes of benzo-fused dehydrotropone which upon the treatment with TCNE (tetracyanoethylene) gave compound **179** .[58]



179

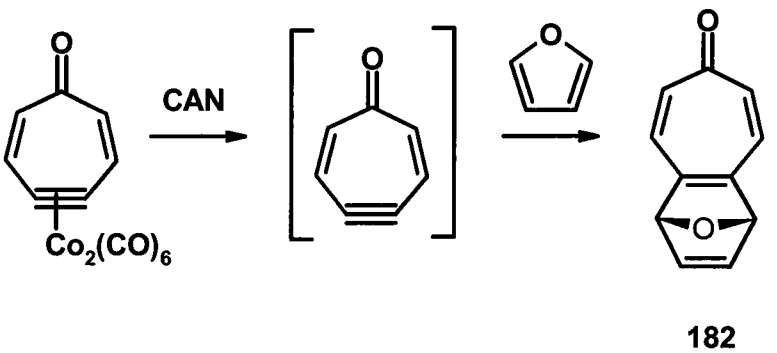
Scheme 4.3 Trimerization reaction of a Pt-complex of benzo-fused dehydrotropone.

Therefore, in principle, considering the known catalytic effect of cobalt on alkyne trimerization, it should be possible to obtain compounds (**180**) and (**181**) upon heating or by exposing compound **117** and **153** to an appropriate oxidizing agent (Scheme 4.4).



Scheme 4.4 Trimerization reaction of **117** and **152**.

The triple bond of these strained cyclic alkyne (**117** or **152**) after generation in situ may be trapped by an appropriate nucleophile (such as Diels-Alder diene traps) to give an access to the smaller cyclic compounds of the troponoid family with potential biological activity.[85] Reaction of dehydrotropone with furan can serve as one such example.



Scheme 4.5. In situ generation of dehydrotropone and its reaction with furan.

REFERENCES

1. Meerwein, H.; van Emster, K. *Chem. Ber.* **1922,** *55*, 2500.

2. Ola, G. A., Surya Prakash, G. K., Eds. *Carbocation Chemistry*, Wiley-Inter science, New York, 2004; pp 26 -29.

3. a) Seyferth, D.; Williams, G. H.; Hallgren, J. E. *J. Am. Chem. Soc.* **1973**, *95*, 226. b) Nicholas, K. M. *Acc. Chem. Res.,* **1987**, *20*, 207. c) Sokolov, V. I.; Barinov, I. V.; Reutov, O. A. *Izv. Akad. Nauk SSSR, Ser. Khim.,* **1982**, 1922; *Bull. Acad. Sci. USSR ,Div. Chem. Sci.,* **1982**, *31*, 1715 (Engl. Transl.) d) Reutov, O. A.; Barinov, I. V.; Chertkov, V. A.; Sokolov, V. I. *J. Organomet. Chem.* **1985**, *297*, C25 (e). Froom, S. F. T.; Green, M.; Nagle, K. R.; Williams, D. J. *J. Chem. Soc., Chem. Commun.,* **1987**, 1305. f) D'Agosino, M. F.; Frampton, S. C.; McGlinchey, M. J. *J. Organomet. Chem.* **1990**, *394*, 145.

4. For thermodynamic stability of carbocations: *a*) Olah, G. A., Schleyer, P.v.R. Eds. *Carbonium Ions,* Vols. I-V, Wiley Interscience, New York, NY, **1968-76** and reviews therein. b) Arnett, E. M.; Petro, C. *J. Am. Chem. Soc.* **1978,** *100*, 5408. c) Deno, N. C.; Jaruzelski, J. J.; Schriesheim. A. *J. Am. Chem. Soc.* **1955,** *77*, 3044. d) Deno, N. C. A.; Schriesheim. J. *J. Am. Chem. Soc.* **1955,** 77, 3051. e) Deno, N. C.; Evans, W. L. *J. Am. Chem. Soc.* **1957**, *79*, 5804. f) For kinetic investigation see: (4a) and (g) Vogel, P. *Carbocation Chemistry.* Elsevier, Amsterdam, **1985**. h) Ritchie. C. D. *Acc. Chem. Res.* **1972**, *5*, 348. Ritchie. C. D. *Can. J. Chem.***1986**, 64, 2239. i) For hydride ion affinity scale see: Anslyn, E. V.; Dougherty, D. A. *Modern Physical Organic Chemistry,* University Science, 2006; pp 88.

5. Mayr, H.; Patz, M.; Gotta, M. F.; Ofiala. A. R. *Pure. Appl. Chem.* **1998**, *70*, 1993.

6. a) Arnett, E. M.; Hofelich, T. C. *J. Am. Chem. Soc.* **1983**, *105,* 2889. b) Deno, N. C.; Richey, H. G.; Liu, J. S.; Lincoln, D. N.; Turner, J. O. *J. Am. Chem. Soc*, **1965**, *87*, 4533. c) For cobalt stabilized cation : Connor, R. E.; Nicholas, K. M. *J. Organomet. Chem.,* **1977**, *125*, C45. d) For tropylium: Doering W. E.; Knox, L. H. *J. Am. Chem. Soc,* **1954**, *76*, 3203. e) Cary, F. A.; Sundberg, R. J. *Advanced organic chemistry A*, 4th Ed. Kluwer, 2000; pp 278.

7. a) Ingold, C. K. *Recl. Trav. Chim. Pays-Bas* **1929**, *48*, 797. b) Ingold, C. K. *J Chem. Soc.* **1933**, 1120. c) Ingold, C. K. *Chem. Rev,* **1934**, *15*, 225.

8. Swain, C. G.; C. B. Scott. *J. Am. Chem. Soc.* **1953**, *75*, 141.

9. a) Mayr, H.; Patz,; M. *Angew. Chem. In. Ed. Engl.* **1994**, *33*, 938. b) Mayr, H.; Kuhn, O.; Gotta, M. F.; Patz, M. *J. Phy. Org .Chem.* **1998**, *11*, 642. c) May, H. *Angew. Chem.* **1990**, 102, 1415; *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 1371. d) Mayr, H.; Bug, T.; Gotta, M. F.; Hering, N.; Irrgang, B.; Janker, B.; Kempf, B.; Loos, R.; Ofial, A. R.; Remennikov, G.; H. Schimmel. *J. Am. Chem. Soc.* **2001**, *123*, 9500. e) Mayr, H.; Kempf, B.; Ofial, A. R. *Acc. Chem. Res.* **2003**, *36*, 66. f) Minegishi, S.; Mayr, H. *J. Am. Chem. Soc.* **2003**, *125*, 286.

10. Holmes, J. D.; Jones, D. A.; Pettit, K. R. *J. Organomet. Chem.* **1965**, *4*, 324.

11. a) Lockwood, R. F.; Nicholas, K. M. *Tetrahedron. Lett.* **1977**, *48*, 4163. Melikyan, G. G.; Nicholas, K. M. *Modern Acetylene Chemistry*, **1995**; pp 99-138. b) McGlinchey, M. J.; Girard, L.; Ruffolo, R. *Coord. Chem. Rev.* **1995**, *143*, 331. c) El-Amouri, H.; Gruselle, M. *Chem. Rev.* **1996**, *96*, 1077.

12. Hill, E.A., Wiesner, R. *J. Am. Chem. Soc.* **1969,** 91, 509.

13. Dunn, J. A.; Hunks, W. J.; Ruffolo, R.; Rigby, S. S.; Brook, M. A.; McGlinchey, M. J. *Organometallics.* **1999,** *18,* 3372.

14. McGlinchey, M. J. *Can. J. Chem.* **2001,** *79*, 1295.

15. Cordier, C.; Gruselle, M.; Vaissermann, J.; Troitskaya, L. L.; Bakhmutov, V. I.; Sokolov, V. I., Jaouen. G. *Organometallics.* **1992**, *11*, *3825.*

16. Nicholas, K. M.; Pettit, R. J. *Organomet. Chem.* **1972**, *44*, C21.

17. For reviews in this area see: 3b and a) Green, J. R. *Curr. Org. Chem.* **2001**, *5*, 809. c) Teobald, B. J. *Tetrahedron.* **2002**, *58*, 4133. d) Fletcher, A. J.; Christie, S. D. R. *J. Chem. Soc., Perkin Trans 1.* **2000**, 1657.

18. Smit, W. A.; Caple, R.; Smoliakova, I. P. *Chem. Rev.* **1994**, *94*, 2359, and references therein

19. a) Gruselle, M.; Cordier, C.; Salmain, M.; El-Amouri, H.; Guerin, C.; Vaissermann, J.; Jaouen, G. *Organometallics* **1990**, *9*, 2993. b) Padmanabhan, S.; Nicholas, K. M. *J. Organomet. Chem.* **1984,** 268, C23.

20. Schreiber, S. L.; Klimas, M. T.; Sammakia, S. J. *J. Am. Chem. Soc.* **1987**, 109, 5749.

21. Schilling, B. E. R.; Hoffmann. R. *J. Am. Chem. Soc.* **1987**, *100*, 6274. b) Schilling, B. E. R.; Hoffmann, R. *J. Am. Chem. Soc.* **1979,** *101*, 3456.

22. Edidin, R. T.; Norton, J. R.; Mislow, K. *Organometallics* **1982**, *1,* 561.

23. Iwashita, Y.; Tamura, F.; Nakamura, A. *Inorg. Chem.* **1969**, *8,* 1179. b) Platts, J. A.; Evans, G. J. S.; Coogan, M. P.; Overgaard, J. *Inorg. Chem.* **2007**, *46*, 6291.

24. Melikyan, G. G.; Bright, S.; Monroe, T.; Hardcastle, K. I.; Ciurash, J. *Angew. Chem. Int. Ed.* **1998**, *37*, 161.

25. a) Gruselle, M.; Kondratenko, M. A.; El-Amouri, H.; Vaissermann, J. *Organometallics.* **1995**, *14,* 5242. b) Kondratenko, M.; El-Hafa, H.; Gruselle, M.; Vaissermann, J.; Jaouen G.; McGlinchey M. J. *J. Am. Chem. Soc.* **1995,** *117*, 6907. c) Aggarwal, R. P.; Connelly, N. G.; Crespo, M. C.; Dunne, B. J.; Hopkins, P. M.; Orpen A. G. *Chem. Commun.* **1989**, 33. d) For mixed Co-Fe complexes see 13a

26. Kuhn, O.; Rau, D.; Mayr, H. *J. Am. Chem. Soc.* **1998**, *120*, 900.

27. El-Amouri, H.; Gruselle, M.; Jaouen, G.; Daran, J.; Vaissermann, *J. Inorg. Chem.* **1990**, *29*, 3238.

28. a) Gelling, B. A.; Went, M. J. *J. Organomet. Chem.* **1992**, 439,189. b) Gelling, A.; Mohrnand, G. F.; Jeffery J. C.; Went, M. J. *J. Chem. Soc. Dalton Trans.* **1993**, 1857.

29. Bennett, S. C.; Phipps, M. A.; Went, M. J. *J. Chem. Soc. Chem. Comm.* **1994**, 225.

30. Gachkova, N.; Cassel, J.; Leue, S.; Kann, N. *J. Comb. Chem.* **2005**, *7*, 449.

31. Krebs, A.; Wilke, J. *Top. Curr. Chem.* **1983**, *109*, 189.

32. Golovko, V.; Hope-Weeks, L. J.; Mays, M. J.; McPartlin, M.; Sloan, A. M.; Woods, A. D. New. *J. Chem.* **2004**, *28*, 527.

33. Iwasawa, N.; Otsuka, M.; Yamashita, S.; Aoki, M.; Takaya. J. *J. Am. Chem. Soc.* **2008**, *130*, 6328.

34. a) Magnus, P.; Carter, R.; Davies, M.; Elliott, J.; Pitterna, T. *Tetrahedron* **1996**, *52*, 6283. b) Schreiber, S. L.; Sammakia, T.; Crowe, W. E. *J. Am. Chem. Soc.* **1986**, *108*, 3128.

35. Green, J. R. *Eur. J. Org. Chem.* **2008**, 6053, and references therein.

36. Palazón, J. M.; Martín, V. S. *Tetrahedron. Lett.* **1995**, *36*, 3549. For the synthesis of cyclic ethers by intramolecular Nicholas reactions, see: a) Mukai, C.; Yamaguchi, S.; Sugimoto, Y.; Miyakoshi, N.; Kasamatsu, E.; Hanaoka, M. *J. Org. Chem.* **2000**, *65*, 6761, and references cited therein. b) Mamajima, A.; Isobe, M. *Org. Lett.* **2006**, *8*, 1205, and references therein.

37. Betancort, J. M.; Martín, T.; Palazón, J. M.; Martín, V. S. *J. Org. Chem.* **2003**, *68*, 3216.

38. Mukai, C.; Yamaguchi, S.; Kim, I. J.; Hanaoka, M. *Chem. Pharm. Bull.* **2001**, 49, 613 and references therein.

39. Crisóstomo, F. R. P.; Martín, T.; Martín, V. S. *Org. Lett.* **2004**, *6*, 565.

40. Hernandez, J. N.; Ramírez, M. A.; Rodríguez, M. L.; Martín, V. S. *Org. Lett.* **2008**, *10*, 2349.

41. Closser, K. D.; Quintal, M. M.; Shea, K. M. *J. Org. Chem.* **2009**, *74*, 3680.

42. Berge, J.; Claridge, S.; Mann, A.; Muller, C.; Tyrrel, E. *Tetrahedron. Lett.* **1997**, *38*, 685. b) Mann, A.; Muller, C.; Tyrrell, E. *J. Chem. Soc. Perkin Trans.* **1998**, 1427 c) Tyrell, E.; Claridge, S.; Davis, R.; Label, J.; Berge J. *Synlett* **1995**, 714.

43. Krafft, M. E.; Cheung, Y. Y.; Wright, C.; Cali, R. *J. Org. Chem.* **1996**, *61*, 3912.

44. Lu, Y.; Green, J. R. *Synlett,* **2001**, 243.

45. Tanino, K.; Shimizu, T.; Miyama, M.; Kuwajima, I. *J. Am. Chem. Soc.* **2000,** *122,* 6116.

46. Christie, S. D. R.; Davoile, R. J. M.; Elsegood, R. J.; Fryatt, R.; Jones, C. F.; Pritchard, G. J. *Chem. Commun.* **2004**, 2474.

47. Lebold, T. P.; Cheryl, C. A.; Kerr, M. A. *Synlett.* **2006**, 364.

48. a) Demirhan, F.; Gelling, A.; Iri li, S.; Jeffery, J. C.; Salek, S. N.; Sentiirk, O. S.; Went, M. J.. *Chem. Sac.* Dalton Trans., **1993**, 2765. b) Bennett, S. C.; Jeffery, J. C.; Went, M. J. *Chem. Sac. Dalton Trans.* **1994,** 44. c) Davies, J. E.; Hope-Weeks, L. J.; Mays, M. J.; Raithby, P. R. *Chem. Commun.*, **2000**, 1411.

49. Hope-Weeks, L. J.; Mays, M. J.; Solan, G. A. *Eur. J. Inorg. Chem.* **2007**, 3101, and references therein.

50. Golovko, V. B.; Mays, M. J.; Solan, G. A. *J. Organomet. Chem*, **2007,** *692*, 4985.

51. a) Guo, R.; Green, J. R. *Chem. Commun.* **1999**, 2503. b) Gibe, R.; Green, J. R. *Chem. Commun.* **2002**, 1550. c) Gibe, R.; Green, J. R.; Davidson, G. *Org. Lett.* **2003**, *5*, 1003.

52. a) Betancort, J. M.; Rodriguez, C. M.; Martín. V. S. *Tetrahedron. Lett.* **1998**, *39*, 9773. b) Palazon, J. M.; Martín. V. S. *Tetrahedron. Lett.* **1995**, *36*, 3549.

53. a) Bradley, D. H.; Khan, M. A.; Nicholas, K. M. *Organometallics* **1989**, *8*, 554. b) Bradley, D. H.; Khan, M. A.; Nicholas, K. M. *Organometallics* **1992,** *11*, 2598. c) Caffyn, A. J. M.; Nicholas, K. M. *J. Am. Chem. Soc.* **1993,** *115*, 6438.

54. a) Jacobi, P. A.; Murphree, S.; Rupprecht, F.; Zheng, W. *J. Org. Chem.* **1996,** *61,* 2413 (b) Jamison, T. F.; Shambayati, S.; Crowe, W. E.; Schreiber, S. L. *J. Am.*

Chem. Soc. **1997,** *119,* 4353. c) Hamajima, A.; Isobe, M. *Angew. Chem. Int. Ed.* **2009**, *48*, 2941. d) Djurdjevic, S.; Green, J. R. *Org. Lett.* **2007**, *9*, 5505. (e) Magnus, P.; Parry, D.; Iliadis, T.; Eisenbeis, S. A.; Fairhurst, R. A. *J. Chem. Soc. Chem. Commun.* **1994**, 1543.

55. a) Melikyan, G. G.; Khan, M. A.; Nicholas K. M. *Organometallics.* **1996,** *14,* 2170 b) Melikyan, G. G.; Deravakian, A. *J. Organomet. Chem.* **1997**, *544*, 143. c) Melikyan, G. G.; Sepanian, S.; Riahi, B.; Villena, F.; Jerome, J.; Ahrens, B.; McClain, R.; Matchett, J.; Scanlon, S.; Abrenica, E.; Paulsen , K.; Hardcastle, K. I. *J. Organomet. Chem.* **2003**, *683*, 324. d) Melikyan, G. G.; Mikailian, B.; Sepanian, R.; Toure, P. *J. Organomet. Chem.* **2009**, *694*, 785. e) Melikyan, G. G.; Villena, F.; Florut, A.; Sepanian, S.; Sarkissian, H.; Rowe, A.; Toure, P.; Mehta, D.; Christian, N.; Myer, S.; Miller, D.; Scanlon, S.; Gruselle, M. P. *Organometallics*, **2006**, *25*, 4680.

56. Malisza, K. L.; Top, S.; Vaissermann, J.; Caro, B.; Senechal-Tocquer, M.; Senechal, D.; Saillard, J. Y.; Triki, S.; Kahlal, S.; Britten, J. F.; McGlinchey, M. J.; Jaouen, G. *Organometallics.* **1995,** *14,* 5273. b) Brownstein, S.; Gabe, E. J.; Hynes, R. C. *Can. J. Chem.***1992,** *70*, 1011.

57. a) Petersen, H.; Kolshorn, H.; Meier, H. *Angew. Chem.* **1978**, *90*, 483. *Angew. Chem. Int. Ed. Engl.* **1978**, *17*, 461. b) Meier, H.; Petersen, H.; Kolshorn, H. *Chem. Ber.* **1980**, *113,* 2398.

58. a) Lu, Z.; Abboud, K. A.; Jones, W. M. *J. Am. Chem. Soc.* **1992**, *114*, 10991. b) Lu, Z.; Jones, W. M. *Organometallics* **1994**, *13*, 1539.c) Klosin, J.; Abboud, K. A.; Jones, W. M. *Organometallics* **1995**, *14*, 2892. d) Klosin, J.; Abboud, K. A.;

Jones, W. M. *Organometallics* **1996,** *15*, 596. e) Klosin, J.; Abboud, K. A.; Jones, W. M. *Organometallics* **1996,** *15,* 2465.

59. Chen, Z.; Wannere, C. S.; Corminboeuf, C.; Puchta, R.; Schleyer, P. v. R. *Chem. Rev.* **2005**, *105*, 3842, and references therein.

60. a) Spitler, E. L.; Johnson, C. A.; Haley. M. M. *Chem. Rev.* **2006**, *106*, 5344, and references therein.

61. a) Boese, R. R. ; Matzger, A. J.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1997**, *119*, 2052. b) Dosa, P. I.; Erben, C.; Iyer, C. V. S.; Vollhardt, K. P. C.; Wasser, I. M. *J. Am. Chem. Soc.* **1999**, *121*, 10430. c) Faust, R. *Angew. Chem., Int. Ed.* **1998**, *37*, 2825.

62. a) Hisaki, I.; Sonoda, M.; Tobe. Y. *Eur. J. Org. Chem.* **2006**, 833, and references therein. b) Jusélius, J.; Sundholm, D. *Phys. Chem. Chem. Phys.* **2001**, *3*, 2433. c) Matzger, A. J.; Vollhardt, K. P. C. *Tetrahedron. Lett.* **1998**, *39*, 6791.

63. a) Shimada, S.; Tanaka, M.; Honda, K. *Inorg. Chim. Acta.* **1997**, *265*, 1. b) Bunz , U. H. F.; Roidl, G.; Adams, R. D. *J. Organomet. Chem.* **2000**, *600*, 56.

64. a) Laskoski, M.; Steffen, W.; Morton, J. G. M.; Smith, M. D.; Bunz, U. H. F. *J. Am. Chem. Soc.* **2002**, *124*, 13814. b) Laskoski, M.; Steffen, W.; Morton, J. G. M.; Smith, M. D.; Bunz, U. H. F. *J. Organomet. Chem.* **2003**, *673*, 25. c) Hodgson, M.; Parker, D.; Taylor, R. J.; Ferguson, G. *Organometallics* **1988**, *7*, 1761.

65. Sautet, P.; Eisenstein, O.; Canadell, E. *New. J. Chem.* **1987**, *11*, 797.

66. Iwasawa, N.; Satoh, H. *J. Am. Chem. Soc.* **1999**, *121,* 7951.

67. Derdau, V.; Laschat, S.; Dix, I. *Organometallics* **1999,** *18,* 3859, and references therein.

68. a) Young, D. G. J.; Burlison, J. A.; Peters, U. *J. Org. Chem.*, **2003**, *68*, 3494. b) Mohamed, A. B. Formation of Cycloheptyne – $Co_2(CO)_6$ Complexes via Nicholas Allylation Reactions and Ring Closing Metathesis. Ph.D. Thesis, University of Windsor, Windsor, ON, September 2005.

69. Green. J. R. unpublished results.

70. Proft F. D.; Geerlings, P. *Chem. Rev.* **2001,** *101,* 1451, and the references therein.

71. Di Martino, J.; Green. J. R. *Tetrahedron.* **2006**, *62*, 1402.

72. Green, J. R.; Pouget, V., unpublished results.

73. Mayr, H.; Muller, K. H.; Ofial, A. R.; Buhl, M. *J. Am. Chem. Soc.* **1999,** *121,* 2418.

74. a) Kruszewski, J.; Krygowski, T. M. *Tetrahedron Lett.* **1972**, 3839. b) Krygowski, T. M.; Cyrański, M. *Tetrahedron.* **1996**, *52*, 1713. c) Cyrański, M.; Krygowski, T. M. *J. Chem. Inf. Comput. Sci.* **1996**, *36*, 1142.

75. a) Pearson, R. G. *J. Org. Chem.* **1987**, **52**, 2131 b) Pearson, R. G. *J. Org. Chem.* **1989**, *54*, 1423. c) Pearson, R. G. *Acc. Chem. Res.* **1993**, *26*, 250.

76. Zhou Z.; Parr, R. G. *J. Am. Chem. Soc.* **1989**, *111,* 7371.

77. Chamizo, J. A.; Morgado, J.; Sosa, P. *Organometallics* **1993**, *12*, 5005.

78. Huang, Y.-Z.; Yang, S.-Y.; Li, X.-Y. *J. Organomet. Chem.* **2004**, *689*, 1050.

79. Zhang, G.; Musgrave, C. B. *J. Phys. Chem. A.* **2007**, *111,* 1554.

80. a) Krygowski, T. M.; Cyrański. M. K. *Chem. Rev.* **2001,** *101,* 1385. b) Glukhovtsev, M. N.; Bach, R. D.; Laiter, S. *J. Mol. Struct. (Theochem.)* **1997,** *417*, 123.

81. Schleyer, P. v. R.; Pühlhofer, F. *Org. Lett.* **2002,** *4*, 2873.

82. a) Heilbronner, H. H. E.; Eschenmoser, A. *Chem. Ind.* **1955**, 415. b) Wong, H. N. C.; Sondheimer, F. *Angew. Chem. Int. Ed. Engl.* **1976**, *15*, 117. c) Chan, T.-L.; Huang, N. Z.; Sondheimer, F. *Tetrahedron* **1983**, *39*, 427. For more information on dehydroannnulene check 61a.

83. Fernandez, A.; Rinco, L.; Almeida, R. *J. Mol. Struct. (Theochem.)* **2009**, *911*, 118.

84. a) Altenbach, H. J.; Korff, R. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 371. b) Aristoff, P. A. *J.Org. Chem.* **1981**, *46*, 1954. c) Mikołajczyk, M.; Mikina, M. *J. Org. Chem.* **1994**, *59*, 6760.

85. a) Zhao. J. *Curr. Med. Chem.* **2007**, *14*, 2597. b) Banwell, M. G. *Aust. J. Chem.* **1991**, *44*, 1. c) Pietra, F. Chem. Rev. **1973**, *73*, 293. d) Banwell, M. G.; Collis, M. P.; Mackay, M. F.; Richards, S. L. *J. Chem. Soc. Perkin Trans* 1. **1993**, 1913.

86. Faitfax, A. J.; Austin, D. J.; Xu, S. L.; Padwa, A. *J. Chem. Soc.,* Perkin Trans 1. **1992**, 2837.

87. Shim, S.-B.; Ko, Y.-J.; Yoo, B.-W.; Lim, C.-K.; Shin. J.-H. *J. Org. Chem.* **2004**, *69*, 8154.

88. Schuster, D. I.; Palmer, J. M.; Dickerman, S. C. *J. Org. Chem.* **1966**, *31*, 4281.

89. Crimmins, M. T.; Zuccarello, J. L.; Cleary, P. A.; Parrish J. D. *Org. Lett.* **2006**, *8*, 159.

90. Wan, W. B.; Chiechi, R. C.; Weakley, T. J. R.; Haley, M. M. *Eur. J. Org. Chem.* **2001**, 3485.

91. Mayr, H.; Kuhn, O.; Schlierf, C.; Ofial, A. R. *Tetrahedron* **2000**, *56*, 4219.

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