Transition-metal mediated cycloaddition reactions of enynes

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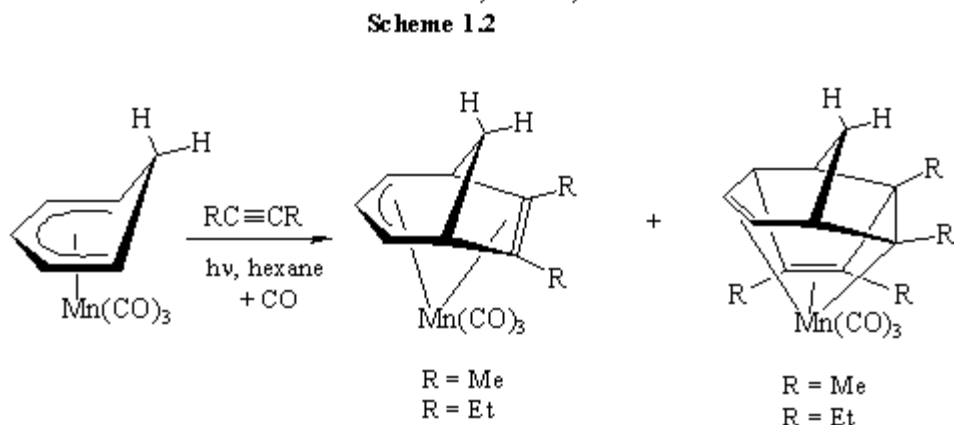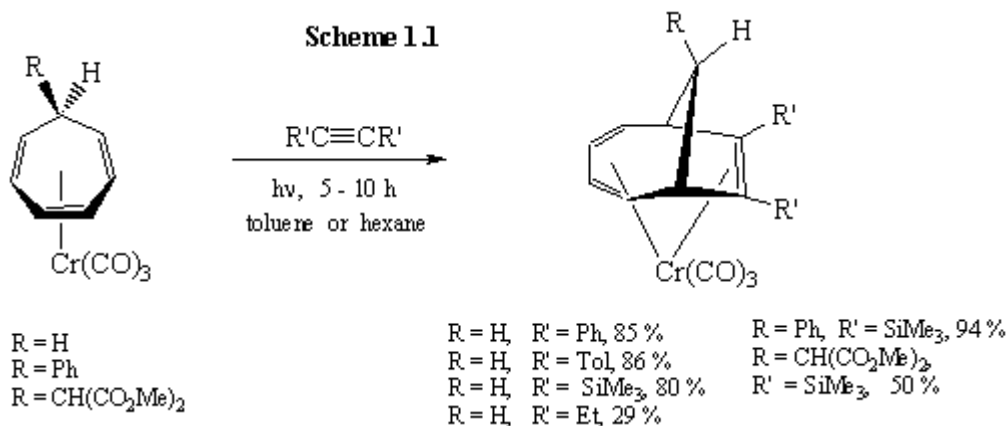[*]Rutgers Undergraduate Research Fellow

Introduction

Purpose

This research project was carried out to investigate transition-metal-mediated cycloaddition reactions between enynes and coordinated polyenyl manifolds (conjugated organic rings).

Background

Cycloaddition reactions are one of the most useful methods for the construction of rings. In the past, several methods were successfully developed for the formation of small-sized (3-6) and large (>10) ring systems (e.g., Diels-Alder reaction). However difficulties were encountered in preparing medium-sized rings (7-10) using these methods. In 1971, a thermally forbidden [6 + 2] cycloaddition was reported to occur by using transition metals under both thermal and photochemical conditions.[1]

The above finding generated interest in these higher-order cycloaddition reactions (e.g., 6 + 2, 6 + 4, 4 + 4, etc.). Since then, different research groups have reported efficient routes to medium-sized rings with high stereoselectivity using these metalmediated processes. Among these, Sheridan and co-workers[2] reported photoinduced [5 + 2] & [6 + 2] cycloaddition reactions between cyclohexadienyl complexes of manganese or triene complexes of chromium with a variety of alkynes (schemes 1.1 & 1.2).

Scheme 1.1

R = H
R = Ph
R = CH(CO₂Me)₂

R = H, R' = Ph, 85 %	R = Ph, R' = SiMe₃, 94 %
R = H, R' = Tol, 86 %	R = CH(CO₂Me)₂
R = H, R' = SiMe₃, 80 %	R' = SiMe₃, 50 %
R = H, R' = Et, 29 %	

Scheme 1.2

R = Me
R = Et

R = Me
R = Et

Similarly, transition-metal mediated cycloaddition (TMMC) reactions of triene complexes of chromium with olefins were also reported by Rigby and coworkers[3] (scheme 1.3).

Scheme 1.3
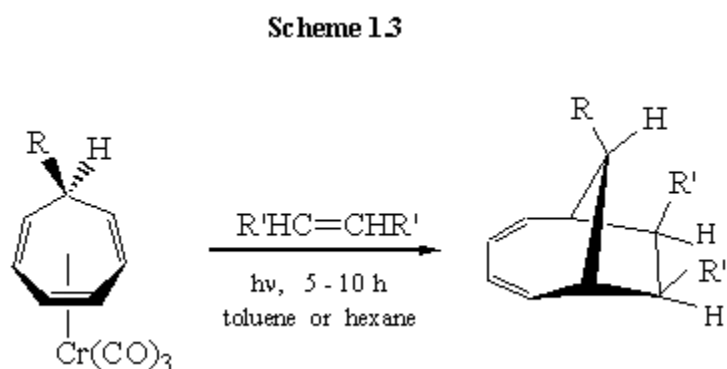
Since both manganese and chromium complexes undergo TMMC reactions with alkynes and alkenes, we have investigated the reactions of enynes (compounds that contain both a triple bond and a double bond), to see whether the alkyne or alkene moiety of the enyne react with the inorganic complexes.

Results and discussion

2

Reaction between tricarbonyl($\square^6$-cycloheptatriene) chromium(0) and 1-phenyl6-heptene-1-yne

Irradiation of a 1:1 mixture of tricarbonyl($\square^6$-cycloheptatriene) chromium(0) (**I**) and 1-phenyl-6-heptene-1-yne with UV light for 10 hours under nitrogen yielded 47% of the single-cycloadduct complex (**II**) after purification by column chromatography.

Scheme 2.1
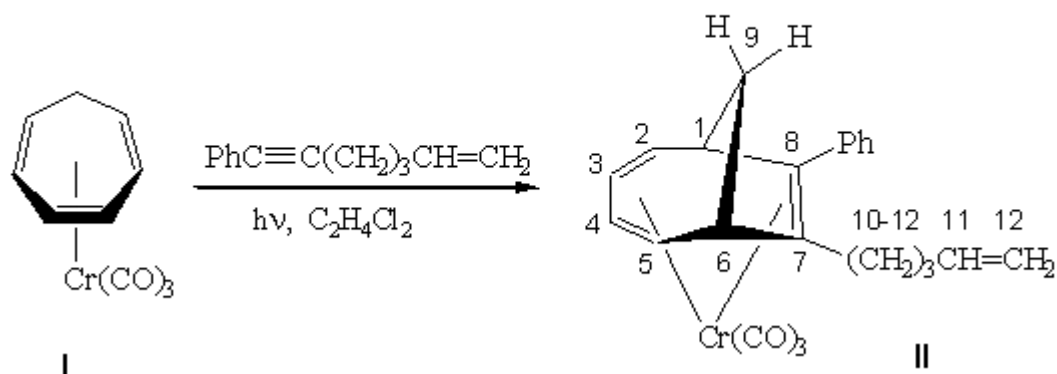
The reaction was monitored by IR spectroscopy. As the reaction progressed, the disappearance of starting material peaks ($\square_{max}$ (CO) (hexane), 1988(vs), 1927(vs), 1904(vs) cm^{-1}) was observed concomitant with the appearance of product **II** peaks ($\square_{max}$ (CO) (hexane), 1974(vs), 1906(vs), 1885(vs) cm^{-1}). The solvent was removed in vacuo and the product was isolated by silica gel/n-hexane column chromatography, loading with toluene, and eluting with n-hexane to first remove the unreacted **I**, then with CH$_2$Cl$_2$ to give product **II** as a red powder. Complex **II** has been characterized using ^{1}H and ^{13}C NMR, and IR spectroscopy.

Given that both the alkyne and alkene groups can undergo photoinduced cycloaddition with **I**, there are a number of possible cycloaddition products. These are shown below:

Scheme 2.2

II

III

IV

V

VI

$(R, R' = Ph, -(CH_2)_3CH=CH_2)$
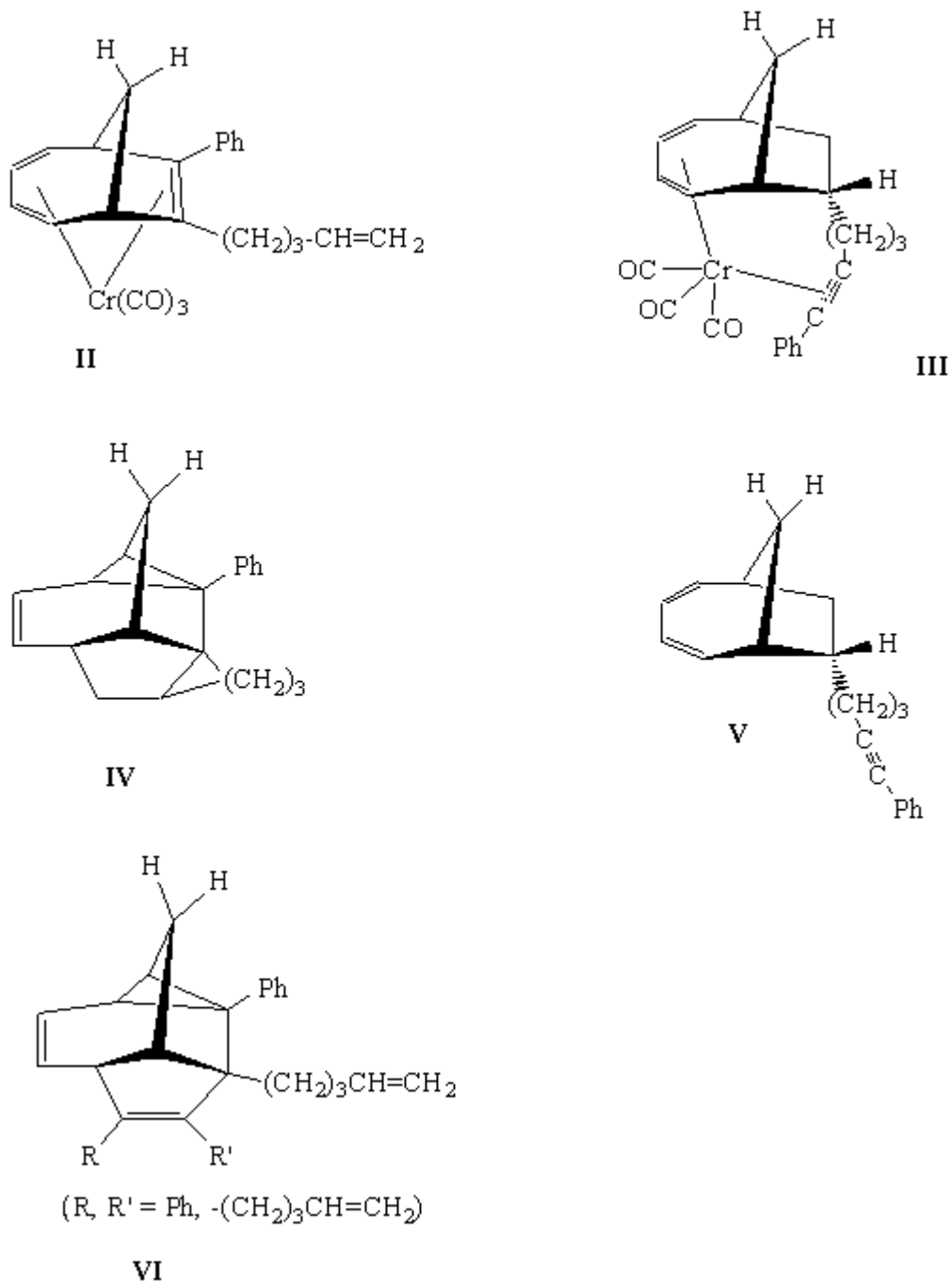
Complex **III** and compound **V** could have been formed by a [6 + 2] cycloaddition of only the olefin of the enyne. Compound **IV** might be formed from further intramolecular homo[6 + 2] addition of the olefin in **II**[4]. Compound **VI** could have formed by double homo[6 + 2] cycloaddition of two molecules of enyne to **I**.

Interestingly, only **II** was formed via a [6 + 2] cycloaddition of the alkyne of the enyne to **I**. Two new carbon-carbon bonds were formed C1-C8 and C6-C7.

Decomplexation of the organic ligand in tricarbonyl($\eta^{2:4}$-7-phenyl-8-pentenebicyclo[4.2.1] nona-2,4,7-triene)chromium(0) (II)

Scheme 2.3
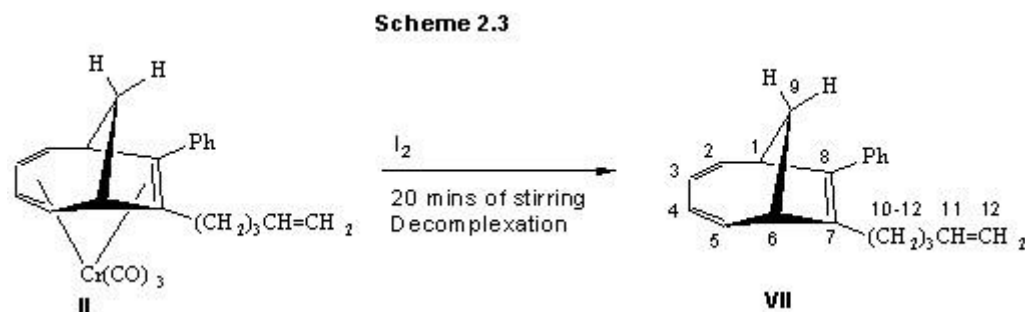
Addition of iodine to a solution of **II** in CH_2Cl_2 at room temperature causes the tricyclic organic ligand **VII** to be decomplexed. The presence of **VII** in the reaction solution was confirmed using Gas Chromatography - Mass Spectroscopy (GCMS). Compound **VII** was isolated as a clear colorless oil in quantitive yield following column chromatography with silica gel, eluting with hexane. Compound **VII** was characterized by GCMS and ^{1}H & ^{13}C NMR spectroscopy. This reaction is significant since it completes a new synthetic pathway for the novel organic ring compound **VII** from **I**.

Thermally induced catalytic [6 + 2] cycloaddition of an enyne to cycloheptatriene

Scheme 2.4
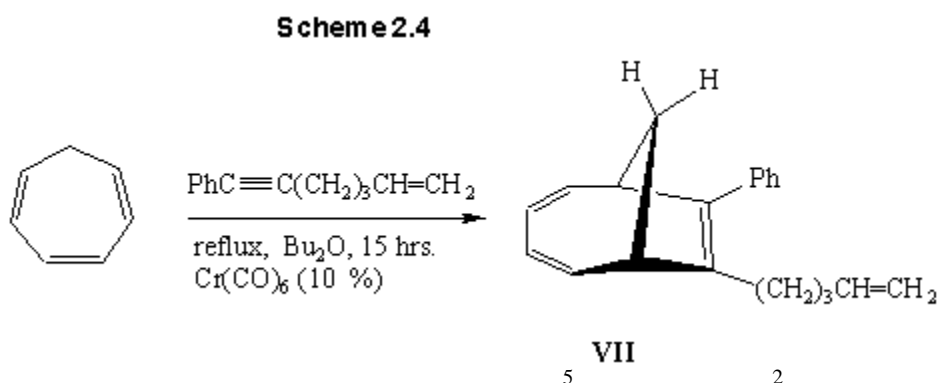
Different research groups, particularly Rigby's and Sheridan's , have reported that [6 + 2] and [6 + 4] cycloaddition reactions can be driven thermally in the presence of a metal catalyst. We have shown that a [6 + 2] cycloaddition reaction also occurs between cycloheptatriene and the enyne. However, the yield for this reaction is not very promising. The reaction has been repeated several times, and the yield of this reaction (calculated by integrating the GC peaks of the enyne and cycloheptatriene)

never exceeded 15%. One possible explanation for this low yield is the interference of the phenyl group of the enyne with the catalyst. The $Cr(CO)_6$ catalyst might coordinate to the phenyl group of the enyne, and prevent the catalyst from mediating the [6 + 2] addition. An experiment has been devised to test this hypothesis (see section 4.2).

Manganese-mediated [5 + 2] cycloaddition reactions between tricarbonyl-(η^5cyclohexadienyl)manganese(I) (VIII) and 1-phenyl-6-heptene 1-yne.

When tricarbonyl- (η^5-cyclohexadienyl)manganese(I)(**VIII**) and 1-phenyl-6heptene 1-yne were irradiated with UV light for 10 hours, a [5 + 2] single cycloadduct (**IX**) (49.5% yield based on enyne) was formed (see scheme 2.5). In addition, a double cycloadduct (**X**) was also formed via [5 + 2],*homo*[5 + 2] cycloaddition, (44.6% yield based on enyne). These two products were characterized by ^{1}H and ^{13}C NMR, 2D NMR and IR spectroscopy, and X-ray diffraction studies.

Scheme 2.5
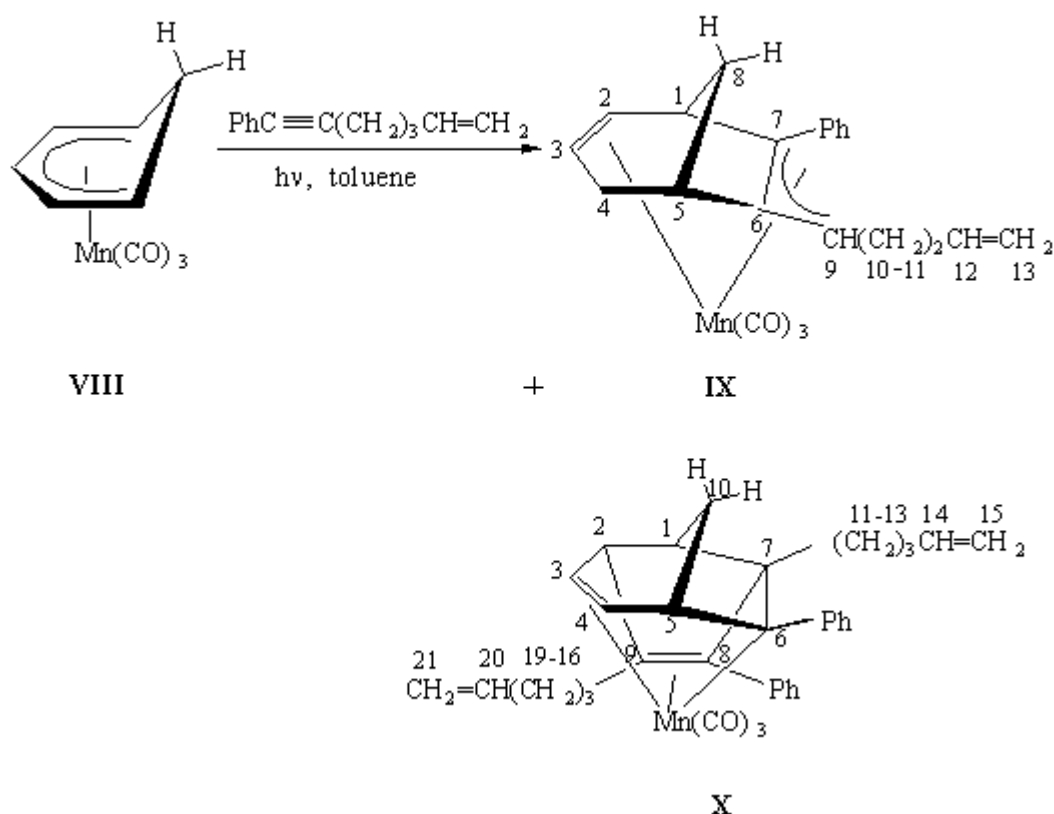
The reaction was monitored by IR spectroscopy, and as the peaks of the starting material disappeared, the gradual appearance of the product peaks was observed. The signals of the double cycloadduct were very similar to those of the single

cycloadduct. The presence of this product was not evident until it was isolated during column chromatography.

Interestingly, compound **IX** is different to previous manganese cyclohexadienylalkyne adducts in that the allyl fragment is exocyclic. This presumably arises via an H-transfer from an initial adduct **XI** as shown in scheme 2.6 below. There is precedent in metal-mediated-cycloaddition reactions for such a H-transfer.[6]
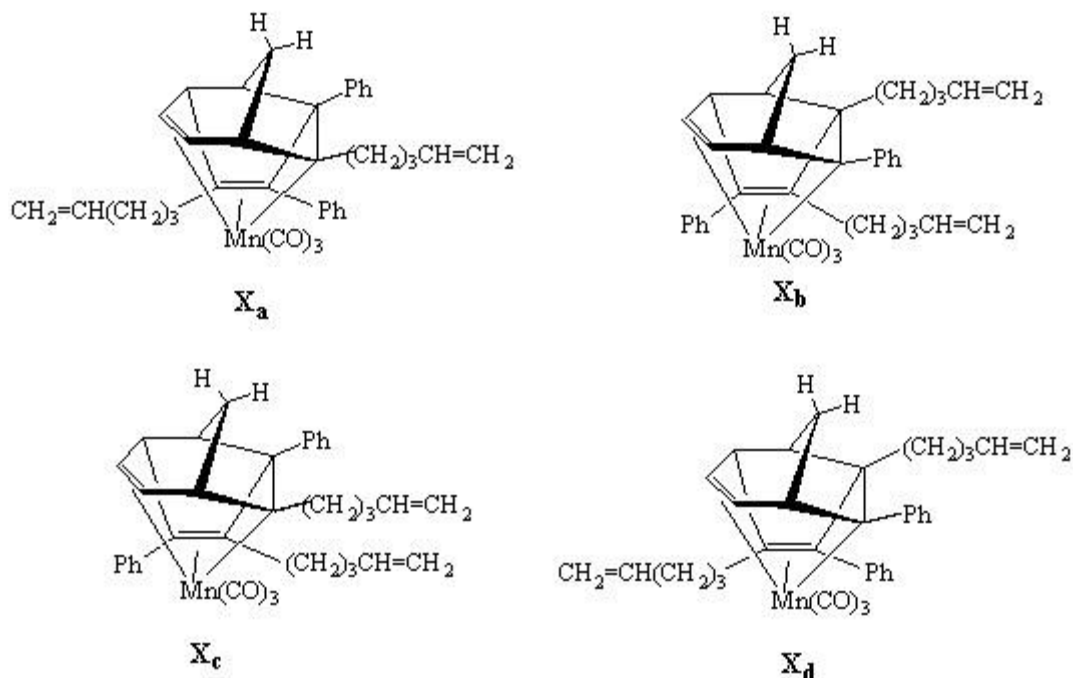
Scheme 2.6
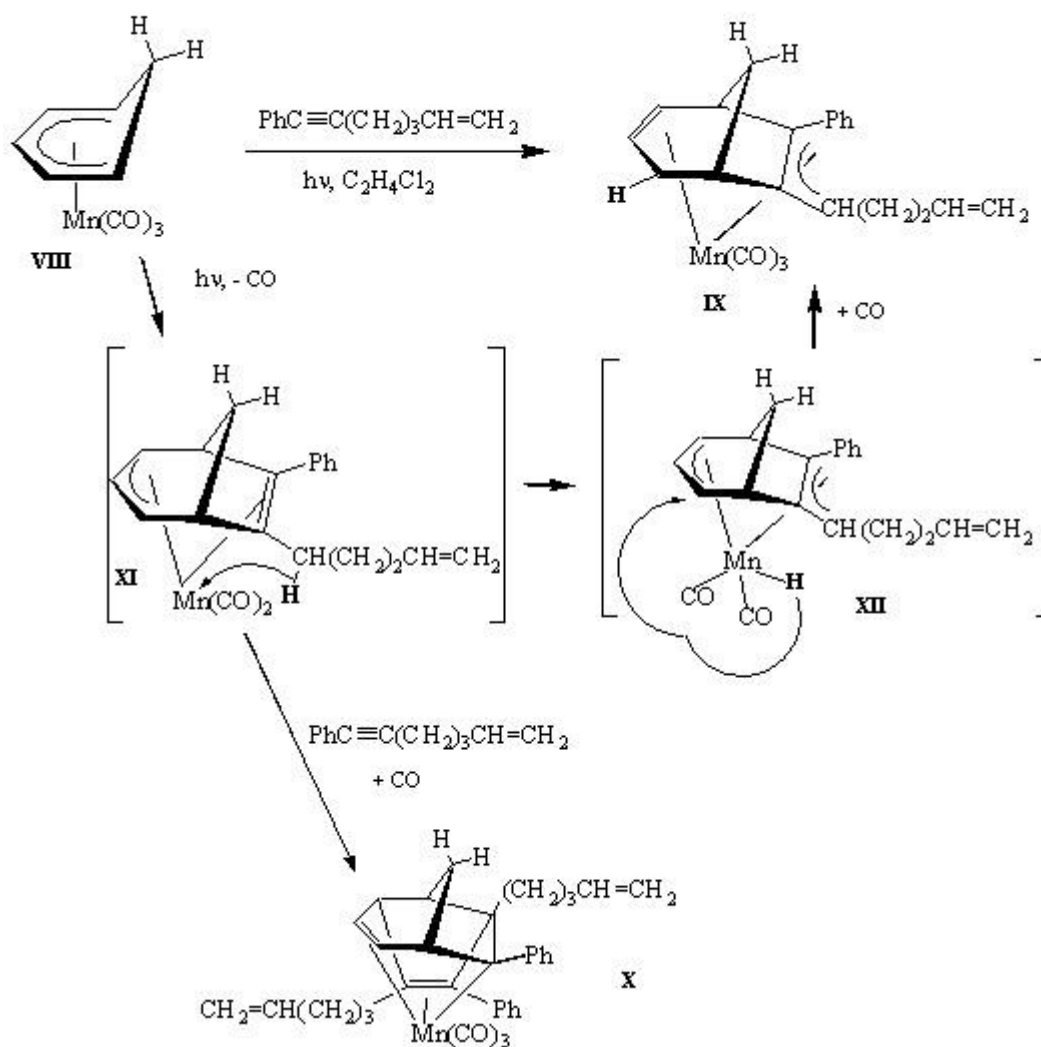
It is also interesting to note that the formation of the double cycloadduct is stereoselective. In fact, of the four possible double cycloadducts as shown below, only **X_d** was formed.

Once again, only the alkyne moiety of the enyne added to the ring systems, even in the double cycloadduct.

Scheme 2.7

From the reactions of enynes with **I** and **VIII**, we observed that <u>only</u> the alkyne moiety of the enyne reacts to give both single and double cycloaddition products. This demonstrates that the alkyne is a better trienophile than the alkene.

Experimental methods

General methods

All chemical procedures described in this report were carried out under an atmosphere of dry nitrogen using standard Schlenk techniques. Some manipulations of air-sensitive complexes were performed inside a Braun MB 150 inert-atmosphere glovebox. The solvents used were dried (over Na/benzophenone for toluene, benzene, THF, diethyl ether; over CaH_2 for n-hexane, CH_2Cl_2; or over K_2CO_3 for acetone), and freshly distilled prior to use. All reagents were purchased from Aldrich Chemical Co. (Milwaukee, WI) or Farchan Laboratory (Gainesville, FL).

IR, ^{1}H and ^{13}C NMR, and GCMS spectra were collected using the following instruments:

- IR: Nicolet 5ZDX FT instrument operated in the transmittance mode.

- ^{1}H and ^{13}C NMR: Varian Inova instrument operated at 500MHz (^{1}H NMR) and 125 MHz (^{13}C NMR).
- GCMS: Hewlett Packard 6890 Gas Chromatograph attached to a HP5973 Mass Selective Detector.

Chromatography was performed on alumina (150 mesh, standard grade, activated, neutral, purchased from Aldrich) or silica gel (230-425 mesh, purchased from Fisher Scientific).

The enyne, 1-phenyl-6-heptene-1-yne was prepared using the procedures described in the literature.[7]

Preparation of compound II

A solution of **I** (228 mg, 1.00 mmol) and 1-phenyl-6-heptene-1-yne (170 mg, 1.00 mmol) in dichloroethane (65 mL) was irradiated (quartz) with UV light for 7 hrs under an inert atmosphere (N_2). Evaporation of the solvent in vacuo and chromatography on a silica gel/n-hexane column (25 x 2 cm), loading with toluene (2 mL) and eluting with n-hexane (to remove unreacted **I**), followed by elution with CH_2Cl_2 gave complex **II** as a red powder following removal of the solvent (yield 188 mg, 47.2%).

Preparation of compound VII

A solution of **II** (122 mg, 0.306 mmol) in CH_2Cl_2 was stirred at room temperature with iodine for 20 min. A greenish precipitate was observed. The solvent was removed in vacuo and the residue chromatographed on silica. Elution with n-hexane gave **VII** as a clear colorless oil in quantitative yield (yield 109 mg).

Preparation of compounds IX and X

A solution of tricarbonyl($\square^6$-cyclohexadienyl)manganese (I) (complex **VIII**) (218 mg, 1.00 mmol) and 1-phenyl-6-heptene-1-yne (170 mg, 1.00 mmol) in dichloroethane (80 mL) was irradiated under UV light for 12 h. Evaporation of the solvent in vacuo and chromatography on alumina, loading with toluene (1 mL) and eluting with n-hexane, removed unreacted **VIII**. Elution with dichloromethane/nhexane (1:19) gave **IX** and **X** as yellow and orange crystals, respectively, after removal of the solvent (yield 193 mg, 49.5% of the single cycloadduct, and 254 mg, 44.6% of the double cycloadduct).

Future work

Migration of the Mn metal group in compound IX

When **IX** is refluxed in toluene, it is possible that there is an intramolecular migration of the $Mn(CO)_3$ to the phenyl group. When a toluene solution of **IX** was

refluxed for 10 hours, its color changed from yellow to reddish-orange. The IR peaks of the three carbonyl groups of **IX** ($\square_{max}$ (CO) (hex) 2007 (vs), 1940 (vs), 1923 (vs) cm^{-1}) gradually disappeared. New peaks were observed at $\square_{max}$ (CO) (hex) 2018 (vs), 2009 (vs), 1941 (vs), 1933 (vs) and 1924 cm^{-1}. These new peaks suggest at least two new compounds are formed. The formation of these new compounds may have resulted from a rearrangement(s) of **IX** involving successive H-shifts as shown in scheme 4.1 below.

Scheme 4.1
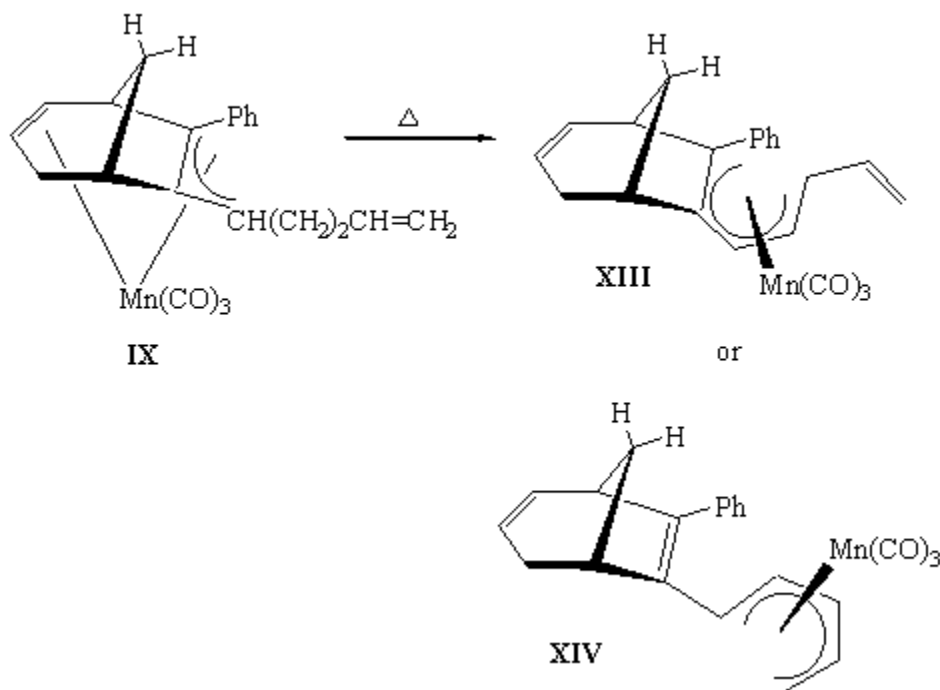
Thin layer chromatography (TLC) of the product mixture with several solvents failed to yield tractable products. Further methods need to be investigated to separate and fully characterize these compounds.

Thermally induced catalytic [6 + 2] cycloaddition of an enyne to cycloheptatriene

As a continuation of sec. 2.3, an experiment should be set up to verify if the phenyl group of the enyne interferes with the catalytic step of the thermally induced catalytic [6 + 2] cycloaddition. Two reactions be tested:

1. Reaction of an alkyne that has a coordinated phenyl group (a phenyl group that is bound to a metal group) with cycloheptatriene;
2. Reaction of an alkyne that has a free phenyl group (a phenyl group that is not bound to a metal group) with cycloheptatriene.

The yield of the former is expected to be higher. The alkynes to be used are tricarbonyl-(η^6-trimethylsilylphenylacetylene)molybdenum(0) and trimethylsilylphenylacetylene. The following scheme summarizes these new reactions.
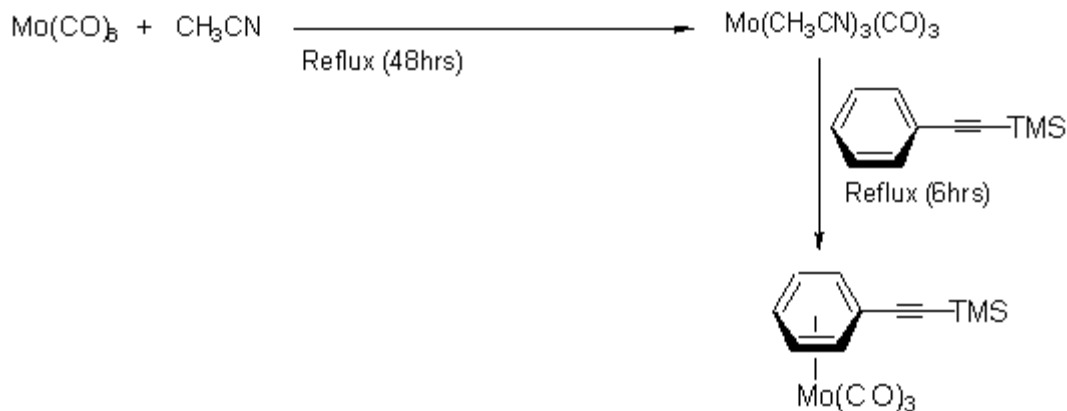
Scheme 4.2

coordinated phenyl group

"free" phenyl group
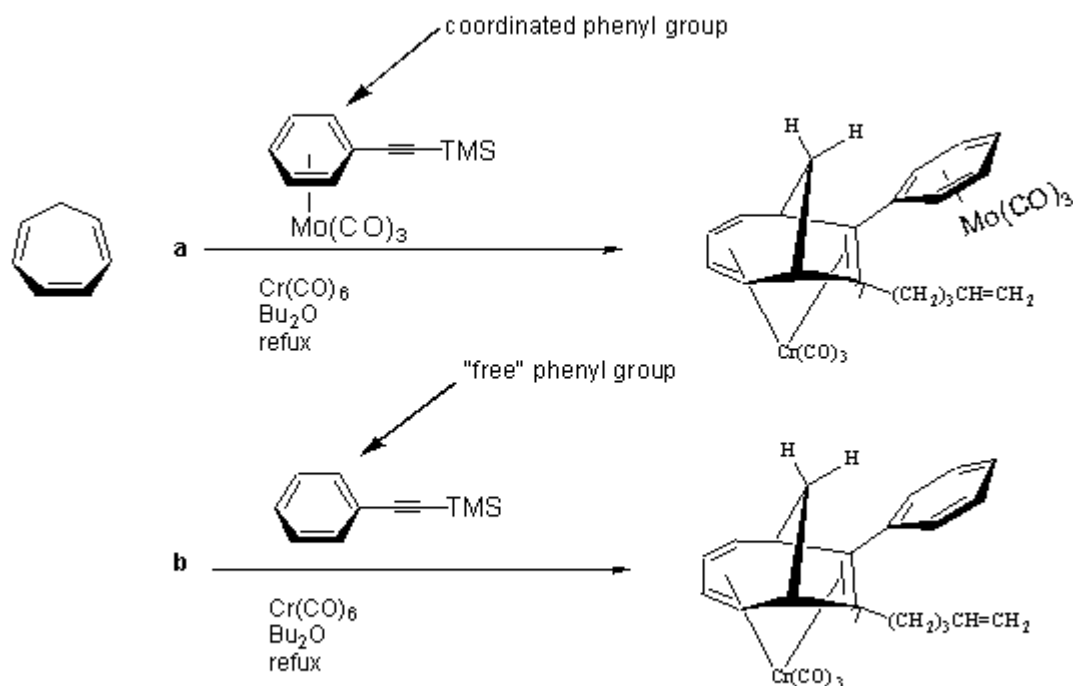
Reaction **a** is expected to have a better yield than **b**.

Tricarbonyl-(η^6-trimethylsilylphenylacetylene)molybdenum(0) can be prepared from $Mo(CO)_6$ as follows:

Scheme 4.3

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