Reactivity of Acyclic (Pentadienyl) iron (1+) Cations with Phosphorous-stabilized Carbon Nucleophiles and with Nitrogen Nucleophiles

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REACTIVITY OF ACYCLIC (PENTADIENYL) IRON (1+) CATIONS WITH PHOSPHOROUS-STABILIZED CARBON NUCLEOPHILES AND WITH NITROGEN NUCLEOPHILES

by

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ABSTRACT

REACTIVITY OF ACYCLIC (PENTADIENYL) IRON (1+) CATIONS WITH PHOSPHOROUS-STABILIZED CARBON NUCLEOPHILES AND WITH NITROGEN NUCLEOPHILES

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A lot of studies regard organoiron compounds have been made in recent years. Nucleophilic addition with soft nucleophiles such as malonate anions or phosphonate stabilized carbon nucleophiles, or harder nucleophiles such as organolithium or Grignard reagents to an acyclic (pentadienyl)iron cation results in the (pentenediyl)iron complexes. Reaction of (pentadienyl)iron complexes with paraformaldehyde via Horner-Emmons olefination will give enolate complex. Oxidation of the enolate leads to the formation of cyclopropane carboxylates. Further oxidation of divinylcyclopropane carboxylates can form cycloheptadiene.

The reacivity of acyclic (pentadienyl)iron cations with nitrogen nucleophiles such as potassium phthalimide were examined, which could be used as potential routes to synthesis natural product. “Click chemistry” was also introduced to see the reactivity of organoiron azide with terminal alkynes.

We have also proposed to synthesize a model of bicycle [4,1,0] heptanes via the ring closing metathesis of vinylcyclopropanes.

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INTRODUCTION

Preparation of (pentadienyl) iron cations

Acyclic (pentadienyl)iron(1+) cations (**1**) were first reported by Pettit and coworkers.[1] The $Fe(CO)_3$ moiety can serve to stabilize carbocation centers adjacent to the diene. Complexes of these types (**1** and **2**), as well as the corresponding cyclic counterpart (**3**) have found great utility in the synthesis of natural products (Figure 1).[2]

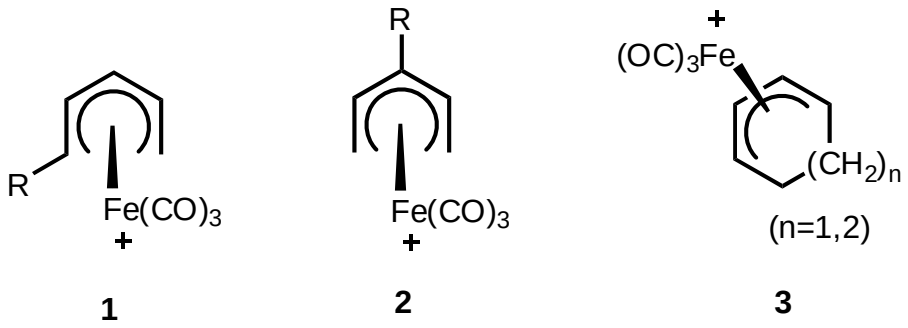
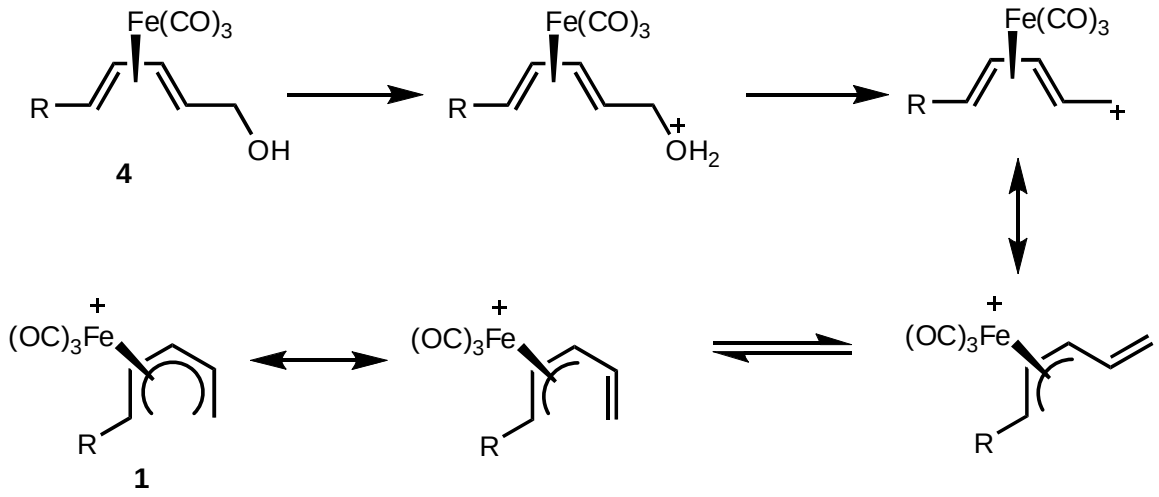


Figure 1: Structures of dienyl-iron complexes

The most convenient method for preparing the acyclic (pentadienyl) iron (1+) cations (**1**) is by acid treatment of a tricarbonyliron complexed pentadienol complex **4** (Scheme 1). Protonation of the alcohol moiety results in the loss of the elements of water, affording cation **1**.[1] Hexafluorophosphoric acid is often the acid of choice because it provides a large noncoordinating anion and affords a stable salt. The reaction can be easily performed on laboratory bench top and requires no purification other than precipitation from the reaction mixture and filtration.



Scheme 1: Mechanism of preparation of acyclic iron cation

Nucleophilic addition to (pentadienyl) iron cations

As indicated in **Figure 2**, five potential acyclic complexes could be generated by nucleophilic addition to an acyclic (pentadienyl) iron cation **1** or **5** on the dienyl ligand.[3] Nucleophilic attack at C-1, C-3, or C-5 can result in diene complexes **6**, **7** and **8** respectively. Correspondingly, nucleophilic addition at C-2 or C-4 can generate (pentenediyl)iron complexes **9** and **10.** The position of the attack is controlled by several factors, including the steric bulk and electronic nature of group R,[4] the "spectator" ligands (L = CO or PPh_3) attached to the iron[4a, 5] and sometimes the solvents used in the reaction,[5b, 6] as well as the nucleophile counter-ion.[5c, 7] Nucleophilic addition generally occurs on the face opposite of the metal group.

More specifically, nucleophilic addition to the 1-methoxycarbonyl cation **11** with soft nucleophiles such as malonate anions often results in (pentenediyl)iron complexes

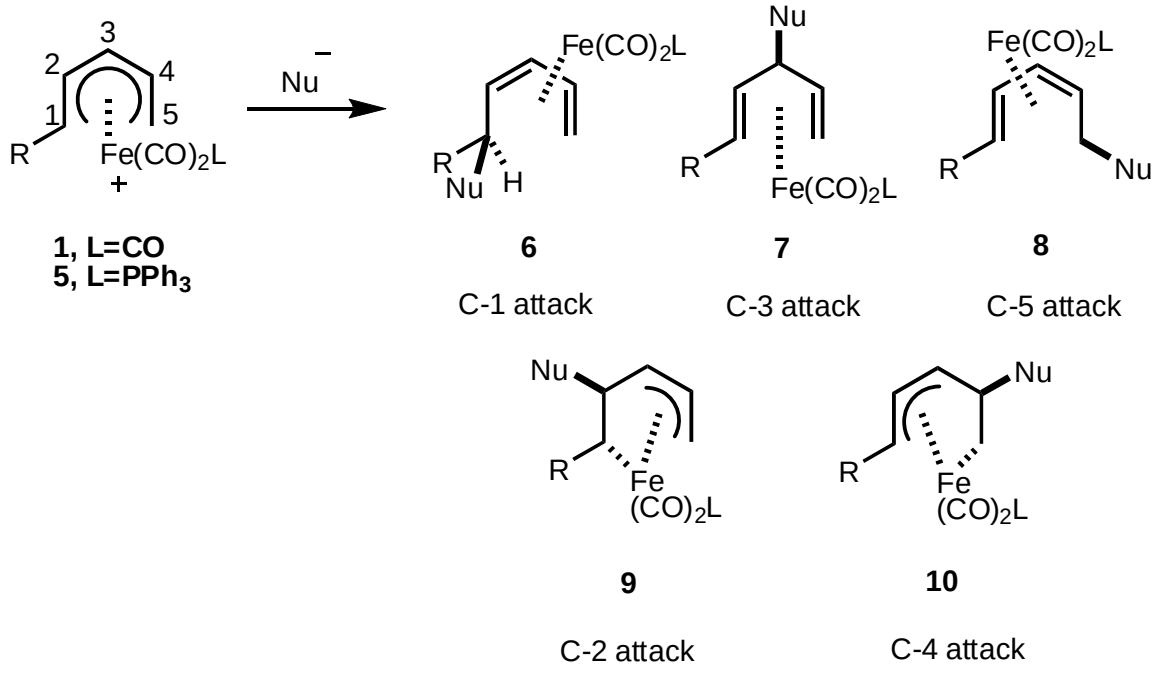
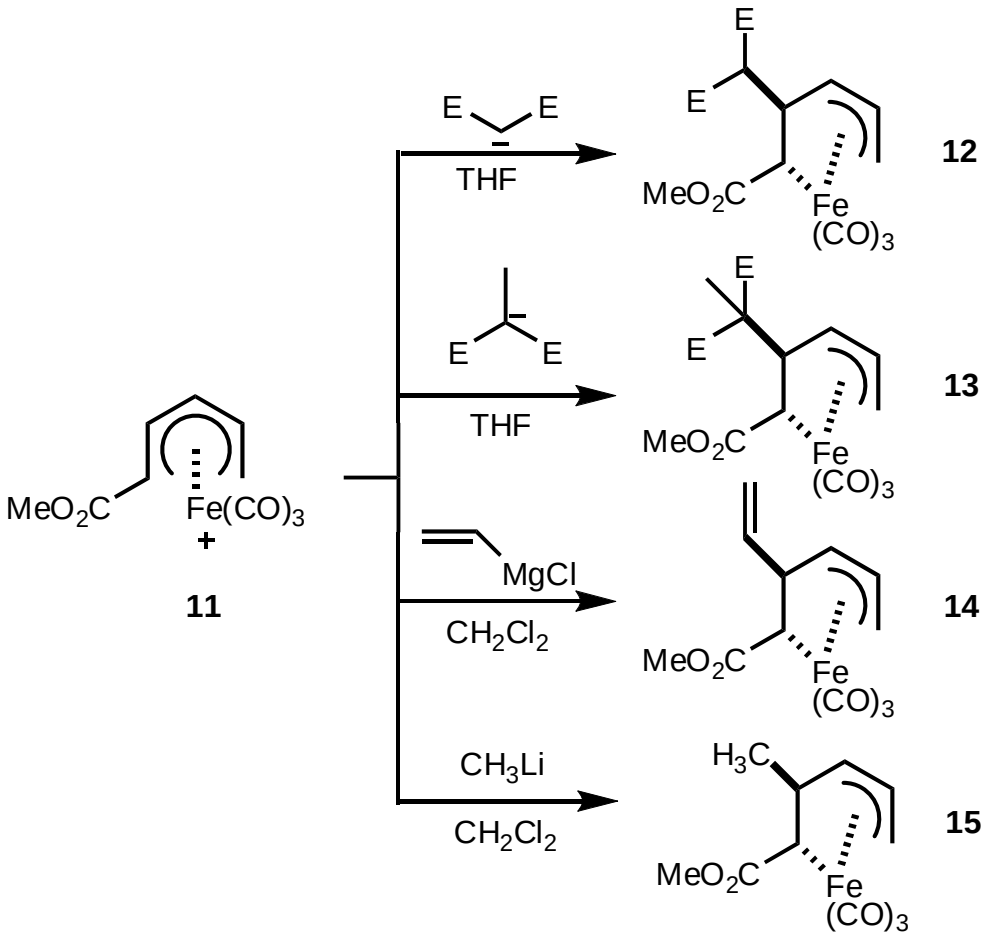


Figure 2

via attack at C-2 (e.g. **12**, **13**, **Scheme 2**).[8] 2-Methyl and 2-vinyl substituted (pentenediyl) iron complexes **15** and **14** were prepared by reaction with organolithium[6] or Grignard reagents[9]. The regioselectivity may be due to initial single electron transfer to cation **11**, followed by collapse of the radical cage.

Nucleophilic addition at the internal carbon (e.g. C-2 of C-4) is inconsistent with frontier orbital theory. By frontier orbital theory, soft nucleophiles will react with cation **11** to give diene complexes via attack at the terminal carbon. The theory of "charge control" is introduced to explain the regioselectivity. Since the methoxycarbonyl group is an electron withdrawing substituent, there is a greater electron donation from metal to the ligand at C-1, C-3 and C-5 which reduces the charge on these carbons. The values of the



Scheme 2

^{13}C NMR data for **11** indicate that C-2 and C-4 appear at the lowest chemical shift (**Figure 3a**).[10a] While the ^{13}C NMR chemical shift of a particular carbon depends on several factors, downfield chemical shifts generally correspond to less electron density at the atom in consideration. Similarly, calculation of the charge distribution over the pentadienyl ligand by density functional theory (B3LYP method, **Figure 3b**) are in concert with the ^{13}C NMR data.[10b] Hence, the soft nucleophiles would attack the most electron deficient carbon-2.

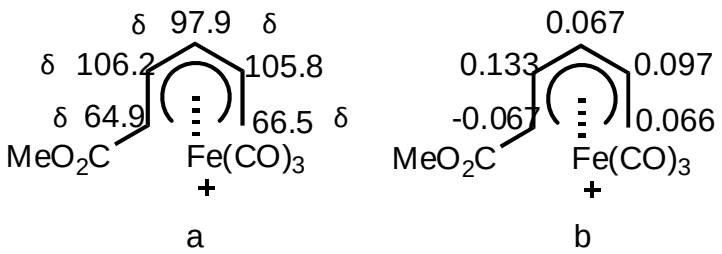
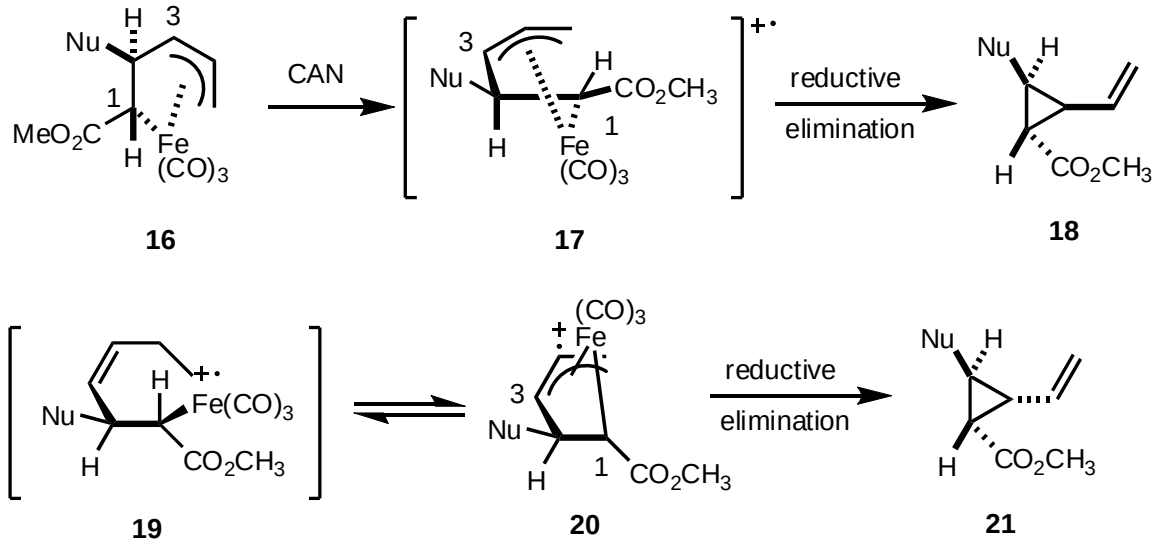


Figure 3 (a) Spectral data of ^{13}C and (b) calculated partial charges

Oxidative decomplexation of (pentenediyl) iron complexes

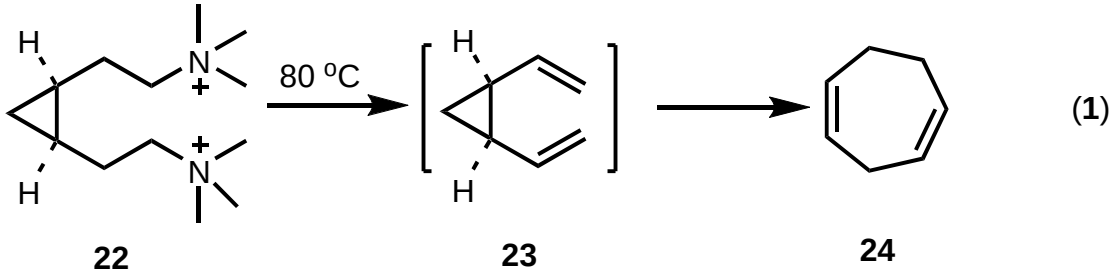
Treatment of (diene) iron complexes with oxidizing agents (e.g. H_2O_2/OH^-) releases the $Fe(CO)_3$ from the iron complex diene.[11] However, oxidation of (pentenediyl) iron complexes **16** leads to the formation of the cyclopropane carboxylate **18** (**Scheme 3**).[8] The oxidation of complex **16** with Ce^{4+} results in reactive intermediate **17** which can undergo reductive elimination to give the cyclopropane. The reductive elimination process to form the cyclopropane is anticipated to proceed with retention of configuration at C1 and C3 such that the nucleophile group is *trans* to the ester group and *cis* to the vinyl group. The present of an electron withdrawing group (e.g. methoxycarbonyl group) at C-1 of **17** retards the rate of CO insertion compared to the rate of reductive elimination. A diastereomeric mixture of cyclopropane is generated from the demetallation of the iron complexes in certain cases. A mechanism involving π-σ-π rearrangement of the oxidized pentenediyl complex, and thus inversion at C3, was proposed to account for the different results.[8b, 9b]



Scheme 3

Cope rearrangement of divinylcyclopropane

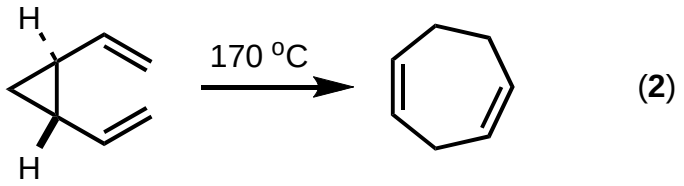
One of the earliest known sigmatropic rearrangements is the Cope rearrangement reported for the conversion of *cis*-divinylcyclopropanes to cyclohepta-1,4-dienes. However mechanistic studies of this divinylcyclopropane isomerization were only begun by the 1960s by Vogel and von Doering.[12]



(**1**)

In 1960, it was reported that treatment of the bis(tetraalkyl)ammonium salt **22** with base gave cyclohepta-1,4-diene **24** via a Hoffman elimination/Cope rearrangement

(**Eq.(1)**). Presumably the divinylcyclopropane intermediate **23** could not be isolated, as it rapidly isomerized under the reaction conditions (80 ℃). The unstable intermediate **23** was isolated and characterized at low temperature in 1973 and the rearrangement was found to be complete below 35 ℃. In contrast to *cis*-divinylcyclopropane **23**, *trans*-divinylcyclopropane **25** is stable and isolable. However, transformation of *trans*-**25** to cyclohepta-1,4-diene **24** can be accomplished at 170 ℃ in 100% yield.[13](**Eq. (2)**).

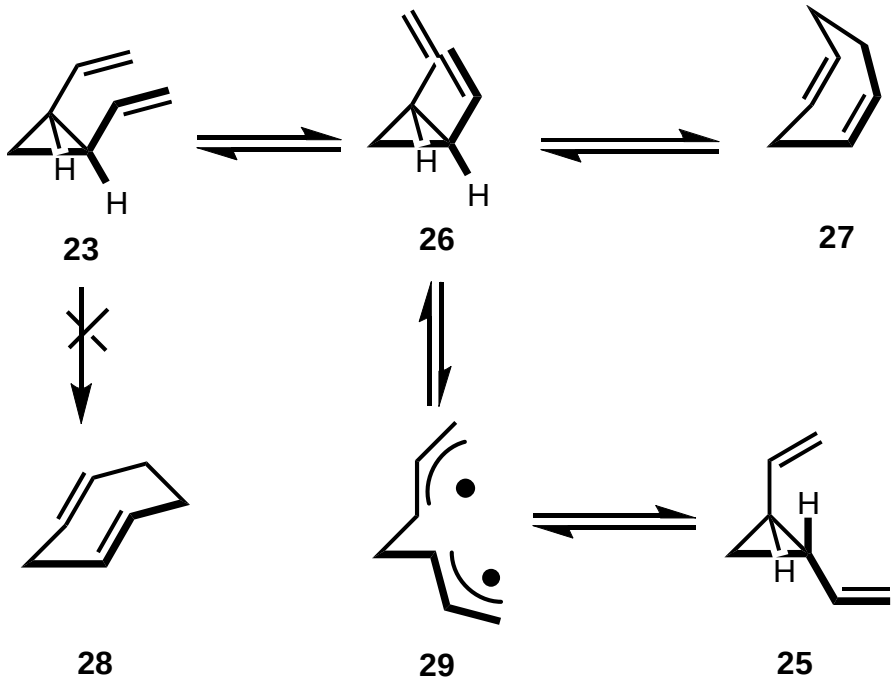


(**2**)

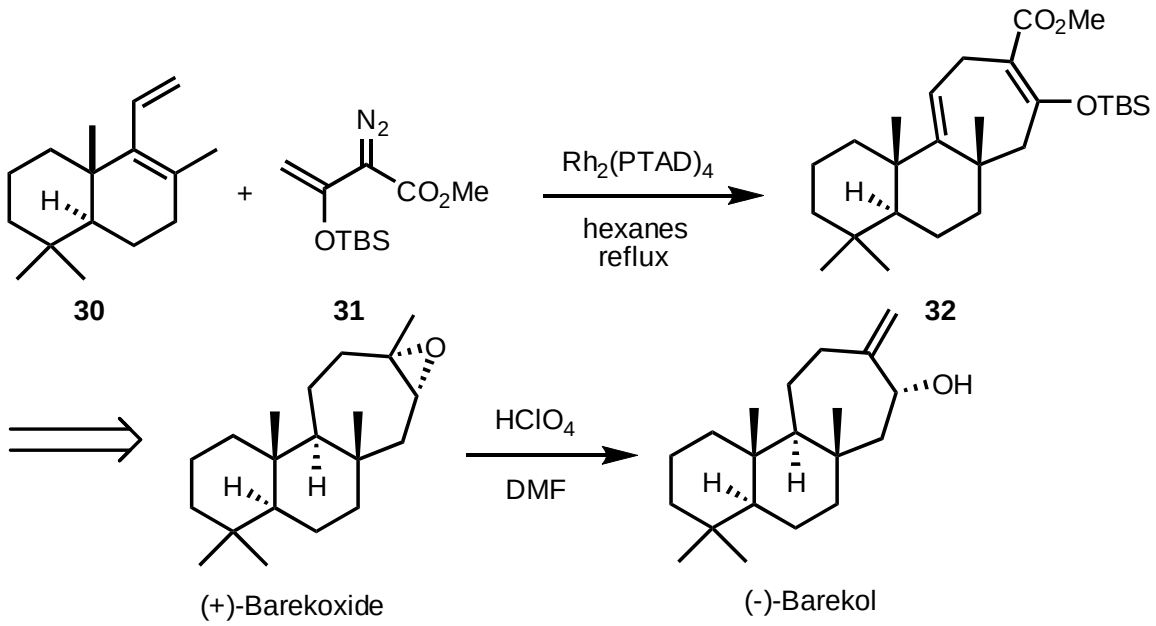
25 **24**

Generally it has been accepted that the Cope rearrangement for *cis*-divinylcyclopropanes is a concerted process that happens through a boat-like transition state (**Scheme 4**), where the double bonds lie over the plane of the cyclopropane ring (**26**). The process through a chair transition state is excluded, as that pathway would generate a highly unstable E, E-cyclohepta-1,4-diene (**28**). In the case of *trans*-cyclopropane (**25**), the conversion from **25** to **27** can be achieved by three steps: (1) formation of a stabilized diradical (**29**), (2) isomerization to *cis*-**26** and (3) Cope rearrangement.

The Cope rearrangement of divinylcyclopropanes is useful for the synthesis of natural products containing seven-membered rings (**Scheme 5**). Recently, (+)-barekoxide and (-)-barekol were synthesized by cyclopropanation followed by Cope rearrangement based on catalyst-controlled formal [4 + 3] cycloaddition.[14]

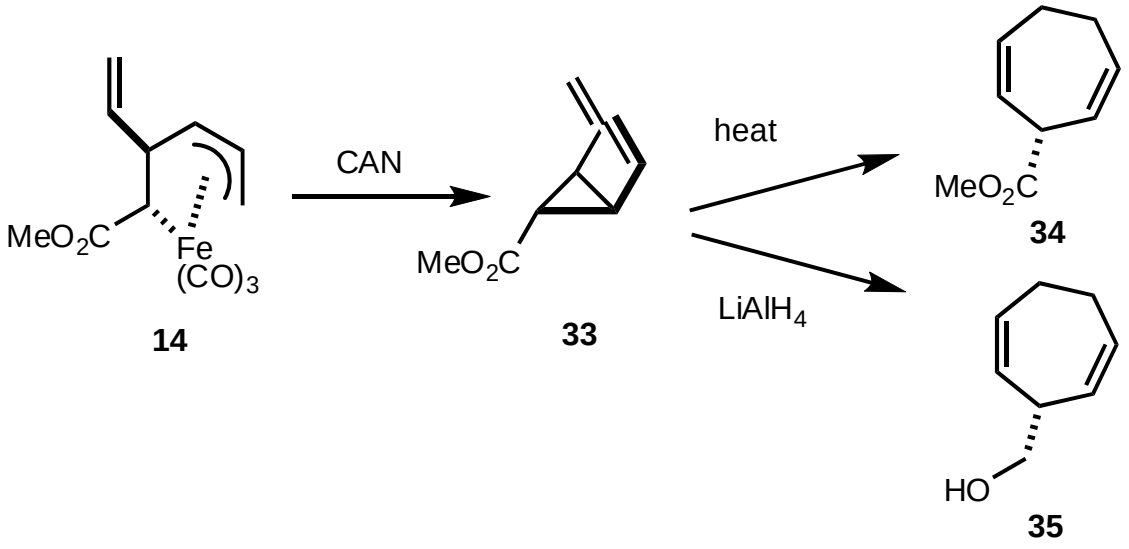


Scheme 4



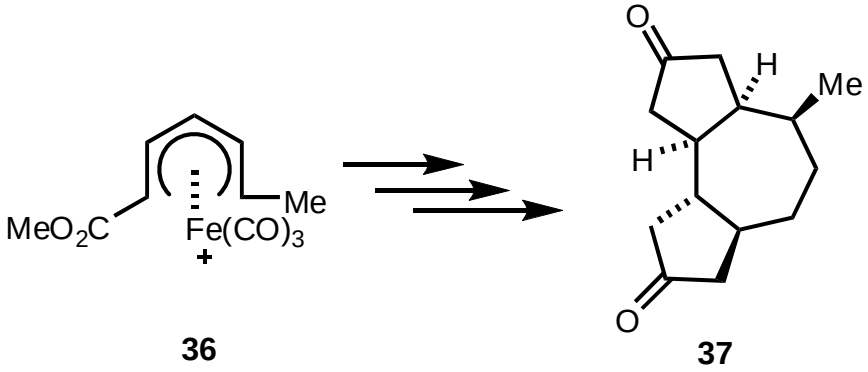
Scheme 5

Oxidatively induced-reductive elimination of (2-alkenyl-3-pentene-1,5-diyl)iron complexes (e.g. **14**) generate the corresponding cis-divinylcyclopropanes (**33**, Scheme **6**).[9] Warming the divinylcyclopropanes carboxylate **33,** or reduction of the ester, followed by Cope rearrangement below room temperature gave the cycloheptadienes **34** or **35** respectively. This methodology has been utilized in a synthesis of the 5-7-5



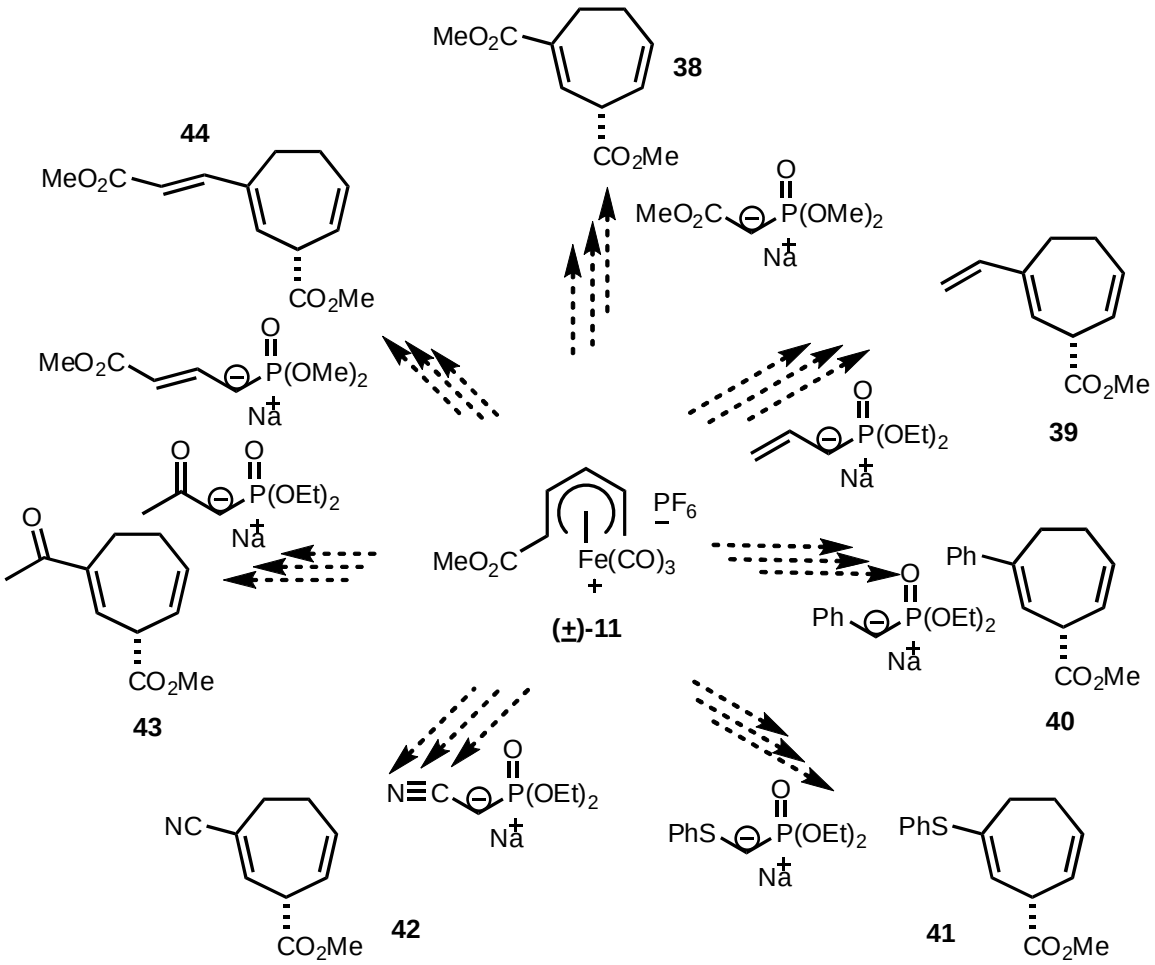
Scheme 6

tricylclic skeleton of cladantholide (**Scheme 7**).[22]



Scheme 7

One short coming of this approach to cycloheptanes is that the addition of alkenyl/cycloalkenyl Grignard reagents to (1-methoxycarbonylpentadienyl)iron(1+) cations proceeds in modest to good yields (39-73%).[9] Additionally the use of Grignard reagents as nucleophiles places inherent limitations on the types of function groups within these nucleophiles. For this reason, one of the aims of this thesis is to develop new methodology for the preparation of (2-alkenyl-3-pentene-1,5-diyl)iron complexes.

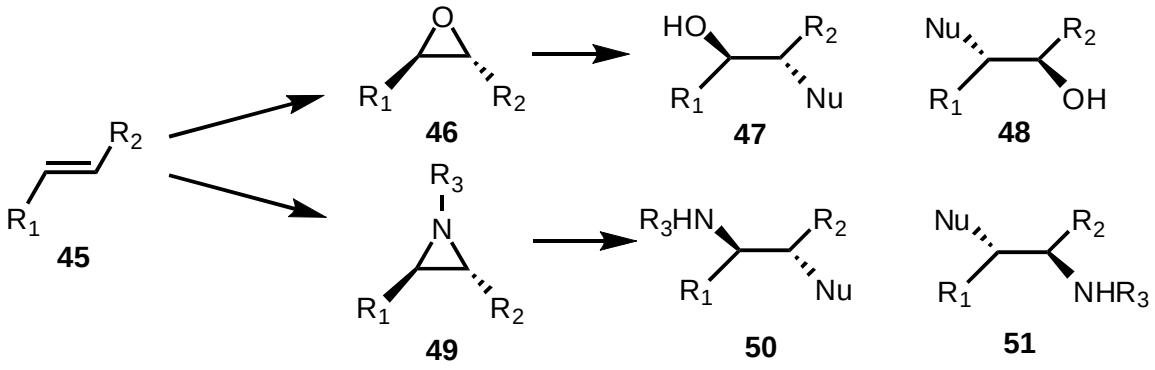


Scheme 8

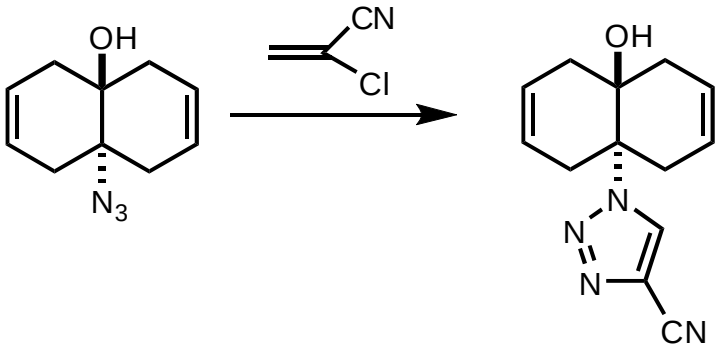
Click chemistry

Click chemistry is a chemical philosophy introduced by K. Barry Sharpless of The Scripps Research Institute in 2001.[15] They describe it as generating substances by joining small units together with heteroatom links (C-X-C). The goal is to develop an expanding set of powerful, selective, and modular "blocks" that work reliably in both small- and large-scale applications. This approach was termed as "click chemistry". This is inspired by the fact that nature also generates substances by joining small modular units.

Generally there are three click chemistry reaction types: (1) nucleophilic opening of spring-loaded rings (**Scheme 9**), (2) cycloaddition reactions (**Eq.(3)**) and (3) "protecting group" reactions.



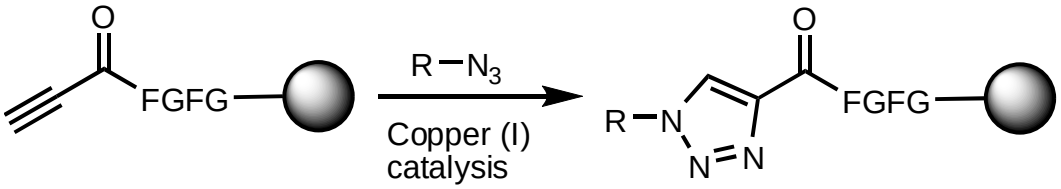
Scheme 9



52 **53** **(3)**

One of the most popular reactions within the click chemistry concept is the azide-alkyne Huisgen cycloaddition using a Cu catalyst at room temperature. The Cu(I)-catalyzed variant[16] was first reported by Morten Meldal and co-workers from Carlsberg Laboratory, Denmark for the synthesis of peptidotriazoles on solid support (**Eq.(4)**).

This is a novel regiospecific copper(I)-catalyzed 1,3-dipolar cycloaddition of terminal alkynes to azides on solid-phase. Primary, secondary, and tertiary alkyl azides, aryl azides, and an azido sugar were used successfully in the copper(I)-catalyzed cycloaddition producing diverse 1,4-disubstituted[1,2,3]-triazoles in peptide backbones or side chains.

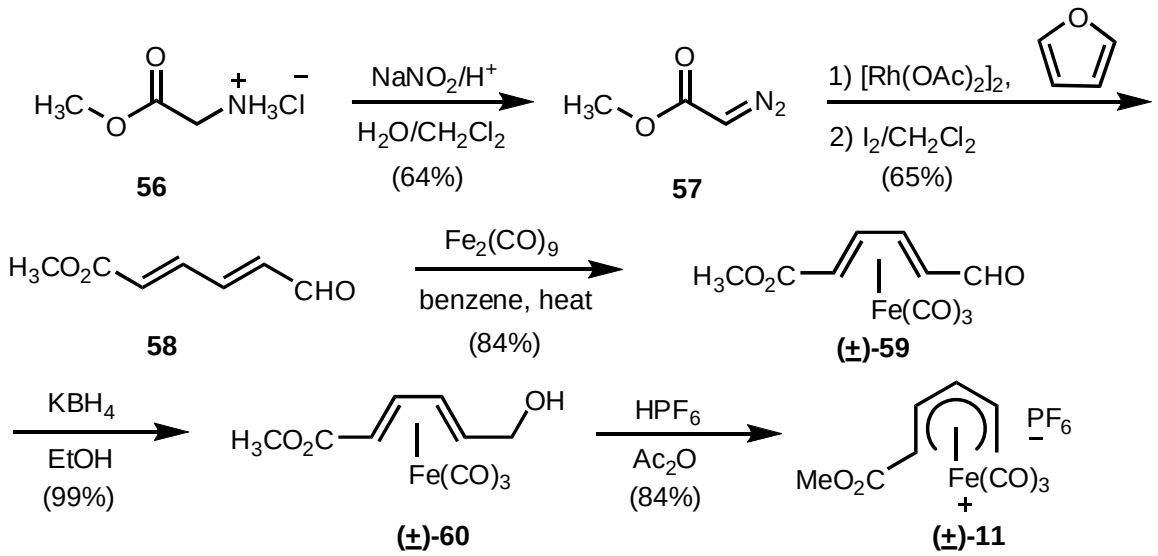


54 **55** **(4)**

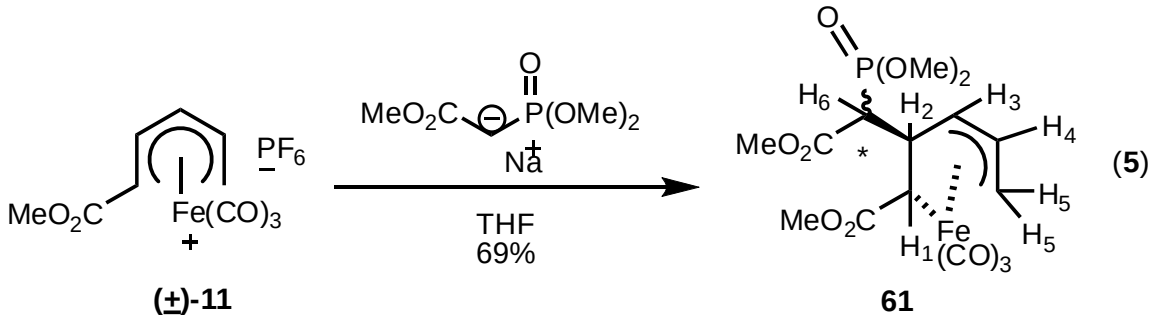
RESULTS and DISCUSSION

Exploration and discovery of new methods for the synthesis of Cycloheptadienes and Cyclohexenones via (Pentadienyl)iron(1+) Cations with Phosphonate Stabilized Carbon Nucleophiles

The racemic-cation **(±)-11** was prepared according to (**Scheme 10**) in a total of 5 steps from commercially available methyl glycinate hydrochloride in good yield. Methyl glycinate hydrochloride reacted with sodium nitrite and H_2SO_4 according to the literature procedure[17] to give methyl diazoacetate. The reaction of diazo compound **57** with furan, catalyzed by rhodium(II)acetate dimer, followed by treatment with a catalytic amount of I_2 gave methyl 6-oxo-2,4-hexadienoate. The diene **58** reacted with $Fe_2(CO)_9$ to give the iron complex **(±)-59**. Reduction of this aldehyde complex by KBH_4 in absolute ethanol gives the dienol complex **(±)-60**. The racemic cation was obtained by protonation/dehydration with HPF_6 in acetic anhydride. Two things should be noticed of these reactions. First, in order to get rid of the acid, the diazo compound should be washed with sufficient saturated aqueous sodium bicarbonate to make sure the Rh-catalyzed diazo cyclopropanation of furan will be successful. Second, the dehydration of alcohol complex **(±)-60** with HPF_6 in acetic anhydride, provides the best yields when performed on small scale.

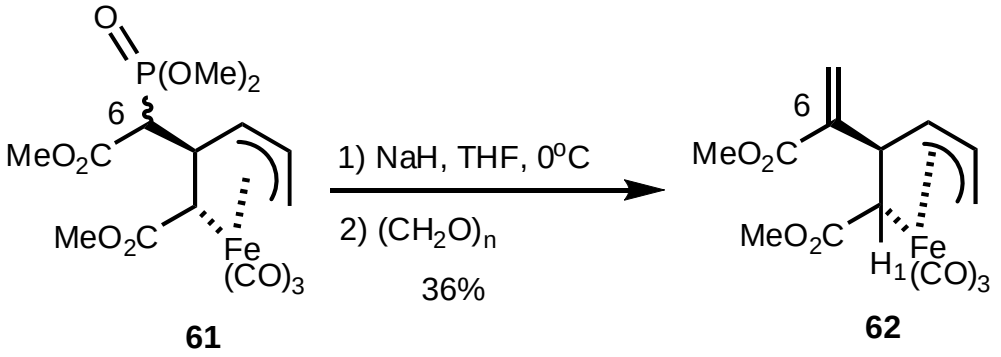


Scheme 10. Preparation of racemic cation



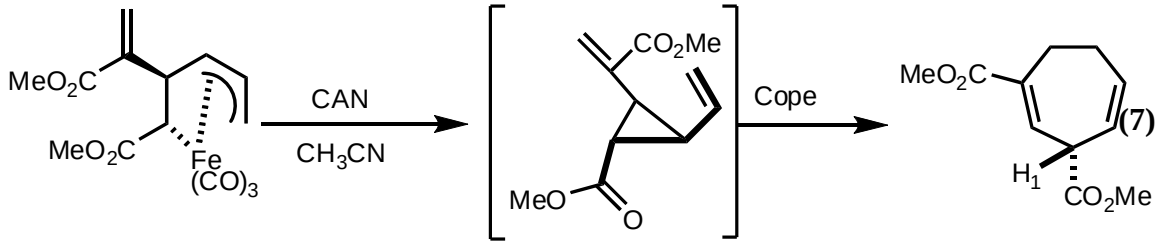
Treatment of (pentadienyl)iron cation**(±)-11** with sodium trimethyl phosphonoacetate, freshly prepared from sodium hydride and trimethyl phosphonoacetate, in anhydrous THF gave the complex **61** in moderate to good yield via nucleophilic attack at C-2. (**Eq.(5)**) Complex **61** was isolated as a mixture of two compound which were diastereomeric at the indicated (*) carbon. The structures of complex **61** were assigned based on their NMR spectral data. The ^{1}H NMR spectrum of the diastereomeric mixture **61** had two high field doublets at δ 0.33 and 0.01 ppm (2xd, J = 8.7 Hz, 1 H total, H-1) which correspond to the hydrogen on the carbon sigma-bound to iron (H_1) of each.[9b]

Additionally, signals at δ 2.67-2.39 ppm (m, 2 H, H-5 exo and H-5 endo) were assigned to the H_5 protons. The newly formed C-C bond was presumed to be *trans* to the iron center by analogy to the nucleophilic addition of other stabilized carbon nucleophiles to **(±)-11**.[4a] The mixture of diastereomeric complexes **61** were not very stable at room temperature and became dark upon standing; it can be kept at -20 ℃ for a long time.



61 **62** (**6**)

Enoate complex **62** was prepared by Horner-Emmons olefination of complex **61** with paraformaldehyde in anhydrous THF (**Eq.(6)**). Since carbon 6 is not a chiral center, complex **62** was afforded as a single pure compound instead of a mixture of diastereomers. The structure of complex **62** was assigned based on its NMR spectral data. The ^{1}H NMR spectrum of **62** contained a high field doublet at δ 0.33 ppm (d, J = 8.8 Hz, 1H) which corresponds to the hydrogen on the carbon sigma-bound to iron (H_1). The signals at δ 6.07 (d, J = 1.8 Hz, 1H) and 5.35 (d, J = 1.8 Hz, 1 H) ppm were assigned to the sp^2 enoate hydrogens.

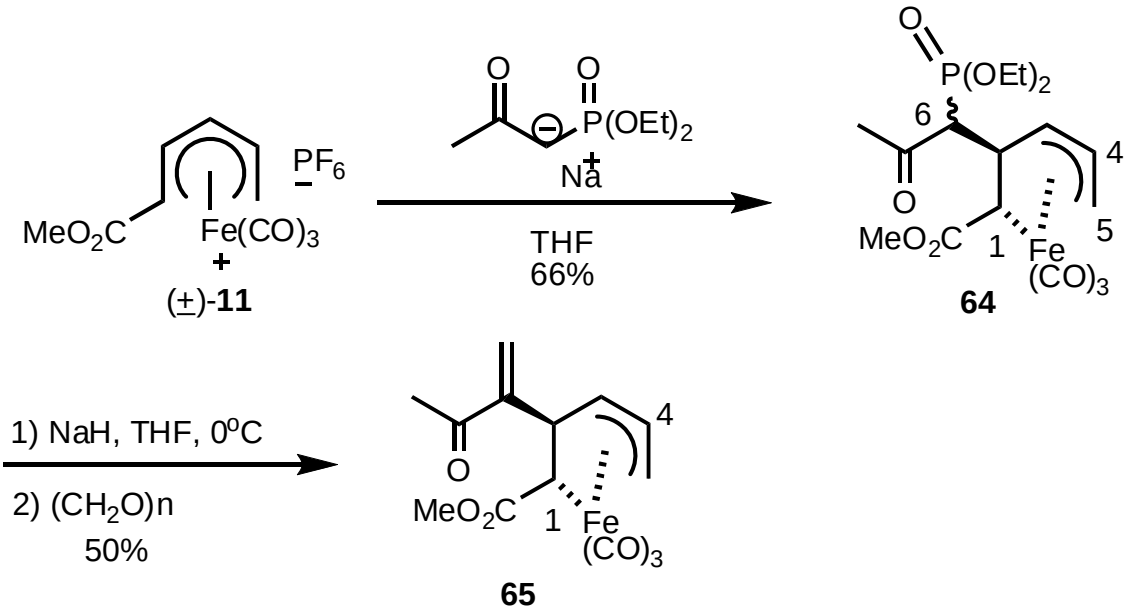


62 **63** **38**

not observed 30%

Cycloheptadienylester **38** was prepared by the oxidation of **62** with cerium ammonium nitrate (CAN) in acetonitrile (**Eq.(7)**). The presumed intermediate divinyl cyclopropane **63** was not observed during the oxidation, and thus it was assumed that it rapidly converted to cycloheptadienyl ester **38** via Cope rearrangement at room temperature. The cycloheptadienyl ester **38** was semi-stable at room temperature and can be kept in the refrigerator for a long time.

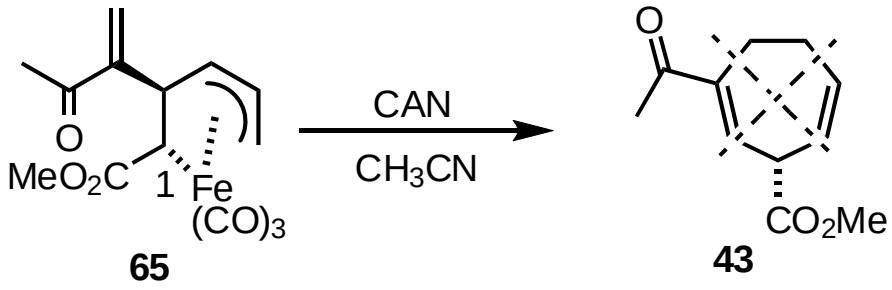
The structure of **38** was assigned based upon its spectral data. The ^{1}H NMR spectrum contained peaks at δ 3.39-3.35 ppm (m, 1 H) which is characteristic of the doubly allylic methane proton H_{1}.[9] The signals at δ 7.31 (d, J = 5.2 Hz, 1 H), 6.41-6.37 (m, 1 H), 6.12-6.06 (m, 1 H) ppm were assigned to the sp^2 olefinic hydrogens.



Scheme 11

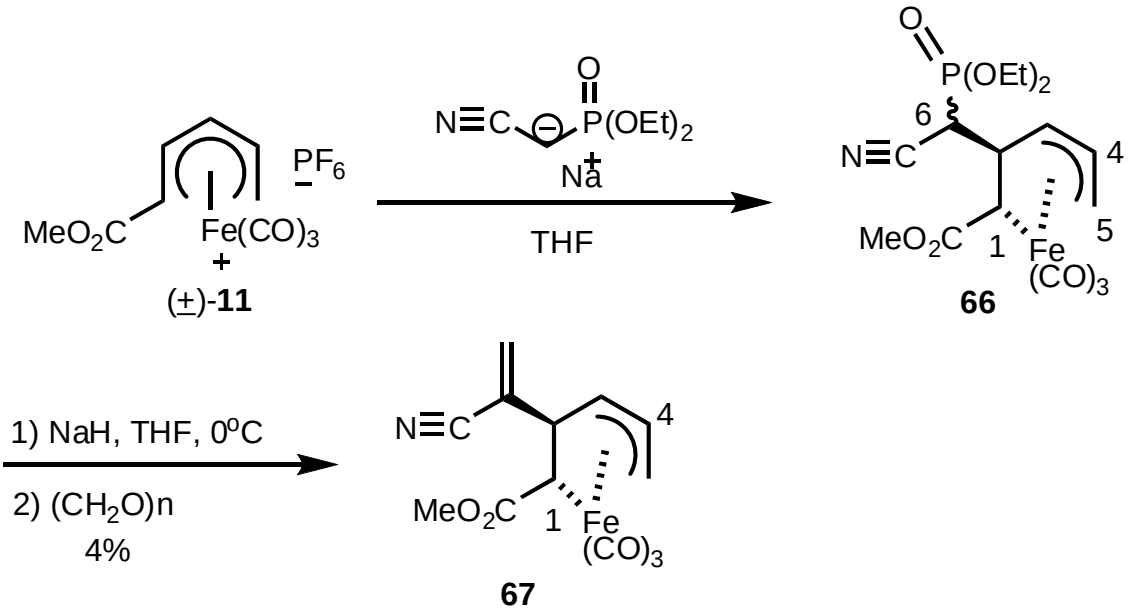
Complex **65** was prepared by a two step sequence from (±)-**11** in moderate to good overall yield. This required nucleophilic addition of sodium diethyl (2-oxopropyl) phosphonate to **(±)-11** in anhydrous THF, followed by Horner-Emmons olefination of the resultant complex with paraformaldehyde (**Scheme 11**). The yield of **64** and **65** were almost the same as compound **61** and **62**. Complex **64** was also obtained as a mixture of diastereomers. The structures of complex **64** were assigned based on their NMR spectral data. The ^{1}H NMR spectrum of **64** contained two high field doublets at δ 0.44 and 0.01 ppm (2xd, J = 8.4 Hz, 1 H total, H-1) which correspond to the hydrogen on the carbon sigma-bound to iron (H_1) and signals at δ 2.98-2.51 (m, 2 H, H-5 exo and H-5 endo) ppm which were assigned to the H_5 protons. It was difficult to assign the signals in the ^{13}C NMR spectrum of **64** to each of the carbon atoms due to the presence of two sets of signals and further complicated by coupling with the phosphorus atom in complex **64**.

Partial ^{13}C NMR data was obtained from the spectrum, signals at δ 210.0 [209.7] ppm were consistent with the ketone carbon and low field signals at δ 203.3 [203.2], 201.9 [201.8], 201.21 [201.20] ppm were assigned to the three CO ligands, signals at 97.0 [96.8] were indication of C-4. The structure of complex **65** was characterized by the ^{1}H NMR signals at δ 0.35 ppm (d, *J* = 8.7 Hz, 1 H) which corresponds to H-1 and δ 5.91 ppm (d, *J* = 1.8 Hz, 1 H), 5.51 (d, *J* = 1.8 Hz, 1H) which correspond to the olefinic hydrogens.



65 **43** **(8)**

Attempted oxidative decomplexation of **60** with cerium ammonium nitrate (CAN) in acetonitrile was fruitless. (**Eq.(8)**) While the starting material decomposed during the reaction, only a complex mixture of unidentified products was obtained.



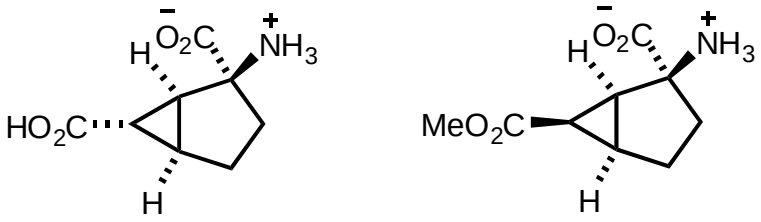
Scheme 12

Complex **67** was prepared by a two step sequence from (±)-**11** in poor yield. This required nucleophilic addition of sodium diethyl (cyanomethyl)phosphonate to **(±)-11** in anhydrous THF, followed by olefination with paraformaldehyde (**Scheme 12**). Products **66** were obtained as a mixture of diastereomers and other byproducts; separation of this mixture was not possible. Further olefination of the unpurified mixture gave a low yield (4%) of compound **67**. The structure of complex **67** was assigned based on its NMR spectral data. The ^{1}H NMR spectrum of **67** had a high field doublet at δ 0.38 (d, J = 8.8 Hz, 1 H) ppm which corresponds to the hydrogen on the carbon sigma-bound to iron (H_1), and the signals at δ 5.71 (d, J = 2.1 Hz, 1 H), 5.54 (d, J = 2.1 Hz, 1 H) ppm correspond to the olefinic hydrogens. Since the overall yield of compound **67** was pretty low, no further oxidation using ammonium nitrate (CAN) was carried out to get the corresponding cycloheptadiene.

The rest of the proposed routes of synthesizing cycloheptadienes were not successful. The major products from the first step nucleophilic attack reaction were diene iron complexes via attack at C-5 instead of sigma-pi iron complexes which result from nucleophilic attack at and C-2. Due to the lack of desired reactivity and poor yields (in certain cases), further work on this project was abandoned for this thesis.

Development of a useful synthetic pathway to bicyclo[4,1,0]heptenes via the ring closing metathesis of vinylcyclopropanes

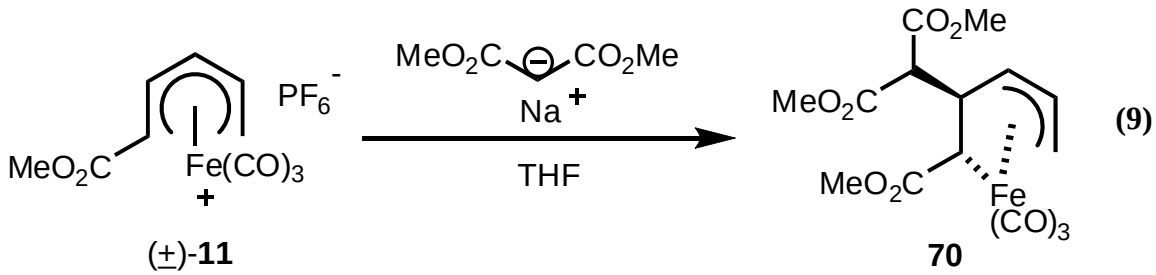
L-Glutamic acid is a ubiquitous neurotransmitter. Several conformationally restricted analogs have been prepared which act as ligands for specific glutamate receptors.[23] For example, LY354740 (**68**) was formed to be a potent and selective



68 **69**

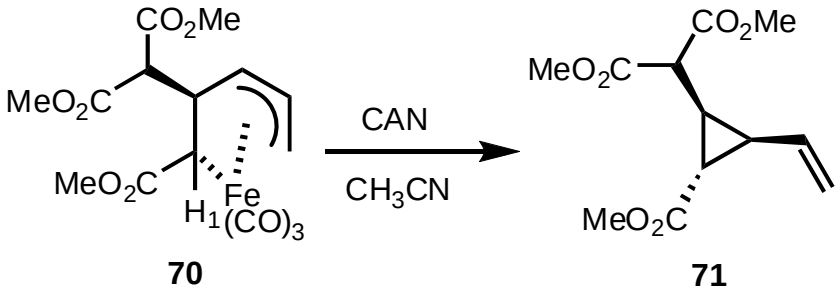
Figure 4

group 2 metabotropic glutamate receptor agonist. [24] The bicyclo[4.1.0]heptanes analog **69** has likewise been prepared, however its biological activity has not been reported. [25] The next section describes model studies toward the preparation of bicyclo[4.1.0]heptanes as the skeleton for **69**.



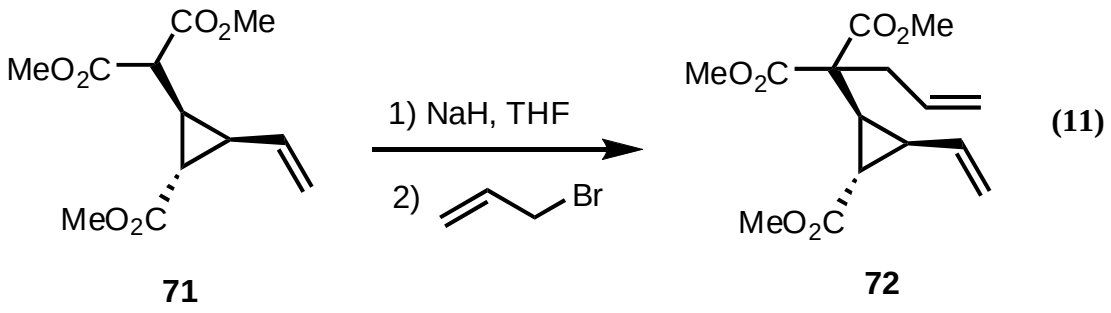
(9)

In a similar fashion, treatment of (pentadienyl) iron (±)-**11** with sodium dimethyl malonate, freshly prepared by sodium hydride and dimethyl malonate, in anhydrous THF gave the complex **70** in good yield (76%) (**Eq.(9)**). The structure of complex **70** was assigned by comparison to the literature spectral data.[4a]



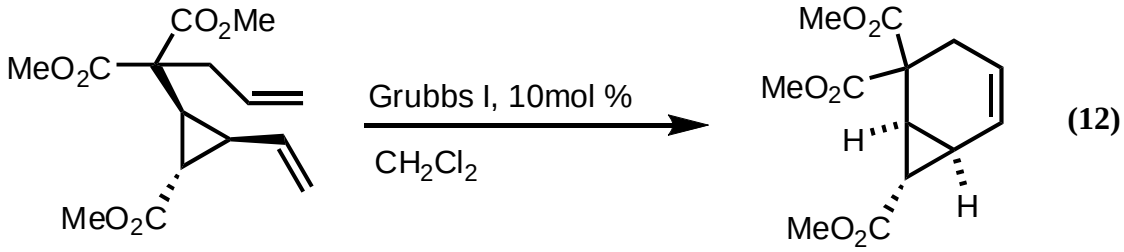
(10)

Oxidative decomplexation of **70** with cerium ammonium nitrate (CAN) in acetonitrile gave cyclopropane **71** in good yield (69%) (**Eq.(10)**). The structure of complex **71** was assigned by comparison of its NMR spectral data with the literature values.[8b]



71 **72** **(11)**

Treatment of compound **71** with sodium hydride in anhydrous THF to generate the anion, followed by reaction with allyl bromide, gave compound **72** (**Eq.(11)**). The yield of this reaction was low (24%). Several variations were attempted to increase the yield: filtrating the allyl bromide through basic aluminum oxide prior to reaction in order to remove any acid; elevating the reaction temperature to 100 ℃; or using tert-butyl lithium instead of sodium hydride as base. None of these variations led to improved yield. The structure of complex **72** was assigned based on its NMR spectral data. The ^{1}H NMR spectrum of **72** had signals at δ 5.79-5.67 (m, 1H), 5.52-5.42 (m, 1H), 5.22 (dt, *J* = 16.8, 1.2 Hz, 1H) and 5.16-5.08 (m, 3H) ppm which correspond to the olefinic hydrogens. The ^{13}C NMR spectrum had signals at δ 173.4, 170.6 ppm which were consistent with the diastereotopic ester carbonyls, and signals at δ 132.5, 132.2, 119.6, 118.4 ppm which correspond to the olefinic sp^2 carbons.

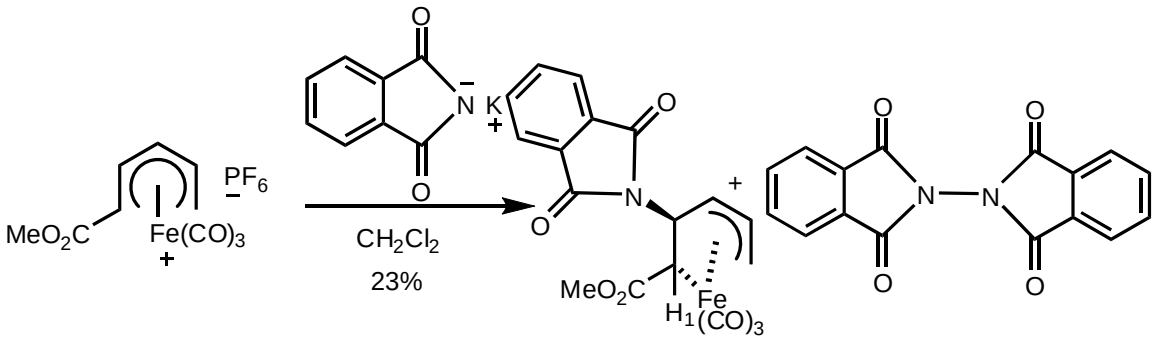


72 **73** **(12)**

Ring-closing metathesis of **72** in the presence of Grubbs first generation Ru catalyst[18] in dichloromethane was successful; albeit in low yield (19%) (**Eq.(12)**). The structure of complex **73** was assigned based on its NMR spectral data. The ^{1}H NMR spectrum of **73** had signals at δ 6.02 (ddd, J = 9.7, 5.8, 3.2 Hz, 1H) and 5.57-5.51 (m, 1H) ppm which correspond to the sp^2 olefinic hydrogens. Compound **73** was not very stable at room temperature and became dark upon standing.

Due to the low yields obtained for the preparation of **72** and **73**, further work on this project was abandoned.

Reacivity of acyclic (pentadienyl) iron (1+) cations with nitrogen nucleophiles

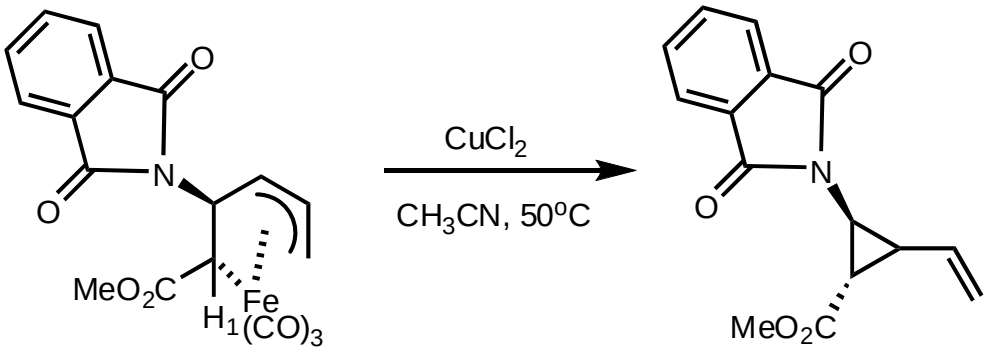


(±)-**11** **74** **75**

Eq.(13)

Treatment of (pentadienyl)iron cation (±)-**11** with potassium phthalimide in anhydrous dichloromethane gave the complex **74** in poor yield (**Eq.(13)**). The crude product was purified by column chromatography over aluminum oxide. The similarity in

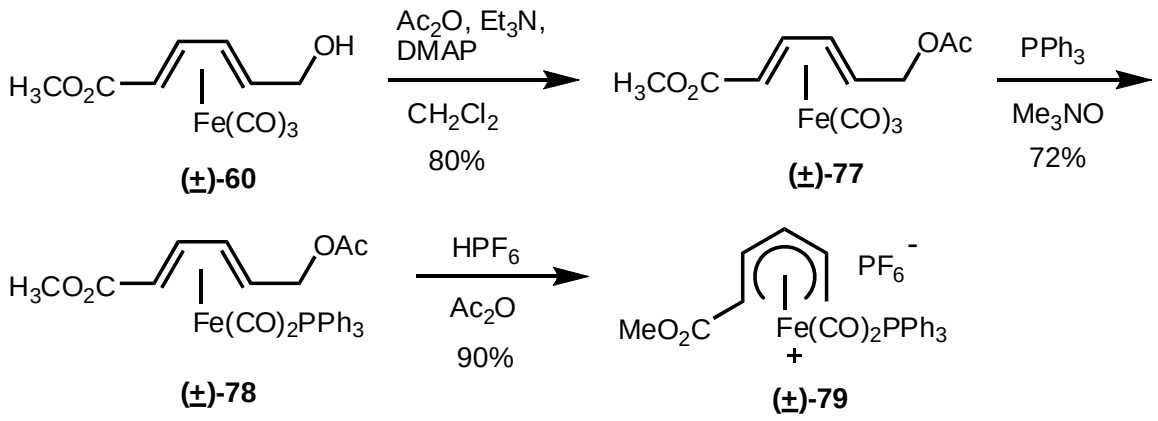
polarity of compound **74** and the phthalimide dimer **75** made separation impossible on silica gel. The structure of complex **74** was assigned based on its NMR spectral data. The ^{1}H NMR spectrum of **74** had high field doublet at δ1.52 ppm (d, J = 10.1 Hz, 1H) which corresponds to the hydrogen on the carbon sigma-bound to iron (H_1). The signals at δ 7.79-7.65 (m, 4H) ppm were consistent with the hydrogens on phthalimide. The ^{13}C NMR spectrum had signals at δ 210.5, 209.1, 203.8 ppm were assigned to the three CO ligands as well as signals at δ 179.3, 167.9 ppm which correspond to the ester and amide carbons. Compound **74** was a yellow solid which is stable at room temperature for a long time.



74 **76** **(14)**

Oxidative decomplexation of compound **74** with copper (II) chloride in anhydrous acetonitrile at 50 ℃ for 1 h gave vinylcyclopropane **76** in low yield (19%) (**Eq.(14)**). Maintaining an anhydrous environment was crucial for this reaction because water reacted with compound **74** and then could be oxidized to aldehyde. The polarity of the aldehyde byproduct was very similar to compound **76**, and thus the separation of these two was very difficult. Since maintaining anhydrous conditions was difficult (even with

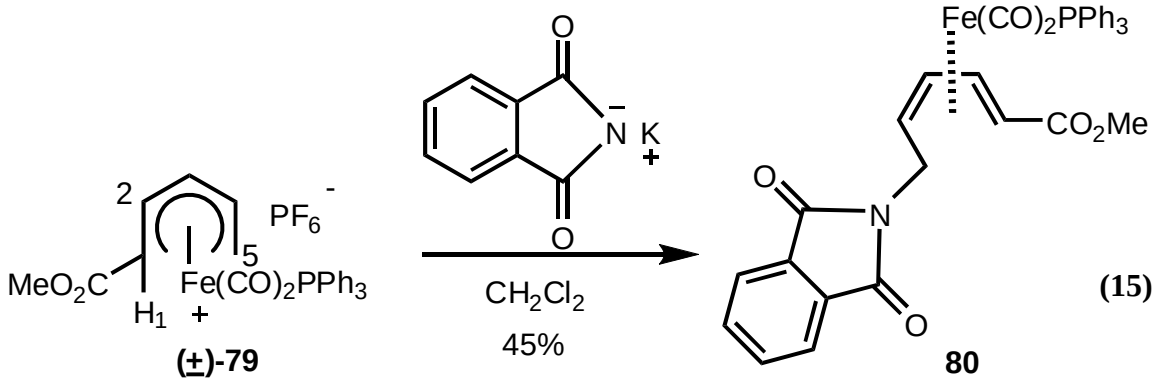
the use of anhydrous CH_3CN), the poor yield of isolated **76** may be due to this inefficiency in chromatographic separation. It was noted that significant amounts of **76** remained in a mixture with the aldehyde byproduct. The structure of complex **76** was assigned based on its NMR spectral data. The ^1H NMR spectrum of **76** had downfield signals at δ 7.85-7.70 (m, 4H) ppm consistent with the hydrogens of the phthalimide group. The signals at δ 5.95-5.82 (m, 1H), 5.43 (ddd, J = 17.2, 1.8, 0.6 Hz, 1H) and 5.24 (ddd, J = 10.3, 1.5, 0.6 Hz, 1H) ppm correspond to the sp^2 olefinic hydrogens.



Scheme 13

The dicarbonyl(triphenylphosphine)-ligated cation **(±)-79** was prepared as indicated in **Scheme 13** according to the literature procedure[20] in a total of 3 steps from compound **(±)-60** in good yield. Compound **(±)-60** reacted with acetic anhydride, triethylamine and DMAP to give the acetylated iron ester complex **(±)-77**. The reaction of iron ester compound **(±)-77** with PPh_3, followed by treatment with trimethylamine N-oxide gave the phosphine ligated compound **(±)-78**. Acetylation prior to ligand displacement was necessary as attempted ligand displacement of **(±)-60** resulted in low yield.[21] Cation **(±)-**

79 was synthesized by protonation/dehydration of **(±)-78** with HPF_6 in acetic anhydride, according to the literature procedure.[20]

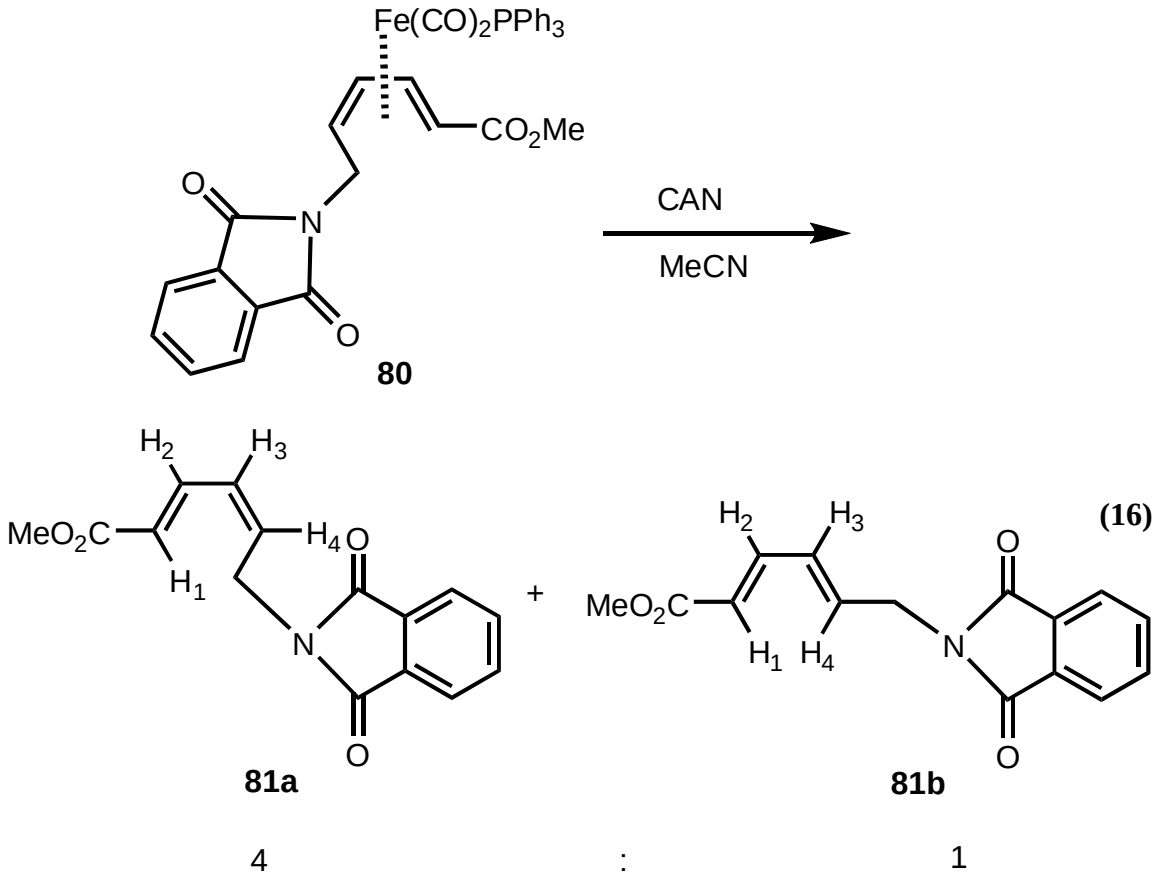


(15)

Reaction of cation **(±)-79** with potassium phthalimide in anhydrous dichloromethane overnight, gave the diene complex **80** in moderate to good yield (**Eq.(15)**). Unlike the reaction of cation **(±)-11** with potassium phthalimide, nucleophilic attack occurred at C-5 (instead of C-2) to form the 2*E*,4*Z*-diene complex. The structure of complex **80** was assigned based on its NMR spectral data. The ^{1}H NMR spectrum of **80** had signals at δ 7.80-7.64 (m, 4H) ppm which were consistent with the hydrogens on phthalimide. The signals at δ 7.50-7.34 (m, 15H) ppm correspond to the hydrogens in PPh_3. Signals at δ 6.02-5.95 (m, 1H) and 4.22-4.08 (m, 1H) are consistent with a (2E,4Z-dienoate) $Fe(CO)_2PPh_3$ complex.[5b] The absence of a doublet peak at high field indicated there was no carbon sigma-bound to iron (H_1).

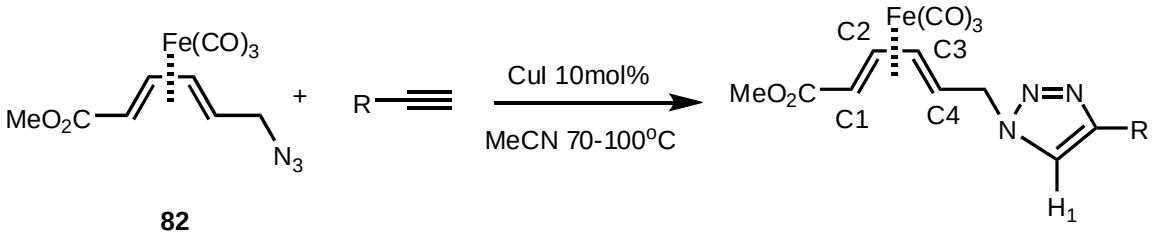
The origins of this difference in regioselectivity for phthalimide nucleophilic attack on **11** (C2) versus **79** (C5) are unclear. One possible explanation is that the increased electron donation from the PPh_3 ligand in **79** places greater electron density

into the pentadienyl ligand. Thus for cation **79**, nucleophilic attack at C5 may be due to frontier orbital control. An alternative rational is that the diene prduct **80** may arise due to thermodynamic control. That is the attack of phthalimide at C2 of **79** may be more rapid than at C5, but that nucleophilic attack at C2 may be reversible (to regenerate **79** and phthalimide) and that eventually slower attack at C5 leads to the more thermodynamically stable diene product **80**. Examples of reversible nucleophilic attack to **79** (but not to **11**) have been previously reported.[5b]

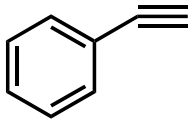
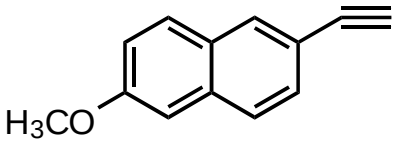
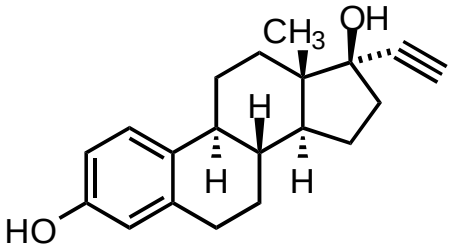


(16)

Oxidative decomplexation of compound **80** with cerium ammonium nitrate (CAN) in anhydrous acetonitrile gave an inseparable mixture of dienes **81a** and **81b** (~4:1 based on ^{1}H NMR integration) (**Eq.(16)**). The structure of complexes **81** were assigned based on their NMR spectral data. The ^{1}H NMR spectrum contained two separate singlet peaks at δ 3.78 (s, 2.4 H, a), 3.72 (s, 0.6 H, b) ppm together totaling 3H which were assigned to the methyl esters of the geometric isomers. The ratio of **81a** and **81b** (4:1) was calculated from integration of these methyl peaks respectively. The major stereoisomer is the *cis*-diene **81a**. The peak at δ 6.30-6.23 (m, 0.8 H, H-3 a) ppm for diene **81a** was assigned to H-3, and its coupling constant was smaller than the peak at δ 6.38-6.30 (m, 0.2 H, H-3 b) ppm. This was the evidence that H-3 was *cis* to H-4 in **81a**.



82

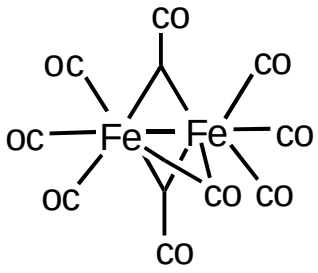
Compound	R	Yield
83		60%
84		48%
85		50%
86		41%[a]
87		36%

[a] The mole ratio of starting material and 1, 4-diethynylbenzene was 1:1

Table 1

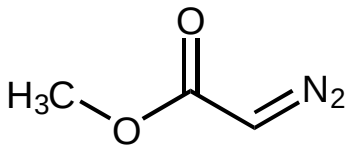
The cycloaddition of tricarbonyl(methyl 6-azido-2,4-hexadienoate)iron **82** with a variety of terminal alkynes under the catalysis of 10 mol% copper (I) iodide in acetonitrile[19] gave the corresponding triazole products **83-87** in moderate to good yield (**Table 1**). This "click chemistry" reaction was pretty clean; almost no byproduct was generated during the reaction. The structure of complexes **83-87** were assigned based on their NMR spectral data. In particular, the ^{1}H NMR spectra of **83-87** had signals at ca. δ 5.9 and 5.55-5.6 ppm which correspond to the protons on C3/C4 of (2*E*,4*E*- hexadienoate) $Fe(CO)_3$ complexes, and the ^{13}C NMR spectrum contained two signals in the range δ 85-86.5 ppm corresponding to C3 and C4 of these complexes. The presence of the 1,4-disubstituted-1,2,3-triazole functionality was identified by a singlet at ca. δ 7.3 ppm in their ^{1}H NMR spectrum as well as signals at ca. 148-149 and 119-120 ppm of their ^{13}C NMR spectra. For complex **86**, the mole ratio of compound **82** and 1,4-diethynylbenzene was 1:1, so instead of obtaining a disubstituted product, compound **86** was the only product. The signal at δ 3.13 ppm (s, 1H) corresponds to the acetylene hydrogen that was not involved in the cycloaddition reaction.

EXPERIMENTAL SECTION



88

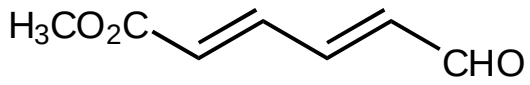
Diiron(0) nonacarbonyl: A clean 1000 mL round bottom flask was charged with glacial acetic acid (500 mL). The solvent was deoxygenated by bubbling N_2 through for approximately 10 min. To this was added iron pentacarbonyl (100 mL) and the mixture was irradiated with an medium pressure Hg arc lamp for 4 h. Diiron nonacarbonyl was formed as golden flakes which were then separated by filtration through a sintered glass funnel. The residue was collected and washed with diethyl ether. The acetic acid-Iron pentacarbonyl filtrate was resubjected to photolysis and the procedure repeated several times. From the 100 g of iron pentacarbonyl, 70 g of diiron nonacarbonyl was obtained. This compound was used in subsequent reactions without further purification or characterization.



57

Methyl diazoacetate: To a three-necked flask equipped with a nitrogen source inlet, an addition funnel, and a cold temperature thermometer, cooled to -5 ℃, was added aqueous methyl glycinate hydrochloride (31.7 g, 99%, 250 mmol) in 63 mL water followed by CH_2Cl_2 (150 mL). An ice-cold solution of sodium nitrite (20.9 g, 99%, 300 mmol) in water (63 mL) was added and the reaction vessel was cooled to -10 ℃. An aqueous solution of H_2SO_4 (5 wt. % 24 g) was added via the addition funned over a 3 min period. During the course of the addition, the temperature inside the reaction flask rose to +3 ℃ and the organic phase became yellow. After the exotherm subsided (~15 min), the biphasic mixture was poured onto ice-cold saturated aqueous sodium bicarbonate solution (250 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (30 mL). The combined organic layers were washed with cold saturated aqueous sodium bicarbonate solution (2 x 250 mL) until the organic layer was no longer acidic as indicated by litmus paper. The organic phase was washed with water (250 mL), dried (Na_2SO_4), and concentrated at aspirator pressure (23 ℃) to give **5** as a yellow oil (15.9 g, 159 mmol, 64%). This compound was used without further purification.

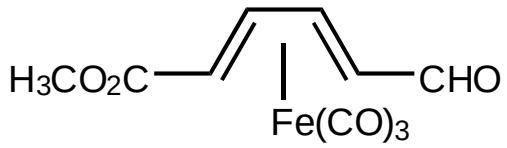
Compound **57**: IR (neat) 3122, 3002, 2957, 2113, 1704 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.75 (s, 1H), 3.76 (s, 3H).



58

Methyl 6-oxohexa-2(*E*), 4(*E*)-dienoate: To a solution of rhodium(II) acetate dimer (30.0 mg, 0.0679 mmol) in furan (65 mL) at room temperature under nitrogen, was added a solution of methyl diazoacetate **57** (6.28 g, 62.7 mmol) in furan (diluted to a total volume of 17.0 mL) via an automatic syringe pump over a 21 h period. The reaction mixture was filtered through SiO_2 using CH_2Cl_2 to rinse the filter pad. The combined filtrate and washings were concentrated, and the resultant yellow oil was reconstituted with fresh CH_2Cl_2 (42 mL). Iodine (0.100 g) was added, and the reaction mixture darkened and became warm. After 90 min, the solution was concentrated and the residue was dissolved in ethyl acetate (50 mL). The organic solution was washed with 10% aqueous sodium thiosulfate solution (50mL) followed by brine (50 mL). The organic phase was dried ($MgSO_4$), concentrated, and adsorbed to SiO_2 using CH_2Cl_2. Purification by column chromatography (SiO_2, hexanes-ethyl acetate gradient = 10:1 → 4:1) gave diene **58** (5.74 g, 41.0 mmol, 65%) as a pale yellow solid.

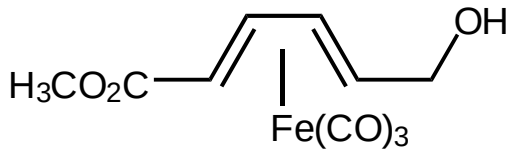
Compound **58:** mp 71-74 ℃; IR (KBr) 3033, 2960, 2862, 2773, 1726, 1686, 1635, 1439, 1233 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.79 (s, 3H), 6.30 (td, *J* = 0.9, 15.3 Hz, 1H), 6.41 (tdd, *J* = 0.9, 7.7, 15.3 Hz, 1H), 7.17 (ddd, *J* = 0.9, 11.2, 15.3 Hz, 1H), 7.42 (ddd, *J* = 0.9, 11.2, 15.3 Hz, 1H), 9.66 (d, *J* = 7.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 52.3, 129.4, 137.1, 140.6, 147.2, 165.8, 192.9.



(±)-59

(±)-Tricarbonyl(methyl 6-oxo-hexa-2(*E*),4(*E*)-dienoate)iron: A round bottom flask was charged with diene **58** (5.93 g, 42.3 mmol), $Fe_2(CO)_9$ (18.9 g, 52.0 mmol), and benzene (140 mL). The reaction mixture was heated to reflux under nitrogen for 2 h during which time the mixture blackened. The reaction was cooled to room temperature and additional $Fe_2(CO)_9$ (6.10 g, 16.8 mmol) was added and the reaction brought back to reflux for 30 min. The reaction mixture was cooled to room temperature and filtered through a bed of SiO_2 using CH_2Cl_2 to rinse the filter pad. The combined filtrate and washings were concentrated to give a black oil which was purified by column chromatography (SiO_2, hexanes-ethyl acetate gradient = 5:1 → 2:1) to give **(±)-59** (9.98 g, 35.6 mmol, 84%) as an orange solid.

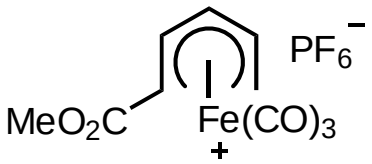
Compound **(±)-59**: mp 83-85 ℃; IR (KBr) 3075, 2952, 2825, 2730, 2701, 2008, 1697, 1679, 1455, 1205 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.47 (dd, *J* = 0.9, 8.1 Hz, 1H), 1.53 (ddd, *J* = 0.9, 3.5, 8.1 Hz, 1H), 3.71 (s, 3H), 5.97-6.09 (m, 2H), 9.43 (d, *J* = 3.5 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 47.9, 52.3, 55.1, 84.8, 88.1, 171.7, 195.5.



(±)-60

(±)-Tricarbonyl(methyl 6-hydroxyhexa-2(*E*),4(*E*)-dienoate)iron ((±)-5): To a mixture of the complexed aldehyde **(±)-59** (9.44 g, 33.7 mmol) in absolute ethanol (166 mL) was added KBH_4 (2.23 g, 40.5 mmol). The reaction mixture was stirred at room temperature for 20 min and was then quenched with water (20 mL). After stirring for an additional 10 min, the solution was diluted with brine (50 mL) and water (50 mL). The organic phase was removed and the aqueous phase extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were dried ($MgSO_4$) and concentrated to give an oil which could be purified by column chromatography (SiO_2, hexanes-ethyl acetate gradient = 3:1 → 1:1) to afford the alcohol complex **(±)-60** (9.37 g, 33.2 mmol, 99%) as an orange syrup.

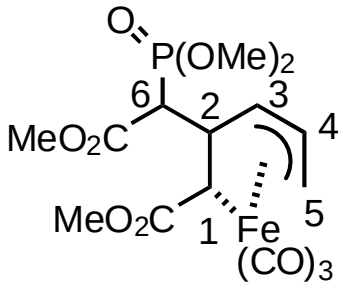
Compound **(±)-60:** IR (neat) 3421, 2954, 2061, 1986, 1709, 1491, 1460, 1340, 1198, 1122, 1009 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.08 (dd, *J* = 1.2, 8.1 Hz, 1H), 1.43 (dddd, *J* = 1.2, 5.5, 6.7, 8.3 Hz, 1H), 1.86 (t, *J* = 5.3 Hz, 1H), 3.66 (s, 3H), 3.68-3.87 (m, 2H), 5.41 (ddd, *J* = 1.0, 5.0, 8.7 Hz, 1H), 5.84 (ddd, *J* = 1.0, 5.0, 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 46.4, 52.0, 62.4, 64.3, 84.4, 85.9, 172.6.



(±)-11

(±)-Tricarbonyl(1-methoxycarbonylpentadienyl)iron(1+) hexafluorophosphate ((±)-11): To a solution of alcohol **(±)-60** (8.96 g, 31.8 mmol) in anhydrous ether (46 mL) and acetic anhydride (9.5 mL) cooled to 0 ℃ was added dropwise an ice-cold solution of aqueous HPF_6 (60 wt. %, 11.0 mL) and acetic anhydride (20 mL). A precipitate developed and the reaction mixture was stirred for 20 min at 0 ℃. The reaction mixture was added to a large excess of ether (1500 mL). The solid salt was collected on a glass frit, washed with several portions of ether, and dried *in vacuo* to afford iron cation **((±)-11)** (11.0 g, 28.8 mmol, 84%) as a microcrystalline yellow solid.

The NMR spectral data for this compound was consistent with the literature values.[6]

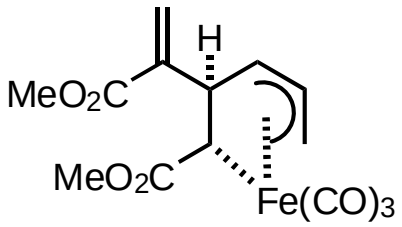


61

Tricarbonyl{1-methoxycarbonyl-2-[1'-(dimethyl phosphinyl)methoxycarbonyl methane]-3-pentene-1,5-diyl}iron: To a stirring suspension of complex **(±)-11** and sodium hydride (50.0 mg, 60% dispersion in mineral oil, 1.25 mmol) in dry THF (30 mL) at 0 ℃ under nitrogen was added trimethylphosphonoacetate (221 mg, 1.21 mmol). The reaction mixture was stirred for 30 min, and then a solution of cation (500 mg, 1.21 mmol) in dry THF (15 mL) was added. The mixture was stirred overnight and then quenched with water. The mixture was diluted with CH_2Cl_2 and the layers were separated. The aqueous layer was extracted once with CH_2Cl_2 and the combined organic extracts were washed once with saturated aqueous sodium chloride, dried ($MgSO_4$), and concentrated. The residue was purified by column chromatography (SiO_2, pure ethyl acetate) to afford the product (372 mg, 0.837 mmol, 69%) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.69-4.39 (m, 2H, H-3 and H-4), 3.81-3.55 (m, 14H, 4xOCH_3, H-2 and H-6), 2.67-2.39 (m, 2H, H-5exo and H-5endo), 0.33 and 0.01 (2 x d, *J* = 8.7 Hz, 1H total, H-1).

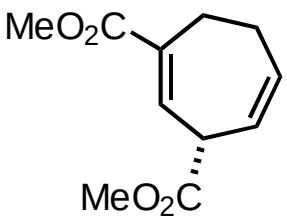
HRMS *m/z* 385.0114 [calcd for $(C_{12}H_{19}O_7PFe)Na^+$ (M+Na^+-3CO) 385.0110].



62

Tricarbonyl [1-methoxycarbonyl-2-(1'-methoxycarbonylethenyl)-3-pentene-1,5-diyl]- iron: To a solution of **61** (371 mg, 0.836 mmol) in dry THF (30 mL) at 0 ℃ was added sodium hydride (42.0 mg, 60% dispersion in mineral oil, 1.05 mmol). The mixture was stirred for 15 min, and then paraformaldehyde (25 mg, 0.83 mmol) was added. The reaction mixture was warmed to room temperature over a 3 h period and then quenched with water. The mixture was diluted with CH_2Cl_2 and the combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated. The residue was purified by column chromatography (SiO_2, hexanes-ethyl acetate = 17:3) to afford the product (104 mg, 0.299 mmol, 36%) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.07 (d, *J* = 1.8 Hz, 1H), 5.35 (d, *J* = 1.8 Hz, 1H), 4.74-4.65 (m, 1H), 4.60 (t, *J* = 7.4 Hz, 1H), 4.14-4.06 (m, 1H), 3.71 (s, 3H), 3.68 (s, 3H), 3.49-3.44 (m, 1H), 2.20 (dd, *J* = 12.2, 2.2 Hz, 1H), 0.33 (d, *J* = 8.8 Hz, 1H). HRMS *m/z* 555.0386 [calcd for $(C_{11}H_{14}O_4Fe)_2Na^+$ (M_2Na^+-6CO) 555.0375].

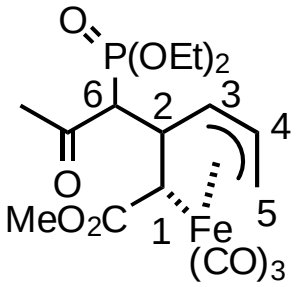


38

1,3-Bis(methoxycarbonyl)-1,4-cycloheptadiene: To a solution of **62** (68.0 mg, 0.196 mmol) in CH_3CN (11 mL) was added, portion wise, cerium ammonium nitrate (430 mg, 0.783 mmol) over a 40 min period. The reaction mixture was monitored by TLC. The mixture was then quenched with water and extracted several times with CH_2Cl_2. The combined extracts were washed with brine, dried ($MgSO_4$), and concentrated. The residue was purified by column chromatography (SiO_2, hexanes-ethyl acetate = 9:1) to afford the product (12 mg, 0.057 mmol, 30%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (d, *J* = 5.2 Hz, 1 H), 6.41-6.37 (m, 1 H), 6.12-6.06 (m, 1 H), 3.78 (s, 3 H), 3.75 (s, 3 H), 3.39-3.35 (m, 1 H), 2.44-2.36 (m, 1 H), 2.34-2.26 (m, 1 H), 2.15-2.07 (m, 2 H).

HRMS *m/z* 443.1676 [calcd for $(C_{11}H_{14}O_4)_2Na^+$ (M_2Na^+) 443.1676].



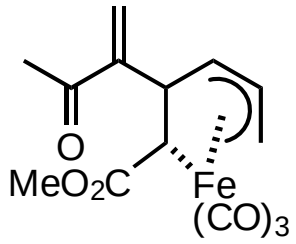
64

Tricarbonyl {2-[1'-(diethylphosphinyl)-2-oxopropyl]-1-methoxycarbonyl-3-pentene-1,5-diyl} iron: To a stirring suspension of **(±)-11** and sodium hydride (50.0 mg, 60% dispersion in mineral oil, 1.25 mmol) in dry THF (30 mL) at 0 ℃ under nitrogen was added diethyl (2-oxopropyl)phosphonate (240 mg, 1.21 mmol). The reaction mixture was stirred for 30 min, and then a solution of cation (500 mg, 1.21 mmol) in dry THF (30 mL) was added. The mixture was stirred overnight and then quenched with water. The mixture was diluted with CH_2Cl_2 and the layers were separated. The aqueous layer was extracted once with CH_2Cl_2 and the combined organic extracts were washed once with saturated aqueous sodium chloride, dried ($MgSO_4$), and concentrated. The residue was purified by column chromatography (SiO_2, pure ethyl acetate) to afford the product (365 mg, 0.801 mmol, 66%) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 4.79-4.50 (m, 2H, H-3 and H-4), 4.29-4.05 (m, 4 H, -OC$\underline{\underline{H}}_2CH_3$), 4.01-3.87 and 3.72-3.63 (m, 2H total, H-2 and H-6), 3.76 and 3.74 (2 x s, 3H total), 2.98-2.51 (m, 2H, H-5 exo and H-5 endo), 2.37 and 2.18 (2 x s, 3H total), 1.48-1.31 (m, 6H, -OCH$_2$C$\underline{\underline{H}}_3$), 0.44 and 0.01 (2 x d, J = 8.4 Hz, 1H total, H-1). ^{13}C NMR (partial, 100 MHz, $CDCl_3$): δ 210.0 [209.7] (-$\underline{\underline{C}}$OMe), {203.3 [203.2], 201.9 [201.8],

201.21 [201.20]} (Fe-CO), 179.6 [179.5] (-$\underline{C}O_2CH_3$), 97.0 [96.8] (C-4), 64.2, 61.7, 61.5, 54.4, 51.3 [51.2] (-$CO_2\underline{C}H_3$), 36.5, 36.1, 32.3, 29.8, 12.5, 11.9 [11.8] (C-1).

HRMS *m/z* 397.0476 [calcd for $(C_{14}H_{23}O_6PFe)Na^+$ ($M+Na^+$-3CO) 397.0474].

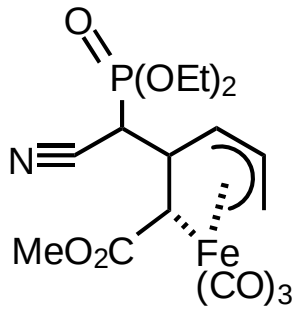


65

Tricarbonyl [1-methoxycarbonyl-2-(1'-methylene-2-oxopropyl)-3-pentene-1,5-diyl] iron: To a solution of **64** (360 mg, 0.789 mmol) in dry THF (30 mL) at 0 ℃ was added sodium hydride (45.0 mg, 60% dispersion in mineral oil, 1.13 mmol). The mixture was stirred for 15 min, and then paraformaldehyde (24 mg, 0.80 mmol) was added. The reaction mixture was warmed to room temperature over a 3 h period and then quenched with water. The mixture was diluted with CH_2Cl_2 and the combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated. The residue was purified by column chromatography (SiO_2, hexanes-ethyl acetate = 17:3) to afford the product (131 mg, 0.395 mmol, 50%) as a yellow oil.

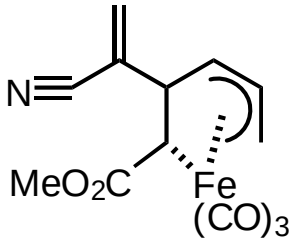
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.91 (d, *J* = 1.8 Hz, 1H), 5.51 (d, *J* = 1.8 Hz, 1H), 4.71-4.55 (m, 2H), 4.19-4.10 (m, 1H), 3.71 (s, 3H), 3.45 (dt, *J* = 8.3, 1.8 Hz, 1H), 2.24 (s, 3H), 2.18 (dd, *J* = 12.1, 2.4 Hz, 1H), 0.35 (d, *J* = 8.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ

210.8, 210.1, 204.0, 198.5, 180.4, 142.9, 124.0, 97.8, 62.4, 54.1, 52.0, 51.6, 40.3, 11.5. HRMS *m/z* 523.0483 [calcd for $(C_{11}H_{14}O_3Fe)_2Na^+$ (M_2Na^+-6CO) 523.0477].



66

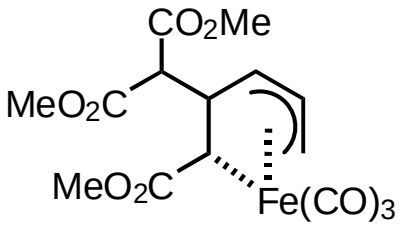
Tricarbonyl {2-[1'-(diethyl phosphinyl)cyanomethyl]-1-methoxycarbonyl-3-pentene-1,5-diyl} iron: To a stirring suspension of **(±)-11** and sodium hydride (50.0 mg, 60% dispersion in mineral oil, 1.25 mmol) in dry THF (30 mL) at 0 ℃ under nitrogen was added diethyl (cyanomethyl)phosphonate (215 mg, 1.21 mmol). The reaction mixture was stirred for 30 min, and then a solution of cation (500 mg, 1.21 mmol) in dry THF (30 mL) was added. The mixture was stirred overnight and then quenched with water. The mixture was diluted with CH_2Cl_2 and the layers were separated. The aqueous layer was extracted once with CH_2Cl_2 and the combined organic extracts were washed once with saturated aqueous sodium chloride, dried ($MgSO_4$), and concentrated. The residue was purified by column chromatography (SiO_2, hexanes-ethyl acetate = 1:1) to afford the product as a mixture of diatereomers. This product was used in the following reaction without further characterization.



67

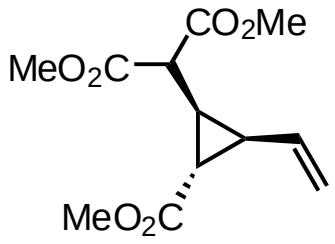
Tricarbonyl [1-methoxy carbonyl-2-(1'-methylene cyano methyl)-3-pentene-1,5-diyl] iron: To a solution of **66** mixture (282 mg) in dry THF (22 mL) at 0 ℃ was added sodium hydride (40 mg, 60% dispersion in mineral oil, 1.0 mmol). The mixture was stirred for 15 min, and then paraformaldehyde (19 mg, 0.63 mmol) was added. The reaction mixture was warmed to room temperature over a 3 h period and then quenched with water. The mixture was diluted with CH_2Cl_2 and the combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated. The residue was purified by column chromatography (SiO_2, hexanes-ethyl acetate = 17:3) to afford the product (7.00 mg, 0.023 mmol 3.5%) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.71 (d, *J* = 2.1 Hz, 1H), 5.54 (d, *J* = 2.1 Hz, 1H), 4.85-4.74 (m, 1H), 4.50-4.42 (m, 1H), 4.07-3.98 (m, 1H), 3.72 (s, 3H), 3.67-3.60 (m, 1H), 2.42 (dd, *J* = 12.3, 2.6 Hz, 1H), 0.38 (d, *J* = 8.8 Hz, 1H).



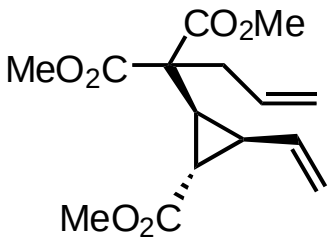
70

Tricarbonyl{1-methoxycarbonyl-2-[2-methoxy-1-(methoxycarbonyl)-2-oxoethyl]-3-pentene-1,5-diyl} iron: To a solution of sodium dimethyl malonate prepared from dimethyl malonate (0.320 g, 2.42 mmol) with sodium hydride (120 mg, 60% dispersion in mineral oil, 3.00 mmol) in THF (120 mL) at 0 ℃ was added solid cation **(±)-11**(0.960 g, 2.33 mmol) in one portion. The mixture was stirred at 0 ℃ for 1 h and 23 ℃ for 18 h, after which water was added and the mixture was extracted with CH_2Cl_2. The combined organic extracts were dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (SiO_2, hexanes-ethyl acetate = 3:1) to afford the product (0.660 g, 1.66 mmol, 76%) as a yellow solid. The NMR spectral data for this compound was consistent with the literature values.[4a]



71

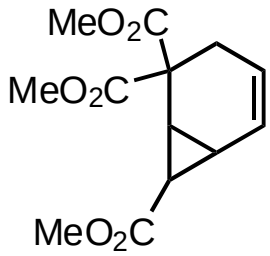
Dimethyl 2-[(2'-ethenyl-3'-methoxycarbonyl)cyclopropyl]propandioate: To a solution of **70** (412 mg, 1.04 mmol) in DMF (28 mL) at room temperature was added in one portion solid cerium ammonium nitrate (1.71 g, 3.11 mmol). After 10 min, an additional portion of CAN (1.71 g, 3.11 mmol) was added and after a further 10 min a final portion of CAN (2.28 g, 4.15 mmol) was added. The reaction mixture was stirred for 3 h, poured into water, and extracted with ether. The combined extracts were washed with water, following brine, dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography (SiO_2, hexanes-ethyl acetate = 10:1) to afford the product (0.18 g, 0.72 mmol, 69%) as a colorless oil. The NMR spectral data for this compound was consistent with the literature values.[8d]



72

Dimethyl 2-[(2'-ethenyl-3'-methoxycarbonyl)cyclopropyl]-2-(2'-propenyl) propandioate: To a solution of **64** (230 mg, 0.900 mmol) in THF (25 mL) under nitrogen was added sodium hydride (44 mg, 60% dispersion in mineral oil, 1.10 mmol) and the mixture stirred for 30 min. Allyl bromide (218 mg, 1.80 mmol) was then added and the mixture stirred at room temperature overnight. The solution was quenched with water, extracted twice with ether, and the combined extracts was washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (SiO_2, hexanes-ethyl acetate = 10:1) to afford the product (64 mg, 0.22 mmol, 24%) as a colorless oil.

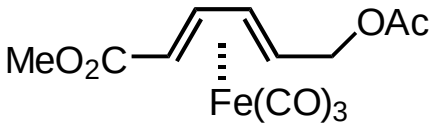
^{1}H NMR (400 MHz, $CDCl_3$): δ 5.79-5.67 (m, 1H), 5.52-5.42 (m, 1H), 5.22 (dt, *J* = 16.8, 1.2 Hz, 1H), 5.16-5.08 (m, 3H), 3.72 (s, 3H), 3.71 (s, 3H), 3.68 (s, 3H), 2.79-2.66 (m, 2H), 2.26 (ddd, *J* = 7.8, 7.8, 7.8 Hz, 1H), 2.18-2.12 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.4, 170.6, 132.5, 132.2, 119.6, 118.4, 56.4, 52.5, 52.0, 40.2, 30.53, 30.45, 24.5. HRMS m/z 319.1152 [calcd for $C_{15}H_{20}O_6Na$ ($M+Na^+$) 319.1152].



73

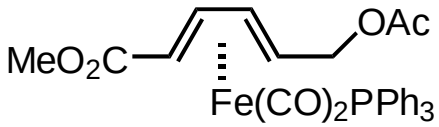
5,5,7-Tris(methoxycarbonyl)bicyclo[4.1.0]hept-2-ene: To a solution of **72** (12 mg, 0.041 mmol) in CH_2Cl_2 (12 mL) was added Grubbs I catalyst (3.33 mg, 10 mol%). The reaction mixture was monitored by TLC. After the mixture had stirred for 1 h, there was no starting material by TLC. The mixture was concentrated and the dark green residue was purified by column chromatography (SiO_2, hexanes-ethyl acetate gradient = 10:1) to afford the product (2 mg, 0.0075 mmol, 19%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.02 (ddd, *J* = 9.7, 5.8, 3.2 Hz, 1H), 5.57-5.51 (m, 1H), 3.77 (s, 3H), 3.75 (s, 3H), 3.69 (s, 3H), 2.74 (ddd, *J* = 17.6, 7.1, 2.3 Hz, 1H), 2.57 (ddd, *J* = 8.9, 4.7, 2.1 Hz, 1H), 2.27 (dt, *J* = 17.6, 2.8 Hz, 1H), 2.11-2.05 (m, 1H), 1.98 (dd, *J* = 5.0, 3.8 Hz, 1H). HRMS m/z 559.1794 [calcd for $(C_{13}H_{16}O_6)_2Na^+$ (M_2Na^+) 559.1786].



(±)-77

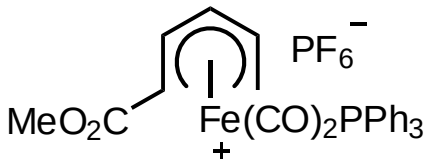
Tricarbonyl(methyl-6-acetoxy-2(E),4(E)-hexadienoate) iron: To a stirring solution of the alcohol complex (8.19 g, 27.6 mmol) in reagent CH_2Cl_2 (262 mL) under nitrogen was added sequentially acetic anhydride (5.7 mL, 98%, 59 mmol), triethylamine (16.2 mL, 99%, 115 mmol), and DMAP (20 mg, 99%, 0.17 mmol). After 50 min, the solution was concentrated to one-half volume and washed with brine. The aqueous phase was back-extracted with CH_2Cl_2. The combined organic phases were dried (Na_2SO_4) and concentrated. Purification of the residue by column chromatography (SiO_2, hexanes-ethyl acetate = 3:1) gave the product (7.47 g, 22.0 mmol, 80%) as an orange oil. The NMR spectral data for this compound was consistent with the literature values.[4a]



(±)-78

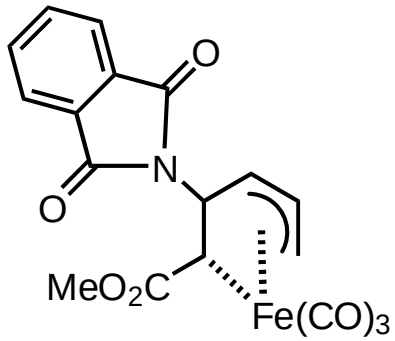
Dicarbonyl(methyl 6-acetoxy-2(E),4(E)-hexadienoate) (triphenylphosphine) iron: To a stirring solution of the tricarbonyliron complex (7.47 g, 22.0 mmol) in reagent acetone (140 mL) under nitrogen was added triphenylphosphine (18.3 g, 99%, 69.1 mmol) in a single portion, followed by trimethylamine N-oxide (7.86 g, 98%, 69.4 mmol) in three

equal portions over a 110 min period. After 160 min from the first addition, the reaction mixture was filtered through a bed of SiO_2, and the filter bed was washed with reagent acetone. The combined filtrate and washings were concentrated to a dark oil, which was purified by column chromatography (SiO_2, hexanes-ethyl acetate = 5:1 → 3:1) to afford the product (9.12 g, 15.9 mmol, 72%) as a yellow-orange solid. The NMR spectral data for this compound was consistent with the literature values.[4a]



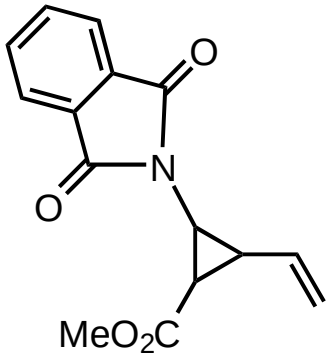
(±)-79

Dicarbonyl(1-methoxycarbonylpentadienyl)(triphenylphosphine)iron(1+)hexafluorophosphate: To a solution of the acetate complex (9.12 g, 15.9 mmol) in ether (85 mL) and acetic anhydride (5.6 mL) cooled to 0 ℃ in an ice bath was added dropwise an ice-cold solution of aqueous HPF_6 (60 wt. %, 5.6 mL) and acetic anhydride (11.3 mL). A precipitate developed and the reaction mixture was stirred for 20 min at 0 ℃. The reaction mixture was added to a large excess of ether (1800 mL). The solid salt was collected on a glass frit, washed with ether (3 x 50 mL), and dried in *vacuo* to afford iron cation (9.48g, 14.7 mmol, 90%) as a yellow powder. The NMR spectral data for this compound was consistent with the literature values.[4a]



74

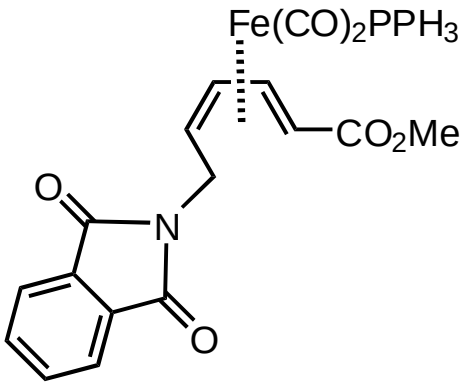
Tricarbonyl(1-methoxycarbonyl-2-phthalimide-3-pentene-1,5-diyl) iron: A 50 mL schlenk flask was charged iron cation **(±)-11**(1.00 g, 2.43 mmol) and anhydrous CH_2Cl_2 (25 mL) at room temperature under nitrogen. Solid potassium phthalimide (674 mg, 3.64 mmol) was added and the mixture was stirred overnight. The mixture was quenched with water, extracted several times with CH_2Cl_2, and the organic layer was washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography (Al_2O_3, hexanes-ethyl acetate = 17:3) to afford the product (170 mg, 0.41 mmol, 23%) as a pale yellow solid. mp 150-152 ℃; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79-7.65 (m, 4H), 5.56 (dd, *J* = 9.8, 7.3 Hz, 1H), 4.87-4.75 (m, 1H), 4.65 (t, *J* = 7.3 Hz, 1H), 3.67 (s, 3H), 3.62 (dd, *J* = 9.1, 1.2 Hz, 1H), 3.49 (dd, *J* = 12.1, 2.3 Hz, 1H), 1.52 (d, *J* = 10.1 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.5, 209.1, 203.8, 179.3, 167.9, 134.4, 131.7, 123.6, 100.9, 64.5, 55.8, 51.7, 47.9, 17.6.



76

(2-Ethenyl-3-methoxycarbonylcyclopropyl)phthalimide: To a solution of phthalimide sigma-pi complex (80 mg, 0.20 mmol) dissolved in anhydrous acetonitrile (10 mL) under nitrogen was added copper(II)chloride (79 mg, 0.59 mmol). The reaction mixture was heated at 50 ℃for 1 h and then concentrated to remove acetonitrile. The residue was dissolved in CH_2Cl_2 and purified by column chromatography (SiO_2, hexanes-ethyl acetate = 10:1) to afford the product (10 mg, 0.037 mmol, 19%) as a colorless oil.

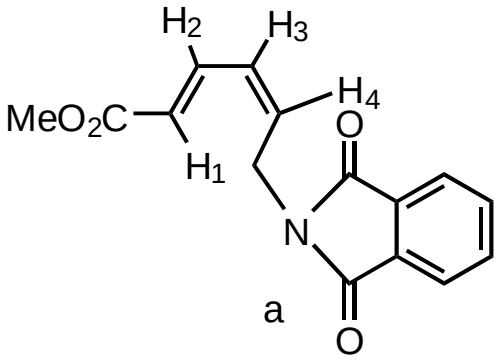
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85-7.70 (m, 4H), 5.95-5.82 (m, 1H), 5.43 (ddd, *J* = 17.2, 1.8, 0.6 Hz, 1H), 5.24 (ddd, *J* = 10.3, 1.5, 0.6 Hz, 1H), 3.75 (s, 3H), 3.60 (dd, *J* = 5.2, 4.4 Hz, 1H), 2.77-2.61 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.2, 170.2, 168.0, 134.3, 131.7, 123.4, 119.0, 52.1, 35.1, 29.8, 26.4. HRMS m/z 565.1588 [calcd for $(C_{15}H_{13}NO_4)_2Na^+$ (M_2Na^+) 565.1581].



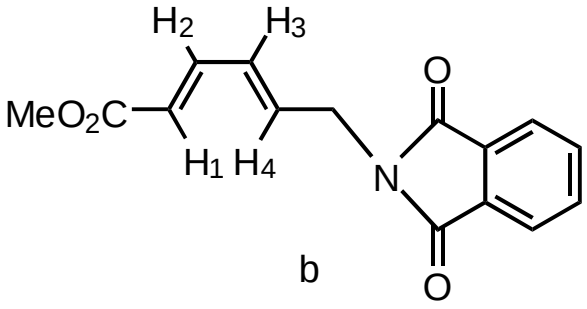
80

Dicarbonyl(methyl 6-phthalimide-2(E),4(E)-hexadienoate)(triphenylphosphine) iron: To a solution of phosphine ligated cation (1.29 g, 2.00 mmol) in anhydrous CH_2Cl_2 (100 mL) under nitrogen was added potassium phthalimide (556 mg, 3.00 mmol). The reaction mixture was stirred overnight then quenched with water. The mixture was extracted three times with CH_2Cl_2, the combined extracts were washed with brine, dried (Na_2SO_4) and concentrated. The residue was dissolved in CH_2Cl_2 and purified by column chromatography (SiO_2, hexanes-ethyl acetate = 3:1) to afford the product (583 mg, 0.900 mmol, 45%) as a yellow solid.

mp 172-178 ℃; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80-7.64 (m, 4H), 7.50-7.34 (m, 15H), 6.02-5.95 (m, 1H), 4.22-4.08 (m, 1H), 4.03-3.87 (m, 1H), 3.70 (s, 3H), 3.28-3.10 (m, 1H), 2.38-2.26 (m, 1H), 1.99-1.81 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.0, 175.1, 167.8, 134.3, 133.8, 133.2(d, *Jpc* = 10.2 Hz), 132.2, 130.2, 128.5(d, *Jpc* = 9.7 Hz), 123.6, 123.1, 91.6, 88.2, 51.4, 39.0, 37.6.

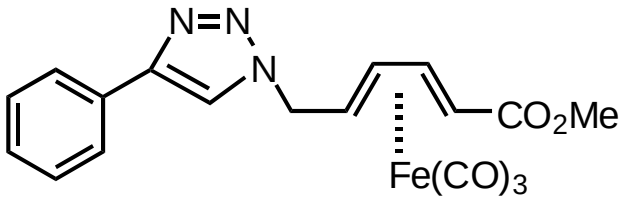


81a



81b

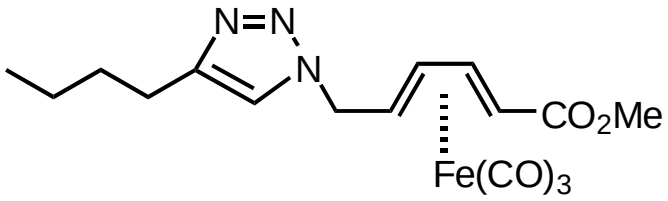
Methyl 6-phthalimide-2,4-hexadienoate: To a solution of **79** (100 mg, 0.160 mmol) in anhydrous acetonitrile (20 mL) was added cerium ammonium nitrate (256 mg, 0.470 mmol). After stirring overnight the mixture was quenched with water and extracted several times with CH_2Cl_2. The combined organic layers were washed with brine, dried (Na_2SO_4) and concentrated. The residue was dissolved in CH_2Cl_2 and purified by column chromatography (SiO_2, hexanes-ethyl acetate = 10:1) to afford a mixture of 4(Z)- and 4(E)-stereoisomers (4:1) (10 mg, 0.037 mmol, 24%) as a pale yellow solid. mp 70-75 ℃. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89-7.70 (m, 4.8 H, H-2a and Phth), 7.22 (dd, *J* = 15.7, 11 Hz, 0.2 H, H-2b), 6.38-6.30 (m, 0.2 H, H-3b), 6.30-6.23 (m, 0.8 H, H-3a), 6.15-6.06 (m, 0.2 H, H-4b), 5.97 (d, *J* = 15.3 Hz, 0.8 H, H-1a), 5.89-5.77 (m, 1 H, H-1b and H-4a), 4.54 (dd, *J* = 7.3, 1.5 Hz, 1.6 H,a), 4.39 (dd, *J* = 6.1, 1.2 Hz, 0.4 H b), 3.78 (s, 2.4 H, a), 3.72 (s, 0.6 H, b).



83

To a solution of tricarbonyl(methyl 6-azido-2,4-hexadienoate)iron (20 mg, 0.065 mmol) in CH_3CN (10 mL) was added phenylacetylene (10 mg, 0.098 mmol) and copper (I) iodide (2 mg, 10 mol%). The mixture was heated to 70 ℃ under nitrogen. After 19 h, the temperature was raised to 100 ℃ and the solution started to reflux. This temperature was maintained for another 5 h. After cooling, the mixture was quenched with H_2O, extracted two times with CH_2Cl_2, the organic layer was washed with brine, and dried (Na_2SO_4). The organic layer was concentrated to give an oil which was purified by column chromatography (SiO_2, hexanes-ethyl acetate gradient = 2:1 → pure ethyl acetate) to afford the product (16 mg, 0.039 mmol, 60%) as a yellow oil.

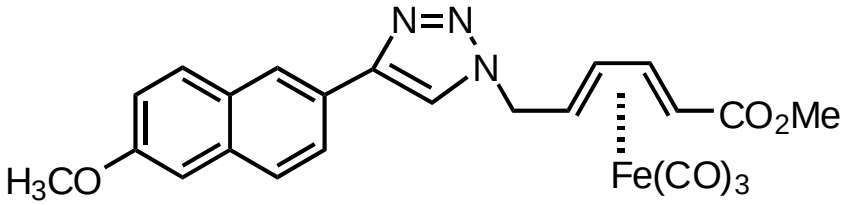
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85-7.79 (m, 3H), 7.46-7.32 (m, 3H), 5.91 (ddd, *J* = 8.6, 5.2, 0.9 Hz, 1H), 5.57 (ddd, *J* = 8.6, 5.2, 0.9 Hz, 1H), 4.60 (dd, *J* = 14.6, 5.9 Hz, 1H), 4.48 (dd, *J* = 14.5, 8.6 Hz, 1H), 3.67 (s, 3H), 1.47-1.38 (m, 1H), 1.15 (dd, *J* = 8.2, 0.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.2, 148.3, 130.6, 129.1, 128.6, 126.0, 119.2, 86.3, 85.8, 55.3, 53.0, 52.0, 47.3.



84

To a solution of tricarbonyl(methyl 6-azido-2,4-hexadienoate)iron (20 mg, 0.065 mmol) in CH_3CN (10 mL) was added 1-hexyne (11 mg, 0.13 mmol) and copper (I) iodide (2 mg, 10 mol%). The mixture was heated at 100 ℃ under nitrogen for 24 h. After cooling, the mixture was quenched with H_2O, extracted two times with CH_2Cl_2, the organic layer was washed with brine, and dried (Na_2SO_4). The organic layer was concentrated to give an oil which was purified by column chromatography (SiO_2, hexanes-ethyl acetate gradient = 2:1 → pure ethyl acetate) to afford the product (12 mg, 0.031 mmol, 48%) as a yellow oil.

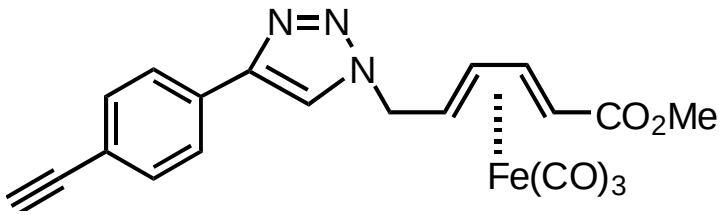
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (s, 1H), 5.89 (dd, *J* = 8.3, 5.1 Hz, 1H), 5.53 (dd, *J* = 8.3, 5.1 Hz, 1H), 4.52-4.38 (m, 2H), 3.66 (s, 3H), 2.72 (t, *J* = 7.8 Hz, 2H), 1.69-1.60 (m, 3H), 1.44-1.33 (m, 2H), 1.12 (d, *J* = 8.3 Hz, 1H), 0.93 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.2, 149.1, 120.3, 86.2, 85.7, 56.0, 52.8, 52.1, 47.1, 31.8, 25.5, 22.4, 13.9.



85

To a solution of tricarbonyl(methyl 6-azido-2,4-hexadienoate)iron (20 mg, 0.065 mmol) in CH_3CN (10 mL) was added 2-ethynyl-6-methoxy-naphthalene (18 mg, 0.099 mmol) and copper (I) iodide (2 mg, 10 mol%). The mixture was heated at 100 ℃ under nitrogen for 24 h. After cooling, the mixture was quenched with H_2O, extracted two times with CH_2Cl_2, the organic layer was washed with brine, and dried (Na_2SO_4). The organic layer was concentrated to give an oil which was purified by column chromatography (SiO_2, hexanes-ethyl acetate gradient = 2:1 → pure ethyl acetate) to afford the product (16 mg, 0.033 mmol, 50%) as a yellow solid.

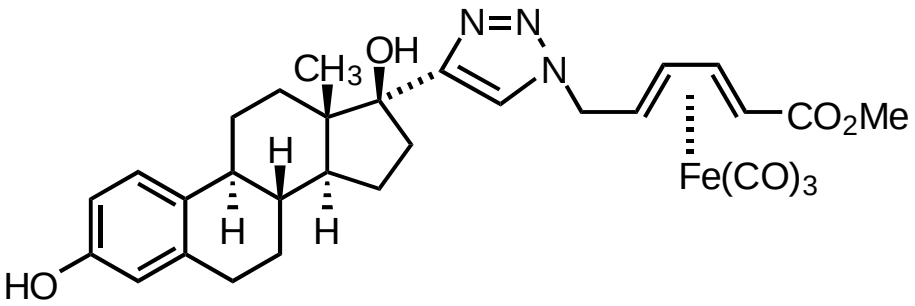
mp 151-154 ℃; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (s, 1H), 7.90-7.86 (m, 2H), 7.80-7.76 (m, 2H), 7.18-7.13 (m, 2H), 5.91 (ddd, *J* = 8.1, 5.2, 1.2 Hz, 1H), 5.58 (ddd, *J* = 8.3, 5.1, 0.8 Hz, 1H), 4.65-4.45 (m, 2H), 3.93 (s, 3H), 3.66 (s, 3H), 1.48-1.41 (m, 1H), 1.16 (dd, *J* = 8.0, 1.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.1, 158.0, 148.4, 134.5, 129.7, 129.0, 127.4, 125.6, 124.4, 124.3, 119.4, 118.9, 105.8, 86.1, 85.6, 55.3, 55.2, 52.8, 51.8, 47.0.



86

To a solution of tricarbonyl(methyl 6-azido-2,4-hexadienoate)iron (21 mg, 0.068 mmol) in CH_3CN (10 mL) was added 1,4-diethynylbenzene (9 mg, 0.071 mmol) and copper (I) iodide (2 mg, 10 mol%). The mixture was heated at 100 ℃ under nitrogen for 24 h. After cooling, the mixture was quenched with H_2O, extracted two times with CH_2Cl_2, the organic layer was washed with brine, and dried (Na_2SO_4). The organic layer was concentrated to give an oil which was purified by column chromatography (SiO_2, hexanes-ethyl acetate gradient = 2:1 → pure ethyl acetate) to afford the product (12 mg, 0.028 mmol, 41%) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82-7.77 (m, 3H), 7.57-7.53 (m, 2H), 5.92 (ddd, *J* = 8.2, 5.0, 0.8 Hz, 1H), 5.57 (dd, *J* = 8.2, 5.1 Hz, 1H), 4.63-4.45 (m, 2H), 3.67 (s, 3H), 3.13 (s, 1H), 1.44-1.37 (m, 1H), 1.15 (dd, *J* = 8.2, 0.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.9, 147.4, 132.7, 130.7, 125.6, 122.0, 119.3, 86.0, 85.6, 83.4, 78.0, 55.0, 52.8, 51.9, 47.1.



87

To a solution of tricarbonyl(methyl 6-azido-2,4-hexadienoate)iron (23 mg, 0.074 mmol) in CH_3CN (10 mL) was added 17α-ethynylestradiol (33 mg, 0.11 mmol) and copper (I) iodide (2 mg, 10 mol%). The mixture was heated at 100 ℃ under nitrogen for 48 h. After cooling, the mixture was quenched with H_2O, extracted two times with CH_2Cl_2, the organic layer was washed with brine, and dried (Na_2SO_4). The organic layer was concentrated to give an oil which was purified by column chromatography (SiO_2, hexanes-ethyl acetate gradient = 2:1 → pure ethyl acetate) to afford the product (16 mg, 0.027 mmol, 36%) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (d, *J* = 4.6 Hz, 1H), 7.05 (d, *J* = 8.4 Hz, 1H), 6.63-6.52 (m, 2H), 5.91 (dd, *J* = 8.2, 5.3 Hz, 1H), 5.55 (dd, *J* = 8.2, 5.3 Hz, 1H), 5.19 (s, 1H), 4.51 (d, *J* = 7 Hz, 1H), 3.67 (s, 3H), 2.85-2.65 (m, 3H), 2.50-2.35 (m, 1H), 2.22-2.06 (m, 2H), 2.03-1.82 (m, 3H), 1.64-1.29 (m, 8H), 1.14 (d, *J* = 8.2 Hz, 1H), 1.05 (s, 3H).* ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.3, 154.3, 153.7, 138.5, 132.7, 126.7, 121.1(121.0), 115.5, 112.9, 86.2, 85.7, 82.8(82.7), 55.7, 53.0, 52.2, 48.7(48.6), 47.5, 47.3, 43.4, 39.7, 38.3(38.2), 33.1, 29.9, 27.5, 26.4, 23.6, 14.4.≠

*Signal for aliphalic hydroxyl not observed.

≠Signals in brackets correspond to diastereomeric complexes.

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