3 + 2 Cycloaddition Reactions of Transition-Metal 2-Alkynyl and η^1-Allyl Complexes and Their Utilization in Five-Membered-Ring Compound Syntheses

MARK E. WELKER

Department of Chemistry, Wake Forest University, Winston-Salem, North Carolina 27109

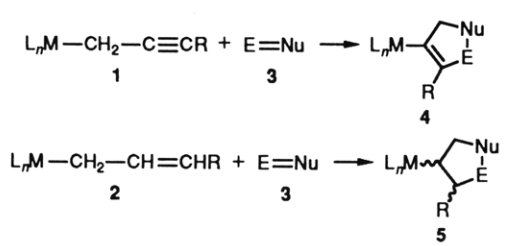
Received August 7, 1991 (Revised Manuscript Received September 26, 1991)

Contents

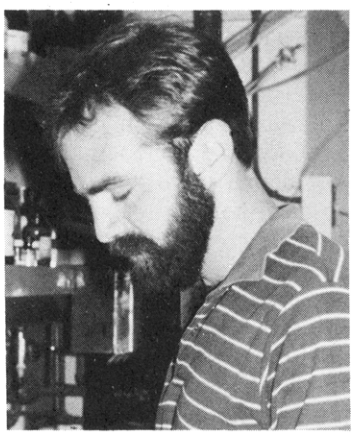
I. Introduction

Cycloaddition reactions between transition-metal 2-alkynyl (**1**) and η^1-allyl complexes (**2**) and unsaturated electrophilic reagents (**3**) have been studied in detail over the last 20 years by a number of research groups. These 3 + 2 cycloaddition reactions have been shown to yield transition-metal-substituted five-membered-ring heterocycles and carbacycles (**4** and **5**) (Scheme I),

SCHEME I



and they offer organic chemists alternative approaches to these ring systems when the metal is subsequently cleaved from the ring.



Mark Welker is Associate Professor of Chemistry at Wake Forest University. He was born in Greensboro, NC in 1958 and received a B.S. in chemistry with highest honors from the University of North Carolina at Chapel Hill in 1981. His Ph.D. work was completed at Florida State University in 1985 under Prof. Lanny S. Liebeskind. After completing a NIH postdoctoral fellowship at the University of California at Berkeley (1986, Prof. K. Peter C. Vollhardt), he joined the faculty at Wake Forest in 1987. His research interests are in the area of transition-metal-mediated organic chemistry.

Andrew Wojcicki last reviewed cycloaddition reactions of transition-metal allyl and propargyl complexes in detail in 1982 (references through 1980).[1] There is a very brief discussion of 3 + 2 cycloaddition reactions of transition-metal propargyls in Wojcicki's recent *Coordination Chemistry Reviews* article.[2] Myron Rosenblum reviewed some of his group's contributions to this field in 1986.[3] 3 + 2 cycloaddition reactions of allyl stannanes with electron deficient alkenes have been reviewed recently and will not be discussed here.[4]

This review will focus primarily on work published since 1980 on 3 + 2 cycloaddition reactions of transition-metal allyl and 2-alkynyl complexes. Some references relevant to the mechanism of these cycloadditions published prior to 1980 will also be cited. In this article, the syntheses of 2-alkynyl and allyl complexes will be briefly reviewed followed by a discussion of recent cycloaddition results. Detailed mechanisms for both the alkynyl and allyl cycloaddition reactions consistent with recent results will be postulated. Finally, demetalation reactions which have been used to yield five-membered-ring carbacycles and heterocycles will be discussed.

II. Early Work

The first reports of 3 + 2 cycloaddition reactions of transition-metal allyl and propargyl complexes ap-

0009-2665/92/0792-0097$10.00/0

peared in the early 1970s. Andrew Wojcicki's group had been investigating insertion of sulfur dioxide (SO_2) into transition-metal alkyl bonds and initially noted unusual rearrangement products from the reactions of transition-metal allyls with SO_2.[5] These rearrangement products were postulated to arise from cyclic transition states. Shortly thereafter, the first 3 + 2 cycloaddition product was reported from the reaction of alkynyl complex $CpFe(CO)_2CH_2C{\equiv}CCH_3$ and SO_2.[6] This cycloaddition product was so unusual and unexpected that its structure had been originally reported incorrectly twice,[7,8] and the structural dilemma was finally solved via X-ray crystallography.[6,9] Wojcicki reviewed his group's early work in this area in 1971.[10]

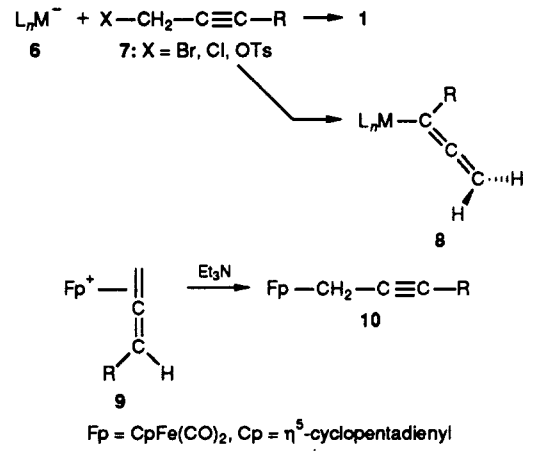
Another 3 + 2 cycloaddition product from the reaction of an alkynyl complex with SO_2 was then reported by Haszeldine in 1971.[11] Also in 1971, Rosenblum's group reported the first 3 + 2 cycloaddition between a transition-metal allyl and an alkene to yield a transition-metal-substituted cyclopentane.[12] At that time, Rosenblum postulated a two-step rather than concerted cycloaddition mechanism for these reactions. Rosenblum reviewed his group's early work in this area in 1974.[13] A large number of publications delineating the scope and mechanism of these cycloaddition reactions appeared during the mid to late 1970s.[14] Much of the work published in this area since 1980 has dealt more with synthetic applications of this cycloaddition and that work will be addressed in detail here.

III. 3 + 2 Cycloaddition Reactions of Transition-Metal 2-Alkynyl Complexes

A. Syntheses of 2-Alkynyl Complexes

Transition-metal 2-alkynyl complexes have been synthesized via two approaches (Scheme II). In all

SCHEME II



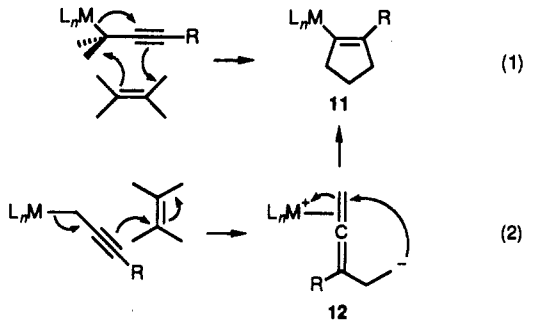
cases to date where preparatively useful amounts of these complexes have been synthesized, they have been prepared via reaction of a solution of a transition-metal anion (6) with a 2-alkynyl bromide, chloride, or tosylate (7).[11,15] In our hands, tosylates routinely produce the highest yields of alkynyl complex.[16] In most instances, there is clean S_N2 displacement of the propargyl leaving group but in a few cases S_N2' attack to yield transition-metal-substituted allenes (8) have also been reported.[14e,15a,16,17] Most transition-metal 2-alkynyl complexes (1) are only slightly air sensitive as solids and may be purified by sublimation or chromatography.

Transition-metal 2-alkynyl complexes (10) have also been prepared via deprotonation of cationic allene complexes (9).[17b,18] Such allene complexes (9) have been prepared via ligand exchange between the Fp(isobutylene) cation[19] and allenes.[17b] This could provide an alternate route to 2-alkynyl complexes which cannot be synthesized directly from the transition-metal anions (6).

B. Cycloaddition Reactions and Mechanistic Implications

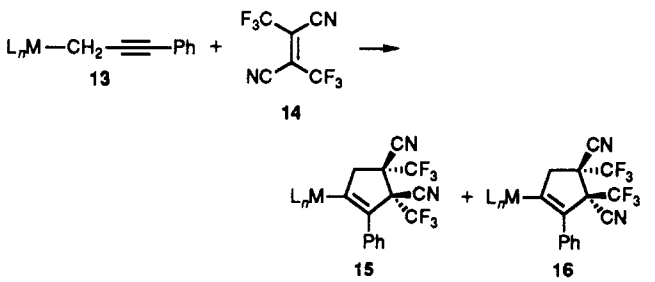
Much of the work published during the 1970s on 3 + 2 cycloaddition reactions of 2-alkynyl complexes was aimed at determining whether these reactions proceed via concerted $\pi 2a + \pi 2s + \sigma 2a$ (Scheme III, eq 1) or

SCHEME III



stepwise reaction mechanisms (Scheme III, eq 2). No spectroscopic evidence for 12 exists and the cycloaddition between $CpFe(CO)_2CH_2C{\equiv}CCH_3$ and SO_2 at −60 °C revealed no evidence of any intermediates by ^1H NMR.[14c]

Prior to 1980, the most convincing evidence that these alkynyl complex cyclizations were stepwise was a modest solvent effect on the rate of the reaction between $CpFe(CO)_2CH_2C{\equiv}CCH_3$ and tetracyanoethylene (TCNE)[20] and a study of the stereochemical outcome of cycloadditions between transition-metal 2-alkynyls (13) and (*E*)- and (*Z*)-1,2-dicyano-1,2-bis(trifluoromethyl)ethylene (14).[14f] In the last study described

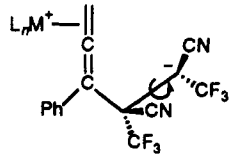


above, both diastereomers (15 and 16) of the cyclized product were observed when starting with either the (*E*)- or (*Z*)-alkene (14), indicating that the reaction proceeded through an intermediate where rotation around the former C=C of the alkene was possible. However, this work was complicated by the fact that pure *E*- or *Z*-14 isomerizes in CH_3CN to a 98:2 mixture of *E*:*Z* over 2 h and this isomerization had been shown to be base or anion catalyzed.[21] Reaction of $CpFe(CO)_2CH_2C{\equiv}CPh$ with *Z*-14 in CH_3CN with a reported reaction time of 15 min yielded a 91:9 mixture of anti:syn (16:15) product. *Z* to *E* isomerization prior to

TABLE I. Relative Rates of Cycloaddition between 1 and 18

	L_nM	R	relative k
1	$(PPh_3)(CO)_4Mn$	Me	>3000
2	$(PPh_3)(CO)_4Mn$	Ph	130
3	$(CO)_5Mn$	Ph	1.0
4	$Cp(CO)_2Fe$	Me	1000
5	$Cp(CO)_2Fe$	Ph	34
6	$Cp(CO)_3Mo$	Me	340
7	$Cp(CO)_2PPh_3Mo$	Ph	540
8	$Cp(CO)_2P(OPh)_3Mo$	Ph	110
9	$Cp(CO)_3Mo$	Ph	11

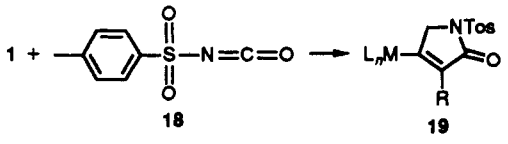
cycloaddition was invoked to explain this but it seems more likely in light of the shortness of this reaction time relative to that required for isomerization, and the fact that the *E* and *Z* isomers react at approximately the same rate, that bond rotation prior to ring closure in **17** more accurately accounts for the observed isomer ratios. The observation that the product ratios (90:10) are <95:5 *E*:*Z* may not be significant in ruling out a concerted mechanism since the reported mass balance for the cycloaddition was <60%.



17

More convincing evidence for some type of nonconcerted cycloaddition mechanism comes from the reaction of $(CO)_5MnCH_2C{\equiv}CPh$ with *E*-**14** where a 90% isolated yield of a 70:30 mixture of anti to syn was reported.[14f] This could only be explained via a concerted cycloaddition mechanism if *Z*-**14** reacted much more rapidly than *E*-**14** in the cycloaddition. It is interesting that the amount of syn product is much greater when $L_nM = (CO)_5Mn$ rather than $Cp(CO)_2Fe$. The rate constant for the ring-closure step for the $Mn(CO)_5$ complexes should be greater than that observed for the $Cp(CO)_2Fe$ complexes since in the allene intermediate (**17**), the allene functions mainly as a σ-donor ligand with the $Mn(CO)_5$ fragment and should be more electrophilic.

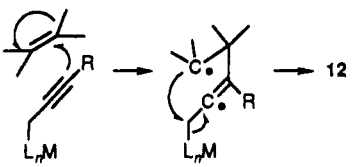
In 1981, Wojcicki et al. reported the results of a kinetic study involving rates of cycloaddition reactions between transition-metal 2-alkynyl complexes (**1**) and *p*-toluenesulfonyl isocyanate (TSI) (**18**).[22] The reac-



18 **19**

tions were found to be first order in both complex and TSI concentration which would be consistent with either a concerted mechanism or a two-step mechanism where the first step (electrophilic attack) is rate limiting. The results reported here showed an even smaller solvent dependence than those reported previously.[20] Also the reaction exhibited the low activation enthalpy and large negative activation entropy which are typical of concerted (Diels–Alder) reactions.[23] This TSI reaction data would only appear to be consistent with a two-step ionic mechanism (Scheme III, eq 2) if the transition state for the rate-determining electrophilic attack was highly ordered and early on the reaction coordinate. The partial loss of alkene stereochemistry seen in Wojcicki's study has also been observed in alkene cycloadditions which proceed through bipolar intermediates but these reactions did show a large solvent dependence.[24] The small solvent rate dependences and the observed loss of stereochemical integrity of alkenes in these cycloadditions would also appear to be consistent with a mechanism invoking a biradical intermediate (**20**) (Scheme IV). Some alkene cycloadditions

SCHEME IV

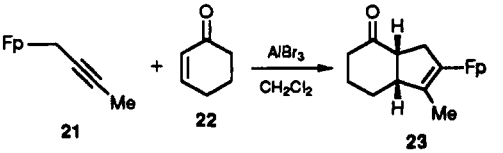


20

have been shown to proceed through biradical intermediates and these reactions also show small solvent effects and partial loss of alkene stereochemistry, depending on the relative rates of bond rotation and ring closure.[25a,b] Bruce, Snow, and co-workers have reported experimental evidence for radical intermediates similar to **20** in reactions between σ-acetylide complexes and TCNE.[25c] The homolytic metal–carbon bond cleavage needed in the ring-closure step has an analogy in the known radical reaction chemistry of related complexes.[26] The mechanistic data available to date on alkynyl complex cyclizations appear to be most consistent with either a two-step ionic reaction with a very early ordered transition state for electrophilic attack or a two-step biradical mechanism with an ordered transition state.

Two trends in the cyclization rate data[22] presented in Table I would be consistent with either an ionic, biradical, or concerted cycloaddition mechanism. Methyl-substituted alkynes are at least 1 order of magnitude more reactive than phenyl-substituted alkynes (compare entries 1 and 2, 4 and 5, and 6 and 9 in Table I). It is not clear whether this is a steric or electronic effect since there is no rate data available on a cyclohexyl- or vinyl-substituted alkyne. When comparing complexes where the alkynyl complex substituent remains constant, the cyclization rates increased as π-acid ligands were replaced by σ-donor ligands (compare entries 3, 5, and 9, 2 and 3, and 7–9).

One of the drawbacks of these alkynyl complex 3 + 2 cycloaddition reactions which has limited their use by synthetic organic chemists is the requirement that the alkene component be very electron deficient. Rosenblum and co-workers reported an attempt to extend the scope of these cycloadditions to less-electron-deficient alkenes in 1982.[27] Cyclohexenone (**22**) was treated with $AlBr_3$ at −78 °C in CH_2Cl_2 followed by addition of 1-Fp-2-butyne (**21**) and warming to 0 °C. *cis*-Hydrindenone product (**23**) was isolated, but the yield was disappointing (20%). This Lewis acid activation

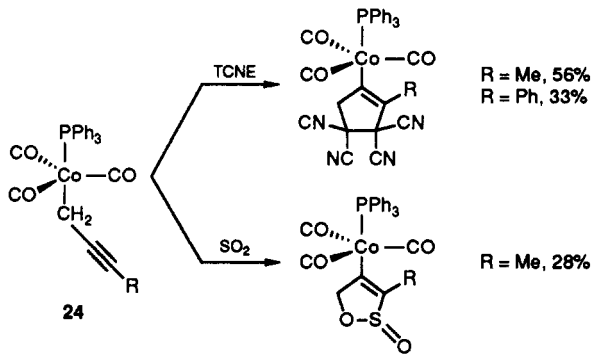


21 **22** **23**

of electrophiles prior to alkyne complex addition

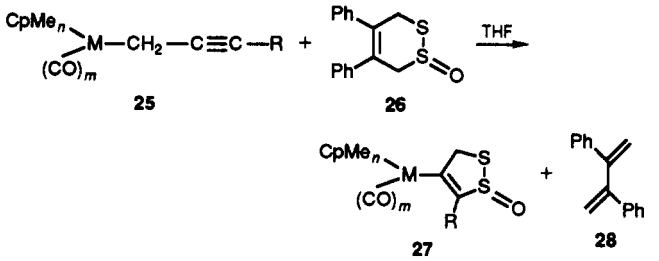
probably represents the best one can do in terms of increasing the electrophilicity of the alkene component.

The problem of limited alkene reactivity has also been solved in the past by increasing the nucleophilicity of the transition-metal alkynyl complex.[22] The increase in nucleophilicity of alkynyl complexes has been achieved by increasing the σ-donor strength of the ligands on the metal. A 2-alkynyl complex which is very nucleophilic and could potentially be made even more so by ligand substitution was recently reported by Ungvary and Wojcicki.[28] These complexes (24) (R = Me, Ph) reacted completely with TCNE in THF at 0 °C in 5 min and with SO_2 in THF at 0 °C in 10 min.



In 1989, we communicated a variant of this alkynyl complex 3 + 2 cycloaddition reaction (Scheme V) which

SCHEME V



yielded transition-metal-substituted five-membered-ring thiosulfinate esters (27).[29]

The 3 + 2 cycloaddition reaction to yield metallothiosulfinate esters (27) depicted in Scheme V requires disulfur monoxide (S_2O) or a disulfur monoxide equivalent. We have previously shown that 4,5-diphenyl-3,6-dihydro-1,2-dithiin 1-oxide (26) serves as a source of S_2O under mild reaction conditions.[29,16,30] We found that all the 2-alkynyl complexes we had prepared reacted with 26 in tetrahydrofuran at 25 °C to yield metallothiosulfinate esters (27) (Table II).

A trend in the relative rates of these cyclizations was observed which bears on a proposed mechanism for this reaction. Increased electron density at the metal center accelerated this reaction. Complexes **27a** and **27b** reacted completely with a slight excess of **26** within 2 h at 25 °C, whereas it was most convenient to use 2 equiv of **26** to effect complete cyclization of **27c–f** in 2 h. Reactions of molybdenum complexes **27f** and **27g** were only 50% complete after 24 h. Similar enhancements in cyclization rates have been reported in transition-metal 2-alkynyl/SO_2 cycloadditions when a CO was replaced by a phosphine.[22] Complexes (27) are all air stable and crystalline and can be chromatographed on silica gel.

The most unusual aspect of this chemistry is that cyclization occurred at room temperature where **26** is

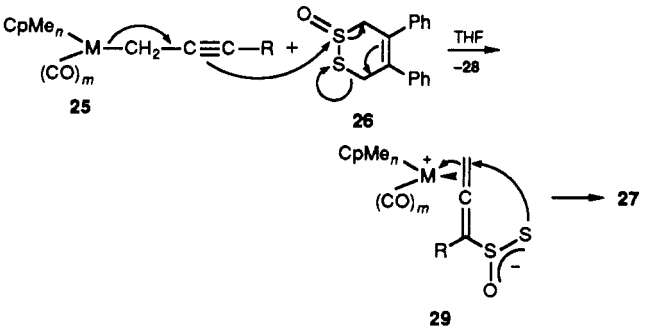
TABLE II. Cyclizations of 2-Alkynyl Complexes (25) with 26

product	M	n	m	R	yield
27a	Fe	5	2	CH_3	74%
27b	Fe	5	2	Ph	81%
27c	Fe	0	2	CH_3	70%
27d	Fe	0	2	Ph	72%
27e	Fe	0	2	$C(CH_3)=CH_2$	56%
27f	Mo	0	3	CH_3	45%[a]
27g	Mo	0	3	Ph	43%[a]

[a] >90% based on recovered alkynyl complex.

stable in solution in the absence of the transition-metal 2-alkynyl complexes. A mechanism which accounts for the observed products and which is consistent with the observed relative rates of cyclization as well as MNDO calculations on the structure of **26**[30b] can be formulated using the two-step ionic reaction mechanism (Scheme III, eq 2) outlined earlier as an analogy (Scheme VI).

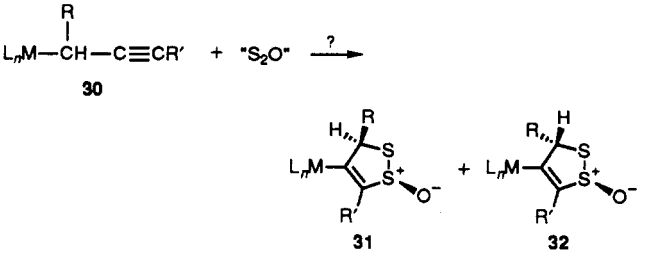
SCHEME VI



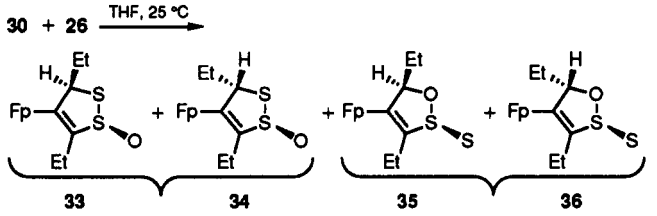
We propose that this cyclization reaction is initiated by nucleophilic attack of 2-alkynyl complexes (25) on **26** at the oxidized sulfur S(1) to form the cationic allene complex (29). Increased electron density on the metal should facilitate this nucleophilic attack. Nucleophilic attack on **26** would result in cleavage of the S(1)–C(6) and S(2)–C(3) bonds in **26** by a formal nucleophile-induced electrocyclic ring opening reaction. Our mechanism invokes an initial nucleophilic attack on the most electrophilic sulfur (S(1)) followed by cleavage of the weak S(1)–C(6) bond rather than the S(1)–S(2) bond. This is consistent with MNDO calculations on **26** which predict a S(2)–C(3) bond order of 0.98 but a S(1)–C(6) bond order of only 0.87.[30b]

To our knowledge, there are no reports of investigation of the diastereoselectivity of 3 + 2 cycloaddition reactions between chiral, racemic transition-metal 2-alkynyl complexes and electrophiles. We were interested in exploring the diastereoselectivity of alkynyl complex/S_2O cycloadditions, and we wanted to get some information about the stabilities of these diastereomeric thiosulfinate esters (31 and 32) if they could be formed (Scheme VII).

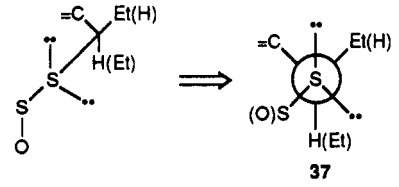
SCHEME VII



Reaction of chiral, racemic 2-alkynyl complex (30) (L_nM = $CpFe(CO)_2$, R = R′ = ethyl) with 26 was studied first because 30 had proven to be a thermally stable alkynyl complex. When 30 was allowed to react with 26 in tetrahydrofuran at 25 °C, the product mixture obtained (33:36) was dependent on reaction time. After 2 h of reaction time, we obtained a 1.3:1 mixture of two diastereomers (34:33) (40%) plus a trace amount of two other complexes (35 and 36). When the reaction

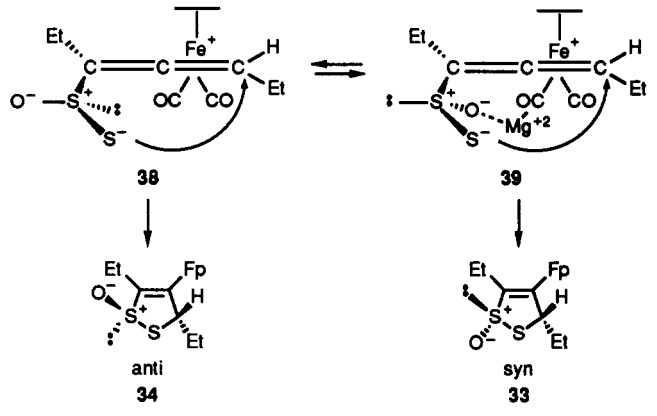


time was increased to 3 h 33/34 were still isolated (40%) (1.3:1, 34:33) in addition to a larger amount of 35/36 (17%, 1.3:1, 35:36). After 6 h of reaction time, 35/36 were the major products (48%, 1.3:1, 35:36) and only a trace of 33/34 were seen in the crude product ^1H NMR. Introduction of a substituent on the carbon next to the nonoxidized sulfur in these thiosulfinate esters (33/34) has obviously affected their stability. We assume that this is a conformational effect similar to those seen in other cyclic thiosulfinate esters[31] where interactions between the sulfur lone pairs and the substituent (37) are responsible for the instability of 33/34.



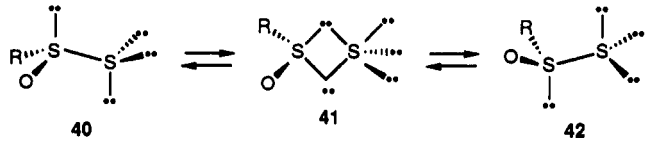
To account for the lack of diastereoselectivity observed in the cyclization of 26 with 30 and to look for a way to improve diastereoselectivity we need to postulate a mechanism for the cycloaddition (Scheme VIII).

SCHEME VIII

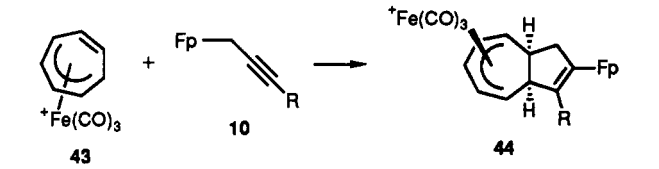


We will assume that these cycloadditions proceed through cationic allene complex intermediates (38 and 39). These allene complexes (38 and 39) should exist predominantly in the conformations shown which place the substituent on the carbon which was α to iron away from the bulky cyclopentadienyl ligand. This has been shown to be the preferred conformation for related cationic $CpFe(CO)_2$(alkene) complexes.[14i] Rotation of the allene around the metal–alkene bond (a process which is rapid for the related tetramethyl allene complex)[17b] would have no effect on the stereochemical outcome of the cycloaddition reaction. If 1,2 shifts of the iron on the allene occurred, this would yield complexes which could not undergo cyclization to yield five-membered-ring products.

We would anticipate that 38 and 39 would be interconvertible via a thermal racemization mechanism (40–42) reported for thiosulfinate esters.[32] There would appear to be little steric or electronic bias to favor either 38 or 39 at equilibrium. We hoped to be able to influence the position of this equilibrium by adding a divalent Lewis acid to coordinate the thiosulfinic acid anion oxygen and a metal carbonyl oxygen thus favoring intermediate (39).[33] When $MgBr_2$ was added to the cyclization reaction syn product (33) (predicted from this model) became the major product (2:1) and the chemical yield improved (95%). The Lewis acid in this case may also be serving to activate 26 toward nucleophilic attack.



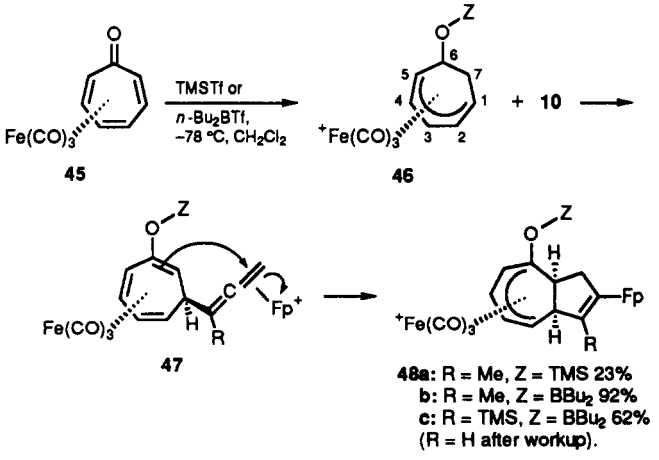
3 + 2 cycloaddition reactions of Fp–2-alkynyl complexes (10) with tropylium iron tricarbonyl cations (43) provide an interesting route to the hydroazulene nucleus (44) which was first communicated in 1976.[34]



More recently, this reaction has been extended to the construction of the guaianolide and pseudoguaianolide sesquiterpene frameworks.[35]

Activation of the tropone iron tricarbonyl complex (45) with TMS triflate or n-Bu_2B triflate yields cation (46) (Z = TMS or n-Bu_2B).[35a] Addition of the 1-Fp-2-alkynyl complexes (10) (R = Me and TMS) yielded the tropone iron tricarbonyl complexes (48) (Scheme IX).

SCHEME IX



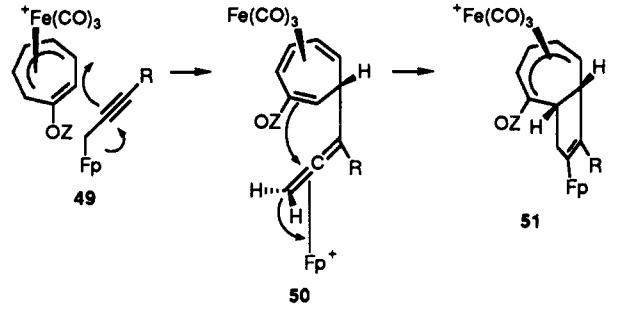
48a: R = Me, Z = TMS 23%
b: R = Me, Z = BBu_2 92%
c: R = TMS, Z = BBu_2 62%
(R = H after workup).

A single regioisomeric cycloadduct with a cis ring junction was isolated from each reaction. Infrared spectroscopic evidence for a cation like 47 was obtained.

The electrophilic attack **46** → **47** is rapid at −78 °C, whereas ring closure **47** → **48** requires reflux (3 h) in CH_2Cl_2. Crossover experiments suggest that the electrophilic attack is irreversible.[35b]

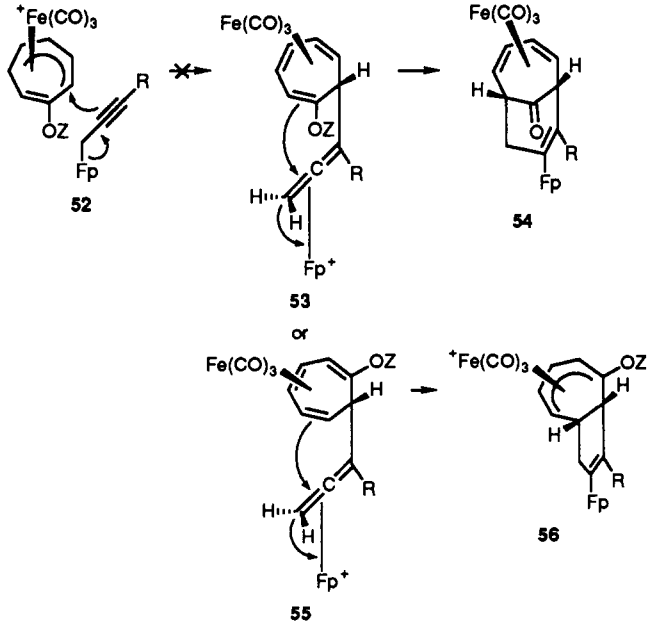
The ring junction stereochemistry in the cycloadducts (**48**) is consistent with previous work[36,27,14h] and can be explained by electrophilic attack on the tropylium cation on the face opposite the $Fe(CO)_3$ fragment with carbon–carbon bond formation anti to Fp (**49**) (Scheme X). This step is followed by ring closure via nucleophilic attack on the Fp allene cation (**50**) on the face opposite Fp.

SCHEME X



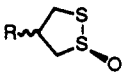
No information exists about the regiochemical makeup of complexes like **46** at equilibrium. The observed cycloadduct regiochemistry (**51**) could be explained if **46** exists as a single regioisomer or if **46** exists as a mixture of regioisomers but reacts with **10** preferentially through the regioisomer depicted (**46**). The observed cycloadduct regiochemistry can only result from initial electrophilic attack at C(1) of **46**. Initial electrophilic attack at C(5) (**52**) would be disfavored on steric grounds and would be expected to lead to the formation of some bridged bicyclic product (**54**) as well as the other regioisomer (**56**) (Scheme XI).

SCHEME XI



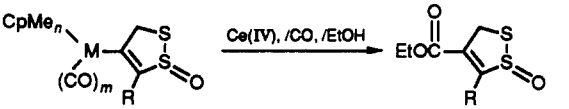
C. Demetalation Reactions

These 3 + 2 cycloaddition reactions are likely to attract greater interest from synthetic organic chemists if the metal can be removed from the cycloadducts in high yield. As part of a general program aimed at synthesizing organosulfur compounds which may be useful as agricultural chemicals or pharmaceuticals, we needed to remove the cyclic thiosulfinate esters from the metal in cyclization products (**27**). We were interested in the heterocyclic ring system contained in complexes (**27**) because it is an analogue of the naturally occurring thiosulfinate esters (**57**, R = CO_2H) (asparagusic acid *S*-oxides, plant growth regulators)[37] and (**57**, R = OH) (brugeriols, isolated from mangroves)[38] and other cyclic thiosulfinate esters have been shown to be tumor growth inhibitors.[39]



57

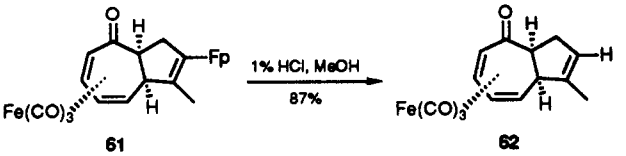
Because of the known ease with which thiosulfinate esters undergo oxidation-induced rearrangements and disproportionations,[40] and the fact that most of the known methods for cleaving metal–carbon bonds in similar complexes are oxidative,[41] we approached the problem of how to remove the thiosulfinate ester from the metal with some caution. Indeed, attempts to cleave the metal–carbon bond in **27d** with halogens (I_2, Br_2, NBS), copper ($CuCl_2$), and iron ($FeCl_3$) reagents under a variety of conditions lead to the isolation of complex mixtures of products. However, when these metallothiosulfinate esters (**27b–e,g**) were treated with ceric ammonium nitrate under 1 atm of CO in ethanol, CO insertion and iron–carbon bond cleavage occurred.[42] This produced the desired five-membered-ring thiosulfinate esters (**58–60**) in good yield (**58** from **27c**, 48%; **59** from **27b,d,g**, 66%, 72%, and 59% respectively, and **60** from **27e**, 58%).



27

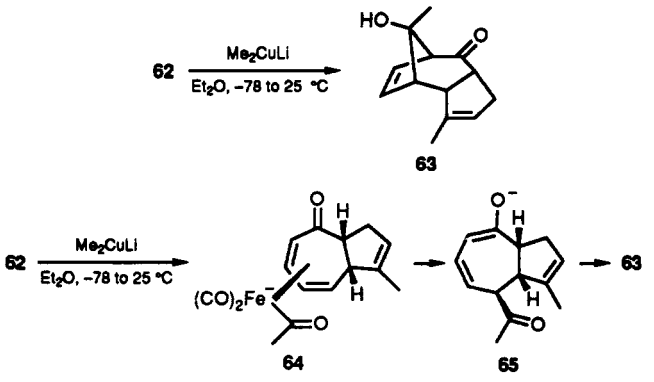
58: R = Me
59: R = Ph
60: R = C(Me)=CH_2

Other recent efforts directed at removal of cycloadducts from the transition metal have focused mainly on allyl rather than alkynyl cycloaddition products. The Fp fragment has been removed from **61** in high yield by exposure to 1% HCl in methanol.[35c] The $Fe(CO)_3$ fragment has been removed from complexes closely related to **62** using ceric ammonium nitrate.[34,35]



61 **62**

Treatment of **62** with lithium dimethylcuprate produced the unexpected tricyclic product (**63**) (82%).[35c] Production of **63** was explained by initial attack of Me_2CuLi on complexed CO to yield anionic acyl (**64**). Reductive elimination from **64** followed by an intramolecular aldol condensation from **65** would produce **63**.

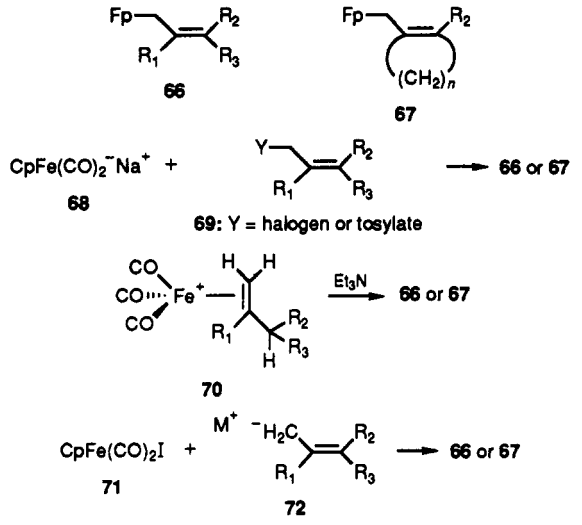


IV. 3 + 2 Cycloaddition Reactions of Transition-Metal η^1-Allyl Complexes

A. Synthesis of η^1-Allyl Complexes

Allyl complexes of the form 66 and 67 can potentially be prepared by one of three methods (Scheme XII): (1)

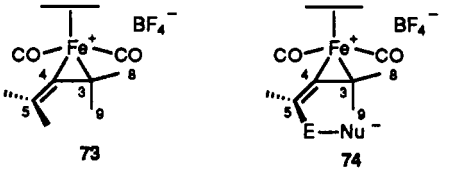
SCHEME XII



reaction of the $CpFe(CO)_2^-Na^+$ salt (68) with appropriately substituted halides or tosylates (69);[43] (2) deprotonation of appropriately substituted cationic alkene complexes (70)[14i] (this would not be useful in cases where mixtures of stereoisomers about the C=C resulted); and (3) reaction of an allylic organometallic nucleophile (72) with $CpFe(CO)_2I$ (71).[44] Route 2 is probably the most practical of the three because of the ease of preparation and stability of the cationic precursors (70). In cases where routes 1 or 3 would be used, the complexes (66 or 67) are best purified by alumina chromatography and immediately used in cyclization reactions.

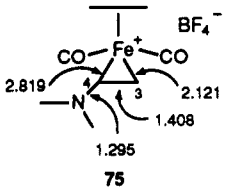
B. A Model for Predicting the Outcome of 3 + 2 Cycloaddition Reactions of Transition-Metal Allyls and Alkynyls

Unlike alkynyl cyclizations, there is no doubt that some allyl complex/electrophile 3 + 2 cycloadditions proceed through a two-step mechanism with a distinct cationic alkene complex intermediate.[14c,j,h] However, with some electrophiles such as TSI, there is no evidence for an ionic intermediate even in allyl cyclizations.[22] In cases where the rate constants for cycloaddition of analogous alkynyl and allyl complexes have been compared they are surprisingly similar.[22] All available information on alkynyl complex cyclizations would indicate that if these cyclizations do proceed stepwise, electrophilic attack is always the rate-determining step and subsequent ring closure is very rapid. Allyl complex 3 + 2 cycloadditions proceed similarly for some electrophiles but there are cases where ring closure rather than electrophilic attack appears to be the rate-limiting step. These observations are consistent with relative rates of electrophilic attack on isolated alkynes and alkenes.[45] Halogenation, for instance, is 10^3–10^5 faster for alkenes than alkynes.[45a] Also, the geometry of the intermediate cationic allene complexes (74) should lead to rapid cyclization for low-valent metal complexes with electron-donating ligands which would not necessarily be expected for the alkene complexes since they have more rotational degrees of freedom. The apparent difference in rate of ring closure from alkenyl and allenyl complexes is best explained by geometrical rather than electronic effects since cationic Fp(alkene) complexes are more susceptible to nucleophilic attack on the complexed double bond than the corresponding allene complexes. Alkoxides attack CO rather than the allene in Fp(allene) cations,[18a] whereas they add cleanly to the alkene in Fp(alkene) cations.[46] The Fp tetramethyl allene BF_4 complex (73) has been structurally characterized and it shows asymmetry in the Fe–C bonds (Fe–C(3), 2.237 Å, and Fe–C(4), 2.063 Å).[47] Similar asymmetry in Fe–C bonds in related Fp complexes could be expected on the basis of comparison of ^{13}C NMR data.[48] The C(5)–C(4)–C(3) bond angle in 73 was 145.7°. The angles between the Fe–C(4)–C(3) plane and the C(4)–C(3)–C(8) and C(4)–C(3)–C(9) planes were 100.8 and 107.1°, respectively. These angles would be expected to be 90° for sp^2 hybridization and 112.6° for sp^3 hybridization at the complexed double bond. This structure for an allene complex (73) and the fact that the C(4)–C(5) bond is a double bond would place the nucleophilic atom of any E=Nu cyclization component in a position which should make ring closure rapid. Another indication of the influence of substituents on the chemistry of the complexed allene is the observation that external nucleophilic attack on the allene in complexes like 73 slows as the size of substituents on the noncoordinated double bond increases.[18b]



The only crystal structure data available on cationic Fp alkene complexes are of heteroatom-substituted alkenes.[49] Complex (75) had a Fe–C(3)–C(4) bond angle of 104.17° indicating that the hybridization in the complexed alkene is close to tetrahedral. Without the additional double bond which is present in the allene, one would expect ring closure to be a less favorable process entropically here than for the allene (74).

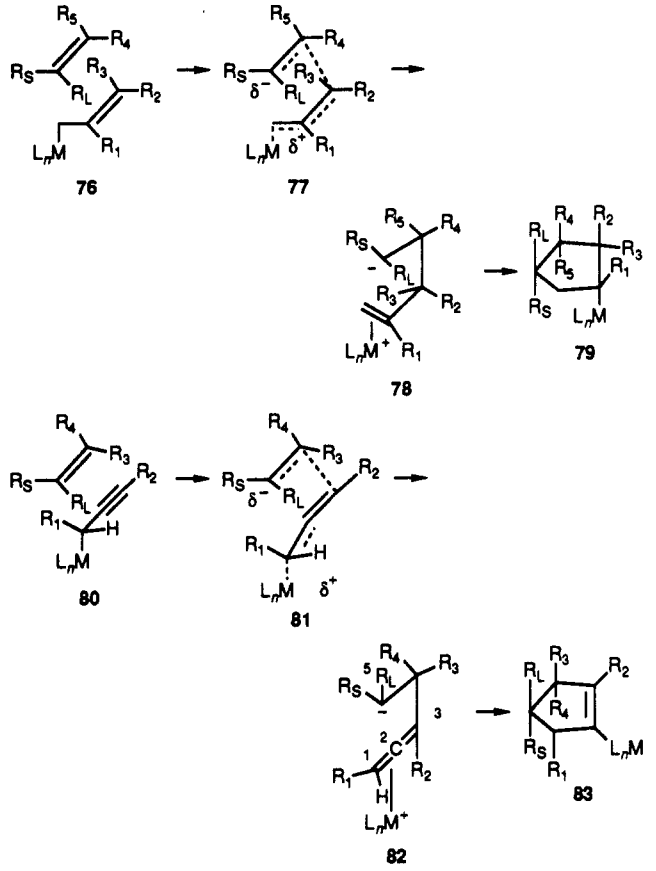
Mechanisms for these cycloadditions which propose extended transition states where large developing charge separations will be present in the transition states and intermediates do not appear to be consistent with rate constant data for these cycloadditions which



75

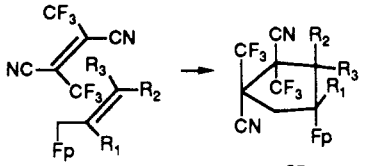
show very little solvent dependence.[20,14f] In an attempt to rationalize the known kinetic data and stereochemical outcomes of transition-metal alkynyl and allyl complex 3 + 2 cycloaddition reactions, we propose the model in Scheme XIII for predicting the major product

SCHEME XIII



of these cycloadditions. This model is similar to the one proposed by Herndon to rationalize allyl tin/electrophile cycloaddition stereochemistry.[4] Initial electrophilic attack on the transition-metal allyl or alkynyl complex occurs from a conformation where the transition metal–carbon σ bond eclipses the p orbitals in the double or triple bond (**76** and **80**). There is ample precedent for this electrophilic attack anti to the transition metal.[14] The most favorable transition state for this electrophilic attack (which accounts for the small solvent rate dependence of these cycloadditions) places the developing negative charge in the electrophile close to the developing positive charge (Coulomb attraction)[24b] on the alkene or allene complex (**77** and **81**). When the allyl or alkynyl complexes and electrophiles are chiral or prochiral, this electrophilic attack proceeds preferentially through the least hindered transition state (R_S and R_L refer to small and large substituents on the reacting alkene). Rosenblum has shown that enolates and other prochiral nucleophiles react with Fp(alkene) cations in both inter- and intramolecular

TABLE III. Cyclization of Fp Allyls (84) with 14



84 85

	R_1	R_2	R_3	yield, %	stereoselectivity
a	H	H	H	94	97:3
b	Me	H	H	79	98:2
c	H	Me	Me	no report	84:16

reactions in a diastereoselective manner and rationalized those results in a similar way.[3,49,50] In allyl or alkynyl complex cyclizations scrambling of stereochemistry at C_5 will occur unless ring closure is fast ($k_{\text{ring closure}} > k_{\text{rotation}} = 10^9\ s^{-1}$).[21] In allyl complex cyclizations, the more electrophilic the cationic alkene complex (**78**), the faster the cyclization (less scrambling of C_5 stereochemistry). In alkynyl complex cyclizations, where geometric constraints are critical, a more electrophilic allenyl complex (**82**) (less back-bonding from L_nM) will have a larger C(1)–C(2)–C(3) bond angle which will retard cyclization (more scrambling of C_5 stereochemistry). Recall that the Fp alkynyl cyclizations with **14** mentioned earlier were much more stereoselective than the cyclizations of the $Mn(CO)_5$ alkynyl complexes.[14f] Rate constants for ring closure in alkynyl complex cyclizations that are significantly greater than those for allyl complex cyclizations would be consistent with the failure to observe allene complex intermediates (**82**).

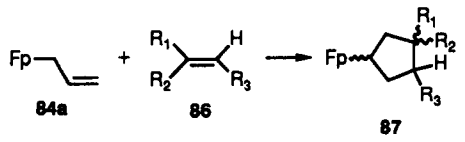
C. Transition-Metal Allyl Complex Cycloaddition Results and Mechanistic Implications

1. Cycloaddition Reactions of Nonheteroatom-Substituted Allyls

Before discussing transition-metal allyl complex 3 + 2 cycloaddition results which have appeared since 1980, a brief review of the allyl cyclizations with **14** mentioned earlier with respect to alkynyl complexes seems in order.[14f] These allyl complex cycloadditions were more stereoselective than the alkynyl cycloadditions and in the one case (entry c, Table III) where preference for facial attack on the alkene can be judged, the major diastereomer (**85c**) (84:16) can be rationalized through a transition state which places the large CF_3 group[51] away from $FpCH_2$.

Wojcicki's 1981 study on cycloaddition rates with TSI (**18**) contained results for allyl complex cycloadditions not mentioned earlier.[22] Complexes with *Z* stereochemistry in the allyl fragment were found to undergo cycloaddition twice as fast as those with *E* stereochemistry. This would be expected for cycloaddition with alkenes but is a surprising result for cycloaddition with the achiral TSI. This rate enhancement is probably caused by relief of strain in the allyl moiety rather than a rate enhancement due to less-hindered electrophile approach. Electron-donating substituents in the allyl fragment accelerated the cycloaddition although steric hindrance to cycloaddition eventually becomes a problem since trisubstituted allyls reacted about $^2/_3$ as fast as disubstituted allyls.

TABLE IV. Reaction of 84a with Electron-Deficient Alkenes 86

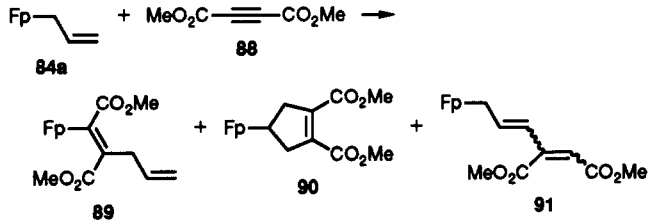


84a 86 87

	R_1	R_2	R_3	yield, %
a	CO_2Et	CN	CO_2Et	81
b	CO_2Et	CO_2Et	H	70
c	CO_2Me	CO_2Me	CO_2Me	50
d	CN	CN	CO_2Et	67
e	CO_2Me	CO_2Me	H	64

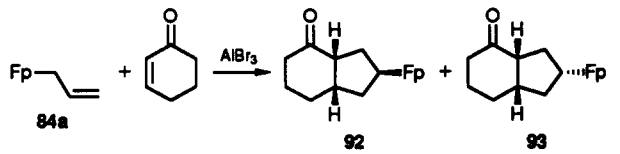
In 1982, Baker et al. reported a series of studies involving cycloaddition of Fp allyl and substituted Fp allyls with a variety of prochiral alkenes. The focus of these studies was on subsequent demetalation reactions rather than the cycloaddition and unfortunately the relative stereochemistries of the diastereomers isolated from the cycloadditions were not determined in many cases.

The first of these studies involved the cycloaddition reactions of the unsubstituted Fp allyl (**84a**).[52] The unsubstituted Fp allyl (**84a**) was treated with several ester- and cyano-substituted alkenes (**86**) and the isolated chemical yields of cycloaddition products were good (Table IV). The only information about the stereochemical outcome of these cycloadditions was that **87a** was a 1:1 mixture of diastereomers. Reaction of **84a** with dimethyl acetylenedicarboxylate yielded the cycloaddition product (**90**) (42%) as well as the zwitterion recombination or insertion product (**89**) (9%) and the proton-transfer product (**91**) (2%). This reaction was much slower than the cycloadditions with alkenes.



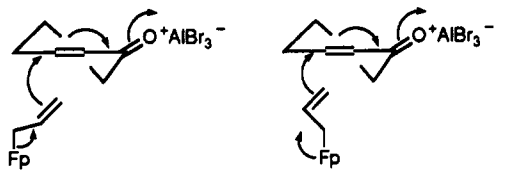
84a 88 89 90 91

Also in 1982, Rosenblum and co-workers reported the results of a series of Lewis acid catalyzed 3 + 2 cycloadditions between the unsubstituted Fp allyl (**84a**) and enones.[27] Reaction of **84a** with cyclohexenone which had been treated with $AlBr_3$ for activation led to the isolation of a 1:1 mixture of two Fp-substituted *cis*-hydrindanone products (**92** and **93**) (45%). Formation



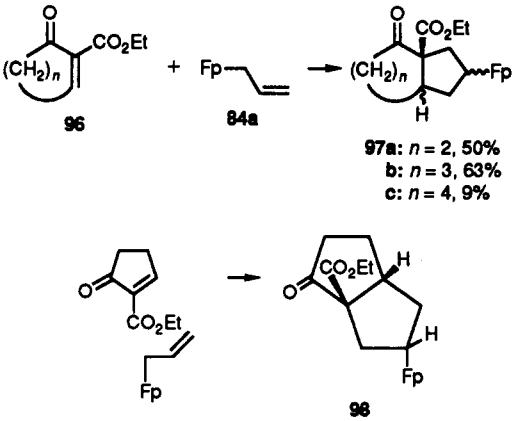
84a 92 93

of these products was explained by attack from either of the two prochiral Fp allyl faces on one prochiral face of the cyclohexenone through an extended transition state (see structures **94** and **95**). An alternative explanation for this stereochemical outcome (which is more consistent with solvent effects on these cycloadditions) would be attack on either of the two prochiral faces of cyclohexenone through an intermediate (**78**) without such large charge separation.



94 95

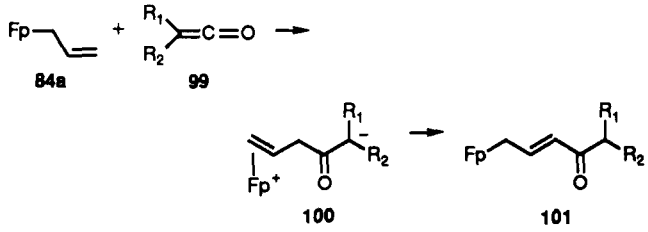
Because the yield of the cyclohexenone cycloaddition was modest and required strong Lewis acid catalysis, Rosenblum and co-workers turned their attention to cyclic enones containing an electron-withdrawing carbethoxy substituent α to the ketone. 2-Carbethoxy-2-cyclopentenone cyclized with **84a** after 24 h in refluxing CH_2Cl_2 to produce a 50% isolated yield of a single diastereomer (**97a**) with cis ring junction stereochemistry. The stereochemistry at the carbon α to iron was not specified but the model proposed earlier for these cycloadditions would predict **98** to be the product. **84b** also cyclized with **96a** to produce a 45% yield of a single diastereomer of unspecified stereochemistry. The model proposed here would predict it to have the same relative stereochemistry as **98**. 2-Carbethoxy-2-cyclohexenone (**96b**) cyclized with **84a** to give two diastereomers (**97b**); however, the relative amounts of each were unreported. They were apparently mistakenly assigned *trans*-hydrindanone structures since subsequent cleavage reactions reportedly yielded *cis*-hydrindanone products. The more puckered cyclohexenone structure would account for less steric differentiation between the ring and the carbethoxy group in the transition state leading to cyclization and yield a mixture of diastereomers. This cycloaddition was found to be very sensitive to steric and electronic effects as more highly substituted enones and Fp allyls failed to cyclize as did the 2-methoxy-substituted Fp allyl.



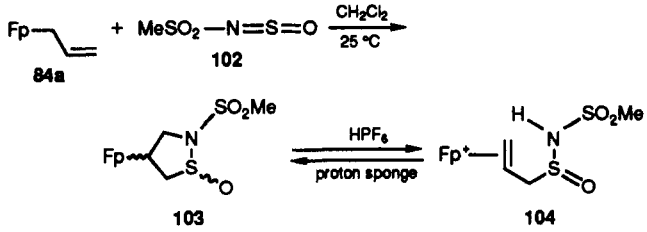
96 84a 97a: n = 2, 50% b: n = 3, 63% c: n = 4, 9% 98

Attempts to synthesize Fp-substituted cyclopentanones via 3 + 2 cycloaddition between **84a** and ketenes failed and instead yielded proton transfer products (**101**). These proton-transfer reactions apparently only become competitive with cyclization when the intermediate carbanion is only stabilized by one adjacent electron-withdrawing group. Since these proton-transfer reactions are probably intermolecular, running the reactions under high dilution conditions may yield cycloaddition products. Alternatively, since cyclohexenone gave cyclization rather than proton-transfer products when used in conjunction with a Lewis acid, ketenes may cyclize with allyls when pretreated with a Lewis acid. The Lewis acid may stabilize

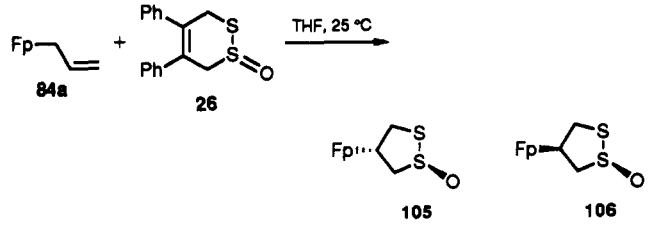
the intermediate anion enough to allow cyclization to become competitive with proton transfer.



In 1983, Wojcicki and co-workers reported a diastereoselective cyclization of **84a** with $MeSO_2NSO$ (**102**) which produced **103** in 66% yield as a 78:22 mixture of diastereomers.[53] The relative stereochemistry of the major diastereomer was undefined. When **103** was treated with HPF_6, cationic alkene complex **104** was isolated in 87% yield.[54] When **104** was treated with proton sponge in THF at −78 °C, **103** was regenerated in 57% isolated yield as a 95:5 mixture of diastereomers. This experiment provides more evidence for cationic alkene complexes as intermediates in these cycloadditions and also demonstrates the possible effect of temperature on the diastereoselectivity of these cycloadditions.

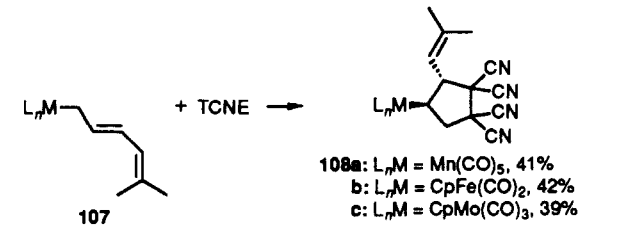


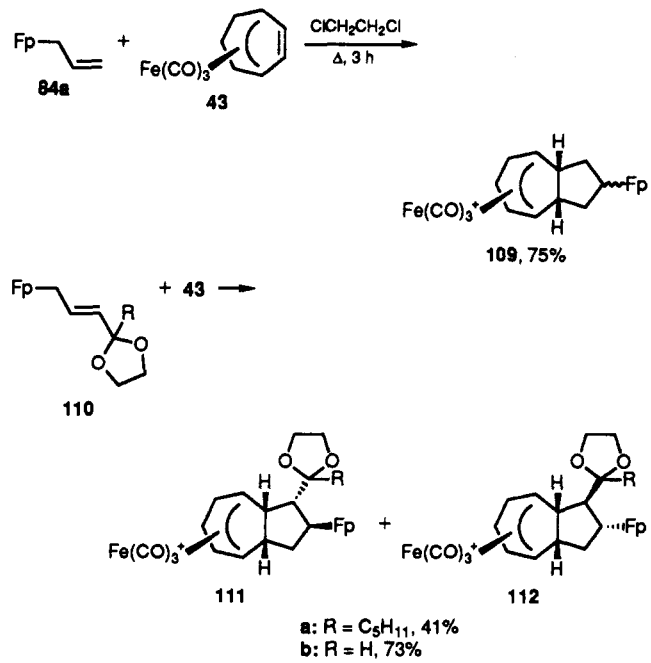
In chemistry related to this, we have found that **84a** reacts with **26** to yield **105** and **106** in 65% yield as a 8:1 (**105**:**106**) mixture of diastereomers.[55] The assignment of relative positions of Fp and O in **105** was based on ^1H NMR coupling constants, NOE experiments, and shift reagent experiments.[37] In light of this information, it would not be surprising if the major diastereomer of **103** also had an anti orientation of Fp and O.



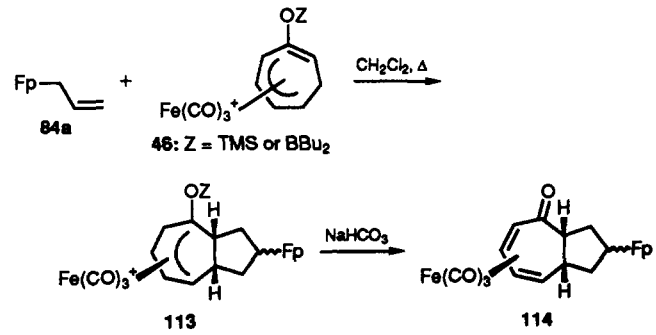
In 1989, Liu and co-workers reported an unusual 3 + 2 cycloaddition reaction between transition-metal η^1-5-methyl-2,4-hexadien-1-yl complexes (**107**) and tetracyanoethylene.[56] Pentadienyl complexes gave 4 + 2 cycloaddition products with TCNE, indicating that the additional alkene substituent present in **107** has rendered 3 + 2 cycloaddition the major reaction pathway. These 3 + 2 cycloadditions were diastereoselective in that the stereochemistry of the transition-metal allyl fragment was retained in the products (**108**).

Fp allyls have been shown to react with a variety of tropylium iron tricarbonyl salts providing an organometallic route to hydroazulene synthesis.[34,35] In the original communication on this work,[34] **84a** was treated with unsubstituted tropylium iron tricarbonyl cation (**43**) to yield **109** as a mixture of epimers at the carbon α to iron. Complexes **109** had the expected cis ring junction stereochemistry (H's syn to $Fe(CO)_3$. The diastereomeric ratio for **109** was unreported and this cyclization would not be expected to be particularly diastereoselective. Acetal- and ketal-substituted allyls (**110**) cyclized with **43** to yield **111** and **112** (ratios unreported).



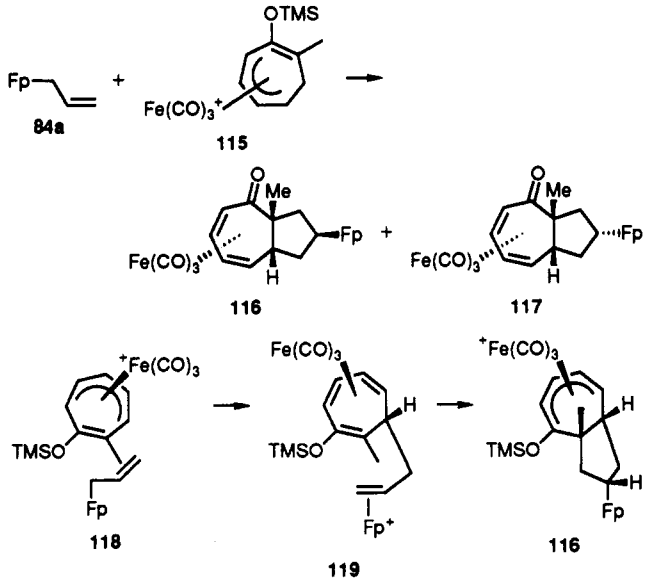


Reaction of activated tropone iron tricarbonyl complex (**46**) with **84a** followed by aqueous $NaHCO_3$ workup yielded **114** (59%) as an undefined mixture of diastereomers (epimers at the carbon α to iron).



Reactions of **84a** with substituted tropylium iron tricarbonyl cations proved to be surprisingly regioselective and in one case diastereoselective. Complex **84a** reacted with TMS-activated cation (**115**) of 2-methyltropone iron tricarbonyl to yield anti (**116**) and syn

(117) diastereomers (2.2:1, 69%). The major diastereomer (116) can be explained through reaction of 84a with 115 through the least hindered transition state (118) that places the electron-rich enol ether near the developing Fp(alkene) cation.



TMS activated 4-methyltropone iron tricarbonyl complex when treated with 84a followed by aqueous $NaHCO_3$ workup produced a cycloadduct in 45% yield as an undefined mixture of diastereomers epimeric at the carbon α to iron.

2. Cycloaddition Reactions of Heteroatom-Substituted Allyls

In 1979, Baker and co-workers first communicated an attempt to extend the scope of allyl complex 3 + 2 cycloaddition reactions by adding electron-donating substituents to the allyl ligand.[14a] The details of those investigations were published in the early 1980s in a series of papers which will be discussed in the following section. These investigations involved the cycloaddition reactions of Fp allyls with methoxy substituents in the 2 and 3 positions of the allyl. This allyl substituent increases the stereochemical complexity of any cycloaddition since an additional chiral center will be formed in the product. As a word of caution, it should be noted that Fp allyls have been reported to isomerize photochemically[26] and in one case isomerize in the presence of base.[14h] These discussions of allyl complex cycloadditions assume reactivity through the original isomer of the Fp allyl starting material. In practice, to insure this is the case, these reactions are best run in the dark in the absence of acid or base.

Reaction of the 3-methoxy-substituted allyl (120) with 86a and 86b was shown to yield separable diastereomers (121a,b and 122a,b).[57] The relative stereochemistry of each diastereomer was determined by ^1H NMR and subsequent chemical reactivity (Table V). Diastereomer 122a eliminated methanol upon attempted alumina chromatography to yield cyclopentene 123.

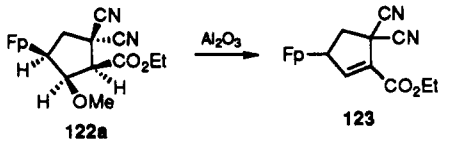
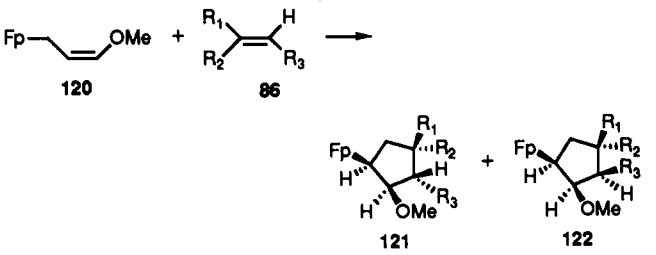


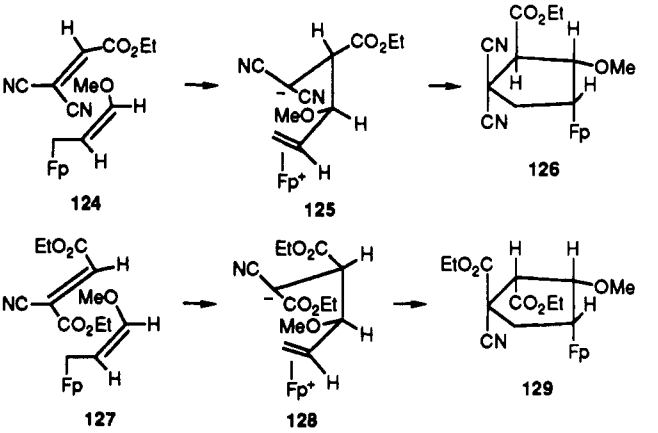
TABLE V. Reactions of 120 with 86



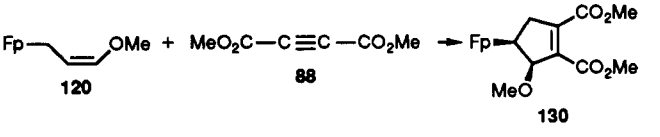
	R_1	R_2	R_3	121, %	122, %
a	CN	CN	CO_2Et	49	36
b	CO_2Et	CN	CO_2Et	33	56
c	CO_2Et	CO_2Et	H	25	
d	CO_2Me	CO_2Me	CO_2Me	16	
e	CO_2Me	CN	CO_2Me	86	

The major diastereomer of each of these cycloadditions can be rationalized through reaction of 120 with 86 through organized transition states resembling 124 and 127 (Scheme XIV) which minimize steric interactions between 120 and 86 in each case. The relative stereochemistry at the carbon bearing R_1 and R_2 was not rigorously proven for 122b, and if ring closure is rapid R_1 and R_3 should still be anti in the product (129). It would appear that $FpCH_2/CO_2Et$ steric interactions are more important than MeO/CO_2Et interactions in determining the major diastereomer formed from the reaction of 120b and 86b.

SCHEME XIV

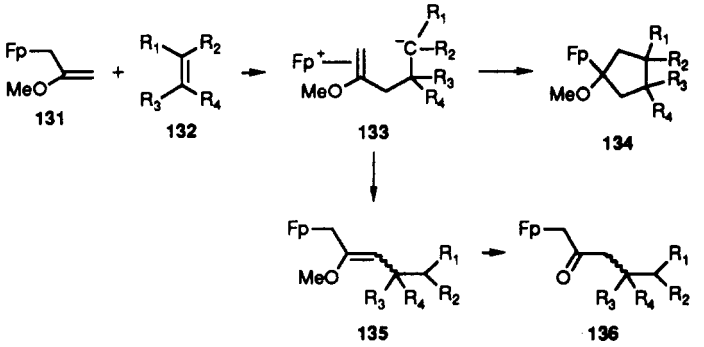


Unfortunately, the electron-donating methoxy in the 3 position of the allyl did not significantly expand the range of alkenes which could be used in this reaction. Low isolated yields of cyclopentanoid products were obtained when diethyl methylenemalonate (86c) and trimethyl ethylenetricarboxylate (86d) were used in the cycloaddition. Complex 120 reacted with 86e to yield 121/122 (86%) as an unspecified mixture of diastereomers. This mixture (121e/122e) was subsequently used in a formal total synthesis of sarkomycin.[58] Dimethyl acetylenedicarboxylate did cyclize with 120 to produce 130 as a single diastereomer in 77% yield.



Attempted cycloaddition reactions using the 2-methoxy-substituted allyl (131) were complicated by the

TABLE VI. Reactions of 131 with 132



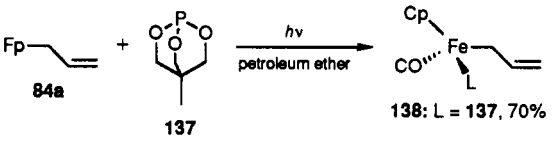
	R_1	R_2	R_3	R_4	solvent	134	135	136	yield, %
a	CO_2Me	CO_2Me	H	CO_2Me	CH_2Cl_2	41	50	9	56
					DMF	22	47	31	49
					THF	6	79	15	53
					C_6H_6	13	82	5	61
b	CN	CN	H	CO_2Et	CH_2Cl_2	100			58
c	CO_2Et	CN	H	CN	CH_2Cl_2	100			71
d	CO_2Et	CO_2Et	CO_2Et	CO_2Et	DMF			100	16
e	CO_2Me	CO_2Me	CO_2Me	CO_2Me	DMF			100	39

presence of large amounts of hydrogen-transfer products (135 and 136).[59] The 2-methoxy-substituted allyl (131) appears to be more nucleophilic than complexes 84a or 120 as evidenced by its reaction with tetracarbomethoxyethylene (Table VI, entry e) which failed to react with either 84a or 120. The alkene complex formed after nucleophilic attack (133) appears to be less electrophilic than nonheteroatom-substituted cationic alkene complexes and this allows intermolecular reactions of 133 to become competitive with cyclization. The only reactions which were clean for cyclization were with dicyanoacrylates (entries b and c, Table VI). The lack of hydrogen transfer in those cases could be accounted for by faster intramolecular cyclization of the less stable anion α to the CN rather than CO_2R.[60] Enol ether hydrolysis product (136) was formed after chromatographic purification and enol ethers (135) could be cleanly converted into ketones (136) by treatment with PTSA in aqueous THF.

3. Effects of Ligand Substitutions on Allyl Complex Cycloadditions

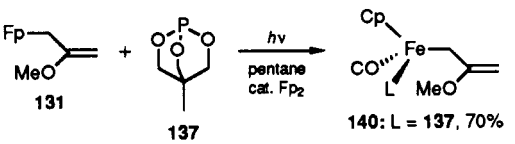
As mentioned earlier, these 3 + 2 cycloadditions have seen limited use to date by synthetic organic chemists because they require very electron deficient alkenes to obtain good yields of cycloadducts. Lewis acid activation of the alkene components and increasing the nucleophilicity of the transition-metal allyls with heteroatom substituents have met with some success. Another possible method of extending the range of alkenes that will participate in this cycloaddition is to increase the nucleophilicity of the allyls by replacing a CO ligand in the Fp complex with a σ-donor ligand such as a phosphine or phosphite. This was first reported in 1980 by Rosenblum and co-workers[61] and has subsequently been extended by Baker.[62] Replacement of CO by a phosphine or phosphite also introduces additional stereochemical complexity to these cycloadditions since the transition metal becomes a chiral center after ligand substitution. The $CpFe(CO)(PR_3)$ moiety's ability to influence the stereochemistry of chiral centers formed in its vicinity could prove helpful in these 3 + 2 cycloadditions.[41c,63]

Rosenblum and co-workers reported the synthesis of the triphenyl phosphite, trimethyl phosphite, and 4-methyl-2,6,7-trioxa-1-phosphabicyclo[2.2.2]octane (137) iron complexes (138).[61] They chose to concentrate their efforts on reactivity studies of the bicyclic phosphite complex (138) because it had the highest thermal stability.

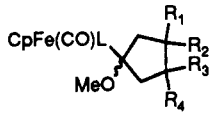


Complex 138 reacted rapidly with tetracyanoethylene at −78 °C to form cycloadduct 139a in 95% yield. Complex 138 reacted with dicyanostyrene (132g) 900 times faster than 84a to afford a single diastereomer(?) (one ^1H NMR Cp resonance reported) (139g) of unspecified stereochemistry (89%). Complex 84a failed to react with (ethoxymethylene)malononitrile (132h), whereas 138 reacted with 132h to produce 139h (85%) as a single diastereomer(?) (one ^1H NMR Cp resonance reported) of unspecified stereochemistry (Table VII). Use of ligand 137 greatly increased the nucleophilicity of the allyl complexes although its ability to influence the stereochemical outcome of these cycloadditions remains unexplored.

In 1983, Baker et al. reported the reaction of the 2-methoxy-substituted allyl (131) with bulky phosphite (137) to yield chiral racemic allyl complex (140) (70%).[62]



Unlike 131, 140 reacted with a variety of electron-deficient alkenes via a 3 + 2 cycloaddition to produce transition-metal-substituted cyclopentenes (141/142) (Table VIII). Linear hydrogen transfer products were minor products if isolated at all. Elimination of methanol from presumed intermediate (143) occurred in all cases. Where R_1 and R_2 differed substantially

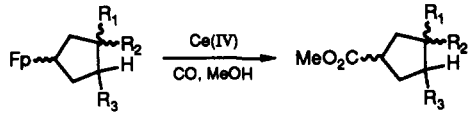


143

in electron-withdrawing ability from R_3 and R_4, elimination occurred exclusively via the more acidic methylene in **143** (Table VIII). Cationic alkene intermediates formed here would be more stable (increased back-bonding) and less electrophilic than Fp(alkene) cations and yet the products here are those of cyclization rather than proton transfer. If proton-transfer products arise via an intermolecular reaction, then this is probably just a steric effect where the bulky phosphite ligand retards proton transfer and cyclization becomes the major reaction pathway. Additionally, with this phosphite the pK_a of protons α to the alkene in cationic alkene complexes increases by 9 relative to the Fp complexes and this would also retard proton transfer.[61]

D. Demetalation Reactions

Baker and co-workers investigated a variety of methods (oxidative carboxylation, acid cleavage, bromination, and β-hydride abstraction) for the removal of functionalized cyclopentanes and cyclopentenes from the transition metals. The cycloaddition products (**87**) of the unsubstituted Fp allyl underwent oxidative carboxylation cleanly overnight at 25 °C under 1 atm of CO in methanol to yield carbomethoxy-substituted cyclopentanes (**144**) in 60–90% yield.[52]

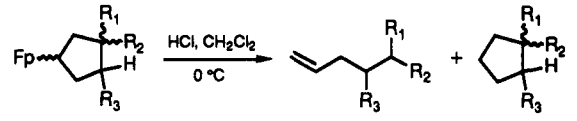


87 144

from **87a** 60%
from **87b** 62%
from **87c** 63%
from **87d** 77%

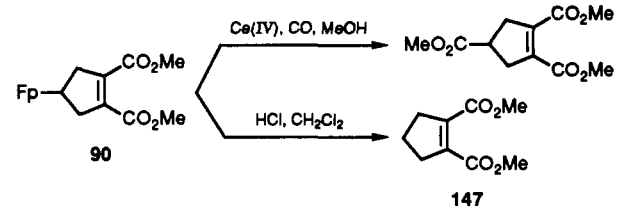
Acid cleavage of the Fp group from **87** was not as clean. The ring-opened product (**145**) was isolated from **87b** as the sole product, and **87a** and **87c** gave mixtures of ring-opened products (**145**) as well as cyclopentanes (**146**). The products from **87a** and **87c** where some cyclopentane-containing products were isolated contain an additional electron-withdrawing group (R_3 = CO_2R). Since the ring-opening reaction is probably initiated by protonation of an ester carbonyl, the introduction of an additional electron-withdrawing group would be expected to slow this process. Cyclopentenes (**147**) were isolated from oxidative carboxylation (87%) and acid cleavage (75%) of **90**.

Bromination of **87** with pyridinium bromide perbromide yielded a diastereomeric mixture of cyclopentyl bromides (**148**) and a mixture of cyclopentenes (**149**). From these experiments it is not possible to determine whether the cyclopentenes are a product of elimination from the bromides or whether they originate via β-hydride elimination from the oxidized Fe(III) species which is presumably an intermediate in this reaction.

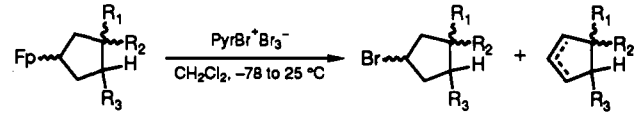


87 145 146

145:146
from **87a** 1:2 60%
from **87b** 1:0 67%
from **87c** 1:1 70%



90 147

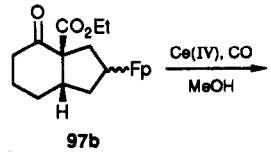


87 148 149

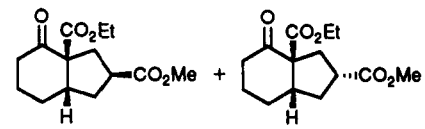
148:149
from **87a** 3:2 32%
from **87b** 13:7 85%
from **87c** 3:1 43%

Attempts to liberate a substituted cyclopentene via trityl cation treatment induced β-hydride abstraction followed by sodium iodide alkene displacement were unsuccessful. Instead the ring-opened product (**145b**) (from **87b**) was isolated in 51% yield. This product (**145b**) is presumably also formed as a result of initial electrophilic attack at the ester carbonyl.

Rosenblum and co-workers reported one example of an oxidative carboxylation in conjunction with their studies aimed at synthesis of the *cis*-hydrindanone nucleus.[27] When a mixture of diastereomers of Fp complex **97b** was treated with ceric ammonium nitrate in methanol, methyl esters **150** and **151** were isolated in 62% yield with no mention of the relative amounts of each diastereomer.



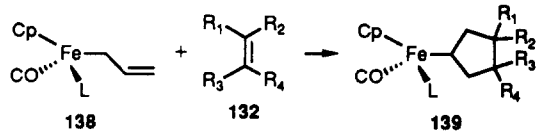
97b



150 151

A variety of transformations of hydroazulene complex (**109**) have been reported.[34] Treatment of **109** with $NaBH_4$ to produce neutral diene complex (**152**) (78%) followed by oxidative carboxylation yielded methyl ester (**153**) (61%). Treatment of **109** with bromine resulted in replacement of the Fp group with Br (62%) (**154**) while leaving the $Fe(CO)_3$ fragment unchanged. Re-

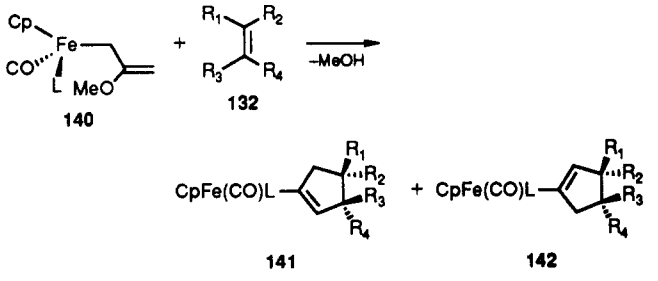
TABLE VII. Reactions of 138 with 132



138 132 139

	R_1	R_2	R_3	R_4	139, %
f	CN	CN	CN	CN	95
g	CN	CN	H	Ph	89
h	CN	CN	H	OEt	85

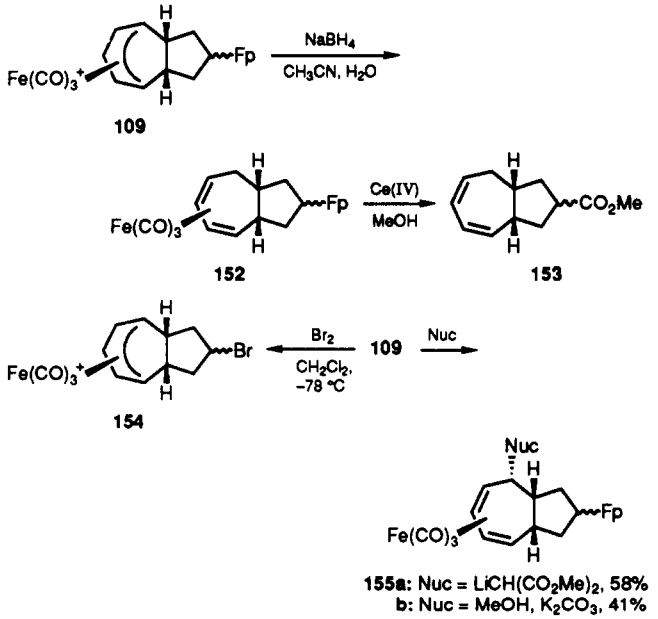
TABLE VIII. Reactions of 140 with 132



140 132 141 142

	R_1	R_2	R_3	R_4	yield, %	141/142
i	CO_2Me	CO_2Me	H	CO_2Me	75	1/1
j	CO_2Me	CN	H	CO_2Me	33	1/1
k	CO_2Et	CN	H	$CH_2CH(S(CH_2)_3S)$	52	0/1
l	CN	CN	H	CO_2Et	70	0/1
m	CN	CN	H	Ph	98	1/1

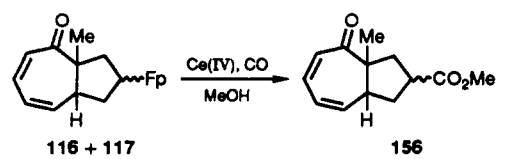
action of **109** with nucleophiles yielded neutral diene substitution products (**155**) with the nucleophile and $Fe(CO)_3$ on opposite sides of the hydroazulene framework.



109 152 153 154

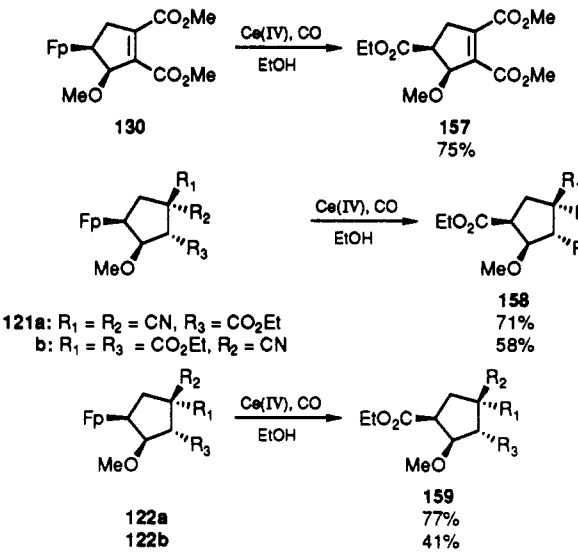
155a: Nuc = $LiCH(CO_2Me)_2$, 58%
b: Nuc = MeOH, K_2CO_3, 41%

In conjunction with their investigation of a synthetic organometallic route to the guaiazulene and guaianolide frameworks, Rosenblum and co-workers[35b,c] reported that the oxidative carboxylation of a mixture of **116** and **117** in methanol produced dienone ester (**156**) as a mixture of diastereomers in 82% yield.



116 + 117 156

Methoxy-substituted cyclopentanoids synthesized by Baker and co-workers were demetalated under a variety of conditions.[57] Oxidative carboxylation of **130** produced cyclopentene **157** and similar treatment of complexes **121** and **122** yielded highly functionalized cyclopentanes (**158** and **159**).



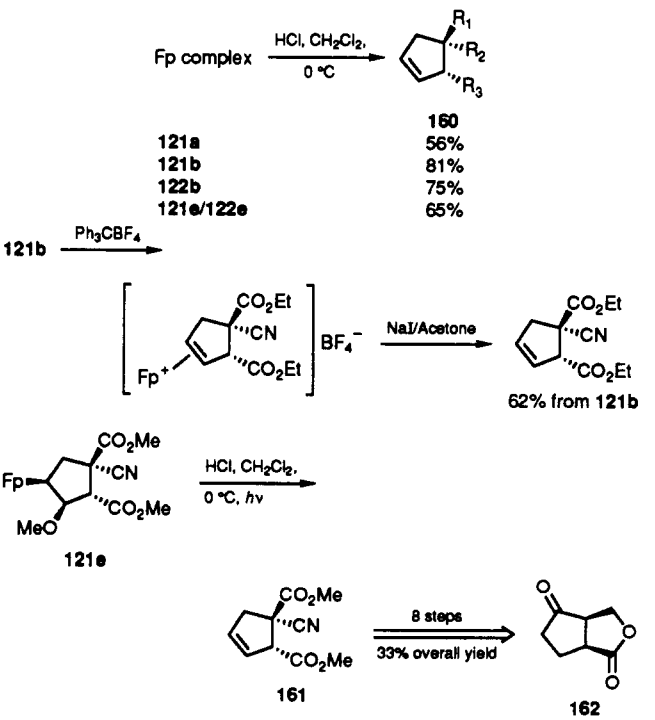
130 157 75%

121a: $R_1 = R_2 = CN$, $R_3 = CO_2Et$
b: $R_1 = R_3 = CO_2Et$, $R_2 = CN$

158 71% 58%

122a 122b 159 77% 41%

Acid treatment of complexes **121** and **122** yielded cyclopentenes (**160**) in high yield as did treatment of **121b** with trityl cation followed by NaI in acetone. Cyclopentene **161** was subsequently converted (8 steps, 33% overall yield) to the keto lactone precursor (**162**) to the antitumor agent sarkomycin.[58]



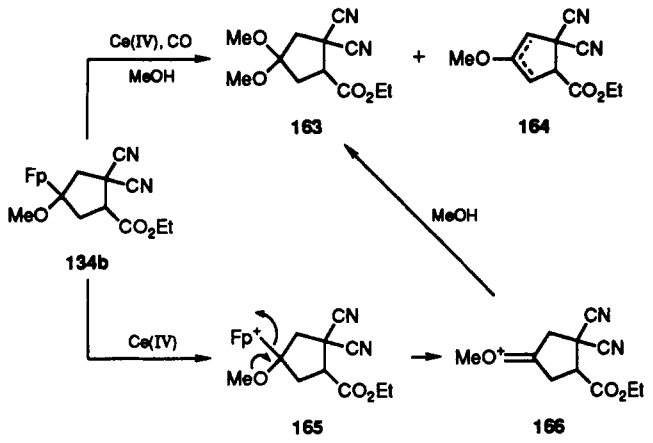
160

121a	56%
121b	81%
122b	75%
121e/122e	65%

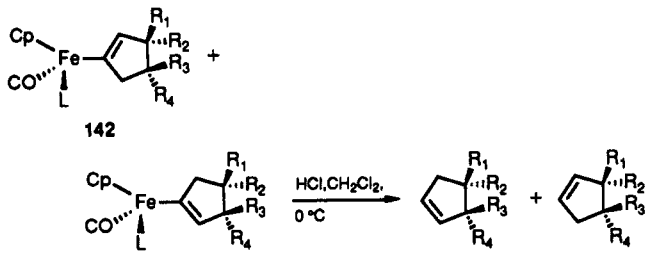
62% from 121b

121e 161 162

Attempted oxidative carboxylation of complex **134b** led to the isolation of ketal (**163**) in addition to enol ethers (**164**) (9:1, 92%).[59] This is a very unusual reaction because Fe–C bond cleavage has occurred without CO insertion. Iron–carbon bond cleavage before CO insertion could be facilitated by electron donation from the heteroatom on the carbon α to iron (**165**).



Lastly, chiral iron-substituted cyclopentenes (141/142) have been converted into cyclopentenes 167 and 168 under mild conditions in good yield.[62]



141/142l	1	1	48%
141j	1	0	84%
142j	0	1	72%
142k	0	1	46%
142l	0	1	60%
141/142m	1	1	81%

V. Summary

In the last 10 years good progress has been made in extending the scope of transition-metal-mediated 3 + 2 cycloaddition reactions. For these reactions to attract more attention from synthetic organic chemists the diastereoselectivities of these cycloadditions must be increased significantly. If the nonextended transition state model for this cycloaddition is correct, diastereoselectivities should increase if the steric requirements of groups in either the transition-metal allyl/alkynyl fragment or the alkene increase. The best hope for extending the range of alkenes which will participate in this cycloaddition seems to be increasing the nucleophilicity of the transition-metal allyl/alkynyl fragment. The use of stable, crystalline, chiral CpFe(CO)(L)(R) (R = allyl or 2-alkynyl ligand) complexes could enhance the diastereoselectivity of these cycloadditions as well as extend the range of alkenes which will participate.[41c,63] That chemistry remains to be explored. More attention should also be focused on developing new methods for removing the cyclopentanes formed from these cycloaddition reactions from the transition-metal fragment under nonoxidative reaction conditions.

Acknowledgments. I am grateful for the help of my co-workers who are in large part responsible for the success of our work in this area and whose names appear in the references. The Research Corporation, the North Carolina Board of Science and Technology, the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the National Science Foundation (Grant No. CHE 8817985 and Chemical Instrumentation Grant No. CHE-9007366) have generously supported our efforts in transition-metal-mediated organic chemistry.

VI. References

(1) Wojcicki, A. *Fundamental Research in Organometallic Chemistry*; Tsutsui, M., Ishii, Y., Yaozeng, H.; Eds.; Van Nostrand Rheinhold Co.: New York, 1982; pp 569–597.
(2) Wojcicki, A. *Coord. Chem. Rev.* **1990**, *105*, 35.
(3) Rosenblum, M. *J. Organometal. Chem.* **1986**, *300*, 191.
(4) Herndon, J. W.; Wu, C.; Harp, J. J.; Kreuzer, K. A. *SYNLETT* **1991**, *2*, 1.
(5) (a) Hartman, F. A.; Pollick, P. J.; Downs, R. L.; Wojcicki, A. *J. Am. Chem. Soc.* **1967**, *89*, 2493. (b) Hartman, F. A.; Wojcicki, A. *Inorg. Chim. Acta* **1968**, *2*, 289.
(6) Churchill, M. R.; Wormald, J.; Ross, D. A.; Thomasson, J. E.; Wojcicki, A. *J. Am. Chem. Soc.* **1970**, *92*, 1795.
(7) Thomasson, J. E.; Wojcicki, A. *J. Am. Chem. Soc.* **1968**, *90*, 2709.
(8) Roustan, J.-L.; Charrier, C. *C.R. Acad. Sci. Ser. C* **1969**, *268*, 2113.
(9) Churchill, M. R.; Wormald, J. *J. Am. Chem. Soc.* **1971**, *93*, 354.
(10) Wojcicki, A. *Acc. Chem. Res.* **1971**, *4*, 344.
(11) Bannister, W. D.; Booth, B. L.; Haszeldine, R. N.; Loader, P. L. *J. Chem. Soc. (A)* **1971**, 930.
(12) Giering, W. P.; Rosenblum, M. *J. Am. Chem. Soc.* **1971**, *93*, 5299.
(13) Rosenblum, M. *Acc. Chem. Res.* **1974**, *7*, 122.
(14) (a) Abram, T. S.; Baker, R. *J. Chem. Soc., Chem. Commun.* **1979**, 267. (b) Abram, T. S.; Baker, R. *Synth. React. Inorg. Met.-Org. Chem.* **1979**, *9*, 471. (c) Chen, L. S.; Su, S. R.; Wojcicki, A. *Inorg. Chim. Acta* **1978**, *27*, 79. (d) Downs, R. L.; Wojcicki, A. *Inorg. Chim. Acta* **1978**, *27*, 91. (e) Cooksey, C. J.; Dodd, D.; Johnson, M. D.; Lockman, B. L. *J. Chem. Soc., Dalton Trans.* **1978**, 1814. (f) Williams, J. P. Wojcicki, A. *Inorg. Chem.* **1977**, *16*, 3116. (g) Chen, L. S.; Lichtenberg, D. W.; Robinson, P. W.; Yamamoto, Y.; Wojcicki, A. *Inorg. Chim. Acta* **1977**, *25*, 165. (h) Cutler, A.; Ehntholt, D.; Giering, W. P.; Lennon, P.; Raghu, S.; Rosan, A.; Rosenblum, M.; Tancrede, J.; Wells, D. *J. Am. Chem. Soc.* **1976**, *98*, 3495. (i) Cutler, A.; Ehntholt, D.; Lennon, P.; Nicholas, K.; Marten, D. F.; Madhavarao, M.; Raghu, S.; Rosan, A.; Rosenblum, M. *J. Am. Chem. Soc.* **1975**, *97*, 3149. (j) Chen, L. S.; Su, S. R.; Wojcicki, A. *J. Am. Chem. Soc.* **1974**, *96*, 5655. (k) Wojcicki, A. *Adv. Organomet. Chem.* **1974**, *12*, 31. (l) Wojcicki, A. *Ann. N.Y. Acad. Sci.* **1974**, *239*, 100.
(15) (a) Roustan, J.-L.; Cadiot, P. *C.R. Acad. Sci. Ser. C* **1969**, *268*, 734. (b) Thomasson, J. E.; Robinson, P. W.; Ross, D. A.; Wojcicki, A. *Inorg. Chem.* **1971**, *10*, 2130.
(16) Raseta, M. E.; Mishra, R. K.; Cawood, S. A.; Welker, M. E.; Rheingold, A. L. *Organometallics* **1991**, *10*, 2936.
(17) (a) Johnson, M. D.; Mayle, C. *J. Chem. Soc., Chem. Commun.* **1969**, 192. (b) Foxman, B.; Marten, D.; Rosan, A.; Raghu, S.; Rosenblum, M. *J. Am. Chem. Soc.* **1977**, *99*, 2160. (c) Cooksey, C. J.; Dodd, D.; Johnson, M. D.; Lockman, B. L. *J. Chem. Soc., Dalton Trans.* **1978**, 1814.
(18) (a) Lichtenberg, D. W.; Wojcicki, A. *J. Organometal. Chem.* **1975**, *94*, 311. (b) Klemarczyk, P.; Rosenblum, M. *J. Org. Chem.* **1978**, *43*, 3488.
(19) (a) Giering, W. P.; Rosenblum, M. *J. Organometal. Chem.* **1970**, *25*, C71. (b) Giering, W. P.; Rosenblum, M. *J. Chem. Soc., Chem. Commun.* **1971**, 441. (c) Laycock, D. E.; Hartgerink, J.; Baird, M. C. *J. Org. Chem.* **1980**, *45*, 291.
(20) Su, S. R.; Wojcicki, A. *Inorg. Chim. Acta* **1974**, *8*, 55.
(21) Proskow, S.; Simmons, H. E.; Cairns, T. L. *J. Am. Chem. Soc.* **1966**, *88*, 5254.
(22) Bell, P. B.; Wojcicki, A. *Inorg. Chem.* **1981**, *20*, 1585.
(23) Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 2nd ed.; Harper & Row: New York, 1981; p 848.
(24) Reviews: (a) Gompper, R. *Angew. Chem., Intl. Ed. Engl.* **1969**, *8*, 312. (b) Huisgen, R. *Acc. Chem. Res.* **1977**, *10*, 117.
(25) (a) Bartlett, P. D. *Q. Rev. Chem. Soc.* **1970**, *24*, 473. (b) Bartlett, P. D. *Pure Appl. Chem.* **1971**, *27*, 597. (c) Bruce, M. I.; Hambley, T. W.; Snow, M. R.; Swincer, H. G. *Organometallics* **1985**, *4*, 494; 501.
(26) Fabian, B. D.; Labinger, J. A. *J. Am. Chem. Soc.* **1979**, *101*, 2239.
(27) Bucheister, A.; Klemarczyk, P.; Rosenblum, M. *Organometallics* **1982**, *1*, 1679.
(28) Ungvary, F.; Wojcicki, A. *J. Organometal. Chem.* **1990**, *396*, 95.
(29) Raseta, M. E.; Cawood, S. A.; Welker, M. E.; Rheingold, A. L. *J. Am. Chem. Soc.* **1989**, *111*, 8268.
(30) (a) Urove, G. A.; Welker, M. E. *Organometallics* **1988**, *7*, 1013. (b) Urove, G. A.; Welker, M. E.; Eaton, B. E. *J. Organometal. Chem.* **1990**, *384*, 105. (c) Brown, D. S.; Owens, C. F.; Wilson,

B. G.; Welker, M. E.; Rheingold, A. L. *Organometallics* **1991**, *10*, 871. (d) Powell, K. R.; Elias, W. J.; Welker, M. E. *J. Organometal. Chem.* **1991**, *407*, 81.
(31) Juaristi, E.; Cruz-Sanchez, J. S. *J. Org. Chem.* **1988**, *53*, 3334 and references therein.
(32) Mikolaczyk, M.; Drabowicz, J. *Top. Stereochem.* **1982**, *13*, 333.
(33) For related examples of metal carbonyl binding, see: Ozin, G. A.; Gil, C. *Chem. Rev.* **1989**, *89*, 1749.
(34) Genco, N.; Morten, D.; Raghu, S.; Rosenblum, M. *J. Am. Chem. Soc.* **1976**, *98*, 848.
(35) (a) Watkins, J. C.; Rosenblum, M. *Tetrahedron Lett.* **1984**, *25*, 2097. (b) Watkins, J. C.; Rosenblum, M. *Tetrahedron Lett.* **1985**, *26*, 3531. (c) Rosenblum, M.; Watkins, J. C. *J. Am. Chem. Soc.* **1990**, *112*, 6316.
(36) Pearson, A. J. *Acc. Chem. Res.* **1980**, *13*, 463.
(37) Yanagawa, H.; Kato, T.; Kitahara, Y. *Tetrahedron Lett.* **1973**, 1073.
(38) Kato, A.; Numata, M. *Tetrahedron Lett.* **1972**, 203.
(39) For a review on the chemistry and biological activities of thiosulfinate esters, see: Isenberg, N.; Grdinic, M. *Int. J. Sulfur Chem.* **1973**, *8*, 307.
(40) For a review on the oxidation, rearrangement, and disproportionation of related organosulfur compounds, see: Freeman, F. *Chem. Rev.* **1984**, *84*, 117.
(41) For some recent relevant examples and a review (41d), see: (a) Barrett, A. G. M.; Mortier, J.; Sabat, M.; Sturgess, M. A. *Organometallics* **1988**, *7*, 2553. (b) Reger, D. L.; Klaeren, S. A.; Babin, J. E.; Adams, R. D. *Organometallics* **1988**, *7*, 181. (c) Liebeskind, L. S.; Welker, M. E.; Fengl, R. W. *J. Am. Chem. Soc.* **1986**, *108*, 6328. (d) Johnson, M. D. *Acc. Chem. Res.* **1978**, *11*, 57.
(42) Reger, D. L.; Mintz, E.; Lebioda, L. *J. Am. Chem. Soc.* **1986**, *108*, 1940.
(43) Green, M. L. H.; Nagy, P. L. I. *J. Chem. Soc.* **1963**, 189.
(44) (a) Green, M. L. H.; Ishaq, M.; Mole, T. *Z. Naturforsch., B* **1965**, *208*, 598. (b) Green, M. L. H.; Mole, T. *J. Organometal. Chem.* **1968**, *12*, 404. (c) Kremer, K. A. M.; Kuo, G.-H.; O'Connor, E. J.; Helquist, P.; Keiber, R. C. *J. Am. Chem. Soc.* **1982**, *104*, 6119. (d) Belmont, J. A.; Wrighton, M. S. *Organometallics* **1986**, *5*, 1421.
(45) (a) Yates, K.; Schmid, G. H.; Regulski, T. W.; Garratt, D. G.; Leung, H.-W.; McDonald, R. *J. Am. Chem. Soc.* **1973**, *95*, 160. (b) Freeman, F. *Chem. Rev.* **1975**, *75*, 439. (c) Noyce, D. S.; Schiavelli, M. D. *J. Am. Chem. Soc.* **1968**, *90*, 1020.
(46) Lennon, P.; Madhavarao, M.; Rosan, A.; Rosenblum, M. *J. Organomet. Chem.* **1976**, *108*, 93.
(47) Foxman, B. M. *J. Chem. Soc., Chem. Commun.* **1975**, 221.
(48) Laycock, D. E.; Baird, M. C. *Inorg. Chim. Acta* **1980**, *42*, 263.
(49) Rosenblum, M.; Chang, T. C. T.; Foxman, B. M.; Samuels, S. B.; Stockman, C. *Organic Synthesis Today and Tomorrow*; Trost, B. M., Hutchinson, C. R., Eds.; Pergamon Press: New York, 1981; pp 47–54.
(50) (a) Lennon, P. J.; Rosan, A.; Rosenblum, M.; Tancrede, J.; Waterman, P. *J. Am. Chem. Soc.* **1980**, *102*, 7033. (b) Chang, T. C. T.; Rosenblum, M.; Samuels, S. B. *J. Am. Chem. Soc.* **1980**, *102*, 5930. (c) Chang, T. C. T.; Rosenblum, M. *J. Org. Chem.* **1981**, *46*, 4103.
(51) Exner, O. *Correlation Analysis in Chemistry, Recent Advances*; Chapman, N. B., Shorter, J., Eds.; Plenum Publishing: New York, 1978; pp 530–531.
(52) Abram, T. S.; Baker, R.; Exon, C. M.; Rao, V. B. *J. Chem. Soc., Perkin Trans. 1*, **1982**, 285.
(53) Leung, T. W.; Christoph, G. G.; Wojcicki, A. *Inorg. Chim. Acta* **1983**, *76*, L281.
(54) Hu, Y.-R.; Leung, T. W.; Su, S.-C. H.; Wojcicki, A.; Calligaris, M.; Nardin, G. *Organometallics* **1985**, *4*, 1001.
(55) Mishra, R. K. M.S. Thesis, Wake Forest University, 1990.
(56) Lee, G.-H.; Peng, S.-M.; Yang, G.-M.; Lush, S.-F.; Liu, R.-S. *Organometallics* **1989**, *8*, 1106.
(57) Baker, R.; Exon, C. M.; Rao, V. B.; Turner, R. W. *J. Chem. Soc., Perkin Trans. 1*, **1982**, 295.
(58) Baker, R.; Keen, R. B.; Morris, M. D.; Turner, R. W. *J. Chem. Soc., Chem. Commun.* **1984**, 987.
(59) Abram, T. S.; Baker, R.; Exon, C. M.; Rao, V. B.; Turner, R. W. *J. Chem. Soc., Perkin Trans. 1*, **1982**, 301.
(60) Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456.
(61) Rosenblum, M.; Waterman, P. S. *J. Organomet. Chem.* **1980**, *187*, 267.
(62) Baker, R.; Rao, V. B.; Erdik, E. *J. Organomet. Chem.* **1983**, *243*, 451.
(63) Davies, S. G. *Aldrichimica Acta* **1990**, *23*, 31 and references therein.