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Catalytic Methods for Metal Carbene Transformations

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Contents

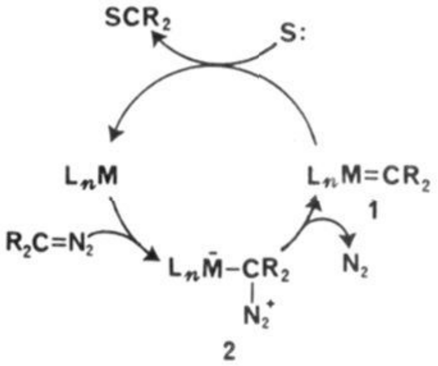
Michael P. Doyle was born in Minneapolis, MN. He received his Bachelor's degree from the College of St. Thomas in 1964 and his Ph.D. from Iowa State University in 1968, where he worked under the direction of Professor Walter S. Trahanovsky. Following a relatively brief postdoctoral engagement with Professor Jan Rocek at the University of Illinois at Chicago Circle, he joined the faculty at Hope College in 1968. In 1984 he moved to Trinity University as the Dr. D. R. Semmes Distinguished Professor of Chemistry. He is the recipient of a Dreyfus Foundation Teacher–Scholar Award (1973) and a Chemical Manufacturers Association Catalyst Award (1982). His research interests include catalytic processes in carbene chemistry and their use in the development of new synthetic methods, chemical and biochemical transformations of nitrogen oxides and dinitrogen compounds, and oxidation–reduction reactions.

I. Introduction

The synthetic uses of organic diazo compounds for carbenoid transformations have undergone a renaissance in recent years as a result of the development of new transition-metal catalysts and the design of effective strategies for their application. Catalytic methods have supplanted thermal and photochemical schemes, and efficient procedures for cyclopropanation, dipolar addition, insertion, and ylide generation have arisen. In addition, recent advances in the mechanistic understanding of transition-metal-catalyzed transformations have removed a significant amount of the voodoo that had been associated with these processes.

Originally suggested by Yates,[1] there is now general agreement that transition-metal catalysts react with diazo compounds to generate transient electrophilic metal carbenes 1. The catalytic activity of transition-metal compounds depends on coordination unsaturation at their metal center which allows them to react as electrophiles with diazo compounds. Electrophilic addition causes the loss of dinitrogen and production of a metal-stabilized carbene 1. Transfer of the carbene entity to an electron-rich substrate completes the catalytic cycle:

$$\underset{1}{L_nM{=}CR_2 \leftrightarrow L_nM^{-}{-}C^{+}R_2}$$



Catalytic methods are most effective when diazo carbonyl compounds are employed, although applications with a limited variety of less stable diazo compounds indicates their general suitability as carbenoid precursors. Alternative carbenoid sources that are synthetically useful for catalytic reactions are not currently available.

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The present review is focused on the generation and synthetic transformations of electrophilic metal carbenes that exemplify the emergence of catalytic methodologies for carbenoid transformations. Earlier reviews emphasized the chemistry of diazo carbonyl compounds,[2] and that by Marchand and MacBrockway in 1974 discussed the unique importance of metal carbenes for molecular constructions with diazo compounds.[3] Partial reviews of catalytic cyclopropanation reactions have also appeared.[4] This review is a critical survey of the literature through 1985 that is intended to identify those factors and conditions which promote effective catalysis in carbenoid transformations of diazo compounds.

II. Catalysts for Carbenoid Transformations

A. Historical Perspective

Metal catalysis in the decomposition of diazo compounds has been known for more than 80 years.[5] Insoluble copper bronze and cupric sulfate dominated their synthetic applications until the 1960s when Nozaki introduced soluble copper chelates such as bis(acetylacetonato)copper(II)[6] and Moser reported the use of soluble (trialkyl and triaryl phosphite)copper(I) catalysts.[7] The introduction of homogeneous catalysts was motivated, in part, by uncertainties with the use of insoluble copper compounds that were regarded as heterogeneous catalysts. Yates had previously suggested that metallic copper participated in the loss of dinitrogen from diazo carbonyl compounds and that the resulting carbene remained bound to the copper surface. Although the carbenoid formalism was generally accepted, the nature of the catalytically active species in these reactions continued to be controversial.[2a] Observations of induction periods,[8] changes in the physical appearance and metallic composition of reaction mixtures,[9] and carbenoid reactions with the ligands originally bound to the metal[10] provided uncertainty as to the actual identity of the catalytically active species.

In 1972 Salomon and Kochi published a benchmark article that has greatly influenced basic understanding of copper catalysis in carbenoid transformations.[11] They discovered that copper triflate (triflate = trifluoromethanesulfonate, OTf) was a very active catalyst for the cyclopropanation of olefins with diazo compounds and that diazo compounds caused reduction of copper(II) to copper(I). This latter discovery was consistent with a prior observation by Wittig and Schwarzenbach,[9a] that copper(II) chloride was reduced to copper(I) chloride by diazo compounds, which fortified their conclusion that copper(I), rather than copper(II), was the active catalyst in carbenoid transformations. However, since copper(I) triflate is relatively difficult to handle,[12] copper(II) triflate, conveniently prepared[13] and reduced in situ by diazo compounds to the copper(I) catalyst, is preferentially employed for carbenoid transformations of diazo compounds.

Between Nozaki's report of Cu(acac)$_2$ and Kochi's development of copper triflate for carbenoid reactions, a number of potentially effective homogeneous catalysts were investigated,[14] but none held synthetic advantage or the promise of unveiling unique mechanistic insight and were not advanced further. During this period, however, Nozaki, Noyori, and co-workers laid the groundwork for effective asymmetric induction in catalytic cyclopropanation reactions with their preparation and use of chiral copper chelates,[15] and Fischer and Dötz demonstrated that stable metal carbenes of chromium, molybdenum, and tungsten underwent stoichiometric carbenoid addition to olefins.[16] This latter discovery prompted extensive development of stable metal carbenes for cyclopropanation along lines that diverged naturally from those taken for their catalytic counterparts (section III.F).

Palladium(II) acetate[17] and rhodium(II) acetate[18] were introduced by Teyssie and co-workers in the early 1970s as alternatives to copper catalysts for carbenoid transformations. They are distinguished from each other by their relative ability to coordinate olefins.[19] Only recently, however, have their unique characteristics for carbenoid transformations been identified.

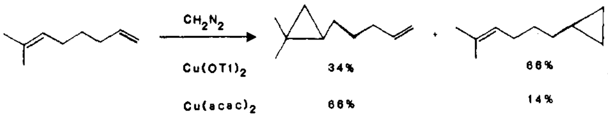
B. Catalysts That Possess More Than One Metal Coordination Site

The capability of copper(I) triflate to coordinate with alkenes[12,20] has distinguished this material from other traditionally employed copper catalysts. The rate for nitrogen loss from diazo compounds in the presence of an alkene is inversely proportional to the alkene concentration[11] which suggests that alkene dissociation precedes electrophilic addition of the catalytically active copper(I) species to the diazo compound ($n \geq 2$):

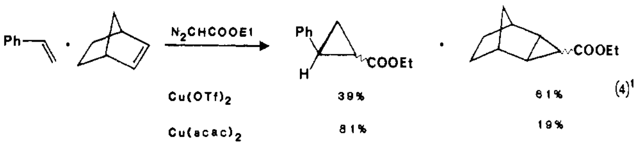
$$(R_2C{=}CR_2)_nCu^+\ {}^-OTf \rightleftharpoons (R_2C{=}CR_2)_{n-1}Cu^+\ {}^-OTf + R_2C{=}CR_2 \quad (1)$$

$$(R_2C{=}CR_2)_{n-1}Cu^+\ {}^-OTf + ZCH{=}N_2 \rightarrow (R_2C{=}CR_2)_{n-1}Cu\text{-}CH(N_2)^+Z\ TfO^- \quad (2)$$

Comparisons of selectivity in cyclopropanation[11,19] have shown that those catalysts that are capable of forming olefin complexes preferentially foster carbenoid addition at the less substituted double bond whereas those which do not form olefin complexes, like Cu(acac)$_2$, favor addition at the more substituted double bond (eq 3 and 4). However, selectivity in competitive cyclopropanation reactions with copper triflate is dependent on the molar ratio of olefins employed, and with ethyl diazoacetate and the styrene/cyclohexene combination, for example, cyclopropanation selectivity for styrene increases from 1.6 to 3.3 as the molar ratio of styrene to cyclohexene is increased from 0.25 to 2.0.[21] Differential olefin coordination of copper(I) during carbenoid addition affects reactivity, but quantitative evaluation of this influence awaits determination.



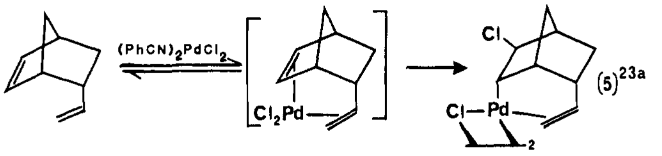
(3)[11]



(4)[19]

Palladium catalysts that are effective for carbenoid reactions include palladium(II) acetate[17,19] and palladium(II) chloride.[22,23] Their similarities as catalysts have been noted,[24] and the ability of palladium(II) compounds to form olefin complexes is well-known.[25,26]

Palladium(II) chloride undergoes Pd–Cl addition with certain dienes (eg., eq 5),[23,27] presumably from the coordinated diene 3, and this transformation complicates its use as a catalyst for carbenoid reactions. In their formation of π-complexes, palladium(II) catalysts resemble copper(I) triflate, which may account for the complimentary selectivities in cyclopropanation reactions that are observed with their use.[19] However, there are significant differences in their coordinating abilities with certain olefins, particularly with bicyclo[2.2.1]hepta-2,5-diene.[12]



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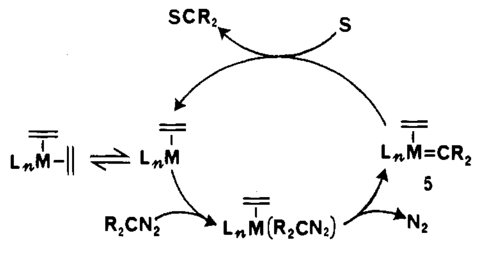
The influence of the coordinated olefin on carbenoid transfer is a fundamental characteristic of these catalysts:



M = Pd in $PdCl_2$, $Pd_3(OAc)_6$

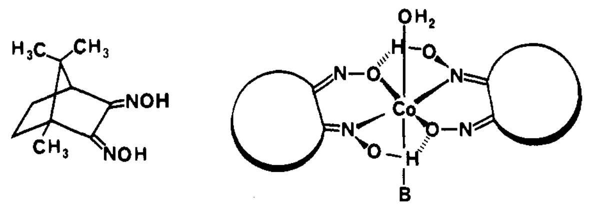
Cu in CuOTf, $CuBF_4$

Steric and/or electronic effects from the coordinated olefin affect reactivity and, in certain cases, selectivity.[22] Lewis bases can replace the coordinated olefin and influence carbenoid transfer, but they also inhibit formation of the carbenoid intermediate. Phosphine ligands on PdX_2 (X = Cl, Br, I), for example, cause a relatively long induction period for nitrogen evolution from ethyl diazoacetate.[22] Entrapment of the phosphine by the diazo compound[28] probably releases the active catalyst:

$$PdX_2(PPh_3)_2 \rightleftharpoons PdX_2(PPh_3) + Ph_3P \quad (6)$$

$$Ph_3P + N_2CHOOEt \rightarrow Ph_3P{=}N{-}N{=}CHCOOEt \quad (7)$$

Bidentate bis(dioximato)cobalt(II) complexes, whose optically active derivatives induce a high degree of enantioselectivity in cyclopropanation reactions with diazo compounds,[29] are square planar with two axial coordination sites.[30] Hexacoordinate Co(II) complexes such as those with bis(dimethylglyoximato)cobalt(II) and its nitrosyl derivative with representative Lewis bases are known, and the lability of the axial ligand has been established.[31] Nakamura and co-workers have found that the addition of a donor molecule such as pyridine to bis[(−)camphorquinone α-dioximato](aqua)cobalt(II), **6** = $Co(\alpha\text{-cqd})_2{\cdot}H_2O$, has a marked effect on enantioselectivity (section III.E) and stereoselectivity in catalytic cyclopropanation reactions.[29a] Its influence is explained by a mechanism in which the olefin that undergoes cyclopropanation causes displacement of the axial ligand by a two-center interaction with the intermediate carbene complex. Although this mechanism may be subject to reinterpretation, the fact remains that ligation which is axial to the carbene ligand influences selectivity.



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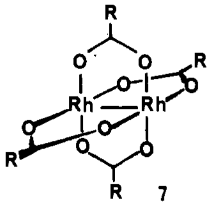
C. Catalysts That Possess Only One Vacant Metal Coordination Site

Rhodium(II) acetate, whose catalytic activity in reactions with diazo compounds was discovered by Teyssie and co-workers,[18] has played a central role in the evolution of a basic understanding of carbenoid transformations. A binuclear compound with four bridging acetate ligands and D_{4h} symmetry,[32] $Rh_2(OAc)_4$ (7) possesses one vacant axial coordination site per metal atom. Rhodium(II) carboxylates are thermally stable and air stable, but they readily form adducts with donor ligands such as nitriles and amines.[33]



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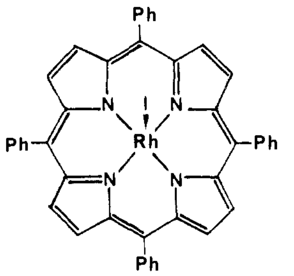
Rhodium(II) acetate does not appear to form olefin complexes in solution,[19,34] although gas–solid-phase measurements have indicated the existence of such complexes.[35] In contrast, olefin coordination by $Rh_2(OOCCF_3)_4$ is readily detectable, and equilibrium constants for association increase with the electron donor ability of alkene substituents.[34] However, only one of the two diaxial coordination sites is occupied by an olefin (eq 8) and, unlike copper triflate, differential olefin coordination does not affect selectivity in carbenoid reactions.[36] As is evident in these results and those by Drago and co-workers,[33] the carboxylate ligand has a strong influence on the electron-pair-acceptor capability of the rhodium(II) center which can be expected to affect reactivity and selectivity in carbenoid transformations.

$$\| + Rh(OOCCF_3)_4Rh \rightleftharpoons \|{-}Rh(OOCCF_3)_4Rh \quad (8)$$

Recently, a number of binuclear carboxamido complexes of rhodium(II) have been synthesized and characterized.[37] Owing to the increased number of possible geometrical isomers for $Rh_2(RNOCR')_4$ (R = H, R′ = CH_3; R = H, R′ = CF_3 R = CF_3, R′ = CH_3), these are structurally complex materials. However, their catalytic activities are comparable to that of $Rh_2(OAc)_4$, and their selectivities in carbenoid transformations increase with the basicity of the free carboxylate/carboxamide ligand.[38]

The hexarhodium(0) carbonyl cluster, $Rh_6(CO)_{16}$, has been reported to be a highly effective homogeneous catalyst for cyclopropanation[24,39] and ylide generation.[40] Carbenoid selectivities obtained with the use of this metal cluster, which are nearly identical with those obtained with $Rh_2(OAc)_4$, point to parallel mechanistic pathways for carbenoid generation and transformations. However, the structure of the actual catalytically active species has not been conclusively determined.

Iodorhodium(III)mesotetraphenylporphyrin (RhTPPI, 8) has also been reported to catalyze transformations of diazo compounds.[41] The first mononuclear rhodium cyclopropanation catalyst, RhTPPI provides an unusual cis(syn) selectivity for reactions of ethyl diazoacetate with olefins. However, the oxidation state of the active catalyst has not been determined. The possible reduction of rhodium(III) to rhodium(II) by diazo compounds, and the lower yields obtained for both cyclpropanation and for carbene dimer formation[42] relative to $Rh_2(OAc)_4$, suggest that the porphyrin ligand may not be inert.



8 RhTPPI

Wulfman and co-workers have maintained that the oxidation state of the active catalyst in carbenoid transformation with $Cu(acac)_2$ and $CuCl{\cdot}P(OR)_3$ is copper(II),[2b,43] and they have argued that under certain conditions diazo compounds undergo nucleophilic addition to a copper–olefin complex.[44] Although $CuCl{\cdot}P(OR)_3$ does not maintain its structural integrity throughout many carbenoid transformations, the catalytically active intermediate in cyclopropanation reactions with ethyl diazoacetate provides the same relative reactivity towards olefins as $Cu(acac)_2$ and $CuSO_4$.[11] That their reaction characteristics differ substantially from copper triflate places them in the category of catalysts that possess only one exchangeable metal coordination site. The oxidation state of the catalytically active intermediate for each of these copper catalysts has not been conclusively determined, but it is unlikely that the oxidation state of the carbene intermediate differs from catalyst to catalyst. The copper(I) oxidation state of even copper(II) β-diketonates such as $Cu(acac)_2$ is accessible.[45] Furthermore, 10 years after the initial proposal[44] there is no evidence that copper(I)–olefin complexes undergo nucleophilic addition by diazo compounds.

D. Evidence for Metal Carbene Involvement in Catalytic Reactions

Metal carbene complexes of transition-metal compounds that are active catalysts for the decomposition of organic diazo compounds have not been isolated or identified. Consequently, evidence for their involvement has arisen indirectly from results obtained in catalytic carbenoid transformations. Carbene dimer formation (eq 9)[42] is characteristic of metal carbene

$$2R_2C{=}N_2 \xrightarrow{ML_n} R_2C{=}CR_2 + 2N_2 \tag{9}$$

intermediates but not conclusive. Similarly, stereospecific cyclopropanation of olefins under reaction conditions that are not conducive to dipolar addition of the diazo compound[46] suggest these intermediates. However, more convincing evidence has been obtained through observation of asymmetric induction in cyclpropane-forming reactions with the use of copper[15,47] or cobalt[29] catalysts (section III.E). Chirality transfer demands that the catalyst is intimately involved at the product-determining stage in cyclopropanation reactions and suggests that free carbenes are not intermediates. That chirality transfer results from the addition of a free (achiral) carbene to a chiral metal–olefin complex is highly unlikely.

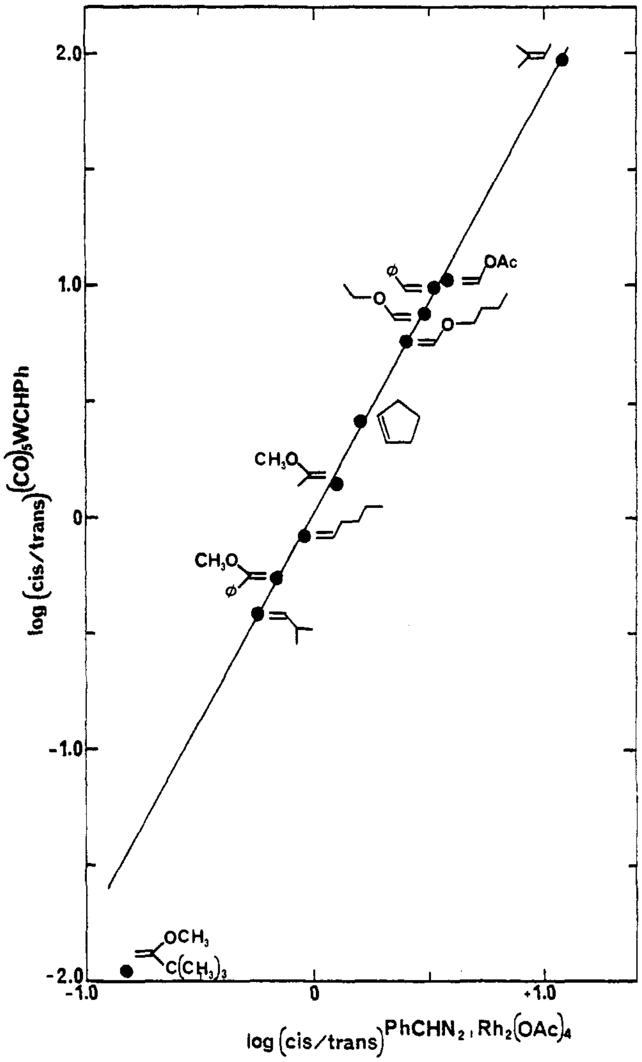
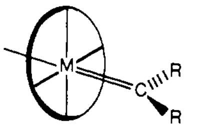


Figure 1. Stereoselectivity correlation in cyclopropanation reactions between $(CO)_5WCHPh$ and $Rh_2(OAc)_4/PhCHN_2$.[21]

Alternatively, if electrophilic metal carbene complexes are intermediates in catalytic reactions, then reactivity–selectivity correlations between known stable metal carbene complexes and assumed structurally similar catalytic intermediates should be observed. Such correlations have been reported by Doyle and co-workers from stoichiometric cyclopropanation reactions of Casey's $(CO)_5WCHPh$[48] and $Rh_2(OAc)_4$-catalyzed reactions of phenyldiazomethane.[21] As indicated by the stereoselectivity correlation in Figure 1,[21] electronic and structural similarities between the carbenes derived from $W(CO)_5$ and $Rh_2(OAc)_4$ are pronounced. A similar correlation between $W(CO)_5$ and $Rh_2(OAc)_4$ has been obtained with the carbene derived from ethyl diazoacetate.[49] Stereoselectivity[24] and regioselectivity[50] correlations for cyclopropane formation between $Rh_2(OAc)_4$-catalyzed reactions of ethyl diazoacetate and those with $CuCl{\cdot}P(O\text{-}i\text{-}Pr)_3$, $Cu(acac)_2$, $Rh_6(CO)_{16}$, $PdCl_2{\cdot}2PhCN$, and $Pd_3(OAc)_6$ catalysts provide their link to metal carbene intermediates.

The combination of chirality transfer and reactivity–selectivity correlations to reactions of structurally defined metal carbenes provides convincing arguments for metal carbene complexes as intermediates in catalytic transformations of diazo compounds. Structural similarities of the metal environments of carbenes associated with $Rh_2(OAc)_4$ and $W(CO)_5$ define the interaction of olefins with the electrophilic carbon center. Accordingly, reactions catalyzed by $Rh_2(OAc)_4$ or $W(CO)_5$ can be viewed as taking place at the carbenic carbon which protrudes from the metal embeded in a wall constructed from its ligands (**9**). In so far as the structures of other metal catalysts fit this description, their reactivities and selectivities will be comparable to those of $Rh_2(OAc)_4$ in carbenoid reactions with differences that are dependent upon the electrophilicity of the metal-stabilized carbene.



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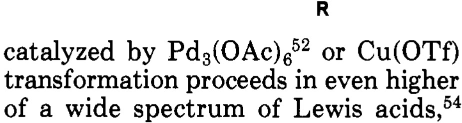
E. Carbenoid Catalysts as Lewis Acids

Although numerous different modes of bonding between a coordinatively unsaturated metal center and a diazo compound may be considered,[51] only the one that results in the loss of dinitrogen and formation of the metal-stabilized carbene accounts for their effective catalysis in carbenoid transformations. The active catalysts in these reactions are Lewis acids, and their turnover of diazo compounds is due, at least in part, to their reactivity as electrophiles. As Lewis acids they are subject to inhibition by Lewis bases including, with catalysts such as copper triflate or rhodium(II) trifluoroacetate, olefins. Rhodium(II) acetate is a superior catalyst for many carbenoid transformations because olefin coordination or association with alkyl halides, ethers, and esters does not occur. Some of the traditional copper catalysts are not inert towards association with these weak bases.

Because they are Lewis acids, transition-metal compounds that are effective catalysts for carbenoid transformations could actually be operating as Lewis acid promoters in much the same manner as BF_3. Such activity appears to explain the formation of oxazoles from nitriles and diazo carbonyl compounds (eq 10) catalyzed by $Pd_3(OAc)_6$[52] or $Cu(OTf)_2$.[53] This same transformation proceeds in even higher yields with any of a wide spectrum of Lewis acids,[54] but especially $BF_3{\cdot}OEt_2$.[55] Furthermore, oxazoles can be prepared directly from ketones and nitriles with the use of $Cu(OTf)_2$.[56] A carbenoid intermediate is not required in this transformation. Instead, as appears to be the case in BF_3-promoted reactions,[55a] the transition metal could activate the nitrile for nucleophilic addition by the diazo carbonyl compound:



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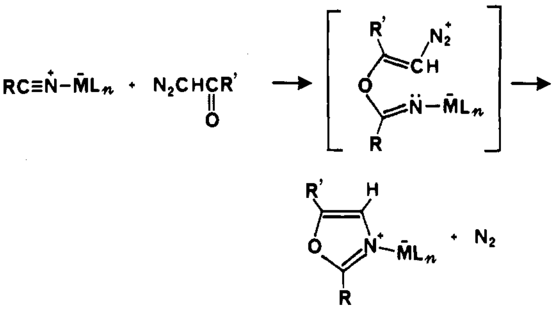
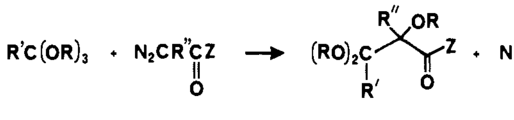


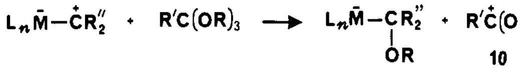
(11)

Alternativily, an electrophilic metal carbene complex could serve as the template upon which oxazole formation occurs.

The same conclusion has been reached for $Cu(OTf)_2$-promoted insertion of diazo compounds into the carbon–oxygen bond of ortho esters (eq 12).[57] But here there is evidence that the metal carbene complex, through alkoxide transfer from the ortho ester (eq 13), generates the active catalyst, a dialkoxycarbenium ion (**10**). Once again $BF_3{\cdot}OEt_2$ is a superior catalyst,[58] but $Rh_2(OAc)_4$, $Rh_6(CO)_{16}$, $CuCl{\cdot}P(OR)_3$, and $PdCl_2{\cdot}2PhCN$ were relatively ineffective.[57] These results point to a gradation in the electrophilicity of catalytically generated metal carbenes that have important implications for catalyst utilization in carbenoid transformations.



(12)

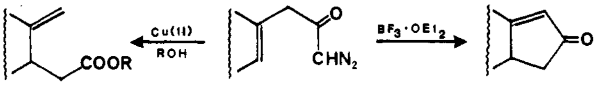


$$L_n\bar{M}-\overset{+}{C}R''_2 + R'C(OR)_3 \longrightarrow L_n\bar{M}-\underset{OR}{\underset{|}{C}}R''_2 + R'\overset{+}{C}(OR)_2$$

10

(13)

The parallel activities of $Cu(OTf)_2$ and $BF_3{\cdot}OEt_2$ are nowhere more pronounced than in the acid-promoted intramolecular cyclization of β,γ-unsaturated diazo ketones. Extensive investigations by Smith and coworkers have demonstrated the utility of these BF_3-promoted cyclizations for the preparation of simple and annulated cyclopentenones,[59] and their discovery of a novel skeletal rearrangement promoted by copper(II) compounds including $CuSO_4$, $Cu(acac)_2$, and $Cu(OTf)_2$, which they termed the *vinylogous Wolff rearrangement* (eq 14),[60] afforded a definite contrast between Lewis acid and transition-metal catalyzed reactions of this class of diazo compounds. However, Doyle and Trudell have reported that $Cu(OTf)_2$ is as effective as $BF_3{\cdot}OEt_2$ in promoting intramolecular cyclization (eq 15).[57] The product and the pathway through which it is obtained



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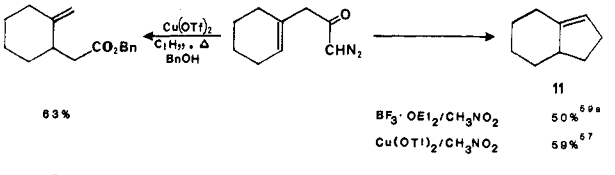
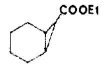
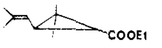
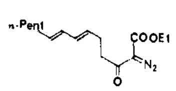
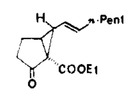
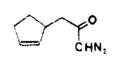
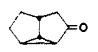
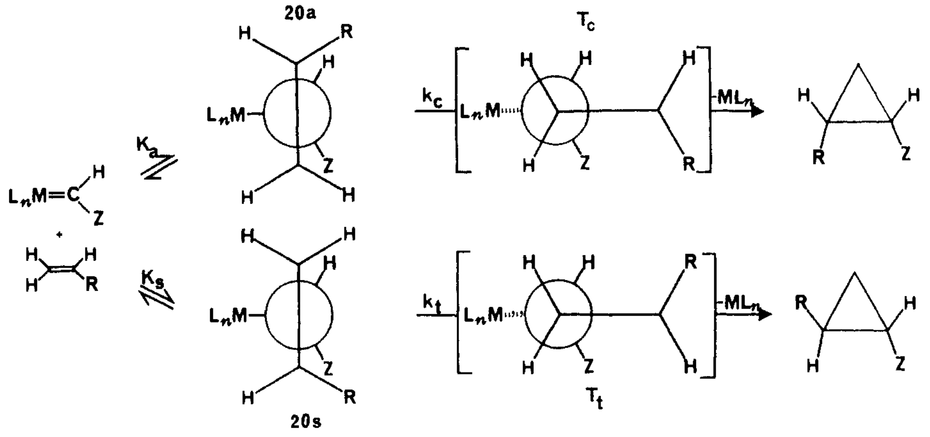


(15)

TABLE I. Cyclopropanation with Heterogeneous and Homogeneous Catalysts

olefin/diazo compd	product	heterogeneous catalyst (ref)	yield, %	homogeneous catalyst (ref)	yield, %
 EDA		Cu, Et_2O, reflux (66)	66	$Rh_2(OAc)_4$, 25 °C (24)	90
 EDA		Cu, 100–130 °C (67)	64	$Rh_2(OAc)_4$, 20 °C (18b)	85
		Cu, $PhCH_3$, reflux (68)	50	$Cu(acac)_2$, PhH, reflux (69)	63
		$CuSO_4$, C_6H_{12}, reflux (70)	67	$Cu(OTf)_2$, CH_3NO_2, 25 °C (57)	90

SCHEME I. Proposed Mechanism for Cyclopropane Formation[21]

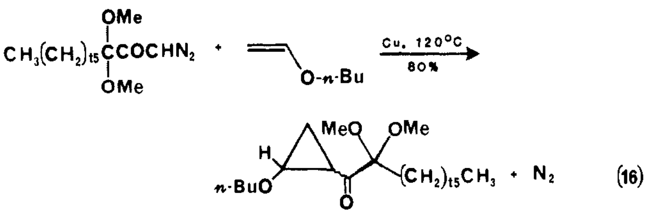


is dependent on the reaction conditions. Doyle and Trudell employed $Cu(OTf)_2$ in anhydrous nitromethane and obtained hydrindanone **11**; the vinylogous Wolff rearrangement takes place in refluxing cyclohexane to which is added an equivalent amount of alcohol. The dichotomy awaits resolution.

III. Catalytic Cyclopropanation Reactions

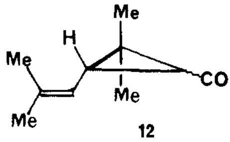
A. Methods

Copper bronze,[61] used as a suspension in refluxing solvent, continues to be a popular catalyst for the cyclopropanation of olefins. Wenkert and co-workers[4a,62] have applied this methodology to the synthesis of a substantial number of cyclopropanes that are synthetic intermediates in the preparation of natural products (e.g., eq 16).[63] Copper bronze was also the catalyst of



(16)

choice for the continuous process synthesis of ethyl chrysanthemate (**12**).[64] An excess of the olefin is



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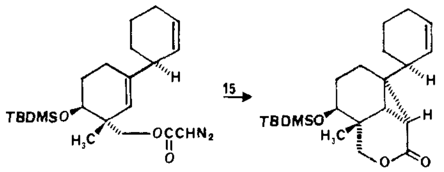
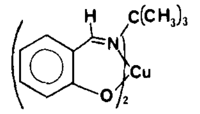
normally employed, and the amount of inexpensive copper bronze required for effective cyclopropanation is ordinarily 1–2 mol percent based on the diazo compound. However, the use of heterogeneous reaction conditions does not always provide optimal yields. Corey and Myers, for example, noted that although copper powder in refluxing toluene converted diazo ester **13** (TBDMS = t-$BuMe_2Si$) to cyclopropyl lactone **14** in 57% yield, the product yield dropped substantially on scaleup.[65] Use of bis(N-*tert*-butylsalicylaldiminato)copper(II), a soluble Nozaki catalyst,[15b] provided **14** in 92% yield. Similar yield improvements with the use of soluble catalysts are being reported with increasing frequency (e.g., Table I). However, Hudlicky and co-workers have found that, whereas $Cu(acac)_2$ is highly effective for intramolecular cyclopropanations of conjugated dienes connected to diazo ketones,[71] useful yields of cyclopropane products were not obtained from structurally similar diazo esters when the same catalyst was employed.[72a] Excess $CuSO_4$ suspended in refluxing benzene together with 15–20 mol



13 14



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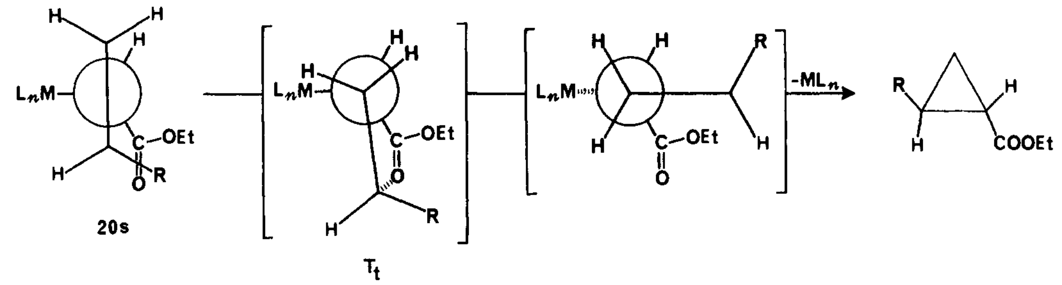
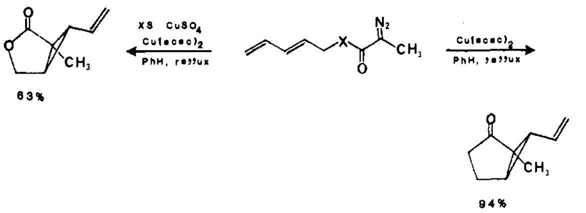
SCHEME II. Preferential Trans-Stereoselectivity in Cyclopropanation by α-Carbonylcarbenes



percent of $Cu(acac)_2$ proved to be suitable for these transformations (eq 17), which apparently have strikingly different requirements compared to cyclopropanation of simple olefins joined to a diazo ester[2c] or to 16, which was converted to cyclopropyl lactone 17 in 92% yield with the use of Nozaki catalyst 15.[65] Hudlicky and co-workers have approached intramolecular diene cyclopropanations of diazo esters and diazo ketones with the use of insoluble $CuSO_4$ in refluxing benzene, and they have reported high-yield conversions for small- and moderate-scale reactions.[72]



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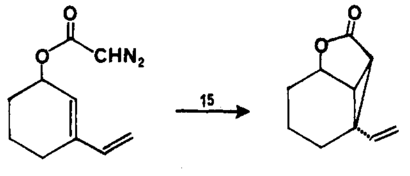
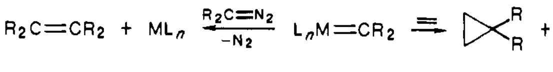


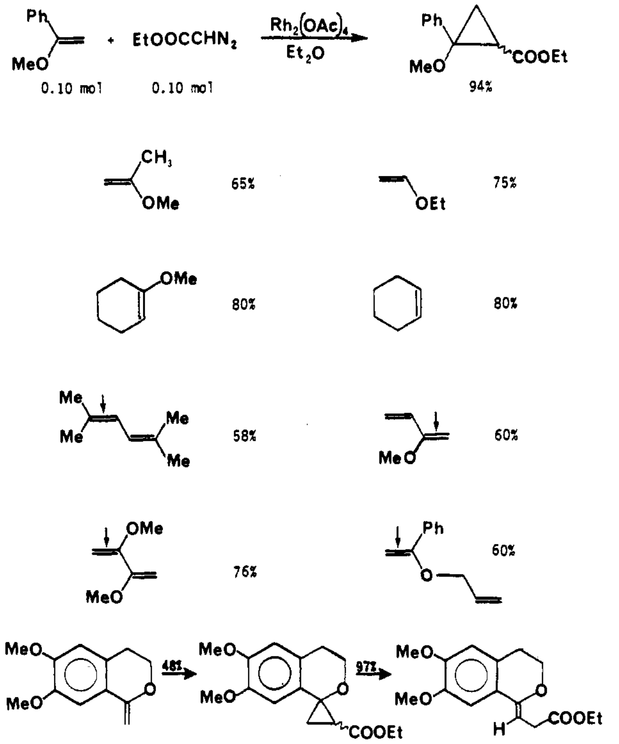
16 17

(18)

Cyclopropane product yields in metal-catalyzed cyclopropanation reactions with diazo compounds are lowered by competitive dimerization of the carbenoid equivalent of the diazo compound.[2] When competition between olefin and diazo compound for the metal carbene (eq 19) is the cause of limited cyclopropane production, merely minimizing the available concentration of the diazo compound should afford optimal yields of cyclopropane products. Thus exact control of the rate of addition of the diazo compound to the reaction medium containing the catalyst and olefin should result in superior cyclopropane yields, even when only equivalent amounts of olefin and diazo compound are employed, and provide economical benefits by limiting the amount of catalyst required for effective cyclopropanations. These advantages have been realized for reactions catalyzed by $Rh_2(OAc)_4$, $Rh_6(CO)_{16}$, and $CuCl{\cdot}P(O\text{-}i\text{-}Pr)_3$.[73] Representative examples of stoichiometric cyclopropanation reactions of ethyl diazoacetate with alkenes include (arrows identify the site of exclusive addition to dienes):



$$R_2C{=}CR_2 + ML_n \xleftarrow[-N_2]{R_2C{=}N_2} L_nM{=}CR_2 \xrightarrow{=} \text{[cyclopropane]}\ + ML_n \quad (19)$$

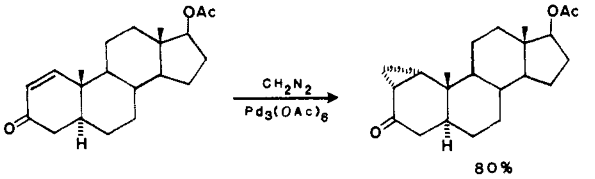


The effect of this control on product yield is dramatically illustrated in results for reactions of 1-methoxycyclohexene with a stoichiometric amount of ethyl diazoacetate: at a $[EDA]/[Rh_2(OAc)_4]$ ratio of 200 and an addition rate of 5 mmol/h, the corresponding cyclopropane product was obtained in 80% yield. With a $[EDA]/[Rh_2(OAc)_4]$ ratio of 2000 and an addition rate of 5 mmol/h, the yield of this product was only 60%. However, by decreasing the rate of addition of ethyl diazoacetate to 0.5 mmol/h, the cyclopropane product could again be isolated in 80% yield. By contrast, control of the rate of addition of the diazo compound has only a marginal influence on cyclopropane product yield in reactions catalyzed by $PdCl_2{\cdot}2PhCN$ or $Cu(OTf)_2$.[24]

Palladium(II) acetate has been advanced as the catalyst of choice for cyclopropanation of terminal olefins[74] and of α,β-unsaturated carbonyl compounds.[75] However, the high yields and selectivities for cyclopropanation of terminal olefins reported for reactions with diazomethane[74] are not duplicated with ethyl diazoacetate.[19] Only styrenes and strained cycloalkenes generally give high yields of cyclopropane products in reactions with ethyl diazoacetate that are catalyzed by

$Pd_3(OAc)_6$, and palladium(II) chloride exhibits similar catalytic behavior.[24] Diethyl maleate and diethyl fumarate, the carbenoid dimers formed from ethyl diazoacetate, inhibit cyclopropanation by palladium(II) acetate,[19] possibly as a result of their coordination to palladium and subsequent reaction with the developing carbenoid on the same metal center. In the presence of relatively unreactive olefins such as cyclohexene, palladium catalysts cause decomposition of ethyl diazoacetate to form as yet uncharacterized polymeric material based on carbethoxycarbene.

The effectiveness of palladium(II) acetate for cyclopropanation of certain α,β-unsaturated carbonyl compounds by either diazomethane or ethyl diazoacetate (eq 20 and 21) is well established.[75] As in reactions with simple olefins, the use of diazomethane generally results in higher product yields. However, neither copper nor rhodium catalysts are similarly effective and, considering the low reactivity of even simple olefins toward cyclopropanation in the presence of palladium catalysts, the apparent ease of cyclopropane formation with α,β-unsaturated carbonyl compounds is surprising. Doyle and co-workers have shown that a variety of transition-metal compounds, but principally $Mo(CO)_6$ and $Mo_2(OAc)_4$, promote cyclopropanation of α,β-unsaturated carbonyl compounds and nitriles,[46,76] and they have demonstrated from kinetic investigations that these reactions occur by dipolar cycloaddition[77] followed by dinitrogen extrusion from the intermediate 1-pyrazoline (eq 22).[46] Whether this is the explanation for the behavior of palladium(II) acetate remains to be established, but metal carbene involvement in the cyclopropanation of α,β-unsaturated carbonyl compounds is by no means certain.



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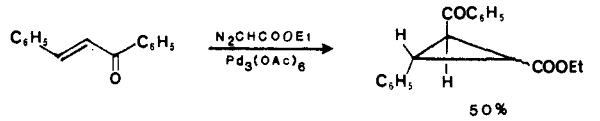

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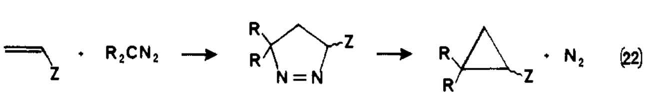


(22)

Although intramolecular cyclopropanation reactions have been advanced to their limits for ease in preparation of diazo carbonyl compounds,[2c] intermolecular reactions have generally been restricted to those between olefins and diazo esters, especially ethyl diazoacetate. Reactions with diazomalonate and diazopyruvate often result in products of carbonyl carbene dipolar addition (sections IV.A and V.B)[4a,b] or carbon–hydrogen insertion (section V.A),[2b] but these products are rarely formed with ethyl diazoacetate. In certain cases, replacement of the ethyl group of ethyl diazoacetate by *n*-butyl has been reported to increase the yield of cyclopropane products,[18b,19] and the cause of the yield increase has been attributed to an increase in the solubility of the intermediate metal carbene.[18b] Because of their relative instability, diazoalkanes have been rarely employed for catalytic transformations, and their responsiveness to different catalysts for cyclopropanation has not been determined.

Olefin reactivities in cyclopropanation reactions are dependent on the catalyst employed. Competitive cyclopropanation of two olefins by diazo compounds in the presence of metal catalysts is ordinarily used to characterize relative reactivities.[11,19,21] However, this data is misleading when the catalyst employed possesses a coordination site for olefin association during carbene transfer because selectivity in competitive cyclopropanation reactions is dependent on the molar ratio of olefins employed.[21] In such cases relative reactivities are accurate only under the conditions employed for their determination. Currently, $Rh_2(OAc)_4$ is the only catalyst for which reliable olefin relative reactivities are available,[21] and the general order for olefin reactivity is reflective of relative rates for electrophilic addition:[78]

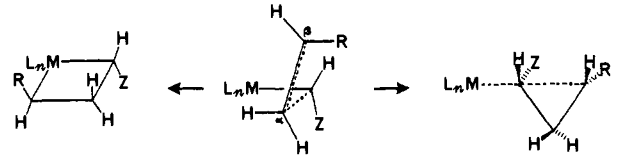
vinyl ethers > styrene > cyclopentene > cyclohexene > 1-hexene

A distinguishing feature of $Rh_2(OAc)_4$ as a cyclopropanation catalyst is that high yields of cyclopropane products can be obtained throughout the spectrum of olefin reactivities.[19,24]

B. Mechanism of Cyclopropanation

Reactivity–selectivity correlations between $(CO)_5WCHPh$ and the combination of $PhCHN_2$ with $Rh_2(OAc)_4$ for reactions with olefins have been obtained (section II.D), and these data implicate metal–carbene involvement in catalytic cyclopropanation reactions. Predominant cis selectivity in cyclopropane formation characterizes both procedures for benzylidene transfer (Figure 1). In contrast, reactions of ethyl diazoacetate with olefins that are catalyzed by either $Rh_2(OAc)_4$ or $W(CO)_5$ favor formation of the trans cyclopropane isomer.[49]

In their initial investigation of the reactions of $(CO)_5WCHPh$ with alkenes, Casey and co-workers found an unexpected preference for the thermodynamically less stable cis cyclopropane isomer, and their systematic survey of the influence of alkene substituents on cyclopropane stereochemistry caused their rejection of metallacyclobutane intermediates as the sole explanation for the observed stereochemical preference.[48] Instead, a stabilizing interaction between the developing electrophilic center of the reacting alkene and the phenyl group was proposed to explain the high cis stereoselectivities for benzylidene transfer from $(CO)_5WCHPh$ and $Cp(CO)_2FeCHPh^+$ to alkenes.[48,79] However, ethylidene transfer reactions of $Cp(CO)_2FeCH(OMe)CH_3$, for which such a stabilizing interaction is not possible, also exhibited a pronounced preference for formation of the cis cyclopropane isomer,[80] and transition state model 17 (e.g., $L_nM = (CO)_5W$, $Cp(CO)_2Fe^+$) was invoked to explain the composite results. According to this model, initial interaction occurs between the electrophilic carbene carbon and one terminus of the reacting alkene. The developing electrophilic center at C_β in 17 may displace ML_n in a frontside manner or by backside attack with synchronous $C_{carbene}$–C_β bond formation (e.g., 18 → *cis*-



19 **17** **18**

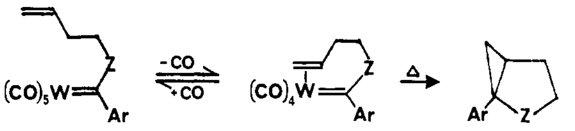
cyclopropane product). Alternatively, a discrete metallocycle (e.g., **19** → *trans*-cyclopropane product) may be formed. As the size of the R group is increased from methyl to *tert*-butyl, the *trans*-cyclopropane isomer becomes the preferred product.

Although this diversity of pathways which includes **18** and **19** accounts for the stereochemistry of cyclopropane formation with alkylidenemetal complexes, it does not explain the predominant trans stereoselectivity observed in catalytic cyclopropanation reactions with diazo carbonyl compounds. To account for this carbenoid-dependent difference in selectivity, Doyle and co-workers proposed an alternate mechanistic model for cyclopropanation.[21] According to this model, cyclopropane formation occurs by initial association of the olefin π bond with the electrophilic center of the metal–carbene complex followed by σ-bond formation with backside displacement of the catalyst (Scheme I). Stabilization of the developing electrophilic center by the electron-donating substituent R determines the motion of the alkene relative to the electrophilic carbon center of the reacting carbene. In proceeding from **20a** to the transition state T_c, the alkene carbon structure moves up relative to the carbenic carbon and concurrently rotates to the T_c configuration in which the original alkene C–C bond axis is parallel to the original metal–carbon bond axis. Similarly, the alkene carbon structure in **20s** moves down relative to the carbenic carbon with rotation to the parallel alignment of T_t. Backside displacement of ML_n by the developing carbenium ion results in cyclopropane formation.

According to this proposal, cyclopropane stereochemistry is determined by a combination of steric and/or electronic interactions at the π complex (**20a** and **20s**) and cyclopropane-forming (T_c and T_t) stages. In the absence of prominant steric interactions between R and Z in the cyclopropane-forming stage, predominant cis stereoselectivity is predicted ($k_t \simeq k_c$, but **20s** is less stable than **20a**) and observed for reactions of monosubstituted alkenes possessing alkyl[80,81] or aryl[21,48,79] substituents. As the size of R is increased, k_c decreases relative to k_t with the resulting decrease in the cis/trans ratio of cyclopropane products. The principal differences between this mechanism and those previously advanced are the proposal of an intermediate that exists in equilibrium with the separated alkene and carbene complex and the absence of a metallacyclobutane intermediate. The π complex of Scheme I may, in fact, be a formalism, although it is a useful one for the prediction of stereoselectivity in catalytic and stoichiometric reactions.

Stereochemical preference for the *trans*-cyclopropane isomer in reactions involving transition-metal-catalyzed reactions of ethyl diazoacetate and related diazo carbonyl compounds appears to be the exception to the model depicted in Scheme I. However, the carbonyl group is a nucleophile that can be expected to influence association between the reacting alkene and the electrophilic carbene. Electronic stabilization of the transition state leading to *trans*-cyclopropane products by interaction of the developing electrophilic carbon of the original alkene with the nucleophilic carbonyl oxygen (T_t is Scheme II), which is only possible in the transition state leading to the trans cyclopropane, accounts for the predominant trans stereoselectivity in these reactions. Accordingly, increasing the nucleophilicity of the carbonyl group should cause an increase in trans selectivity. Also, alkenes such as vinyl ethers whose substituents can stabilize a developing electrophilic carbon center should be least affected by interaction with the carbonyl substituent of the metal carbene (section III.C).

Metal–carbene–alkene complexes have often been invoked as intermediates in metal-catalyzed cyclopropanation reactions.[7,15,19] Until recently, their existence has been hypothetical, based on arguments derived from selectivities in product formation. However, Casey and co-workers have prepared stable tungsten–carbene–alkene complexes **21** from their



(23)

22 **21** **23**

corresponding pentacarbonyltungsten carbenes **22** by thermolysis and observed their decomposition to cyclopropane products (eq 23, Z = O, NMe).[82] Cyclopropane formation was found to be autocatalytic, and a chain mechanism involving $W(CO)_4$ was proposed[83]

$$\mathbf{22} \rightarrow \mathbf{21} + CO \tag{24}$$

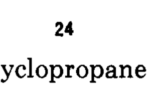
$$\mathbf{21} \rightarrow \mathbf{23} + W(CO)_4 \tag{25}$$

$$\mathbf{22} + W(CO)_4 \rightarrow \mathbf{21} + W(CO)_5 \tag{26}$$

$$\mathbf{22} + W(CO)_5 \rightarrow \mathbf{21} + W(CO)_6 \tag{27}$$

Introduction of any agent that can trap the reactive $W(CO)_4$ and $W(CO)_5$ intermediates effectively shuts down the autocatalytic decomposition and greatly inhibits the decomposition of **22**. The composite data are consistent with the intervention of a tungsten–carbene–alkene complex in cyclopropane formation but, considering the slow rate for exchange of carbon monoxide on pentacarbonyltungstencarbenes,[84] the relevance of these intermediates to cyclopropanation reactions of carbene complexes such as $(CO)_5WCHPh$[48] and to catalytic cyclopropanation reactions remains to be determined.

Doyle, Wang, and Loh have recently reported that stable palladium chloride complexes of dienes[27] such as **24** and **25** do not react with ethyl diazoacetate and do



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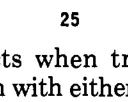


25

not form cyclopropane products when treated with ethyl diazoacetate in combination with either $Rh_2(OAc)_4$ or $PdCl_2 \cdot 2PhCN$.[23] These results are inconsistent with intermolecular electrophilic carbene addition to a coordination olefin as well as with electrophilic addition of the coordinated olefin to the diazo compound. Although collapse of a metal–carbene–alkene complex

TABLE II. Cyclopropanation Reactions of Ethyl Diazoacetate at 25 °C. Influence of Reaction Catalyst on Stereoselectivity[24]

	trans/cis (anti/syn)					
alkene	$Rh_2(OAc)_4$	$Rh_6(CO)_{16}$	$Cu(OTf)_2$	$CuCl\cdot P(O\text{-}i\text{-}Pr)_3$	$Cu(acac)_2$[a]	$PdCl_2\cdot 2PhCN$
ethyl vinyl ether	1.7	1.7	2.4[b]	1.9	1.6[c]	1.5
styrene	1.6	1.7	1.9[b]	2.8	2.6	1.6
3,3-dimethyl-1-butene	4.2	4.5	5.5	7.3	10.4	2.5
cyclohexene	3.8	3.9	6.8	6.8	6.5	2.2
2,5-dimethyl-2,4-hexadiene	1.8	1.9	2.3	2.7	1.8	2.3[d]
% yield range	81–93	42–88	54.97	23–88	15–76	20–52
av % yield	88	73	75	51	40	36

[a] Reactions performed at 60 °C. [b] Reactions performed at 0 °C. [c] Reaction performed at 25 °C. [d] The cis isomer undergoes chloropalladation (ref 85).

TABLE III. Cyclopropanation Reactions of Ethyl Diazoacetate at 25 °C. Influence of Rhodium Catalyst on Stereoselectivity

	trans/cis (anti/syn)			
alkene	$Rh_2(NHCOCH_3)_4$[a]	$Rh_2(OAc)_4$[b]	$Rh_2(OOCC_3F_7)_4$[a]	RhTPPI[c]
ethyl vinyl ether	2.8	1.6	1.3	
styrene	2.1	1.6	1.1	0.88
3,3-dimethyl-1-butene	4.9	2.9[a]	1.5	
cyclohexene	10	3.8	1.9	1.2
bicyclo[2.2.1]hept-2-ene	3.6	2.0[a]	1.5	0.54

[a] Reference 38. [b] Reference 24. [c] Reference 41.

remains a mechanistic possibility for catalytic cyclopropanation reactions with copper triflate and palladium(II) acetate or chloride, the absence of an intermolecular counterpart weakens arguments for their involvement. Catalyst-dependent selectivity differences in cyclopropanation reactions, such as have been reported for copper triflate (eq 3), may be due to electronic influences of the metal or to steric influences derived, at least in part, from olefin coordination to a metal carbene complex (eq 5).

C. Stereoselectivity

The attractiveness of catalytic cyclopropanation reactions for organic syntheses has been limited by low stereoselectivities associated with the transformation. In fact, few reports have documented isomer distribution. However, sufficient data is now available to evaluate the influence of catalyst, diazo compound, and olefin on stereoselectivity.

In reactions with diazo esters, copper catalysts generally provide a higher trans selectivity than do either $Rh_2(OAc)_4$ or $Rh_6(CO)_{16}$ which, in turn, are superior to palladium(II) catalysts (Table II). Stereoselectivities are invariant to changes in catalyst concentration, to the rate of addition of the diazo compound, and to the molar ratio of olefin to diazo compound,[24] except with palladium(II) chloride which causes "isomerization" of vinylcyclopropanes.[85] Stereochemical results from cyclopropanation reactions with 22 olefins have been found to correlate through the simple linear relationship

$$(\text{isomer ratio})^{\text{catalyst}} = S \times (\text{isomer ratio})^{Rh_2(OAc)_4}$$

where S, the index of relative stereoselectivity, is equal to 1.7 for $CuCl\cdot P(O\text{-}i\text{-}Pr)_3$, 1.0 for $Rh_6(CO)_{16}$, and 0.59 for $PdCl_2\cdot 2PhCN$.[24] Surprisingly, there is little difference in selectivity between $Rh_2(OAc)_4$ and $Rh_6(CO)_{16}$ or between various copper catalysts, including $Cu(OTf)_2$. Rhodium(II) acetate and $W(CO)_5$ also produce nearly identical isomer distributions in reactions with ethyl diazoacetate ($S = 0.9$).[49] However, product yields are dependent on the catalyst employed, and rhodium(II) carboxylates are superior.

Electronic effects from ligands bound to dimeric rhodium(II) influence carbene stabilization and, as seen from the range of cyclopropanation stereoselectivities in Table III, afford more exact control than is obtained with the selection of copper and palladium catalysts (Table II). Stereoselectivities for production of the more stable trans or anti cyclopropane isomer are greater with rhodium(II) acetamide than with even copper catalysts, and they are less than even palladium(II) chloride when rhodium(II) perfluorobutyrate is employed. Electronic effects of these ligands are apparently manifest in the carbene and influence the closeness of approach by the olefin to the electrophilic carbene center. The mesotetraphenylporphyrin complex 8 (RhTPPI) actually causes a reversal of predominant stereoselectivity in reactions of ethyl diazoacetate with certain olefins,[41] but this catalyst may affect selectivities differently than do rhodium(II) carboxylates or carboxamides. The influence of rhodium(II) carboxylate ligands on stereoselectivities in the synthesis of chrysanthemic and permethric esters has been reported,[64c,86] and a slight preference for the Z isomers was observed with the use of rhodium(II) (L-(+)-2-(tetrachlorophthalimido)propionate.[86]

For catalytic reactions with diazocarbonyl compounds, Scheme II predicts that increasing the size of the carbonyl substituent and increasing the nucleophilicity of the α-carbonyl group should lead to an increase in trans(anti) selectivity. These effects are observed (Table IV). 2,3,4-Trimethyl-3-pentyl diazoacetate is superior to *tert*-butyl diazoacetate in causing an increase in trans(anti) selectivity as a result of steric effects,[87] and *N*,*N*-dimethyldiazoacetamide, whose carbonyl oxygen is more nucleophilic, exhibits even greater selectivity in the cyclopropanation of cis olefins. However, increasing the size of amide substituents or employment of rhodium(II) acetamide with *N*,*N*-dimethyldiazoacetamide does not lead to further dramatic increases in selectivity.

The influence of olefin structure on stereoselectivity is relatively weak. Heteroatom substituents such as

TABLE IV. Cyclopropanation Reactions Catalyzed by $Rh_2(OAc)_4$ at 25 °C. Influence of Diazo Compound on Stereoselectivity

	trans/cis (anti/syn)			
alkene	N_2CHPh[a]	$N_2CHCOOEt$[b]	$N_2CHCOOCMe(i\text{-}Pr)_2$[c]	$N_2CHCONMe_2$[d]
ethyl vinyl ether	0.33	1.7	2.3	1.8
n-butyl vinyl ether	0.40	1.7	2.0	1.7
styrene	0.30	1.6	2.4	2.2
cyclohexene	(0.63)[e]	3.8	9.5	12
2,5-dimethyl-2,4-hexadiene		1.8	1.8	1.1

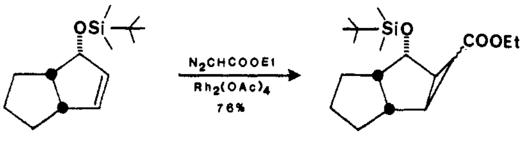
[a] Reference 21. [b] Reference 24. [c] Reference 87. [d] Reference 38. [e] Stereoselectivity for cyclopentene. With ethyl diazoacetate, value is 2.1 (anti/syn).

TABLE V. Cyclopropanation Reactions of Ethyl Diazoacetate at 25 °C. Influence of Reaction Catalyst on Regioselectivity

	regioselectivity (A/B)				
diene	$Rh_2(OAc)_4$	$Rh_6(CO)_{16}$	$Cu(OTf)_2$	$CuCl{\cdot}P(O\text{-}i\text{-}Pr)_3$	$PdCl_2{\cdot}2PhCN$
isoprene (**28**)[a]	1.6	1.6	2.0	1.9	0.54
trans-piperylene (**29**)[a]	7.5	8.2		10	3.4
limonene (**30**)[b,c]	2.5	2.8	3.9	4.7	1.7
5-methylenebicyclo[2.2.1]hept-2-ene (**31**)[b,c]	2.3	2.2	1.0	2.5	0.16
bicyclo[4.3.0]nona-3,6-diene (**32**)[b]	6.0	6.2	3.2	2.1	4.1

[a] Reference 24. [b] Reference 94. [c] Reference 49.

oxygen in vinyl ethers[24,88] and silyl enol ethers[89] offer advantages in reactivity but not in selectivity. However, increasing the steric bulk of the olefinic substituent does result in enhancement of the relative percentage of the sterically less encumbered cyclopropane product, and cis-disubstituted olefins are among the most sensitive to catalyst-dependent changes in selectivity. Rhodium(II) acetate has recently been reported to catalyze cyclopropanation of ethyl diazoacetate exclusively from the convex side of a bicyclo[3.3.0]octene (e.g., eq 28),[90] although both carboxylate epimers were obtained (anti/syn = 4). However, the anti isomer is formed exclusively by $Rh_2(OAc)_4$-catalyzed cyclopropanation of 1,3-cyclohexadiene with *tert*-butyl diazopyruvate.[91]



26 **27** (28)

Stereoselectivity increases with decreasing temperature, and the direction of this increase is dependent on the carbene. With phenylcarbene cis(syn) selectivity is enhanced,[21] and trans(anti) selectivity also increases to a small extent with decreasing temperature.[24] However, the use of temperature as a controlling influence of stereoselectivity is limited by the rate for carbenoid generation with diazo compounds.

D. Regioselectivity

A considerable amount of information is available on the regioselectivity of cyclopropanation reactions.[49,50,92,93] Doyle and co-workers have reported that regioselectivities for copper- and palladium-catalyzed reactions of monosubstituted 1,3-butadienes with ethyl diazoacetate correlates with those for rhodium(II) acetate by the relationship

$$(\text{isomer ratio})^{\text{catalyst}} = R \times (\text{isomer ratio})^{Rh_2(OAc)_4}$$

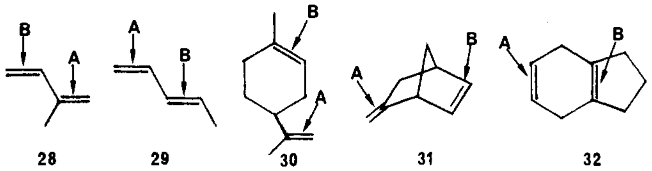
where R, the index of relative regioselectivity, is equal to 1.4 for $CuCl{\cdot}P(O\text{-}i\text{-}Pr)_3$, 1.1 for $Rh_6(CO)_{16}$, and 0.5 for $PdCl_2{\cdot}2PhCN$.[50] Regioselectivity increases with substituents at the 2-position in the order Me < Ph < Cl < OMe, and exclusive cyclopropanation at the 1,2-double bond is observed with 2-methoxy-1,3-butadiene. In contrast, selectivity for cyclopropanation at the 3,4-double bond of 1-substituted-1,3-butadienes follows the order MeO < Me < Ph < Cl. Inversion of the order for the methoxy substituent of 1- and 2-substituted butadienes is an anomaly.

TABLE VI. Cyclopropanation Reactions of Ethyl Diazoacetate at 25 °C. Influence of Rhodium Catalyst on Regioselectivity

	regioselectivity (A/B)		
diene	$Rh_2(NHCOCH_3)_4$[a]	$Rh_2(OAc)_4$[b]	$Rh_2(OOCC_3F_7)_4$[a]
isoprene (**28**)	2.1	1.7	1.2
trans-piperylene (**29**)	13	7.5	3.7
limonene (**30**)	2.8	2.5	1.5
5-methylene-bicyclo[2.2.1]-hept-2-ene (**31**)	5.2	2.3	2.0
bicyclo[4.3.0]nona-3,6-diene (**32**)	8.3	6.0	3.3
myrcene (**34**)[a]	10.4 (1.5)[c]	6.0 (1.3)[c]	3.5 (1.1)[c]

[a] References 36 and 38. [b] Reference 49. [c] Regioselectivity (A_2/A_1).

Regioselectivity for intermolecular cyclopropanation is determined primarily by electronic influences of the catalyst, carbene substituents, and olefin. Dienes **28**–**32** are representative, and their regioselectivites in reactions with ethyl diazoacetate are responsive to the catalyst employed (Table V). At least with $Rh_2(OAc)_4$, relative reactivities for model compounds reflect regioselectivities. Differences in olefin reactivities have been attributed to electronic influences on the transition state for cyclopropanation.[49] A transition state with little charge development at the olefinic carbons (**33a**, e.g., $ML_n = PdCl_2$) favors cyclopropanation at double bond B in **28** and **31**, whereas a transition state with



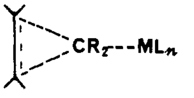
28 **29** **30** **31** **32**

TABLE VII. Cyclopropanation Reactions Catalyzed by $Rh_2(OAc)_4$ at 25.0 °C. Influence of Diazo Compound on Regioselectivity

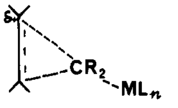
diene	regioselectivity (A/B)		
	N_2CPh_2[a]	$N_2CHCOOEt$[b]	$N_2CHCONMe_2$[c]
isoprene (**28**)	2.6	1.7	2.5
trans-piperylene (**29**)	100	7.5	
5-methylenebicyclo-[2.2.1]hept-2-ene (**31**)	100	2.3	12

[a] Reference 94. [b] References 24 and 49. [c] Reference 38.

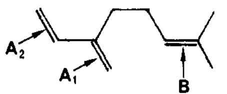
considerable charge development (**33b**, e.g., ML_n = $Rh_2(OAc)_4$) favors cyclopropanation at double bond A in these same compounds. Regioselectivity in cyclopropanation of other dienes reflects their responsiveness to electronic and steric effects in the transition state for addition.[24,50] Decreasing the electrophilicity of the intermediate metal carbene increases selectivity (Tables VI and VII). With the triene myrcene (**34**), the diene functional group is more reactive than the trisubstituted double bond, and regioselectivity for cyclopropanation of the diene is proportional to that observed with isoprene (Table VI); both selectivities increase with decreasing electrophilicity of the dimeric rhodium(II) catalyst.



33a



33b



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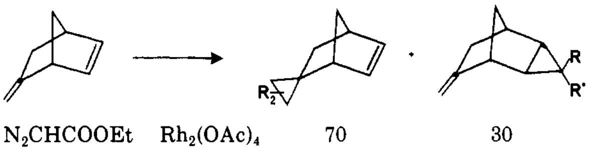
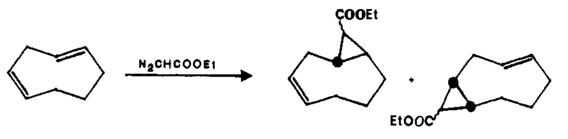
The response of dienes possessing a strained carbon–carbon double bond toward regioselective cyclopropanation by palladium(II) and rhodium(II) catalysts is inverted, and the extent of this inversion is enhanced with diazo compounds whose substituents offer greater carbene stabilization than does carbalkoxy.[23] With 5-methylenebicyclo[2.2.1]hept-2-ene, for example, preferential electrophilic carbene addition occurs at the exocyclic double bond with $Rh_2(OAc)_4$ (eq 29), but PdCl₂·2PhCN directs cyclopropanation to the endocyclic double bond. This selectivity is enhanced with diphenyldiazomethane. However, (*E*,*Z*)-1,5-cyclodecadiene undergoes selective cyclopropanation of the *E* double bond with $Pd_3(OAc)_6$ (eq 30).[93] The reason for this disparate reactivity may be related to the "free" carbene character of the transition state for cycloaddition.



(29)

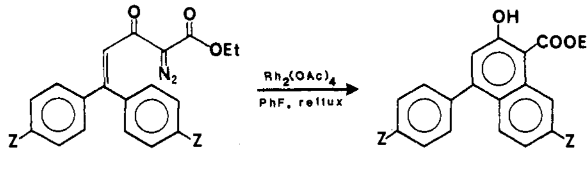
$N_2CHCOOEt$	$Rh_2(OAc)_4$	70	30
	$PdCl_2{\cdot}2PhCN$	14	86
Ph_2CN_2	$Rh_2(OAc)_4$	99	1
	$PdCl_2{\cdot}2PhCN$	2	98

Ring size determines regioselectivity in intramolecular cyclopropanation reactions.[2c] The formation of bicyclic compounds with five-, six-, and even seven-membered rings has been reported, and five-membered ring formation is favored over the production of seven-membered rings.[71,72] Bicyclo[2.1.0]pentanone derivatives have been proposed as intermediates, but they have not been isolated in the presence of a cyclopropanation catalyst.[2c,60,71a] Taylor and Davies have disclosed a novel route to 4-aryl-2-hydroxy-1-naphthoates by intramolecular "cyclopropanation" of aromatic compounds using rhodium(II) acetate as the catalyst (eq 31).[95] Since the intermolecular counterpart of this process produces cycloheptatrienes (from diazo esters and rhodium(II) trifluoroacetate),[96] the formation of **35** is presumably a consequence of the lower energy pathway leading to aromatization.



(30)

$Rh_2(OAc)_4$	50	50
$Cu(OTf)_2$	50	50
$Pd_3(OAc)_6$	2	98

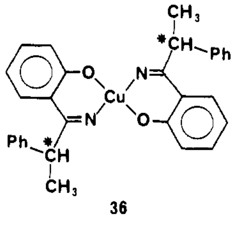


(31)

35, 90% (Z = H)
97% (Z = Cl)
76% (Z = OMe)

E. Enantioselectivity

Nozaki and co-workers were the first to recognize the potential of chiral catalysts for asymmetric cyclopropanation,[15] but their early results with the copper(II) chelates (*R*)- and (*S*)-bis(N-α-phenethylsalicylaldiminato)copper(II) (**36**) were disappointing. Low optical yields were obtained from reactions of selected olefins with either ethyl diazoacetate or diazomethane, although they were nearly identical but opposite in configuration with (*R*)- and (*S*)-**36**. Moser reported even lower optical yields (3%) than those obtained with **36** (6%) for the cyclopropanation of styrene by ethyl diazoacetate using [(−)-tribornyl phosphite]copper(I) chloride **37**.[7] The first breakthrough occurred in 1975 when Aratani reported that copper chelate **38** produced optical yields as high as 68% in reactions of ethyl diazoacetate with 2,5-dimethyl-2,4-hexadiene.[97] Predominant formation of (1*S*,3*S*)-*trans*- and (1*S*,3*R*)-*cis*-chrysanthemic acid ester was observed with (*S*)-**38**, and



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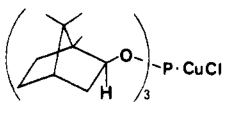

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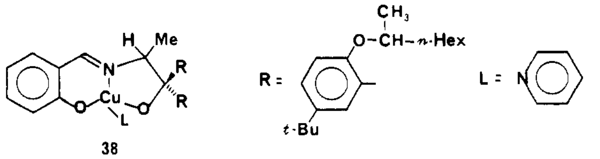

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TABLE VIII. Cyclopropanation of 2,5-Dimethyl-2,4-hexadiene with Alkyl Diazoacetates Catalyzed by (*R*)-38[98]

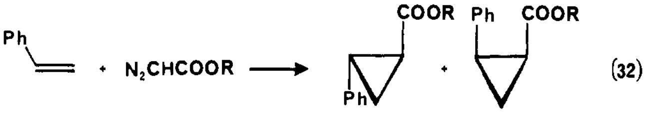
	crysanthemate ester		enantiomeric excess, %	
N_2CHOOR, R =	yield, %	trans/cis	trans	cis
d-menthyl	64	2.6	90	59
d,l-menthyl	67	4.3	90	75
1-adamantyl	82	5.2	85	46
cyclohexyl	71	1.4	70	58
2,3-dimethyl-2-butyl	71	3.6	85	43
tert-butyl	74	3.0	75	46
ethyl	54	1.04	68	62

(*R*)-**38** produced esters of opposite chirality. As expected, the optical activity of the product increased with the bulkiness of substituent R.

Increasing the size of the alkyl group of the diazoacetate ester led to further increases in the optical purities of chrysanthemate esters from those with **38** and ethyl diazoacetate (Table VIII).[98] A 90% enantiomeric excess of (1*S*,3*S*)-*trans* alkyl chrysanthemate is obtained with menthyl diazoacetate, and the (1*S*,3*R*)-*cis* isomer is produced in as high as 75% enantiomeric excess. Lower optical yields were obtained from the cyclopropanation of 1,1-dichloro-4-methyl-1,3-pentadiene leading to permethric acid.[99]

Table VIII also describes the dramatic influence of alkyl group structure on stereoselectivity. The observed increase in trans selectivity with increasing size of the alkyl substituents suggests a higher degree of sensitivity of the bulky alkyl substituent to catalyst **38** than to structurally simpler catalysts such as $Rh_2(OAc)_4$ (Table IV). However, the increases in percent enantiomeric excess do not parallel the observed increases in stereoselectivity which suggests that size alone does not determine enantioselectivity.

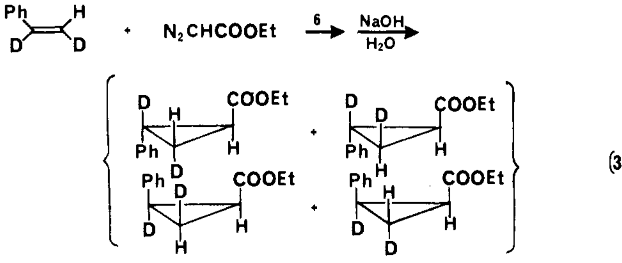
Asymmetric induction from the use of Nakamura's chiral cobalt catalyst, $Co(\alpha\text{-cqd})_2\cdot H_2O$ (**6**),[29] is at least as good as that from **38**[99] for the cyclopropanation of styrene (eq 32), α-methylstyrene, or 1,1-diphenylethylene, but the use of this catalyst is restricted to a limited selection of conjugated olefins.[29a] Methyl α-phenylacrylate undergoes cobalt-catalyzed cyclopropanation readily with ethyl diazoacetate at 0 °C, but vinyl ethers and even norbornadiene are not cyclopropanated. Pyrazoline intermediates were ruled out, but the aberent reactivity of **6** towards alkenes has not been explained. A cobalt–carbene complex with a low barrier to rotation about the metal–carbene bond, similar to that proposed for octaethylporphinatocobalt(II) in its reactions with ethyl diazoacetate,[100] was invoked to explain enantioselectivity derived from the use of **6**.



(32)

		% ee	% ee
R = neopentyl	**6**	88	81
R = *l*-menthyl	(*R*) - **38**	69	54
R = *l*-menthyl	(*S*) - **38**	81	78

Nakamura found that enantioselectivity increased with an increase in the bulkiness of the ester group of diazoacetate, but in his investigation stereoselectivity paralled enantioselectivity.[29b] Also, addition of a donor molecule to the cobalt(II) catalyst caused a marked change in enantioselectivity for the cyclopropanation of styrene, which with β- or γ-picoline reversed the configuration of the prevailing enantiomer. Most interestingly, geometrical isomerization of *cis*-styrene-d_2 occurred during but not prior to carbenoid cyclopropanation (eq 33) and was explained as due to cobaltacyclobutane formation by either a symmetry-allowed $[2_s + 2_a]$ cycloaddition or a biradical process.

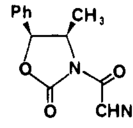


(33)

However, Brookhart has observed the same isomeration in stoichiometric reactions of $Cp(CO)_2FeCHPh^+$ with *cis*-styrene-d_1,[101] and his explanation allows for bond rotation of the alkene after attachment to the electrophilic carbene. An alternate explanation is available from an extension of Scheme I.

A novel pattern of enantioselectivities was recently reported by Laidler and Milner using chiral copper(II) Schiff base catalysts derived from L-phenylalanine and aromatic aldehydes.[102] Although cyclopropane yields and enantiomeric excesses were low, both the degree and direction of optical induction were found to depend upon the olefin. An explanation was provided that concurs with π-complex formation (Schemes I and II) as the initial metal carbene–olefin interaction.

Asymmetric induction with the use of chiral diazo compounds and an achiral catalyst was attempted recently. Doyle and co-workers have reported the synthesis of chiral *N*-(diazoacetyl)oxazolidones **39** and **40**



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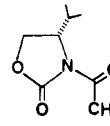

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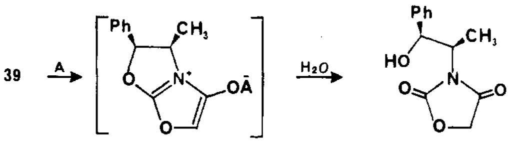
and their use in the $Rh_2(OAc)_4$-catalyzed cyclopropanation of styrene.[103] Although optical yields were moderate (13% ee of the 1*R*,2*R* enantiomer and 14% ee of the 1*R*,2*S* enantiomer) and products of the same chirality were produced from **39** and **40**, product yields were low because of competing intramolecular association of the oxazolidone carbonyl group with the carbenoid center (e.g., eq 34, A = $Rh_2(OAc)_4$). However, the observed enantioselectivity with **39** or **40** is far greater than that previously obtained with 1-menthyl diazoacetate (0.7% ee using copper powder).[98]



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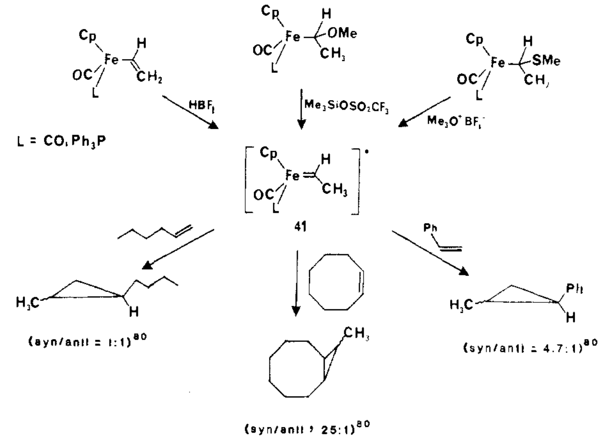
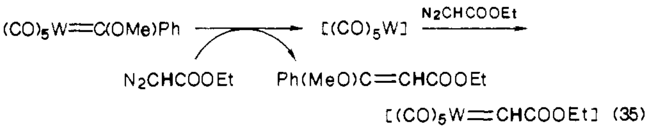
F. Stoichiometric Metal Carbene Reagents

Electrophilic metal carbene complexes, particularly those of chromium, tungsten, and iron, have been designed for use as highly versatile and selective stoichiometric cyclopropanation reagents.[104,105] Those possessing an α-heteroatom substituent such as oxygen are stable, isolable reagents, although poor cyclopropanating agents, whereas metal carbene complexes without a stabilizing α-heteroatom substituent are unstable, but they are good cyclopropanating agents. Basically, three methods are available for the generation of these carbene reactants:[79-81,106-108]



Cyclopentadienyliron carbene complexes afford greater stereoselectivity in cyclopropanation reactions than do carbene complexes of tungsten, and a high degree of enantioselectivity is obtained when L in 41 is a chiral phosphine.[109]

Stoichiometric metal carbene reagents with destabilizing electron withdrawing substituents such as 42 which are accessible from diazo carbonyl compounds have not been prepared, although a stable Fischer carbene has been used to generate such a reagent as a catalytic intermediate (eq 35).[49] The Fischer carbene



$$(CO)_5W{=}C(OMe)Ph \xrightarrow[N_2CHCOOEt \qquad Ph(MeO)C{=}CHCOOEt]{} [(CO)_5W] \xrightarrow{N_2CHCOOEt} [(CO)_5W{=}CHCOOEt] \quad (35)$$

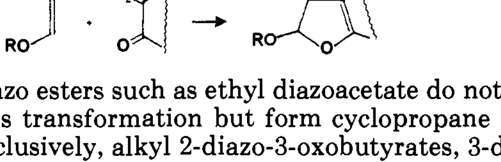
42

was described as a "procatalyst" for the generation of the active cyclopropanation agent. That the selectivities for cyclopropanation observed for 42 and for $N_2CHOOEt/Rh_2(OAc)_4$ were nearly identical supports the basic mechanistic similarity of catalytic and stoichiometric methods for cyclopropanation. Given the scope and limitations of the two methodologies, they remain complementary.

IV. Dipolar Addition

A. Dihydrofuran Formation

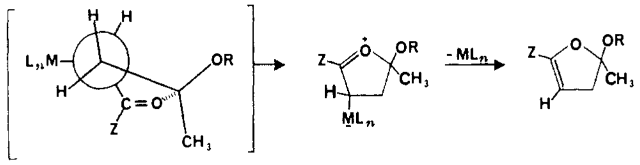
Alkyl vinyl ethers react with certain diazo carbonyl compounds to form dihydrofurans in what is formally a 1,3-dipolar addition reaction (eq 36).[110] Although



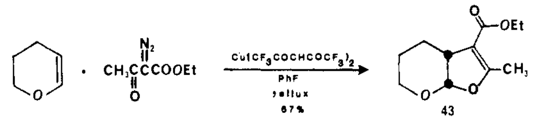
(36)

diazo esters such as ethyl diazoacetate do not undergo this transformation but form cyclopropane products exclusively, alkyl 2-diazo-3-oxobutyrates, 3-diazo-2,4-pentanedione, and even diazo ketones[21,111] undergo the dipolar addition process preferentially. Developed and utilized as an advantageous methodology for dihydrofuran formation by Wenkert,[4a,b,63,111] the addition transformation has been thoroughly investigated by Alonso and co-workers.[110]

SCHEME III. Proposed Mechanism for Dihydrofuran Formation[21]



Dipolar addition is restricted to vinyl ethers, including furans, and is regiospecific with vinyl ethers but not with furans. Diazo ketones of varied structures are required (eq 37–40); diazo esters, including diazomalonate, do not undergo this transformation. Originally copper bronze and $(MeO)_3P{\cdot}CuI$ were the preferred catalysts, but recently $Cu(acac)_2$, $Cu(CF_3COCHCOCF_3)_2$, and $Rh_2(OAc)_4$ have also been used. Alonso has reported that $Cu(CF_3COCHCOCF_3)_2$ is superior to $Cu(acac)_2$.[110]



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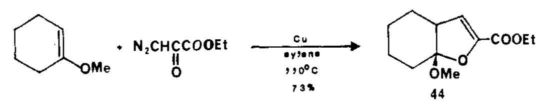

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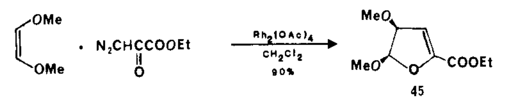

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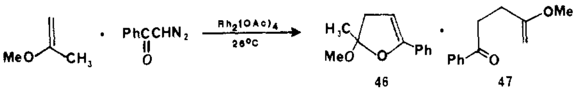


46 47

(40)[21]

malonate, do not undergo this transformation. ...

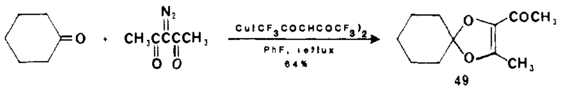
The apparent dipolar addition has been explained as an extension of Scheme II.[21] Increased stabilization that is provided to the developing electrophilic center of the reacting olefin by the carbonyl group can be expected to alter the reaction course by forming dihydrofuran products (Scheme III). Vinyl ethers allow greater charge development in the transition state, and the ketone carbonyl group is more nucleophilic than that of an ester. As seen in eq 40, dipolar addition is competitive in certain cases with an apparent carbon–hydrogen insertion process (section V.B).

B. 1,3-Dioxole Formation

Aldehydes and ketones react with either 2-diazo-3-oxobutyrate or 3-diazo-2,4-pentanedione in the presence of copper(II) chelates to form 1,3-dioxoles exclusively (eq 41–43).[113-115] Although sensitive to steric influences

48

(41)[114]



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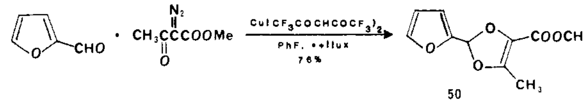

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(43)[115]

from the carbonyl compound, this transformation is general for even α,β-unsaturated aldehydes. Copper(II) hexafluoroacetylacetonate is superior to other copper chelates, and copper(II) triflate was not effective.[115] Simple diazo esters and diazomethane led to complex mixtures of products.[114] Synchronous [1,3]-dipolar cycloaddition of the keto carbenoid intermediate or the production of a short-lived ylide intermediate accounts for available data.[115]

V. *Insertion Reactions*

A. Carbon-Hydrogen Insertion

Originally based on the use of copper catalysts,[2] the insertion of metal-associated carbenes into carbon-hydrogen bonds has undergone a renaissance with the advent of rhodium(II) carboxylate catalysts. Intermolecular carbon-hydrogen insertion into paraffins by diazoacetate esters (eq 44) has been achieved with

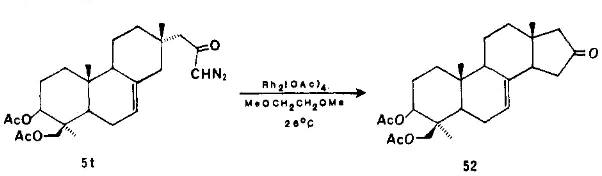
$$RH + N_2CHCOOEt \xrightarrow{Rh_2(OOCCF_3)_4} RCH_2COOEt + N_2 \qquad (44)$$

rhodium(II) trifluoroacetate.[116] A large excess of the alkane is required to prevent oligomerization of the carbene, and product yields are dependent on the catalyst employed, but rhodium(II) perfluoroalkanoates are clearly effective. Regioselectivities for these insertion reactions are also catalyst dependent, and the 9-triptycene (9-TRP) rhodium(II) carboxylate alkyl group affords both efficient conversions and a higher selectivity for insertion into primary C-H bonds:[117]

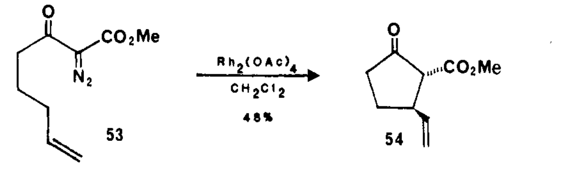
	$CH_3\text{-}\overset{H_3C}{CH}\text{-}\overset{CH_3}{CH}\text{-}CH_3$		$CH_3\text{-}\overset{CH_3}{CH}\text{-}CH_2\text{-}CH_3$			
$Rh_2(OOCCF_3)_4$	88	12	5	25	66	4
$Rh_2(OOC\text{-}9\text{-}TRP)_4$	67	33	18	18	27	37

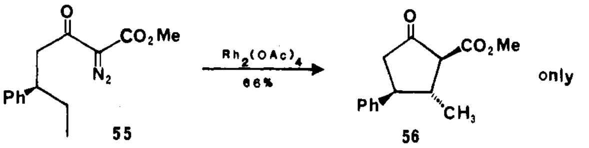
Analogous effects have been observed with the use of RhTPPI 8.[118]

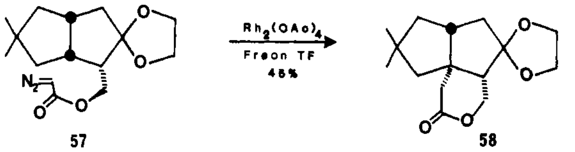
Intramolecular C-H insertions of carbenes are synthetically important, and they have also evolved with the use of rhodium(II) carboxylates. Wenkert was the first to report the effectiveness of $Rh_2(OAc)_4$.[119] The conversion of a isopimaradiene system **51** into a steroid skeleton **52** (eq 45) was achieved in 60% yield with this catalyst, and poor yields characterized the $CuSO_4$-catalyzed process. Taber and co-workers have undertaken a comprehensive examination of this methodology.[120-122] They employed α-diazo-β-keto esters for intramolecular C-H insertion and found that these diazo compounds undergo highly selective conversions to cyclopentanone derivatives. Carbon-hydrogen insertion competes effectively with other carbenic processes, even at the allylic position of **53** (eq 46),[120] and occurs with a high degree of diastereoselectivity (eq 47).[122] Exclusive formation of the cyclopentanone ring coupled with the high reaction diastereoselectivity suggests a chairlike transition state for the insertion reaction.[122] However, whereas acyclic systems show a substantial preference for five-membered ring formation, the same is not necessarily true for cyclic systems (eq 48).[123]



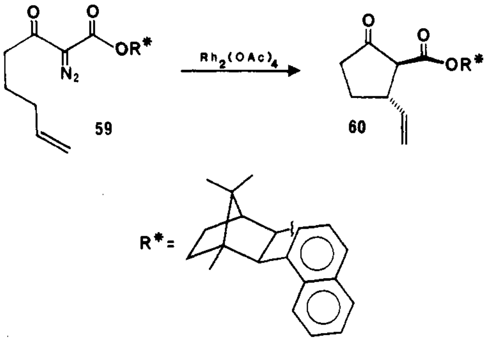
5t 52 (45)[119]





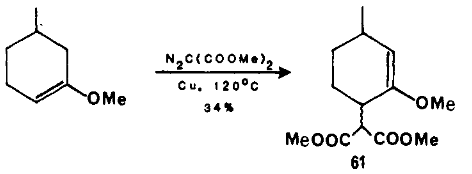


Taber and Raman recently reported a high degree of enantioselectivity in C-H insertion reactions of α-diazo-β-keto esters bearing a chiral alkyl ester group derived from camphor (e.g., eq 49).[121] The diastereoselectivity for the conversion of **59** → **60** was 92:8, and these esters are conveniently separated by HPLC.



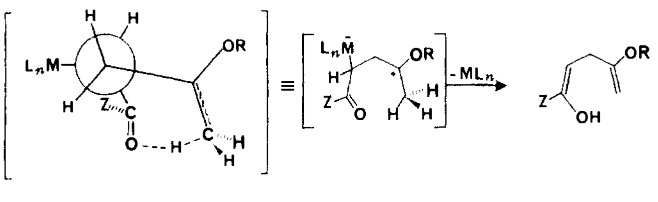
B. Apparent Allylic C-H Insertion

When cyclohexene is treated with dialkyl diazomalonate in the presence of copper catalysts, a formal carbene carbon-hydrogen insertion product is formed in addition to the anticipated cyclopropane derivative.[124] The origin of this insertion product has been the subject of considerable speculation,[2b,44] and only recently has the question been resolved. In the meantime, a select number of synthetically useful insertion reactions began to appear (e.g., eq 50)[63] which suggested a commonality of mechanism with cyclopropanation and dihydrofuran formation (e.g., eq 40). However, evidence accumulated thus far indicates that the occurrence of this insertion process is limited.



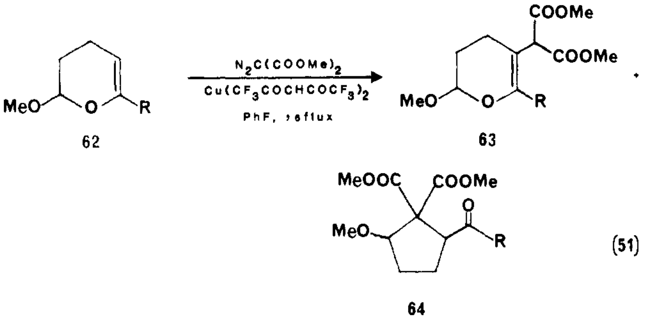
Ethyl diazopyruvate[125] and ethyl diazoacetate[24] do not form these insertion products in any meaningful yield under normal cyclopropanation conditions. Only dia-

SCHEME IV. Proposed Mechanism for Apparent Allylic C-H Insertion[21]

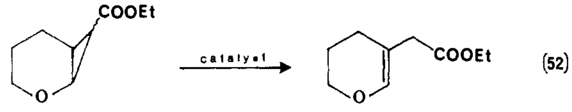


zomalonates and α-diazoacetophenone[21] appear to be capable of generating apparent allylic carbon–hydrogen insertion products, but only with certain alkenes. Even dicyclopropylethylene does not yield these products when treated with dimethyl diazomalonate in the presence of $Cu(acac)_2$.[126] Doyle and co-workers have proposed that these products arise in competition with cyclopropanes and/or dihydrofurans by hydrogen transfer in the transition state encompassing the interacting metal–carbene and alkene (Scheme IV). The apparent limitations to this transformation may be related to the basicity of the carbonyl group and the orientation of the allylic C–H bond relative to the base.

Recently, Alonso and Garcia reported that 2-alkoxydihydropyrans **62** undergo apparent vinyl C–H insertion and novel addition–rearrangement in catalytic reactions (eq 51: a, R = H; b, R = CH_3).[127] The oxocyclopropane–vinyl ether rearrangement (e.g., eq 52) had been previously described by Doyle and van Leusen as a general reaction,[88,128] and the viability of this transformation was confirmed by Alonso and Garcia. However, their interpretation of this process was that the oxocyclopropane underwent Lewis acid-catalyzed ring opening, rather than metal insertion,[88] and this explanation is probably correct for common cyclopropanation catalysts.

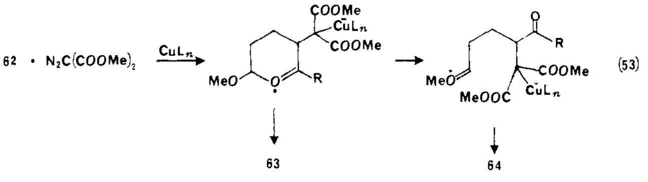


(51)



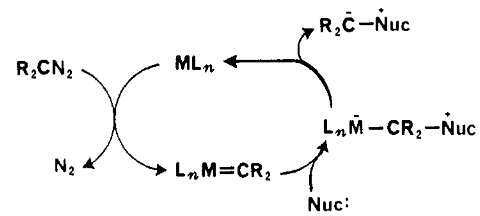
(52)

The molar ratio of **63** to **64** was highly dependent on the reaction solvent, decreasing with increasing polarity, indicating the participation of charged species in the metal-catalyzed addition of diazo compounds to electron-rich olefins.[127] A possible explanation for the production of **63** and **64** was proposed (eq 53). Taken together with Schemes I–IV, all modes of reaction observed for metal carbenes with olefins can now be explained.



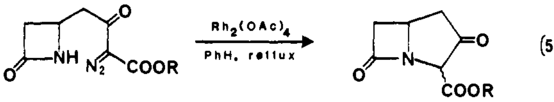
(53)

SCHEME V. Catalytic Generation of Ylides



C. Nitrogen–Hydrogen Insertion

The advent of $Rh_2(OAc)_4$ as an effective catalyst for carbenoid transformations resulted in extensive uses of this methodology for carbenoid insertion into polar bonds. Teyssie's report of its use for insertion into the hydroxyl bond[18a] initiated the widespread use of this catalyst for O–H[129] and N–H insertion reactions.[130,131] Probably the most significant example of intramolecular N–H insertion is the key step (eq 54) in the Merck synthesis of carbapenams.[130] Similar examples using a variety of catalytic methods have been reported.[132–135]



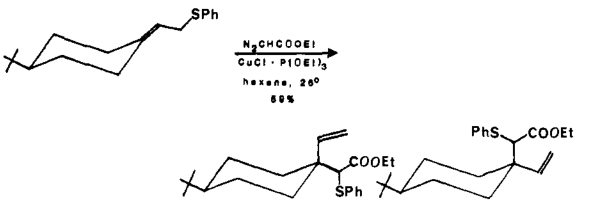
(54)

VI. Catalytic Methods for Ylide Generation and Rearrangements

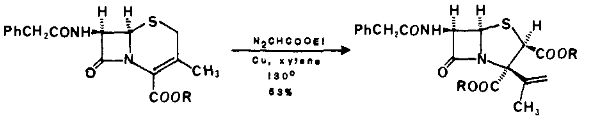
A. [2,3]-Sigmatropic Rearrangement

Carbenoid entry into reactive ylides is a useful alternative to the widely employed base-promoted technologies.[136] Although suitable for ylide production, carbenes generated photochemically and thermally in the presence of organic compounds containing heteroatoms are relatively indiscriminate.[137,138] The potentially more general catalytic approach to carbenoid generation began to evolve with the use of copper catalysts[139–145] and, as with catalytic cyclopropanation reactions, the discovery of $Rh_2(OAc)_4$ as a highly effective catalyst for ylide generation[40,146] accelerated the use of this methodology. In the catalytic approach, diazo compounds combine with the transition-metal catalyst to form the reactive electrophilic carbene complex. Nucleophilic addition followed by dissociation of the catalytically active metal species and ylide complete the catalytic cycle (Scheme V).

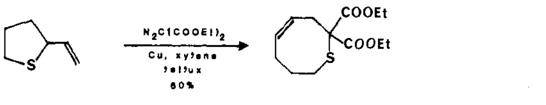
The symmetry-allowed [2,3]-sigmatropic rearrangement[147] is a facile bond reorganization process for catalytically generated ylides. Copper catalysts have been employed for the generation of allylic sulfur ylides and their subsequent [2,3]-sigmatropic rearrangement in a variety of synthetic applications (e.g., eq 55–57). However, as Vedejs has pointed out,[149] copper catalysts are not generally successful for these transformations since high yields for synthetic conversions such as that in eq 57 could not be achieved, and analogous reactions with diazo ketones were unsuccessful. Rhodium(II) acetate has greater potential for these transformations (eq 58 and 59), and its use allows these reactions to take place under milder conditions than necessitated by the use of copper. The rhodium carbonyl cluster $Rh_6(CO)_{16}$



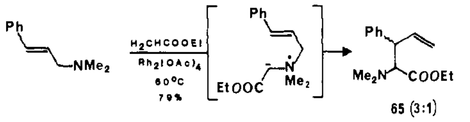
91 : 9 (55)[143]



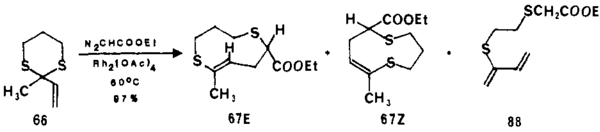
(56)[147]



(57)[148]



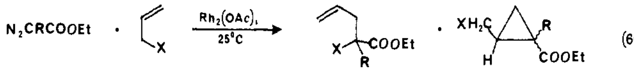
65 (3:1) (58)[40]



66 67E 67Z 88 (59)[150]

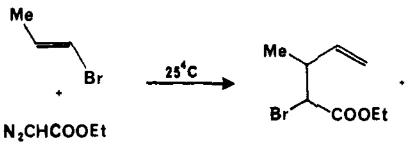
is also useful for the generation and rearrangement of ylides from allyl sulfides and amines, and in some cases is superior to $Rh_2(OAc)_4$.[40] In general, catalysts that are effective for cyclopropanation are at least as active for ylide generation from allyl sulfides.[151,152] Elimination reactions of intermediate ylides such as in the conversion of **66** to **68** can be competitive with [2,3]-sigmatropic rearrangement (**67**/**68** = 3.4).[150] However, cyclopropanation is not competitive with ylide generation from allylamines or sulfides.

Ando and co-workers were the first to show that the copper-salt-catalyzed decomposition of diazo esters in the presence of allyl halides could be used to enter halonium ylides.[145] Here cyclopropanation is competitive with the generation and rearrangement of ylides. Recent systematic investigations by Doyle, Tamblyn, and Bagheri with rhodium and copper catalysts have shown that the product distribution is dramatically dependent on the nucleophilicity of the halide (eq 60), on the diazo compound, and on the catalyst.[40] With crotyl bromide, for example, the rhodium(II)-acetate-catalyzed decomposition of ethyl diazoacetate exhibits competition between only cyclopropanation and the [2,3]-sigmatropic rearrangement (eq 61), whereas copper catalysts employed under the same conditions generate the product from direct carbon–heteroatom insertion (**70**) as well as **69** and **71**.[40] These results and those from analysis of diastereoselectivity in the formation of **69** (1.2 with $Rh_2(OAc)_4$ and 0.8–0.9 with copper catalysts) indicate that the copper catalysts, and also $Rh_2(OAc)_4$ at or above 40 °C, are capable of carbon–bromide bond cleavage from the bromide-associated metal carbene (Scheme VI) prior to metal dissociation of the reactive ylide.

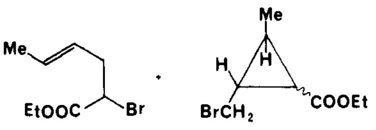


(60)

R = H	X = I	98%	100	0
H	Br	76%	28	72
H	Cl	95%	5	95
COOEt	Br	92%	93	7



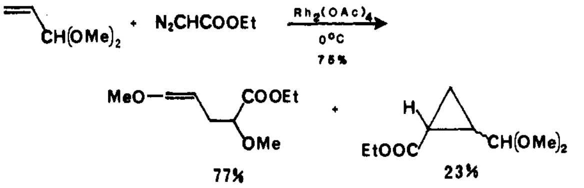
69



70 71 (61)

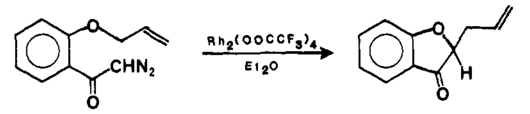
catalyst	69, %	70, %	71, %
$Rh_2(OAc)_4$	67	0	33
$Cu(acac)_2$	43	45	7
$CuCl \cdot P(O\text{-}i\text{-}Pr)_3$	32	53	6
Cu bronze	34	52	7

Allyl ethers are like allyl chlorides in their preference for cyclopropanation. However, allyl acetals undergo ylide generation in $Rh_2(OAc)_4$-catalyzed reactions with diazo esters, and subsequent production of 2,5-dialkoxy-4-alkenoates by the [2,3]-sigmatropic rearrangement occurs in moderate to good yields (e.g., eq 62).[150]

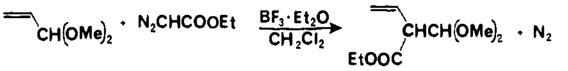


77% 23% (62)

Like those with allyl halides, reactions with acetals are dependent on the catalyst, diazo compound, acetal, and temperature. Stevens rearrangement products are observed in certain cases, even with $Rh_2(OAc)_4$ catalysis. That ylides derived from allyl acetals undergo preferential rearrangement in competition with cyclopropanation, whereas those from the corresponding allyl ethers are relatively unresponsive to ylide rearrangement, demonstrates that heteroatom substitution at the allylic carbon accelerates the [2,3] sigmatropic rearrangement. However, the ylide rearrangement in intramolecular reactions of diazo allyl ethers appears to be highly favored (e.g., eq 63).[153] Lewis acid catalyzed reactions of allyl acetals with diazo compounds take a completely different pathway to form β,γ-unsaturated acetals (e.g., eq 64).[154]



(63)

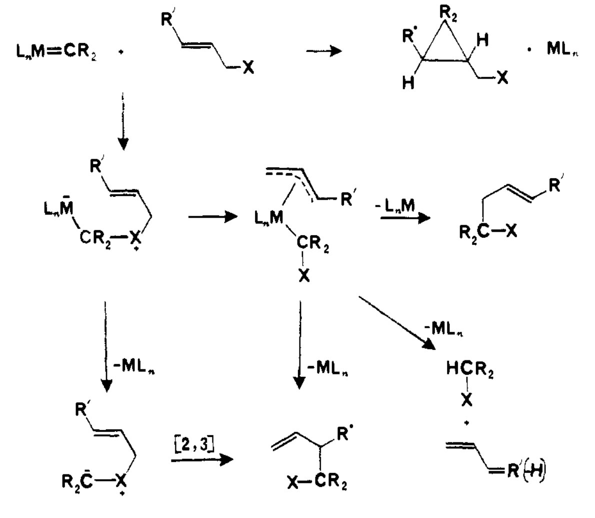


(64)

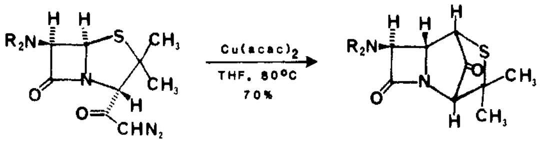
B. Ylide Intermediates in Carbon–Heteroatom Insertion and Miscellaneous Transformation

Effective ylide generation in transition-metal-catalyzed reactions of diazo compounds depends on the

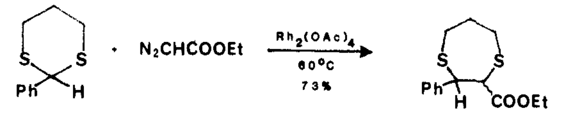
SCHEME VI. Competition between [2,3] and [1,2] Rearrangements



catalyst, diazo compound, heteroatom, and competition with such transformations as cyclopropanation. With sulfides and amines, ylide formation occurs exclusively and, in the absence of an allylic double bond to direct bond migration, 1,2-carbon shifts (Stevens rearrangements) occur (e.g., eq 65 and 66). The potential complexity of these transformations is suggested by the conversion of 72 to 73, which must have occurred by elimination–addition from the intermediate ylide in order to produce the observed stereochemical result.[155] As suggested by the formation of 68 from 66 in eq 59, elimination can also compete with 1,2-bond migration.[150] Kirmse and co-workers have recently confirmed the relative unreactivity of ethers towards ylide generation in $Rh_2(OAc)_4$-catalyzed reactions,[156] but they did observe that insertion of methylene into the carbon–oxygen bond occurs selectively and in preference to carbon–hydrogen insertion.

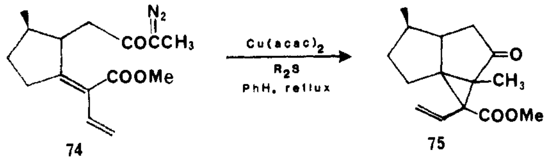


72 73 (65)[154]



(66)[150]

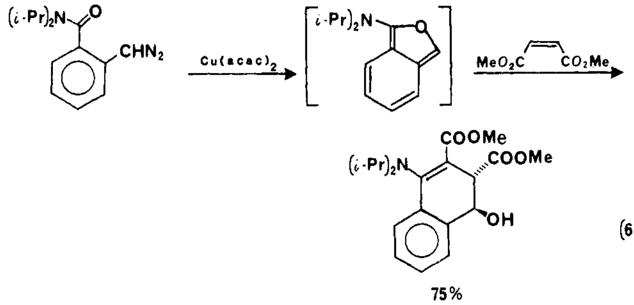
Hudlicky and Short have apparently successfully employed ylide intermediates for intramolecular cyclopropanation of an α,β-unsaturated ester (eq 67).[157]



74 75 (67)

In the absence of either dimethyl sulfide or diphenyl sulfide, the yield of 75 was very low; in their presence, the yield was improved. A combination of $Cu(acac)_2$ and $CuSO_4$ effected smooth conversion of 74 to 75.

In a novel application of carbenoid methodologies, Beak and Chen have used *o*-diazobenzamides to form 2-azaisobenzofurans which can be trapped in situ by dienophiles to form 3,4-dihydronaphthalenes (eq 68).[158] This approach to annelation of tertiary aromatic amides allows addition of a formyl carbon and a dienophile to complete a six-membered ring.



(68)

VII. Summary

What began as a convenient entry to vaguely defined carbenoid species in addition reactions with alkenes has become a highly versatile methodology for organic synthesis. Effective transition-metal catalysts are now available for transformations ranging from cyclopropanation and dipolar addition to insertion reactions and ylide generation/rearrangement. For most of these processes rhodium(II) carboxylates offer considerable advantages in reaction conditions and conversion yields over alternative copper or palladium catalysts. Electrophilic metal carbene intermediates are implicated in these reactions, and their reactivities are principle determinants of selectivity.

Although breakthroughs have recently been made in the design of rhodium catalysts and diazo compounds for control of regioselectivity and stereoselectivity,[159] there is room for improvement, and the same statement can be made about cobalt or copper catalysts in enantioselective cyclopropanation reactions. The architecture of the metal carbene complex in its interaction with the reacting substrate will be a major consideration in future designs, and both electronic and steric factors can be employed to influence selectivity. With certain diazo compounds and alkenes, dipolar addition and/or apparent allylic carbon–hydrogen insertion occur in lieu of cyclopropanation, but effective catalytic control of these alternative transformations has not yet been realized.

Ylide generation is one of the newest successful applications of catalytic methods. In addition to ylides derived from sulfides and tertiary amines, which are accessible in base-promoted methodologies, those from bromides, iodides, and even acetals can be generated from diazo compounds with rhodium(II) carboxylates. Both the [2,3]-sigmatropic rearrangement and the [1,2]-Stevens rearrangement are viable transformations with apparent synthetic advantages.

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Hudlicky, Ph. Teyssie, and E. Wenkert for their exchange of information.

VIII. ***References***

(1) Yates, P. *J. Am. Chem. Soc.* **1952**, *74*, 5376.
(2) (a) Dave, V.; Warnhoff, E. *Org. React. (N.Y.)* **1970**, *18*, 217. (b) Wulfman, D. S.; Linstrumelle, G.; Cooper, C. F. In *The Chemistry of Diazonium and Diazo Groups*; Patai, S., Ed.; Wiley: New York, 1978; Part 2, Chapter 18. (c) Burke, S. D.; Grieco, P. A. *Org. React. (N.Y.)* **1979**, *26*, 361.
(3) Marchand, A. P.; MacBrockway, N. *Chem. Rev.* **1974**, *74*, 431.
(4) (a) Wenkert, E. *Acc. Chem. Res.* **1980**, *13*, 27. (b) Wenkert, E. *Heterocycles* **1980**, *14*, 1703. (c) Doyle, M. P. In *Catalysis of Organic Reactions*; Augustine, R. L., Ed.; Marcel Dekker: New York, 1985; Chapter 4.
(5) Silberrad, O.; Roy, C. S. *J. Chem. Soc.* **1906**, *89*, 179.
(6) Nozaki, H.; Moriuti, S.; Yamabe, M.; Noyori, R. *Tetrahedron Lett.* **1966**, 59.
(7) Moser, W. R. *J. Am. Chem. Soc.* **1969**, *91*, 1135, 1141.
(8) (a) House, H. O.; Blankley, C. J. *J. Org. Chem.* **1968**, *33*, 53. (b) D'yakonov, I. A.; Vitenberg, A. G.; Komendantov, M. I. *J. Org. Chem., USSR* **1965**, *1*, 1193.
(9) (a) Wittig, G.; Schwarzenbach, K. *Justus Liebigs Ann. Chem.* **1961**, *650*, 1. (b) Bacon, R. G. R.; Hill, H. A. O. *Quart. Rev. (London)* **1965**, *19*, 95. (c) Komendantov, M. I.; D'yakonov, I. A.; Smirnova, T. S. *J. Org. Chem., USSR* **1966**, *2*, 561.
(10) (a) House, H. O.; Fischer, W. F., Jr.; Gall, M.; McLaughlin, T. E.; Peet, N. P. *J. Org. Chem.* **1971**, *36*, 3429. (b) Cowan, D. O.; Couch, M. M.; Kopecky, K. R.; Hammond, G. S. *J. Org. Chem.* **1964**, *29*, 1922. (c) D'yakanov, I. A.; Vitenberg, A. G. *J. Org. Chem., USSR* **1967**, *3*, 1115.
(11) Salomon, R. G.; Kochi, J. K. *J. Am. Chem. Soc.* **1973**, *95*, 3300.
(12) Salomon, R. G.; Kochi, J. K. *J. Am. Chem. Soc.* **1973**, *95*, 1889.
(13) Salomon, R. G.; Salomon, M. F.; Heyne, T. R. *J. Org. Chem.* **1975**, *40*, 756.
(14) (a) Armstrong, R. K. *J. Org. Chem.* **1966**, *31*, 618. (b) Bogdanovic, B.; Kröner, M.; Wilke, G. *Justus Liebigs Ann. Chem.* **1966**, *199*, 1.
(15) (a) Nozaki, H.; Moriuti, S.; Takaya, H.; Noyori, R. *Tetrahedron Lett.* **1966**, 5239. (b) Nozaki, H.; Takaya, H.; Moriuti, S.; Noyori, R. *Tetrahedron* **1968**, *24*, 3655. (c) Noyori, R.; Takaya, H.; Nakanishi, Y.; Nozaki, H. *Can. J. Chem.* **1969**, *47*, 1242.
(16) (a) Fischer, E. O.; Dötz, K. H. *Chem. Ber.* **1970**, *103*, 1273. (b) Dötz, K. H.; Fischer, E. O. *Ibid.* **1972**, *105*, 1356.
(17) Paulissen, R.; Hubert, A. J.; Teyssie, Ph. *Tetrahedron Lett.* **1972**, 1465.
(18) (a) Paulissen, R.; Reimlinger, H.; Hayez, E.; Hubert, A. J.; Teyssie, Ph. *Tetrahedron Lett.* **1973**, 2233. (b) Hubert, A. J.; Noels, A. F.; Anciaux, A. J.; Teyssie, Ph. *Synthesis* **1976**, 600.
(19) Anciaux, A. J.; Hubert, A. J.; Noels, A. F.; Petiniot, N.; Teyssie, Ph. *J. Org. Chem.* **1980**, *45*, 695.
(20) (a) Salomon, R. G.; Kochi, J. K. *J. Organomet. Chem.* **1974**, *64*, 135. (b) Wallraff, G. M.; Boyd, R. H.; Michl, J. *Ibid.* **1983**, *105*, 4550.
(21) Doyle, M. P.; Griffin, J. H.; Bagheri, V.; Dorow, R. L. *Organometalics* **1984**, *3*, 53.
(22) Nakamura, A.; Koyama, T.; Otsuka, S. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 593.
(23) Doyle, M. P.; Wang, L. C.; Loh, K.-L. *Tetrahedron Lett.* **1984**, *25*, 4087.
(24) Doyle, M. P.; Dorow, R. L.; Buhro, W. E.; Griffin, J. H.; Tamblyn, W. H.; Trudell, M. L. *Organometalics* **1984**, *3*, 44.
(25) Hartley, F. R. *Chem. Rev.* **1973**, *73*, 163.
(26) (a) Wakatsuki, Y.; Nozakura, S.; Murahashi, S. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 3426. (b) Baenziger, N. C.; Richards, G. F.; Doyle, J. R. *Acta Crystallogr.* **1965**, *18*, 924. (c) Aikens, D. A.; Murray, R. C. *Inorg. Chem.* **1969**, *8*, 539.
(27) (a) Wipke, W. T.; Goeke, G. L. *J. Am. Chem. Soc.* **1974**, *96*, 4244. (b) Heumann, A.; Reglier, M.; Waegell, B. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 866. (c) Wright, L. L.; Wing, R. M.; Rettig, M. F. *J. Am. Chem. Soc.* **1980**, *102*, 5950. (d) Wright, L. L.; Wing, R. M.; Rettig, M. F. *Ibid.* **1982**, *104*, 610.
(28) (a) Freeman, B. H.; Lloyd, D.; Singer, M. I. C. *Tetrahedron* **1974**, *30*, 211. (b) Wittig, G.; Haag, W. *Chem. Ber.* **1955**, *88*, 1654.
(29) (a) Nakamura, A.; Konishi, A.; Tsujitani, R.; Kudo, M.; Ctsuka, S. *J. Am. Chem. Soc.* **1978**, *100*, 3449. (b) Nakamura, A.; Konishi, A.; Tatsuno, Y.; Otsuka, S. *Ibid.* **1978**, *100*, 3443, 6544. (c) Tatsuno, Y.; Konishi, A.; Nakamura, A.; Otsuka, S. *J. Chem. Soc., Chem. Commun.* **1974**, 588.
(30) Schrauzer, G. N.; Windgassen, R. J. *Chem. Ber.* **1966**, *99*, 602.
(31) (a) Doyle, M. P.; Pickering, R. A.; Dykstra, R. L.; Cook, B. R. *J. Am. Chem. Soc.* **1982**, *104*, 3392. (b) Doyle, M. P.; Pickering, R. A.; Cook, B. R. *J. Inorg. Biochem.* **1983**, *19*, 329.
(32) (a) Felthouse, T. R. *Prog. Inorg. Chem.* **1982**, *29*, 73. (b) Cotton, F. A.; Walton, R. A. *Multiple Bonds Between Metal Atoms*; Wiley: New York, 1982; p 311. (c) Boyar, E. B.; Robinson, S. D. *Coord. Chem. Rev.* **1983**, *50*, 109.
(33) (a) Drago, R. S.; Long, J. R.; Cosmano, R. *Inorg. Chem.* **1982**, *21*, 2196; (b) 1981, *20*, 2920. (c) Drago, R. S.; Tanner, S. P.; Richman, R. M.; Long, J. R. *J. Am. Chem. Soc.* **1979**, *101*, 2897.
(34) Doyle, M. P.; Colsman, M. R.; Chinn, M. S. *Inorg. Chem.* **1984**, *23*, 3684.
(35) Schurig, V.; Bear, J. L.; Zlatkis, A. *Chromatographia* **1972**, *5*, 301.
(36) Doyle, M. P.; Harn, N. K., unpublished results.
(37) (a) Charan, M. Y.; Zhu, T. P.; Lin, X. Q.; Ahsan, M. Q.; Bear, J. L.; Kadish, K. M. *Inorg. Chem.* **1984**, *23*, 4538. (b) Bear, J. L.; Zhu, T. P.; Malinski, T.; Dennis, A. M.; Kadish, K. M. *Ibid.* **1984**, *23*, 674. (c) Dennis, A. M.; Korp, J. D.; Bernal, I.; Howard, R. A.; Bear, J. L. *Ibid.* **1983**, *22*, 1522. (d) Duncan, J.; Malinski, T.; Zhu, T. P.; Hu, Z. S.; Kadish, K. M.; Bear, J. L. *J. Am. Chem. Soc.* **1982**, *104*, 5507. (e) Kadish, K. M.; Lancon, D.; Dennis, A. M.; Bear, J. L. *Inorg. Chem.* **1982**, *21*, 2987. (f) Dennis, A. M.; Howard, R. A.; Lancon, D.; Kadish, K. M.; Bear, J. L. *J. Chem. Soc., Chem. Commun.* **1982**, 339.
(38) Doyle, M. P.; Loh, K.-L., unpublished results.
(39) Doyle, M. P.; Tamblyn, W. H.; Buhro, W. E.; Dorow, R. L. *Tetrahedron Lett.* **1981**, *22*, 1783.
(40) Doyle, M. P.; Tamblyn, W. H.; Bagheri, V. *J. Org. Chem.* **1981**, *46*, 5094.
(41) (a) Callot, H. J.; Piechocki, C. *Tetrahedron Lett.* **1980**, *21*, 3489. (b) Callot, H. J.; Metz, F.; Piechocki, C. *Tetrahedron* **1982**, *38*, 2365.
(42) Shankar, B. K. R.; Shechter, H. *Tetrahedron Lett.* **1982**, *23*, 2277.
(43) (a) Wulfman, D. S.; Peace, B. W. *Tetrahedron Lett.* **1972**, 3903. (b) Wulfman, D. S.; Thinh, N. V.; McDaniel, R. S., Jr.; Peace, B. W.; Jones, M. T.; Heitsch, C. W. *J. Chem. Soc., Dalton Trans.* **1975**, 522.
(44) Wulfman, D. S.; McDaniel, R. S., Jr.; Peace, B. W. *Tetrahedron* **1976**, *32*, 1241.
(45) Morris, M. L.; Koob, R. D. *Inorg. Chem.* **1985**, *24*, 1769.
(46) Doyle, M. P.; Dorow, R. L.; Tamblyn, W. H. *J. Org. Chem.* **1982**, *47*, 4059.
(47) (a) Aratani, T.; Yoneyoshi, Y.; Nagase, T. *Tetrahedron Lett.* **1975**, 1707; **1977**, 2599; (b) **1982**, *23*, 685.
(48) Casey, C. P.; Polichnowski, S. W.; Shusterman, A. J.; Jones, C. R. *J. Am. Chem. Soc.* **1979**, *101*, 7282.
(49) Doyle, M. P.; Griffin, J. H.; Conceicão, J. *J. Chem. Soc., Chem. Commun.* **1985**, 328.
(50) Doyle, M. P.; Dorow, R. L.; Tamblyn, W. H.; Buhro, W. E. *Tetrahedron Lett.* **1982**, *23*, 2261.
(51) Hillhouse, G. L.; Haymore, B. L. *J. Am. Chem. Soc.* **1982**, *104*, 1537.
(52) Paulissen, R.; Moniotte, Ph.; Hubert, A. J.; Teyssie, Ph. *Tetrahedron Lett.* **1974**, 3311.
(53) Moniotte, Ph. G.; Hubert, A. J.; Teyssie, Ph. *J. Organomet. Chem.* **1975**, *88*, 15.
(54) (a) Doyle, M. P.; Oppenhuizen, M.; Elliott, R. C.; Boelkins, M. R. *Tetrahedron Lett.* **1978**, 2247. (b) Kitatani, K.; Hiyama, T.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 1647.
(55) (a) Doyle, M. P.; Buhro, W. E.; Davidson, J. G.; Elliott, R. C.; Hoekstra, J. W.; Oppenhuizen, M. *J. Org. Chem.* **1980**, *45*, 3657. (b) Ibata, T.; Sato, R. *Chem. Lett.* **1978**, 1129.
(56) Nagayoshi, K.; Sato, T. *Chem. Lett.* **1983**, 1355.
(57) Doyle, M. P.; Trudell, M. L. *J. Org. Chem.* **1984**, *49*, 1196.
(58) (a) Schönberg, A.; Praefcke, K. *Tetrahedron Lett.* **1964**, 2043. (b) Schönberg, A.; Praefcke, K. *Chem. Ber.* **1966**, *99*, 196.
(59) (a) Smith, A. B., III; Toder, B. H.; Branca, S. J.; Dieter, R. K. *J. Am. Chem. Soc.* **1981**, *103*, 1996. (b) Smith, A. B., III; Dieter, R. K. *Ibid.* **1981**, *103*, 2009, 2017. (c) Smith, A. B., III; Dieter, R. K. *Tetrahedron* **1981**, *37*, 2407.
(60) (a) Smith, A. B., III *J. Chem. Soc., Chem. Commun.* **1974**, 695. (b) Smith, A. B., III; Toder, B. H.; Branca, S. J. *J. Am. Chem. Soc.* **1976**, *98*, 7456. (c) Branca, S. J.; Lock, R.; Smith, A. B., III *J. Org. Chem.* **1977**, *42*, 3165. (d) Smith, A. B., III; Toder, B. H.; Branca, S. J. *J. Am. Chem. Soc.* **1984**, *106*, 3995. (e) Smith, A. B., III; Toder, B. H.; Richmond, R. E.; Branca, S. J. *Ibid.* **1984**, *106*, 4001.
(61) Fuson, R. C.; Cleveland, E. A. *Organic Synthesis*; Wiley: New York, 1955; Collect. Vol. III, p 339.
(62) Wenkert, E.; Greenberg, R. S.; Raju, M. S. *J. Org. Chem.* **1985**, *50*, 4681.
(63) Wenkert, E.; Alonso, M. E.; Buckwalter, B. L.; Sanchez, E. L. *J. Am. Chem. Soc.* **1983**, *105*, 2021.
(64) (a) Shim, K. Y.; Martin, D. J. DOS 21 23 989, 1970; Stauffer Chem. Co. (b) Nurrenbach, A.; Boll, W. DOS 24 00 188, 1974; BASF AG. (c) Milner, D. J.; Holland, D.; Runcorn, C. DOS 28 10 098, 1978; Imperial Chem. Ind.
(65) Corey, E. J.; Myers, A. G. *Tetrahedron Lett.* **1984**, *33*, 3559.
(66) Kirmse, W.; Pook, K.-H. *Chem. Ber.* **1965**, *98*, 4022.

(67) Henne, A. L.; Chanan, H. H.; Turk, A. *J. Am. Chem. Soc.* **1944**, *66*, 1944.

(68) Taber, D. F. *J. Am. Chem. Soc.* **1977**, *99*, 3513.

(69) Kondo, K.; Umenoto, T.; Takahatake, Y.; Tunemoto, D. *Tetrahedron Lett.* **1977**, 113.

(70) Russell, G. A.; McDonnell, J. J.; Whittle, P. R.; Givens, R. S.; Keske, R. C. *J. Am. Chem. Soc.* **1971**, *93*, 1452.

(71) (a) Hudlicky, T.; Sheth, J. P.; Gee, V.; Barnvos, D. *Tetrahedron Lett.* **1979**, 4889. (b) Hudlicky, T.; Koszyk, F. J.; Kutchan, T. M.; Sheth, J. P. *J. Org. Chem.* **1980**, *45*, 5020. (c) Hudlicky, T.; Koszyk, F. J.; Dochwat, D. M.; Cantrell, G. L. *Ibid.* **1981**, *46*, 2911.

(72) (a) Hudlicky, T.; Reddy, D. B.; Govindan, S. V.; Kulp, T.; Still, B.; Sheth, J. P. *J. Org. Chem.* **1983**, *48*, 3422. (b) Hudlicky, T.; Ranu, B. C.; Naqvi, S. M.; Srnak, A. *Ibid.* **1985**, *50*, 123. (c) Hudlicky, T.; Govindan, S. V.; Frazier, J. O. *Ibid.* **1985**, *50*, 4166. (d) Hudlicky, T.; Kwart, L. D.; Tiedje, M. H.; Ranu, B. C.; Short, R. P.; Frazier, J. O.; Rigby, L. H. *Synthesis*, in press.

(73) Doyle, M. P.; van Leusen, D.; Tamblyn, W. H. *Synthesis* **1981**, 787.

(74) Suda, M. *Synthesis* **1981**, 714.

(75) (a) Majchrzak, M. W.; Kotelko, A.; Lambert, J. B. *Synthesis* **1983**, 469. (b) Mende, U.; Radüchel, B.; Skuballa, W.; Vorbrüggen, H. *Tetrahedron Lett.* **1975**, 629.

(76) Doyle, M. P.; Davidson, J. G. *J. Org. Chem.* **1980**, *45*, 1538.

(77) Huisgen, R. *Pure Appl. Chem.* **1981**, *53*, 171.

(78) Freeman, F. *Chem. Rev.* **1975**, *75*, 439.

(79) Brookhart, M.; Humphrey, B. H.; Kratzer, H. J.; Nelson, G. O. *J. Am. Chem. Soc.* **1980**, *102*, 7802.

(80) Brookhart, M.; Tucker, J. R.; Husk, G. R. *J. Am. Chem. Soc.* **1983**, *105*, 258.

(81) Brookhart, M.; Tucker, J. R.; Husk, G. R. *J. Am. Chem. Soc.* **1981**, *103*, 979.

(82) (a) Casey, C. P.; Shusterman, A. J.; Vollendorf, N. W.; Haller, K. J. *J. Am. Chem. Soc.* **1982**, *104*, 2417. (b) Casey, C. P.; Vollendorf, N. W.; Haller, K. J. *Ibid.* **1984**, *106*, 3754.

(83) Casey, C. P.; Shusterman, A. J. *Organometallics* **1985**, *4*, 736.

(84) Casey, C. P.; Cesa, M. C. *Organometallics* **1982**, *1*, 87.

(85) (a) Williams, J. L.; Rettig, M. F. *Tetrahedron Lett.* **1981**, *22*, 385. (b) Ahmad, M. U.; Backvall, J.-E.; Nordberg, R. E.; Norin, T.; Stromberg, S. *J. Chem. Soc., Chem. Commun.* **1982**, 321.

(86) Demonceau, A.; Noels, A. F.; Anciaux, A. J.; Hubert, A. J.; Teyssie, P. *Bull. Soc. Chim. Belg.* **1984**, *93*, 949.

(87) Doyle, M. P.; Chinn, M. S., unpublished results.

(88) Doyle, M. P.; van Leusen, D. *J. Org. Chem.* **1982**, *47*, 5326.

(89) Kunkel, E.; Reichelt, I.; Reissig, H.-U. *Justus Leibigs Ann. Chem.* **1984**, 512.

(90) (a) Piers, E.; Jung, G. L.; Moss, N. *Tetrahedron Lett.* **1984**, *25*, 3959. (b) Piers, E.; Moss, N. *Ibid.* **1985**, *26*, 2735. (c) Piers, E.; Maxwell, A. R.; Moss, N. *Can. J. Chem.* **1985**, *63*, 555.

(91) Mueller, L. G.; Lawton, R. G. *J. Org. Chem.* **1979**, *44*, 4741.

(92) (a) De Smet, A.; Anteunis, M.; Tavernier, D. *Bull. Soc. Chim. Belg.* **1975**, *84*, 67. (b) Decock-Le Reverend, B.; Durand, M. *C.R. Acad. Sci. Paris, Serie C* **1975**, *280*, 209. (c) Decock-Le Reverend, B.; Durand, M.; Merenyi, R. *Bull. Soc. Chim. Fr.* **1978**, *78*, 369.

(93) Anciaux, A. J.; Demonceau, A.; Noels, A. F.; Warin, R.; Hubert, A. J.; Teyssie, P. *Tetrahedron* **1983**, *39*, 2169.

(94) Doyle, M. P.; Wang, L. C., unpublished results.

(95) Taylor, E. C.; Davies, H. M. L. *Tetrahedron Lett.* **1983**, *24*, 5453.

(96) Anciaux, A. J.; Demonceau, A.; Hubert, A. J.; Noels, A. F.; Pertiniot, N.; Teyssie, Ph. *J. Chem. Soc., Chem. Commun.* **1980**, 765.

(97) Aratani, T.; Yoneyoshi, Y.; Nagase, T. *Tetrahedron Lett.* **1975**, 1707.

(98) Aratani, T.; Yoneyoshi, Y.; Nagase, T. *Tetrahedron Lett.* **1977**, 2599.

(99) Aratani, T.; Yoneyoshi, Y.; Nagase, T. *Tetrahedron Lett.* **1982**, *23*, 685.

(100) Johnson, A. W.; Ward, D. *J. Chem. Soc., Perkin Trans. 1* **1975**, 2076.

(101) Brookhart, M.; Kegley, S. E.; Husk, G. R. *Organometalics* **1984**, *3*, 650.

(102) Laidler, D. A.; Milner, D. J. *J. Organomet. Chem.* **1984**, *270*, 121.

(103) Doyle, M. P.; Dorow, R. L.; Terpstra, J. W.; Rodenhouse, R. A. *J. Org. Chem.* **1985**, *50*, 1663.

(104) Casey, C. P. In *Reactive Intermediates*; Jones, M., Jr., Moss, R. A., Eds.; Wiley: New York, 1985; Vol. 3, Chapter 4.

(105) Dötz, K. H. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 587.

(106) (a) Casey, C. P.; Miles, W. H.; Tukada, H. *J. Am. Chem. Soc.* **1985**, *107*, 2924. (b) Casey, C. P.; Miles, W. H. *Organometalics* **1984**, *3*, 808. (c) Casey, C. P.; Miles, W. H.; Tukada, H.; O'Connor, J. M. *J. Am. Chem. Soc.* **1982**, *104*, 3761.

(107) (a) Brookhart, M.; Studabaker, W. B.; Husk, G. R. *Organometalics* **1985**, *4*, 943. (b) Brookhart, M.; Kegleym, S. E.; Husk, G. R. *Ibid.* **1984**, *3*, 650.

(108) Kremer, K. A. M.; Helquist, P. *J. Organomet. Chem.* **1985**, *285*, 231. (b) Kuo, G.-H.; Helquist, P.; Kerber, R. C. *Organometalics* **1984**, *3*, 806. (c) Kremer, K. A. M.; Kuo, G.-H.; O'Connor, E. J.; Helquist, P.; Kerber, R. C. *J. Am. Chem. Soc.* **1982**, *104*, 6119. (d) Kremer, K. A. M.; Helquist, P.; Kerber, R. C. *Ibid.* **1981**, *103*, 1862.

(109) Brookhart, M.; Timmers, D.; Tucker, J. R.; Williams, G. D.; Husk, G. R.; Brunner, H.; Hammer, B. *J. Am. Chem. Soc.* **1983**, *105*, 6721.

(110) (a) Alonso, M. E.; Morales, A.; Chitty, A. W. *J. Org. Chem.* **1982**, *47*, 3748. (b) Alonso, M. E.; Jano, P.; Hernandez, M. I.; Greenberg, R. S.; Wenkert, E. *J. Org. Chem.* **1983**, *26*, 3047.

(111) Dowd, P.; Kaufman, C.; Paik, Y. H. *Tetrahedron Lett.* **1985**, 2283.

(112) Wenkert, E.; Alonso, M. E.; Buckwalter, B. L.; Chou, J. K. *J. Am. Chem. Soc.* **1977**, *99*, 4778.

(113) Alonso, M. E.; Jano, P. *J. Heterocyclic Chem.* **1980**, *17*, 721.

(114) Alonso, M. E.; Chitty, A. W. *Tetrahedron Lett.* **1981**, *22*, 4181.

(115) Alonso, M. E.; Garcia, M. del C.-; Chitty, A. W. *J. Org. Chem.* **1985**, *50*, 3445.

(116) Demonceau, A.; Noels, A. F.; Hubert, A. J.; Teyssie, P. *J. Chem. Soc., Chem. Commun.* **1981**, 688.

(117) Demonceau, A.; Noels, A. F.; Hubert, A. J.; Teyssie, P. *Bull. Soc. Chim. Belg.* **1984**, *93*, 945.

(118) Callot, H. J.; Metz, F. *Tetrahedron Lett.* **1982**, 4321.

(119) Wenkert, E.; Davis, L. L.; Mylari, B. L.; Solomon, M. F.; da Silva, R. R.; Shulman, S.; Warnet, R. J.; Ceccherelli, P.; Curini, M.; Pellicciari, R. *J. Org. Chem.* **1982**, *47*, 3242.

(120) Taber, D. F.; Petty, E. H. *J. Org. Chem.* **1982**, *47*, 4808.

(121) Taber, D. F.; Raman, K. *J. Am. Chem. Soc.* **1983**, *105*, 5935.

(122) Taber, D. F.; Ruckle, R. E., Jr. *Tetrahedron Lett.* **1985**, *26*, 3059.

(123) Cane, D. E.; Thomas, P. J. *J. Am. Chem. Soc.* **1984**, *106*, 5295.

(124) Wulfman, D. S.; McGibbony, B. G.; Steffen, E. K.; Thinh, N. V.; McDaniel, R. S., Jr.; Peace, B. W. *Tetrahedron* **1976**, *32*, 1257.

(125) Alonso, M. E.; Jano, S. P.; Hernandez, M. I. *J. Org. Chem.* **1980**, *45*, 5299.

(126) Alonso, M. E.; Gomez, M. *Tetrahedron Lett.* **1979**, 2763.

(127) Alonso, M. E.; Garcia, M. del C.- *J. Org. Chem.* **1985**, *50*, 988.

(128) Doyle, M. P.; van Leusen, D. *J. Am. Chem. Soc.* **1981**, *103*, 5917.

(129) (a) Ikota, N.; Takamura, N.; Young, S. D.; Ganem, B. *Tetrahedron Lett.* **1981**, *22*, 4163. (b) Noels, A. F.; Demonceau, A.; Petiniot, N.; Hubert, A. J.; Teyssie, Ph. *Tetrahedron* **1982**, *38*, 2733.

(130) Ratcliffe, R. W.; Salzmann, T. N.; Christensen, B. G. *Tetrahedron Lett.* **1980**, *21*, 31.

(131) Moody, C. J.; Pearson, C. J.; Lawton, G. *Tetrahedron Lett.* **1985**, *26*, 3171.

(132) Knierzinger, A.; Vasella, A. *J. Chem. Soc., Chem. Commun.* **1984**, 9.

(133) Andrus, A.; Christensen, B. G.; Heck, J. V. *Tetrahedron Lett.* **1984**, *25*, 595.

(134) Buynak, J. D.; Pajouhesh, H.; Lively, D. L.; Ramalakshi, Y. *J. Chem. Soc., Chem. Commun.* **1984**, 948.

(135) Yamamoto, S.; Itani, H.; Takahashi, H.; Tsuji, T.; Nagata, W. *Tetrahedron Lett.* **1984**, *25*, 4545.

(136) (a) Pine, S. H. *Org. React.* **1970**, *18*, 403. (b) Trost, B. M.; Melvin, L. S. *Sulfur Ylides*; Academic Press: New York, 1975. (c) Jemison, R. W.; Laird, T.; Ollis, W. E.; Sutherland, I. O. *J. Chem. Soc., Perkin Trans. 1* **1980**, 1436, 1450.

(137) (a) Ando, W. *Acc. Chem. Res.* **1977**, *10*, 179. (b) Ando, W. In *The Chemistry of Diazonium and Diazo Groups*; Patai, S., Ed.; Wiley: New York, 1978; Chapter 9.

(138) Iwamura, H.; Imahashi, Y.; Kushida, K.; Aoki, K.; Satoh, S. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 1690.

(139) D'yakonov, I. A.; Domareva, T. V. *Zh. Obshch. Khim.* **1955**, *25*, 934, 1486.

(140) Phillips, D. D.; Champion, W. C. *J. Am. Chem. Soc.* **1956**, *78*, 5452.

(141) Parham, W. E.; Groen, S. H. *J. Org. Chem.* **1966**, *31*, 1694.

(142) Kirmse, W.; Arold, H. *Chem. Ber.* **1968**, *191*, 1008.

(143) Andrews, G.; Evans, D. A. *Tetrahedron Lett.* **1972**, 5121.

(144) Ando, W.; Kondo, S.; Nakayama, K.; Ichibori, K.; Kohoda, H.; Yamato, H.; Imai, I.; Nakaido, S.; Migita, T. *J. Am. Chem. Soc.* **1972**, *94*, 3870.

(145) Ando, W.; Yagihara, T.; Kondo, S.; Nakayama, K.; Yamato, H.; Nakaido, S.; Migita, T. *J. Org. Chem.* **1971**, *36*, 1732.

(146) Gillespie, R. J.; Murray-Rust, J.; Murray-Rust, P.; Porter, A. E. A. *J. Chem. Soc., Chem. Commun.* **1978**, 83.

(147) Yoshimoto, M.; Ishihara, S.; Nakayama, E.; Soma, N. *Tetrahedron Lett.* **1972**, 2923.

(148) Vedejs, E.; Hagen, J. P. *J. Am. Chem. Soc.* **1975**, *97*, 6878.

(149) Vedejs, E. *Acc. Chem. Res.* 1984, *17*, 358.
(150) Doyle, M. P.; Griffin, J. H.; Chinn, M. S.; Van Leusen, D. *J. Org. Chem.* **1984**, *49*, 1917.
(151) Tamblyn, W. H.; Hoffmann, S. R.; Doyle, M. P. *J. Organomet. Chem.* **1981**, *216*, C64.
(152) McCrindle, R.; Sneddon, D. W. *J. Organomet. Chem.* **1985**, *282*, 413.
(153) Doyle, M. P.; DeVries, K., unpublished results.
(154) Doyle, M. P.; Trudell, M. L.; Terpstra, J. W. *J. Org. Chem.* **1983**, *48*, 5146.
(155) Ernest, I. *Tetrahedron* **1977**, *33*, 547.
(156) Kirmse, W.; Chiem, P. V.; Schurig, V. *Tetrahedron Lett.* **1985**, *26*, 197.
(157) Hudlicky, T.; Short, R. P. *J. Org. Chem* .**1982**, *47*, 1522.
(158) Beak, P.; Chen, C.-W. *Tetrahedron Lett.* **1983**, *24*, 2945.
(159) Callot, H. J.; Metz, F. *Tetrahedron* **1985**, *41*, 4495.