It is intersting to note, however, that it may be difficult to lose a proton entirely from the coordination sphere of either complex in eq 18 (e.g., eq 19), as the four π

$$W(CH\text{-}t\text{-}Bu)(NR)L_2Cl_2 \rightarrow$$
$$W(C\text{-}t\text{-}Bu)(NR)L_2Cl + HCl \quad (19)$$

components of the $W\equiv C\text{-}t\text{-}Bu$ triple bond and those of the $W\equiv NR$ pseudo triple bond would then have to compete with each other for d orbitals of π symmetry.

Recently[45] a variation of the reaction shown in eq 18 has been employed to prepare a precursor to a wide variety of complexes of the type $W(CH\text{-}t\text{-}Bu)(NAr)X_2$ (eq 20; Ar = 2,6-diisopropylphenyl). That in which X

$$W(C\text{-}t\text{-}Bu)(dme)Cl_3 + (Me_3Si)NH(2,6\text{-}C_6H_3\text{-}i\text{-}Pr_2) \rightarrow$$
$$W(C\text{-}t\text{-}Bu)(HN\text{-}2,6\text{-}C_6H_3\text{-}i\text{-}Pr_2)(dme)Cl_2 \quad (20)$$

is $OCMe(CF_3)_2$ is a relatively efficient catalyst for the metathesis of cis-2-pentene and the most successful so far for the metathesis of methyl oleate. If $Me_3SiCH=CH_2$ is added to $W(CH\text{-}t\text{-}Bu)(NAr)[OCMe(CF_3)_2]_2$, then a tungstacyclobutadiene complex can be isolated whose structure is a distorted trigonal bipyramid in which the bent WC_3 ring is found to occupy equatorial positions (cf. Figure 2). Interestingly, $W(CH\text{-}t\text{-}Bu)(NAr)(O\text{-}t\text{-}Bu)_2$ does *not* react with ordinary olefins. Therefore the principles of olefin metathesis appear to parallel those of acetylene metathesis; five-coordinate trigonal bipyramidal metallacyclic intermediates seem to be

favorable, and more electron-withdrawing alkoxide ligands produce more active catalysts.

Comments and Conclusions

It is especially pleasing to see how the chemistry of molybdenum and tungsten alkylidyne complexes is developing in relation to other chemistry characteristic of the heavier, earlier transition metals, i.e., that of alkylidene complexes and complexes that contain a metal–metal triple bond. High-oxidation-state alkylidyne complexes, like alkylidene complexes, appear to be "natural products" in organometallic chemistry involving alkyl complexes in this part of the periodic table, even in circumstances that one might think would yield solely reduced species. We expect that much of what has been learned can be extended to rhenium(7+) chemistry, if suitable starting materials can be synthesized. This approach to high-oxidation-state organometallic chemistry is revealing new molecules, unique types of bonding of carbon-containing fragments to metals, and potentially useful stoichiometric reactions. An important future direction is the application of what we have learned toward the controlled design of metathesis catalysts with well-defined and predictable properties.

(45) Schaverien, C. J.; Dewan, J. C.; Schrock, R. R. *J. Am. Chem. Soc.* 1986, *108*, 2771.

Electrophilic Metal Carbenes as Reaction Intermediates in Catalytic Reactions

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Catalytic methods for the decomposition of diazo compounds have been know for more than 80 years, and their uses for a variety of carbenoid transformations are well established.[1] The term "carbenoid" was first applied to these processes in 1966[2] to infer that the reacting species was neither a free carbene nor an activated diazo compound but, rather, a carbene bound to a transition metal, as originally suggested by Yates in 1952.[3] This model was adopted for catalytic cyclopropanation reactions with limited evidence, primarily based on asymmetric induction through the the use of chiral copper and cobalt catalysts,[4] that supported the actual participation of the metal during addition to olefins. The discovery of stable metal carbene complexes and demonstration of their compatibility for stereospecific olefin cyclopropanation[5] lent further support to transient metal carbene intermediates in catalytic processes. However, metal carbene involve-

(1) (a) Dave, V.; Warnhoff, E. *Org. React. (N.Y.)* 1970, *18*, 217. (b) Burke, S. D.; Grieco, P. A. Ibid. 1979, *26*, 361. (c) Marchand, A. P.; MacBrockway, N. *Chem. Rev.* 1974, *74*, 431. (d) Wenkert, E. *Acc. Chem. Res.* 1980, *13*, 27. (e) Doyle, M. P. In *Catalysis of Organic Reactions*; Augustine, R. L., Ed.; Marcell Dekker: New York, 1985; Chapter 4.
(2) Nozaki, H.; Moriuti, S.; Takaya, H.; Noyori, R. *Tetrahedron Lett* 1966, 5239.
(3) Yates, P. *J. Am. Chem. Soc.* 1952, *74*, 5376.
(4) (a) Nozaki, H.; Takaya, H.; Moriuti, S.; Noyori, R. *Tetrahedron* 1968, *24*, 3655. (b) Nakamura, A.; Konishi, A.; Tsujitani, R.; Kudo, M.; Otsuka, S. *J. Am. Chem. Soc.* 1978, *100*, 3449. (c) Arantani, T.; Yoneyoshi, Y.; Nagase, T. *Tetrahedron Lett* 1982, *23*, 685. (d) Laidler, D. A.; Milner, D. J. *J. Organomet. Chem.* 1984, *270*, 121.
(5) (a) Casey, C. P. In *Reactive Intermediates*; Jones, M., Jr., Moss, R. A., Eds.; Wiley: New York, 1985; Vol. 3, Chapter 4. (b) Dötz, K. H. *Angew. Chem., Int. Ed. Engl* 1984, *23*, 587. (c) Brookhart, M.; Studabaker, W. B.; Husk, G. R. *Organometallics* 1985, *4*, 943. (d) Kuo, G.-H.; Helquist, P.; Kerber, R. C. *Ibid.* 1984, *3*, 806. (e) Casey, C. P.; Miles, W. H. *Ibid.* 1984, *3*, 808.

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ment in catalytic reactions has yet to be demonstrated by direct observation.

The discovery by Teyssie and co-workers that rhodium(II) acetate, a binuclear rhodium compound with one available coordination site per metal center, is an exceptionally effective catalyst for a wide variety of catalytic transformations involving diazo compounds[6] holds singular importance in the history of this developing methodology. Rhodium(II) acetate is not susceptible to redox transformations with diazo compounds, does not form π complexes with olefins, and is resistant to carboxylate exchange under ordinary catalytic conditions. We have found that even when employed with catalyst to diazo compound molar ratios as low as 0.0005, product yields from $Rh_2(OAc)_4$-catalyzed cyclopropanation reactions (e.g., eq 1) are not

$$\text{(1)}$$
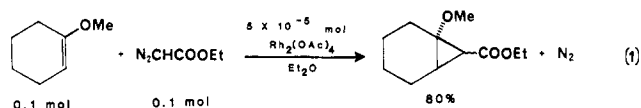
diminished.[7] Previously, heterogeneous catalysts that included copper bronze and cupric sulfate were believed to be the most effective in reactions with diazo compounds,[1] although homogeneous catalysts that originated with Nozaki's copper chelates[8] and Moser's soluble $CuCl \cdot P(OR)_3$[9] offered some advantages in selectivity for cyclopropanation. A variety of transition metal compounds, including $Cu(OTf)_2$ ($Tf = CF_3SO_2$),[10] $Pd_3(OAc)_6$,[11] and $Rh_6(CO)_{16}$[12] were introduced as catalysts for carbenoid reactions, but none of these have the general suitability of the rhodium(II) carboxylates.

Synthetic uses for metal-catalyzed decomposition of diazo compounds are not limited to cyclopropanation, even though the focus of mechanistic investigations has been centered on these transformations. Insertion reactions, including those into alkane C–H bonds (eq 2)[13]

$$\text{(2)}^{13b}$$

$$\text{(3)}^{14}$$

$$\text{(4)}^{15}$$

$$\text{(5)}^{16a}$$
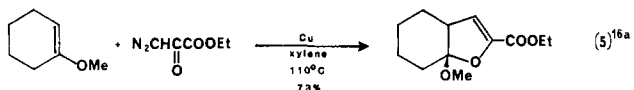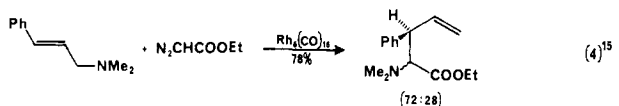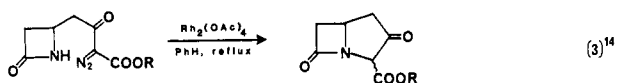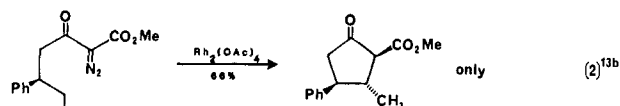
(6) (a) Paulissen, R.; Reimlinger, H.; Hayez, E.; Hubert, A. J.; Teyssie, Ph. *Tetrahedron Lett.* 1973, 2233. (b) Hubert, A. J.; Noels, A. F.; Anciaux, A. J.; Teyssie, Ph. *Synthesis* 1976, 600. (c) Anciaux, A. J.; Demonceau, A.; Hubert, A. J.; Noels, A. F.; Petiniot, N.; Teyssie, Ph. *J. Chem. Soc., Chem. Commun.* 1980, 765.

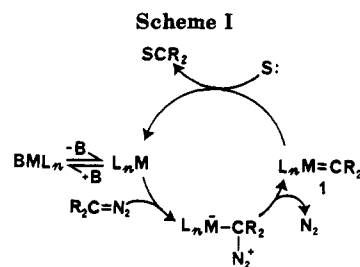(7) Doyle, M. P.; van Leusen, D.; Tamblyn, W. H. *Synthesis* 1981, 787.

(8) Nozaki, H.; Moriuti, S.; Yamabe, M.; Noyori, R. *Tetrahedron Lett.* 1966, 59.

(9) Moser, W. R. *J. Am. Chem. Soc.* 1969, 91, 1135, 1141.

(10) Salomon, R. G.; Kochi, J. K. *J. Am. Chem. Soc.* 1973, 95, 3300.

(11) Paulissen, R.; Hubert, A. J.; Teyssie, Ph. *Tetrahedron Lett.* 1972, 1465.

(12) Doyle, M. P.; Tamblyn, W. H.; Buhro, W. E.; Dorow, R. L. *Tetrahedron Lett.* 1981, 22, 1783.

Scheme I

or amide N–H bonds (eq 3),[14] ylide generation and rearrangement (eq 4),[15] and transformations involving formal dipolar addition (eq 5)[16] characterize the catalytic methodology and have been attributed to the involvement of metal carbenes. Rhodium(II) acetate is applicable for all of these processes, but other transition-metal compounds having varied activities have also been used. Our efforts have been directed to mechanistic developments that provide a predictive understanding of these catalytic processes.

The catalytic activity of transition-metal compounds depends on the coordination unsaturation at their metal center which allows them to react with diazo compounds as electrophiles. Addition to the diazo compound is believed to cause the loss of dinitrogen and production of an electrophilic metal-stabilized carbene **I** whose transfer of the carbene entity to an electron-rich substrate completes the catalytic cycle (Scheme I). Lewis bases may compete with the diazo compound for the available coordination site on the electrophilic transition metal but, so long as this inhibition is reversible, the chemical outcome of the transformation is not altered.

We recognized that if metal carbenes were intermediates in catalytic processes, the structural rigidity of $Rh_2(OAc)_4$ (2)[17] could provide the basis for a link with
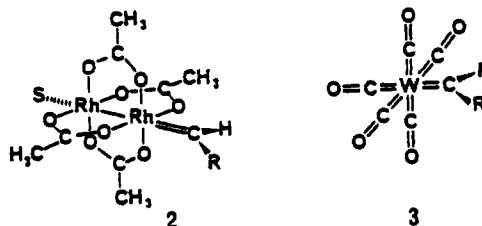
known stable metal carbenes of $(CO)_5W$ (3)[18] and from $Rh_2(OAc)_4$ to other metal catalysts. Carbenes associated with $(CO)_5W$ and $Rh_2(OAc)_4$ were expected to maintain their structural integrity about the metal center during carbene addition to olefins. Accordingly, their reactions could be viewed as taking place at the

(13) (a) 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. (b) Taber, D. F.; Ruckle, R. E., Jr. *Tetrahedron Lett.* 1985, 26, 3059. (c) Demonceau, A.; Noels, A. F.; Hubert, A. J.; Teyssie, P. *J. Chem. Soc., Chem. Commun.* 1981, 688.

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

(15) Doyle, M. P.; Tamblyn, W. H.; Bagheri, V. *J. Org. Chem.* 1981, 46, 5094.

(16) (a) Wenkert, E.; Alonso, M. E.; Buckwalter, B. L.; Sanchez, E. L. *J. Am. Chem. Soc.* 1983, 105, 2021. (b) Alonso, M. E.; Garcia, M. del C.; Chitty, A. W. *J. Org. Chem.* 1985, 50, 3445.

(17) (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.
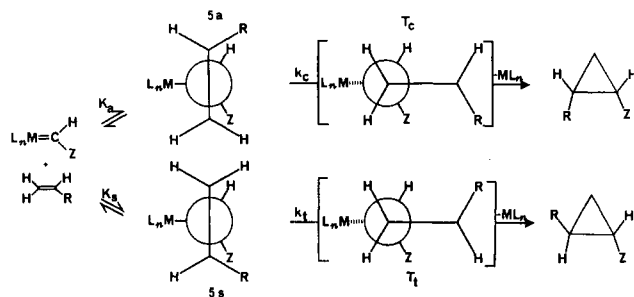
(18) Casey, C. P.; Polichnowski, S. W.; Shusterman, A. F.; Jones, C. R. *J. Am. Chem. Soc.* 1979, 101, 7282.

Figure 1. Stereoselectivity correlation in cyclopropanation reactions between $(CO)_2WCHPh$ and $Rh_2(OAc)_4/PhCHN_2$.

carbenic carbon which protrudes from the metal embedded in a wall constructed from its ligands (4). In

so far as the structures of other metal catalysts fit this description, their reactivities and selectivities should be comparable to those of $Rh_2(OAc)_4$ in carbenoid reactions with differences that are dependent on the electrophilicity of the metal-stabilized carbene. In this Account we describe the development of this connection and its implications for optimization of carbenoid transformations through control of reactivity and selectivity in catalytic reactions of diazo compounds.

Reactivity–Selectivity Correlations for Metal Carbenes in Catalytic Reactions

Reactivity–selectivity correlations have provided proven interlinks to specific reaction intermediates for a variety of chemical transformations. We have employed these same methods to ascertain the nature of the reaction intermediate in $Rh_2(OAc)_4$-catalyzed reactions of phenyldiazomethane with alkenes through comparisons with identical transformations of Casey's $(CO)_5WCHPh.$[19] This tungsten-stabilized phenylcarbene has been characterized, and its reactions with a variety of alkenes produce phenylcyclopropanes whose

(19) Doyle, M. P.; Griffin, J. H.; Bagheri, V.; Dorow, R. L. *Organometallics* **1984**, *3*, 53.

Scheme II

Figure 2. Correlation of stereoselectivities for cyclopropanation reactions of ethyl diazoacetate catalyzed by $Rh_2(OAc)_4$ with those catalyzed by $CuCl\cdot P(O\text{-}i\text{-}Pr)_3$ (▲), $Rh_6(CO)_{16}$ (●), $(CO)_5W$ (○), and $PdCl_2\cdot 2PhCN$ (■).

predominant stereochemistry is cis(syn).[18] As seen from the data in Figure 1, stereoselectivities for cyclopropanation by the two methods correlate linearly with a slope of 1.78 in this log–log plot. Furthermore, their relative reactivities towards pairs of olefins are also linearly related.

We have recently extended cyclopropanation stereoselectivity correlations between $Rh_2(OAc)_4$ and $(CO)_5W$ to ethoxycarbonylcarbene.[20] The heteroatom-stabilized carbene $(CO)_5WC(OMe)Ph$ was employed as a "procatalyst" (Scheme II). Electrophilic addition of the Fischer carbene to ethyl diazoacetate resulted in dinitrogen extrusion and the formation of both a vinyl ether and the highly electrophilic $(CO)_5W,$[21] whose catalytic activity for olefin cyclopropanation was demonstrated. Here trans (anti) selectivity was favored for addition (Figure 2). Taken together with asymmetric induction in cyclopropanation reactions through the use of chiral catalysts,[4] these reactivity–selectivity correlations provide convincing arguments for metal carbene intermediates.

The relative reactivities of alkenes in cyclopropanation reactions of diazo compounds are de-

(20) Doyle, M. P.; Griffin, J. H.; Conceicão, J. *J. Chem. Soc., Chem. Commun.* **1985**, 328.

(21) Casey, C. P.; Bertz, S. H.; Burkhardt, T. J. *Tetrahedron Lett.* **1973**, 1421.

Table I.
Stereoselectivity Enhancement in Catalytic Cyclopropanation of Styrene[a]

catalyst	$N_2CHCOOEt$	$N_2CHCOOCMe(i\text{-}Pr)_2$	$N_2CHCONMe_2$	$N_2CHCON(i\text{-}Pr)_2$
$Rh_2(OOCC_3F_7)_4$	1.1	1.0	1.5	12
$Rh_2(OAc)_4$	1.6	2.4	2.2	64
$Rh_2(NHCOCH_3)_4$	2.1	4.4	2.4	114

Scheme III

pendent on the catalyst employed. Competitive cyclopropanation of two olefins in the presence of metal catalysts is ordinarily used to characterize these reactivities.[10,22] However, this data can be misleading when the catalyst possesses a coordination site for olefin association during carbene transfer because, as we discovered with $Cu(OTf)_2$,[19] selectivity in competitive cyclopropanation reactions is dependent on the molar ratio of olefins employed. Currently, $Rh_2(OAc)_4$ is the only catalyst for which reliable olefin relative reactivities are available,[22,23] and their general order is consistent with electrophilic addition.

Selectivity correlations in cyclopropanation reactions of diazo compounds between those catalyzed by $Rh_2(OAc)_4$ and a variety of alternative catalysts have been obtained,[23,24] and they provide these catalysts with their link to metal carbene intermediates established in the $Rh_2(OAc)_4$-catalyzed reactions. Stereoselectivities are invarient to changes in catalyst concentration, to the rate of addition of the diazo compound, and to the molar ratio of olefin to diazo compound. However, in reactions of alkenes with diazo esters, copper catalysts generally provide a higher trans (anti) selectivity than do either $Rh_2(OAc)_4$ or $Rh_6(CO)_{16}$ which, in turn, are superior to palladium(II) catalysts.[23] Stereochemical results from cyclopropanation reactions of ethyl diazoacetate with olefins correlate (Figure 2) through the linear relationship $I_{cat(i)} = SI_0$, where I_{cat} is the trans/cis (anti/syn) isomer ratio for a given catalyst i, and I_0 is the same ratio for the reference catalyst, $Rh_2(OAc)_4$. S, the selectivity index, is equal to 1.7 for $CuCl\cdot P(O\text{-}i\text{-}Pr)_3$, 1.0 for $Rh_6(CO)_{16}$, 0.9 for $(CO)_5W$, and 0.59 for $PdCl_2\cdot 2PhCN$. A similar relationship is observed for cyclopropanation of dienes,[24] and values for the corresponding regioselectivity indices are nearly the same for these catalysts as their stereoselectivity indices. Apparently those factors that control selectivity in cyclopropanation reactions catalyzed by $Rh_2(OAc)_4$ are the same, differing only in degree, as those that control selectivity in cyclopropanation reactions catalyzed by alternative transition-metal compounds.

Mechanism of Cyclopropanation and Its Implications

We have developed a mechanistic model for cyclopropanation to explain the observed carbenoid-dependent differences in selectivity.[19] Accordingly, cyclopropane formation is proposed to occur by initial association of the olefin π bond with the electrophilic center of the metal carbene followed by σ-bond formation with backside displacement of the catalyst (Scheme III). Orientation of the olefin with respect to carbene substituents either at the π-complex, when transition-state (T_t and T_c) energies are nearly equal, or in the transition state, when their respective energies differ as a result of interactions between R and Z, determines the predominance of one cyclopropane isomer over the other. Only **5a** proceeding through T_t can form the *cis*-cyclopropane isomer, but **5a** and **5s** are interconnected through the separated metal carbene and olefin so that factors which inhibit one pathway enhance the other. In the absence of prominant steric interactions between R and Z in the transition state, predominant cis (syn) stereoselectivity is predicted ($k_t \simeq k_c$, but **5s** is less stable than **5a**) and observed.[19] As the size of R is increased (Et < i-Pr < t-Bu), k_c decreases relative to k_t with the resulting decrease in the cis/trans ratio of cyclopropane products. The π complex of Scheme III may, in fact, be a formalism, but it is a useful one for the prediction of stereoselectivity in cyclopropanation reactions. Alternative mechanisms have been proposed to explain these stereochemical results,[18,25] and that offered by Brookhart is, like Scheme III, consistent with all available data for cyclopropanation by aryl- or alkylcarbenes. The principal differences between Scheme III and those previously advanced are the proposal of an intermediate that exists in equilibrium with the separated metal carbene and alkene and the absence of a metallocyclobutane intermediate.

Stereochemical preference for the *trans*-cyclopropane isomer in catalytic reactions involving ethyl diazoacetate and related diazo carbonyl compounds appears to be the exception to the model depicted in Scheme III. 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 in Scheme IV), which is only possible in the transition state leading to the trans cyclopropane, accounts for the predominant trans stereoselectivity in these reactions. An intramolecular counterpart for carbonyl association with a metal carbene intermediate is seen in the results of $Rh_2(OAc)_4$-catalyzed decomposition of oxazolidone **6**, whose

(22) (a) Anciaux, A. J.; Hubert, A. J.; Noels, A. F.; Petiniot, N.; Teyssie, Ph. *J. Org. Chem.* **1980**, *45*, 695. (b) Anciaux, A. J.; Demonceau, A.; Noels, A. F.; Warin, R.; Hubert, A. J.; Teyssie, P. *Tetrahedron* **1983**, *39*, 2169.

(23) Doyle, M. P.; Dorow, R. L.; Buhro, W. E.; Griffin, J. H.; Tamblyn, W. H.; Trudell, M. L. *Organometallics* **1984**, *3*, 44.
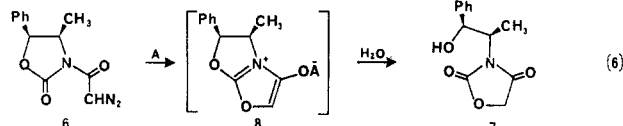
(24) Doyle, M. P.; Dorow, R. L.; Tamblyn, W. H.; Buhro, W. E. *Tetrahedron Lett.* **1982**, *23*, 2261.

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

Scheme IV

5 s

T_t
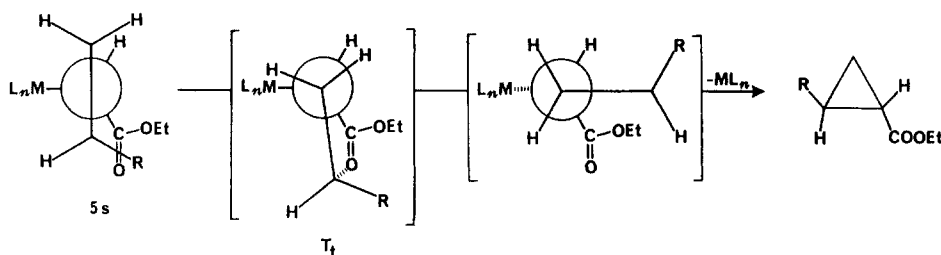
hydration product **7** suggests the oxazolium ion **8** (eq 6, A = Rh$_2$(OAc)$_4$).[26] Accordingly, increasing the nu-

(6)

6   8   7

cleophilicity of the carbonyl group and the size of the group attached to it should cause an increase in trans selectivity, and this prediction has been verified (Table I). The amide carbonyl group, which is more nucleophilic than that of an ester, enhances trans (anti) selectivity so that, by also expanding the size of the dialkylamino group, the relative percentage of the trans isomer from Rh$_2$(OAc)$_4$-catalyzed cyclopropanation of styrene is increased from 62 with ethyl diazoacetate to greater than 98 with *N,N*-diisopropyldiazoacetamide. Furthermore, decreasing the electrophilicity of the carbenic carbon by alteration of the electron-withdrawing properties of the bridging ligand for the dirhodium complex also enhances trans stereoselectivity.

Scheme IV is consistent with dipolar addition of carbonyl carbenes to vinyl ethers (e.g., eq 5) and also outlines an explanation for the apparent allylic carbon–hydrogen insertion by certain diazo carbonyl compounds (**9** in eq 7).[19] Although diazo esters such as

(7)

9
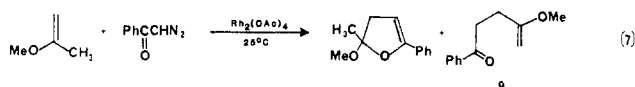
ethyl diazoacetate are immune to these transformations and undergo cyclopropanation exclusively, alkyl 2-diazo-3-oxobutyrates, 3-diazo-2,4-pentanedione, and even conjugated diazo ketones react with vinyl ethers to yield dihydrofuran products.[1d,16,19] Dialkyl diazomalonate and α-diazoacetophenone are capable of generating apparent allylic carbon–hydrogen insertion products.[16a,19,27] We have explained the apparent dipolar addition as due to increased stabilization provided to the developing electrophilic center of the reacting olefin by the carbonyl group. Since vinyl ethers allow greater charge development in the transition state, and conjugation with a carbonyl or phenyl group affords enhanced product stabilization, dihydrofuran formation is favored over cyclopropanation. Allylic C–H insertion has been proposed to result from hydrogen transfer in the transition state encompassing the interacting carbonyl carbene and alkene.[19] The formation of dihydrofuran or insertion products may be regarded as arising through competitive association/proton abstraction by the carbonyl group with the developing

(26) Doyle, M. P.; Dorow, R. L.; Terpstra, J. W.; Rodenhouse, R. A. *J. Org. Chem.* **1985**, *50*, 1663.
(27) Wulfman, D. S.; McGibbony, B. G.; Steffen, E. K.; Thinh, N. V.; McDaniel, R. S., Jr.; Peace, B. W. *Tetrahedron* **1976**, *32*, 1257.

Scheme V

10 + N$_2$C(COOMe)$_2$

11   12
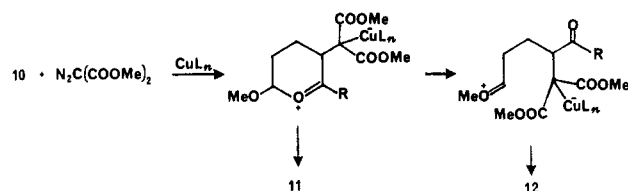
carbocation in the transition state. Alternatively, both processes may result from a fully developed carbocation intermediate.

Recently, Alonso and Garcia reported that 2-alkoxydihydropyrans **10** undergo apparent vinyl carbon–hydrogen insertion and a novel addition–rearrangement in catalytic reactions (eq 8: **a**, R = H; **b**, R = CH$_3$).[28]

(8)

10   11   12
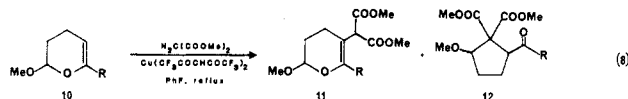
We had previously shown that 2-alkoxycyclopropane-carboxylate esters underwent transition-metal-catalyzed rearrangement to vinyl ethers (the oxocyclopropane-vinyl ether rearrangement)[29] which is an apparent compliment to the formation of **11** (e.g., eq 9). The

(9)
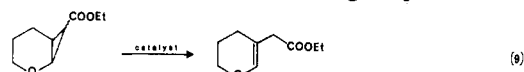
generality of this process has been established, and [Rh(CO)$_2$Cl]$_2$, PtCl$_2$·2PhCN, and [Ru(CO)$_3$Cl$_2$]$_2$ were found to be the most active catalysts. Although metal insertion was proposed to account for the accumulated data,[29b] Lewis acid catalyzed ring opening remains a viable alternative with certain transition metal catalysts.

The explanation of the formation of **11** and **12** by Alonso and Garcia (Scheme V)[28] has provided a view of the extreme in metal carbene–alkene interactions. The molar ratio of **11** and **12** 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. Taken together with those previously discussed, all known modes of reaction with olefins can now be explained as electrophilic processes of metal-stabilized carbenes, but it is only vinyl ethers in combination with diazo carbonyl compounds that show the broad spectrum of synthetically useful pathways that are competitive with cyclopropanation. Apparent nucleophilic carbenoid additions to α,β-unsaturated esters and nitriles have been shown to occur by dipolar addition of diazocarbonyl compounds with subsequent extrusion of dinitrogen.[30]

(28) Alonso, M. E.; Del Carmen Garcia, M. *J. Org. Chem.* **1985**, *50*, 988.
(29) (a) Doyle, M. P.; van Leusen, D. *J. Am. Chem. Soc.* **1981**, *103*, 5917. (b) Doyle, M. P.; van Leusen, D. *J. Org. Chem.* **1982**, *47*, 5326.

Metal Carbenes

Table II.
Regioselectivity Enhancement in Catalytic Cyclopropanation[a]

diene	catalyst	$N_2CHCOOEt$	$N_2CHCOOCMe(i\text{-}Pr)_2$	$N_2CHCONMe_2$	$N_2CHCON(i\text{-}Pr)_2$
(structure)	$Rh_2(OOCC_3F_7)_4$	1.3	1.1	1.9	0.5
	$Rh_2(OAc)_4$	1.7	1.4	2.5	2.2
	$Rh_2(NHCOCH_3)_4$	2.0	1.3	2.7	3.0
(structure)	$Rh_2(OOCC_3F_7)_4$	2.0	2.4	5.1	4.6
	$Rh_2(OAc)_4$	2.3	3.9	12	18
	$Rh_2(NHCOCH_3)_4$	4.0	7.0	16	22

[a] Results of N. K. Harn, K.-L. Loh, and L. C. Wang.

The electrophilic character of metal carbene intermediates in catalytic reactions is reflected in their regioselectivities for cyclopropanation of dienes. Our focus here is the carbenic carbon whose electrophilicity is primarily determined by electronic influences of the catalyst, carbene substituents, and olefin. Isoprene and 5-methylenebicyclo[2.2.1]hept-2-ene are representative, and their regioselectivities in reactions with ethyl diazoacetate are responsive to the catalyst employed (Table II). We have attributed differences in olefin reactivities to electronic influences on the transition state for cyclopropanation.[31] A transition state with little charge development at the olefinic carbons (13a,
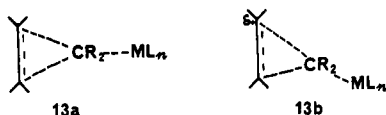
e.g., ML_n = $PdCl_2$) favors cyclopropanation at double bond B, whereas a transition state with considerable charge development (13b, e.g., ML_n = $Rh_2(OAc)_4$) favors addition to double bond A in these same compounds (Table II). Decreasing the electrophilicity of the intermediate metal carbene increases selectivity but, as is evident in reactions of isoprene with N,N-diisopropyldiazoacetamide, steric effects also play a role in regioselectivity determinations.

The response of dienes towards 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 carboalkoxy.[31] With 5-methylenebicyclo[2.2.1]hept-2-ene and ethyl diazoacetate, for example, preferential electrophilic carbene addition (70%) occurs at the exocyclic double bond with $Rh_2(OAc)_4$ (eq 10), but $PdCl_2 \cdot 2PhCN$ directs cyclo-

propanation to the endocyclic double bond (86%). These opposite selectivities are exclusive with diphenyldiazomethane. The reason for the disparate reactivity may be related to the "free" carbene character of the transition state for cycloaddition which, in turn, is related to the extent of carbene stabilization by the metal.
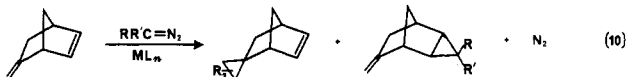
Metal–carbene–alkene complexes have often been invoked as intermediates in metal-catalyzed cyclopropanation reactions.[9,22] Until recently, their existence

has been hypothetical, based on arguments derived from selectivities in product formation. However, Casey and co-workers have prepared stable tungsten–carbene–alkene complexes 14 from their corresponding pentacarbonyltungsten carbenes 15 by thermolysis and observed their decomposition to cyclopropane products (eq 11, Z = O, NMe).[32]
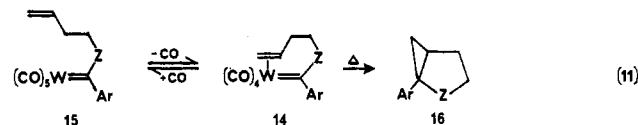
We have recently reported that stable palladium chloride complexes of dienes such as 17 or 18 do not

react with ethyl diazoacetate and do not form cyclopropane products when treated with ethyl diazoacetate in combination with $Rh_2(OAc)_4$ or $PdCl_2 \cdot 2PhCN$.[31] These results are inconsistent with intermolecular electrophilic carbene addition to a coordinated olefin as well as with electrophilic addition of the coordinated olefin to the diazo compound. Although collapse of a metal–carbene–alkene complex remains a mechanistic possibility for catalytic cyclopropanation reactions with copper triflate and palladium(II) acetate or chloride which are capable of forming such complexes, the absence of an intermolecular counterpart to eq 11 weakens arguments for their involvement.

Catalytic Generation of Ylides and Their Rearrangements

Carbenoid entry into reactive ylides is a useful alternative to the widely employed base-promoted techniques.[33] Although suitable for ylide production, carbenes generated photochemically and thermally from diazo compounds are relatively indiscriminate.[34] The potentially more general catalytic approach to carbenoid generation began to evolve with the use of copper catalysts[35] and, as with catalytic cyclopropanation re-

(30) (a) Doyle, M. P.; Davidson, J. G. *J. Org. Chem.* 1980, 45, 1538. (b) Doyle, M. P.; Dorow, R. L.; Tamblyn, W. H. *J. Org. Chem.* 1982, 47, 4059.
(31) Doyle, M. P.; Wang, L. C.; Loh, K.-L. *Tetrahedron Lett.* 1984, 2, 4087.

(32) Casey, C. P.; Shusterman, A. J. *Organometallics* 1985, 4, 736.
(33) (a) Pine, S. H. *Org. React. (N.Y.)* 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.
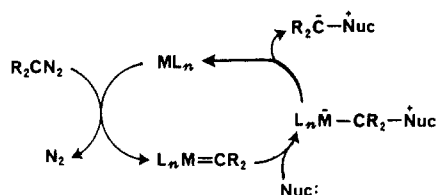(34) (a) Ando, W. *Acc. Chem. Res.* 1977, 10, 179. (b) Ando, W. In *The Chemistry of Diazonium and Diazo Groups*; Patai, S., Ed.; Wiley: New York, 1978; Chapter 9.
(35) (a) D'yakonov, I. A.; Domareva, T. V. *Zh. Obshch. Khim.* 1955, 25, 934, 1486. (b) Phillips, D. D.; Champion, W. C. *J. Am. Chem. Soc.* 1956, 78, 5452. (c) Parham, W. E.; Groen, S. H. *J. Org. Chem.* 1966, 31, 1694. (d) Kirmse, W.; Arold, H. *Chem. Ber.* 1968, 191, 1008. (e) Andrews, G.; Evans, D. A. *Tetrahedron Lett.* 1972, 5121.

Scheme VI

actions, the discovery of $Rh_2(OAc)_4$ as a highly effective catalyst for ylide generation accelerated the use of this methodology.[15,36]   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 from the associated ylide complete the catalytic cycle (Scheme VI).

The symmetry-allowed [2,3]-sigmatropic rearrangement is a facile bond reorganization process for catalytically generated ylides. Copper catalysts have been employed for the generation of allylic sulfur ylides whose subsequent [2,3]-sigmatropic rearrangements have a variety of synthetic applications (e.g., eq 12,13).
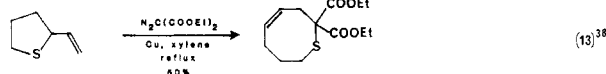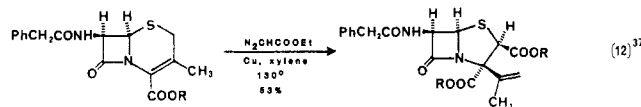
However, as Vedejs has pointed out,[39] copper catalysts are not generally successful for these transformations since optimization of synthetic conversions such as that in eq 13 were unsatisfactory, and analogous reactions with diazoketones were unsuccessful. We have found that rhodium(II) acetate has greater potential (e.g., eq 14),[40] and its use allows these reactions to take place
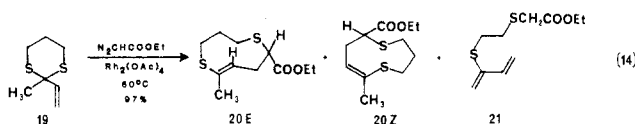
under milder conditions than necessitated by the use of copper. The rhodium carbonyl cluster $Rh_6(CO)_{16}$ is also useful for ylide generation and rearrangement with allyl sulfides and amines (eq 4), and in some cases it is superior to $Rh_2(OAc)_4$.[15] In general, catalysts that are effective for cyclopropanation are at least as active for ylide generation with allyl sulfides.[41]   Elimination reactions of intermediate ylides such as in the conversion of 19 to 21 can be competitive with [2,3]-sigmatropic rearrangement (20/21 = 3.4).[40] 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 15).

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.[42]   Here there is no comparable base-promoted methodology, but cyclopropanation is competitive with ylide generation and rearrangement. Our recent systematic investigations with rhodium and copper catalysts have shown that the product distribution is dramatically dependent on the nucleophilicity of the halide (eq 16), on the diazo compound, and on

R = H	X = I	98%	100	0
H	Br	76%	28	72
H	Cl	95%	5	95
COOEt	Br	92%	93	7
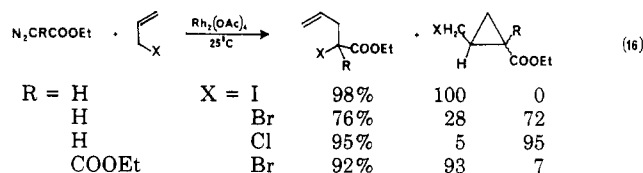
the catalyst.[15] With crotyl bromide, for example, the rhodium(II) acetate catalyzed decomposition of ethyl diazoacetate exhibits competition between only cyclopropanation and the [2,3]-sigmatropic rearrangement (eq 17: 67% 22, 33% 24), whereas copper catalysts
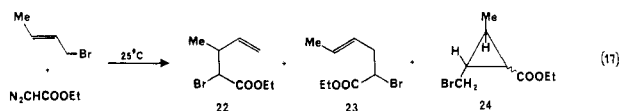
employed under the same conditions produce the product from direct carbon–heteroatom insertion (23: 33%) as well as 22 and 24.[15] These results indicate that the copper catalysts, and also $Rh_2(OAc)_4$ at or above 40 °C, are capable of carbon–bromide bond cleavage from the bromide-associated metal carbene and, therefore, are not suitable for synthetic applications of ylide transformations.   Competitive cyclopropanation diminishes the general suitability of $Rh_2(OAc)_4$, but the use of rhodium(II) perfluorobutyrate substantially increases the relative yield of the ylide-derived product, even with allyl chlorides (>88% with dimethyl diazomalonate), and this catalyst can now be regarded as superior to $Rh_2(OAc)_4$ for ylide generation.

Allyl ethers resemble allyl chlorides in their preference for cyclopropanation. However, allyl acetals undergo ylide generation in $Rh_2(OAc)_4$-catalyzed reactions with diazoesters, and subsequent production of synthetically useful 2,5-dialkoxy-4-alkenoates by the [2,3]-sigmatropic rearrangement occurs in moderate to good yields (e.g., eq 18).[40] Like those with allyl halides,
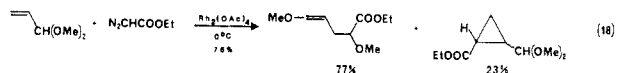
reactions with acetals are dependent on the catalyst, diazo compound, acetal, and temperature. Stevens arrangement products are observed in certain cases, even with $Rh_2(OAc)_4$ catalysis. That ylides derived from allyl acetals undergo preferential rearrangement in competition with cyclopropanation, whereas those from the corresponding allyl ethers in intermolecular processes are relatively unresponsive to ylide rear-

(36) Gillespie, R. J.; Murray-Rust, J.; Murray-Rust, P.; Porter, A. E. A. *J. Chem. Soc., Chem. Commun.* 1978, 83.
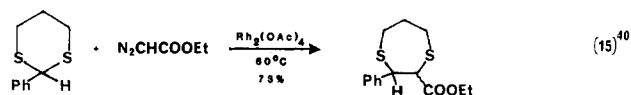
(37) Yoshimoto, M.; Ishihara, S.; Nakayama, E.; Soma, N. *Tetrahedron Lett.* 1972, 2923.

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

(39) Vedejs, E. *Acc. Chem. Res.* 1984, 17, 358.

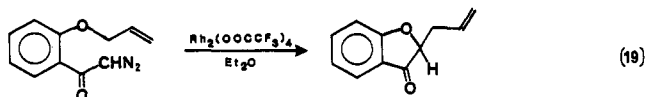(40) Doyle, M. P.; Griffin, J. H.; Chinn, M. S.; van Leusen, D. *J. Org. Chem.* 1984, 49, 1917.

(41) Tamblyn, W. H.; Hoffmann, S. R.; Doyle, M. P. *J. Organomet. Chem.* 1981, 216, C64.

(42) (a) Ando, W.; Yagihara, T.; Kondo, S.; Nakayama, K.; Yamato, H.; Nakaido, S.; Migita, T. *J. Org. Chem.* 1971, 36, 1732. (b) Ando, W.; Kondo, S.; Nakayama, K.; Kohoda, H.; Yamato, H.; Imai, I.; Nakaido, S.; Migita, T. *J. Am. Chem. Soc.* 1972, 94, 3870.

rangement, demonstrates that heteroatom substitution at the allylic carbon accelerates the [2,3]-sigmatropic rearrangement. However, ylide generation and rearrangement in intramolecular reactions of diazo allyl ethers (e.g., eq 19) occur without competition from cy-


clopropanation. Parenthetically, Lewis acid catalyzed reactions of allyl acetals with diazo compounds take a completely different pathway to form β,γ-unsaturated acetals (e.g., eq 20).[43]
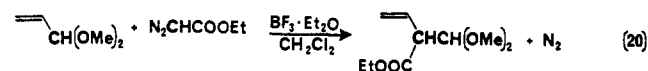


Carbenoid Catalysts as Lewis Acids

Although numerous different modes of bonding between a coordinatively unsaturated metal center and a diazo compound may be considered, 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[10] or rhodium(II) trifluoroacetate,[44] 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.

Because they are Lewis acids, some of the transition-metal compounds that are effective catalysts for carbenoid transformations actually operate as Lewis acid promoters in much the same manner as BF_3. Such activity appears to explain the formation of oxazoles from nitriles and diazocarbonyl compounds (eq 21)
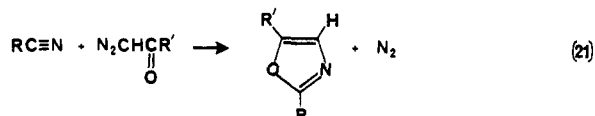
catalyzed by $Pd_3(OAc)_6$ or $Cu(OTf)_2$,[45] which have been interpreted in terms of metal carbene intermediates. This same transformation proceeds in even higher yields with any of a wide spectrum of Lewis acids,[46] but especially $BF_3 \cdot OEt_2$.[47]

The same conclusion has been reached for $Cu(OTf)_2$-promoted carbenoid insertion of diazo compounds into the carbon–oxygen bond of ortho esters (eq 22),[48] but here there is evidence that the metal carbene,
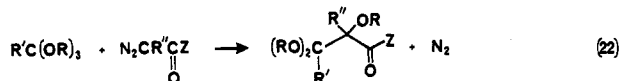
(43) Doyle, M. P.; Trudell, M. L.; Terpstra, J. W. *J. Org. Chem.* **1983**, *48*, 5146.

(44) Doyle, M. P.; Colsman, M. R.; Chinn, M. S. *Inorg. Chem.* **1984**, *23*, 3684.

(45) Paulissen, R.; Moniotte, Ph.; Hubert, A. J.; Teyssie, Ph. *Tetrahedron Lett.* **1974**, 3311. (b) Moniotte, Ph. G.; Hubert, A. J.; Teyssie, Ph. *J. Organomet. Chem.* **1975**, *88*, 15.

(46) (a) Doyle, M. P.; Oppenhuizen, M.; Elliott, R. C.; Boelkins, M. R. *Tetrahedron Lett.* **1978**, 2247. (b) Kitatani, K.; Hiyame, T.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 1647.

(47) (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.
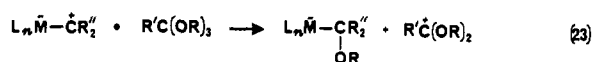
through alkoxide transfer from the ortho ester (eq 23), generates the active catalyst, a dialkoxycarbenium ion. Once again $BF_3 \cdot OEt_2$ is a superior catalyst,[49] but $Rh_2(OAc)_4$, $Rh_6(CO)_{16}$, $CuCl \cdot P(OR)_3$, and $PdCl_2 \cdot 2PhCN$ are relatively ineffective.[48] These results point to a gradation in the electrophilicity of catalytically generated metal carbenes that have important implications for catalyst utilization in carbenoid transformations.

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 A. B. Smith and co-workers have demonstrated the utility of these BF_3-promoted cyclizations for the preparation of simple and annulated cyclopentenones,[50] 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 24),[51] afforded a definite contrast
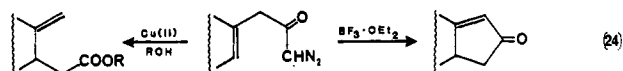
between Lewis acid promoted and transition-metal-catalyzed reactions of this class of diazo compounds. However, we have reported that $Cu(OTf)_2$ is as effective as $BF_3 \cdot OEt_2$ in promoting intramolecular cyclization (eq 25).[48] The product and the pathway through which it
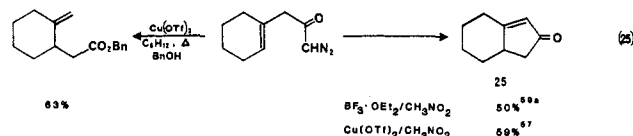
is obtained is dependent on the reaction conditions. We employed $Cu(OTf)_2$ in anhydrous nitromethane and obtained hydrindanone **25**; the vinylogous Wolff rearrangement takes place in refluxing cyclohexane to which is added an equivalent amount of alcohol. The dichotomy awaits resolution.

Concluding Remarks

Metal-stabilized carbene intermediates are generated from diazo compounds by the catalytic action of a select number of transition metal compounds of which the rhodium(II) carboxylates and carboxamides are the most versatile. They are highly electrophilic reagents, capable of a broad spectrum of chemical transformations, whose uses in organic syntheses are rapidly emerging. Still, although we now understand many of the factors responsible for their reactivity and selectivity, many opportunities for further development of this methodology remain.

The catalytic approach to metal carbene transformations is dependent on the availability of suitable carbenoid precursors and, because of their ease of

(48) Doyle, M. P.; Trudell, M. L. *J. Org. Chem.* **1984**, *49*, 1196.

(49) Schönberg, A.; Praefcke, K. *Chem. Ber.* **1966**, *99*, 196.

(50) (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.

(51) (a) Smith, A. B., III; Toder, B. H.; Branca, S. J. *J. Am. Chem. Soc.* **1984**, *106*, 3995. (b) Smith, A. B., III; Toder, B. H.; Richmond, R. E.; Branca, S. J. *Ibid.* **1984**, *106*, 4001.

preparation and stability, diazo carbonyl compounds are most amenable to synthetic utilization. Their aliphatic counterparts, including diazomethane, are less stable and, consequently, they are more prone to undergo preferential dimerization or polymerization in the presence of a transition metal catalyst. Stoichiometric methods based on the direct use of metal carbenes are presently better adapted for aliphatic carbenoid addition reactions.

The attractiveness of catalytic cyclopropanation reactions for organic synthesis has been limited by low selectivities associated with the transformation. Now, however, control of stereoselectivity and regioselectivity can be achieved through the use of structurally modified catalysts and diazo compounds.[52]

(52) Catalysts that enhance syn selectivity have recently been reported: Callot, H. J.; Metz, F. Tetrahedron 1985, 41, 4495.

Catalytic entry to ylide intermediates has perhaps the greatest potential for new synthetic developments. Rhodium catalysts are superior to previously employed copper catalysts, and even ylide generation from allyl halides and ethers can now be conveniently achieved without excessive competition from cyclopropanation. Although current examples of ylide transformations in catalytic reactions are limited to the [2,3]-sigmatropic rearrangement and direct insertion, a variety of other processes should also be possible.

Stereo- and Regiocontrol by Complex Induced Proximity Effects: Reactions of Organolithium Compounds

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The sensible idea that chemical reactions can be promoted by structures which bring potentially reactive groups close together emerged naturally as chemists applied models of bonding to understanding reaction pathways. The famous Fisher "lock and key" model for enzyme action, the well-recognized advantages of intramolecularity, and the often-invoked chelate and complexation effects embody proximity as an important factor for understanding and controlling the course of chemical reactions.[1]

In organolithium chemistry mechanistic rationales of regio- and stereochemical results often involve bonding between lithium and electron pairs of substrates in critical intermediates.[2] For example, reviews of ortho-lithiations of aromatic compounds and of lithiations and additions to nonaromatic compounds suggest complexation to be a major effect in many cases.[3] Such ideas are firmly based on information from X-ray spectroscopy about the structure of lithium in solids, the propensity of lithium for association in solution, and theoretical calculations of lithium binding in the gas phase.[4]

In most cases association between lithium and the functional group of a substrate enforces not only proximity but also resonance, stereoelectronic, inductive, and steric effects. As a result, evaluation of the relative contributions of these factors can be difficult.

Biographies of the authors have appeared previously.

However, reactions have been described which suggest that a complex-induced proximity effect (CIPE), operating in a preequilibrium complex, can be as important as the classical effects in controlling the course of the ensuing transformations.

One of the clearer demonstrations of dominance by a CIPE process is the β-lithiation of γ,δ-unsaturated

(1) For recent discussions and diverse applications of this ubiquitous concept, see: (a) Menger, F. M. Acc. Chem. Res. 1985, 18, 128. (b) Weinreb, S. M. Ibid. 1985, 18, 16. Kozikowski, A. P. Ibid. 1984, 17, 410. Magnus, P.; Gallagher, T.; Brown, P.; Pappalardo, P. Ibid. 1984, 17, 35. (c) Hibbert, F. Ibid. 1984, 17, 115. (d) Breslow, R. Ibid. 1980, 13, 170. (e) Mutterties, E. Chem. Soc. Rev. 1982, 11, 283. (f) Houk, K. N.; Paddon-Row, M. N.; Rondan, N. G.; Wu, Y. D.; Brown, F. K.; Spellmeyer, D. C.; Metz, J. T.; Li, Y.; Lancharich. Science 1986, 231, 1108. (g) Beak, P.; Ziegler, J. M. J. Org. Chem. 1981, 46, 614.

(2) (a) Wakefield, B. J. Chemistry of Organolithium Compounds; Pergamon: Oxford, 1974. (b) Meyers, A. I. Acc. Chem. Res. 1978, 11, 375.

(3) (a) Gschwend, H. W.; Rodriquez, H. R. Org. React. (N.Y.) 1979, 26, 1. H. Gilman [Gilman, H.; Marten, J. W. Org. React. N.Y. 1954, 8, 258] credits Roberts and Curtin [Roberts, J. D.; Curtin, D. Y. J. Am. Chem. Soc. 1946, 68, 1658] for demonstrating this effect in ortho lithiations. (b) Klumpp, G. W. Rec. Trav. Chim. Pays-Bas 1986, 105, 1.

(4) For recent examples and leading references, see: Amstuz, R.; Laube, T; Schweizer, W. B.; Seebach, D.; Dunitz, J. D. Helv. Chim. Acta 1984, 67, 224. Jastrzebski, J. T. B. H.; van Koten, G.; Konijn, M.; Stem, C. H. J. Am. Chem. Soc. 1982, 104, 5490. Al-Aseer, M. A.; Allison, B. D.; Smith, S. G. J. Org. Chem. 1985, 50, 2715. Frankel, G.; Henrichs, M.; Hewitt, M.; Su, B. M. J. Am. Chem. Soc. 1984, 106, 255. Laube, T.; Dunitz, J. D.; Seebach, D. Helv. Chim. Acta 1985, 68, 1373. Jackman, L. M.; Scormoutzous, L. M. J. Am. Chem. Soc. 1984, 106, 4627. Buese, M. A.; Hogen-Eisch, T. E. Ibid. 1985, 107, 4509. McGarrity, J. F.; Ogle, C. A.; Brich, Z.; Looli, H. R. Ibid. 1985, 107, 1810. Kaufmann, E.; Clark, T.; Schleyer, P. v. R. J. Am. Chem. Soc. 1984, 106, 1856. Streitwieser, A., Jr. Acc. Chem. Res. 1984, 17, 353, and references cited therein.