

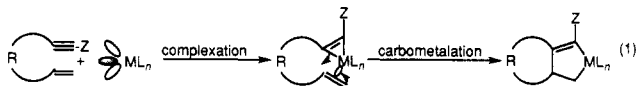
Patterns of Stoichiometric and Catalytic Reactions of Organozirconium and Related Complexes of Synthetic Interest

EI-ICHI NEGISHI^{*,†} AND TAMOTSU TAKAHASHI[‡]

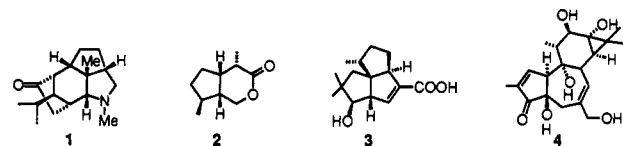
Department of Chemistry, Purdue University, West Lafayette, Indiana 47907, and Coordination Chemistry Laboratories, Institute for Molecular Science, Myodaiji, Okazaki 444, Japan

Received July 27, 1993

Over the past two decades organozirconium compounds have emerged as synthetically useful reagents and intermediates.^{1,2} Most of the investigations in the 1970s and early 1980s were focused on the chemistry of Zr(IV) compounds.² We became interested in the chemistry of Zr(II) compounds with the notion of developing a facile bicyclization reaction of enynes promoted by "Zr^{II}Cp₂" and related to the Co-promoted enyne bicyclization reaction.³ We reasoned that it would be desirable to generate a complex that can serve as an equivalent to or a source of a 14-electron species with two valence-shell empty orbitals and at least one filled nonbonding orbital for the presumed π complexation-carbometalation sequence shown in eq 1.



Experimentally, a ZrCp₂ equivalent, i.e., "ZrCp₂", generated by treatment of Cp₂ZrCl₂ with Mg and HgCl₂⁴ or 2 equiv of *n*-BuLi⁵ has proved to be effective in converting a variety of enynes^{6,7} and diynes^{5,7} into the corresponding zirconabicycles in high yields.⁸ The enyne bicyclization reaction has been shown to be readily applicable to the synthesis of various types of natural products, such as dendrobine⁹ (1), iridomyecine¹⁰ (2), pentalenic acid¹¹ (3), and phorbol¹² (4). This and the related chemistry of alkyne-zirconocenes including benzyne-zirconocenes have been extensively investigated and reviewed.¹³⁻¹⁶



In this Account, reactions of coordinatively unsaturated zirconocene derivatives are systematically surveyed

Ei-ichi Negishi obtained his baccalaureate degree from the University of Tokyo (1958), moved to the United States as a Fulbright scholar (1960), and obtained a Ph.D. degree from the University of Pennsylvania (1963). After 3 years at Teijin, Ltd., Tokyo, he joined Professor Herbert C. Brown's research group at Purdue University as a postdoctoral associate and then served as his personal assistant, followed by a move to Syracuse University (Assistant Professor, 1972; Associate Professor, 1976). He returned to Purdue University in 1979 as a Professor. His research interests range from C₁ chemistry to the selective synthesis of natural products using organometallics.

Tamotsu Takahashi received the bachelor's (1978) and Ph.D. degrees (1983) from the University of Tokyo. He was a Research Associate in Professor Yasuzo Uchida's group at the University of Tokyo and then a Postdoctoral Associate in Professor Ei-ichi Negishi's group 1984-1986 at Purdue University. He returned to the University of Tokyo and stayed there until the end of 1990. He moved to the Institute for Molecular Science in 1991, where he is an Associate Professor. He is a recipient of the Progress Award in Synthetic Organic Chemistry, Japan (1993).

and discussed with emphasis on the conversion of dialkylzirconocenes into alkene-zirconocenes and interconversions among alkene-zirconocenes and five-membered zirconacycles.

Reactions of Dialkylzirconocenes

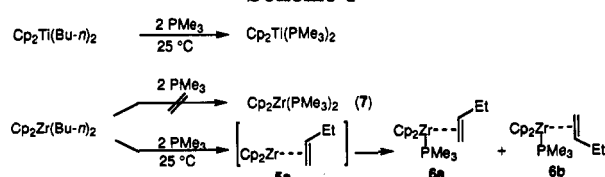
Treatment of Cp₂ZrCl₂ in THF with 2 equiv of *n*-BuLi at -78 °C gives Cp₂Zr(Bu-*n*)₂.⁵ The Zr-C bonds of Cp₂Zr(Bu-*n*)₂ and other dialkylzirconocenes act as typical polar metal-carbon bonds in some reactions. Thus, their protonolysis and deuteration with HCl and DCl, respectively, give Cp₂ZrCl₂ and the corresponding protonated and deuterated alkanes, respectively, while their iodolysis provides Cp₂ZrI₂ and iodoalkanes in high yields. Unlike RZrCp₂Cl,^{2c} which is thermally stable at room temperature, dialkylzirconocenes containing one or more β C-H bonds are thermally labile. The corresponding dialkylhafnocenes, e.g., Cp₂Hf(Bu-*n*)₂, are more stable and readily characterized at room

[†] Purdue University.

[‡] Institute for Molecular Science.

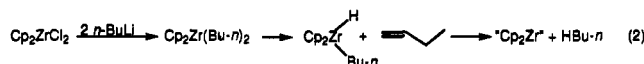
- (1) For background information on organozirconium compounds, see: (a) Wailes, P. C.; Courts, R. S. P.; Weigold, H. *Organometallic Chemistry of Titanium, Zirconium and Hafnium*; Academic Press: New York, 1974. (b) Cardin, D. J.; Lappert, M. F.; Raston, C. L. *Chemistry of Organozirconium and Hafnium Compounds*; John Wiley & Sons: New York, 1986. (2) For our previous reviews, see: (a) Negishi, E.; Takahashi, T. *Aldrichimica Acta* 1985, 18, 31. (b) Negishi, E.; Takahashi, T. *Synthesis* 1988, 1, 1. (c) For a review, see: Schwartz, J.; Labinger, J. A. *Angew. Chem., Int. Ed. Engl.* 1976, 15, 333. (3) (a) Khand, I. V.; Knox, G. R.; Pauson, P. L.; Watts, W. E.; Foreman, M. I. *J. Chem. Soc., Perkin Trans. 1* 1973, 977. (b) For a review, see: Schore, N. E. In *Comprehensive Organic Synthesis*; Paquette, L. A., Ed.; Pergamon Press: New York, 1991; Vol. 5, Chapter 9.1. p 1037. (4) Thanedar, S.; Farona, M. F. *J. Organomet. Chem.* 1982, 235, 65. (5) Negishi, E.; Cederbaum, F. E.; Takahashi, T. *Tetrahedron Lett.* 1966, 27, 2829. (6) (a) Negishi, E.; Holmes, S. J.; Tour, J. M.; Miller, J. A. *J. Am. Chem. Soc.* 1985, 107, 2568. (b) Negishi, E.; Swanson, D. R.; Cederbaum, F. E.; Takahashi, T. *Tetrahedron Lett.* 1987, 28, 917. (c) Negishi, E.; Sawada, H.; Tour, J. M.; Wei, Y. *J. Org. Chem.* 1988, 53, 913. (d) Negishi, E.; Holmes, S. J.; Tour, J. M.; Miller, J. A.; Cederbaum, F. E.; Swanson, D. R.; Takahashi, T. *J. Am. Chem. Soc.* 1989, 111, 3336. (7) (a) Nugent, W. A.; Thorn, D. L.; Harlow, R. L. *J. Am. Chem. Soc.* 1987, 109, 2788. (b) Fagan, P. J.; Nugent, W. A. *J. Am. Chem. Soc.* 1988, 110, 2310. (c) RajanBabu, T. V.; Nugent, W. A.; Taber, D. F.; Fagan, P. J. *J. Am. Chem. Soc.* 1988, 110, 7128. (8) Negishi, E. In *Comprehensive Organic Synthesis*; Paquette, L. A., Ed.; Pergamon Press: New York, 1991; Vol. 5, p 1163. (9) Mori, M.; Uesaka, N.; Shibasaki, M. *J. Org. Chem.* 1992, 57, 3519. (10) Agnel, G.; Owczarczyk, Z.; Negishi, E. *Tetrahedron Lett.* 1992, 33, 1543. (11) Agnel, G.; Negishi, E. *J. Am. Chem. Soc.* 1991, 113, 7424. (12) Wender, P. A.; McDonald, F. E. *J. Am. Chem. Soc.* 1990, 112, 4956. (13) Takahashi, T.; Swanson, D. R.; Negishi, E. *Chem. Lett.* 1987, 623. (14) Erker, G.; Kropp, K. *J. Am. Chem. Soc.* 1979, 101, 3659. (15) McDade, C.; Bercaw, J. E. *J. Organomet. Chem.* 1985, 279, 281. (16) (a) Buchwald, S. L.; Watson, B. T.; Huffman, J. C. *J. Am. Chem. Soc.* 1986, 108, 7411; 1987, 109, 2544. (b) Buchwald, S. L.; Lum, R. T.; Dewan, J. C. *J. Am. Chem. Soc.* 1986, 108, 7441. (c) For a review, see: Buchwald, S. L.; Nielsen, R. B. *Chem. Rev.* 1988, 88, 1047.

Scheme 1



temperature. Those dialkylzirconocenes lacking β C–H bonds, e.g., Cp_2ZrMe_2 and $\text{Cp}_2\text{Zr}(\text{CH}_2\text{Ph})_2$, are stable for at least days and weeks at room temperature,¹ indicating that, unlike the corresponding titanocene derivatives,¹⁷ dialkylzirconocenes do not readily undergo α -H abstraction reactions.

β -Hydrogen Abstraction. In our initial study, we tentatively presented a dissociative path for the decomposition of $\text{Cp}_2\text{Zr}(\text{Bu}-n)_2$, in which free 1-butene and free ZrCp_2 are at least momentarily formed (eq 2). However, our subsequent studies have shown that decomposition of this and other dialkylzirconocenes proceeds nondissociatively,¹⁸ without producing free alkenes or ZrCp_2 itself, an elusive 14-electron species. Thus, for example, in the decomposition reaction of $\text{Cp}_2\text{Zr}(\text{Oct}-n)_2$ in the presence of $\text{D}_2\text{C}=\text{CH}(\text{Hex}-n)$, incorporation of $\text{D}_2\text{C}=\text{CH}(\text{Hex}-n)$ into the ZrCp_2 -containing compound lags far behind the decomposition reaction itself.¹⁸ In view of the nondissociative nature of the reaction, the term β -H abstraction has been chosen over β -elimination mainly to distinguish this process from that shown in eq 2 in which 1-butene is at least momentarily eliminated from di- n -butylzirconocene.



The initial product obtained by decomposition of $\text{Cp}_2\text{Zr}(\text{Bu}-n)_2$ was thermally labile and has not been identified. However, it must be $\text{Cp}_2\text{Zr}(\text{H}_2\text{C}=\text{CHEt})$ (5), a 16-electron species, since our study^{6d} and that of Binger¹⁹ have fully identified the corresponding PMe_3 -stabilized complex 6 as a roughly 85:15 mixture of 6a and 6b (Scheme 1). Our initial interpretation that thermal decomposition of $\text{Cp}_2\text{Zr}(\text{Bu}-n)_2$ in the presence of 2 equiv of PMe_3 would give $\text{Cp}_2\text{Zr}(\text{PMe}_3)_2$ (7) was erroneous,¹⁸ even though the corresponding reaction of $\text{Cp}_2\text{Ti}(\text{Bu}-n)_2$ in the presence of PMe_3 has since been shown to give $\text{Cp}_2\text{Ti}(\text{PMe}_3)_2$.¹⁹ The available data are consistent with the β -H abstraction path shown in eq 3.²⁰ In the absence of any indication for the existence of two discrete species, we tentatively adopt the resonance hybrid between 5a and 5b as the structure of 5 and use either 5a or 5b for the sake of simplicity without giving any preference to one or the other.

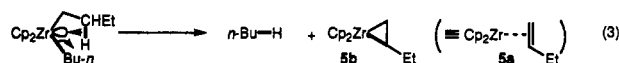
The following features of β -H abstraction are worth noting: (i) (1-Butene)zirconocene (5) can be signifi-

(17) Petasis, N. *Abstracts of Papers*, 205th National Meeting of the American Chemical Society, Denver, CO, March 28–April 2, 1993; American Chemical Society: Washington, DC, 1993; ORGN 96.

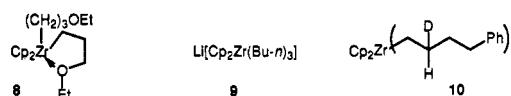
(18) Negishi, E.; Swanson, D. R.; Takahashi, T. *J. Chem. Soc., Chem. Commun.* 1990, 1254.

(19) Binger, P.; Müller, P.; Berm, R.; Rufinska, A.; Gabor, B.; Krüger, C.; Betz, P. *Chem. Ber.* 1989, 122, 1035.

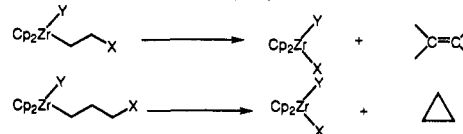
(20) For related reactions of other zirconocenes derivatives, see: (a) Buchwald, S. L.; Nielsen, R. B.; Dewan, J. C. *J. Am. Chem. Soc.* 1987, 109, 1590. (b) Buchwald, S. L.; Nielsen, R. B. *J. Am. Chem. Soc.* 1988, 110, 3171. (c) Buchwald, S. L.; Watson, B. T.; Wannamaker, M. W.; Dewan, J. C. *J. Am. Chem. Soc.* 1989, 111, 4486.



cantly stabilized through complexation with PMe_3 to produce 6; yet the β -H abstraction reaction is neither driven nor facilitated by PMe_3 , since the rates of decomposition of dialkylzirconocenes are essentially unaffected by the presence of PMe_3 .²¹ In fact, $\text{Cp}_2\text{Zr}(\text{Bu}-n)_2$ or even sterically less hindered Cp_2ZrMe_2 shows no sign of interaction with PMe_3 by NMR. Therefore, the role of PMe_3 is merely to act as a stabilizing ligand for alkene–zirconocenes, e.g., 6, after their formation. (ii) Comparison of the relative rates of decomposition of several dibutylzirconocenes and Cp_2ZrMeBu relative to those of Cp_2ZrEt_2 and Cp_2ZrMeEt , respectively, indicate the following order of reactivity of alkyl groups as β -H donors: *sec*-Bu > *t*-Bu \geq Et > *n*-Bu > *i*-Bu.²¹ Clearly, this order does not correlate with the overall steric requirements of these groups. In a more generalized sense, the following order has been observed in the great majority of cases,²¹ and it provides reasonable predictions: β -CH₃ > β -CH₂ > β -CH. This order appears to reflect the ease of agostic interaction between a β C–H bond and a Zr empty orbital, and localized steric factors must be primarily responsible for the observed order. However, electronic factors can also play a significant role. Thus, for example, PhCH_2CH_2 , a β -CH₂ group, is a somewhat better β -H donor than Et, a β -CH₃ group, presumably due to benzylic stabilization in the styrene–zirconocene complexes.²¹ (iii) The significance of a Zr empty orbital in the β -H abstraction reaction is also indicated by the following facts. The half-life of bis(3-ethoxypropyl)zirconocene (8) is 700 times as long as that of $\text{Cp}_2\text{Zr}(\text{Bu}-n)_2$, suggesting a stabilization through chelation.²¹ Similarly, treatment of Cp_2ZrCl_2 with 3 equiv of *n*-BuLi gives a thermally stable species in 50–60% yield, which has been tentatively identified as 9.²¹ (iv) The decomposition reaction of 10 displays a significant isotope effect ($k_{\text{H}}/k_{\text{D}} = 5.7$).²¹



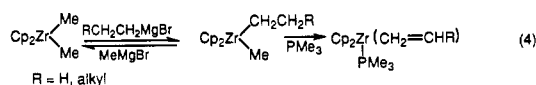
Elimination Reactions. Alkylzirconocene derivatives containing β - and γ -heteroatoms, such as halogens, are prone to β - and γ -elimination processes, respectively¹ (Scheme 2). An increasing number of synthetically useful reactions, which are thought to proceed via β - or γ -elimination, have been developed in recent years, as discussed later.

 Scheme 2^a


^a X = halogens, oxygen, and other heteroatom groups. Y = ligand.

Transmetalation and “Ate” Complexation. Treatment of Cp_2ZrMe_2 with Grignard reagents in the presence of PMe_3 provides alkene–zirconocene– PMe_3 complexes in good yields along with MeMgBr .²² The

reaction must proceed via transmetalation, which may in turn proceed via "ate" complexation, although no clear-cut indication has been shown by NMR spectroscopy for the formation of zirconate complexes (eq 4). The reaction provides an alternate route to alkene-zirconocenes.



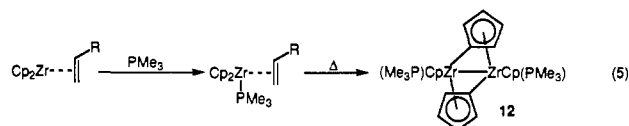
More reactive organolithiums have shown clear signs of "ate" complexation with diorganyl zirconocenes.¹ In addition to Li[Cp₂Zr(Bu-*n*)₃] (9), the reaction of Cp₂ZrCl₂ with 3 equiv of LiC≡CR, where R = Ph, Hex-*n*, or C(Me)=CH₂, gives products tentatively identified as Li[Cp₂Zr(C≡CR)₃] (11).²³ In contrast with 9, the alkyne-containing complexes 11 are thermally labile, and they undergo an interesting migration reaction.²³ Both transmetalation and "ate" complexation, especially readily reversible versions, appear to play important roles in both stoichiometric and catalytic reactions of zirconocene derivatives, as discussed later.

In addition to protonolysis (deuterolysis) and halogenolysis, several synthetically important processes that dialkylzirconocenes can undergo have emerged: β-H abstraction, β- and γ-elimination reactions involving heteroatoms, transmetalation, and "ate" complexation. With the exception of cyclopropanation via γ-elimination, none of these reactions as such provide a means of constructing new organic skeletons via C-C bond formation. Nonetheless, they play crucial roles in conjunction with some skeleton-constructing processes, such as carbometalative ring expansion, reductive elimination, and migratory insertion.

Reactions of Alkene-Zirconocenes

Alkene-zirconocene complexes having 16 Zr valence electrons have proved to be highly reactive species, which can effectively act as loosely clad analogs of the 14-electron ZrCp₂. Throughout our investigation, ZrCp₂ itself has remained elusive. In the absence of added reagents, alkene-zirconocene complexes tend to readily decompose at room temperature. Even their PMe₃ complexes have been shown to irreversibly decompose to give 12^{18,24} (eq 5). It now appears that the key to observing synthetically useful Zr^{II}Cp₂ reactions is to generate 16-electron Zr^{II}Cp₂ derivatives of sufficient reactivity, e.g., 5, in the presence of the substrates with which they are to react, while avoiding their unwanted decomposition to give "dead" dimers, e.g., 12. The alkene ligand of an alkene-zirconocene complex can be readily released as a free alkene or the corresponding alkane by treatment of the complex with I₂ or HCl, respectively.

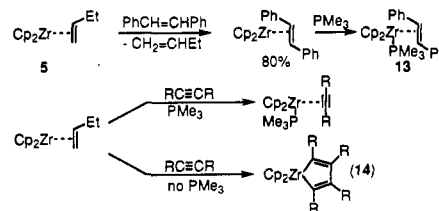
Although the development of synthetically interesting reactions of alkene-zirconocene complexes has chronologically lagged behind that of alkyne-zirconocene^{8,16}



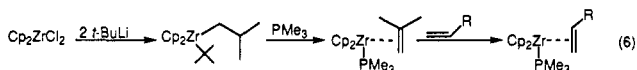
and conjugated diene-zirconocene^{25,26} complexes, studies over the past several years have shown that they indeed participate in many synthetically interesting reactions.

Alkene Displacement. In contrast with alkynes on Zr, alkenes can be readily displaced by alkenes, alkynes, and other π compounds. Typically, the reaction of Cp₂Zr(Bu-*n*)₂ used as a source of (1-butene)zirconocene (5) with stilbene gives (stilbene)zirconocene in 80% yield.¹³ Its PMe₃ complex 13 has yielded one of the first X-ray structures of alkene-zirconocene complexes²⁷ along with Cp₂Zr(CH₂=CH₂)PMe₃.²⁸ A related reaction of 5 with alkynes in the presence of a phosphine provides a convenient route to alkyne-zirconocene-phosphine complexes. In the absence of a phosphine, the reaction is dominated by the formation of the alkyne-alkyne coupling product 14¹³ (Scheme 3). The scope of the

Scheme 3



alkene displacement route to alkene-zirconocene complexes can be significantly expanded by the use of a weaker alkene ligand, e.g., isobutylene²⁹ (eq 6).



Formation of Five-Membered Zirconacycles via Carbometalative Ring Expansion. In the initial phase of our investigation, we envisioned the ring expansion reactions of zirconacyclopropenes and zirconacyclopropanes depicted in Scheme 4. Although this generalized scheme might suggest that the formation of five-membered zirconacycles via this route would be complicated by difficulties associated with "pair"-selectivity, regioselectivity, and stereoselectivity, investigations by us and others over the past several years indicate that many of these reactions are surprisingly

(25) (a) Yasuda, H.; Kajihara, Y.; Mashima, K.; Nagasuma, K.; Nakamura, A. *Chem. Lett.* 1981, 671. (b) Kai, Y.; Kanehisa, N.; Miki, K.; Kasai, N.; Mashima, K.; Nagasuma, K.; Yasuda, H.; Nakamura, A. *Chem. Lett.* 1982, 1979. (c) Kai, Y.; Kanehisa, N.; Miki, K.; Kasai, N.; Akita, M.; Yasuda, H.; Nakamura, A. *Bull. Chem. Soc. Jpn.* 1983, 56, 3735.

(26) (a) Skibbe, V.; Erker, G. *J. Organomet. Chem.* 1983, 241, 15. (b) Erker, G.; Engel, K.; Atwood, J. L.; Hunter, W. E. *Angew. Chem., Int. Ed. Engl.* 1983, 22, 494. (c) Erker, G.; Dorf, U. *Angew. Chem., Int. Ed. Engl.* 1983, 22, 777.

(27) (a) Takahashi, T.; Uchida, Y.; Uchida, T.; Negishi, E. 13th International Conference on Organometallic Chemistry, Torino, Sept 1988; Abstract 187. (b) Takahashi, T.; Murakami, M.; Kunishige, M.; Saburi, M.; Uchida, Y.; Kozawa, K.; Uchida, T.; Swanson, D. R.; Negishi, E. *Chem. Lett.* 1989, 761.

(28) Alt, H. G.; Denner, C. E.; Thewalt, U.; Rausch, M. D. *J. Organomet. Chem.* 1988, 356, C83.

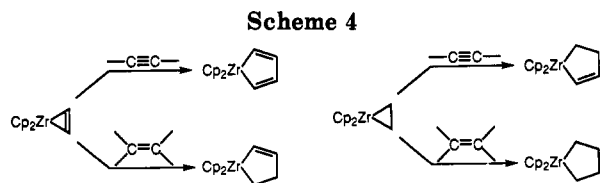
(29) Swanson, D. R.; Negishi, E. *Organometallics* 1991, 10, 825.

(21) Negishi, E.; Nguyen, T.; Maye, J. P.; Choueiri, D.; Suzuki, N.; Takahashi, T. *Chem. Lett.* 1992, 2367.

(22) Takahashi, T.; Nitto, Y.; Seki, T.; Saburi, M.; Negishi, E. *Chem. Lett.* 1990, 2259.

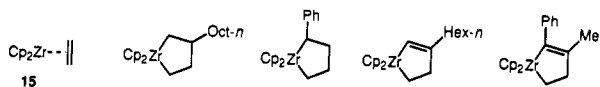
(23) Takagi, K.; Rousset, C. J.; Negishi, E. *J. Am. Chem. Soc.* 1991, 113, 1440.

(24) Kool, L. B.; Rausch, M. D.; Alt, H. G.; Herberhold, M.; Thewalt, U.; Honold, B. *J. Organomet. Chem.* 1986, 310, 27.

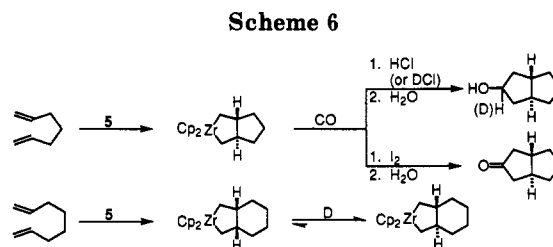
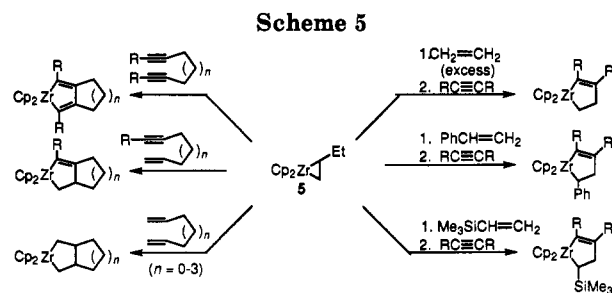


selective with respect to the selectivity aspects mentioned above. Regardless of the "pair"-selection types, alkyl substituents in alkenes and alkynes strongly prefer to be β to Zr, while aryl, alkenyl, alkynyl, and silyl groups strongly favor the α position. The former must be largely steric in origin, while the latter must be largely electronic. Furthermore, two substituents in zirconacyclopentanes strongly favor being trans to each other.

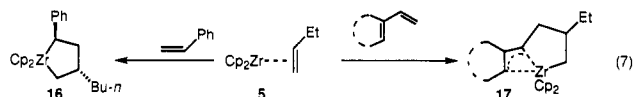
The "pair"-selectivity aspect of these reactions is mostly dictated by the relative rates of ligand displacement and carbometalative ring expansion processes. In cases where the alkene ligand of an alkene-zirconocene is tightly bound and not displaced by an added alkene or alkyne, a strictly "pair"-selective formation of a zirconacyclopentane or zirconacyclopentene would result (type I process). Indeed, the reaction of (ethylene)zirconocene (15) with many alkenes and alkynes has provided a "pair"-selective route to various five-membered zirconacycles, such as those shown below.^{30,31} The high "pair"-selectivities and regioselectivities observed in these reactions strongly suggest that these products must have been formed under kinetically controlled, nonequilibrating conditions.



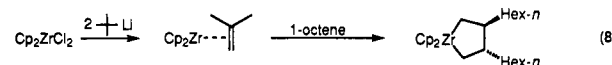
The reaction of (1-butene)zirconocene (5) with styrene gives predominantly 16 along with rather minor amounts ($\sim 5\%$ each) of the two possible homo-coupled products.^{32a} However, this cannot be a type I reaction, because, in the presence of 1 equiv of 1-octene, it gives a 1:1 mixture of 16 and the corresponding 1-octene-styrene cross-coupling products, indicating that 1-butene in 5 is readily displaced and that 16 is formed under equilibrating conditions. The selective formation of 16 in preference to the two possible homo-coupled products is readily explained as follows. Provided that the molar ratio of 1-butene to styrene is 1, the amounts of the two homo-coupled products must be equal. Of the three possible products, the 1-butene dimerization product must be relatively destabilized due to the absence of an α -Ph group exerting benzylic stabilization. This, in turn, also disfavors the styrene dimerization products due to the constraint mentioned above. This leads to a selective formation of 16. On this basis, it is readily expected that the reaction of 5 with conjugated dienes that can exert allylic stabilization is even more "pair"-selective. Indeed, the formation of 17 from 5 (eq 7) is $>95\%$ "pair"-selective.^{32b} These "pair"-selective reactions which proceed under equilibrating



conditions and incorporate the original alkene in the five-membered zirconacycles are herein referred to as type II processes.



In cases where the original alkene is readily displaceable, the use of 2 equiv or more of an alkene or alkyne can lead to selective homo-coupling without incorporation of the original alkene (type III process). 1-Butene and isobutylene are typical examples of readily displaceable alkenes. The formation of 14 from 5 in Scheme 3 is a typical example of this process along with that shown in eq 8.^{32a}



One of the synthetically most attractive types of ring expansion reactions of alkene-zirconocene complexes is represented by the "pair"-selective and regioselective bicyclization reactions of nonconjugated enynes,^{6,7} diynes,⁵⁻⁷ and dienes^{33,34} induced by 5 (type IV process) (Scheme 5). In the latter, the zirconabicyclo[3.3.0] systems strongly favor *trans* fusion, whereas the [4.3.0] homologs favor *cis* fusion. The latter, however, has been shown to be a kinetic phenomenon.^{34d} Carbonylation with retention of stereochemistry provides a route to *trans*-fused bicyclo[3.3.0]octanes,³³ which are otherwise not readily accessible (Scheme 6). Significantly, allylic substituents in enynes and dienes end up *cis* to the adjacent bridgehead hydrogen in the products,^{33,35} permitting diastereoselective construction of substituted fused bicycles and polycycles.^{10,11} Although generally more difficult, the intermolecular version of the "pair"-selective type IV process may also be observed, provided that the initial alkene displacement

(30) Takahashi, T.; Seki, T.; Nitto, Y.; Saburi, M.; Rousset, C. J.; Negishi, J. *Am. Chem. Soc.* 1991, 113, 6266.

(31) (a) Takahashi, T.; Kageyama, M.; Denisov, V.; Hara, R.; Negishi, E. *Tetrahedron Lett.* 1993, 34, 687. (b) Copéret, C.; Negishi, E.; Xi, Z.; Takahashi, T. *Tetrahedron Lett.* 1994, 35, 695.

(32) (a) Swanson, D. R.; Rousset, C. J.; Negishi, E.; Takahashi, T.; Seki, T.; Saburi, M.; Uchida, Y. *J. Org. Chem.* 1989, 54, 3521. (b) Negishi, E.; Miller, S. R. *J. Org. Chem.* 1989, 54, 6014.

(33) Rousset, C. J.; Swanson, D. R.; Lamaty, F.; Negishi, E. *Tetrahedron Lett.* 1989, 30, 5105.

(34) For related studies by other workers, see: (a) Gell, I.; Schwartz, J. J. *Chem. Soc., Chem. Commun.* 1979, 244. (b) Yasuda, H.; Nagasuna, K.; Akita, M.; Lee, K.; Nakamura, A. *Organometallics* 1984, 3, 1470. (c) Nugent, W. A.; Taber, D. F. *J. Am. Chem. Soc.* 1989, 111, 6435. (d) Akita, M.; Yasuda, H.; Yamamoto, H.; Nakamura, A. *Polyhedron* 1991, 10, 1.

(35) Lund, E. C.; Livinghouse, T. *J. Org. Chem.* 1989, 54, 4487.

Table 1. Some Distinctive Features of Various Types of Ring Expansion Reactions of Alkene-Zirconocene Complexes

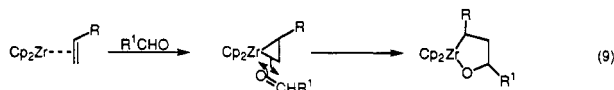
type	displacement of the initial alkene	pair-selectivity	equilibrating or not
I	no	very high (~100%)	no
II	no	high	yes
III	yes	homo-coupling	a
IV	yes	high	b
V	b	low	yes

^a Not pertinent. ^b Depends on the substrates.

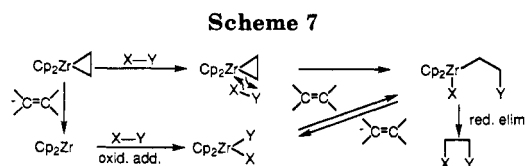
is followed by either a type I or type II process. Some such reactions have indeed been observed in the reaction of **5** with ethylene, styrene, or (trimethylsilyl)ethylene followed by addition of an alkyne³⁶ (Scheme 5).

In the absence of strongly directing and controlling factors, coupling between two π -compounds gives mixtures of the three possible products (type V process). Thus, the reaction of $\text{Cp}_2\text{Zr}(\text{Bu-}n)_2$ with 1 equiv of 1-octene gives a nearly statistical 2:1:1 mixture of the cross-coupled and the two homo-coupled products.^{32a} Some distinctive features of the five types of processes discussed above are summarized in Table 1.

Polar Addition Reactions of Alkene-Zirconocenes. Alkene-zirconocenes generated in the presence of aldehydes undergo an addition reaction, shown in eq 9.³⁷ Its regioselectivity is opposite to that in the alkene-alkene coupling reaction (e.g., eq 8). Although not yet firmly established, it must be a kinetically controlled, nonequilibrating process, in which interaction between the less hindered C-Zr bond and the C=O group must be sterically favored. Aside from this reaction, little is known about other polar addition reactions of alkene-zirconocenes. This area clearly deserves further exploration.



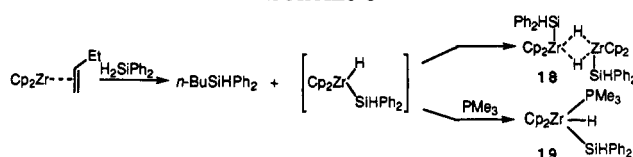
Reactions of Alkene-Zirconocenes with Single-Bonded Reagents (X-Y). In analogy with the ring expansion (Scheme 4) and polar addition reactions (eq 9), the Zr-C bonds of zirconacycloprenes and zirconacycloprenes should, in principle, be capable of reacting with various single-bonded reagents X-Y, where X and Y are H, C, Si, Sn, N, O, S, and halogens. Alternatively, alkene-zirconocenes and alkyne-zirconocenes may release ZrCp_2 , which may then undergo oxidative addition with X-Y (Scheme 7).



Treatment of alkene-zirconocenes with I_2 releases the corresponding alkenes with the concomitant formation of Cp_2ZrI_2 . In our recent study of ZrCp_2 -

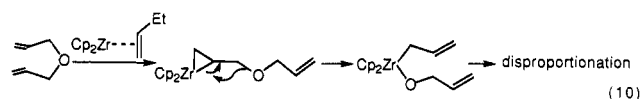
(36) Takahashi, T.; Xi, Z.; Rousset, C. J.; Suzuki, N.; *Chem. Lett.* 1993, 1001.

(37) Takahashi, T.; Suzuki, N.; Hasegawa, M.; Nitto, Y.; Aoyagi, K.; Saburi, M. *Chem. Lett.* 1992, 331.

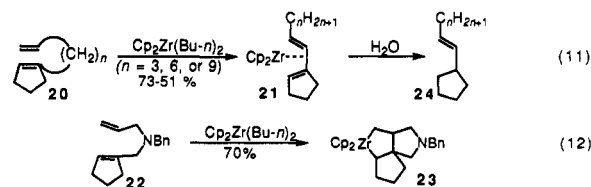
Scheme 8

catalyzed hydrosilation of alkenes,^{38,39} we treated $\text{Cp}_2\text{Zr}(\text{Bu-}n)_2$ with 2 equiv of H_2SiPh_2 . This reaction produced not only $n\text{-BuSiHPh}_2$ but also a yellow crystalline compound, **18**, in 85% yield. The same reaction run in the presence of PMe_3 produces **19** (90% yield). The results indicate that (1-butene)zirconocene reacts with H_2SiPh_2 via oxidative addition (Scheme 8). Oxidative addition of H_2 to Zr(II) species has also been reported.^{40,41}

Another pattern for oxidative addition was accidentally discovered in an attempt to cyclize diallyl ether by its reaction with $\text{Cp}_2\text{Zr}(\text{Bu-}n)_2$.³³ The reaction gave allyl(allyloxy)zirconocene, which subsequently disproportionated (eq 10). This reaction and a related oxidative addition reaction of propargyl ethers have been developed into a convenient route to allyl- and propargylzirconocene derivatives.⁴²



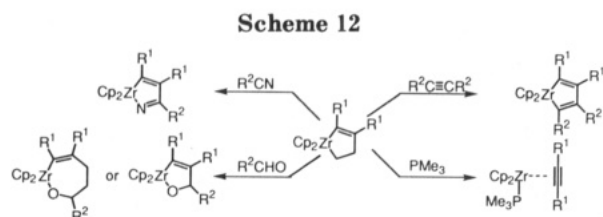
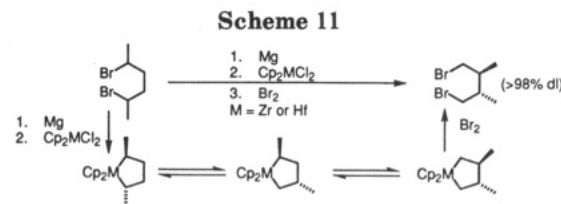
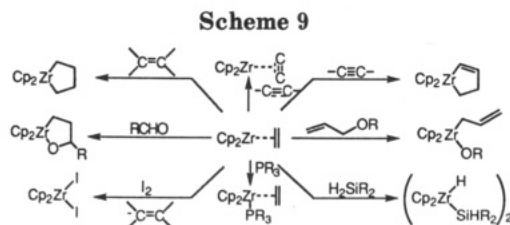
Regioisomerization. In view of the β C-H agostic interaction discussed earlier, the allylic C-H activation by Zr in alkene-zirconocenes is readily expected. In conjunction with a Ti-catalyzed alkene isomerization reaction, a related but very inefficient reaction catalyzed by Cp_2Zr derivatives has been briefly described.⁴³ This type of regioisomerization can indeed take place in the absence of any other more facile processes and/or in the presence of some functionalities in alkene-zirconocenes promoting regioisomerization. Specifically, the reaction of a series of compounds represented by **20** with $\text{Cp}_2\text{Zr}(\text{Bu-}n)_2$ fails to produce the expected bicyclization products but gives the corresponding conjugated diene-zirconocenes **21**, even though a N-containing analog **22** smoothly bicyclizes to give **23**^{44a} (eqs 11 and 12). Interestingly, protonolysis of **21** selectively products **24**, corresponding to partial hydrogenation of the more hindered double bonds of conjugated dienes.^{44b}



Some representative reactions of alkene-zirconocenes are summarized in Scheme 9.

(38) Takahashi, T.; Hasegawa, M.; Suzuki, N.; Saburi, M.; Rousset, C. J.; Fanwick, P. E.; Negishi, E. *J. Am. Chem. Soc.* 1991, 113, 8564.

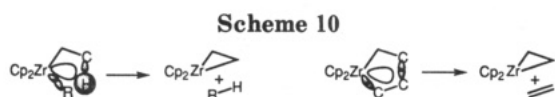
(39) For related studies by others, see: (a) Mu, Y.; Aitken, C.; Cote, B.; Harrod, J. F.; Samuel, E. *Can. J. Chem.* 1991, 69, 264. (b) Kesti, M. R.; Abdulrahman, M.; Waymouth, R. M. *J. Organomet. Chem.* 1991, 417, C12. (c) Kesti, M. R.; Waymouth, R. M. *Organometallics* 1992, 11, 1095. (d) Corey, J. Y.; Zhu, X. H. *Organometallics* 1992, 11, 672.



Reactions of Zirconacyclopentanes and Zirconacyclopentenenes

Zirconacyclopentanes and zirconacyclopentenenes prepared via alkene–zirconocenes and other suitable precursors are cyclic analogues of dialkylzirconocenes and alkyl(alkenyl)zirconocenes. Thus, they undergo many reactions of the latter classes of compounds, such as protonolysis, deuteration, halogenolysis, carbonylation, and transmetalation.²

Cleavage of C_β–C'_β Bonds Leading to Ring Contraction. One of the major differences between acyclic diorganylzirconocenes and the corresponding five-membered zirconacycles is that, whereas acyclic diorganylzirconocenes readily undergo β -H abstraction, their cyclic counterparts do not.⁴⁵ Due to conformational constraints, the H–C_β bonds of zirconacyclopentanes and zirconacyclopentenenes cannot readily adopt a coplanar relationship with the other Zr–R bond and a Zr empty orbital, which disfavors β -H abstraction. This very conformational restriction, however, makes readily available a similar coplanar relationship involving the Zr, C_α, C_β, and C'_β atoms. It is therefore not surprising to observe the ring-contraction reaction shown in Scheme 10.^{46,47} In this scheme, the Zr empty orbital lying inside the zirconacyclopentane ring is poised to interact with the C_β–C'_β bond. As such, this process is nothing but the microscopic reversal of the carbometallative ring expansion process discussed earlier. This process itself most probably is thermodynamically unfavorable. However, its kinetic accessibility leads to a number of synthetically attractive processes.



We have indeed observed over the past several years (i) the ring contraction reaction of zirconacyclopentanes and hafnacyclopentanes to produce the corresponding

(40) Takahashi, T.; Suzuki, N.; Kageyama, M.; Nitto, Y.; Saburi, M.; Negishi, E. *Chem. Lett.* **1991**, 1579.

(41) (a) Manriquez, J. M.; McAlister, D. R.; Sanner, R. D.; Bercaw, J. E. *J. Am. Chem. Soc.* **1976**, *98*, 6733; **1978**, *100*, 2716. (b) Gell, K. I.; Posin, B.; Schwartz, J.; Williams, G. M. *J. Am. Chem. Soc.* **1982**, *104*, 1846.

(42) (a) Ito, H.; Taguchi, T.; Hanzawa, Y. *Tetrahedron Lett.* **1992**, *33*, 1295. (b) Ito, H.; Nakamura, T.; Taguchi, T.; Hanzawa, Y. *Tetrahedron Lett.* **1992**, *33*, 3769. (c) Ito, H.; Taguchi, T.; Hanzawa, Y. *J. Org. Chem.* **1993**, *58*, 774.

(43) Yasuda, H.; Kajihara, Y.; Mashima, K.; Nagasuna, K.; Lee, K.; Nakamura, A. *Organometallics* **1982**, *1*, 388.

(44) (a) Maye, J. P.; Negishi, E. *Tetrahedron Lett.* **1993**, *34*, 3359. (b) Maye, J. P.; Negishi, E. *J. Chem. Soc., Chem. Commun.* **1993**, 1830.

(45) For a study on titanacyclopentanes, see: McDermott, J. X.; Wilson, M. E.; Whitesides, G. M. *J. Am. Chem. Soc.* **1976**, *98*, 6529.

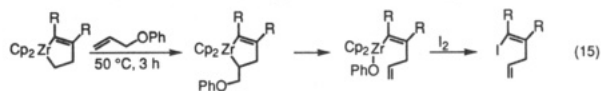
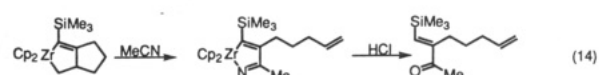
(46) Erker, G.; Dorf, U.; Rheingold, A. L. *Organometallics* **1988**, *7*, 138.

(47) For related processes involving other transition metals, see: (a) Grubbs, R. H.; Miyashita, A. *J. Am. Chem. Soc.* **1978**, *100*, 1300. (b) McLain, S. J.; Wood, C. D.; Schrock, R. R. *J. Am. Chem. Soc.* **1979**, *101*, 4558.

alkene–metallocene–phosphine complexes^{18,48} (eq 13), (ii) skeletal rearrangement involving “apparent” migration of substituents⁴⁹ (Scheme 11), and (iii) displacement of alkene components of metallacycles by external π -compounds^{64,31,50} (Scheme 12). The ring contraction reaction shown in eq 13 provides the fourth route to alkene–zirconocene complexes along with those shown in Scheme 1 (β-H abstraction), eq 4 (transmetalation–abstraction), and Scheme 3 (alkene displacement). The skeletal rearrangement has been shown to proceed stepwise by NMR spectroscopic analysis of the regioisomerization reaction of hafnocene derivatives⁴⁹ (Scheme 11).



Following an accidental initial finding, shown in eq 14,^{6d} we have extensively developed in recent years various alkene–displacement reactions, shown in Scheme 12.³¹ In this scheme, the zirconacyclopentene intermediates are readily generated *in situ* by successive treatment of Cp₂ZrCl₂ with 2 equiv of EtMgBr and alkynes. Since the final products in most cases do not contain the dimethylene moiety, it acts as a “dummy” group, which amounts to an inexpensive phosphine substitute. Higher alkyls, e.g., *n*-Bu, except PhCH₂CH₂, Me₃SiCH₂CH₂, etc., may not readily be used in place of Et, because they tend to participate in the type III and V cyclization processes discussed earlier. In the reaction of zirconacyclopentenenes with aldehydes, either five-membered (at ≥50 °C) or seven-membered (at ≤25 °C) products may be obtained, depending on the reaction temperature. Significantly, the alkene displacement reactions can lead to further transformations of synthetic utility, as shown in eq 15.⁵⁰



In summary, zirconacyclopentanes and zirconacyclopentenenes share many reactions with their acyclic counterparts. Instead of undergoing β -H abstraction, however, these cyclic compounds readily undergo C_β–C'_β bond cleavage leading to ring contraction, skeleton rearrangement, and alkene displacement. Some of

these reactions induce further transformations of synthetic interest. To our knowledge, no $C_{\beta}-C'_{\beta}$ bond cleavage reaction of zirconacyclopentadienes has been reported.

Catalytic Reactions Involving Alkene-Zirconocenes

We have previously developed some $ZrCp_2$ -catalyzed reactions of organometals containing Al^{51-53} and Zn ,⁵⁴ which most probably occur via nonredox processes involving only Cp_2Zr^{IV} species as active catalysts. Recent studies by us and others indicate that the scope of the $ZrCp_2$ -catalyzed reactions can be significantly expanded through further utilization of Cp_2Zr^{II} species. Furthermore, some previously known Cp_2Zr -catalyzed reactions that were thought to involve only Cp_2Zr^{IV} catalysts have been shown to involve Cp_2Zr^{II} species as well. In such catalytic reactions, β -H abstraction and $C_{\beta}-C'_{\beta}$ bond cleavage represent important reductive processes, while carbometalative ring expansion and oxidative addition play crucial roles as oxidative processes.

Also significant are some nonredox processes, such as "ate" complexation, transmetalation, and elimination reactions. Needless to say, these reductive and oxidative processes must be combined in appropriate manners in order to devise catalytic processes of the redox type. The Dzhemilev ethylmagnesiumation of alkenes⁵⁵ is superficially related to the previously developed Cp_2ZrCl_2 -catalyzed carboalumination of alkynes,⁵¹ but it displays some features that cannot be readily explained in terms of a simple ethyl-metal bond addition to alkenes. For example, it does not work with $MeMgBr$. Higher alkylmagnesium halides undergo a different head-to-tail alkene dimerization reaction.⁵⁶ Through our systematic investigations discussed in the previous

(48) Takahashi, T.; Tamura, M.; Saburi, M.; Uchida, Y.; Negishi, E. *J. Chem. Commun.* **1989**, 852.

(49) Takahashi, T.; Fujimori, T.; Seki, T.; Saburi, M.; Uchida, Y.; Rousset, C. J.; Negishi, E. *J. Chem. Soc., Chem. Commun.* **1990**, 182.

(50) Suzuki, N.; Kondakov, D. Y.; Takahashi, T. *J. Am. Chem. Soc.* **1993**, *115*, 8485.

(51) (a) Negishi, E.; Van Horn, D. E. *J. Am. Chem. Soc.* **1977**, *99*, 3168. (b) Okukado, N.; Van Horn, D. E.; Klima, W. L.; Negishi, E. *Tetrahedron Lett.* **1978**, 1027. (c) Negishi, E.; Okukado, N.; King, A. O.; Van Horn, D. E.; Spiegel, B. I. *J. Am. Chem. Soc.* **1978**, *100*, 2254.

(52) (a) Van Horn, D. E.; Negishi, E. *J. Am. Chem. Soc.* **1978**, *100*, 2252. (b) Negishi, E. *Pure Appl. Chem.* **1981**, *53*, 2333. (c) Negishi, E.; Van Horn, D. E.; Yoshida, T. *J. Am. Chem. Soc.* **1985**, *107*, 6639.

(53) Negishi, E.; Yoshida, T. *Tetrahedron Lett.* **1980**, *21*, 1501.

(54) Negishi, E.; Van Horn, D. E.; Yoshida, T.; Rand, C. L. *Organometallics* **1983**, *2*, 563.

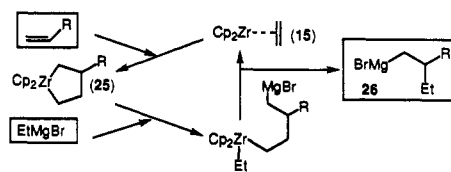
(55) (a) Dzhemilev, V. M.; Vostrikova, O. S.; Sultanov, R. M. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1983**, 219. (b) Dzhemilev, V. M.; Vostrikova, O. S.; Tolstikov, G. A. *J. Organomet. Chem.* **1986**, *304*, 17.

(56) Rousset, C. J.; Negishi, E.; Suzuki, N.; Takahashi, T. *Tetrahedron Lett.* **1992**, *33*, 1965.

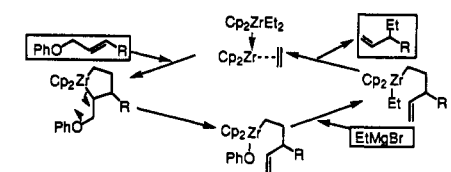
(57) For related studies by others, see: (a) Knight, K. S.; Waymouth, R. M. *J. Am. Chem. Soc.* **1991**, *113*, 6268. (b) Hoveyda, A. H.; Xu, Z. *J. Am. Chem. Soc.* **1991**, *113*, 5079. (c) Lewis, D. P.; Muller, D. M.; Whitby, R. J.; Jones, R. V. H. *Tetrahedron Lett.* **1991**, *32*, 6797. (d) Hoveyda, A. H.; Morken, J. P.; Houry, A. F.; Xu, Z. *J. Am. Chem. Soc.* **1992**, *114*, 6692.

(58) Negishi, E.; Rousset, C. J.; Maye, J. P.; Choueiry, D.; Suzuki, N.; Takahashi, T. Submitted for publication.

Scheme 13

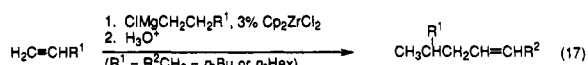
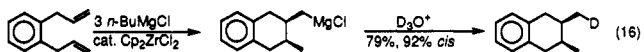


Scheme 14



sections, we have found⁵⁰ the following stoichiometric processes. (i) The reaction of Cp_2ZrCl_2 with $EtMgBr$ produces (ethylene)zirconocene via β -H abstraction of Cp_2ZrEt_2 . (ii) (Ethylene)zirconocene (15) reacts with 1-alkenes in a "pair"-selective and regioselective manner to give 25. (iii) The zirconacyclopentane 25 reacts, in turn, with $EtMgBr$ to give 26 and 15 via selective transmetalation and β -H abstraction. When these stoichiometric processes i-iii are linked together, they add up to the Dzhemilev ethylmagnesiumation catalyzed by Cp_2ZrCl_2 ^{55,57} (Scheme 13).

This study triggered our subsequent investigations of Cp_2Zr^{II} -catalyzed reactions including (i) a related diene cyclization reaction⁵⁸ (eq 16), (ii) head-to-tail alkene dimerization⁵⁶ (eq 17), (iii) regioselective ethylation of allyl ethers⁵⁰ (Scheme 14), (iv) hydrogenation of alkenes⁴⁰ (eq 18), and (v) hydrosilylation of alkenes³⁸ (eq 19).



In summary, a novel catalytic concept involving redox processes of Cp_2Zr -containing compounds has been recognized. It not only helps explain some previously known but puzzling catalytic processes but also has led to the discovery and development of new catalytic processes. Undoubtedly, many additional catalytic processes of this class will be discovered and developed in the future.

We are deeply indebted to a number of co-workers who have worked on the chemistry of Cp_2Zr^{II} species. Their names are indicated in our papers cited herein. Studies at Purdue have been mainly supported by the National Science Foundation and those in Japan by the Ministry of Education, Science and Culture and the Kawakami Memorial Foundation.