Nonconcerted Paths for Reactions of Alkene-Zirconocene Complexes

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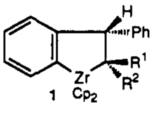
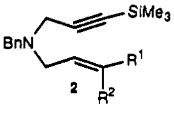
Concerted reaction paths have been implicated in various reactions of alkyne–zirconocene derivatives including benzyne–zirconocenes.[1] Thus, for example, Cp_2ZrPh_2, where Cp = η^5-C_5H_5, was reported to react with (*E*)- and (*Z*)-stilbenes to give stereospecifically **1a** and **1b**, respectively.[2] Similarly, the $ZrCp_2$-promoted bicyclization reaction of **2** proceeds with stereochemical retention to give the corresponding isomers of **3**.[3] On the other hand, the stereochemistry of reactions of alkene–zirconocene derivatives with respect to the *E–Z* configuration of the starting alkenes has remained essentially unknown.



1

a: R^1 = Ph, R^2 = H
b: R^1 = H, R^2 = Ph



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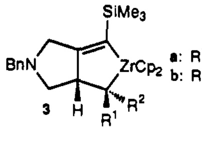
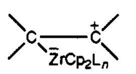


3

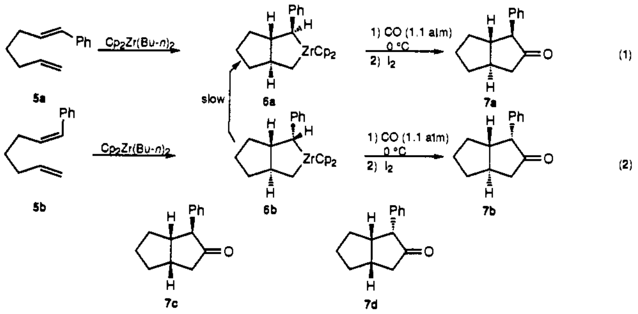
a: R^1 = Me, R^2 = H
b: R^1 = H, R^2 = Me

We now report that, *although the reactions of alkene–zirconocenes can, in some cases, proceed stereospecifically, they can also undergo stereoisomerization leading to nonstereospecific but often highly stereoselective processes*, which most likely proceeds via novel dipolar zirconate species represented by **4**.

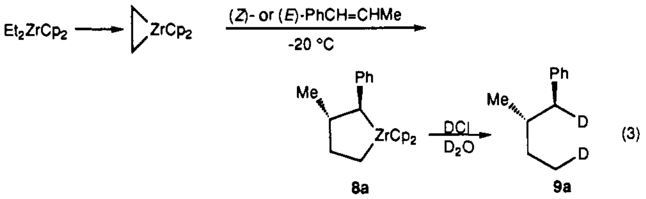


4 (L_n = ligands and $ZrCp_2$-containing groups)

The reaction at −78 to 23 °C of **5a** and **5b** with *n*-Bu_2ZrCp_2, generated *in situ* by treating Cl_2ZrCp_2 with *n*-BuLi in THF at −78 °C,[4] produced **6a** and **6b**, respectively. Compound **6a** was obtained in 85% NMR yield as a >96% stereoisomerically pure species, while **6b** was obtained in 93% NMR yield, as a 10:1 mixture of **6b** and **6a** after 1 h at 23 °C. Carbonylation of **6a** and **6b** with 1.1 atm of CO at 0 °C followed by iodinolysis[5] gave **7a** and **7b**, respectively. Compound **7a** was isolated in 70% yield as a >97% stereoisomerically pure species, while the product derived from **6b** was 90–95% isomerically pure **7b** contaminated with **7a** (5–10%). The stereochemical assignments of these compounds were in part based on NMR spectroscopy. The identity of **7a** was confirmed by its X-ray analysis. The unusual *trans* stereochemistry for ring fusion[6] was further established by synthesizing the two *cis*-fused isomers **7c** and **7d** from previously reported 2-phenylbicyclo[3.3.0]oct-1-en-3-one[4b] by its reduction with 3 equiv of $LiAlH(OMe)_3$ and 1.5 equiv of CuBr[7] and hydrogenation with H_2 (10 psi) over $Pd/BaSO_4$ in EtOAc at 25 °C, respectively. These results clearly demonstrate that *the formation of zirconacyclopentane derivatives via $ZrCp_2$-promoted alkene–alkene coupling can proceed stereospecifically.*



Surprisingly, the reaction of Et_2ZrCp_2 with (*E*)- or (*Z*)-β-methylstyrene was *>98% stereoselective but nonstereospecific*, producing **8a** in high yields. Its deuterolysis gave **9a**, which was ≥96% *erythro*.[8] The sharply contrasting results in eqs 2 and 3 prompted us to further examine the reaction shown in eq 2, which indeed revealed a slow but significant isomerization of **6b** into **6a**. Over 48 h at 23 °C, the ratio of **6a** to **6b** changed from 1:10 to 9:1. These results clearly indicate that *the thermodynamically less stable stereoisomer of zirconacyclopentane derivatives can isomerize to the more stable stereoisomer.* To our knowledge, this kind of stereoisomerization of metallacyclopentanes appears to be unprecedented.



We have further found that, in addition to (*Z*)-stilbene,[3] various olefins, such as (*Z*)-PhCH═CHMe, (*Z*)-PhCH═CHSiMe$_3$, and (*E*)-cyclooctene,[9] undergo stereoisomerization catalyzed by *n*-Bu_2ZrCp_2. A 1:1 mixture of (*Z*)-PhCH═CHPh and (*Z*)-PhCD═CDPh gave a 1:1 mixture of the corresponding *E* isomers under the influence of *n*-Bu_2ZrCp_2 without a sign of H–D scrambling. Coupled with the fact that there is no allylic hydrogen, two commonly observed transition-metal-mediated stereoisomerization processes, i.e., hydrometalation–dehydrometalation and allylic C–H oxidative addition–reductive elimination,[10] are ruled

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(1) For reviews, see: (a) Negishi, E.; Takahashi, T. *Aldrichimica Acta* **1985**, *18*, 31. (b) Negishi, E.; Takahashi, T. *Synthesis* **1988**, 1. (c) Negishi, E. *Chem. Scr.* **1989**, *29*, 457. (d) Buchwald, S. L.; Nielsen, R. B. *Chem. Rev.* **1988**, *88*, 1047.

(2) Kropp, K.; Erker, G. *Organometallics* **1982**, *1*, 1246. See, however, Erker, G.; Rosenfeldt, F. *J. Organomet. Chem.* **1982**, *224*, 29.

(3) Negishi, E.; Swanson, D. R.; Cederbaum, F. E.; Takahashi, T. *Tetrahedron Lett.* **1987**, *28*, 917. See also McDade, C.; Bercaw, J. E. *J. Organomet. Chem.* **1985**, *279*, 281.

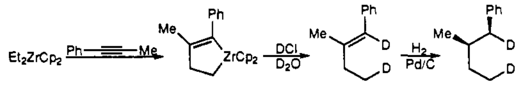
(4) (a) Negishi, E.; Cederbaum, F. E.; Takahashi, T. *Tetrahedron Lett.* **1986**, *27*, 2829. (b) Negishi, E.; Holmes, S. J.; Tour, J. M. Miller, J. A.; Cederbaum, F. E.; Swanson, D. R.; Takahashi, T. *J. Am. Chem. Soc.* **1989**, *111*, 3336.

(5) Swanson, D. R.; Rousset, C. J.; Negishi, E.; Takahashi, T.; Seki, T.; Saburi, M.; Uchida, Y. *J. Org. Chem.* **1989**, *54*, 3521.

(6) (a) Rousset, C. J.; Swanson, D. R.; Lamaty, F.; Negishi, E. *Tetrahedron Lett.* **1989**, *30*, 5105. (b) Nugent, W. A.; Taber, D. F. *J. Am. Chem. Soc.* **1989**, *111*, 6435.

(7) Semmelhack, M. F.; Stauffer, R. D.; Yamashita, A. *J. Org. Chem.* **1977**, *42*, 3180.

(8) The *threo* isomer of **9a** was prepared as follows for spectral comparison.



(9) For its preparation, see: Carbally, R. P.; Perkins, M. J.; Elnitski, A. P. *J. Chem. Soc., Perkin Trans. 1* **1979**, 793.

(10) For papers presenting such mechanisms for a different Ti- or Zr-catalyzed alkene isomerization reaction, see: (a) Akita, M.; Yasuda, H.; Nagasuna, K.; Nakamura, A. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 554. (b) Maye, J. P.; Negishi, E. *Tetrahedron Lett.* **1993**, *34*, 3359.

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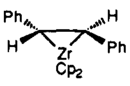
out. However, isomerization of simple alkyl-substituted alkenes is indeed complicated and even dominated by a more conventional regio- and stereoisomerization process.[10] A detailed NMR study of the isomerization reaction of (*Z*)-stilbene in the presence of 1 equiv of preformed (*E*)-(PhCH=CHPh)ZrCp$_2$ (**10**) has revealed that the stereoisomerization reaction is first order in (*Z*)-stilbene and second order in **10**. Critically important here is that *this isomerization proceeds associatively.*



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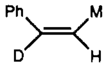

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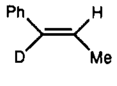

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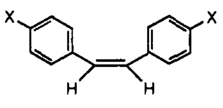
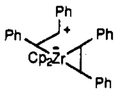


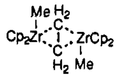
13

a: X = H
b: X = Me
c: X = F
d: X = Cl
e: X = CF$_3$

In principle, alkene stereoisomerization may involve one or more of C–H and σ and/or π C–C bond cleavages. To rigorously probe this point, we chose (*Z*)-PhCD=CHMe[11] (**11**) as a readily accessible, regio- and stereodefined *Z* olefin containing four different groups around the C=C bond. Its stereoisomerization using 10 mol % of *n*-Bu$_2$ZrCp$_2$ produced the *E* isomer **12** without a sign of the formation of any species arising from changes in atom-linking sequences. *The results rule out all but the π-bond cleavage mechanisms*, for which the homolytic and heterolytic extremes may be considered. Neither Me$_2$ZrCp$_2$ nor tetramethylenezirconocene in the presence of an excess of ethylene catalyzed *Z*-to-*E* isomerization of stilbene at 23 °C. In fact, no reaction was observed. These results indicate that as such neither dialkylzirconocenes nor zirconacyclopentanes are isomerization catalysts. Since ^{1}H NMR analysis of the isomerization reaction mixtures revealed the presence of alkene–ZrCp$_2$ complexes, e.g., **10**, as the predominant ZrCp$_2$ derivatives, they most likely serve as the active catalysts. In order for dialkylzirconocenes and zirconacyclopentanes to act as catalyst precursors, they must therefore be convertible to alkene–ZrCp$_2$ complexes. To further probe the mode of interaction between an alkene and an alkene–ZrCp$_2$, especially the sign and extent of charge buildup on an alkenyl C and Zr, *p,p'*-disubstituted (*Z*)-stilbenes (>98% *Z*) containing Me, F, Cl, and CF$_3$ (**13**) were prepared by partial reduction of the corresponding tolans which, in turn, were prepared by the Pd(PPh$_3$)$_4$-catalyzed reaction of (—ZnC≡C—)$_n$ with aryl iodide (2 equiv).[12] Isomerization of **13** was carried out in 2:1 THF–C$_6$D$_6$ at 23 °C using the corresponding stilbene–ZrCp$_2$ generated *in situ* from 1 molar equiv each of **13** and (*n*-Bu)$_2$ZrCp$_2$ as the isomerization agent, and its progress was monitored by ^{1}H NMR spectroscopy. Under these conditions **13e** remained essentially unchanged over several hours. In the other cases, the signals for the *E* isomer emerged and grew at the expense of those of the *Z* isomer, while those for the (*E*)-stilbene-ZrCp$_2$ remained essentially constant. No other stilbene-containing or -derived species were detectable. The pseudo-first-order rate constants observed with **13a–d** are 1.19×10^{-3} (**13a**), 1.84×10^{-3} (**13b**), 4.56×10^{-4} (**13c**), and 2.79×10^{-5} (**13d**) s^{-1}. Although a clear-cut linear free energy relationship is not observed, it is not surprising, considering the reactant structures and the nature of interactions. Nonetheless, the overall trend in substituent effects seems unmistakable and points to the involvement of benzyl cationic species. One associative process we initially considered involves **14** as a transient species. However, the second-order rate dependence[13] on Cp$_2$Zr(PhCH=CHPh) is clearly inconsistent with this view. Our recent elucidation of the structure of (Cp$_2$ZrMe)$_2$(CH$_2$=CH$_2$) (**15**) by NMR and X-ray analyses[14] prompts us to propose **16** as an active species consistent with all of the data presented herein.[15] The modes of alkene–ZrCp$_2$ interaction and alkene stereoisomerization reflected in **14** and **16** are essentially the same. Significantly, however, dimerization of Cp$_2$Zr(PhCH=CHPh) as depicted in **17** represents a plausible, novel mode of activation of one Zr center as an electrophile by the other. The opportunity for possible, extensive electron delocalization in **16** may also favor the proposed 2:1 interaction.



14



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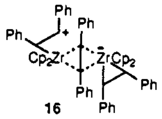
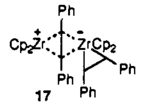


16



17

In summary, the reaction of alkene–zirconocenes with alkenes can, in some cases, lead to the formation of zirconacyclopentanes *via* concerted C–Zr bond addition to alkenes, which is thought to involve donation of alkene π-electrons and back-donation of C–Zr bonding electrons.[1] In cases where the back-donation is hindered due to steric and other factors, the alkene–zirconocenes presumably act merely as electron-accepting Lewis acids, leading to the formation of zirconates represented by **4**. This process can be facilitated through dimeric interaction as in **16**. In addition to inducing *E*–*Z* isomerization, **4** could, in some cases, ring-expand to provide zirconacyclopentanes via a polar path, for which the reaction shown in eq 3 is a possible candidate. These polar processes represent yet another novel reaction pattern that ZrCp$_2$ derivatives display and show some striking contrasts between alkene–zirconocenes and their alkyne counterparts.

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Supplementary Material Available: Experimental details including the stereoisomerization of (*Z*)-stilbenes and IR and NMR data for **5a,b**, **6a,b**, **7a-d**, **9a**, and other compounds (11 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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(11) Compound **11** was prepared as a 9:1 mixture of the *Z* and *E* isomers by the reaction of ethylidenetriphenylphosphorane with PhCDO, which in turn was prepared by oxidation of PhCD$_2$OH with PCC.

(12) King, A. O.; Negishi, E.; Villani, F. J., Jr.; Silveira, A., Jr. *J. Org. Chem.* **1978**, *43*, 358.

(13) As suggested by a referee, the apparent second-order dependence on Cp$_2$Zr(PhCH=CHPh) may be due to LiCl generated as a byproduct in the reaction of Cp$_2$ZrCl$_2$ with *n*-BuLi. However, addition of LiCl (4 equiv) did not affect the rate of reaction.

(14) Takahashi, T.; Kasai, K.; Suzuki, N.; Nakajima, K.; Negishi, E. *Organometallics*, in press. See also: (a) Kaminsky, W.; Kopf, J.; Sinn, H.; Vollmer, H.-J. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 629. (b) Cotton, F. A.; Kibala, P. A. *Inorg. Chem.* **1990**, *29*, 3192.

(15) A search for bimetallic intermediates was urged by a referee, whom we thank.