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Regioselective Bond Cleavage of Vinylcyclopropane Derivatives with the "Zirconocene–Butene" Complex

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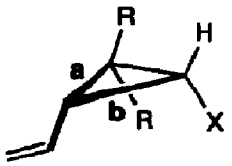
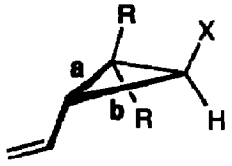
Abstract: *The regioselective bond cleavage of vinylcyclopropanes with zirconocene–butene complex gave η^3- and/or η^1-allylic zirconocene derivatives depending on the substitutional pattern of the cyclopropyl ring. The reactions and characterization of the complexes were carried out.*

Vinylcyclopropane (homobutadiene) constitutes conjugation between vinyl and cyclopropyl groups due to the internal strain of the cyclopropyl group that imparts p-characterics to the ring. Owing to this feature of vinylcyclopropanes, reactions using various transition metals have been studied and applied to organic synthesis.[1]

Recently the structures and reactivity of zirconocene–conjugated diene complexes have been studied by several groups.[2] In spite of the characteristic feature of vinylcyclopropane mentioned above, to our knowledge, there is no report on the reactions of vinylcyclopropane derivatives with the zirconocene–butene complex ("Cp_2Zr" = the equivalent of zirconocene) which can be easily generated *in situ* from zirconocene dichloride and 2 equiv n-butyllithium.[3] Vinylcyclopropane derivatives should thus react with "Cp_2Zr" to form the zirconocene–homobutadiene complex. As part of our work in organic synthesis using low-valent early transition metals,[4] we report herein the regioselective bond cleavage of vinylcyclopropane derivatives **1**[5] with "Cp_2Zr" and consequent zirconocene complex formations.



cis-**1**

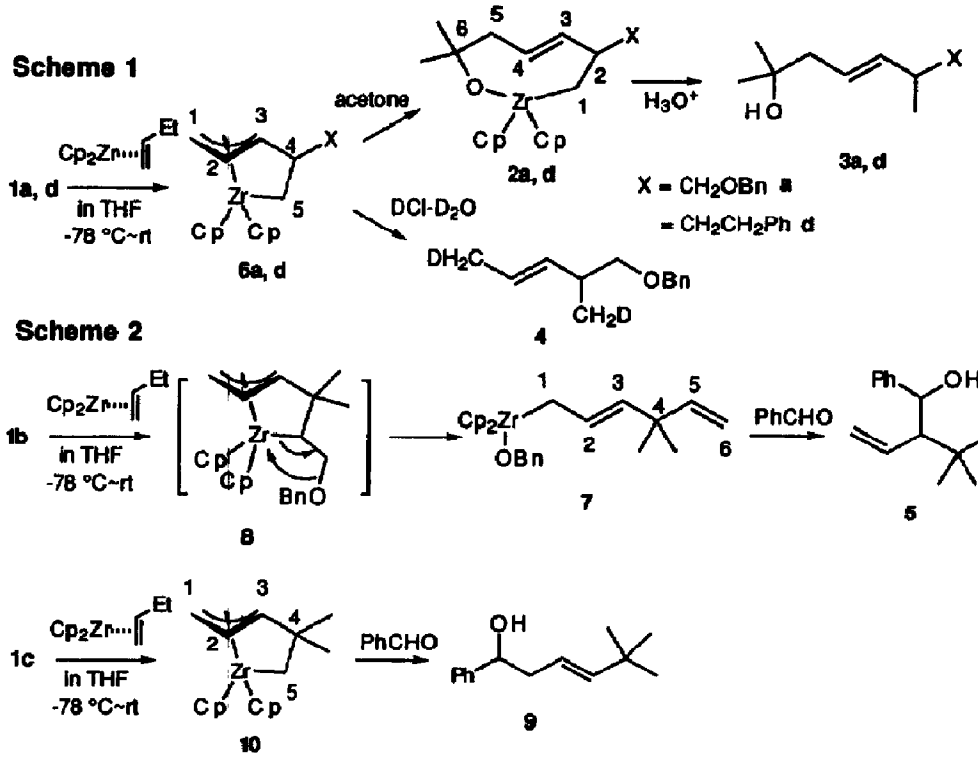


trans-**1**

a R=H, X=CH_2OBn
b R=Me, X=CH_2OBn
c R=Me, X=H
d R=H, X=CH_2CH_2Ph

The treatment of *cis*- or *trans*-**1a** with a stoichiometric amount of "Cp_2Zr" in THF (-78 °C ~ room temperature) and subsequent addition of acetone at 0 °C to the reaction mixture gave zirconacycle **2a** whose double bond was confirmed to be (*E*)-geometry (J = 15.1 Hz).[6] Acidic hydrolysis of **2a** gave **3a**[7] in 86 % yield from *cis*-**1a** and 48 % yield from *trans*-**1a**. Quenching of the reaction mixture with deuterium (10 % DCl–D_2O), instead of acetone, indicated the efficient introduction of deuteriums one by one into two methyl carbons of **4**, thus demonstrating the selective cleavage of bond a of the cyclopropyl ring of **1a** (Scheme 1).[7] In the reactions of *cis*- or *trans*-**1b** and **1c** with "Cp_2Zr" and subsequent reaction with benzaldehyde, the selective cleavage of cyclopropyl bond b was confirmed by isolation of compound **5**[7] (80 % from *cis*-**1b**, 26 % from *trans*-**1b**) and **9** (41 % from **1c**) (Scheme 2). The oxygen functionality in **1a** or **1b** which can

coordinate to zirconium metal has no effect on the cleavage of the cyclopropyl bond since **1d** reacts with "Cp_2Zr" to give **3d** without significant difference (84 % from *cis*-**1d** and 45 % from *trans*-**1d**). It should be pointed out that the *cis*- isomer gives consistently higher yield of the carbonyl adduct than *trans*- isomer.[8] It is obvious that the less substituted bond of the two cyclopropyl bonds concerned (bond **a** or **b**) is cleaved selectively. The present reactions demonstrate the requirement for the vinyl group by recovery of the starting material in reactions of cyclopropane derivatives which possess no vinyl substituent.[9]



The structures of the organozirconium intermediates (η^3–π allylic zirconium and/or η^1–σ allylic zirconium derivatives) were deduced from the incorporation of deuterium, the carbonyl addition products and NMR analyses (COSY, HETCOR and DEPT) of the intermediates. NMR spectral data of the reactive organozirconium intermediates derived from **1a** and **1c** indicated the presence of (*E*) η^3–π allylic zirconium complexes **6a** and **10**.[10] (*E*)-Stereochemistry of complexes **6a** and **10** was supported by the coupling constant (**6a**; 16.1 Hz, **10**; 16.9 Hz) between two vinyl protons, 2 and 3. The intermediate **7** derived from **1b** was confirmed to have the (*E*) η^1–σ allylic zirconium structure by NMR spectra.[11] The intermediate **7** was formed through β–alkoxyl elimination in the primarily formed (*E*) η^3–π allylic zirconium complex **8** (Scheme 2).

(*E*)-Stereochemistry of intermediates **6a** and **10** suggests that the selective scission of the cyclopropyl bond (**a** or **b**) and complex formation are brought about by "Cp_2Zr"-approach to vinyl and cyclopropyl bonds of *anti*-vinylcyclopropane derivatives **1** from the less sterically hindered site (Figure 1).[12] In these models, **A** and **B**, the steric bulk of substituents (R or X) on the cyclopropyl ring exerts influence on the approach of "Cp_2Zr" to vinylcyclopropane derivative. Therefore, a balance of steric bulkiness of substituents on the

cyclopropyl ring is important for the selective bond cleavage and complexation of vinylcyclopropene derivatives **1** with "Cp_2Zr". Compounds **1a** and **1d** thus sterically prefer complexation **B** while **1b** and **1c** sterically prefer **A**.

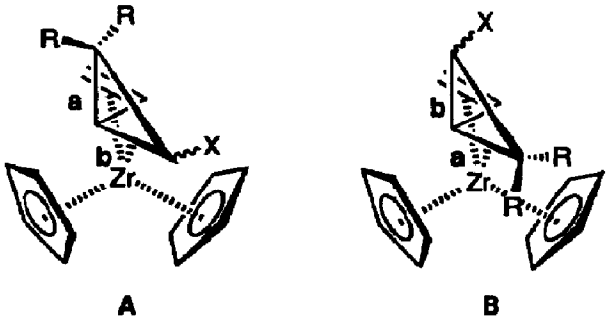


Figure 1 Complexation of Vinylcyclopropane Derivatives with "Cp_2Zr".

In conclusion, the regioselective bond scission of vinylcyclopropane derivatives by "Cp_2Zr" occurrs under the influence of the substituent which has critical steric effect on the direction of the approaching "Cp_2Zr" to vinylcyclopropane. Application of the present results to organic synthesis is currently under way and the results will be reported in due course.

References and Notes

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4. For a review, see; Ito, H.; Hanzawa, Y.; Taguchi, T. *J. Syn. Org. Chem. Jpn* **1994**, *52*, 217-225 and the references cited therein. See also; Ito, H.; Ikeuchi, Y.; Taguchi, T.; Hanzawa, Y.; Shiro, M. *J. Am. Chem. Soc.* **1994**, *116*, 5469-5470.
5. Compounds **1a**, **c** and **d** were prepared by the Simmons-Smith cyclopropanation ($Et_2Zn/CH_2I_2/Et_2O$) of the corresponding allylic alcohols, Swern oxidation of the alcohol and olefination (CH_2I_2, Zn/Me_3Al or Wittig olefination). Compound **1b** was prepared by the following reactions: 1)

dimethylcyclopropanation of (*Z*)- or (*E*)-benzyloxycrotonate with diphenylsulfonium isopropylide, 2) reduction (DIBAL-H/CH_2Cl_2), 3) Swern oxidation and 4) olefination (CH_2I_2, Zn/Me_3Al).

6. **2a** ^1H NMR (d_6 benzene) δ; 0.59 (dd, 1H, *J*=12.2, 2.8Hz, H_1), 0.98 (s, 3H, Me), 1.05 (s, 3H, Me), 1.25 (t, 1H, *J*=12.2Hz, $H_{1'}$), 1.71 (t, 1H, *J*=11.5Hz, H_5), 2.09 (dd, 1H, *J*=11.5, 3.8Hz, $H_{5'}$), 2.97 (m, 1H, H_2), 3.48 (dd, 1H, *J*=9.1, 8.0Hz), 3.57 (dd, 1H, *J*=10.1, 5.4Hz), 4.62 (s, 2H, benzylic), 4.86 (dd, 1H, *J*=15.1, 10.1Hz, H_3), 5.21 (ddd, 1H, *J*=15.1, 11.5, 3.8Hz, H_4), 5.73 (s, 5H, Cp), 5.76 (s, 5H, Cp), 7.15-7.50 (m, 5H). ^{13}C NMR (d_6 benzene) ppm; 30.1, 32.2, 36.2 (C_1), 46.2 (C_2), 47.7 (C_5), 73.0, 79.5, 79.8 (C_6), 109.7, 110.7, 122.8 (C_4), 123.4, 127.8, 128.5, 140.1, 143.5 (C_3).
7. Structures of the new compounds were confirmed by IR, NMR, MS and elemental analysis.
8. Although the precise reason is unclear, this observation may be related to the diastereomeric nature of **6a**, **d** and **8** or steric effect of the trans substituent at the stage of complexation (Figure 1).
9. Vinylcyclobutane derivative was recovered under the same reaction conditions.
10. NMR data of major diastereomeric isomer of **6a**: ^1H NMR (d_6 benzene) δ; -1.08, (dd, 1H, *J*=11.0, 9.5Hz, H_5) -0.72 (dd, 1H, *J*=9.5, 8.6Hz, $H_{5'}$), 1.17 (dd, 1H, *J*=15.2, 3.4Hz, H_1), 2.25 (dd, 1H, *J*=7.7, 3.4Hz, $H_{1'}$), 2.58 (m, 1H, H_4), 2.73 (dd, 1H, *J*=16.1, 10.0Hz, H_3), 3.45 (dd, 1H, *J*=9.1, 8.0Hz), 3.58 (dd, 1H, *J*=9.1, 4.6Hz), 4.42 (ddd, 1H, *J*=16.1, 15.2, 7.7Hz, H_2), 4.62 (s, 2H), 5.14 (s, 5H, Cp), 5.29 (s, 5H, Cp). ^{13}C NMR (d_6 benzene) ppm; -25.4 (C_5), 41.5 (C_4), 43.2 (C_1), 73.1, 74.6 (C_3), 79.9, 104.0 (Cp), 104.6 (Cp), 110.7 (C_2) and aromatic carbons.
Intermediate **10**: ^1H NMR (d_6 benzene) δ; -0.94 (d, 1H, *J*=10.0Hz, H_5), -0.81 (d, 1H, *J*=10.0Hz, $H_{5'}$), 1.00 (s, 3H, Me), 1.28 (dd, 1H, *J*=14.2, 4.5Hz, H_1), 1.37 (s, 3H, Me), 2.21 (dd, 1H, *J*=7.7, 4.5Hz, $H_{1'}$), 3.03 (d, 1H, *J*=16.9Hz, H_3), 4.21 (ddd, 1H, *J*=16.9, 14.2, 7.7Hz, H_2), 5.19, (s, 5H, Cp), 5.27 (s, 5H, Cp). ^{13}C NMR (d_6 benzene) ppm; -14.8 (C_5), 26.1 (Me), 33.4 (C_4), 37.2 (Me), 40.6 (C_1), 83.5 (C_3), 104.0 (Cp), 104.2 (C_2), 104.5 (Cp). See also the reported NMR data of related system; (a) Erker, G.; Engel, K.; Dorf, U.; Atwood, J. L.; Hunter, W. E. *Angew. Chem. Suppl.* **1982**, 1974-1983. (b) Luker, T.; Whitby, R. J. *Tetrahedron Lett.* **1994**, *35*, 785-788.
11. Intermediate **7**: ^1H NMR (d_6 benzene) δ; 1.31 (s, 6H, 2Me), 1.96 (dd, 2H, *J*=8.5, 1.2Hz, H_1), 4.88 (s, 2H), 5.04 (dd, 1H, *J*=10.5, 1.6Hz, H_6), 5.17 (dd, 1H, *J*=17.4, 1.6Hz, $H_{6'}$), 5.21 (dd, 1H, *J*=15.3, 1.2Hz, H_3), 5.78 (s, 10H, 2Cp), 5.91 (dt, 1H, *J*=15.3, 8.5Hz, H_2), 6.11 (dd, 1H, *J*=17.4, 10.5Hz, H_5), 7.16-7.31 (m, 5H). ^{13}C NMR (d_6 benzene) ppm; 28.4 (Me), 39.3 (C_4), 44.2 (C_1), 75.7, 109.3 (C_6), 111.2 (Cp), 111.7, 134.9, 149.5 and aromatic carbons.
12. The conformation of vinylcyclopropane is known to exist as a mixture of two conformers at room temperature in a gaseous phase, ~70 % *anti* - and ~30 % *gauche*-form. (a) De Meijere, A.; Lüttke, W. *Tetrahedron* **1969**, *25*, 2047-2058. (b) Trætteberg, M.; Bakken, P.; Almenningen, A.; Lüttke, W. *J. Molecular Structure* **1988**, *189*, 357-371. *anti*-Conformation of *cis*-1-methyl-2-vinylcyclopropane is also predicted to be the lowest energy conformer. See; Loncharich, R. J.; Houk, K. N. *J. Am. Chem. Soc.* **1988**, *110*, 2089-2092 and the references cited therein.

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