# Carbon–Carbon Bond Formation between α-Chloro Ethers and Alkyl- and Alkenylzirconocenes

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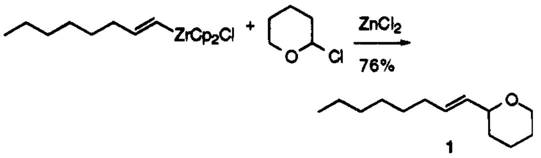
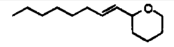
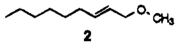
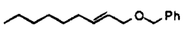
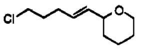
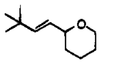
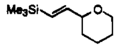
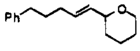
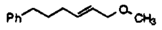
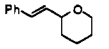
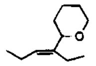
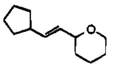
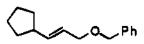
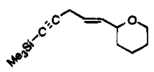
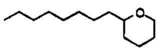
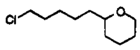
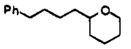
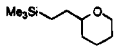
α-Halo ethers are useful synthetic intermediates.[2] Carbon–carbon bond formation between α-halo ethers and organometallics leads to many useful products.[3] However, a completely general protocol for reaction of α-halo ethers with both alkyl- and alkenylorganometallics has not been reported.[2,4] Alkyl- and alkenylzirconocene chlorides, $RZrCp_2Cl$, are readily available from alkenes and alkynes.[5] As part of our program to develop new reactions of zirconocene organometallics,[6] we became interested in the reaction of alkyl- and alkenylzirconocene chlorides with α-chloro ethers since this would represent a new carbon–carbon bond-forming reaction. In this paper, we report the results of the reaction of organozirconocene chlorides with α-chloro ethers to provide ethers and *trans*-allylic ethers.

When 1-octenylzirconocene chloride was reacted with 2-chlorotetrahydropyran (2-Cl-THP), the cross-coupled product, **1**, was isolated in 10–25% yield. This is interesting because carbon–carbon bond formation occurred without addition of another metal salt. Although zirconium is an electropositive early transition element, the carbon–zirconium bond is generally not reactive toward carbon electrophiles. Very few electrophiles react directly at the Zr–C bond.[7] This is possibly due to the bulky nature of the cyclopentadienyl rings and the occupied coordination sites around the metal, forming high kinetic barriers to reaction.[5c] In our case, although some product was formed by direct reaction of $RZrCp_2Cl$ with 2-Cl-THP, a complex mixture was obtained. Transmetalation is a way to increase reactivity.[8] Zinc, nickel, and copper and more recently silver have enjoyed considerable success, and organozirconocenes in the presence of these salts react with a variety of electrophiles.[5c,8,9] When our reaction was repeated in the presence of $ZnCl_2$, a mildly exothermic reaction ensued from which the *trans* allylic ether, **1**, was obtained in good yield (eq 1).



**1** (1)

**Table 1. Ethers from α-Chloro Ethers and $RZrCP_2Cl$**

| Entry | Acetylene/Alkene | α-Chloro ether | Conditions | Product | Yield, %[a] |
|---|---|---|---|---|---|
| 1 | 1-octyne | 2-Cl-THP | A[b] | <br>**1** | 76 |
| 2 | 1-octyne | $ClCH_2OCH_3$ | A[b] | <br>**2** | 63 |
| 3 | 1-octyne | $ClCH_2OCH_2Ph$ | A[b] | <br>**3** | 55 |
| 4 | 5-chloro-1-pentyne | 2-Cl-THP | A[b] | <br>**4** | 62 |
| 5 | 3,3-dimethyl-1-propyne | 2-Cl-THP | A[b] | <br>**5** | 82 |
| 6 | trimethylsilyl-acetylene | 2-Cl-THP | A[b] | <br>**6** | 75 |
| 7 | 5-phenyl-1-pentyne | 2-Cl-THP | A[b] | <br>**7** | 69 |
| 8 | 5-phenyl-1-pentyne | $ClCH_2OCH_3$ | A[b] | <br>**8** | 55 |
| 9 | phenylacetylene | 2-Cl-THP | A[b] | <br>**9** | 77 |
| 10 | 3-hexyne | 2-Cl-THP | A[b] | <br>**10** | 45 |
| 11 | cyclopentyl-acetylene | 2-Cl-THP | A[b] | <br>**11** | 67 |
| 12 | cyclopentyl-acetylene | $ClCH_2OCH_2Ph$ | A[b] | <br>**12** | 75 |
| 13 | 5-trimethylsilyl-1,4-pentadiyne | 2-Cl-THP | A[b] | <br>**13** | 92 |
| 14 | 1-octene | 2-Cl-THP | B[c] | <br>**14** | 75 |
| 15 | 5-chloro-1-pentene | 2-Cl-THP | B[c] | <br>**15** | 83 |
| 16 | 4-phenyl-1-butene | 2-Cl-THP | B[c] | <br>**16** | 65 |
| 17 | vinyltrimethyl-silane | 2-Cl-THP | B[c] | <br>**17** | 81 |

[a] Isolated after silica gel column chromatography (ether:hexane, 3:97). [b] Condition A: $HZrCp_2Cl$ (1.05 mmol), alkyne (1 mmol), THF (1 mL), 25 °C, 1 h; $ZnCl_2$ (0.50 mL, 1 M in ether), α-chloro ether (1 mmol), 5 min. [c] Condition B: Same quantities as in A except that hydrozirconation required 12 h, and CuCl (10 mol % was used).

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(1) Present address: Department of Chemistry, California Institute of Technology, Pasadena, CA 91125.

(2) For a review: (a) Benneche, T. *Synthesis* **1995**, 1.

(3) (a) Friedel–Crafts: Kajigaeshi, S.; Kadowaki, T.; Nishida, A; Fujisaki, S.; Noguchi, M. *Synthesis* **1984**, 335. (b) Halogen–metal exchange: Cheshire, D. R. In *Comprehensive Organic Synthesis;* Trost, B. M., Ed.; Pergamon Press: Oxford, 1991; Vol. 3, p 194.

(4) Alkenylalanes have been reacted with chloromethyl ethyl ether: Zweifel, G.; Lynd, R. A *Synthesis* **1976**, 816.

(5) (a) Negishi, E.; Takahashi, T. *Synthesis* **1988**, 1. (b) Schwartz, J.; Arvanitis, G. M.; Smegel, J. A.; Meier, I. K.; Clift, S. M.; Van Engen, D. *Pure Appl. Chem.* **1988**, *60*, 65. (c) Negishi, E.; Takahashi, T. *Aldrichim. Acta* **1985**, *18*, 31. (d) Dzhemilev, U. M.; Vostrikova, O. S.; Ibragimov, A. G. *Russ. Chem. Rev.* **1986**, *55*, 66. (e) Cardin, D. J.; Lappert, M. F.; Raston, C. L. *Chemistry of Organo–Zirconium and Hafnium Compounds;* Ellis Horwood Limited: Chichester, 1986.

(6) (a) Zheng, B.; Srebnik, M. *J. Org. Chem.* **1995**, *60*, 1912. (b) Zheng, B.; Srebnik, M. *J. Org. Chem.* **1995**, *60*, 3278.

(7) Some examples are: (a) CO insertion: Bertelo, C. A.; Schwartz, J. *J. Am. Chem. Soc.* **1975**, *97*, 228. (b) Isocyanate insertion: Buchwald, S. L.; LaMaire, S. J. *Tetrahedron Lett.* **1987**, *28*, 295. (c) $CO_2$, isocyanates, and ethylene carbonate insertions into Zr–C bond of imine chlorides: Gately, D. A.; Norton, J. R.; Goodson, P. A *J. Am Chem. Soc.* **1995**, *117*, 986 and references cited therein.

(8) For a recent review of transmetalation reactions involving zirconium, see: Wipf, P. *Synthesis* **1993**, 537.

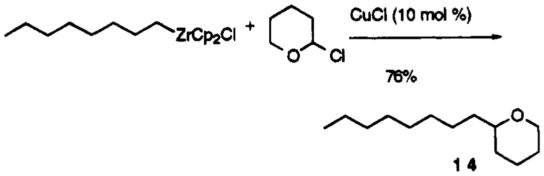
(9) (a) Maeta, H.; Hashimoto, T.; Hasegawa, T.; Suzuki, K. *Tetrahedron Lett.* **1992**, *33*, 5965. (b) Wipf, P.; Xu, W. *J. Org. Chem.* **1993**, *58*, 825.

0022-3263/95/1960-6260$09.00/0

Whether this is due to transmetalation from zirconium to zinc or to increased activity of the halo ether complexed to the zinc to form an alkoxycarbenium salt[10] is at present not clear.

Coupling of alkenylzirconocene chlorides with α-chloro ethers under zinc catalysis is a general reaction, proceeding in good to excellent yields. In all cases, the *trans* geometry of the alkenylzirconocene was retained in the products of the reaction, allylic ethers, that are useful intermediates in their own right.[11] Noteworthy is that the reaction worked well for an internal alkenylzirconocene derived from 3-hexyne, but in lower yield (Table 1, entry 10, 45%), and for a hindered alkenylzirconocene (Table 1, entry 5, 82%). Other α-chloro ethers may be used. Chloromethyl methyl ether and benzylchloromethyl ether were all coupled successfully (Table 1). Copper salts were not as effective as zinc salts in the reaction of alkenylzirconocenes with α-chloro ethers.

To make the reaction truly general, we also sought to develop a procedure for cross-coupling alkylzirconocenes with α-chloro ethers. In the absence of additives, alkylzirconocene chlorides did not react at all with 2-Cl-THP. Surprisingly, zinc salts were completely ineffective. On the other hand, of a series of copper salts, CuCl proved to be a very reactive catalyst (eq 2).[12] Results are summarized in Table 1.



(2)

In summary, a new carbon–carbon bond-forming reaction between organozirconocene chlorides and α-chloro ethers has been developed. Zinc catalysis works best for alkenylzirconocenes, while copper(I) is suitable for alkylzirconocene-derived reagents. The reason(s) for this selectivity is not obvious, and experiments are underway to exploit the differentiation.

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[10] Olah, G. A.; Svoboda, J. J. *Synthesis* **1973**, 52.

[11] Schlosser, M. In *Organometallics in Synthesis;* Schlosser, M. Ed.; Wiley: Chichester, 1994; p 120.

[12] CuI, CuBr, CuCN, and CuOTf were ineffective. Cu(I) phosphines, prepared according to the method of Churchhill et al. (Churchill, M. R.; DeBoer, B. G.; Mendak, S. J. *Inorg. Chem.* **1978**, *17*, 1945), were also ineffective.