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Tandem Inter-Intramolecular Allylation of Zirconacyclopentadienes: Pathway to Vinylcyclohexadienes and Methylenecycloheptadienes.

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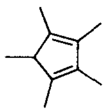
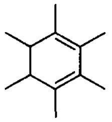
Abstract: Copper-catalyzed or mediated reaction of zirconacyclopentadienes with allylic dichlorides afforded vinylcyclohexadienes or methylenecycloheptadienes. © 1997 Elsevier Science Ltd.

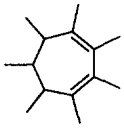
The formation of cyclized compounds is an essential process in organic synthesis, and metallacycles can be important intermediates in transition metal-catalyzed or -mediated cyclizations.[1] Of special interest is the synthesis of cyclic dienes (cyclopentadienes, cyclohexadienes, and cycloheptadienes) which can be used as intermediates for the construction of more complex polycyclic molecules.[2] One possible and most direct approach to the synthesis of cyclic dienes is the utilization of reactions of five-membered metallacycles, e.g., zirconacycles.



5- membered

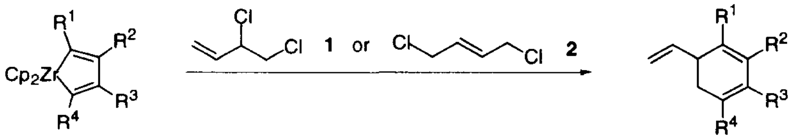


6- membered

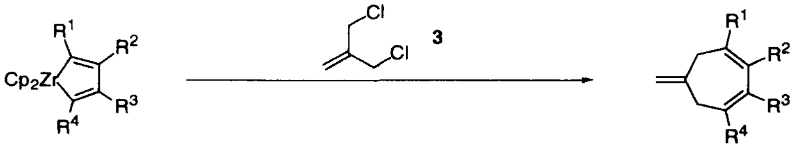


7- membered

In order to prepare cyclopentadienes from five-membered zirconacycles, a one-carbon unit building block is required. For six-membered and seven-membered cyclic dienes, two-carbon unit and three-carbon unit building blocks are necessary. Recently we have reported the preparation of cyclopentadienes by copper-catalyzed reaction of zirconacyclopentenes with acyl chlorides[3] or by the reaction of zirconacyclopentadienes with ethyl propynoate (one-carbon unit building block).[4] We also reported the synthesis of cyclohexadienes by the copper-mediated Michael reaction of zirconacyclopentadienes to ethyl maleate or fumarate (two-carbon unit building block).[5] In this paper we would like to report a reaction of zirconacyclopentadienes[6] with difunctional allyl chlorides **1-3**[7] behaving as a two-carbon unit building block (eq 1) or a three-carbon unit building block (eq 2) in the formation of 6- and 7-membered ring compounds.[8]



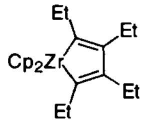
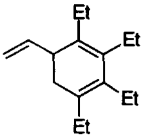
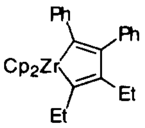
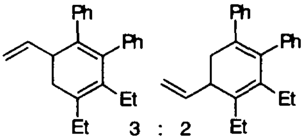
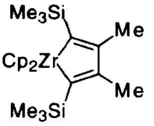
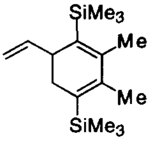
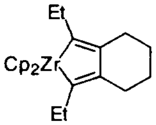
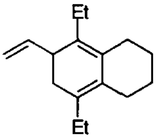
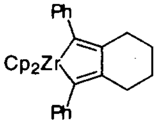
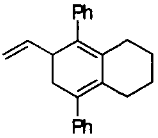
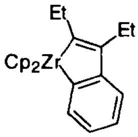
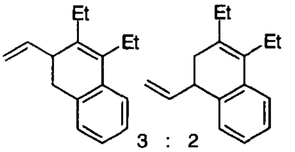
(1)



(2)

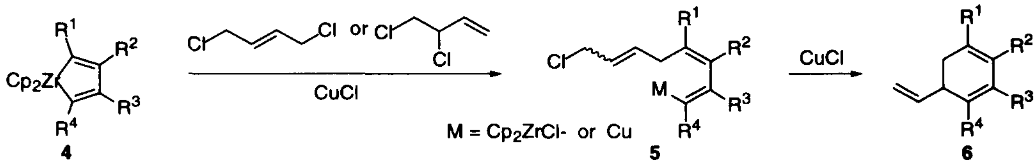
The results concerning the copper-catalyzed or -mediated formation of vinylcyclohexadienes are presented in Table 1. Generally, various zirconacyclopentadienes (monocyclic, bicyclic, and indenyl)) reacted with **1** or **2** using a catalytic or a stoichiometric amount of CuCl. The latter gave higher yields of products. Interestingly, in the case of trimethylsilyl-substituted zirconacyclopentadienes the desired product was obtained only with a stoichiometric amount of CuCl. The use of a catalytic amount of CuCl either afforded very low yield of the product (<10%) or the reaction did not proceed at all. As expected, the reaction of unsymmetrically substituted zirconacyclopentadienes afforded a mixture of two regioisomers.

Table 1. Formation of vinylcyclohexadienes by the reaction of zirconacyclopentadienes with 3,4-dichloro-1-butene (**1**) and 1,4-dichloro-2-butene (**2**).

Zirconacyclopentadiene	Allyl chloride	CuCl /equiv.	T/ °C	t /h	Product	Yield /%[a]
	1 1 2	0.1 2 0.1	-78 to rt rt rt	6 3 3		66 (41) 87 (59) 58 (40)
	1	0.1	-78 to rt	12	 3 : 2	73 (61)
	1	2	rt	6		(60)
	1	2	0	1		58 (37)
	1 1	2 0.1	0 rt	1 6		(61) (57)
	1	0.1	-78 to rt	24	 3 : 2	57 (46)

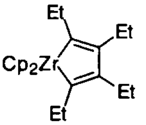
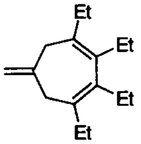
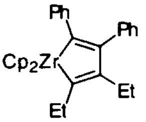
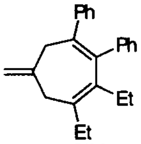
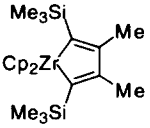
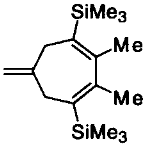
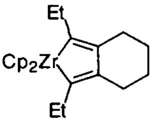
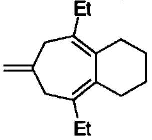
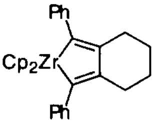
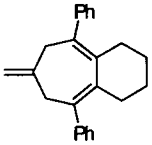
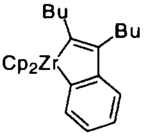
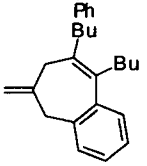
[a] GC yield. Isolated yields are given in parentheses.

The reaction mechanism of this cyclization involves an inter-intramolecular reaction sequence. The essential step is transmetallation of the Zr-C bonds of zirconacyclopentadienes **4** to more reactive Cu-C bonds as we have reported.[9] Thus, in the first step, zirconacyclopentadiene reacts with **1** via S_N2' substitution after transmetallation to Cu, giving intermediate **5** which undergoes intramolecular reaction via S_N2' substitution to afford the vinylcyclohexadiene **6**.[10] It is interesting that when **2** is used, the first reaction must proceed via S_N2 substitution in order to form intermediate **5** that is able to undergo the cyclization.



The results of the formation of methylenecycloheptadienes are summarized in Table 2. Various zirconacyclopentadienes participated in the reaction to give the desired products in good yields. Surprisingly, in this case better yields are obtained with a catalytic amount of CuCl.

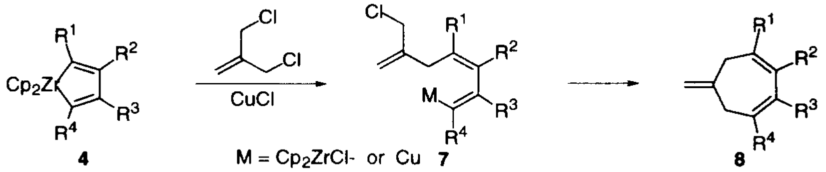
Table 2. Formation of methylenecycloheptadienes by the reaction of zirconacyclopentadienes with 3-chloro-2-chloromethyl-1-propene (**3**).

Zirconacyclopentadiene	CuCl/equiv.	t /h	Product	Yield/%[a]
	0.1	1		87 (62)
	0.1	3		66 (47)
	0.1	1		(51)
	0.1	3		(50)
	0.1 2	6 1		71 (64) 56
	0.1	3		79 (59)

[a] GC yield. Isolated yields are given in parentheses. In all cases reactions were conducted at room temperature.

The reaction mechanism of the reaction of zirconacyclopentadienes with **3** is similar to that for vinylcyclohexadienes giving intermediate **7** instead of **5**. The compound **7** undergoes intramolecular reaction in the presence of CuCl to afford the methylenecycloheptadiene **8**.[11] S_N2 and S_N2' substitutions similarly in both steps produce the same products.

Lower yields in some cases can be attributed to the intermolecular side reactions that produce products with high molecular weights. Indeed, formation of a small amount of polymeric materials was observed.



Generally, this protocol offers a convenient and simple pathway to the direct transformation of zirconacyclopentadienes to 6- and 7-membered cyclic diene compounds.

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6. a) Negishi, E.; Swanson, D. R.; Cederbaum, F. E.; Takahashi, T. *Tetrahedron Lett.*, **1986**, *27*, 2829. b) Negishi, E.; Tour, J. M.; Miller, J. A.; Cederbaum, F. E.; Swanson, D. R.; Takahashi, T. *J. Am. Chem. Soc.*, **1989**, *111*, 3336. c) Xi, Z.; Hara, R.; Takahashi, T. *J. Org. Chem.* **1995**, *60*, 4444. For zirconaindene compound see: Buchwald, S.L.; Watson, B.T. *J. Am. Chem. Soc.* **1986**, *108*, 7411.
7. Takahashi, T.; Kotora, M.; Kasai, K.; Suzuki, N. *Organometallics* **1994,** *13*, 4183.
8. **Typical experimental procedure:** To solution of zirconacyclopentadiene (1mmol) in THF (5 mL) was added the corresponding allyl dichloride (125 mg, 1.0 mmol), and copper(I) chloride (10 mg, 0.1 mmol) and the reaction mixture was stirred until the consumption of the starting compounds (see Table I and II for conditions). Then the reaction mixture was quenched by 3*N* HCl and extracted (hexane, 3 x 5 mL). Organic fractions were collected, washed with a solution of $NaHCO_3$, dried ($MgSO_4$), and concentrated *in vacuo*. Products were isolated by Kugelrohr distillation or column chromatography.
9. For other CuX-catalyzed or -mediated reactions of organozirconium compounds see: a) Venanzi, L.M.; Lehman, R.; Keil, R.; Lipshutz, B.H. *Tetrahedron Lett.* **1992**, *33*, 5857. b) Takahashi, T.; Kotora, M.; Kasai, K.; Suzuki, N. *Tetrahedron Lett.* **1994**, *35*, 5685. c) Honda, T.; Mori, M. *Organometallics* **1994,** *13*, 5464. d) Kasai, K.; Kotora, M.; Suzuki, N.; Takahashi, T. *J. Chem. Soc., Chem. Commun.*, **1995**, 109. e) Lipshutz, B.H.; Segi, M. *Tetrahedron* **1995**, *51*, 4407. f) Takahashi, T.; Hara, R.; Nishihara, Y.; Kotora, M. *J. Am. Chem. Soc.* **1996**, *118*, 5154. g) Dekura, F.; Honda, T.; Mori, M. *Chem. Lett.* **1997**, 825.
10. **5-Ethenyl-1,2,3,4-tetraethyl-1,3-cyclohexadiene:** ^1H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 0.92 (t, J = 7.6 Hz, 3H), 0.95 (t, J = 7.6 Hz, 3H), 0.97 (t, J = 7.6 Hz, 3H), 1.02 (t, J = 7.6 Hz, 3H), 1.75-2.40 (m, 10H), 2.45-2.55 (m, 1H), 4.83 (dd, J = 10.5, 2.2 Hz, 1H), 4.95 (ddd, J = 17.3, 2.0, 0.9 Hz, 1H), 5.72 (ddd, J = 17.2, 9.9, 8.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si) δ 13.00, 14.82, 15.35, 15.42, 20.32, 20.72, 24.95, 26.48, 34.10, 41.62, 113.16, 130.29, 131.95, 133.16, 134.91, 139.79; HRMS for $C_{16}H_{26}$ calcd 218.2033, found 218.2034.
11. **6-Methylene-1,2,3,4-tetraethyl-1,3-cycloheptadiene:** ^1H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 0.88 (t, J = 7.5 Hz, 6H), 1.01 (t, J = 7.5 Hz, 6H), 2.1-2.2 (m, 8H), 2.5-2.8 (br s, 4H), 4.55-5.60 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, Me_4Si) δ 13.96(2C), 14.23(2C), 21.87(2C), 27.04(2C), 40.83(2C), 104.96, 135.92(2C), 136.85(2C), 160.48; HRMS calcd for $C_{16}H_{26}$ 218.2033, found: 218.2032.

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