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# Zirconium Mediated Synthesis. Convergent Access to Terminal Trienes, Dienes, and Dienynes.

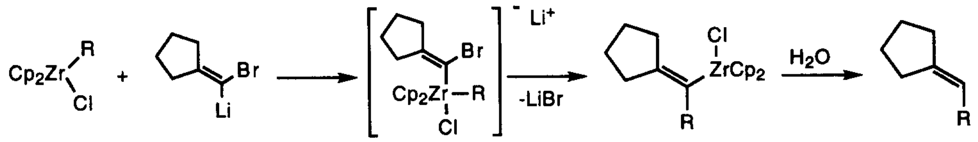
**Aleksandr Kasatkin and Richard J. Whitby***

Department of Chemistry, The University, Southampton, SO17 1BJ, U. K.

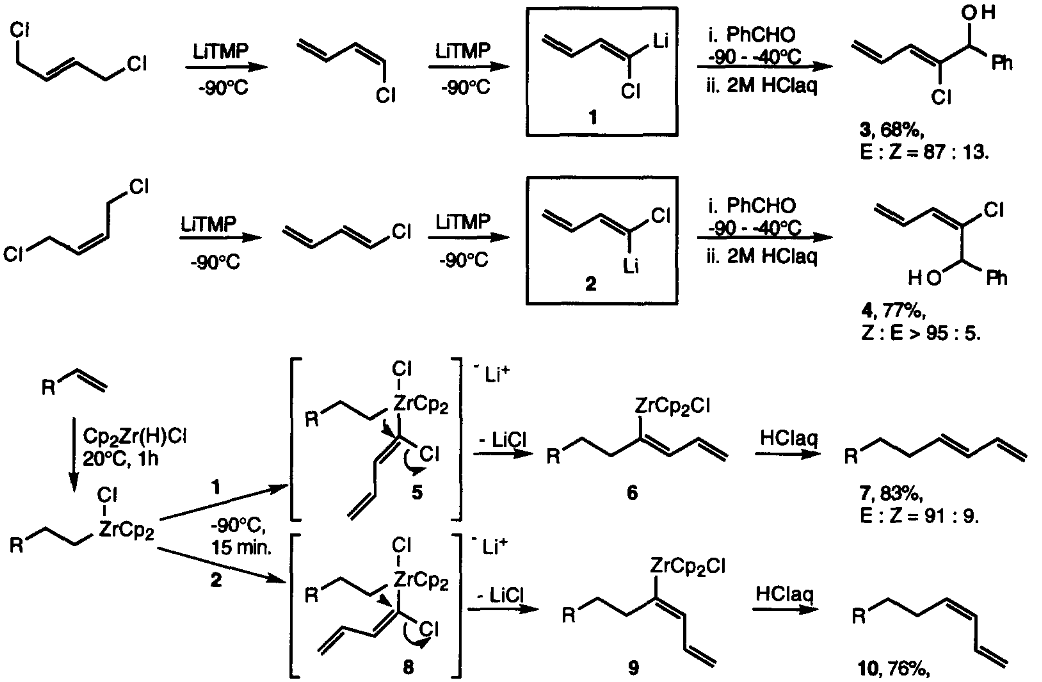
***Abstract:*** Treatment of alkyl, vinyl, or alkynyl zirconocenes with (*E*)- or (*Z*)-1,4-dichloro-2-butene and 2 equivalents of lithium 2,2,6,6-tetramethylpiperidide gave (3*E*)- or (3*Z*)-1,3-dienes, 1,3,5-trienes, or 1,3-dien-5-ynes in good yields and stereoselectivity. © 1997 Elsevier Science Ltd.

Hydrozirconation of alkenes and alkynes with the Schwartz reagent ($Cp_2Zr(H)Cl$, Cp = $C_5H_5$) to give alkyl- and vinyl-zirconocene chlorides is a well established synthetic method.[1] To be useful in organic synthesis methods for further elaboration of the organozirconium species are needed. Carbon-carbon bond forming reactions include carbonylation, isocyanide insertion, and copper, nickel, and palladium catalysed reactions.[1] A particularly interesting elaboration method was reported by Negishi[2] when he showed that a variety of α-haloorganolithium species inserted into the carbon-zirconium bond to form a new organometallic (e.g. Eq. 1). We have applied this type of reaction to the elaboration of zirconacycles.[3] We now describe the use of the novel, and easily generated, carbenoid species (*E*)- or (*Z*)-1-lithio-1-chlorobutadienes for the elaboration of acyclic organozirconium species to afford terminal dienes, trienes, and dienynes.[4]

**Eq. 1.**



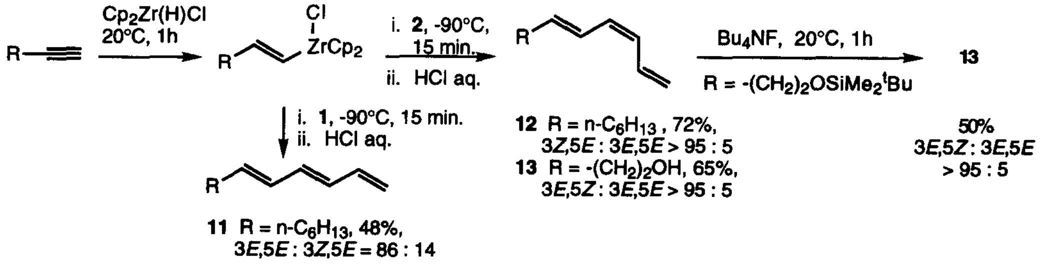
The base induced elimination of HX from (*E*)- or (*Z*)-1,4-dihalo-2-butene is known to give predominantly (*Z*)- or (*E*)-1-halobutadiene respectively.[5] α-Deprotonation of vinylhalides has also been described.[6] Treatment of (*E*)- or (*Z*)-1,4-dichloro-2-butene with two equivalents of lithium 2,2,6,6-tetramethylpiperidide (LiTMP) at -90°C gave stereoselectively (*Z*)- or (*E*)-1-chloro-1-lithio-1,3-butadienes (**1** and **2**). Trapping with benzaldehyde to afford the chlorodienes **3** and **4**[7] confirmed the formation and sterochemistry of the novel carbenoids. The formation of **1** is notable as the first successful deprotonation of a (*Z*)-chloroalkene with a hydrogen *trans* to the chlorine.[8] Hydrozirconation[9] of 1-octene to give $Cp_2Zr(octyl)Cl$ followed by insertion



**Scheme 1.** Solvent tetrahydrofuran throughout. R = n-$C_6H_{13}$.

of **1** or **2** (generated *in situ* from 1.3 equivalents of the dichlorides and 2.6 equivalents of LiTMP) and aqueous work-up gave the (*E*)- or (*Z*)-dienes **7** or **10** in good isolated yield and isomeric purity (Scheme 1). The reaction presumably occurs *via* formation and 1,2-metallate rearrangement of the '18-electron' complexes **5** and **8** to give organozirconium species **6** and **9**. The formation of **6** and **9** were proven by work-up with $DCl/D_2O$ to give >95% deuterium incorporation at the indicated site. These results prove that with zirconium the 1,2-metallate rearrangement of **5** or **8** goes with inversion of configuration at the $sp^2$ carbon centre.[10] Reaction of (*E*)-1,4-dibromo-2-butene and two equivalents of LiTMP with $Cp_2Zr(octyl)Cl$ proceeds less stereoselectively to give a mixture of **7** and **10** (**7** : **10** = 76 : 24) in 76% total yield.

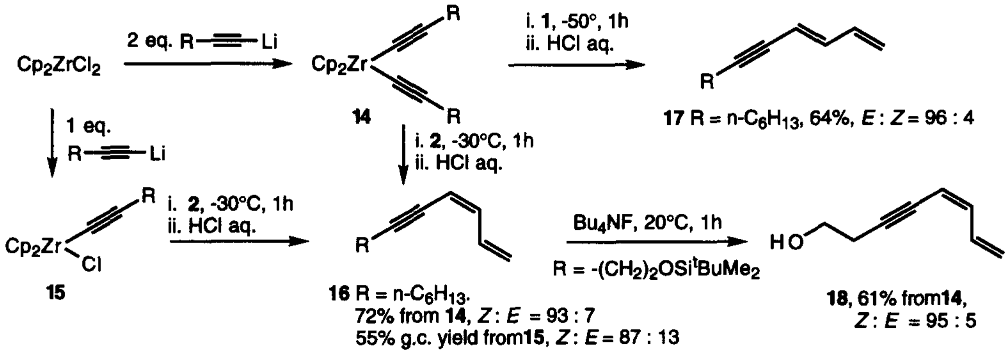
In a similar way hydrozirconation of 1-octyne followed by insertion of **1** or **2** and aqueous work-up gave the stereodefined 1,3,5-trienes **11** and **12** (Scheme 2). The incorporation of functional groups is important for further applications of this chemistry so we investigated 3-butyne-1-ol as the hydrozirconation substrate.



**Scheme 2.** Solvent tetrahydrofuran throughout.

Reaction of the alcohol with 2.3 equivalents of $Cp_2Zr(H)Cl$ followed by 1.3 equivalents of the carbenoid **2** and protonolysis gave (3*E*,5*Z*)-3,5,7-octatrien-1-ol (**13**) in good yield and stereoselectivity. Careful control of the quantity of $Cp_2Zr(H)Cl$ was required to prevent over-reduction of the alkyne and subsequent formation of 5,7-octadien-1-ol. Hydrozirconation of 1-*tert*-butyldimethylsiloxy-3-butyne followed by insertion of **2**, protonolysis, and deprotection also gave **13**.

Access to (5*Z*)-1,3,5-trienes was desired to complete the scope of the synthetic method. Di(1-octynyl)zirconocene (**14**) was readily prepared *in situ* from the lithiated alkyne and zirconocene dichloride. Treatment with 1.3 equivalents (based on zirconium) of the lithium carbenoid **2** followed by aqueous work-up gave (*Z*)-1,3-dodecadien-5-yne (**16**) in good yield (72%) based on $Cp_2ZrCl_2$ but only 36% yield based on the alkyne. Use of 2 equivalents of the carbenoid did not increase the yield of **16** implying that only one of the two alkyne moieties in **14** reacts. Reaction of (1-octynyl)zirconocene chloride (**15**) (generated *in situ* from zirconocene dichloride and one equivalent of the lithiated alkyne) with **2** followed by protonolysis gave **16** in an improved yield of 55% based on the alkyne. In similar fashion reaction of **14** with **1** gave (*E*)-1,3-dodecadien-5-yne (**17**) in reasonable yield, and good stereoselectivity. Use of 1-*tert*-butyldimethylsiloxy-3-butyne as the acetylenic component and **2** as the carbenoid gave (*Z*)-5,7-octadien-3-yn-1-ol (**18**) after deprotection. Reduction of 1,3-dien-5-ynes to (5*Z*)-1,3,5-trienes with activated zinc is well known.[11]



**Scheme 3.** Solvent tetrahydrofuran throughout.

We have described a one-pot synthesis of terminal diene, dienyne, and triene components found in many natural products including pheromones and perfumery compounds[12] using novel butadienyl metal carbenoids. The potential of a carbon-zirconium bond in the initial insertion products for further elaboration[1] will provide an important future extension of this chemistry.

*Preparation of (3Z, 5E)-1,3,5-dodecatriene.*

To a stirred suspension of $Cp_2Zr(H)Cl$ (0.260 g, 1.00 mmol) in THF (12.0 mL) was added 1-octyne (0.091 g, 0.83 mmol). The mixture was stirred at 20°C for 1h to give a clear yellow solution of the alkenylzirconium compound. After cooling to -90°C (*Z*)-1,4-dichloro-2-butene (0.135 g, 1.08 mmol) was added followed by a solution of LiTMP [preformed from TMP (0.305 g, 2.16 mmol) and BuLi (0.86 mL, 2.5 M in hexane, 2.16 mmol) in THF (2.0 mL)]. The reaction mixture was stirred at -90°C for 15 min then hydrolysed by the addition of 2M HClaq (8.0 mL). After extraction with diethyl ether (12 mL) the organic layer was washed with

2M HCl (2 x 10 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography (Silica gel, 40 - 60 petroleum ether) to afford (3*Z*, 5*E*)-1,3,5-dodecatriene (0.104 g, 76% yield).

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## References and Notes

1. Wipf, P.; Jahn, H. *Tetrahedron* **1996**, *52*, 12853.
2. Negishi, E.; Akiyoshi, K.; O'Connor, B.; Takagi, K.; Wu, G. *J. Am. Chem. Soc.* **1989**, *111*, 3089.
3. Luker, T.; Whitby, R. J. *Tetrahedron Lett.* **1994**, *35*, 785 and 9465; **1995**, *36*, 4109; **1996**, *37*, 7661. Gordon, G. J.; Whitby, R. J. *Synlett* **1995**, 77.
4. Recent approaches to these structures involve palladium or nickel catalysed coupling reactions e.g. (a) Tellier, F.; Descoins, C.; Sauvêtre, R. *Tetrahedron* **1991**, *47*, 7767. (b) Alami, M.; Gueugnot, S.; Domingues, E.; Linstrumelle, G. *Tetrahedron* **1995**, *51*, 1209. (c) Huynh, C.; Alami, M.; Linstrumelle, G. *Synth. Commun.* **1994**, *24*, 2273. (d) Alami, M.; Crousse, B; Linstrumelle, G. *Tetrahedron Lett.* **1994**, *35*, 3543. (e) Alexakis, A.; Barthel, A.; Normant, J. F.; Fugier, C.; Leroux, M. *Synth. Commun.* **1992**, *22*, 1839.
5. Heasley, V. L.; Lais, B. R. *J. Org. Chem.* **1968**, *33*, 2571. Keegstra, M. A.; Verkruijsse, H. D.; Andringa, H.; Brandsma, L. *Synth. Commun.* **1991**, *21*, 721. Ref. 4e.
6. Köbrich G.; Trapp, H. *Chem. Ber.* **1966**, *99*, 670 and 680. Köbrich, G.; Flory, K. *Chem. Ber.*, **1966**, *99*, 1773.
7. All organic compounds were characterised by g.c. and high field $^1H$ and $^{13}C$ NMR. If novel IR, LRMS and either HRMS or elemental analysis were also obtained. All yields are for isolated pure materials except where stated. Isomer ratio's were determined by g.c. or NMR. Assignment of (*E*)- or (*Z*)-stereochemistry is based on $^1H$-$^1H$ coupling constants and comparison of carbon-13 NMR with authentic materials, or the homologous undeca-1,3,5-trienes and undeca-1,3-dien-5-ynes: Mitsudo, T.; Nakagawa, Y.; Watanabe, K.; Hori, Y.; Misawa, H.; Watanabe, H.; Watanabe, Y. *J. Org. Chem.*, **1985**, *50*, 565. Pfueller, U.; Schulze, K.; Muehlstaedt, M. *Z. Chem.* **1978**, 18, 59. Ref. 4a-c. The stereochemistry of **3** and **4** follow from the $\gamma$-gauche effect in the carbon-13 NMR - the CH(OH) carbons coming at $\delta_C$ 77.27 and 70.88 p.p.m. respectively.
8. For example the deprotonation of (*Z*)-1-chloro-1-alken-3-ynes reportedly fails whereas the (*E*)-isomers work well: Alami, M.; Crousse, B.; Linstrumelle, G. *Tetrahedron Lett.* **1995**, *36*, 3687.
9. $Cp_2Zr(H)Cl$ (Schwartz reagent) was purchased from Aldrich. Generally around 1.3 eq. were required for complete consumption of the substrate (monitored by g.c.).
10. Inversion of configuration of the $sp^2$ carbon in this type of rearrangement has been established for reactions involving copper, aluminium, zinc, and boron: Kocienski, P.; Barber, C. *Pure and Appl. Chem.* **1990**, *62*, 1933. Harad, T.; Hara, D.; Hattori, K.; Oku, A. *Tetrahedron Lett.* **1988**, *29*, 3821. Miller, J. A. *J. Org. Chem.* **1989**, *54*, 998. Zweifel, G.; Arzoumanian, H. *J. Am. Chem. Soc.* **1967**, *89*, 5086.
11. Boland, W.; Schroer, N.; Sieler, C.; Fiegel, M. *Helv. Chim. Acta.* **1987**, *70*, 1025. Morris, S. G.; Herb, S. F.; Magidman, P.; Luddy, F. E. *J. Am. Oil Chem. Soc.* **1972**, *49*, 92. Also ref. 4a and 4b.
12. Chrétien-Bessière, Y.; Garnero, J.; Benezet, L.; Peyron, L. *Bull. Soc. Chim. Fr.* **1967**, 97. Naves, Y. R. *Bull. Soc. Chim. Fr.* **1967**, 3152. Moore, R. E. *Acc. Chem. Res.* **1977**, *10*, 40. Tellier, F.; Descoins, C. *Tetrahedron Lett.* **1990**, *31*, 2295.
13. D. A. Fletcher, R. F. McMeeking and D. Parkin, *J. Chem. Inf. Comput. Sci.*, **1996**, *36*, 746.

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