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Elaboration of Zirconacyclopentanes by Sequential Insertion of Lithium Chloroallylide and Ketones or Aldehydes.

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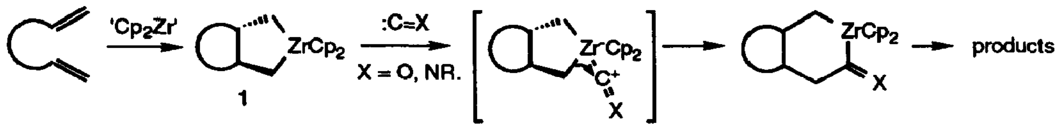
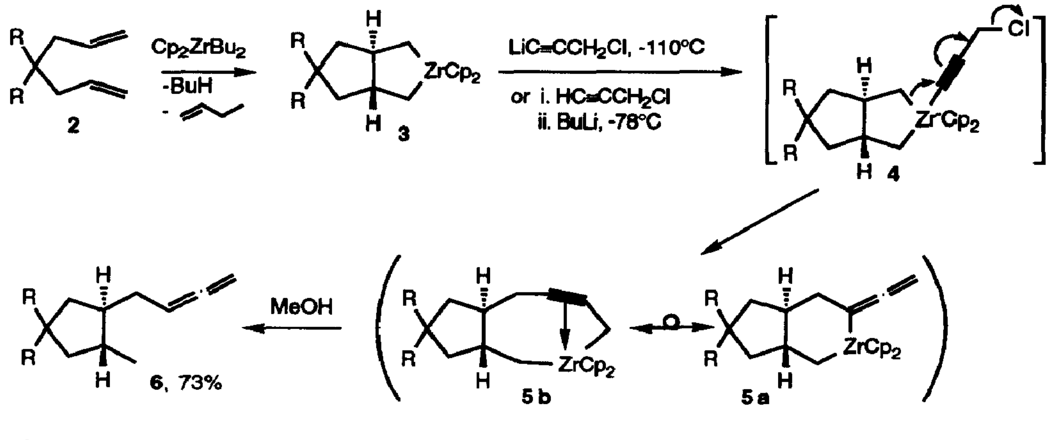
Abstract. Insertion of lithium chloropropargylide or lithium chloroallylide into bicycliczirconacyclopentanes gives 1-zirconacyclooct-3-ynes or -3-enes respectively. The former give allenes on protonolysis. The latter react further with ketones or aldehydes to afford 1-zircona-2-oxa-5-decenes which give (E)-homoallyic alcohols on aqueous work-up. With aldehydes moderate 1,6-diastereocontrol is observed.

The intramolecular co-cyclisation of 1,n-dienes on a zirconocene template (Eq. 1) is an emerging technology for the synthesis of carbocyclic and heterocyclic systems[1]. One limitation to the efficient use of the metal is that the remaining carbon-zirconium bonds of the metallacycles are unreactive towards conventional electrophiles such as carbonyl compounds and alkyl halides. The only carbon-carbon bond forming reactions which have been reported are the insertion of carbon monoxide[1a] and various isocyanides[2] which afford cyclopentanones and cyclopentanols, and elaborated cyclopentylamines respectively. The successful insertion of these reagents is due to their carbenic character - donation of an electron pair to the 16 electron zirconium centre in **1** to form an unstable 18-electron zirconate complex is followed by migratory insertion of the reagent into the carbon-zirconium bond. In a seminal paper Negishi reported[3] the insertion of various metal carbenoids into the carbon-metal bond of acyclic zirconocene chlorides which probably follows a similar mechanism. We now report the first[4] insertion of metal carbenoids into zirconacyclopentanes, and further elaboration of some of the products.

Eq. 1.

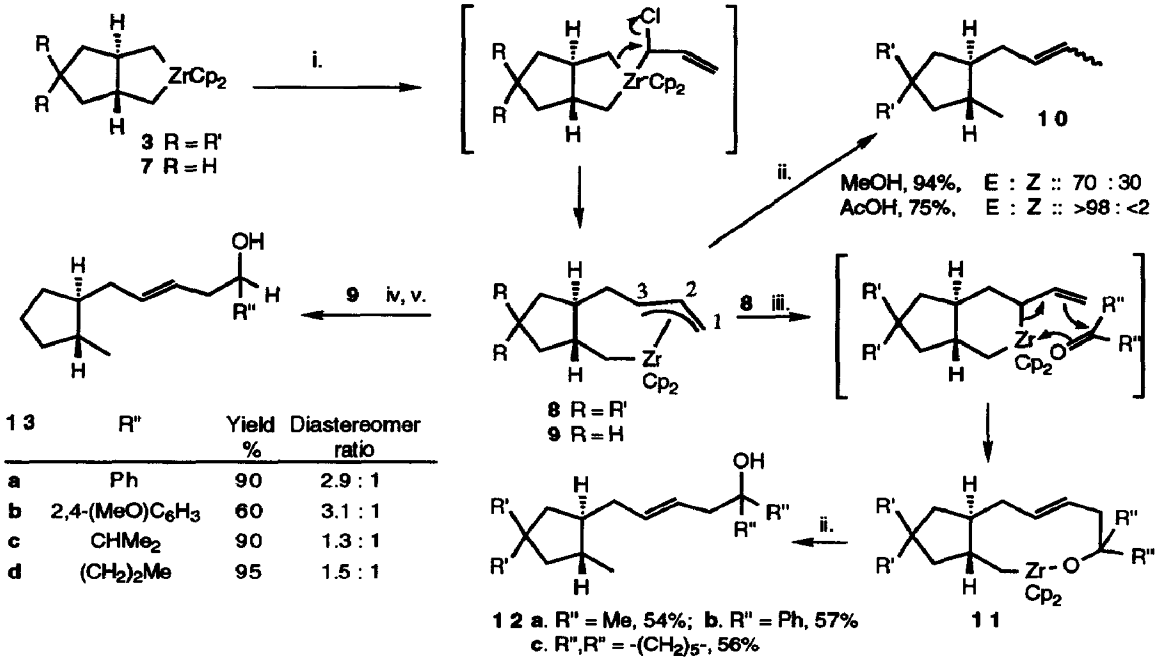


Addition of lithium chloropropargylide[5] to the zirconacycle **3** (formed *in-situ*[1a]) afforded the ring-expanded[5] product **5** (Scheme 1) in a remarkably clean reaction, presumably *via* formation of the zirconate complex **4** followed by migratory insertion[6]. NMR studies on **5** suggest that it is best viewed as the cycloalkyne isomer **5a** rather than the allene form **5b**[7]. Most characteristic are the quaternary carbon resonances at δ_C (75MHz, C_6D_6) 99.94 and 106.42 ($C{\equiv}C$) together with the $C{\equiv}C\underline{CH_2}Zr$ at δ_C 38.35 (δ_H (300MHz, C_6D_6) 2.522 & 2.269). Quenching with methanol afforded the allene product **6**[8] in good overall yield from the diene **2**. Experimentally the reaction was simplified by the *in-situ* formation of the lithium chloropropargylide by the addition of butyl lithium to the premixed propargyl chloride and zirconacycle **3** at -78°C, avoiding the need for very low temperatures.



Scheme 1. R,R =- $CH_2OCMe_2OCH_2$-

Reaction between the zirconacycle **3** and lithium chloroallylide[9], most conveniently generated *in-situ*, gave the inserted product **8**[10] (Scheme 2). **8** may be viewed as an (E)-1-zirconacyclooct-3-ene or as the η^3-allyl structure drawn[11] - the 'allyl' signals appearing at δ_C (75MHz, C_6D_6) 120.13 (C-2), 92.28 (C-3), and 42.53 (C-1); δ_H (300MHz, C_6D_6) 3.05 (H-3, dd, J 6.6, 15.4), 4.45 (H-2, ddd, J 15.4, 13.2, 8.8), 2.16 (H-1, dd, J 3.7, 8.8 Hz), 1.1 (H-1, unresolved). The 15Hz coupling between the vinyl protons (H-2,H-3) support the *trans* configuration. Protonation of **8** with methanol gave a 70:30 mixture of the E and Z isomers of the internal alkene product **10**. Quenching with acetic acid gave only the E isomer.



13	R"	Yield %	Diastereomer ratio
a	Ph	90	2.9 : 1
b	2,4-$(MeO)C_6H_3$	60	3.1 : 1
c	$CHMe_2$	90	1.3 : 1
d	$(CH_2)_2Me$	95	1.5 : 1

Scheme 2. R' = -$CH_2OCMe_2OCH_2$-. *Reagents and conditions:* i. CH_2=$CHCH_2Cl$, $^iPr_2NLi$ or LiTMP, -78°C - r.t., THF; ii. MeOH or AcOH, 16h, r.t.; iii. Me_2CO, benzene, 80°C *or* Ph_2CO or cyclohexanone, toluene, 48h, 110°C; iv. RCHO, $BF_3.Et_2O$, THF, -40 - 20°C, 3 h; v. MeOH, $NaHCO_3$aq., 12h, r.t.
Yields are based on the starting dienes **2** or 1,6-heptadiene (precursor of **7**).

Although simple alkyl- and vinyl- zirconium species do not react with carbonyl compounds[12] allyl zirconium species are reactive[13]. Heating the zirconacycle **8** with acetone (12h, 80°C, benzene) gave clean conversion into a new zirconacycle **11a**, probably *via* a 'decalin' type transition state (Fig.1). The 15Hz coupling constant between the vinylic protons of **11a** confirmed the expected *trans*-configuration of the double bond. Work-up with methanol gave the organic product **12a** in 54% overall yield from the diene **2**. Cyclohexanone and diphenylketone also underwent insertion to afford the corresponding elaborated cyclopentanes although more vigorous conditions were required (48h, 120°C, toluene).

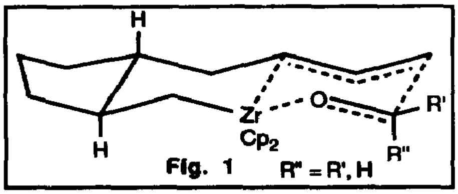
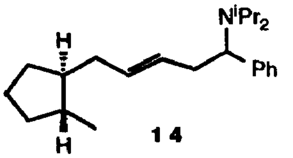


Fig. 1 R'' = R', H

Attempts to insert benzaldehyde into **8** initially failed, probably because of preferential reaction with the cyclopentadienyl unit to afford fulvenes. Addition of $BF_3.Et_2O$ allowed the reaction to proceed but *trans*-acetalisation between the acetonide moiety of **8** and benzaldehyde complicated the reaction. Cocyclisation of 1,6-heptadiene to form the zirconacycle **7** followed by lithium chloroallylide insertion gave the allyl complex **9** which avoids this problem. Reaction with benzaldehyde in the presence of 1 eq. $BF_3.Et_2O$ followed by aqueous work-up gave the hoped for product **13a** (45%) together with the amine **14** (36%). **14** presumably results from insertion into **9** of the iminium ion $[PhCH{=}N^iPr_2]^+$ formed *in-situ* from benzaldehyde and the diisopropylamine remaining in solution from the metallation step. The diisopropylamine could be removed before the aldehyde insertion reaction, but it was experimentally simpler to use the anion of the less nucleophilic amine 2,2,6,6-tetramethylpiperidine (TMP). Under these optimised conditions the benzaldehyde inserted product **13a** was obtained in a remarkably efficient 90% overall yield from 1,6-heptadiene. Three separate reactions have been used, and three new C-C bonds formed in this one-pot reaction.



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The degree of diastereoinduction obtained in the insertion step was determined by high resolution carbon 13 NMR[14] to be 2.9 : 1, the identity of the minor isomer being confirmed by Mitsonobu - inversion[15] of the hydroxyl in **13a**. Although moderate, this degree of 1,6-acyclic diastereocontrol is rare and indicates the potential of remote diastereoconrol mediated by a transition metal template[16]. It is possible that the diastereocontrol arises from the '*trans*-decalin' type transition state (fig. 1, with the aldehyde R'' group lying in an equatorial position) but the presence of BF_3, and the successful insertion of the iminium species **14** both argue against the requirement for coordination of the carbonyl oxygen to zirconium.

Insertion of 2,4-dimethoxybenzaldehyde (1.1 eq) gave a similar result to benzaldehyde but alkyl aldehydes gave poor yields. Fortunately increasing the amount of the aldehyde and $BF_3.Et_2O$ to 3.5 equivalents gave the excellent yields reported (Scheme 2).

Conclusion.

We have demonstrated that readily available zirconacyclopentanes may be ring-expanded by the insertion of lithium chloropropargylide and lithium chlororallylide. In the latter case further elaboration *via* insertion of ketones and aldehydes provides efficient use of the metal. An overall moderate 1,6-diastereocontrol mediated by the metal template is notable.

Typical experimental: *Synthesis of 13a.*

To a stirred solution of zirconocene dichloride (0.293 g, 1 mmol) in THF (5 ml) under argon at -78°C was added dropwise n-BuLi (0.8 ml of a 2.5M soln. in hexanes, 2 mmol). After 20 min 1,6-heptadiene (0.096 g, 1 mmol) in THF (3 ml) was added and the reaction mixture warmed to room temperature over 2 h. After cooling to -78°C allyl chloride (0.084 g, 1.1 mmol) followed by LiTMP (1.1 mmol, generated from the amine and BuLi in 2 ml THF at 0°C) were added dropwise and after 15 min the reaction mixture allowed to warm to room temperature. After cooling to -78°C benzaldehyde (0.12 g, 0.11 ml, 1.1 mmol) and $BF_3.Et_2O$ (0.16 g, 0.14 ml, 1.1 mmol) were added and the solution warmed to room temperature over 1.5 h. The reaction mixture was quenched by the addition of methanol (3 ml) and $NaHCO_3aq$ (15 ml) and stirred at room temperature for 15h. Extractive work-up and chromatography (SiO_2, 10-15% diethyl ether in light petroleum) gave the alcohol **13a** as a colourless oil (0.220 g, 90%).

Acknowledgements.

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References

1. a. Rousset, C.J.; Swanson, D.R.; Lamaty, F.; Negishi, E. *Tetrahedron Lett.* **1989**, *30*, 5105; b. Takahashi, T.; Seki, T.; Nitto, Y.; Saburi, M.; Rousset, C.J.; Negishi, E. *J. Am. Chem. Soc.* **1991**, *113*, 6266; c. Nugent, W.A.; Taber, D.F. *J. Am. Chem. Soc.* **1989**, *111*, 6435; d. Taber, D.F., Louey, J.P.; Lim, J.A. *Tetrahedron Lett.* **1993**, *34*, 2243; e. Mori, M.; Uesaka, N.; Shibasaki, M. *J. Org. Chem.* **1992**, *57*, 3519; *f. Akita, M; Yasuda, H.; Yamamoto, H.; Nakamura, A. Polyhedron* **1991**, *10*, 1; g. Knight, K.S.; Waymouth, R.M. *J. Am. Chem. Soc.* **1991**, *113*, 6268; h. Kemp, M.; Whitby, R.J.; Coote, S.J. *Synlett, in press.*
2. Davis, J. M; Whitby, R. J.; Jaxa-Chamiec, A. *Tetrahedron Lett.* **1992**, *33*, 5655.
3. Negishi, E.; Akiyoshi, K.; O'Conner, B.; Takagi, K.; Wu, G. *J. Am. Chem. Soc.* **1989**, *111*, 3089.
4. The formation of a hafnacyclobutane in the reaction between (ethylene)hafnocene and methylenetriphenylphosphorane may be viewed as a carbenoid ring expansion: Erker, G.; Czisch, P.; Krüger, C.; Wallis, J.M. *Organometallics* **1985**, *4*, 2059;
5. Zweifel, G.; Backlund, S.J.; Leung, T. *J. Am. Chem. Soc.* **1978**, *100*, 5561.
6. Also described as 1,2-metallate rearrangements this reaction type has found recent use in organic synthesis: review: Kocienski, P.; Barber, C. *Pure and Appl. Chem.* **1990**, *62*, 1933. These are also the basis of much boron chemistry - see ref 9 and therin.
7. The very slow protonolysis of **5** with methanol (10 h at r.t. c.f. a few seconds for **3**) suggests that it is better viewed as an η^3-bonded system. The probable first step of protonolysis - donation of the hydroxyl-oxygen lone pair to the zirconium centre - should be inhibited in such electronically saturated (18 electron) complexes. For an η^3-allenyl zirconocene complex see: Blosser, P.W.; Gallucci, J.C.; Wojcicki, A. *J. Am. Chem. Soc.* **1993**, *115*, 2994.
8. All organic compounds gave satisfactory ^1H NMR, ^{13}C NMR, IR and Mass spectra including HRMS.
9. *In-situ* lithiated allyl chloride has recently been used to homologate boron compounds and to ring expand boracyclanes: Brown, H.C.; Rangaishenvi, M.V.: Jayaraman, S. *Organometallics* **1992**, *11*, 1948; Brown, H.C.; Jayaraman, S. *Tetrahedron Lett.* **1993**, *34*, 3997.
10. Related homologous systems (monocyclic 1-zircona-3-heptenes) have been formed by the insertion of alkenes into zirconocene-diene complexes. (a). Erker, G.; Engel, K.; Dorf, U.; Atwood, J.L.; Hunter, W.E. *Angew. Chem. Suppl.* **1982**, 1974-1983. Nakamura has shown that these insert carbonyl compounds to give structures related to **10**. (b) Yasuda, H.; Okamoto, T.; Mashima, K.; Nakamura, A. *J. Organomet. Chem.* **1989**, *363*, 61.
11. A homologous (7 member ring) zirconacycle prepared by the insertion of ethylene into zirconocene butadiene has been characterised as an (E)-η^3-allyl complex by crystal structure determination: ref 10a.
12. The reaction of acyclic Cp_2ZrRCl with aldehydes may be catalysed by $AgClO_4$: Marta, H.; Hashimoto, T.; Hasegawa, T.; Suzuki, K. *Tetrahedron Lett.* **1992**, *33*, 5965.
13. Ito, H.; Taguchi, T.; Hanzawa, Y. *Tetrahedron Lett.* **1992**, *33*, 1295.
14. Bucker AC300, 75MHz, 32K FID zero-filled to 64K. The largest seperation of diastereomer peaks was 0.07 p.p.m. The given ratios are the average from several pairs of signals using deconvolution to determine peak areas.
15. Mitsonobu, O. *Synthesis* **1981**, 1.
16. For a zirconium mediated 1,5-diastereoinduction see Erker, G; Sosna, F; Betz, P.; Werner, S.; Kruger, C. *J. Am. Chem. Soc.* **1991**, *113*, 564.

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