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Insertion of (*E*)-(1,2-dihalovinyl)lithium and (2-haloethynyl)lithium into zirconacycles

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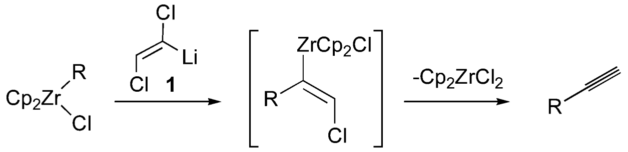
Insertion of (*E*)-(1,2-dihalovinyl)lithium into zirconacyclopentenes was followed by elimination of halide to afford an alkyne which inserts intramolecularly into the resulting carbon–zirconocenium bond to give a methylenecyclopentene, whereas insertion of (2-haloethynyl)lithium gives the same product *via* a zirconocene alkenylidene.

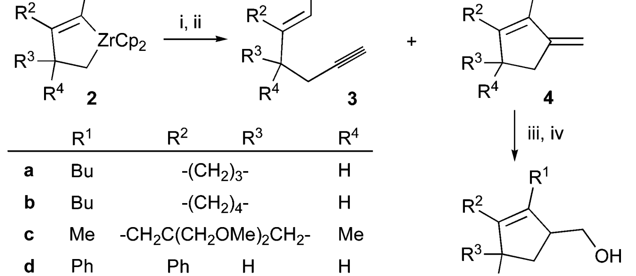
We have shown that insertion of a range of carbenoids (1-lithio-1-halo species) provides a useful method for further elaboration of 5-membered zirconacycles.[1] We have also described the insertion of (*E*)-(1,2-dichlorovinyl)lithium (**1**) into acyclic organozirconocene chlorides to afford terminal alkynes *via* elimination of the initially formed β-chloroalkenylzirconium species (Scheme 1).[2] We now report unexpected products when the equivalent insertion was applied to the elaboration of zirconacycles.

Zirconacyclopentenes **2** were formed by intramolecular co-cyclisation of 1,6- or 1,7-enynes using zirconocene(but-1-ene)[3a] (**2a–d**) or by addition of alkynes to *in situ* generated zirconocene-(ethylene) (**2e,f**).[3b] The zirconacycles were cooled to −78 °C before addition of (*E*)-1,2-dichloroethene followed by dropwise addition of lithium diisopropylamide (LDA) to generate the carbenoid **1**[4] *in situ*. Aqueous work-up gave a mixture of the expected alkynes **3** and the unexpected methylidenecyclopentenes **4** (Scheme 2; Table 1, entries 1, 3–5, 8, 11). The ratios of **3**:**4** were estimated by GC† of crude reaction products since compounds **4** partially decomposed on chromatography. In cases where the methylidenecyclopentenes **4** could not be obtained analytically pure, the stable derivatives **5** were formed by *in situ* hydroboration/oxidation.

A reasonable mechanism for the formation of **4** is insertion of carbenoid **1** into **2** to afford six-membered zirconacycle **7**, which eliminates the anti-periplanar chloride to give the zirconocenium species **8** (Scheme 3). There is now competition between trapping of the zirconocenium species with an anion to give a stable species which affords **3** on work up, and intramolecular insertion of the initially formed alkyne into the carbon–zirconocenium bond to afford **9** and hence methylidenecyclopentene **4** on work-up. Both the presence and stereochemistry of the carbon-zirconium bond in **9e** were confirmed by deuteration (MeOD–D_2O) to afford **14e**. We have observed a similar intramolecular insertion of an alkyne into a carbon–zirconocenium bond during elaboration of cyclic η^3-propargyl zirconacycles with aldehydes/$BF_3·Et_2O$[5] and related intermolecular additions are known.[6]



Scheme 1 Insertion of (*E*)-(1,2-dichlorovinyl)lithium into acyclic organozirconocenes.



	R^1	R^2	R^3	R^4
a	Bu	$-(CH_2)_3-$		H
b	Bu	$-(CH_2)_4-$		H
c	Me	$-CH_2C(CH_2OMe)_2CH_2-$		Me
d	Ph	Ph	H	H
e	Pr	Pr	H	H

Scheme 2 *Reagents and conditions*: (i) XCH=CHX, LDA, −78 °C, THF; (ii) MeOH/$NaHCO_3$ (aq.); (iii) 9-BBN (1 equiv.) or $BH_3·SMe_2$ (0.33 equiv.), THF; (iv) NaOH, H_2O_2.

Ring strain in bicyclo[3.3.0]octenes inhibits formation of the cyclisation products **4a** and **c** compared with the unstrained bicyclo[4.3.0]nonene (**4b**) and monocycles **4d** and **4e** (Table 1, entries 1 and 4, *cf.* 3, 8 and 11).

We then examined the use of 1,2-dibromoethene, commercially available as a 2:1 mixture of (*Z*):(*E*) stereoisomers, as a carbenoid precursor, and found that it substantially increased the ratio of **4**:**3** (Table 1, entries 2, 6, 7, 9, 10). The result was synthetically useful, but rather surprising as we would expect (*Z*)-(1,2-dibromovinyl)lithium to eliminate LiBr very rapidly to afford bromoethyne. Furthermore working up the reaction from **2e** with MeOD–D_2O afforded **4e** with complete deuterium incorporation at one of the methylene positions, and remarkably around 85% incorporation at the other *i.e.* approximately a 15:85 mixture of **14e** and **15e** (Scheme 3) was formed. To clarify matters we treated (*Z*)-1,2-dichloroethene with 2 equiv. LDA at −78 °C for 10 min to afford (2-chloroethynyl)lithium, as confirmed by trapping an aliquot with $PhMe_2SiCl$. Subsequent addition of a pre-cooled solution of the zirconacycle **2e** and stirring at −78 °C gave good conversion into the methylenecyclopentene **4e** after quenching. Work-up with MeOD–D_2O gave > 95% deuterium incorporation at both methylene protons (*i.e.* **15e**).

A mechanism which explains the formation of cyclised products **4** by insertion of 1-lithio-2-haloethyne, and in particular the formation of bis-deuterated compound **15** on work-up with D_2O is given in Scheme 3. The rearrangement of **10** to **11** has precedent

Table 1 Insertions into zirconacyclopentenes

Entry	Substrate	Reagent[a]	Ratio of **3**:**4**[b]	Yield **3**[c] (%)	Yield **4**[c] (%)	Yield **5**[c] (%)
1	**2a**	Cl (2 equiv.)	3:5	26	—	—
2	**2a**	Br (2 equiv.)	0:1	—	—	36
3	**2b**	Cl (2 equiv.)	0:1	—	—	41
4	**2c**	Cl (2 equiv.)	2:3	27	17	—
5	**2c**	Cl (4 equiv.)	2:7	33	32	—
6	**2c**	Br (2 equiv.)	1:22	—	66	—
7	**2c**	Br (2 equiv.)	1:22	—	—	36
8	**2d**	Cl (2 equiv.)	1:3	33	38	—
9	**2d**	Br (2 equiv.)	1:7	15	24	—
10	**2d**	Br (2 equiv.)	1:7	—	—	40
11	**2e**	Cl (1 equiv.)	0:1		74[d]	38
12	**2e**	Cl* (1 equiv.)	0:1		56[d]	

[a] LDA (1 equiv.) added to: Cl = (*E*)-HClC=CHCl, Br = 1:2 (*E*)-:(*Z*)-HBrC=CHBr, Cl* = ClC≡CH. [b] Determined by GC of the crude reaction mixture. [c] Isolated yields from the enyne or alkyne precursors of zirconacycles **2**. [d] NMR yield.

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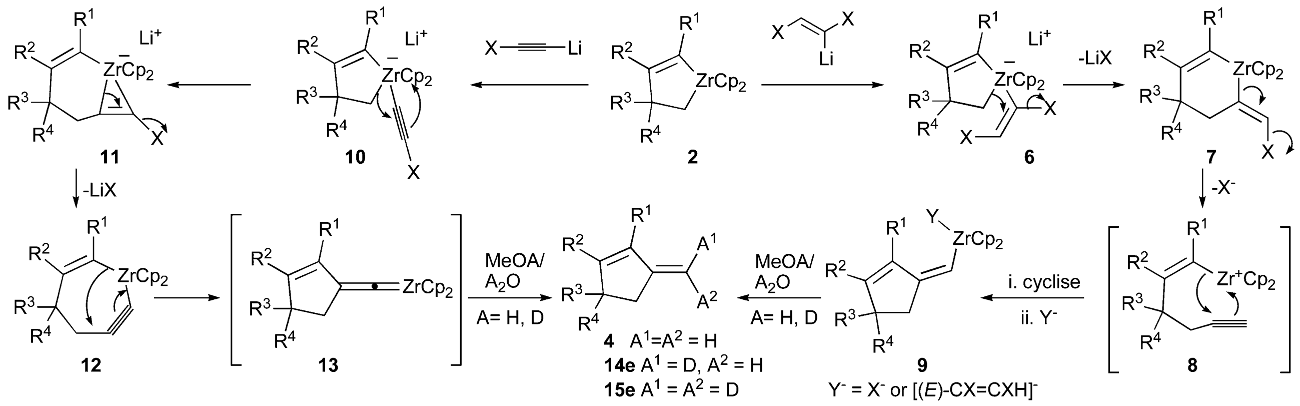
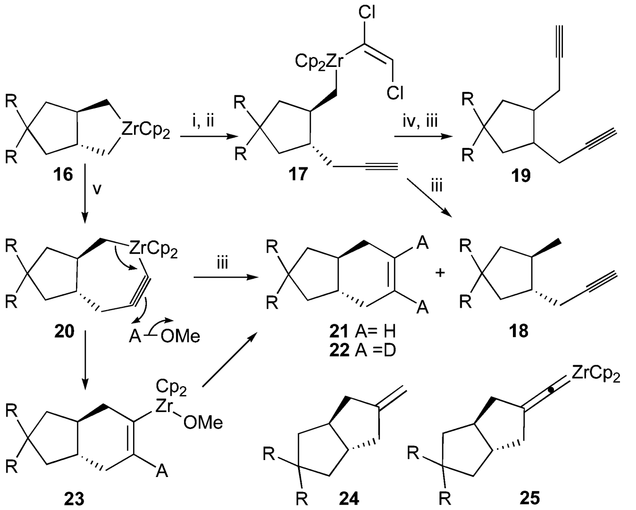


Scheme 3 Two mechanisms for formation of methylenecyclopentenes.

from the work of Negishi on insertion of lithiated aryl alkynes into zirconacycles, although the latter requires hours at room temperature.[7] Elimination of chloride from **11** is analogous to the known rearrangement of 2-chlorozirconacyclopropanes.[8] The rearrangement of **12** to the zirconocene alkenylidene **13** is unprecedented but, calculations indicate, thermodynamically favourable.‡ Zirconium alkenylidene complexes have not previously been reported even as intermediates, although zirconium alkylidenes are known.[9] It is likely that **13** will dimerise to form a 1,3-bis(zircona-)cyclobutane, though we could not observe it by NMR spectroscopy.

Insertion of carbenoid **1** into zirconacyclopentane **16**, derived by co-cyclisation of 4,4-bis(methoxymethyl)-1,6-heptadiene with zirconocene(1-butene), followed by protic quench at −70 °C yielded alkyne **18** (43%) together with the bis-alkyne **19** (7%) (Scheme 4). Two equivalents of the carbenoid were required for optimum yields. Warming the reaction mixture to room temperature for 16 h before quenching gave predominantly **19** (49%, *cf.* 11% **18**) which suggests the complex **17** incorporating a second molecule of carbenoid as the major neutral intermediate formed, and that room temperature was required for its rearrangement/elimination.[10] Isolated yields of **18** and **19** were 45 and 37% under the respective conditions. No cyclisation to form the methylidenecyclopentane **24** analogous to the formation of **4** occurred.‡ Insertion of (2-chloroethynyl)lithium also gave **18** (41% isolated yield), but unexpectedly also cyclohexene **21** (16% yield).§ Work-up of the reaction mixture with $MeOD–D_2O$ gave the bis-deuterated product **22** (> 95% D). The most likely mechanism is insertion of $ClC\equiv CLi$ into **16** to give zirconacycloheptyne **20** which unlike the analogous zirconacycle **12** does not rearrange to the alkenylidene **25**.‡ Protonation of the alkyne moiety of **20** could induce cyclisation to afford **23** and hence **21**/**22**. The ratio of **18** to **21** formed does not change significantly when the reaction mixture is kept at room temperature for 2 h before quenching implying that cyclisation only occurs on work-up. Bis-alkyne **19** is not formed even when a large excess of $ClC\equiv CLi$ is used.



Scheme 4 R = CH_2OMe. *Reagents and conditions*: (i) (*E*)-HClC=CHCl; (ii) LDA, −78 °C; (iii) MeOA, A_2O (A = H, D); (iv) 25 °C, 2 h; (v) $ClC\equiv CLi$.

In conclusion we have discovered several novel transformations of zirconacycles which imply the formation of unprecedented zirconocene alkenylidene and 1-zircona-2-cycloheptyne intermediates, as well as useful multi-component coupling reactions, in the insertion of (*E*)-(1,2-dihalovinyl)lithium and (2-haloethynyl)lithium into zirconacycles.

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Notes and references

† GC carried out on Hewlett Packard 6890 with 30 m HP5 column, He as carrier gas, 80–250 °C at 25 °C min^{-1}, FID detection.

‡ DFT calculations carried out with B3LYP/6-31G* method using Spartan04 for Windows (Wavefuntion Inc.) indicate that **20** is 26 kJ mol^{-1} more stable than **25** whereas **12** (R^1 = R^2 = Me, R^3 = R^4 = H) is 62 kJ mol^{-1} less stable than **13**.

§ Identity of **21**, and absence of **24** were confirmed by their independent synthesis.

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