Tandem insertion of allenyl carbenoids and aldehydes into zirconacycles: an unexpected cyclisation

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Allenyl carbenoids (3-chloro-1-lithioalk-1-ynes) insert into zirconacyclopentanes and zirconacyclopentenes to afford cyclic η^3-allenyl/prop-2-ynyl zirconocene complexes which give allenyl, alkynyl or cyclised-alcohol products on addition of aldehydes activated with boron trifluoride–diethyl ether.

The formation of zirconacyclo-pentanes and -pentenes by co-cyclisation of 1,*n*-dienes and 1-en-*n*-ynes, or reaction of zirconocene η^2-alkene or -alkyne complexes with alkenes or alkynes comprises a useful C–C bond forming method.[1] For efficient use in organic synthesis methods for further elaboration of the carbon–zirconium bonds in these intermediates are required. Carbonylation,[2] isocyanide insertion,[3] addition of aldehydes,[4] and copper catalysed reactions[5] have been reported recently. We have described the tandem insertion of lithium chloroallylides and a variety of electrophiles into mono- and bicyclic zirconacyclo-pentanes and -pentenes to provide highly elaborated organic products.[6] We have also reported the insertion of prop-2-ynyl carbenoids (1-chloro-1-lithioalk-2-ynes) into zirconacycles.[7] We now describe the tandem insertion of allenyl carbenoids (3-chloro-1-lithioalk-1-ynes) and aldehydes into zirconacycles to afford a variety of alkyne, allene, and unexpected cyclised products.

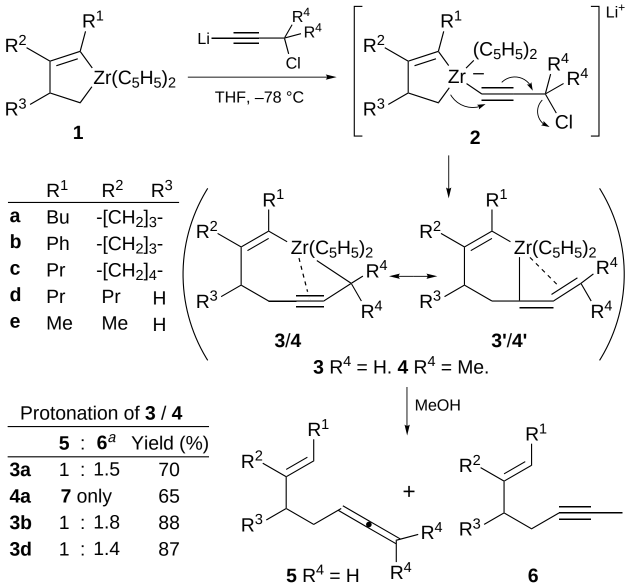
A variety of zirconacyclopentenes **1** were synthesised, either by intramolecular co-cyclisation of 1,6- or 1,7-enynes induced by zirconocene but-1-ene,[8] or by addition of alkynes to *in situ* generated zirconocene ethylene.[9] After cooling to −78 °C, dropwise addition of 3-choroprop-1-yne followed by lithium 2,2,6,6-tetramethylpiperidide generated the unstable allenyl carbenoid, 1-lithio-3-chloroprop-1-yne, which underwent insertion into the alkyl C–Zr bond of the zirconacyclopentenes **1**, presumably *via* an 18 electron zirconate intermediate **2**, to afford the ring expanded products **3a–e** (Scheme 1). In the same way insertion of 1-lithio-3-chloro-3-methylbut-1-yne gave the zirconacycles **4a** and **4e**. The bonding in the zirconocene η^3-prop-2-ynyl/allenyl complexes **3** and **4** may be described in terms of the two contributing resonance structures **3**/**4** and **3′**/**4′** (Scheme 1).[7,10] Relative contributions of the two structures vary. The ^{13}C NMR shifts of the prop-2-ynyl/allenyl components of **3a** (δ_C = 103.3, 104.3 and 46.8) and **4a** (δ_C = 127.9, 176.6 and 87.3) demonstrate the much greater contribution of the allenyl form when R^4 = Me. η^3-Prop-2-ynyl/allenyl complexes of transition metals are rare, and have recently been reviewed.[11]

Protonation of **3a**,**b**, and **e** required several hours stirring with excess methanol and gave a mixture of terminal allene **5** and internal alkyne **6** products,† favouring the later (Scheme 1). Protonation of **4a** was fast, and gave exclusively the allene **7**.

Reaction of the η^3-prop-2-ynyl complexes **3** and **4** with aldehydes activated with boron trifluoride–diethyl ether was examined. For example **3a** gave an excellent overall yield (based on the starting enyne) of the allenol **8a** (R^5 = Pr) when reacted with butyraldehyde (Scheme 2). The regiochemistry of addition to the η^3-moiety is the opposite of that observed in the elaboration of analogous η^3-allyl complexes.[6] Much to our surprise reaction of **3a** with benzaldehyde gave a quite different product which proved to be the cyclised dienol alcohol **9a** (R^5 = Ph). Generally, reaction of complexes **3** with alkyl aldehydes gave only the allene product **8**, whereas benzaldehyde gave either the dienol **9**, or a mixture of **8** and **9** (Table 1). The *gem*-dimethyl substituted complexes **4a** and **4e** gave only the dienols **10** with either aliphatic, or aromatic aldehydes (Table 1).

In addition to extensive NMR studies (including H–H and C–H COSY) on most of the allenol and dienol products, the structure of **9d** (R^5 = Ph) was further proven through degradation. Ozonolysis followed by dimethyl sulfide work-up gave undeca-4,5,8-trione and 3-phenyl-3-hydroxypropanal. The stereochemistry of the exocyclic alkene in **10e** (R^5 = Ph) was proven by NOE studies, in particular a 9.6% enhancement between the vinylic methyl group and the adjacent vinylic hydrogen. All the dienol products were formed as single isomers.

A likely mechanism for the cyclisation to afford the dienol products **9** and **10** is given in Scheme 3. Addition of the boron trifluoride complex of the aldehyde to the terminus of the prop-2-ynyl system generates both an alkyne, and a cationic

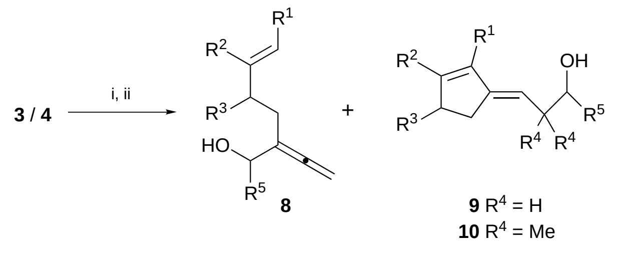


	R^1	R^2	R^3
a	Bu	-[CH$_2$]$_3$-	
b	Ph	-[CH$_2$]$_3$-	
c	Pr	-[CH$_2$]$_4$-	
d	Pr	Pr	H
e	Me	Me	H

Protonation of **3** / **4**

	5 : **6**^{a}	Yield (%)
3a	1 : 1.5	70
4a	**7** only	65
3b	1 : 1.8	88
3d	1 : 1.4	87

Scheme 1 Ratios determined from ^{1}H NMR of the crude products



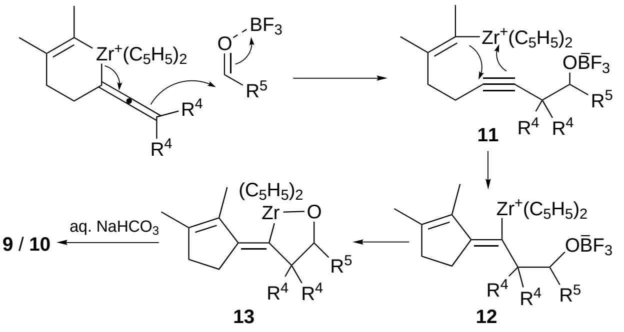
Scheme 2 *Reagents and conditions*: i, R^{5}CHO, BF$_3$·Et$_2$O, −78 °C to room temp., 2 h; ii, aq. NaHCO$_3$, room temp., 16 h

zirconium species. Intramolecular insertion of the pendant alkyne into the carbon–cationic zirconocene bond in **11** to give **12** has some precedent.[12] The final step, formation of the oxazirconacycle **13** (which is likely to be relatively stable towards hydrolysis), is speculation, but may explain why work-up with D_2O or MeOD fails to give deuterated product (DCl causes decomposition).

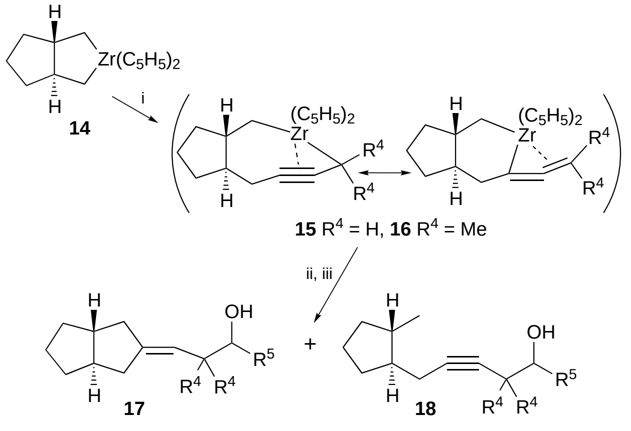
Table 1. Results of $R^5CHO/BF_3{\cdot}Et_2O$ addition to **3/4**

Substrate	R^5	Product	Yield (%)[a]
3a	Pr	**8**	83
3a	Ph	**9**	51[c]
3a	Bu^i	**8**	74
4a	Ph	**10**	61
4a	Bu^i	**10**	74
3c	Ph	**8** : **9** :: 2.4 : 1.0[b]	61
3d	Ph	**8** : **9** :: 1.0 : 5.0[b]	71
3d	Pr	**8**	76
3e	Pr	**8**	84
4e	Ph	**10**	68

[a] Of **8** + **9**, or **10** based on enyne for **a** and **c**, and $(C_5H_5)_2ZrCl_2$ for **d** and **e**. 1.5 equiv. of aldehyde/$BF_3{\cdot}Et_2O$ used with aromatic aldehydes, 3.0 equiv. with aliphatic. [b] Determined from ^1H NMR of crude product. [c] Unstable to chromatography.



Scheme 3 Possible mechanism for dienol formation



Scheme 4 *Reagents and conditions*: i, $R^4{}_2ClCC{\equiv}CH$, LiTMP, −78 °C, THF; ii, R^5CHO, $BF_3{\cdot}Et_2O$, −78 °C to room temp.; iii, aq. $NaHCO_3$

Table 2. Aldehyde addition to **15** and **16**

Substrate	R^4	R^5	Products	Yield (%)[a]	**17 : 18**
15	H	Bu^i	**17a/18a**	23	1 : 1.3
15	H	Ph	**18b**	75	0 : 1
16	Me	Bu^i	**17c/18c**	72	1 : 1.3
16	Me	Ph	**17d/18d**	81	1[b] : 10.6

[a] Combined yield of pure **17** + **18** before separation. [b] Not isolated pure.

Application of the tandem insertion of 1-lithio-3-chloroalk-1-ynes and aldehydes to zirconacyclopentane systems highlighted further reactivity and product selectivity variations. Co-cyclisation of hepta-1,6-diene using zirconocene but-1-ene gave the zirconacycle **14**. Insertion of 1-lithio-3-chloroprop-1-yne or 1-lithio-3-chloro-3-methylbut-1-yne afforded the ring expanded zirconacycles **15** and **16** respectively (Scheme 4). Addition of aldehydes activated with boron trifluoride–diethyl ether gave the bicyclic enol products **17** and/or the alkynols **18** (Table 2). Both products arise from insertion at the terminus of the prop-2-ynyl system in marked contrast to the results from unsaturated zirconacycles (Table 1). The structure of **17c** was proven by ozonolysis to give bicyclo[3.3.0]octan-3-one and 2,2,5-trimethyl-3-hydroxyhexanal, each prepared by independent synthesis.

In summary, we have shown that the insertion of 1-lithio-3-chloroalk-1-ynes (allenyl carbenoids) into zirconacyclopentenes and pentanes affords unusual cyclic η^3-prop-2-ynyl/allenyl complexes. Further elaboration by the addition of boron trifluoride activated aldehydes gives a variety of products, some of which result from intramolecular insertion into a proposed intermediate cationic zirconocene.

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Footnotes

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† All organic compounds were characterised (^1H and ^{13}C NMR, IR, MS and HRMS) as pure compounds with the exception of **17a** which decomposed during seperation from **18a**. The compounds **18a**, **c** and **d** were seperated *via* their $Co_2(CO)_6$ adducts.

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