Tandem prop-2-ynyl carbenoid–aldehyde insertion into zirconacycles

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Insertion of 1-lithio-1-chloroalk-2-ynes into zirconacycles gives cyclic zirconocene η³-prop-2-ynyl/allenyl complexes which afford useful organic products on protonation or Lewis acid induced addition of aldehydes.

The co-cyclisation of alkenes and alkynes induced by the zirconocene equivalent, zirconocenebut-1-ene (generated *in situ* from dibutylzirconocene—the 'Negishi reagent'[1]) is a useful method for carbon–carbon bond formation.[2] Efficient use of the transition metal requires productive methods for elaboration of the intermediate zirconacycles. Although conventional electrophiles such as alkyl halides are unreactive, reagents with carbenic reactivity such as carbon monoxide and isocyanides insert into the carbon–zirconium bonds very rapidly.[3] We recently reported[4] the insertion of lithium chloroallylides into zirconacycles to afford η³-allylzirconium species which could be further elaborated by the addition of a variety of electrophiles. We now describe the extension of this insertion reaction to 1-chloro-1-lithioalk-2-ynes (prop-2-ynyl carbenoids) to give novel η³-prop-2-ynyl/allenyl zirconium species, and their further elaboration.

Co-cyclisation of hepta-1,6-diene using zirconocenebut-1-ene gave the zirconacyclopentane **1**. Addition of 1-chlorohept-2-yne followed by a solution of lithium 2,2,6,6-tetramethylpiperidide (LiTMP) at −78 °C gave clean conversion into a 1:1 mixture of the diastereoisomeric zirconacyclohexanes **3** and **4**, presumably *via* the 'ate' complex **2**. Since both the carbenoid and the zirconacycle are chiral, but racemic, the 1:1 ratio of **3**:**4** suggests that there is little 'chiral recognition' between the carbenoid and zirconacycle, and little equilibration of the 'ate' complex **2** which could favour one of the two diastereoisomers on rearrangement. Heating the mixture of **3** and **4** did not cause any change in the isomer ratio. The complexes **3** and **4** were remarkably resistant to protonolysis showing no change after eight days dissolved in CD₃OD–C₆D₆ (1:2) (*cf.* **1** which protonates in < 2 min). Acetic acid caused rapid protonation of **4** (< 5 min at room temp.) to give **5**† and **6** (2:1) but left **3** untouched. Aqueous work-up followed by recrystallisaton of the crude product from hexane gave **3** as fine white crystals in an overall yield of 27%. The crystallisation liquor was purified by column chromatography to yield 1-methyl-2-(oct-3-ynyl)cyclopentane **5** (31%) and 1-methyl-2-(octa-2,3-dienyl)cyclopentane **6** (14%). Protonation of **3** with acetic acid took 24 h to reach completion and gave a 1:1.5 mixture of **5** and **6**.

The NMR shifts of the prop-2-ynyl unit in both **3** (δ_C 73.6, 115.1, 122.3) and **4** (δ_C 76.7, 121.1, 123.2) are consistent with η³-bonding (*i.e.* with a substantial contribution from the η³-allenyl representation **3′**/**4′**), and are comparable to those in (C₅H₅)₂Zr(Me)(η³-CH₂C≡CPh) (δ_C 55.5, 114.2, 120.5) reported by Wojecicki.[5] The small number of known η³-prop-2-ynyl complexes of transition metals have recently been reviewed.[6] The relative stereochemistries of **3** and **4** were tentatively assigned as shown based on the marked difference in stability towards hydrolysis. In **3** (chair zirconacyclohexane) the alkyne moiety is ideally positioned for donation of electron density into the empty orbital on zirconium[7] whereas in **4** the zirconacyclohexane ring must adopt a higher energy twisted boat conformation (Fig. 1).‡ We have previously noted a correlation between an 18 electron configuration at a zirco-

nocene centre, and stability of carbon–zirconium bonds towards hydrolysis[8] and believe that hydrolysis occurs *via* the 16 electron η¹-prop-2-ynyl forms of **3** and **4**, more readily attained by the later. By analogy with our successful elaboration of cyclic zirconocene allyl complexes with aldehydes activated with BF₃·Et₂O[4] we exposed the mixture of **3** and **4** to these conditions, but no reaction occurred. The products isolated after aqueous work-up comprised **5**, **6** and **3**.

We next examined the insertion of prop-2-ynyl carbenoids into unsaturated zirconacycles. Treatment of the bicyclic zirconacyclopentenes **7a** and **7b**, derived from the intramolecular co-cyclisation of enynes, with 1-chloro-3-phenyl-prop-2-yne or 1-chlorohept-2-yne and LiTMP at −78 °C gave clean conversion to the ring expanded zirconacycles **8a–c**, each as a 1:1 mixture of diastereoisomers (Scheme 2). Protonolysis of **8a** with methanol was selective for one diastereoisomer (< 5 min for complete protonation of one isomer, half life of around 4 h at room temp. for the other). Unfortunately, we could not cleanly isolate a single isomer which made assignment of NMR data difficult. To avoid the problem we synthesised the monocyclic zirconium species **7c**[9] and treated it with various prop-2-ynyl carbenoids to give the single isomer ring expanded products **8d–g** in quantitative yield by NMR spectroscopy. Protonation of the zirconacycles **8a–f** gave alkyne **9** and/or allene products **10** in good yields (Table 1), the ratio of products
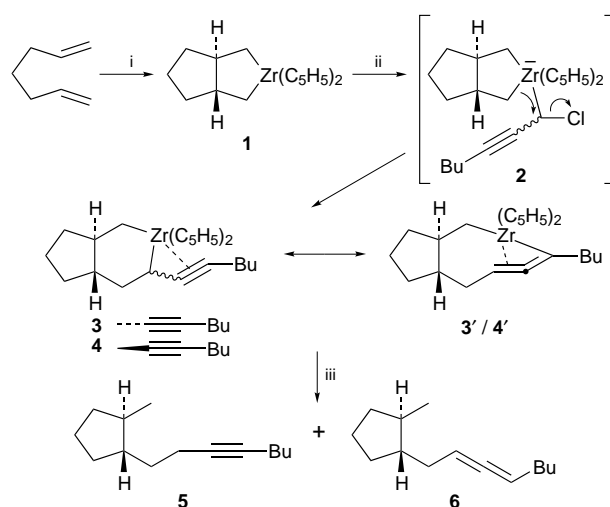
Scheme 1 *Reagents and conditions*: i, (C₅H₅)₂ZrCl₂ + 2 BuLi, THF, −78 °C to room temp; ii, BuC≡CCH₂Cl, THF, LiTMP, −78 °C to room temp; iii, AcOH
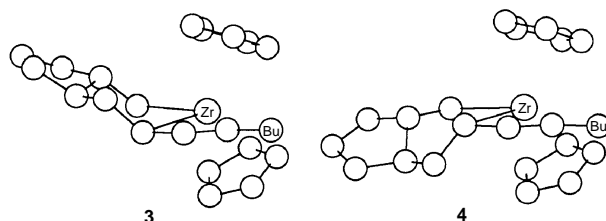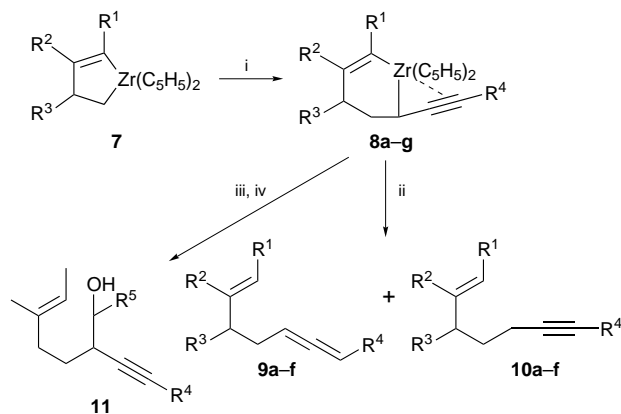

Fig. 1 Minimum energy conformations of **3** and **4** from ZINDO calculations

Scheme 2 *Reagents and conditions*: i, R⁴C≡CCH₂Cl or MeC≡CCH₂O-CO(NPr^{i}₂), LiTMP, THF, −78 °C; ii, NaHCO₃ aq. or HCl aq. or MeOH or AcOH; iii, R⁵CHO, BF₃·Et₂O or TiCl₄, 10 h, room temp; iv, NaHCO₃ aq.

Table 1 Definition of **7–10** and protonation results

R¹	R²	R³	**7**	R⁴	**8**	Quench	Yield (%)^a **9 + 10**	Ratio^b **9 : 10**
Bu	–(CH₂)₃–		**7a**	Bu	**8a**	NaHCO₃aq.	76	21:79
Bu	–(CH₂)₃–		**7a**	Bu	**8a**	AcOH	—	0:100
Bu	–(CH₂)₃–		**7a**	Bu	**8a**	MeOH	—	63:37
Bu	–(CH₂)₃–		**7a**	Ph	**8b**	NaHCO₃aq.	86	52:48
Bu	–(CH₂)₃–		**7a**	Ph	**8b**	HCl aq.	—	48:52
Bu	–(CH₂)₃–		**7a**	Ph	**8b**	AcOH	—	15:85
Bu	–(CH₂)₃–		**7a**	Ph	**8b**	MeOH	—	83:17
Ph	–(CH₂)₃–		**7b**	Ph	**8c**	AcOH	90	13:87
Ph	–(CH₂)₃–		**7b**	Ph	**8c**	MeOH	86	79:21
Me	Me	H	**7c**	Ph	**8d**	AcOH	79	14:86
Me	Me	H	**7c**	Ph	**8d**	MeOH	71	93:7
Me	Me	H	**7c**	SiMe₃	**8e**	AcOH	81	0:100
Me	Me	H	**7c**	SiMe₃	**8e**	MeOH	75	0:100
Me	Me	H	**7c**	Me	**8f**	AcOH	68	0:100
Me	Me	H	**7c**	Me	**8f**	MeOH	74	70:30
Me	Me	H	**7c**	Bu	**8g**	—^{c}		

^{a} Yield of pure mixture of **9** and **10** before separation. ^{b} From ¹H NMR spectra of the crude product. ^{c} Protonation not attempted.

Table 2 Reaction of **8d–g** with R⁵CHO to give **11**

R⁴	R⁵	Lewis acid	Yield of **11** (%)	Dr^a
Bu	Ph	TiCl₄	86	1:2.9
Bu	Ph	BF₃·Et₂O	77	1:1.2
Ph	Ph	TiCl₄	76	1:4.2
Ph	C≡CC₅H₁₁	BF₃·Et₂O	88	1:2.3
SiMe₃	Ph	BF₃·Et₂O	36	1:1.4
Me	Ph	BF₃·Et₂O	61	1:1.1

^{a} Diastereoisomer ratio, measured by NMR.

proving to be dependent on the reagent. Quenching with acetic acid favoured formation of the alkyne (exclusive for R⁴ = alkyl or SiMe₃), whereas MeOH favoured the allene, except for the trimethylsilyl substituted case when only the alkyne was obtained.

Reaction of the η³-prop-2-ynyl complexes **8e–g** with aldehydes in the presence of BF₃·Et₂O or TiCl₄ gave adducts **11** in good yield (Table 2), as a mixture of diastereoisomers. Somewhat better diastereocontrol was found using TiCl₄ as the Lewis acid. The regiochemistry of insertion into the η³-prop-2-ynyl system is opposite to that previously observed with the analogous η³-allyl complexes.[4] The zirconabicycle **8a** also
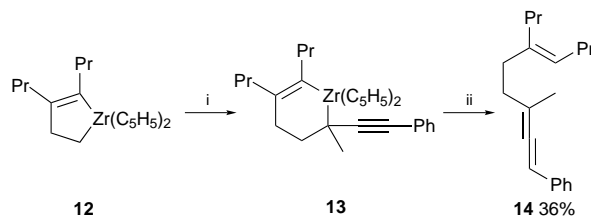
Scheme 3 *Reagents and conditions*: i, PhC≡CCHMeCl, THF, LiTMP, −78 °C; ii, MeOH, −78 °C to room temp.

reacted with aldehydes, but the increased number of diastereoisomeric products formed prevented proper characterisation.

Finally we examined the insertion of a secondary prop-2-ynyl carbenoid, derived by deprotonation of 1-phenyl-3-chlorobut-1-yne, into the zirconacycle **12**. Insertion occurred readily, but the intermediate zirconacycle **13** was too unstable for NMR characterisation, probably due to β-hydride elimination from the methyl group. Protonation with methanol gave exclusively the allene **14**, confirming that insertion had occurred and illustrating that steric hinderence in the carbenoid is well tolerated (Scheme 3).

We have demonstrated a new method for the elaboration of zirconacycles to provide organic products in good yields. We have also synthesised and characterised a range of novel η³-prop-2-ynyl/allenyl zirconacycles, some of which are remarkably unreactive towards air and water.

Footnotes

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† All organic compounds were fully characterised (high field ¹H and ¹³C NMR, IR, MS, and HRMS) as pure compounds, with the exception of the diastereoisomers of **11** which were not separated.

‡ Structures based on ZINDO (INDO/1)[10] calculations carried out using CACHE software (Oxford Molecular). The calculations indicate that **4** is 6.4 kJ mol⁻¹ higher in energy than **3**, and that the chair form of **4** with the alkyne axial, and not coordinated to the metal, is 23 kJ mol⁻¹ higher in energy than the η³-prop-2-ynyl boat form.

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