Organozirconate Chemistry

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Coupling Reactions of Zirconate Complexes Induced by Carbonyl Compounds**

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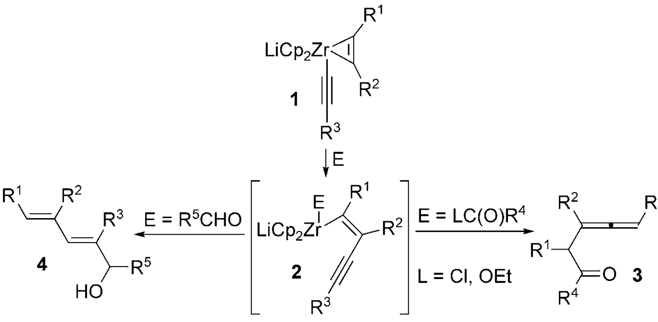
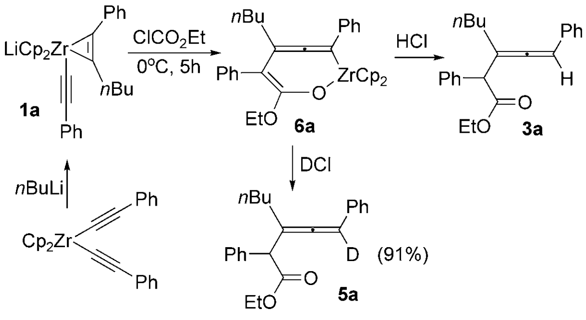
During the past few decades the chemistry of 16-electron organozirconocene complexes has been extensively explored and a tremendous number of applications in synthetic chemistry have been found.[1] However, organozirconate complexes, which usually have an 18-electron configuration with two cyclopentadienyl (Cp) rings, three Zr–C bonds, and alkali counter ions, have rarely been explored in spite of being the supposed intermediates in a number of stoichiometric and catalytic reactions, and able to form C–C bonds through a successful 1,2-migration of organozirconates.[2–4] Our research group has an interest in the above mentioned subjects, and we have recently reported[5] that by adding quinone as an oxidant to a mixture of alkynylzirconates then zirconocenendiyne compounds are afforded: these compounds can be converted into various endiynes through coupling reaction with electrophiles. These results prompted us to further study the chemistry of organozirconate complexes. Herein, we report the coupling reactions of three-membered alkynylzirconates induced by carbonyl compounds. The unique features of this reaction involve the carbonyl compound acting as an electrophile, participating in the reaction with zirconates, and also inducing the coupling of an alkynyl group and an sp^2-hybridized carbon atom of zirconacyclopropene. To the best of our knowledge, this type of reaction has not been reported. When acyl compounds were used as electrophiles, then functionalized allenes were formed. When aldehydes were used as electrophiles, then dienols were formed. These outcomes are illustrated in Scheme 1.



Scheme 1. Diverse reactivity of zirconates.

The reaction of zirconate **1a**, which was generated by the treatment of *n*BuLi with bis(phenylethynyl)zirconocene at room temperature,[6] with chloroformate at 0 °C for five hours afforded allene **3a** in 73 % yield after hydrolysis. Quenching the reaction mixture with DCl in D_2O provided allene **5a** in a comparable yield with 91 % deuterium incorporation. This result indicates that the zirconium-containing complex **6a** is formed (Scheme 2).

Oxazirconacycle **6a** was formed in 74 % yield (based on NMR spectroscopy). The ^1H NMR spectrum of **6a** showed a singlet resonance at $\delta = 5.96$ ppm, which was assigned to the protons on the Cp ring. In the ^{13}C NMR spectrum, the signal for the carbon atoms in the Cp ring appeared at $\delta = 104.5$ ppm, and the signal for the allenic-type sp-hybridized carbon atom appeared at $\delta = 198.5$ ppm. The carbon signals in Zr–*C*(Ph) and –*C*(OEt)O appeared at $\delta = 149.5$ and 169.6 ppm, respectively.



Scheme 2. The reaction with chloroformate.

The allene group is a versatile functionality because it is useful as either a nucleophile or an electrophile as well as a substrate for cycloaddition reactions. This multiple reactivity make allenes as excellent candidates for synthetic manipulation.[7] The reaction described here allowed the efficient synthesis of various substituted allenes. A variety of acyl compounds were subjected to this novel reaction and all reactions afforded analogous products in good to high yields after hydrolysis. Notably, the acyl compounds induced

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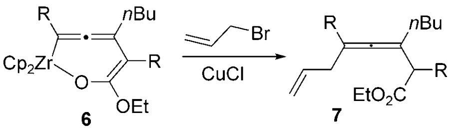
coupling between an alkynyl group and an sp^2-hybridized carbon atom with high regioselectivity. This result is due to the higher reactivity of the carbon atom attached to the alkyl group as compared to the carbon atom attached to the aryl group. The representative results are summarized in Table 1. Chloroformates afforded the corresponding allenes in 47–61 % yields (Table 1, entries 1–5). The addition of esters similarly gave allenes in good yields (Table 1, entries 6–8). The diethylcarbamyl chloride afforded the corresponding product in 55 % yield (Table 1, entry 9). When acyl chloride and anhydride were treated with zirconates under similar reaction conditions the desired products were not observed.

The remaining Zr–C bond of oxazirconacycle **6** was further treated with allyl bromide in the presence of one equivalent of CuCl[8] and afforded fully substituted allenes **7a** and **7b** in moderate yields, respectively (Scheme 3).



7a: R = Ph, yield = 59% (43%)
7b: R = pBuC$_6$H$_4$, yield = 58% (45%)

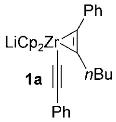
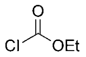
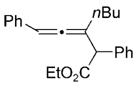
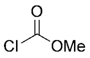
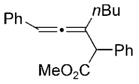
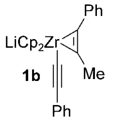
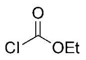
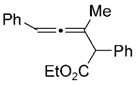
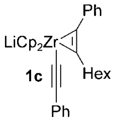
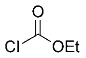
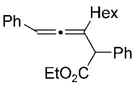
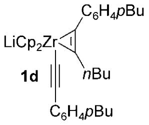
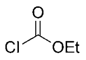
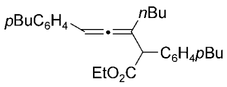
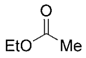
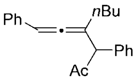
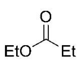
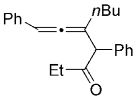
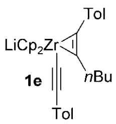
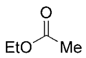
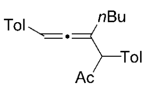
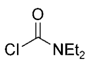
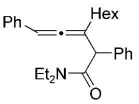
Scheme 3. The reaction of oxazirconacycle **6** with allyl bromide (yield of isolated product given in parentheses).

Based on the above results, we propose the following mechanism for this reaction (Scheme 4). The zirconate $[\mathrm{LiCp_2Zr(C{\equiv}CR^3)(R^1C{=}CR^2)}]$ **1** undergoes a coupling reaction to give intermediate **2** in the presence of an acyl compound. The intermediate **2** reacts with an acyl compound through nucleophilic substitution to form **8** with elimination of a lithium salt and then undergoes cyclic oxidation/rearrangement (path a) to give **6**. Alternatively, intermediate **8** undergoes oxidative coupling of the carbonyl and alkenyl groups to give oxazirconacycle **9** with an alkynyl moiety at the α position (path b),[9] which subsequently rearranges to **6**. Hydrolysis of **6** affords the product **3**.

In light of the unusual reactivity of the organozirconate, we further investigated the reaction of zirconate **1a** with benzaldehyde (Scheme 5). Interestingly, dienol **4a** was formed in good yield after hydrolysis. Deuteriolysis instead of hydrolysis afforded the dideuterated compound **10a** in 66 % yield with 93 % and 97 % deuterium incorporation. The structure of product **4a** was confirmed by ^{1}H NMR, ^{13}C NMR, HSQC, HMBC, and NOESY experiments.[10]

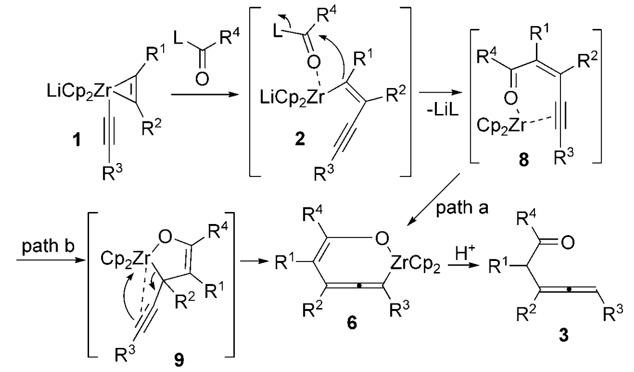
Intermediate **11a** was also characterized by NMR spectroscopy. The ^{1}H NMR spectrum of **11a** showed two signals at $\delta = 5.72$ and 6.00 ppm which are assigned to the protons of two Cp rings, and a resonance at $\delta = 5.39$ ppm is assigned to the proton in $-$OC*H*Ph. In the ^{13}C NMR spectrum, the signals for the carbon atoms of the Cp ring appear at $\delta =$ 111.0 and 111.6 ppm, and the resonance for the carbon atoms of the diene appear at $\delta = 146.9$, 150.4, 154.8, and 183.4 ppm.

Table 1: Formation of functionalized allenes by the reaction of zirconates with acyl compounds.

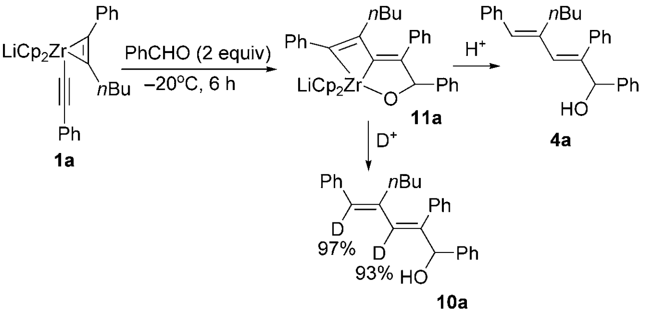
Entry	Zirconate	Acyl compound	Product[a]	Yield [%][b]
1	 **1a**		**3a** 	73(57)
2	**1a**		**3b** 	65(47)
3	 **1b**		**3c** 	76(61)
4	 **1c**		**3d** 	69(53)
5	 **1d**		**3e** 	67(52)
6	**1a**		**3f** 	46(32)
7	**1a**		**3g** 	44(28)
8	 **1e**		**3h** 	40(31)
9	**1c**		**3i** 	67(55)

[a] Single isomer, the stereoselectivity was not defined. [b] Yield is based on ^{1}H NMR spectroscopy, yield of isolated product given in parentheses. Hex = hexyl, Tol = tolyl.

A variety of aromatic aldehydes were subjected to the reaction. The results were summarized in Table 2. Aromatic aldehydes bearing a chlorine, fluorine, or phenyl group were treated with zirconates and led to the corresponding products in good yields (Table 2, entries 3–6, and 8). The p-methylbenzaldehyde was treated with zirconates and led to the

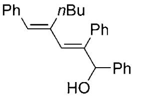
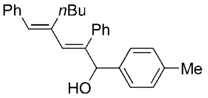
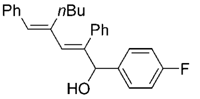
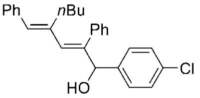
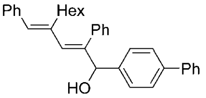
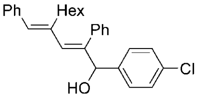
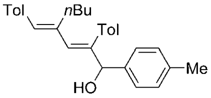
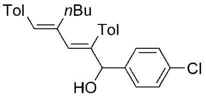


Scheme 4. Proposed mechanism for the reaction with acyl compounds.



Scheme 5. The reaction with benzaldehyde.

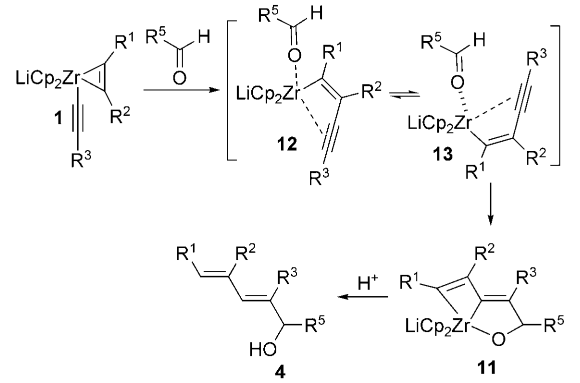
Table 2: Formation of dienols by the reaction of zirconates with aldehydes.

Entry	Ziconate	Aldehyde	Product		Yield [%][a]
1	**1a**	PhCHO	**4a**		66(54)
2	**1a**	p-MeC$_6$H$_4$CHO	**4b**		51(45)
3	**1a**	p-FC$_6$H$_4$CHO	**4c**		69(57)
4	**1a**	p-ClC$_6$H$_4$CHO	**4d**		66(50)
5	**1c**	p-PhC$_6$H$_4$CHO	**4e**		64(52)
6	**1c**	p-ClC$_6$H$_4$CHO	**4f**		70(59)
7	**1e**	p-MeC$_6$H$_4$CHO	**4g**		46(37)
8	**1e**	p-ClC$_6$H$_4$CHO	**4h**		65(50)

[a] Yield is based on ^{1}H NMR spectroscopy; yield of isolated product given in parentheses.

corresponding products in moderate yields (Table 2, entries 2 and 7). When aliphatic aldehydes were treated with zirconates under similar reaction conditions, the desired products were not observed, but aldol products were obtained.

These results indicate that aldehydes behaved differently to acyl compounds. A plausible reaction mechanism is shown in Scheme 6. Firstly, the oxygen atom of the carbonyl group coordinates to zirconate **1** and induces coupling of the alkynyl and an sp^2-hybridized carbon atom of zirconacyclopropene to give intermediate **12**, which forms an equilibrium between **13**. In this case, the reaction pathway differs from the reaction with acyl compound. A possible explanation is that the nucleophilicity of the carbon atom attached to zirconium is not high enough to react with an aldehyde. On the other hand, oxidative coupling of an aldehyde and an alkyne on the zirconocene(II) is preferred.[11] The intermediate **13** undergoes oxidative coupling to form **11**. Hydrolysis of **11** affords the product **4**.[12]



Scheme 6. Plausible mechanism for the formation of dienols.

In summary, we have demonstrated a novel coupling reaction of alkynylzirconate complexes with carbonyl compounds. A unique feature of this reaction is that carbonyl compounds not only participated in the reaction with zirconates but also induced coupling of an alkynyl and alkenyl group of zirconoacyclopropene with high regioselectivity. In this reaction, two alkyne groups, introduced as to alkynyllithiums and an organolithium, and carbonyl compounds were selectively coupled in one-pot by the reaction of [Cp$_2$ZrCl$_2$] to afford highly substituted allene and dienol derivatives. Investigation of the reaction mechanism and further application of this chemistry are in progress.

Experimental Section

Typical procedure for the reaction of alkynylzirconates with acyl compounds: nBuLi (4.5 mmol, 1.6 M solution in hexane) was added to a solution of phenylacetylene (3.0 mmol) at −78 °C and stirred for 1 h. Then [Cp$_2$ZrCl$_2$] (1.5 mmol) was added and the solution was stirred at −78 °C for 1 h then warmed to room temperature and kept at this temperature for 12 h. After cooling the reaction mixture to 0 °C, ethyl chloroformate (1.0 mmol) was added and the reaction mixture was stirred for 5 h. The reaction mixture was quenched with 6 N HCl and extracted with ethyl acetate. The organic extract was dried over $MgSO_4$, and the filtrate was concentrated under reduced pressure. Purification of the residue by column chromatography on silica gel (hexane/ethyl acetate 50:1) afforded **3a** as yellow liquid (190 mg) in 57 % yield.^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si): $\delta = 0.82$ (t, $^3J_{HH} = 7.2$ Hz, 3H), 1.12 (t, $^3J_{HH} = 7.2$ Hz, 3H), 1.21–1.44 (m, 4H), 2.05 (dt, $^3J_{HH} = 7.3$ Hz, $^2J_{HH} = 2.4$ Hz, 2H), 4.00 (dq, $^3J_{HH} = 7.0$ Hz, $^2J_{HH} = 10.8$ Hz, 1H), 4.04 (dq, $^3J_{HH} = 7.0$ Hz, $^2J_{HH} = 10.8$ Hz, 1H), 4.33 (q, $^4J_{HH} = {}^5J_{HH} = 2.4$ Hz, 1H), 6.22 (q, $^4J_{HH} = {}^5J_{HH} = 2.4$ Hz, 1H), 7.27–7.33 ppm (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$, Me_4Si): $\delta = 14.0$, 14.1, 22.5, 29.8, 31.7, 55.9, 61.2, 98.1, 108.5, 126.7, 126.8, 127.4, 128.2, 128.5, 129.0, 135.0, 137.0, 171.8, 203.4 ppm. HRMS calcd for $C_{23}H_{26}O_2$ ($[M]^+$): 334.1933; found: 334.1925.

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Keywords: acyl compounds · aldehydes · allenes · dienols · organozirconates

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