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LETTERS

C–C bond formation using allylic organozirconium compounds. Nucleophilic additions on to isolated and in situ generated η^5-pentadienyl-Fe(CO)$_3$/Fe(CO)$_2$PPh$_3$(+1) cations

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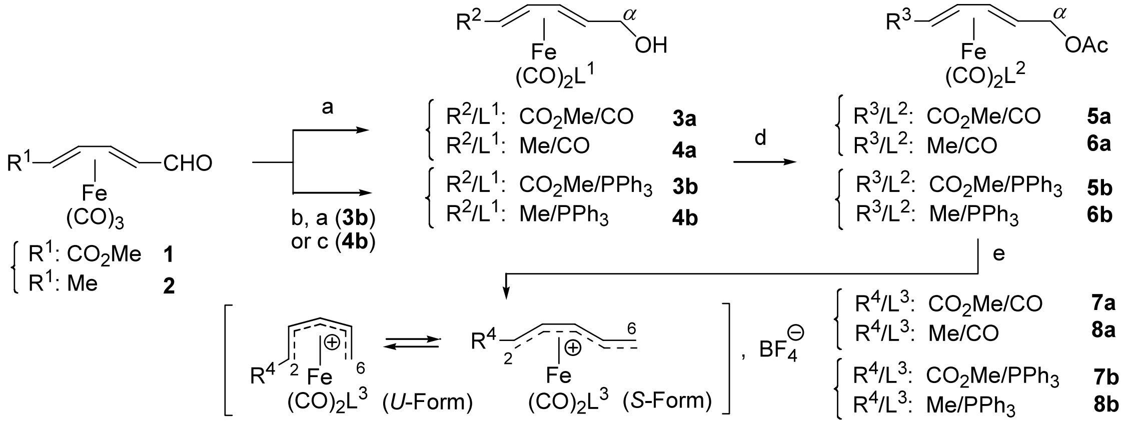
Abstract—Two nucleophilic allylic organozirconium compounds **9**–**10** (R^5: Me and *t*Bu) have been reacted with acyclic isolated η^5-pentadienyl-Fe(CO)$_3$/Fe(CO)$_2$PPh$_3$(+1) cations or with these intermediates *generated* in situ (Uemura-like conditions). Depending on reaction conditions, iron-complexed η^4-dienyl-Fe(CO)$_3$/Fe(CO)$_2$PPh$_3$ and σ,η^3-π-allyl-Fe(CO)$_3$/Fe(CO)$_2$PPh$_3$ condensation products have been selectively isolated and fully characterized.

Organometallic η^4-dienyl-Fe(CO)$_3$ complexes are useful intermediates which have found multiple uses in organic chemistry and asymmetric synthesis due to their particular protecting and stereodirecting properties.[1] Interestingly, if unsymmetrically substituted, these complexes are homochiral and can be resolved using various resolution methods.[1] Moreover, carbocations located close to the coordination site are known to be strongly stabilized by anchimeric assistance from the iron atom. For example, related η^5-pentadienyl-Fe(CO)$_3$(+1) cationic complexes of type **7a**–**8a** (equilibrium between *U*- and *S*-forms,[1c–e] Scheme 1) are known to add a great variety of *C*- and heteronucleophiles (Nu) in an *anti* manner.

Within this class of iron-complexed electrophiles, isolated *cisoid U*-shaped cations generally afford (*E*,*E*)-/(*E*,*Z*)-η^4-dienyl complexes (Nu *anti* attack at C2/6 cation extremities), σ,η^3-π-allyl derivatives (Nu *anti*



Scheme 1. *Reagents and conditions*: (a) NaBH$_4$, MeOH, 0–20°C, 0.5 h, 84–98%; (b) PPh$_3$, Me$_3$NO, MeCOMe, reflux, 3 h, 72–74%; (c) **4b**: DIBAL-H, anh. CH$_2$Cl$_2$, −78°C, 0.5 h, 86%; (d) Ac$_2$O, anh. pyridine, 0–20°C, 14 h, 77–95%; (e) 50% aq. HBF$_4$, Ac$_2$O/anh. Et$_2$O, −15°C, 0.5 h, 80–91%.

Keywords: organozirconium compounds; (η^5-pentadienyl)Fe(CO)$_3$/Fe(CO)$_2$PPh$_3$(+1) cations; carbon–carbon bond formation.

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attack at internal cation C3/C5) or mixtures of them, depending on nucleophiles, on substituents of the dienyl ligand, and, on reaction conditions.[1] Average condensation yields, and disappointing regio- and diene (*E*,*E*)-/(*E*,*Z*)-selectivities generally limit the synthetic interest of additions onto *isolated* cations.[1c–e] By contrast, iron-complexed esters **5a**–**6a** and α-substituted analogs can be ionized by Lewis or protic acids *in the presence of trapping nucleophiles*.[2] *Transoid S*-shaped cations are generated in situ by smooth heterolysis of the C_α–O bond, and are trapped regioselectively by trialkylaluminiums, allylTMS, allylSn*n*Bu$_3$ and enol silyl ethers. η^4-Dienyl-$Fe(CO)_3$ iron-complexed products are obtained with sole (*E*,*E*)-diene geometry and an overall retention of configuration at C_α.[2]

To the best of our knowledge, C–C bond formation mediated by nucleophilic additions of allylic organozirconium species onto η^5-pentadienyl-iron complexed cations has not previously been reported.

The main purposes of this letter are (1) to investigate the basic reactivity and selectivity trends of such nucleophilic additions; (2) to prove clearly that η^5-pentadienyl-iron complexed cations can be generated *in situ in the presence of allylic organozirconium species and successfully trapped by them*, and, finally, (3) to provide a first preliminary result that will pave the way to similar organozirconium-based *intramolecular* condensations.

More specifically, this study emphasizes the reaction of the two allylzirconocene compounds **9**–**10** with η^5-pentadienyl-$Fe(CO)_3$/$Fe(CO)_2PPh_3$(+1) cations **7a**–**b**/**8a**–**b** (equilibrium of *cisoid*/*transoid U*-/*S*-forms, Scheme 1) containing a CO_2Me/Me electron withdrawing/electron donating substituent at C2. The organozirconium nucleophiles **9**–**10** have been classically prepared by oxidative addition of Negishi's reagent Cp_2Zr(1-butene) ('Cp_2Zr' equivalent), respectively, to *O*-TMS and *O*-TBDMS allyl alcohols[3] (Cp_2ZrCl_2/2 *n*BuLi, PhMe or THF, −78°C: 1 h→20°C: 3 h).

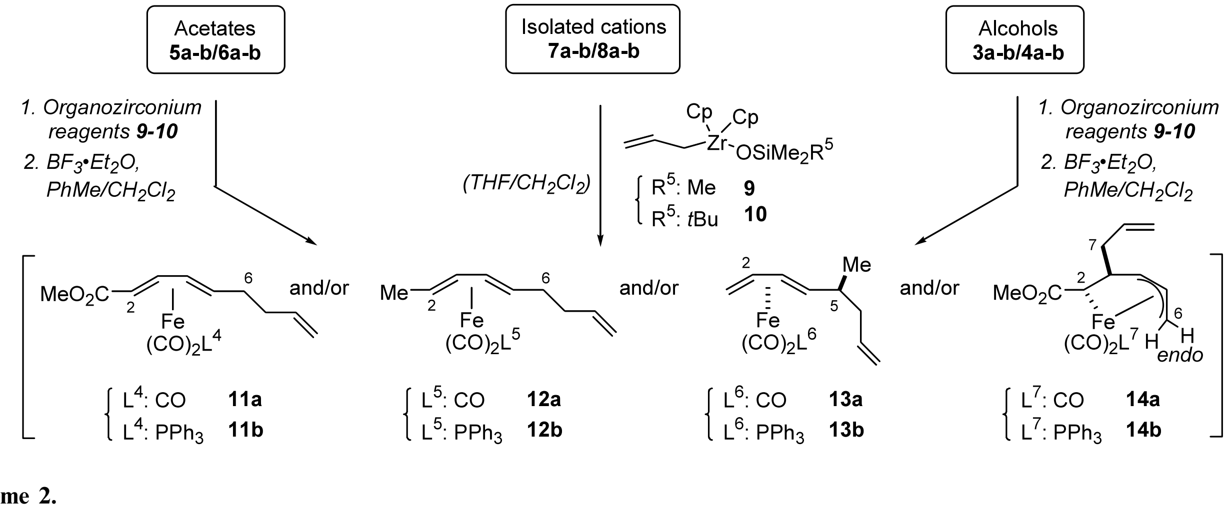
Iron complexed alcohols **3a**–**b**/**4a**–**b**, related acetates **5a**–**b**/**6a**–**b**, and isolated *U*-cations **7a**–**b**/**8a**–**b** (dehydration of alcohols **3a**–**b**/**4a**–**b**; Ac_2O/anhydrous Et_2O, 50% aqueous HBF_4, yield range: 80–91%) have been readily prepared from the two $Fe(CO)_3$-precursors **1** and **2** (Scheme 1). Some of these organometallic compounds have been previously described.[4]

Two experimental protocols have been tested (Scheme 2). First, *isolated cisoid U*-cations **7a**–**b**/**8a**–**b** (1.0 mmol) were reacted with allylzirconocene compounds **9**–**10** (1.0 mmol, CH_2Cl_2/THF, 0°C, 2–3 h). In a second approach, the same cations **7a**–**b**/**8a**–**b** were generated in situ by acid-mediated ionization of precursor alcohols **3a**–**b**/**4a**–**b** or acetates **5a**–**b**/**6a**–**b** (1.0 mmol) using $BF_3\cdot OEt_2$ (2.0 mmol) *in the presence of the same allylzirconocene reagents* **9**–**10** as the trapping nucleophiles (1.0 mmol, PhMe/CH_2Cl_2, 0°C, 2–3 h).

Several interesting conclusions may be drawn from Table 1. The allylzirconocene **10** reacted with the *S*-form of the isolated cation **7a** solely at the unsubstituted less hindered C6 to afford the (2*E*,4*E*)-η^4-dienyl-$Fe(CO)_3$ complex **11a** (40% yield, entry 1). Signals for protons H_3 (^1H NMR, 600 MHz, $CDCl_3$, $\delta = 6.03$ ppm, ddd, $J = 8.5$, 5.0 and 1.0 Hz), H_4 ($\delta = 5.30$ ppm, dd, $J = 8.0$ and 5.0 Hz), *endo*-H_2 ($\delta = 2.18$ ppm, dd, $J = 8.5$ and 1.5 Hz), and *endo*-H_5 ($\delta = 2.71$ ppm, dddd, $J = 9.5$, 8.0, 5.0 and 1.5 Hz), are characteristic of an (*E*,*E*)-conjugated complexed diene.[5]

Contrary to this Zr-based nucleophile, Donaldson reported that allylTMS showed *no diene selectivity* affording an inseparable 1.0/1.6 mixture of **11a** and of its (2*E*,4*Z*)-isomer.[6] Additionally, it is worthy to note that reactions of organocadmium and organo-/alkynyl cuprate *C*-nucleophiles with the same isolated cation **7a** afforded only (2*E*,4*Z*)-condensation complexes while sodiomalonates and alkynyl cerium reagents lead respectively to σ,η^3-π-allyl derivatives and mixtures of σ,η^3-π-allyl derivatives with (2*E*,4*Z*)-complexes.[1c–e]

Interestingly, the allylzirconocene **9**, which is less hindered at the Zr atom (OTMS versus OTBDMS ligand), afforded a 1/5 separable mixture of the same complex **11a** and of the diastereoisomerically pure σ,η^3-π-allyl



Scheme 2.

Table 1. Condensations of allylzirconocene compounds **9**/**10** on to η^5-pentadienyl-cations **7a**–**b**/**8a**–**b**

Entry	*U*-Cation (R^4)	Alcohol (R^2)	Acetate (R^3)	Product	Reagent **9** (%)[a]	Reagent **10** (%)[a]
1	**7a** (CO_2Me)	–	–	**11a**	–	40
2	**8a** (Me)	–	–	**12a**+**13a**: 1/1	–	23[b]
3	**7b** (CO_2Me)	–	–	**14b**	–	88
4	**8b** (Me)	–	–	**13b**	–	80
5	–	**3b** (CO_2Me)	–	**11b**	–	32
6	–	**4b** (Me)	–	**12b**	–	27
7	–	–	**5b** (CO_2Me)	**11b**	–	65
8	–	–	**6b** (Me)	**12b**	–	48
9	**7b** (CO_2Me)	–	–	**14b**	86	–
10	**8b** (Me)	–	–	**13b**	79	–
11	–	–	**5b** (CO_2Me)	**11b**	65	–
12	–	–	**6b** (Me)	**12b**	46	–
13	**7a** (CO_2Me)	–	–	**11a**+**14a**: 1/5	50[b]	–

[a] Yields of isolated pure products.

[b] Complexes **11a** and **14a**, **12a** and **13a** have been isolated and characterized separately.

complex **14a** (50% global yield, entry 13). To the best of our knowledge, the fact that steric hindrance at the metal atom of zirconated *C*-nucleophiles can help to modulate addition regioselectivity is without any precedence. Most likely, compound **14a** resulted from a nucleophilic attack at internal C3 of *U*-**7a** *anti* to the $Fe(CO)_3$ unit.[1d] The highly shielded signals of H_2 (δ = 0.03 ppm, d) and of H_4-H_6 (η^3-σ-allyl system, δ = 4.42, 4.50, 2.46 and 3.54 ppm) have been well characterized by 2D $^1H/^1H$ and 2D $^1H/^{13}C$ homo-/heteronuclear correlations.[1e] ^{13}C NMR signals of the highly shielded C2 (75 MHz, $CDCl_3$, δ = 13.81 ppm) and of carbons C4–C6 (η^3-σ-allyl system, δ = 66.90, 98.33 and 54.95 ppm) confirmed this structure.[1e] The *anti* addition has been unambiguously established in the following way. Preliminary molecular mechanics calculations (PC Model software, 8.0 version, Serena Software, Bloomington, USA) performed on **14a** and its (C2,C3)-*syn* isomer indicated that the *endo* H_6 should be proximal to the C7 methylene solely for **14a**. Confirmation came from a 2D NOESY experiment ($CDCl_3$, 600 MHz) showing strong correlations between this proton and the two H_7 hydrogens.

Condensations of the two allylzirconocene compounds **9** and **10** onto the isolated *U*-cation **7b** were found to be more efficient, independent of the ligand pattern at Zr, and *totally C3 regioselective*, affording the diastereoisomerically pure PPh_3-containing σ,η^3-π-allyl derivative **14b** (entries 3 and 9, **10**: 88% yield, **9**: 86% yield). $^1H/^{13}C$ NMR data similar to those of **14a** as well as 2D $^1H/^1H$ and 2D $^1H/^{13}C$ correlations confirmed its structure. This trend toward better yields and regioselectivities introduced by the PPh_3 ligand[1e] can again be observed when reacting isolated cations *U*-**8a** and *U*-**8b** with reagents **9** and **10**. A 1/1 mixture of 4*E*-disubstituted and diastereoisomerically pure 3*E*-monosubstituted complexes **12a** and **13a**[6] were obtained when allylzirconocene **10** reacted on to isolated *U*-**8a** (entry 2, 23% global yield, **12a**: $J_{H4–H5}$ = 8.0 Hz, **13a**: $J_{H3–H4}$ = 9.0 Hz). These complexes arose most likely from the nucleophilic addition of reagent **10** at the C6 and C2 extremities of the more reactive *S*-form of cation **8a**. Again, ^1H NMR data of complex **13a**, previously obtained by an *anti* addition of allylTMS onto isolated *U*-**8a**, matched our own results.[6] This additional observation ensured the *anti* assignment made along this series.

This same addition performed on the *isolated* PPh_3-containing cation *U*-**8b** was found to be independent of the ligand pattern at zirconium and *totally C2 regioselective*. It afforded the diastereoisomerically pure 3*E*-iron complexed triene **13b** (*anti* addition onto the *S*-form of cation *U*-**8b**, $J_{H3–H4}$ = 8.5 Hz; entries 4 and 10, **10**: 80% yield, **9**: 79% yield).

We next examined our second approach involving *transoid S*-cations **7a**–**b**/**8a**–**b** generated in situ from alcohols **3a**–**b**/**3a**–**b** or acetates **5a**–**b**/**6a**–**b** ($BF_3{\cdot}OEt_2$ activation, Uemura-like conditions[2]) *in the presence of allylzirconocenes* **9**–**10**. When compared to data involving isolated cations, quite different but complementary results were obtained. Surprisingly, the η^4-dienyl-$Fe(CO)_3$ alcohols **3a**–**4a** and acetates **5a**–**6a** did not undergo ionization, even in the presence of $BF_3{\cdot}OEt_2$ in excess (2.0 versus 5.0 equiv., results not shown in Table 1). Most likely, this is due to extra-complexations of $BF_3{\cdot}OEt_2$.

On the contrary, the better cation-stabilizing effect of a PPh_3 ligand can be demonstrated in the $Fe(CO)_2PPh_3$ series versus the $Fe(CO)_3$ one.[1e,4d] For example, alcohols **3b** and **4b** afforded, respectively, the (2*E*,4*E*)-iron complexed trienes **11b** and **12b** in low yields (entries 5 and 6, **11b**: 32%, **12b**: 27%, $J_{H4–H5}$ = 8.0 and 9.0 Hz). As expected in the *transoid* cation series, nucleophilic attack of zirconocene **10** was totally regioselective toward the C6 carbon of *transoid S*-cations **7b** and **8b**. Neither σ,η^3-π-allyl derivative **14b** (entry 3) nor (*3E*)-monosubstituted complex **13b** (entry 4) were detected. Condensation results involving the allylzirconocene reagent **10** were significantly improved when using complexed acetates **5b**/**6b** instead of complexed alcohols **3b**/**4b** as cation precursors (entries 5–6, **10**: **11b**/**12b**: 32%/27% versus entries 7–8, **10**: **11b**/**12b**: 65%/48%). A similar trend in reactivity was also found for the allylzirconocene reagent **9** (entries 11–12, **9**: **11b**/**12b**: 65%/46%).

Finally, the PPh_3-iron complexed methyl ether (1.0 mmol) prepared from **4b** ($CH(OMe)_3$, cat. APTS, CH_2Cl_2, 0°C, 92%) was mixed with OTMS-allyl alcohol (1.0 mmol, PhMe: 8.0 mL) and added with the Negishi reagent (3.0 mmol, 0°C). Formation of the allylic zirconium reagent **9** (3 h, 20°C) occurred *in the presence of the PPh_3-iron complexed cation precursor*. After medium cooling at −78°C, $BF_3{\cdot}Et_2O$ (4.0 mmol) was added to ionize the *O*-methylated complex. The expected nucleophilic addition onto the *S*-shaped cation **8b** generated *in situ* was complete after 30 min at 0°C (TLC monitoring) to selectively afford the (2*E*,4*E*)-$Fe(CO)_2PPh_3$ triene **12b** in a good 87% yield. This result validated conditions resembling the intramolecular variant of those nucleophilic condensations. On-going work towards homochiral medium-sized carbocycles will be reported soon using this synthetic variant.

In conclusion, two nucleophilic allylzirconocene compounds **9** and **10** have been reacted with isolated or *in situ* generated η^5-pentadienyl-$Fe(CO)_3$/$Fe(CO)_2PPh_3(+1)$ cations **7a**–**b**/**8a**–**b** to afford η^4-dienyl- or σ,η^3-π-allyl-$Fe(CO)_3$/$Fe(CO)_2PPh_3$ condensation products, depending on the reaction conditions. If compared to the η^5-pentadienyl-$Fe(CO)_3(+1)$ series, η^5-pentadienyl-$Fe(CO)_2PPh_3(+1)$ cations have been found to react more selectively and more efficiently.[7]

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7. The new compounds have been fully characterized (TLC and/or HPLC, FT-IR, high-field $^1H/^{13}C$ NMR, EI/DCI-MS, microanalyses and/or high-resolution FAB-MS).