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Effect of lithium chloride on allylation of zirconacyclopentadienes

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Abstract—The effects of lithium chloride on the allylation of zirconacyclopentadienes with allylic halides in the presence of CuCl have been studied. It is found that mono-allylation products are formed predominantly in the absence of lithium chloride, while the presence of lithium chloride leads to the formation of di-allylation products.

Zirconacyclopentadienes, which have two metal–sp^2 carbon bonds, are very useful intermediates in organic synthesis. They can be readily prepared in high yields by the reaction of two alkynes or a diyne with reduced zirconium species[1–3] and are frequently used in situ with the salts generated as a result of the reaction. Several reactions of zirconacyclopentadienes with organic halides have been reported. Di-alkylation (involving formation of two C–C bonds)[4] or mono-alkylation (only one C–C bond is formed)[5] products are formed, depending on the type of substrates. However, the effect of salts on the alkylation of zirconacyclopentadienes[6] with organic halides[4a] has not been studied, although the effect of salts on organic and organometallic chemistry is evident.[7]

Takahashi et al. have reported that the reaction of zirconacyclopentadienes **1** with 2 equiv of allylic halides in the presence of CuCl and LiCl gave di-allylation products **2** in high yields.[4a] During the course of our studies[4f] of this allylation reaction, we found that the reaction of zirconacyclopentadienes, prepared using EtMgBr, with 2 equiv of allylic halides and CuCl gave mono-allylation products **3** in the absence of LiCl (Scheme 1).

Our initial goal was to prepare unsymmetrical di-allylation products from unsymmetrical zirconacyclopentadienes. We carried out the allylation of zirconacyclopentadiene **1a**, prepared using ethylmagnesium bromide,[3d] with 2,3-dibromopropene following the procedure reported by Takahashi et al. Unexpectedly mono-allylation product **3a** was obtained in a good yield with high regioselectivity. The reaction conditions were varied by changing the amount of CuCl and 2,3-dibromopropene and also by increasing the reaction temperature; however only mono-allylation was observed. A series of reactions involving different zirconacyclopentadienes prepared from Cp_2ZrCl_2/EtMgBr/alkynes and various allylic halides were carried out. The results are shown in Table 1. It is clear that the mono-allylation reaction proceeded in good yield in most cases.

The major difference between this procedure and the Takahashi procedure was in the preparation of zirconacyclopentadiene. Our procedure generated magnesium bromide as a byproduct while the literature one produced lithium chloride. We deduced that the different salts may have some effect on the formation of the products.

To clarify whether magnesium salt has any effect on the allylation reaction, the magnesium salt, generated from the preparation of zirconacyclopentadiene **1b** using ethylmagnesium bromide, was removed by precipitation with 1,4-dioxane before CuCl and 2,3-dibromopropene were added to the reaction mixture. Mono-allylation product was again formed (Table 2, entry 2). This indicated that the reaction of zirconacyclopentadiene with allylic halide yields mono-allylation product **3b** independent of the magnesium salt.

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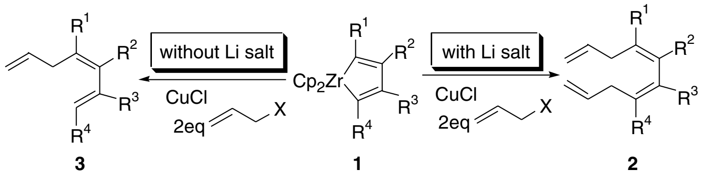
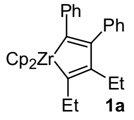
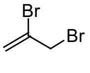
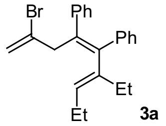
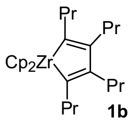
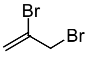
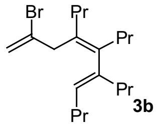
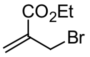
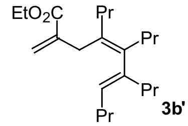
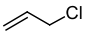
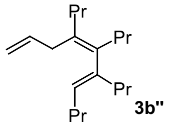
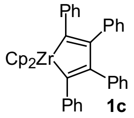
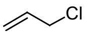
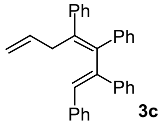
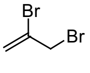
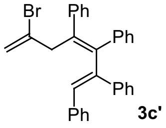
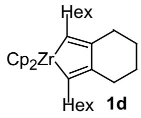
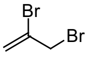
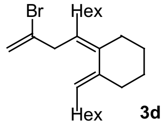


Scheme 1.

Table 1. Formation of mono-allylation products from zirconacyclopentadienes

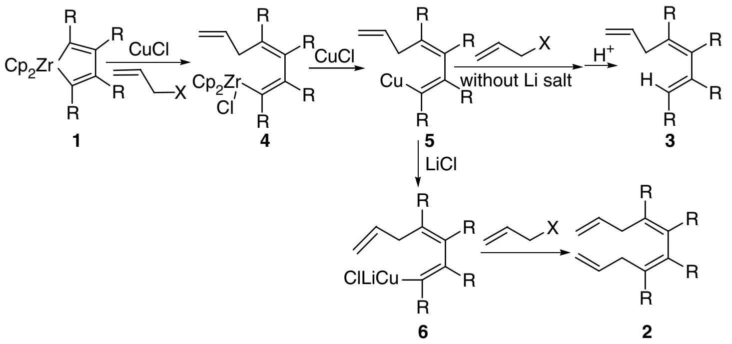
Zirconacyclopentadienes[a]	Allylic halides	CuCl (equiv)	Time (h)	1,4,6-Heptatriene	Yield (%)[b]
 **1a**		1	12	 **3a**	52 (35)
		2	12		50
 **1b**		1	6	 **3b**	62 (45)
		2	6		54[c]
1b		1	6	 **3b'**	78 (62)
1b		0.2	12	 **3b''**	71 (56)
 **1c**		1	12	 **3c**	— (51)
1c		1	12	 **3c'**	— (59)
		2	12		— (57)
 **1d**		1	12	 **3d**	— (25)

[a] All zirconacyclopentadienes were prepared in situ from Cp_2ZrCl_2 + EtMgBr (2 equiv) + alkynes by methods in the literature. All allylation reactions were carried out at room temperature in the presence of CuCl.

[b] GC yields. Isolated yields are shown in parentheses.

[c] Diallylation product 13% (GC yield).

In order to see whether lithium salt has any effect on the allylation, zirconacyclopentadiene **1b** was prepared using Takahashi's method[4a] using *n*-BuLi in THF. LiCl formed as byproduct was removed by changing the solvent from THF to anhydrous ether (LiCl precipitated out upon cooling).[8] The reaction solvent was then



Scheme 2.

Table 2. Effect of metal salt on the allylation of zirconacyclopentadiene **1b**

Entry		Diallylation product (%)[e]	Mono-allylation product **3b** (%)[e]
1[a]	No Li^+ with Mg^{2+}	—	62
2[b]	No Li^+ no Mg^{2+}	—	40
3[c]	No Li^+ no Mg^{2+}	Trace **2b**	45
4[d]	With Li^+ no Mg^{2+}	61% **2b**	—

Unless otherwise noted, zirconacyclopentadiene was prepared in situ from Cp_2ZrCl_2 + EtMgBr (2 equiv) + 4-octyne (2 equiv). All allylation reactions were carried out at room temperature using CuCl, THF, 2 equiv of 2,3-dibromopropened.

[a] Allylation reaction proceed in situ.

[b] Allylation reaction proceed after removing Mg^{2+} by 1,4-dioxane.

[c] Zirconacyclopentadiene was prepared in situ from Cp_2ZrCl_2 + *n*-BuLi (2 equiv) + 4 octyne (2 equiv) in THF. LiCl was removed by changing the solvent from THF to Et_2O and cooling.

[d] Anhydrous LiCl was added after Mg^{2+} had been removed by 1,4-dioxane.

[e] GC yields.

replaced with THF before CuCl and 2,3-dibromopropene were added. Mono-allylation product **3b** was formed as a major product, with only a trace amount of di-allylation product **2b** (entry 3), indicating that lithium salt has a significant effect on the formation of the di-allylation product.

To further confirm the effect of lithium salt on the allylation of zirconacyclopentadienes, **1b** was prepared using EtMgBr, but LiCl was added to the reaction mixture after magnesium salt had been removed. Only di-allylation product was formed (entry 4). The result is consistent with that of the literature procedure, implying that lithium salt has a dramatic effect on the allylation of zirconacyclopentadiene and plays an important role in the formation of the di-allylation product.[4a,f] The experimental results are summarized in Table 2.

Recently the facile transmetallation of Zr–C bonds of zirconacyclopentadiene to give more reactive Cu–C bonds has been reported.[4a,b] Thus, in this work, it is proposed that zirconacyclopentadiene **1** reacted with allylic halide via S_N2' substitution after transmetallation to Cu, to give intermediate **4** (Scheme 2). Then a second transmetallation from Zr to Cu occurred to give **5**. In the presence of lithium chloride, organocopper intermediate **6**[9] may be responsible for the formation of di-allylation product **2**. A possible reason for the formation of di-allylation product may be the increased nucleophilicity and solubility of organocopper compound **6** due to the presence of lithium chloride. In contrast, without lithium salt, organocopper **5** does not undergo a second allylation.

In summary, the reactions of zirconacyclopentadienes with allylic halides in the presence of CuCl and in the absence of lithium salt, give mono-allylation product with or without magnesium salt. Di-allylation products result in the presence of lithium salt, either generated in situ or externally added to the reaction system.

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