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A novel reaction of titanacyclopentenes and aldehydes with or without Lewis acids

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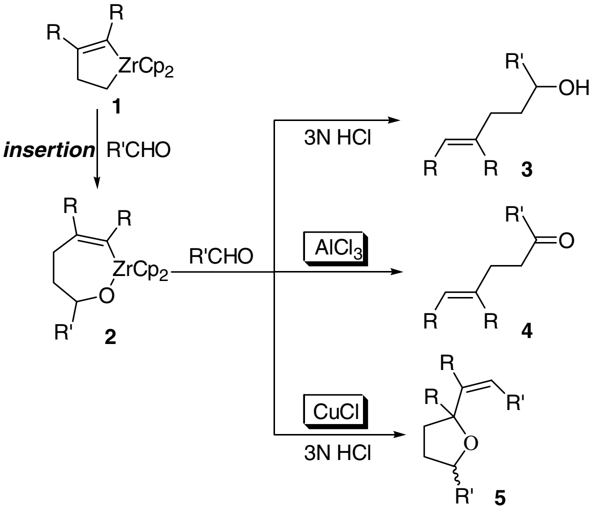
Abstract—Oxatitanacyclopentenes were prepared in high yields from the reaction of aldehydes with titanacyclopenetens via substitution of ethylene. No insertion product was obtained in this reaction. The combination of alkynes and aldehydes played an important role in the successive formation of oxatitanacyclopentenes. Some oxatitanacyclopentenes are very stable and can be purified using column chromatography. The cooperation between Ti and LA led to very different results from that between Zr and LA.

We have recently demonstrated that a combination of transition-metal-mediated C–C bond forming reaction with Lewis-acid-mediated organic transformation is a powerful strategy leading to unprecedented reaction patterns and synthetically useful methodologies.[1–5] Thus, zirconacyclopentenes **1**, prepared in situ from Cp_2ZrEt_2 (Takahashi reagent) and alkynes, reacted with aldehydes via insertion reaction to afford oxazirconacycloheptenes **2**, which gave homoallylic alcohols **3** upon hydrolysis with 3 N HCl.[6,7] However, in the presence of Lewis acids, instead of **3**, homoallyl ketones **4** or tetrahydrofurans **5** were obtained in excellent yields (Scheme 1).[3,4] Prompted by these interesting results,[1–5] we initiated a project on reactions between titanacyclopentenes **6** and aldehydes with or without the presence of Lewis acids, for the following reasons: (1) although Cp_2Zr and Cp_2Ti are both group IV metals, their reactivity are frequently found remarkably different, (2) compared with many reports about the reaction of Cp_2Zr–zirconacyclopentenes,[2–8] few reports have appeared about reactions of Cp_2Ti–titanacyclopentenes,[9–12] an immediate analogy of zirconacyclopentenes. In this Letter, preliminary results about reaction of Cp_2Ti–titanacyclopetenes with aldehydes in the presence and in the absence of Lewis acids are reported.



Scheme 1.

Titanacyclopentenes **6** could be readily prepared in excellent yields from $Cp_2TiCl_2/2EtMgBr$ at −30 °C as demonstrated by NMR and GC.[9c] As shown in Scheme 1, zirconacyclopentenes **1** underwent insertion reaction of aldehydes at 0 °C affording the corresponding seven-

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Keywords: Lewis acid mediated reaction; Indene; Insertion; Titanacyclopentene.

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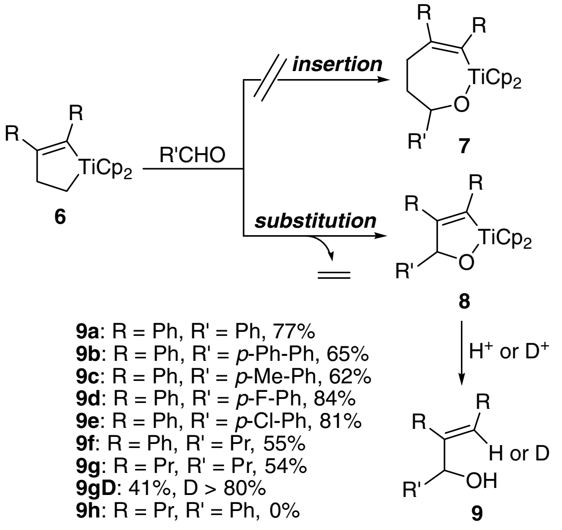
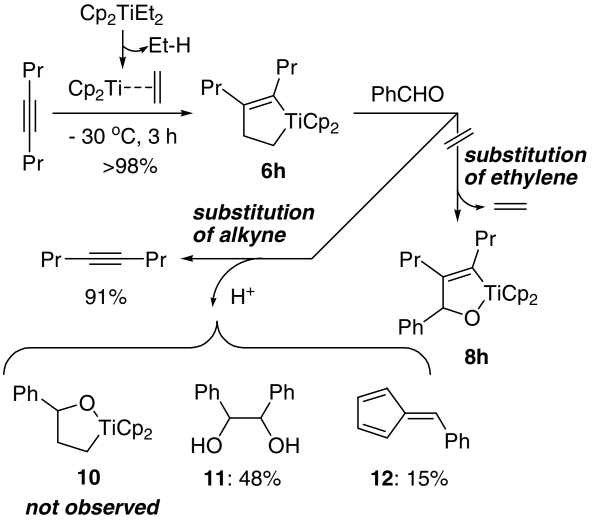


Scheme 2.

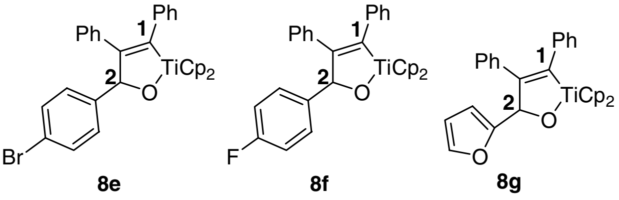
membered zirconacycles **2** in high yields.[6,7] However, surprisingly, titanacyclopentenes **6** did not undergo any insertion reaction with aldehydes under a variety of reaction conditions, including change of reaction temperatures, reaction time, amount of reagents, etc.[12] Instead, substitution reaction of the ethylene molecule by the aldehyde always took place at higher temperatures to afford the five-membered oxatitanacyclopentenes **8** (Scheme 2). Hydrolysis of the reaction mixtures with aqueous 3 N HCl gave their corresponding allylic alcohols **9**.[13] This reactivity is very different from that of its analogous **1**, although **1** could also undergo substitution reaction with aldehydes at higher temperatures.[14] The relatively space-demanding character of Ti is proposed to be responsible for this exclusive substitution reaction. This substitution reaction of **6** with aldehydes affording **8** represents the first example of this kind.

The combination of alkynes and aldehydes was found to be crucial for the formation of oxa-intermediates **8**. For examples, the combination between diphenylacetylene and aromatic aldehydes afforded alcohols (**9a**–**e**) in high to excellent isolated yields. However, the yields of hydrolyzed products **9** were relatively lower in cases of coupling between diphenylacetylene and aliphatic aldehydes (**9f**) or coupling between 4-octyne and aliphatic aldehyde (**9g**, **9gD**). The uttermost case is shown in Scheme 3. When titanacyclopentene **6h** possessing two propyl substituents was treated with aromatic aldehydes, such as PhCHO, totally no coupling product **9h** was obtained. Instead, substitution of the original 4-octyne was completed, regenerating 4-octyne in more than 90% recovered yield. The oxatitanacyclopentane **10** was not obtained either. The pinacol coupling product (**11**) of aldehydes and the fulvene derivative (**12**) formed from an aldehyde and the Cp_2Ti were isolated in 48% and 15% yields, respectively. Although we are not sure about the fate of Cp_2Ti moiety, these results suggest that low-valent Ti species must be formed in the reaction mixture and the coordination mode of Cp ligands must be also changed.[15,16]



Scheme 3.

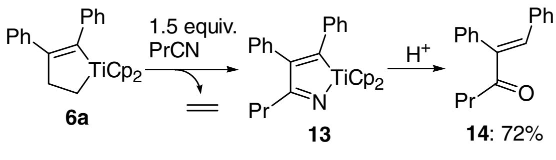
Table 1. Selected NMR data for complexes **8e**–**8g** (unit: ppm)



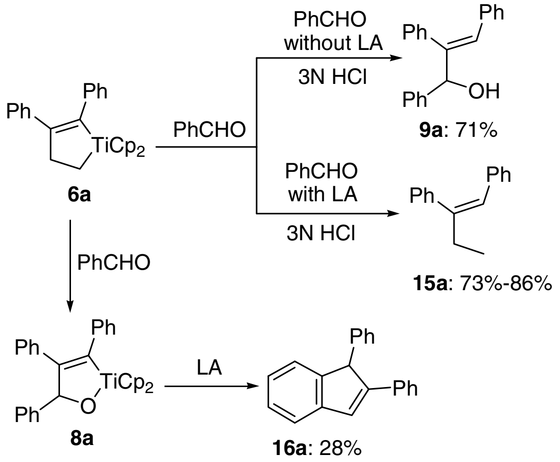
		8e	8f	8g
^{1}H NMR	Cp	6.39, 6.38	6.40, 6.38	6.30, 6.34
	CH-2	6.18	6.20	6.13
^{13}C NMR		**8e**	**8f**	**8g**
	Cp	116.4, 115.4	116.3, 115.3	116.5, 116.1
	C-1	195.8	195.5	196.1
	CH-2	89.8	89.9	82.1

It was interesting to find out that, probably due to the high oxo-philic nature of Ti, several oxatitanacyclopentenes **8** (Table 1. Full NMR data and spectra can be found in the Supplementary data) are very stable, even column chromatograph could be used to purify them. However, they gradually decomposed with time; thus attempts to determine their structures by single-crystal X-ray structural analysis generally failed in vain.[17]

Titanacyclopentenes were found to react also with organonitriles to afford α,β-unsaturated ketones upon hydrolysis. As demonstrated in Scheme 4, **6a** reacted with PrCN via substitution of ethylene to afford azati-



Scheme 4.



Scheme 5.

tanacyclopentadiene **13**, which after long-time hydrolysis (9 h) gave product **14** in 72% isolated yield.[14]

We then carried out reactions of **6a** (R = Ph) with PhCHO in the presence of a variety of Lewis acids, such as $AlCl_3$, $EtAlCl_2$, BF_3, and CuCl. Surprisingly, hydrolysis of the reaction mixtures gave **15a** as the major product in 73–86% isolated yields (Scheme 5). This result is in contrast with the usual activity of adduct of carbonyl compounds with Lewis acids (LA). Insertion products **7** were expected because the aldehyde was activated by forming the adduct. However, this result indicated that even the substitution reaction was blocked. With this information in hand, we first generated oxatitanacyclopentene **8a**, followed by treatment with Lewis acids. The result was again a surprise and gave an indene derivative **16a** in 28% isolated yields along with several unknown products. Although the function of Lewis acids in this reaction is not yet clear, our preliminary results suggest that the cooperation between Cp_2Ti and LA must lead to very different results from that between Cp_2Zr and LA as we already observed.

Further investigation into the reaction chemistry of titanacycles and the Lewis acid-mediated reactions of titanacycles with a variety of organic substrates are in progress.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.06.149.

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