Allenation of Carbonyl Compounds with Alkenyltitanocene Derivatives

Nicos A. Petasis* and Yong-Han Hu

Department of Chemistry and Loker Hydrocarbon Research Institute, University of Southern California, Los Angeles, California 90089-1661

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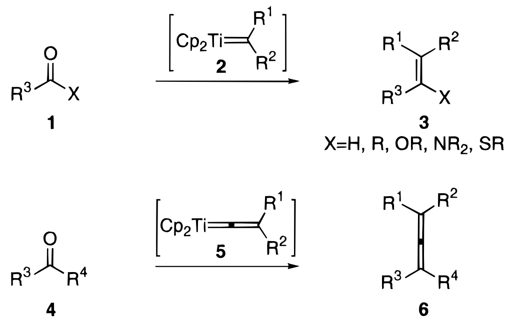
The conversion of carbonyl compounds **1** to olefins **3** via titanocene alkylidene intermediates **2** is an important process with numerous applications in organic synthesis.[1] In recent years, we have been involved with the development of new and practical methods for carrying out this type of titanium-mediated transformation, which is suitable not only for the olefination of aldehydes and ketones but also for heteroatom-substituted carbonyls.[2] Herein we report the analogous conversion of aldehydes and ketones **4** to allenes **6** via a titanocene alkenylidene intermediate **5**.

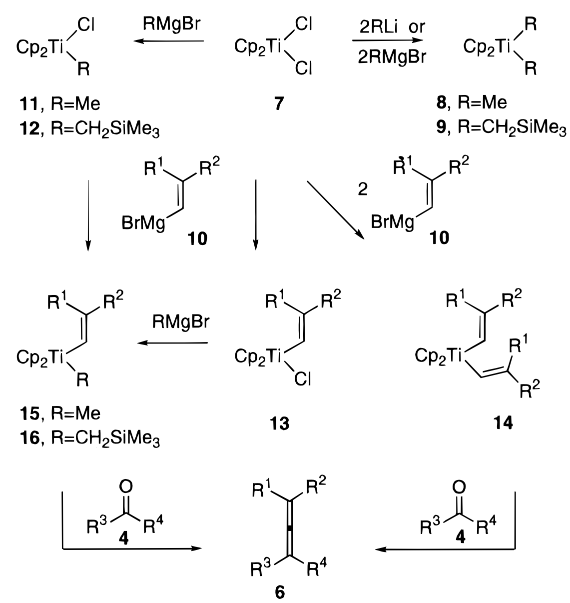


The bis(pentamethylcyclopentadienyl)titanium vinylidene analog of **5** was studied extensively by Beckhaus.[3] Although this species reacted with alkynes[3g] to give the corresponding titanacyclobutenes, when it was reacted with carbonyl compounds it generated a titanocene enolate species instead of allenes.[3d] A similar carbonyl enolization was previously observed with the bis(pentamethylcyclopentadienyl) analog of **2**.[4] In contrast, as described below, carbonyl allenations proceed quite efficiently with the less hindered titanocene alkenylidene intermediate **5**, formed in situ from several alkenyltitanocene precursors.

Although some of the hydrocarbyltitanocenes that we used as precursors of **2** (e.g., **8**,[2a] **9**[2d]) are quite stable at room temperature and can even tolerate air and water, the analogous precursors of **5**, namely the dialkenyl titanocenes **14**, are too unstable and could not be isolated in a similar manner. These compounds, however, prepared from titanocene dichloride (**7**) with 2 equiv of an alkenylmagnesium bromide **10**, could be reacted in situ at 0 °C with carbonyl compounds **4** to give the corresponding allenes (**6**). Similarly, the alkylalkenyl titanocenes **15** and **16**, prepared from the monochloro titanocenes **11**−**13**, were also quite unstable for normal isolation.[5] These mixed derivatives, which could be beneficial in cases involving more valuable alkenyl groups, can be prepared by adding 1 equiv of **10** to preformed **11**[6] or **12**[7] or by the one-pot consecutive addition of 1 equiv of **10** to form **13**, followed by the addition of 1 equiv of the second organomagnesium bromide. Despite the facile decomposition of **14**−**16**, a useful allenation process can still be accomplished if these alkenyl titanocenes are prepared at low temperature and used directly without isolation.[8]

Table 1. Allenation of Carbonyl Compounds with Alkenyltitanocenes 14−16

entry	titanocene			ketone		allene	yield (%)
		R^1	R^2	R^3	R^4		
1	**14a**	H	H	Ph	Me	**6a**	89
2	**14b**	H	Me	Ph	Me	**6b**	83
3	**14c**	Me	Me	Ph	Me	**6c**	79
4	**15a**	H	H	Ph	Me	**6a**	89
5	**15a**	H	H	Ph	Ph	**6d**	86
6	**15b**	H	Me	Ph	Me	**6b**	88
7	**15b**	H	Me	Ph	Ph	**6e**	80
8	**15c**	Me	Me	Ph	Ph	**6f**	85
9	**16a**	H	H	Ph	Me	**6a**	84
10	**16a**	H	H	Ph	Ph	**6d**	89



Tables 1 and 2 show several examples of this chemistry, which gives good yields of allenes from a variety of

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(5) Even the corresponding bis(pentamethylcyclopentadienyl)vinyl titanocenes decompose readily at or below room temperature: Luinstra, G. A.; Teuben, J. H. *Organometallics* **1992**,*11*, 1793.

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(8) Typical procedure (Table 1, entry 2): To a solution of titanocene dichloride (500 mg, 2.0 mmol) in THF (20 mL) stirred at −40 °C under nitrogen was added dropwise 1-propenylmagnesium bromide (8.03 mL, 0.5 M solution in THF, 4.0 mmol). After the mixture was warmed to 0 °C over 1.5 h, acetophenone (0.117 mL, 1.0 mmol) was added, and stirring was continued at rt monitored by TLC. Concentration of the solution (to 1 mL), dilution with hexane (30 mL), removal of the titanocene byproduct by filtration, solvent evaporation, and flash column chromatography (silica, hexane) gave the allene product (120 mg, 83%).

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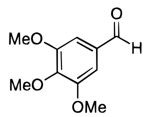
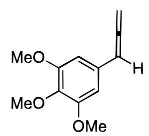
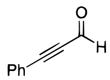
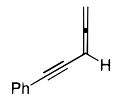
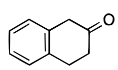
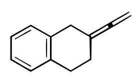
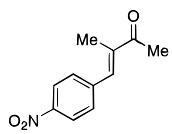
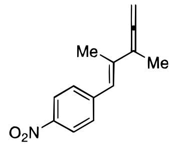
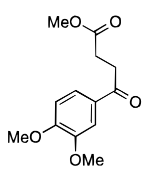
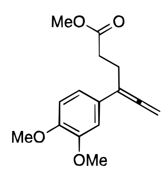
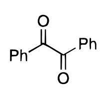
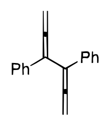
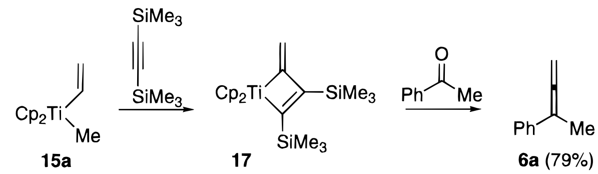
Table 2. Allenation of carbonyl compounds with alkenyl titanocenes 15a and 16a

Entry	Carbonyl Compd	Titanocene	Allene	Yield (%)
1		**15a**		88
2		**16a**		77
3		**16a**		40
4		**15a**		72
5		**16a**		81
6		**15a** (2.2 equiv.)		55

carbonyl compounds.[9] The reaction is quite clean and works well with several types of ketones, including aryl, diaryl, and nitroaryl, as well as α,β-unsaturated carbonyl derivatives and readily enolizable ketones. Moreover, this process selectively allenates ketonic carbonyls in the presence of ester carbonyls (Table 2, entry 5). With 1,2-diketones (Table 2, entry 6), both carbonyls can be allenated to form the corresponding diallene product. Although titanium-mediated olefinations generally work well with esters and lactones,[1,2] the present allenation process is more difficult on these carbonyls, due to facile product decomposition.

The intermediacy of a titanocene vinylidene complex **5** was confirmed by reacting **15a** with bis(trimethylsilyl)-acetylene to form the corresponding titanacyclobutene adduct **17**. Similar to tris(trimethylsilyl)titanacyclobutene,[2g] reaction of **17** with acetophenone gave allene **6a** in good yield.



Overall, this titanium-mediated carbonyl allenation process is a convenient and efficient way to prepare a variety of allenes and may also be suitable for the synthesis of more functionalized derivatives. Unlike other methods for the synthesis of allenes,[10] which often involve multiple steps or form mixtures with alkynes, dienes, or other byproducts, the allenation of carbonyls[11] offers a direct and versatile approach to this increasing useful functionality. While earlier work by Negishi[11a] and Grubbs[11b] has shown the viability of titanium-mediated carbonyl allenations, the method described herein offers a simple and experimentally more convenient approach to this process.

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Supporting Information Available: Additional experimental procedures and spectroscopic data of selected compounds (4 pages).

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(9) All products gave satisfactory spectroscopic and analytical data.

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