J. Am. Chem. Soc. **1995**, *117*, 3881−3882 3881

New, Efficient Method for the Synthesis of Allyltitanium Compounds from Allyl Halides or Allyl Alcohol Derivatives *via* Oxidative Addition. A Highly Efficient and Practical Synthesis of Homoallyl Alcohols

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Received December 16, 1994

Allyltitanium compounds have attracted considerable interest as synthetic reagents because of their advantages in comparison to other allylmetal compounds in terms of chemo-, regio-, diastereo-, and enantioselectivity.[1] η^1-Allyltitanium compounds have been prepared by treatment of L_3TiCl ($L = OR^2$ or $NR_2{}^3$) or L_4Ti ($L = OR$ or NR_2)[4] with allylmetal compounds such as allyllithium and -magnesium compounds. η^3-Allyltitanium compounds of the type $Cp_2Ti(\eta^3\text{-allyl})$ can be synthesized by hydrotitanation of conjugated dienes by Cp_2TiH generated *in situ* by the reaction of Cp_2TiCl_2 with alkyl Grignard reagents or by the reaction of Cp_2TiCl_2 with 2 equiv of allylmetal compounds.[5] Oxidative addition of allyl halides (allyl-X) to $Cp_2Ti(\eta^3\text{-allyl}')$ providing $Cp_2Ti(\eta^1\text{-allyl})X$ compounds was also reported.[6]

Reported here is a new, efficient synthetic method for preparation of allyltitanium compounds from allyl halides or allyl alcohol derivatives by oxidative addition to a titanium(II) compound.

To a mixture of $Ti(O\text{-}i\text{-}Pr)_4$ and 3-halo-1-propene or 2-propen-1-ol derivatives in ether was added 2 equiv of *i*-PrMgBr at −50 °C. After the reaction mixture was stirred for 1 h at −40 to −50 °C, benzaldehyde was added and the reaction mixture was stirred for 30 min to provide 1-phenyl-3-buten-1-ol in the yields shown in Table 1. These results indicated the formation of an allyltitanium compound, and this in turn reacted with benzaldehyde to afford the addition product.

It can be seen from Table 1 that the allyl derivatives which can be used for the reaction include halide, acetate, carbonate, phenyl ether, sulfonate, and phosphate. In regard to starting titanium compounds, in addition to $Ti(O\text{-}i\text{-}Pr)_4$, $ClTi(O\text{-}i\text{-}Pr)_3$ also gave good results, while use of $Cl_2Ti(O\text{-}i\text{-}Pr)_2$ or $TiCl_4$ resulted in a rather low yield. Moreover, the Grignard reagent used affected the reaction yield seriously: *i*-PrMgX (X = Cl or Br) gave an excellent yield, EtMgBr provided a good but somewhat inferior yield, and *n*-PrMgBr resulted in a poor yield under the same reaction conditions and needed a higher reaction temperature to get an excellent yield, while *i*-BuMgBr did not afford the product even under strained conditions.

Table 1. Synthesis of an Allyltitanium Compound and Its Reaction with Benzaldehyde Leading to 1-Phenyl-3-buten-1-ol[a]

reactn conditns			
starting compds			
X in $CH_2{=}CHCH_2X$	Ti compd	Grignard reagent	1-phenyl-3-buten-1-ol % yield[b]
Br	$Ti(O\text{-}i\text{-}Pr)_4$	*i*-PrMgBr	94
Br	$ClTi(O\text{-}i\text{-}Pr)_3$	*i*-PrMgBr	92[c]
Br	$Cl_2Ti(O\text{-}i\text{-}Pr)_2$	*i*-PrMgBr	12[c]
Br	$TiCl_4$	*i*-PrMgBr	20[c]
Br	$Ti(O\text{-}i\text{-}Pr)_4$	*i*-PrMgCl	93
Br	$Ti(O\text{-}i\text{-}Pr)_4$	EtMgBr	72[c]
Br	$Ti(O\text{-}i\text{-}Pr)_4$	*n*-PrMgBr	10[c] (93)[c,d]
Br	$Ti(O\text{-}i\text{-}Pr)_4$	*i*-BuMgBr	trace
I	$Ti(O\text{-}i\text{-}Pr)_4$	*i*-PrMgBr	96
Cl	$Ti(O\text{-}i\text{-}Pr)_4$	*i*-PrMgBr	92
OAc	$Ti(O\text{-}i\text{-}Pr)_4$	*i*-PrMgBr	61
OC(O)OEt	$Ti(O\text{-}i\text{-}Pr)_4$	*i*-PrMgBr	74
OPh	$Ti(O\text{-}i\text{-}Pr)_4$	*i*-PrMgBr	89
OTs	$Ti(O\text{-}i\text{-}Pr)_4$	*i*-PrMgBr	57
$OP(O)(OEt)_2$	$Ti(O\text{-}i\text{-}Pr)_4$	*i*-PrMgBr	83

[a] All reactions were carried out using 1.0 equiv of allylic compound, 1.0 equiv of titanium compound, 2.0 equiv of Grignard reagent, and 0.7 equiv of benzaldehyde. An allyltitanium compound was prepared at −50 to −40 °C (1 h), and then benzaldehyde was added at −40 °C unless stated otherwise. [b] Isolated yield based on benzaldehyde. [c] Yield was determined by 300 MHz ^{1}H-NMR analysis of the crude product using an internal standard. [d] An allyltitanium compound was prepared at −25 to −15 °C (1 h), and then benzaldehyde was added at −15 °C.

There are many precedents in the synthesis of allyl organometallic compounds by the reaction of low-valent metal compounds with allyl halides and in their application in organic synthesis.[7] To a lesser extent, the synthesis of allylmetal compounds as nucleophilic species from allyl acetates,[8] allyl phosphates,[9] allyl sulfonates,[10] allyl ethers,[11] and allyl alcohols[12] has also been reported. The synthesis of nucleophilic allylmetal compounds from allyl carbonates, however, has not been reported. From a synthetic point of view, the result that an allyl acetate and a carbonate provide an allyltitanium compound is especially noteworthy, because various kinds of regio- and stereodefined allyl acetates and carbonates can be prepared from readily available allyl alcohols.

Table 2 summarizes the results of the reaction using a variety of allylic and carbonyl compounds. It can be seen from Table 2 that various kinds of allyltitanium compounds can be readily prepared from the corresponding allylic compounds, including those containing a functional group which are not accessible by transmetalation using organolithium or -magnesium compounds (entries 17 and 18), and thus opens a way to prepare a variety of homoallylic alcohols by successive treatment with aldehydes or ketones.

It can also be seen from Table 2 that the reaction of benzaldehyde with the titanium compound derived from either 2-buten-1-yl ethyl carbonate or 1-buten-3-yl ethyl carbonate provided, irrespective of the starting carbonate, only the corresponding β-methylhomoallyl alcohol with a *anti*:*syn* ratio of 75:25, and the latter gave the better yield (entries 10 and 11). The tendency of α-substituted allylic carbonates to give better yields than γ-substituted allylic carbonates was more remarkable in the case of 3-phenyl-2-propenyl *vs* 1-phenyl-2-

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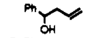
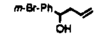
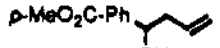
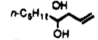
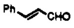
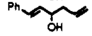
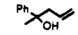
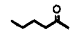
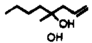
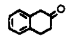
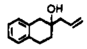
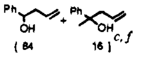
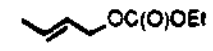
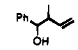
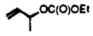
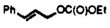
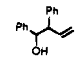
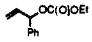
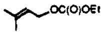
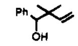
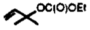
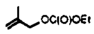
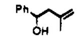
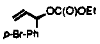
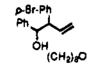
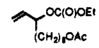
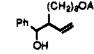
Table 2. Synthesis of Homoallylic Alcohols Using a Variety of Allylic and Carbonyl Compounds[a]

entry	allylic compound	carbonyl compound	product	% yield[b]	(*anti* : *syn*)[c]
1		PhCHO		94	
2		*m*-Br-PhCHO		80	
3		*p*-MeO$_2$C-PhCHO		77	
4		*n*-C$_5$H$_{11}$CHO		87	
5				88	
6				85	
7				82	
8				92	
9[d]		PhCHO + 	 (84 16)[c,f]	91[e]	
10		PhCHO		50	(75 : 25)[g]
11		PhCHO		74	(75 : 25)
12		PhCHO		23	(>97 : 3)
13		PhCHO		73	(>97 : 3)
14		PhCHO		12	
15		PhCHO		56	
16		PhCHO		45 (73)[h] (94)[i]	
17		PhCHO		83	(>97 : 3)
18		PhCHO		76	(77 : 23)

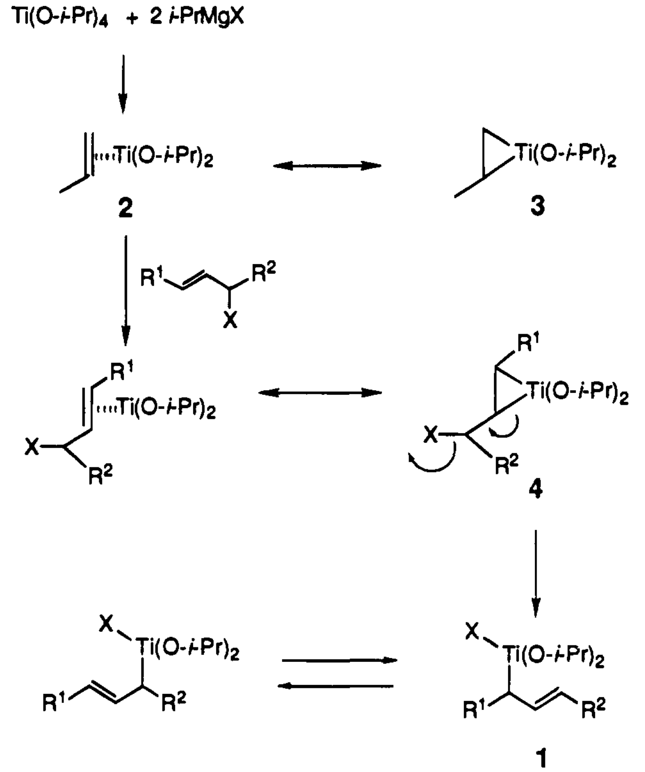
[a] Reaction conditions: allylic compound:Ti(O-*i*-Pr)$_4$:*i*-PrMgBr:carbonyl compound = 1.0:1.0:1.9−2.0:0.7 was used. An allyltitanium compound was prepared at −50 to −40 °C (1 h), and then a carbonyl compound was added at −40 °C. [b] Isolated yield unless stated otherwise, and based on the carbonyl compound. [c] Determined by 300 MHz ^{1}H-NMR analysis of the crude product. The relative stereochemistry was determined as shown in ref 15. [d] To an equimolar mixture of the carbonyl compounds was added a solution of the allyltitanium compound (1 equiv) at −78 °C. [e] Yield was determined by 300 MHz ^{1}H-NMR analysis of the crude product using an internal standard. [f] The ratio 84:16 was reported for the reaction of $H_2C{=}CHCH_2Ti(O\text{-}i\text{-}Pr)_3$ prepared by the transmetalation reaction of ClTi(O-*i*-Pr)$_3$ with $H_2C{=}CHCH_2MgCl$.[1a,c] [g] The ratio 80:20 was reported for the reaction of $CH_3CH{=}CHCH_2Ti(O\text{-}i\text{-}Pr)_3$ prepared by the transmetalation reaction.[16] [h] Allylic compound:Ti(O-*i*-Pr)$_4$:*i*-PrMgBr:PhCHO = 2.0:1.0:2.0:0.7 was used. [i] Allylic compound:Ti(O-*i*-Pr)$_4$:*i*-PrMgBr:PhCHO = 1.0:2.3:4.6:0.7 was used.

propenyl carbonate (entry 12 *vs* 13) and also 3-methyl-2-buten-1-yl *vs* 2-methyl-3-buten-2-yl carbonate (entry 14 *vs* 15). These results, indicating that the same allyltitanium compounds were obtained from γ- and α-substituted allylic substrates but the latter afforded better yields, gave some insight into the reaction mechanism (*vide infra*).

It should be noted that the allylic titanium compounds thus synthesized showed reactivity similar to those obtained by the reaction of ClTi(O-*i*-Pr)$_3$ with allyllithium or -magnesium compounds.[2] Thus, they afforded the addition products in excellent yields by the reaction with not only aldehydes and simple ketones (entries 1, 4, 6, and 7 in Table 2) but also enolizable ketones (entry 8), and they underwent 1,2-addition with α,β-unsaturated carbonyl compounds (entry 5). Moreover, they showed high chemoselectivity (entries 2, 3, and 9) and good diastereoselectivity (entries 10, 12, 17, and 18).

It has been shown that the reaction of alkyl Grignard reagents with alkanoic acid methyl esters in the presence of Ti(O-*i*-Pr)$_4$ or ClTi(O-*i*-Pr)$_3$ produces substituted cyclopropanols, and the process is proposed to be mediated by the titanacyclopropane intermediate **3**.[13]

Scheme 1



1

Thus, although the precise structure of the allyltitanium compounds derived here and the reaction mechanism to lead to them must await further study, the results obtained here can be explained by the formation of η^1-allyltitanium compound **1** according to the mechanism shown in Scheme 1. The reaction of Ti(O-*i*-Pr)$_4$ with 2 equiv of *i*-PrMgBr furnishes the corresponding (η^2-olefin)titanium complex **2**, which can also be regarded as titanacyclopropane complex **3**. Further, the olefin exchange with allyl compounds added leads to new titanacyclopropane **4**, which is followed by β-elimination to afford **1**.[14] The exchange step might be sensitive to the steric accessibility of the double bond of allylic compounds, and sterically more hindered substrates resulted in lower yields, as observed in entries 10 *vs* 11, 12 *vs* 13, and 14 *vs* 15.

In summary, we have developed a highly efficient method for the synthesis of a variety of allyltitanium compounds, including those having functional groups, by the reaction of allylic halides or allylic alcohol derivatives with Ti(O-*i*-Pr)$_4$/2 *i*-PrMgBr reagent, which opens up a practical way to prepare various kinds of homoallylic alcohols. We are continuing to investigate the scope of these reactions, with special regard to the functional group compatibility of the reaction. We are also conducting the reaction of Ti(O-*i*-Pr)$_4$/2 *i*-PrMgBr, a synthetically practical Ti(II)-equivalent reagent, with unsaturated compounds other than allylic compounds such as alkynes and propargyl alcohol derivatives.

Supplementary Material Available: Experimental and spectral data for the new compounds (2 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

JA944047U

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[14] A similar reaction mechanism was proposed for the preparation of allylzirconium compounds by the reaction of Cp$_2$Zr(*n*-Bu)$_2$ with allyl ethers; see ref 11.

[15] Stereochemistries of the products were determined in comparison with the spectral data in the literatures. For entries 10 and 11, see ref 9a. For entries 12 and 13: Coxon, J. M.; Simpson, G. W.; Steel, P. J.; Trenerry, V. C. *Aust. J. Chem.* **1984**, *37*, 65. For entries 17 and 18, stereochemistries of the products were speculated in analogy with other compounds.

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