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An Efficient Method for Conversion of 1-Alken-3-yl Carbonates to 1-Alkenes and 3-Chloro-1-alkenes *via* Allyltitaniums

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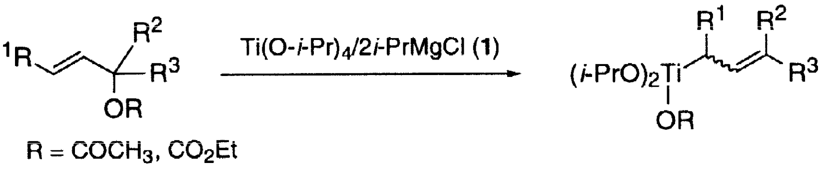
Abstract

Hydrolysis and halogenolysis of the allyltitaniums derived from allylic carbonates and a $Ti(O\text{-}i\text{-}Pr)_4$ / 2 i-PrMgCl reagent proceed with high regio- and stereoselectivity, thus providing an efficient method for converting 1-alken-3-yl carbonates to 1-alkenes or 3-chloro-1-alkenes.

Keywords: titanium and compounds; alkenes; halogens and compounds; steroids and sterols

Use of allyltitanium complexes as a nucleophilic reagent in organic synthesis has attracted much interest. However, the synthetic application so far reported has been limited to their addition reactions to carbonyl compounds and imines which proceed highly selectively [1]. The paucity of relevant data on the reaction of allyltitaniums with electrophiles other than carbonyl compounds and imines is probably due to the fact that allyltitaniums have been usually prepared by transmetallation reaction using the corresponding organolithium or -magnesium compounds, and it has been considered that it offers no definite synthetical advantage to carry out the reaction after the transmetallation to titanium. Recently, we have developed a direct method for synthesizing allyltitaniums from readily available allylic alcohol derivatives [2]. Thus, the reaction of a $Ti(O\text{-}i\text{-}Pr)_4$ / 2 i-PrMgX (X = Cl or Br) reagent (**1**) with allylic carbonates or acetates proceeds *via* an oxidative addition pathway to furnish allyltitanium complexes in excellent yields (eq 1). With this direct and easy access to a variety of allyltitaniums, we thought that the reaction with electrophiles other than carbonyl compounds and imines might prove worthwhile from the synthetic viewpoint [3]. Reported here are the results of the hydrolysis and halogenolysis (eq 2, Table 1).



(1)

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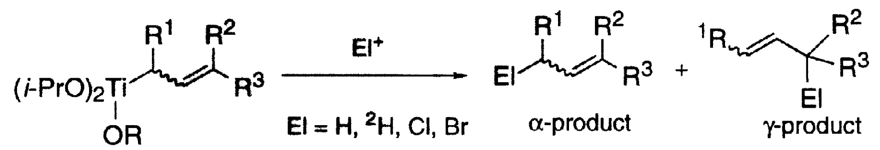
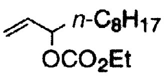
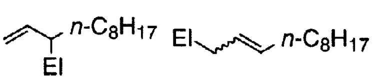
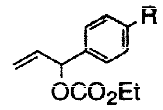
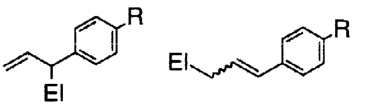
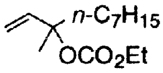
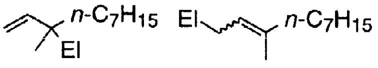
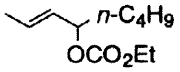
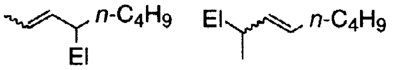
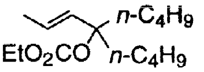
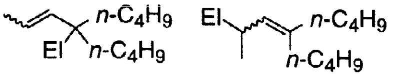


(2)

After the reaction of **1** with ethyl 1-undecen-3-yl carbonate, the reaction mixture was quenched with aqueous HCl to afford 1-undecene (γ-protonated product) and 2-undecene (α-protonated product) in a ratio of 92:8 in excellent combined yield (entry 1 in Table 1). Naturally, [3-^{2}H]-1-undecene was obtained highly predominantly by quenching the reaction mixture with ^2H_2O (entry 2). Meanwhile, treatment of the reaction mixture with NCS provided γ- and α-chlorinated products in a ratio of 95:5 in 77% combined yield (entry 3). The reaction with Br_2 or NBS, however, resulted in rather low regioselectivity (entries 4 and 5); this might be due to the isomerization of the resulting α-brominated product to γ-

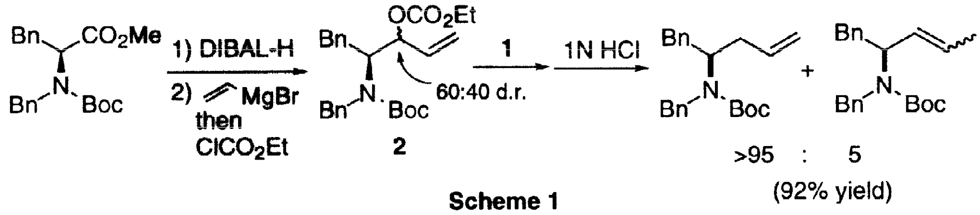
Table 1. Hydrolysis and Halogenolysis of Allyltitanium Compounds[a]

Entry	Substrate	Electrophile	Products		
				Regioselectivity[b] γ- : α-product	Yield, %[c]
					
1		H_2O	El = H	92 : 8	86
2		^2H_2O	El = ^{2}H	92 : 8	84[d]
3		NCS	El = Cl	95 : 5	77
4		Br_2	El = Br	50 : 50	~80[e]
5		NBS	El = Br	75 : 25	~80[e]
					
6	R = H	H_2O	El = H	96 : 4	87
7	R = H	^2H_2O	El = ^{2}H	96 : 4	84[d]
8	R = I	1N HCl	El = H	96 : 4	71
					
9		H_2O	El = H	92 : 8	80
10		^2H_2O	El = ^{2}H	92 : 8	75[d]
11		NCS	El = Cl	95 : 5	81[e,f]
12		H_2O	El = H	 50 : 50	51[g]
13		H_2O	El = H	 85 : 15	~30[e,g]

[a] Reaction procedure: A mixture of the substrate (1.0 mmol), Ti(O-*i*-Pr)$_4$ (1.5 mmol) and *i*-PrMgCl (2.8 mmol) in ether (8 mL) was stirred for 2~3 h at -50~-40 °C. After cooling to -78 °C, aqueous 1N HCl (3 mL) for hydrolysis, ^2H_2O (0.5 mL) for deuterolysis, or halogenating reagent (1.5 mmol) for hologenolysis was added and the resulting mixture was warmed to 0 °C over 1~2 h. After addition of 1N HCl (6 mL), usual extractive workup followed. [b] Determined by 300 MHz ^{1}H NMR and/or GC analysis. [c] Total isolated yield after column chromatography unless otherwise indicated. [d] >95% ^{2}H. [e] NMR yield determined using an internal standard. [f] Owing to somewhat low stability on column chromatography, pure compounds could not be isolated. [g] Starting allylic carbonate was recovered in 20% yield for entry 12 and 11% yield for entry 13.

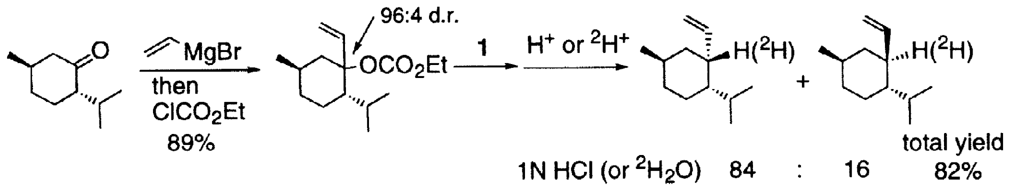
brominated ones *via* 1,3-allylic rearrangement [4]. Similarly, 3-aryl-1-propene (entries 6 and 8) and their deuterated derivatives (entry 7) were obtained highly selectively from ethyl 1-aryl-2-propen-1-yl carbonate *via* the corresponding allyltitaniums [5] A similar regioselection was observed with a carbonate of tertiary allyl alcohol. Thus, the reaction of **1** with ethyl 3-methyl-1-decen-3-yl carbonate afforded highly predominantly a γ-protonated or -deuterated product by the hydrolysis or deuterolysis (entries 9 and 10), and a γ-chlorinated product after the reaction with NCS (entry 11). Since allyltitaniums are readily isomerized *via* 1,3-rearrangement, hydrolysis of 1,3-disubstituted allyltitaniums derived from the secondary allylic carbonate having an internal double bond afforded two olefinic regioisomers in almost equal amounts (entry 12). Meanwhile, the hydrolysis of 1,3,3-trisubstituted allyltitaniums derived from the corresponding tertiary allylic carbonate proceeded with rather good regioselectivity, but is not so attractive from a synthetic viewpoint, to afford the γ-protonated product mainly (entry 13). Thus, in conclusion, a new highly selective one-pot method for converting 1-alken-3-yl carbonates to 1-alkenes [6,7] and 3-chloro-1-alkenes has been developed. The following features are especially noteworthy: (i) 1-Alkenes having ^{2}H at the C-3 position can easily be synthesized. (ii) The method allows access to tertiary allylic chlorides, selective preparation of which by existing procedures is difficult [8].

Since the starting allylic carbonates can be obtained readily from the corresponding carbonyl compounds and a vinyl Grignard reagent, the present method might find varied utility in organic synthesis, and reported next are a few further applications. Scheme 1 demonstrates the derivatization of amino acid to 4-amino-1-alkene. Thus, *N*-protected phenylalanine was converted into carbonate **2** in 72% yield by the conventional procedure, and which, in turn, was treated with **1** to provide, after hydrolysis, the corresponding 4-amino-1-alkene in 92% yield.



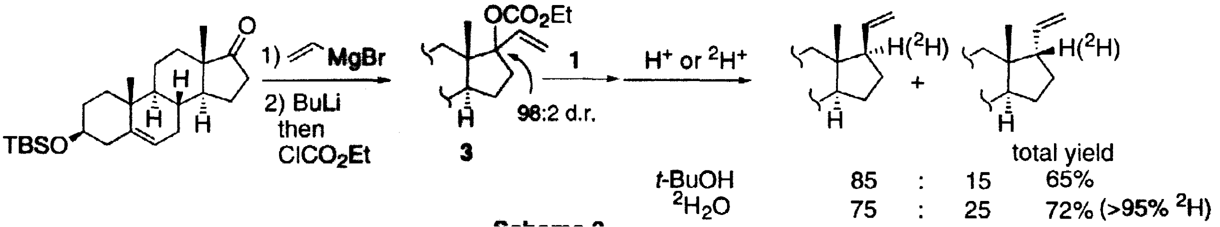
Scheme 1

The synthetic transformations summarized in Schemes 2 and 3 show that the reaction can be used for diastereoselective introduction of a vinyl moiety onto a five- or six-membered substituted cycloalkanone ring by using the carbonyl moiety as a clue. Thus, starting from *l*-menthone, (1*S*,2*R*,3*R*)-1-isopropyl-2-vinyl-4-methylcyclohexane was obtained highly selectively (Scheme 2) [9]. Noteworthy here is the fact that use of a bulky



Scheme 2

proton source such as *t*-BuOH rather than H_2O for the hydrolysis afforded higher diastereoselectivity. Similarly, the reaction with the carbonate **3**, prepared from the *t*-butyldimethylsilyl ether of dehydroepiandrosterone, afforded the *t*-butyldimethylsilyl ether of pregna-5,20-diene-3β-ol [10] selectively after hydrolysis [11,12] Although the diastereoselectivity is not so high in this case, it should be noted that the ^2H-labeled steroid derivative can readily be synthesized by quenching with ^2H_2O.



Scheme 3

The regiochemistry of the hydrolysis and halogenolysis of allyltitaniums observed here can be explained as follows. The hydrolysis proceeds through the coordination of the H_2O to the titanium and the following S_E2'-type cleavage through a cyclic 6-membered transition state (Fig. 1, **a**) [13] Meanwhile, the chlorination with NCS proceeds according to the S_E2' mechanism *via* a halogenium cation intermediate (Fig. 1, **b**) [14].

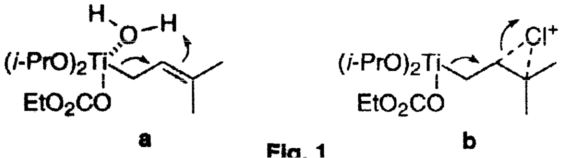


Fig. 1

References and Footnotes

[1] Reetz MT. Organotitanium Reagents in Organic Synthesis, Berlin/Heidelberg: Springer-Verlag, 1986. Yamamoto, Y.; Asao, N. *Chem. Rev.* 1993;93:2207-2293.

[2] (a) Kasatkin A, Nakagawa T, Okamoto S, Sato F. J. Am. Chem. Soc. 1995;117:3881-3882. (b) Gao Y, Sato F. J. Org. Chem. 1995;60:8136-8137. (c) Kasatkin A, Sato F. Angew. Chem., Int. Ed. Engl. 1996;35:2848-2849. (d) Hikichi S, Gao Y, Sato F. Tetrahedron Lett. 1997;38:2867-2870. (e) Teng X, Kasatkin A, Kawanaka Y, Okamoto S, Sato F. Tetrahedron Lett. 1997;38:8977-8980.

[3] For the reaction with aldehydes, see references 2a, 2c, 2d and 2e. For the reaction with imines, see references 2b and 2d.

[4] Valkanas G, Waight ES. J. Am. Chem. Soc. 1959:2720-2727 and references cited therein.

[5] The reaction with NCS afforded a mixture of α- and γ-chlorinated products in a variable ratio because of instability of the resulting 3-chloro-3-aryl-1-propene which can easily rearrange to 1-chloro-3-aryl-2-propenes even under neutral conditions. See, ref. 4.

[6] For metal-catalyzed or -mediated regioselective conversion of allylic alcohol derivatives to alkenes, see: Pd-catalyzed reduction; (a) Tsuji J, Minami I, Shimizu I. Synthesis, 1986:623-627. (b) Mandai T, Suzuki S, Murakami T, Fujita M, Kawada M, Tsuji J. Tetrahedron Lett. 1992;33:2987-2990. (c) Mandai T, Matsumoto T, Kawada M, Tsuji J. J. Org. Chem. 1992;57:6090-6092. (d) Mandai T, Matsumoto T, Kawada M, Tsuji J. Tetrahedron, 1994;50:475-486. Protonation of allylsamariums; (e) Tabuchi T, Inanaga J, Yamaguchi M. Tetrahedron Lett. 1986;27:601-602. (f) Yoshida A, Hanamoto T, Inanaga J, Mikami K. Tetrahedron Lett. 1998;39:1777-1780.

[7] Hydrolysis of allylzirconium compounds derived from allylic ethers and $Cp_2Zr(\eta^2$–butene) was reported to afford a mixture of two possible regioisomers. See: Ito H, Taguchi T, Hanzawa Y. Tetrahedron Lett. 1992;33:1295-1298.

[8] To the best of our knowledge, selective synthesis of tertiary allylic halides has not been reported.

[9] Stereochemistry of the products was assigned based on ^1H NMR analysis.

[10] Pregna-5,20-diene-3β-ol was identified as the aglycone of muricin from the Pacific gorgonian *Muricea fruticosa*, which displayed antifungal activity and specific inactivation of rabbit and rat liver cytochromes P-450. (a) Bandurraga MM, Fenical W. Tetrahedron, 1985;41;1057-65. (b) Dawe RD, Wright JLC. Can. J. Chem. 1987;65:666-669. (c) Halpert J, Jaw JY, Balfour C. Mol. Pharmacol. 1988;34:148-156.

[11] The 17*R* (17β) configuration of the major product was confirmed by converting to the known pregna-5,20-diene-3β-ol by treatment with aqueous HCl and comparison of its ^1H NMR data with those reported in the literature (ref. 10b).

[12] Diastereoselective Pd-catalyzed reduction of a similar substrate providing the corresponding 1-alkene has been reported, see ref. 6b.

[13] A similar transition state model as that shown in Fig. 1 has been used for explanation of the regioselective hydrolysis of allylsamarium compounds. See ref. 6f.

[14] Similar S_E2' halodemetallation reactions of allenylstannyl compounds have been reported. Cochran JC, Kuivila HG. Organometallics, 1982;1:97-103 and references cited therein.