Reaction of Vinyltitanium(IV) Species Prepared by the Alkylation of Titanium–Vinylcarbene Complexes

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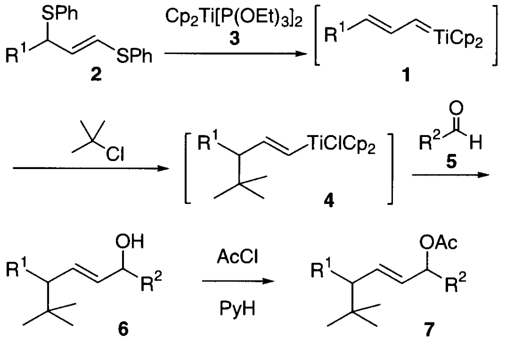
Vinyltitanium(IV) species prepared by the alkylation of titanium–vinylcarbene complexes with *tert*-butyl chloride reacted with aldehydes to give allylic alcohols. The reaction of vinyltitanium species with terminal alkynes produced conjugated dienes, in which a vinyl group regioselectively bonded to the unsubstituted side of carbon–carbon triple bond.

Reactions of organotitanium reagents have been studied and employed as useful synthetic tools because of their characteristic reactivities.[1] For example, alkyltitanium reagents are capable of differentiating between aldehydes and ketones leading to the formation of secondary alcohols on treatment with keto aldehydes.[2] Allyltitanium reagents are used for the stereoselective preparation of *anti*-homoallyl alcohols.[3] On the contrary, the chemistry of vinyltitanium species has not been fully studied yet. As for the addition to carbonyl compounds, it remains unclear whether vinyltitanium reagents react with carbonyl compounds regardless of their ligands other than vinyl group. Seebach et al. reported that they were unable to add non-heterosubstituted vinyltitanium reagent to carbonyl compound.[4] On the other hand, recently Sato and co-workers reported that the trimethylsilyl group substituted vinyltitanium species prepared by the protonation of titanacyclopropene[5] and bicyclic alkoxytitanacyclopentenes[6] reacted with various electrophiles including aldehydes. Taguchi et al. also reported the reaction of the vinyltitanium intermediate formed by the intramolecular carbotitanation of the titanium enolate of alkynylmalonate with benzaldehyde.[7]

The thermal stability of vinyltitanium reagents is another issue of crucial importance for their use in organic synthesis. Cyclohexenyltriisopropoxytitanium was found to be thermally unstable and form the oxidative coupling product upon warming above –60 °C.[4] It is also known that unsubstituted trichlorovinyltitanium is thermally unstable and decomposes above –30 °C.[8] On the contrary, Cardin and Norton reported that trichloro(2-methyl-1-phenylprop-1-enyl)titanium was thermally stable and survived without decomposition for 3 h at 65 °C and for 0.5 h at 80 °C.[9] However the reactivity of their vinyl titanium reagent has not been studied yet.

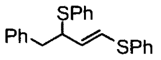
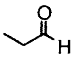
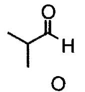
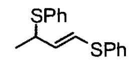
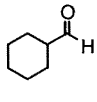
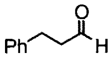
In the course of study on the reactions of titanium–carbene complexes,[10] we found that titanium–vinylcarbene complexes **1**, formed by the desulfurization of 1,3-bis(phenylthio)propene derivatives **2** with the low-valent titanium species $Cp_2Ti[P(OEt)_3]_2$ **3**, reacted with *tert*-alkyl chlorides to form terminal olefins regioselectively.[11] On the basis of the fact that the deuterium was incorporated at the terminal sp^2 carbon when the reaction was quenched with D_2O, we tentatively assume that the vinyltitanium species **4** is formed as an initial product. Considering the uncertainty of the reactivity of vinyltitanium species described above, we have studied the reactions of the intermediary organotitanium species with various organic compounds. Here we wish to describe the results of their addition to aldehydes and alkynes.

Desulfurization of 4-phenyl-1,3-bis(phenylthio)but-1-ene (**2a**) with titanocene(II) reagent **3** (3.5 equiv) at 0 °C for 10 min produced the vinyl carbene complex. After the treatment of the carbene complex with *tert*-butyl chloride (2 equiv) at 0 °C for 30 min, the resulting organotitanium species was further treated with propionaldehyde **5a** (1 equiv / 0 °C; 30 min then room temperature; 1 h) to produce the allylic alcohol **6a** which was isolated as the acetate **7a** (AcCl; 4 equiv / PyH / room temperature; 1.5 h) in 49% overall yield from **2a** (Scheme 1). In a similar manner, the reactions of several vinylcarbene complexes with aliphatic aldehydes were performed. In all the cases examined, the allylic acetates were obtained in reasonable overall yields (Table 1). The NMR spectra of these compounds indicate that they consist of only *E*-isomers. On the other hand, it was found that the allylic alcohol **6** was not produced by the reaction of **4** with benzaldehyde.



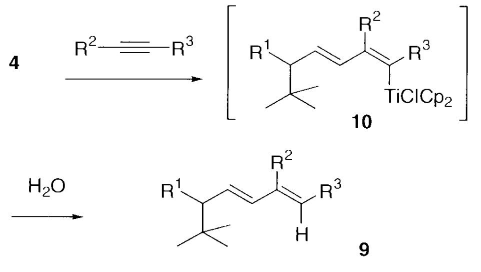
Scheme 1.

Table 1. Reaction of Vinyltitanium **4** with Aldehydes **5**

Entry	1,3-Bis(phenylthio)-alkene **2**	Aldehyde **5**		Product **7** (Yield[a] / %; Ratio of diastereomers)
1	 **2a** (*E* only)		**5a**	**7a** (49; 69 : 31)
2	**2a**		**5b**	**7b** (48; 68 : 32)
3	 **2b** (*E* : *Z* = 94 : 6)		**5c**	**7c** (48; 58 : 42)
4	**2b**		**5d**	**7d** (52; 53 : 47)

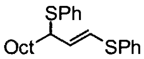
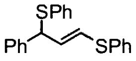
[a]Overall yield from **2**.

Carbometallation of alkynes with vinylmetal species is a useful method for the preparation of conjugated dienes. However only a limited number of such reactions have been explored. Normant and co-workers reported the addition of alkenyl cuprates to unsubstituted and heteroatom substituted acetylenes.[12] Klei and Teuben showed that the reaction of (1-methylprop-1-enyl)titanocene with diphenylacetylene produced the *syn*-adduct, which afforded the diene upon hydrolysis.[13] Therefore we were interested in the reaction of the vinyltitanium(IV) species **4** with alkynes **8** (Scheme 2). Although the treatment of **4** prepared from **2c** with diphenylacetylene **8a** afforded the conjugated diene **9a** as a mixture of the stereoisomers[14] in 38% yield (Table 2, Entry 1), aliphatic internal alkyne was found to be unreactive towards the vinyltitanium species **4**. We found, however, that terminal alkynes **8b–d** did react with **4** to form the *E*,*E*-dienes **9** in good overall yields with complete regio- and stereo-selectivity.[15] The formation of *trans*-carbon–carbon double bond is explained well by the *syn*-addition of the vinyltitanium species **4**.[16] The regioselectivity of the present reaction is of special interest. The reaction of organometallic reagents with terminal alkynes is usually complicated by formation of the two possible regioisomers, and an organic group tends to add to the substituted side of triple bond.[12,17] The regioselectivity of the present reaction is deferent from the conventional reactions; a vinyl group selectively attacks at the terminus of alkyne.



Scheme 2.

Table 2. Reaction of Vinyltitanium **4** with Alkynes **8**

Entry	1,3-Bis(phenylthio)-alkene **2**	R^2—≡—R^3 **8**	Product **9** (Yield[a] / %)
1	 **2c** (*E* only)	**8a:** R^2=Ph, R^3=Ph	**9a** (38)[b]
2	**2a** (*E* only)	**8b:** R^2=H, R^3=$CH_3(CH_2)_5$	**9b** (55)[c,d]
3	**2a** (*E* only)	**8c:** R^2=H, R^3=$(CH_3)_3Si$	**9c** (68)[c]
4	**2c** (*E* only)	**8d:** R^2=H, R^3=Ph	**9d** (58)
5	 **2d** (*E* : *Z* = 94 : 6)	**8c**	**9e** (72)

[a] Overall yield from **2**. [b] A mixture of the 1*E*,3*E*- and 1*Z*,3*E*-isomers (ratio of the two isomers = 63 : 37). [c] Contaminated with 3-*tert*-butyl-4-phenylbut-1-ene. The yield was corrected for the contaminant. [d] The NMR spectrum contained some unidentified signals.

Although more work will be required to elucidate the relationship between the structure and reactivity of vinyltitanium species, the present study demonstrates potential utility of vinyltitanium compounds as reagents in organic synthesis. Further study on their preparation and reaction is currently underway.

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14 The ratio of two isomers was found to be variable in the different runs, indicating the isomerization of the initial product during work-up and isolation.
15 The typical experimental procedure is as follows: Magnesium turnings (51 mg, 2.1 mmol; purchased from Nakarai Tesque Inc. Kyoto, Japan), finely powdered molecular sieves 4 A (175 mg), and Cp_2TiCl_2 (436 mg, 1.75 mmol) were placed in a flask and dried by heating with a heat gun under reduced pressure (2–3 mmHg). During this procedure, care was taken not to sublime Cp_2TiCl_2. After cooling, THF (3.5 mL) and $P(OEt)_3$ (0.60 mL, 3.5 mmol) were added successively with stirring at room temperature under argon. After 3 h, **2c** (186 mg, 0.5 mmol) in THF (1.5 mL) was added to the mixture at 0 °C, and stirring was continued for 10 min. Then *tert*-butyl chloride (46 mg, 0.5 mmol) in THF (1 mL) was added and the reaction mixture was stirred for 1 h. A THF (1 mL) solution of **8d** (102 mg, 1 mmol) was added and the mixture was stirred for 30 min at the same temperature and then at 25 °C for 1.5 h. The reaction was quenched by addition of 1 M NaOH (20 mL), and the resulting insoluble materials were filtered off through Celite and washed with ether (10 mL). The organic materials were extracted with ether (3 × 20 mL), and the extract was dried (Na_2SO_4). After removal of solvent, the residue was purified by PTLC (hexane) to give **9d** (90 mg, 58%).
16 When the reaction of **2a** with (trimethylsilyl)acetylene **8c** was quenched with D_2O, 5-benzyl-6,6-dimethyl-1-(trimethylsilyl)[1-^{2}H]hepta-1,3-diene was obtained in 55% yield (85% deuterium incorporation), indicating the formation of the dienyltitanium species **10**.
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