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A novel propargyltitanation of acetylenes. Heteroatom substituent-dependent manifold in intermolecular coupling of allene and acetylene

Ryoichi Tanaka,[a] Misa Sasaki,[a] Fumie Sato[b,*] and Hirokazu Urabe[a,b,*]

[a] *Department of Biological Information, Graduate School of Bioscience and Biotechnology, Tokyo Institute of Technology, 4259 Nagatsuta-cho, Midori-ku, Yokohama, Kanagawa 226-8501, Japan*

[b] *Department of Biomolecular Engineering, Graduate School of Bioscience and Biotechnology, Tokyo Institute of Technology, 4259 Nagatsuta-cho, Midori-ku, Yokohama, Kanagawa 226-8501, Japan*

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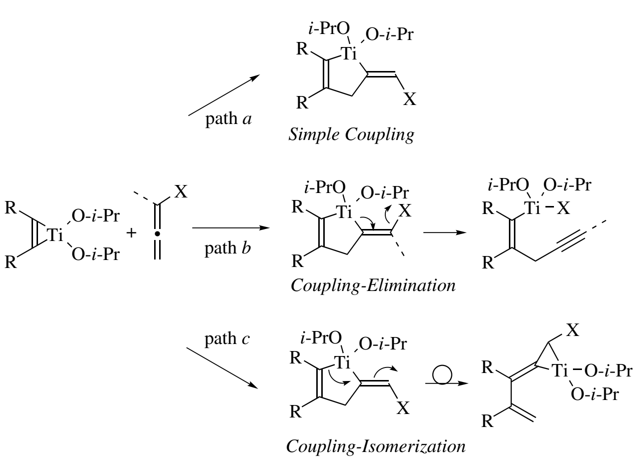
Abstract—Titanium alkoxide-mediated coupling of functionalized allenes and acetylenes afforded various types of products, and the first propargyltitanation of acetylenes was achieved by the appropriate choice of allenes.

Allenes occupy a unique position in metal-promoted ene–yne coupling reactions.[1] As far as the group 4 metal-mediated coupling reactions are concerned,[2,3] the behavior of functionalized allenes such as those having a heteroatom substituent has not been focused on in these reactions. We report herein that the reactions of such functionalized allenes proceed in three different ways as formulated in Scheme 1, which involves a simple coupling reaction (path *a*), a coupling–elimination sequence (path *b*), or a coupling followed by isomerization of the molecular structure (path *c*).

Silylacetylene **2** was first titanated with Ti(O-*i*-Pr)4/2 *i*-PrMgCl (**1**)[4] to generate acetylene complex **3**,[4a,b,d] which was then allowed to react with (phenylsulfenyl)allene **4**[5] or its silylated homologue **8**[5] at −50 °C (Scheme 2).[6] Both reactions proceeded in a regioselective manner with respect to the acetylene and allene to give coupling products. However, while nonsilylated allenes **4a**,**b** afforded 1,4-dienes **6a**,**b** having a (*Z*)-vinylsulfide moiety after hydrolysis (i.e., Scheme 1, path *a*), the silylated allene **8** experienced elimination of the sulfenyl group to give 1,4-enyne **11** (Scheme 1, path *b*). In the former reaction, no elimination product such as **7**, an authentic sample of which was prepared by desilylation of **11**, was detected even under forcing reaction conditions (up to room temperature). The stereochemistry of the olefinic linkage of **6a**,**b**, and **11** was unambiguously determined by ^{1}H NMR spectroscopy. Considering the most likely structure of the intermediate **9**, where the bulky silyl group is located *trans* to the titanium atom on the resultant olefin,[2] we could conclude that the *cis*-elimination from **9** to **10** promoted by the silyl group is a favorable path.



Scheme 1. Variation of reaction patterns.

Keywords: Alkynes; Allenes; Carbometallation; Metallacycle; Titanium and compounds.

[*] Corresponding authors. E-mail addresses: fsato@bio.titech.ac.jp; hurabe@bio.titech.ac.jp

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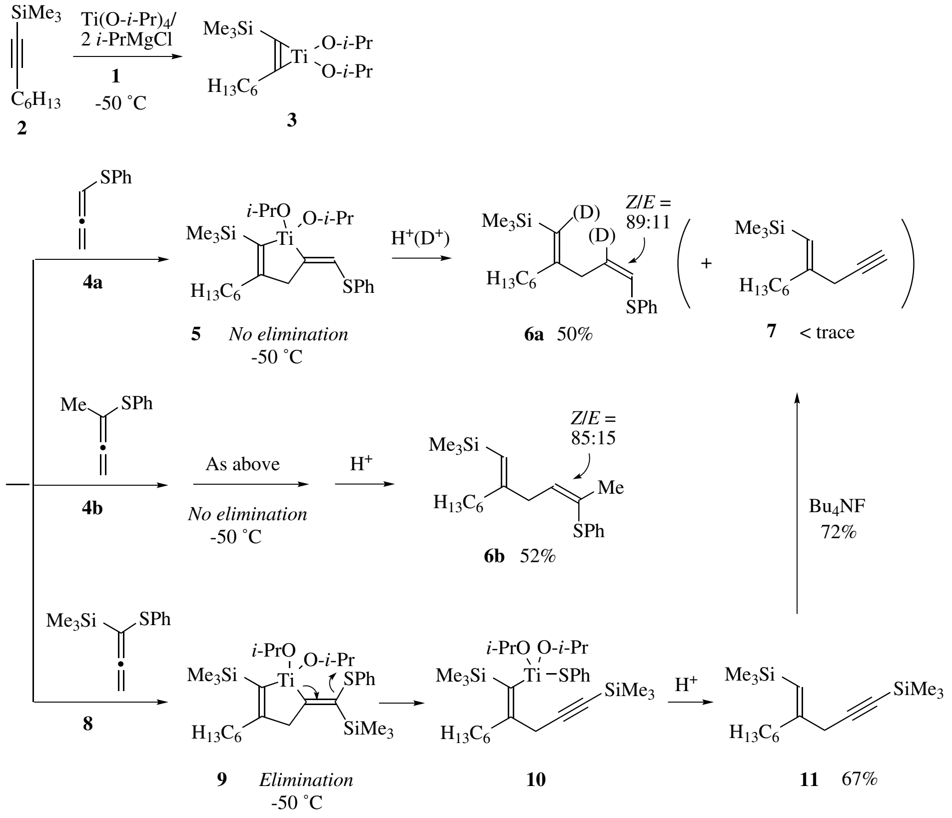
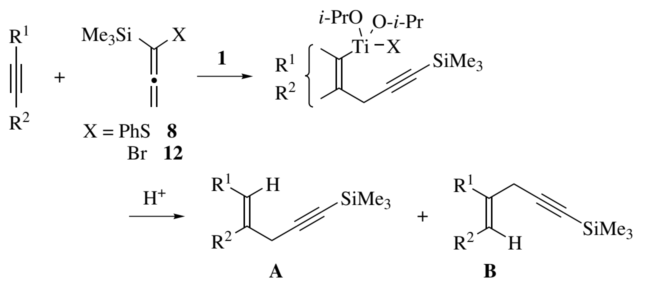


Scheme 2. Stereochemical requirement for elimination.

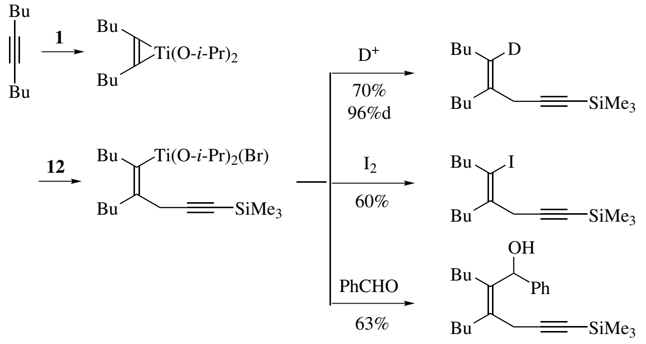
From the synthetic point of view, the smooth conversion from acetylene **2** to metalated enyne **10** with allene **8** illustrates the first propargyltitanation of acetylenes.[7] In order to establish the generality of this propargyltitanation, variations of the allenic reagents and acetylenic substrates were examined as summarized in Table 1, where the feasibility and regioselectivity of the reaction were accessed by hydrolytic workup. Actually, bromo(silyl)allene **12**[5,8] is a convenient alternative of **8**, although, in a couple of cases (entries 3 and 5), the regioselectivity (**A**:**B**) is less satisfactory than that attainable by **8**. With the appropriate choice of the allenic reagent, unsymmetrical acetylenes in entries 3, 5, 6, and 7 showed good to virtually complete regioselectivities, which proved that the preparation of various stereo-defined 1,4-enynes is viable.

Table 1. Regiochemistry in the synthesis of skip-type enynes



Entry	R^1	R^2	X = SPh (**8**)		X = Br (**12**)	
			A:**B**	Yield (%)[a]	**A**:**B**	Yield (%)[a]
1	Bu	Bu	—	65	—	70
2	Ph	Ph			—	90
3	$SiMe_3$	C_6H_{13}	Exclusively **A**	67	71:29	50
4	TBS	C_6H_{13}			77:23	74
5	Ph	Bu	83:17	76	47:53	59
6	$SiMe_3$	Ph	Exclusively **A**	51	Exclusively **A**	73
7	$SiMe_3$	CO_2Bu-*t*			Exclusively **A**	68

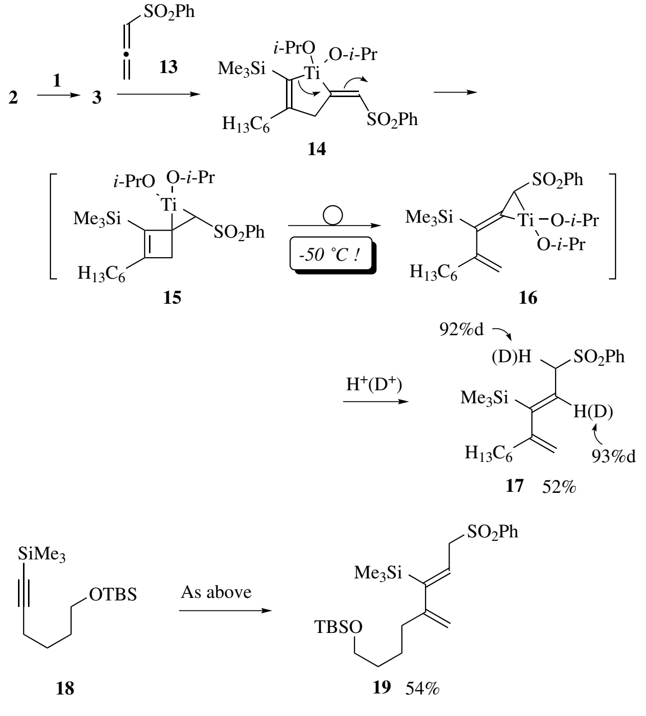
[a] Isolated yield.



Scheme 3. Further synthetic transformations based on the propargyltitanation.

In the above transformations, the intermediate vinyltitanium species was always hydrolyzed, but it allows the second coupling reaction with electrophiles such as D$^+$, iodine, or an aldehyde,[9] to effect the double carbon–carbon bond formation and functionalization of acetylenes as exemplified in Scheme 3.

Like the case of nonsilylated allene **4**, allene **13**[5] did not release the sulfonyl group, but the product obtained after hydrolytic workup was, surprisingly, a new conjugated diene **17** (Scheme 4; hence, path *c* in Scheme 1). This compound is most likely produced via the intramolecular addition of the vinyltitanium bond to the vinylsulfone moiety (**14** → **15**), followed by the electrocyclic ring opening of the resulting cyclobutene (**15** → **16**) and hydrolysis (**16** → **17**). The result of deuteriolysis also supports the proposed reaction intermediates. For another example, the functional group of acetylene **18** survived the reaction conditions to give the product **19**. When compared with a related ring-opening reaction of other metalated cyclobutenes, which proceeded at a temperature higher than +50 °C,[10] the low-temperature ring opening of **15** even at −50 °C is noteworthy and suggests the importance of the particularly metalated structure of **15** and/or **16**.[11]



Scheme 4. The coupling of allene followed by isomerization.

In conclusion, the titanium-mediated intermolecular coupling of functionalized allenes and acetylenes proceeded in a few different ways. The appropriate choice of a heteroatom substituent of allenes promoted the elimination of the Ti–heteroatom element to achieve the novel propargyltitanation of acetylenes. Further investigation on the utility of these allene–acetylene coupling reactions is now in progress.

Acknowledgements

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