Coupling reaction of terminal allenes with themselves or acetylenes mediated by $(\eta^2\text{-propene})Ti(OPr^i)_2$: some new selectivities and synthetic application

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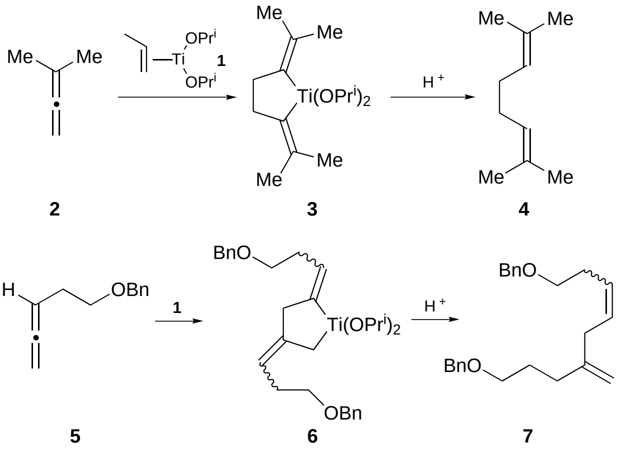
Treatment of an allene alone or with an acetylene with $(\eta^2\text{-propene})Ti(O\text{-}i\text{-}Pr)_2$ generates a new titanacycle, which reacts with some electrophiles to give useful intermediates for organic synthesis.

Low-valent early transition metal complexes are well known to effect the coupling reactions of olefins and acetylenes to yield metallacycles *via* olefin– (or acetylene)–metal intermediates, which show wide application in organic synthesis.[1] Although some examples of allene coupling reactions based on $(C_5H_5)_2Ti$– or $(C_5H_5)_2Zr$–allene complexes have been documented,[2–4]† the small number of reactions utilizing just allenes as the starting material (rather than any other appropriate precursors) and, accordingly, the critical issues in organic synthesis of regio- and stereo-selectivity and the feasibility of the reaction with respect to various substrates, have not been sufficiently investigated. As some of the aforementioned cyclometallation reactions have recently been carried out with an inexpensive, readily available low-valent titanium species, $(\eta^2\text{-propene})Ti(OPr^i)_2$ **1**,[5] we reinvestigated the coupling reaction of allenes themsleves and with other unsaturated compounds by taking advantage of this new method.

The homo-coupling reaction of 1,1-dimethylallene **2** with **1** proceeded at −50 °C for 2 h to give the symmetrically substituted **3** having two vinyl–metal bonds as a virtually single isomer (Scheme 1) as shown by the production of **4** (Table 1, entry 1) in accord with precedents of the $(C_5H_5)_2Ti$- or $(C_5H_5)_2Zr$-mediated reactions.[2,3*a*,4*b*] However, mono-substituted allene **5**[6] showed a completely different regioselectivity from **2** to give the titanabicycle **6**, which was identified by isolation of **7** as a mixture of *E*- and *Z*-olefinic isomers after aqueous workup (Table 1, entry 2). The latter regioselectivity is not seen in the homo-coupling reactions of representative types of allenes mediated by a low-valent titanium complex having cyclopentadienyl ligands.[2]

The *E*/*Z* ratio of the double bond in the above product could be controlled by the use of a silylallene.[7*c*] Thus, treatment of **8**[8] with **1** under the same conditions as above initiated cyclization to afford the single product **10** after aqueous workup (Scheme 2 and entry 3, Table 1). The internal double bond of **10** had exclusively the *Z* configuration, as determined *via* examination of the coupling constants and an NOE study in the ^{1}H NMR spectrum. The titanacycle structure **9**‡ was verified by deuterolysis that gave the bis-deuterated product [$^2H_2$]-**10** (93 atom% at each position) as a single regioisomer.



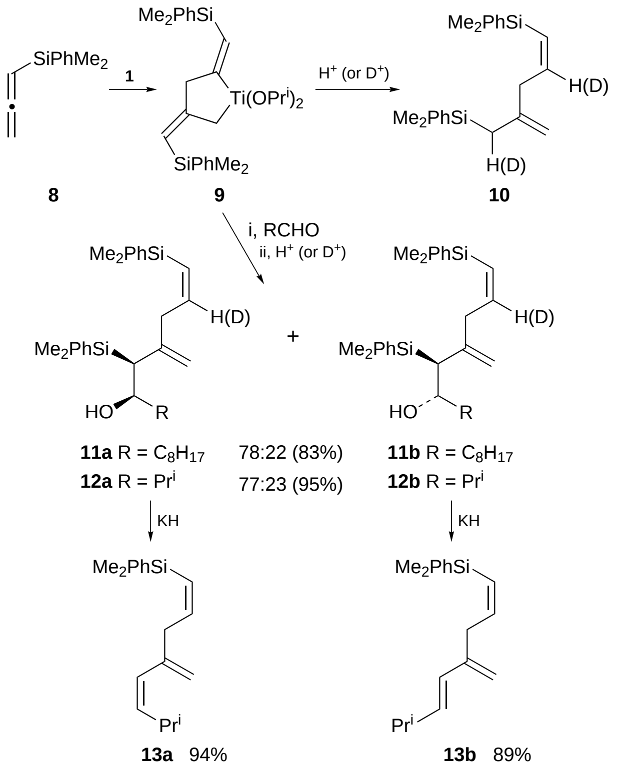
Scheme 1

Table 1 Coupling of allene mediated by **1**

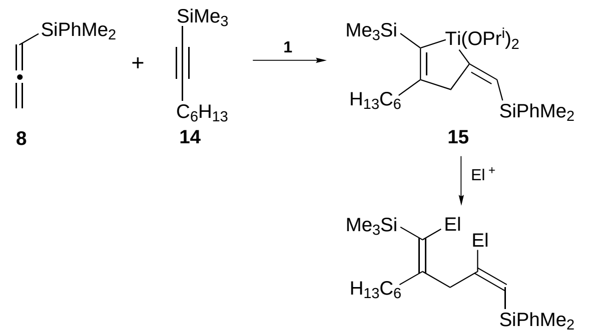
Entry	Allene	Product	Yield (%)
1	**2**	**4**	75
2	**5**	**7**	65[a]
3	**8**	**10**	80[b]

[a] $E:Z$ ratio = 24 : 76 (or *vice versa*). [b] *Z* isomer only.

More importantly, addition of **9** to aldehydes proceeded in a regioselective manner to give the adducts **11** and **12** as an approximately 3 : 1–4 : 1 mixture of diastereoisomers, which could be separated on silica gel. The addition of the vinyl–titanium bond in **9** to the aldehyde was not observed,[5*b*,9] although its presence was confirmed by the subsequent workup with deuteriochloric acid to give the product **12** having vinylic deuterium (93 atm%). Upon treatment with KH in THF,[10] the



Scheme 2



16 El = H 94%
17 El = D 94% 97–99 atom% D
18 El = I 54%

Scheme 3

major stereoisomer **12a** afforded the *Z,Z*-triene **13a**, while the minor **12b** gave *Z,E*-**13b**. These results not only established the orientation of the hydroxy group in **12** (and, hence, **11** by analogy) based on the well-precedented stereochemical course of the Peterson olefination,[10] but also demonstrated a synthetic application of the homo-coupling of the allene followed by aldehyde addition for the stereoselective preparation of trienes.

The hetero-coupling reaction between an allene and an acetylene is another important feature of the transformation involving allenes.[3a,4]† However, little information is available on the regio- and stereo-chemical aspects of the coupling reaction starting from unsymmetrical allenes and acetylenes.[4b] Thus, we first attempted the reaction of unsymmetrical substrates, a mono-substituted allene **8** and silylacetylene **14**, and found that the desired products **16** could be obtained in good yield and as an essentially single stereoisomer (Scheme 3). The stereochemistry of both double bonds in **16** was elucidated by ^{1}H NMR analysis. The high regioselectivity found for this unsymmetrical acetylene, as verified by the absence of another regioisomer, is also noteworthy. The presence of the intermediate titanacycle **15** was confirmed by the deuterolysis (1 M DCl) and iodinolysis (excess I_2) to give the bis-deuterated **17** and diiodide **18** in good yields.

This coupling reaction seems to be general for various substrates, as shown in Table 2. Alkylallene **5** preferentially affords the product **20** having an *E*-disubstituted double bond when reacted with di*alkyl*acetylene **19** (Table 2, entries 1 and 2), but gives **21** carrying a *Z*-disubstituted olefin with *silyl*acetylene **14** (entry 3), both in good yields. Alkoxyallene **22**[11] was able to participate in this coupling reaction as well. Although the yield of **23** is not particularly good due to partial decomposition of the allene in the presence of the titanium alkoxide, the exclusive *Z*-olefinic preference found in the product is somewhat amazing, provided that the stereoselectivity was simply controlled by the steric hindrance of the allenic substituent, which is usually less pronounced in the following order: trialkylsilyl > *n*-alkyl > *n*-alkyloxy (*cf.* entries 3–5). The resultant *cis*-vinyl ether moiety may be stereospecifically replaced by a carbon chain with a Grignard reagent under nickel catalysis[12] or hydrolyzed to aldehyde.

The coupling reaction based on allenes described herein, which enables the selective construction of a carbon framework and the facile introduction of an electrophile, is a synthetically useful entry to the metal-promoted coupling reactions of unsaturated compounds.

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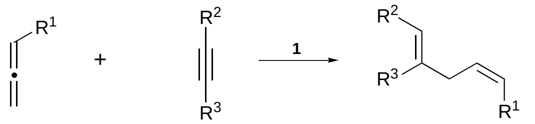
Table 2 Coupling of allene and acetylene mediated by **1**[a]



5 $R^1 = (CH_2)_2OBn$
8 $R^1 = SiPhMe_2$
22 $R^1 = OC_8H_{17}$

14 $R^2 = SiMe_2$, $R^3 = C_6H_{13}$
19 $R^2 = R^3 = Bu$

16, **20**, **21**, **23**

Entry	Allene	Acetylene	Product	*E*:*Z* ratio[b]	Yield (%)[c]
1	**5**	**19**	**20**	64:36	74
2	**5**	**19**[d]	**20**	64:36	70
3	**5**	**14**	**21**	25:75	72
4	**8**	**14**	**16**	*Z* only	94
5	**22**	**14**	**23**	*Z* only	45

[a] Allene (1.5 equiv.) and acetylene (1.0 equiv.), unless otherwise stated. [b] Refers to double bond substituted with R^1. [c] Isolated yields based on limiting substrate. [d] Allene (1.0 equiv.) and acetylene (1.5 equiv.).

Footnotes and References

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† The *intra*molecular cyclization of allenes and acetylenes has also been documented (ref. 7).

‡ Two simple rules, namely that (i) the formation of the transient allene–titanium complex takes place from the less hindered side and (ii) the titanium atom is better located at the less crowded terminus of the allylic system (ref. 9), support the depicted structure of **9** (and also **6**) over the other possible isomeric formulations.

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