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# Scandium-Catalyzed Regio- and Stereospecific Methylalumination of Silyloxy/Alkoxy-Substituted Alkynes and Alkenes

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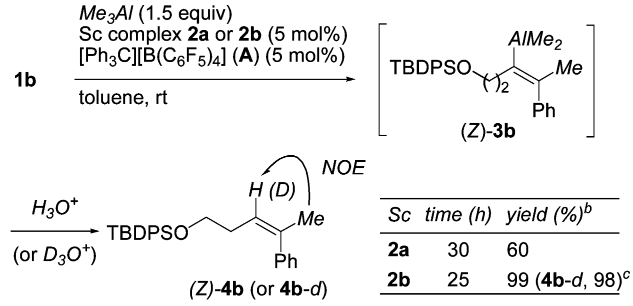
Carbometalation, particularly methylalumination, of alkynes is one of the most efficient methods for the synthesis of polysubstituted alkenes, especially those with branching methyl groups (an important class of structural units that are found in many biologically active natural compounds).[1,2] Similarly, the methylalumination of alkenes is also of considerable importance in synthetic organic chemistry.[3,4] The catalysts reported to date for these reactions have been based mainly on group-4 metal complexes.[2,4] In contrast, the use of rare-earth (group 3 and lanthanide) metal-based catalysts for the carbometalation of alkynes or alkenes has not been reported previously. Although group-4 metal catalysts are useful, they have limitations. The search for new catalysts for the carbometalation of alkynes and alkenes is of obvious interest and importance.

Recently, cationic rare-earth metal alkyl complexes have emerged as a novel class of catalysts for olefin polymerization.[5,6] In contrast, their potential as catalysts in organic synthesis remains almost unexplored.[7] We report here that the cationic half-sandwich alkylscandium complexes generated from dialkyl precursors such as $(C_5Me_4R)Sc(CH_2C_6H_4NMe_2\text{-}o)_2$ (R = Me, $SiMe_3$)[6c] can serve as excellent catalysts for the methylalumination of alkynes and alkenes, particularly those having an ether tether group, to afford the corresponding methylalumination products with unprecedented regio- and stereoselectivity.

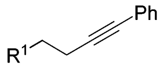
We first examined the methylalumination of 1,4-diphenylbut-1-yne (**1a**) using the cationic scandium species prepared in situ by the reaction of bis(aminobenzyl)scandium complex **2a** or **2b** with $[Ph_3C][B(C_6F_5)_4]$ (**A**).[6c] However, this reaction showed poor selectivity, yielding an inseparable mixture of two regioisomers (∼2:1) in a low yield (∼20%). Surprisingly to us, when an internal alkyne having a tethered siloxy group, such as **1b**, was reacted with $Me_3Al$ in the presence of **2a**/**A** (5 mol %), the reaction proceeded in a regio- and stereoselective manner to give exclusively the *Z* isomer of the hydromethylation product **4b** after hydrolysis (Scheme 1). The $C_5Me_5$-ligated complex **2b** showed a higher activity than the $C_5Me_4SiMe_3$ analogue **2a** under the same conditions, giving **4b** quantitatively in 25 h at room temperature. In these reactions, the methyl group was introduced to the alkyne carbon distal from the tethered silyl ether. The nuclear Overhauser effect (NOE) experiment showed that the double bond in the product **4b** has a *Z* configuration. Treatment of the reaction mixture with $DCl/D_2O$ afforded deuterated (*Z*)-**4b**-*d* in 98% yield (>98% D content). These results indicate that $Me_3Al$ probably undergoes syn addition to the alkyne moiety to give (*Z*)-**3b** as an intermediate. Neither the neutral dialkyl complex (**2a** or **2b**) nor the activator (**A**) showed any catalytic activity when used alone, suggesting that a cationic scandium alkyl species is essential for this reaction.

***Scheme 1.*** Sc-Catalyzed Carboalumination of **1b**[a]

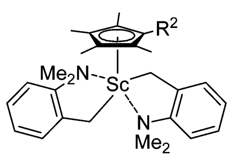


| Sc | time (h) | yield (%)[b] |
|---|---|---|
| **2a** | 30 | 60 |
| **2b** | 25 | 99 (**4b**-*d*, 98)[c] |

[a] TBDPS = *tert*-$BuPh_2Si$. [b] Isolated yield. [c] The reaction mixture was treated with 20% $DCl/D_2O$.



**1a**, $R^1$ = Ph
**1b**, $R^1$ = OTBDPS



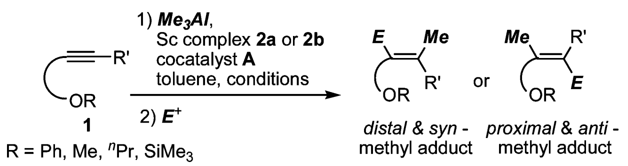
**2a**, $R^2$ = $SiMe_3$
**2b**, $R^2$ = $CH_3$

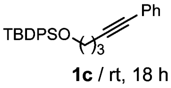
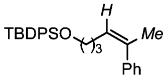
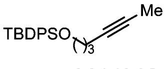
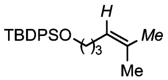
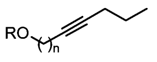
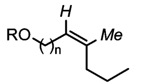
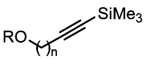
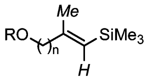
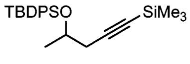
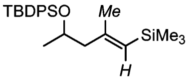
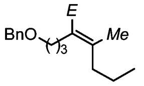
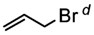
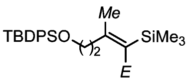
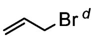
Various internal alkynes having an ether tether group could be used in the present reaction. Some representative results are summarized in Table 1. Generally, in the reactions of phenyl- or alkyl-substituted alkynes such as **1c**−**g**, the methyl group was introduced to the C≡C carbon atom distal from the ether group in a syn fashion to give exclusively the corresponding *Z* alkenes in high yields after hydrolysis (Table 1, entries 1−5).[8,9] In contrast, methylalumination of trimethylsilyl (TMS)-substituted alkynes such as **1h**−**l** took place in an anti-selective manner with introduction of the methyl group to the carbon atom proximal to the tethered ether group (Table 1, entries 6−10).[10,11] Under similar conditions, the Zr-catalyzed reactions were found to show much lower activity and lower selectivity. In a comparison experiment, the methylalumination of **1g** catalyzed by $Cp_2ZrCl_2$ (a representative Zr catalyst) yielded a mixture of the two regioisomers in a much lower yield (<10%). The use of Wipf's improved procedure[12] led to a better yield (75%) but no regioselectivity (∼1:1).

In the present Sc-catalyzed methylaluminations of alkynes, the resulting alkenylalane intermediates could be trapped in "one pot" by various electrophiles. In contrast with the conventional Zr-catalyzed reactions,[13] removal of the solvent or unreacted $Me_3Al$ was not required for the subsequent cross-coupling reactions because the Sc-catalyzed methylalumination reactions could be carried out in an inert solvent (toluene) with only a slight excess of $Me_3Al$ (∼1.1 equiv). Thus, treatment of the alkenylalane generated from **1g** with paraformaldehyde, allyl bromide, and iodobenzene gave the corresponding syn adducts **6a**, **6b**, and **6c** with introduction of the electrophile at the carbon atom proximal to the tethered benzyloxy group (Table 1, entries 11−13). Analogously, the alkenylalane prepared from **1h** reacted with iodine, paraformalde-

10.1021/ja909126k

***Table 1.*** Sc-Catalyzed Methylalumination of Alkynes[a]



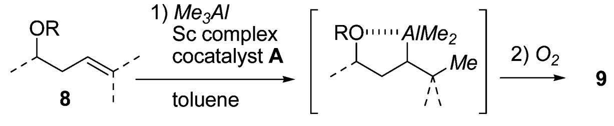
| entry | alkyne / conditions | Sc | $E^+$ | product (yield) |
|---|---|---|---|---|
| 1 | <br>**1c** / rt, 18 h | **2b** | $H_3O^+$ | <br>**4c** (98%) |
| 2 | <br>**1d** / 40 °C, 24 h | **2b** | $H_3O^+$ | <br>**4d** (83%) |
| 3 | <br>**1e** (n = 2, R = Bn)<br>40 °C, 41 h | **2b** | $H_3O^+$ | <br>**4e** (87%) |
| 4 | **1f** (n = 3, R = TBDPS)<br>40 °C, 6 h | | | **4f**(82%) |
| 5 | **1g** (n = 3, R = Bn)<br>rt, 6 h | | | **4g**(100%) |
| 6 | <br>**1h** (n = 2, R = TBDPS)<br>rt, 5h | **2a** | $H_3O^+$ | <br>**5h** (100%) |
| 7 | **1i** (n = 1, R = TBDPS)<br>rt, 5 h | | | **5i** (100%) |
| 8 | **1j** (n = 3, R = TBDPS)<br>rt, 6 h | | | **5j** (100%) |
| 9 | **1k** (n = 4, R = TBDMS[b])<br>rt, 14 h | | | **5k** (93%) |
| 10 | <br>**1l** / rt, 19 h | **2a** | $H_3O^+$ | <br>**5l** (99%) |
| 11 | **1g** / rt, 6 h | **2b** | HCHO [c] | <br>**6a** ($E$ = CH$_2$OH, 84%) |
| 12 | **1g** | |  Br [d] | **6b** ($E$ = allyl, 90%) |
| 13 | **1g** | | Ph-I [e] | **6c** ($E$ = Ph, 77%) |
| 14 | **1h** / rt, 5 h | **2b** | $I_2$ | <br>**7a** ($E$ = I, 100%) |
| 15 | **1h** | | HCHO [c] | **7b** ($E$ = CH$_2$OH, 81%) |
| 16 | **1h** | |  Br [d] | **7c** ($E$ = allyl, 100%) |

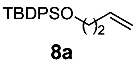
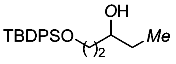
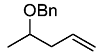
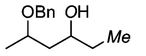
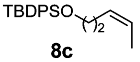
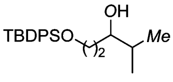
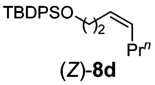
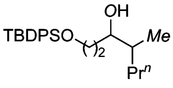
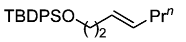
[a] Methylaluminations were carried out using 1.1−1.5 equiv of $Me_3Al$, 5 mol % Sc precatalyst, and 5 mol % **A**. For details, see the Supporting Information. [b] TBDMS = *tert*-BuMe$_2$Si. [c] Using 1.1 equiv of BuLi. [d] CuCl (30 mol %) catalyst. [e] $ZnCl_2$ (1.1 equiv) + $Pd(PPh_3)_4$ (5 mol %) catalyst.

hyde, and allyl bromide to afford the corresponding anti adducts **7a**, **7b**, and **7c** with introduction of the electrophiles at the carbon atom distal from the tethered siloxy group (Table 1, entries 14−16).

The usefulness of the present Sc-based catalyst system was further demonstrated by the methylalumination of alkenes. The homoallylic alcohol derivative **8a** reacted smoothly and regioselectively with $Me_3Al$ in the presence of **2a**/**A** (5 mol %), affording the secondary alcohol **9a** in 93% isolated yield after oxidation of the resulting alkylalane species (Table 2, entry 1). It is noteworthy that the $AlMe_2$ unit was introduced at the internal carbon atom in this reaction. This is in sharp contrast with what was observed in the Zr-catalyzed methylalumination of **8a**, in which the aluminum atom was introduced at the terminal carbon.[14] The methylaluminations of secondary homoallylic ether **8b** and internal alkenes **8c** and **8d** also proceeded similarly (Table 2, entries 2−5).[15] In each case, the $AlMe_2$ unit was introduced at the C═C carbon atom proximal to the ether group to give the corresponding secondary alcohol in high yield after oxidation.

***Table 2.*** Sc-Catalyzed Methylalumination of Alkenes[a]



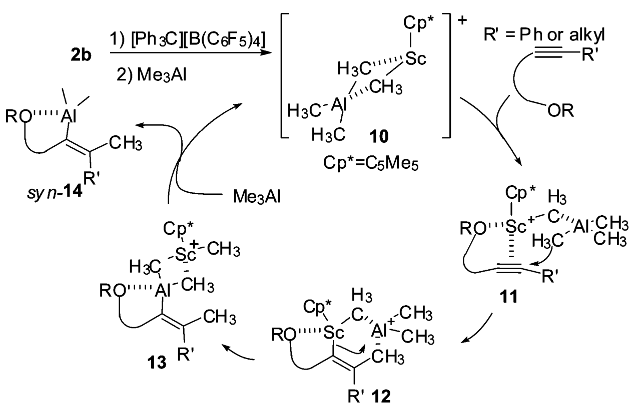
| entry | alkene | Sc | conditions | product (yield) |
|---|---|---|---|---|
| 1 | <br>**8a** | **2a** | rt, 12 h | <br>**9a** (93%) |
| 2 | <br>**8b** | **2a** | rt, 18 h | <br>**9b** (83%)[b] |
| 3 | <br>**8c** | **2a** | 50 °C, 14 h | <br>**9c** (94%) |
| 4 | <br>($Z$)-**8d** | **2a** | 50 °C, 24 h | <br>**9d** (86%)[c] |
| 5 | <br>($E$)-**8d** | **2b** | 50 °C, 24 h | **9d** (80%)[d] |

[a] Methylaluminations were carried out using 1.5 equiv of $Me_3Al$, 5 mol % Sc precatalyst, and 5 mol % **A**. Oxidative workup was carried out at 0 °C. For details, see the Supporting Information. [b] The diastereomeric ratio (dr) of **9b** was 1:1 (as determined by $^1$H NMR analysis). [c] dr = ~1.6:1. [d] dr = ~1:1.4.

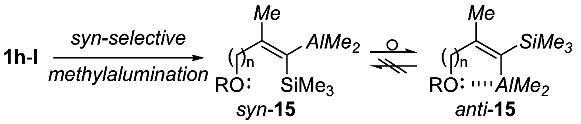
Although the mechanistic details of the present Sc-catalyzed reactions are yet not clear, it seems certain that the tethered oxygen atom in the alkyne or alkene plays a crucially important role. A likely mechanism for the reaction of alkyl- or phenyl-substituted alkynes is proposed in Scheme 2. In the presence of $Me_3Al$ and $[Ph_3C][B(C_6F_5)_4]$, the bis(alkyl)scandium complex **2b** may undergo alkyl ligand exchange and alkyl abstraction to afford cationic heteronuclear Sc/Al complex **10**.[16] Coordination of an ether-tethered alkyne to the metal center may take place through both the oxygen atom and the C≡C unit to give the intermediary complex **11.** Subsequent migratory addition of a methyl group to the C≡C unit in **11** would afford vinylscandium intermediate **12**. Intramolecular transmetalation in **12** should give the syn methylalumination product **13**, which upon reaction with $AlMe_3$ could yield alkenylalane *syn*-**14** and regenerate **10**. The regioselective methylalumination of alkenes **8a**−**d** (Table 2) could take place through a similar pathway.

In the case of TMS-substituted alkynes **1h**−**l** (Table 1, entries 6−10), the reaction may take place similarly.[10] However, the strong electronic effect of the TMS substituent[17] could direct the aluminum

*Scheme 2.* Possible Mechanism for the Reaction



unit to the TMS-substituted carbon atom to afford *syn*-**15** (eq 1). Because of its intrinsically unstable 1-silyl-1-metalloalkene structure,[18] the initially formed *syn*-**15** could undergo rapid isomerization to give *anti*-**15**, which is stabilized by the intramolecular coordination of the oxygen atom to the Al atom.[19]



In summary, we have demonstrated that cationic alkylscandium species such as that generated from the in situ reaction of **2a** or **2b** with **A** can serve as a highly effective catalyst system for the regio- and stereoselective carboalumination of internal akynes and alkenes having an ether tether group. In most cases, the regio- and stereoselectivity are unique and could not be achieved using previously known catalysts. The resulting vinylalane species in the carboalumination of alkynes can be easily transformed to the corresponding tetrasubstituted alkenes through one-pot, stereospecific coupling reactions with electrophiles. The oxidation of the alkylalane species formed in the carboalumination of alkenes selectively affords the corresponding secondary alcohols. Studies of the use of the cationic rare-earth metal alkyls for other synthetic organic reactions are in progress.

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**Supporting Information Available:** Experimental details and compound characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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