Science "Summer" Seminar

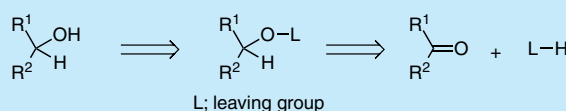## Carbonyl Olefination (3)

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1. Designing of Synthetic Organic Reactions

In the two preceding issues, some problems encountered in carbonyl olefination were discussed. At the end of this series, an approach to developing new synthetic reactions is described in connection with the reaction mechanism of carbonyl olefination. For good understanding of organic reactions and creating new synthetic methods, it is important to focus on the most basic principle of each reaction mechanism. For example, most oxidation of alcohols can be regarded as elimination of a leaving group on oxygen and α-proton as shown in Scheme 1. Indeed, the treatment of geraniol with bromocopper(II) *tert*-butoxide (**1**) produces geranial (Scheme 2).[1] The oxidation is assumed to proceed via the formation of copper(II) alkoxide **2** and following elimination of copper hydride **3**. Based on this simple idea, oxidations of amines,[2] α-amino acids,[3] amides,[4] α-hydroxy acids,[3] and *trans*-cyclic diols[5] have been achieved (Scheme 3). The copper(II)-promoted transformation of hydrazones into *gem*-dichlorides and the preparation of dithioortho esters by the copper(II)-promoted reaction of lithium alkoxides with tributyl[bis(phenylthio)methyl]stannane described in the previous issue have also been developed as parts of this study.


Scheme 1
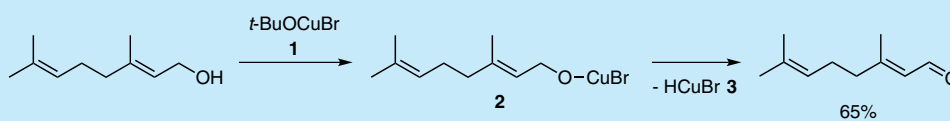
Scheme 2
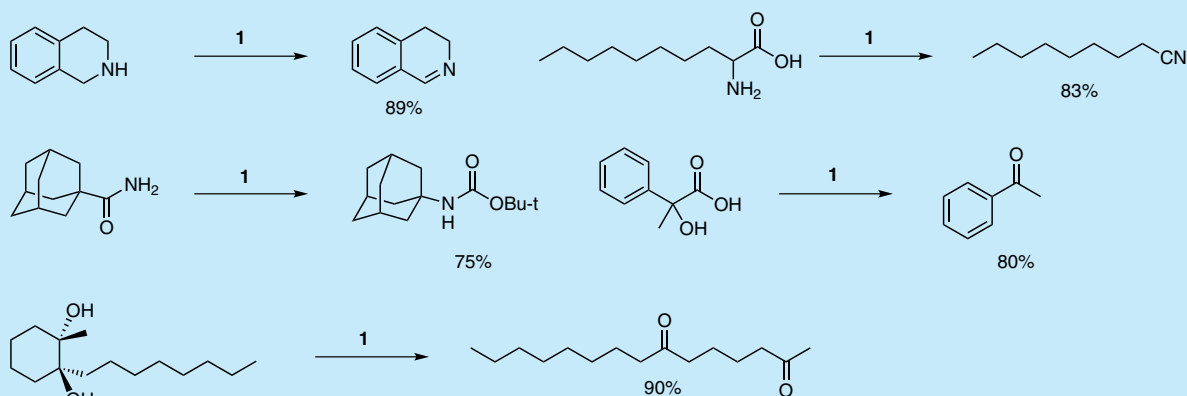
**Scheme 3**

2. Oxatitanacyclobutane

The intermediates of carbonyl olefination using titanium-carbene complexes **4** are suggested to be oxatitanacyclobutanes **5** and the following elimination of titanocene oxide **6** affords olefins (Scheme 4). Simply stated, the Wittig and Peterson reactions also proceed via the formation of similar oxaheterocycles **7**, **8** and subsequent deoxygenation process. Thus, it is likely that new carbonyl olefination is realized by designing novel oxametallacyclobutanes which contain a highly oxophilic element. Such an approach would enable us to overcome some difficulties in carbonyl olefination described in the foregoing two issues.


Scheme 4
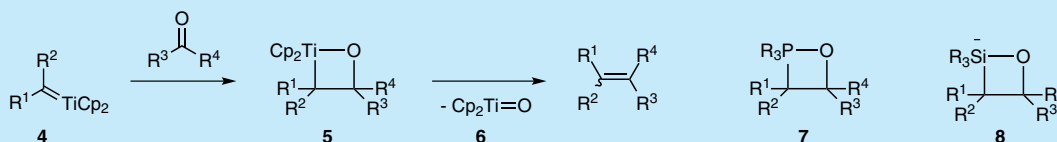
Designing new reactive intermediates is a powerful tool to create synthetic organic reactions, and indeed, various four-membered titanacycles which are analogous to the titanacycles **5** are the intermediates of a variety of molecular transformations. A typical example is illustrated in Scheme 5. The titanium carbene complex bearing an allylsilane moiety **4a** generated from the corresponding unsaturated thioacetal results in the formation of unsaturated oxasilacycle **9** through the formation of titanacyclobutane **10** and extrusion of methylidenetitanocene.[7] The metathesis-type degradation of titanacyclobutene **11**, generated by the reaction of the carbene complex **4b** with acetylene, in contrast, produces the new carbene complex **12** with two-carbon homologation, and hence the carbene complexes generated from thioacetals act as initiators for the polymerization of acetylene. Under appropriate reaction conditions, such polymerization produces a conductive polyacetylene film **13** (Scheme 6).[8] The carbene complex **4c** also reacts with the δ-iodonitrile to form the azatitanacyclobutene **14**. Its ring opening produces the titanium vinylimido complex **15** which affords the cyclohexanone after intramolecular alkylation and hydrolysis (Scheme 7).[9]


Scheme 5

Scheme 6

Scheme 7
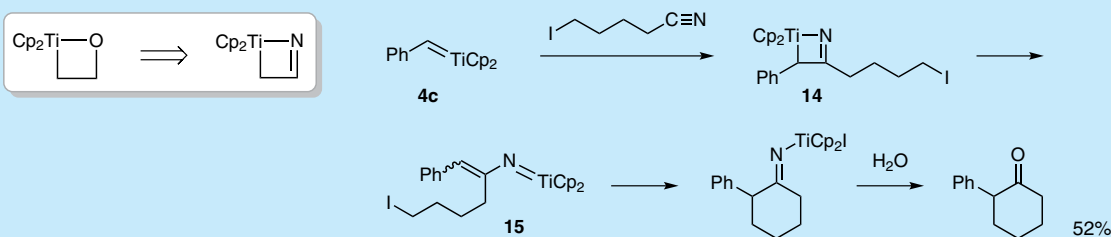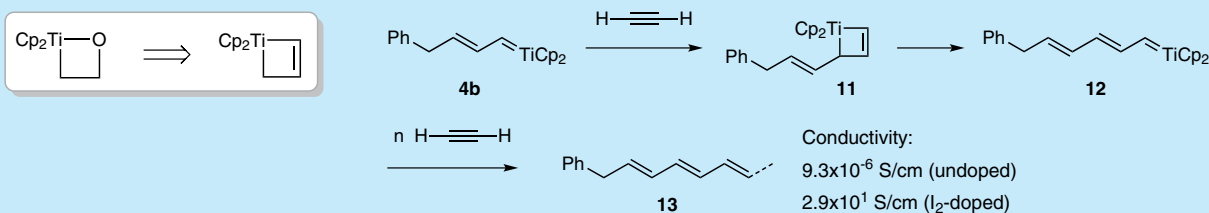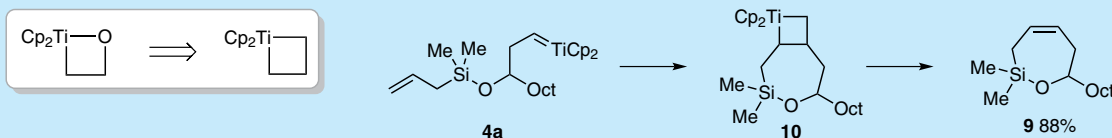
A new stereoselective carbon-carbon bond formation has been realized through the further modification of titanacyclobutene intermediates. The allenyltitanocene **16** is formed by the reaction of carbene complex **4d** with the alkynyl sulfone **17** followed by the β-elimination of a methylsulfonyl group from the resulting titanacyclobutene **18**. The organotitanium species **16** reacts with 2-cyclohexene to afford *tert*-homopropargyl alcohol **19** with high diastereoselectivity (Scheme 8).[10]

Scheme 8
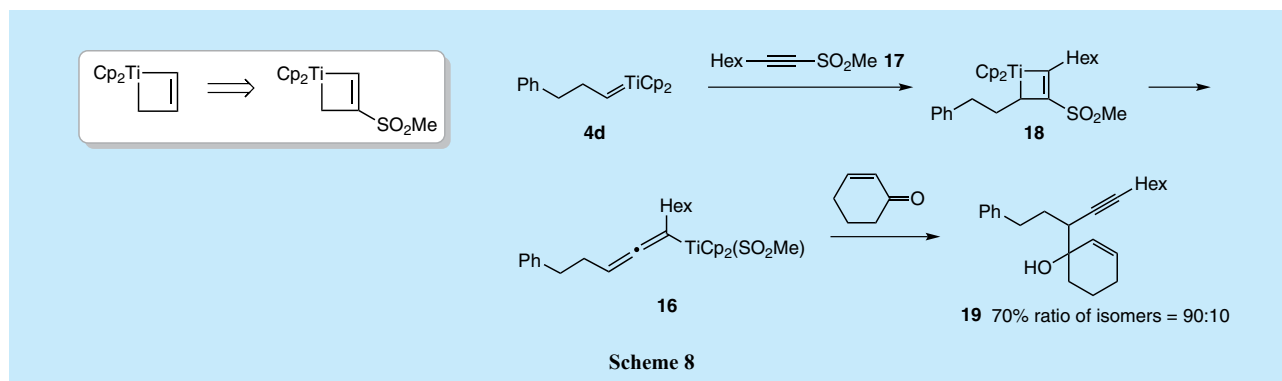
In general, the reaction of allylmetals with ketones is less diastereoselective than their reaction with aldehydes. On the basis of the high diastereoselectivity observed in the reaction of allenyltitanocene **16** with 2-cyclohexenone, the highly stereoselective[11] or stereospecific[12] allylations of various ketones have also been established (Scheme 9).
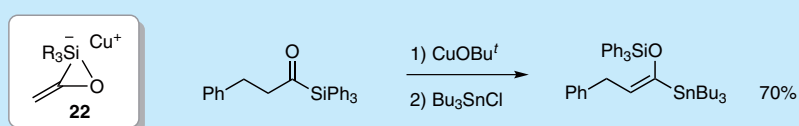

Scheme 9
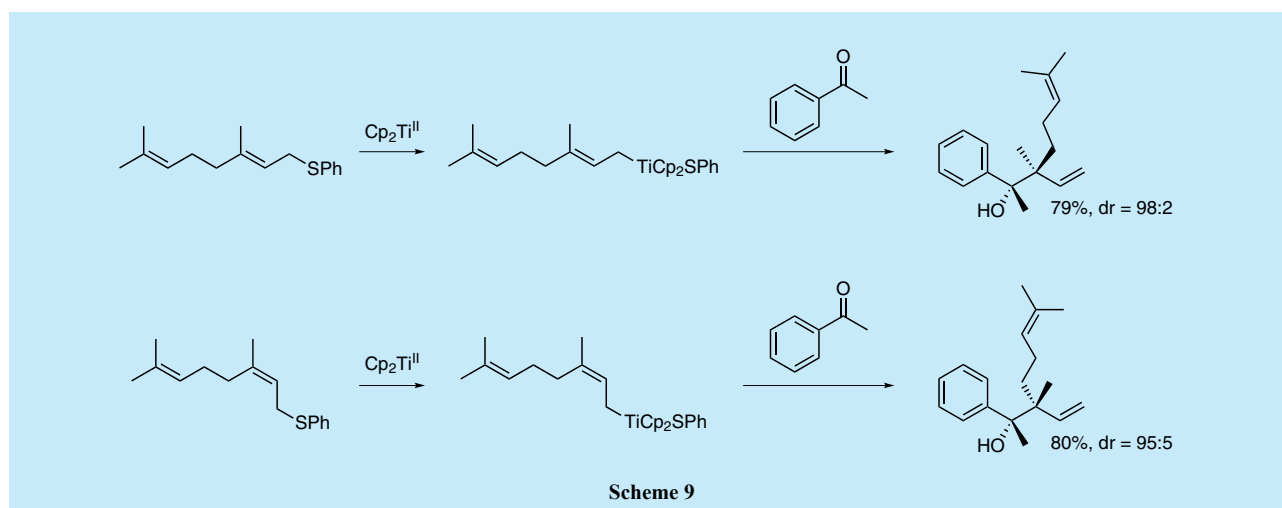
3. Oxasilacycles

A slight modification of the four-membered silicates **8** brings a new cross-coupling reaction of alkenylsilanes. The cyclic silicate **20** with a copper(I) counterion undergoes the transmetallation between silicon and copper to form alkenylcopper species **21** (Scheme 10).[13] The organocopper compound thus formed is reactive toward organic halides, and thus the similar processes are promising as new methods for the stereoselective formation of highly substituted olefins. The three-membered homologues **22** (Scheme 11),[14] the unsaturated analogues **23** (Scheme 12),[15] and their five-membered homologues **24** (Scheme 13),[16] **25** (Scheme 14)[17] are assumed to be the intermediates of the reactions which produce silyl enol ethers and highly substituted olefins with extremely high stereoselectivity.
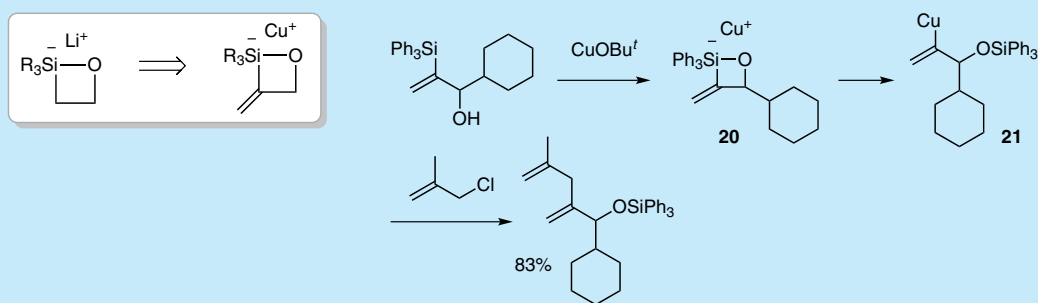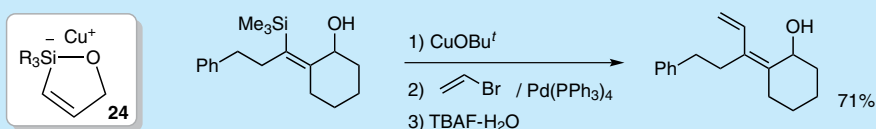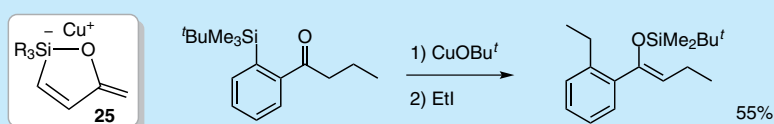
Scheme 10

Scheme 11
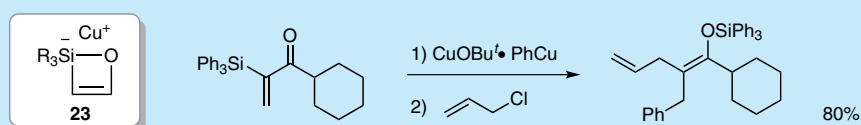
Scheme 12

Scheme 13

Scheme 14

4. Concluding Remarks

As described above, the designing of various oxametallacycles opens the possibility to create new molecular transformations. Our carbonyl olefination utilizing titanium carbene complexes has been developed based on the unanticipated finding that alkenylcyclopropanes are produced by the reaction of β,γ-unsaturated thioacetals with titanocene(II)‑ 1-butene complex.[18] This finding further enabled us to develop a variety of synthetic reactions through the process of designing new reaction intermediates. Such "designing reaction intermediate approach" to create new synthetic methods might be somewhat unique to our group and, of course, each researcher in this field has his/her own way of doing research. It is my hope that our "way of doing research" described in this serial can be of some help for you to do your research work.

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Introduction of the author :

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Takeshi Takeda obtained his Ph.D. (1977) in chemistry from Tokyo Institute of Technology. He joined the University of Tokyo as an Assistant Professor in 1977. After a half year of postdoctoral work at University of California, Los Angeles, he moved to Tokyo University of Agriculture and Technology as an Associate Professor in 1981. He was appointed to a Professor-ship in 1994.
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