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Award Accounts

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Organic Syntheses Utilizing Titanium Carbene Complexes

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Synthetic reactions utilizing titanium carbene complexes prepared by the desulfurizative titanation of thioacetals and related organosulfur compounds with the titanocene(II) species $[Cp_2Ti\{P(OEt)_3\}_2]$ are described. The Wittig type olefination of carbonyl compounds including carboxylic acid derivatives with the titanium carbene complexes affords a variety of olefinic compounds. The reaction is successfully applied to the intramolecular carbonyl olefination of carboxylic acid derivatives, giving various carbo- and hetero-cycles. The organotitanium species generated by the treatment of *gem*-dihalides and certain alkyl halides with the titanocene(II) species are also useful for the transformation of carbonyl compounds into highly substituted olefins or into olefins bearing a bulky substituent.

The alkylidenetitanocenes generated from thioacetals react with olefins in both inter- and intramolecular fashions to give olefin metathesis products. The ring-closing olefin metathesis of the carbene complexes formed from thioacetals having a terminal olefin provides a variety of unsaturated heterocyclic compounds. On the other hand, cyclopropanation proceeds when terminal olefins are treated with alkenyl- and alkynyl-carbene complexes. Cyclopropanes are also obtained by treatment of *gem*-dihalides having a terminal carbon–carbon double bond.

The carbene complexes are also highly reactive toward triple bonds. Their reactions with nitriles afford the acylation products after hydrolysis of intermediary titanium vinylimido complexes. The reactions of the carbene complexes with internal alkynes via the formation of titanacyclobutene intermediates afford conjugated dienes with high stereoselectivity, whereas metathesis polymerization proceeds to give *trans*-polyacetylene when the carbene complexes are treated with excess acetylene. The carbene complexes also react with *t*-alkyl halides and group 14 metal hydrides.

The discovery of active organometallic species presents a constant challenge to the chemists who desire to establish efficient methods for the construction of carbon frameworks of organic molecules. In this context, we have studied the preparation of organometallic compounds by the desulfurizative metallation of organosulfur compounds with low-valent metal species.[1] In 1996 our account entitled "Organic Synthesis Utilizing 2-Phenylthiocyclobutyl Ketones" appeared in *Synlett*.[2] The article focuses on syntheses of the titled compounds by [2 + 2]cycloaddition of 1-alkenyl sulfides with vinyl ketones and their applications to organic synthesis. In its "concluding remarks", we described an unusual formation of cyclopropanes by the treatment of unsaturated thioacetals with titanocene(II)–olefin complexes (Fig. 1). The story described here is a sequel of this extraordinary finding.

What is most interesting in the above finding is how the cyclopropanation proceeds. We assumed that the reduction of the unsaturated thioacetal **1a** with the titanocene(II) species **2** produced the titanium alkenylcarbene complex **3a**, which reacts with the coordinated terminal olefin to afford the alkenylcyclopropane **4a** via the formation of the titanacyclobutane intermediate **5a** (Scheme 1).[3] On the basis of this assumption, we have studied the generation of titanium carbene complexes by the desulfurization of organosulfur compounds with the low-valent titanium species and their application to organic syntheses.

Much attention has been focused on the synthetic application of metal–carbene complexes in a wide range of stoichiometric and catalytic reactions.[4] These complexes are subdivided into two categories; the Fischer-type complexes and the Schrock-type complexes. The carbene complexes having a low-valent late transition metal center, π-acceptor ligands, and π-donor substituents on the carbene carbon are called the Fischer-type carbene complexes; these are electrophilic at the carbene carbon atom. The Schrock-type carbene complexes are usually high-valent early transition metal species without π-accepting ligands and are essentially nucleophilic in nature.

Titanium carbene complexes are typical nucleophilic complexes; their basic skeleton, methylidenetitanocene **6**, was first generated by the α-elimination of dimethyltitanocene **7**.[5] Around the same time, Tebbe and co-workers also described the formation of such species by treatment of so-called the Tebbe reagent **8** with a Lewis base (Scheme 2).[6] A modified method for the preparation of aluminum-free methylidenetitanocene **6** by thermolysis of titanacyclobutanes **5**, which are ob-

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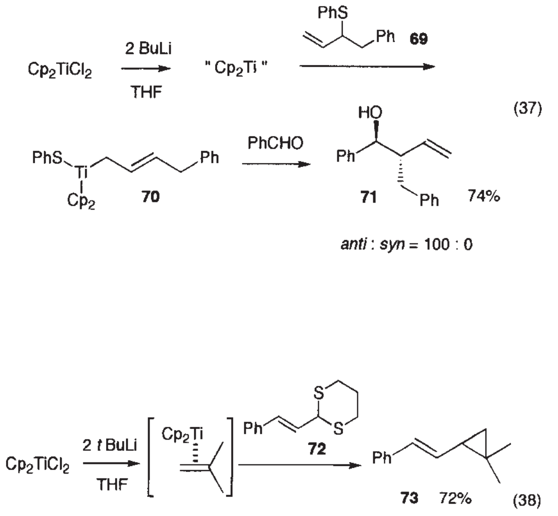
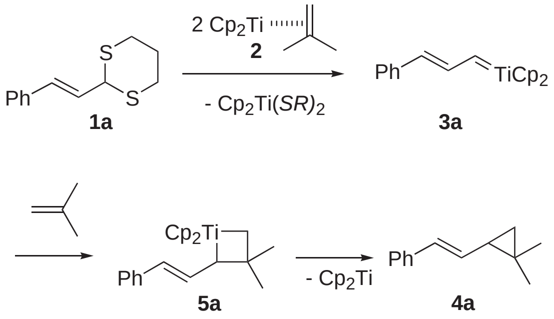
In the course of another study on the desulfurizative metallation of organosulfur compounds, we recently found that the treatment of allyl sulfides **69** with the low-valent titanium species prepared by the reaction of titanocene dichloride with butyllithium produced the allyltitanium compounds **70** which afford *anti*-homoallyl alcohols **71** with high regio and diastereoselectivity on treatment with aldehydes (eq 37).[39] On the other hand, much to our surprise, the similar reactions of thioacetals of α,β-unsaturated aldehydes **72** and their analogues, substituted 1,3-bis(phenylthio)-1-propenes, gave the alkenylcyclopropanes **73** (eq 38).[40]



We now believe that interesting and synthetically useful reactions must be developed by the combined use of organosulfur and organometallic compounds as exemplified in the last two equations.

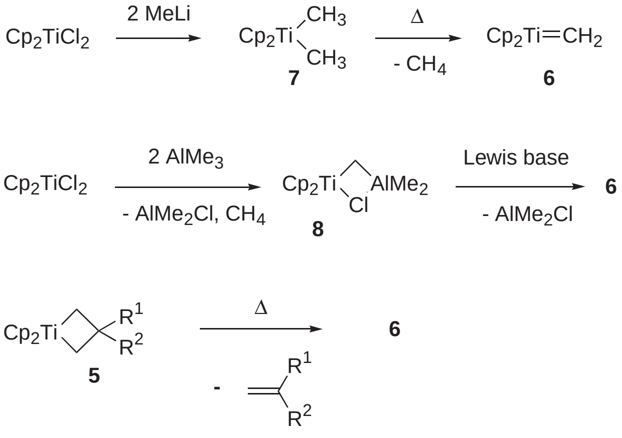
Fig. 1.



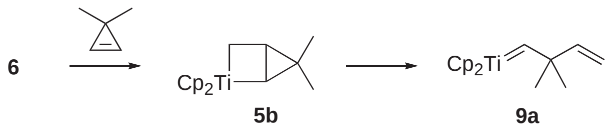
Scheme 1.

tained by reaction of the Tebbe reagent with appropriate olefins, was also reported by Grubbs and his co-workers.[7] The most fundamental titanium carbene complex **6** has been employed as a synthetic reagent or catalyst in a wide range of organic syntheses such as carbonyl methylenation and olefin metathesis.[8]

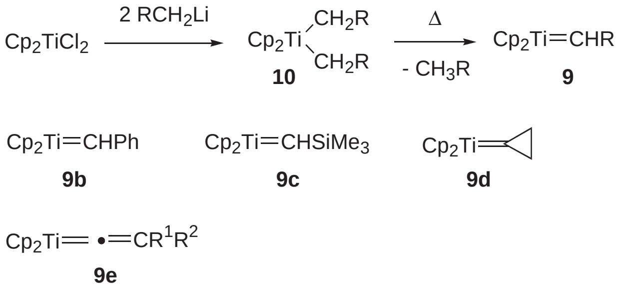
On the contrary, the preparation of its higher homologues, alkylidenetitanocenes **9**, has still been largely restricted. Grubbs et al. reported in 1986 the preparation of **9** by the metathesis of the methylidene complex **6** with strained olefins.[9] For example, **9a** is prepared by the reaction of **6** with 3,3-dimethylcyclopropene via the formation of the titanacyclobutane **5b**



Scheme 2.



Scheme 3.



Scheme 4.

(Scheme 3). The method, however, has only limited application. In the early 90's, Petasis and co-workers developed the preparation of alkylidenetitanocenes **9** by the α-elimination of dialkyltitanocenes **10** (Scheme 4).[10] Unfortunately, their method can be applied for the preparation of only a limited number of carbene complexes, such as titanocene–benzylidene **9b**, –trimethylsilylmethylidene **9c**, –cyclopropylidene **9d**, and –vinylidene **9e** complexes.

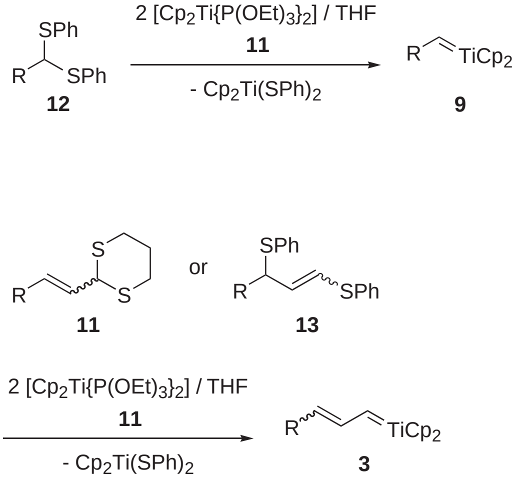
1. Formation of Alkylidenetitanocenes by the Desulfurizative Titanation of Thioacetals

As described above, the preparation of alkylidenetitanocenes was still a longstanding problem when we started this study. We expected that the desulfurizative titanation of thioacetals would become a versatile way for the preparation of such active species. Our reaction (Scheme 1), however, suffers a fatal flaw as a procedure for the preparation of titanium carbene complexes: an olefin is inevitably produced when the low-valent titanium species **2** is prepared by the reaction of titanocene dichloride with alkyllithiums (Scheme 5) and, consequently, the carbene complex reacts with the olefin as it is formed. Then the first problem that needed to be overcome was to establish a method for the preparation of an olefin-free

Scheme 5.

$$\mathrm{Cp_2TiCl_2} + \mathrm{Mg} + 2\,\mathrm{P(OEt)_3} \xrightarrow[\text{THF / rt, 2- 3 h}]{\textit{Molecular Sieves 4A}} [\mathrm{Cp_2Ti\{P(OEt)_3\}_2}]\ \mathbf{11}$$

Scheme 6.



Scheme 7.

titanocene(II) reagent.

Two methods for the generation of such titanocene(II) species by the reduction of titanocene dichloride with sodium[11] or magnesium[12] in the presence of trimethyl phosphite or trimethylphosphine have already appeared. These methods, however, seemed to be either too time-consuming or too costly for our purposes. We then examined an alternative method for the preparation of low-valent titanium species and found that the titanocene(II) complex $[\mathrm{Cp_2Ti\{P(OEt)_3\}_2}]$ **11** is formed by the reduction of titanocene dichloride with magnesium in the presence of triethyl phosphite. Unfortunately, however, the preparation was not reproducible, and we sometimes observed no reaction even after two or three days. We assumed that a trace amount of water would retard the reduction and examined the use of molecular sieves as a drying agent. As expected, the reduction of titanocene dichloride was completed within a short period of time under the reaction conditions to produce the titanocene(II) reagent **11** (Scheme 6).[13]

As is explained in the later sections, the desulfurizative titanation of thioacetals **12** with the titanocene(II) reagent **11** was found to be a convenient procedure for the preparation of a variety of titanium carbene complexes **9** (Scheme 7). Titanium alkenylcarbene complexes **3** have also been prepared by the treatment of unsaturated thioacetals **1** or related organosulfur compounds **13** with **11**. Since the reactivity of thioacetals toward the low-valent titanium **11** is largely dependent on the substituent on sulfur, the use of appropriate thioacetals is of crucial importance in this system; for the preparation of alkylidene complexes **9**, the corresponding diphenyl thioacetals **12** are starting materials of choice. No alkylidene complexes are formed from dialkyl thioacetals. In the case of the generation of α,β-unsaturated carbene complexes **3**, trimethylene thioacetals of α,β-unsaturated aldehydes **1** or 1,3-bis(phenylthio)propene derivatives **13** can be employed. The reactivity profile of these active species toward organic molecules has become clear; they react with various organic compounds including ones bearing a carbon-heteroatom or carbon–carbon multiple bond.

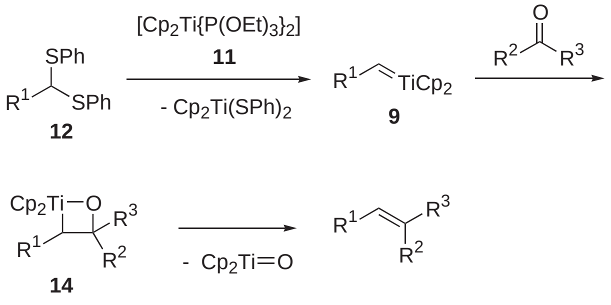
2. Carbonyl Olefination[14]

2.1 Intermolecular Carbonyl Olefination. Olefination of carbonyl compounds is one of the most fundamental organic transformations and has been extensively studied since its discovery by Wittig in the early 1950s.[15] The Wittig,[16] Horner–Wadsworth–Emmons,[17] Peterson,[18] and Julia[19] reactions are frequently employed for this transformation. However, these conventional reactions suffer one serious disadvantage, in that the acylation of the carbanions used tends to proceed in preference to the Wittig-type olefination of carbonyl compounds when the reactions are applied to carboxylic acid derivatives.

One of the most characteristic reactions of nucleophilic transition metal carbene complexes is the Wittig-like olefination of carbonyl compounds. These reactions have an advantage over the conventional carbonyl olefinations in that not only aldehydes and ketones but also carboxylic acid derivatives are transformed into heteroatom-substituted olefins. Accordingly, if the organotitanium species generated from thioacetals **12** are alkylidenetitanocenes **9**, one would expect that the treatment of such species with carbonyl compounds would afford the olefins via the oxatitanacyclobutane intermediates **14** (Scheme 8).

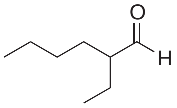
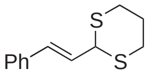
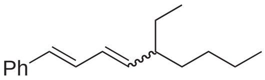
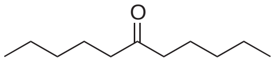
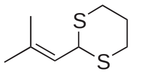
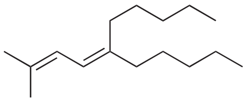
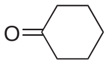
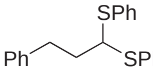
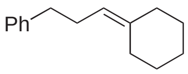
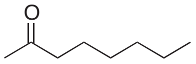
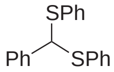
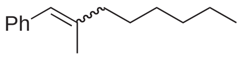
Indeed, the successive treatment of thioacetals **12** with the titanocene(II) **11** and carbonyl compounds did produce a variety of olefinic compounds (Table 1).[13] Thioacetals of α,β-unsaturated aldehydes **1** can also be employed for the reaction. The olefination of esters, lactones, thiol esters,[20] and amides[21] also proceed to afford the corresponding heteroatom-substituted olefins with *Z*-stereoselectivity (Table 2). The characteristic features of this new carbonyl olefination are that it is operationally straightforward and that it requires neither a strong base nor a pyrophoric reagent.

As for the alkylidenation of carboxylic acid derivatives, Takai, Utimoto, and their co-workers reported the olefination using a $\mathrm{RCHBr_2}$–$\mathrm{TiCl_4}$–Zn(Pb)–TMEDA system.[22] Petasis



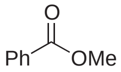
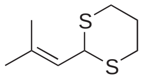
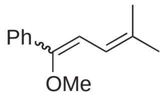
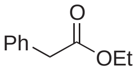
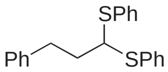
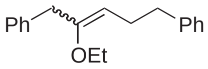
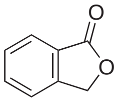
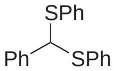
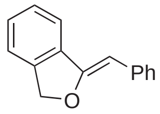
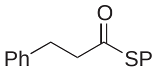
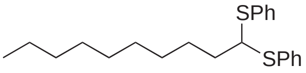
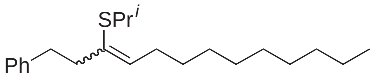
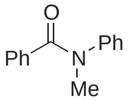
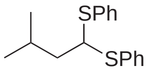
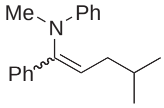
Scheme 8.

Table 1. Olefination of Aldehydes and Ketones

Carbonyl compound	Thioacetal	Product	Yield/%; *E*:*Z*
	 **1a**		77
	 **1b**		88
	 **12a**		69
	 **12b**		80; 54:46

Reaction conditions: 1) Thioacetal; 1.1 equiv/**11**; 3 equiv/THF/rt, 10 min. 2) Carbonyl compound/rt, 30 min.

Table 2. Olefination of Carboxylic Acid Derivatives

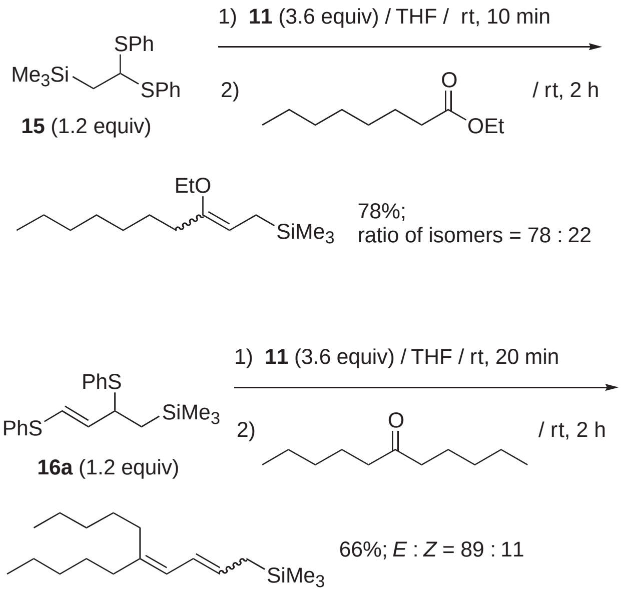
Carbonyl compound	Thioacetal	Product	Yield/%; *E*:*Z*
	 **1b**		73; 23:77
	 **12a**		75; 14:86
	 **12b**		75; <1:>99
	 **12c**		84; 19:81
	 **12d**		76; <1:>99[a)]

Reaction conditions: 1) Thioacetal; 1.1–1.5 equiv/**11**; 3–4.5 equiv/THF/rt, 5–10 min. 2) Carbonyl compound/rt, 30 min or reflux, 1–2 h. a) Ratio of isomers.

and co-workers also reported the carbonyl olefination with some alkylidenetitanocenes prepared from dialkyltitanocenes having no β-hydrogen.[10] As compared with these procedures, carbonyl olefination utilizing thioacetals enjoys an advantage that a variety of thioacetals and related organosulfur compounds are easily obtainable from various starting materials. The following equations exemplify the wide synthetic applications of the present method; carbonyl compounds are transformed into allylsilanes[23] and dienylsilanes[24] using trialkylsilyl group-substituted organosulfur compounds **15** and **16a**, which are easily prepared by the alkylation of bis(phenylthio)methane and 1,3-bis(phenylthio)propene with trialkylsilylmethyl iodide, respectively (Scheme 9).

Another application of our carbonyl olefination is the preparation of enol ethers and alkenyl sulfides using dithio- and trithioorthoformates **17a** and **18** as carbene complex precursors (Scheme 10).[25] This procedure provides a convenient way for the preparation of 1,2-diheteroatom-substituted olefins from carboxylic acid derivatives.

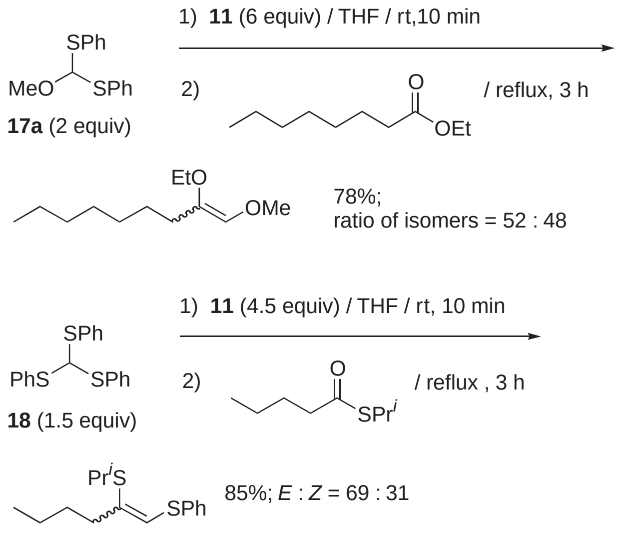
However a serious drawback remained in the above procedure for the preparation of alkoxy group substituted carbene complexes; it is difficult to introduce a variety of alkoxy groups to the olefinating agents due to lack of easy access to dithioorthoformates **17**. Preparation of **17** is generally performed by the reaction of alkyl dichloroalkyl ethers[26] with alkali metal thiolates. However, this route cannot be applied for synthesis of dithioorthoformates bearing an acid labile alkoxy group. We solved this problem based on our previous findings in organotin chemistry;[27] a variety of dithioorthoformates **17** including the ones bearing a terminal olefin moiety or an acid-sensitive 2-trimethylsilylethoxy group were obtained by the copper(II) salt-promoted oxidative coupling of lithium alkoxides with readily available bis(phenylthio)methyltributylstannane **19** (Scheme 11). The titanocene(II)-promoted car-



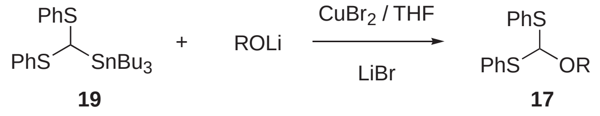
Scheme 9.

bonyl olefination using these organosulfur compounds gave the corresponding enol ethers in good yields (Table 3).[28]

In the olefination of esters and lactones with (alkoxymethylidene)titanocenes **20**, the *E*-isomers always predominated. The stereoselectivity observed in the formation of 1,2-dialkoxy olefins is different from that found in the alkylidenation of carboxylic acid derivatives with alkylidenetitanocenes, in which *Z*-isomers are always dominant products.[13,20] This is probably due to the unfavorable formation of the oxatitanacyclobutane intermediate **14b**, which is destabilized by the dipole–dipole repulsion between two alkoxy substituents. Therefore the *E*-isomers are produced via the preferential formation of the titanacycle intermediate **14a** (Scheme 12).



Scheme 10.

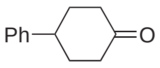
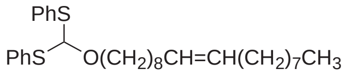
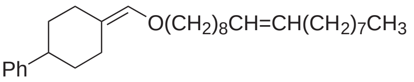
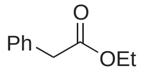
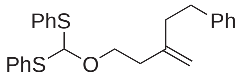
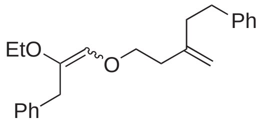
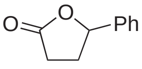
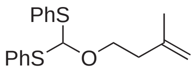
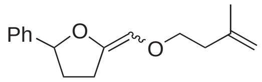
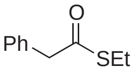
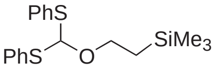
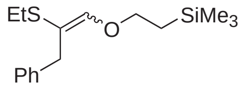
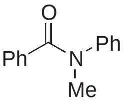
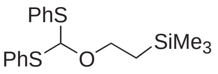
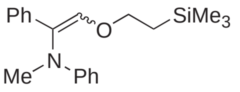


Scheme 11.

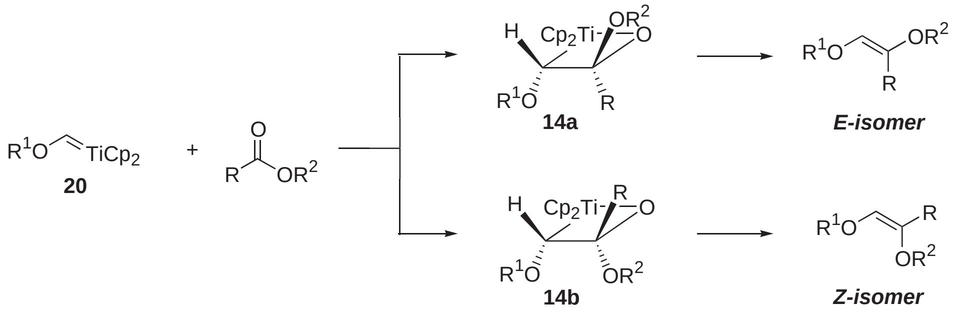
The above investigation indicates that the synthetic application of the carbonyl olefination utilizing a thioacetal–titanocene(II) system will be further developed by exploring new methods for the preparation of various thioacetals and their analogues.

2.2 Intramolecular Carbonyl Olefination. Although many methods for the olefination of carbonyl compounds have been developed, the intramolecular carbonyl olefination of carboxylic acid derivatives has remained as a big issue to be solved. For example, intramolecular carbonyl olefinations of esters using the phosphorous-stabilized carbanions are general-

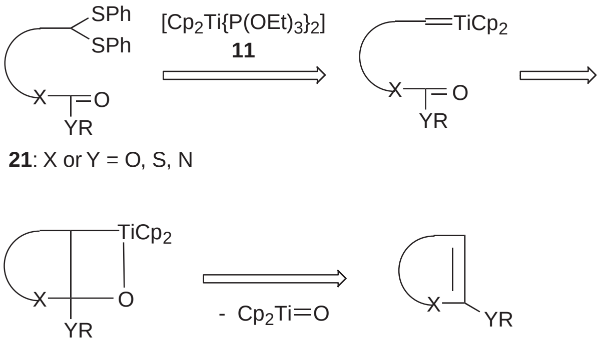
Table 3. Transformation of Carbonyl Compounds into Enol Ethers

Carbonyl compound	Dithioorthoformate **17**	Product	Yield/%; *E*:*Z*
			56
			80; 62:38
			52; 62:38
			81; 83:17
			64[a]

Reaction conditions: 1) Dithioorthoformate; 1.5 equiv/**11**; 3 equiv/THF/25 °C, 10 min. 2) Carbonyl compound/reflux, 3 h.
a) Single isomer. The configuration was not determined.



Scheme 12.

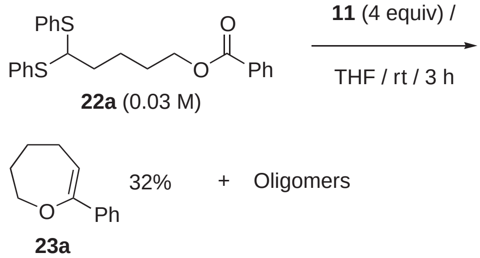


Scheme 13.

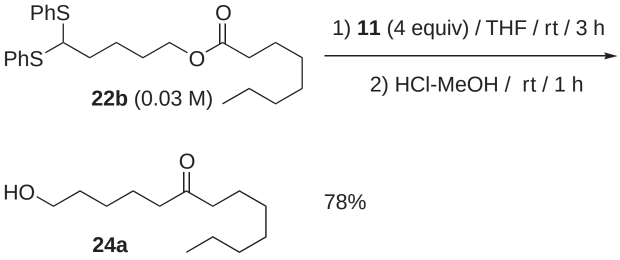
ly unsuccessful because these reactions end up with the formation of acylation products.[29] Only the preparation of certain five- and six-membered cyclic compounds, in which the formation of double bond is facilitated with π-conjugation with a carbonyl group or an aromatic ring, has been achieved.[30] Although the intramolecular carbonyl olefination of amides is one of the most attractive routes for the construction of nitrogen heterocycles, the Wittig and related reactions are employed only for the formation of aromatic rings such as indoles and the unsaturated cyclic compounds in which the formed double bond is stabilized with π-conjugation. The intramolecular Peterson[31] and McMurry[32] reactions are also employed for the preparation of indoles and pyrroles. Although the intramolecular carbonyl olefinations via the formation of transition metal carbene complexes and related reactive species have been investigated,[33] the application of these methods is largely restricted by inaccessibility of appropriate starting materials which must possess both a carbonyl group and a precursor of organometallic species.

Thioacetal is a typical protecting group of carbonyl compounds and is fairly stable under either acidic or basic conditions. Therefore, carboxylic acid derivatives having a thioacetal moiety **21** are readily obtained using various starting materials and can be subjected to intramolecular carbonyl olefination (Scheme 13).

We first examined the titanocene(II)-promoted reaction of ω,ω-bis(phenylthio)alkyl alkanoates **22**, the esters having a thioacetal moiety in their alcohol part. Unfortunately, however, our expectations were disappointed; the reaction of **22a** is rather complicated by the formation of oligomeric vinyl ethers and the cyclic vinyl ether **23a** was obtained only in moderate yield even under high dilution conditions (Scheme 14). The



Scheme 14.

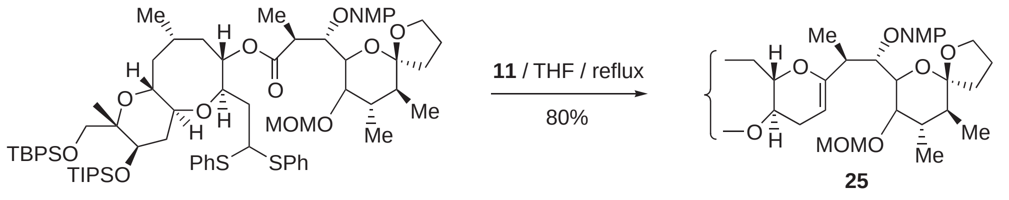


Scheme 15.

multi-component mixture of the vinyl ethers obtained from **22b** were hydrolyzed to afford the ω-hydroxy ketone **24a** in good overall yield (Scheme 15).[34]

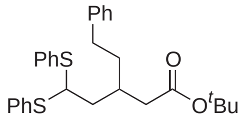
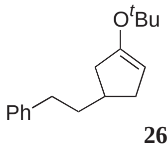
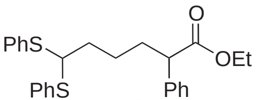
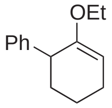
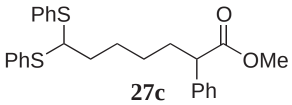
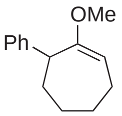
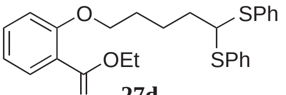
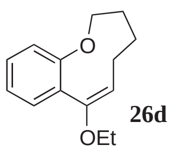
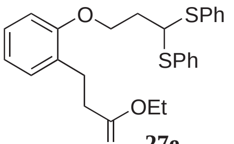
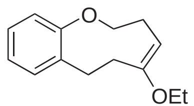
It is well known that the success in the construction of cyclic molecules by intramolecular reaction is largely dependent on the conformation of the substrates. Indeed, despite our disappointing results, Hirama and his co-workers showed that the formation of the J-ring of ciguatoxin **25** was successfully achieved using a thioacetal–titanocene(II) system (Scheme 16).[35] Their success was encouraging for us because it indicated that our thinking was not widely wrong.

Indeed, contrary to our above results, the vinyl ethers of cyclic ketones **26** were produced in good yields by the reactions of alkyl ω,ω-bis(phenylthio)alkanoates **27** having a thioacetal function in their carboxylic acid part (Table 4).[36] These results indicate that the success of the intramolecular carbonyl olefination largely depends on the structure of the substrate. As noted above, the advantage of the present preparation is that the starting materials are easily prepared by the use of organosulfur building blocks. Thus the esters **27d** and **27e** obtained by the Williamson ether synthesis utilizing ω,ω-bis(phenylthio)-alkanols were transformed into the nine-membered cyclic vinyl ethers **26d** and **26e** with high stereoselectivity.



Scheme 16.

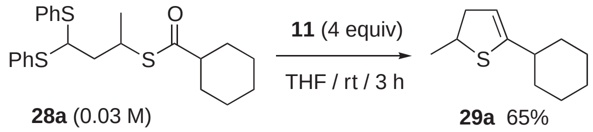
Table 4. Intramolecular Carbonyl Olefination of Alkyl ω,ω-Bis(phenylthio)alkanoates **27**

ω,ω-Bis(phenylthio)alkanoate **27**	Product **26**	Yield/%
 **27a**	 **26a**	75
 **27b**	 **26b**	53
 **27c**	 **26c**	73
 **27d**	 **26d**	70
 **27e**	 **26e**	67

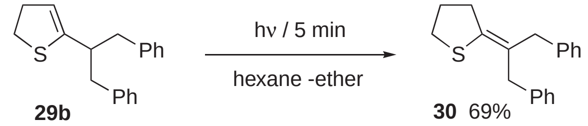
Thioacetal; 0.03 M/**11**; 4 equiv/THF/rt, 3–5 h or reflux, 2–5 h.

Another successful intramolecular carbonyl olefination utilizing a thioacetal–titanocene(II) system is the preparation of five-membered heterocyclic compounds. The treatment of the thiol ester bearing a thioacetal moiety **28a** with the titanocene(II) reagent **11** gave the dihydrothiophene **29a** in good yield (Scheme 17).[37] Although 2,3-dihydrothiophene is one of the most fundamental sulfur-containing heterocycles, its chemistry has not been fully studied yet. This is evidently due to the lack of any appropriate methods for the preparation of the dihydrothiophene derivatives. Actually, during this study, we found an interesting photochemical isomerization reaction: the 5-substituted 2,3-dihydrothiophene **29b** obtained were susceptible to sunlight, and easily isomerized to the exocyclic olefin **30** by a brief irradiation with a high-pressure mercury lamp under air (Scheme 18).

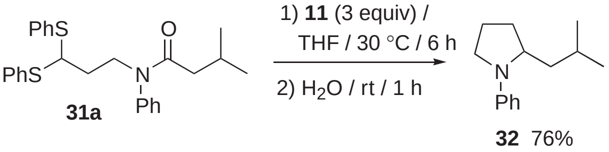
Next, we tried to prepare 5-membered unsaturated nitrogen heterocycles by the intramolecular carbonyl olefination of *N*-[3,3-bis(phenylthio)propyl]anilides **31**. Contrary to our expectation, the pyrrolidine derivative **32** was obtained by the reaction of the anilide **31a** with the titanocene(II) reagent **11** under high dilution conditions, followed by the treatment with water (Scheme 19).[21] We tentatively assume that the initially formed dihydropyrrole is reduced by the action of a certain titanium hydride species generated from the divalent titanocene **11** and water.



Scheme 17.



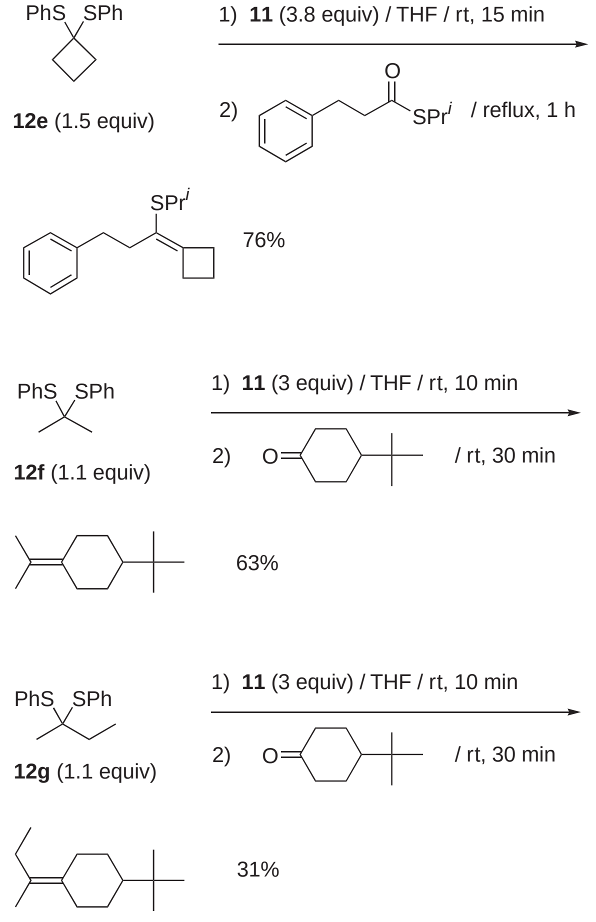
Scheme 18.



Scheme 19.

2.3 Carbonyl Olefination Using Organic Halides. Since the conventional olefin-forming reactions are seriously affected by steric hindrance, the yields are generally very low in the case of tetrasubstituted olefins.[38] For example, reactions of phosphoryl-stabilized carbanions and α-silyl carbanions proceed smoothly only when one alkyl group is present at the central carbon of these carbanions; hence preparation and reaction of these species possessing two α-alkyl substituents have seldom been the subjects of synthetic work. Only α-phosphoryl-[39] and α-silyl-carbanions,[40] in which substituents present minimal steric hindrance to the approaching carbonyl compound, have been prepared and employed for carbonyl olefination. Unfortunately our thioacetal–[$Cp_2Ti\{P(OEt)_3\}_2$] procedure also suffers a similar disadvantage. Although the carbonyl olefination using diphenyl thioacetals prepared from less hindered ketones such as cyclobutanone **12e**[41] or acetone **12f**[13] gave tetrasubstituted olefins in good yields, a further increase in steric bulk of the substituent largely decreases the yield as seen in the carbonyl olefination utilizing **12g** (Scheme 20). In the case of the thioacetals prepared from dialkyl ketones, alkenyl and alkyl sulfides were preferentially produced and no formation of carbene complex was observed.[42]

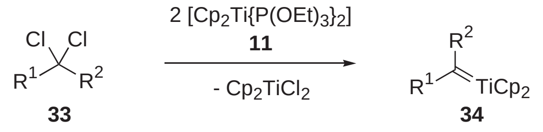
Then we turned our attention to the synthesis of highly substituted olefins using *gem*-dihalides **33**. Since the carbon–halogen bond would be more easily reduced with titanocene(II) **11** than the carbon–sulfur bond of thioacetal, the alkylidenetitanocene having an α-substituent **34** or its equivalent would be formed by the treatment of *gem*-dihalide having two alkyl substituents **33** with **11** (Scheme 21). The preparation of highly substituted dihalides **33** in pure form is generally difficult owing to the concomitant formation of vinyl halides. Fortunately, around the same time we found an operationally straightforward and inexpensive method for the preparation of *gem*-dihalides **33** without contamination of vinyl halides. The method consists of the formation of the hydrazone **35** from the corresponding ketone and its treatment with copper(II) halide–triethylamine in methanol (Scheme 22).[43]



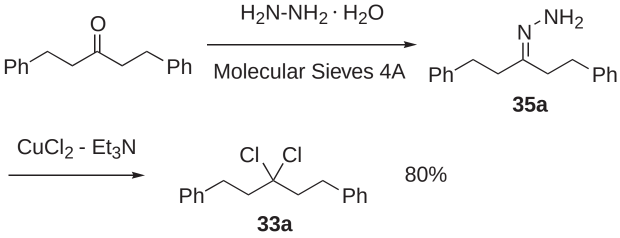
Scheme 20.

As was expected, the organotitanium species generated by the treatment of *gem*-dihalides **33** with the titanocene(II) species reacted with ketones, esters, and lactones to produce tetrasubstituted olefins and trisubstituted vinyl ethers in good yields (Table 5).[40]

This procedure was successfully extended to the dichloromethylidenation of ketones using carbon tetrachloride (Scheme 23).[44] Although the Wittig type reaction using dihalomethylenephosphorane or lithium salt of diethyl dichloro-

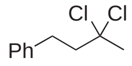
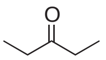
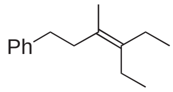
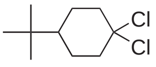
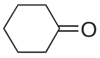
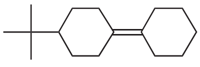
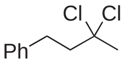
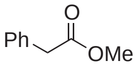
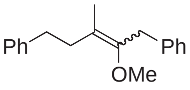
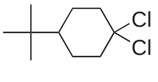
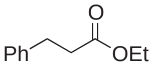
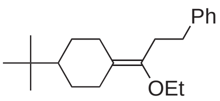
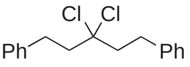
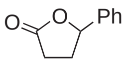
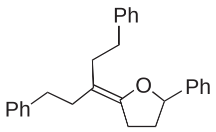


Scheme 21.

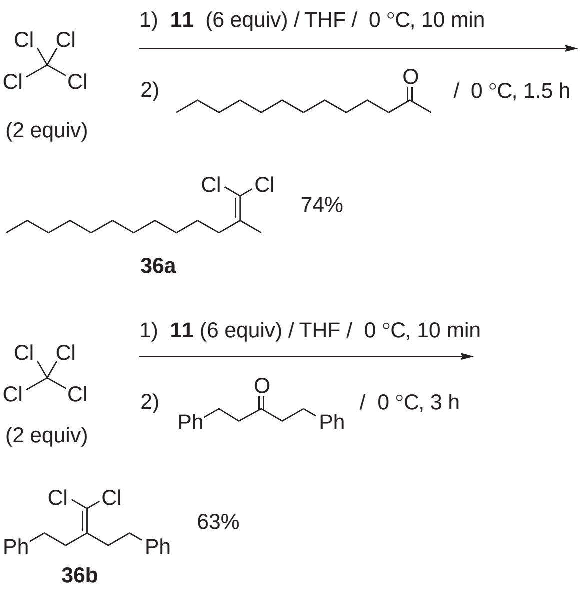


Scheme 22.

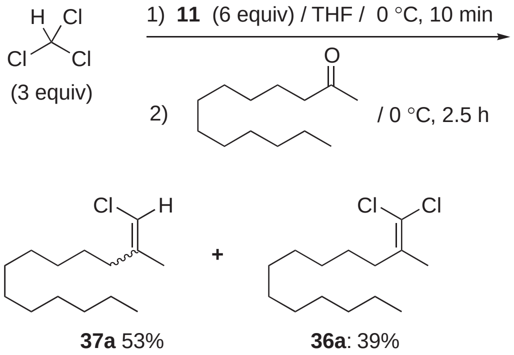
Table 5. Carbonyl Olefination Utilizing a *gem*-Dichloride–Titanocene(II) System

gem-Dichloride **33**		Carbonyl compound	Product	Yield/%; ratio of isomers
	**33b**			59
	**33c**			73
	**33d**			83; 62:38
	**33e**			81
	**33a**			72

Reaction conditions: 1) Dichloride; 2 equiv/**11**; 6 equiv/THF/rt, 20 min. 2) Carbonyl compound/0 °C, 1 h.



Scheme 23.

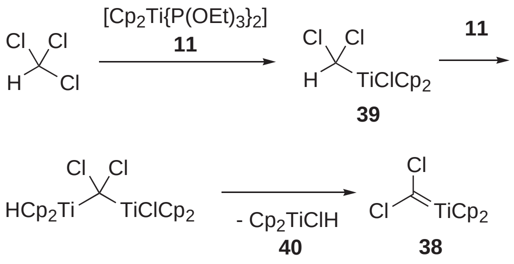


Scheme 24.

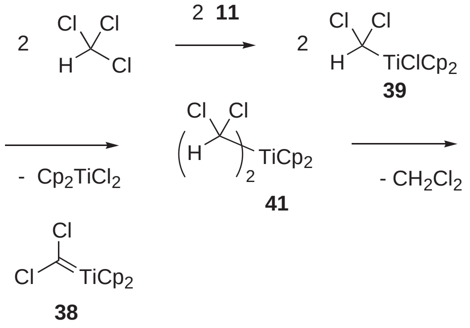
methanephosphonate,[45] and the Peterson olefination using (dichlorotrimethylsilylmethyl)lithium[46] are frequently employed for the conversion of carbonyl compounds into 1,1-dihaloalkenes **36**, attempts to prepare the highly substituted dichlorides, such as **36b** in Scheme 23, from dialkyl ketones are generally unsuccessful. The dichloromethylidenation utilizing a carbon tetrachloride–titanocene(II) system enjoys an advantage that the dichloro olefins are obtained even when sterically hindered dialkyl ketones are employed.

One might imagine that the olefination of ketones with a chloroform–titanocene(II) system affords the corresponding vinyl chlorides **37**. Although 2-tridecanone was transformed into the vinyl chloride **37a** on treatment with the reagents, it was found that a considerable amount of the 1,1-dichloroalkene **36a** was also produced as a by-product (Scheme 24).[44]

The formation of **36** implies that (dichloromethylidene)titanocene **38** is generated by the reaction of chloroform with the low valent titanium **11**. We initially assumed that such species was formed by the oxidative addition of C–H bond of the dichloromethyltitanocene chloride **39** to **11** and following elimination of titanocene hydride **40**, as depicted in Scheme 25. However, at a later time, we came up with another reasonable explanation for the reaction, in which the disproportionation of



Scheme 25.



Scheme 26.

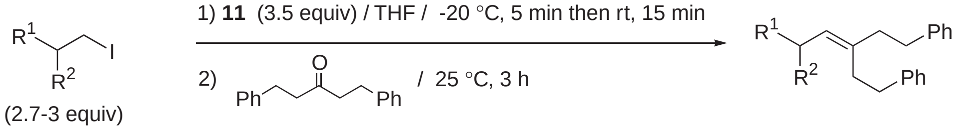
39 gave bis(dichloromethyl)titanocene **41** and titanocene dichloride. The following α-elimination of **41** gave the (dichloromethylidene)titanocene **38** (Scheme 26).

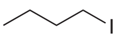
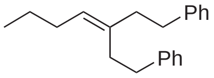
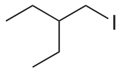
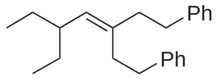
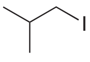
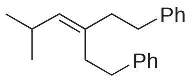
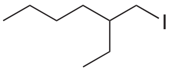
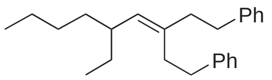
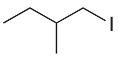
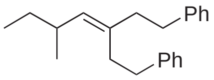
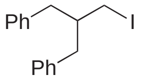
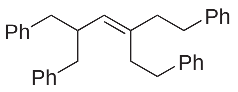
This hypothesis was quite attractive for us because it indicated that titanium carbene complexes would be generated by the treatment of simple alkyl halides with the titanocene(II) reagent **11**. We were disappointed, however, that the successive treatment of butyl iodide with **11** and 1,5-diphenyl-3-pentanone gave no olefination product. We further continued the study along this line, and a successful result was obtained when alkyl halides possessing a substituent at the carbon β to halogen were employed (Table 6).[47] The yield of carbonyl olefination is largely dependent on the bulkiness of the substituent; it increases with increase in the carbon numbers of the main chain and substituent, and it is maximized when the halide has an ethyl group as a β-substituent. Generally, a carbene complex cannot be formed by α-elimination of a transition metal complex possessing alkyl groups with β-hydrogen due to the preferential β-elimination.[4] Thus, this finding is of special interest because it demonstrates that the titanium carbene complexes are produced by α-elimination of dialkyltitanocene even when the alkyl substituent has a β-hydrogen.

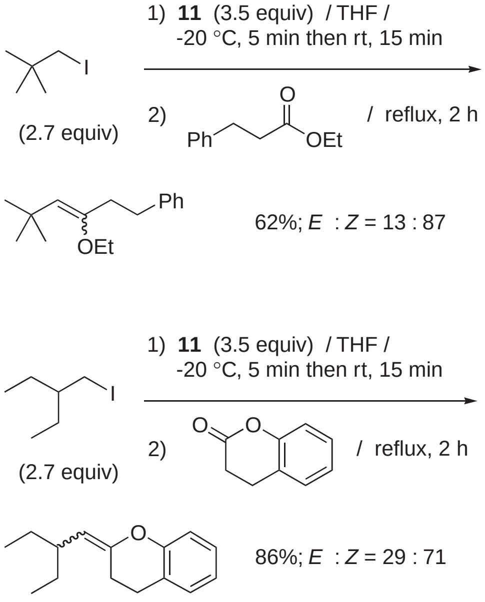
As shown in the following scheme, the Wittig-like olefination of a variety of carbonyl compounds is accomplished by the use of readily available alkyl halides bearing a β-substituent without any pre-transformation. The conversion of carbonyl compounds into the bulky *t*-butyl group substituted olefins was also attained by the use of neopentyl iodide (Scheme 27).

Similarly the organotitanium reagents generated by the treatment of alkyl chloromethyl ethers such as **42a** with **11** is employed for the alkoxymethylenation of carbonyl compounds, leading to the formation of enol ethers or 1,2-dialkoxy-1-alkenes (Scheme 28).[48] It is obvious that this new olefination procedure largely simplifies the conventional Wittig route, as shown in Scheme 29.

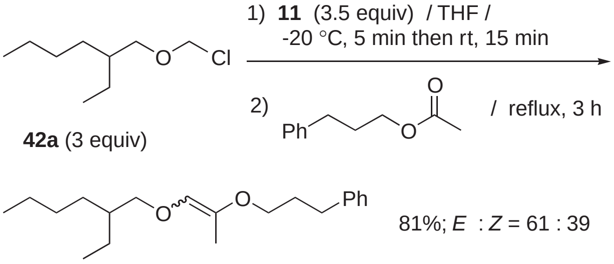
Table 6. Olefination of 1,5-Diphenyl-3-pentanone with Various Alkyl Iodides



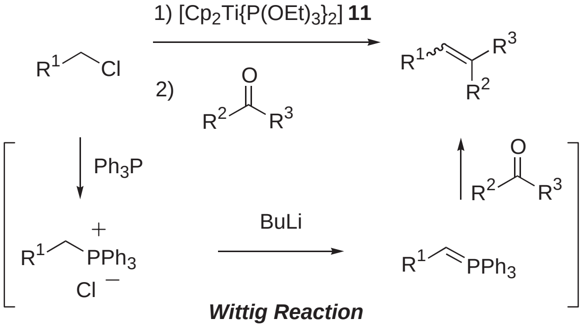
Alkyl iodide	Product (Yield/%)		Alkyl iodide	Product (Yield/%)	
		(—)			(64)
		(15)			(66)
		(42)			(60)



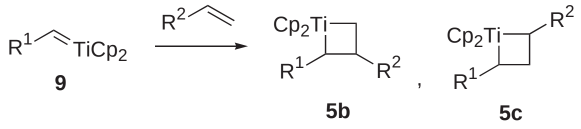
Scheme 27.



Scheme 28.



Scheme 29.



Scheme 30.

3. Reaction of Carbene Complexes with Olefins[49]

3.1 Olefin Metathesis. One of the characteristic features of transition metal carbene complexes is that they readily react with non-polar carbon–carbon multiple bonds as well as with polar multiple bonds such as those in carbonyl compounds. Then we examined the reaction of titanium carbene complexes generated from thioacetals with terminal olefins. The reaction, however, gave multi-component mixtures of unsaturated hydrocarbons. It is assumed that this complexity would arise, at least in part, from lack of regioselectivity in the formation of titanacyclobutane intermediates **5b** and **5c**, which may decompose to form new carbene complexes and olefins by a metathesis-type degradation process (Scheme 30).

We then examined the influence of substituents of olefins on the geometry of the intermediate titanacycles **5**. We found that the γ-substituted allylsilane **43** was stereoselectively obtained when allyltriisopropylsilane was employed as an olefin component (Scheme 31).[50] The by-product, homoallylsilane **44**, is assumed to be produced by the β-elimination of the intermediary titanacyclobutane **5d** (Scheme 32). The formation of these organosilicon compounds indicates that the titanacycle **5d** is produced with high regioselectivity.

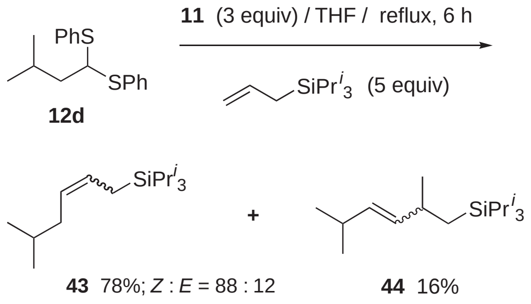
A similar metathesis between the carbene complexes **9** generated from thioacetals **12** and ethylene that gives terminal olefins is regarded as an equivalent to the Wittig-type methylenation of "protected aldehydes". For example, the thioacetal **12h** was transformed into the corresponding olefin by simple treatment with **11** under ethylene (Scheme 33).

In this reaction, half of the ethylene is introduced into the terminal olefin via the formation of titanacyclobutane intermediate **5**, followed by the extrusion of methylidenetitanocene **6** (Scheme 34).[51] Another conceivable mode of degradation of titanacyclobutanes **5** is the expulsion of a titanocene(II) species via β-elimination[52] leading to the formation of terminal olefins with two-carbon homologation. In the first report on the preparation and reactions of the Tebbe reagent **7**, the formation of propene by the reaction of methylidenetitanocene **6** with ethylene was described.[6] Despite the potential synthetic utility of this two-carbon homologation, the process has not been thoroughly studied so far. We were intrigued with such a process because it is regarded as a formal carbenoid insertion reaction of alkylidenetitanocenes with vinylic C–H bond of ethylene.

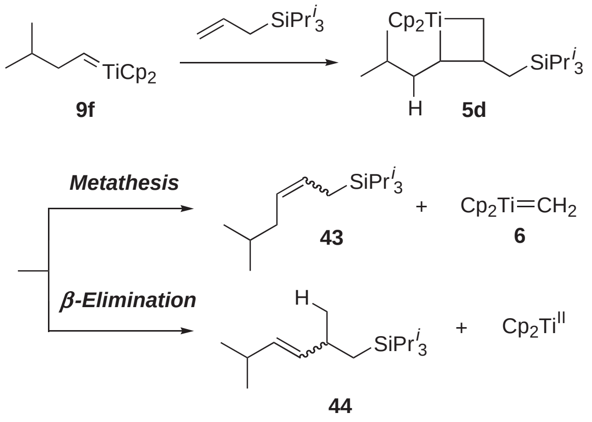
After detailed examination of the reaction conditions, we found that the terminal olefin with two-carbon homologation was selectively produced when triethyl phosphite-free titanocene(II) species **2** was employed for the desulfurization of the thioacetal **12i** (Scheme 35).[51]

We also found that a similar reaction of alkylidenetitanocenes with styrene derivatives produced (*E*)-1-aryl-1-alkenes with high stereoselectivity: the treatment of the thioacetal **12h** with **2** in the presence of styrene gave the β-substituted styrene along with a small amount of its isomer (Scheme 36).[53] The success of the reaction utilizing the unsymmetrical olefins is due to the regioselective formation of titanacyclobutane intermediate **5e** and its β-elimination via the selective scission of the titanium–benzyl bond (Scheme 37).

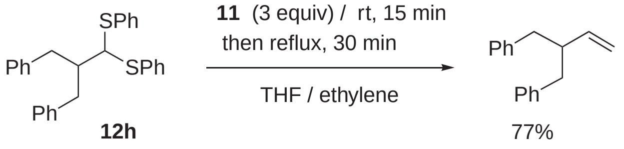
Another approach to regioselective formation of titanacycle intermediate **5** is to modify the reaction in an intramolecular fashion. In recent years, the transition metal catalyzed ring-closing metathesis (RCM) of dienes is frequently employed for the preparation of various cyclic compounds.[54] Nicolaou et al. reported the preparation of cyclic ethers from unsaturated esters by RCM using the Tebbe reagent **8** or dimethyltitanocene **7** as a promoter; in this reaction the alkylidenetitanocene



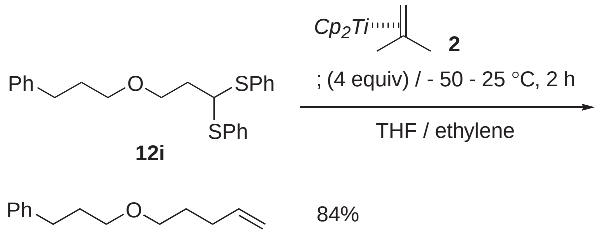
Scheme 31.



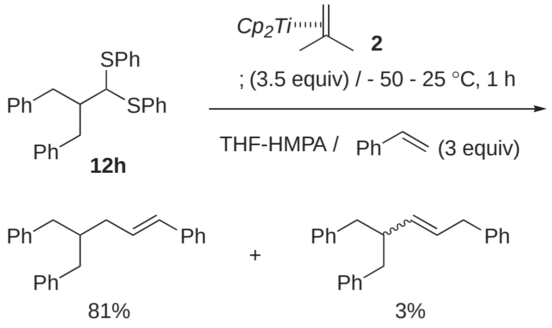
Scheme 32.



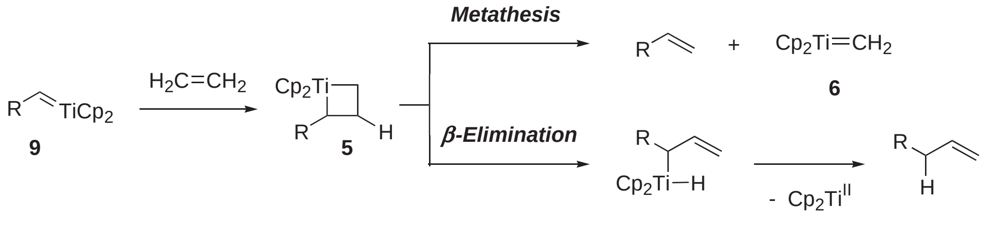
Scheme 33.



Scheme 35.

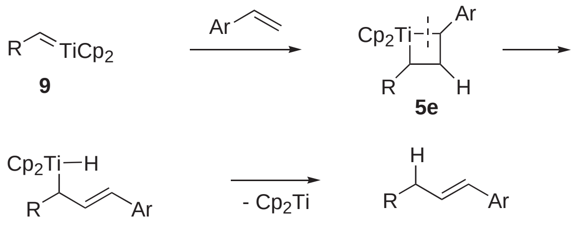


Scheme 36.

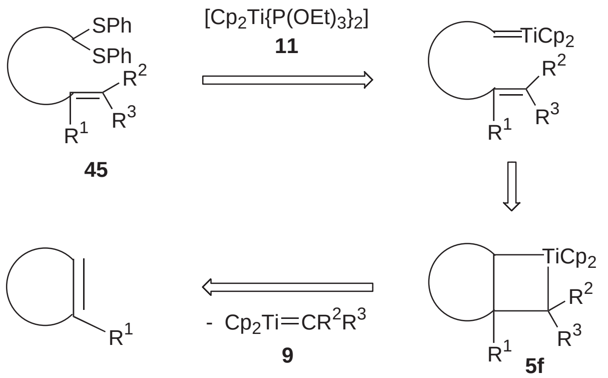


Scheme 34.

was suggested to serve as an intermediate.[55] The success of the above intermolecular metathesis between the titanium carbene complexes generated from thioacetals with olefins prompted us to explore RCM using thioacetals that have a carbon–carbon double bond **45**. This transformation proceeds via the formation of titanacyclobutane intermediate **5f** by the reaction of titanium–carbene complex with an internal double bond and the subsequent elimination of alkylidenetitanocene **9** (Scheme 38).[56]

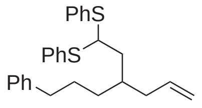
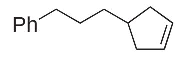
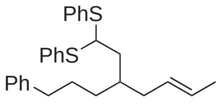
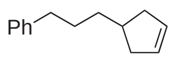
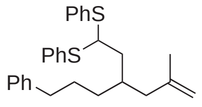
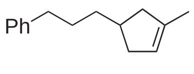
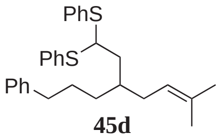
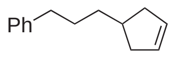


Scheme 37.



Scheme 38.

Table 7. Formation of Cyclopentenes by the Titanocene(II)-Promoted Reaction of Thioacetals Bearing a Carbon–Carbon Double Bond **45**

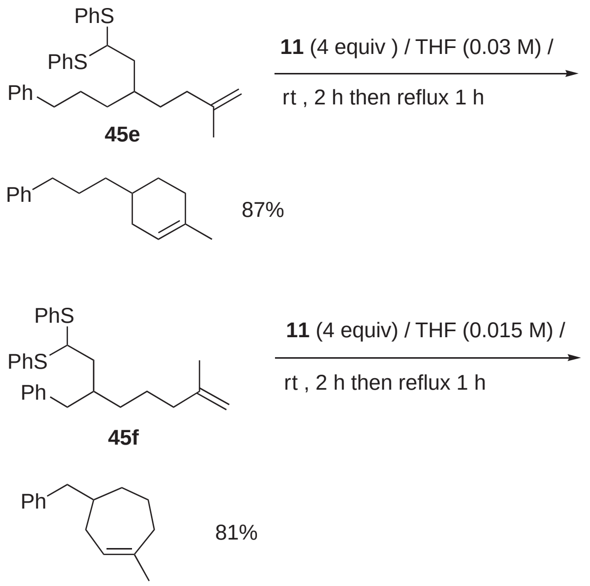
Thioacetal **45**	Product	Yield/%
 **45a**		71
 **45b**		67
 **45c**		87
 **45d**		8

Thioacetal; 0.1–0.03 M/**11**; 3 equiv/THF/rt, 1–2 h then reflux, 1 h.

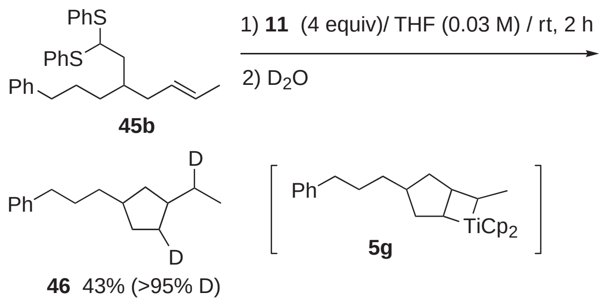
The substituent effect of the formation of cyclopentenes by the titanocene(II)-promoted reaction of the thioacetals **45** is summarized in Table 7. Taking into account the reaction pathway depicted in Scheme 38, we can explain the substituent effect of methyl groups observed in the above reactions by the extent of the retrograde reaction between the product, cycloalkene, and the alkylidenetitanocene **9**. In the case of **45d**, the steric repulsion between the two terminal methyl substituents of **45d** and Cp rings on titanium makes the formation of titanacycle **5f** unfavorable. The titanocene(II)-promoted cyclization of unsaturated thioacetals can be applied to the preparation of larger rings such as six and seven-membered cycloalkenes (Scheme 39).

In order to confirm the proposed mechanism, we treated the unsaturated thioacetal **45b** with the low-valent titanocene **11** at room temperature and then we quenched the reaction with D_2O to give the dideuteriocyclopentane **46** along with the RCM product (Scheme 40). The formation of **46** indicates that the reaction proceeds via the formation of titanacyclobutane intermediate **5g**.

The RCM of unsaturated thioacetals **45** enjoys an advantage that a diphenyl thioacetal moiety is easily introduced to organ-



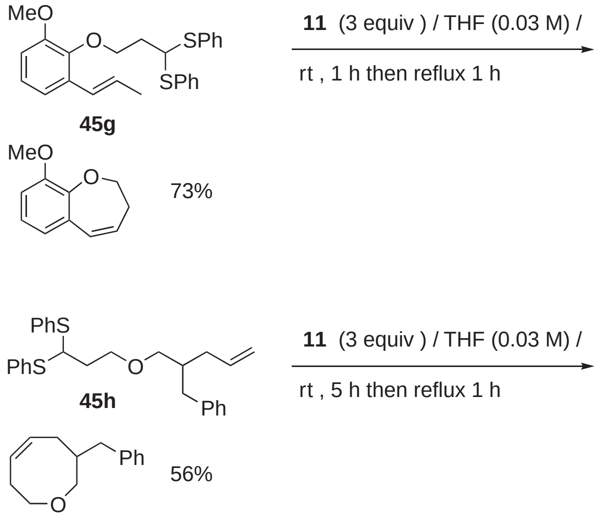
Scheme 39.



Scheme 40.

ic molecules by alkylation of bis(phenylthio)methane or treatment of carbonyls with thiophenol, and hence it is a strong synthetic tool for the construction of a variety of cyclic compounds including heterocycles. This idea was substantiated when the unsaturated ethers were treated with the titanocene(II) species; seven- and eight-membered cyclic ethers were obtained from the unsaturated thioacetals **45g** and **45h** (Scheme 41).[57]

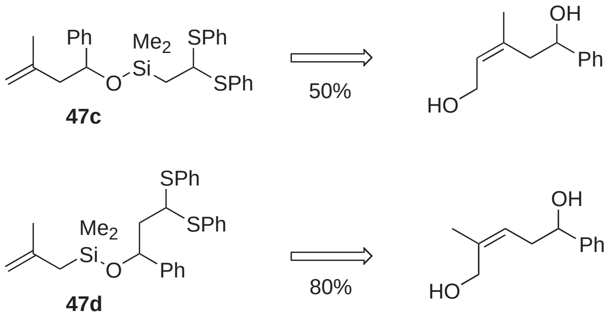
An interesting application of this cyclic ether synthesis is the stereoselective preparation of olefinic diols.[58] The unsaturated silyl ethers **47** were cyclized by the simple treatment with the titanocene(II) species **11**. The Tamao–Fleming oxidation[59] of the products, the cyclic allylsilanes **48**, gave the diols with complete *Z*-stereoselectivity (Scheme 42). As shown in Scheme 42, two types of starting materials can be employed for the present preparation. The first approach includes the cyclization of [2,2-bis(phenylthio)ethyl](but-3-enyloxy)dimethylsilane **47a** (Route A). The second starting material is the allylsilyl ether of 3,3-bis(phenylthio)propanol **47b** (Route B). These two types of cyclization are complementary to each other when the trisubstituted olefins are to be prepared, as exemplified by the reactions of **47c** and **47d** (Scheme 43).



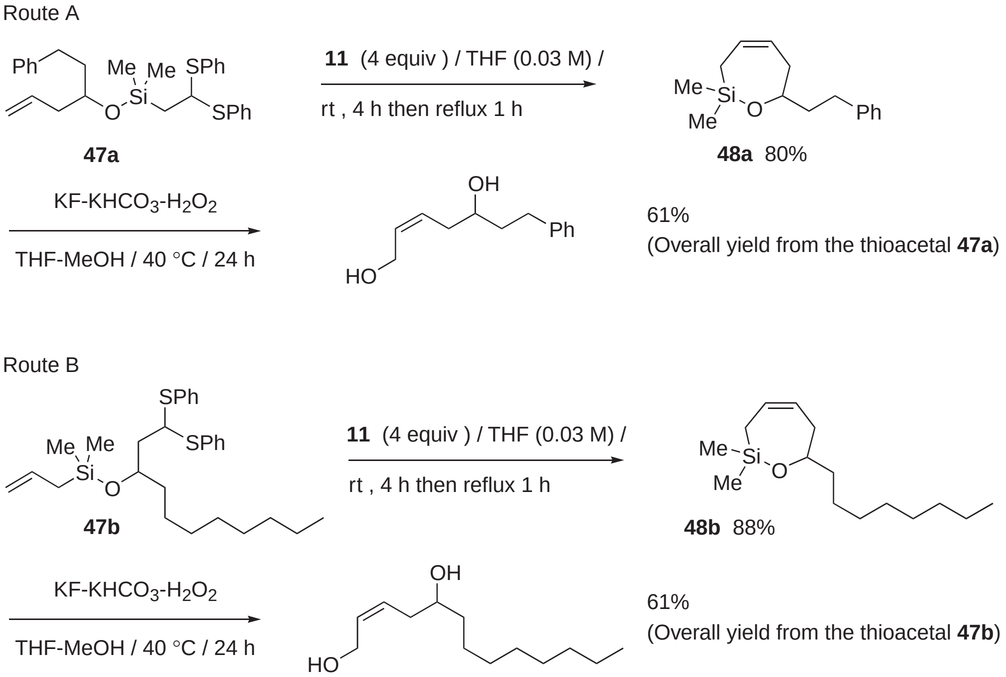
Scheme 41.

The titanocene(II)-promoted ring-closure of unsaturated thioacetals can also be employed for the synthesis of nitrogen heterocycles. Seven- and eight-membered monocyclic amines as well as ones fused with a benzene ring can be synthesized by the present method (Scheme 44).[60] Cyclization of the sulfide having a thioacetal moiety and a terminal double bond **45k** affords the corresponding cyclic sulfides as well.[57]

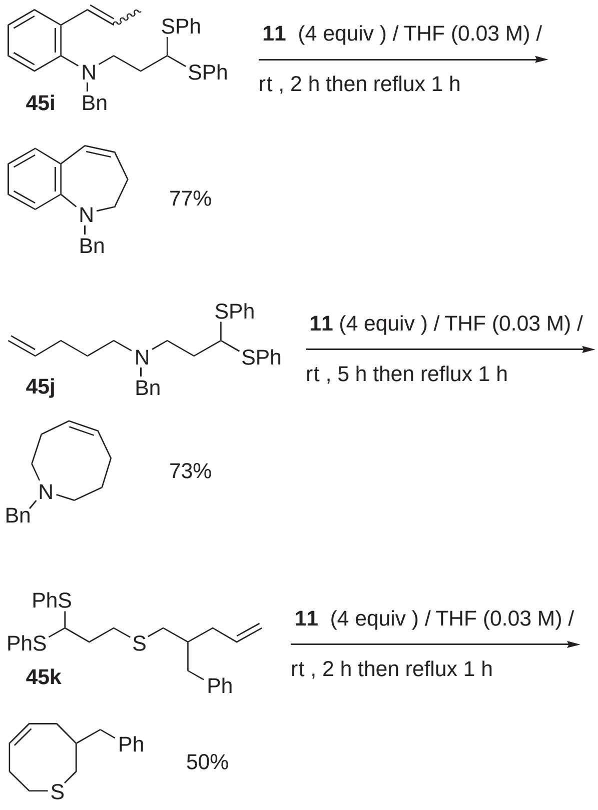
3.2 Cyclopropanation. As noted in the former section, the treatment of *gem*-dihalides **33** with the titanocene(II) reagent **11** produces the organotitanium species, which serve as highly substituted alkylidenetitanocenes **34**. Based on the above successful results of RCM using unsaturated thioacetals **45**, we investigated the reaction of *gem*-dihalides carrying a terminal



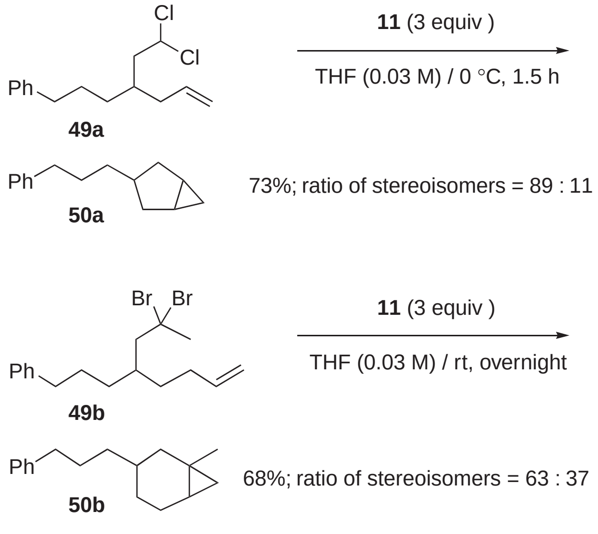
Scheme 43.



Scheme 42.



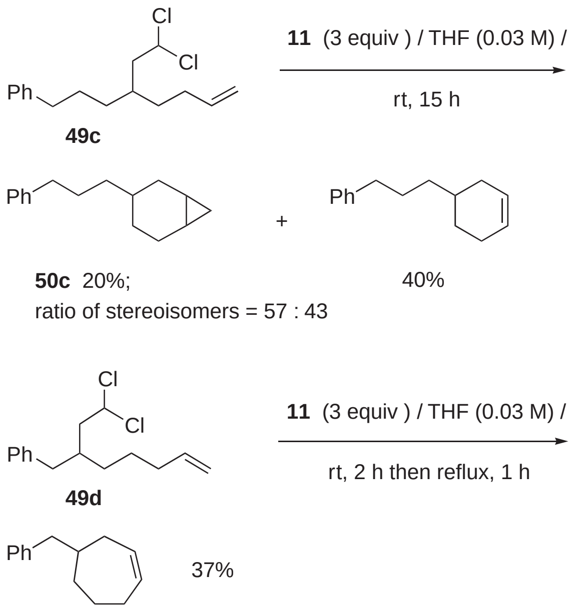
Scheme 44.



Scheme 45.

double bond **49** with **11**. We found that, unlike the reaction of the thioacetals **45**, the cyclopropanes, bicyclo[3.1.0]hexane and bicyclo[4.1.0]heptane derivatives **50a** and **50b**, were produced by the treatment of **49a** and **49b** with **11**, respectively (Scheme 45).[61]

The mode of the reaction of 7,7-dihalo-1-heptene derivatives was largely dependent on the substituent at the carbon α to the halogen; the reactions of the *gem*-dichloride **49c** having no substituent at the 7-C position gave the cyclohexene as a major product. Furthermore, the treatment of the 8,8-dichloro-1-octene derivative **49d** with the titanocene(II) reagent **11** preferentially produced the RCM product, though the reaction was rather complicated (Scheme 46).



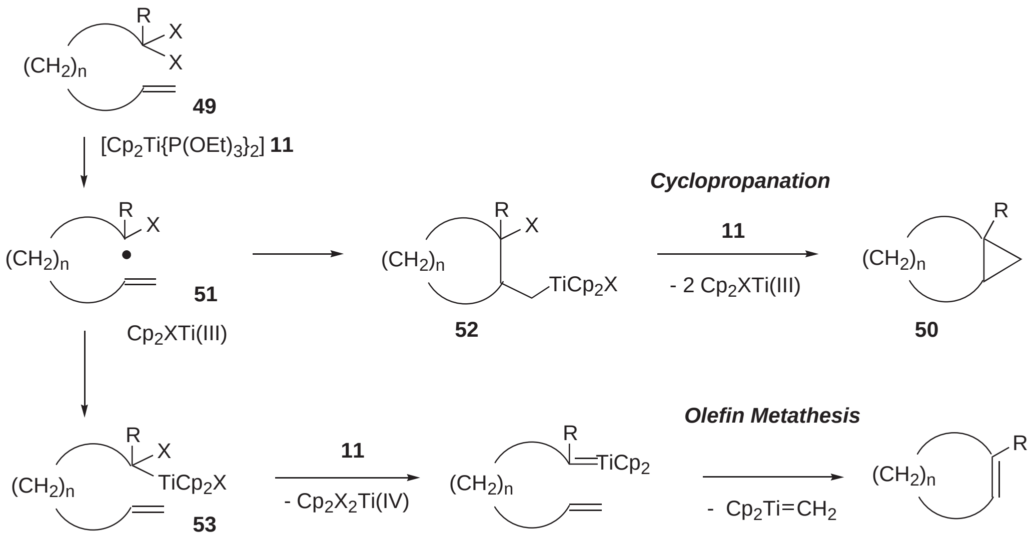
Scheme 46.

These results teach us the difference between the oxidative addition processes of thioacetals and *gem*-dihalides to the low-valent titanium species **11**. We assume that the oxidative addition of thioacetal to **11** would proceed through three-center addition or S_N2 process.[62] On the contrary, the above formation of the bicyclic compounds is accounted for nicely if the oxidative addition of *gem*-dihalides to **11** proceeds through radical mechanism. One-electron oxidation of **11** by the *gem*-dihalide **49** as a result of a halogen atom transfer forms the radical species **51** and titanocene(III) halide. In the cases of the 6,6-dihalo-1-alkenes and certain 7,7-dihalo-1-heptene derivatives such as **49a** and **49b**, the intermediate free radical rearranges to the cyclic radical, which combines with the trivalent titanocene halide to give the γ-haloalkyltitanocene **52**. The subsequent intramolecular reductive coupling of **52** with an additional equivalent of **11** affords the cyclopropane **50** (Scheme 47). If the titanium compound **53** is formed prior to the cyclization, the RCM product is produced via the carbene complex.

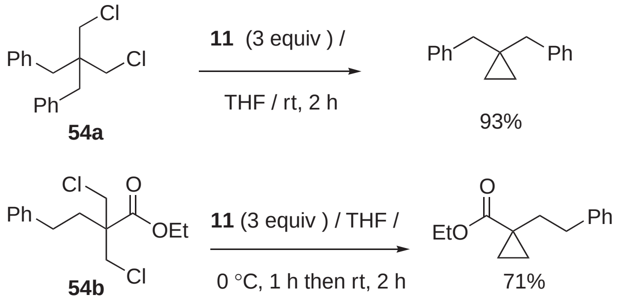
On the basis of the above mechanism, we examined the intramolecular reductive coupling of 1,3-dihalides **54** with the titanocene(II) reagent **11**. As was expected, the treatment of **54a** with **11** gave the cyclopropane in high yield (Scheme 48).[63] The present reductive coupling showed tolerance to ester groups, so the cyclopropanecarboxylic acid ester is obtained from the dihalo ester **54b**.

When 1,2-disubstituted cyclopropanes are produced, the *trans*-isomers are formed preferentially regardless of the stereoisomeric purity of the starting material, as shown in Scheme 49. These results indicate that the reaction proceeds via the formation of γ-haloalkyltitanium intermediate **55** through an atom transfer process which involves a radical intermediate **56** (Scheme 50).

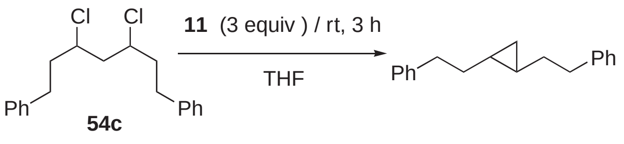
As was mentioned in the beginning of this article, alkenylcyclopropanes **4** are produced by the reaction of alkenyl thio-



Scheme 47.

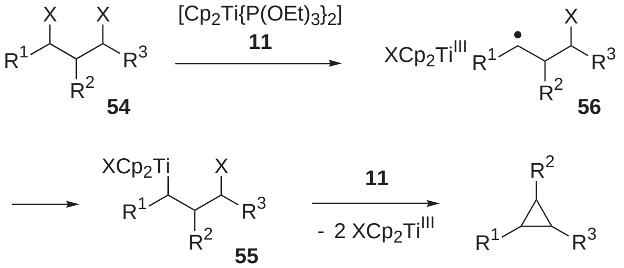


Scheme 48.



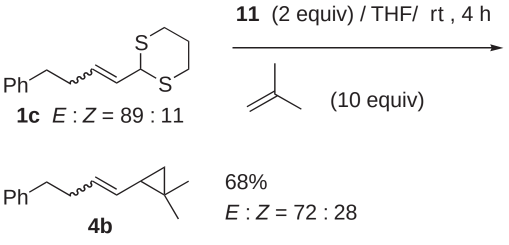
Ratio of isomers	Yield / %	*trans* : *cis*
49 : 51	84	92 : 8
61 : 39	86	91 : 9
81 : 19	85	92 : 8

Scheme 49.

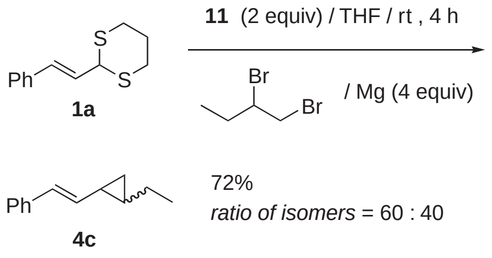


Scheme 50.

acetals **1** with the olefin complexes of titanocene(II) generated by the reaction of titanocene dichloride with 2 equiv of alkyllithiums. The preparation of different cyclopropane derivatives



Scheme 51.



Scheme 52.

4 is conveniently performed using the olefin-free titanocene(II) reagent **11**. The treatment of β,γ-unsaturated thioacetal **1c** with **11** in the presence of isobutene afforded **4b** in good yield (Scheme 51).[64]

Because 1,2-dibromides are easily reduced with magnesium to form olefins, they can be substituted for the olefins in this reaction by adding them to the reaction mixture before the reduction of titanocene dichloride (Scheme 52). This alternative is extremely convenient when volatile olefins such as ethylene are used.

The cyclopropanes **4** were obtained in better yields when 1,3-bis(phenylthio)propene derivatives such as **13a** were used as carbene complexes precursors (Scheme 53). This might be due to the fact that phenylthio group serves as a better leaving group than alkylthio group.

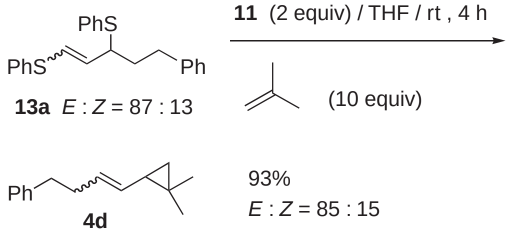
The present method can be employed for the preparation of various cyclopropane derivatives; the cyclopropyl group substituted allylsilane **57** is readily obtained by using the bissulfide **16b** (Scheme 54).[24]

Although several reports on the syntheses of alkynylcyclopropanes possessing an additional hydroxy,[65] alkenyl,[66] or alkynyl[67] substituent have appeared, only a limited number of methods for the preparation of unfunctionalized alkynylcyclopropanes have been reported.[68] Then we examined the preparation of such compounds utilizing our titanium carbene chemistry and found that the preferential cyclopropanation proceeded when the β,γ-acetylenic thioacetals **58a** and **58b** were treated with the titanocene(II) species **11** in the presence of terminal olefins (Scheme 55).[69] The alkynylcyclopropane **59a** that possessed no additional substituent on the cyclopropane ring was produced only in poor yield by the treatment of **58a** with **11** at ambient temperature under ethylene. However, **59a** was obtained in acceptable yield when the reaction was carried out at higher temperature.

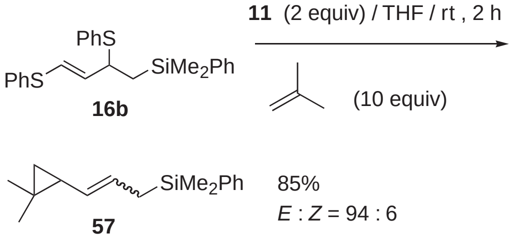
As described in this section, the mode of degradation of titanacyclobutane intermediates **5** formed from titanocene carbene complexes with olefins has become clear. They are classified into three categories: metathesis type degradation, β-elimination, and reductive elimination (Scheme 56). The metathesis between titanium carbene complexes and olefins has already been extensively studied, while the latter two types of reactions have been well established through our study.

4. A Broad Range of Reactivity of Alkylidenetitanocenes

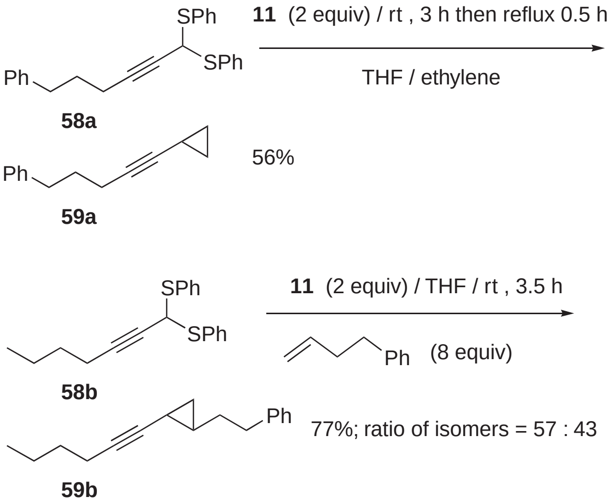
4.1 Reactions with the Organic Compound Bearing a Triple Bond. The reaction of methylidene complex of titanium **6** with alkanenitrile was first reported by Eisch and Piotrowski.[70] Doxsee and his co-workers investigated the reactions of intermediary vinylimido complexes of titanium and reported the formal [4 + 2] cycloadditions with ketones, nitriles, and imines.[71] Therefore, we became interested in whether titanocene–alkylidenes **9** react with alkanenitriles in the same manner as the methylidene complex. We found that the reaction of the carbene complexes **9**, prepared from thioacetals such as **12a** and **12b**, with alkanenitriles and the following hydrolysis produced the ketones (Scheme 57).[72]



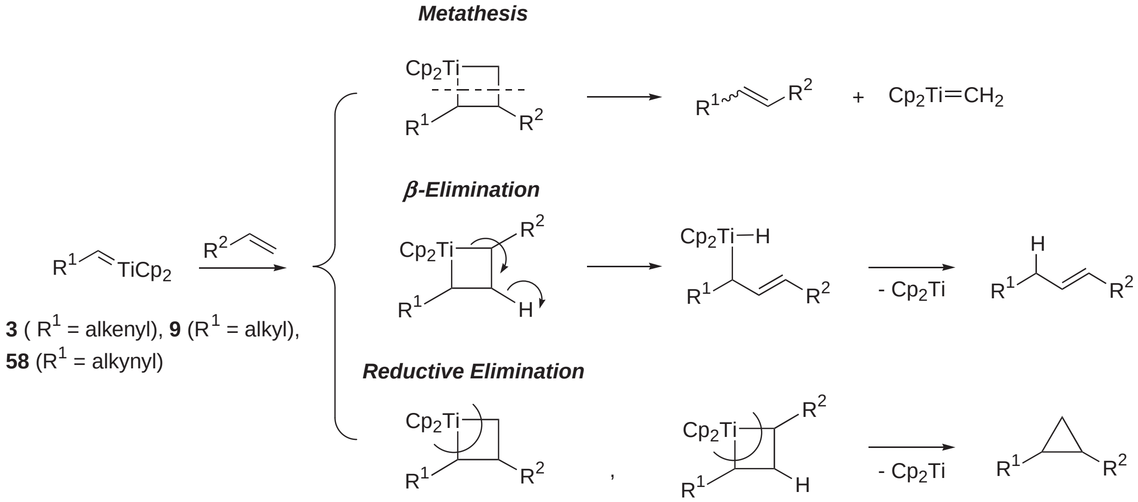
Scheme 53.



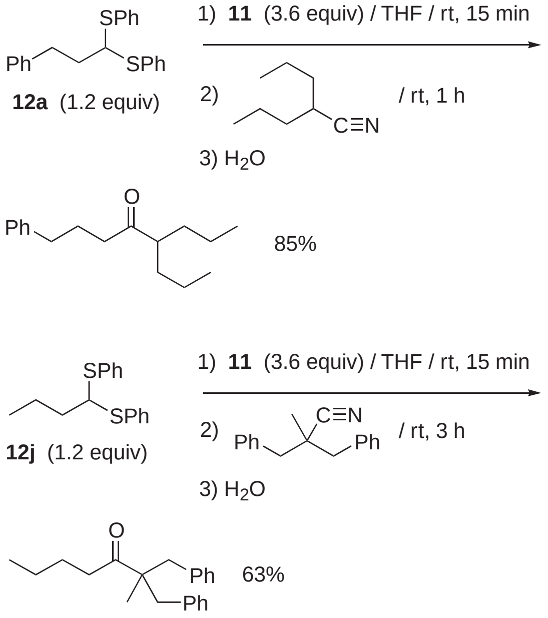
Scheme 54.



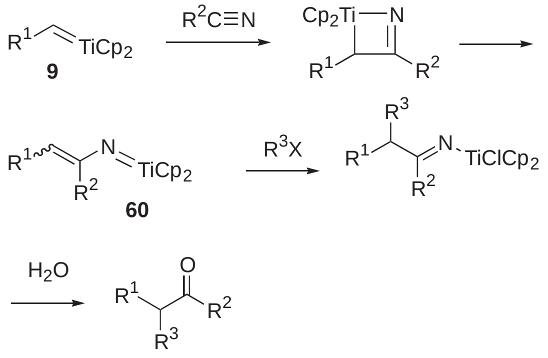
Scheme 55.



Scheme 56.



Scheme 57.

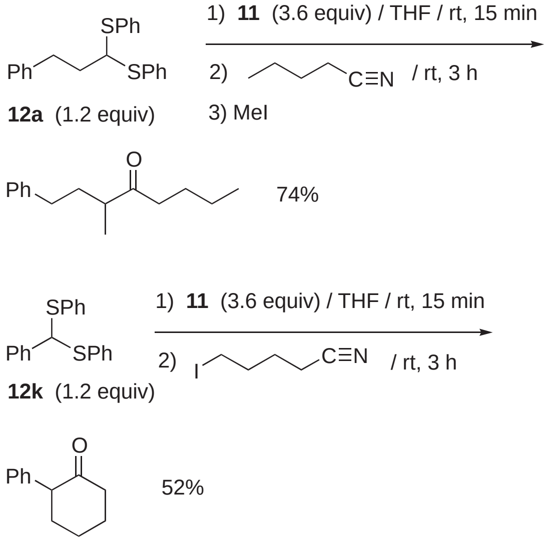


Scheme 58.

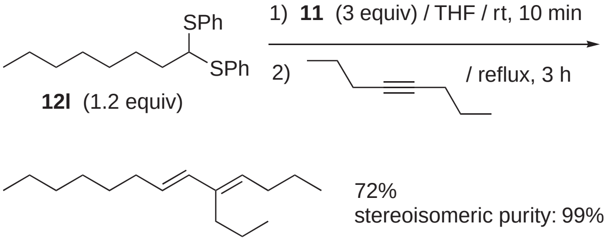
The preparation of ketones by addition of organometallic compounds such as Grignard reagents to alkanenitriles is often affected by steric hindrance, and the yields are generally low in the case of α,α-disubstituted alkanenitriles.[73] The most remarkable feature of the above transformation of nitriles to ketones using thioacetals is the generality in the choice of substrates; ketones are obtained in good yields even when the sterically hindered alkanenitriles are employed.

The above results suggest that the reaction proceeds through the formation of vinylimido complex **60**, similar to the reaction of methylidenetitanocene **6** (Scheme 58). Indeed, the treatment of the organotitanium intermediate generated from the thioacetal **12a** and valeronitrile with methyl iodide gave the monoalkylated ketone (Scheme 59). When 5-iodovaleronitrile was employed, the alkylation proceeded in an intramolecular fashion to give the cyclohexanone derivative.

The reactivity toward carbon–carbon triple bond is also an interesting issue in the chemistry of titanium carbene complexes. The formation of titanacyclobutenes by the reaction of methylidenetitanocene **6** with alkynes[74] and their reactions with carbonyl compounds and nitriles have been extensively studied. These reactions were found to be useful for the preparation of various organic compounds such as β,γ-unsaturated ketones[75] and conjugated dienes.[76] Despite these extensive studies, there was no report on the reaction of alkylidenetitanocene **9** with alkyne when we started this study. We were interested in the formation of α-substituted titanacyclobutenes **61** and their reactions with organic compounds having a multiple bond, such as carbonyl compounds.



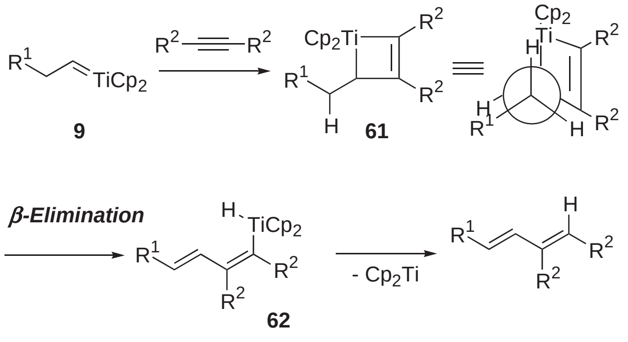
Scheme 59.



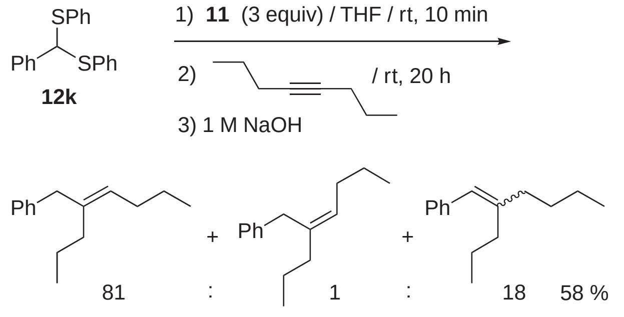
Scheme 60.

Contrary to our expectation, the titanocene(II)-promoted reaction of thioacetals with internal alkynes gave conjugated dienes. The reaction of the thioacetal **12l** with 4-octyne proceeded with high stereoselectivity, giving the *E*,*E*-isomer with 99% selectivity (Scheme 60).[77] When an unsymmetrical alkyne was employed, the reaction proceeded with mixed regioselectivity. For example, 3-pentylundeca-2,4-diene and 7-methylpentadeca-6,8-diene were formed in a ratio of 57:43 by the reaction of the thioacetal **12l** with 2-octyne.

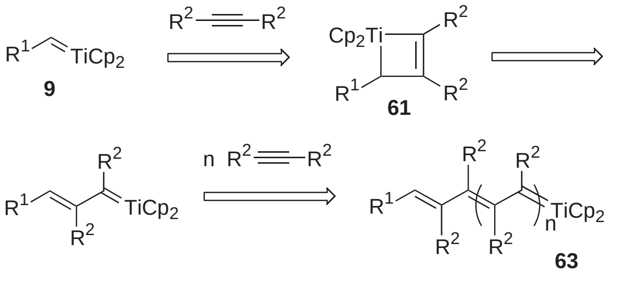
The stereoselective formation of conjugated dienes is well explained by the reaction pathway depicted in Scheme 61. The reaction of alkylidenetitanocene **9**, formed from thioacetal **12**, with an alkyne produces the titanacyclobutene intermediate **61**. Its β-hydride elimination from the most stable conformation affords the *Z*-vinyltitanium species **62**. Subsequent reductive elimination gives the diene with retention of configuration of the trisubstituted double bond. This reaction pathway was supported by the fact that the reaction of benzaldehyde diphenyl thioacetal **12k** with oct-4-yne gave the structurally isomeric alkenes, which are formed by protonation of the titanacyclobutene intermediate (Scheme 62).



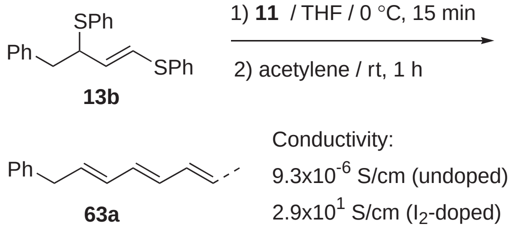
Scheme 61.



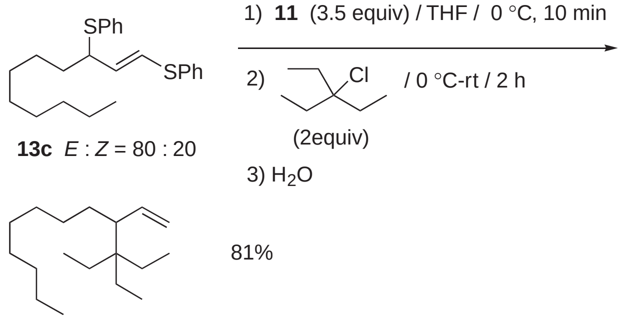
Scheme 62.



Scheme 63.



Scheme 64.



Scheme 65.

As described in Section 3, we observed two major types of degradation of titanacyclobutanes **5**: metathesis and β-elimination. We therefore expected that metathesis type degradation of titanacyclobutene **61** might proceed under certain reaction conditions. Such degradation of **61** is of special interest because the product is also a carbene complex, which further reacts with an alkyne to form a homologous titanacycle. It is reasonable to assume that the sequence of the formation and ring-opening of the titanacyclobutene affords polyacetylene **63** (Scheme 63).

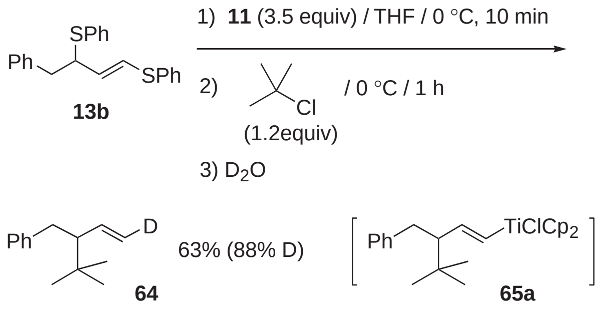
Polymerization of alkyne through this process was realized by using unsubstituted acetylene.[78] Under certain conditions, the alkylidenetitanocene-initiated polymerization of acetylene gave free-standing conducting films. The spectroscopic analysis of these films indicated that they consist of *trans*-polyacetylene (Scheme 64).

Since the discovery of the Shirakawa method using the concentrated Zieglar–Natta catalyst,[79] various catalysts and procedures for the preparation of conductive films by polymerization of acetylene have been extensively explored.[80] Thanks to the mechanism, the polymerization utilizing the titanium carbene complexes enjoys an advantage over conventional procedures in that it provides polyacetylenes possessing a specific end group that originated from the initiators.

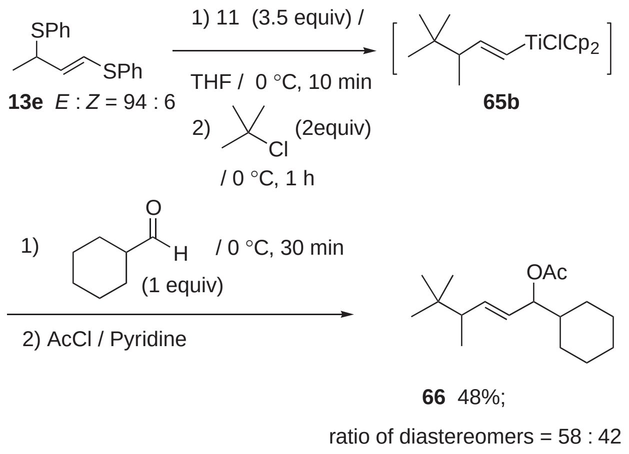
4.2 Alkylation. Organotitanium species such as methyltitanium reagents or titanium enolates react with tertiary halides to afford the substitution products.[81] Considering these results, we expected that the carbene complexes generated from thioacetals would be reactive toward tertiary alkyl halides because the metal carbenes like alkylidene–titanocene **9** are regarded as Schrock type complexes and would behave as excellent nucleophiles. Contrary to our expectation, the reactions of carbene complexes **9** formed from saturated thioacetals **12** did not react with any alkyl halide under the various reaction conditions. We found, however, that the alkenylcarbene complexes **3**, formed from 1,3-bis(phenylthio)propene derivatives **13**, did react with *t*-alkyl chlorides, as exemplified in Scheme 65.[82] As is the case with the cyclopropanation, a similar alkylation of β,γ-unsaturated thioacetals **1** gave the alkylation products in somewhat lower yields. The alkylation proceeds with extremely high regioselectivity; the alkyl halide attacks only at the substituted side of the allylic system even when highly sterically hindered tertiary halides are employed.

In order to determine the reaction pathway, we quenched the reaction of the bissulfide **13b** with *t*-butyl chloride with excess D_2O. The formation of the *trans*-deuterio olefin **64** indicates that the reaction proceeds via the formation of *trans*-vinyltitanium species **65** (Scheme 66).

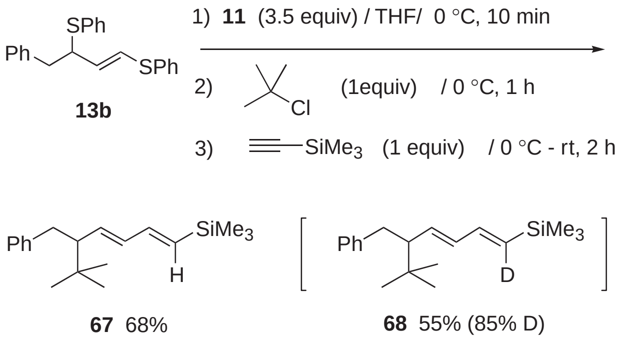
As noted above, the reactions of alkyltitanium compounds have been extensively studied and are employed for various organic syntheses. On the contrary, the chemistry of vinyltitanium species has not been fully studied yet. For example, it remains unclear whether vinyltitanium reagents react with carbonyl compounds regardless of their structures. Although Seebach et al. described that they were unable to add a non-heterosubstituted vinyltitanium reagent to carbonyl com-



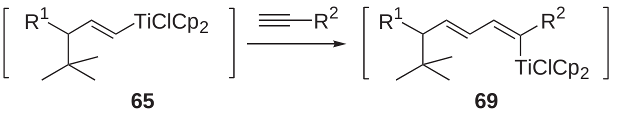
Scheme 66.



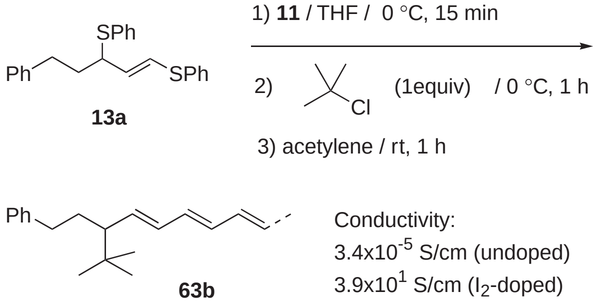
Scheme 67.



Scheme 68.



Scheme 69.



Scheme 70.

pound,[83] Sato and co-workers reported the reactions of trimethylsilyl group substituted vinyltitanium species prepared by protonation of titanacyclopropene[84] and bicyclic alkoxytitanacyclopentenes[85] 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.[86] Thermal stability of vinyltitanium reagents also remains uncertain.[83,87]

We therefore studied the reactions of the vinyltitanium species **65** generated by the tertiary alkylation of alkenylcarbene complexes with aldehydes and alkynes.[88] The treatment of **65b** with cyclohexanecarboxaldehydes produced the allylic alcohol, which was isolated as the acetate **66** in reasonable overall yield (Scheme 67). The reaction is highly stereoselective, and only the *E*-isomer of **66** was isolated.

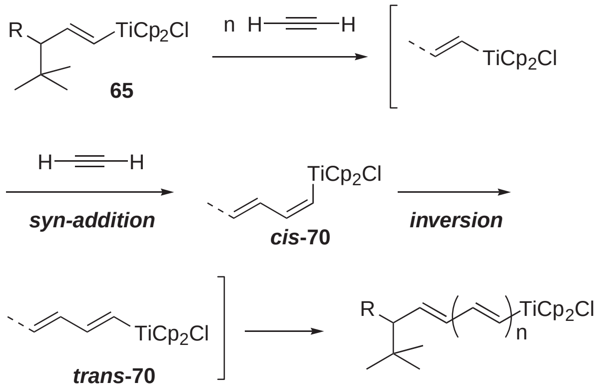
Further, we found that the carbometallation of terminal alkynes with the vinylmetal species **65a** generated from the bissulfide **13b** proceeded to form the *E*,*E*-diene **67** in good overall yield with complete regio- and stereoselectivity (Scheme 68). When the reaction was quenched with D_2O, the deuterated diene **68** was produced. Therefore the formation of *trans*-carbon–carbon double bond is explained well by the *syn*-addition of **65** to form the dienyltitanocene **69** (Scheme 69).

The regioselectivity observed in this reaction is of special interest. The carbometallation 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.[89] On the contrary, a vinyl group selectively attacks at the terminus of alkyne in our reaction.

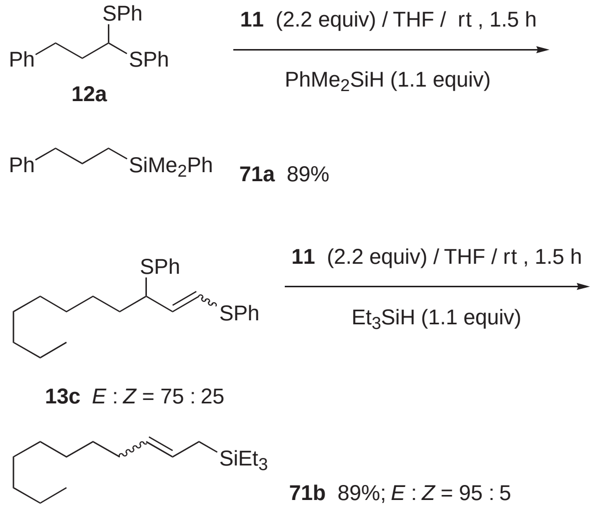
The fact that the vinyltitanium species **65** reacts with one equivalent of terminal alkyne and no oligomer was produced indicates that the dienyltitanium species **69** bearing a substituent at the carbon α to the titanium atom is far less reactive than the species possessing no substituent. Therefore one might imagine that successive carbotitanation would proceed to form polyacetylene **63** when the vinyltitanium species **65** is treated with excess acetylene. On the basis of the above hypothesis, we examined the polymerization of acetylene using **65** generated from the bissulfide **12a** as an initiator. As was expected, it gave the conductive film of polyacetylene **63b** with *trans* configuration (Scheme 70).[78]

We initially anticipated that the polymerization would proceed by the successive *syn*-addition of the propagation species to afford polyacetylene with *cis* configuration, just like the above carbotitanation of vinyltitaniums **65** with terminal alkynes. Although the detailed mechanism is uncertain at present, the following explanation for the formation of *trans*-polyacetylene would be plausible. The inversion of the *cis*-macrovinyltitanium species ***cis*-70** to the thermodynamically more stable ***trans*-70** proceeds prior to the next carbotitanation with acetylene, hence all-*trans*-polyacetylene **63b** is formed as depicted in Scheme 71.

4.3 Carbenoid Insertion-Type Reaction. It is well known



Scheme 71.



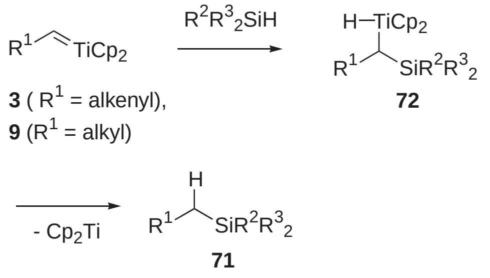
Scheme 72.

that group 14 organometallic compounds are produced by the transition metal-catalyzed reactions of diazo compounds with triorganosilanes, germanes, and stannanes.[90] The Fischer carbene complexes also react with silanes and stannanes to form such compounds.[91] Therefore, we assumed that the reaction of carbene complexes **3** and **9** formed from organosulfur compounds with group 14 metal hydrides would become an alternative way for the preparation of tetraorganosilanes and related organometallics.

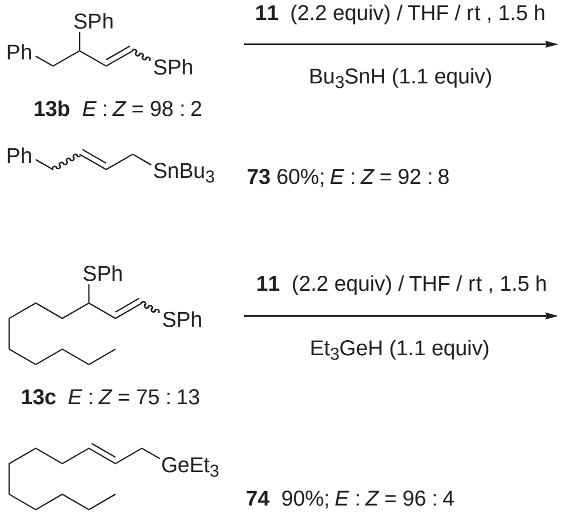
As would be expected, when the desulfurization of the thioacetal **12a** with the titanocene(II) species **11** was carried out in the presence of dimethylphenylsilane, the corresponding tetraorganosilane **71a** was obtained in good yield (Scheme 72).[92] This procedure is applicable to the preparation of the allylsilane **71b** by use of the bissulfide **13c**.

We assume that the tetraorganosilanes are formed by a [2 + 1] carbenoid insertion-type reaction of titanium–carbene complexes (Scheme 73). The carbene complexes **3** and **9** react with trialkylsilanes to form the α-silylalkyltitanium species **72**. The following elimination of the titanocene(II) species affords tetraorganosilanes **71**.

Similar reactions of the carbene complexes generated from 1,3-bis(phenylthio)propene derivatives **13b** and **13c** with tibutylstannane or triethylgermane also gave the corresponding allylstannane **73** or allylgermane **74** (Scheme 74).



Scheme 73.



Scheme 74.

5. Concluding Remarks

The chemistry described here started with a finding of some unusual formations of cyclopropanes from alkenyl thioacetals. Although it was a casual discovery, we believed that it involved a significant process, formation of titanium carbene complexes, and expected that a wide range of organic syntheses might be realized by using such active organometallic species. Fortunately, our study along this line brought about substantial results. Now a variety of titanium carbene complexes are readily available from thioacetals and related organosulfur compounds. The reductive metallation of organic halides with the titanocene(II) reagent has become an alternative way for the preparation of alkylidenetitanocenes. These new organotitanium reagents have already found widespread use in organic synthesis. Nonetheless, we expect that many exciting possibilities still remain to be explored in this chemistry. So keeping my fingers crossed, I wonder hopefully whether I would have a chance to write another sequel of this story.

I am very grateful to my enthusiastic co-workers who participated in this chemistry; their names appear in the reference section. In particular, I thank Dr. Tooru Fujiwara (currently at Chemipro Kasei), Dr. Yasuo Horikawa (currently at Bridgestone Corporation), and Dr. Akira Tsubouchi for their excellent contributions to this study. This work was supported financially by the Ministry of Education, Culture, Sports, Science and Technology.

References

1 a) T. Takeda, K. Ando, A. Mamada, and T. Fujiwara, *Chem. Lett.*, **1985**, 1149. b) T. Takeda, H. Oshima, M. Inoue, A. Togo, and T. Fujiwara, *Chem. Lett.*, **1987**, 1345. c) T. Takeda, S. Ogawa, N. Ohta, and T. Fujiwara, *Chem. Lett.*, **1987**, 1967. d) J. Yamaguchi, Y. Tamada, and T. Takeda, *Bull. Chem. Soc. Jpn.*, **66**, 607 (1993). e) T. Takeda, I. Miura, Y. Horikawa, and T. Fujiwara, *Tetrahedron Lett.*, **36**, 1495 (1995).

2 T. Takeda and T. Fujiwara, *Synlett*, **1996**, 481.

3 Y. Horikawa, T. Nomura, M. Watanabe, I. Miura, T. Fujiwara, and T. Takeda, *Tetrahedron Lett.*, **36**, 8835 (1995).

4 F. Z. Dörwald, "Metal Carbenes in Organic Synthesis," WILEY-VCH, Weinheim (1999), p. 78.

5 a) G. J. Erskine, D. A. Wilson, and J. D. McCowan, *J. Organomet. Chem.*, **114**, 119 (1976). b) G. J. Erskine, J. Hartgerink, E. L. Weinberg, and J. D. McCowan, *J. Organomet. Chem.*, **170**, 51 (1979).

6 F. N. Tebbe, G. W. Parshall, and G. S. Reddy, *J. Am. Chem. Soc.*, **100**, 3611 (1978).

7 a) K. A. Brown-Wensley, S. L. Buchwald, L. Cannizzo, L. Clawson, S. Ho, D. Meinhardt, J. R. Stille, D. Straus, and R. H. Grubbs, *Pure Appl. Chem.*, **55**, 1733 (1983). b) E. V. Anslyn and R. H. Grubbs, *J. Am. Chem. Soc.*, **109**, 4880 (1987).

8 a) R. H. Grubbs and S. H. Pine, "Comprehensive Organic Synthesis," ed by B. M. Trost, Pergamon Press, New York (1991), Vol. 5, p. 1115. b) S. H. Pine, *Org. React.*, **43**, 1 (1993). c) J. R. Stille, "Comprehensive Organometallic Chemistry II," ed by E. W. Abel, F. G. A. Stone, and G. Wilkinson, Pergamon Press, Oxford (1995), Vol. 12, p. 577. d) N. A. Petasis, "Transition Metals for Organic Synthesis," ed by M. Beller and C. Bolm, Wiley-VCH, Weinheim (1999), p. 361.

9 a) L. R. Gilliom and R. H. Grubbs, *Organometallics*, **5**, 721 (1986). b) J. R. Stille and R. H. Grubbs, *J. Am. Chem. Soc.*, **108**, 855 (1986). c) J. R. Stille, B. D. Santarsiero, and R. H. Grubbs, *J. Org. Chem.*, **55**, 843 (1990).

10 a) N. A. Petasis and E. I. Bzowej, *J. Org. Chem.*, **57**, 1327 (1992). b) N. A. Petasis and I. Akiritopoulou, *Synlett*, **1992**, 665. c) N. A. Petasis and E. I. Bzowej, *Tetrahedron Lett.*, **34**, 943 (1993). d) N. A. Petasis, J. P. Staszewski, and D.-K. Fu, *Tetrahedron Lett.*, **36**, 3619 (1995). e) N. A. Petasis and Y.-H. Hu, *J. Org. Chem.*, **62**, 782 (1997).

11 M. Chang, P. L. Timms, and R. B. King, *J. Organomet. Chem.*, **199**, C3 (1980).

12 L. B. Kool, M. D. Rausch, H. G. Alt, M. Herberhold, U. Thewalt, and B. Wolf, *Angew. Chem., Int. Ed. Engl.*, **24**, 394 (1985).

13 Y. Horikawa, M. Watanabe, T. Fujiwara, and T. Takeda, *J. Am. Chem. Soc.*, **119**, 1127 (1997).

14 T. Takeda and A. Tsubouchi, "Modern Carbonyl Olefination," ed by T. Takeda, Wiley-VCH, Weinheim (2004), p. 151.

15 G. Wittig and G. Geissler, *Liebigs Ann. Chem.*, **1953**, 44.

16 A. Maercker, *Org. React.*, **14**, 270 (1965).

17 W. S. Wadsworth, Jr., *Org. React.*, **25**, 73 (1977).

18 D. J. Ager, *Org. React.*, **38**, 1 (1990).

19 a) P. J. Kociénsky, *Chem. Ind.*, **1981**, 548. b) P. J. Kociénsky, *Phosphorus Sulfur Relat. Elem.*, **24**, 97 (1985). c) P. J. Kociénsky, "Comprehensive Organic Synthesis," ed by B. M. Trost and I. Fleming, Pergamon Press, New York (1991), Vol. 6, p. 987. d) N. S. Simpkins, "Sulfones in Organic Synthesis, Tetrahedron Organic Chemistry Series 10," Pergamon Press, London (1993).

20 T. Takeda, M. Watanabe, N. Nozaki, and T. Fujiwara, *Chem. Lett.*, **1998**, 115.

21 T. Takeda, J. Saito, and A. Tsubouchi, *Tetrahedron Lett.*, **44**, 5571 (2003).

22 a) T. Okazoe, K. Takai, K. Oshima, and K. Utimoto, *J. Org. Chem.*, **52**, 4410 (1987). b) K. Takai, Y. Kataoka, T. Okazoe, and K. Utimoto, *Tetrahedron Lett.*, **29**, 1065 (1988). c) K. Takai, O. Fujimura, Y. Kataoka, and K. Utimoto, *Tetrahedron Lett.*, **30**, 211 (1989). d) K. Takai, M. Tezuka, Y. Kataoka, and K. Utimoto, *Synlett*, **1989**, 27. e) K. Takai, T. Kakiuchi, Y. Kataoka, and K. Utimoto, *J. Org. Chem.*, **59**, 2668 (1994).

23 T. Takeda, M. Watanabe, Md. A. Rahim, and T. Fujiwara, *Tetrahedron Lett.*, **39**, 3753 (1998).

24 T. Takeda, Y. Takagi, N. Saeki, and T. Fujiwara, *Tetrahedron Lett.*, **41**, 8377 (2000).

25 Md. A. Rahim, H. Taguchi, M. Watanabe, T. Fujiwara, and T. Takeda, *Tetrahedron Lett.*, **39**, 2153 (1998).

26 H. Gross, A. Rieche, E. Höft, and E. Beyer, *Org. Synth.*, Coll. Vol. **V**, 365 (1973).

27 a) T. Takeda, T. Inoue, and T. Fujiwara, *Chem. Lett.*, **1988**, 985. b) T. Takeda, S. Ogawa, M. Koyama, K. Kato, and T. Fujiwara, *Chem. Lett.*, **1989**, 1257. c) T. Takeda, A. Nakayama, T. Furukawa, and T. Fujiwara, *Tetrahedron Lett.*, **31**, 6685 (1990). d) J. Yamaguchi, Y. Takagi, A. Nakayama, T. Fujiwara, and T. Takeda, *Chem. Lett.*, **1991**, 133. e) T. Takeda, F. Kanamori, M. Masuda, and T. Fujiwara, *Tetrahedron Lett.*, **32**, 5567 (1991). f) T. Takeda, Y. Takagi, H. Takano, and T. Fujiwara, *Tetrahedron Lett.*, **33**, 5381 (1992).

28 T. Takeda, K. Sato, and A. Tsubouchi, *Synthesis*, **2004**, 1457.

29 For example, see: H. O. House and H. Babad, *J. Org. Chem.*, **28**, 90 (1963).

30 P. J. Murphy and S. E. Lee, *J. Chem. Soc., Perkin Trans. 1*, **1999**, 3049.

31 G. Bartoli, M. Bosco, R. Dalpozzo, and P. E. Todesco, *J. Chem. Soc., Chem. Commun.*, **1988**, 807.

32 For example: a) A. Fürstner, A. Ptock, H. Weintritt, R. Goddard, and C. Krüger, *Angew. Chem., Int. Ed. Engl.*, **34**, 678 (1995). b) A. Fürstner and A. Hupperts, *J. Am. Chem. Soc.*, **117**, 4468 (1995). c) A. Fürstner, A. Ernst, H. Krause, and A. Ptock, *Tetrahedron Lett.*, **52**, 7329 (1996).

33 a) G. C. Fu and R. H. Grubbs, *J. Am. Chem. Soc.*, **115**, 3800 (1993). b) M. Mortimore and P. Kociénski, *Tetrahedron Lett.*, **29**, 3357 (1998).

34 Md. A. Rahim, T. Fujiwara, and T. Takeda, *Tetrahedron*, **56**, 763 (2000).

35 a) T. Oishi, H. Uehara, Y. Nagumo, M. Shoji, J.-Y. Le Brazidec, M. Kosaka, and M. Hirama, *Chem. Commun.*, **2001**, 381. b) M. Hirama, T. Oishi, H. Uehara, M. Inoue, M. Maruyama, H. Oguri, and M. Satake, *Science*, **294**, 1904 (2001).

36 Md. A. Rahim, H. Sasaki, J. Saito, T. Fujiwara, and T. Takeda, *Chem. Commun.*, **2001**, 625.

37 Md. A. Rahim, T. Fujiwara, and T. Takeda, *Synlett*, **1999**, 1029.

38 a) D. H. R. Barton and B. J. Willis, *J. Chem. Soc., Perkin Trans. 1*, **1972**, 305. Symmetrical sterically hindered olefins can be prepared by the McMurry coupling. For reviews, see: b) J. E. McMurry, *Chem. Rev.*, **89**, 1513 (1989). c) M. Ephritikhine and C. Villiers, "Modern Carbonyl Olefination," ed by T. Takeda, Wiley-VCH, Weinheim (2004), p. 223.

39 For examples: a) G. Wittig and D. Wittenberg, *Liebigs Ann. Chem.*, **606**, 1 (1957). b) A. Mondon, *Liebigs Ann. Chem.*,

603, 115 (1957). c) U. H. M. Fagerlunt and D. R. Idler, *J. Am. Chem. Soc.*, **79**, 6473 (1957). d) A. W. Johnson, *J. Org. Chem.*, **24**, 282 (1959). e) A. A. Bothner-By, C. Naar-Colin, and H. Günther, *J. Am. Chem. Soc.*, **84**, 2748 (1962). f) H. J. Bestmann and H. Häberlein, *Z. Naturforsh., B: Anorg. Chem., Org. Chem.*, **17**, 787 (1962). g) G. Wittig and A. Haag, *Chem. Ber.*, **96**, 1535 (1963). h) H. J. Bestmann, *Angew. Chem.*, **77**, 651 (1965). i) K. V. Scherer, Jr. and R. S. Lunt, III, *J. Org. Chem.*, **30**, 3215 (1965). j) K. Sisido and K. Utimoto, *Tetrahedron Lett.*, **7**, 3267 (1966). k) E. J. Corey and G. T. Kwiatkowski, *J. Am. Chem. Soc.*, **88**, 5652 (1966). l) D. Redmore, *J. Org. Chem.*, **34**, 1420 (1969).

40 For examples: a) S. Halazy, W. Dumont, and A. Krief, *Tetrahedron Lett.*, **22**, 4737 (1981). b) T. Cohen, J. P. Sherbine, J. R. Matz, R. R. Hutchins, B. M. McHenry, and P. R. Willey, *J. Am. Chem. Soc.*, **106**, 3245 (1984). c) B. Halton, C. J. Randall, and P. J. Stang, *J. Am. Chem. Soc.*, **106**, 6108 (1984). d) W. H. Richardson and S. A. Thomson, *J. Org. Chem.*, **50**, 1803 (1985). e) D. J. Ager, *J. Chem. Soc., Perkin Trans. 1*, **1986**, 183.

41 T. Fujiwara, N. Iwasaki, and T. Takeda, *Chem. Lett.*, **1998**, 741.

42 T. Takeda, R. Sasaki, and T. Fujiwara, *J. Org. Chem.*, **63**, 7286 (1998).

43 a) T. Takeda, R. Sasaki, A. Nakamura, S. Yamauchi, and T. Fujiwara, *Synlett*, **1996**, 273. b) T. Takeda, R. Sasaki, S. Yamauchi, and T. Fujiwara, *Tetrahedron*, **53**, 557 (1997).

44 T. Takeda, Y. Endo, A. C. S. Reddy, R. Sasaki, and T. Fujiwara, *Tetrahedron*, **55**, 2475 (1999).

45 a) A. J. Speziale, G. J. Marco, and K. W. Ratts, *J. Am. Chem. Soc.*, **82**, 1260 (1960). b) D. Seyferth, S. O. Grim, and T. O. Read, *J. Am. Chem. Soc.*, **83**, 1617 (1961). c) A. J. Speziale and K. W. Ratts, *J. Am. Chem. Soc.*, **84**, 854 (1962). d) R. Rabinowitz and R. Marcus, *J. Am. Chem. Soc.*, **84**, 1312 (1962). e) F. Ramirez, N. B. Desai, and N. McKelvie, *J. Am. Chem. Soc.*, **84**, 1745 (1962). f) N. S. Isaacs and D. Kirkpatrick, *J. Chem. Soc., Chem. Commun.*, **1972**, 443. g) E. J. Corey and P. L. Fuchs, *Tetrahedron Lett.*, **13**, 3769 (1972). h) R. L. Soulen, S. C. Carlson, and F. Lang, *J. Org. Chem.*, **38**, 479 (1973). i) D. Seyferth and R. S. Marmor, *J. Organomet. Chem.*, **59**, 237 (1973). j) G. H. Posner, G. L. Loomis, and H. S. Sawaya, *Tetrahedron Lett.*, **16**, 1373 (1975). k) J. Villieras, P. Perriot, and J. F. Normant, *Synthesis*, **1975**, 458. l) P. Savignac, J. Petrova, M. Dreux, and P. Coutrot, *Synthesis*, **1975**, 535. m) B. A. Clement and R. L. Soulen, *J. Org. Chem.*, **41**, 556 (1976). n) P. Savignac and P. Coutrot, *Synthesis*, **1976**, 197. o) W. G. Salmond, *Tetrahedron Lett.*, **18**, 1239 (1977). p) G. Burton, J. S. Elder, S. C. M. Fell, and A. V. Stachulski, *Tetrahedron Lett.*, **29**, 3003 (1988). q) P. Vinczer, S. Struhar, L. Novak, and C. Szantay, *Tetrahedron Lett.*, **33**, 683 (1992). r) R. Waschbüsch, J. Carran, A. Marinetti, and P. Savignac, *Chem. Rev.*, **97**, 3401 (1997).

46 A. Hosomi, M. Inaba, and H. Sakurai, *Tetrahedron Lett.*, **24**, 4727 (1983).

47 T. Takeda, K. Shimane, K. Ito, N. Saeki, and A. Tsubouchi, *Chem. Commun.*, **2002**, 1974.

48 T. Takeda, T. Shono, K. Ito, H. Sasaki, and A. Tsubouchi, *Tetrahedron Lett.*, **44**, 7897 (2003).

49 T. Takeda, "Titanium and Zirconium in Organic Synthesis," ed by I. Marek, Wiley-VCH, Weinheim (2002), p. 480.

50 T. Fujiwara, M. Takamori, and T. Takeda, *Chem. Commun.*, **1998**, 51.

51 A. Tsubouchi, E. Nishio, Y. Kato, T. Fujiwara, and T. Takeda, *Tetrahedron Lett.*, **43**, 5755 (2002).

52 R. H. Grubbs, "Comprehensive Organometallic Chemistry," ed by E. W. Abel, F. G. A. Stone, and G. Wilkinson, Pergamon, Oxford (1982), Vol. 8, p. 532.

53 A. Tsubouchi, E. Nishio, K. Arai, and T. Takeda, *Lett. Org. Chem.*, **1**, 357 (2004).

54 For examples: a) M. Schuster and S. Blechert, *Angew. Chem., Int. Ed. Engl.*, **36**, 2036 (1997). b) R. H. Grubbs and S. Chang, *Tetrahedron*, **54**, 4413 (1998). c) A. Fürstner, *Top. Catal.*, **4**, 285 (1998). d) D. L. Wright, *Curr. Org. Chem.*, **3**, 211 (1999). e) M. E. Maier, *Angew. Chem., Int. Ed.*, **39**, 2073 (2000). f) M. D. McReynolds, J. M. Dougherty, and P. R. Hanson, *Chem. Rev.*, **104**, 2239 (2004). g) A. Deiters and S. F. Martin, *Chem. Rev.*, **104**, 2199 (2004).

55 K. C. Nicolaou, M. H. D. Postema, and C. F. Claiborne, *J. Am. Chem. Soc.*, **118**, 1565 (1996).

56 T. Fujiwara and T. Takeda, *Synlett*, **1999**, 354.

57 T. Fujiwara, Y. Kato, and T. Takeda, *Tetrahedron*, **56**, 4859 (2000).

58 T. Fujiwara, K. Yanai, K. Shimane, M. Takamori, and T. Takeda, *Eur. J. Org. Chem.*, **2001**, 155.

59 K. Tamao, N. Ishida, Y. Ito, and M. Kumada, *Org. Synth.*, Coll. Vol. **VIII**, 315 (1993).

60 T. Fujiwara, Y. Kato, and T. Takeda, *Heterocycles*, **52**, 147 (2000).

61 T. Fujiwara, M. Odaira, and T. Takeda, *Tetrahedron Lett.*, **42**, 3369 (2001).

62 J. K. Kochi, "Organometallic Mechanisms and Catalysis," Academic Press, New York (1978), p. 138.

63 T. Takeda, K. Shimane, T. Fujiwara, and A. Tsubouchi, *Chem. Lett.*, **2002**, 290.

64 Y. Horikawa, T. Nomura, M. Watanabe, T. Fujiwara, and T. Takeda, *J. Org. Chem.*, **62**, 3678 (1997).

65 a) J. Salaün, *J. Org. Chem.*, **41**, 1237 (1976). b) J. Salaün and J. Ollivier, *Nouv. J. Chim.*, **5**, 587 (1981). c) N. Iwasawa, T. Matsuo, M. Iwamoto, and T. Ikeno, *J. Am. Chem. Soc.*, **120**, 3903 (1998).

66 H. Hauptmann, *Tetrahedron*, **32**, 1293 (1976).

67 a) M. Franck-Neumann, P. Geoffroy, and J. J. Lohmann, *Tetrahedron Lett.*, **24**, 1775 (1983). b) M. Franck-Neumann and P. Geoffroy, *Tetrahedron Lett.*, **24**, 1779 (1983).

68 a) W. Schoberth and M. Hanack, *Synthesis*, **1972**, 703. b) C. E. Hudson and N. L. Bauld, *J. Am. Chem. Soc.*, **94**, 1158 (1972). c) V. Dalacker and H. Hopf, *Tetrahedron Lett.*, **15**, 15 (1974). d) T. Liese and A. de Meijere, *Angew. Chem., Int. Ed. Engl.*, **21**, 65 (1986). e) W. Weber and A. de Meijere, *Chem. Ber.*, **118**, 2450 (1985). f) T. Liese and A. de Meijere, *Chem. Ber.*, **119**, 2995 (1986). g) G. Bengtson, S. Keyaniyan, and A. de Meijere, *Chem. Ber.*, **119**, 3607 (1986).

69 a) T. Takeda, S. Kuroi, K. Yanai, and A. Tsubouchi, *Tetrahedron Lett.*, **43**, 5641 (2002). b) T. Takeda, S. Kuroi, M. Ozaki, and A. Tsubouchi, *Org. Lett.*, **6**, 3207 (2004).

70 J. J. Eisch and A. Piotrowski, *Tetrahedron Lett.*, **24**, 2043 (1983).

71 a) K. M. Doxsee and J. B. Farahi, *J. Am. Chem. Soc.*, **119**, 7239 (1988). b) K. M. Doxsee and J. B. Farahi, *J. Chem. Soc., Chem. Commun.*, **1990**, 1452. c) K. M. Doxsee, J. B. Farahi, and H. Hope, *J. Am. Chem. Soc.*, **113**, 8889 (1991).

72 T. Takeda, H. Taguchi, and T. Fujiwara, *Tetrahedron Lett.*, **41**, 65 (2000).

73 a) M. J. Jorgenson, *Org. React.*, **18**, 51 (1970). b) F. J. Weiberth and S. S. Hall, *J. Org. Chem.*, **52**, 3901 (1987).

74 a) F. N. Tebbe, G. W. Parshall, and D. W. Ovenall, *J. Am.*

Chem. Soc., **101**, 5074 (1979). b) F. N, Tebbe and R. L. Harlow, *J. Am. Chem. Soc.*, **102**, 6149 (1980). c) T. R. Howard, J. B. Lee, and R. H. Grubbs, *J. Am. Chem. Soc.*, **102**, 6876 (1980). d) E. V. Anslyn and R. H. Grubbs, *J. Am. Chem. Soc.*, **109**, 4880 (1987). e) J. D. Meinhart, E. V. Anslyn, and R. H. Grubbs, *Organometallics*, **8**, 583 (1989). f) N. A. Petasis and D.-K. Fu, *Organometallics*, **12**, 3776 (1993). g) K. M. Doxsee, J. J. J. Juliette, J. K. M. Mouser, and K. Zientara, *Organometallics*, **12**, 4682 (1993).

75 a) J. D. Meinhart and R. H. Grubbs, *Bull. Chem. Soc. Jpn.*, **61**, 171 (1988). b) K. M. Doxsee and J. K. M. Mouser, *Organometallics*, **9**, 3012 (1990).

76 K. M. Doxsee and J. K. M. Mouser, *Tetrahedron Lett.*, **32**, 1687 (1991).

77 T. Takeda, H. Shimokawa, Y. Miyachi, and T. Fujiwara, *Chem. Commun.*, **1997**, 1055.

78 Y. Takagi, N. Saeki, A. Tsubouchi, H. Murakami, Y. Kumagai, and T. Takeda, *J. Polym. Sci., Polym. Chem. Ed.*, **40**, 2662 (2002).

79 H. Shirakawa, *Angew. Chem., Int. Ed.*, **40**, 2575 (2001).

80 For examples: a) L. B. Luttinger, *Chem. Ind.*, **1960**, 1135. b) G. P. Pez, *J. Am. Chem. Soc.*, **98**, 8072 (1976). c) S. L. Hsu, A. J. Signorelli, G. P. Pez, and R. H. Baughman, *J. Chem. Phys.*, **69**, 106 (1978). d) M. Monkenbusch, B. S. Morra, and G. Wegner, *Makromol. Chem., Rapid Commun.*, **3**, 69 (1982). e) L. Terlemezyan and M. Mihailov, *Makromol. Chem., Rapid Commun.*, **3**, 613 (1982). f) Z. Shen, M. Yang, M. Shi, and Y. Cai, *J. Polym. Sci., Polym. Lett. Ed.*, **20**, 411 (1982). g) Y. Cao, R. Qian, F. Wang, and X. Zhao, *Makromol. Chem., Rapid Commun.*, **3**, 687 (1982). h) I. Kmínek and J. Trekoval, *Makromol. Chem., Rapid Commun.*, **7**, 53 (1986). i) H. Naarmann and N. Theophilou, *Synth. Met.*, **22**, 1 (1987). j) N. Basescu, Z.-X. Liu, D. Moses, A. J. Heeger, H. Naarmann, and N. Theophilou, *Nature*, **327**, 403 (1987). k) A. Munardi, N. Theophilou, R. Aznar, J. Sledz, F. Schué, and H. Naarmann, *Makromol. Chem.*, **188**, 395 (1987). l) J. Tsukamoto, A. Takahashi, and K. Kawasaki, *Jpn. J. Appl. Phys.*, **29**, 125 (1990). m) K. Akagi, G. Piao, S. Kaneko, K. Sakamaki, H. Shirakawa, and M. Kyotani, *Science*, **282**, 1683 (1998).

81 M. T. Reetz, "Organotitanium Reagents in Organic Synthesis," Springer-Verlag, Berlin (1986), p. 199.

82 T. Takeda, N. Nozaki, N. Saeki, and T. Fujiwara, *Tetrahedron Lett.*, **40**, 5353 (1999).

83 B. Weidmann, C. D. Maycock, and D. Seebach, *Helv. Chim. Acta*, **64**, 1552 (1981).

84 H. Urabe, T. Hamada, and F. Sato, *J. Am. Chem. Soc.*, **121**, 2931 (1999).

85 H. Urabe and F. Sato, *J. Am. Chem. Soc.*, **121**, 1245 (1999).

86 O. Kitagawa, T. Suzuki, T. Inoue, and T. Taguchi, *Tetrahedron Lett.*, **39**, 7357 (1998).

87 a) B. J. Hewitt, A. K. Holliday, and R. J. Puddephatt, *J. Chem. Soc., Dalton Trans.*, **1973**, 801. b) D. J. Cardin and R. J. Norton, *J. Chem. Soc., Chem. Commun.*, **1979**, 513.

88 T. Takeda, N. Saeki, Y. Takagi, and T. Fujiwara, *Chem. Lett.*, **2000**, 1198.

89 a) J. F. Normant and A. Alexakis, *Synthesis*, **1981**, 841. b) E. Negishi, *Pure Appl. Chem.*, **53**, 2333 (1981). c) P. Knochel, "Comprehensive Organic Synthesis," ed by B. M. Trost and I. Fleming, Pergamon, Oxford (1991), Vol. 4, p. 865. d) E. Negishi and D. Y. Kondakov, *Chem. Soc. Rev.*, **1996**, 417.

90 a) F. Rijkens, M. J. Janssen, W. Drenth, and G. J. M. Van Der Kerk, *J. Organomet. Chem.*, **2**, 347 (1964). b) D. Seyferth, R. Damrauer, J. Y.-P. Mui, and T. F. Jula, *J. Am. Chem. Soc.*, **90**, 2944 (1968). c) H. Watanabe, T. Nakano, Y. Araki, H. Matsumoto, and Y. Nagai, *J. Organomet. Chem.*, **69**, 389 (1974). d) V. Bagheri, M. P. Doyle, J. Taunton, and E. E. Claxton, *J. Org. Chem.*, **53**, 6158 (1988). e) O. Andrey, Y. Landais, and D. Planchenault, *Tetrahedron Lett.*, **34**, 2927 (1993). f) Y. Landais and D. Planchenault, *Tetrahedron Lett.*, **35**, 4565 (1994). g) Y. Landais, D. Planchenault, and V. Weber, *Tetrahedron Lett.*, **35**, 9549 (1994). h) O. Andrey, Y. Landais, D. Planchenault, and V. Weber, *Tetrahedron*, **51**, 12083 (1995). i) J.-P. Barnier and L. Blanco, *J. Organomet. Chem.*, **514**, 67 (1996). j) R. T. Buck, M. P. Doyle, M. J. Drysdale, L. Ferris, D. C. Forbes, D. Haigh, C. J. Moody, N. D. Pearson, and Q.-L. Zhou, *Tetrahedron Lett.*, **37**, 7631 (1996). k) Y. Landais, L. Parra-Rapado, D. Planchenault, and V. Weber, *Tetrahedron Lett.*, **38**, 229 (1997). l) H. M. L. Davies, T. Hansen, J. Rutberg, and P. Bruzinski, *Tetrahedron Lett.*, **38**, 1741 (1997). m) Y. Landais and D. Planchenault, *Tetrahedron*, **53**, 2855 (1997).

91 a) J. A. Connor, P. D. Rose, and R. M. Turner, *J. Organomet. Chem.*, **55**, 111 (1973). b) J. A. Connor, J. P. Day, and R. M. Turner, *J. Chem. Soc., Dalton Trans.*, **1976**, 108. c) J. A. Connor, J. P. Day, and R. M. Turner, *J. Chem. Soc., Dalton Trans.*, **1976**, 283. d) E. Nakamura, K. Tanaka, and S. Aoki, *J. Am. Chem. Soc.*, **114**, 9715 (1992). e) C. C. Mak and K. S. Chan, *J. Chem. Soc., Perkin Trans. 1*, **1993**, 2143. f) C. C. Mack, M. K. Tse, and K. S. Chan, *J. Org. Chem.*, **59**, 3585 (1994). g) C. A. Merlic and J. Albaneze, *Tetrahedron Lett.*, **36**, 1007 (1995). h) C. A. Merlic and J. Albaneze, *Tetrahedron Lett.*, **36**, 1011 (1995).

92 T. Takeda, N. Nozaki, and T. Fujiwara, *Tetrahedron Lett.*, **39**, 3533 (1998).

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