J. prakt. Chem. 339 (1997) 304–314

Journal für praktische Chemie
Chemiker-Zeitung

Übersichtsartikel · Review Article

Cycloadditions of Allylsilanes. Part 10 [1]

Stereoselective Construction of Ring Systems by Cycloaddition Reactions of Allyltriisopropylsilane

H.-J. Knölker

Karlsruhe, Institut für Organische Chemie, Universität

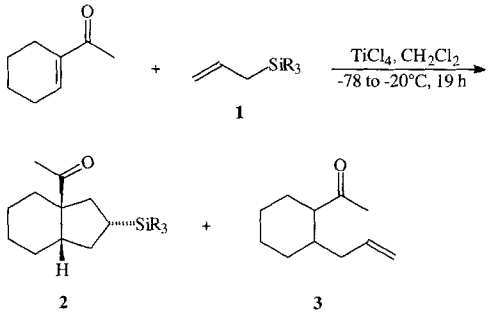
Received January 23rd, 1997

Dedicated to Professor Ekkehard Winterfeldt on the Occasion of his 65th Birthday

Abstract. Allyltriisopropylsilane is a useful reagent for the stereoselective construction of various ring systems by Lewis acid promoted formal cycloaddition reactions. The reaction of allyltriisopropylsilane as a synthetic equivalent of a 1,3-dipole in [3+2] and [3+3] cycloadditions provides cyclopentanes, tetrahydrofurans, and tetrahydronaphthalenes. [2+2] and [2+3] Cycloadditions of allyltriisopropylsilane as a synthetic equivalent of a 1,2-dipole provide cyclobutanes, oxetanes, azetidines, and dihydrofurans.

1 Introduction

In this article a brief overview on the utility of allyltriisopropylsilane as a building block for diverse cycloaddition reactions is given. Allylsilanes represent versatile reagents for organic synthesis and therefore have found many applications, e.g. in stereoselective additions to carbonyl groups or electron-deficient double bonds [2]. The nucleophilic introduction of allyl groups is achiev-ed on reaction of electrophilic centers with allyltrimethylsilane, which can be activated *in situ* either by fluoride ions or Lewis acids [3]. The Hosomi–Sakurai reaction, a Lewis acid promoted conjugate addition of allyltrimethylsilane to α,β-unsaturated ketones or alde-hydes, and the corresponding intramolecular version have been utilized for many elegant stereoselective syn-theses [4]. In some cases silylcyclopentanes were obtained as by-products of the Hosomi–Sakurai reaction: thus, the addition of 1-acetylcyclohex-



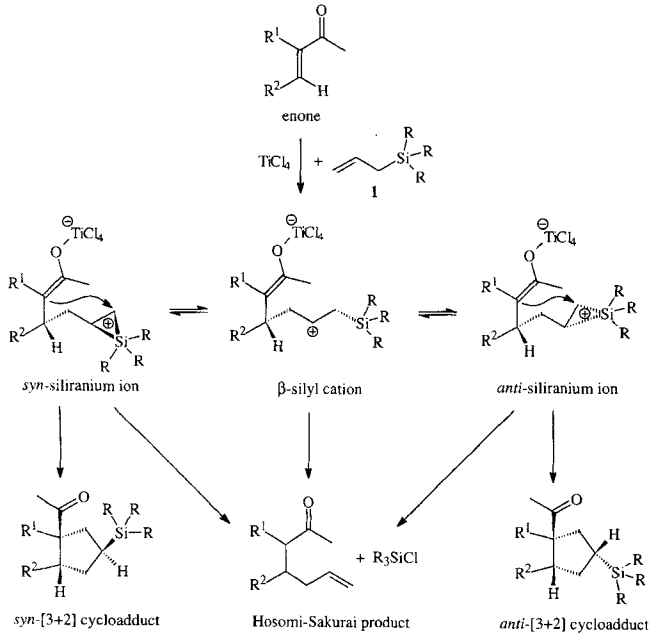
Scheme 1

ene and allyltrimethylsilane **1a** afforded 1-acetyl-8-trimethylsilylbicyc-lo[4.3.0]nonane **2a** along with 1-acetyl-2-allylcyclohexane **3** (Scheme 1, Table 1) [5–8].

Table 1 [3+2] Cycloaddition of allylsilanes **1** and 1-acetylcyclohexene

1	R	2, Yield (%)	3, Yield (%)
a	CH_3	18	76
b	*i*-Pr	86	2

In an extensive optimization it was shown, that the yield of the bicyclic product **2** strongly depends on the steric demand of the silyl moiety [1, 9]. With bulky alkyl groups R at the silicon atom the cycloadduct **2** was obtained in better yields [10]. Using allyltriisopropylsilane **1b** as the reagent, the cycloadduct **2b** was obtained in 86% yield as a single diastereoisomer with *anti* stereochemistry provided that optimized reaction conditions (addition of 1.5 equivalents of **1b** at –78 °C and subsequent reaction for 19 h at –20 °C) are applied [1, 9]. The prefixes *anti* and *syn* denote the position of the triisopropylsilyl group relative to the carbonyl group.



Scheme 2

The titanium tetrachloride promoted nucleophilic attack of the allylsilane **1** at the β-position of the enone generates a β-silyl cation (Scheme 2). This intermediate is stabilized by forming a siliranium ion, which represents a bridged non-classical pentavalent silicon cation [5, 8, 9]. The two diastereoisomeric siliranium ions, having *syn*- and *anti*-stereochemistry, are interconverted *via* the β-silyl cation. Intermolecular nucleophilic attack at the silicon atom of any of the three cationic intermediates by a chloride ion provides the Hosomi–Sakurai product along with the trialkylchlorosilane. Intramolecular nucleophilic attack of the titanium enolate at the primary carbon atom of the siliranium ions provides the [3+2] cycloadducts. The cyclization of the siliranium ion induces a cationic 1,2-silyl shift, which may be considered a sila-Wagner–Meerwein rearrangement, and proceeds highly stereospecific. For stereoelectronic reasons the cyclization of the *anti*-siliranium ion leading to the *anti*-[3+2] cycloadduct is strongly preferred. Using allyltrimethylsilane **1a** ($R=CH_3$) the nucleophilic attack of a chloride ion at the silicon atom readily occurs and the Hosomi–Sakurai reaction becomes the major course of the addition. However, with allyltriisopropylsilane **1b** (R = *i*-Pr) the nucleophilic attack at the silicon is inhibited and thus, the formal [3+2] cycloaddition is the dominant pathway of the reaction.

The conclusion which could be drawn from this observation was, that allyltriispropylsilane **1b**, which is commercially available [11], represents a useful novel reagent for the annulation of silylcyclopentanes. While allyltrimethylsilane **1a** reacts as an allylanion, e.g. in 1,2-additions to carbonyl groups or in the classical Hosomi–Sakurai reaction, allyltriisopropylsilane **1b** represents the synthetic equivalent of a 2-silyl-substituted 1,3-dipole (Fig. 1).

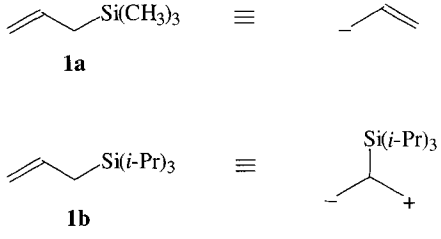


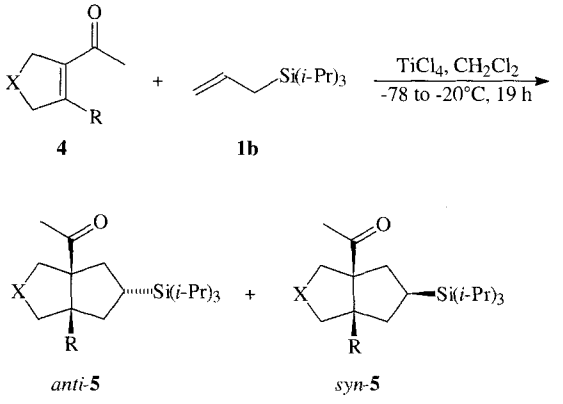
Fig. 1

2 Reactions of Allyltriisopropylsilane as a Formal 1,3-Dipole

2.1 [3+2] *Cycloadditions with Conjugated Enones to Cyclopentanes*

Using a broad range of 1-acetylcycloalkenes **4** of different ring sizes as starting materials the method was extended to a general and highly stereoselective synthesis of bicyclo[n.3.0]alkanes **5** (Scheme 3, Table 2) [1, 9]. These annulations provide in most cases exclusively the *anti* diastereoisomer, only if the optimized reaction conditions are used. Danheiser obtained the cycloadduct **5b** in 45% yield as a 11.5:1 mixture of the *anti* and *syn* diastereoisomers on reaction at –25 °C for 30 min [12]. The stereochemistry of the products was

unambiguously confirmed by X-ray crystal structure determinations of the corresponding triphenylsilyl derivatives, which are all crystalline, and a comparison of their ^{13}C NMR data with those of the triisopropylsilyl derivatives **5** [1]. Only the cycloadditions with the 1-acetylcyclopentenes **4a** and **4d** afforded the *syn* diastereoisomer as a minor by-product. This loss of diastereoselectivity is explained by a steric effect: in the products *anti*-**5a** and *anti*-**5d** the bulky triisopropylsilyl group is in the *endo* position of the bicyclo[3.3.0]octane framework, representing the sterically more hindered diastereoisomers [1, 9, 13]. Further applications of the [3+2] cycloaddition of allyltriisopropylsilane and α,β-unsaturated ketones to the synthesis of the bicyclo[3.3.0]octane ring system are described below.

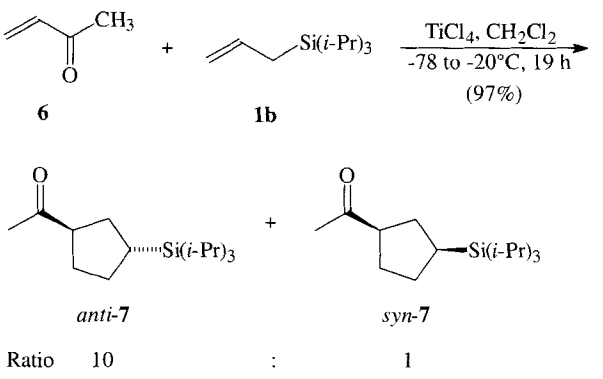


Scheme 3

Table 2 [3+2] Cycloaddition of allyltriisopropylsilane **1b** and 1-acetylcycloalkenes **4**

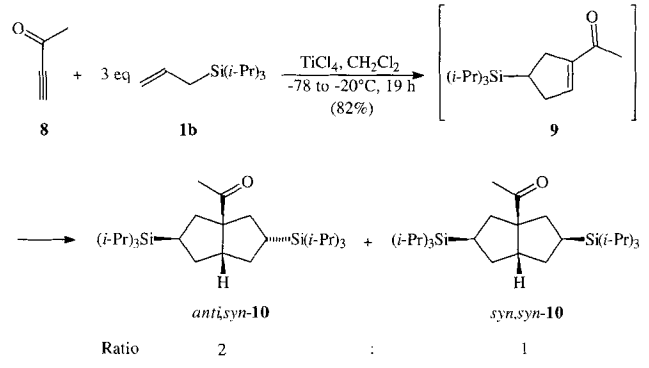
4	X	R	5, Yield (%)	Stereochemistry
a	CH_2	H	71	*anti*/*syn* = 3:1
b	$(CH_2)_2$	H	86	*anti*
c	$(CH_2)_3$	H	68	*anti*
d	CH_2	CH_3	92	*anti*/*syn* = 5:1
e	$(CH_2)_2$	CH_3	46	*anti*
f	$(CH_2)_3$	CH_3	54	*anti*

Methyl vinyl ketone **6** as an example of an acyclic enone provided under the same optimized reaction conditions almost quantitatively the cyclopentane **7** with a 10:1 ratio in favor of the *anti* diastereoisomer (Scheme 4) [13]. A lower yield (77%) but a higher stereoselectivity (99:1) for the cycloaddition of allyltriisopropylsilane **1b** with methyl vinyl ketone **6** was reported by Danheiser using different conditions (reaction at –78 °C for 2 h) [12, 14]. Panek described an application of this methodology to the asymmetric synthesis of cyclopentanes by Lewis acid promoted conjugate addition reaction of chiral (*E*)-crotylsilanes with α,β-unsaturated aldehydes and methyl vinyl ketone [15].



Scheme 4

Domino reactions offer the possibility for multiple bond formations and thus, the construction of polycyclic ring systems in a one-pot reaction [16]. The Weiss reaction represents an example for such a process, where in a sequence of aldol and Michael reactions the bicyclo[3.3.0]octane framework is furnished by the generation of four carbon–carbon bonds starting from one central C_2-unit (glyoxal) and two C_3-moieties (dimethyl 3-oxoglutarate) [17]. We devised a novel one-pot construction of the bicyclo[3.3.0]octane ring system by forming four carbon–carbon bonds in a domino [3+2] cycloaddition of two molecules of allyltriisopropylsilane and butynone as the central C_2 building block (Scheme 5) [18].



Scheme 5

The two consecutive [3+2] cycloadditions became possible by the reaction of an excess of allyltriisopropylsilane **1b** with butynone **8**, which generates both five-membered rings sequentially in a Lewis acid promoted domino [3+2] cycloaddition of two molecules of **1b** with the alkyne **8**. The 1-acetyl-3,7-bis(triisopropylsilyl)-*cis*-bicyclo[3.3.0]octane **10** was obtained in 82% yield as a mixture of diastereoisomers containing *anti*,*syn*-**10** and *syn*,*syn*-**10** in a 2:1 ratio and additionally traces of the *anti*,*anti*-diastereoisomer [18]. Using only 1.5 equivalents of allyltriisopropylsilane **1b** the silylcyclopentene

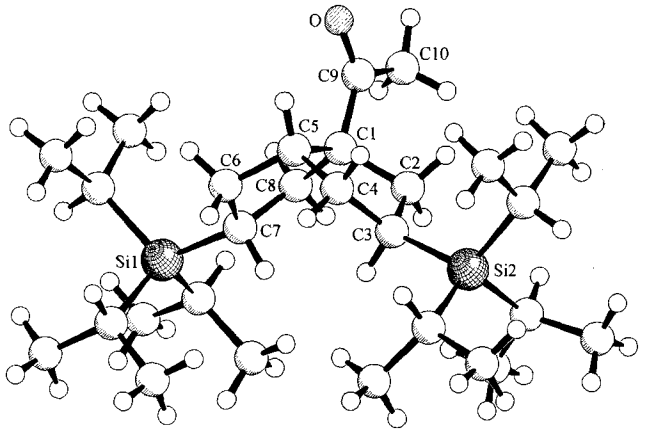
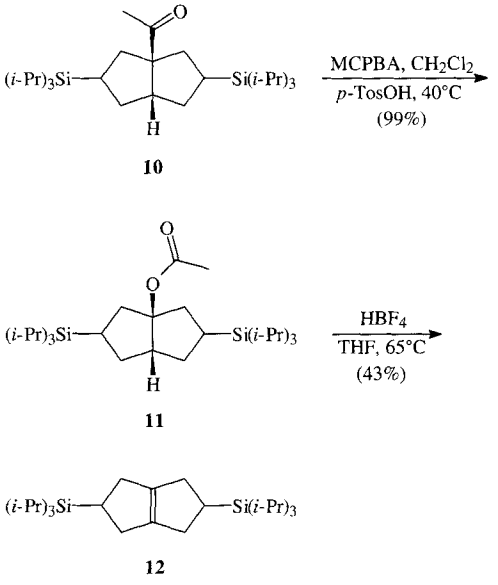
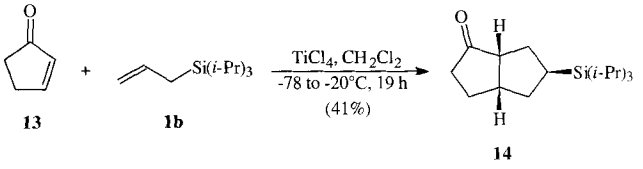


Fig. 2 Molecular structure of *syn,syn*-**10** in the crystal (triclinic, space group: P $\bar{1}$, Z = 2). Selected bond lenghts (Å): C1-C2 1.545(5), C2-C3 1.499(5), C3-C4 1.515(5), C4-C5 1.514(5), C5-C6 1.522(5), C6-C7 1.509(5), C7-C8 1.516(5), C1-C8 1.538(5), C1-C5 1.551(5), Si1-C7 1.888(4), Si2-C3 1.891(4) [19].



Scheme 6



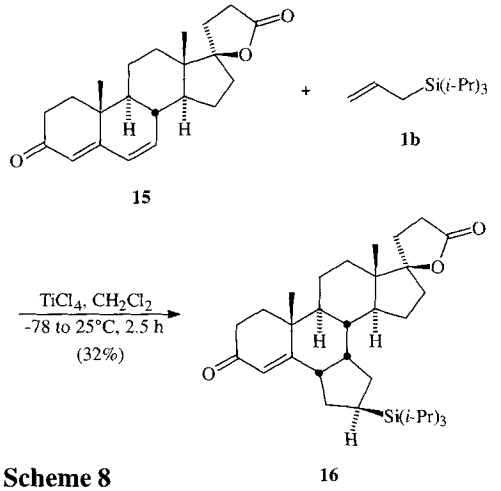
Scheme 7

9 could be isolated. The isolation of this intermediate of the domino [3+2] cycloaddition supported the proposed sequence of reactions leading to **10**. Resubmission of the silylcyclopentene **9** to the reaction with titanium tetrachloride and **1b** afforded the bicyclo[3.3.0]octane **10**. The structural assignments were based on the ^{13}C NMR spectra, which show that the non-symmetrical isomer *anti,syn*-**10** is the major product, and an X-ray crystal structure determination of *syn,syn*-**10** (Fig. 2) [19]. The X-ray analysis confirmed that the two bulky triisopropylsilyl groups are on the *exo* face of the bicyclo[3.3.0]octane framework of the minor diastereoisomer.

Compound **10** exhibited useful reactivity in further synthetic transformations (Scheme 6) [18]. Regioselective Baeyer–Villiger rearrangement to the 1-acetoxy derivative **11** was achieved with *m*-chloroperbenzoic acid. Subsequent elimination of acetic acid afforded the bicyclo[3.3.0]octene **12**. The *meso* compound **12** was obtained as a mixture of two diastereoisomers because the two triisopropylsilyl groups are either on the same face or on opposite faces of the molecule.

Only a few examples have been reported so far for the cycloaddition of 2-cycloalkenones and allyltriisopropylsilane **1b**. The reaction of 2-cyclopentenone **13** with **1b** afforded under the standard reaction conditions the 7-triisopropylsilyl-*cis*-bicyclo[3.3.0]octan-2-one **14** as a single diastereoisomer, again with an *anti* arrangement of the silyl moiety and the carbonyl group (Scheme 7) [8]. For the cycloadditions of **1b** and 2-cycloalkenones however, this mode of stereoselectivity leads to the sterically less hindered products with an *exo*-orientation of the triisopropylsilyl group.

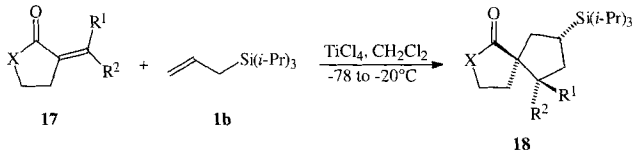
The cycloaddition of allyltriisopropylsilane **1b** with the steroiddienone **15**, which was kindly provided by Dr. G. Sauer (Schering AG, Berlin), demonstrated that this methodology could be extended to a system containing a further double bond (Scheme 8) [8]. The hexacyclic product **16** derives from an initial 1,6-addition of the allylsilane to the linear conjugated dienone as



Scheme 8

known for classical Hosomi–Sakurai reactions. Also in this vinylogous case of the [3+2] cycloaddition of allyltriisopropylsilane **1b** with enones the *anti* stereoselectivity is maintained.

The reaction of allyltriisopropylsilane **1b** with 2-alkylidenecycloalkan-1-ones **17** of various ring sizes (five- to eight-membered rings) in presence of titanium tetrachloride using the standard conditions provides a simple and quantitative access to the spiro[4.n]alkanones **18** (Scheme 9, Table 3) [20]. These cycloadditions again exhibited the preferred *anti* selectivity with respect to the orientation of the triisopropylsilyl group. The syn-



17 1b 18

Scheme 9

thesis of the spiro[4.4]nonane derivative **18a** demonstrated the feasibility of generating two contiguous quaternary carbon centers by spiroannulation of **1b**. Reaction of (*R*)-(+)-pulegone **17c** with **1b** afforded the spiro[4.5]decane **18c** as a 2:1 mixture of diastereoisomers [13]. This lack of stereoselectivity results from approach of the allyltriisopropylsilane *syn* or *anti* relative to the methyl group of pulegone while the *anti* arrangement of silyl and carbonyl group is maintained for both isomers. The cycloadditions of **1b** with the enones **17d** and **17e**, having *E*- and *Z*-configurated exocyclic double bonds respectively, provided with high selectivity the spiro[4.4]nonanes **18d** and **18e** with only minor amounts of the alternative diastereoisomer in either case [20]. This result confirms the high degree of stereospecificity for the construction of three stereogenic centers which can be achieved in this type of spiroannulation. The stereochemical assignments are based on the ^{13}C NMR spectra and an X-ray crystal structure investigation of the 2,4-dinitrophenylhydrazone derivative of **18d**, which confirmed the *anti* arrangement of both, the triisopropylsilyl group and the isopropyl group, relative to the carbonyl group (Fig. 3) [20].

The [3+2] cycloaddition of allyltriisopropylsilane **1b** with 2-methylene-1-tetralone **19** provided compound **20** with the same stereoselectivity (Scheme 10) [20].

Polyspirocyclic ring systems having several contiguous quaternary carbon centers are available in a one-pot process by two consecutive [3+2] cycloadditions of allyltriisopropylsilane **1b** at 2,5-diisopropylidenecyclopentanone **21** (Scheme 11). The two diastereoisomeric spirotricyclic products *anti,anti*-**22** and *anti,syn*-**22** are obtained in 66% yield and in a ratio of 1.4:1 in favor of the symmetrical structure as deduced from the

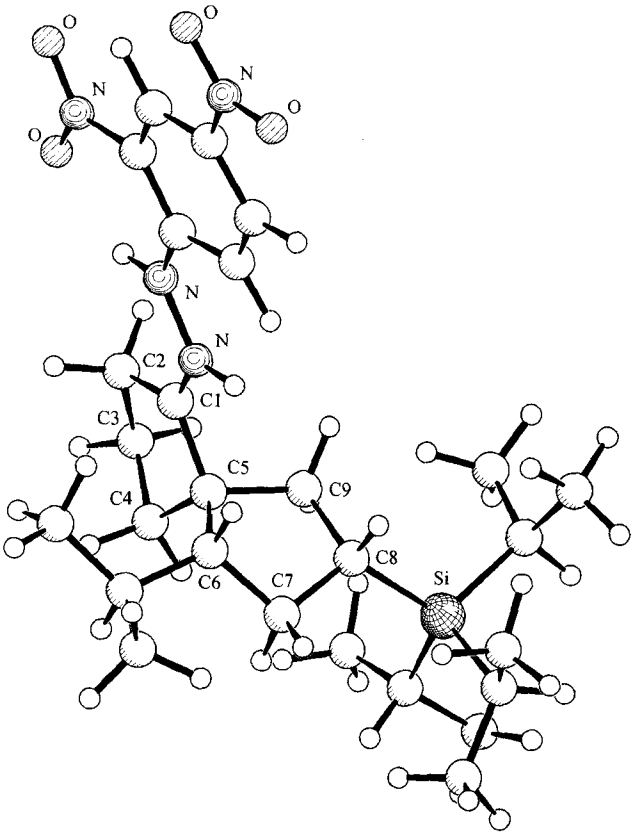
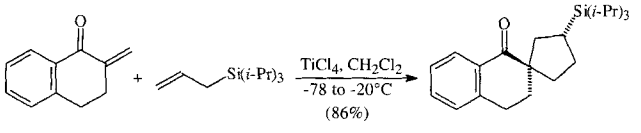


Fig. 3 Molecular structure of the 2,4-dinitrophenylhydrazone derivative of **18d** in the crystal (monoclinic, space group: $P2_1/n$, Z = 8, the asymmetric unit contains two independent molecules). Selected bond lenghts (Å): C1-C2 1.510(4), C2-C3 1.534(5), C3-C4 1.528(4), C4-C5 1.541(4), C5-C6 1.546(4), C6-C7 1.532(4), C7-C8 1.531(4), C8-C9 1.549(4), C5-C9 1.566(4), Si-C3 1.887(3) [20].

Table 3 [3+2] Cycloaddition of allyltriisopropylsilane **1b** and 2-alkylidenecycloalkan-1-ones **17**

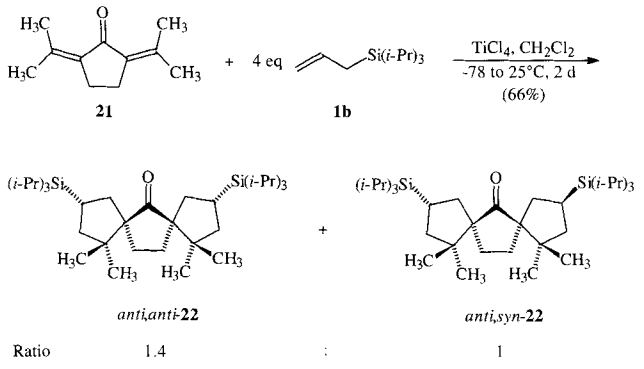
17	X	R^1	R^2	**18**, Yield (%)	Products (ratio)
a	$C(CH_3)_2$	H	H	98	**18a** (–)
b	CH_2	CH_3	CH_3	95	**18b** (–)
c	$CH_2C(H)(CH_3)$	CH_3	CH_3	97	**18c** (2 : 1)
d	CH_2	H	*i*-Pr	100	**18d/18e** (7:1)
e	CH_2	*i*-Pr	H	100	**18e/18d** (30:1)
f	$(CH_2)_3$	H	H	100	**18f** (–)
g	$(CH_2)_4$	H	H	98	**18g** (–)



19 1b 20

Scheme 10

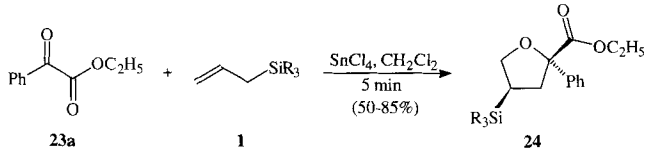
^{13}C NMR spectrum. Polyspiranes are of structural interest and represent useful starting materials for the synthesis of propellanes [21].



Scheme 11

2.2 *[3+2] Cycloadditions with Carbonyl Functions to Tetrahydrofurans*

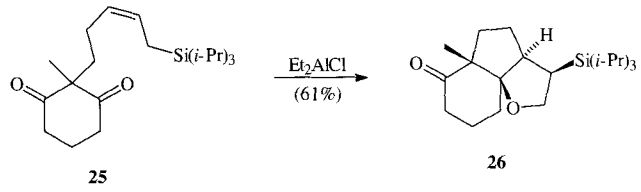
It has been shown by Akiyama that the Lewis acid promoted [3+2] cycloaddition of allylsilanes **1** (R_3 = Me_3, Me_2Ph, Me_2t-Bu, Ph_2t-Bu) and the α-ketoester **23a** provides a stereoselective access to trisubstituted tetrahydrofurans **24** (Scheme 12) [22]. In this case an initial 1,2-addition of the allylsilane onto the carbonyl group is followed by a cationic 1,2-shift of the silyl group.



Scheme 12

This method has been utilized for the enantioselective synthesis of polysubstituted tetrahydrofuran derivatives. Akiyama achieved an asymmetric synthesis of tetrahydrofurans by diastereoselective [3+2] cycloaddition of allylsilanes **1** and α-keto esters bearing an optically active cyclitol. Removal of the chiral auxiliary afforded silyl-substituted tetrahydrofurans of high enantiomeric purity [23]. Panek previously reported the synthesis of almost enantiomerically pure tetrasubstituted tetrahydrofurans by a double stereodifferentiation in the Lewis acid promoted addition of chiral (*E*)-crotylsilanes to (*S*)-(benzyloxy)propanal [24].

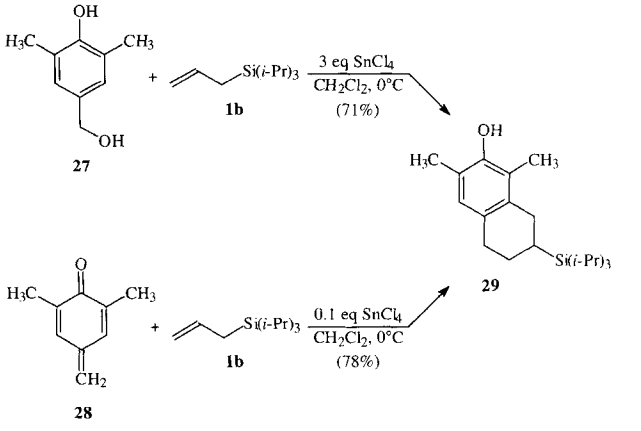
An elegant intramolecular version of this reaction has been described recently by Schinzer (Scheme 13) [25]. The substituted allyltriisopropylsilane **25**, which is appended to a cyclohexan-1,3-dione in an appropriate distance, undergoes in presence of the Lewis acid diethylaluminum chloride a diastereoselective transformation to the tricyclic furan derivative **26**. An intramolecular 1,2-addition of the allylsilane at the carbonyl group proceeding *via* a *synclinal* transition state and subsequent cyclization by nucleophilic attack of the alkoxide with concomitant 1,2-migration of the triisopropylsilyl group rationalizes the formation of **26**.



Scheme 13

2.3 *[3+3] Cycloadditions with Benzylic Cations to Tetrahydronaphthalenes*

Formal [3+3] cycloadditions of allyltriisopropylsilane **1b** with benzylic cations have been used by Angle for the synthesis of tetrahydronaphthalenes (Scheme 14) [26]. In these reactions either the benzylic alcohols or the quinone methides served as precursors for the benzylic cations. The tetrahydronaphthalene **29** was prepared in high yield by reaction of the benzylic alcohol **27** or the quinone methide **28** with allyltriisopropylsilane **1b**. The major advantage of the quinone methide route is, that catalytic amounts of the Lewis acid (0.1 equivalent of tin tetrachloride) can be employed.



Scheme 14

A competing reaction pathway (reaction of **1b** as a formal 1,2-dipole in a [2+3] cycloaddition, see below) afforded in some cases dihydro-1*H*-indenes as by-products.

3 Reactions of Allyltriisopropylsilane as a Formal 1,2-Dipole

Besides their ability to function as a synthetic equivalent of an allyl anion (e.g. in the synthesis of homoallylic alcohols by 1,2-additions to carbonyl compounds or in the Hosomi–Sakurai reaction) and as a synthetic equivalent of a 2-silyl-substituted 1,3-dipole (compare the cycloadditions described above), there exists a third mode of reactivity for allylsilanes in their Lewis acid mediated reactions with carbonyl compounds: the cycloaddition of allylsilane as a formal 1,2-dipole without a cationic 1,2-silyl shift (Fig. 4).

1b

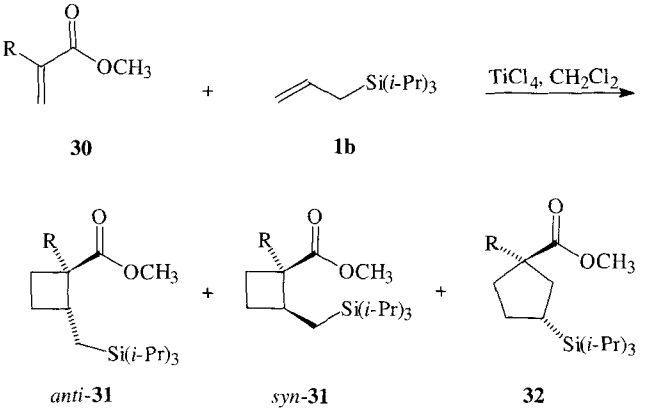
Fig. 4

The positive charge in the intermediate is again stabilized by the so-called „β-effect" of the silicon atom and the proposed siliranium ion is intramolecularly attacked by the enolate at the secondary carbon atom resulting in the formation of a triisopropylsilylmethyl-substituted ring system.

It is important to note at this point that, before the first report on the [3+2] cycloaddition of allylsilanes in Lewis acid promoted reactions appeared [5], several silylmethyl-substituted cyclobutanes were erroneously reported as products of the Lewis acid promoted reaction of allylsilanes with enones [27]. Later on all these silylmethylcyclobutanes [27] were reassigned to silylcyclopentanes [8, 9, 28] based on the original findings [5]. In spite of these structural corrections it was subsequently shown that the [2+2] cycloaddition of allylsilanes in Lewis acid promoted reactions does occur with appropriate systems as discussed in this chapter. The [2+2] and [3+2] cycloaddition reactions of allylsilanes which are not mediated by Lewis acids are not considered in this article [29].

3.1 *[2+2] Cycloadditions with Unsaturated Esters to Cyclobutanes*

Our group has demonstrated that the titanium tetrachloride promoted cycloaddition of allyltriisopropylsilane **1b** with the methyl acrylates **30** provided a mixture of the two diastereoisomeric silylmethylcyclobutanes *anti*-**31** and *syn*-**31** and minor amounts of the silylcyclopentane **32** (Scheme 15, Table 4) [30]. Here, the prefixes *anti* and *syn* denote the position of the triisopropylsilylmethyl group relative to the methoxycarbonyl group. The structures and the stereochemistry of these products were assigned based on the ^{13}C NMR data and an X-ray crystal structure determination of a derivative of the triphenylsilyl analogue of *anti*-**31b** [30]. Addition of **1b** to the titanium tetrachloride complex of methyl acrylate **30a** gives a cyclobutane/cyclopentane ratio of **31a/32a** > 21:1 and a ratio of the two diastereoisomeric cyclobutanes of *anti*-**31a**/*syn*-**31a** = 1:1.25. An extensive investigation revealed that the product distribution significantly depends on the reaction temperature. Higher temperatures favor both, the formation of the five-membered ring product **32a** relative to the four-membered ring product **31a** and the cyclization to *syn*-**31a** relative to *anti*-**31a**. The same trend applies to the cycloaddition of methyl methacrylate **30b**. These results suggest that the silylmethylcyclobutane represents the kinetic product of this reaction whereas the silylcyclopentane is the thermodynamically controlled product. This assumption was confirmed by the transformation of both diastereoisomeric cyclobutanes *anti*-**31a** and *syn*-**31a** into **32a** on treatment with titanium tetrachloride in dichloromethane at reflux. Related [2+2] cycloadditions of allyltriisopropylsilane **1b** were subsequently reported by other groups [31].

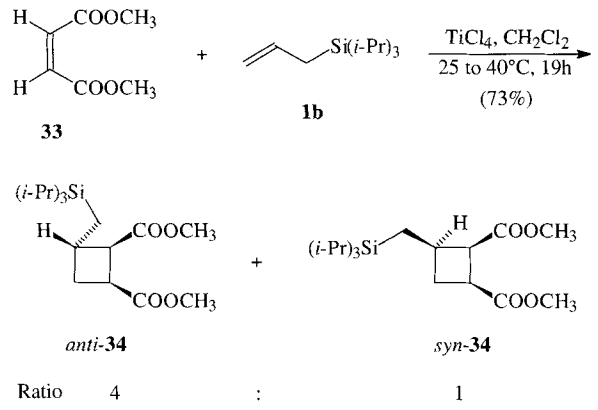


Scheme 15

The stereospecificity of the Lewis acid promoted [2+2] cycloaddition of allyltriisopropylsilane was shown by reaction of **1b** with dimethyl maleate **33** in presence of titanium tetrachloride (Scheme 16). The product was obtained as a 4:1 mixture of the diastereoisomers *anti*-**34** and *syn*-**34**. However, the *cis* relationship of the two

Table 4 [2+2] Cycloaddition of allyltriisopropylsilane **1b** and methyl acrylates **30**

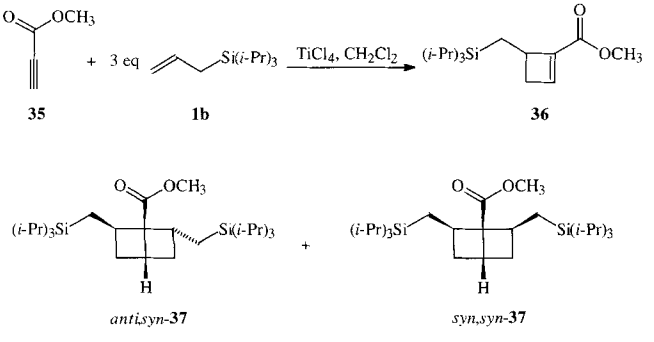
30	R	Reaction conditions	Yield (%)	Product ratio *anti*-**31**:*syn*-**31**:**32**
a	H	−40 °C to 0 °C, 19 h	100	9.5 : 11.9 : 1
a	H	40 °C, 3 h	97	1.7 : 6.3 : 1
b	CH_3	−78 °C to −20 °C, 19 h	40	8.6 : 1.0 : 1.1
b	CH_3	−78 °C to 40 °C, 19 h	57	5.4 : 1.0 : 13



Scheme 16

methoxycarbonyl groups was maintained in both isomers [30].

In analogy to the domino [3+2] cycloaddition of allyltriisopropylsilane with an alkynoic ketone (see chapter 2.1.) we developed a domino [2+2] cycloaddition by reaction with an alkynoic ester. The cycloaddition of methyl propynoate **35** even with an excess of **1b** under the standard conditions (titanium tetrachloride, –78 °C to –20 °C, 19 h) afforded almost quantitatively the triisopropylsilylmethylcyclobutene **36** (Scheme 17, Table 5). However, when applying more vigorous conditions the second [2+2] cycloaddition at the intermediate cyclobutene **36** occurred. Reaction for 19 h in dichloromethane at reflux provided the bicyclo[2.2.0]hexane **37** in 64% yield along with 34% of the cyclobutene **36** [30].



Scheme 17

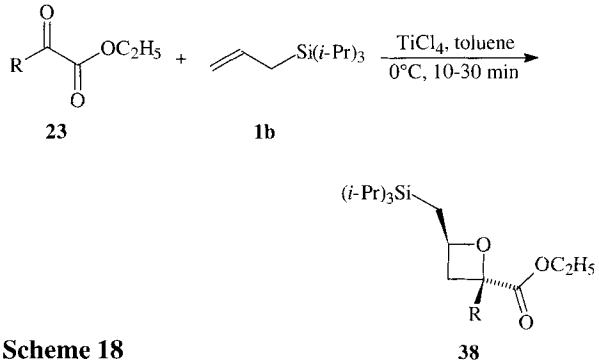
The bicyclo[2.2.0]hexane was obtained as a mixture of two diastereoisomers in a ratio of 3:1. As previously described for the [3+2] domino cycloaddition reaction of **1b**, the two diastereoisomeric products of the [2+2] domino cycloaddition were easily distinguished by their ^{13}C NMR spectra, which revealed that again the major isomer has a non-symmetrical structure. Thus, the major isomer of the bicyclo[2.2.0]hexane has the structure *anti,syn*-**37** and the minor isomer was assigned the *syn,syn* arrangement of both silylmethyl groups.

Table 5 [2+2] Cycloaddition of allyltriisopropylsilane **1b** and methyl propynoate **35**

Reaction conditions	**36**, Yield (%)	**37**, Yield (%)	Ratio *anti,syn*-**37**: *syn,syn*-**37**
–78 °C to –20 °C, 19 h	98	–	–
25 °C to 40 °C, 19 h	34	64	3 : 1

3.2 *[2+2] Cycloadditions with Carbonyl Functions to Oxetanes*

Akiyama reported the stereoselective construction of oxetanes by titanium tetrachloride promoted [2+2] cycloaddition of allylsilanes with α-ketoesters [32]. As the [2+2] cycloaddition of allylsilanes with α,β-unsaturated esters augments the [3+2] cycloaddition with enones, this novel reaction complements the [3+2] cycloaddition with carbonyl functions to tetrahydrofurans (see chapter 2.2.). In a reaction which is initiated by a 1,2-addition at the carbonyl function the allyltriisopropylsilane **1b** reacts as a formal 1,2-dipole and thus generates the oxetane ring (Scheme 18). Addition of **1b** to the α-keto esters **23** (**a**: R=C_6H_5, **b**: R=CH_3) in presence of titanium tetrachloride stereoselectively afforded the oxetanes **38** in high yields (**38a**: R=C_6H_5, 74% yield; **38b**: R=CH_3, 95% yield). The stereochemistry of the oxetanes was assigned based on NOE experiments.

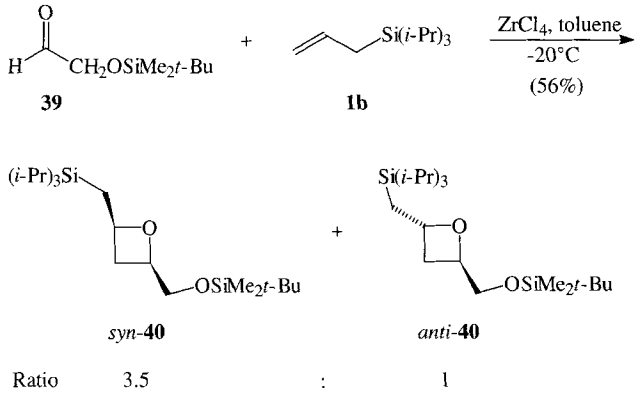


Scheme 18

Important for the reversal from [3+2] cycloaddition to [2+2] cycloaddition was the change of the Lewis acid from tin tetrachloride to titanium tetrachloride and the use of toluene as solvent instead of dichloromethane. Moreover, the formation of the oxetanes is preferred at lower reaction temperatures while at higher temperatures the amount of tetrahydrofuran increased [32]. This

observation indicates that the four-membered ring (oxetane) represents the kinetic and the five-membered ring (tetrahydrofuran) the thermodynamically controlled product of the reaction. The same trend was previously found for the conjugate cycloaddition of allyltriisopropylsilane to α,β-unsaturated carbonyl compounds generating either cyclobutanes or cyclopentanes (see above) [30].

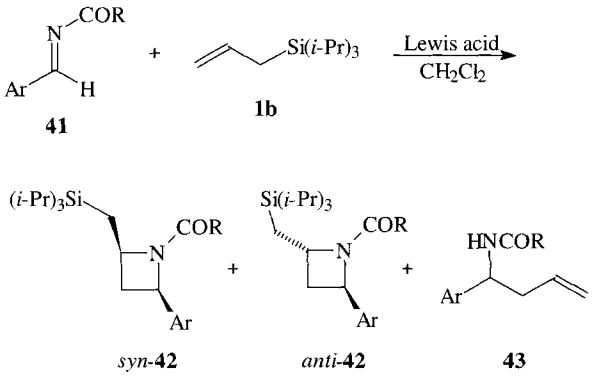
Recently Akiyama described the zirconium tetrachloride promoted [2+2] cycloaddition of allyltriisopropylsilane **1b** with the α-silyloxyaldehyde **39** which provided in 56% yield the diastereoisomeric oxetanes *syn*-**40** and *anti*-**40** in a ratio of 3.5:1 (Scheme 19) [33]. The stereochemical assignment was based on NOE studies. This result demonstrates for the first time that aldehydes may participate in the Lewis acid promoted [2+2] cycloaddition of allylsilanes provided that appropriate reaction conditions (i.e. zirconium tetrachloride as Lewis acid) are applied.



Scheme 19

3.3 *[2+2] Cycloadditions with N-Acylaldimines to Azetidines*

A further example for the construction of four-membered ring heterocycles by [2+2] cycloaddition of allyltriisopropylsilane **1b** has recently been reported by Uyehara [34]. The reaction of **1b** with *N*-acylaldimines **41** in presence of Lewis acid afforded the diastereoisomeric azetidines *syn*-**42** and *anti*-**42** (Scheme 20, Table 6). The stereochemical assignment was again based on NOE experiments.



Scheme 20

The best results were obtained when the reaction was carried out first for 1 h at –78 °C and subsequently completed at room temperature. It was also found that the use of boron trifluoride etherate suppressed the formation of the allyl derivative **43** and gave better yields of the azetidines **42** [34]. The complementary [3+2] cycloaddition to pyrrolidines by boron trifluoride etherate promoted reaction of *N*-alkoxycarbonylaldimines with chiral crotylsilanes was previously reported by Panek [35].

3.4 *[2+3] Cycloadditions with 1,3-Dicarbonyl Compounds to Dihydrofurans*

In these reactions five-membered rings are formed by cycloaddition of allyltriisopropylsilane, which serves as a formal 1,2-dipole, with 3-carbon dipolarophiles. For clarity of nomenclature, the term [2+3] cycloaddition is suggested for these annulations in order to distinguish from the [3+2] cycloadditions of allyltriisopropylsilane as a 1,3-dipole described in the chapters 2.1 and 2.2.

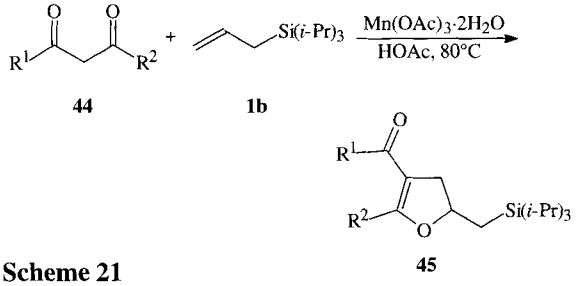
Table 6 [2+2] Cycloaddition of allyltriisopropylsilane **1b** and *N*-acylaldimines **41**

41	Ar	R	Reaction conditions	Yields (%) *syn*-**42**	*anti*-**42**	**43**
a	*p*-$CH_3OC_6H_4$	*t*-Bu	$TiCl_4$, –78 °C, 1 h and 25 °C, 17 h	40	11	–
a	*p*-$CH_3OC_6H_4$	*t*-Bu	$BF_3{\cdot}OEt_2$, –78 °C, 3 h	22	9	–
a	*p*-$CH_3OC_6H_4$	*t*-Bu	$BF_3{\cdot}OEt_2$, –78 °C, 1 h and 25 °C, 39 h	49	32	–
b	*p*-$CH_3OC_6H_4$	C_6H_5	$TiCl_4$, –78 °C, 1 h and 25 °C, 24 h	23	29	18
b	*p*-$CH_3OC_6H_4$	C_6H_5	$BF_3{\cdot}OEt_2$, –78 °C, 1 h and 25 °C, 24 h	45	23	–
c	C_6H_5	C_6H_5	$TiCl_4$, –78 °C, 1 h and 25 °C, 48 h	–	8	32
c	C_6H_5	C_6H_5	$BF_3{\cdot}OEt_2$, –78 °C, 1 h and 25 °C, 24 h	30	36	–

Table 7 [2+3] Cycloaddition of allyltriisopropylsilane **1b** and 1,3-dicarbonyl compounds **44**

44	R^1	R^2	**45**, Yield (%)
a	C_6H_5	C_6H_5	67
b	CH_3	OC_2H_5	76

The oxidative addition of 1,3-dicarbonyl compounds with allyltriisopropylsilane as described by Hwu afforded dihydrofurans (Scheme 21, Table 7) [36]. These reactions are initiated by one-electron oxidizing agents, e.g. ceric ammonium nitrate and manganese(III) acetate. Removal of a hydrogen atom from the 1,3-dicarbonyl compound generates a radical which adds to the double bond of the allylsilane. Subsequent cyclization, second SET oxidation, and proton loss terminate the reaction. Thus, reaction of **1b** with either 1,3-diphenyl-1,3-propanedione **44a** or ethyl acetoacetate **44b** in presence of 2.4 equivalents of manganese(III) acetate in acetic acid at 80 °C gave the triisopropylsilylmethyldihydrofurans **45a** and **45b** in high yields.



Scheme 21

4 Conclusion

While allyltrimethylsilane represents a useful synthetic equivalent for an allylanion, e.g. in the allylation of carbonyl compounds or in the Hosomi–Sakurai reaction, allyltriisopropylsilane may be used as a synthetic equivalent of a 2-silyl-substituted 1,3-dipole or a silylmethyl-substituted 1,2-dipole in Lewis acid promoted formal cycloadditions. The silylmethyl-substituted cyclobutanes and oxetanes resulting from [2+2] cycloadditions with electron-deficient olefins and carbonyl groups are the kinetic products of these annulations. Using equilibrating conditions rearrangement to the silyl-substituted cyclopentanes and tetrahydrofurans occurs. These thermodynamically controlled products derive from a [3+2] cycloaddition of the allyltriisopropylsilane with concomitant cationic 1,2-silyl shift. The present experimental data suggest that the same applies for the [2+2] cycloaddition of allyltriisopropylsilane to silylmethyl-substituted azetidines and the [3+2] cycloaddition to silyl-substituted pyrrolidines.

The construction of complex polycyclic ring systems in one-pot reactions becomes feasible by sequential cycloadditions of allyltriisopropylsilane. The domino [3+2] cycloaddition with butynone to a bicyclo[3.3.0] octane, the domino [2+2] cycloaddition with methyl propynoate to a bicyclo[2.2.0]hexane, and the synthesis of a polyspirocyclic ring system by consecutive [3+2] cycloadditions with a 2,5-bisalkylidenecyclopentanone demonstrate the flexibility of these reactions and their utility for organic synthesis.

For potential applications of the allylsilane cycloadditions to natural product synthesis it is crucial that the sterically hindered silyl groups are removed from the cycloaddition products. A useful method for removal of the silyl moiety is the oxidative cleavage of the carbon–silicon bond developed independently by Fleming and Tamao [37, 38], which offers an excellent tool for the conversion of silyl groups into hydroxy groups [39]. Recently, this reaction was applied to transform methyldiphenylsilyl- and triphenylsilyl-substituted cyclopentanes to the corresponding cyclopentanols [40].

I am grateful to my coworkers who have contributed to this project: Jörn–Bernd Pannek, Norbert Foitzik, Regina Graf, and Günter Wanzl. I also wish to thank Professor Hansgeorg Schnöckel, Institute of Inorganic Chemistry, University of Karlsruhe, and Professor Peter G. Jones, Institute of Inorganic and Analytical Chemistry, Technical University of Braunschweig, for the X-ray crystal structure determinations. Our work on the cycloadditions of allylsilanes was supported by the Deutsche Forschungsgemeinschaft (Gerhard–Hess-Förderpreis) and the Fonds der Chemischen Industrie. We thank Dr. G. Sauer (Schering AG, Berlin) for a generous gift of the steroid dienone **15**.

References

[1] Part 9: H.–J. Knölker, N. Foitzik, H. Goesmann, R. Graf, P. G. Jones, G. Wanzl, Chem. Eur. J. **3** (1997) 538

[2] H. Sakurai, Pure Appl. Chem. **54** (1982) 1; A. Hosomi, Acc. Chem. Res. **21** (1988) 200; I. Fleming, J. Dunoguès, R. Smithers, Org. React. **37** (1989) 57; I. Fleming in „Comprehensive Organic Synthesis", ed. C. H. Heathcock, Pergamon, Oxford 1991, vol. 2, p. 563; C. E. Masse, J. S. Panek, Chem. Rev. **95** (1995) 1293; E. Langkopf, D. Schinzer, Chem. Rev. **95** (1995) 1375

[3] D. Schinzer, J. Prakt. Chem. **336** (1994) 375

[4] A. Hosomi, H. Sakurai, J. Am. Chem. Soc. **99** (1977) 1673; T. A. Blumenkopf, C. H. Heathcock, J. Am. Chem. Soc. **105** (1983) 2354; D. Schinzer, Synthesis **1988**, 263; G. Majetich in „Organic Synthesis, Theory and Applications", ed. T. Hudlicky, JAI Press, Greenwich (CT) 1989, vol. 1, p. 173

[5] H.–J. Knölker, P. G. Jones, J.–B. Pannek, Synlett **1990**, 429

[6] H.–J. Knölker, P. G. Jones, J.–B. Pannek, A. Weinkauf,

Synlett **1991**, 147
[7] H.–J. Knölker in „Organic Synthesis *via* Organometallics", eds. K. H. Dötz and R. W. Hoffmann, Vieweg, Braunschweig 1991, p. 119; H.–J. Knölker, Synlett **1992**, 371
[8] H.–J. Knölker, N. Foitzik, R. Graf, J.–B. Pannek, P. G. Jones, Tetrahedron **49** (1993) 9955
[9] H.–J. Knölker, N. Foitzik, H. Goesmann, R. Graf, Angew. Chem. **105** (1993) 1104; Angew. Chem., Int. Ed. Engl. **32** (1993) 1081; this work was presented first at the 8th ORCHEM meeting in Bad Nauheim, September 24–26, 1992
[10] G. Hagen, H. Mayr, J. Am. Chem. Soc. **113** (1991) 4954
[11] Aldrich Chemical Co.: Allyltriisopropylsilane (art. 33,806-0)
[12] R. L. Danheiser, B. R. Dixon, R. W. Gleason, J. Org. Chem. **57** (1992) 6094
[13] H.–J. Knölker, R. Graf, Tetrahedron Lett. **34** (1993) 4765
[14] R. L. Danheiser, T. Takahashi, B. Bertók, B. R. Dixon, Tetrahedron Lett. **34** (1993) 3845
[15] J. S. Panek, N. F. Jain, J. Org. Chem. **58** (1993) 2345
[16] For reviews, see: T.–L. Ho, Tandem Organic Reactions, Wiley, Chichester, 1992; L. F. Tietze, U. Beifuss, Angew. Chem. **105** (1993) 137; Angew. Chem., Int. Ed. Engl. **32** (1993) 131
[17] R. Mitschka, J. Oehldrich, K. Takahashi, J. M. Cook, U. Weiss, J. V. Silverton, Tetrahedron **37** (1981) 4521; S. H. Bertz, J. M. Cook, A. Gawish, U. Weiss, Org. Synth. **64** (1986) 27
[18] H.–J. Knölker, R. Graf, Synlett **1994**, 131
[19] H.–J. Knölker, E. Baum, R. Graf, unpublished results
[20] H.–J. Knölker, P. G. Jones, R. Graf, Synlett **1996**, 1155
[21] L. Fitjer, H. Monzó–Oltra, M. Noltemeyer, Angew. Chem. **103** (1991) 1534; Angew. Chem., Int. Ed. Engl. **30** (1991) 1492; B. M. Trost, Y. Shi, J. Am. Chem. Soc. **115** (1993) 9421; L. Fitjer, M. Majewski, H. Monzó-Oltra, Tetrahedron **51** (1995) 8835
[22] T. Akiyama, K. Ishikawa, S. Ozaki, Chem. Lett. **1994**, 627
[23] T. Akiyama, T. Yasusa, K. Ishikawa, S. Ozaki, Tetrahedron Lett. **35** (1994) 8401
[24] J. S. Panek, M. Yang, J. Am. Chem. Soc. **113** (1991) 9868; J. S. Panek, R. Beresis, J. Org. Chem. **58** (1993) 809
[25] D. Schinzer, G. Panke, J. Org. Chem. **61** (1996) 4496
[26] S. R. Angle, J. P. Boyce, Tetrahedron Lett. **35** (1994) 6461
[27] R. Pardo, J.–P. Zhara, M. Santelli, Tetrahedron Lett. **1979**, 4557; A. Hosomi, H. Kobayashi, H. Sakurai, Tetrahedron Lett. **21** (1980) 955; S. Danishefsky, M. Kahn, Tetrahedron Lett. **22** (1981) 485; H. O. House, P. C. Gaa, D. VanDerveer, J. Org. Chem. **48** (1983) 1661; G. Majetich, J. Defauw, C. Ringold, J. Org. Chem. **53** (1988) 50; K. Nickisch, H. Laurent, Tetrahedron Lett. **29** (1988) 1533; G. Majetich, K. Hull, D. Lowery, C. Ringold, J. Defauw in „Selectivities in Lewis Promoted Reactions", ed. D. Schinzer, Kluwer, Dordrecht 1989, p. 169; G. Majetich, J.–S. Song, C. Ringold, G. A. Nemeth, Tetrahedron Lett. **31** (1990) 2239
[28] G. Majetich, J.–S. Song, C. Ringold, G. A. Nemeth, M. G. Newton, J. Org. Chem. **56** (1991) 3973; G. Majetich in „Strategies and Tactics in Organic Synthesis", ed. T. Lindberg, Academic Press, San Diego 1991, vol. 3, p. 295
[29] G. D. Hartmann, T. G. Traylor, Tetrahedron Lett. **1975**, 939; M. Ochiai, M. Arimoto, E. Fujita, J. Chem. Soc. Chem. Commun. **1981**, 460; S. Ohashi, W. E. Ruch, G. B. Butler, J. Org. Chem. **46** (1981) 614; S. Imazu, N. Shimizu, Y. Tsuno, Chem. Lett. **1990**, 1845; R. Huisgen, R. Brückner, Tetrahedron Lett. **31** (1990) 2553
[30] H.–J. Knölker, G. Baum, R. Graf, Angew. Chem. **106** (1994) 1705; Angew. Chem., Int. Ed. Engl. **33** (1994) 1612
[31] H. Monti, G. Audran, J.–P. Monti, G. Léandri, Synlett **1994**, 403; G. P. Brengel, C. Rithner, A. I. Meyers, J. Org. Chem. **59** (1994) 5144
[32] T. Akiyama, M. Kirino, Chem. Lett. **1995**, 723
[33] T. Akiyama, M. Yamanaka, Synlett **1996**, 1095
[34] T. Uyehara, M. Yuuki, H. Masaki, M. Matsumoto, M. Ueno, T. Sato, Chem. Lett. **1995**, 789
[35] J. S. Panek, N. F. Jain, J. Org. Chem. **59** (1994) 2674
[36] J. R. Hwu, C. N. Chen, S.-S. Shiao, J. Org. Chem. **60** (1995) 856
[37] I. Fleming, R. Henning, H. Plaut, J. Chem. Soc. Chem. Commun. **1984**, 29; I. Fleming, P. E. J. Sanderson, Tetrahedron Lett. **36** (1987) 4229; I. Fleming, R. Henning, D. C. Parker, H. E. Plaut, P. E. J. Sanderson, J. Chem. Soc., Perkin Trans. 1 **1995**, 317
[38] K. Tamao, T. Kakui, M. Akita, T. Iwahara, R. Kanatani, J. Oshida, M. Kumada, Tetrahedron **39** (1983) 983; K. Tamao, N. Ishida, T. Tanaka, K. Kumada, Organometallics **2** (1983) 1694; K. Tamao, N. Ishida, J. Organomet. Chem. **269** (1984) C37
[39] For recent reviews, see: I. Fleming, Chemtracts-Organic Chemistry **9** (1996) 1; G. R. Jones, Y. Landais, Tetrahedron **52** (1996) 7599
[40] H.–J. Knölker, G. Wanzl, Synlett **1995**, 378; for a more recent example, see: G. P. Brengel, A. I. Meyers, J. Org. Chem. **61** (1996) 3230

Address for correspondence:
Prof. Dr. Hans–Joachim Knölker
Institut für Organische Chemie
Universität Karlsruhe
Richard–Willstätter-Allee
D-76131 Karlsruhe
Telefax: Int. Code + (721)698529