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[3+2] Cycloadditions of Allylsilanes, Part 3.[1]
Diastereoselective Construction of Two Contiguous Quaternary Carbon Centers by [3+2] Cycloaddition of Allyltrisisopropylsilane

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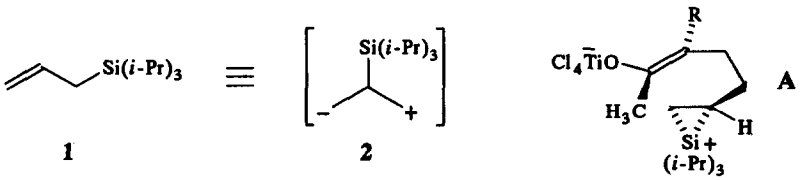
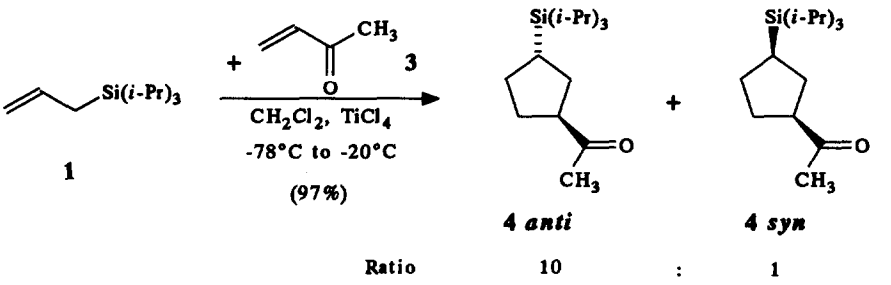
Abstract: A diastereoselective synthesis of 1,2-annulated and spiroannulated bicyclic ring systems with concomitant generation of two contiguous quaternary carbon atoms is achieved by [3+2] cycloaddition of allyltrisisopropylsilane to the appropriate enones.

We recently found a novel cyclopentane annulation by [3+2] cycloaddition of allylsilanes to enones.[2] Subsequent to our preliminary communication several further examples for this hitherto unprecedented mode of reactivity of allylsilanes have been reported.[3] Similar reactions of allylstannanes have been observed with α,β-unsaturated acyliron complexes.[4] One of the major features of the [3+2] cycloaddition of allylsilanes is the high degree of stereospecificity with respect to the stereogenic centers formed in this process. For stereoelectronic reasons the favored diastereoisomer always exhibits an *anti* arrangement of the silyl group and the alkanoyl group. In most of the cases which we have investigated the *anti* stereoisomer represents the only one which could be isolated.[1,2,5] The competing Sakurai reaction[6] which takes advantage of an allylsilane as an allyl anion equivalent can be almost completely suppressed by the introduction of sterically demanding substituents at the silicon atom.[1] Therefore, the allyltrisisopropylsilane **1** represents a very useful synthetic equivalent for the 2-silyl-substituted 1,3-dipole **2**.



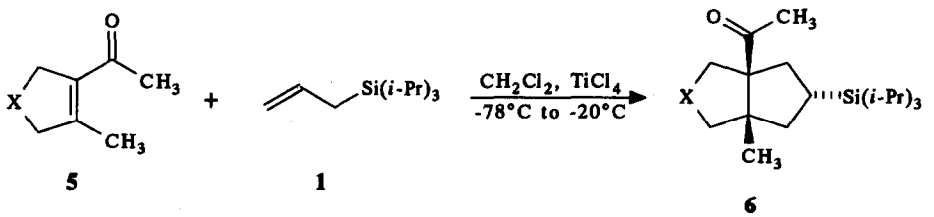
1 **2**

The annulation involves a cationic 1,2-silyl shift which we suggest to proceed *via* an intermediate bridged non-classical pentavalent silicon cation **A**.[7] The stereoelectronic requirements for cyclization of **A** also explains the preferred mode of stereospecificity which is observed in these cyclizations. We found that a broad variety of α,β-unsaturated carbonyl compounds provide the corresponding cycloaddition products on Lewis acid mediated reaction with **1**. These cycloadditions proceed under mild conditions to give in some cases virtually quantitative yields. Thus, using our optimized standard procedure[1] the reaction of methyl vinyl ketone **3** with **1** affords quantitatively the cyclopentane **4** with a 10 : 1 ratio in favor of the *anti* diastereoisomer (Scheme 1). Both *anti* and *syn* diastereoisomers are characterized by their ^{13}C-NMR spectra.[8]



Scheme 1

The utility of this process for the diastereoselective construction of bicyclic ring systems of different ring size by [3+2] cycloaddition of allylsilanes to 1-acetylcycloalkenes has recently been demonstrated.[1] In this paper we wish to report the application of this process for annulations directed towards the synthesis of bicyclic ring systems with the concomitant diastereoselective construction of two contiguous quaternary carbon centers. First, we investigated the reaction of allyltrisisopropylsilane **1** with 1-acetyl-2-methyl-cycloalkenes **5**[9,10] of different ring size which provides the bicyclic products **6** (Scheme 2, Table 1).



Scheme 2

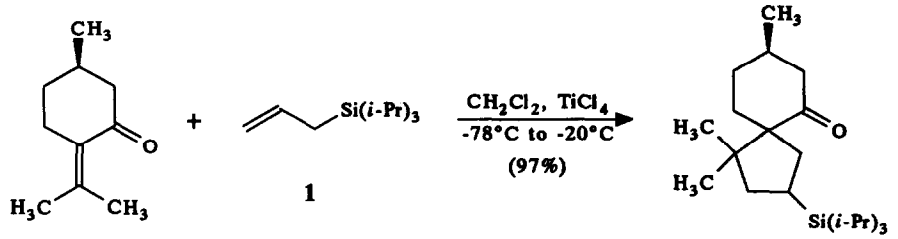
Table 1. [3+2] Cycloadditions of Allyltrisisopropylsilane to 1-Acetyl-2-methylcycloalkenes

	X	Synthesis of **5**	Yield of **6**	Stereochemistry
a	CH_2	*Ref.* [9]	92%	*anti/syn* = 5 : 1
b	$(CH_2)_2$	*Ref.* [10]	46%	*anti*
c	$(CH_2)_3$	*Ref.* [10]	54%	*anti*

The cycloaddition of **1** to 1-acetyl-2-methylcyclopentene **5a** affords the bicyclic product **6a** in the highest yield. This increased reactivity of the five-membered ring double bond is explained by strain release on the addition of allylsilane. However, only a 5 : 1 ratio in favor of the *anti* diastereoisomer is obtained. This low selectivity is a consequence of the steric hindrance caused by the trisisopropylsilyl group in the *endo*-position of a bicyclo[3.3.0]octane ring. The higher homologues **5b** and **5c** provide the hydrindane **6b** and the hydroazulene **6c** in lower yield but with complete stereospecificity. The structural assignments are based on correlation of the ^{13}C-NMR data[11] with the data of related compounds[1] previously reported.

The $TiCl_4$-promoted reaction of (R)-(+)-pulegone with allyltrisisopropylsilane **1** affords quantitatively the spiro[4.5]decane **7** (Scheme 3). Compound **7** is obtained as a 2 : 1 mixture of two enantiopure diastereoisomers, which are separated by flash chromatography on silica gel. The ^{13}C-NMR data suggest that

the *anti*-selectivity of the silyl group relative to the alkanoyl group is maintained and that the two products result from the addition of the 1,3-dipole **2** *syn* and *anti* with respect to the methyl group of pulegone.[12]



(R)-(+)-Pulegone **7**

Scheme 3

The last example emphasizes the utility of the [3+2] cycloaddition of allylsilanes for the generation of annulated ring systems with sterically crowded substituents. Moreover, it indicates for the first time the tremendous power that this process has for the construction of spirocyclic ring systems. Spiroannulations of this type are of potential value for natural product synthesis, since the spiro[4.5]decane framework is found in several biologically active sesquiterpenes (*e.g.* α-acoradiene[13]). Further applications of this methodology are in progress and will be reported in due course.

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8. ^{13}C-NMR data and the results of the DEPT experiments (100 MHz, $CDCl_3$) of the cyclopentanes **4**.
4 ***anti*** (major diastereoisomer): 11.3 (3 CH), 19.1 (6 CH_3), 22.5 (CH), 28.7 (CH_3), 30.3 (CH_2), 30.5 (CH_2), 31.1 (CH_2), 52.6 (CH), 211.1 (C=O).
4 ***syn*** (minor diastereoisomer): 12.3 (3 CH), 17.7 (6 CH_3), 24.1 (CH), 28.5 (CH_2), 29.0 (CH_3), 29.1 (CH_2), 33.2 (CH_2), 53.8 (CH), 211.2 (C=O).
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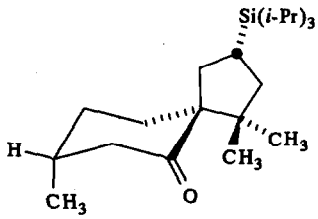
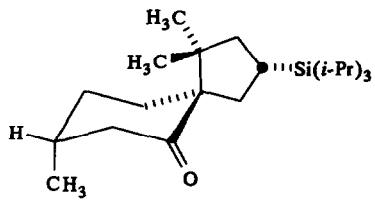
11. ^{13}C-NMR data and results of DEPT experiments (100 MHz, $CDCl_3$) of the bicyclo[n.3.0]alkanes **6**.
6a ***anti*** (major diastereoisomer): 11.4 (3 CH), 19.2 (6 CH_3), 23.7 (CH_2), 23.8 (CH), 24.7 (CH_3), 29.0 (CH_3), 38.0 (CH_2), 41.9 (CH_2), 42.9 (CH_2), 46.1 (CH_2), 57.0 (C), 68.0 (C), 213.4 (C=O).
6a ***syn*** (minor diastereoisomer): 11.4 (3 CH), 19.2 (6 CH_3), 20.8 (CH), 25.1 (CH_3), 26.3 (CH_2), 29.3 (CH_3), 39.0 (CH_2), 40.9 (CH_2), 43.0 (CH_2), 45.8 (CH_2), 56.5 (C), 68.3 (C), 213.7 (C=O).
6b: 11.1 (3 CH), 15.5 (CH), 19.3 (6 CH_3), 21.7 (CH_2), 22.2 (CH_2), 24.4 (CH_3), 28.1 (CH_3), 33.4 (CH_2), 33.7 (CH_2), 37.3 (CH_2), 39.8 (CH_2), 43.3 (C), 59.7 (C), 211.9 (C=O).
6c: 11.3 (3 CH), 19.3 (CH, 6 CH_3), 23.9 (CH_2), 24.8 (CH_2), 28.92 (CH_3), 28.94 (CH_3), 31.2 (CH_2), 37.4 (CH_2), 38.9 (CH_2), 39.9 (CH_2), 44.3 (CH_2), 47.7 (C), 64.4 (C), 212.5 (C=O).
12. The spiro[4.5]decane **7** consists of a 2 : 1 mixture of two enantiopure diastereoisomers. Provided that the complete stereoselectivity control of the *anti* arrangement of the trisisopropylsilyl group relative to the ketone is retained, it can be concluded that the two stereoisomers result from the lack of stereoselectivity control by the methyl group of pulegone in the spirocyclization step.





This assignment is supported by the ^{13}C-NMR data and the DEPT experiments (100 MHz, $CDCl_3$).
7a (major diastereoisomer: less polar product; $[\alpha]_D$ = +3.45°, 20°C, $CHCl_3$, *c* 3.85): 11.16 (3 CH), 17.1 (CH), 19.3 (6 CH_3), 21.8 (CH_3), 23.7 (CH_3), 27.3 (CH_3), 31.1 (CH_2), 32.8 (CH_2), 33.7 (CH), 38.1 (CH_2), 43.5 (CH_2), 44.0 (C), 48.7 (CH_2), 60.8 (C), 213.3 (C=O).
7b (minor diastereoisomer: more polar product; $[\alpha]_D$ = +1.99°, 20°C, $CHCl_3$, *c* 5.52): 11.25 (3 CH), 18.4 (CH), 19.3 (6 CH_3), 22.2 (CH_3), 25.5 (CH_3), 26.5 (CH_3), 31.7 (CH_2), 33.9 (CH), 37.6 (CH_2), 40.4 (CH_2), 44.8 (C), 46.6 (CH_2), 50.6 (CH_2), 59.7 (C), 213.9 (C=O).
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