Pergamon

Tetrahedron Letters 40 (1999) 2557–2560

TETRAHEDRON LETTERS

New Synthesis of Silylcyclopropanols via Titanium(II)-Mediated Coupling of Vinylsilanes and Esters

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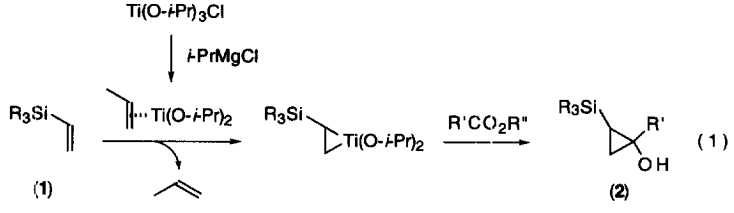
Received 24 December 1998; revised 20 January 1999; accepted 22 January 1999

Abstract

A variety of silylcyclopropanols were conveniently prepared from vinylsilanes, carboxylic esters, and a titanium(II) species prepared *in situ* from Ti(O-*i*-Pr)3Cl and *i*-PrMgCl. The compatibility of some functional groups and the stereochemistry of the products are disclosed. In addition, a few synthetic applications are also illustrated.

Keywords: cyclopropanation; cyclopropanes; silicon and compounds; stereoselection; titanium and compounds

Cyclopropanols and their derivatives such as *O*-silylated ones are useful intermediates in organic synthesis [1]. In addition to known methods for their synthesis [2], considerable progress has been achieved in their accessibility by the recently introduced inter- or intramolecular coupling reaction of terminal alkenes and esters under the influence of a titanium(II) species, generated *in situ* from $Ti(OR)_4$ and a Grignard reagent [3-5]. Functionalized alkenes should make it possible to introduce a functional group directly onto the cyclopropane ring. However, the proper choice of the olefinic component is critical, particularly in the intermolecular reaction, in order to efficiently generate the desired olefin-titanium complex via the ligand exchange reaction that is basically under equilibrium. So far, styrene [6] and conjugated dienes [7] fulfill this requirement to give the corresponding cyclopropanols having a phenyl or vinyl group β to the hydroxy group. Gratifyingly, our latest study along this line revealed that vinylsilanes **1** are also a suitable candidate for this process as shown in eq 1 to give silylcyclopropanols **2** [8].



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PII: S0040-4039(99)00201-4

The transformation of eq 1, which can be carried out by a simple experimental procedure, shows general applicability with respect to a few types of vinylsilanes as well as several kinds of esters. Table 1 summarizes the results. In addition to (trimethylsilyl)cyclopropanols, [(alkoxy)dimethylsilyl]cyclopropanols **2k** and **2l** could be obtained as well (entries 11 and 12). The oxidative conversion of the latter silyl group to a hydroxy group may be feasible [9]. The presence of an additional functional group in esters such as olefin, alkyl bromide, and phenyl ether does not impede with the reaction at all (entries 7-10). To our surprise, methyl 6-heptenoate (entry 7), for which the intramolecular cyclopropanol formation would be a quite preferred path [4], did undergo the intermolecular reaction to give the corresponding silylcyclopropanol without any complication. A hindered ester participated in the reaction, but it caused a change in the stereochemistry of the product (entry 6 and *vide infra*).

As far as the diastereoselectivity of the reaction is concerned, the selectivity generally falls within a good level, favoring *trans* relationship between the silyl and hydroxy groups in most cases where the alkyl side chain is not sterically demanding (all entries except entry 6) and, contrarily, *cis* for a sterically encumbered *tert*-butyl group (entry 6). The relative stereochemistries have been unambiguously determined in representative cases by nOe study of the ^{1}H NMR spectroscopy as shown in Fig 1. As the major isomers **2a-e**, **2g**, and **2i-k** of other products in Table 1 as well as **2h** and **2l** in Fig 1 always behaved as a more polar component on silica gel chromatography (TLC or preparative) than the minor isomers, as readily expected based on the degree of steric shielding of the hydroxy group, the stereochemical assignments to the major and minor isomers of these products were made as shown in Table 1 by analogy. This fact also means that the stereoisomers were successfully separated by flash chromatography on silica gel to pure fractions (of the major isomers).

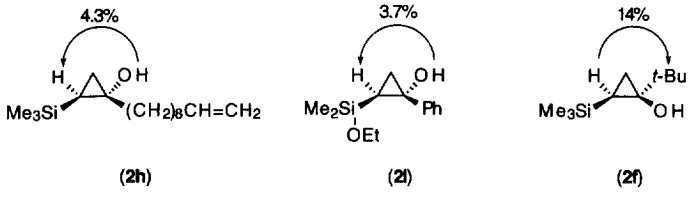


Figure 1. Values in % refer nOe enhancements.

Silylated compounds are useful intermediates in organic synthesis [10]. In order to disclose the advantage of silylcyclopropanols [11], fundamental transformations of silylcyclopropanols are exemplified in eq 2. The silyl group seems to control the regioselective scission of the carbon-carbon bond in Me3Si-C-C-OH to give β-silylketones under acidic conditions. Another example is the Peterson-like olefination to give a cyclopropene in good yield [12]. Further study for these and other reactions based on silylcyclopropanols is now in progress and the results will be reported in due course.

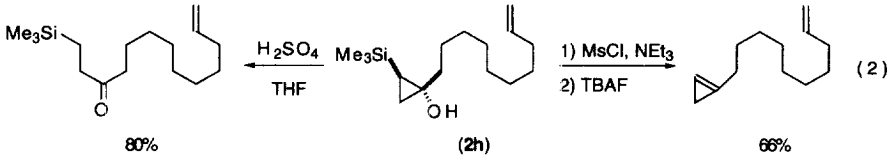
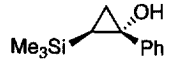
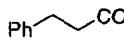
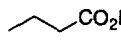
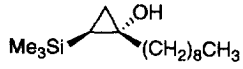
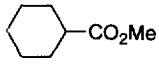
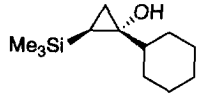
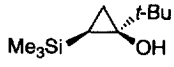
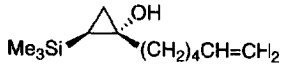
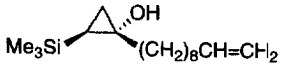
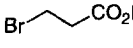
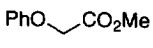
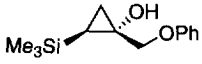
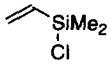
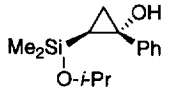
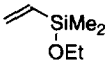
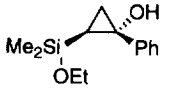


Table1. Synthesis of Silylcyclopropanols via Titanium(II)-Mediated Coupling of Vinylsilanes and Esters.[a]

Entry	Vinylsilane	Ester	Major isomer of the product		*Trans/cis* ratio of the crude product[b]	Yield of major isomer (%)[c]
1	 (**1a**)	$PhCO_2Et$		(**2a**)	93 : 7	88
2	**1a**			(**2b**)	81 : 19	76
3	**1a**			(**2c**)	87 : 13	80
4	**1a**	$CH_3(CH_2)_8CO_2Me$		(**2d**)	88 : 12	74
5	**1a**			(**2e**)	81 : 19	62
6	**1a**	t-$BuCO_2Me$		(**2f**)	7 : 93	82
7	**1a**	$CH_2=CH(CH_2)_4CO_2Me$		(**2g**)	88 : 12	62
8	**1a**	$CH_2=CH(CH_2)_8CO_2Me$		(**2h**)	87 : 13	81
9	**1a**			(**2i**)	77 : 23	42
10	**1a**			(**2j**)	88 : 12	55
11	 (**1b**)	$PhCO_2Et$		(**2k**)	85 : 15	62 (18)[d]
12	 (**1c**)	$PhCO_2Et$		(**2l**)	65 : 35	31 (30)[d]

[a]See eq 1 and the typical experimental procedure. [b]Determined by ^1H NMR spectroscopy. *Trans/cis* refers to the relationship between the silyl and hydroxy groups. [c]Isolated yields. [d]Yield of the recovered ester in parentheses.

Typical procedure for the preparation of 2a. To a stirred solution of Ti(O-*i*-Pr)3Cl (1.50 mL of a 1.0 M solution in hexane, 1.5 mmol) in Et_2O (10 mL) was added *i*-PrMgCl (2.2 mL of a 1.30 M solution in ether, 2.9 mmol) at -60 °C under argon. Ten minutes later, a mixture of vinyl(trimethyl)silane (0.22 mL, 1.5 mmol) and ethyl benzoate (0.14 mL, 1.0 mmol) was added to the solution. The reaction mixture was then warmed up to -25 °C over 30 min and was stirred at -25 °C ~ -20 °C for 1 h and finally at room temperature for 1 h. After water (0.5 mL) in THF (2.0 mL) was added at room temperature, the heterogeneous mixture was stirred for 0.5 h. The resultant suspension was filtered through a pad of Celite, which was subsequently washed with ether. The combined filtrate and ethereal fractions were concentrated *in vacuo* to afford a crude oil, ^{1}H NMR analysis of which showed the diastereomeric ratio to be 93:7. Purification by column chromatography on silica gel (pretreated with 1% NEt3 in hexane and eluted with hexane/ether 8:1) afforded pure **2a** as a colorless oil (182 mg, 88%). TLC (Merck#1.05554, hexane/ether 3:1): R_f 0.30 (major isomer **2a**) and 0.70 (minor isomer). **2a**: IR (neat): 3323, 3026, 1942, 1248 cm^{-1}; ^{1}H NMR (300 MHz) δ -0.30 (s, 9 H), 0.54 (dd, *J* = 8.7, 12 Hz, 1 H), 1.14 (dd, *J* = 4.5, 8.7 Hz, 1 H), 1.24 (dd, *J* = 4.5, 12 Hz, 1 H), 1.57 (s, 1 H), 7.26-7.45 (m, 5 H); ^{13}C NMR (75 MHz) δ -1.87, 15.35, 16.01, 62.37, 127.94, 128.38, 128.70, 141.69. Another (minor) isomer: ^{1}H NMR (300 MHz) (a characteristic peak is shown) δ 0.29 (dd, *J* = 9, 11 Hz).

It should be noted that, when the above reaction was carried out by the routine procedure (addition of *i*-PrMgCl *to a mixture of* Ti(O-*i*-Pr)4, olefin, and ester) adopted from our and other groups' protocol [4,8], the yield of **2a** apparently decreased.

Acknowledgment. We thank the Ministry of Education, Science, Sports and Culture (Japan) for financial support.

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