

USE OF ALLYLSILANES AS A NEW TYPE OF SILYLATING AGENT FOR  
ALCOHOLS AND CARBOXYLIC ACIDS

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**Summary:** A new convenient route to silyl ethers and esters from alcohols and carboxylic acids using allylsilanes in the presence of an acid catalyst in acetonitrile was developed. The present method is also applicable to *t*-butyldimethylsilylation.



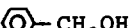

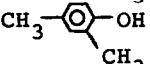
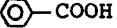
Trimethylsilyl group is the most versatile one for protection of various hydroxy functions in organic synthesis as well as chromatographic analyses of organic compounds. Several silylating agents such as chlorotrimethylsilane, hexamethyldisilazane, and *N,O*-bis(trimethylsilyl)acetamide etc. have been developed and become available on a commercial scale.<sup>1,2</sup> For trimethylsilyl ethers and esters, the most common preparative method is chlorotrimethylsilane/pyridine system. However, it is accompanied by the formation of voluminous pyridine salt as a by-product and requires a careful filtration of the salt before isolating the silylated compounds. The product yields are not so high in most cases. Another trimethylsilylation with hexamethyldisilazane in the presence of an acid catalyst involves refluxing of the reaction mixture at 130 °C for several hours to drive off the resulting ammonia. These silicon reagents, which contain relatively labile Si-Cl or Si-N bond toward oxygen nucleophiles, are susceptible to hydrolysis even with the atmospheric moisture during silylation reaction or prolonged storage. More recently, two new silylating methods using trimethylsilylacetate<sup>3</sup> or hexamethyldisiloxane<sup>4</sup> have been reported.

In order to improve a few drawbacks described above, our interest was focused on a new type of silylating procedure using the alternative readily available organosilane containing Si-C bond only. Since 1974,

allyltrimethylsilane has been shown to be an effective reagent for introducing the allyl group into carbon electrophiles<sup>5</sup> and widely employed for various synthetic transformations.<sup>6</sup> We now report here that the reaction of alcohols and carboxylic acids with allylsilanes in the presence of an acid catalyst results a quantitative formation of the corresponding silylated derivatives without any by-product.

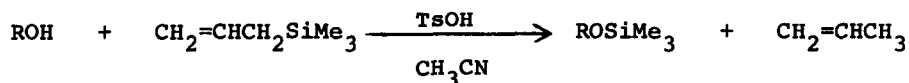
When a mixture of alcohol (10 mmol), allyltrimethylsilane<sup>7</sup> (12 mmol), and p-toluensulfonic acid (0.2 mmol, 0.02 equiv.) in acetonitrile (10 ml) was heated at 70 - 80 °C with stirring, the reaction immediately occurred and propene gas was evolved.<sup>8</sup> The progress of reaction was conveniently monitored by GLC.

Table 1 Conversion of alcohols and carboxylic acids into silyl ethers and esters

Entry	Substrate	Time (h)	Yield <sup>a</sup> (%)	Bp °C/mmHg
1	$n\text{-C}_7\text{H}_{15}\text{OH}$	2.0	95	83 - 85/21
2	$\text{CH}_3(\text{CH}_2)_5\text{CH}(\text{OH})\text{CH}_3$	2.5	88	90 - 92/26
3	1-Menthol	2.0	87	87 - 88/8
4		2.0	91	68 - 70/26
5		1.5	93	78 - 79/22
6		1.5	95	96 - 97/24
7		8.0	86	102 - 103/20
8		2.5	96	105 - 106/21
9	Borneol	2.0	89	92 - 93/12
10	$n\text{-C}_5\text{H}_{11}\text{COOH}$	2.5	88	79 - 81/19
11		2.0	87	97 - 99/10

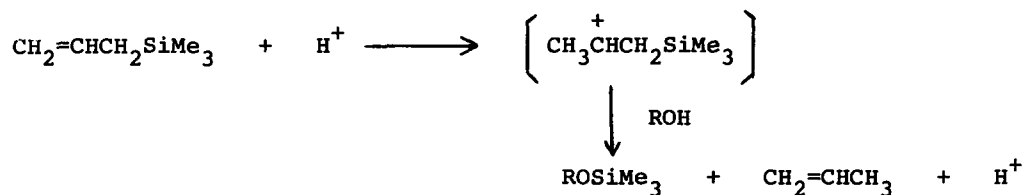
<sup>a</sup> Yields are for isolated products by distillation. In all cases, the silyl ethers and esters were identified by comparison with authentic samples.

The silylation was essentially completed within 1.5 - 3.0 h.



The reaction mixture was almost pure acetonitrile solution of the silyl ether. To neutralize the catalyst, an equivalent amount of pyridine (0.2 mmol) was added to the solution. Then direct distillation of the resulting solution under reduced pressure gave the desirable trimethylsilyl ether in an excellent yield.<sup>9</sup> The results are summarized in Table 1. Similarly, the treatment of carboxylic acids with this reagent in acetonitrile afforded the corresponding trimethylsilyl carboxylates quantitatively (entry 10, 11). On the contrary, thiophenol was not silylated with this reagent.

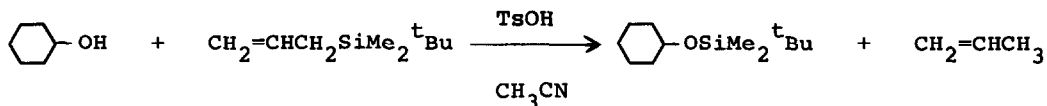
From the following three points, i) allyltrimethylsilane is very stable in water, alcohols, and carboxylic acids, ii) p-toluenesulfonic acid acts as a catalyst, iii) acetonitrile proves to be the most suitable solvent in this reaction than others such as benzene, carbon tetrachloride, and chloroform, we propose the following mechanism for the present alcohol silylation.



It involves an initial formation of cationic species generated by protonation at  $\gamma$ -carbon atom in the allylsilane followed by a subsequent nucleophilic attack of alcohol on the silicon atom to produce the silyl ether and propene.

On the other hand, Corey et al. have shown that sterically hindered t-butyldimethylsilyl group is useful for protecting hydroxy functions because of its extreme stability toward solvolysis.<sup>11</sup> Besides the original method using t-butyldimethylchlorosilane/imidazole, two improved reagents such as the silyl perchlorate/pyridine<sup>12</sup> and the chlorosilane/4-dimethylaminopyridine<sup>13</sup> have been developed for the silylation. The chlorosilane is very hygroscopic. We now recommend allyl-t-butyldimethylsilane<sup>14</sup> as a new effective reagent for introducing the hindered silyl group. The reaction of cyclohexanol with this

reagent at 70 - 80 °C for 2.5 h gave the t-butyldimethylsilyl ether (74 - 76 °C/8 mmHg) in 95 % yield.



Our new simple route to trialkylsilyl ethers and esters using allylsilanes is of considerable use because of the availability and stability of reagents, the lack of by-product, and the high yield of products.

#### References and Notes

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- 7 Allyltrimethylsilane is commercially available from Aldrich Chemical Company, Inc. and also is easily prepared from chlorosilane and allyl bromide in THF by the Grignard reaction.
- 8 The propene generated was identified as 1,2-dibromopropane by the reaction with bromine.
- 9 To our knowledge, this is the first example of acid-catalyzed alcohol silylation with allylsilane, although [1,3]allylic rearrangement was reported utilizing protodesilylation of allylsilanes with p-toluenesulfonic acid in benzene.<sup>10</sup>
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- 14 The allylsilane (a colorless liquid, bp 65 - 66 °C/47 mmHg) was prepared from the chlorosilane and allyl bromide by a similar method in the case of ref. 7.

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