

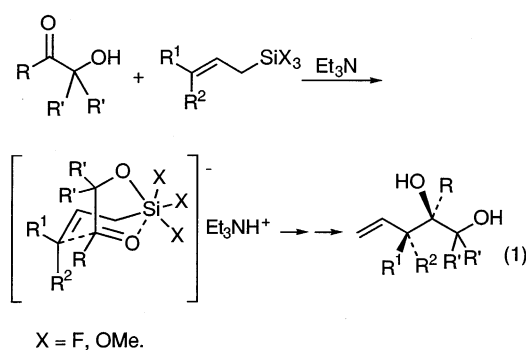
## Stereoselective Allylation of $\beta$ -Hydroxy- and $\beta$ -Amino- $\alpha,\beta$ -enones with Allyltrifluorosilane/Triethylamine Systems<sup>1</sup>

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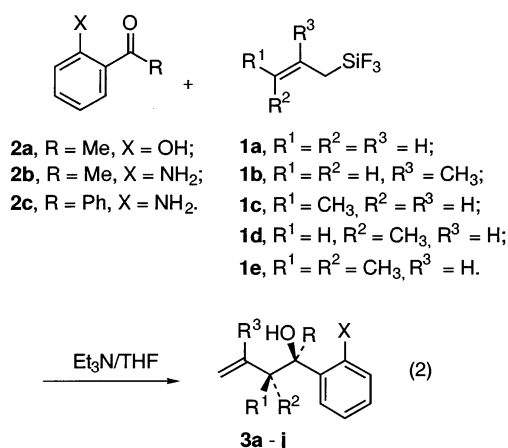
Reactions of allyltrifluorosilanes with  $\beta$ -functional- $\alpha,\beta$ -enones such as *o*-hydroxy- and *o*-aminophenyl ketones and 1,3-diketones in the presence of triethylamine yielded the corresponding tertiary homoallyl alcohols in regiospecific and highly diastereoselective manner.

Allylation of aldehydes with pentacoordinate allylsilicates offers a useful method for regiospecific and highly diastereoselective synthesis of homoallyl alcohols.<sup>2</sup> Recently, we have reported that treatment of  $\alpha$ -hydroxy ketones with allyltrifluorosilanes and allyltrialkoxysilanes in the presence of triethylamine causes unique allylation with stereo-regulation at three carbon centers via the 1,3-bridged cyclohexane-like transition state as shown in Eq 1.<sup>3</sup> Although the allylation was not applicable to aliphatic  $\beta$ - and  $\gamma$ -hydroxy ketones, *o*-hydroxyacetophenone was allylated under similar conditions rather exceptionally. As an extension of our study of synthetic application of pentacoordinate allylsilicates we report an efficient allylation of  $\beta$ -functional- $\alpha,\beta$ -enones such as *o*-hydroxy- and *o*-aminophenyl ketones and 1,3-diketones with the allyltrifluorosilane/triethylamine reagent systems.



Reactions of allyltrifluorosilanes with *o*-hydroxy- and *o*-aminophenyl ketones in the presence of triethylamine yielded the corresponding tertiary homoallyl alcohols **3** in regiospecific and highly diastereoselective manner as shown in Eq 2. The results are summarized in Table 1. Typically, 2-(2-hydroxyphenyl)-4-methylpent-4-en-2-ol (**3a**) was prepared by the following procedure: To a mixture of **2a** (264 mg, 1.5 mmol), triethylamine (303 mg, 3.0 mmol), and THF (5 ml), **1b** (420 mg, 3.0 mmol) was added. After stirring for 48 h at ambient temperature, the reaction mixture was chromatographed on a short column of silica gel. The pure product was obtained by Kugelrohr distillation in 90% yield.<sup>4</sup> Reactivity of the allyltrifluorosilanes with *o*-hydroxyacetophenone and *o*-aminophenyl ketones was very sensitive to the steric bulkiness of the substituents. Thus, for completion of the reaction of *o*-hydroxyacetophenone with prenyltrifluorosilane, heating the

mixture for 40 h was required, while the reactions of other allyltrifluorosilanes took place at room temperatures. *o*-Aminophenyl ketones **2b** and **2c** did not react with either (*Z*)-crotyltrifluorosilane (**1d**) or prenyltrifluorosilane (**1e**).

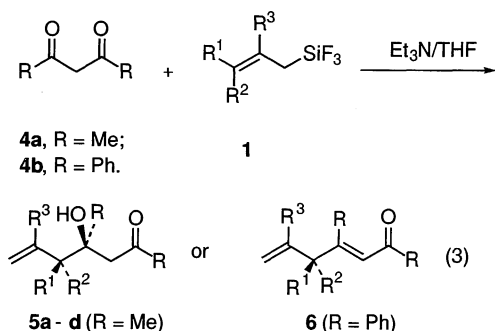


**Table 1.** Allylation of *o*-Functional Phenylketones

Entry	Ketone	Allyl-silane	Reaction Conditions <sup>a</sup>	Product	Isolated Yield/%
1	<b>2a</b>	<b>1b</b>	rt, 48 h	<b>3a</b>	90
2	<b>2a</b>	<b>1c<sup>b</sup></b>	rt, 48 h	<b>3b</b>	90 <sup>c</sup>
3	<b>2a</b>	<b>1d<sup>d</sup></b>	rt, 48 h	<b>3c</b>	83 <sup>c</sup>
4	<b>2a</b>	<b>1e</b>	reflux, 36 h	<b>3d</b>	90
5	<b>2b</b>	<b>1a</b>	rt, 40 h	<b>3e</b>	63
6	<b>2b</b>	<b>1b</b>	reflux, 29 h	<b>3f</b>	65
7	<b>2b</b>	<b>1c<sup>e</sup></b>	rt, 40 h	<b>3g</b>	68
8	<b>2b</b>	<b>1d<sup>d</sup></b>	reflux, 96 h	<b>3h</b>	0
9	<b>2c</b>	<b>1a</b>	rt, 40 h	<b>3i</b>	56
10	<b>2c</b>	<b>1e</b>	reflux, 40 h	<b>3j</b>	0

a) The following molar ratio of reagents were used: allyl-silane/ketone/triethylamine = 2.0/1.0/2.0. b) A mixture of **1c/1d** = 97/3. c) The other diastereomer was not detected by capillary glc. d) A mixture of **1c/1d** = 5/95. e) A mixture of **1c/1d** = 88/12. f) The diastereomer ratio determined by capillary glc.

Allylation of 1,3-diketones was also attainable with the present reagent systems because the corresponding  $\beta$ -hydroxy- $\alpha,\beta$ -enones exist in equilibrium. Pentane-2,4-dione (**4a**) reacted very smoothly with various allyltrifluorosilanes to give the corresponding allylated  $\beta$ -hydroxy ketones **5** in good to fair yields (Table 2),<sup>5</sup> while the reaction of 1,3-diphenylpropane-1,3-dione (**4b**) with **1e** gave **6<sup>o</sup>** in a high yield. The reactions of **1a - 1d** with **4b** proceeded but gave unidentified complex mixtures probably via dehydration during work-up.

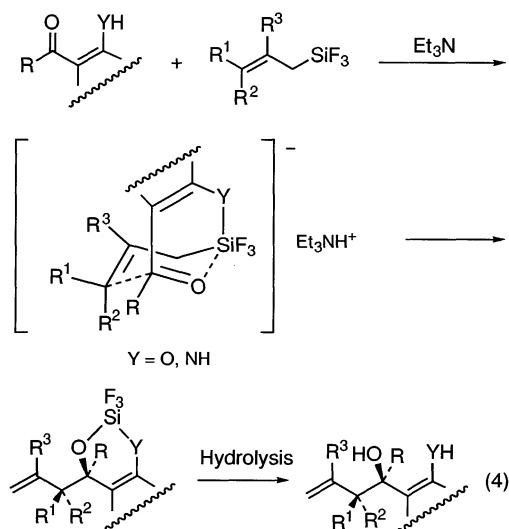
**Table 2.** Allylation of 1,3-Diketones

Entry	Ke- tone	Allyl- silane	Reaction Conditions <sup>a</sup>	Pro- duct	Isolated Yield/%
1	<b>4a</b>	<b>1a</b>	rt, 34 h	<b>5a</b>	81
2	<b>4a</b>	<b>1b</b>	rt, 5 h	<b>5b</b>	48
3	<b>4a</b>	<b>1c<sup>b</sup></b>	rt, 48 h	<b>5c</b>	45 (6/94) <sup>c</sup>
4	<b>4a</b>	<b>1d<sup>d</sup></b>	rt, 48 h	<b>5d</b>	61 (99/1) <sup>c</sup>
5	<b>4b</b>	<b>1e</b>	reflux, 48 h	<b>6</b>	90

a) The following molar ratio of reagents were used: allylsilane/ketone/triethylamine = 2.0/1.0/2.0. b) A mixture of **1c/1d** = 97/3. c) The diastereomer ratio determined by capillary glc. d) A mixture of **1c/1d** = 5/95.

The C-C bond formation of these allylation occurs at the  $\gamma$ -position of the allylsilanes; no regioisomers other than those shown in Eqs 2 and 3 were detected.

The crotylation is highly diastereoselective. Comparison of the <sup>1</sup>H and <sup>13</sup>C NMR spectra for the crotylation products of **2a** and **4a** revealed that the major diastereomers produced from **1c** and **1d** are different from each other (Entries 2 and 3 in Table 1 and Entries 3 and 4 in Table 2). Since **3b/3c** and **5c/5d** lack vicinal hydrogens at the two chiral centers, the usual method of the stereochemical assignment of the diastereomers using <sup>1</sup>H NMR coupling constants cannot be applied here. The tentative assignments of these adducts are shown in Eqs 2 and 3, on the basis of the assumption of the bicyclic transition state shown in Eq 4, which is similar to that proposed for the allylation of  $\alpha$ -hydroxy ketones.<sup>3</sup>



Simple  $\beta$ -hydroxy alkylketones such as 4-hydroxybutan-2-one and 4-hydroxy-4-methylpentan-2-one did not react with **1c** under similar reaction conditions; the severe steric repulsion between R<sup>3</sup> group of the allylsilane and endo hydrogens at the bridging alkyl chain in the bicyclic transition state may hamper the facile allylation.

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## References and Notes

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- 3a**: <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  9.25 (brs, 1H), 7.13 (ddd, J = 7.77, 7.50, 1.59 Hz, 1H), 7.03 (dd, J = 7.77, 1.59 Hz, 1H), 6.83 (dd, J = 8.05, 1.05 Hz, 1H), 6.80 (ddd, 8.05, 7.50, 1.59 Hz, 1H), 4.97 (brs, 1H), 4.77 (s, 1H), 2.95 (brs, 1H), 2.77 (d, J = 13.6 Hz, 1H), 2.47 (d, J = 13.7 Hz, 1H), 1.64 (s, 3H), 1.63 (s, 3H); <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>)  $\delta$  155.7, 141.8, 129.4, 128.8, 126.2, 119.3, 117.6, 116.4, 77.3, 49.8, 29.4, 24.6.
- 5c**: <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  5.73 (ddd, J = 16.8, 10.6, 8.8 Hz, 1H), 5.02 (dm, J = 10.6 Hz, 1H), 5.01 (dm, J = 16.8 Hz, 1H), 3.88 (s, 1H), 2.69 (d, J = 17.3 Hz, 1H), 2.50 (d, J = 17.3 Hz, 1H), 2.37 (dq, J = 8.8, 6.9 Hz, 1H), 2.15 (s, 3H), 1.12 (s, 3H), 1.03 (d, J = 6.9 Hz, 3H); <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>)  $\delta$  211.9, 140.9, 116.0, 73.5, 51.1, 47.9, 32.2, 23.1, 14.5. **5d**: <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>)  $\delta$  5.85 (ddd, 17.1, 10.5, 8.2 Hz, 1H), 5.06 (dm, J = 10.5 Hz, 1H), 5.05 (dm, J = 17.1 Hz, 1H), 3.75 (s, 1H), 2.66 (d, J = 16.9 Hz, 1H), 2.52 (d, J = 16.9 Hz, 1H), 2.26 (dq, J = 8.2, 7.0 Hz, 1H), 2.18 (s, 3H), 1.18 (s, 3H), 1.01 (d, J = 7.0 Hz, 3H); <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>)  $\delta$  211.4, 140.0, 115.7, 73.2, 50.2, 47.7, 32.1, 24.5, 14.4.
- 6**: <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  7.8 - 7.0 (m, 10H), 6.85 (s, 1H), 6.02 (dd, J = 9.9 and 17.3 Hz, 1H), 5.15 (d, J = 9.9 Hz, 1H), 5.10 (d, J = 17.3 Hz, 1H), 1.24 (s, 6H). <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>)  $\delta$  193.3, 161.9, 145.5, 138.4, 138.4, 132.5, 128.7, 128.5, 128.2, 127.2, 126.9, 123.7, 112.7, 43.5, 26.4.