Stereoselective Allylation of β-Hydroxy- and β-Amino-α,β-enones with Allyltrifluorosilane/Triethylamine Systems[1]

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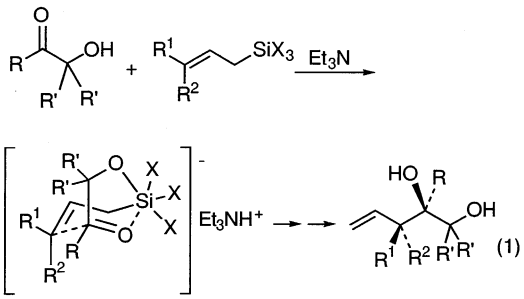
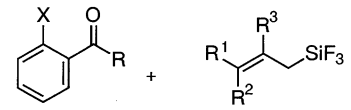
Reactions of allyltrifluorosilanes with β-functional-α,β-enones such as *o*-hydroxy- and *o*-aminophenyl ketones and 1,3-diketones in the presence of triethylamine yielded the corresponding tertiary homoallyl alcohols in regiospecific and highly diastereoselective manner.

Allylation of aldehydes with pentacoordinate allylsilicates offers a useful method for regiospecific and highly diastereoselective synthesis of homoallyl alcohols.[2] Recently, we have reported that treatment of α-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.[3] Although the allylation was not applicable to aliphatic β- and γ-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 β-functional-α,β-enones such as *o*-hydroxy- and *o*-aminophenyl ketones and 1,3-diketones with the allyltrifluorosilane/triethylamine reagent systems.

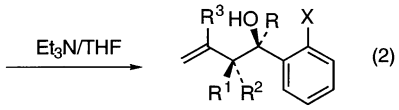


Reactions of allyltrifluorosilanes with *o*-hydroxy- and *o*-aminophenyl ketones in the presence of triethylamine yielded the corresponding tertiary homoallyl alcohols **3** in regiospecific and highly diastereoselective manner as shown in Eq 2. The results are summarized in Table 1. Typically, 2-(2-hydroxyphenyl)-4-methylpent-4-en-2-ol (**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.[4] 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**).



2a, R = Me, X = OH;
2b, R = Me, X = NH_2;
2c, R = Ph, X = NH_2.

1a, $R^1 = R^2 = R^3 = H$;
1b, $R^1 = R^2 = H$, $R^3 = CH_3$;
1c, $R^1 = CH_3$, $R^2 = R^3 = H$;
1d, $R^1 = H$, $R^2 = CH_3$, $R^3 = H$;
1e, $R^1 = R^2 = CH_3$, $R^3 = H$.



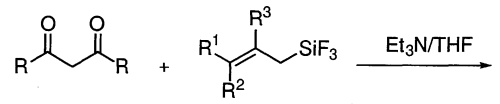
3a - j

Table 1. Allylation of *o*-Functional Phenylketones

Entry	Ketone	Allyl-silane	Reaction Conditions[a]	Product	Isolated Yield/%
1	**2a**	**1b**	rt, 48 h	**3a**	90
2	**2a**	**1c**[b]	rt, 48 h	**3b**	90[c]
3	**2a**	**1d**[d]	rt, 48 h	**3c**	83[c]
4	**2a**	**1e**	reflux, 36 h	**3d**	90
5	**2b**	**1a**	rt, 40 h	**3e**	63
6	**2b**	**1b**	reflux, 29 h	**3f**	65
7	**2b**	**1c**[e]	rt, 40 h	**3g**	68 (92/8)[f]
8	**2b**	**1d**[d]	reflux, 96 h	**3h**	0
9	**2c**	**1a**	rt, 40 h	**3i**	56
10	**2c**	**1e**	reflux, 40 h	**3j**	0

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 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 β-hydroxy-α,β-enones exist in equilibrium. Pentane-2,4-dione (**4a**) reacted very smoothly with various allyltrifluorosilanes to give the corresponding allylated β-hydroxy ketones **5** in good to fair yields (Table 2),[5] while the reaction of 1,3-diphenylpropane-1,3-dione (**4b**) with **1e** gave **6**[6] in a high yield. The reactions of **1a** - **1d** with **4b** proceeded but gave unidentified complex mixtures probably via dehydration during work-up.



4a, R = Me;
4b, R = Ph.

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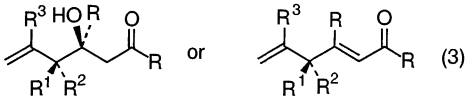


5a - d (R = Me) **6** (R = Ph) (3)

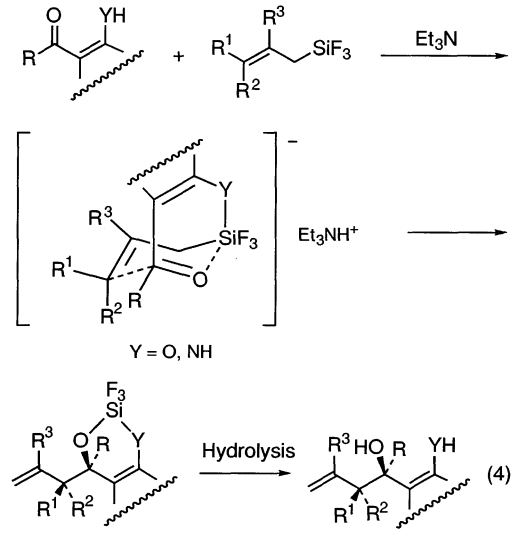
Table 2. Allylation of 1,3-Diketones

Entry	Ketone	Allylsilane	Reaction Conditions[a]	Product	Isolated Yield/%
1	**4a**	**1a**	rt, 34 h	**5a**	81
2	**4a**	**1b**	rt, 5 h	**5b**	48
3	**4a**	**1c**[b]	rt, 48 h	**5c**	45 (6/94)[c]
4	**4a**	**1d**[d]	rt, 48 h	**5d**	61 (99/1)[c]
5	**4b**	**1e**	reflux, 48 h	**6**	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 γ-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 ^{1}H and ^{13}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 ^{1}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 α-hydroxy ketones.[3]



(4)

Simple β-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^3 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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4 **3a**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 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); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 155.7, 141.8, 129.4, 128.8, 126.2, 119.3, 117.6, 116.4, 77.3, 49.8, 29.4, 24.6.

5 **5c**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 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); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 211.9, 140.9, 116.0, 73.5, 51.1, 47.9, 32.2, 23.1, 14.5. **5d**: ^{1}H NMR (600 MHz, $CDCl_3$) δ 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); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 211.4, 140.0, 115.7, 73.2, 50.2, 47.7, 32.1, 24.5, 14.4.

6 **6**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 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). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 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.