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Communication

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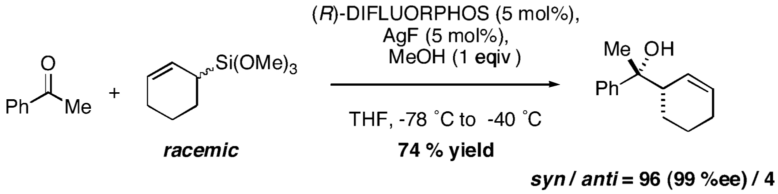

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Silver-Catalyzed Asymmetric Sakurai−Hosomi Allylation of Ketones

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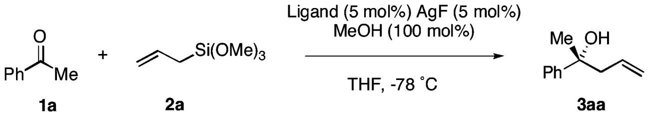
Chiral homoallylic alcohols represent a class of compounds that can be widely used in the synthesis of biologically active compounds.[1] Catalytic asymmetric Sakurai−Hosomi allylation is one of the most reliable methods for providing these compounds and has the advantage of having inexpensive, nontoxic, and stable allyltrialkylsilanes[2] and allyltrialkoxysilanes[3] as nucleophiles. Although excellent asymmetric Sakurai−Hosomi allylations of aldehydes have been developed with these reagents, there are few examples[3b,4,5] of catalytic asymmetric allylation of simple ketones despite the attractive structure of the chiral tertiary homoallylic alcohols in organic synthesis.[6]

Many chiral silver-mediated asymmetric reactions have recently been reported from our[7] and other laboratories.[8] We herein report the development of a new catalyst system and its application to the highly regio-, diastereo-, and enantioselective Sakurai−Hosomi allylation of simple ketones.

Initially we tested Sakurai−Hosomi allylation with acetophenone and allyltrimethoxysilane using a catalytic amount of AgF and (*R*)-BINAP (**4**) in MeOH.[3a] The desired product was not obtained at all even under reflux conditions. Athough AgF is not soluble in an aprotic solvent such as THF, the complex of AgF and **4** prepared in MeOH is easily dissolved in THF. Further, the desired tertiary alcohol with 63% ee was obtained by using this complex (Table 1, entry 1). It is noteworthy that the product obtained was the tertiary alcohol, not the silylated product. The alcoholic proton of this product must originate from a small amount of MeOH used for preparation of the catalyst. This observation indicated that the proton transfer from MeOH should be much faster than silyl transfer (Figure 1).[3b,6a,9] Therefore, an additional equivalent of MeOH improved the yield of the product significantly (entry 2).

We recently documented that more than three complexes between silver and diphosphine exist (Figure 2). According to these studies, different reactivity and selectivity were given by different complexes, and it is important to generate a single silver complex to achieve a high stereoselective reaction.[7b] A survey of the ^{31}P NMR of 1:1 mixtures of AgF and ligands revealed that (*R*)-DIFLUORPHOS (**7**) gave predominantly complex **A**, which is presumably due to the poor electron donation ability of the phosphorus atoms.[10] Significant improvement of enantioselectivity was observed by using this solution.[11] Finally, 86% ee was obtained by conducting the reaction at −90 °C (entry 6). Using 2 mol % of catalyst provided the same level of yield and enantioselectivity (entry 7).

Table 1. Optimal Reaction Conditions[a]



entry	ligand	catalyst, mol %	temp, °C	yield, %	ee, %[b]
1[c]	**4**	5	−78	35	63
2	**4**	5	−78	90	63
3	**5**	5	−78	90	46
4	**6**	5	−78	95	74
5	**7**	5	−78	96	82
6	**7**	5	−90	40	86
7	**7**	2	−78	86	81

[a] Reaction was conducted with 2.0 equiv of allyltrimethoxysilane at −78 °C for 12 h under Ar atmosphere. [b] The ee value was determined by HPLC. [c] No addition of MeOH.

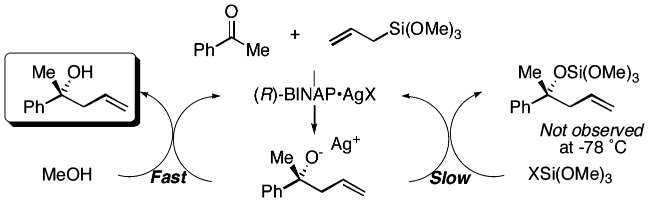


Figure 1. Proposed catalytic cycle.

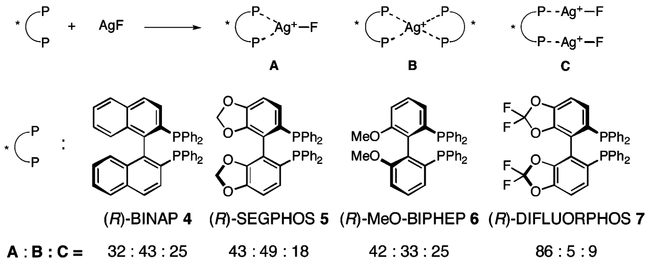


Figure 2. Ratio of three silver ligand complexes. A 1:1 mixture of AgF ligand was used. The ratio of **A**/**B** was determined by ^{31}P NMR at −78 °C. See details in Supporting Information.

As summarized in Table 2, the catalytic enantioselective allylation of a variety of ketones was carried out using these conditions. Although reactions proceed smoothly with either electron-withdrawing or -donating groups attached to the aromatic ring, the electron-withdrawing group gave higher enantioselectivity (entry 1). Remarkably, more than 90% ee was obtained from various aromatic cyclic ketones (entries 6−9). Only the 1,2-addition took place exclusively with both cyclic and acyclic conjugate enones (entries 10−14). It is noteworthy that excellent enantiomeric excesses (up to 96% ee) were observed in the reactions with a series of α-halo unsaturated ketones.

Condensation of γ-substituted allyl metal reagents with simple ketones is a challenging problem with regard to regio- (α/γ) and stereoselectivity (*E*/*Z* or *anti*/*syn*).[3b,12] The reactions between acetophenone and various allyltrimethoxysilanes were investigated using our new catalyst system (Table 3). Crotyltrimethoxysilane gave branched syn products with high enantioselectivity from both *E*- and *Z*-isomers. Surprisingly, starting from racemic allylsilanes such as **2d**−**e**, we observed the optically pure product almost exclusively. Thus, in sharp contrast with the previous study of the SE′ allylation using a combination of chiral allylsilanes and Lewis acid,[1] the present catalyst provides high diastereo- and enantioselectivity *regardless of chirality of the starting allylsilane*. We may

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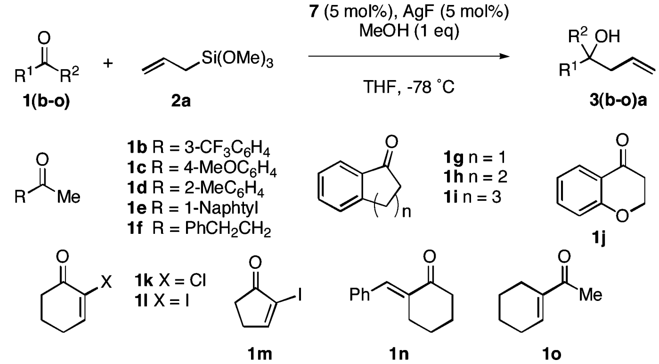
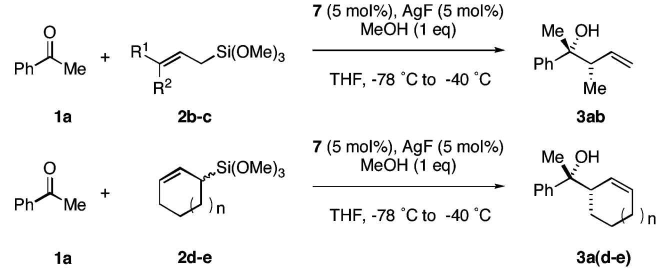
Table 2. Substrate Scope[a]



entry	ketone	product	yield, %	ee, %[b]
1	**1b**	**3ba**	92	90
2	**1c**	**3ca**	63	78
3	**1d**	**3da**	62	92
4	**1e**	**3ea**	98	95
5	**1f**	**3fa**	42	65
6	**1g**	**3ga**	89	91
7	**1h**	**3ha**	63	93
8	**1i**	**3ia**	78	92
9	**1j**	**3ja**	74	92
10	**1k**	**3ka**[d]	97	96
11	**1l**	**3la**[d]	92	96
12	**1m**	**3ma**[d]	92	94
13	**1n**	**3na**[d]	96	84
14[c]	**1o**	**3oa**[d]	56	95

[a] Reaction was conducted with 5 mol % of catalyst, 2.0 equiv of allyltrimethoxysilane at −78 °C for 12 h under Ar atmosphere. [b] The ee value was determined by HPLC or GC. [c] A quantity of 4.0 equiv of allyltrimethoxysilane was used. [d] Only 1,2-adduct was observed.

Table 3. Catalytic Diastereo- and Enantioselective Allylation[a]

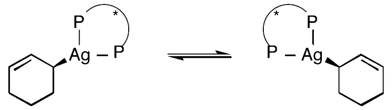


entry	allylsilane	yield %	syn/anti[b]	ee, %[c]
1	**2b** R1 = Me, R2 = H	60	90/10	95
2	**2c** R1 = H, R2 = Me	95	90/10	93
3	**2d** *n* = 1	72	96/4	98
4[d]	**2d** *n* = 1	74[e]	96/4	99
5	**2e** *n* = 3	97	>99/1	98

[a] Reaction was conducted with 5 mol % of catalyst, 3.0 equiv of allylsilane at −40 °C for 36 h under Ar atmosphere. [c] Diastereomer ratio was determined by ^{1}H NMR. [b] The ee value was determined by HPLC. [c] Major isomer. [d] A quantity of 0.5 equiv of allylsilane was used. [e] Determined from allylsilane.

therefore conclude that allylsilvers rapidly interconvert between two diastereomeric complexes (eq 1).[13]

In summary, we have developed a new AgF catalyst and demonstrated high enantioselective allylation of simple ketones.



(1)

Catalyst turnover was increased by the addition of MeOH, and the system was further improved based on the structure of the complex of silver and ligand. The allylation uniformly provided optically active syn isomers. Detailed mechanisms of this reaction including allylation from racemic allylsilane are now under investigation.

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Supporting Information Available: Experimental procedures, spectral data for all new compounds, and characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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