

Superacid Catalysis of the Addition of Allylsilanes to Carbonyl Compounds

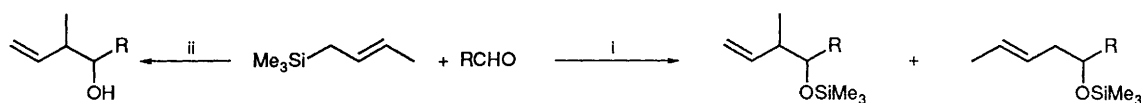
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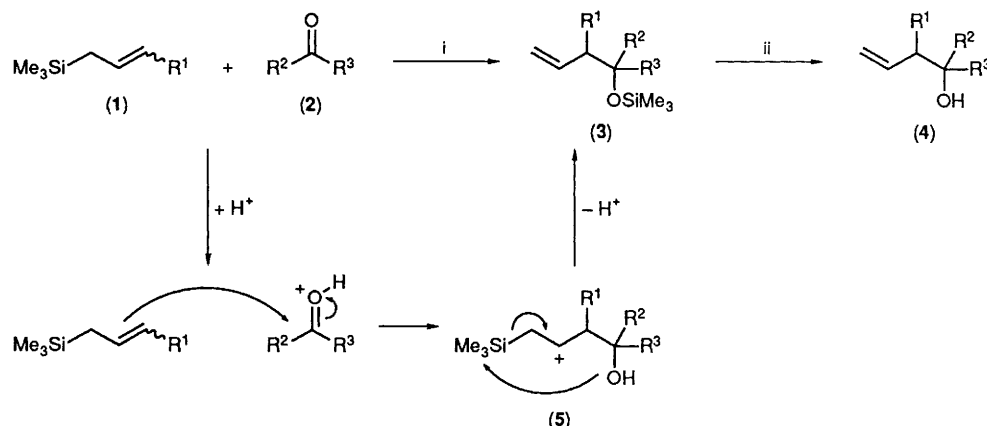
The superacid $\text{TfOH}_2^+\text{B(OTf)}_4^-$ ($\text{Tf} = \text{CF}_3\text{SO}_2$) was found to catalyse the addition of trialkylallylsilanes to aldehydes and a ketone (the Sakurai reaction) at levels of *ca.* 0.5 mol%; the reactions were clean, high-yielding, and regioselective with respect to allylic inversion.

The addition of trialkylallylsilanes to aldehydes and ketones (the Sakurai reaction) is widely appreciated as a mild method of C–C bond formation. It can be induced either by stoichiometric amounts of Lewis acids, or by catalytic quantities of fluoride ions (*e.g.* Scheme 1).¹ Both methods have disadvantages. In the former the presence of large amounts of oxophilic metal ions can cause difficulties,² while the latter lacks regioselectivity with respect to allylic inversion³ (Scheme 1). As far as we are aware, catalysis of the Sakurai reaction by Brønsted acids has not previously been reported. This is perhaps unsurprising, as allylsilanes are known to be decomposed rapidly by strong protic acids.⁴ However, we now report a remarkably clean, efficient, and regioselective version of the Sakurai reaction induced by catalytic amounts (<1%) of the superacid $\text{TfOH}_2^+\text{B(OTf)}_4^-$ ($\text{Tf} = \text{CF}_3\text{SO}_2$).⁵

The original motivation behind this work was the search for Lewis acids which would act catalytically in the Sakurai reaction, and from which enantioselective catalysts might be developed. We were pleased to discover that, for the reaction between allyltrimethylsilane and benzaldehyde in dichloromethane, Bu_2BOTf and $(-)\text{-(IPC)}_2\text{BOTf}$ ⁶ (IPC = isopinocampheyl) had modest activity at levels of *ca.* 10 mol %. Improved activity was shown by solutions of the latter to which TfOH had been added. However, none of these catalysts was enantioselective, and an ¹¹B NMR investigation suggested that catalytic activity was closely tied to the presence of a sharp singlet at $\delta -3.31$ ppm in dichloromethane ($\text{BF}_3\cdot\text{OEt}_2$ as reference). As this corresponded closely to the reported spectrum of $\text{TfOH}_2^+\text{B(OTf)}_4^-$,⁵ we prepared a pure sample of this superacid from BBr_3 and TfOH and tested its activity. Our results are summarised in Scheme 2 and Table 1.



Scheme 1. Reagents and conditions: i, cat. $\text{Bu}_4\text{N}^+\text{F}^-$; ii, TiCl_4 (1 equiv.), then aqueous work-up.



Scheme 2. Reagents and conditions: i, CH_2Cl_2 , room temp., $\text{TfOH}_2^+\text{B}(\text{OTf})_4^-$ (0.005 equiv.); ii, acidic hydrolysis (see Table 1).

Table 1. Results from the Sakurai reaction between allylsilanes (1) and carbonyl compounds (2), catalysed by $\text{TfOH}_2^+\text{B}(\text{OTf})_4^-$.^a

Entry	R^1	R^2, R^3	% Yield of (3)	% Yield of (4) ^b
1	H	Ph, H	60 ^c	95 ^d
2	H	<i>c</i> - C_6H_{11} , H	79 ^c	81 ^d
3	H	Bu ^t , H		86 ^e
4	H	PhCH ₂ CH ₂ , H		76 ^d
5	H	Pr ⁱ , H		77 ^f
6	H	Bu ⁿ , H		60 ^f
7	H	<i>p</i> -MeOCOC ₆ H ₄ , H		85 ^{d,c}
8	H	<i>p</i> -O ₂ NC ₆ H ₄ , H		95 ^d
9	H	<i>p</i> -ClC ₆ H ₄ , H		60 ^{g,d}
10	H	-[CH ₂] ₅ -		80 ^{h,c}
11	Me	Ph, H		80 ^{e,c}

^a For most cases, conditions for the allylation reaction were as given in the text. Exceptions are indicated. ^b Unless otherwise stated, the crude alcohols were clean by ^1H NMR and TLC and needed no further purification. Losses on work-up and evaporation are presumed to account for the missing material in such cases. All alcohols are known compounds. ^c Purified by flash chromatography. ^d Desilylation in aq. HCl -MeOH- CH_2Cl_2 . ^e Desilylation in aq. HCl -MeOH- Et_2O . ^f Desilylation in aq. HCl - Et_2O ; purified by distillation. ^g Reaction time for allylation 72 h. ^h Conditions for allylation: 3 mol% catalyst, -40°C , reaction time 1.5 h. Quenching the reaction mixture with aq. NaHCO_3 gave alcohol (4) directly.

In a typical experiment, an allylsilane (1) (2 mmol) and an aldehyde (2, $\text{R}^3 = \text{H}$) (1 mmol) were dissolved in dry dichloromethane at room temperature, and the superacid (0.005 mmol) was added *via* a microsyringe. After *ca.* 3 min, analysis by TLC indicated complete conversion of the aldehyde to the silyl ether (3, $\text{R}^3 = \text{H}$), contaminated by a small amount of the alcohol (4, $\text{R}^3 = \text{H}$). At this stage, (3) could be isolated by quenching the reaction mixture with aqueous NaHCO_3 , followed by flash chromatography (Table 1, entries 1 and 2). Alternatively, the crude product could be desilylated under acidic conditions to give alcohols (4). In many cases the alcohols were pure by TLC and ^1H NMR spectroscopy, implying that the reactions were clean and

quantitative. In the reaction of crotyltrimethylsilane with benzaldehyde (entry 11), the product (4, $\text{R}^1 = \text{Me}$, $\text{R}^2 = \text{Ph}$, $\text{R}^3 = \text{H}$) was contaminated by <1% of its regioisomer (6).

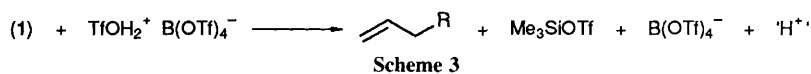
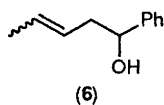
The reaction seems quite broad in scope. The major limitation so far revealed is that, in susceptible cases, the acidic conditions seem to promote the elimination of water (or Me_3SiOH) from the product. Thus the method was unsuccessful with crotonaldehyde and cinnamaldehyde. The one ketone tried, cyclohexanone, gave a low yield at room temperature but a good result at -40°C (entry 10).

We have performed a number of experiments aimed at clarifying the mechanism of the reaction. TfOH (7 mol %) proved capable of catalysing the addition of allyltrimethylsilane to benzaldehyde, but only slowly (incomplete reaction after 24 h at room temperature). We presume that its action is due to protodesilylation of the allylsilane yielding $\text{Me}_3\text{Si-OTf}$, which was shown to be a similarly poor catalyst in a separate experiment.[†] A $^1\text{H}/^{11}\text{B}$ NMR study revealed that the superacid also caused protodesilylation of allyltrimethylsilane, but only reacted rapidly with one equivalent of the latter. Solutions formed from a 1:1 mixture of allylsilane and superacid were active catalysts.

Taken together, the results suggest that in the reaction mixture the allylsilane may react with the superacid according to Scheme 3, and that the resulting proton is donated to the aldehyde/ketone to initiate the catalytic cycle shown in Scheme 2.[‡] The allylsilane is presumably unable to quench this proton because its counterion is the highly non-nucleophilic $\text{B}(\text{OTf})_4^-$, which cannot be used to remove the Me_3Si group. It is the final step of the mechanism [(5) \rightarrow (3)] which differentiates this reaction from the traditional version involving stoichiometric quantities of Lewis acids. In the latter case, the oxygen becomes bound to an oxophilic metal ion with a bulky co-ordination sphere, which is not easily replaced by the trimethylsilyl group.

[†] Similar (if anything, poorer) results with this catalyst were obtained by Noyori and co-workers.⁷

[‡] Although Scheme 2 shows a two-step mechanism for the addition, the possibility of a single-step reaction *via* a cyclic transition state should also be recognised.



In conclusion, this work indicates that superacids, normally regarded as highly aggressive reagents (capable, for example, of catalysing the rearrangement of hydrocarbons⁸) may also be applicable to delicate and specific transformations in organic synthesis. Proton catalysis of the addition of organometallic reagents to carbonyl compounds has very little precedent,[§] and the reaction should prove useful as a benchmark for mechanistic studies on Lewis acid catalysis.

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§ We are aware of one example, an intramolecular addition of an allylstannane to an aldehyde.⁹

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- 8 For an example, see O. Farooq, S. M. F. Farnia, M. Stephenson, and G. A. Olah, *J. Org. Chem.*, 1988, **53**, 2840.
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