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General and convenient TsOH-induced allylboration of ketones

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ABSTRACT

TsOH-induced allylation of various ketones with air- and moisture-stable potassium allyltrifluoroborate is described.

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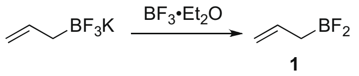
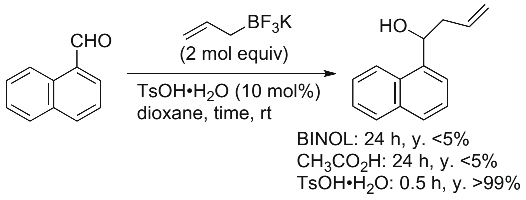
The allylation of ketones is one of the most important carbon–carbon bond-forming reactions, because homoallylic alcohols possessing a tetrasubstituted carbon are potentially useful synthetic intermediates.[1,2] Among various allylmetal reagents, potassium allyltrifluoroborate[3] is preferred given the recent demand for safe and sustainable organic synthesis, because this reagent is air-stable. As part of our research on the development of catalytic synthetic reactions in which the catalyst is composed of elements of a high Clarke number,[4,5] we herein report the general and convenient TsOH-induced allylation of ketones by potassium allyltrifluoroborate.

Since it has been reported that a Lewis acid such as $BF_3{\cdot}Et_2O$ immediately converts potassium allyltrifluoroborate into allyl difluoroborane (**1**), the *air- and moisture-sensitive* trivalent borane (Scheme 1),[3] we undertook allylation of ketones with the combination of Brønsted acids and potassium allyltrifluoroborate.[6,7] The effect of Brønsted acids in the allylboration[8] using the test substrate 1-naphthoaldehyde was first investigated. As shown in Scheme 2, $TsOH{\cdot}H_2O$ was found to be the most effective catalyst among the acids employed.



Scheme 1.



Scheme 2. Effects of Brønsted acids in allylboration.

Encouraged by the result with $TsOH{\cdot}H_2O$, we turned our attention to the allylboration of ketones (Table 1). The allylation of ketone **2** with 2 mol equiv of potassium allyltrifluoroborate and 20 mol % of $TsOH{\cdot}H_2O$ at 40 °C was carried out in several solvents (entries 1–5): using 10 mol % of $TsOH{\cdot}H_2O$ or lowering the temperature from 40 °C to rt resulted in a sluggish reaction. All the solvents evaluated produced the desired allylated products. Toluene was found to exhibit a high reaction rate (entry 5: 3 h, y. 90%). The generality of this allylboration under the optimized reaction conditions was then tested with a variety of other ketones. Acyclic **3**–**5**, easily enolizable **6**, and cyclic ketones **7** and **8** gave good yields of the corresponding allylated products (entries 6–11). Acetophenone derivatives (**9a–c**) could also be used, giving the corresponding allylated products in good yields (entries 12–14). The α,β-unsaturated ketone **10** was allylated in only the 1,2-mode, and no 1,4-addition product was observed (entry 15).

A ^{11}B NMR (CD_3CN, 40 °C) study was performed on the mixture of potassium allyltrifluoroborate and $TsOH{\cdot}H_2O$. CD_3CN was chosen as the solvent for ^{11}B NMR measurements because of the solubility for potassium allyltrifluoroborate: no ^{11}B NMR data were available because of low solubility of potassium allyltrifluoroborate in toluene-d_8. The chemical shift ($\delta = -7.10$ ppm, q, $J = 61.7$ Hz) of the mixture compared to that of the potassium allyltrifluoroborate[9] alone showed no change in the chemical shift.[10] Taking these results into consideration, a possible active nucleophile appears to be potassium allyltrifluoroborate (*not the trivalent borane* **1**) as shown in Figure 1, although further investigation is needed.

In summary, we developed a generally and conveniently semi-catalytic allylation to various ketones of potassium allyltrifluoroborate using $TsOH{\cdot}H_2O$.[11] Investigation of a catalytic asymmetric allylboration of ketones with a novel chiral sulfonic acid is in progress.[12]

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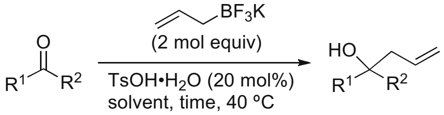
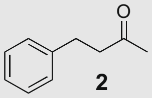
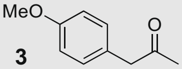
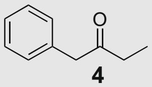
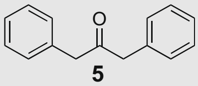
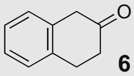
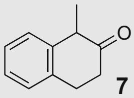
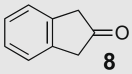
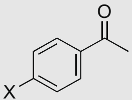
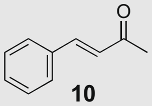
Table 1
Allylboration to ketones with TsOH·H_2O



Entry	Ketone	Solvent	Time (h)	Yield (%)
1	 **2**	Dioxane	14	59[a]
2	**2**	PrOH	24	19[a]
3	**2**	CH_3CN	24	68[a]
4	**2**	DMF	24	23[a]
5	**2**	Toluene	3	90
6	 **3**	Toluene	4	85
7	 **4**	Toluene	6	82
8	 **5**	Toluene	5	85
9	 **6**	Toluene	6	81
10	 **7**	Toluene	6	91[b]
11	 **8**	Toluene	20	82
12	 **9**: X= OMe (**a**)	Dioxane[c]	24	73[a]
13	**9b**: X = H	Toluene	24	81
14	**9c**: X = Cl	Toluene	24	90
15	 **10**	Dioxane[c]	14	84

[a] Remainder of mass balance was the starting ketone.

[b] Diastereoselectivity is 17:1, although the stereochemistry was not determined.

[c] The use of toluene in place of dioxane as a solvent gave less satisfactory results.

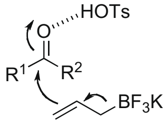


Figure 1. Possible reaction mechanism.

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11. *Representative procedure for the allylboration of benzylacetone* (**2**) *(entry 5)*: To a stirred solution of TsOH·H_2O (7.6 mg, 0.0400 mmol) in toluene (0.60 mL) were added potassium allyltrifluoroborate (59.2 mg, 0.400 mmol) and benzylacetone (**2**) (30 μL, 0.200 mmol) at rt. The reaction mixture was stirred for 3 h at 40 °C, allowed to cool, diluted with aq $NaHCO_3$, and extracted with EtOAc. The organic extracts were washed with brine, dried (Na_2SO_4), and concentrated. Purification by SiO_2 column (pretreated with 1% Et_3N in hexane, hexane/EtOAc = 15:1) afforded 3-methyl-1-phenylhex-5-ene-3-ol (35.3 mg, 90%) as a colorless oil.
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