Tetrahedron Letters 50 (2009) 2320–2321

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

General and convenient TsOH-induced allylboration of ketones

Hiroaki Matsuoka[a], Kazuhiro Kondo[a,b,*]

[a] Graduate School of Medical Sciences, Nagoya City University, 1 Azakawasumi, Mizuho-ku, Nagoya 467-8601, Japan
[b] Graduate School of Pharmaceutical Sciences, Nagoya City University, 3-1 Tanabe-dori, Mizuho-ku, Nagoya 467-8603, Japan

ARTICLE INFO

Article history:
Received 12 February 2009
Revised 23 February 2009
Accepted 24 February 2009
Available online 6 March 2009

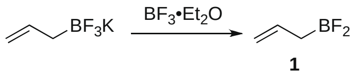
ABSTRACT

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

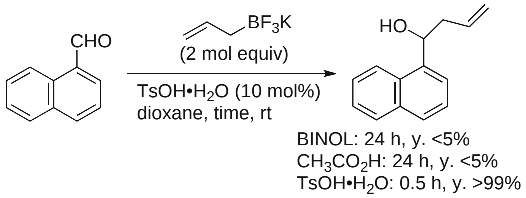
The allylation of ketones is one of the most important carbon–carbon bond-forming reactions, because homoallylic alcohols possessing a tetrasubstituted carbon are potentially useful synthetic intermediates.[1,2] Among various allylmetal reagents, potassium allyltrifluoroborate[3] is preferred given the 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.

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).



Scheme 1.



Scheme 2. Effects of Brønsted acids in allylboration.

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.

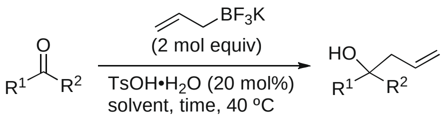
In summary, we developed a generally and conveniently semi-catalytic allylation to various ketones of potassium allyltrifluoroborate using $TsOH{\cdot}H_2O$.[11] Investigation of a catalytic asymmetric allylboration of ketones with a novel chiral sulfonic acid is in progress.[12]

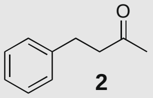
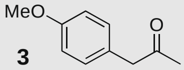
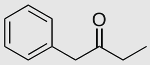
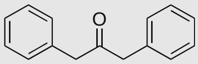
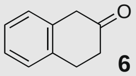
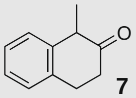
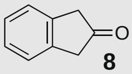
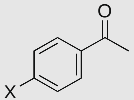
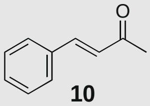
---

* Corresponding author.
E-mail address: kazu@gakushikai.jp (K. Kondo).

0040-4039/$ - see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2009.02.226

Table 1
Allylboration to ketones with $TsOH{\cdot}H_2O$



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.

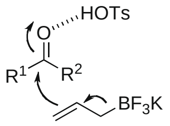


Figure 1. Possible reaction mechanism.

Acknowledgment

We thank Professor Toyohiko Aoyama (Graduate School of Pharmaceutical Sciences, Nagoya City University) for his very important support in various ways.

References and notes

1. Only one example of synthetically useful and general catalytic allylation of ketones (achiral version): (a) Yamasaki, S.; Fujii, K.; Wada, R.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2002**, *124*, 6536–6537; For other catalytic allylations of ketones (achiral version), see: (b) Hosomi, A.; Shirahata, A.; Sakurai, H. *Tetrahedron Lett.* **1978**, 3043–3046; (c) Ishihara, K.; Hiraiwa, Y.; Yamamoto, H. *Synlett* **2001**, 1851–1854; (d) Barker, T. J.; Jarvo, E. R. *Org. Lett.* **2009**, *11*, 1047–1049.
2. (a) Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207–2293; (b) Denmark, S. E.; Fu, J. *Chem. Rev.* **2003**, *103*, 2763–2793.
3. For a recent review, see: Darses, S.; Genet, J. P. *Chem. Rev.* **2008**, *108*, 288–325.
4. Ni-Catalyzed arylation to aldehydes of arylboron reagents: (a) Arao, T.; Kondo, K.; Aoyama, T. *Tetrahedron Lett.* **2007**, *48*, 4115–4117; (b) Yamamoto, K.; Tsurumi, K.; Sakurai, F.; Kondo, K.; Aoyama, T. *Synthesis* **2008**, 3585–3590; (c) Sakurai, F.; Kondo, K.; Aoyama, T. *Chem. Pharm. Bull.*, in press.
5. N-Heterocyclic carbene as nucleophilic organocatalyst: (a) Fukuda, Y.; Maeda, Y.; Ishii, S.; Kondo, K.; Aoyama, T. *Synthesis* **2006**, 589–590; (b) Fukuda, Y.; Maeda, Y.; Kondo, K.; Aoyama, T. *Chem. Pharm. Bull.* **2006**, *54*, 397–398; (c) Fukuda, Y.; Maeda, Y.; Kondo, K.; Aoyama, T. *Synthesis* **2006**, 1937–1939; (d) Fukuda, Y.; Kondo, K.; Aoyama, T. *Synthesis* **2006**, 2649–2652.
6. For Lewis acid- or PTC-catalyzed allylations to aldehydes using potassium allyltrifluoroborate: (a) Batey, R. A.; Thadani, A. N.; Smil, D. V. *Tetrahedron Lett.* **1999**, *40*, 4289–4292; (b) Batey, R. A.; Thadani, A. N.; Smil, D. V.; Lough, A. J. *Synthesis* **2000**, 990–998; (c) Thadani, A. N.; Batey, R. A. *Org. Lett.* **2002**, *4*, 3827–3830.
7. With allyl-9-BBN and no catalyst, allylboration of α-amono ketones: Pace, R. D.; Kabalka, G. W. *J. Org. Chem.* **1995**, *60*, 4838–4844.
8. Catalytic enantioselective allylboration of benzylic and allylic ketones with the combination of 2,2′-di-Br-BINOL and allyldiisopropoxyboron, the trivalent borane, has been reported: Lou, S.; Moquist, P. N.; Schaus, S. E. *J. Am. Chem. Soc.* **2006**, *128*, 12660–12661.
9. The NMR data of potassium allyltrifluoroborate in CD_3CN at rt have been reported.[6b]
10. ^{11}B chemical shifts were referenced to BF_3 (δ = −8.70 ppm) in $CDCl_3$.
11. *Representative procedure for the allylboration of benzylacetone* (**2**) *(entry 5)*: To a stirred solution of $TsOH{\cdot}H_2O$ (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.
12. Successful examples for catalytic enantioselective allylation of ketones: (a) Wada, R.; Oisaki, K.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2004**, *126*, 8910–8911; (b) Kim, J. G.; Waltz, K. M.; Garcia, I. F.; Kwiatkowski, D.; Walsh, P. J. *J. Am. Chem. Soc.* **2004**, *126*, 12580–12585; (c) Wadamoto, M.; Yamamoto, H. *J. Am. Chem. Soc.* **2005**, *127*, 14556–14557; (d) Ref. 8.; (e) Casolari, S.; D'Addario, D.; Tagliavini, E. *Org. Lett.* **1999**, *1*, 1061–1063.