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cis-Dihydroxylation of Unsaturated Potassium Alkyl- and Aryltrifluoroborates

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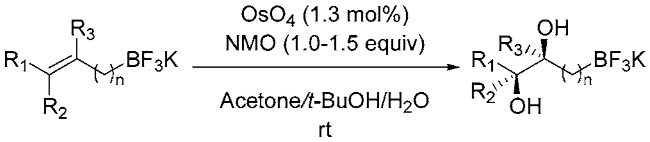
ABSTRACT

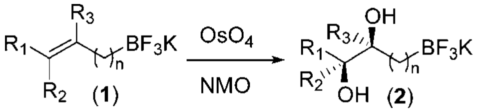


The *cis*-dihydroxylation of olefin-containing potassium alkyl- and aryltrifluoroborates proceeds readily in moderate to excellent yields. The resulting diols are efficient coupling partners in Suzuki–Miyaura-type reactions with both alkenyl and aryl bromides.

Organoboron compounds have been widely used in organic synthesis.[1] The utility of these organometallic reagents as synthetic tools is often based on the ability of the carbon−boron bond to be oxidized.[2] It is this characteristic that also limits the opportunity to perform oxidative transformations on other functional groups present in the molecule while still preserving the valuable carbon−boron bond. Common oxidizing reagents are often too powerful and are not well tolerated by many organoboron compounds. Only a few examples of this type of transformation have been reported.[3,4]

Organotrifluoroborate salts are unique organoboron compounds, notable for their stability to moisture and air.[5] They are powders or crystalline solids that are easy to access and handle, and these properties have made them attractive synthetic intermediates. The chemistry of these compounds has been expanded to various applications, including Suzuki−Miyaura coupling reactions,[5a] rhodium-catalyzed 1,4-additions,[6] as well as allylation of aldehydes[7] and *N*-toluenesulfonylimines.[8]

Our group has focused on expanding the chemistry of organotrifluoroborates to processes in which the carbon−boron bond remains intact. The epoxidation of olefin-containing potassium organotrifluoroborates demonstrated the tolerance of such organoboron compounds to oxidative conditions such as MCPBA and dimethyldioxirane.[9] These results led us to consider other oxidative reactions. This paper describes our initial results toward the *cis*-dihydroxylation of olefin-containing potassium organotrifluoroborates. We also demonstrate that the diols produced through this method are valuable synthetic intermediates.



(1)

The *cis*-dihydroxylation of olefins is one of the most widely used reactions for the synthesis of vicinal diols.[10]

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(1) (a) Cragg, G. M. *Organoboranes in Organic Synthesis*; Marcel Decker: New York, 1973. (b) Brown, H. C. *Organic Syntheses via Boranes*; Wiley-Interscience: New York, 1975.

(2) Oxidizing and Reducing Agents. In *Handbook of Reagents for Organic Synthesis*; Burke, S. D., Danheiser, R. L., Eds.; Wiley: Chichester, U.K., 1999.

(3) de Filippis, A.; Morin, C.; Thimon, C. *Synth. Commun.* **2002**, *32*, 2669.

(4) Matteson, D. S. *J. Organomet. Chem.* **1999**, *581*, 51.

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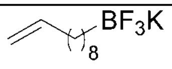
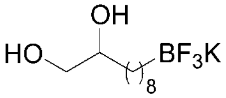
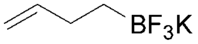
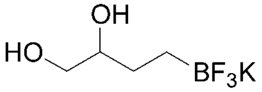
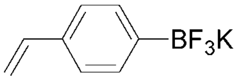
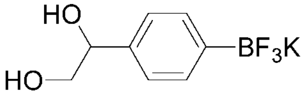
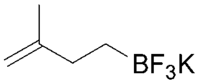
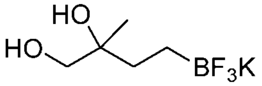
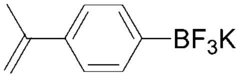
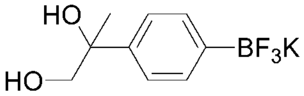
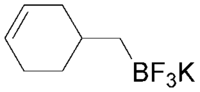
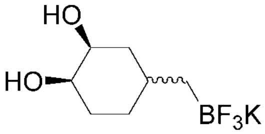
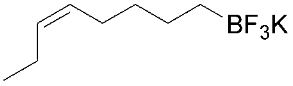
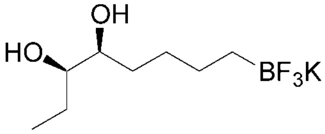
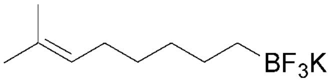
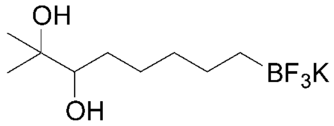
Table 1. Dihydroxylation of Potassium Alkyl- and Aryltrifluoroborates[a]

entry	substrate	time (h)	product	yield (%)[c]
1[b]	 (**1a**)	2	 (**2a**)	75
2	 (**1b**)	3	 (**2b**)	88
3	 (**1c**)	2	 (**2c**)	84
4	 (**1d**)	4	 (**2d**)	30
5	 (**1e**)	6	 (**2e**)	56
6[c]	 (**1f**)	2	 (**2f**)	53[f]
7	 (**1g**)	1	 (**2g**)	71
8[c,d]	 (**1h**)	6	 (**2h**)	69

[a] The reactions were conducted using OsO_4 (1.3 mol %), *N*-methylmorpholine *N*-oxide (1.0−1.5 equiv), and an acetone/*t*-BuOH/water mixture (18:1:1) at room temperature. [b] Solvent ratio was 4.5:1:1. [c] Solvent ratio was 60:1:1. [d] OsO_4 (0.62 mol %). [e] Isolated yields. [f] Mixture of diastereomers in a 2:1 ratio.

Catalytic OsO_4 and *N*-methylmorpholine *N*-oxide (the Upjohn process) have been widely applied after the initial publication of this method.[11] This process provides the advantage of minimizing overoxidation.[10] With these factors in mind, we explored the use of these reagents to accomplish the dihydroxylation of unsaturated organotrifluoroborates (eq 1). Acetone, *t*-BuOH, and water are solvents commonly used in this reaction,[10] and based on our prior experience with the epoxidation reaction, we knew that the appropriate solvent ratio would facilitate isolation of the diol by precipitation.[9] The required potassium organotrifluoroborate salts were prepared following literature protocols[12] involving transmetalation of Grignard reagents with trimethyl borate[13] or hydroboration of alkenes with the Snieckus reagent[14] (diisopropylprenylborane). This was followed by hydrolysis and subsequent treatment with KHF_2. The products were powders or crystalline white solids that were stored on the benchtop without detectable degradation.

As outlined in Table 1, initial studies were directed toward sterically unhindered organotrifluoroborates containing a remote monosubstituted olefin. The dihydroxylation of potassium 9-decenyltrifluoroborate **1a** proceeded in very good yield using 1.3 mol % of OsO_4 and a 4.5:1:1 acetone:*t*-BuOH:water solvent mixture at room temperature (entry 1). The product was easily isolated as an analytically pure white solid in 75% yield by a simple filtration. The use of ^1H, ^{13}C, ^{19}F, and ^{11}B NMR as well as elemental analysis corroborated formation of the diol and retention of the valuable trifluoroborate moiety.

We subsequently investigated the dihydroxylation of potassium 4-butenyltrifluoroborate **1b** (entry 2), in which the olefin is closer to the electron-rich boron atom. The reaction

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(11) (a) Upjohn (W. P. Schneider, A. V. McIntosh) US 2.769.824. (b) VanRheennen, V.; Kelly, R. C.; Cha, D. Y. *Tetrahedron Lett.* **1976**, *17*, 1973.

(12) (a) Vedejs, E.; Fields, S. C.; Hayashi, R.; Hitchcock, S. R.; Powell, D. R.; Schrimpf, M. R. *J. Am. Chem. Soc.* **1999**, *121*, 2460. (b) Garrett, C. E.; Fu, G. C. *J. Org. Chem.* **1996**, *61*, 1, 3224. (c) Pereira, S.; Srebnik, M. *J. Am. Chem. Soc.* **1996**, *118*, 8, 909. (d) Vedejs, E.; Chapman, R. W.; Fields, S. C.; Lin, S.; Schrimpf, M. R. *J. Org. Chem.* **1995**, *60*, 0, 3020. (e) Kabalka, G. W.; Narayana, C.; Reddy, N. K. *Synth. Commun.* **1994**, *24*, 1019. (f) Burgess, K.; Ohlmeyer, M. J. *Chem. Rev.* **1991**, *91*, 1179. (g) Männing, D.; Nöth, H. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 878. (h) Brown, H. C.; Bhat, N. G.; Somayaji, V. *Organometallics* **1983**, *2*, 1311.

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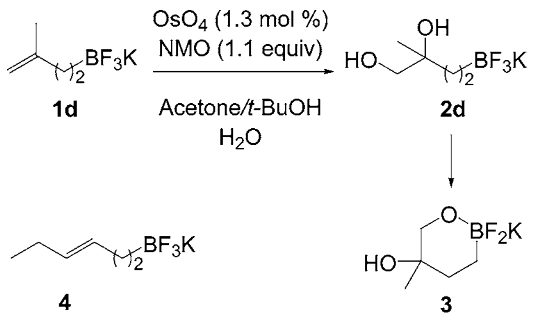
proceeded smoothly as expected to give the diol in excellent yield. Optimization was required only of the solvent ratio to a mixture of 18:1:1 acetone/*t*-BuOH/water. This new solvent mixture became our standard condition because it facilitated isolation of the diols. In addition, the dihydroxylation of potassium 4-vinylphenyltrifluoroborate **1c** (entry 3) demonstrated that the same reaction conditions are applicable to aryltrifluoroborates.

Our next aim was to carry out the dihydroxylation on more highly substituted olefins. Interestingly, 1,1-disubstituted alkyltrifluoroborate **1d** (entry 4) proved to be sensitive to the reaction conditions. The apparent low yield reflects the inability of all of the product to precipitate in pure form from the reaction mixture. Thus, the majority of the product coprecipitated with an impurity that could not be separated from the desired dihydroxytrifluoroborate under several different isolation protocols. On the basis of ^{1}H, ^{11}B, and ^{19}F NMR, we suspect cyclized product **3** as the impurity (Scheme 1), which would be generated by displacement of a fluoride by one of the hydroxy groups of the diol. Similar behavior was also observed in the dihydroxylation of organotrifluoroborate **4**.

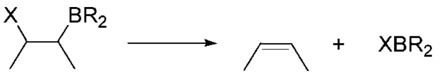
Scheme 1



Nevertheless, 1,1-disubstituted olefins can be successfully dihydroxylated and isolated as shown by aryltrifluoroborate **1e** (entry 5). Diols from 1,2-disubstituted olefin-containing organotrifluoroborates were also obtained in good yield (entries 6 and 7). Trisubstituted olefins are usually challenging substrates in *cis*-dihydroxylation.[10,15] This problem has been attributed to slow hydrolysis of the intermediate osmate(VI) ester, which results in low turnover in the catalytic cycle.[10,16] The dihydroxylation of potassium 7-methyl-6-octenyl trifluoroborate **1h**, containing a trisubstituted olefin, was achieved in good yield without the need to facilitate the hydrolysis process (entry 8).

The lower yields for diols **2e**, **2g**, and **2h** can be attributed to difficulties associated with isolation. These products did not precipitate readily.

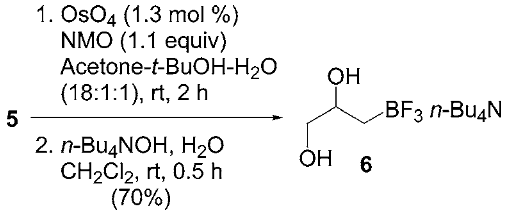
The dihydroxylation of potassium allyltrifluoroborate was of particular interest because the diol produced contains a heteroatom β to the boron. Normally, organoboron compounds with an electronegative atom, such as oxygen, at the β-position eliminate rapidly via tetracoordination to the boron (eq 2).[4] This elimination process has been attributed to the thermodynamic stability of the boron−oxygen bond.[15] To the best of our knowledge, only limited examples of this type of organoboron compound have been reported.[15,17]



(2)

In the event, dihydroxylation of potassium allyltrifluoroborate, **5**, proceeded smoothly under the reaction conditions described previously (Scheme 2).

Scheme 2



Isolation of diol **6** was easily achieved using the cation exchange protocol reported by Batey and Quach.[18] Tetracoordination of the boron atom by fluoride as well as the strength of the B−F bond prevented oxidative cleavage and protonolysis of the trifluoroborate moiety in this and our earlier examples;[6] these characteristics have now been employed to prevent β-elimination as well.

The Suzuki−Miyaura-type coupling of potassium organotrifluoroborates has been the subject of extensive study in our group.[5a] Dihydroxylated alkyl- and aryltrifluoroborates were anticipated to be good coupling partners. The presence of free hydroxy groups was deemed unlikely to present a problem because the cross-coupling reactions are often run using alcohols as solvents. Therefore, the diols were subjected to the cross-coupling reactions without the use of protecting groups. The optimized reaction conditions reported by our group for the Suzuki−Miyaura-type coupling reaction between alkyltrifluoroborates and aryl bromides employ $PdCl_2(dppf)\cdot CH_2Cl_2$ (9 mol %) and $CsCO_3$ (3 equiv) as a base, heated to reflux in a 10:1 THF:H_2O mixture.[19] Thus, with the potassium dihydroxytrifluoroborate **2b** in hand, we conducted a cross-coupling reaction with 4-cyanophenyl bromide under these conditions to afford 4-cyanophenyl-1,2-butanediol **7** in 65% yield after column chromatography (eq 3).

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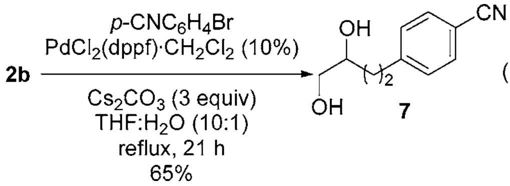
(16) (a) Akashi, K.; Palermo, R. E.; Sharpless, B. K. *J. Org. Chem.* **1978**, *43*, 2063. (b) Sharpless, B. K.; Akashi, K. *J. Am. Chem. Soc.* **1976**, *98*, 1986.

(17) Pereira, S.; Srebnik, M. *Tetrahedron Lett.* **1996**, *37*, 3283.

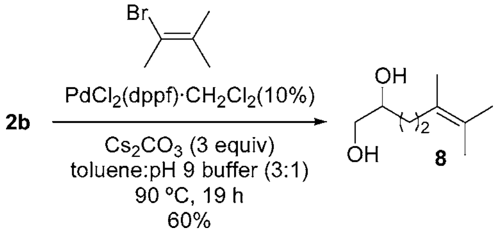
(18) Batey, R. A.; Quach, T. D. *Tetrahedron Lett.* **2001**, *42*, 9099.

(19) (a) Molander, G. A.; Ito, T. *Org. Lett.* **2001**, *3*, 393. (b) Molander, G. A.; Yun, C.-S.; Ribagorda, M.; Biolatto, B. *J. Org. Chem.* **2003**, *68*, 5534.



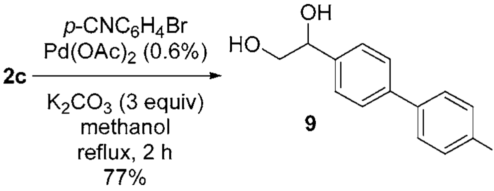
7 (3)

The cross-coupling of alkyltrifluoroborates with alkenyl bromides is part of ongoing research.[20] The ideal conditions to date [$PdCl_2(dppf)\cdot CH_2Cl_2$ (10 mol %), Cs_2CO_3 (3 equiv), toluene/pH 9 buffer (3:1), 90 °C] were used to couple potassium 3,4-dihydroxybutyltrifluoroborate (**2b**) with 3-bromo-2-methyl-2-butene, affording the product in good yield (eq 4). This reaction is particularly relevant because it provides an efficient alternative to selective dihydroxylation at a single olefinic site within a diene or polyene system.



8 (4)

The Suzuki coupling of aryltrifluoroborates with aryl bromides has also been successfully developed by our group.[21] Therefore, potassium 4-(1′,2′-dihydroxyethyl)phenyltrifluoroborate, **2c**, was reacted with 4-cyanophenyl bromide under the previously optimized conditions [$Pd(OAc)_2$ (0.5 mol %), K_2CO_3 (3 equiv), methanol, reflux] to afford the biaryl **9** in good yield (eq 5).



9 (5)

In summary, the first *cis*-dihydroxylation of potassium alkyl- and aryltrifluoroborates has been achieved. The reaction is general for both sterically unhindered and hindered olefins. The olefin-containing organotrifluoroborate salts are readily available by the Grignard approach or selective hydroboration of dienes. The diols were isolated as highly pure solids. Their versatility and value as synthetic units was also demonstrated. We successfully accomplished Suzuki–Miyaura-type coupling reactions of the dihydroxylated trifluoroborates. The cross-coupling reactions were carried out without the need for protecting groups. Studies directed toward the asymmetric version of this reaction are underway.

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Supporting Information Available: Full experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

OL052549E

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[20] Dave Seapy, unpublished results.

[21] Molander, G. A.; Biolatto, B. *J. Org. Chem.* **2003**, *68*, 4302.