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Allylation and highly diastereoselective *syn* or *anti* crotylation of *N*-toluenesulfonylimines using potassium allyl- and crotyltrifluoroborates

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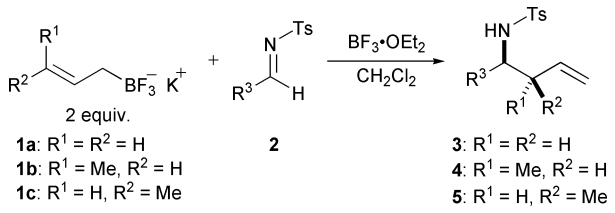
Received (in Corvallis, OR, USA) 11th March 2004, Accepted 6th April 2004
First published as an Advance Article on the web 11th May 2004

Air and moisture stable potassium allyl- and crotyltrifluoroborates undergo addition to *N*-sulfonyl and *N*-sulfinyl aldimines in the presence of Lewis acids, to provide the corresponding homoallylic amines in high yields and excellent diastereoselectivity.

Homoallylic amines are important synthetic targets, particularly as intermediates for alkaloid syntheses. One of the most general strategies for their formation is the addition of organometallic reagents toward imines.[1] However, the allylation and diastereospecific crotylation of imines and their derivatives has been less successful than the well-established analogous addition of allyl- and crotylorganometallics to carbonyl compounds,[2] because of the poor electrophilicity of imines and the tendency of enolizable imines to undergo deprotonation rather than addition.[3] Examples of diastereoselective allylations and crotylations of C=N bonds, include the use of B, Si, Zn, and Sn reagents.[4] Several recent strategies have emerged to allow enantioselective allylations and crotylations, including chiral base assisted addition of trichloroallyl and crotylsilanes to hydrazones,[5] Pd catalyzed addition of trimethylallylsilanes[6] and stannanes[7] to imines, and the addition of chiral allylboranes to *N*-silylimines.[8] We now report a general solution to the allylation and diastereoselective crotylation of imines, as well as an auxiliary based approach for the synthesis of chiral homoallylamines, using conveniently handled air and water stable boron reagents.

We have recently shown that potassium allyl- and crotyltrifluoroborates **1a–c** add to carbonyl compounds either under Lewis acid catalysis[9] or in biphasic and aqueous media.[10] A significant advantage of these species are their air and water stability, and in the case of **1b–c** their configurational stability. Preliminary studies on the addition of **1a–c** to simple imines, such as PhCH=NPh, led to disappointing results with the formation of the corresponding homoallylic alcohols, occurring as a result of *in situ* hydrolysis of the imines. To overcome this problem we evaluated the use of more stable imine derivatives, such as *N*-tosylimines, which were found to be sufficiently electrophilic to undergo allylation and highly diastereoselective crotylation using potassium ally/crotyltrifluoroborates in the presence of a Lewis acid (Scheme 1). Initial attempts at the addition of 1 equiv. potassium allyltrifluoroborate **1a** to *N*-tosylimine **2a** using 1 equiv. $BF_3{\cdot}OEt_2$ yielded the desired adduct in moderate yield (*i.e.* 50%) after prolonged reaction times. However, with 2 equiv. of **1a**, allylation proceeded with full conversion in 2 days. The transformation can also be achieved in comparable yield using a catalytic amount of $BF_3{\cdot}OEt_2$ (10 mol%). Alkyl, aryl and heterocyclic sulfonylimines were allylated in this manner, giving homoallylic amines in high isolated yields (Table 1). The reaction conditions are mild and even enolizable imines such as **2e** react in good yield (Table 1, entry 5). Reaction of the salt **1a** does not occur in the absence of a Lewis acid catalyst even at elevated temperatures. This feature distinguishes the reactivity of **1** from most allyl boron compounds, which do not require such activation.



Scheme 1 Allylation and crotylation of *N*-toluenesulfonylimines **2** with potassium allyl- and crotyltrifluoroborates **1** using a catalytic amount of $BF_3{\cdot}OEt_2$ (10 mol%).

Crotylation of aliphatic, aromatic, and heterocyclic *N*-tosylimines using potassium (*Z*)- and (*E*)-crotyltrifluoroborate and the developed conditions was found to work equally well with either stoichiometric or catalytic amounts of $BF_3{\cdot}OEt_2$, leading to products **4** and **5**, respectively, in high yields and with excellent diastereoselectivities (Table 2). The use of (*Z*)-crotyltrifluoroborate **1b** led to the preferential formation of *anti* homoallylic amines **4**, whereas the (*E*)-crotyltrifluoroborate **1c** afforded the *syn* products **5**. The relative stereochemistry of adducts **4c** and **5c** were determined by comparison of ^{1}H NMR spectra to reported authentic compounds.[11,12] These observations are consistent with the intermediacy of allylboron difluoride, formed *in situ* by Lewis acid promoted removal of fluoride from salt **1**, and addition via a

Table 1 Allylation of *N*-toluenesulfonylimines **2** by potassium allyltrifluoroborate **1a** (R^1 and R^2 = H) under Lewis acid catalysis

Entry	R^3	Homoallylic amine	Yield[a](%)
1	Ph	**3a**	92
2	4-ClC_6H_4	**3b**	99
3	2-furanyl	**3c**	96
4	Chx	**3d**	91
5	*n*Bu	**3e**	78
6	*t*Bu	**3f**	88[b]
7	4-$MeOC_6H_4$	**3g**	96

[a] Isolated yields. [b] 1 equiv. of $BF_3{\cdot}OEt_2$ was used.

Table 2 Crotylations of *N*-toluenesulfonylimines **2** by potassium (*Z*)- and (*E*)-crotyltrifluoroborate **1b/c** under Lewis acid catalysis[a]

Entry	R^1	R^2	R^3	Homoallylic amine	Yield[b] (%)	*Syn*:*anti*[c]
1	Me	H	Ph	**4a**	94	3 :97
2	H	Me	Ph	**5a**	92	91 : 9
3	Me	H	4-ClC_6H_4	**4b**	99	< 2: : 98
4	H	Me	4-ClC_6H_4	**5b**	99	96 : 4
5	Me	H	2-furanyl	**4c**	99	4 : 96
6	H	Me	2-furanyl	**5c**	98	95 : 5
7	Me	H	Chx	**4d**	97	< 2 : 98
8	H	Me	Chx	**5d**	98	> 98: : 2
9	Me	H	*n*Bu	**4e**	63	< 2 : 98
10	H	Me	*n*Bu	**5e**	99	> 98 : 2
11	Me	H	*t*Bu	**4f**	90	< 2 : 98
12	H	Me	*t*Bu	**5f**	54	3 : 1

[a] $BF_3{\cdot}OEt_2$ (10 mol%). [b] Isolated yields. [c] Detemined by ^{1}H NMR.

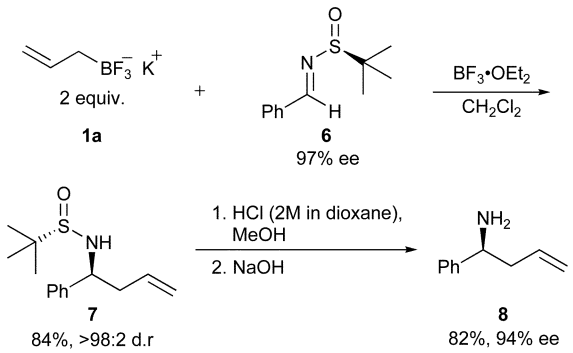
DOI: 10.1039/b403759f

Zimmerman–Traxler chair-like transition state. In the reaction of the sterically hindered sulfonylimine **1f** with (*E*)-crotyltrifluoroborate **1c** significant amounts of the *anti*-product **5f** were observed (Table 2, entries 12). In this case some reaction *via* a boat-like transition state is possible due to the destabilization of the chair-like transition state, because of an unfavourable 1,2- axial–equatorial interaction between the *t*Bu group and the methyl group in **1c**.[3a]

The success of the allyl/crotylation of *N*-tosylimines **2** using the salts **1**, prompted us to extend the use of allyl/crotylation reagents to the synthesis of chiral homoallylic amines. We envisaged that Ellman's chiral *N*-*tert*-butanesulfinamides[13] could serve as useful precursors, having successfully been employed in diastereoselective additions of various organometallic reagents (*e.g.* Grignard regents[14] and organolithiums[15]). Interestingly, only allyl Grignard reagents have been added to *N*-sulfinylimines[14b,16] and crotylations of these compounds have not been previously explored. Sulfinylimine **6** was synthesized according to the literature procedure.[17] Under the conditions developed for the allyl/crotylation of *N*-tosylimines **2**, the allylation of sulfinylimine **6** proceeded smoothly to give the desired product **7** as a single diastereomer as observed by ^{1}H NMR (Scheme 2). The acid-labile chiral auxiliary was readily cleaved by treatment of the product with acid. The corresponding optically active homoallylic amine **8** was then obtained in good yield after neutralization.[8c,18]

In conclusion, we have established an efficient protocol for the synthesis of protected homoallylic amines using potassium allyl- and crotyltrifluoroborates. These reagents offer advantages over existing allylboron reagents, including high yielding additions and excellent levels of diastereocontrol in the case of crotylation reactions. An auxiliary base approach using *N*-*tert*-butanesulfinamides provides a convenient approach to the enantioselective synthesis of primary homoallylic amines.

This work was supported by the Natural Sciences and Engineering Research Council of Canada (NSERC). S.-W. Li thanks the University of Toronto for fellowship support. R.A.B. gratefully acknowledges receipt of a Premier's Research Excellence Award. We thank Dr A. B. Young for mass spectrometric analysis.



Scheme 2 Asymmetric synthesis of homoallylic amine **7** utilizing potassium allyltrifluoroborate **1a**.

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