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Room-Temperature Rhodium-Catalyzed Asymmetric 1,4-Addition of Potassium Trifluoro(organo)borates

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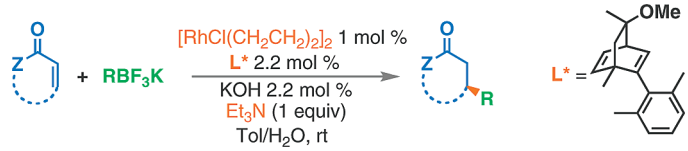
ABSTRACT



For the first time the room-temperature rhodium-catalyzed asymmetric 1,4-addition of potassium aryltrifluoroborates to α,β-unsaturated substrates is described. Thanks to the use of a chiral diene as ligand for rhodium and triethylamine as base, to facilitate transmetalation of the boron species, high yields and enantioselectivities were generally achieved. Moreover, the use of such tetravalent boron species offers some improvements compared to the use of boronic acids in term of stability and ease of purification.

1,4-Addition of organometallic reagents (Michael-type additions) to electron-deficient alkenes catalyzed by transition metals has emerged as a powerful tool in organic synthesis for making carbon−carbon bonds, allowing the introduction of a β-substituent to a Michael acceptor with concomitant enantioselective control of the newly created carbon−carbon bond.[1] Useful examples include the asymmetric 1,4-addition of organozinc reagents catalyzed by chiral copper complexes or of organoboranes catalyzed by chiral rhodium complexes.[1]

The success of these reactions relies on the development of chiral ligands adapted to the metal complexes, including phosphorus-, nitrogen-, and oxygen-containing chiral ligands. In asymmetric rhodium-catalyzed reactions, it has recently been shown that the use of chiral dienes[2] allowed very efficient reactions with organoboronic acids at rt and reached high levels of enantioselectivity in either the addition to Michael acceptors[3] or the addition to imines.[4] In that field, we have shown that C_1-symmetric chiral dienes, which are easily available in a few steps, were also adapted in the rhodium-catalyzed 1,4-addition to electron-deficient alkenes.[5]

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In our continuing interest in rhodium-catalyzed reactions with organoboron derivatives,[6] we showed that potassium trifluoro(organo)borates could be used efficiently in rhodium-catalyzed processes.[7,8] The use of such boron ate complexes is more attractive because of their higher stability and ease of preparation and purification. However, even if high levels of enantioselectivity were achieved using an atropoisomeric ligand such as binap or MeO-biphep, elevated temperatures were necessary for the reaction to proceed, which could be problematic for sensitive substrates.

In this Letter, we report the room-temperature rhodium-catalyzed addition of potassium trifluoro(organo)borates to α,β-unsaturated substrates using chiral diene ligands and using triethylamine as an additive, representing the first room-temperature transition-metal-catalyzed reaction using potassium aryltrifluoroborates.

We evaluated the possibility of conducting rhodium-catalyzed 1,4-additions of RBF_3K using several conditions in the addition of trifluoro(phenyl)borate (**2a**) to cyclohexenone (**1b**) (Scheme 1). It appeared that in the absence of any added base, transmetalation of organotrifluoroborates to several rhodium(I) precursors did not occur at rt, and as described by Corey and co-workers for the addition of alkenyltrifluoroborates,[9] the addition of triethylamine allowed the reaction to occur at rt (Table 1). However, in the presence of chiral phosphorus ligands (entries 1−6) and contrary to the addition of alkenyltrifluoroborates to α,β-unsaturated substrates,[9] the reaction was very sluggish and the enantioselectivity low, one exception being difluorphos ligand in term of enantioselectivity and chiral phosphoramidite ligand for the yield (entries 4 and 6). We were pleased to find that the use of chiral diene **4**[5] allowed the reaction to proceed efficiently at rt, giving **3ba** in a 85% yield and an ee of 96%. As observed in the addition of boronic acids under similar conditions,[5] chiral diene ligand **4**, bearing two *o*-methyl substituents on the aromatic ring, was found to be the most suited in the reaction, affording the highest levels of enantioselectivity. Other organic and inorganic bases were evaluated, and aliphatic tertiary amines were found to be the most suited; triethylamine being the cheapest was kept for the rest of the study.

Under these conditions and using 2 mol % rhodium catalyst in association with 2.2 mol % of chiral diene **4**, a variety of potassium trifluoro(organo)borates added to different cyclic enones with high enantioselectivity levels (Table 2). Addition of potassium aryltrifluoroborates occurred readily on cyclopentenone (**1a**), affording enantioenriched products with good yields and enantioselectivities ranging from 93% to 97% (entries 1−5). Good yields and high enantioselectivities could also be achieved on the six-membered enones (entries 6−10), but the ee's were lower on the seven-membered one (entries 11−13),

Scheme 1. Rhodium-Catalyzed 1,4-Addition of RBF_3K

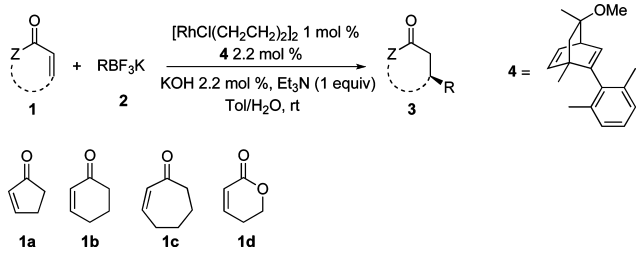
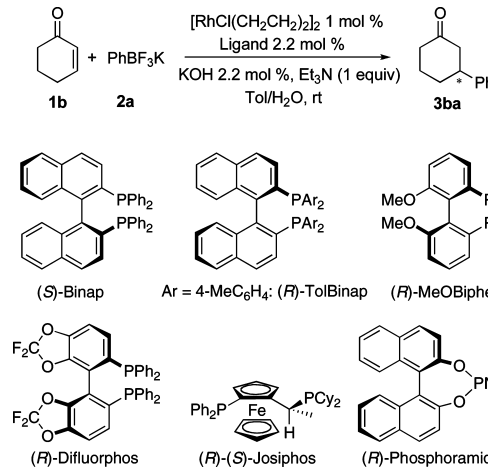


Table 1. Influence of the Chiral Ligand on the Room-Temperature Addition of **2a** to **1b**[a]



entry	ligand	yield of **3ba**[b]	ee[c]
1	(*S*)-binap	21	71 (*S*)
2	(*R*)-Tol-binap	0	
3	(*R*)-MeO-biphep	18	10 (*R*)
4	(*R*)-difluorphos	14	98 (*R*)
5	(*R*)-(*S*)-josiphos	0	
6	(*R*)-phosphoramidite	60	81 (*R*)
7	**4**	85	96 (*S*)

[a] Reactions conducted on 0.5 mmol of **1b**, 2 equiv of **2a**, [RhCl$(CH_2CH_2)_2]_2$ 2 mol % Rh, 2.2 mol % of chiral ligand, KOH 2.2 mol %, and 1 equiv of Et_3N in toluene/H_2O 4:1 (1 mL) at rt. [b] Isolated yields of 1,4-adduct **3**. [c] Enantiomeric excesses determined by chiral HPLC.

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Table 2. Rhodium-Catalyzed Addition of $ArBF_3K$ to Cyclic Enones and Lactones[a]

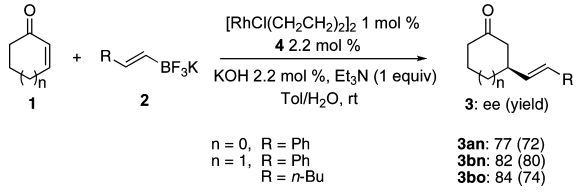
entry	1	2	product 3	ee (yield)[b]
1	**1a**	**2a**	**3aa**	93 (99)
2	**1a**	**2c**	**3ac**	93 (61)
3	**1a**	**2e**	**3ae**	95 (97)
4	**1a**	**2f**	**3af**	93 (40)
5	**1a**	**2j**	**3aj**	97 (81)
6	**1b**	**2a**	**3ba**	96 (85)
7	**1b**	**2b**	**3bb**	96 (80)
8	**1b**	**2d**	**3bd**	96 (66)
9	**1b**	**2g**	**3bg**	92 (92)
10	**1b**	**2h**	**3bh**	95 (63)
11	**1c**	**2a**	**3ca**	84 (84)
12	**1c**	**2i**	**3ci**	80 (43)
13	**1c**	**2k**	**3ck**	90 (75)
14	**1d**	**2a**	**3da**	91 (51)[c]

[a] Reactions conducted on 0.5 mmol of **1**, 2 equiv of **2**, $[RhCl(CH_2CH_2)_2]_2$ 2 mol % Rh, 2.2 mol % of chiral ligand, KOH 2.2 mol %,and 1 equiv of Et_3N in toluene/H_2O 4:1 (1 mL) at rt. [b] Isolated yields of 1,4-adduct **3**. Enantiomeric excesses determined by chiral HPLC. [c] Reaction conducted at 80 °C without Et_3N.

as observed by others.[2,3] We also evaluated the reactivity of cyclic lactones under these conditions. However, disappointing results were observed using triethylamine as a base and decomposition of the lactone occurred even at rt. This decomposition may be explained by the presence of some trivalent fluoroborane Lewis acid in the reaction medium together with the base. In the absence of any added base but conducting the reaction at higher temperature, lactone **1d** participated in the reaction, and the addition of trifluoro(phenyl)borate (**2a**) afforded the expected product **3da** with a 91% ee. However, under identical conditions, five-membered ring lactone furan-2(5*H*)-one failed to give any addition adduct.

Under these conditions, potassium alkenyltrifluoroborates also added to cyclohexenones (Scheme 2). Good yields were

Scheme 2. Rhodium-Catalyzed 1,4-Addition of Potassium Alkenyltrifluoroborates



generally achieved on five- and six-membered substrates using chiral diene **4**, although the enantioselectivity levels were lower than those obtained with aryltrifluoroborates. Further studies are underway to optimize the chiral diene for these substrates.

We have conducted preliminary experiments to elucidate the role played by the added base. Contrary to the observation of Corey et al. on a rhodium chloride precursor, we did not observe any reaction when the model complex $[RhOH(cod)]_2$ was treated at rt with Et_3N.[9] On the other hand, when 4-$FC_6H_4BF_3K$ was reacted with 1 equiv of Et_3N in benzene-d_6/D_2O at rt, a new boron ate complex was formed [^{19}F NMR $\delta = -118.7$ (1F, m) and -135.6 (2F, br q), ^{11}B NMR, $\delta = 4.6$ (br)] that was the only observable boron compound, along with unreacted starting trifluoroborate (Figure 1); no other boron species

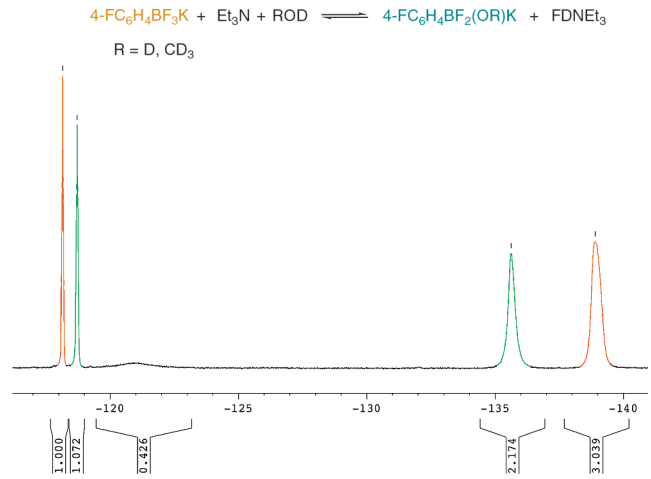


Figure 1. Reaction of potassium aryltrifluoroborates with protic solvents in the presence of triethylamine (R = D represented).

could be observed.[10] ^1H NMR spectra and ESI analysis also revealed the formation of Et_3NH^+.

Formation of this borate was not complete (52% conversion in 1 h), and by ^1H, ^{19}F, and ^{11}B NMR analysis the structure of this new tetravalent boron species was attributed to 4-$FC_6H_4BF_2(OD)^-$. When the same experiment was conducted using methanol as cosolvent, formation of 4-$FC_6H_4BF_2(OCD_3)^-$ was also observed [^{19}F NMR, $\delta = -119.5$ (1F, m) and -148.3 (2F, br q), ^{11}B NMR, $\delta = 4.6$ (br)], along with starting material (57% conversion). Indeed, and as suggested by others,[11] it appears that, at rt, potassium aryltrifluoroborates does not transmetalate directly to rhodium(I), but a monohydroxyborate is certainly the boron species that effects the transmetalation step.

We have thus described for the first time the room-temperature rhodium-catalyzed asymmetric 1,4-addition of potassium aryltrifluoroborates to α,β-unsaturated substrates. Thanks to the use of chiral diene as ligand for rhodium and triethylamine as base, to facilitate transmetalation of the boron species, high yields and enantioselectivities were generally achieved. Moreover, the use of such tetravalent boron species offers some improvements compared to the

(10) See Supporting Information.

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use of boronic acids in terms of stability and ease of purification.[7]

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Supporting Information Available: Experimental procedures and description of compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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