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Carbonylative 1,4-addition of potassium aryltrifluoroborates to vinyl ketones†

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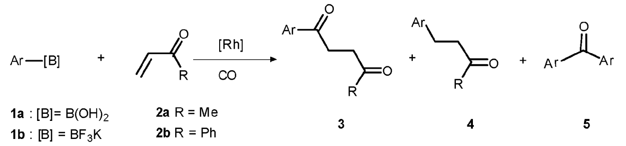
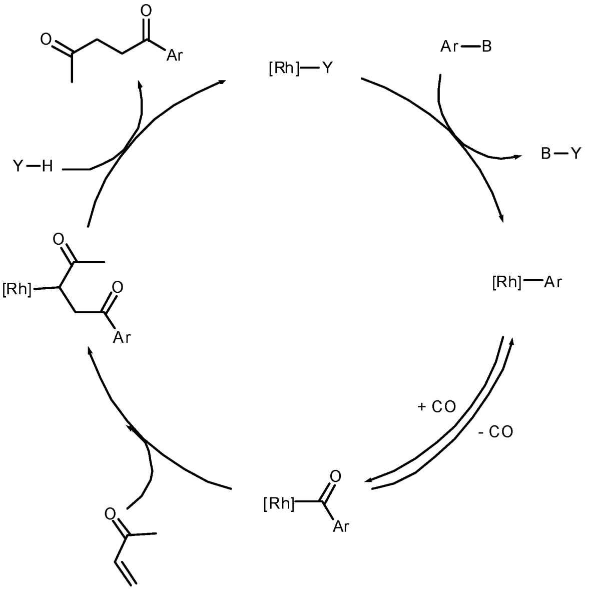
Potassium aryltrifluoroborates have proven to be useful reagents for the carbonylative aroylation of vinyl ketones; this study broadens the scope of potassium aryltrifluoroborates in homogeneous catalysis and shows that the solvent can act as the proton source for this family of reactions.

Potassium aryltrifluoroborates, of general formula $ArBF_3K$, have been used as alternative starting substrates to arylboronic acids in relatively few metal catalysed transformations.[1] They were, for example, successfully involved in palladium catalysed coupling reactions and in the 1,4-addition reactions of aryl moieties to α,β-unsaturated ketones and esters.[2] They are easily prepared as pure crystalline compounds from arylboronic acids or esters by reaction with KHF_2 as a fluorine source. Alternative synthetic pathways like the direct borylation of arenes followed by reaction with KHF_2 are also available in order to avoid the preliminary preparation of arylboronic acid. Arylboronic acids are, in contrast to potassium aryltrifluoroborates, often obtained as mixtures with their anhydride forms (boroxines). This is somewhat problematic for the interpretation of catalytic results as the nature of the organoboron which reacts is not clearly defined.[3] Furthermore, unlike arylboronic acids which can liberate water molecules through dehydration, potassium aryltrifluoroborates are water free and are potentially better partners in reactions that are limited by the presence of water. In relation to this property, the trifluoroborate group can be used to protect the boron and allow other reactions on the organic part such as metal halogen exchange,[4] oxidation,[5] epoxidation[6] or dihydroxylation.[7] The trifluoroborate remains intact and can be further involved in a subsequent C–C coupling reaction.



Scheme 1 The 1,4-carbonylative addition of arylboron derivatives to methyl vinyl ketone.



Scheme 2 Catalytic cycle proposed for the carbonylative addition of organoboron derivatives to methyl vinyl ketone.

However, we have recently shown that under CO pressure, the combination of a rhodium salt with arylboronic acids leads to the formation of Rh–acyl intermediates.[8] These catalytically generated acyl anion equivalents can react with α,β-unsaturated ketones,[9] alkynes[10] and diazabicycles.[11] For instance, the carbonylative addition of arylboronic acid **1a** to the methyl vinyl ketone **2a** yields 1,4-diketone **3** as the major product along with the side products **4** and **5** (Scheme 1). The proposed catalytic cycle (see Scheme 2: B = $B(OH)_2$) involves a boron to rhodium transmetallation step followed by sequential CO and α,β-unsaturated ketone insertion. The catalytic cycle ends with a protonation, releasing the diketone **3** and the starting rhodium species. However using arylboronic acids, the source of the proton (Y–H in Scheme 2) involved in the last step of this cycle remains unclear. Either methanol, the arylboronic acid or water (resulting from $ArB(OH)_2$ dehydration) can act as a proton source. When using potassium aryltrifluoroborates **2b**, the acidic proton can only come from the alcoholic solvent. Thus, if reaction does take place with this reagent, we will have more insight into the reaction's mechanism and, in addition, we will broaden the use of potassium aryltrifluoroborates in the field of carbonylation reactions.‡

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Table 1 Rhodium catalysed aroylation reaction of methyl vinyl ketone with potassium phenyltrifluoroborate under CO pressure[a]

Entry	P_{CO}/atm	T/°C	**3**[b] (%)	**4**[b] (%)	**5**[b] (%)
1	20	80	75	8	2
2[c]	20	80	75	8	6
3	5	80	68	18	7
4	40	80	62	2	4
5	20	50	85	2	<2
6	20	100	56	4	6
7[c]	20	100	30	2	33

[a] Reactions were carried out using potassium phenyltrifluoroborate (1.5 mmol), methyl vinyl ketone (3 mmol), 0.5% $[Rh(cod)Cl]_2$ + 2% PPh_3, 10 mL methanol and the appropriate CO pressure and reaction temperature for 18 h. [b] Yields determined by GC and based on the quantity of potassium phenyltrifluoroborate. [c] The reaction was performed with 1.5 mmol of phenylboronic acid in place of potassium phenyltrifluoroborate.

Table 2 Rhodium catalysed aroylation reaction of methyl vinyl ketone with potassium phenyltrifluoroborate with various solvents[a]

Entry	Solvent	**3**[b] (%)	**4**[b] (%)	**5**[b] (%)
1	THF	0	0	0
2	Toluene	0	0	0
3	Acetone	0	0	0
4	THF–H_2O (9 : 1)	23	4	<2
5	Toluene–H_2O (9 : 1)	28	6	8
6	Acetone–H_2O (9 : 1)	0	0	0
7	MeOH	75	8	2
8	EtOH	72	6	4
9	*n*-PrOH	72	6	3
10	*n*-BuOH	73	8	6
11	i-PrOH	61	8	12
12	*n*-PrOH[c]	61	4	<2
13	*n*-BuOH[c]	62	5	<2

[a] Reactions were carried out using potassium phenyltrifluoroborate (1.5 mmol), methyl vinyl ketone (3 mmol), 0.5% $[Rh(cod)Cl]_2$ + 2% PPh_3, 10 mL solvent with 20 bar of CO at 80 °C for 18 h. [b] Yields determined by GC and based on the quantity of potassium phenyltrifluoroborate. [c] The reaction was performed with 1.5 mmol of phenylboronic acid in place of potassium phenyltrifluoroborate.

Preliminary experiments were carried out with potassium phenyltrifluoroborate under the optimized reaction conditions for arylboronic acids. Using 1.5 mmol of potassium phenyltrifluoroborate and 3 mmol of methyl vinyl ketone in 10 mL of MeOH under 20 bar CO at 80 °C overnight, yields **3** as the main product in 75% yield, the by-products **4** and **5** being only obtained in limited amounts (Table 1; entry 1). These results are comparable with those obtained with phenylboronic acid (compare in Table 1; entries 1 and 2).

The proportions in **3**, **4** and **5** are very dependent on the reaction conditions. The reaction is more selective for the carbonylated derivative **3** with high CO pressure and satisfactory selectivities are obtained with 20 bar of CO (Table 1; entries 1, 3 and 4) as higher pressures do not give significant improvements. The reaction temperature has a more drastic effect on the selectivity. At 50 °C, the reaction went to completion within 16 hours and gave the highest yield of **3**. Indeed, at this temperature, extremely low amounts of side products **4** and **5** are formed. At higher reaction temperatures (*ca.* 100 °C) the yield of **3** is significantly reduced. However, compared to the results obtained with phenylboronic acid, the loss of yield is much less significant with the potassium phenyltrifluoroborate salt (Table 1; compare entries 6 and 7). In particular, with the latter, the amount of diphenylketone remains limited.

The reactivity observed with potassium phenyltrifluoroborate as partner of the reaction was strongly dependent on the nature of the solvent. Aprotic solvents such as THF, toluene and acetone are completely inefficient for the reaction (Table 2; entries 1–3). The starting materials are water free and a proton source is needed for the reaction. Moreover potassium phenyltrifluoroborate is largely insoluble in THF and toluene. The addition of water as proton source and solubilizing media allows the formation of the reaction products albeit in quite low yields (Table 2; entries 4–6) except in acetone which clearly inhibits the reaction.

Finally, alcoholic solvents appear to be the best media (Table 2; entries 7–11). Most of them allow the formation of **3** in high yields. Lower yields are usually obtained with phenylboronic acids if an alcohol other than methanol is used (Table 2; compare entries 9 and 10 with 12 and 13). However, the use of *n*-propanol or *n*-butanol has the advantage over methanol, in addition to their lower toxicity, that the fluorous containing boron salts obtained as by-products precipitate and thus can be easily removed from the reaction medium by a simple filtration.

Different aryltrifluoroborate salts were reacted with methyl vinyl ketone or phenyl vinyl ketone with optimum reaction conditions. The reaction temperature used was 80 °C in order to insure a complete reaction overnight. The resulting 1,4-diketones **3** were either purified by silica gel column chromatography or crystallized from the reaction mixture. Electron-donating substituents on the phenyl group of the organoboron derivative induce a high selectivity in carbonylated product **3** *versus* the non-carbonylated product **4**. The highest yields are obtained with potassium *p*-tolyltrifluoroborate salt or potassium *p*-methoxyphenyltrifluoroborate salt with a very limited amount of non-carbonylated derivative **4** (Table 3; compare entries 2 and 3 with entry 5). Sterically hindered *ortho*-substituted aryltrifluoroborate salts are in

Table 3 Rhodium catalysed aroylation reaction of vinyl ketones with potassium aryltrifluoroborate under CO pressure[a]

Entry	Ar	R	**3** (%)	**4**[b] (%)	**5**[b] (%)
1	Ph	Me	70[b]	5	3
2	4-MeC_6H_4	Me	72[b]	6	<2
3	4-$MeOC_6H_4$	Me	78[b]	5	<2
4	4-FC_6H_4	Me	74[b]	5	3
5	4-ClC_6H_4	Me	54[b]	12	3
6	2-MeC_6H_4	Me	15[b]	68	4
7	Ph	Ph	55[c]	<2	<2
8	4-MeC_6H_4	Ph	62[c]	<2	<2
9	4-ClC_6H_4	Ph	59[c]	11	<2
10	4-FC_6H_4	Ph	52[c]	<2	<2

[a] The reaction was carried out using potassium aryltrifluoroborate (1.5 mmol), methyl vinyl ketone (3 mmol) or phenyl vinyl ketone (1.5 mmol), 0.5% $[Rh(cod)Cl]_2$ + 2% PPh_3, 10 mL MeOH and 20 bar of CO at 80 °C for 18 h. [b] Yields determined by GC and based on the quantity of potassium aryltrifluoroborate. [c] Isolated yield after crystallization from the reaction mixture.

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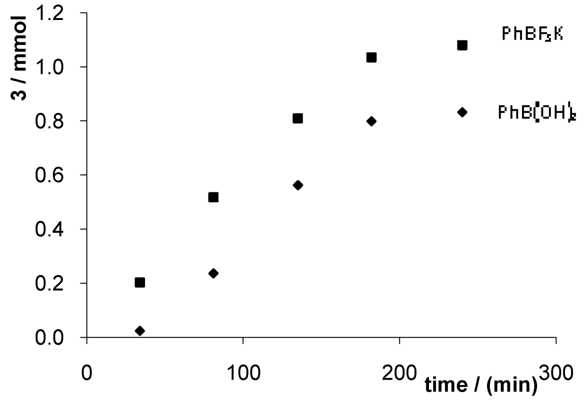

Fig. 1 Reaction profiles obtained with phenylboronic acid and potassium phenyltrifluoroborate at 80 °C (1.5 mmol of boron derivative, 3 mmol of methyl vinyl ketone, 0.25% [Rh(cod)Cl]$_2$, 1.5% PPh$_3$, 20 bar CO, 50 mL MeOH).

contrast more difficult to carbonylate and a large amount of the non-carbonylated product **4** is for example obtained from potassium *o*-tolyltrifluoroborate. This by-product formation largely accounts for the low yield in derivative **3**; however, the selectivity can be further improved by using higher carbon monoxide pressures. The same trend is observed with phenyl vinyl ketone (Table 3; entries 7 to 10) and methyl vinyl ketone (Table 3; entries 1 to 6). The products obtained from phenyl vinyl ketone are easily isolated as they are readily crystallized from methanol upon cooling to room temperature whereas those obtained from methyl vinyl ketone have to be purified by silica gel column chromatography.

The kinetic profiles of the reaction with phenylboronic acid and potassium phenyltrifluoroborate at 80 °C under 20 bar of CO in 50 mL MeOH also showed a strong similarity (Fig. 1). Although the reaction with the phenylboronic acid needs a short induction period which is not observed with potassium phenyltrifluoroborate, the overall reaction rates are identical in both cases. This indicates that a common intermediate is probably involved in the rate limiting step.

Additional experiments indeed showed that the overall kinetics of the reaction under these conditions is dependent on the methyl vinyl ketone and rhodium concentrations but not on the organoboron concentration, suggesting that the transmetallation step is not rate determining. This is also consistent with the fact that the two overall reaction rates are similar. The same intermediate possessing a Rh–COAr moiety is probably obtained from both organoboron reagents, and the reaction of this intermediate with the enone is suggested to be the slowest step of the catalytic cycle.

We have found that potassium aryltrifluoroborates can be efficiently used in the 1,4-carbonylative addition of organoboron derivatives to methyl vinyl ketone and phenyl vinyl ketone. The reaction proceeds with good yields and efficiently affords the corresponding 1,4-diketones. The involvement of the water free potassium phenyltrifluoroborate in the reaction indicates that the alcohol can act as a proton donor. Although alcohols are weak acids compared to water, the protonation occurs efficiently. The reaction rates obtained with potassium phenyltrifluoroborates and with phenylboronic acid are similar indicating the involvement of a probable identical intermediate in the rate limiting step of the reaction.

Experimental

For a typical catalytic run

A 50 mL stainless steel autoclave equipped with a magnetic stirrer bar was charged with potassium phenyltrifluoroborate (1.5 mmol), [Rh(cod)Cl]$_2$ (0.0075 mmol; 1% Rh) and PPh$_3$ (0.03 mmol). The solids were degassed by three vacuum nitrogen cycles. A mixture of methyl vinyl ketone (3 mmol) and MeOH (10 mL; distilled over Mg) was thus added under nitrogen. The autoclave was pressurized to 20 bar with CO and the mixture was agitated and warmed at 80 °C for 18 h. After cooling to room temperature, the reactor was vented and 145 μL of undecane used as internal standard were added to the yellow methanol solution before analysis by GC.

Notes and references

‡ To the best of our knowledge, there is no example in the literature of carbonylation reactions involving potassium aryltrifluoroborate salts.

1 (*a*) S. Darses and J.-P. Genêt, *Eur. J. Org. Chem.*, 2003, 4313; (*b*) G. A. Molander and N. Ellis, *Acc. Chem. Res.*, 2007, **40**, 275; (*c*) H. A. Stefani, R. Cella and A. S. Vieira, *Tetrahedron*, 2007, **63**, 3623; (*d*) S. Darses and J.-P. Genêt, *Chem. Rev.*, 2008, **108**, 288.

2 (*a*) R. A. Batey, A. N. Thadani and D. V. Smil, *Org. Lett.*, 1999, **1**, 1683; (*b*) M. Pucheault, S. Darses and J.-P. Genêt, *Tetrahedron Lett.*, 2002, **43**, 6155; (*c*) M. Pucheault, S. Darses and J.-P. Genêt, *Eur. J. Org. Chem.*, 2002, 3552; (*d*) L. Navarre, S. Darses and J.-P. Genêt, *Eur. J. Org. Chem.*, 2004, 69.

3 J. M. Murphy, C. C. Tzschucke and J. F. Hartwig, *Org. Lett.*, 2007, **9**, 757.

4 G. A. Molander and N. M. Ellis, *J. Org. Chem.*, 2006, **71**, 7491.

5 G. A. Molander and D. E. Petrillo, *J. Am. Chem. Soc.*, 2006, **128**, 9634.

6 G. A. Molander and M. Ribagorda, *J. Am. Chem. Soc.*, 2003, **125**, 11148.

7 G. A. Molander and R. Figueroa, *Org. Lett.*, 2006, **8**(1), 75.

8 M. Sauthier, Y. Castanet and A. Mortreux, *Chem. Commun.*, 2004, 1520.

9 H. Chochois, M. Sauthier, E. Maerten, Y. Castanet and A. Mortreux, *Tetrahedron*, 2006, **62**, 11740.

10 (*a*) Ö. Aksin, N. Dege, L. Artok, H. Türkmen and B. Çetinkaya, *Chem. Commun.*, 2006, 3187; (*b*) J. Dheur, M. Sauthier, Y. Castanet and A. Mortreux, *Adv. Synth. Catal.*, 2007, **349**(16), 2499; M. Kuş, Ö. A. Artok, F. Ziyanak and L. Artok, *Synlett*, 2008, 2587.

11 F. Menard, C. F. Weise and M. Lautens, *Org. Lett.*, 2007, **9**, 5365.

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