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Access to Stereodefined Trisubstituted Alkenes *via* Rhodium-Catalyzed 1,4-Addition of Potassium Trifluoro(organo)-borates to Baylis–Hillman Adducts

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Abstract: In the presence of a rhodium catalyst, unactivated Baylis–Hillman adducts reacted regioselectively with potassium trifluoro(organo)borates to afford stereodefined trisubstituted alkenes with good yields. This highly efficient reaction (aerobic conditions, low temperature, absence of added phosphane ligand) is believed to proceed *via* a 1,4-addition/β-hydroxy elimination mechanism.

Keywords: alkenes; Baylis–Hillman adduct; conjugate addition; homogeneous catalysis; organotrifluoroborates; rhodium

The Baylis–Hillman (BH) reaction is a very useful and operationally simple reaction allowing carbon-carbon bond formation under mild conditions.[1] The reaction products, called Baylis–Hillman adducts, are highly functionalized substrates bearing both allyl alcohol and α,β-unsaturated ester moieties. Indeed, they have been further functionalized *via* palladium-catalyzed Heck reactions[2] or Friedel–Crafts reactions.[3] S_N2'[4] or π-allyl-type[5] reactions have also been described on BH adducts, but the allyl alcohol moiety had to be further transformed to carbonate or acetate, which are better leaving groups. For example, Kabalka et al. recently reported palladium-catalyzed cross-coupling reactions of BH acetates with bis(pinacolato)diboron[6] or potassium trifluoro(organo)borates,[7,8] allowing the formation of stereodefined alkenes *via* π-allylpalladium intermediates. In terms of atom economy,[9] the use of unactivated BH adducts would be more desirable but they are generally less reactive in transition metal-catalyzed reactions.

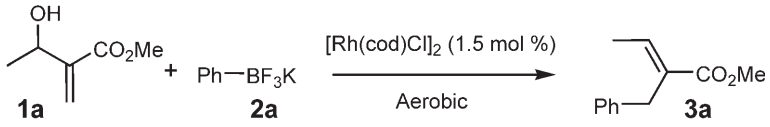
In our continuous interest in rhodium-catalyzed reactions with organoboron derivatives,[10,11] we recently showed that organoboronic acids added to BH adducts in the presence of a rhodium complex, affording stereodefined trisubstituted (*E*)-alkenes under mild conditions *via* an unusual mechanism.[12] In this reaction, the use of potassium trifluoro(organo)borates would be more attractive because of their higher stability and ease of preparation and purification.[8] Moreover, these compounds have found to be highly suited in rhodium-catalyzed processes.[10,13]

In this paper, we report for the first time the reaction of potassium trifluoro(organo)borates with unactivated BH adducts catalyzed by phosphine ligand-free rhodium complexes under aerobic conditions[14] to afford (*E*)-trisubstituted alkenes.

In order to determine the optimal parameters for the addition, several conditions were evaluated using potassium trifluoro(phenyl)borate (**2a**) and **1a** as model reaction partners. Among the catalyst precursors tested (rhodium, palladium and ruthenium complexes) rhodium(I) complexes appeared to be the most suited to accomplish the reaction. Particularly, the commercially available and easily prepared rhodium dimer $[Rh(cod)Cl]_2$ allowed the reaction to go to completion, even in the absence of added phosphane ligand.[15] With this rhodium pre-catalyst in hand, several conditions (solvent and temperature) were evaluated to improve the overall efficiency of this catalytic process (see Table 1 for selected examples).

From these results, it appeared that the presence of a protic solvent was essential to achieve high conversion of the starting BH adduct (entries 1–3 compared to entry 4) but isolated yields were relatively modest, because of the decomposition of the substrate with long reaction times. The combination of a protic solvent and toluene, a solvent usually used in 1,4-addition using potassium trifluoro(organo)borates,[10] as reaction medium afforded improved isolated yields. Among the binary mixtures evaluated, a toluene/methanol mixture proved to be highly suited in achieving high yields and isomeric ratios (99/1) in favor of the (*E*) isomer. Even if the reaction was

Table 1. Optimization of the reaction conditions.[a]



1a 2a 3a

Entry	Solvent	T [°C]	Time [h]	Conv. (yield) [%]	E/Z
1	Water	55	26	90 (47)	98/2
2	Methanol	55	60	84	98/2
3	Ethanol	55	5	61	98/2
4	Toluene	55	40	2	–
5	Toluene/MeOH (1:1)	55	4	30	99/1
6	Toluene/MeOH (1:1)	70	4	98 (86)	99/1
7	Toluene/EtOH (1:1)	70	5	45	98/2

[a] Reactions were conducted using 0.5 mmol BH adduct **1a**, 1 mmol of **2a** with 1.5 mol % $[Rh(cod)Cl]_2$.
[b] Conversion determined by GC. Isolated yield of BH adduct **3a** in parentheses.
[c] Determined by GC/MS and ^1H NMR.

slightly sluggish at 50 °C (reaction time of 20 h), increased reactivity was achieved at 70 °C, keeping high levels of the E/Z ratio.

The generality of this reaction was evaluated under these optimized conditions: $[Rh(cod)Cl]_2$ as catalyst precursor in toluene/methanol at 70 °C. It appeared that these conditions proved to be general, independent of the nature of the BH adduct or potassium aryltrifluoroborate employed (Table 2).

Very high yields were generally achieved independent of the electronic nature of the aryltrifluoroborate and, to a given BH adduct, isomeric ratios were constant. Concerning the BH adduct partner, either aliphatic (entries 1–8) or aromatics substrates (entries 9–12) participated equally well, in sharp contrast with the palladium-catalyzed reaction of the BH adduct.[7] From these results it also appeared that increasing steric hindrance of the aliphatic R^1 moiety resulted in a slight decrease of the isomeric ratio: from more than 99/1 (entries 1–4) to 96/4 (entries 5–6), still in favor of the (E) isomer. The same trend was observed using organoboronic acids as reaction partners.[12] It is also important to note that higher yields, but comparable E/Z ratios, were generally observed using potassium trifluoro(organo)borates compared to boronic acids: for example, in the addition to BH substrate **1c**, a 70% yield of alkene **3i** was achieved using phenylboronic acid, whereas the yield was improved to 96% using the potassium trifluoro(phenyl)-borate derivative (entry 8).

Due to their ready availability and higher stability compared to trivalent organoboron derivatives, the reactivity of potassium alken-1-yltrifluoroborates[8] was also evaluated in this reaction (Table 3).

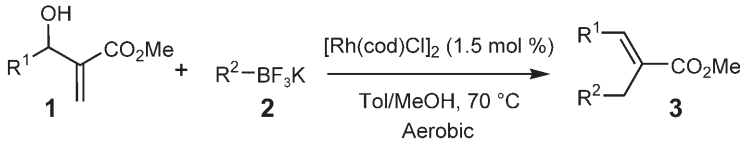
Indeed, under the current aerobic conditions, alkenyltrifluoroborates added smoothly to BH adducts affording useful 1,4-dienes in high yields and high stereoselectivity on both double bonds: the (E)-alkene from the acrylate moiety while maintaining the geometry of the incoming organometallic partner. Particularly, potassium vinyltrifluoroborate[16] also participated in this reaction, affording the expected coupling adduct **3q** in 44% yield. Thus, using this efficient catalytic reaction, highly functionalized 1,4-dienes were easily accessible from readily available reagents: an aldehyde, a Michael acceptor (the BH reagent) and a potassium alkenyltrifluoroborate.

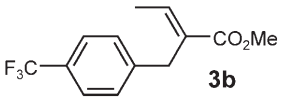
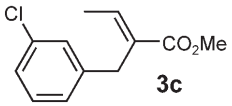
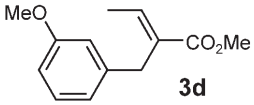
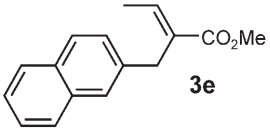
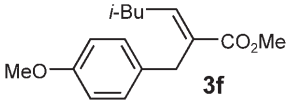
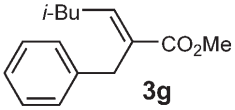
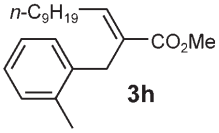
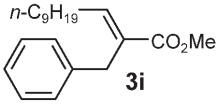
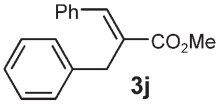
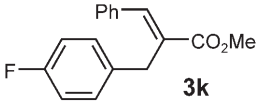
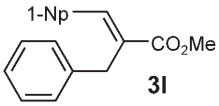
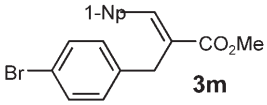
Concerning the mechanism of this rhodium-catalyzed reaction, it is expected to be analogous to our previously described reaction involving trivalent boronic acids derivatives: a tandem 1,4-addition/β-hydroxy elimination-type mechanism instead of a π-allyl-type reactivity.[12] The involvement of such a mechanism was confirmed by the high regioselectivity of the reaction involving deuterated substrate **1f**. Indeed, the reaction of potassium trifluoro(phenyl)borate (**2a**) with **1f** in the presence of the rhodium dimer $[Rh(cod)Cl]_2$ in toluene/methanol afforded exclusively the Michael adduct **3r** in 71% yield, deuterium atoms being positioned on the vinylic moiety and not at the benzylic position (Scheme 1).

This high regioselectivity excluded a true π-allyl-type mechanism, where deuterium incorporation should have appeared in both positions. Thus, the reaction should involve regioselective 1,4-addition of the organometallic reagent followed by an unusual β-hydroxy elimination, generating the expected alkene and a hydroxorhodium complex suited for a transmetallation reaction with an organoboron species[17] (Scheme 2).

In this reaction on BH adducts, an α,β-unsaturated ester is generated which could participate to a novel rhodium-catalyzed 1,4-addition[10,11g] with remaining potassium trifluoro(organo)borate present in the reaction medium. However, in all the reactions examined, the bis-addition compound was never observed on substituted BH adducts, probably because the generated trisubsti-

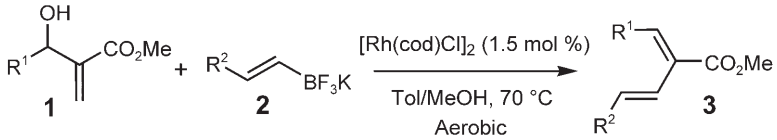
Table 2. Aerobic rhodium-catalyzed addition of potassium aryltrifluoroborates to BH adducts.[a]

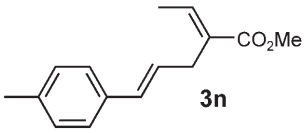
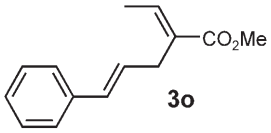
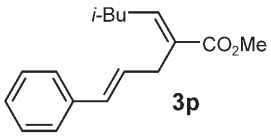
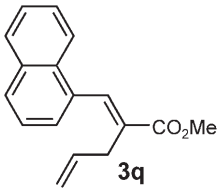


Entry	Product	Yield[b] [%]	*E*/*Z*[c] [%]
1	 **3b**	63	99/1
2	 **3c**	58	99/1
3	 **3d**	85	99/1
4	 **3e**	98	99/1
5	 **3f**	70	96/4
6	 **3g**	91	96/4
7	 **3h**	90	96/4
8	 **3i**	96	96/4
9	 **3j**	98	97/3
10	 **3k**	98	98/2
11	 **3l**	98	98/2
12	 **3m**	98	97/3

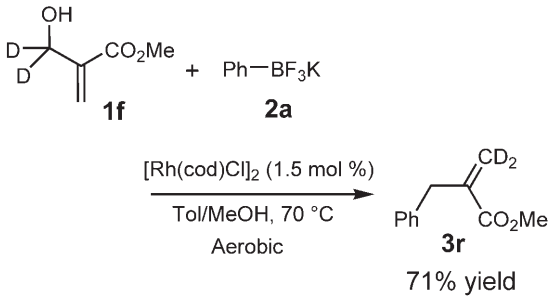
[a] Reactions were conducted using 0.5 mmol BH adduct **1**, 1 mmol of R^2-BF_3K **2** with 1.5 mol % $[Rh(cod)Cl]_2$ at 70 °C in 2 mL toluene/methanol (1:1).
[b] Isolated yield of adduct **3**.
[c] Determined by GC/MS and ^1H NMR.

Table 3. Aerobic rhodium-catalyzed addition of potassium alkenyltrifluoroborates to BH adducts.[a]

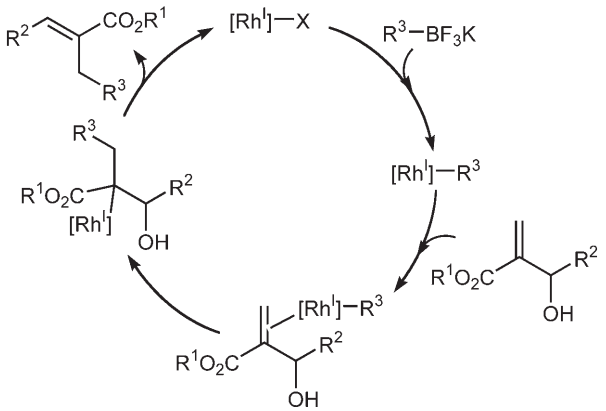


Entry	Product	Yield[b] [%]	*E*/*Z*[c] [%]
1	 **3n**	91	99/1
2	 **3o**	84	98/2
3	 **3p**	94	96/4
4	 **3q**	44[d]	99/1

[a] Reactions were conducted using 0.5 mmol BH adduct **1**, 1 mmol of R^2-BF_3K **2** with 1.5 mol% $[Rh(cod)Cl]_2$ at 70 °C in 2 mL toluene/methanol 1:1.
[b] Isolated yield of adduct **3**.
[c] Determined by GC/MS and ^1H NMR.
[d] Reaction conducted with three equivalents of potassium trifluoro(vinyl)borate.



Scheme 1. Regioselectivity of the addition.

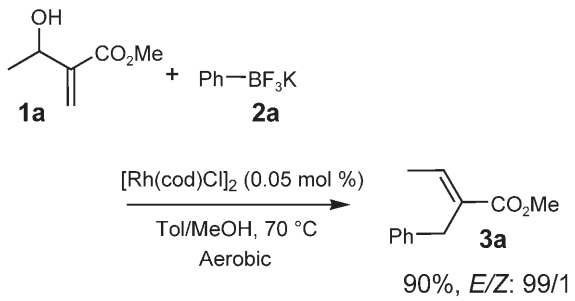


Scheme 2. Proposed mechanism.

tuted alkene intermediate is too crowded to participate in a novel insertion.[18]

To further demonstrate the utility of the present procedure for the formation of (*E*)-trisubstituted alkenes, larger scale reaction was conducted with low catalyst loading (Scheme 3). Reaction of BH adduct **1a** (5 mmol) with potassium trifluoro(phenyl)borate **2a** furnishes **3a** in 90% yields and using 0.1 mol % of rhodium and unchanged isomeric ratio (99/1) in favor of the (*E*) isomer.

We have thus described an highly efficient reaction allowing an access to stereodefined trisubstituted alkenes from easily available BH adducts and potassium trifluoro-



Scheme 3. Catalyst loading.

(organo)borates. Compared to their trivalent congeners, trifluoroborate derivatives show several advantages in term of stability and ease of preparation and purification.[8] Moreover, higher yields were generally achieved using these boron ate complexes. This reaction, involving a 1,4-addition/β-hydroxy elimination mechanism, occurs under mild and aerobic conditions in the absence of added phosphane ligand. We hope this methodology would provide new opportunities in organic synthesis due to its high versatility and the readily availability of the reagents.

Experimental Section

Typical Procedure for the Reaction of Potassium Trifluoro(organo)borates with Baylis–Hillman Adducts

A mixture of the Baylis–Hillman adduct (0.5 mmol), potassium trifluoro(organo)borate (2 equivalents), $[Rh(cod)Cl]_2$ (3.6 mg, 1.5 mol %) were placed in a flask and then methanol (1 mL) and toluene (1 mL) were added at room temperature. The flask, equipped with a condenser, was placed in a preheated oil bath at 70 °C and the mixture was stirred until completion of the reaction (followed by GC analysis). Purification by silica gel chromatography (cyclohexane/ethyl acetate) afforded analytically pure products.

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