Synthesis of *gem*-Difluoroalkenes via β -Fluoride Elimination of Organorhodium(I)

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Treatment of α -(trifluoromethyl)styrenes with arylboronic esters and MeMgCl in the presence of a rhodium(I) catalyst affords *gem*-difluoroalkenes. The reaction proceeds through the addition of arylrhodium(I) species across the electron-deficient carbon–carbon double bond and the subsequent β -fluoride elimination.

The rhodium-catalyzed addition reactions of organoboron reagents to unsaturated functionalities have grown dramatically in organic synthesis.¹ The reaction generally proceeds via a transmetalation step generating an organorhodium(I) species from Rh^{I} -OR (OR = hydroxy or alkoxy) and organoboron followed by a carborhodation step onto various unsaturated functional groups. For regeneration of the RhI-OR species, there are two major elementary steps available. One is protodemetalation by a proton source, i.e., water or an alcohol that is present as a co-solvent or an additive,² and the other is β -oxygen elimination from a β -oxy-substituted organorhodium(I) intermediate.³ We have described a variety of catalytic reactions which proceed through a sequential carborhodation/ β -oxygen elimination pathway.⁴ As a continuation of our studies on rhodium-catalyzed addition reactions, we report herein a new rhodium-catalyzed addition reaction of arylboronic esters to α -(trifluoromethyl)styrenes,⁵ in which an organorhodium(I) intermediate undergoes β -fluoride elimination⁶ to afford gemdifluoroalkenes.7

A mixture of α -(trifluoromethyl)styrene (1a) and phenylboronic acid (2a, 3 equiv) in 1,4-dioxane was heated at 100 °C in the presence of [Rh(OH)(cod)]₂ (5 mol % Rh, cod = cycloocta-1,5-diene). An aqueous workup afforded a mixture of products 4aa (39%), 5aa (2%), and 6aa (22%) (Table 1, Entry 1). Scheme 1 depicts the pathways conceivable for the formation of the products. Initially, an alkylrhodium(I) intermediate A arises from regioselective 1,2-addition of phenylrhodium(I) species across the electron-deficient carbon–carbon double bond of 1a. Whereas β -fluoride elimination takes place with A to afford the product 4aa, β -hydride elimination of A gives the product 5aa.⁸ On the other hand, protodemetalation of A by H₂O or 2a forms 6aa.

When phenylboronic ester **3a** (PhBneo = 5,5-dimethyl-2phenyl-1,3,2-dioxaborinane) was used in place of phenylboronic acid (**2a**), the formation of **6aa** was diminished and the yield of **4aa** increased to 60% (Table 1, Entry 2). Next, the effect of several additives was examined (Entries 3–7). Among them, the use of methylmagnesium chloride gave a better yield of **4aa**.⁹ We assume that the Mg–F interaction activates the C–F bond to promote the β -fluoride elimination step.¹⁰ The product **4aa** was obtained in 73% yield even with 1.5 equiv of phenylboronate **3a** (Entry 8).

A control experiment was carried out using a combination

Table 1. Optimization of reaction conditions^a

C Ph	Pł F₃ [R ≫ 10	hB(OR) ₂ hX(cod)] ₂ Dioxane 0 °C, 12 h	C Ph ⁺ Ph	F₃ → + Ph	CF ₃ Ph	Ph
Entry	v	2a or 3a	Additive	GC yield/% ^b		
	Х	PhB(OR) ₂ (equiv)	(3 equiv)	4aa	5aa	6aa
1	OH	PhB(OH) ₂ (3.0)	none	39	2	22
2	OH	PhBneo (3.0)	none	60	5	8
3	OH	PhBneo (3.0)	CsF	55	1	4
4	Cl	PhBneo (3.0)	CsF	51	4	4
5	Cl	PhBneo (3.0)	NaOEt	37	3	0
6	Cl	PhBneo (3.0)	MeLi	60	5	0
7	Cl	PhBneo (3.0)	MeMgCl	72	2	0
8	Cl	PhBneo (1.5)	MeMgCl	73	1	0

^aReaction conditions: **la** (0.2 mmol), **2a** or **3a**, additive (0.6 mmol), $[RhX(cod)]_2$ (5.0 µmol, 5 mol % Rh) in dioxane (4 mL) at 100 °C for 12 h. ^bGC analysis (J&W DB-1).



Scheme 1. Plausible reaction pathways.

of methylboronic ester and phenylmagnesium chloride (eq 1). The sequential arylation/ β -fluoride elimination reaction proceeded under similar conditions to give **4aa** in 67% yield. This result indicated generation of magnesium methyl(phenyl)borate from organoboronic esters and Grignard reagents.¹¹

Under the optimized reaction conditions using MeMgCl as the activator, a wide range of arylboronic esters **3b–3i** participated in the reaction with **1a** to furnish *gem*-difluoroalkenes **4ab–4ai** (Table 2).

The scope of the substrate **1** was also examined (Table 3). The methoxy-substituted substrate **1b** was more reactive than the substrates having electron-withdrawing substituents **1c–1e** (Entries 1–4). No reaction took place with alkyl-substituted substrate **1g** (Entry 6).

When α -(difluoromethyl)styrenes **7a** and **7b** were subjected to similar reaction conditions, β -fluoride elimination occurred

Table 2. Scope of arylboronate reagents 3^{a}

CF ₃	+ Ar-	-B´O_	2.5 mol % 3.0 equiv l Dioxane,	[RhCl(cod)] ₂ MeMgCl 100 °C, 12 h	Ph F Ar
1a	3 ((1.5 equiv)			4
Entry		А	r	Product	Yield/% ^b
1	3b	4-Me-C	$_{6}H_{4}$	4ab	78
2	3c	$4-F-C_6H$	I_4	4ac	77
3	3d	$3-Cl-C_6$	H_4	4ad	79
4	3e	3-MeO-	C_6H_4	4ae	77
5	3f	3-CN-C	$_{6}H_{4}$	4af	55°
6	3g	3-MeO ₂	$C-C_6H_4$	4ag	74 ^c
7	3h	2-Me-C	$_{6}H_{4}$	4ah	75
8	3i	$2-Cl-C_6$	H_4	4ai	48

^aReaction conditions: **1a** (0.5 mmol), **3** (0.75 mmol), MeMgCl (1.5 mmol), [RhCl(cod)]₂ (12.5 μ mol, 5 mol% Rh) in dioxane (10 mL) at 100 °C for 12 h unless otherwise noted. ^bIsolated material of >95% purity. °**3** (1.5 mmol).

Table 3. Scope of substrates 1^a

CF₃	+ Ph-B, 0		2.5 mol % [RhCl(cod)] ₂ 3.0 equiv MeMgCl		F F	
Ar' 🚿			Dioxane,	100 °C, 12 h	Ar Ph	
1	3a (3	.0 equiv)			4	
Entry		A	Ar	Product	Yield/% ^b	
1	1b	4-MeC	$-C_6H_4$	4ba	80	
2	1c	4-F-C	$_{5}H_{4}$	4ca	60	
3	1d	4-Br–0	C_6H_4	4da	61	
4	1e	4-CN-	C_6H_4	4ea	54	
5	1f	2-Napł	nthyl	4fa	88	
6	1g	<i>n</i> -C ₁₀ H	I ₂₁	4ga	0	

^aReaction conditions: **1a** (0.2 mmol), **3a** (0.6 mmol), MeMgCl (0.6 mmol), [RhCl(cod)]₂ (5.0 μ mol, 5 mol % Rh) in dioxane (4 mL) at 100 °C for 12 h unless otherwise noted. ^bIsolated material of >95% purity.

selectively to produce fluoroalkenes **8aa** and **8ba** in good yield as a single stereoisomer (E/Z = >95: 5, eq 2).¹²

CF ₂ H	2.5 mol % [RhCl(cod)] ₂ 3.0 equiv MeMgCl	I F	
R (3.0 equiv)	Dioxane, 100 °C, 12 h	R ^{Ph}	(2)
7a (R = Ph) 7b (R = 2-Naphthyl)		8aa 80% 8ba 83%	

In summary, we have demonstrated that the rhodiumcatalyzed addition of arylboronic esters to α -(trifluoromethyl)styrenes provides a new synthetic route to *gem*-difluoroalkenes.¹³ This catalytic process presents a rare example of β fluoride elimination of an organorhodium(I) complex.

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