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Critical Role of Catalysts and Boranes for Controlling the Regioselectivity in the Rhodium-Catalyzed Hydroboration of Fluoroolefins

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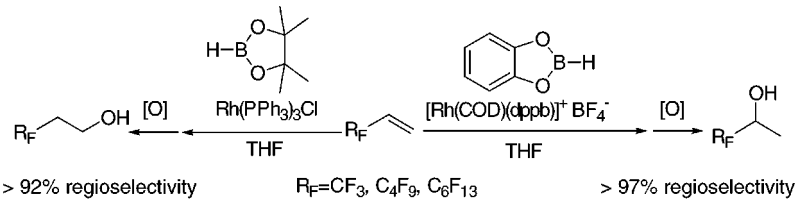
ABSTRACT



Catalytic hydroboration of perfluoroalkylethylenes ($R_FCH{=}CH_2$) with cationic and neutral rhodium complexes allows for selective access to either regioisomeric alcohol after hydroboration with catechol- and pinacolboranes, followed by oxidation with alkaline hydrogen peroxide.

The introduction of fluorine in place of hydrogen often improves the biological properties of organic molecules.[1] Furthermore, fluorinated compounds are increasingly being used in analytical, materials, and polymer chemistry due to their unique properties.[1] Accordingly, many effective methods for fluoroorganic synthesis have been reported.[2] However, organoboranes have not been pursued in this respect until recently,[3] although they are routinely used in many synthetic laboratories. The Markovnikov hydroboration of perfluoroalkylethylenes, such as 3,3,3-trifluoropropene, has been known for four decades.[4] We reexamined the hydroboration of 3,3,3-trifluoropropene and observed that $HBCl_2$ and $HBBr_2$ provide Markovnikov products more selectively than previously reported for BH_3.[5] In continuation of our research on the utilization of organoboranes for the synthesis of fluoroorganic compounds,[6] we desired a simple, direct method for selective access to the anti-Markovnikov isomer as well. However, these 1°-fluoroalkyl boranes could not be

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(6) Ramachandran, P. V.; Brown, H. C. *Enantiocontrolled Synthesis of Fluoro-Organic Compounds: Stereochemical Challenges and Biomedical Targets*; Soloshonok, V. A., Ed.; John Wiley and Sons Ltd.: 1999.

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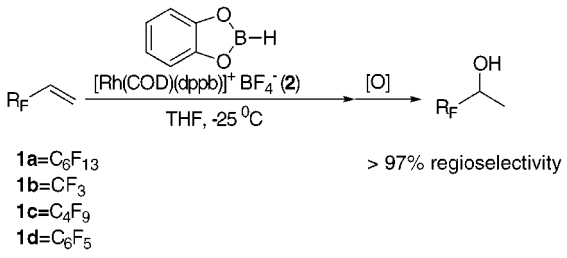
produced by uncatalyzed hydroboration due to the low reactivity of these fluorinated olefins toward sterically hindered hydroborating reagents such as 9-BBN and Sia_2BH.

Since the pioneering discovery by Männing and Nöth that rhodium catalysts facilitate the hydroboration of alkenes with catecholborane,[7] there have been notable developments of both achiral and chiral versions of this reaction with variation in the catalysts, substrates, and boranes.[8] It has been shown that transition-metal-catalyzed and uncatalyzed hydroboration reactions proceed via different mechanisms, periodically resulting in opposite regiochemical outcomes.[9] Sneddon and co-workers had previously reported, as part of their extensive study, the first rhodium-catalyzed hydroboration of 3,3,3-trifluoropropene with borazine for use in materials chemistry.[10] With this background, we decided to undertake a systematic study of the rhodium-catalyzed hydroboration of fluoroolefins to complement the uncatalyzed procedure. Herein, we wish to report the critical importance of rhodium catalysts and boranes in achieving high levels of selectivity for *both* regioisomers.

As previously reported by Evans and co-workers, cationic rhodium complexes were the most active for the hydroboration of alkenes.[11] We chose these types of catalysts due to the intrinsic lower reactivity of the electron deficient fluoroolefins. To enhance the convenience of isolation, we selected 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro-1-octene (**1a**) and 2′,3′,4′,5′,6′-pentafluorostyrene (**1d**), as representative examples of an aliphatic and aromatic perfluoroethylene ($R_FCH{=}CH_2$).

The hydroboration of **1a** at room temperature with 1 mol % of $[Rh(COD)(dppb)]^+BF_4^-$ (**2**) and catecholborane (CBH) in THF was complete in 0.25 h (^{11}B δ 34.5). Alkaline H_2O_2 oxidation furnished the product alcohols in 71% isolated yield. Gas chromatography (GC) revealed a moderate excess, 72%, of the 2°-alcohol with 28% of the 1°-alcohol (Scheme 1). Decreasing the reaction temperature to 0 °C increased

Scheme 1



the regioselectivity to 9:1. Subsequent lowering of the temperature to −25 °C produced essentially pure 2°-alcohol.

(7) Männig, D.; Nöth, H. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 879.
(8) For the most recent comprehensive review, see: Beletskaya, I.; Pelter, A. *Tetrahedron* **1997**, *53*, 4957.
(9) (a) Hayashi, T.; Matsumoto, Y.;. Ito, Y. *Tetrahedron: Asymmetry* **1991**, *2*, 601. (b) Evans, D. A.; Fu, G. C.; Hoyveda, A. H. *J. Am. Chem. Soc.* **1988**, *110*, 6917. (c) Evans, D. A.; Fu, G. C.; Anderson, B. A. *J. Am. Chem. Soc.* **1992**. *114*, 6679.
(10) Frazen, P. J.; Sneddon, L. G. *Organometallics* **1994**, *13*, 2867.

The generality of this reaction was demonstrated by carrying out the hydroboration of 3,3,3-trifluoropropene (**1b**) and 3,3,4,4,5,5,6,6,6-nonafluoro-1-hexene (**1c**) which provided similar results. The hydroboration of **1d** produced optimal results (≥97% 2°-product) at room temperature. The results are summarized in Table 1.

Table 1. $[Rh(COD)(dppb)]^+BF_4^-$-Catalyzed Hydroboration of Perfluoroalkyl(aryl)ethylenes with CBH in THF

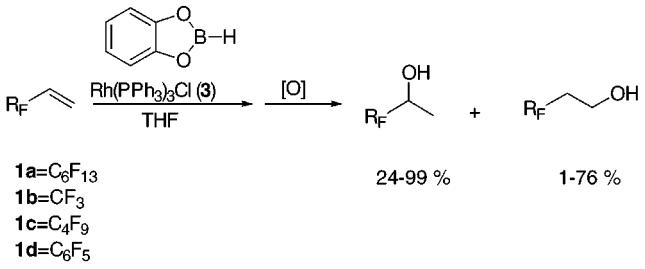
no.	R_F	T, °C	time (h)	yield (%)[a]	2°-ol	1°-ol
1a	C_6F_{13}	20	0.25	82 (71)	72	28
1a	C_6F_{13}[b]	20	0.25	84 (72)	75	25
1a	C_6F_{13}	0	0.50	84 (74)	90	10
1a	C_6F_{13}	−25	0.75	89 (77)	98	2
1a	C_6F_{13}[b]	−25	0.75	87 (74)	98	2
1b	CF_3	−25	0.75	87	97	3
1c	C_4F_9	−25	0.75	84 (73)	99	1
1d	C_6F_5	20	0.25	89 (80)	97	3
1d	C_6F_5[b]	20	0.25	91 (82)	97	3

[a] GC (isolated). [b] $Rh(NBD)(dppb)^+BF_4^-$ used as catalyst.

We surmised that altering the electronics and sterics of the catalyst could impede secondary and impose selective primary insertion of the fluoroalkene into the rhodium complex. Accordingly, we selected Wilkinson's catalyst ($Rh(PPh_3)_3Cl$ (**3**) due to the metal coordinated anion and large cone angle of the PPh_3 ligands.

The hydroboration of **1a** with 1 mol % of **3** and 1.5 equiv of CBH in THF was complete in 0.5 h (^{11}B NMR δ 34.5 ppm). Alkaline H_2O_2 oxidation provided an excess of the 1°-alcohol (76% vs 24%) in 60% isolated yield. Contrary to the cationic catalysts, lowering the temperature had very little effect on selectivity. Hydroboration was also performed with **1b** and **1c**, and we observed a modest effect of the R_F chain length on the regioselectivity (Scheme 2).

Scheme 2



However, hydroboration of **1d** still provided the Markovnikov product (79%) which improved to >99% upon the addition of excess PPh_3. The results are compiled in Table 2.

(11) Evans, D. A.; Fu, G. C.; Hoyveda, A. H. *J. Am. Chem. Soc.* **1992**, *114*, 6671.

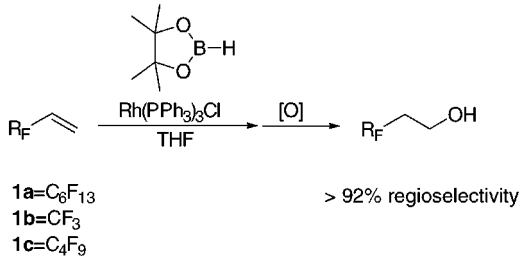
Table 2. $Rh(PPh_3)_3Cl$ (1 mol %) Catalyzed Hydroboration of Perfluoroalkyl(aryl)ethylenes with CBH

no.	R_F	T, °C	time (h)	yield (%)[a]	2°-ol	1°-ol
1a	C_6F_{13}	20	0.5	71 (60)	24	76
1a	C_6F_{13}[b]	20	3	74 (64)	31	69
1a	C_6F_{13}	0	1	79 (67)	36	64
1b	CF_3	20	1	71	47	53
1b	CF_3[c]	20	1	73	45	55
1c	C_4F_9	20	1	74 (62)	38	62
1d	C_6F_5	20	0.5	79 (70)	79	21
1d	C_6F_5[c]	20	0.5	81 (72)	>99	<1

[a] GC (isolated) yield. [b] 0.1 mol % of catalyst. [c] 2 equiv of PPh_3.

Gratified by the partial success achieved, we chose to study the effect of variation in the hydroborating reagents. Wilkinson's catalyst (**3**) had previously been reported to accelerate the hydroboration of simple olefins and acetylenes with pinacolborane (PBH).[12] On the basis of this result, we envisaged that a bulkier borane might lead to the desired anti-Markovnikov product. Indeed, the hydroboration of **1a** (1.5 equiv) with PBH in the presence of 2 mol % of **3** provided the 1°-product in 71% isolated yield and 97% regioisomeric purity! Having attained our goal, we examined other perfluoroalkylethylenes **1b** and **1c**, and the results were similar (Scheme 3).

Scheme 3



The hydroboration of **1d** produced a majority (60 vs 25%) of the 1°-boronate ester along with 15% of a β-styrenyl boronate ester side product. The results are summarized in Table 3.

Table 3. $Rh(PPh_3)_3Cl$ (2 mol %) Catalyzed Hydroboration of Perfluoroalkyl(aryl)ethylenes with PBH at Room Temperature

no.	R_F	time (h)	yield (%)[a,b]	2°-ol	1°-ol
1a	C_6F_{13}	2.5	76 (71)	3	97
1b	CF_3	2	73	8	92
1c	C_4F_9	2.5	74 (68)	4	96
1d	C_6F_5[c]	2.5	70 (61)	25	60

[a] GC (isolated) yield. [b] Yield based on PBH. [c] Isolated as boronate esters.

On the basis of previous mechanistic studies,[9c] we offer the following rationale for our observations (Figure 1). The

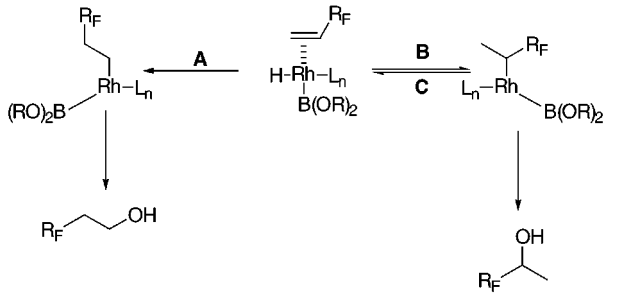


Figure 1.

cationic rhodium catalyst **2** preferentially forms the sterically hindered 2°-alkyl rhodium complex due to the electronic effect exerted by the R_F groups (pathway **B**). In addition, reductive elimination must be more facile than a β-H elimination (**C**) followed by a primary reinsertion sequence (**A**). However, similar to that of styrene, the catalyst binds as a more stable η-3 complex with **1d**, and the corresponding reductive elimination provides the Markovnikov product exclusively.

Upon the reaction of **3** and CBH**,** olefins **1a**−**c** presumably undergo both 1°- and 2°-insertions (pathways **A** and **B**). Reductive elimination of the hindered 2°-alkyl complex may procee at a rate comparable to or even faster than that of pathway **C**, to account for the production of 2°-alcohol. For the hydroboration with PBH, there are two distinct possibilities. A highly selective (>92%) primary insertion takes place due to the steric hindrance of the rhodium−borane complex (path **A**), followed by elimination providing the 1°-product. However, we cannot discount the possibility of an initial olefin insertion pattern similar to CBH, followed by a rapid isomerization of the very sterically congested 2°-alkyl complex placing the metal on the least hindered carbon (pathway **C** and then **A**). Subsequent reductive elimination would yield the 1°-product in high regioselectivity.

In conclusion, we have realized our goal of preparing anti-Markovnikov perfluoroalkyl boranes via neutral Rh-mediated catalytic hydroboration with pinacolborane.[13] In addition, we have also shown that the Markovnikov products can be obtained via cationic Rh-catalyzed hydroboration with catecholborane at low temperatures. Thus we have discovered the first example of direct access to either regioisomer for the catalytic hydroboration of aliphatic olefins by varying the catalyst and borane. Given the importance of fluorine-

(12) Pereira, S.; Srebnik, M. *J. Am. Chem. Soc.* **1996**, *118*, 909.

(13) A typical experimental procedure for the hydroboration of fluoroalkenes with Wilkinson's catalyst and PBH is as follows. Wilkinson's catalyst (2 mol %) was placed and weighed in a 50-mL round-bottom flask under argon followed by 3 mL of dry THF. Pinacolborane (3 mmol) was then added to this solution and maintained at room temperature. After 5 min, **1a** (4.5 mmol) was added slowly and the solution was stirred until the reaction was complete by ^{11}B NMR (δ 33.4). The boronate ester was then oxidized by adding 3 mL of 3 M NaOH and 3 mL of 30% H_2O_2, slowly. The crude product was analyzed by GC to give 97% of the 1°-alcohol and 3% of the 2°-alcohol with a combined isolated yield of 71%.

(14) Brown, H. C. *Organic Syntheses via Boranes*; Wiley-Interscience: New York, 1975. Reprinted edition, Vol. 1. Aldrich Chemical Co. Inc., Milwaukee, WI, 1997. Chapter 9.

containing molecules in agricultural, medicinal, and materials chemistry, we believe these results will lead to the synthesis of various fluoroorganic molecules via established organoborane chemistry.[14]

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