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New insights on the asymmetric hydroboration of perfluoroalkenes

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Enantioselective access to Markovnikov regioisomeric perfluoroalcohols is achieved in the presence of chiral cationic rhodium complexes and specific hydroborating reagents.

The directing effects of electronegative substituents on 2-substituted-1-alkenes can substantially modify the regioselectivity expected both in the transition-metal catalysed[1] and uncatalysed[2,3] hydroboration reaction. The reversal of the regioselectivity from Markovnikov "B–H" addition in unfunctionalised terminal olefins to the anti-Markovnikov manner in perfluoroalkylethylenes,[4] makes it possible to add the borane at the 2-position. However, other factors that must be taken into account for the control of regioselectivity in the hydroboration of fluoroolefins are the hydroborating reagents, the reaction temperature and the electronic nature of the rhodium complex when it is used as a catalyst precursor, Scheme 1.

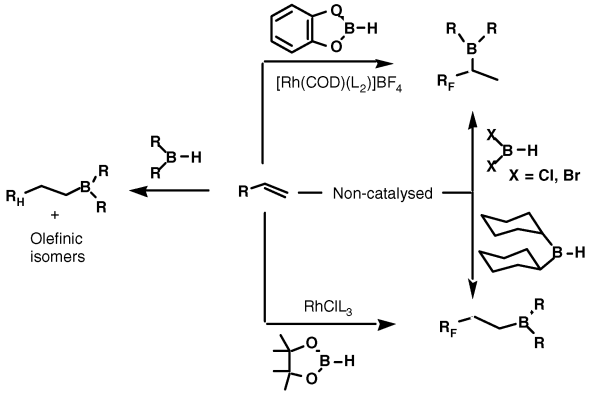
The regioselectivity for a series of fluorinated terminal olefins can be controlled by choosing the appropriate reaction conditions. This makes it possible to synthesise the suitable anti-Markovnikov fluoroalkylborane isomers.[1] However, this process has not been subjected to an asymmetric catalytic version in order to get the chiral product. Due to the synthetic utility of chiral fluoroorganic compounds,[5] both in biological and analytical applications, we decided to undertake for the first time a systematic study of the asymmetrically rhodium-catalysed hydroboration of perfluoroalkylethylenes.

On the basis of the observations by P. V. Ramachandran and H. C. Brown that cationic Rh(I) complexes are effective for the Markovnikov hydroboration/oxidation of perfluoroalkyl-ethylenes when catecholborane is used as reagent,[1] we decided to examine how a cationic catalytic system modified with a chiral diphosphine ligand affected the process (Scheme 2). In order to make a comparison with previous studies where dppb was used as bidentate ligand, we chose (*R*)-BINAP because both ligands make a 7-membered chelate with rhodium in the complex.

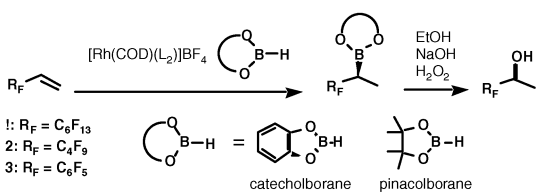
We started by examining the hydroboration/oxidation of a model substrate 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro-1-octene, **1**, with 1 mol% of [Rh(COD)(*R*)-(BINAP)]BF_4 and catecholborane (Scheme 2). As is shown in Table 1, the reaction was almost complete within 1 h at room temperature (entry 1). Regioselection on the secondary alcohol was favoured and increased at low reaction temperatures (entries 2 and 3). Similar behaviour was attributed to the catalytic system [Rh(COD)(dppb)]BF_4 (entries 4–6),[1] although in the latter case the regioselectivity was almost quantitative. When (*R*)-BINAP was used instead of dppb as the chiral ligand, enantiomeric excesses were between 60 and 65.5%, under those reaction conditions.

In contrast to the cationic catalysts, a preferentially primary insertion has been detected of the fluoroalkene into the neutral-Rh complex formed from [Rh(μ-Cl)(COD)]$_2$–2 equiv. (*R*)-BINAP. However, it had very little effect on enantioselectivity, as the e.e. values remained about 60.5% (Table 1, entry 7). The neutralising influence of chlorine as a coordinated counterion was confirmed in a new experiment where the salt $BnMe_3NCl$ was added to the catalytic system [Rh(COD)(*R*)-(BINAP)]BF_4, and the products were distributed in a very similar way to when the neutral system was used (Table 1, entry 8). A complete undesired regioselection towards the primary alcohol was obtained when the sterically hindered borane pinacolborane was used instead of catecholborane as the hydroborating reagent in the presence of [Rh(COD)(*R*)-(BINAP)]BF_4 (entry 9).

The generality of this reaction was demonstrated by carrying out the hydroboration of 3,3,4,4,5,5,6,6,6-nonafluoro-1-hexene, **2**. The results were similar to those when catecholborane was used as the hydroborating reagent (Table 1, entry 10). Alkene isomerization was not observed during the reaction, in contrast to the observed trend with hydroboration of unfunctionalized alkenes.[6]



Scheme 1



Scheme 2

Table 1 Rh–BINAP-catalysed enantioselective hydroboration/oxidation of perfluoroalkylolefins with catecholborane[a]

Entry	Catalytic system [Rh(COD)L–L]-BF_4	R_F	*T*/°C	Yield[b] (%)	2°-alcohol[b] (%)	e.e.[b] (%)
1	(*R*)-BINAP	C_6F_{13}	20	99	70	62(+)
2	″	″	0	99	84	65.5(+)
3	″	″	−78	23	81	60(+)
4[c]	dppb	″	20	82	72	—
5[c]	″	″	0	84	90	—
6[c]	″	″	−25	89	98	—
7[d]	(*R*)-BINAP	″	20	99	46	60.5(+)
8[e]	″	″	20	99	35	50(+)
9[f]	″	″	20	99	0	—
10	″	C_4F_9	0	99	80	64(+)
11	″	C_6F_5	20	86	97	19.5[g]

[a] Standard conditions: olefin/catecholborane/Rh complex = 1/1.1/0.01. Solvent: THF. *T*: 20 °C. Time: 1 h. [b] Determined by GC with chiral column FS-Cyclodex B-IP, 50 m × 0.25 mm. [c] Ref. 1 with 2 mol% of catalyst. [d] Precursor of catalyst: [Rh(μ-Cl)(COD)]$_2$/(*R*)-BINAP. [e] Addition of 0.03 mmol of $BnMe_3NCl$. [f] Pinacolborane. [g] (*R*) Enantiomer.

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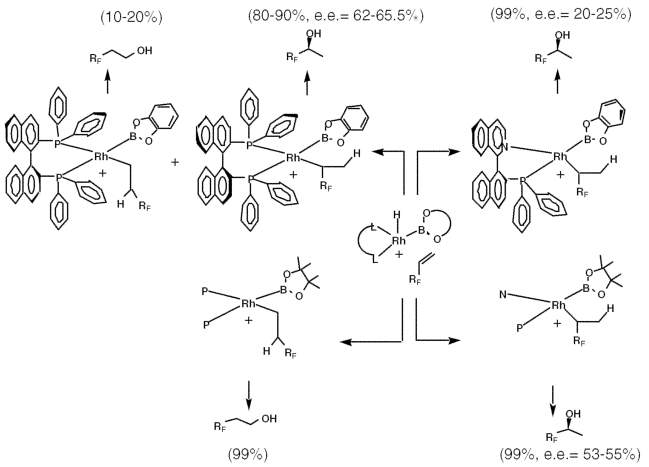
Attending to the fact that the steric factors of the catalyst alter as much as the electronics in the substrate the access to the sterically hindered 2-perfluoroalkyl-rhodium intermediate, we studied the influence of the QUINAP derived Rh-catalyst[7] on the regio- and stereoselectivity of the hydroboration reaction. Using catecholborane as the hydroborating reagent, **1** and **2** were transformed into their corresponding alcohols with complete regioselectivity (Table 2, entries 1 and 3). However the induced chirality was lower than the chirality provided by the analogue (*R*)-BINAP derived Rh-catalyst, even at low temperatures (entry 2). We then conducted the hydroboration of **1** and **2** with the more sterically demanding hydroborating reagent pinacolborane, and surprisingly we also obtained the secondary perfluoroalkylborane quantitatively, with e.e. values up to 55% (entries 4 and 5). Symmetrically internal alkyl pinacolboronate products could be previously formed in the presence of $[RhCl(CO)(PPh_3)_2]$ and $[NiCpCl(PPh_3)Cl]$ but not with $[RhCl(PPh_3)_3]$.[8]

It should be pointed out that both cationic Rh-catalytic systems behave differently towards the formation of the secondary-alkyl rhodium complex due principally to the steric properties of the hydroborating reagent involved in the intermediates. As can be seen in Scheme 3, the use of pinacolborane provides almost exclusively the secondary insertion of the perfluoroalkenes on the "(*S*)-QUINAP–Rh" catalyst, but the primary insertion of the same substrates on the "(*R*)-BINAP–Rh" catalyst. Presumably the most congested "(*R*)-BINAP–Rh–pinacolboryl" intermediate could be the reason for the terminal olefin insertion. However it cannot be excluded that this product may also be the result of the isomerization of a plausible secondary alkyl–rhodium intermediate into the primary alkyl–rhodium, throughout a β-H elimination process, which could also be favoured by the steric demand around the metal. A high and complete degree of the secondary alkyl–rhodium complex is obtained by using both "(*R*)-BINAP–Rh" and "(*S*)-QUINAP–Rh" complexes, respectively, when catecholborane is involved in the reaction. In these cases, the lower steric demand around the reaction site leads to placement of the metal at the most hindered carbon, as is expected because of the electronic effect exerted by the fluorinated alkene.

Table 2 Rh–QUINAP-catalysed enantioselective hydroboration/oxidation of perfluoroalkenes[a]

Entry	Hydroborating reagent	R_F	*T*/°C	Yield[b] (%)	2°-alcohol[b] (%)	e.e.[b] (%)
1	catecholborane	C_6F_{13}	20	99	99	20(+)
2	″	″	0	99	99	19(+)
3	″	C_4F_9	20	99	99	25(+)
4	pinacolborane	C_6F_{13}	20	99	99	55(+)
5	″	C_4F_9	20	99	99	53.5(+)
6	catecholborane	C_6F_5	20	97	97	18[c]

[a] Standard conditions: olefin/catecholborane/Rh complex = 1/1.1/0.02. Solvent: THF. *T*: 20 °C. Time: 1 h. [b] Determined by GC with chiral column FS-Cyclodex B-IP, 50 m × 0.25 mm. [c] (*S*) Enantiomer.



Scheme 3

To obtain a total picture of the process, it should be mentioned that the oxidation of the secondary alkyl–rhodium intermediate, obtained from both chiral complexes, "(*S*)-QUINAP–Rh" and "(*R*)-BINAP–Rh", provided principally the same (+)-enantiomer. This contrasts substantially with the trend observed in the hydroboration/oxidation of styrene, where the "(*S*)-QUINAP–Rh" catalyst provided the (*S*)-1-phenylethanol and the "(*R*)-BINAP–Rh" catalyst provided the (*R*)-enantiomer.[9] The enantiodifferentiation in the case of the vinylarenes has been previously explained by some intermolecular π–π stacking interaction between the ligand and the substrate.[10] The lack of phenyl groups in the perfluoroalkenes **1** and **2** suggests that the coincidence in the main enantiomer formed could be due to the configuration of the Rh–H fragment when it is transferred to the coordinated alkenes. This extreme is confirmed by an additional experiment, where 2′,3′,4′,5′,6′-pentafluorostyrene was subjected to the hydroboration/oxidation reaction with catecholborane and both chiral catalytic systems. In accordance with the regioselective trend observed with the hydroboration of vinylarenes, the aromatic perfluoroalkene gave the (*S*) enantiomer product in presence of the "(*S*)-QUINAP–Rh" and the (*R*) enantiomer with (*R*)-BINAP (Table 1, entry 11, Table 2, entry 6, respectively).

The consistently moderate e.e. values (55–65%) obtained here in the hydroboration of aliphatic perfluoroalkenes are even higher than those observed in the aromatic perfluoroalkenes (18–19.5%), and in electron-deficient vinylarenes such as 3,5-bis-trifluoromethylstyrene (5%), and 2,6-difluorostyrene (< 15%).

The results show how asymmetry can be induced in the hydroboration of perfluoroalkenes. The search for new systems to improve the e.e. is in progress.

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