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Catalytic asymmetric hydroboration of heterofunctional allylic substrates: an efficient heterogenized version

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Abstract—The hydroboration of heterofunctional allylic systems with catecholborane (HBcat) using neutral and cationic rhodium complexes modified with P–P and P–N bidentate chiral ligands has been described in order to produce the secondary heteroorganoboronate ester as a major product with moderate enantioselectivity. The immobilization of cationic chiral rhodium complexes onto clays has beneficial effects on the recyclability and reuse of the catalytic system in particular for the hydroboration of allyl aryl sulfones.

1. Introduction

Regiochemical control in the hydroboration reaction of vinylarenes can be assessed by a catalytic system, providing suitable access to secondary organoboronate compounds.[1] Alternatively, the electronic properties of heterofunctional vinylic substrates, such as perfluoroalkenes[2] and aryl vinyl sulfides,[3] allow strong regiocontrol toward the secondary isomer formation, in the catalytic hydroboration with catecholborane (HBcat, cat = 1,2-$O_2C_6H_4$). This particular electronic influence from heteroatom-containing substrates has also been observed in the catalyzed hydroboration of aryl allyl sulfones ($PhSO_2CH_2CH{=}CH_2$)[4] and allyl sulfonamides ($ArSO_2NRCH_2CH{=}CH_2$; R = H, Ph, Bz)[5] using the precursors [$RhCl(PPh_3)_3$] and [$HRh(PPh_3)_3$] as catalysts; this is in contrast to the catalytic hydroboration of 1-phenylprop-2-ene where mixtures of linear and branched product were formed simultaneously.[6]

The regioselectivity toward the secondary regioisomer has permitted the study of the asymmetric version of the catalyzed hydroboration/oxidation of vinylarenes.[7] However, to the best of our knowledge, the asymmetric version of the catalytic hydroboration reaction of heteroatom-containing substrates has only been carried out in the case of perfluoroalkenes[8] and aryl allyl sulfones[9] by our group. Since heteroorganoboronate esters are extensively applied in medicine[10] and organic synthesis,[11] we wanted to extend this study to the catalytic hydroboration of heterofunctional allylic substrates, in order to see the influence of the electronic properties of the O, N, and S heteroatoms on the regiocontrol, and in the stereocontrol. In these cases where the catalytic system provides an efficient and selective route to the corresponding secondary organoboronate product, we explored the recovery and recycling of the active metal species involved. The immobilization of chiral rhodium-complexes onto clays had provided clear advantages in the past toward the asymmetric hydroboration of vinylarenes,[12] such as an improved stability of the metal species under air, easy separation from the reaction mixture by simple filtration and recycling for consecutive runs without the loss of activity, regio- and stereoselectivity. Indeed, there are few examples of recovery of the catalyst in hydroboration reactions,[13] but even less on the recycling capability. The most recent work by Leitner et al. using the biphasic IL/$scCO_2$ methodology is one of the few examples.[14] It is also noteworthy that none of these previous attempts[13,14] for recycling the catalytic system was studied under the asymmetric version.

2. Results and discussion

The use of ionic Rh(I) compounds modified with chiral ligands such as (*R*,*R*)-BDPP and (*S*)-QUINAP (Fig. 1) has already been demonstrated to catalyze aryl allyl sulfones with a total conversion and high regioselectivity but moderate enantiomeric excesses.[9] This previous work, was in agreement with Wescott's[5] observations on the hydroboration of allyl sulfonamides, as far as the requirement

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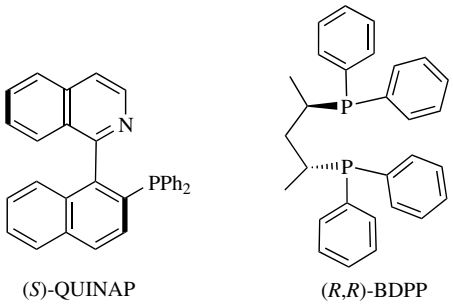


Figure 1.

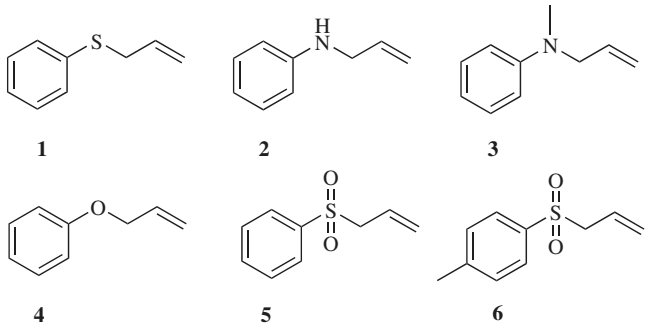


Figure 2.

of an excess of hydroborating reagent is concerned, to keep the catalytic activity high enough.

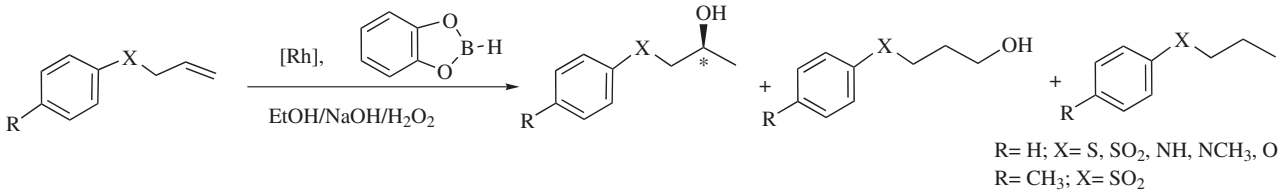
When the catalytic hydroboration/oxidation (Scheme 1) was performed on a series of heterofunctional allylic substrates (Fig. 2) using cationic Rh complexes modified with (*R*,*R*)-BDPP and an excess of HBcat as a hydroborating reagent, conversion of the substrates was completed after 1 h (Table 1).

The regiocontrol of the hydroboration/oxidation reaction seems to depend on the electronic influence of the heterofunctional group which plays a decisive role in obtaining the desired branched product. As a general behavior, the sulfone group of substrates **5** and **6** selectively induced the Markovnikov alcohol product (Table 1, entries 1 and 3). However, the analogue sulfide substrate **1** showed a lower regiocontrol giving a few percentage of the secondary alcohol but linear and hydrogenated product instead (Table 1, entry 5). When the cationic rhodium-complex was modified with (*S*)-QUINAP, the percentage of the branched organoboronate product was slightly improved upon. In the case of substrates *N*-allylaniline **2** and *N*-allyl-*N*-methylaniline **3**, with both cationic and neutral complexes, the regiocontrol was only moderate, although the hydrogenated byproduct was almost not observed (Table 1, entries 7–14). This is in contrast with Wescott's[5] observations on the catalytic hydroboration of allyl sulfonamides which show a competing isomerization reaction as the main reason for the branched isomer formation in high yields. In fact, they proposed a tandem isomerization/hydroboration catalytic reaction whereby a rhodium-hydride complex could be involved in the in situ transformation of allyl sulfonamides to the *N*-prop-1-en-1-yl sulfonamide $ArSO_2NHCH{=}CHCH_3$ and *N*-propylidene sulfonamide $ArSO_2N{=}CHCH_2CH_3$. While the secondary heteroorganoboronate was explained as the main product of the hydroboration of $ArSO_2NHCH{=}CHCH_3$, the hydroboration of $ArSO_2N{=}CHCH_2CH_3$ provided the hydrogenation product.

The hydroboration/oxidation of phenyl allyl ether **4** with neutral and ionic rhodium complexes, showed a similar activity and selectivity to *N*-allyl-*N*-methylaniline **3** (Table 1, entries 15–18). We observed that in both cases, the modification of rhodium complexes with (*S*)-QUINAP provided larger percentages of the secondary alcohol than with (*R*,*R*)-BDPP as the chiral ligand.

The enantioselectivities obtained were moderate and were determined either from the ^1H NMR spectra in the presence of the chiral shift reagent $Eu(TFC)_3$ or by CG with a chiral column. Contrary to the electronic influence of the heterofunctional group on the branched isomer formation, the enantioselectivity was not affected. When the catalytic system was $[Rh(COD)_2]BF_4$/(*R*,*R*)-BDPP the ee values were found to be between 22% and 32% for the secondary alcohol obtained from substrates **1**–**6**. However, lower ee values could be obtained for the same substrates with the catalytic system $[Rh(COD)_2]BF_4$/(*S*)-QUINAP. For the allyl phenyl ether substrate **4**, the use of neutral and ionic complexes modified with (*S*)-QUINAP afforded higher asymmetric induction than cationic complex $[Rh(COD)_2]BF_4$, modified with (*R*,*R*)-BDPP (Table 1, entries 15 and 18).

In order to perform the heterogenized version of the catalytic asymmetric hydroboration of heterofunctional allylic systems, we selected the Rh(I) catalytic system that showed the highest activity and selectivity. We tested the long-term stability of $[Rh(COD)_2]BF_4$/(*R*,*R*)-BDPP and its recovery and reuse in consecutive runs by its immobilization in the smectita clay montmorillonite MK-10 (MK-10), previously treated at 100 °C for 24 h. To immobilize the ionic rhodium complex into the MK-10, the colored solution of the metal



Scheme 1.

Table 1. Homogeneous asymmetric hydroboration/oxidation of aryl allyl systems with neutral and cationic rhodium catalytic precursor[a]

Entry	Catalytic system	Substrate	Secondary alcohol[b] (%)	ee[c] (%)	Linear alcohol[b] (%)	Hydrogenated product[b] (%)
1	$[Rh(COD)_2]BF_4$/(*R*,*R*)-BDPP	**5**	99	32 (*S*)	1	—
2[e]	$[Rh(COD)_2]BF_4$/(*S*)-QUINAP	**5**	85	12 (*R*)	15	—
3	$[Rh(COD)_2]BF_4$/(*R*,*R*)-BDPP	**6**	98	34 (*S*)	—	2
4[e]	$[Rh(COD)_2]BF_4$/(*S*)-QUINAP	**6**	70	16 (*R*)	30	—
5	$[Rh(COD)_2]BF_4$/(*R*,*R*)-BDPP	**1**	7[f]	—	67	25
6	$[Rh(COD)_2]BF_4$/(*S*)-QUINAP	**1**	30[f]	—	30	40
7	$[Rh(COD)_2]BF_4$/(*R*,*R*)-BDPP	**2**	67	23 (*S*)	33	—
8	$[Rh(\mu\text{-}Cl)(COD)]_2$/(*R*,*R*)-BDPP	**2**	62	12 (*S*)	35	3
9	$[Rh(COD)_2]BF_4$/(*S*)-QUINAP	**2**	60	20 (*R*)	39	1
10	$[Rh(\mu\text{-}Cl)(COD)]_2$/(*S*)-QUINAP	**2**	74	23 (*R*)	23	3
11	$[Rh(COD)_2]BF_4$/(*R*,*R*)-BDPP	**3**	41	22 (*S*)	59	—
12	$[Rh(\mu\text{-}Cl)(COD)]_2$/(*R*,*R*)-BDPP	**3**	22	23 (*S*)	88	—
13	$[Rh(COD)_2]BF_4$/(*S*)-QUINAP	**3**	51	26 (*R*)	49	—
14	$[Rh(\mu\text{-}Cl)(COD)]_2$/(*S*)-QUINAP	**3**	57.5	22 (*R*)	42.5	—
15	$[Rh(COD)_2]BF_4$/(*R*,*R*)-BDPP	**4**	40	15 (*S*)[d]	60	—
16	$[Rh(\mu\text{-}Cl)(COD)]_2$/(*R*,*R*)-BDPP	**4**	24	22 (*S*)[d]	76	—
17	$[Rh(COD)_2]BF_4$/(*S*)-QUINAP	**4**	61	23 (*R*)[d]	39	—
18	$[Rh(\mu\text{-}Cl)(COD)]_2$/(*S*)-QUINAP	**4**	68	25 (*R*)[d]	32	—

[a] Standard conditions: substrate/HBcat/Rh precursor = 1:3:0.0075, solvent: THF, *T*: 25 °C; *t*: 1 h. Oxidative workup with EtOH/NaOH/H_2O_2.
[b] Conversion, selectivities calculated by ^1H NMR in $CDCl_3$. Characterization was made in comparison with pure products, Refs. 16 and 17.
[c] Enantiomeric excess of the branched alcohol determined by ^1H NMR in the presence of chiral shift reagent Eu(TFC)$_3$. Absolute configuration was assigned by comparison with Ref. 15.
[d] Enantiomeric excess of the branched alcohol was determined by GC with a chiral column, on derivative alcohols. Absolute configuration was assigned by comparison with Ref. 15.
[e] Ref. 9.
[f] Branched organoboronate products.

Table 2. Heterogenized asymmetric hydroboration/oxidation of aryl allyl sulfones[a]

Entry[a]	Catalytic system	Substrate	Run	Conversion[b] (%)	Branched[b] (%)	ee[c] (%)	Linear[b] (%)
1	[Rh((*R*,*R*)-BDPP)$(COD)_2$]BF_4/MK-10	**5**	1	100	93	32 (*S*)	7
			2	100	98	34 (*S*)	2
			3	100	94	36 (*S*)	6
			4	89.5	97	29 (*S*)	3
2	[Rh((*R*,*R*)-BDPP)$(COD)_2$]BF_4/MK-10	**6**	1	100	>99	30 (*S*)	—
			2	100	>99	28 (*S*)	—
			3	100	>99	25 (*S*)	—

[a] Standard conditions: substrate/HBcat = 1:3 and 1.5% of catalytic precursor immobilized in 250 mg of MK-10, solvent: THF, *T*: 25 °C; *t*: 2 h. Oxidative work-up with EtOH/NaOH/H_2O_2.
[b] Conversion, selectivities calculated by ^1H NMR in $CDCl_3$. Characterization was made in comparison with pure products, Ref. 17.
[c] Enantiomeric excess of the branched alcohols was determined by ^1H NMR in the presence of chiral shift reagent Eu(TFC)$_3$. Absolute configuration was assigned by comparison with Ref. 15.

compound in anhydrous dichloromethane with MK-10 was stirred for 24 h at room temperature, under nitrogen, following a solvent-impregnation methodology.[12,18] The high superficial area of the montmorillonite allows an immobilization via adsorption of the cationic complex and thus permitting an easy accessibility of the substrate to the immobilized complex.

The experiments with the heterogenized rhodium catalytic system [Rh((*R*,*R*)-BDPP)$(COD)_2$]BF_4/MK-10 were carried out using the previously optimized conditions for the homogeneous version in the hydroboration/oxidation of both allyl phenyl sulfone **5** and allyl aryl sulfone **6** with HBcat. The results are shown in Table 2.

The activities, selectivities, and enantioselectivities were similar to those of the homogeneous catalytic system from the first run and were maintained during four consecutive runs (Table 2). Leaching of the catalyst was not observed. These results show the capability of the [Rh((*R*,*R*)-BDPP)(COD)]BF_4/MK-10 catalytic system to be recovered and reused in the asymmetric catalytic hydroboration/oxidation reaction of allyl aryl sulfone for more than four runs, obtaining the secondary alcohol as the major product with moderate enantiomeric excess.

3. Conclusion

We can conclude that the regioselectivity toward the secondary heteroorganoboronate ester in the hydroboration of heterofunctional allylic substrates, is controlled by the nature of the heteroatom, following the order: $SO_2 > NH > N(CH_3) \sim O \gg S$. However, the enantioselec-

tivity seems to be controlled by the chiral ligand and the nature of the complex giving in all the cases moderated enantiomeric excess. The cationic rhodium complex modified with (*R,R*)-BDPP was immobilized in MK-10 and employed in the heterogenized hydroboration/oxidation reaction of the allyl aryl sulfones showing an efficient recovery and reuse of the catalytic system without the loss of activity and selectivity.

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