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COMMUNICATION

Chiral *N*-*tert*-butanesulfinyl α,β-unsaturated ketimine: a simple and highly effective olefin/sulfinimide hybrid ligand for asymmetric 1,4-additions†

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One novel type of chiral olefin/sulfinimide hybrid ligands has been developed through a simple one-step condensation of α,β-unsaturated ketones with *tert*-butanesulfinamide and utilized successfully for rhodium-catalyzed asymmetric conjugated additions to furnish the desired adducts in high yields with excellent ee's.

Chiral olefin ligands have become one type of important ligands for asymmetric catalysis.[1] Numerous chiral dienes,[2] phosphorus/olefin,[3] and nitrogen/olefin[4] hybrid ligands have been well developed and successfully utilized for various transition-metal-catalyzed asymmetric reactions. However, hybrid olefin ligands contained other coordination elements have rarely been reported. Until very recently, Knochel,[5] Xu,[6] and our group[7] independently and simultaneously reported the development of chiral hybrid sulfur-olefin ligands **1–3** for rhodium-catalyzed asymmetric 1,4-additions (Fig. 1).[8] Promising activity and selectivity have been achieved for this novel type of ligands. Interestingly, both ligands **2a** and **3** were employed the chiral *tert*-butanesulfinamide as the key moieties.[9,10] Because of the intriguing features such as the readily available chiral source and the ease of synthesis, further exploring *tert*-butanesulfinamide incorporated novel olefin ligands is important and attractive.

In our previous work, we found that the sulfur chirality of ligands **3** played a crucial role for the observed high enantioselectivity, while the allyl carbon chirality had little impact on both activity and selectivity.[7] This would suggest that elimination of this stereochemical element might have no effect on the outcome. Hence, we envisaged that ligands **3** could be simplified as more practical ligands **4** which could be easily prepared by a one-step condensation of chiral *tert*-butanesulfinamide with a variety of α,β-unsaturated ketones or aldehydes. In addition, we predict that ligands **4** would still maintain high activity and selectivity for rhodium-catalyzed asymmetric conjugated additions (Scheme 1). Herein, we wish to report our efforts on this subject.

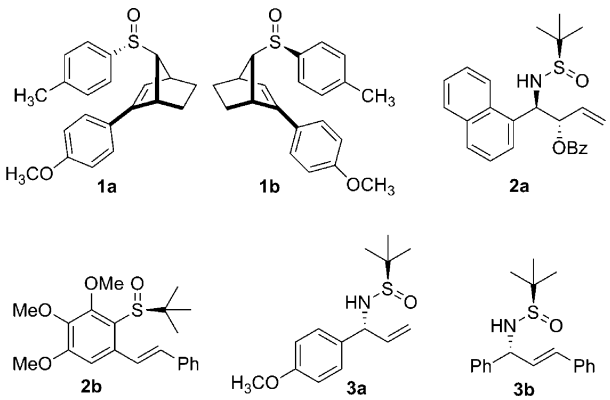
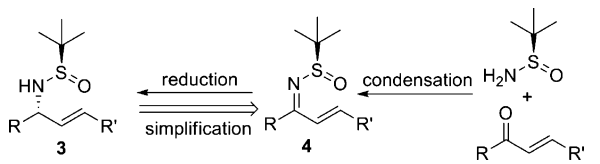


Fig. 1 Chiral olefin/sulfur ligands developed recently.



Scheme 1 Strategy for the development of chiral olefin/sulfinimide hybrid ligands.

Initially, a well-known compound[11] **4a** obtained by the condensation of chalcone with (*R*)-*tert*-butanesulfinamide was subjected to Rh(I)-catalyzed asymmetric 1,4-addition to evaluate the effect of directly using *N*-*tert*-butanesulfinyl α,β-unsaturated ketimine as ligand. It was found that the reaction of phenylboronic acid (**6a**) and 2-cyclohexenone (**5a**) went smoothly to furnish product **7a** in quantitative conversion with 92% ee (Scheme 2). In comparison with the previously reported ligand **3b**, under the same conditions, ligand **4a** gave a better reactivity with only a slightly lower ee (Scheme 2). This promising result encouraged us to prepare a variety of chiral olefin/sulfinimide hybrid ligands by a one-step condensation of (*R*)-*tert*-butanesulfinamide with α,β-unsaturated ketones or an aldehyde according to the well established methodology (Fig. 2).[11,12]

Further study on the optimization of the reaction conditions showed that the enantioselectivity could be improved to 97% when the reaction of 2-cyclohexenone (**5a**) and phenylboronic

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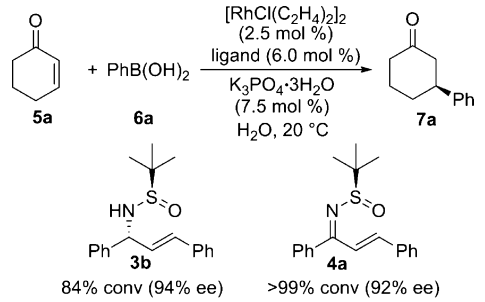
† Electronic supplementary information (ESI) available: The procedure for Rh(I)-catalyzed conjugated addition and the characterization and data for the determination of enantiomeric excess of addition products along with the NMR spectra. See DOI: 10.1039/c1ob05971h



Scheme 2 Initial study with chiral olefin/sulfinimide hybrid ligand.

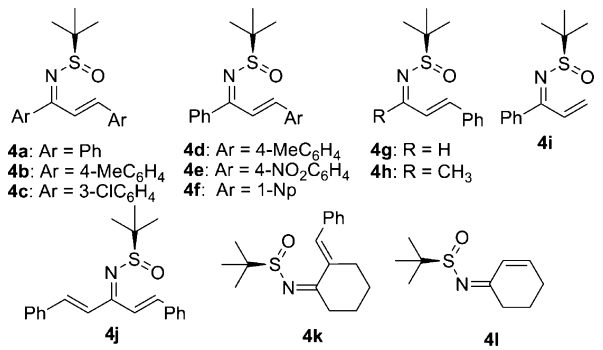


Fig. 2 Selected chiral olefin/sulfinimide hybrid ligands.

Table 1 Evaluation of chiral olefin/sulfinimide hybrid ligands[a]

Entry	Ligand	Conv (%)[b]	ee (%)[c]
1	**4a**	>99	97
2	**4b**	88	97
3	**4c**	40	94
4	**4d**	79	96
5	**4e**	46	96
6	**4f**	86	96
7	**4g**	44	97
8	**4h**	35	85
9	**4i**	17	65
10	**4j**	44	95
11	**4k**	>99	83
12	**4l**	*NR*[d]	*ND*[e]

[a] All the reactions were carried out with 2-cyclohexenone (**5a**) (0.33 mmol), phenylboronic acid (**6a**) (0.50 mmol), $K_3PO_4{\cdot}3H_2O$ (0.025 mmol), $[RhCl(C_2H_4)_2]_2$ (0.005 mmol), ligand (0.012 mmol) in MeOH (1.5 mL) at 30 °C under argon for 4 h. [b] The conversion was determined by crude ^1H NMR. [c] The ee was determined by chiral HPLC. [d] No reaction. [e] Not determined.

acid (**6a**) was carried out under the catalysis of Rh/**4a** complexes (3.0 mol %) in MeOH at 30 °C for 4 h (Table 1, entry 1). To search for better ligands, chiral ligands **4b–l** were then subjected to this reaction under the optimal conditions. As shown in Table 1, the majority of ligands modified rhodium catalysts can promote this reaction to furnish the desired adduct **7a** in 17–99% conversions with 65–97% ee's (Table 1, entries 2–11). Ligand **4g** derived from (*E*)-cinnamaldehyde gave 44% conversion with 97% ee (Table 1, entry 7). Hybrid ligands incorporated with terminal or tri-substituted olefins can also promote this reaction (Table 1, entries 9 and 11). While ligand **4l** prepared from 2-cyclohexenone was not a suitable ligand (Table 1, entry 12). After a careful evaluation, ligand **4a** proved to be the best ligand to afford the highest reactivity and enantioselectivity (Table 1, entry 1).

Table 2 Rhodium-catalyzed asymmetric 1,4-addition[a]

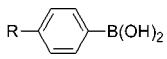
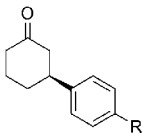
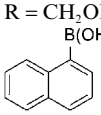
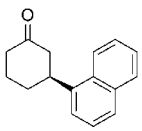
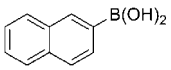
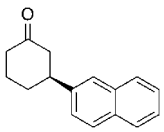
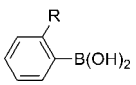
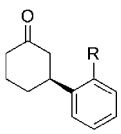
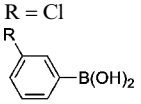
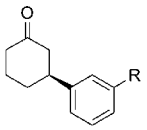
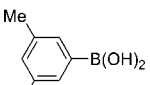
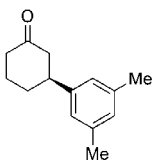
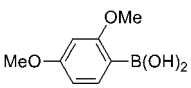
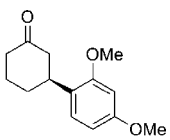
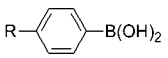
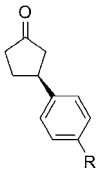
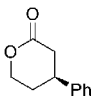
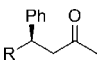
Entry	Boronic acid (**6**)	Product (**7**)[d]	Yield (%)[e]	ee (%)[f]
				
1	R = H		90	96
2	R = Me		99	96
3[b]	R = Ph		96	98
4[b]	R = F		73	96
5[c]	R = CF_3		61	96
6[c]	R = Ac		57	94
7[c]	R = CH_2OH		99	95
8			88	95
9			67	92
				
10	R = OMe		72	92
11	R = Me		96	90
12[c]	R = Cl		91	94
				
13	R = Me		99	96
14[c]	R = F		77	96
15			84	97
16[b]			48	90

Table 2 (*Contd.*)

Entry	Boronic acid (**6**)	Product (**7**)[d]	Yield (%)[e]	ee (%)[f]
				
17	R = H		98	91
18	R = Me		91	89
19[b]	$PhB(OH)_2$		81	97
				
20[b]	$PhB(OH)_2$	R = *n*-C_3H_7	88	60
21[b]		R = *n*-C_5H_{11}	84	60

[a] All the reactions were carried out with enone **5** (0.40 mmol), arylboronic acid **6** (0.60 mmol), $K_3PO_4{\cdot}3H_2O$ (0.030 mmol), $[RhCl(C_2H_4)_2]_2$ (0.006 mmol), ligand **4a** (0.0144 mmol) in MeOH (1.5 mL) at 30 °C under argon for 5 h unless other noted. [b] 5.0 mol % of catalyst and $K_3PO_4{\cdot}3H_2O$ (7.5 mol %) as base. [c] 5.0 mol % of catalyst and CsF (0.6 mmol) as base. [d] The absolute configuration was determined by comparing the optical rotation with the reported one. [e] Yield based on enone **5**. [f] The ee was determined by chiral HPLC.

The substrate scope for ligand **4a** in Rh(I)-catalyzed 1,4-additions was subsequently investigated. As shown in Table 2, in most cases, it was found that ligand **4a** was highly effective for the reactions between 2-cyclohexenone (**5a**) and electron-rich arylboronic acids to give the corresponding products in high yields with excellent ee's, but exhibited relatively lower activity for electron-poor arylboronic acids where 5 mol % of catalyst loading and/or 1.5 equiv of CsF were required (Table 2, entries 1–14). Other cyclic enones are also suitable substrates for this reaction to furnish the corresponding products in 81–98% yields with 89–97% ee's (Table 2, entries 17–19). It is worth noting that ligand **4a** can be also applied to the Rh(I)-catalyzed asymmetric addition of phenylboronic acid (**6a**) to linear enones to give the desired adducts in good yields with moderate ee's (Table 2, entries 20, 21).

Conclusion

In summary, a variety of chiral olefin/sulfinimide hybrid ligands has been successfully developed by a simple one-step condensation of α,β-unsaturated ketones and readily available (*R*)-*tert*-butanesulfinamide. This novel type of ligands exhibited promising activity and enantioselectivity for rhodium-catalyzed asymmetric 1,4-additions to afford the desired products in high yields with up to 98% ee. The ease of synthesis and the diverse structures make this type of ligands attractive for other transition-metal-catalyzed asymmetric reactions.

Acknowledgements

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