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Asymmetric allyltributylstannane addition to ketones catalyzed by chiral PYBOX–In(III) complex immobilized in ionic liquid

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Abstract—An indium complex of chiral PYBOX was applied in the catalytic asymmetric allylation of ketones in the ionic liquid. It was found that this chiral indium complex was strong enough to promote the reaction of ketones with allyltributylstannane smoothly. The products were obtained in moderate to high enantioselectivities, and the chiral catalyst immobilized in the ionic liquid could be reused with comparable enantioselectivities and yields.
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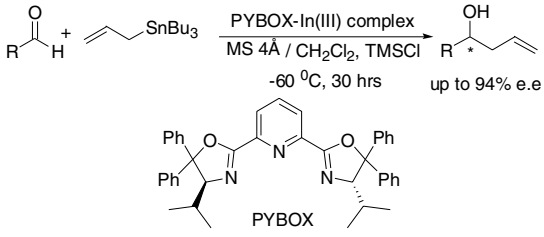
Catalytic enantioselective additions of carbon-based nucleophiles to carbonyl groups constitute an important class of carbon–carbon bond-forming reactions that are of great value in synthetic organic chemistry.[1] The enantioselective allylation of aldehydes and ketones has attracted significant attention, for the optically active secondary and tertiary homoallylic alcohols that are versatile building blocks for the enantioselective synthesis of many biologically active compounds. Therefore, many methods have been developed for the enantioselective synthesis of this class of compounds. However, very few catalytic enantioselective allylation of ketones have been achieved successfully.[2] To the best of our knowledge, strong allylation reagents such as tetraallyl stannane should be needed in these processes mainly due to the significant difference in reactivity between aldehydes and ketones.[3]

Recently, we disclosed a practical catalytic enantioselective allylation of aldehydes with allyltributyl stannane in the presence of the chiral tetraphenyl substituted (*S*)-*i*-PrPYBOX–In(III) complex (Scheme 1).[4] The products could be obtained in good yields and excellent enantiomeric excess when the reaction was carried out in ionic liquids.[5] Further study regarding the recycle of the catalytic system revealed that the chiral In(III) complex in ionic liquid could be reused with good yields and ee values. This observation led us to examine the possibility of realizing the catalytic enantioselective allylation of ketones.



Scheme 1.

Herein, we present the catalytic enantioselective allylation of ketones with allyltributyl stannane by the aid of the chiral tetraphenyl substituted (*S*)-*i*-PrPYBOX–In(III) complex in an ionic liquid (Scheme 2).

We envisioned that the indium(III) complex prepared from indium triflate and the tetraphenyl substituted (*S*)-*i*-PrPYBOX should work as a catalyst to promote the allyltributyl stannane addition to ketones in ionic liquids. A few of the reaction conditions were screened using acetophenone as a model substrate. In the

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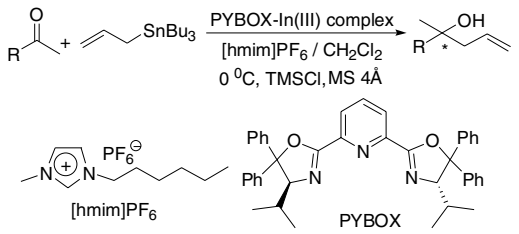


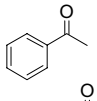
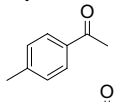
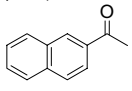
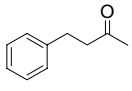
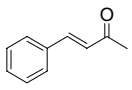
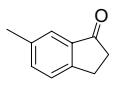
Scheme 2.

presence of 20 mol % catalyst formed in situ from the chiral tetraphenyl substituted (*S*)-*i*-PrPYBOX and indium triflate, the reaction worked enantioselectively to provide the product with the best result (82% yield, 65% ee) in [hmim]PF_6/CH_2Cl_2 at 0 °C. To our delight, the reaction mixture was extracted several times with dry hexane to give the [hmim]PF_6 containing chiral In(III) complex, which could be reused with comparable enantioselectivity and yield for four successive runs (65% ee and 82% yield, 62% ee and 80% yield, 60% ee and 81% yield, 56% ee and 79% yield).

Under the optimized conditions, the asymmetric catalytic system was examined with other ketones. The results are presented in Table 1.

It was found that this chiral indium complex was strong enough to promote all the reactions of various ketones with allyltributylstannane smoothly. The cyclic ketone, 1-indanone, was an excellent substrate for our catalyst, exhibiting an enantioselectivity of 93% with 82% yield (entry 6). Employing α-tetralone resulted in slightly lower enantioselectivity (81% ee, entry 8). The catalytic allylation of aromatic ketones worked well in terms of asymmetric induction and aliphatic ketones exhibited less satisfactory enantioselectivity (entries 4 and 5). In the reaction with α,β-unsaturated aldehydes, the 1,2-addition reaction proceeded exclusively (entry 5).

Table 1. Enantioselective allylations of ketones catalyzed by chiral In(III) complex in ionic liquid

Entry	Ketone	Yield[a,c] (%)	ee[b] (%)
1		82	65 (*R*)
2		78	71 (*R*)
3		80	62 (*R*)
4		74	56 (*S*)
5		68	55 (*S*)
6		82	93 (*R*)
7		58	91 (*R*)
8		74	81 (*R*)

[a] Isolated yield.
[b] The ee values were determined on HPLC.
[c] All the products are characterized by ^1H NMR, ^{13}C NMR, FTIR and mass spectrometry.

In conclusion, a highly catalytic enantioselective allylation of ketones was developed to give enantiomerically enriched homoallylic alcohols with moderate to high enantiomeric excess in an ionic liquid. Further study regarding the recycle of the catalytic system was revealed that the chiral In(III) complex in the ionic liquid could be reused with comparable yields and ee values.

Typical experimental procedure: To an oven dried 5 mL round-bottomed flask equipped with a magnetic stirring bar were added $In(OTf)_3$ (16.9 mg, 0.03 mmol, 0.2 equiv) and 4 Å molecular sieve (120 mg). The solid was azeotropically dried with anhydrous tetrahydrofuran twice (2 mL × 2) prior to the addition of [hmim]PF_6 (0.5 mL) and dichloromethane (0.5 mL). PYBOX (20 mg, 0.033 mmol, 0.22 equiv) was added and the mixture was stirred under nitrogen at room temperature for 2 h to afford a white suspension. A mixture of acetophenone (18 μL, 0.15 mmol, 1 equiv) and TMSCl (23 μL, 0.18 mmol, 1.2 equiv) in dichloromethane (0.2 mL) was added to the resulting suspension and stirred for 10 min. The mixture was then cooled to 0 °C for 15 min followed by addition of allyltributyl stannane (57 μL, 0.18 mmol, 1.2 equiv). The reaction mixture was stirred at 0 °C for 70 h, then dichloromethane was removed in vacuo; the reaction mixture was extracted with dry hexane (5 × 5 mL). The combined hexane was treated with saturated sodium bicarbonate solution at room temperature for 30 min, washed with brine, dried over Na_2SO_4, filtered and concentrated in vacuo. The residual crude product was purified via silica gel chromatography to afford the homoallylic alcohol as a colourless oil (82% yield and 65% ee).

After the reaction mixture was washed with dry hexane (5 × 5 mL), the catalytic system was azeotropically dried with anhydrous tetrahydrofuran twice (2 mL × 2). A second run was performed under identical reaction conditions and resulted in the formation of the product in 83% yield and 62% ee.

(*R*)-2-Phenyl-4-penten-2-ol (entry 1): ^1H NMR (300 MHz, $CDCl_3$): δ 7.21–7.48 (m, 5H), 5.57–5.72 (m, 1H), 5.10–5.18 (m, 2H), 2.70 (dd, $J = 13.9$, 6.3 Hz, 1H), 2.51 (dd, $J = 13.6$, 8.0 Hz, 1H), 2.08 (s, 1H), 1.56 (s, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 147.6, 133.6, 128.1, 126.6, 124.7, 119.4, 73.6, 48.4, 29.8; FTIR (neat): 3415, 3075, 2974, 1640, 1445, 914, 766, 700 cm^{-1}. HRMS Calcd for $C_{11}H_{14}O$ [M−H_2O]: 144.0939, found: 144.0934. The enantiomeric excess was determined by HPLC analysis employing a Daicel Chiralcel OJ column

(hexane–*i*-propanol 98:2, 1.0 mL/min: $t_1 = 7.76$ min for *S* enantiomer, $t_2 = 10.39$ min for *R* enantiomer).

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