Synthesis of Ru–Coordinating Helical Polymer and Its Utilization as a Catalyst for Asymmetric Hydrogen-transfer Reaction

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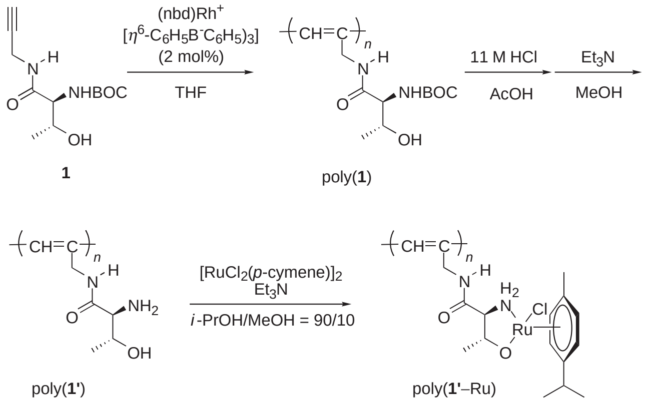
An L-threonine-based helical poly(*N*-propargylamide)–Ru complex was synthesized, and used as a catalyst for hydrogen-transfer reaction of ketones. The enantiomeric excess (ee) values of the formed alcohols ranged from 12 to 36%. On the other hand, an Ru complex with a low-molecular-weight model ligand gave an alcohol with ee as low as 1.8%.

Polymer-supported catalysts attract much attention due to easy recoverability from reaction mixtures, recyclability, and unusual activity due to polymer effect.[1] Attempts have been made to induce chirality into reaction products by immobilizing optically active functional groups on crosslinked polystyrene (PS) beads. Recent examples include PS-supported phosphine–phosphite–Rh complex for olefin hydroformylation,[2] PS-supported diamino–Ru complex for ketone hydrogenation,[3] PS-supported diphenyl prolinol for ketone reduction,[4] and PS-supported *cinchona* ammonium salts for benzylation of glycine derivatives.[5] Though there are several reports concerning polymer-supported catalysts carrying chiral substituents in the side chain, only a few attempts have been made to utilize the main chain chirality of polymers. Takata and co-workers have synthesized helical polymers of binaphthyl salen–Zn[6] and Mn[7] complexes, and examined asymmetric addition and olefin epoxidation using the polymer complexes as catalysts. Yashima et al. have utilized helical poly[*N*-(4-ethynylbenzyl)ephedrine] as a polymeric catalyst for enantioselective addition of dialkylzincs to benzaldehyde.[8] We have reported that poly(*N*-propargylamides) carrying appropriate chiral substituents take a helical structure with predominantly one-handed screw sense. This helix is stabilized by intramolecular hydrogen bonding between the amide groups in the side chains along with steric repulsion.[9] We have also synthesized poly(*N*-propargylamides) derived from some amino acids to find that they transform the structure from helix to random coil, or from helix to helix with opposite helical senses caused by external stimuli such as heat,[10] photoirradiation,[11] solvent,[10,12] and pH.[13] It is expected to utilize amino acid-based helical poly(*N*-propargylamides) as reactive and functional polymers. In this article, we wish to report the synthesis of a helical poly(*N*-propargylamide–Ru complex), and evaluation of its catalytic activity in the asymmetric hydrogen-transfer reaction of ketones to produce chiral alcohols, which are important intermediates in pharmaceutical, agrochemical, flavor, and fragrance industries.[14]

Scheme 1 illustrates the synthetic route for the poly(*N*-propargylamide–Ru complex). L-Threonine-based *N*-propargylamide **1** was synthesized by the condensation of *N*-*tert*-butoxycarbonyl-L-threonine with propargylamine, and it was polymerized with a rhodium zwitterion catalyst in THF to give poly(**1**) with number-average molecular weight of 10,000 quantitatively.[15] It was confirmed that poly(**1**) took a helical structure with predominantly one-handed screw sense from its large specific rotation ($[\alpha]_D = -218°$) as compared to that of **1** ($[\alpha]_D = -12°$), and intense Cotton effect ($[\theta] = -18{,}000\,\mathrm{deg{\cdot}cm^2/dmol}$) at 350 nm, which arises from the conjugated polyacetylene backbone. The *tert*-butoxycarbonyl (BOC) group of poly(**1**) was removed using HCl, and then the resulting polymer with ammonium structure was neutralized with triethylamine to obtain poly(**1′**) carrying chiral *β*-amino alcohol moiety.[16] This structure is suitable to form a ruthenium complex with chiral *N*,*O*-ligand, which has achieved excellent ee values in ketone reduction so far.[17] In the present study, the polymer–ruthenium complex [poly(**1′**–Ru)] was obtained by the reaction of poly(**1′**) with $[RuCl_2(p\text{-cymene})]_2$.[18] The content of incorporated ruthenium was 45%, which was calculated from the weight of ash determined by elemental analysis of the polymer complex. It is considered that poly(**1′**–Ru) carries ruthenium chelated with the amino alcohol moiety as illustrated in Scheme 1. The ^{1}H NMR spectrum reasonably supported the formation of the polymer complex. Figure 1 depicts the CD and UV–vis spectra of poly(**1′**–Ru). It exhibited intense CD signals at 270, 310, and 400 nm based on the conjugated polyacetylene backbone, indicating that it takes a helical structure with predominantly one-handed screw sense. Thus, we could synthesize a helical polymer carrying ruthenium in the side chain.



Scheme 1. Synthesis of poly(**1′**–Ru).

Table 1 summarizes the results of asymmetric hydrogen-transfer reaction of ketones using poly(**1′**–Ru) as a catalyst. The corresponding alcohols were obtained in 23–48% yields. The ee values of the alcohols were 12–36%, which were determined by chiral HPLC. In the reaction of acetophenone, the predominant enantiomer was (*R*)-2-phenylethanol, which was confirmed by comparison with the authentic sample. The highest ee was achieved in the reaction of 2-acetonaphthone. We also

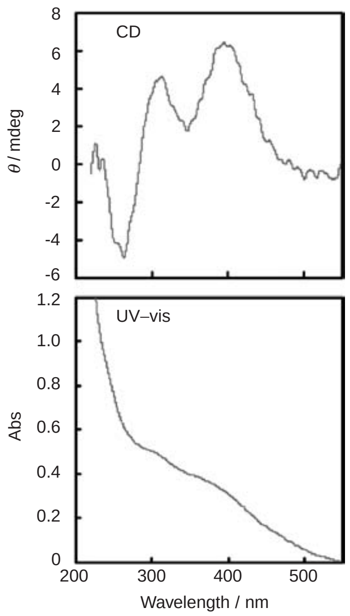
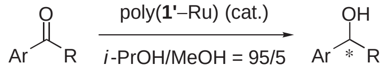


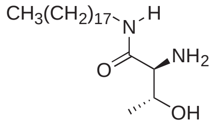
Figure 1. CD and UV–vis spectra of poly(**1′**–Ru) measured in *i*-propanol/methanol = 95/5 in the presence of 10 equiv. of *t*-BuOK.

Table 1. Asymmetric hydrogen-transfer reaction of ketones catalyzed by poly(**1′**–Ru)[a]



Ketone	Yield[b]/%	ee[c]/%
Acetophenone	23	28
1-Acetonaphthone	39[d]	19
2-Acetonaphthone	48	36
1-Indanone	43	12

[a] Conditions: [ketone]$_0$ = 0.10 M, [poly(**1′**–Ru)] = 1 mM (repeating unit), [*t*-BuOK] = 10 mM, solvent *i*-PrOH/MeOH = 95/5 (v/v), 50 °C, 24 h, under N_2. [b] Determined by GC. [c] Determined by HPLC equipped with DAICEL CHIRALPAK IA eluted with hexane/ethyl acetate = 98/2–95/5 (volume ratio). [d] Isolated yield.



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Scheme 2.

examined the hydrogen-transfer reaction of acetophenone with a chiral amino alcohol **2**–Ru complex to find that it induced chirality in the formed alcohol as low as 1.8% ee (Scheme 2). This result suggests that the helical structure of poly(**1′**–Ru) is effective to enhance the catalytic ability for chiral induction.

In summary, we have demonstrated the synthesis of an L-threonine-based helical poly(*N*-propargylamide)–ruthenium complex, and its application as a catalyst for asymmetric hydrogen-transfer reaction of ketones. We believe that tuning the ligand structure improves the synergistic effect of chiralities of the side chain and helical main chain of the polymer, results in higher efficiency of chiral induction.

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15 Details of the synthesis and polymerization of **1** have been reported. See: F. Sanda, H. Araki, and T. Masuda, *Macromolecules*, **37**, 8510 (2004).
16 Poly(**1**) (484 mg, 2 mmol–repeating unit) was dissolved in acetic acid (15 mL). 11 M HCl (15 mL) was added to the poly(**1**) solution, and the resulting mixture was stirred at room temperature for 30 min. It was concentrated by a rotary evaporator, and the residue was dissolved in methanol. An excess amount of triethylamine was added to the solution, and it was poured into acetone to precipitate poly(**1′**). ^{1}H NMR (400 MHz, CD_3OD): δ 1.32 (broad s, -CH_3, 3H), 3.5–4.4 (m, -CH_2-, >CH-O-, >CH-N<, 4H), 6.2 (broad s, -CH=C<, 1H).
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18 A solution of triethylamine (101 mg, 1 mmol) in 2-propanol (9 mL) was added to a solution of poly(**1′**) (30 mg, 0.2 mmol–repeating unit) and [$RuCl_2$(*p*-cymene)]$_2$ (61 mg, 0.1 mmol) in methanol (1 mL). The resulting mixture was stirred at 50 °C overnight, then concentrated by a rotary evaporator. The residue was poured into ether to precipitate poly(**1′**–Ru). ^{1}H NMR (400 MHz, D_2O): δ 1.4 (broad s, -CH_3), 2.4 (broad s, -CH_3, -$CH(CH_3)_2$), 3.5 (broad s), 5.2–6.2 (broad m).

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