Advanced Synthesis & Catalysis

DOI: 10.1002/adsc.201500539

Synthesis of Chiral Polyethers Containing Imidazolidinone Repeating Units and Application as Catalyst in Asymmetric Diels–Alder Reaction

Shinichi Itsuno,[a,*] Tatsuaki Oonami,[a] Nagisa Takenaka,[a] and Naoki Haraguchi[a]

[a] Department of Environmental & Life Sciences, Toyohashi University of Technology, Toyohashi 441-8580, Japan
Fax: (+81)-532-44-6813; e-mail: itsuno@ens.tut.ac.jp

Received: June 3, 2015; Revised: September 28, 2015; Published online: December 9, 2015

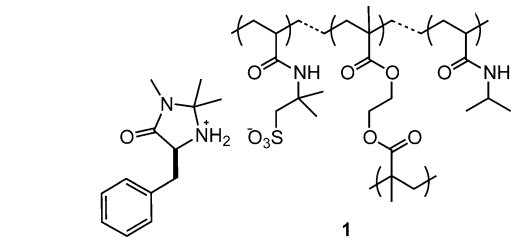
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201500539.

Abstract: In this study, enantiopure imidazolidinones containing two hydroxyphenyl groups were synthesized, and the Williamson synthesis of the chiral bisphenols thus prepared with dihalides afforded polyethers containing chiral imidazolidinone repeating units. These chiral imidazolidinone polyethers exhibited excellent catalytic activity in the asymmetric Diels–Alder reaction. With the use of these polymeric catalysts, enantioselectivities up to 99% were obtained, higher than those obtained by the corresponding monomeric imidazolidinone catalyst in homogeneous solution. The polymeric catalysts were found to be insoluble in commonly used organic solvents, and they could be repeatedly used without the loss of activity.

Keywords: asymmetric catalysis; Diels–Alder reaction; enantioselectivity; organocatalysis; polymers

Introduction

Chiral imidazolidinones[1,2] developed by MacMillan have been known to be excellent organocatalysts for several asymmetric transformations such as Diels–Alder cycloaddition,[3] Friedel–Crafts alkylation,[4] 1,3-dipolar cycloaddition,[5] intramolecular Michael addition,[6] α-chlorination,[7] and α-fluorination.[7] Although high enantioselectivities have been obtained in various asymmetric reactions by the use of these chiral imidazolidinone catalysts, in most cases, a high catalyst loading of 20 mol% is usually required for facilitating a reaction at a reasonable rate. Furthermore, column chromatography is necessary for separating the catalyst before product isolation. In addition, it is typically difficult to recover and reuse the catalyst. The immobilization of a chiral imidazolidinone catalyst may provide potential solutions to the above-mentioned challenges.[8] Several approaches for immobilizing the imidazolidinone catalyst onto solid supports have been reported.[9,10,11,12] We have also synthesized a polymer-immobilized chiral imidazolidinone **1** (Figure 1) by stable ionic bond formation between imidazolidinone and polymeric sulfonate.[13] On the other hand, if the chiral imidazolidinone is incorporated into the polymer main chain as a repeating unit, the microenvironment around the chiral imidazolidinone moiety in the polymer would be different from that in the monomer in solution. Furthermore, the microenvironment in the polymer may affect catalytic activity and enantioselectivity. The use of chiral main-chain polymeric catalysts in asymmetric reactions has positively affected these reactions.[8] Appropriately designed polymeric catalysts can provide high stereoselectivity in asymmetric reactions.



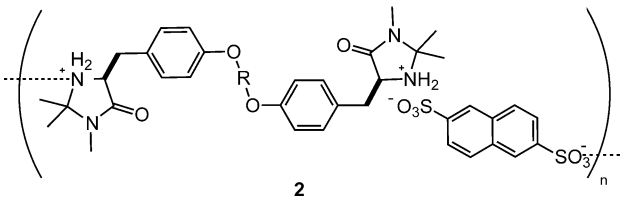


Figure 1. Polymer-immobilized imidazolidinones by using ionic bonds.

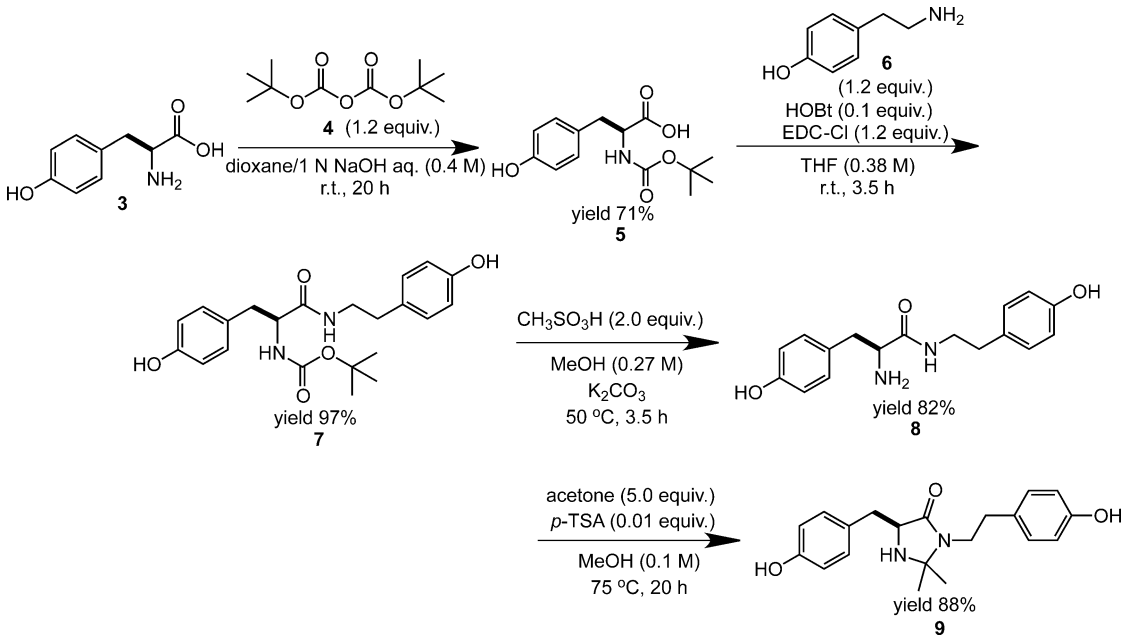
Previously, we have developed such main-chain polymers of a chiral imidazolidinone catalyst **2** (Figure 1) by ionic bond formation between imidazolidinone and sulfonate.[14] Since the secondary amino group of imidazolidinone easily forms the corresponding sulfonates, the reaction between the imidazolidinone dimer and disulfonic acid smoothly occurs to afford chiral polymers containing chiral imidazolidinone sulfonate moieties as repeating units in their main-chain structure. The main chain of the chiral polymer contains ionic bonds. This chiral ionic polymer with a unique main-chain structure was successfully utilized as an organocatalyst in asymmetric Diels–Alder reaction. Some of the chiral ionic polymeric catalysts exhibit slightly higher enantioselectivity than that exhibited by the original monomeric catalyst in the asymmetric reaction.[14] However, the catalytic activity of the chiral imidazolidinone catalyst is affected by its salt structure. The change of the counter anion sometimes dramatically affects enantioselectivity. Sulfonate has always acted as the counter anion of the previously developed polymer.[14]

In this study, we aim to synthesize chiral imidazolidinone polymers having structures composed of various counter anions. Such chiral imidazolidinone polymers can be utilized as catalysts for various asymmetric reactions with a wide range of substrates. The introduction of polymerizable functional groups on the chiral imidazolidinone would make it possible to synthesize chiral polymers containing imidazolidinone as the main-chain repeating unit. The secondary amino groups of imidazolidinone moieties in the polymer chain are easily modified to their salts by acid treatment. Various imidazolidinone salts structures can be prepared by using these polymers. For the synthesis of such chiral imidazolidinone polymers, we chose a strategy that involves the synthesis of polyethers. Surprisingly, the synthesis of chiral polyethers has not been extensively investigated. Some stereoregular polyethers have been investigated for the polymerization of substituted epoxides.[15,16,17] However, the synthesis of chiral polyethers by the Williamson reaction has not been reported. We have synthesized bisphenol-type chiral imidazolidinones. Under Williamson reaction conditions, the polycondensation of the chiral bisphenol thus prepared and dihalide afforded chiral polyethers. In this study, we report the synthesis of chiral bisphenols containing an imidazolidinone structure and their polymerization with dihalide to afford chiral imidazolidinone polyethers. The catalytic activity of the chiral imidazolidinone polyethers was examined for the Diels–Alder reaction of cinnamaldehyde and cyclopentadiene.

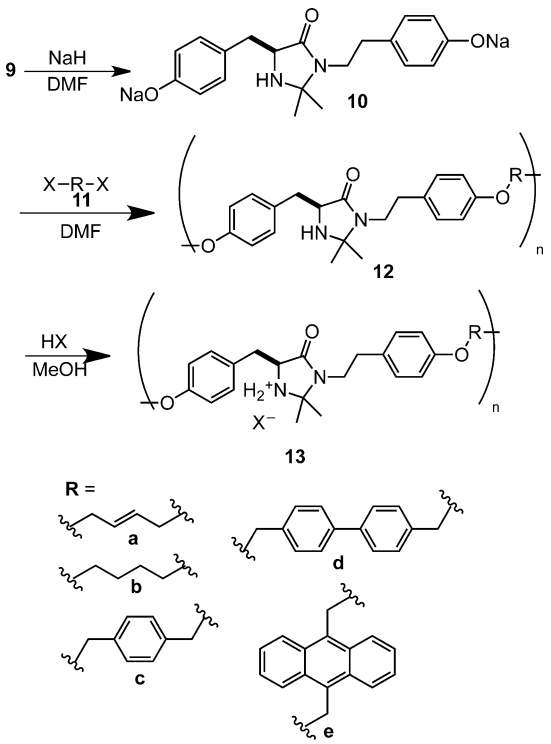
Results and Discussion

Synthesis of Chiral Polyethers Containing Imidazolidinone Repeating Units

Bisphenol-type chiral imidazolidinone **9** was synthesized as shown in Scheme 1. (*S*)-Tyrosine **3** is an α-amino acid containing a hydroxyphenyl group. Another hydroxyphenyl group was introduced by using 4-hydroxyphenylethylamine (tyramine, **6**). (*S*)-*N*-Boc-tyrosine (**5**)[18] was treated with **6** in the presence of 1-



Scheme 1. Synthesis of bisphenol-type chiral imidazolidinone monomer **9**.



Scheme 2. Synthesis of chiral polyethers.

hydroxybenzotriazole (HOBt) and the water-soluble carbodiimide, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC-HCl), to give **7**. The *N*-Boc group from **7** was deprotected to afford α-amino amide **8** having two hydroxyphenyl groups. The reaction of α-amino amide **8** with acetone afforded the desired bisphenol-type chiral imidazolidinone monomer **9**. Details of the synthesis of **9** are described in the Supporting Information.

Generally, bisphenols have been known to be excellent monomers for the synthesis of polycarbonates[19,20] and epoxy resins.[21] Various types of polyethers and poly(ether ketone)s have also been synthesized from bisphenols.[22,23,24] However, the synthesis of chiral polyethers has not been extensively studied. We have recently demonstrated the synthesis of chiral polyethers from *Cinchona* alkaloid derivatives.[25] The repeated Williamson reaction between the diol of the *Cinchona* alkaloid dimer and dihalide afforded chiral polyethers in good yield. In this paper, we applied the same methodology to the synthesis of chiral imidazolidinone polymers.

As shown in Scheme 2, the disodium diphenoxide **10** of chiral imidazolidinone **9** was allowed to react with dihalide **11** to afford the corresponding chiral polyether **12**. The treatment of **12** with acid (HX) resulted in the formation of imidazolidinone salt in each repeating unit of **13**. In this polymer, the chiral imidazolidinone (MacMillan) catalyst is fixed as the repeating unit in the main chain of chiral polymer **13**, which was used as a chiral catalyst for enantioselective reactions including the Diels–Alder reaction. The polymerization of **10** with **11** smoothly occurred to afford chiral polyether **12** in high yield (Table 1). Various types of dihalides including allylic dihalide, alkyl dihalide, and benzylic dihalides were used to prepare chiral polyethers **12**. Table 1 summarizes the molecular weight and molecular weight distribution of the chiral imidazolidinone polyethers **12**. Chiral polyether **12** containing an aromatic linker (**12c**, **12d**, **12e**) exhibited relatively poor solubility in DMF. The molecular weight of the soluble part of these polymers was determined by SEC. The treatment of chiral polyether **12** with acid (HX) yielded polymers **13** having a salt structure.

To evaluate the catalytic activity of the chiral monomeric and polymeric imidazolidinones, the enantioselective Diels–Alder reaction between **19** and **20** was investigated. The Diels–Alder reaction afforded cyclic adduct **21** in quantitative conversion with 93% *ee* by the use of the original MacMillan-HCl catalyst **14** (Figure 2), derived from (*S*)-phenylalanine (Table 2, entry 1).[3] Toluenesulfonate imidazolidinone catalyst **15** (Figure 2) showed similar enantioselectivity for the *endo* adduct (92% *ee*) and somewhat lower enantioselectivity for the *exo* adduct (88% *ee*) (entry 2). Since we used the (*S*)-tyrosine derivative for polymer synthesis, imidazolidinones (**16**–**18**, Figure 2) derived from (*S*)-tyrosine were applied to the same reaction. The asymmetric reaction smoothly proceeded with these catalysts at room temperature to afford chiral cyclic adducts **21** in almost quantitative conversion.

Table 1. Synthesis of chiral polymer **12** from **10** and dihalides **11**.

Entry	Dihalide	Polymer	Yield [%]	M_n[a]	M_w[a]	M_w/M_n[a]
1	**11a**	**12a**	92	18000	42000	2.4
2	**11b**	**12b**	94	17000	28000	1.6
3	**11c**	**12c**[b]	95	12000	37000	3.1
4	**11d**	**12d**[b]	92	6800	8700	1.3
5	**11e**	**12e**[b]	87	5100	5400	1.1

[a] Determined by SEC using DMF as a solvent at a flow rate of 1.0 mL min^{-1} at 40 °C (polystyrene standard).
[b] Partially insoluble in DMF.

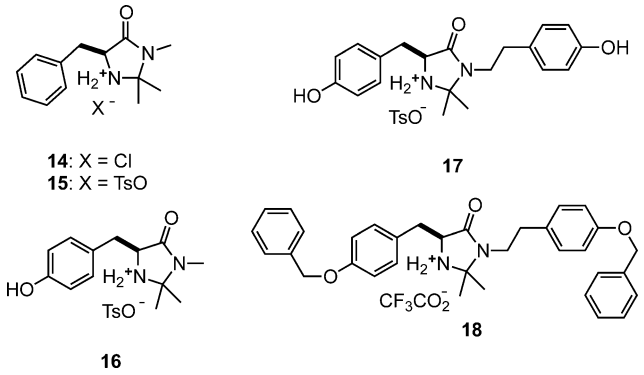


Figure 2. Chiral imidazolidinones.

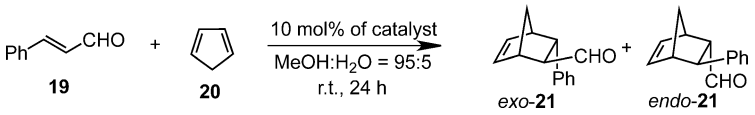
Imidazolidinone catalysts **17** and **18** are model compounds for the polymeric catalyst (entries 4 and 5).

Then, we investigated the use of chiral imidazolidinone salt polymers **13** in the same asymmetric Diels–Alder reaction. Although chiral imidazolidinone salt polymers **13** were totally insoluble in the MeOH:H_2O = 95:5 used for the asymmetric reaction, the reaction smoothly occurred in the presence of **13**. For example, in the presence of **13a-TsO**, the reaction proceeded in MeOH/water = 95:5 at room temperature to afford the corresponding chiral cyclic adduct in 70% yield with 77% *ee* for the *endo* adduct and 67% *ee* for the *exo* adduct (Table 3, entry 1).

As compared with the use of monomeric catalysts **14**–**17**, the use of polymeric chiral catalyst **13a-TsO** exhibited lower enantioselectivity. The structure of the achiral linker R (Scheme 2) in polymer **13** affected the enantioselectivity of the reaction. The polymer-containing butylene chain (**13b-TsO**) exhibited high enantioselectivity (entry 2). Although chiral polymer **13c-TsO** containing a *p*-xylyl linker exhibited decreased enantioselectivity (entry 3), **13d-TsO** and **13e-TsO** exhibited enantioselectivities higher than 80% for both *endo* and *exo* isomers of the product (entries 4 and 5, respectively).

The activated iminium ion, formed by the condensation of chiral imidazolidinone and cinnamaldehyde, underwent reaction with **20** to yield the cyclic adduct. The counter anion of the iminium cation should affect the enantioselectivity. To examine the effect of the counter anions, we tested several counter anions for this reaction. Table 4 summarizes the results obtained using different counter anions. No major differences

Table 2. Asymmetric Diels–Alder reaction using chiral imidazolidinone catalysts.



Entry	Chiral imidazolidinone	Yield [%][a]	21		
			exo/*endo*[b]	*exo ee* [%][c]	*endo ee* [%][c]
1[d]	**14**	94	1.3/1	93	93
2[e]	**15**	94	55/45	88	92
3	**16**	94	55/45	92	88
4	**17**	92	65/35	89	93
5	**18**	94	51/43	92	94

[a] Isolated yield.
[b] Determined by ^{1}H NMR.
[c] Determined by GC (CHIRALDEX β-PH).
[d] See ref.[3]
[e] See ref.[1]

Table 3. Asymmetric Diels–Alder reaction with chiral polymeric catalyst **13-TsO**.

Entry	Chiral polymeric imidazolidinone	Catalyst loading [mmol g^{-1}]	Yield [%][a]	21		
				exo/*endo*[b]	*exo ee* [%][c]	*endo ee* [%][c]
1	**13a-TsO**	1.77	67	58/42	67	77
2	**13b-TsO**	1.76	86	60/40	75	86
3	**13c-TsO**	1.63	61	53/47	73	77
4	**13d-TsO**	1.45	53	53/47	83	82
5	**13e-TsO**	1.40	80	59/41	80	83

[a] Isolated yield.
[b] Determined by ^{1}H NMR.
[c] Determined by GC (CHIRALDEX β-PH).

Table 4. Effect of counter anion on the asymmetric Diels–Alder reaction.

Entry	Chiral polymeric imidazolidinone	X^-	Catalyst loading [mmol g^{-1}]	**21**			
				Yield [%][a]	*exo*/*endo*[b]	*exo ee* [%][c]	*endo ee* [%][c]
1	**13c-BF_4**	BF_4^-	1.89	94	54/46	80	91
2	**13c-TFA**	$CF_3CO_2^-$	1.80	94	59/41	93	97
3	**13c-MsO**	$CH_3SO_3^-$	1.86	94	57/43	85	96
4	**13c-TsO**	$TolSO_3^-$	1.63	61	53/47	73	77
5	**13c-Cl**	Cl^-	2.09	94	61/39	86	95
6	**13c-ClO_4**	ClO_4^-	1.84	94	55/45	76	92

[a] Isolated yield.
[b] Determined by ^{1}H NMR.
[c] Determined by GC (CHIRALDEX β-PH).

Table 5. Effect of trifluoroacetate complexes of polymeric imidazolidinones on the asymmetric Diels–Alder reaction.

Entry	Chiral polymeric imidazolidinone	Catalyst loading [mmol g^{-1}]	**21**			
			Yield [%][a]	*exo*/*endo*[b]	*exo ee* [%][c]	*endo ee* [%][c]
1	**13a-TFA**	1.97	99	57/43	86	95
2	**13b-TFA**	1.97	68	59/41	83	91
3	**13c-TFA**	1.80	99	59/41	93	97
4	**13d-TFA**	1.58	94	61/39	85	91
5	**13e-TFA**	1.52	69	59/41	90	95

[a] Isolated yield.
[b] Determined by ^{1}H NMR.
[c] Determined by GC (CHIRALDEX β-PH).

were observed in the catalytic activity and enantioselectivity of polymeric catalysts **13c**, except for the toluenesulfonate polymer **13c-TsO**, upon the use of which the reactivity and enantioselectivity decreased (Table 4, entry 4). Moreover, of the polymeric catalysts used in this study, trifluoroacetate polymer **13c-TFA** exhibited the highest enantioselectivities for both diastereomers of product **21** (entry 2).

Trifluoroacetates of other polymeric imidazolidinones were also investigated as catalysts in the asymmetric Diels–Alder reaction. Table 5 summarizes the results. The combination of chiral imidazolidinone polymer **12c** and TFA afforded polymeric catalyst **13c-TFA**, which exhibited the highest enantioselectivities for both enantiomers of the Diels–Alder adduct **21** (Table 5, entry 3).

Polymeric chiral imidazolidinone catalysts **13** were insoluble not only in commonly used organic solvents such as dichloromethane, acetonitrile, ethyl acetate, and methanol but also in water. Even though they formed a completely heterogeneous system, the asymmetric reaction smoothly occurred at room temperature, as shown in Table 3, Table 4 and Table 5. After the completion of the reaction, the polymeric catalyst was easily separated by simple filtration or decantation. Table 6 shows the recyclability of the polymeric catalyst as well as the effect of temperature on enantioselectivity. The recovered polymer **13c-TFA** was reused for the same reaction and exhibited high catalytic activity (Table 6, entry 2). The third cycle of reuse led to a decrease in the catalytic activity and enantioselectivity (entry 3). The same polymeric catalyst **13c-TFA** was used in the asymmetric Diels–Alder reactions of 2,3-dimethylbutadiene and acrolein (Scheme 3) and exhibited high catalytic activity (entry 4).

The asymmetric reaction using **13c-TFA** still proceeded at 0 °C. Almost perfect enantioselectivity was observed for the *endo* isomer of the cyclic adduct **21** at 0 °C (entry 5). The recovered polymer **13c-TFA** was treated with TFA and used for the same reaction. High catalytic activity and enantioselectivity were maintained with the polymeric catalyst (entries 5 and 6).

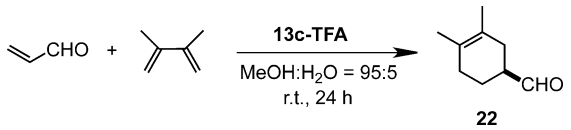
Conclusions

We have successfully synthesized chiral imidazolidinone polyethers **12** by the Williamson reaction of chiral bisphenol-type monomer **9** with achiral dihalides **11**. This is the first example of the synthesis of chiral imidazolidinone polyethers. The treatment of polymers **12** with acid afforded amine salt polymers **13**. These polymers exhibited excellent catalytic activities in the enantioselective Diels–Alder reaction of (*E*)-cinnamaldehyde and cyclopentadiene. High enantioselectivities were observed with the use of **13**. The

Table 6. Recycle use of polymeric imidazolidinone **13c-TFA** in the asymmetric Diels–Alder reaction.

Entry	Temperature [°C]	Time [h]	Product	Yield [%][a]	*exo*/*endo*[b]	*exo ee* [%][c]	*endo ee* [%][c]
1	25	24	**21**	94	59/41	93	97
2[d]	25	24	**21**	94	58/42	87	93
3[e]	25	48	**21**	90	58/42	82	87
4[f]	25	24	**22**	94	-	97	
5	0	24	**21**	81	57/43	96	99
6[g]	0	24	**21**	89	54/46	96	99
7[h]	0	24	**21**	90	53/47	96	98

[a] Isolated yield.
[b] Determined by ^{1}H NMR.
[c] Determined by GC (CHIRALDEX β-PH).
[d] **13c-TFA** used in entry 1 was reused.
[e] **13c-TFA** used in entry 2 was reused.
[f] Diels–Alder reaction between acrolein and 2,3-dimethylbutadiene.
[g] **13c-TFA** used in entry 4 was retreated with TFA and reused.
[h] **13c-TFA** used in entry 6 was retreated with TFA and reused.



Scheme 3. Asymmetric Diels–Alder reaction of acrolein and 2,3-dimethylbutadiene with **13c-TFA**.

structure of **11** and acid HX affected the enantioselectivity. The enantioselective Diels–Alder reaction smoothly occurred in the presence of **13c-TFA**, and higher yields and enantioselectivities (up to 99% *ee*) were observed in comparison with those observed with the use of low-molecular-weight catalysts (**14**, **15**, **16**) in solution. The polymeric catalyst was insoluble in solvent and easily recovered by simple decantation. The acid retreatment of the recovered polymeric catalyst enabled us to repeatedly use the catalyst without the loss of catalytic activity. Chiral imidazolidinone salts exhibit excellent catalytic activity in several asymmetric reactions. Currently, investigation of the catalytic activity of chiral imidazolidinone polymers in various asymmetric transformations other than the Diels–Alder reaction is underway in our laboratory.

Experimental Section

Materials and General Considerations

All solvents and reagents were purchased from Sigma–Aldrich, Wako Pure Chemical Industries, Ltd., or Tokyo Chemical Industry (TCI) Co., Ltd. at the highest available purity and were used as received, unless otherwise noted. Reactions were monitored by thin-layer chromatography using precoated silica gel plates (Merck 5554, 60F254). Column chromatography was performed using a silica gel column (Wakogel C-200, 100–200 mesh). Melting points were recorded using a Yanaco micro melting apparatus and are uncorrected. NMR spectra were recorded on JEOL JNM-ECS400 spectrometers in $CDCl_3$ or DMSO-d_6 at room temperature operating at 400 MHz (^{1}H) and 100 MHz (^{13}C{^{1}H}). TMS was used as an internal standard for ^{1}H NMR and $CDCl_3$ for ^{13}C NMR. Chemical shifts were reported in ppm using TMS as a reference, and the *J* values were recorded in Hertz. IR spectra were recorded on a JEOL JIR-7000 FTIR spectrometer and are reported in cm^{-1}. Elemental analyses (carbon, hydrogen, nitrogen) were performed on a Yanaco-CHN coder MT-6 analyzer. HR-MS (ESI) spectra were recorded on a microTOF-Q II HRMS/MS instrument (Bruker). GC analyses were performed using a Shimadzu capillary gas chromatograph GC-2014 equipped with a capillary column (CHIRALDEX β-PH, 30 m × 0.25 mm). Size exclusion chromatography (SEC) was performed using a Tosoh instrument with HLC 8020 UV (254 nm) or refractive index detection. DMF was used as the carrier solvent at a flow rate of 1.0 mL min^{-1} at 40 °C. Two polystyrene gel columns of bead size 10 μm were used. A calibration curve was made to determine the number-average molecular weight (M_n) and molecular weight distribution (M_w/M_n) values with polystyrene standards. Optical rotation was recorded using a JASCO DIP-149 digital polarimeter using a 10 cm thermostatted microcell.

Synthesis of Chiral Polymer 12a

First, NaH (30 mg, 1.3 mmol) at 0 °C was added to a DMF solution of **9** (136 mg, 0.4 mmol). Second, the reaction mixture was stirred at 0 °C for 1 h, and *trans*-1,4-dibromo-2-butene (84.8 mg, 0.4 mmol) was added. Next, the mixture was stirred at room temperature for 20 h. Finally, diethyl ether (20 mL) was added to the reaction mixture to precipitate the chiral polymer, which was washed with water and ether. Polymer **12a** was obtained as a solid; yield: 179 mg (99%). ^{1}H NMR (400 MHz, DMSO): $\delta = 1.07$ (s, 3H, CH_3), 1.13 (s, 3H, CH_3), 2.61–2.2.76 (m, 3H, CH_2CH_2), 2.86–2.97 (m, 1H, CH_2N), 3.03–3.18 (m, 1H, CH_2Ph), 3.22–3.31 (m, 1H, CH), 3.54 (s, 1H, CH), 4.53 (s, 4H, CH_2CH), 6.02 (s, 2H, $CHCH_2$), 6.78–6.90 (m, 4H, Ar),7.09 (d, $J = 7.9$ Hz, 2H, Ar), 7.16 (d, $J = 7.9$ Hz, 2H, Ar); ^{13}C NMR: (100 MHz, DMSO): $\delta = 27.0$, 28.7, 34.7, 37.5, 42.7, 59.9, 68.1, 76.7,

115.3, 115.4, 129.3, 130.8, 131.4, 131.6, 132.2, 157.6, 157.7, 174.6; M_n (SEC) = 1.8×10^4; $M_w/M_n = 2.4$.

Enantioselective Diels–Alder Reaction of (*E*)-Cinnamaldehyde (19) with Cyclopentadiene (20) using 15

First, *p*-toluenesulfonic acid monohydrate (19.0 mg, 0.1 mmol) was added to a solution of **9** (39.0 mg, 0.1 mmol) in methanol (1.0 mL). Next, the resulting mixture was stirred for 2 h at room temperature. Finally, the solvent was evaporated and the residue dried under vacuum to afford catalyst **17**. ^{1}H NMR (400 MHz, DMSO): $\delta = 1.41$ (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 2.65–2.76 (m, 3H, CH_2CH_2), 2.78–2.88 (m, 1H, CH_2N), 3.23–3.45 (m, 2H, CH_2Ph), 4.43 (s, 1H, CH), 6.69 (d, $J = 8.2$ Hz, 2H, Ar), 6.74 (d, $J = 8.5$ Hz, 2H, Ar), 7.04 (d, $J = 8.2$ Hz, 2H, Ar), 7.14 (d, $J = 8.2$ Hz, 2H, Ar), 9.27 (s, 1H, ArOH), 9.38 (s, 1H, ArOH); ^{13}C NMR: (100 MHz, DMSO): $\delta = 24.3$, 25.4, 34.1, 34.5, 42.6, 49.6, 58.3, 77.9, 116.2, 116.3, 127.0, 129.5, 130.7, 131.2, 156.9, 157.5.

First, after dissolving **17** in MeOH/H_2O = 95/5 (v/v) (1.0 mL), **19** (146 mg, 1.0 mmol) and **20** (206 mg, 3 mmol) were added. Second, the reaction mixture was stirred for 24 h at room temperature and diluted with Et_2O and washed with H_2O and brine. Next, the organic layer was dried over $MgSO_4$, filtered, and concentrated. Finally, the product dimethyl acetal was hydrolyzed by stirring the crude product mixture in CH_2Cl_2:H_2O:TFA (1:0.5:0.25 mL) for 2 h at room temperature, followed by neutralization with a saturated $NaHCO_3$ aqueous solution and extraction with Et_2O. The Diels–Alder adduct was purified by silica gel chromatography (ethyl acetate/hexane = 1/19). Products *exo*-**21** and *endo*-**21** were obtained as colorless liquids; yield: 92%. The *exo*/*endo* ratio was determined to be 65/35 by ^{1}H NMR by comparing the proton signals of the aldehyde. The enantiomeric excess was determined by GC analysis (Astec CHIRALDEX B-PH: injection temperature 180 °C, detection temperature 180 °C, column temperature was increased from 120 °C to 150 °C at 5 °C min^{-1} and then 180 °C at 1 °C min^{-1}): retention times: 26.2 min [*exo*(2*R*)], 26.8 min [*exo*(2*S*)], 27.3 min [*endo*(2*R*)], and 27.7 min [*endo*(2*S*)].

General Procedure for Enantioselective Diels–Alder Reaction of 19 with 20 using Polymeric Catalyst 13

First, trifluroacetic acid (TFA, 50 μL, 0.6 mmol) was added to a suspension of **12a** (49 mg, 0.13 mmol) in methanol (1.0 mL) Second, the reaction mixture was stirred for 2 h at room temperature. Third, the solvent was evaporated and the reesidue dried under vacuum to afford **13a**-**TFA** as a pale yellow solid, which was suspended in MeOH/H_2O = 95/5 (v/v) (1.0 mL). Then, **19** (146 mg, 1.0 mmol) and **20** (206 mg, 3 mmol) were added to the suspension. Next, the reaction mixture was stirred for 24 h at room temperature and filtered through a glass filter to separate polymeric catalyst **13a**-**TFA**, which was washed with Et_2O. Finally, the organic layer of the filtrate was dried over $MgSO_4$, filtered, and concentrated. The product dimethyl acetal was hydrolyzed by stirring the crude product mixture in CH_2Cl_2:H_2O:TFA (1:0.5:0.25 mL) for 2 h at room temperature, followed by neutralization with a saturated $NaHCO_3$ aqueous solution and extraction with Et_2O. The Diels–Alder adduct was purified by silica gel chromatography (ethyl acetate/hexanes = 1/19). Products *exo*-**21** and *endo*-**21** were obtained as colorless liquids; yield: 94%. The *exo*/*endo* ratio was determined to be 57/43 by ^{1}H NMR by comparing the proton signals of the aldehyde. The enantiomeric excess (86% *ee* for *exo* adduct, 95% *ee* for *endo* adduct) was determined by GC analysis (Astec CHIRALDEX B-PH: injection temperature 180 °C, detection temperature 180 °C, column temperature was increased from 120 °C to 150 °C at 5 °C min^{-1} and then 180 °C at 1 °C min^{-1}): retention times: 26.2 min [*exo*(2*R*)], 26.8 min [*exo*(2*S*)], 27.3 min [*endo*(2*R*)], and 27.7 min [*endo*(2*S*)].

Acknowledgements

This study has been supported by JSPS KAKENHI (Grant-in-Aid for Scientific Research)) Grant Number 15K05517 and MEXT KAKENHI (Grant-in-Aid for Scientific Research on Innovative Areas) Grant Number 15H00732.

References

[1] G. Lelais, D. W. C. MacMillan, *Aldrichimica Acta* **2006**, *39*, 79–87.
[2] T. D. Beeson, A. Mastracchio, J. Hong, K. Ashton, D. W. C. MacMillan, *Science* **2007**, *316*, 582–585.
[3] K. A. Ahrendt, C. J. Borths, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2000**, *122*, 4243–4244.
[4] N. A. Paras, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2002**, *124*, 7894.
[5] S. P. Brown, N. C. Goodwin, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2003**, *125*, 1192.
[6] M. T. Hechevarria Fonseca, B. List, *Angew. Chem.* **2004**, *116*, 4048–4050; *Angew. Chem. Int. Ed.* **2004**, *43*, 3958–3960.
[7] Y. Huang, A. M. Walji, C. H. Larsen, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2005**, *127*, 15051.
[8] S. Itsuno, M. M. Hassan, *RSC Adv.* **2014**, *4*, 52023–52043.
[9] a) P. Riente, J. Yadav, M. A. Pericas, *Org. Lett.* **2012**, *14*, 3668–3671; b) V. Chiroli, M. Benaglia, A. Puglisi, R. Porta, P. Jumde, A. Mandoli, *Green Chem.* **2014**, *16*, 2798–2806.
[10] H. Hagiwara, T. Kuroda, T. Hoshi, T. Suzuki, *Adv. Synth. Catal.* **2010**, *352*, 909–916.
[11] T. Mitsudome, K. Nose, T. Mizugaki, K. Jitsukawa, K. Kaneda, *Tetrahedron Lett.* **2008**, *49*, 5464–5466.
[12] V. Chiroli, M. Benaglia, F. Cozzi, A. Puglisi, R. Annunziata, G. Celentano, *Org. Lett.* **2013**, *15*, 3590–3593.
[13] N. Haraguchi, Y. Takemura, S. Itsuno, *Tetrahedron Lett.* **2010**, *51*, 1205–1208.
[14] N. Haraguchi, H. Kiyono, Y. Takemura, S. Itsuno, *Chem. Commun.* **2012**, *48*, 4011–4013.
[15] C. C. Price, R. Spector, A. L. Tumolo, *J. Polym. Sci. Part A-1* **1967**, *5*, 407–416.
[16] T. Tsuruta, *Pure. Appl. Chem.* **1981**, *53*, 1745–1752.
[17] T. Hagiwara, M. Ishimori, T. Tsuruta, *Makromol. Chem.* **1981**, *182*, 501–511.
[18] M. Biswas, A. Saha, M. Dule, T. K. Mandal, *J. Phys. Chem. C* **2014**, *118*, 22156–22165.

[19] W. Zhai, J. Yu, W. Ma, J. He, *Macromolecules* **2007**, *40*, 73.
[20] a) S. Fukuoka, M. Tojo, H. Hachiya, M. Aminaka, K. Hasegawa, *Polym. J.* **2007**, *39*, 91–114; b) H. Baick, W. J. Yang, Y. G. Ahn, K. H. Song, K. Y. Choi, *J. Appl. Polym. Sci.* **2015**, *132*, 41609/1–41609/10.
[21] Z. Wu, J. Li, Z. Wang, *Polym. Adv. Technol.* **2015**, *26*, 153–159.
[22] T. Na, K. Shao, J. Zhu, H. Sun, D. Xu, Z. Zhang, C. M. Lew, G. Zhang, *J. Power Sources* **2013**, *230*, 290–297.
[23] N. Hurduc, A. Daoudi, J. M. Buisine, V. Barboiu, C. I. Simionescu, *Eur. Polym. J.* **1998**, *34*, 123–125.
[24] M. Wu, J. Guo, H. Jing, *Catal. Commun.* **2008**, *9*, 120–125.
[25] S. Itsuno, D. K. Paul, M. Ishimoto, N. Haraguchi, *Chem. Lett.* **2010**, *39*, 86–87.

