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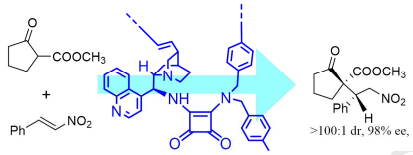

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Design and synthesis of cinchona-based chiral hyperbranched polymers and their application in asymmetric reactions

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ABSTRACT

Cinchona-based chiral hyperbranched polymers (HBPs) were designed and successfully synthesized via the Mizoroki-Heck (MH) coupling reaction. **AB$_2$** and **A$_2$B**-type chiral monomers were prepared from cinchona squaramide derivatives, where **A** (vinyl) reacted only with **B** (iodophenyl) under MH reaction conditions. The chiral HBPs obtained by the MH polymerization contained cinchona squaramide moieties and demonstrated excellent diastereoselectivity and enantioselectivity in asymmetric Michael addition reactions of methyl 2-oxocyclopentanecarboxylate and *trans*-β-nitrostyrene. These newly designed HBPs were structurally robust and could be reused for further reaction without losing their catalytic activity.

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1. Introduction

Hyperbranched polymers (HBPs), which are highly branched three-dimensional macromolecules, have attracted significant attention for various applications.[1, 2] Compared to linear polymers, HBPs possess properties analogous to those of dendrimers, such as fragile molecular entanglement, higher viscosity, higher solubility, and large numbers of functional groups, because they have diverse branching points and terminal groups.[3-8] As dendrimers have precise molecular weights and exact numbers of repeating units, they require multistep synthesis with isolation and purification at each step.[3,9-11] Further, this process is time consuming and difficult to scale up. In contrast, the preparation of HBPs is suitable for large-scale production, even though the resulting HBPs constitute a mixture of chains with different molecular weights.[12] The highly branched tree-like structure is an important and unique characteristic of HBPs, which differentiates them from linear and cross-linked polymers.[1] Various kinds of achiral HBPs have been prepared.[1,2,13-21] Although these have promising potential in asymmetric reactions, the number of synthesized chiral HPBs is limited. We have previously prepared chiral branched polymers from $\mathbf{A_2}$ and $\mathbf{B_3}$ monomers.[22] In the $\mathbf{A_2}$ + $\mathbf{B_3}$ approach, network polymers may form by crosslinking and there is often very little control over the molar mass and topology.

In this study, we have focused on the $\mathbf{AB_2}$ approach to prepare a novel type of chiral HBPs. The $\mathbf{AB_2}$ monomer yields an HBP with **A** as the focal unit. The Mizoroki-Heck (MH) coupling is one of the most efficient C-C bond forming reactions.[23] It proceeds smoothly between olefinic compounds and an aromatic iodide. We have reported several types of cinchona-based linear polymers using MH polymerization.[24-26] The MH reaction was performed between an aryl or alkenyl halide and a terminal olefin of the cinchona-derived iodide and olefinic double bond in the presence of a Pd catalyst to produce a substituted olefin.[23] The reaction afforded high yields and showed high functional group selectivity.[23]

Cinchona alkaloid derived organocatalysts possess a C3-vinyl group that can be used as a MH reactive site. Several types of cinchona-based chiral organocatalysts have been developed for asymmetric catalysis.[27] For example, cinchona squaramide derivatives have shown excellent catalytic activities in asymmetric transformations. In this study, we chose the cinchona squaramide structure as the chiral catalyst site of the chiral HBPs.

Chiral HBP catalysts are different from the classical polymer-supported cinchona catalysts.[28-32] In this study, we designed the chiral $\mathbf{AB_2}$ monomer using cinchona alkaloid squaramide. We applied MH polymerization technique to prepare chiral HBPs. Two iodophenyl groups were introduced into the cinchona squaramide derivative to obtain the $\mathbf{AB_2}$ monomer. One component self-polycondensation of $\mathbf{AB_2}$ monomer gives an HBP having focal site **A** and surface (terminal) functional groups **B**. The $\mathbf{A_2B}$ monomer can also be polymerized to give another type of chiral HBP, which possess focal site **B** and surface (terminal) functional groups **A**.

In both chiral HBPs derived from $\mathbf{AB_2}$ and $\mathbf{A_2B}$ polymerization, each branching point involves a catalytic active site. The catalyst conformation in the interior branches may be uniform or different from that of the corresponding low molecular weight catalysts in homogeneous solution and the linear polymer catalysts. The interior cavities of HBP can provide a suitable microenvironment for asymmetric transformations. Based on this rationale, we synthesized novel chiral cinchona-based $\mathbf{AB_2}$ and $\mathbf{A_2B}$ monomers and conducted their MH polymerization. We subsequently applied these chiral HBPs in asymmetric catalysis and evaluated their catalytic performance.

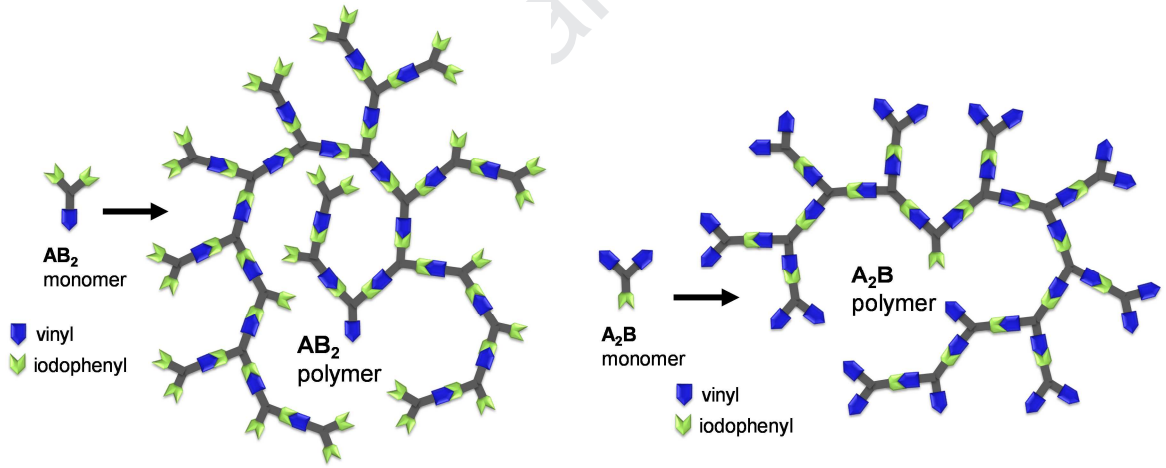


Figure 1. Chiral hyperbranched polymer (HBP) catalysts.

2. Results and Disscussions

Novel chiral HBPs containing cinchona squaramide moieties were designed and synthesized via the MH coupling polymerization. The monomer for the chiral HBPs was a cinchona squaramide derivative having an iodophenyl group. Cinchona squaramide **4** having two iodophenyl groups was equivalent to an $\mathbf{AB_2}$-type monomer for MH polymerization. Similarly, monomer **7** with two cinchona squaramide units and one iodophenyl group was an $\mathbf{A_2B}$-type monomer. Polymerization of these monomers to HBPs is illustrated in Figure 1. One component and one step self-polycondensation is one of the easiest methods to obtain novel chiral HBPs.

For the synthesis of $\mathbf{AB_2}$ monomer **4**, a bis-iodophenyl component is required. Bis(4-iodobenzyl)amine **1** was synthesized from 4-iodobenzylamine via the Fukuyama secondary amine synthesis method.[33] Then, squaramide squarate **2** was synthesized by reacting **1** with an equimolar amount of diethyl squarate. $\mathbf{AB_2}$ monomer **4** was finally obtained by the reaction of **2** with 9-amino substituted cinchonidine **3** (Scheme 1).

The $\mathbf{A_2B}$ type squaramide **7** was synthesized by the reaction of (5-iodo-1,3-phenylene)dimethanamine **5** with cinchonidine squaramide **6** (Scheme 2). For comparison of the catalytic

performances of the Chiral HBPs and a linear polymer, we also synthesized monoiodobenzyl squaramide **10** from 4-iodobenzyl amine **8** and **3** (Scheme 3).

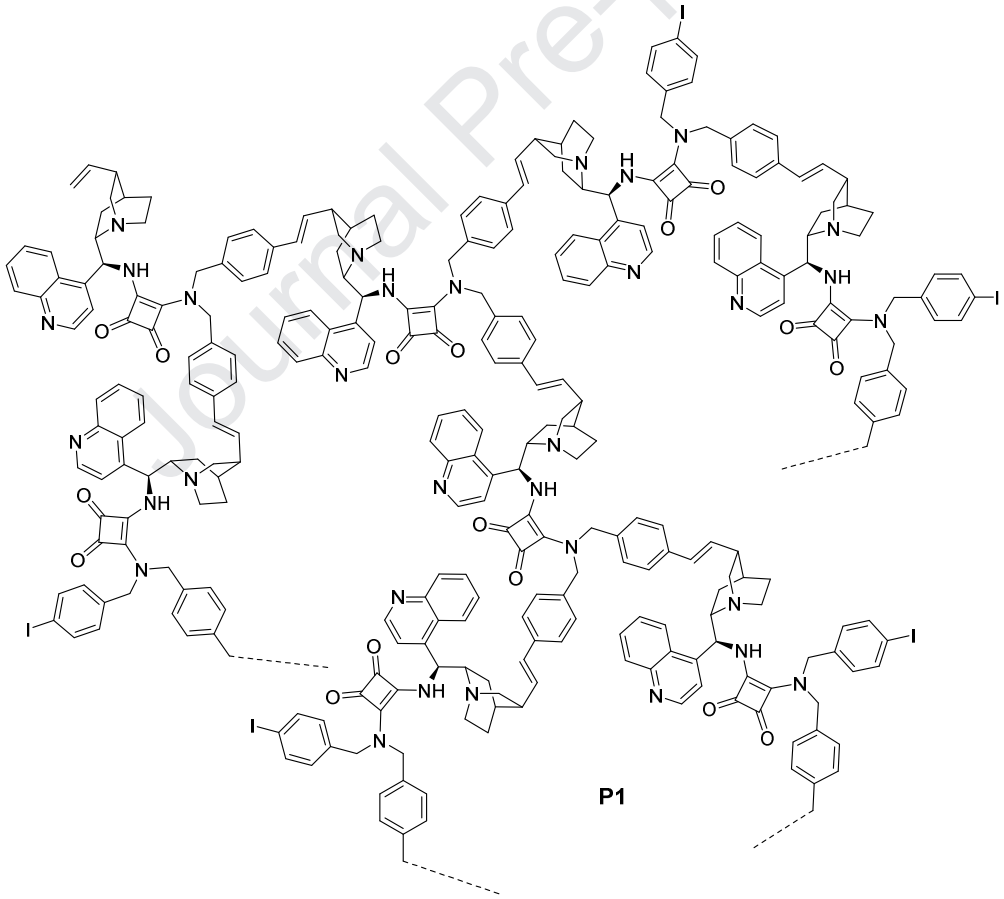
2.1 Preparation of chiral cinchona-based squaramide HBPs

The synthesized chiral monomers contain both an iodophenyl group and an olefinic double bond. These functional groups are suitable for the MH reaction. In the presence of $Pd(OAc)_2$, monomer **4** underwent the MH reaction to give the corresponding chiral HBP **P1** in quantitative yield, as shown in Table 1. The MH polymerization conditions were established for the synthesis of chiral cinchona squaramide polymers using a two component polycondensation system.[24] We applied these polymerization conditions to the synthesis of chiral HBPs. Similarly, monomer **7** was polymerized under these MH conditions to give **P2**. Linear polymer **PL** was also prepared by the MH polymerization. The obtained chiral HBPs were soluble in DMF and DMSO, and insoluble in other commonly used organic solvents such as CH_2Cl_2, $CHCl_3$, MeOH, EtOAc, and THF. Figure 2 shows the structure of chiral HBP **P1** and **P2** and linear polymer **PL**. The yield and molecular weight of the HBPs and linear polymer are summarized in Table 1.

Table 1. Synthesis of chiral HBPs **P1**, **P2** and linear polymer **PL** from cinchona squaramide **4, 7, 10** and their GPC data.

Entry	Squaramide	Chiral HBP	Yield [%]	M_n[d]	N[e]	M_w[d]	M_w/M_n[d]
1[a]	**4**	**P1**	99	20000	35	23000	1.14
2[b]	**7**	**P2**	99	88000	183	125000	1.43
3[c]	**10**	**PL**	99	10000	21	15000	1.48

[a] Polymerization was carried out with squaramide **4** (0.31 mmol), triethylamine (0.61 mmol) in DMF (3.5 mL) in the presence of 10 mol% $Pd(OAC)_2$.
[b] Polymerization was carried out with squaramide **7** (0.14 mmol), triethylamine (0.28 mmol) in DMF (3.0 mL) in the presence of 10 mol% $Pd(OAC)_2$.
[c] Polymerization was carried out with squaramide **10** (0.41 mmol), triethylamine (0.82 mmol) in DMF (4.0 mL) in the presence of 10 mol% $Pd(OAC)_2$.
[d] Determined by SEC using DMF as a solvent at a flow rate of 1.0 mL min^{-1} at 40 °C (polystyrene standard).
[e] Average number of catalyst unit per chain calculated from M_n.



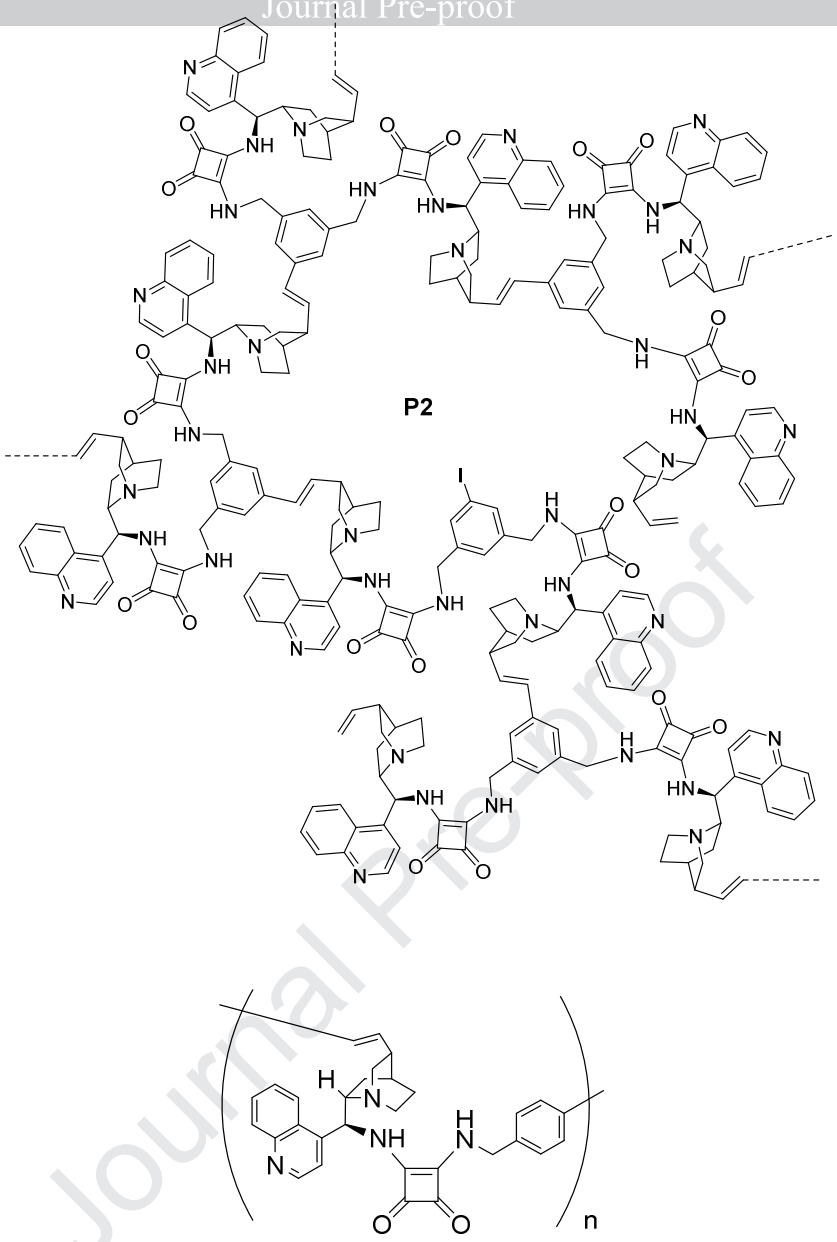
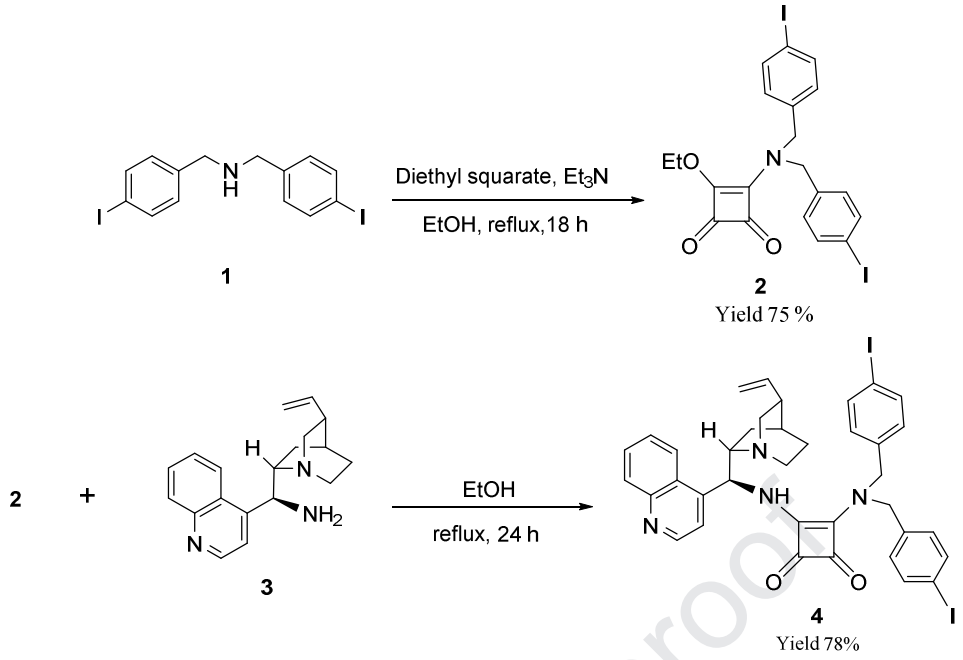


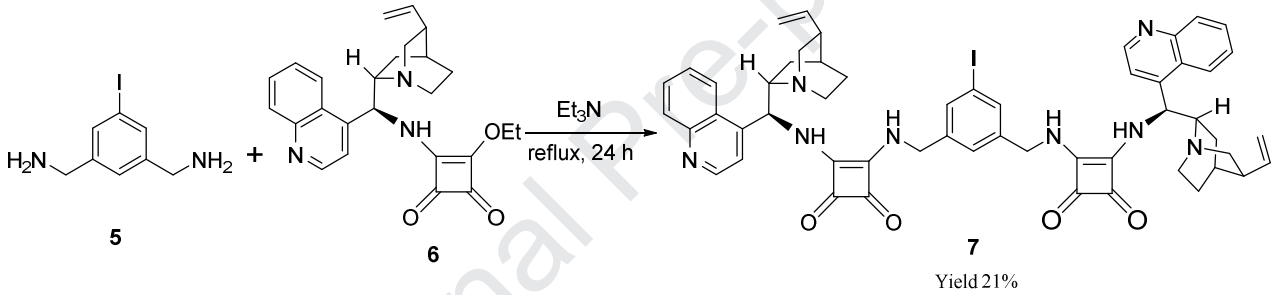
Figure 2. Structures of chiral HBPs, **P1** and **P2**, and chiral linear polymer **PL.**

2.2 Asymmetric Michael addition of methyl 2-oxocyclopentanecarboxylate to trans-β-nitrostyrene

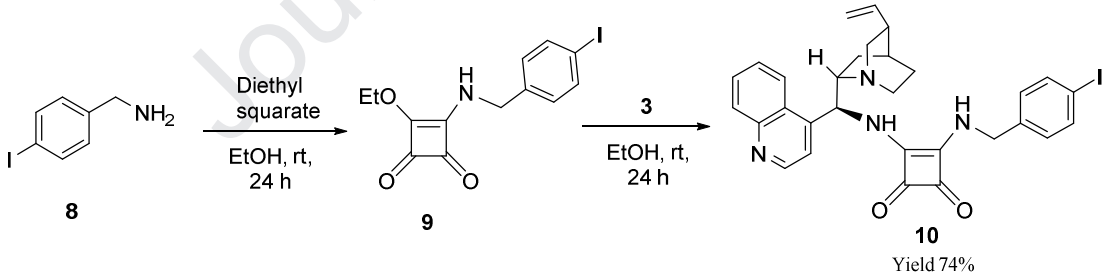
We tested the catalytic activity of the chiral HBP catalyst **P1** (5 mol %, calculated from the unit molecular weight of the polymer catalyst)) in the asymmetric Michael addition reaction of methyl 2-oxocyclopentanecarboxylate **11** and *trans*-β-nitrostyrene **12** (Scheme 4). Although **P1** was insoluble in solvent used for the asymmetric reaction, the reaction under the heterogeneous condition proceeded smoothly to give the corresponding Michael adduct **13** in 93% yield with excellent diastereoselectivity (diastereomer ratio (*dr*) >100:1). Enantioselectivity (in terms of enantiomeric excess, *ee*) of the major diastereomer was 98% (Table 2 entry 2). The results of the asymmetric reaction are summarized in Table 2. The catalytic activity of another HBP **P2** was almost equivalent to that of **P1** (entry 3). We also used a linear polymer catalyst **PL** for the same reaction. A similar result of high stereoselectivity was obtained with **PL** (entry 4). Further, all synthesized polymeric catalysts **P1**, **P2**, and **PL** showed excellent catalytic activity with higher stereoselectivity compared to the corresponding low molecular weight catalyst **4** (entry 1).



Scheme 1. Synthesis of squaramide **4**.



Scheme 2. Synthesis of squaramide **7**.

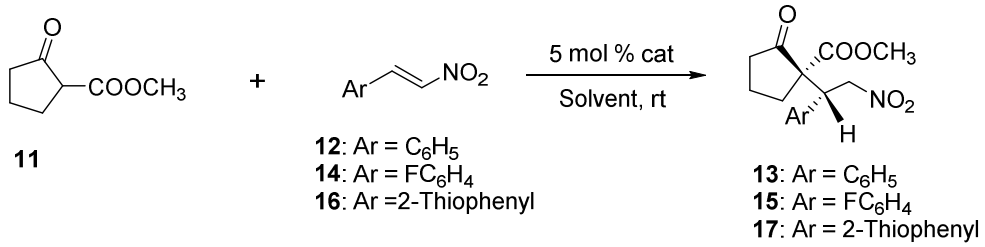


Scheme 3. Synthesis of squaramide **10**.

The effect of solvents on the catalytic performance was surveyed using **P1**. In hexane, both the yield and diastereoselectivity were low (entry 5). In contrast, both THF and methanol as solvents led to high yields with low diastereoselectivity (entries 6 and 7). Interestingly, enantioselectivities higher than 99% *ee* were attained for the major diastereomer in these solvents (entries 5–7). Lowering the reaction temperature to 0 °C in methanol afforded somewhat higher diastereoselectivity compared to that obtained at room temperature (entry 8). Two other nitroolefins, **14** and **16**, were tested for the asymmetric reaction with **P1** in CH_2Cl_2 and methanol. Similar trends in the catalytic activity and stereoselectivity was observed in these cases (entries 9–12).

2.3 *Recyclability of chiral HBPs*

Chiral HBP catalysts were mostly insoluble in commonly used organic solvents, except for DMF and DMSO. In spite of the heterogeneous system, the asymmetric reaction with chiral HBP catalysts proceeded smoothly to give the product. The insoluble catalyst could be easily separated and recovered after completion of the reaction via simple filtration. Recovered polymeric catalyst **P1** was reused in the same reaction in methanol to examine its recyclability. **P1** could be recycled four times and the results of the recycling experiments are summarized in Table 3. Even after recycling for four catalytic runs, the catalytic activity and stereoselectivity were still maintained.



Scheme 4. Enantioselective Michael addition of methyl 2-oxocyclopentanecarboxylate **11** to *trans*-β-nitrostyrene **12**.

Table 2. Asymmetric Michael addition reaction of **11** with nitroolefins using HBP catalysts.[a]

Entry	Catalyst	Solvent	Michael acceptor	Product	Reaction time [h]	Yield[b] [%]	*dr*[c] [%]	*ee*[c] [%]
1	**4**	CH_2Cl_2	12	13	48	85	56:1	98
2	**P1**	CH_2Cl_2	12	13	24	93	>100:1	98
3	**P2**	CH_2Cl_2	12	13	24	90	>100:1	98
4	**PL**	CH_2Cl_2	12	13	24	92	>100:1	98
5	**P1**	Hexane	12	13	48	64	34:1	99
6	**P1**	THF	12	13	24	91	51:1	>99
7	**P1**	MeOH	12	13	19	91	42:1	>99
8[d]	**P1**	MeOH	12	13	24	70	97:1	>99
9	**P1**	CH_2Cl_2	14	15	24	93	>100:1	98
10	**P1**	MeOH	14	15	24	90	54:1	91
11	**P1**	CH_2Cl_2	16	17	24	92	>100:1	98
12	**P1**	MeOH	16	17	24	89	36:1	94

[a]Asymmetric reaction was carried out with **11** (0.5 mmol), nitroolifin (0.55 mmol) and 5 mol% catalyst in solvent (2.0 mL) at room temperature.
[b]Isolated yield of the product after column chromatography.
[c] Enantioselectivity (*ee*) and *dr* value were determined using HPLC (Chiralcel OD-H column).
[d] Reaction was performed at 0 °C.

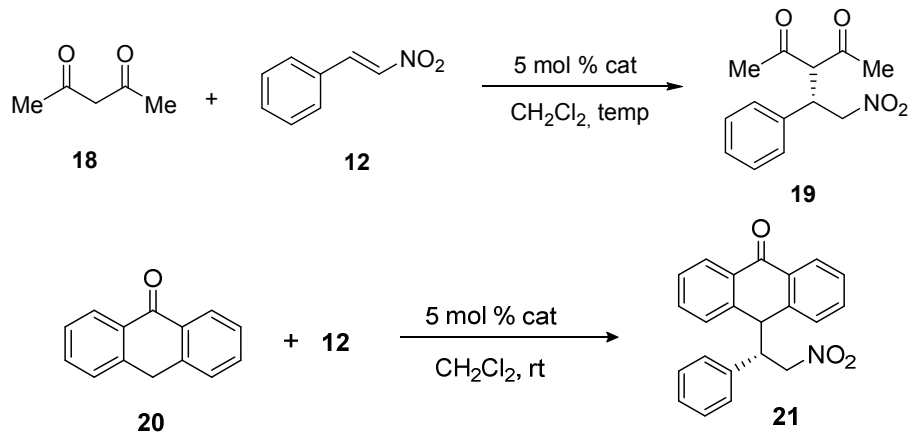
Table 3. Recyclability of chiral HBP **P1** in enantioselective Michael addition reaction of **11** and *trans*-β-nitrostyrene in methanol.[a]

Entry	Reaction time [h]	Yield[b] [%]	*dr*[c] [%]	*ee*[c] [%]
Fresh polymer	19	91	42:1	>99
Cycle 1	24	85	47:1	92
Cycle 2	24	86	39:1	94
Cycle 3	24	88	36:1	99
Cycle 4	24	86	30:1	99

[a]Asymmetric reaction was carried out with **11** (0.5 mmol), **12** (0.55 mmol) and 5 mol% catalyst in methanol (2.0 mL) at room temperature.
[b]Isolated yield of the product after column chromatography.
[c]Enantioselectivity (ee) and *dr* values were determined using HPLC (Chiralcel OD-H column).

2.4 Asymmetric Michael addition reaction of other active methylene compounds to trans-β-nitrostyrene

Other active methylene compounds (**18** and **20**) were examined as Michael donors in the asymmetric addition reaction. In the presence of the low molecular weight cinchona squaramide catalysts **4**, **7**, and **10**, the reaction of acetylacetone **18** and **12** proceeded smoothly to give the chiral adduct **19** (Table 4, entries 1–3). Cinchona squaramide **10** gave the best enantioselectivity among these catalysts (entry 3). The corresponding chiral polymeric catalysts **P1**, **P2**, and **PL** were then applied in the same reaction. These chiral HBP catalysts showed excellent performance in the asymmetric reaction. When **P1** was used as a catalyst in CH_2Cl_2, chiral product **19** was obtained in 83% yield after 24 h even under heterogeneous conditions and gave high enantioselectivity (81%, entry 4). Enantioselectivity improved to 85% when this reaction was performed at 0 °C, although the reaction time was prolonged to 48 h (entry 7). At 50 °C, *ee* was reduced to 77% (entry 8). Using HBP **P2**, the reaction resulted in 88% yield with 58% *ee* (entry 5). The corresponding linear polymer catalyst **PL** gave the product **19** with almost similar catalytic activity and enantioselectivity (entry 6). A suitable microenvironment was created for the asymmetric reaction in the chiral polymer network in the case of catalyst **P1**. The Michael addition of anthrone **20** to β-nitrostyrene **12** was also examined using the polymeric catalysts. The HBP **P1** catalyst showed higher enantioselectivity compared to other polymeric catalysts (entries 9–11).



Scheme 5. Asymmetric Michael addition reaction using chiral HBP catalysts.

Table 4. Asymmetric Michael addition reaction using chiral low molecular weight catalysts and HBP catalysts.[a]

Entry	Catalyst	Michael donor	Product	Temperature [°C]	Reaction time [h]	Yield[b] [%]	*ee*[c][%]
1	**4**	**18**	**19**	rt	24	92	36
2	**7**	**18**	**19**	rt	24	91	76
3	**10**	**18**	**19**	rt	24	90	95
4	**P1**	**18**	**19**	rt	24	89	81
5	**P2**	**18**	**19**	rt	24	88	58
6	**PL**	**18**	**19**	rt	24	85	58
7	**P1**	**18**	**19**	0	48	77	85
8	**P1**	**18**	**19**	50	24	86	77
9[d]	**P1**	**20**	**21**	rt	20	82	61
10[d]	**P2**	**20**	**21**	rt	16	80	16
11[d]	**PL**	**20**	**21**	rt	16	79	47

[a]Asymmetric reaction was carried out with **18** (0.275 mmol), **12** (0.25 mmol) and 5 mol% catalyst in CH_2Cl_2 (2.0 mL).
[b]Isolated yield of the product after column chromatography.
[c] Enantioselectivity (*ee*) was determined using HPLC (Chiralpak AD-H and Chiralpak AS-H columns for entries 9–11).
[d]Asymmetric reaction was carried out with **20** (0.24 mmol), **12** (0.20 mmol) and 5 mol% catalyst in CH_2Cl_2 (2.0 mL).

3. Conclusion

We synthesized novel chiral HBPs from cinchona squaramide monomers **4** and **7** possessing both vinyl (**A**) and iodophenyl (**B**) groups in their structure. These $\mathbf{AB_2}$ and $\mathbf{A_2B}$ monomers were successfully polymerized by the MH coupling reaction between the **A** and **B** functionalities to give chiral HBPs **P1** and **P2**, respectively. The chiral HBPs (**P1**, **P2**) prepared by one step MH polymerization were used as catalysts in asymmetric Michael reactions. The reactions occurred smoothly to give the corresponding chiral product. In case of the reaction between methyl 2-oxocyclopentanecarboxylate **11** and *trans*-β-nitrostyrene **12**, the HBP catalysts showed high catalytic activity with excellent diastereoselectivity and enantioselectivity. Reactions between some other substrate combinations also occurred smoothly with the HBP catalysts. **P1** exhibited superior selectivity in these reactions. Interestingly, the HBP catalysts gave higher diastereoselectivity compared to that obtained with the low-molecular-weight catalyst **4**. Somewhat higher catalytic activity was also observed with HBP catalyst. Precise control of the catalyst conformation may be possible in case of polymer catalyst. These results show that the design of chiral HBP catalyst may lead the development of high performance polymeric catalyst.The HBP catalysts were easily recovered from the reaction mixture and reused several times without any decrease in catalytic activity and stereoselectivity.

4. Experimental Section

4.1 material and methods

All reagents and solvents were purchased from Sigma Aldrich, Wako Pure Chemical Industries, Ltd., or Tokyo Chemical Industry (TCI) Co., Ltd. To monitor the progress of the reactions, thin layer chromatography (TLC) was performed using pre-coated silica gel plates (Merck TLC silica gel, 60F254). To purify the synthesized compounds, column chromatography was performed using a silica gel column (Wakogel C-200, 100–200 mesh). NMR spectra were recorded on JEOL JNM-ECS400 and JEOL JNM-ECX500 spectrometers in $CDCl_3$ or DMSO-d_6 at room temperature operated at 400 MHz (^{1}H) and 500 MHz (^{1}H), and 400 MHz (^{13}C{^{1}H}) and 500 MHz (^{13}C{^{1}H}), respectively. Chemical shifts are reported in parts per million (ppm) using tetramethylsilane (TMS) as a reference and the *J* values are reported in Hertz (Hz). IR spectra were recorded using KBr pellets on a JASCO FT/IR-230 spectrometer and the wavenumbers are reported in cm^{-1}. HRMS (ESI and APCI) data was obtained using a Bruker micro OTOF II HRMS instrument. High-performance liquid chromatography (HPLC) was performed on a Jasco HPLC system composed of a DG-980-50 three-line degasser, an HPLC pump (PU-980), and CO-2065 column oven equipped with a chiral column (Chiralcel OD-H, Chiralpak AD-H, and Chiralpak AS-H, Daicel) using hexane/2-propanol as the eluent at a flow rate of 1.0 mL/min and 0.7 mL/min at room temperature. For peak detection, a Jasco UV-975 UV detector

was used. Size exclusion chromatography (SEC) was performed using a Tosoh instrument with HLC 8020 UV (254 nm) or a refractive index detector. Two polystyrene gel columns with a bead size of 10 μm were used and dimethylformamide (DMF) was used as the carrier solvent at a flow rate of 1.0 mL min^{-1} at 40 °C. A calibration curve was established to determine the number average molecular weight (M_n) and molecular weight distribution (M_w/M_n) values by comparison with polystyrene standards. Optical rotations were determined on a JASCO DIP-149 digital polarimeter using a 10 cm thermostatted microcell.

4.2 Synthesis of squaramide 2

In a 30 mL flask, 5.0 mmol (734 μL) of diethylsquarate and 15 mL of ethanol were mixed. Next, 2.0 mmol of triethyl amine was added and to the stirred solution, 1.0 mmol (449 mg) of bis(4-iodobenzyl)amine **1** was added slowly. The mixture was stirred at reflux for ~18 h under Ar. Subsequently, the solution was cooled to room temperature. Eventually, off-white crystals were formed, which were filtered and dried. Yield: 430 mg (75%). R_f: 0.43 (hexane/EtOAc = 2.0/1.0); mp: 145–149 ºC; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.44 (t, *J* = 7.2 Hz, 3H), 4.37 (s, 2H), 4.67 (s, 2H), 4.81 (q, *J* = 6.8 Hz, 2H), 6.95 (dd, *J* = 7.6 Hz and 14.4 Hz, 4H), 7.71 (dd, *J* = 8.4 Hz and 12.4 Hz, 4H); ^{13}C NMR (400 MHz, $CDCl_3$): δ 15.99, 50.58, 51.20, 70.32, 94.39, 130.05, 130.69, 134.25, 134.37, 138.27, 138.39, 171.95,176.79, 182.80, 188.68; IR (KBr): *ν* = 3076, 2979, 2880, 2081, 1908, 1800, 1702, 1562, 1460, 1383, 1282, 1183, 1069, 984, 889, 795, 719, 628, 532 cm^{-1}; HRMS (APCI) *m/z* for $C_{20}H_{18}I_2NO_3$ [M^+H^+] calcd. 573.9376, found 573.9371.

4.3 Synthesis of squaramide 4

Compound **2** (410 mg, 0.714 mmol) was mixed with 10 mL of ethanol in a 30 mL volumetric flask. To the stirred solution, 0.862 mmol (253 mg) of **3** in 10 mL ethanol was added slowly. The mixture was stirring at reflux for ~24 h under Ar. A white precipitate was formed, and it was filtered, washed with ethanol, and dried to obtain **4** (460 mg, 78%) as a white solid. R_f: 0.48 (CH_2Cl_2/MeOH = 9.0/1.0; mp: 229–232 ºC. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.90 (m, 1H), 1.29 (m, 2H), 1.57 (m, 4H), 2.27 (br,1H), 2.57–3.14 (m, 4H), 4.59 (br, 4H), 4.93 (m, 2H), 5.63 (m, 1H), 6.95 (d, *J* = 8.0 Hz, 4H), 7.72 (m, 8H), 8.14 (d, *J* = 8.0 Hz, 1H), 8.86 (d, *J* = 4.4 Hz, 1H); ^{13}C NMR (500 MHz, $CDCl_3$): δ 25.9, 27.31, 27.69, 39.54, 40.77, 56.0, 94.20, 114.90, 123.57, 127.16, 129.56, 135.32, 138.41, 141.20, 149.99, 167.46, 168.0, 182.87, 183.50. IR (KBr): *ν* = 3324, 3065, 2933, 2862, 1788, 1667, 1561, 1484, 1343, 1285, 1182, 1088, 981, 839, 771, 649, 564 cm^{-1}; HRMS (APCI) *m/z* for $C_{37}H_{35}I_2N_4O_2$ [M^+H^+] calcd. 821.0849, found 821.0844; $[\alpha]^{23.7}_D$ = –166 (*c* 0.22, DMF).

4.4 Synthesis of chiral cinchona-based squaramide hyperbranched polymers via the MH polymerization

In a 30 mL flask, squaramide **4** (250 mg, 0.305 mmol) and two equivalents of triethylamine (85.0 μL, 0.610 mmol) were mixed together. Next, palladium acetate (10 mol%) and DMF solvent (3.5 mL) were added and the reaction mixture was stirred for 48 h at 100 °C. Subsequently, the solution was concentrated by evaporation and poured into diethyl ether. The precipitated polymer was collected by filtration and washed with diethyl ether (3×60 mL) and water (40 mL). Next, the compounds were dried in a vacuum oven to afford the **P1** as a light brown solid. Yield: 245 mg; ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.83, 1.20–2.00, 4.62, 6.38, 6.80–8.20, 8.92; IR (KBr): *ν* = 3586, 3470, 2933, 2862, 2385, 2114, 1790, 1673, 1582, 1431, 1319, 1257, 1143, 1059, 969, 844, 767, 620 cm^{-1}; $[\alpha]^{23.9}_D$ = −22.1(*c* 0.05, DMF); M_n (SEC) = 20000; M_w/M_n = 1.14.
The other two chiral HBPs used in this study were synthesized by following this procedure.

*4.5 Synthesis of **P2***

Squaramide **7** (140 mg, 0.139 mmol) and double amount of triethyl amine (38 μL, 0.279 mmol) were taken in 20 mL flask. After adding palladium acetate (10 mol %) and DMF (3 mL) reaction mixture was stirred for 48 hours at 100 ^{o}C. Subsequently, the solution was concentrated by evaporation and poured into diethyl ether. The precipitated polymer was collected by filtration and washed with diethyl ether (3×60 mL) and water (40 mL). After that the compounds were dried over in vacuum oven to afford the **P2** as a light brown Solid. Yield: 138 mg; ^{1}H NMR (500 MHz, DMSO-d_6); *δ* 0.72-2.0, 2.95, 4.65, 5.01, 5.86, 6.39, 7.0-8.58, 8.98; IR (KBr); *ν* = 3470, 3223, 2936, 2866, 2128, 1797, 1671, 1619, 1530, 1428, 1240, 1084, 979, 814, 767, 619 cm^{-1}. $[\alpha]^{24.1}_D$ = –104 (*c* 0.02, DMF). M_n (SEC) = 88000; M_w/M_n = 1.43.

*4.6 Synthesis of **PL***

Squaramide **10** (250 mg, 0.414 mmol) and triethyl amine (115.8 μL, 0.828 mmol) were taken in a 20 mL flask and palladium acetate (10 mol %) and DMF (4 mL) were added in the reaction mixture and it was stirred for 48 hours at 100 ^{o}C. Subsequently, the solution was concentrated by evaporation and poured into diethyl ether. The precipitated polymer was collected by filtration and washed with diethyl ether (3×60 mL) and water (40 mL). After that the compounds were dried over in vacuum oven to afford the **PL** as a light brown Solid. Yield: 248 mg; ^{1}H NMR (400 MHz, DMSO-d_6): *δ* 0.93-1.93, 2.95, 4.65, 6.41, 7.0–8.60, 8.44; IR (KBr): *ν* = 3469, 3222, 2935, 1797, 1673 1590, 1459, 1348, 1242, 973, 846, 768, 617, 529 cm^{-1}; $[\alpha]^{24.3}_D$ = –101 (*c* 0.035, DMF); M_n (SEC) = 10000; M_w/M_n = 1.48

4.7 Enantioselective Michael addition reaction of Methyl 2-oxocyclopentanecarboxylate to trans-β-nitrostyrene

trans-β-Nitrostyrene **12** (82.1 mg, 0.55 mmol) and the HBP (5 mol%, calculated from the unit molecular weight of the polymer catalyst) were added to a reaction vessel with 2.0 mL of solvent. Methyl 2-oxocyclopentanecarboxylate **11** (63 μL, 0.50 mmol) was added via a syringe into the resulting solution. The reaction was stirred at room temperature and its progress was monitored by TLC. The reaction mixture was then filtered, and the filtrate was concentrated in vacuo. The crude compound was purified by column chromatography on silica gel (100–200 mesh) using hexane/EtOAc = 6.0/1.0 as the eluent to afford the addition product **13** as a colorless oil. The enantioselectivity (*ee*) and diastereomeric ratio (*dr*) were determined using HPLC on a Chiralcel OD-H column using solvent mixture hexane:2-propanol=4:1. Experiments to understand the effect of the solvent, substrate scope, and recyclability were conducted according to this procedure.

4.8 Enantioselective Michael addition reaction between acetylacetone and trans-β-nitrostyrene

trans-β-Nitrostyrene **12** (37.3 mg, 0.25 mmol) and the HBP (5 mol%) were added to a reaction vessel with 1.0 mL of CH_2Cl_2. Next, acetylacetone **18** (30.6 μL, 0.275 mmol) was added using a syringe into the resulting solution. The reaction was stirred at room temperature and monitored using TLC. The reaction mixture was then filtered, and the filtrate was concentrated in vacuo. The crude compound was purified by column chromatography using hexane/EtOAc/CH_2Cl_2 = 6.0/1.0/1.0 as the eluent on silica gel (100-200 mesh) to afford the addition product **19** as a white solid. The *ee* values were determined using HPLC on a Chiralpak AD-H column using solvent mixture hexane:2-propanol=9:1.

4.9 Enantioselective Michael addition reaction between anthrone and trans-β-nitrostyrene

trans-β-Nitrostyrene **12** (29.8 mg, 0.20 mmol) and the HBP catalyst (5.0 mol%) were added to a reaction vessel with 2.0 mL of CH_2Cl_2. Anthrone **20** (46.6 mg, 0.24 mmol) was added to the resulting solution. The reaction was stirred at room temperature and monitored using TLC. The reaction mixture was then filtered, and the filtrate was concentrated in vacuo. The crude product was purified by column chromatography on silica gel (100–200 mesh) using hexane/EtOAc = 5.0/1.0 as the eluent to afford **21** as a white solid. The *ee* was determined using HPLC on a Chiralpak AS-H column using solvent mixture hexane:2-propanol=5:1.

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Design and synthesis of cinchona-based chiral hyperbranched polymers and their application in asymmetric reactions

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Highlights

- Chiral hyperbranched polymers (HBPs) having cinchona squaramide.
- Highly stereoselective chiral HBPs by one step self-polycondensation.
- Robust and reusable HBP catalyst for asymmetric Michael reaction.

Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: