**Article**

**ADMET Polymerization of Dimeric Cinchona Squaramides for the Preparation of a Highly Enantioselective Polymeric Organocatalyst**

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**Abstract:** Under the acyclic diene metathesis (ADMET) reaction condition, the C3-vinyl groups of cinchona alkaloids readily react with each other to form a C-C bond. A novel type of cinchona alkaloid polymers was synthesized from dimeric cinchona squaramides using the Hoveyda-Grubbs’ second-generation catalysts (HG$_2$) by means of ADMET reaction. The chiral polymers, containing cinchona squaramide moieties in their main chains, were subsequently employed as catalysts for the enantioselective Michael reaction to give the corresponding chiral adducts in high yields with excellent enantioselectivity and diastereoselectivity. Both enantiomers from the asymmetric Michael reaction were distinctively prepared while using the polymeric catalysts, possessing pseudoenantiomeric structures. The catalysts were readily recovered from the reaction mixture and recycled several times due to the insolubility of the cinchona-based squaramide polymers.

**Keywords:** ADMET; cinchona alkaloid; squaramide; polymeric organocatalyst; Michael addition; pseudoenantiomer

**1. Introduction**

Polymeric catalysts have been widely used in organic syntheses. Their easy recoverability, applicability to continuous flow systems, and simple modification and control of their microenvironment have attracted significant attention [1,2]. Chiral catalysts, for asymmetric syntheses, require the precise control of the reaction microenvironment to optimize the catalyst performance. Cinchona alkaloid and its derivatives have demonstrated their splendid catalytic activity in many kinds of enantioselective reactions. The polymeric version of the cinchona alkaloid compounds, as catalysts, has been highly desired. We prepared various chiral polymeric catalysts, possessing cinchona alkaloid moieties in their main chains, by various kinds of polymerization techniques, such as etherification [3], ion-exchange [4,5], and neutralization [6,7]. These optically active polymeric catalysts have been employed in enantioselective reactions, including C-C bond forming reactions. The utilization of the chiral main-chain polymeric catalysts confirmed their splendid catalytic activity in enantioselective reactions. In several cases, superior ability in stereoselections was achieved with the optically active main-chain polymeric catalysts. From these results, the catalytic moiety should have reasonable conformation in the optically active polymer main-chain. These results also facilitated the development of novel optically active polymeric catalyst. We recently initiated the application of Mizoroki–Heck (MH) coupling reaction to polymer synthesis of cinchona alkaloid derivatives [8–10]. The preparation of optically active polymeric catalysts requires the chiral functionalities to act as a catalytic active site, which must be maintained during and after the polymer synthesis. A chiral monomer requires extra functionalities for a polymerization that is not associated with catalytically active functionalities.
The polymerization reaction conditions must be tolerant to these active functional groups. Moreover, the MH reaction fulfills these requirements. The copolymerization of the dimers [11] of cinchona alkaloid derivatives and aromatic diiodide in the presence of a Pd catalyst produced chiral polymers in good yield. This polymerization effectively utilized the C3-vinyl group of the cinchona alkaloid compounds.

The acyclic diene metathesis (ADMET) polymerization is another possible polymerization that utilizes the C3-vinyl group of cinchona alkaloid. Dimers of cinchona squaramide derivatives [8,10] possess vinyl groups in both cinchona moieties and they are considered to be optically active diene. ADMET polymerization does not require other monomers, such as 1,4-diiodobenzene, which are required in MH polymerization. Since the dimers of cinchona alkaloid always contain two vinyl groups, they can be polymerized directly under the condition of ADMET reaction. The concept of ADMET has been discussed in scientific literature since the 1970s [12–14]. The first successful ADMET polymerization was reported by Wagner’s group in 1987. ADMET polymerization is highly tolerant to various functionalities and it proceeds under mild polymerization conditions [3]. In 1991, Wagner et al. reported the reaction mechanism of the ADMET polymerization [15]. This polymerization method can be used to give a different kinds of polymers and polymer architectures that cannot be accomplished with other polymerization methods. Different kinds of polymers, such as unsaturated poly[carbo(dimethyl)silanes] [16], unsaturated polyethers [17–19], hydrocarbons [20], unsaturated polycarbonates [21], unsaturated polyamines [22], unsaturated polycetals [23], organoboronates [24], carbosilane-/carbosiloxane-based homopolymers/copolymers [25], and unsaturated polyesters [26] were prepared by the Wagener group. Most of the polymers, which were synthesized using ADMET polymerization, were optically inactive polymers. One exception is the chiral polymers synthesized from -amino acid derivatives [27]. The ADMET polymerization technique has not been adopted in the synthesis of optically active polymers derived from cinchona alkaloid until our recent publication of preliminary results of the polymerization [28]. Cinchona alkaloids and their derivatives are widely employed for the preparation of different types of catalysts, and their most important application is as chiral organocatalysts in asymmetric reactions [29–35]. Since cinchona alkaloids exhibit various functionalities, such as a quinuclidine tertiary N, secondary alcohol, a quinoline ring, and a vinylic unit, it was feasible to modify their functionalities for the design of novel polymeric catalysts [34–36]. Rawal et al. successfully introduced cinchona squaramide derivatives as important organocatalysts by their pioneering work [37], and exhibited outstanding catalytic performance for enantioselective C-C bond forming reaction, such as the Michael-type reactions [38,39]. The cinchona-based squaramides contain an acidic NH that can be a hydrogen bond donor, and the quinuclidine tertiary nitrogen could also be a hydrogen bond acceptor and a base in enantioselective Michael reactions. A number of modifications of the catalyst have been reported after Rawal’s group initiated the excellent work on cinchona alkaloid squaramide organocatalysts. Various catalysts containing cinchona alkaloid squaramide have been developed and used for different types of asymmetric reactions [40–48].

In this paper, we describe the ADMET polymerization of cinchona squaramide dimers using the Hoveyda–Grubbs second-generation catalysts to prepare novel optically active polymeric catalysts. We applied these optically active polymeric catalysts for the enantioselective Michael type reactions to examine the catalytic performance and stereoselectivity. The enantioselective Michael reaction is one of the most important C-C bond forming reactions for the construction of chiral building blocks. Because the resulting ADMET polymeric organocatalysts were insoluble in some generally utilized organic solvents, we also examined their recyclability.

2. Results and Discussion

Synthesis of Dimeric Cinchona Squaramides and Their Corresponding Polymers by ADMET Polymerization

Cinchona-based squaramide dimers (1–3) (Figure 1) were prepared from dimethylsquarate and the C9-amino substituted cinchona alkaloids according to the literature procedures [8]. The C9-amino derivatives were synthesized by the Mitsunobu-type azide formation, followed by the Staudinger
reaction according to the previously reported procedure [37,45]. Dimers 1 (a cinchonine-derived catalyst), 2C (a cinchonidine-derived catalyst), and 2Q (a quinine-derived catalyst) were successfully prepared. Another dimeric cinchona squaramide (3), which contained a chiral diamine moiety between two squaramides, was also synthesized [10]. The treatment of the two equivalents of dimethylsquarate with (1R,2R)-1,2-diamino-1,2-diphenylethane afforded the bissquaramide. Subsequently, the C9-aminated quinine could react with the chiral bissquaramide to afford 3 in good yield.

![Figure 1. Dimeric cinchona squaramides 1–3.](image)

The dimeric cinchona squaramides that are shown in Figure 1 possess two olefinic double bonds in their structures. These squaramides are chiral dienes and they amenable to ADMET polymerization. A variety of diene compounds has been polymerized under the ADMET reaction condition to afford the polymers [15–22]. We synthesized the chiral polymers by repetitive ADMET reactions of 1–3. The ADMET polymerization of 1–3 with catalyst HG2A readily proceeded in dry DMF, affording chiral polymers P1–3, respectively, which contained cinchona squaramides in repeated units, in their main chains (Scheme 1). Further, the copolymerization of 2C and achiral triallyl ether (4) was also performed to prepare a hyperbranched polymer (P4). After the copolymerization, the reaction mixture was poured into ether to precipitate the product polymer. P1–3 were soluble in dichloromethane (DCM), methanol (MeOH), CDCl3, as well as in highly polar solvents, such as DMF and DMSO. P4 was slightly soluble in these solvents. All of the polymers were insoluble in generally employed organic solvents, including ether, tetrahydrofuran (THF), hexane, toluene, acetonitrile, and EtOAc.

Table 1 summarizes the results of the ADMET polymerizations of different cinchona squaramides with HG2. First, we examined the condition for the polymerization of the dimeric cinchona squaramides. Different reaction conditions were examined while using 2Q, as shown in Table 1. In DMF, 2Q was polymerized using catalyst HG2A (5 mol%) to give the quinine-derived polymer (P2Q) with 81% yield (entry 1). It was also observed that a low concentration of 2Q afforded a low yield of P2Q (entry 2). Moreover, HG2A achieved better results than HG2B (Figure 2). We observed that the ADMET polymerization of 2Q proceeded readily in toluene at 100 °C. After 9 h stirring at the same temperature, P2Q was generated with a 92% isolated yield (entry 6). Polymerization at 85 °C caused a lowering of the yield in prolonged reaction time (entry 7). Other dimeric cinchona squaramides were also polymerized to afford their corresponding chiral ADMET polymers under the optimized condition for the polymerization of 2Q (entries 8–11). All of the polymers obtained by ADMET polymerization possessed $M_n > 40,000$, except for P3.
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7g P2Q 2Q Toluene 25 52 49,000 56,000 1.14
8 P1 1 Toluene 9 77 47,000 49,000 1.04
9 P1 1 DMF 24 74 41,000 47,000 1.14
10 P2Q 2Q o-Dichloro benzene 24 77 56,000 74,000 1.32
11 P2Q 2Q Toluene 9 92 42,000 46,000 1.10
12 P1 1 DMF 9 92 42,000 46,000 1.10

Scheme 1. Synthesis of P1–P4 from 1–4, using HG2.

Figure 2. Hoveyda-Grubbs 2nd generation catalysts (HG2).
When CHF Catalysts decreased with increasing temperature. Interestingly, the high ee for the reaction in EtOAc, ether, toluene, and hexane. However, high chiral product with high enantioselectivity (entry 4). Relatively prolonged reaction times were required because they are generally used organic solvents. Among these solvents, acetonitrile, THF, EtOAc, hexane, dichloromethane, ether, hexane, and toluene were employed. Among these solvents, the low-molecular-weight catalyst (1) in MeOH to afford the product (7) with 91% yield and 93% enantiomeric excess (ee) of the major diastereomers (7a and c) (Table 2, entry 1). The corresponding P1 successfully catalyzed the reaction in the same solvent to yield 6 in good yield and high stereoselectivities (entry 2). The solvent effect on the catalytic performance of P1 was also investigated. MeOH, acetonitrile, THF, EtOAc, hexane, dichloromethane, ether, hexane, and toluene were employed, because they are generally used organic solvents. Among these solvents, P1 was partially soluble in MeOH, DCM, and CDCl3. P1 was insoluble in the other solvents utilized and the reaction proceeded in heterogeneous condition. However, P1 was swollen well in these solvents. Highly catalytic activity was obtained, even in heterogeneous condition. In DCM, its diastereoselectivity improved and higher enantioselectivity (97% ee) for the major diastereomer was achieved using (entry 3). Under a heterogeneous condition, in THF, the asymmetric reaction readily proceeded to afford the chiral product with high enantioselectivity (entry 4). Relatively prolonged reaction times were required for the reaction in EtOAc, ether, toluene, and hexane. However, high ees were obtained in all cases (entries 5–8). Toluene afforded poor isolated yield and decreased in diastereoselectivity with P1 (entry 7). When CH3CN was used as a solvent for the enantioselective reaction, the reaction was completed in 9 h at room temperature (entry 9). Very high diastereoselectivity (1::100) was achieved with P1 in acetonitrile. In this case, the ee of the major diastereomers was 95%. The temperature effect on the catalyst performance in acetonitrile was also investigated. The reaction was performed in the range of −10 to 80 °C (entries 9–12) to see the temperature effect on the stereoselectivity. The diastereoselectivity decreased with increasing temperature. Interestingly, the high ee of 95% was still achieved at 80 °C.

![Scheme 2. Asymmetric Michael addition of 5 and 6 to yield 7a–d.](image-url)

Table 1. Synthesis of P1–P4 by acyclic diene metathesis (ADMET) polymerization.

| Entry | Polymer | Diene | Solvent | Time (h) | Yield (%) | $M_n$ b | $M_w$ b | $M_w/M_n$ b |
|-------|---------|-------|---------|----------|-----------|---------|---------|-------------|
| 1 d   | P2Q     | 2Q    | DMF     | 24       | 81        | 49,000  | 58,000  | 1.18        |
| 2 c d | P2Q     | 2Q    | DMF     | 24       | 70        | 44,000  | 52,000  | 1.18        |
| 3 c d f | P2Q    | 2Q    | DMF     | 24       | 58        | 46,000  | 53,000  | 1.15        |
| 4 d f | P2Q     | 2Q    | o-Dichlorobenzene | 24 | 77 | 56,000 | 74,000 | 1.32 |
| 5     | P2Q     | 2Q    | Toluene | 24       | 92        | 42,000  | 46,000  | 1.10        |
| 6     | P2Q     | 2Q    | Toluene | 24       | 52        | 49,000  | 56,000  | 1.14        |
| 7     | P1      | 1     | Toluene | 24       | 93        | 47,000  | 49,000  | 1.04        |
| 8     | P2C     | 2C    | Toluene | 24       | 86        | 74,000  | 75,000  | 1.01        |
| 9     | P3      | 3     | Toluene | 24       | 70        | 9000    | 19,000  | 2.19        |

*Polymerization was performed in 0.5 mL of solvent at 100 °C using 0.2 mmol of 1–3 in the presence of HG2A (5 mol%). ° Determined by SEC, using DMF (0.5 wt%, LiCl) as an eluent at a flow rate of 1.0 mL/min at 40 °C (the calibration curve was made the use of polystyrene standards). $Dichlorobenzene 24 77 56,000 74,000 1.32$. $\text{P1} \text{ catalyst was employed. } ^{g} \text{ HG}_{2}B \text{ was employed as a catalyst. } ^{h} \text{ Polymerization was performed at 85 °C.}$
Table 2. Asymmetric Michael addition of 5 and 6 using the ADMET polymeric catalyst.

| Entry | Catalyst | Solvent | Temp (°C) | Reaction Time (h) | Yield (%)<sup>b</sup> | dr<sup>c</sup> | % ee<sup>c</sup> |
|-------|----------|---------|-----------|-------------------|---------------------|----------|-----------|
| 1     | P1       | MeOH    | 25        | 6                 | 91                  | 1:14     | 93        |
| 2     | P1       | MeOH    | 25        | 6                 | 77                  | 1:12     | 87        |
| 3     | P1       | DCM     | 25        | 30                | 52                  | 1:81     | 97        |
| 4     | P1       | THF     | 25        | 7                 | 89                  | 1:80     | 99        |
| 5     | P1       | EtOAc   | 25        | 27                | 34                  | 1:62     | 92        |
| 6     | P1       | ether   | 25        | 20                | 87                  | 1:45     | 97        |
| 7     | P1       | Toluene | 25        | 24                | 29                  | 1:3      | 90        |
| 8     | P1       | Hexane  | 25        | 24                | 84                  | 1:38     | 96        |
| 9     | P1       | Acetonitrile | 25 | 9               | 97                  | 1:100    | 95        |
| 10    | P1       | Acetonitrile | 0    | 24               | 92                  | 1:100    | 96        |
| 11    | P1       | Acetonitrile | −10  | 24               | 99                  | 1:89     | 99        |
| 12    | P1       | Acetonitrile | 80   | 6                | 78                  | 1:16     | 95        |
| 13<sup>e</sup> | 2C | DCM    | 25        | 4                 | 95                  | >100:1   | 98        |
| 14    | P2C      | Acetonitrile | 25 | 9               | 75                  | 68:1     | 91        |
| 15<sup>d</sup> | 2Q | DCM    | 25        | 2                 | 95                  | 79:1     | 91        |
| 16<sup>d</sup> | P2Q | DCM    | 25        | 48                | 45                  | 59:1     | 96        |
| 17    | P3       | acetonitrile | 25 | 9               | 67                  | 95:1     | 97        |
| 18    | P4       | acetonitrile | 25 | 20              | 85                  | 24:1     | 99        |

<sup>a</sup> Reactions were performed with 5 (0.50 mmol), 6 (0.55 mmol), and a polymeric catalyst (5 mol%) in solvent (2.5 mL).

<sup>b</sup> Isolated yield of the product after purification by column chromatography.

<sup>c</sup> The diastereomeric ratio (dr) and ee were determined by chiral HPLC (Chiralcel OD-H, Supplementary Materials).

<sup>d</sup> See ref. [21].

<sup>e</sup> See ref. [48].

Cinchonine and cinchonidine are pseudoenantiomers. When 2C was employed, the major products of the asymmetric Michael addition were 7b and 7d (entry 13). The corresponding polymeric catalyst P2C also afforded the same isomers (entry 14). Quinine possesses the same configuration as cinchonine. 2Q and its corresponding polymeric catalyst (P2Q) catalyzed the reaction in the same direction of stereo selection (entries 15 and 16). We introduced a chiral diamine moiety (C9-aminated quinine) between cinchonidine squaramide (chiral bissquaramide) to afford 3, which was thereafter polymerized under an ADMET condition to produce P3. The same asymmetric reaction was observed with P3 as a catalyst. When compared to P2C, somewhat higher diastereoselectivity was achieved with P3 (entry 17). Another chiral polymer (P4) was prepared by the copolymerization of 3 and 4. Although the diastereoselectivity decreased, an excellent ee was achieved with P4 (entry 18).

The asymmetric reactions proceeded in a heterogeneous system since the chiral ADMET polymers were insoluble in most of the generally utilized organic solvents. The utilization of P1 facilitated the easy separation of the catalyst from the reaction mixture by filtration. The recyclability test was, therefore, performed with P1 in acetonitrile at room temperature. At the end of the reaction, the polymer was readily separated from the reaction mixture and washed with ether three times. The recovered polymer was employed in subsequent reactions. Although the third and fourth reuse cycles exhibited lower ee (Table 3, entries 3 and 4) than the first and second, the catalytic performance of P1 was maintained for several cycles.

Table 3. Recycling of P1.

| Cycle | Yield (%)<sup>b</sup> | dr<sup>c</sup> | % ee<sup>c</sup> |
|-------|-----------------------|----------------|------------------|
| original | 97                    | 1:100          | 95               |
| 1      | 73                    | 1:54           | 97               |
| 2      | 93                    | 1:59           | 97               |
| 3      | 90                    | 1:59           | 94               |
| 4      | 82                    | 1:46           | 93               |
| 5      | 72                    | 1:51           | 95               |

<sup>a</sup> Reactions were performed with 5 (0.50 mmol), 6 (0.55 mmol), and P1 (5 mol%) in CH₃CN (2.5 mL) at 25 °C.

<sup>b</sup> Isolated yield of the product 7 after purification by column chromatography.

<sup>c</sup> dr and ee were determined by chiral HPLC (Chiralcel OD-H).
Finally, we applied P$_1$ as a polymeric organocatalyst in the asymmetric Michael addition of various kinds of substrates. The reaction between ethyl 2-oxocyclopanecarboxylate and 6 proceeded readily in acetonitrile to afford the corresponding asymmetric product 8 in good yield and excellent diastereoselectivity of >100:1, $dr$, and high $ee$ (Scheme 3). Further, 6 was allowed to react with two other Michael donors, including pentane-2,4-dione and anthrone. In the case of anthrone, product 10 was obtained with low enantiopurity. The Michael donor (5) readily reacted with 4-fluoro-trans-$\beta$-nitrostyrene, 4-methyl-trans-$\beta$-nitrostyrene, and (2-nitrovinyl)thiophene in the presence of P$_1$ to afford the Michael adducts (11, 12, and 13) with good yields and high $ees$. The stereoselectivity of the chiral product that was obtained from methyl-trans-$\beta$-nitrostyrene was not determined due to the incomplete separation of the products by chiral HPLC analysis.

![Scheme 3](image_url)

**Scheme 3.** Asymmetric Michael addition reaction involving different combinations of the Michael donors and acceptors, using P$_1$. Reactions were conducted with the Michael donor (0.50 mmol), Michael acceptor (0.55 mmol), and P$_1$ (5 mol%) in acetonitrile (2.5 mL) at 25 °C. Isolated yield of the product after purification by column chromatography. $dr$ and $ee$ were determined by chiral HPLC (Chiralcel OD-H) for compounds 8, 11–13; Chiralcel AD-H for compound 9 and Chiralcel AS-H for compound 10. $^d$ $dr$ and $ee$ were not determined due to the incomplete separation of the products by chiral HPLC.

3. **Materials and Methods**

3.1. **Materials and General Considerations**

All of the solvents and reagents were purchased from Sigma Aldrich (St. Luis, MO, USA), Wako Pure Chemical Industries, Ltd. (Tokyo, Japan), or Tokyo Chemical Industry (TCI) Co., Ltd. (Tokyo, Japan). in the highest available purity and they were utilized as received. The reactions were monitored by thin-layer chromatography (TLC) using precoated silica gel plates (Merck 5554, 60F254). Column chromatography was performed using a silica gel column (Wakogel C-200, 100–200 mesh). The NMR spectra were recorded on JEOL JNM-ECS400 spectrometers in deuterated chloroform (CDCl$_3$) or deuterated dimethyl sulfoxide (DMSO-$d_6$) solvent at room temperature operating at 400 ($^1$H) and 100 MHz ($^{13}$C[1H]). Tetramethylsilane (TMS) and CDCl$_3$ were used as the internal standards for $^1$H and $^{13}$C NMR, respectively. The chemical shifts are reported in parts per million (ppm) while using TMS as a reference, and the $J$ values are reported in hertz (Hz). The infrared (IR) spectra were recorded on a JEOL JIR-7000 Fourier-transform (FT)–IR (FT–IR) spectrometer and they were reported in reciprocal centimeters (cm$^{-1}$). High-performance liquid chromatography (HPLC) was
performed on a Jasco HPLC system consisting of a DG-980-50 three-line degasser, PU-980 HPLC pump, and CO-965 column oven and equipped with a chiral column (Chiralpak OD-H, AD-H Daicel), using hexane/2-propanol as the eluent. A Jasco UV-975 UV detector was employed for peak detection. Size-exclusion chromatography (SEC) was performed using a Tosoh HLC 8020 instrument with UV (254 nm) for refractive index detection. Dimethylformamide (DMF) with 0.5 wt% LiCl/LiBr was used as the carrier solvent at a flow rate of 1.0 mL min⁻¹ at 40 °C. Two polystyrene gel columns with 10 μm beads were utilized. A calibration curve was generated for determining the number average molecular weight (Mn) and molecular weight distribution (Mw/Mn), using polystyrene standards. The optical rotation was recorded on a JASCO DIP-149 digital polarimeter using a 10 cm thermostated microcell.

### 3.2. Synthesis of Cinchona-Based Squaramide Containing the Chiral ADMET Polymer

#### 3.2.1. Polymer P1

Squaramide 1 (133.0 mg, 0.200 mmol), HG₂A (6.26 mg, 0.010 mmol), and toluene (0.5 mL) were collected in a dried Schlenk tube, after which they were set in an oil bath with a condenser. The Schlenk tube was connected to continuous N₂ gas flow. The reaction mixture was stirred for 9 h after setting the desired reaction temperature (100 °C). Thereafter, the reaction mixture was cooled to room temperature and then poured into diethyl ether (50 mL). Next, the solid polymer product was purified by reprecipitation in diethyl ether (70–80 mL) three times. The precipitate was filtered out and vacuum-dried at 40 °C for 3 h to afford the desired polymer (P1 with 77% yield as a brownish solid), which is an ADMET polymeric organocatalyst. [α]D²⁵ = +90.99 (c 0.175 g/dL in DMF at 26.0 °C).

1H NMR (400 MHz, DMSO-d₆, 25 °C); δ 8.37, 8.43, 8.84, 8.98 (1H), 7.48–8.26 (aromatic H), 5.71–6.08 (vinylc H), 5.43 (2H), 5.02–5.15 (m, 2H), 3.05, 2.89, 2.72, 2.67, 2.34, 2.10, 1.55, 1.45, 1.26, 0.93, 0.76, and 0.65 (quinuclidine H) ppm. IR (KBr): ν = 3380, 3208, 2936, 2863, 1793, 1672, 1360, 1258, 1239, 1085, 1030, 975, 848, 692, and 624 cm⁻¹. Mₙ (SEC) = 4.7 × 10⁴, Mₙ/Mₚ = 1.04.

Other optically active polymers were prepared from different cinchona-based squaramides (1–3) with HG₂A while using the same process. Table 1 summarizes the relevant results.

#### 3.2.2. Representative Procedure for the Asymmetric Michael Reaction between β-Ketoesters and Trans-β-Nitrostyrene to Yield Nitroolefins Using P1

Methyl 2-oxocyclopentanecarboxylate (5) (63 µL, 0.50 mmol) and trans-β-nitrostyrene (6) (82.05 mg, 0.55 mmol) were placed in a vessel with 2.5 mL of a solvent. Subsequently, P1 (5 mol%) was added to the mixture. The reaction mixture was then stirred at 25 °C for a specified time. The solvent was evaporated with a rotary evaporator after the complete consumption of 5, which was monitored by TLC. The residue was washed with ether, which was subsequently separated by decantation. Unused P1 was recovered for reuse. The collected ether solution was concentrated in vacuo, and the crude product was purified by silica gel column chromatography (100–200 mesh) with hexane/ethyl acetate (EtOAc), 6.0/1.0, as the eluent to afford 7 as a colorless oil. ¹H NMR (400 MHz, 25 °C, CDCl₃); δ = 7.29–7.23 (m, 5H), 5.14 (dd, J = 13.8 Hz, 3.8 Hz, 1H), 5.00 (dd, J = 13.8 Hz, 10.7 Hz, 1H), 4.08 (dd, J = 10.8 Hz, 3.8 Hz, 1H), 3.74 (s, 3H), 2.38–2.33 (m, 2H), and 2.04–1.84.

Additional asymmetric Michael additions were similarly performed and the results are summarized in Tables 2 and 3, as well as in Scheme 3.

### 4. Conclusions

In summary, we successfully synthesized chiral cinchona squaramide polymers P1–P3 by ADMET polymerization. The vinyl group in cinchona alkaloid exhibited good reactivity in ADMET polymerization when HG₂ was employed to afford the optically active polymers in high yields. The copolymerization with triallyl ether also readily proceeded to afford P4. Asymmetric Michael reaction of 5 with 6 was efficiently catalyzed by the cinchona squaramide polymers to afford the Michael adducts with high stereoselectivity and isolated yields. P1a afforded 7a and c as major...
diastereomers, while P2C, P2Q, P3, and P4 afforded 7b and d. Both pseudoenantiomeric polymeric catalysts exhibited excellent performance in the same asymmetric reaction with high stereoselectivity. Different stereoisomers can be obtained by the proper selection of the catalytic structure of the cinchonidine and cinchonine derivatives. The recovery of the catalysts from the reaction mixture was dramatically improved by using the insoluble polymeric organocatalysts. These catalysts can be reused several times in the same asymmetric reaction without any significant loss in their catalytic activity.

**Supplementary Materials:** The following are available online at [http://www.mdpi.com/2073-4344/10/5/591/s1](http://www.mdpi.com/2073-4344/10/5/591/s1), details and data supplemental to the main text is shown here.

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