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Asymmetric Induction in the Base-Catalyzed Reactions Using Polymer-Supported Quinines with Spacer Groups

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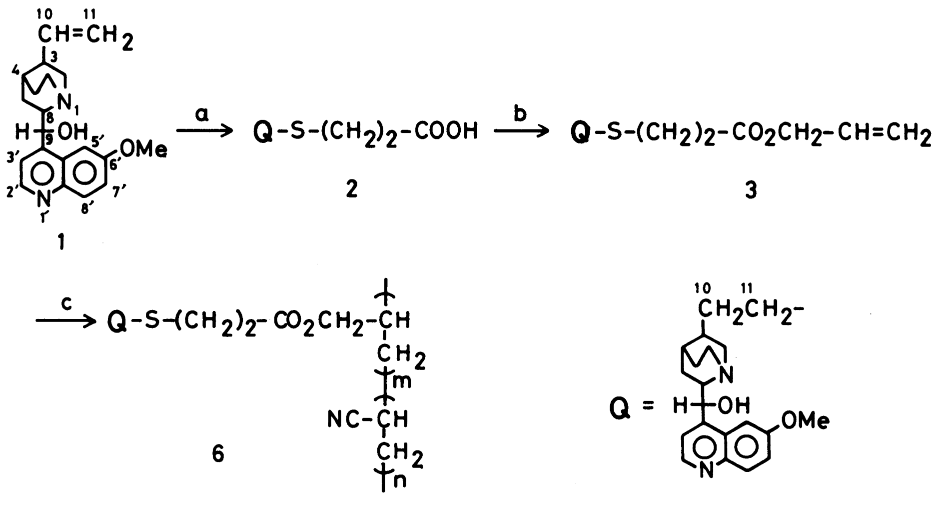
New polymer-supported quinines having the spacer groups were synthesized and utilized for three types of base-catalyzed asymmetric reactions. Insertion of the spacer groups leads to improve the stereoselectivity in comparison with the polymer-catalyst with no spacer groups.

Cinchona alkaloid and its derivertives have been used as chiral catalysts in asymmetric reactions because of their unique stereochemical properties.[1—3] We also investigated the methanolysis of cyclic anhydrides using cinchona alkaloids as catalysts.[4] In order to obtain more easy-to-handle catalysts, many workers[5—9] have prepared polymer-supported cinchona alkaloids. In particular, Kobayashi et al. synthesized chiral functionalized polymers having relatively higher stereoselectivity by copolymerization with acrylonitrile and the vinyl group of the alkaloids.[7] But the utilization of a Kobayashi's polymers for the methanolysis of *cis*-2,4-dimethylglutaric anhydride resulted in low steroselectivity.

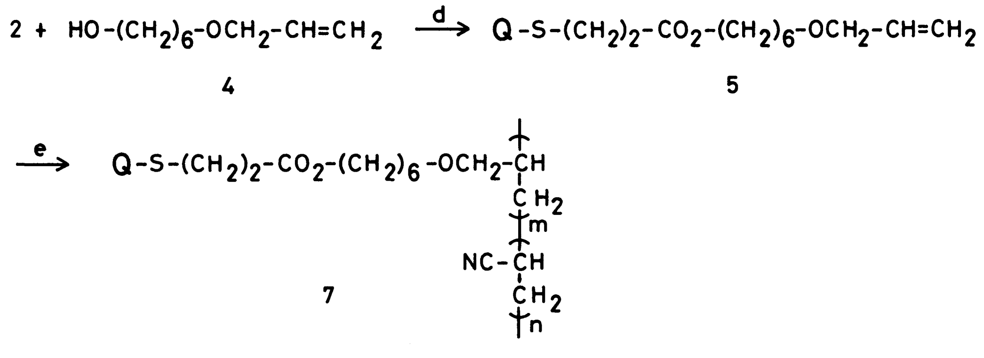
It has been found that the reactivity of catalyst or reagent is often reduced by being polymer-supported. One approach to overcome this drawback is introduction of spacer group between catalytic center and polymer matrix. By inserting a spacer group, the reactivity[10—13] and/or selectivity[14] can be improved. This also holds the case with immobilized enzymes.[15] Thus we prepared the polymer-supported quinine derivatives with spacer groups of various length, and applied them for three types of asymmetric base-catalyzed reactions.

Results and Discussion

Preparation of Polymer-Supported Quinines with Spacer Groups. The synthetic strategy is shown in Schemes 1—3. Our first attempt to submit methyl 3-mercaptopropionate to the reaction with quinine (**1**) was unsuccessful. But 3-mercaptopropionic acid easily reacted with **1** in the presence of 2,2′-azobisisobutyronitrile (AIBN) as a radical initiator to give the carboxylic acid derivative **2** as a colorless powder in 91% yield. In order to introduce a polymerizable double bond, esterification of **2** with allyl alcohol by the use of thionyl chloride afforded **3** having a spacer group as long as 8-atoms from the quinuclidine ring of quinine in 72% chemical yield. The carboxylic acid **2** was also esterified by the Mitsunobu reaction with the alcohol **4** derived from 6-chloro-1-hexanol to give the ester **5** having a spacer group of 15-atoms length in 94% yield. Copolymerization of quinine derivatives **3** and **5** with acrylonitrile in dry DMF afforded the polymers **6** and **7**, respectively. The crude polymers were reprecipitated and Soxhlet-extracted to remove unreacted monomers. The alkaloid content of **6** and **7** were determined by elemental analyses to be 1.10 and 1.24 mol%, respectively. These values were lower than

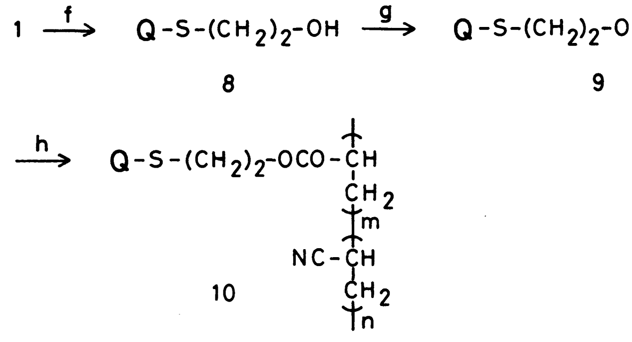


Scheme 1. (a): $HSCH_2CH_2COOH$, AIBN; 91%, (b): $HOCH_2CH=CH_2$, $SOCl_2$; 72%, (c): $CH_2=CHCN$. AIBN; 57%.



$$2 + \mathrm{HO{-}(CH_2)_6{-}OCH_2{-}CH{=}CH_2} \xrightarrow{d} \mathrm{Q{-}S{-}(CH_2)_2{-}CO_2{-}(CH_2)_6{-}OCH_2{-}CH{=}CH_2}$$

Scheme 2. (d): Diethyl azodicarboxylate, PPh3; 94%, (e): CH2=CHCN, AIBN; 43%.



$$1 \xrightarrow{f} \mathrm{Q{-}S{-}(CH_2)_2{-}OH} \xrightarrow{g} \mathrm{Q{-}S{-}(CH_2)_2{-}OCOCH{=}CH_2}$$

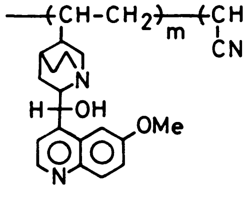
Scheme 3. (f): HSCH2CH2OH, AIBN; 77%, (g): diethyl azodicarboxylate, CH2=CHCOOH, PPh3; 67%, (h): CH2=CHCN, AIBN; 57%.

Table 1. Physical Properties of Polymer-Supported Quinines with Spacer Groups

Polymer-catalyst	Spacer length	Initial molar ratio[a]	$[\alpha]_D$[b]/°	Elemental analysis/% C	H	N	Alkaloid content/mol%
6	8	1 : 19	−5.6[c]	67.41	5.78	24.44	1.10
7	15	1 : 19	−6.5	67.62	5.95	23.81	1.24
10	7	1 : 9	−26.0	65.82	6.15	17.69	8.04
11	0	1 : 19	−10.4[d]	68.33	5.93	24.39	1.99

a) Initial molar ratio of monomer **1**, **3**, **5**, and **9** vs. acrylonitrile. b) Measured in DMF at 25 °C. c) At 27 °C. d) At 28 °C.

that expected from the initial alkaloid concentration (5 mol%) in the reaction mixture. Therefore we synthesized another copolymer with higher alkaloid content. The monomer having an acryloyl group was prepared which can polymerize with acrylonitrile more easily than simple terminal double bond.[16] Then, **1** was allowed to react with 2-mercaptoethanol to give **8**.[17] The compound **8** was converted to the acrylic ester **9** by the selective esterification of the primary hydroxyl group by the Mitsunobu reaction. It is worth noting that the secondary hydroxyl group of quinine moiety was exclusively esterified when **8** was treated with acryloyl chloride. Copolymerization of **9** with acrylonitrile (1:9 molar ratio) afforded the copolymer **10** having an alkaloid content of 8.04 mol%, which agreed with the initial molar ratio in the reaction mixture. To evaluate the spacer effect, we also synthesized the polymer **11** having no spacer group according to the Kobayashi's method.[18] The



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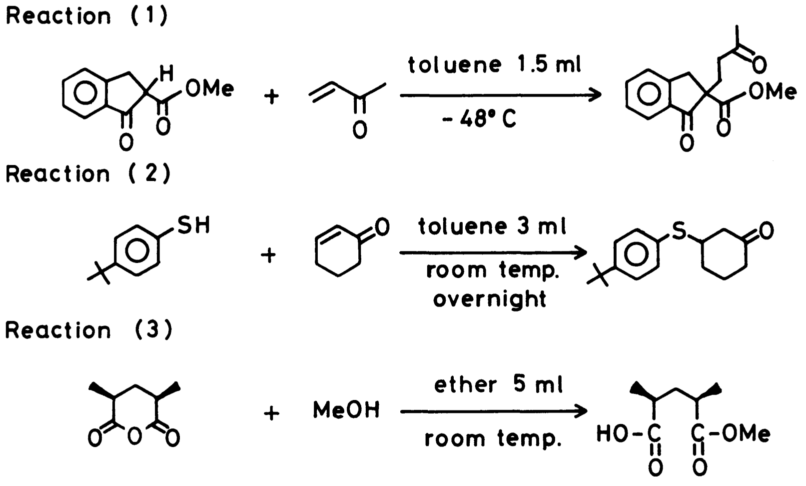
conditions employed in polymerizations and some properties of the polymers **6**, **7**, **10**, and **11** are compiled in Table 1.

Asymmetric Reactions Catalyzed by Polymer-Supported Quinine with Spacer Groups. Polymers **6**, **7**, **10**, and **11** were used as catalysts for three types of



Scheme 4.

Table 2. Asymmetric Addition of Methyl 1-Oxo-2-indancaboxylate to 3-Buten-2-one Catalyzed by Polymers **6**, **7**, **10**, and **11**; the Reaction (1)[a)]

Entry	Catalyst	Spacer length	Reaction period/h	Isolated yield/%	$[\alpha]^{25}_{578}$/°	e.e.[b)] /%	Abs. config.
1	**7**	15	28	88	−50.4	65	*S*
2	**6**	8	28	96	−47.4	62	*S*
3	**10**	7	6.6d	2[c)]	—[d)]	—	—
4	**11**	0	28	99	−37.8	49	*S*
5	**5**	—	14	quant.	−58.1	75	*S*
6	**3**	—	14	quant.	−58.7	76	*S*
7	**9**	—	27	quant.	−57.9	75	*S*
8	**1**	—	28	quant.	−58.7	76	*S*
9	**10**	7	3.9d	92	−34.4	45	*S*

a) The reaction temperature was −48 °C for Entries 1—8 and room temperature for the Entry 9. b) Based on $[\alpha]^{\mathrm{r.t.}}_{578} = -77°$ (*c* 2, benzene) for the optically pure product. c) Determined by HPLC. d) Not measured.

base-catalyzed reactions including the Michael addition of methyl 1-oxo-2-indancarboxylate to 3-buten-2-one (Reaction (1)),[1)] the conjugated addition of *p-t*-butylbenzenethiol to 2-cyclohexenone (Reaction (2)),[2)] and the methanolysis of *cis*-2,4-dimethylglutaric anhydride (Reaction (3)).[4)]

The results of the Reaction (1) catalyzed by polymers **6**, **7**, **10**, and **11** are shown in Table 2. The reaction was also effected using monomeric alkaloids **1**, **3**, **5**, and **9** for comparison. The monomers **3**, **5**, and **9**, as well as **1**, promoted the reaction to give the adduct quantitatively with 75—76% optical purity. Elongation of spacer arms from the (C)-3 vinyl group of quinine did not reduce the stereoselectivity (Table 2, Entries 5—8). In other words, the conformation of the catalytic center of quinine, around the hydroxyl group and nitrogen atom of quinuclidine moiety, was kept unaltered. Polymer-catalysts **6**, **7**, and **11** on the other hand, gave the product with 88—99% yield, and somewhat lower asymmetric yields than the corresponding monomers. The polymers **6** and **7** with spacer groups showed higher stereoselectivity 62 and 65% than **11** with no spacer 49% (Table 2, Entries 1, 2 vs. 4).

The results of the Reaction (2) are shown in Table 3. The monomers **1**, **3**, **5**, and **9**, gave the addition product in high chemical yield with 25—45% e.e. Polymers **6**, **7**, and **11** also catalyzed the reaction with 89—98% chemical yield. But the optical purities were extremely reduced in comparison with their monomeric counterparts **1**, **3**, **5**, and **9**, respectively. The reason for this phenomena is unclear at present, but at least the result can not be attributed to spontaneous reaction in the presence of polymer matrix, since poly(acrylonitrile) itself has no catalytic activity (Table 3, Entry 5). Thus the polymer-catalysts, with or without spacer group, were found to be unsuitable so far as this asymmetric reaction.

On the other hand, polymers **6**, **7**, **10**, and **11** were good catalysts for the Reaction (3) as shown in Table 4. Although they showed lower stereoselectivity than the corresponding monomers **1**, **3**, **5**, and **9**,

Table 3. Asymmetric Addition of Thiol Catalyzed by Polymers **6**, **7**, **10**, and **11**; the Reaction (2)

Entry	Catalyst	Spacer length	Isolated yield/%	$[\alpha]^{25}_{578}$/°	e.e.$^{a)}$ /%	Abs. config.
1	**7**	15	89	+ 5.8	8	*R*
2	**6**	8	90	+ 4.8	6	*R*
3	**10**	7	7$^{b)}$	—$^{c)}$	—	—
4	**11**	0	98	+ 4.2	5	*R*
5	poly(AN)$^{d)}$	—	7$^{b)}$	—$^{c)}$	—	—
6	**5**	—	83	+19.4	25	*R*
7	**3**	—	96	+27.1	35	*R*
8	**9**	—	87	+23.1	30	*R*
9	**1**	—	97	+31.5	41	*R*

a) Based on $[\alpha]^{21}_{578}=+77°$ (*c* 1, CCl_4) for optically pure product. b) Determined by HPLC. c) Not measured. d) Poly(acrylonitrile) containing no quinine moiety.

Table 4. Asymmetric Methanolysis of an Acid Anhydride Catalyzed by Polymers **6**, **7**, **10**, and **11**; the Reaction (3)

Entry	Catalyst	Spacer length	Reaction period$^{a)}$ /day	e.e.$^{b)}$ /%	Selectivity$^{c)}$
1	**7**	15	4.0	32	*R*-side
2	**6**	8	3.8	22	*R*-side
3	**10**	7	8.6$^{d)}$	20	*R*-side
4	**11**	0	2.6	14	*R*-side
5	**5**	—	1.5	12	*R*-side
6	**3**	—	2.0	57	*R*-side
7	**9**	—	2.0	29	*R*-side
8	**1**	—	3.8	50	*R*-side
9$^{e)}$	**7**	15	9.0	28	*R*-side
10$^{e)}$	**6**	8	12.2	33	*R*-side

a) Conversion = >95%. b) Determined by HPLC after converting the product to the diastereometric amide ester. c) We define the selectivity as *R*-side when the caboxyl group next to the asymmetric center with *R*-configuration was attacked preferentially by the nucleophile. d) The reaction was worked up at a conversion of ca. 40% and the e.e. was determined. e) Reuse of catalyst.

respectively, the effect of the spacer group was also observed clearly. The stereoselectivity of the reaction was improved from 14 to 22% e.e. by inserting a spacer group with 8-atoms length, moreover by inserting a 15-atoms-spacer the steroselectivity was raised up to 32% (Table 4, Entries 1, 2, and 4).

The polymer **10**, having another type of spacer group containing acryloyl moiety had a lower activity as to all the three Reactions (1)—(3). However, when the reaction was carried out at room temperature, the polymer **10** slowly catalyzed the Reaction (1) to give the *S* enantiomer of methyl 2-(3-oxobutyl)-1-oxo-2-indancarboxylate with 45% e.e. (Table 2, Entry 9). The similar feature was also observed for the Reaction (3) (Table 4, Entry 3). This indicates that configurational environment of the alkaloid moieties in polymer **10** was retained after the copolymerization in spite of their low catalytic activity.

One of the advantage of polymer-catalysts is that they can be recovered by filtration and reused. Thus the recovered polymers **6** and **7** were reused as the catalysts in the Reaction (3). As shown in Table 4, although the recovered **6** and **7** exhibited lower catalytic activity, the stereoselectivities were comparable with the first usages. (Table 4, Entries 9 and 10 vs. 1 and 2).

In summary, polymer-supported quinines were prepared in which the spacer arms was elongated to remote the catalytic center from polymer chain. Those polymers were found to be good catalysts for the three types of asymmetric reactions as well, and by inserting spacer groups, enantioselectivities were approached to those of the corresponding non-immobilized catalysts.

Experimental

General Procedure. The spectroscopic and analytical instruments were: ^{1}H NMR, Varian EM-360 (60 MHz), VXR-200 (200 MHz), and JEOL GX-400 (400 MHz); ^{13}C NMR, Varian VXR-200 (50 MHz) and JEOL GX-400 (100 MHz); IR, Hitachi 215; Elemental Analysis, Yanaco MT-3; MS, JEOL JMS-DX-300; Optical Rotation, Perkin-Elmer 241; GLC, Shimadzu GC-4B; HPLC, JASCO BIP-I. NMR spectra were measured in $CDCl_3$ with TMS as internal standard throughout unless otherwise specified. Toluene and methanol were distilled over CaH_2. Diethyl ether and THF were distilled from benzophenone ketyl before use. Acrylonitrile was distilled and immediately used for polymerization.

11-(2-Carboxyethylthio)-10,11-dihydroquinine (2): A mixture of **1** (9.73 g, 30 mmol), 3-mercaptopropionic acid (31.67 g, 300 mmol), and 2,2′-azobisisobutyronitrile (AIBN) (0.99 g, 6 mmol) in benzene (80 ml) was heated at 70 °C for 17 h under Ar atmosphere. The reaction mixture was extracted with 2 M† HCl (3×50 ml). The combined extracts were washed with ether (2×50 ml) and made alkaline (pH 8)

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† 1 M=1 mol dm^{-3}.

with Na_2CO_3 powder to afford **2** as viscous semisolid. It became powder by cooling at 4 °C overnight. The powder was collected and dried, and used for the next step without further purification; 10.55 g (82%): $[\alpha]^{25}_{D}$ 211° (*c* 1.022, 0.1 M HCl); ^{1}H NMR (200 MHz, DMSO-d_6) δ=1.30—3.55 (19H, m, H of quinuclidine ring and spacer arms), 3.91 (3H, s, CH_3O), 5.54 (1H, d, *J*=4.4 Hz, H-9), 6.15 (3H, br s, OH and COOH), 7.37 (1H, dd, *J*=9.2 and 2.5 Hz, H-7′), 7.50 (1H, d, *J*=2.5 Hz, H-5′), 7.54 (1H, d, *J*=4.7 Hz, H-3′), 7.92 (1H, d, *J*=9.2 Hz, H-8′), 8.68 (1H, d, *J*=4.7 Hz, H-2′); ^{13}C NMR (50 MHz, DMSO-d_6) δ=21.427, 24.991, 26.705, 26.972, 28.969, 33.537, 33.592, 35.724, 41.844, 55.652, 56.051, 59.605, 68.936, 102,143, 118.958, 121.119, 126.501, 131.106, 143.768, 147.363, 148.007, 157.073, 174.080; MS (30 eV) *m/z* (rel intensity) 430 (M$^+$; 6), 242 (8), 44 (100); Found: *m/z* 430.1927. Calcd for $C_{23}H_{30}N_2O_4S$: M, 430.1927; IR (KBr) 3410 (OH), 1620 cm^{-1} (C=O).

11-[2-(Allyloxycarbonyl)ethylthio]-10,11-dihydroquinine (3): To a suspension of **2** (2.50 g, 5.81 mmol) in allyl alcohol (40 ml), was added thionyl chloride (1.45 g, 12.16 mmol) at 0 °C with stirring. Then the mixture was stirred at room temperature for 3 h. The resulting mixture was evaporated and quenched with 1 M NaOH at 0 °C, followed by extraction with CH_2Cl_2 (4×25 ml). The extracts were washed with brine and dried (Na_2SO_4). Evaporation followed by column chromatography on silica gel (eluent, $CHCl_3$(70)–MeOH(2)–NEt_3(1)) and concentration gave **3** as a syrup; 1.96 g (72%): $[\alpha]^{28}_{D}$ −122° (*c* 0.968, EtOH); ^{1}H NMR (400 MHz) δ=1.35—1.82, 2.32, 2.58, 2.99—3.05, and 3.47 (13H, m, H of quinuclidine ring and H-10), 2.41 (2H, m, H-11), 2.57 (2H, m, $C\underline{H}_2CO_2$), 2.71 (2H, m, $SC\underline{H}_2CH_2CO_2$), 3.90 (3H, s, CH_3O), 4.56 (2H, m, *J*=5.9 and 1.5 Hz, allyl H), 5.21 (1H, m, *J*=10.3, 2.5, and 1.5 Hz, (*Z*)-vinyl H), 5.29 (1H, m, *J*=17.1, 3.2, and 1.5 Hz, (*E*)-vinyl H), 5.36 (1H, br s, OH), 5.50 (1H, d, *J*=3.4 Hz, H-9), 5.88 (1H, m, *J*=17.1, 10.3, and 5.9 Hz, =CH), 7.21 (1H, d, *J*=2.4 Hz, H-3′), 7.25 (1H, dd, *J*=9.3, and 2.9 Hz, H-7′), 7.44 (1H, d, *J*=4.4 Hz, H-5′), 7.87 (1H, d, *J*=9.3 Hz, H-8′), 8.43 (1H, d, *J*=4.9 Hz, H-2′); ^{13}C NMR (100 MHz) δ=20.959, 25.512, 26.987, 27.483, 30.022, 34.182, 34.255, 34.678, 43.144, 55.681, 57.739, 59.695, 65.036, 70.670, 100.839, 117.798, 117.973, 120.980, 125.899, 130.905, 131.416, 143.530, 146.493, 146.741, 157.162, 170.662; MS (30 eV) *m/z* (rel intensity) 470 (M$^+$; 27), 282 (42), 32 (100); Found: *m/z* 470.2235. Calcd for $C_{26}H_{34}N_2O_4S$: M, 470.2239; IR (liquid) 3080 (OH), 1735 cm^{-1} (C=O).

6-Allyloxy-1-hexanol (4): The allyl ether **4** was prepared from 6-chloro-1-hexanol and allyl alcohol through its THP ether; 2.20 g (37% from 6-chloro-1-hexanol): bp (bath) 142—148 °C/13 mmHg[††]; ^{1}H NMR (200 MHz) δ=1.20—1.60 (8H, m, CH_2×4), 2.65 (1H, s, OH), 3.22—3.68 (4H, m, OCH_2×2), 4.83—4.92 (2H, m, allyl H), 5.05—5.26 (2H, m, CH_2=), 5.70—5.95 (1H, m, =CH).

11-[2-[6-(Allyloxy)hexyloxycarbonyl]ethylthio]-10,11-dihydroquinine (5): The carboxylic acid **2** (2.50 g, 5.81 mmol), **4** (1.10 g, 6.98 mmol), and triphenylphosphine (1.83 g, 6.98 mmol) were suspended in dry THF (60 ml), and diethyl azodicarboxylate (1.21 g, 6.98 mmol) was added dropwise to the mixture at 0 °C with stirring over a period of 15 min. The mixture was stirred overnight at room temperature and evaporated to dryness, and extracted with 2 M HCl (4×25 ml). The combined acid extract was washed with ether (6×35 ml) and made alkaline with NaOH pellet, and extracted with CH_2Cl_2 (4×25 ml). The extract was washed with brine and dried (Na_2SO_4). Evaporation gave **5**; 3.12 g (94%): $[\alpha]^{24}_{D}$ −101° (*c* 1.156, EtOH); ^{1}H NMR (400 MHz) δ=1.30—1.85, 2.35, 2.61, 3.02—3.08, and 3.47 (21H, m, H of quinuclidine ring, H-10, and CH_2×4), 2.42 (2H, t, *J*=7.3 Hz, H-11), 2.53 (2H, t, *J*=7.3 Hz, $C\underline{H}_2CO_2$), 2.70 (2H, t, *J*=7.3 Hz, $SC\underline{H}_2CH_2CO_2$), 3.40 (2H, t, *J*=6.4 Hz, $C\underline{H}_2OCH_2$–CH=), 3.87 (3H, s, CH_3O), 3.94 (2H, m, *J*=5.4 and 1.5 Hz, allyl H), 4.05 (2H, t, *J*=6.8 Hz, $CO_2OC\underline{H}_2$), 4.88 (1H, br s, OH), 5.16 (1H, m, *J*=10.3 and 1.5 Hz, (*Z*)-vinyl H), 5.25 (1H, m, *J*=17.1, 3.4, and 1.5 Hz, (*E*)-vinyl H), 5.52 (1H, m, H-9), 5.90 (1H, m, *J*=17.1, 10.3, and 5.4 Hz, =CH), 7.22 (1H, d, *J*=2.4 Hz, H-5′), 7.27 (1H, dd, *J*=9.3, and 2.4 Hz, H-7′), 7.46 (1H, d, *J*=4.4 Hz, H-3′), 7.90 (1H, d, *J*=9.3 Hz, H-8′), 8.51 (1H, d, *J*=4.4 Hz, H-2′); ^{13}C NMR (50 MHz) δ=21.404, 25.688, 25.835, 25.908, 27.157, 28.013, 28.586, 29.683, 30.196, 34.452, 34.631, 34.882, 43.627, 55.805, 58.202, 59.876, 64.770, 70.242, 71.580, 71.811, 101.370, 116.688, 118.423, 121.382, 126.527, 131.343, 134.941, 144.029, 147.326, 147.725, 157.657, 171.846; MS (70 eV) *m/z* (rel intensity) 570 (M$^+$; 4), 382 (5), 32 (100); Found: *m/z* 570.31328. Calcd for $C_{32}H_{46}N_2O_5S$: M, 570.31278; IR (liquid) 3150 (OH), 1740 cm^{-1} (C=O).

Alkaloid 3-Acrylonitrile Copolymer (6): The alkaloid **3** (1.91 g, 4.06 mmol), acrylonitrile (4.09 g, 77.14 mmol), and AIBN (0.018 g, 0.11 mmol) in dry DMF (14.8 ml) were heated at 60 °C for 21 h under Ar atmosphere. The reaction mixture was poured into boiling MeOH (1000 ml). Precipitated polymer was filtered, reprecipitated twice and Soxhlet-extracted with MeOH (5 h) to remove unreacted monomers. The residue was dried (over P_2O_5 in vacuo at 70 °C (4 h)), to give the polymer **6**; 3.39 g (57%): $[\alpha]^{27}_{D}$ −5.6° (*c* 1.022, DMF); Elemental analysis. Found: C, 67.41; H, 5.78; N, 24.44%; Alkaloid content 1.10 mol%.

Alkaloid 5-Acrylonitrile Copolymer (7): The alkaloid **5** (2.58 g, 4.52 mmol), acrylonitrile (4.56 g, 85.89 mmol), and AIBN (0.021 g, 0.13 mmol) in dry DMF (17.5 ml) were heated at 60 °C for 22 h under Ar atmosphere. The same purification process described above afforded the polymer **7**; 3.08 g (43%): $[\alpha]^{25}_{D}$ −6.5° (*c* 1.086, DMF); Elemental analysis. Found: C, 67.62; H, 5.95; N, 23.81%; Alkaloid content 1.24 mol%.

11-(2-Hydroxyethylthio)-10,11-dihydroquinine (8): Quinine (**1**) (9.73 g, 30 mmol), 2-mercaptoethanol (18.75 g, 240 mmol), and AIBN (0.99 g, 6 mmol) in benzene (80 ml) were heated at 70 °C for 28 h under Ar atmosphere. The reaction mixture was extracted with 2 M HCl (2×50 ml). The extracts were washed with ether (2×50 ml), and made alkaline with NaOH pellet. The liberated oil was taken up with CH_2Cl_2 (3×50 ml). The combined extracts were washed with brine and dried (Na_2SO_4). Evaporation and chromatography on silica gel (eluent $CHCl_3$(70)–MeOH(2)–NEt_3(1)) afforded **8** as a syrup; 9.25 g (77%): $[\alpha]^{25}_{D}$ −108° (*c* 1.030, EtOH), (Ref. 17 $[\alpha]^{25}_{D}$ −140.6° (EtOH)); ^{1}H NMR (400 MHz) δ=1.22—1.80, 2.26, 2.52, 2.90—3.00, and 3.48 (13H, m, H of quinuclidine ring and H-10), 2.37 (2H, m, H-11), 2.59 (2H, t, *J*=6.4 Hz, SCH_2), 3.63 (2H, t, *J*=6.4 Hz, CH_2O), 3.83 (3H, s, CH_3O), 4.36 (1H, br s, OH), 5.49 (1H, m, H-9), 5.59 (1H, br s, OH), 7.13—7.26, 7.43, 8.79, and 8.42 (5H, m, H of quinoline ring); ^{13}C NMR (50 MHz) δ=20.880,

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[††] 1 mmHg=133.322 Pa.

25.633, 27.945, 29.956, 34.586, 35.154, 43.189, 55.742, 58.157, 59.681, 60.700, 68.403, 71.322, 101.509, 118.476, 121.377, 126.532, 130.996, 143.709, 147.110, 148.461, 157.733; MS (70 eV) *m/z* (rel intensity) 402 (M^+; 57), 357 (49), 214 (100).

11-[2-(Acryloyloxy)ethylthio]-10,11-dihydroquinine (9): To a suspension of **8** (4.00 g, 9.94 mmol), acrylic acid (0.745 g, 10.33 mmol), and triphenylphosphine (2.71 g, 10.33 mmol) in dry THF (100 ml), was added dropwise a solution of diethyl azodicarboxylate (1.80 g, 10.33 mmol) in dry THF (5 ml) with stirring at 0 °C over a period of 15 min. The mixture was stirred at 0 °C for 30 min and then at room temperature overnight. The reaction mixture was evaporated to dryness. The residue was dissolved in 2 M HCl (80 ml). Aqueous layer was washed with ether (6×30 ml), made alkaline with Na_2CO_3 powder and extracted with CH_2Cl_2 (2×50 ml). The extracts were washed with brine and dried (Na_2SO_4), and the solvent was evaporated. The residue was flush chromatographed on silica gel (eluent $CHCl_3$-(50)–MeOH(2)–NEt_3(1)) to afford **9**; 3.02 g (67%): $[\alpha]_D^{25}$ −105° (*c* 1.044, EtOH); ^1H NMR (400 MHz) δ=1.34—1.83, 2.38, 2.61, 3.02—3.08, and 3.53 (13H, m, H of quinuclidine ring and H-10), 2.45 (2H, t, *J*=7.3 Hz, H-11), 2.70 (2H, t, *J*=6.8 Hz, SCH_2), 3.84 (3H, s, CH_3O), 4.23 (2H, a, *J*=6.8 Hz, CH_2O), 5.56 (2H, m, H-9 and OH), 5.80 (1H, m, *J*=10.3, 2.4, and 1.5 Hz, (*Z*)-vinyl H), 6.07 (1H, m, *J*=17.1 and 10.3 Hz, =CH), 6.34 (1H, m, *J*=17.1 and 1.5 Hz, (*E*)-vinyl H), 7.21 (1H, d, *J*=2.9 Hz, H-5′), 7.23 (1H, dd, *J*=9.3 and 2.4 Hz, H-7′), 7.46 (1H, d, *J*=4.4 Hz, H-3′), 7.86 (1H, d, *J*=9.3 Hz, H-8′), 8.45 (1H, d, *J*=4.4 Hz, H-2′); ^{13}C NMR (50 MHz), δ=20.931, 25.543, 27.738, 30.221, 30.403, 33.723, 34.431, 43.182, 55.699, 58.008, 59.781, 63.433, 71.111, 101.338, 118.456, 121.338, 126.457, 128.059, 131.142, 131.142, 143.832, 147.202, 148.059, 157.676, 165.846; MS (70 eV) *m/z* (rel intensity) 456 (M^+; 87), 357 (99), 268 (100); Found: *m/z* 456.20527. Calcd for $C_{25}H_{32}N_2O_4S$: M, 456.20817; IR (liquid) 3160 (OH), 1725 cm^{-1} (C=O).

Alkaloid 9-Acrylonitrile Copolymer (10): A solution of the alkaloid **9** (1.95 g, 4.27 mmol), acrylonitrile (2.04 g, 38.40 mmol), and AIBN (0.012 g, 0.07 mmol) in dry DMF (10.0 ml) was heated at 65 °C for 42 h under Ar atmosphere. The same purification process described for the polymer **5** gave the polymer **10**; 2.29 g (57%): $[\alpha]_D^{25}$ −26.0° (*c* 1.008, DMF); Elemental analysis. Found: C, 65.82; H, 6.15; N, 17.69%; Alkaloid content 8.04 mol%.

Quinine-Acrylonitrile Copolymer (11): According to reported procedure,[18] a mixture of **1** and acrylonitrile (1 : 19) was copolymerized in dry DMF. The crude polymer was purified as above to give the polymer **11** having no spacer; 8.09 g (29%): $[\alpha]_D^{28}$ −10.4° (*c* 1.00, DMF); Elemental analysis. Found: C, 68.33; H, 5.93; N, 24.39%; Alkaloid content 1.99 mol%.

Asymmetric Addition of Methyl 1-Oxo-2-indancarboxylate Catalyzed by 7. Typical Procedure for the Reaction (1): A mixture of the polymer-catalyst **7** (59.0 mg, 0.0125 mmol of alkaloid), methyl 1-oxo-2-indancarboxylate (47.5 mg, 0.25 mmol), and freshly distilled 3-buten-2-one (35.0 mg, 0.50 mmol) in dry toluene (1.5 ml) was stirred at −48 °C. The conversion was monitored by HPLC (hexane(100)–*i*-PrOH(5), detect at 280 nm). Evaporation of the filtrate afforded the pure adduct and its optical rotation was measured at 578 nm (25 °C) in benzene. The purity and structural integrity were certified by ^1H NMR and TLC.

Asymmetric Addition of the Thiol Catalyzed by 6. Typical Procedure for the Reaction (2): A mixture of the polymer catalyst **6** (80.0 mg, 0.015 mmol), *p-t*-butylbenzenethiol (301 mg, 1.81 mmol), and 2-cyclohexenone (150 mg, 1.56 mmol) in dry toluene (3 ml) was stirred overnight at room temperature. The reaction mixture was washed successively with 2 M HCl (2×10 ml), 2 M KOH (2×10 ml), and brine (1×10 ml) followed by drying over Na_2SO_4. Then the optical rotation was measured at 578 nm (25 °C) in CCl_4.

Asymmetric Methanolysis of the Acid Anhydride Catalyzed by 6. Typical Procedure for the Reaction (3): The polymer-catalyst **6** (52.6 mg, 0.01 mmol of alkaloid), *cis*-2,4-dimethylglutaric anhydride (14.2 mg, 1.0 mmol), and dry methanol (32.0 mg, 1.0 mmol) in dry ether (5 ml) were allowed to react at room temperature. The conversion was monitored by GLC (2% XE-60, 2 m, 160 °C). After removing polymer-catalyst by filtration, the half-ester obtained was converted to the diastereomeric amide ester using (*R*)-1-(1-naphthyl)ethylamine.[4] The diastereomeric ratio of the amide ester was determined by HPLC (hexane(100)–*i*-PrOH(6), detection at 280 nm).

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