Asymmetric Diels-Alder Reactions of Some Chiral Dienophiles Derived from Cinchona Alkaloids

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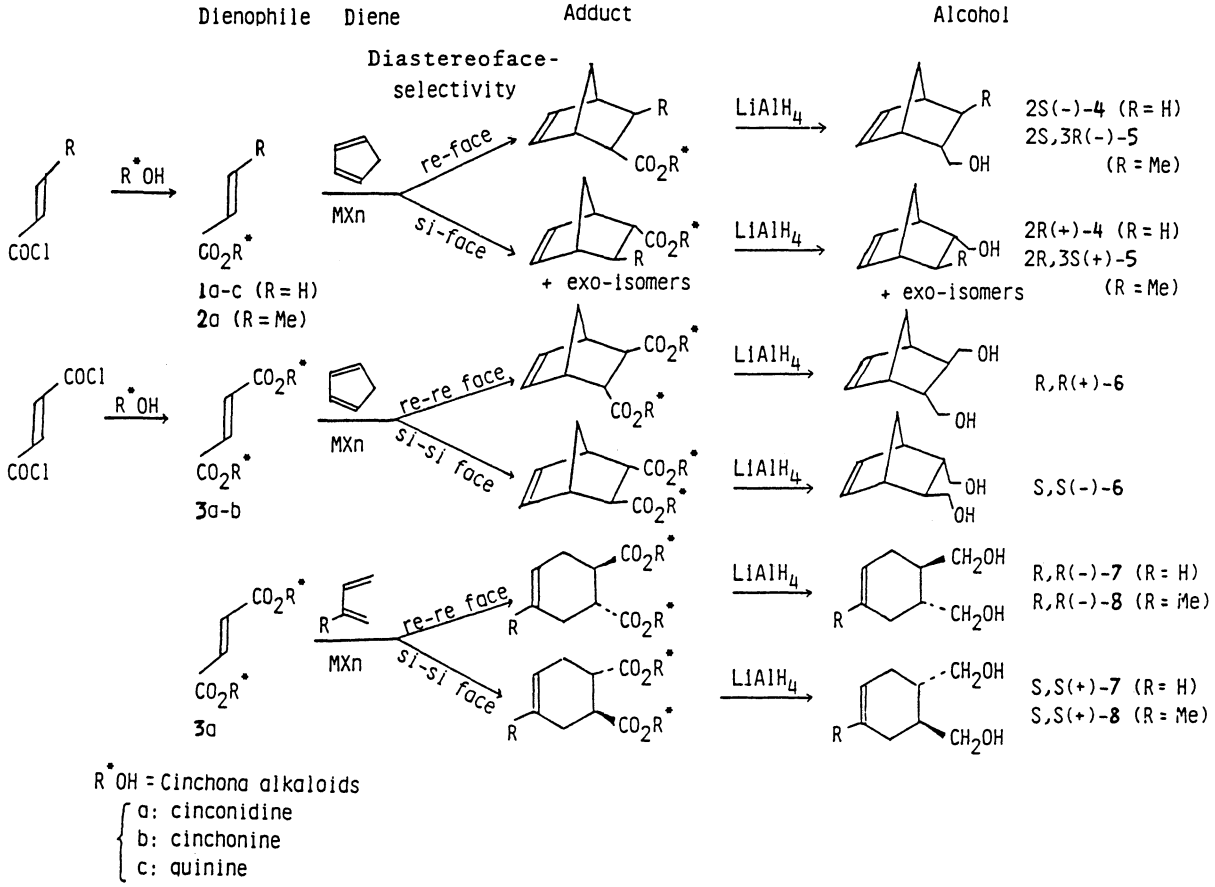
(Received September 11, 1987)

Acrylates, crotonate, and fumarates derived from cinchona alkaloids were easily prepared. The highly *re*-facial selective additions of the dienophiles derived from cinchonidine or quinine to some dienes were achieved in the presence of $SnCl_4$. Similarly, *si*-facial selective additions were also achieved by the use of cinchonine instead of cinchonidine or quinine as a chiral auxiliary alcohol with equal ease. The inverse diastereofacial selectivity was observed by the use of $TiCl_4$ instead of $SnCl_4$ as a Lewis acid in the case of the reaction of the acrylates cited above with cyclopentadiene. It was suggested by the infrared spectra of the dienophile-$SnCl_4$ complexes and by some circumstantial evidence that in the complexes, $SnCl_4$ coordinates with the oxygen atom of the C-O bond (not C=O bond) and probably also with the nitrogen atom of the quinuclidine framework to form a rigid five-membered ring structure.

The Diels-Alder reactions have been of considerable interest in organic syntheses. Recently, extensive efforts have been made concerning the asymmetric Diels-Alder reaction; cycloadducts with high stereoselectivity have been obtained by a variety of reactions.[1,2] Many kinds of auxiliary groups have been used.

Unfortunately, though, because of the limited availability of the auxiliary, only one of enantiomers of an auxiliary or one of the alternative topological counterparts has often been used as a chiral auxiliary, and only products enriched in one enantiomer have been synthesized. We aimed at the use of chiral auxiliary alcohols which 1) are readily available in both antipodal forms, 2) give their crystalline dienophiles, and 3) are removed easily from the final products without chromatography.

Thus, we made use of cinchona alkaloids as an auxiliary alcohol which seem to have the following merits: a) Several diastereomers are commercially available



Scheme 1.

in optically pure forms and can be directly treated with acids or acid chlorides to give the corresponding esters as dienophiles. b) The rigid structure containing the quinuclidine framework is capable of forming stable complexes with a suitable Lewis acid. In this paper we describe the highly diastereofacial selective Diels-Alder reactions of the dienophiles derived from cinchona alkaloids with some dienes.

Results and Discussion

The acrylic, crotonic, and fumarylic esters of cinchona alkaloids were prepared as dienophiles in high yields by reactions of the corresponding acid chlorides with cinchona alkaloids in THF followed by treatment with Et_3N in $CHCl_3$. The Diels-Alder reaction of the dienophiles with various dienes is shown in the Scheme 1 and Tables 1, 2. The reaction of cinchonidine acrylate (**1a**) with cyclopentadiene followed by a reduction of the adduct with $LiAlH_4$ (Table 1) was undertaken so as to determine the effects of the characteristics of the Lewis acid, solvents, and cinchona alkaloids used as auxiliary alcohol, as well as the reaction temperature on the chemical yield and the diastereofacial selectivity.

Lewis Acid. The extent and direction of the diastereoface-selection and the rate in the reaction of **1a** with cyclopentadiene varied greatly with the nature and quantity of the Lewis acid used. A low chemical yield and low diastereofacial selectivity were observed for a reaction using $BF_3 \cdot Et_2O$, $AlCl_3$, and $ZrCl_4$ as the Lewis acid, and upon a thermal reaction at −20 °C (entries 2 and 4—6). The use of $SnCl_4$ (entry 3) was found to greatly increase not only the chemical yield but also the diastereofacial selectivity, giving 2*S*(−)-2-hydroxymethyl bicyclo[2.2.1]hept-5-ene (**4**) with 93% *re*-facial selection of **1a** after a reduction of the adduct with $LiAlH_4$. The use of $TiCl_4$ or $BF_3 \cdot Et_2O$ (entries 6 and 7) instead of $SnCl_4$ caused a decrease in the endo as well as the diastereofacial selectivity to give **4**, which is unexpectedly enriched in the 2*R*(+)-enantiomer with *si*-facial selection, in low chemical yield. A reversal in the diastereoface-selection of dienophile by the different Lewis acids used is very unique in an asymmetric Diels-Alder reaction, and only one has been reported (T. Poll et al.[8] in 1984). A similar reversal was further observed in reactions using cinchonine acrylate (**1b**) and quinine acrylate (**1c**) as dienophiles (entries 18, 19, 21, and 22). The quantiy of $SnCl_4$ was found to strongly affect the diastereofacial selectivity. Generally, the selectivity was enhanced by increasing the mole equivalent of $SnCl_4$ toward **1a**; the highest value,

Table 1. Asymmetric Diels-Alder Reactions of **1a**—**c**[a] and **2a**[b] with Cyclopentadiene (5 mol equiv)

Entry	Dienophile	Lewis acid (mol equiv)	Reaction temp/°C (time/h)	Solvent	Yield/%[c]	endo/exo	Endo-isomer	
							%ee[d]	Abs. config.[e]
1	**1a**	None	+20(24)	CH_2Cl_2	95	87/13	20	2*S*(−)
2	**1a**	None	−20(7)	CH_2Cl_2	3	92/8	—	—
3	**1a**	$SnCl_4$(1.5)	−20(5)	CH_2Cl_2	70	96/4	93	2*S*(−)
4	**1a**	$AlCl_3$(1.5)	−20(6)	CH_2Cl_2	11	94/6	20	2*S*(−)
5	**1a**	$ZrCl_4$(1.5)	−20(6)	CH_2Cl_2	21	97/3	6	2*S*(−)
6	**1a**	$BF_3 \cdot Et_2O$(1.5)	−20(6)	CH_2Cl_2	18	92/8	13	2*R*(+)
7	**1a**	$TiCl_4$(1.5)	−20(6)	CH_2Cl_2	35	88/12	33	2*R*(+)
8	**1a**	$SnCl_4$(0.5)	−20(6)	CH_2Cl_2	45	96/4	42	2*S*(−)
9	**1a**	$SnCl_4$(1.0)	−20(6)	CH_2Cl_2	64	95/5	80	2*S*(−)
10	**1a**	$SnCl_4$(2.0)	−20(6)	CH_2Cl_2	65	95/5	90	2*S*(−)
11	**1a**	$SnCl_4$(1.5)	0(4)	CH_2Cl_2	64	95/5	91	2*S*(−)
12	**1a**	$SnCl_4$(1.5)	−45(6)	CH_2Cl_2	82	96/4	93	2*S*(−)
13	**1a**	$SnCl_4$(1.5)	−70(6)	CH_2Cl_2	58	97/3	92	2*S*(−)
14	**1a**	$SnCl_4$(1.5)	−20(5)	PhCl	72	96/4	90	2*S*(−)
15	**1a**	$SnCl_4$(1.5)	−20(5)	PhMe	66	96/4	86	2*S*(−)
16	**1a**	$SnCl_4$(1.5)	−20(5)	Xylene	45	96/4	82	2*S*(−)
17	**1b**	None	+20(24)	CH_2Cl_2	90	87/13	13	2*R*(+)
18	**1b**	$SnCl_4$(1.5)	−20(5)	CH_2Cl_2	79	96/4	88	2*R*(+)
19	**1b**	$TiCl_4$(1.5)	−20(6)	CH_2Cl_2	37	84/16	49	2*S*(−)
20	**1c**	None	+20(24)	CH_2Cl_2	90	87/13	13	2*S*(−)
21	**1c**	$SnCl_4$(1.5)	−20(5)	CH_2Cl_2	69	96/4	82	2*S*(−)
22	**1c**	$TiCl_4$(1.5)	−20(6)	CH_2Cl_2	44	86/14	34	2*R*(+)
23	**2a**	$SnCl_4$(1.6)	0(3)	CH_2Cl_2	38	93/7	70	2*S*,3*R*(−)
24	**2a**	$SnCl_4$(1.6)	−20(3)	CH_2Cl_2	67	93/7	93	2*S*,3*R*(−)
25	**2a**	$SnCl_4$(1.6)	−40(3)	CH_2Cl_2	27	93/7	85	2*S*,3*R*(−)

a) **1a**: cinchonidine acrylate; **1b**: cinchonine acrylate; **1c**: quinine acrylate. b) **2a**: cinchonidine crotonate. c) Combined yield (by GLC) of endo and exo alcohols. d) HPLC analysis of the corresponding chiral Pirkle's carbamate.[3] e) Assigned by means of chiroptic measurements of endo alcohols (2-hydroxymethyl bicyclo[2.2.1]hept-5-ene (**4**)[4] for entries 1—22 and 2-hydroxymethyl-3-methylbicyclo[2.2.1]hept-5-ene (**5**)[5] for entries 23—25.

Table 2. Asymmetric Diels-Alder Reactions of **3a** and **b**[a] with Some Dienes in CH_2Cl_2

Entry	Dienophile	Diene (mol equiv)	Lewis acid (mol equiv)	Reaction temp/°C (time/h)	Yield/%[b]	%ee[c]	Abs. config.[d]
26	**3a**	(5)	$SnCl_4$(1.5)	−20(4)	62	25	*R,R*(+)
27	**3a**	(5)	$SnCl_4$(3.0)	−20(4)	61	67	*R,R*(+)
28	**3a**	(5)	$SnCl_4$(3.0)	0(4)	63	38	*R,R*(+)
29	**3a**	(5)	$SnCl_4$(3.0)	−45(4)	96	95	*R,R*(+)
30	**3a**	(5)	$SnCl_4$(3.0)	−70(8)	62	90	*R,R*(+)
31	**3b**	(5)	$SnCl_4$(3.0)	−45(4)	74	93	*S,S*(−)
32	**3a**	(30)	$SnCl_4$(3.0)	0(4)	44	94	*R,R*(−)
33	**3a**	(30)	$SnCl_4$(3.0)	−20(4)	46	92	*R,R*(−)
34	**3a**	(20)	$SnCl_4$(3.0)	0(4)	71	98	*R,R*(−)
35	**3a**	(20)	$SnCl_4$(3.0)	−20(4)	70	99	*R,R*(−)
36	**3a**	(20)	$SnCl_4$(3.0)	−40(4)	30	99	*R,R*(−)

a) **3a**: cinchonidine fumarate; **3b**: cinchonine fumarate. b) GLC yields. c) HPLC analysis of the corresponding chiral Pirkle's carbamates.[3] d) Assigned by means of chiroptic measurements of alcohols (2,3-bis(hydroxymethyl)bicyclo[2.2.1]hept-5-ene (**6**)[6] for Entries 26—31, 1,2-bis(hydroxymethyl)-4-cyclohexene (**7**)[7] for Entries 32 and 33, and 1,2-bis(hydroxymethyl)-4-methyl-4-cyclohexene (**8**)[7] for Entries 34—36).

up to 93%, was recorded by carring out the reaction in the presence of 1.5 mol equiv of $SnCl_4$ (entry 3). On the other hand, in a reaction of cyclopentadiene with cinchonidine fumarate (**3a**), containing two pieces of the cinchonidine group, the highest value, up to 95% (entry 29 in Table 2), was recorded by carring out the reaction in the presence of 3 mol equiv of $SnCl_4$ toward **3a**. Thus, the use of 1.5 mol equiv mol of $SnCl_4$ toward per cinchona alkaloid group was found to be most efficient regarding asymmetric Diels-Alder reactions of the dienophile derived from cinchona alkaloids with diene.

Reaction Temperature. No evident temperature dependency in $SnCl_4$-promoted reactions (Tables 1 and 2), excluding the reaction of cinchonidine fumarate (**3a**) with cyclopentadiene, was observed between 0 and −45 °C, mainly because of its heterogeneity in the reaction media.

Solvent Effect. As can be seen in entries 14—16, increasing the density of π-electrons in the aromatic solvents (chlorobenzene, toluene, and xylene) caused a stepwise decrease, mainly in the chemical yield. This decrease may be attributable to the increased donating ability of these solvents to the acryloyl group in cinchonidine acrylate (**1a**) coordinated by $SnCl_4$.[9]

Cinchona Alkaloids as Chiral Auxiliary and the Diastereofacial Selectivities of Their Dienophiles. Three commercially available cinchona alkaloids (cinchonidine, cinchonine, and quinine) were selected as auxiliary alcohols. The dienophiles, **1a** and **1c**, derived from cinchonidine and quinine, respectively, containing the same configuration (8α ,9*R*), gave 2*S*(−)-**4** with a high *re*-facial selection upon reacting with cyclopentadiene in the presence of $SnCl_4$, followed by a reduction with $LiAlH_4$.

As expected, **1b** (antipode of **1a**) derived from cinchonine (8α, 9*S*) gave 2*R*(+)-**4** with a *si*-facial selection

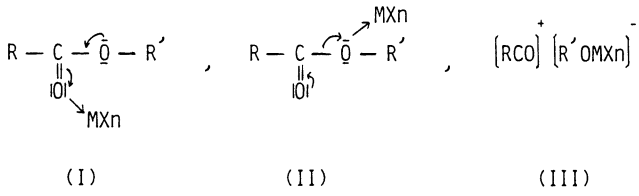


Fig. 1. Ester-Lewis acid complexes.

with equal ease (entry 18). Similarly, a highly *re-re* facial selective addition was achieved upon the reaction of cinchonidine fumarate (**3a**) with cyclopentadiene in the presence of $SnCl_4$ to yield 2*R*,3*R*(+)-2,3-bis(hydroxymethyl)bicyclo[2.2.1]hept-5-ene (**6**) followed by a reduction with $LiAlH_4$ (entry 29 in Table 2). A *si-si* facial selective addition was also achieved by the use of cinchonine fumarate (**3b**) instead of **3a** as a dienophile (entry 30 in Table 2). In the other reactions (entries 23—25 in Table 1 and 32—36 in Table 2), it was further confirmed that when cinchonidine was used as a chiral auxiliary alcohol, a high *re* (or *re-re*)-facial selection of the dienophiles used could be achieved in reactions with various dienes in the presence of $SnCl_4$.

Therefore, both diastereoface-differential Diels-Alder reactions were achieved by the use of the dienophiles derived from (8α, 9*R*) and (8α, 9*S*)-cinchona alkaloids in the presence of $SnCl_4$.

Structure of the Dienophile-$SnCl_4$ Complexes. Regarding the structures and infrared spectra of the ester-Lewis acid complexes, three structures (**I—III**) shown in Fig. 1 have been considered.[10]

A lengthening of the C=O bond (shift of the $\nu_{C=O}$ band to lower frequency), and a shortening of the C(O)-O bond (shift of the $\nu_{C(O)-O}$ band to higher frequency) are anticipated by a coordination of the Lewis acid with acyl-oxygen (structure **I**),[10] which has been

found in most cases of the ester-Lewis acid complexes.

On the other hand, the reverse is anticipated by a coordination with the alkyl-oxygen (structure **II**), which has been postulated in various reports.[11-13] However, it is apparently unprecedented in an identified form, with the exception of some cases that are somewhat different from structure **II** (i.e., the intramolecular hydrogen bonding to alkyl-oxygen in certain steroid hydroxy-esters,[14] the infrared spectra of which shows the $\nu_{C=O}$ band raised by 8—13 cm^{-1} and the $\nu_{C(O)-O}$ band lowered by 10—14 cm^{-1}, compared with the bands in esters with no hydrogen bonding to the alkyl-oxygen, were reported; also, the coordination of Cu with the nitrogen atom of amide in *N,N*-di(2-pyridylmethyl)amide-Cu(II) complexes,[15] the infrared spectrum of which shows the $\nu_{C=O}$ band raised by 26 cm^{-1} compared with that in free amide, was reported).

The acylinium ion in structure **III** would require the presence of the $\nu_{C\equiv O}$ band near 2190 cm^{-1}, which was observed in $[MeCO]^+[BF_4]^-$.[16]

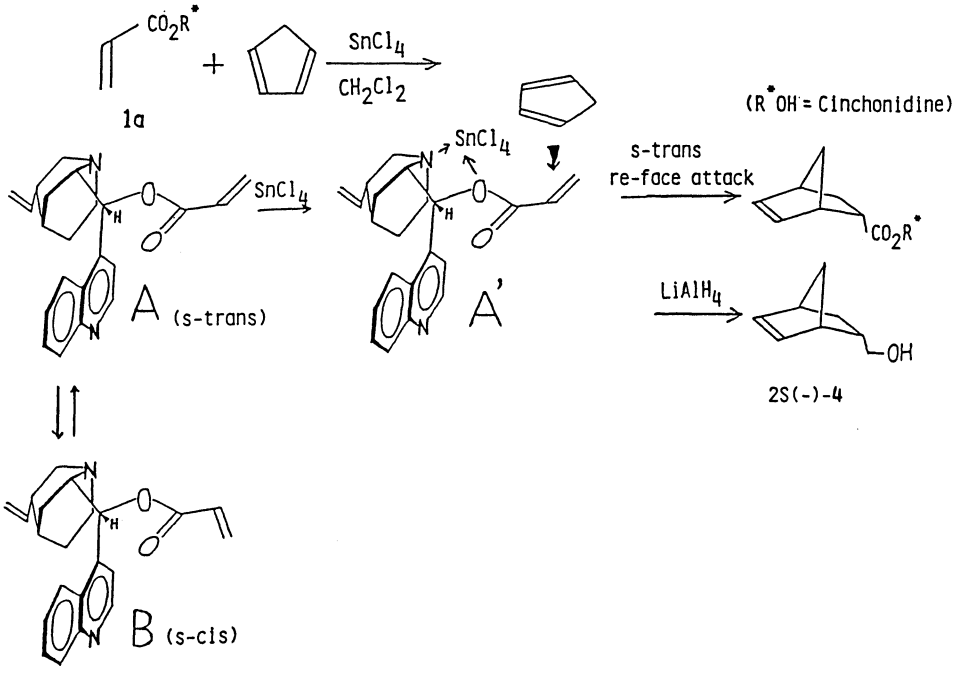
Now, the addition of $SnCl_4$ to **1a** in CH_2Cl_2 gave insoluble solids, the **1a**-$SnCl_4$ complex; the infrared spectrum (Nujol mulls) showed the $\nu_{C=O}$ band at 1738 cm^{-1}, raised by 20 cm^{-1}, and the $\nu_{C(O)-O}$ band at 1155 cm^{-1}, lowered by 25 cm^{-1}, compared with the bands in **1a**. The direction and extent of the shifts of these bands caused by adding $SnCl_4$ to **1a** agreed with that in the reports[14,15] cited regarding structure **II** (mentioned above), suggesting that $SnCl_4$ coordinates with the oxygen atom of the C-O bond (not C=O bond) in the **1a**-$SnCl_4$ complex.

On the other hand, the addition of $SnCl_4$ to a simple acrylate, methyl acrylate, in CH_2Cl_2 gave a homogeneous solution; the infrared spectrum showed the $\nu_{C=O}$ band at 1658 cm^{-1}, lowered by 67 cm^{-1}, and the $\nu_{C(O)-O}$ band at 1340 cm^{-1}, raised by 135 cm^{-1}, compared with the bands in free methyl acrylate, showing that $SnCl_4$ coordinates with the carbonyl-oxygen in the methyl acrylate-$SnCl_4$ complex.

The difference of the **1a**-$SnCl_4$ complex from the methyl acrylate-$SnCl_4$ complex in the infrared spectrum mentioned above may be caused by the presence of a quinuclidine framework in **1a**, suggesting that $SnCl_4$ coordinates not only with the oxygen atom in the C-O bond, but also with the nitrogen atom of the framework in the **1a**-$SnCl_4$ complex to form a rigid five-membered ring.

Assuming that $SnCl_4$ ordinarily coordinates with the carbonyl-oxygen and also with nitrogen atom, it is anticipated that a seven-membered ring structure is formed, resulting in the synthesis of **4** rich in the 2*R*(+)-enantiomer with a *si*-facial selection upon the reaction of **1a** with cyclopentadiene in the presence of $SnCl_4$ followed by reduction with $LiAlH_4$. However, our result (entry 3) showed a synthesis of 2*S*(−)-enantiomer with *re*-facial selection. Therefore, the coordination of $SnCl_4$ with the carbonyl-oxygen in the **1a**-$SnCl_4$ complex could be contradicted by the configuration of product **4**, and also the absence of the $\nu_{C=O}$ band near 1658 cm^{-1}, which was observed in the methyl acrylate-$SnCl_4$ complex mentioned above.

Similarly, the coordination of $SnCl_4$ with only the nitrogen atom in the **1a**-$SnCl_4$ complex could also be contradicted by the fact that $SnCl_4$ significantly promotes the rate in the reaction of **1a** with cyclopentadiene (entries 2 and 3), suggesting that $SnCl_4$ coordinates with the cabonyl-oxygen or the oxygen atom of the C-O bond.



Scheme 2.

Therefore, according to the infrared spectrum of the **1a**-$SnCl_4$ complex and the circumstantial evidence described above, it was suggested that $SnCl_4$ in the complex probably coordinates with the nitrogen atom of the quinuclidine framework and also with the oxygen atom, which is situated at the δ-position, counted from the nitrogen atom of the framework, of the C-O bond (not C=O bond), to form a rigid five-membered ring structure.

Reaction Models. For the purpose of illustrating the $SnCl_4$-promoted high diastereofacial selectivity descrived above, we referred to several models regarding the reaction of **1a** or **3a** with cyclopentadiene in the presence of $SnCl_4$.

Concerning the structures of the esters in solution or in solids, it has been widely accepted as a result of a spectral study[17] that the ester exists in solution as an equilibrium mixture of s-trans and s-cis conformations, in which the former is thermodynamically more stable, and by an X-ray analysis[18] that the ester exists in solids as s-trans conformation.

Now, cinchonidine acrylate (**1a**) dissolves in CH_2Cl_2 and seems to exists as an equilibrium mixture of the s-trans conformation **A** and the s-cis conformation **B** in Scheme 2, where the former is more stable (as mentioned above). Therefore, cyclopentadiene attacks **1a** more from the less-hindered *re*-face of conformation **A** than from the less-hindered *si*-face of conformation **B**, to yield **4** enriched in 2*S*(−)-enantiomer in the thermal reaction (entry 1), followed by reduction with $LiAlH_4$.

On the other hand, the addition of $SnCl_4$ to **1a** in CH_2Cl_2 gave solids that were insoluble in CH_2Cl_2. In solids composed of the **1a**-$SnCl_4$ complex, **1a** exists mainly as a s-trans conformation (as mentioned above) to yield conformation **A′**.

Therefore, cyclopentadiene selectively attacks **1a** in the presence of $SnCl_4$ from the less-hindered *re*-face of conformation **A′** to yield 2*S*(−)-**4** with a high diastereofacial selectivity, followed by a reduction with $LiAlH_4$.

Similarly, cyclopentadiene attacks cinchonidine fumarate (**3a**), in which two pieces of the cinchonidine group cover the *si-si* face by a cooperative blocking effect,[19] selectively from the less-hindered *re-re* face of conformation **C**, according to Scheme 3, to yield *R,R*(+)-**6** followed by a reduction with $LiAlH_4$.

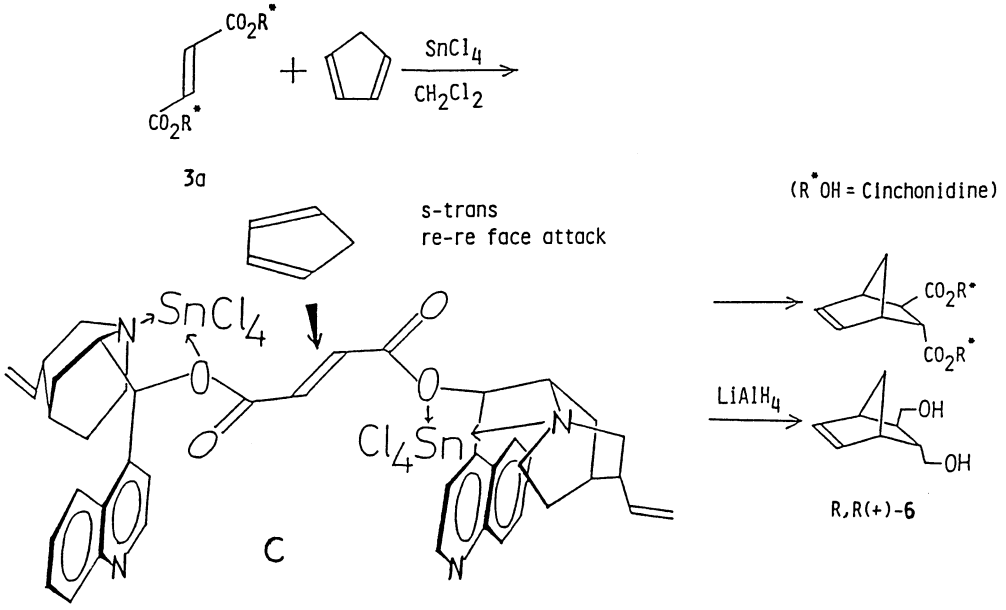
Experimental

General. The preparation of dienophiles, the Diels-Alder reaction and reduction of the adduct with $LiAlH_4$ were carried out under an atmosphere of argon.

Materials. Solvents and dienes were dried in the usual manner and distilled just before use. $SnCl_4$, $TiCl_4$, $BF_3 \cdot Et_2O$, acryloyl chloride, crotonyl chloride, and fumaroyl dichloride were also distilled under argon just before use. $AlCl_3$ and $ZrCl_4$ were purified by sublimation. Chiral 1-(1-naphthyl)ethyl isocyanate was obtained from the Aldrich Chemical Company and used without further purification.

Measurements. The melting point (uncorrected) were determined in a sealed tube with a Yamato melting-point apparatus. The IR spectra and the optical rotations were recorded with a Hitachi infrared spectrophotometer (EPI-G3) and a Union 101 polarimeter, respectively. The gas chromatographs were recorded with a Shimadzu gas chromatograph (GC-8A) using a column packed with 10% PEG-20M on Chromosorb W AW. The high-performance liquid chromatography (HPLC) was recorded with a Kyowa Seimitsu liquid chromatograph (column packed with SiO_2; eluents: hexane-ethyl acetate for entries 1—25 in Table 1 or hexane-ethanol for entries 26—36 in Table 2).

Dienophiles. Preparation of Cinchonidine Acrylate (1a) as a Typical Procedure. To a stirred solution of cinchonidine (25 g, 85 mmol) in THF (600 ml) was slowly added a solution of acryloyl chloride (5.8 ml, 71 mmol) in THF (50



Scheme 3.

ml) at 0 °C in the dark. The mixture was stirred for 24 h at 0 °C—r.t. in a dark room. After concentration under reduced pressure and a subsequent addition of $CHCl_3$ (50 ml) to the residual mass, Et_3N (19.8 ml, 142 mmol) was added dropwise under stirring at 0 °C. Stirring was continued for 2 h at r.t. and then acetone (500 ml) was added to the mixture. After cooling in a refrigerator overnight, precipitates composed of Et_3NHCl and excess cinchonidine were filtered off. The filtrate was evaporated and the pale-yellow residual mass was twice recrystallized from hexane-isopropyl alcohol to give white crystals **1a**; yield: 20 g (80%); mp 113—114 °C; $[\alpha]_D^{25}$ +10.5° (*c* 1.5, $CHCl_3$); IR(Nujol mulls); 1718 ($\nu_{C=O}$) and 1180 cm^{-1} ($\nu_{C(O)-O}$); Found: C, 75.64; H, 7.11; N, 7.98%. Calcd for $C_{22}H_{24}N_2O_2$: C, 75.86; H, 6.90; N, 8.05%. The other dienophiles: cinchonidine crotonate (**2a**); yield: 82%; mp 152—153 °C; $[\alpha]_D^{25}$ +38.0 (*c* 1.5, $CHCl_3$; IR(Nujol mulls) 1720 ($\nu_{C=O}$) and 1177 cm^{-1} ($\nu_{C(O)-O}$); Found: C, 75.91; H, 7.41; N, 7.53%. Calcd for $C_{23}H_{26}N_2O_2$: C, 76.21; H, 7.23; N, 7.73%. Cinchonidine fumarate (**3a**); yield: 78%; mp 221—223 °C; $[\alpha]_D^{25}$ +81.2° (*c* 1.5, $CHCl_3$); IR (Nujol mulls) 1718 ($\nu_{C=O}$) and 1167 cm^{-1} ($\nu_{C(O)-O}$); Found: C, 75.50; H, 6.70; N, 8.43%. Calcd for $C_{42}H_{44}N_4O_4$: C, 75.42; H, 6.63; N, 8.38%. Cinchonine fumarate (**3b**); yield: 86%; mp 104—107 °C; $[\alpha]_D^{25}$ +40.5° (*c* 1.5, $CHCl_3$); IR (Nujol mulls) 1720 ($\nu_{C=O}$) and 1164 cm^{-1} ($\nu_{C(O)-O}$); Found: C, 75.25; H, 7.10; N, 7.90%. Calcd for $C_{42}H_{44}N_4O_4$: C, 75.42; H, 6.63; N, 8.38%. Cinchonine acrylate[20] (**1b**); mp 63—64 °C; $[\alpha]_D^{25}$ +81.6° (*c* 1.5, $CHCl_3$), which was reported to be an oily material, $[\alpha]_D^{20}$ +80° (*c* 2, $CHCl_3$), and quinine acrylate[21] (**1c**) were also prepared by a similar procedure.

Asymmetric Diels-Alder Reaction. $SnCl_4$-Promoted Addition of 1a to Cyclopentadiene (Entry 3) as a Typical Procedure. To a stirred solution of **1a** (1.04 g, 3 mmol) in CH_2Cl_2 (18 ml) was added cyclopentadiene (1.2 ml, 15 mmol) at −70 °C. Subsequently, a solution of $SnCl_4$ (0.52 ml, 4.5 mmol) in CH_2Cl_2 (6 ml) was added dropwise to the mixture at −20 °C. The increase in the temperature of the mixture and the appearance of pale-yellow precipitates were noted as the addition of $SnCl_4$ proceeded.

After stirring for 5 h at −20 °C, Et_3N (2.5 ml, 18 mmol) and H_2O (1 ml) were added to the mixture. Excess cyclopentadiene was then removed in vacuo. To the resulting mass were added CH_2Cl_2 (200 ml), Et_3N (2.5 ml, 18 mmol), and saturated aq. NH_4Cl (20 ml), and stirred for 1 h. The two layers were separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic phases were washed (H_2O), dried (Na_2SO_4), and evaporated to dryness. After the residue was treated with $LiAlH_4$ (1.5 g, 40 mmol) in ether for 20 h, the excess $LiAlH_4$ was decomposed by saturated aq. NH_4Cl, then acidified to pH 2—3. The two layers were separated and the aqueous layer was extracted with ether. The combined organic phases were washed (H_2O), dried (Na_2SO_4), concentrated, and distilled under reduced pressure to give the alcohol **4**, containing some of its exo isomer, as shown by GLC analysis. After removing the exo isomer by preparative GLC, the endo alcohol was treated with chiral 1-(1-naphthyl)ethyl isocyanate in benzene at 80 °C to give chiral carbamate for an HPLC analysis.[3] The other reactions were carried out in a similar way according to Scheme 1 and are shown in Tables 1 and 2 together with the results.

Dienophile-Lewis Acid Complexes. Preparation of 1a-$SnCl_4$ Complex as a Typical Procedure. To a stirred solution of **1a** (0.52 g, 1.5 mmol) in CH_2Cl_2 (10 ml) was added $SnCl_4$ (0.26 ml, 2.25 mmol). The mixture was stirred for 1 h at r.t. A cream-colored complex was filtered, washed (CH_2Cl_2), and dried in vacuo. Yield 1.03 g (93%); Decomp: 183 °C; IR(Nujol mulls) 1738 ($\nu_{C=O}$) and 1155 cm^{-1} ($\nu_{C(O)-O}$); Found: Cl, 28.6%. Calcd for $C_{44}H_{48}N_4O_4Cl_8Sn_3$ (**1a**-1.5 $SnCl_4$): Cl, 28.8%

The other complexes of some dienophiles with $SnCl_4$ or $TiCl_4$ were prepared in a similar way, and the infrared spectra showed similarly the $\nu_{C=O}$ band shifted to a higher frequency and the $\nu_{C(O)-O}$ band shifted to a lower frequency, compared with the bands in the corresponding free dienophiles.

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