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Asymmetric Synthesis of Methylenecyclobutanes and Their Transformation to Medium-sized Carbocyclic Compounds.#

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Key Words
chiral titanium reagent; catalytic asymmetric [2+2] cycloaddition reaction; cationic cyclization; methylenecyclobutanes

Abstract: *The catalytic asymmetric [2+2] cycloaddition proceeds between 3-(2-alkenoyl)-1, 3-oxazolidin-2-ones and 1, 2-propadienyl sulfides having various substituents at 1-position, affording methylenecyclobutane derivatives with high optical purity. Seven and eight membered carbocycles with chiral side chains are prepared by the ring cleavage reaction and successive cationic cyclization of the chiral methylenecyclobutane derivatives having ω-alkenyl substituents.*

Catalytic asymmetric reaction is one of the efficient methods for the preparation of optically active compounds.[1] In our laboratory, the development of asymmetric reactions for construction of chiral carbon skeletons has been investigated by the use of a chiral titanium reagent generated from $TiCl_2(OPr^i)_2$ and a chiral 1,4-diol **1**[2] which is derived from dimethyl tartrate. The chiral titanium catalyst is generated in situ by mixing the 1,4-diol **1** and $TiCl_2(OPr^i)_2$, and promotes some asymmetric carbon-carbon bond forming reactions such as Diels-Alder reaction,[3] intramolecular ene reaction,[4] and hydrocyanation of aldehydes.[5] In addition, the asymmetric [2+2] cycloaddition reaction proceeds with the catalyst between vinyl sulfides and 3-(2-alkenoyl)-1,3-oxazolidin-2-ones, affording various cyclobutanes with high optical purity.[6] For example, optically active methylenecyclobutane derivatives are synthesized from 1,2-propadienyl sulfides and 3-(2-alkenoyl)-1,3-oxazolidin-2-ones.[6c, 7] In the previous paper, the preparation of chiral methylenecyclobutanes was investigated by employing a limited number of 1,2-propadienyl sulfides such as 1-trimethylsilyl, 1-trimethylstannyl, and 1-benzyl substituted 1,2-propadienyl sulfides.[6c, 7] Herein, we wish to report the asymmetric [2+2] cycloaddition reaction of various 1,2-propadienyl sulfides and the transformation of the optically active methylenecyclobutanes having ω-alkenyl side chains to medium-sized carbocyclic compounds.

[2+2] Cycloaddition reaction

For screening the generality of the [2+2] cycloaddition reaction, 1-methyl **2a**, 1-isopropyl **2b**, 1-(ω-alkenyl) **2c-2f**, 1-(1-cyclopentenyl)ethyl **2g**, 1-(4-butynyl) **2h**, and 1-(dimethyl(2-propenyl)silyl) **2i** 1-methylthio-1,2-propadienes[6c, 8] were prepared and subjected for the reaction with methyl (*E*)-4-oxo-4-(2-oxo-1,3-oxazolidin-3-yl)-2-butenoate (**3a**) or 3-acryloyl-1,3-oxazolidin-2-one (**3b**) in the presence of Lewis acids.

Dedicated in honor of Professors R. Noyori and K. B. Sharpless on the occasion of the award of the *Tetrahedron Prize* for 1993.

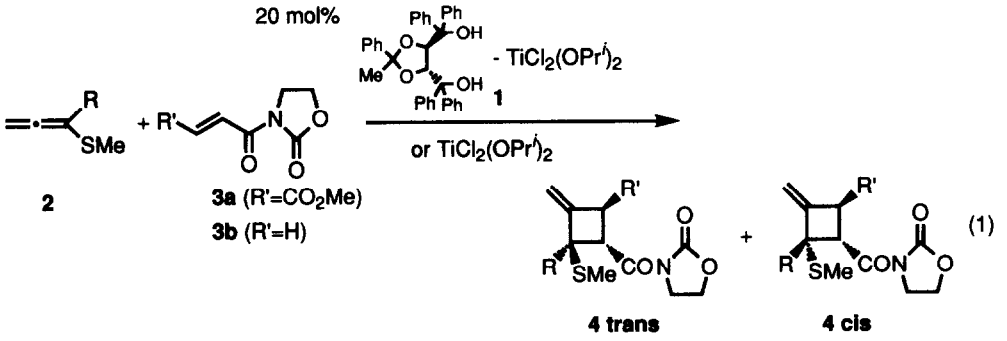


Table 1. [2+2] cycloaddition reaction between the acrylic acid derivative **3** and 1,2-propadienylsulfide **2**

R		3	Conditions[a]	Yield /%		trans : cis[b]	Optical Yield /%ee trans	cis
Me	(2a)	3a	A	98	(4a)	50:50	95	97
			B	98		80:20		
Pr^i	(2b)	3a	A	95	(4b)	73:27	95	95
			B	98		80:20		
n=1	(2c)	3a	A	98	(4c)	68:32	97	>98
			B	95		80:20		
2	(2d)	3a	A	94	(4d)	65:35	91	95
			B	98		80:20		
3	(2e)	3a	A	98	(4e)	63:37	98	88
			B	92		80:20		
4	(2f)	3a	A	95	(4f)	65:35	98	97
			B	92		80:20		
	(2g)	3a	A	88	(4g)	67:33	98	97
			B	90		80:20		
	(2h)	3a	A	98	(4h)	50:50	95	97
			B	98		67:33		
Me, Me Si	(2i)	3a	A	98	(4i)	<2:>98	-	>98
			B	98		<2:>98		
Me_3Si[c]	(2j)	3a	A	98	(4j)	<2:>98	-	>98
			B	98		<2:>98		
	(2e)	3b	A	86	(4k)	20:80	98	97
			B	85		29:71		

a) Condition A: 20 mol% of **1** -$TiCl_2(OPr^i)_2$, toluene-P.E. (1:1), MS 4A.
B: 1.1eq. $TiCl_2(OPr^i)_2$, toluene.

b) Isomer ratio is determined by ^{1}H-NMR (500MHz).

c) Data from ref. 6.

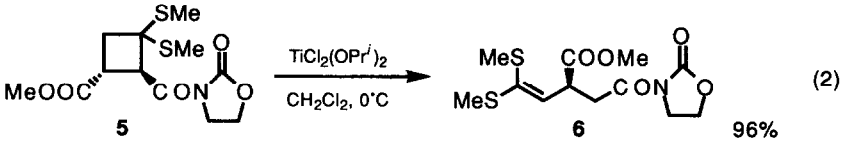
The chiral catalyst was generated by mixing $TiCl_2(OPr^i)_2$ and 1.1 molar amounts of the chiral diol **1** in toluene at room temperature for 30 min in the presence of MS 4A. To the solution of the chiral titanium reagent was added oxazolidin-2-one derivative **3** and a petroleum ether (P.E.) solution of 1,2-propadienylsulfide **2** at 0 °C (conditions A). The reaction was completed with a catalytic amount of the chiral titanium reagent within 10-12 h to afford methylenecyclobutane derivatives **4** in good to excellent yield. The results of the [2+2] cycloaddition reaction by the use of the chiral titanium reagent are exhibited in Table 1.

As for diastereo- and enantio-selectivity, the reaction of 1-trimethylsilyl or 1-allyldimethylsilyl substituted 1,2-propadienylsulfide (**2i**, **2j**) with **3a** afforded only a cis-isomer with complete enantioselectivity. Though the reaction of the other 1,2-propadienylsulfides afforded mixtures of trans- and cis-isomers,[9] each isomer had excellent optical purity. In the case of **2i**, having both allylsilane and 1,2-propadienylsulfide moieties, [2+2] cycloaddition reaction proceeded without the Sakurai-type Michael reaction of the allyl group.[10] Thus, various 1,2-propadienylsulfides having alkyl, ω-alkenyl, ω-alkynyl and alkylsilyl substituents can be successfully utilized in the asymmetric [2+2] cycloaddition, and the corresponding methylenecyclobutane derivatives are prepared in good yield with high optical purity.

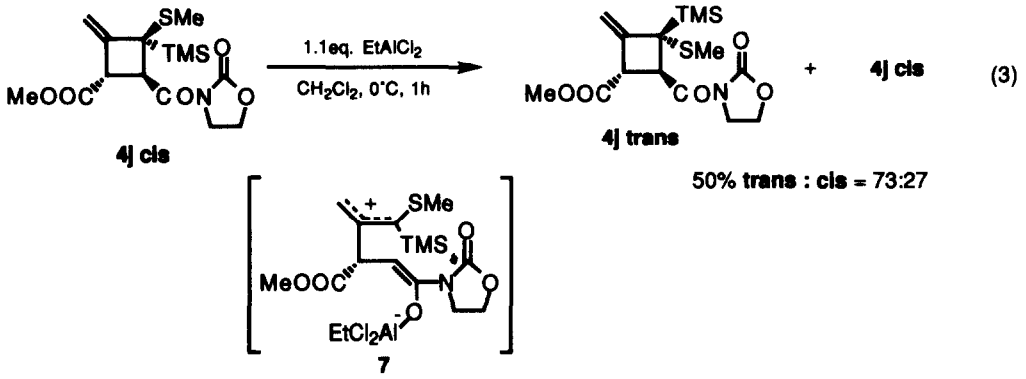
This [2+2] cycloaddition reaction also proceeded by achiral Lewis acids, but the choice of the appropriate Lewis acid was crucial to obtain methylenecyclobutanes in good yield. In the reaction between **3a** and 1,2-propadienylsulfides **2**, the use of $EtAlCl_2$ afforded a rather complex mixture probably because $EtAlCl_2$ also promoted the ring cleavage of the resulting methylenecyclobutanes (vide infra). $TiCl_2(OPr^i)_2$ was utilized as a suitable Lewis acid for the preparation of racemic methylenecyclobutanes. That is, in the presence of an equimolar amount of $TiCl_2(OPr^i)_2$, 1,2-propadienylsulfides **2** reacted with **3** within 1-2 h to afford the corresponding methylenecyclobutane derivatives **4** in good to excellent yield (conditions B).

The rearrangement of optically active cyclobutanes to medium-sized rings

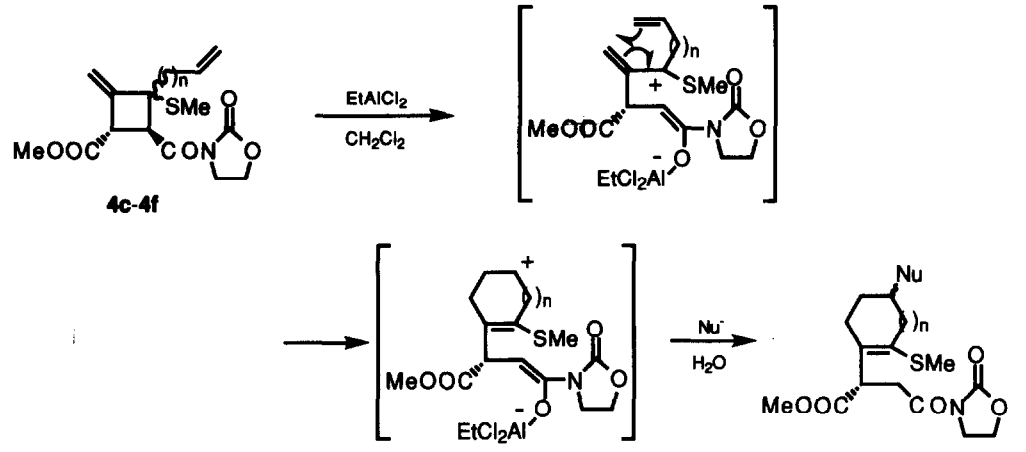
A cyclobutanone dithioacetal **5** prepared from ketene dimethyldithioacetal and 3-(2-alkenoyl)-1,3-oxazolidin-2-one derivative by the catalytic action of the chiral titanium reagent is rather acid sensitive.[6c] For instance, **5** was transformed to the ring-opened product **6** by the treatment with an equimolar amount of $TiCl_2(OPr^i)_2$ in dichloromethane (Eq. 2) which is a slightly stronger Lewis acid than the chiral titanium reagent.



Methylenecyclobutanes **4** are not so unstable as the cyclobutanone dithioacetal **5** that **4** was recovered unchanged by treatment with the titanium reagents.[9] However, the diastereomeric isomerization was observed when the methylenecyclobutane derivative **4j cis** was treated with $EtAlCl_2$, which is stronger Lewis acid than $TiCl_2(OPr^i)_2$, yielding a 27 : 73 mixture of **4j cis** and **4j trans** isomers in 50% yield (Eq. 3). This isomerization suggested that the ring cleavage and closure reactions via the zwitterion intermediate **7** occur upon treatment of the methylenecyclobutane **4** with the Lewis acid $EtAlCl_2$.



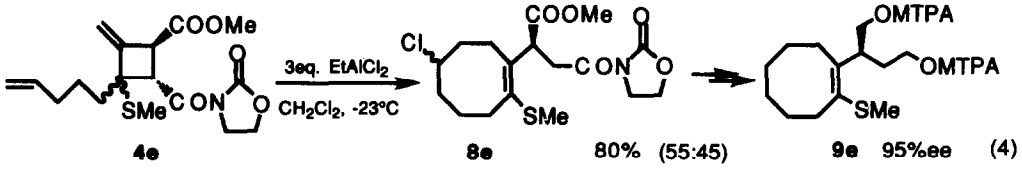
Based on these observations, it was postulated that if the side chain of the methylenecyclobutanes has an olefinic moiety at a suitable position, the cationic cyclization would proceed via the zwitterion intermediate as shown in Scheme 1. The methylenecyclobutane derivatives **4c-4f** having ω-alkenyl substituents were, therefore, subjected to the rearrangement reaction promoted by $EtAlCl_2$.



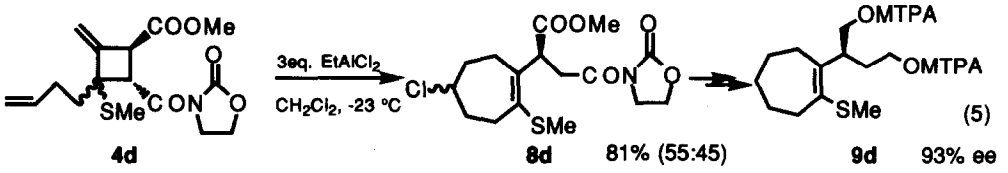
Scheme 1

A mixture of diastereomers of the 4-pentenyl substituted methylenecyclobutane **4e** (trans:cis=63:37) was treated with an equimolar amount of $EtAlCl_2$ in dichloromethane. As expected, the ring cleavage and the subsequent cationic cyclization occured affording a chlorocyclooctene derivative **8e** in 30% yield. The yield was improved to 80% when **4e** was added to the dichloromethane solution containing 3 molar amounts of $EtAlCl_2$ at -23 °C (Eq. 4).

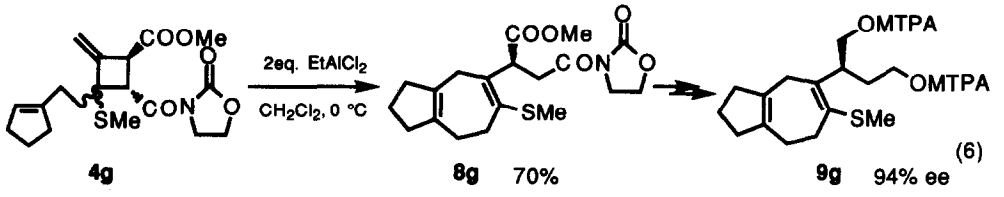
The optical purity of **8e** was elucidated as 95% by the conversion to the bis(+)-MTPA ester **9e**, indicating that the optical purity was maintained through the skeletal transformation.



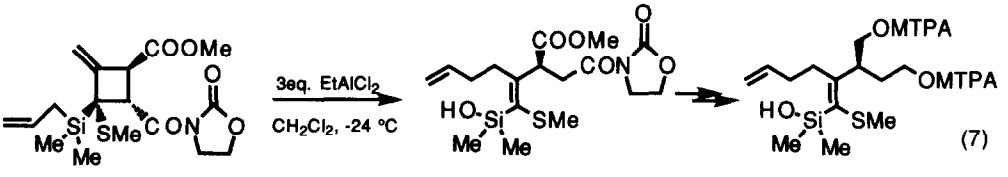
Next, methylenecyclobutanes having 2-propenyl, 3-butenyl and 5-hexenyl substituents (**4c**, **4d**, **4f**) were prepared and treated with 3 molar amounts of $EtAlCl_2$ at -23 °C in dichloromethane solution. In the reactions of **4c** and **4f**, the desired cyclohexene and cyclononene derivatives were not obtained. Rather, many unidentified products were formed. In the reaction of 3-butenyl substituted derivative **4d**, the reaction was completed within 20 min at -23 °C, affording a chlorocycloheptene derivative **8d** in 81% yield as a diastereomer mixture (55:45). The cycloheptene **8d** was converted to the bis(+)-MTPA ester **9d** and the optical purity was found to be 93% ee (Eq. 5).



This method was also applied to the formation of a bicyclic compound. Thus, methylenecyclobutane **4g**, that has a cyclopentenylethyl substituent gave the bicyclo[5.3.0]decane derivative **8g** in 70% yield with 94% optical purity (Eq. 6).



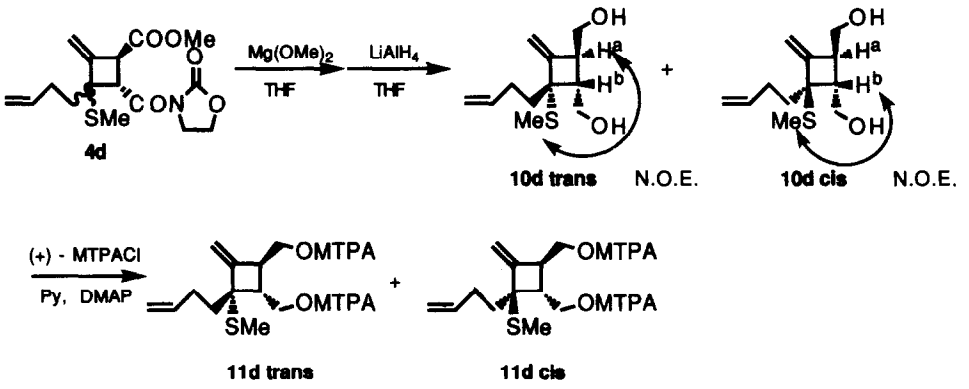
By the rearrangement of the methylenecyclobutane derivative **4i** having an allylsilane moiety, silanol **8i** was obtained in 88% yield instead of the ring-closure compound. The enantiomeric purity of **8i** was shown to be 97% ee by converting it to the bis (+)-MTPA ester **9i** (Eq. 7).



Determination of the stereochemistry and the optical purity of methylenecyclobutanes

The stereochemistry of the methylenecyclobutane derivatives **4a-i** was determined as follows. The methylenecyclobutane derivatives were converted to the corresponding diols **10a-i** by treatment with $Mg(OMe)_2$ and then with $LiAlH_4$. The **trans** and **cis** diastereomers of the diols **10a-10i** were separated by column or thin layer chromatography.

All the protonresonances for the two diastereomers having 3-butenyl substituent **10d trans** and **10d cis** were assigned by ^1H-^1H COSY spectra. The relative stereochemistry was determined for each diastereomer by the observed NOE in the NOESY spectra as shown in Scheme 2.

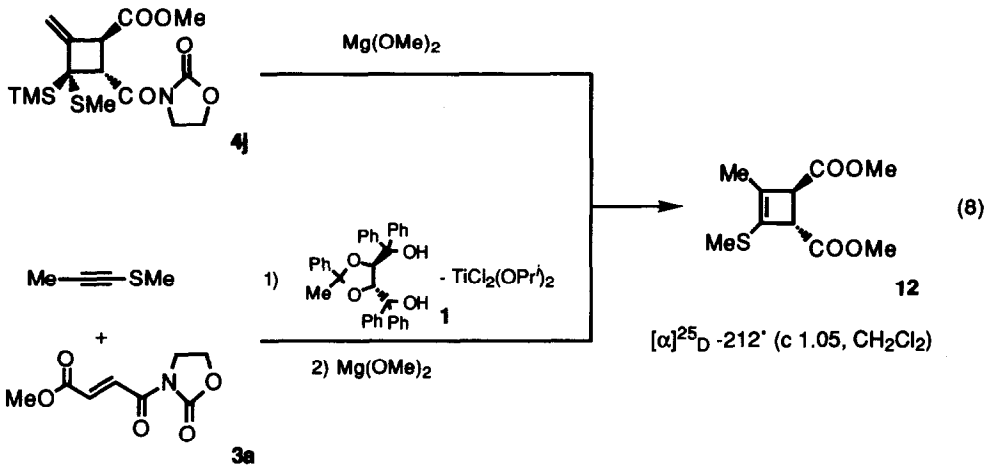


Scheme 2

The ^1H-NMR spectra of the other diols **10a-c, 10e-i** show the same pattern in the chemical shifts and multiplicities as those of **10d**, because the difference between **10d** and the other diols **10** is only the substituent at a side chain. This observation indicated that the methylenecyclobutanes situate almost the same conformation around the cyclobutane framework in **10**. The remarkable difference of chemical shifts was observed between H^a and H^b protons of the trans and cis diols: That is, in the ^1H-NMR spectrum of the major isomer **10d trans**, in which methylthio and oxazolidinylcarbonyl groups are trans, H^a proton appears at 2.9 ppm and H^b proton at 2.5 ppm, whereas H^a proton appears at 3.2 ppm and H^b at 2.3 ppm in the minor isomer **10d cis**. Accordingly, the isomer having higher field H^a proton and lower field H^b proton was determined to be the isomer in which methylthio and oxazolidinylcarbonyl groups are trans. The assignment of the trans and cis isomers of **10** based on ^1H-NMR also coincides with the mobility of each isomer on the thin layer chromatography, namely each **10 cis** isomer is more polar than the trans isomer.

The optical purity of methylenecyclobutanes **4a-4i** and the product **8i** were determined by ^1H-NMR analysis of the corresponding bis-(+)-MTPA ester **11a-11i** and **9i**.

It is known that in the Lewis acid-catalyzed asymmetric Diels-Alder and [2+2] cycloaddition reactions, the *re*-face of the α-carbon of the alkenoyl group in **3** is always attacked preferentially if the (*R*, *R*)-1,4-diol **1** is present as chiral auxiliary.[3, 6] The same sense of enantioselection is expected in the present formation of methylenecyclobutanes **4a-4i**. In fact, the cyclobutene derivative **12**, that was derived in 26% yield from **4j** by the treatment with $Mg(OMe)_2$ at room temperature, showed the same optical rotation ($[\alpha]^{25}_D$ -212° (c 1.05, CH_2Cl_2)) as **12** derived from the [2+2] cycloadduct of **3a** and 1-methylthio-1-propyne.[6c] Thus, the absolute stereochemistry of methylenecyclobutane **4j** was assigned as (1*S*, 2*S*, 3*S*).



Conclusion

The catalytic asymmetric [2+2] cycloadditions reported herein proceed with high enantioselectivity. The synthesis has wide generality for preparing optically active methylenecyclobutanes by the reaction of 1,2-propadienyl sulfides and the oxazolidinone derivatives of α,β-unsaturated carboxylic acids in the presence of a chiral titanium catalyst. Methylenecyclobutanes having ω-alkenyl substituents rearrange upon treatment with $EtAlCl_2$ to afford seven and eight membered ring compounds with a chiral side chain.

Experimental

General. NMR spectra were recorded on Bruker AM500 spectrometer using tetramethylsilane as the internal standard. $CDCl_3$ was used as solvent. IR spectra were measured with Horiba FT-300S spectrometer. High-resolution mass spectra (HRMS) were recorded on JEOL JMS-D300 mass spectrometer operating at 70 eV. The optical rotations were measured with JASCO DIP-370 polarimeter. Melting points and boiling points were uncorrected.

Column chromatography was conducted on silica gel (E. Merck, 7734, 70-230 mesh) and Florisil (Wako, 100-200 mesh) and medium pressure column chromatography was performed with the YHLC-254 system of YAMAZEN Corp. Preparative thin-layer chromatography (TLC) was carried out on a silica gel (Wakogel B-5F).

Dichloromethane was distilled from P_2O_5, then from CaH_2, and dried over MS4A. Toluene and petroleum ether were distilled and dried over MS 4A. Tetrahydrofuran (THF) and diethyl ether (Et_2O) were freshly distilled from sodium diphenylketyl. Dichlorodiisopropoxytitanium ($TiCl_2(OPr^i)_2$) was prepared from titanium(IV) chloride and titanium(IV) isopropoxide according to the literature method.[3g] All the operations were carried out under an argon atmosphere. Methyl (*E*)-4-oxo-4-(2-oxo-1,3-oxazolidin-3-yl)-2-butenoate (**3a**)[3c] and 3-acryloyl-1,3-oxazolidin-2-one (**3b**)[11] were prepared by the literature procedure.

Purification of the chiral 1,4-diol (1).

(2*R*,3*R*)-1,1,4,4-tetraphenyl-2,3-(1-phenylethylidene)dioxy-1,4-butanediol (**1**) was prepared according to the method in the paper.[3c]

The crude mixture (about 10g) is purified by silica gel column chromatography (SiO_2, ca. 500mL) by the use of the following solvent; 1) hexane 1600 mL, 2) hexane 1800 mL, Et_2O 20 mL, 3) hexane 1000 mL, Et_2O 16 mL, 4) hexane 1000 mL, Et_2O 20 mL. The product is eluted in the 3) and 4) fractions. About 7g is recovered. The purified product 1 g is dissolved in the mixture of hexane 5 mL and 2-propanol 4 mL with gentle warming. White precipitates (2-propanol inclusion complex) are formed after standing overnight. The precipitates are collected, washed with small amount of hexane and dried in vacuo for 5 h which weigh 0.67g. The precipitates are composed of the 2:1-3:1 mixture of the chiral diol **1** and 2-propanol. 2-Propanol is removed azeotropically with benzene by evaporation under reduced pressure several times and the product is dried in vacuo.

Preparation of 1-substituted-1,2-propadienylsulfides

3-Methylthio-1,2-butadiene (2a) and **4-methyl-3-methylthio-1,2-pentadiene (2b)** were prepared by our reported procedure.[8]

3-Methylthio-1,2,8-nonatriene (2f)

To a THF solution (5 mL) of diisopropylamine 625 mg (6.17 mmol), a hexane solution of *n*-BuLi 3.8 mL (1.66 mol/L, 6.15 mmol) was added at 0 °C and the reaction mixture was stirred for 10 min. To the reaction mixture was added a THF (2 mL) solution of 3-methylthio-1-propyne[6c] 536 mg (6.22 mmol) at -78 °C. After the reaction mixture was stirred for 1h, a THF (2 mL) solution of 6-bromo-1-hexene 1.0 g (6.13 mmol) was added to the reaction mixture, which was warmed to 0 °C. After the mixture was stirred for an additional hour, the reaction was quenched with pH 7 phosphate buffer and the organic materials were extracted with diethyl ether. The combined extracts were washed with brine and dried over Na_2SO_4. After evaporation of the solvent, the crude products were purified by bulb to bulb distillation to afford **2f** (665 mg, 3.96 mmol, 64%). Other sulfides **2c-e, g-j** were prepared by use of the corresponding halides such as 3-bromo-1-propene, 4-bromo-1-butene, 5-bromo-1-pentene, 1-cyclopentenylethylbromide,[12] 5-iodohexyn and chlorodimethyl(2-propenyl)silane.

Spectral Data

3-Methylthiohexa-1,2,5-triene (2c) yield 72%, bp 90 °C/1.0 mmHg (bulb to bulb distillation), IR (neat) cm^{-1} 3078, 2976, 2918, 1944, 1639, 1429, 916; ^1H NMR δ= 2.13 (3H, s), 2.89-2.91 (2H, m), 4.98 (2H, t, J=2.9 Hz), 5.05 (1H, dd, J=10.0, 1.0 Hz), 5.09 (1H, dd, J=13.0, 1.5 Hz), 5.83 (1H, ddt, J_d=13.0, 10.0 Hz, J_t=6.8 Hz); ^{13}C NMR δ= 15.50, 37.61, 81.32, 102.58, 116.61, 134.65, 202.49; HRMS Calcd. for $C_7H_{10}S$: M, 126.0504. Found: m/z 126.0515.

3-Methylthiohepta-1,2,6-triene (2d) yield 75%, bp 100 °C/0.8 mmHg (bulb to bulb distillation), IR (neat) 2976, 1940, 1641, 1435, 914, 864 cm^{-1} ; ^1H NMR δ= 2.12 (3H, s), 2.20-2.32 (4H, m), 4.95 (1H, dd, J=10.1, 1.0 Hz), 4.97 (2H, t, J=2.5 Hz), 5.02 (1H, dd, J=17.0, 1.6 Hz), 5.80 (1H, ddt, J_d=17.0, 10.1 Hz, J_t=6.1 Hz); ^{13}C NMR δ= 15.42, 32.14, 32.33, 81.33, 104.55, 115.06, 137.49, 202.23; HRMS Calcd. for $C_8H_{12}S$: M, 140.0661. Found: m/z 140.0659.

3-Methylthioocta-1,2,7-triene (2e) yield 85%, bp 125 °C/0.8 mmHg (bulb to bulb distillation), IR (neat) 2976, 2921, 1943, 1639, 1435, 912, 862 cm^{-1} ; ^1H NMR δ= 1.55-1.70 (2H, m), 2.01-2.10 (2H, m), 2.11 (3H, s), 2.12-2.23 (2H, m), 4.90-

5.50 (4H, m), 5.70-5.85 (1H, m); ^{13}C NMR δ= 15.42, 27.28, 32.38, 32.99, 81.07, 103.89, 114.81, 138.28, 202.17; HRMS Calcd. for $C_9H_{14}S$: M, 154.0817. Found: m/z 154.0829.

3-Methylthionona-1,2,8-triene (2f) yield 68%, bp 105 °C/0.4 mmHg (bulb to bulb distillation), IR (neat) cm^{-1} 2927, 1944, 1641, 1435, 912, 862; ^1H NMR δ= 1.35-1.45 (2H, m), 1.50-1.57 (2H, m), 2.00-2.06 (2H, m), 2.12-2.17 (2H, m), 2.12 (3H, s), 4.92 (1H, ddt, J_d=10.3, 3.0 Hz, J_t=1.6 Hz), 4.96 (2H, t, J=2.9 Hz), 4.98 (1H, ddt, J_d=17.9, 3.0 Hz, J_t=1.6 Hz), 5.78 (1H, ddt, J_d=17.9, 10.3 Hz, J_t=6.5 Hz); ^{13}C NMR δ= 15.4, 27.5, 28.2, 32.8, 33.4, 81.0, 104.0, 114.4, 138.8, 202.1; HRMS Calcd. for $C_{10}H_{16}S$: M, 168.0974. Found: m/z 168.0971.

5-(1-Cyclopentenyl)-3-methylthiopenta-1,2-diene (2g) yield 48%, bp 140 °C/0.5 mmHg (bulb to bulb distillation), IR (neat) cm^{-1} 3284, 2946, 2921, 1936, 1435, 960, 862; ^1H NMR δ= 1.80-1.83 (2H, m), 2.13 (3H, s), 1.90-2.30 (8H, m), 4.98 (2H, t, J=2.9 Hz), 5.35 (1H, br); ^{13}C NMR δ= 15.49, 23.39, 29.74, 31.42, 32.46, 35.10, 81.20, 103.96, 123.80, 143.59, 202.23; HRMS Calcd. for $C_{11}H_{16}S$: M, 180.0974. Found: m/z 180.0976.

3-Methylthioocta-1,2-dien-7-yne (2h) yield 75%, bp 150 °C/1.5 mmHg (bulb to bulb distillation), IR (neat) cm^{-1} 3298, 2919, 1946, 1430, 970, 866, 638; ^1H NMR δ= 1.74 (2H, quint., J=7.2 Hz), 1.93 (1H, t, J=2.7 Hz), 2.12 (3H, s), 2.20-2.27 (4H, m), 4.97 (2H, t, J=2.9 Hz); ^{13}C NMR δ= 15.42, 17.68, 26.84, 31.86, 68.58, 81.35, 83.92, 103.21, 202.13; HRMS Calcd. for $C_9H_{12}S$: M, 152.0661. Found: m/z 152.0666.

1-(Dimethyl-2-propenylsilyl)-1-methylthio-1,2-propadiene (2j) yield 85%, bp 125 °C/0.5 mmHg (bulb to bulb distillation), IR (neat) 2964, 1922, 1630, 1251, 835 cm^{-1} ; ^1H NMR δ= 0.15 (6H, s), 1.67 (2H, d, J=8.0 Hz), 2.17 (3H, s), 4.72 (2H, s), 4.85 (1H, d, J=10.3 Hz), 4.88 (1H, d, J=18.0 Hz), 5.77 (1H, ddt, J_d=18.0, 10.3 Hz, J_t=8.0 Hz); ^{13}C NMR δ= -3.89. -3.89, 15.14, 22.66, 75.88, 93.90, 113.79, 134.03, 204.13; HRMS Calcd. for $C_9H_{16}SSi$: M, 184.0828. Found: m/z 184.0760.

Typical procedure for the catalytic asymmetric [2+2] cycloaddition reaction. (Table 1, **4d**, condition A)

Chiral titanium reagent was prepared by stirring a toluene (5mL) solution of $TiCl_2(OPr^i)_2$ (125 mg, 0.53 mmol) and the chiral diol **1** (305 mg, 0.58 mmol) at room temperature for 30 min. To a flask containing MS 4A (powder, 100 mg) was added successively a part of the solution of the above chiral titanium reagent (1.0 mL, 0.10 mmol), toluene (1.5 mL) and petroleum ether (2.0 mL). To this solution was added methyl (*E*)-4-oxo-4-(2-oxo-1,3-oxazolidin-3-yl)-2-butenoate (**3a**) (103.8 mg, 0.502 mmol) and 2 mL of toluene and a petroleum ether solution (3 mL) of 3-methylthio-1,2,6-heptatriene (**2d**) 92 mg (0.65 mmol) at 0 °C. After stirring for 10 h, the reaction was quenched with pH 7 phosphate buffer and inorganic precipitates were removed by filtration. The organic materials were extracted with ethyl acetate and the extracts were washed with brine and dried over Na_2SO_4. After evaporation of the solvent, the crude products were purified by TLC (hexane : ethyl acetate = 1 : 1) to afford the mixture of **4d trans** and **4d cis** (159 mg, 94%, **4d trans** : **4d cis** = 65 : 35). The ratio of **4d trans** and **4d cis** was determined by 500 MHz ^1H-NMR.

Typical procedure for the [2+2] cycloaddition reaction. (Table 1, **4d**, condition B)

To a toluene solution (2mL) of $TiCl_2(OPr^i)_2$ (246 mg, 1.04 mmol) and methyl (*E*)-4-oxo-4-(2-oxo-1,3-oxazolidin-3-yl)-2-butenoate (**3a**) (183 mg, 0.92 mmol), a toluene solution (3 mL) of 3-methylthio-1,2,6-heptatriene (**2d**) (142 mg, 1.01 mmol) was added at 0 °C. After stirring for 2 h, the reaction was quenched with pH 7 phosphate buffer and inorganic precipitates were removed by filtration. The organic materials were extracted with ethyl acetate and the extracts were washed with brine and dried over Na_2SO_4. After evaporation of the solvent, the crude products were purified by TLC (hexane : ethyl acetate = 1 : 1) to afford the mixture of

4d trans and **4d cis** (294 mg, 98%, **4d trans** : **4d cis** = 80 : 20). The ratio of **4d trans** and **4d cis** was determined by 500 MHz ^{1}H-NMR.

Spectral Data

Cis- and trans-isomers of **4a-h, 4k** were not separated by TLC.

Methyl (1*R*, 2*R*)-3-methyl-4-methylene-3-methylthio-2-(2-oxo-1,3-oxazolidin-3-ylcarbonyl)cyclobutanecarboxylate (4a) (**trans** : **cis** = 50 : 50 (Conditions A), 80 : 20 (Conditions B)) IR (neat) cm^{-1} 2925, 1786, 1736, 1691; ^{1}H NMR major δ= 1.65 (3H, s), 2.00 (3H, s), 3.69 (3H, s), 4.00-4.08 (2H, m), 4.35-4.43 (2H, m), 4.47 (1H, dt, J_d=8.0, J_t=3.2 Hz), 4.67 (1H, d, J=8.0 Hz), 5.06 (1H, d, J=3.2 Hz), 5.30 (1H, d, J=3.2 Hz), minor δ= 1.33 (3H, s), 2.08 (3H, s), 3.69 (3H, s), 3.93-4.07 (2H, m), 4.28 (1H, dt, J_d=8.3, J_t=3.2 Hz), 4.35-4.43 (2H, m), 5.08 (1H, d, J=8.3 Hz), 5.10 (1H, d, J=3.2 Hz), 5.26 (1H, d, J=3.2 Hz); ^{13}C NMR major δ= 12.23, 27.44, 42.70, 43.39, 44.53, 52.15, 56.77, 62.25, 108.94, 147.35, 153.17, 169.88, 170.72, minor δ= 13.04, 22.63, 42.67, 43.55, 44.53, 50.27, 55.74, 61.93, 108.04, 146.97, 153.03, 169.35, 170.17; Found: C, 51.55; H, 5.67; N, 4.92; S, 10.78 %. Calcd. for $C_{13}H_{17}O_5NS$: C, 52.16; H, 5.72; N, 4.68; S, 10.71 %.

Methyl (1*R*, 2*R*)-3-isopropyl-4-methylene-3-methylthio-2-(2-oxo-1,3-oxazolidin-3-ylcarbonyl)cyclobutanecarboxylate (4b) (**trans** : **cis** = 73 : 27 (Conditions A), 80 : 20 (Conditions B)) IR (neat) cm^{-1} 2971, 2927, 1782, 1736, 1691; ^{1}H NMR major δ= 1.00 (3H, d, J=6.6 Hz), 1.05 (3H, d, J=6.6 Hz), 1.98 (3H, s), 2.12 (1H, qq, J=6.6, 6.6 Hz), 3.67 (3H, s), 3.90-4.10 (2H, m), 4.31 (1H, ddd, J=7.9, 1.1, 1.1 Hz), 4.35-4.45 (2H, m), 5.03 (1H, dd, J=2.8, 1.1 Hz), 5.03 (1H, d, J=7.9 Hz), 5.40 (1H, dd, J=2.8, 1.1 Hz), minor δ= 0.78 (3H, d, J=6.7 Hz), 0.98 (3H, d, J=6.8 Hz), 2.04 (3H, s), 2.35 (1H, qq, J=6.7, 6.8 Hz), 3.66 (3H, s), 3.83-4.10 (2H, m), 4.10-4.16 (1H, m), 4.25-4.43 (2H, m), 4.80-4.82 (1H, m), 5.12 (1H, d, J=10.2 Hz), 5.38 (1H, d, J=2.7 Hz); ^{13}C NMR major δ= 13.50, 17.77, 18.34, 34.12, 42.99, 44.44, 45.17, 52.14, 62.18, 64.89, 111.92, 143.50, 153.30, 170.36, 170.52, minor δ= 10.99, 17.93, 18.14, 30.72, 42.92, 44.35, 44.44, 52.14, 61.84, 68.60, 110.22, 144.31, 153.06, 170.25, 170.55; HRMS Calcd. for $C_{15}H_{21}O_5NS$: M, 327.1141. Found: m/z 327.1148.

Methyl (1*R*, 2*R*)-4-methylene-3-methylthio-2-(2-oxo-1,3-oxazolidin-3-ylcarbonyl)-3-(2-propenyl)cyclobutanecarboxylate (4c) (**trans** : **cis** = 68 : 32 (Conditions A), 80 : 20 (Conditions B)) IR (neat) cm^{-1} 2987, 2921, 1780, 1736, 1689; ^{1}H NMR major δ= 2.04 (3H, s), 2.66 (1H, dd, J=14.3, 6.5 Hz), 2.76 (1H, dd, J=14.3, 7.7 Hz), 3.73 (3H, s), 4.00-4.13 (2H, m), 4.35-4.45 (3H, m), 4.78 (1H, d, J=7.5 Hz), 5.10-5.25 (3H, m), 5.46 (1H, dd, J=2.9, 1.3, Hz), 5.83-5.95 (1H, m), minor δ= 2.13 (3H, s), 2.41 (1H, dd, J=14.7, 8.3 Hz), 2.59 (1H, ddt, J_d=14.8, 5.7 Hz, J_t=1.6 Hz), 3.74 (3H, s), 3.90-4.00 (2H, m), 4.30-4.45 (3H, m), 5.10-5.25 (3H, m), 5.40-5.50 (1H, m), 5.75-5.85 (1H, m); ^{13}C NMR major δ=13.06, 42.76, 42.93, 44.16, 47.98, 52.07, 58.72, 61.89, 111.66, 119.12, 133.08, 144.29, 153.15, 169.82, 170.34, minor δ=11.66, 39.49, 42.50, 43.56, 47.98, 52.14, 60.30, 62.29, 109.41, 116.02, 132.57, 144.88, 153.64, 169.75, 170.07 ; HRMS Calcd. for $C_{15}H_{19}O_5NS$: M, 325.0985. Found: m/z 325.0987.

Methyl (1*R*, 2*R*)-3-(3-butenyl)-4-methylene-3-methylthio-2-(2-oxo-1,3-oxazolidin-3-ylcarbonyl)cyclobutanecarboxylate (4d) (**trans** : **cis** = 65 ; 35 (Conditions A), 80 : 20 (Conditions B)) IR (neat) cm^{-1} 2992, 2923, 1786, 1734, 1691; ^{1}H NMR major δ= 1.90 (1H, dt, J_d=7.7 Hz, J_t=11.2 Hz), 1.98 (3H, s), 1.95-2.20 (2H, m), 2.25-2.38 (1H, m), 3.69 (3H, s), 3.98-4.09 (2H, m), 4.40 (2H, t, J=8.6 Hz), 4.44 (1H, ddd, J=7.8, 1.3, 1.3), 4.78 (1H, d, J=7.8 Hz), 4.87 (1H, dd, J=10.3, 1.7 Hz), 4.95-5.02 (1H, m), 5.03 (1H, dd, J=3.0, 1.3 Hz), 5.39 (1H, dd, J=3.0, 1.3 Hz), 5.76 (1H, ddt, J_d=16.4, 10.3 Hz, J_t=6.3 Hz) minor δ= 1.45-1.55 (1H, m), 2.08 (3H, s), 1.95-2.20 (2H, m), 2.25-2.38 (1H, m), 3.68 (3H, s), 3.90-4.00 (2H, m), 4.25-4.45 (3H, m), 4.92-4.98 (2H, m), 5.09 (1H, dd, J=3.3, 1.2 Hz), 5.13 (1H, d, J=7.8 Hz), 5.34 (1H, dd, J=3.3, 1.3 Hz), 5.69 (1H, ddt, J_d=16.4, 10.3 Hz, J_t=6.3 Hz); ^{13}C NMR major δ= 13.03, 29.17, 37.54, 42.77, 44.44, 47.38, 52.22, 59.44, 62.27, 110.89, 114.72, 137.90, 144.56, 153.23, 169.73, 170.52, minor δ= 11.81, 28.94, 31.65, 33.99, 43.28, 43.78, 52.20, 61.35, 61.92,

109.68, 115.06, 137.63, 144.70, 153.08, 169.78, 170.15; Found: C, 56.51; H, 6.20; N, 4.30; S, 9.54 %. Calcd. for $C_{16}H_{21}O_5NS$: C, 56.62; H, 6.24; N, 4.13; S, 9.45 %.

Methyl (1*R*, 2*R*)-4-methylene-3-methylthio-2-(2-oxo-1,3-oxazolidin-3-ylcarbonyl)-3-(4-pentenyl)cyclobutanecarboxylate (4e) (**trans : cis** = 63 : 37 (Conditions A), 81 : 19 (Conditions B)) IR (neat) cm^{-1} 2983, 2925, 1782, 1736, 1689; ^1H NMR major δ= 1.40-2.20 (6H, m), 2.01 (3H, s), 3.72 (3H, s), 4.00-4.07 (2H, m), 4.38-4.46 (3H, m), 4.81 (1H, d, J=7.7 Hz), 4.91-5.00 (2H, m), 5.05 (1H, dd, J=3.2, 1.2 Hz), 5.42 (1H, dd, J=3.0, 1.2 Hz), 5.77 (1H, ddt, J_d=16.9, 10.3 Hz, J_t=6.6 Hz), minor δ= 1.40-2.20 (6H, m), 2.11 (3H, s), 3.71 (3H, s), 3.90-4.07 (2H, m), 4.25 (1H, dt, J_d=8.7 Hz, J_t=1.0 Hz), 4.38-4.46 (2H, m), 4.91-5.00 (2H, m), 5.11 (1H, d, J=3.0 Hz), 5.16 (1H, d, J=8.7 Hz), 5.36 (1H, d, J=3.0 Hz), 5.70-5.75 (1H, m); ^{13}C NMR major δ= 12.97, 23.91, 33.56, 37.64, 42.72, 44.34, 47.43, 52.11, 59.66, 62.23, 110.73, 114.54, 136.44, 144.71, 153.17, 169.80, 170.47, minor δ= 11.71, 23.61, 33.62, 37.64, 43.09, 43.60, 47.43, 52.11, 61.62, 61.67, 109.30, 114.70, 136.06, 144.97, 153.03, 169.77, 170.11; Found: C, 57.60; H, 6.53; N, 4.18; S, 9.31 %. Calcd. for $C_{17}H_{23}O_5NS$: C, 57.77; H, 6.56; N, 3.96; S, 9.07 %.

Methyl (1*R*, 2*R*)-3-(5-hexenyl)-4-methylene-3-methylthio-2-(2-oxo-1,3-oxazolidin-3-ylcarbonyl)cyclobutanecarboxylate (4f) (**trans : cis** = 65 : 35 (Conditions A), 80 : 20 (Conditions B)) IR (neat) cm^{-1} 2979, 2927, 1780, 1736, 1689; ^1H NMR major δ= 1.20-2.10 (8H, m), 2.00 (3H, m), 3.71 (3H, m), 4.00-4.10 (2H, m), 4.35-4.42 (1H, m), 4.41 (2H, t, J=8.3 Hz), 4.80 (1H, d, J=10.8 Hz), 4.89 (1H, d, J=10.8 Hz), 4.94 (1H, d, J=16.9 Hz), 5.03-5.04 (1H, m), 5.41 (1H, dd, J=2.8, 1.0 Hz), 5.77 (1H, ddt, J_d=16.9, 10.8 Hz, J_t=6.6 Hz), minor δ= 1.20-2.10 (8H, m), 2.09 (3H, m), 3.70 (3H, m), 3.90-4.00 (2H, m), 4.20-4.40 (1H, m), 4.35-4.45 (2H, m), 4.85-4.95 (2H, m), 5.08-5.12 (1H, m), 5.14 (1H, d, J=7.7 Hz), 5.31 (1H, d, J=10.8 Hz), 5.65-5.75 (1H, m); ^{13}C NMR major δ= 12.78, 24.01, 28.65, 33.28, 34.46, 42.60, 44.17, 46.33, 51.95, 59.56, 62.14, 110.52, 114.00, 138.97, 144.70, 153.08, 169.62, 170.30 minor δ=11.53, 23.85, 28.74, 33.28, 38.06, 42.68, 43.53, 47.33, 51.95, 61.52, 61.77, 109.03, 114.27, 138.35, 144.97, 152.93, 169.60, 169.96; HRMS Calcd. for $C_{18}H_{25}O_5NS$: M, 367.1455. Found: m/z 367.1453.

Methyl (1*R*, 2*R*)-3-(2-cyclopentenylethyl)-4-methylene-3-methylthio-2-(2-oxo-1,3-oxazolidin-3-ylcarbonyl)cyclobutanecarboxylate (4g) (**trans : cis** = 67 : 33 (Conditions A), 80 : 20 (Conditions B)) IR (neat) cm^{-1} 2949, 2922, 1784, 1736, 1691; ^1H NMR major δ= 1.74-1.84 (2H, quint., J=7.4 Hz), 1.98 (3H, s), 1.90-2.40 (8H, m), 3.69 (3H, s), 4.00-4.10 (2H, m), 4.35-4.46 (3H, m) 4.78 (1H, d, J=7.6 Hz), 5.03 (1H, dd, J=3.0, 1.0 Hz), 5.28-5.30 (1H, m), 5.39 (1H, dd, J=3.0, 1.3 Hz), minor δ= 1.55-1.65 (2H, m), 1.98 (3H, s), 1.90-2.40 (8H, m), 3.68 (3H, s), 3.90-4.00 (2H, m), 4.20-4.46 (3H, m) 5.05-5.10 (1H, m), 5.13 (1H, d, J=8.7 Hz), 5.20-5.50 (1H, m), 5.33-5.35 (1H, m); ^{13}C NMR major δ=12.89, 23.18, 26.25, 32.24, 35.13, 36.47, 42.70, 44.32, 47.39, 52.07, 59.51, 62.19, 110.76, 123.13, 143.72, 144.59, 153.12, 169.65, 170.41, minor δ=11.68, 23.13, 26.03, 32.27, 35.06, 35.13, 43.15, 43.70, 47.39, 52.05, 61.32, 61.65, 109.40, 123.37, 143.42, 144.79, 153.01, 170.05, 170.41; HRMS Calcd. for $C_{19}H_{25}O_5NS$: M, 379.1455. Found: m/z 379.1456.

Methyl (1*R*, 2*R*)-4-methylene-3-methylthio-2-(2-oxo-1,3-oxazolidin-3-ylcarbonyl)-3-(4-pentynyl)-cyclobutanecarboxylate (4h) (**trans : cis** = 50 : 50 (Conditions A), 67 : 33 (Conditions B)) IR (neat) cm^{-1} 3290, 2924, 1778, 1734, 1687; ^1H NMR major δ= 1.50-1.62 (2H, m), 1.70-1.95 (2H, m), 1.90 (1H, t, J=2.5 Hz), 1.97 (3H, s), 2.09-2.15 (1H, m), 2.17 (1H, dt, J_d=2.5 Hz, J_t=6.7 Hz), 3.67 (3H, s), 3.97-4.06 (2H, m), 4.33-4.42 (3H, m), 4.72 (1H, d, J=7.7 Hz), 5.03 (1H, dd, J=2.4, 1.0 Hz), 5.37 (1H, dd, J=2.4, 1.0 Hz), minor δ=1.50-1.62 (2H, m), 1.70-1.95 (2H, m), 1.90 (1H, t, J=2.5 Hz), 2.06 (3H, s), 2.09-2.15 (1H, m), 2.21 (1H, dt, J_d=2.5 Hz, J_t=6.7 Hz), 3.67 (3H, s), 3.90-4.00 (2H, m), 4.21 (1H, dt, J_d=8.7 Hz, J_t=3.0 Hz), 4.33-4.42 (2H, m), 5.06 (1H, dd, J=3.0, 1.0 Hz), 5.11 (1H, d, J=8.7 Hz), 5.32 (1H, dd, J=3.0, 1.0 Hz); ^{13}C NMR major δ=12.97, 18.37, 23.78, 37.33, 42.77, 44.45, 47.31, 52.19, 59.35, 62.28, 68.43, 84.10, 110.86, 144.38, 153.23, 169.62, 170.46, minor δ=11.76, 18.50, 23.76, 33.75, 42.28, 43.78, 47.31, 52.19, 61.20, 61.93, 68.74, 83.65, 109.61, 144.72, 153.07, 169.74, 170.10; HRMS Calcd. for $C_{17}H_{21}O_5NS$: M, 351.1141. Found: m/z 351.1150.

Methyl (1*R*, 2*R*, 3*S*)-4-methylene-3-methylthio-2-(2-oxo-1,3-oxazolidin-3-ylcarbonyl)-3-(dimethyl-2-propenylsilyl)cyclobutanecarboxylate (4i) IR (neat) cm^{-1} 2925, 1738, 1691, 1660; ^1H NMR δ= 0.84 (3H, s), 0.89 (3H, s), 1.68 (2H, d, J=8.0 Hz), 1.99 (3H, s), 3.67 (3H, s), 4.04 (2H, t, J=8.0 Hz), 4.40 (2H, t, 8.0 Hz), 4.42 (1H, ddd, J=7.0, 1.9, 1.1), 4.79 (1H, d, J=10.2 Hz), 4.82 (1H, d, J=16.9), 4.89 (1H, dd, J=2.1, 1.9 Hz), 5.04 (1H, d, J=7.0 Hz), 5.47 (1H, dd, J=2.1, 1.1 Hz), 5.70 (1H, ddt, J_d=16.9, 10.2 Hz, J_t=8.0 Hz); ^{13}C NMR δ= -5.55, -5.51, 12.34, 20.54, 42.81, 45.71, 45.81, 49.02, 52.13, 62.14, 112.81, 113.87, 134.48, 143.01, 153.10, 170.36, 171.46; HRMS Calcd. for $C_{17}H_{25}O_5NSSi$: M, 383.1224. Found: m/z 383.1223.

(1*R*)-3-(3-Methylene-2-(methylthio)-2-(4-pentenyl)-1-cyclobutanecarbonyl)-1,3-oxazolidin-2-one (4k) (trans : cis = 20 : 80 (Conditions A), 29 : 71 (Conditions B)) IR (neat) cm^{-1} 2925, 1738, 1691, 1660; ^1H NMR major δ= 1.20-2.10 (6H, m), 2.08 (3H, s), 2.56 (1H, ddt, J_d=15.3, 8.6 Hz, J_t=2.1 Hz), 3.11 (1H, ddt, J_d=15.3, 8.6 Hz, J_t=2.8 Hz), 4.00-4.05 (2H, m), 4.31-4.60 (2H, m), 4.77 (1H, dd, J=8.6, 8.6 Hz), 4.88-5.01 (4H, m), 5.72 (1H, ddt, J_d=16.9, 10.2 Hz, J_t=6.7 Hz), minor δ= 1.20-2.10 (6H, m), 1.96 (3H, s), 2.62 (1H, ddt, J_d=16.2, 8.9 Hz, J_t=2.5 Hz), 3.23 (1H, ddt, J_d=16.2, 9.2 Hz, J_t=2.9 Hz), 3.90-3.99 (2H, m), 4.31-4.60 (3H, m), 4.88-5.01 (4H, m), 5.77 (1H, ddt, J_d=17.0, 10.2 Hz, J_t=6.7 Hz); ^{13}C NMR major δ=11.70, 23.80, 29.04, 33.63, 33.80, 40.75, 42.80, 81.81, 82.12, 107.54, 114.58, 138.36, 147.44, 153.32, 171.59, minor δ= 12.82, 24.03, 28.82, 33.63, 33.80, 38.39, 45.49, 81.45, 83.59, 108.96, 114.60, 138.53, 147.96, 153.47, 171.51; HRMS Calcd. for $C_{15}H_{21}O_3NS$: M, 295.1243. Found: m/z 295.1234.

General procedure for the ring cleavage reaction and the rearrangement reaction. (10e)

To a CH_2Cl_2 solution (3 mL) of $EtAlCl_2$ (0.86 mL, 0.93 mol/L in hexane, 0.80 mmol) was added a CH_2Cl_2 (2mL) solution of methyl (1*R*,2*R*)-4-methylene-3-methylthio-2-(2-oxo-1,3-oxazolidin-3-yl)butanoate (**4e**) (94.3 mg, 0.267 mmol) dropwise at -23 °C or 0 °C (in the case of **4g**). After the reaction mixture was stirred for 20 min, the reaction was quenched with a 10 mL of sat. $NaHCO_3$. After filteration of the inorganic precipitates, organic materials were extracted 3 times with CH_2Cl_2, dried over Na_2SO_4. After evaporation of the solvent, the crude products were purified by TLC (hexane : ethyl acetate = 2 : 1) to afford the compound **10e** (82.5 mg, 0.211 mmol, 80%). This procedure was also applied to **4d** and **4i**.

Spectral Data

Methyl (2*R*)-2-(5-chloro-1-cycloheptenyl-2-methylthio)-4-(2-oxo-1,3-oxazolidin-3-yl)butanoate (8d) Diastereomer ratio is 55 : 45. IR (neat) cm^{-1} 2950, 2927, 1784, 1734, 1699, 1390, 762, 733, 702; ^1H NMR δ= 1.50-2.10 (7H, m), 2.16 (3H, s), 2.30-2.47 (2H, m), 2.65 (1H x 0.45, dd, J=7.4, 4.8 Hz), 2.70 (1H x 0.55, dd, J=7.6, 4.8 Hz), 2.71-2.80 (1H, m), 3.57-3.64 (1H, m), 3.62 (3H x 0.55, s), 3.64 (3H x 0.45, s), 3.94-4.07 (2H, m), 4.15-4.20 (1H x 0.45, m), 4.20-4.23 (1H x 0.55, m), 4.35-4.39 (2H, m), 4.78 (1H, dd, J=9.8 1.7 Hz); ^{13}C NMR major δ= 15.77, 25.46, 29.38, 35.07, 35.31, 35.48, 42.34, 45.69, 52.01, 62.15, 62.98, 136.28, 139.64, 153.45, 170.96, 172.97 Minnor 15.75, 25.67, 29.91, 35.01, 35.43, 35.67, 42.34, 45.67, 52.06, 62.15, 63.06, 136.10, 139.72, 153.48, 170.96, 172.88; Found: C, 51.00; H, 5.96; N, 3.98; S, 8.24 %. Calcd. for $C_{16}H_{22}O_5NSCl$: C, 51.13; H, 5.90; N, 3.73; S, 8.53 %.

Methyl (2*R*)-2-(6-chloro-1-cyclooctenyl-2-methylthio)-4-(2-oxo-1,3-oxazolidin-3-yl)butanoate (8e) Diastereomer ratio is 55 : 45. IR (neat) cm^{-1} 2947, 2925, 1781, 1734, 1697, 1389, 761, 737, 704; ^1H NMR δ= 1.60-2.30 (10H, m), 2.19 (3H x 0.55, s), 2.18 (3H x 0.45, s), 2.42-2.54 (2H, m), 2.83 (1H x 0.45, dd, J=8.0, 4.0 Hz), 2.98 (1H x 0.55, dd, J=8.0, 4.0 Hz), 3.68 (3H x 0.55, s), 3.70 (3H x 0.45, s), 3.70-3.80 (1H, m), 3.95-4.10 (1H, m), 4.40 (2H, dd, J=7.9, 7.9 Hz), 4.64 (1H x 0.45, dd, J=10.5 4.0 Hz), 4.81 (1H x 0.55, dd, J=10.5 4.0 Hz); ^{13}C NMR major δ= 15.77, 25.46, 29.38, 35.07, 35.31, 35.48, 42.34, 45.69, 52.01, 62.15, 62.98, 136.28, 139.64, 153.45, 170.96, 172.97, minor δ= 15.75, 25.67, 29.91,

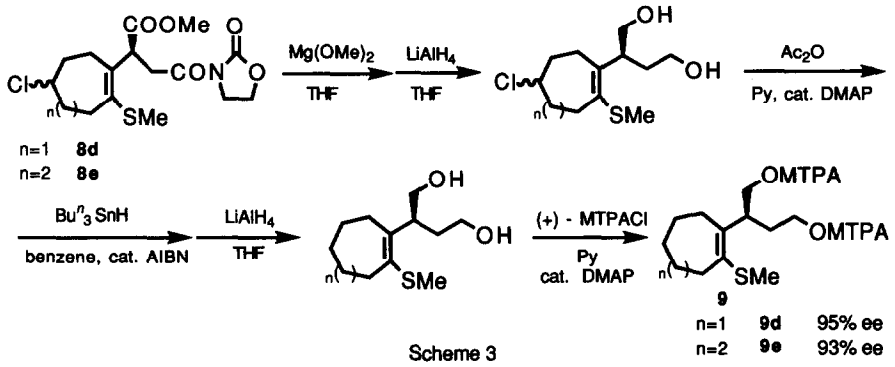
35.01, 35.43, 35.67, 42.34, 45.67, 52.06, 62.15, 63.06, 136.10, 139.72, 153.48, 170.96, 172.88; Found: C, 52.36; H, 6.16; N, 3.56; S, 8.37 %. Calcd. for $C_{17}H_{24}O_5NSCl$: C, 52.37; H, 6.20; N, 3.59; S, 8.22 %.

Methyl (2*R*)-2-(4-methylthiobicyclo[5.3.0]deca-3,7-dien-3-yl)-4-oxo-4-(2-oxo-1,3-oxazolidin-3-yl)butanoate (8g) IR (neat) cm^{-1} 2949, 2925, 1780, 1732, 1699, 1389; ^1H NMR δ= 1.55-1.75 (2H, m), 1.90-2.90 (10H, m), 2.19 (3H, s), 3.61 (3H, s), 3.55-3.75 (2H, m), 3.70-4.05 (2H, m), 4.30-4.45 (2H, m), 4.76 (1H, dd, J=10.2 4.5 Hz); ^{13}C NMR δ= 15.99, 21.03, 27.58, 28.86, 30.70, 35.79, 36.48, 36.67, 42.37, 45.22, 52.04, 62.14, 130.74, 133.71, 135.07, 139.38, 153.50, 171.20, 173.22; HRMS Calcd. for $C_{19}H_{25}O_5NS$: M, 379.1455. Found: m/z 379.1451.

Methyl (2*R*)-3-(1-dimethylhydroxysilyl-1-methylthiomethylene)-2-[2-oxo-2-(2-oxo-1,3-oxazolidin-3-yl)ethyl]heptanoate (8j) IR (neat) cm^{-1} 3210, 2952, 2923, 1780, 1731, 1701, 1390, 1227; ^1H NMR δ= 0.31 (3H, s), 0.32 (3H, s), 2.03-2.12 (1H, m), 2.12-2.22 (1H, m), 2.16 (3H, s), 2.33 (1H, ddd, J=13.5, 11.2, 5.3 Hz), 2.40 (1H, ddd, J=13.5, 11.4, 5.5 Hz), 2.56 (1H, br), 2.73 (1H, dd, J=17.9, 3.2 Hz), 3.66 (3H, s), 3.90 (1H, dd, J=17.9, 10.4 Hz), 3.95-4.04 (2H, m), 4.40 (2H, t, J=8.1 Hz), 4.84 (1H, dd, J=10.4, 3.2), 4.96 (1H, d, J=10.2 Hz), 5.00 (1H, d, J=16.8 Hz), 5.75 (1H, ddt, J_d=16.8, 10.2 Hz, J_t=6.5 Hz); ^{13}C NMR δ= 1.75, 1.82, 19.78, 33.86, 34.74, 36.75, 42.46, 45.68, 52.17, 62.22, 115.36, 135.19, 137.26, 153.55, 159.36, 171.24, 173.16; HRMS Calcd. for $C_{17}H_{27}O_6NSSi$: M, 401.1329. Found: m/z 401.1335.

Determination of the optical purity of the rearrangement product

The optical purity of cycloheptene and cyclooctene **8d** and **8e** was determined as follows. **8d** and **8e** were converted to the dimethyl esters by the treatment with $Mg(OMe)_2$. These were reduced to the corresponding diols with $LiAlH_4$. After acetylation of the diols, reduction with Bu^n_3SnH and then $LiAlH_4$, followed by the treatment with (+)-MTPACl and pyridine, gave the bis-(+)-MTPA esters **9d** and **9e**. The optical purity was determined by ^1H-NMR analysis of the methyl proton of the methoxyl group of **9d** or the methylthio group of **9e**.

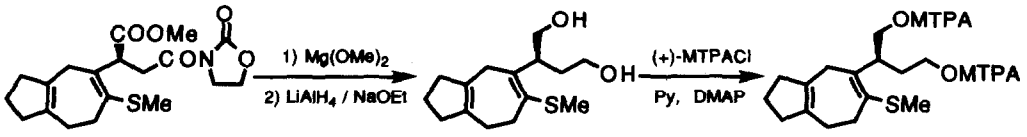


Scheme 3

Bicyclo[5.3.0]decane derivative **8g** was converted to the dimethyl ester by the treatment with $Mg(OMe)_2$. The reduction with $LiAlH_4$ did not give the corresponding diol, but the reduction with $LiAlH_4$ and NaOEt afforded the desired diol in 50% yield.[13] The ^{13}C-NMR analysis of the bis(+)-MTPA ester **9g** revealed the optical purity as 94%.

In the rearrangement to form bicyclo[5.3.0]decane **8g**, a slight loss of the optical purity was observed. Thus, the optical purity of **8g** is 94% ee, in spite of the high optical purity of the [2+2] cycloadducts **4g trans**

and **4g cis** (**trans** : **cis** = 67 : 33, **4g trans** = 98% ee, **4g cis** = 97% ee). This is probably due to partial racemization during the reduction of the dimethyl ester with $LiAlH_4$ and NaOEt.



8g **9g** 94%ee

Scheme 4

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9) When a mixture of diastereomers (trans:cis=63:37) of the chiral **4e** which was prepared from the method described in condition A in Table 1(the asymmetric [2+2] reaction) was treated with $TiCl_2(OPr^i)_2$ under the reaction condition B, the starting material was recovered without the change of the diastereomer ratio. When achiral **4e** (trans:cis=80:20) which was prepared under the condition B was treated with the chiral titanium reagent, no change of the diastereomer ratio was observed. This result indicates **4cis** and **4trans** were produced under the conditions of the kinetic control in the reactions catalyzed by titanium reagents.

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