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A New Methodology for the Stereoselective Synthesis of 4-Substituted Butenolides: Asymmetric Michael Addition Reaction of 2-(Trimethylsilyloxy)furans to Oxazolidinone Enoates

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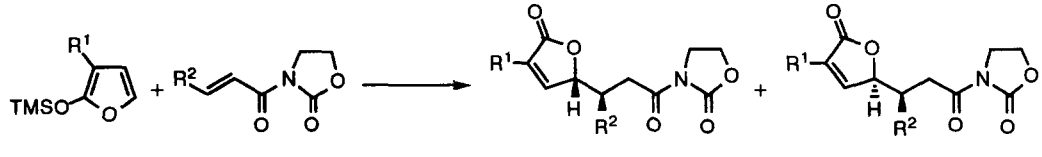
Abstract: Chiral Lewis acid promoted Michael addition of 2-(trimethylsilyloxy)furans to oxazolidinone enoates (**2**) in the presence of hexafluoroisopropanol proceeded stereoselectively to give 4-substituted butenolides in good yields. A 1:1 complex prepared *in situ* from $Sc(OTf)_3$ and 3,3'-bis(diethylaminomethyl)-1,1'-bi-2-naphthol **5b** showed excellent *anti*-selectivity and moderate enantioselectivity, while $Cu(OTf)_2$-bis(oxazoline) complex exhibited excellent enantioselectivity and moderate to good *anti*-selectivity. © 1997 Elsevier Science Ltd.

Butenolides exist as subunits of many natural products[1] and also serve as the precursors for the synthesis of densely substituted chiral γ–lactone compounds.[2] Therefore, much effort has been directed toward exploitation of the methodology for efficient synthesis of chiral butenolides. 2-(Trialkylsilyloxy)furans have been widely used for this purpose, since they are nucleophiles and react with various electrophiles such as ketone,[3] aldehyde,[3a,4] acetal,[3a,5] nitrone,[6] enone[7], and allyl halide[8] in the presence of Lewis acid to afford the corresponding 4–substituted butenolides. In these reactions, Michael reaction has an advantage over the other reactions, because it provides the butenolide bearing a C4-substituent functionalized at its terminal carbon which allows the further extension of the substituent. Accordingly, Michael reaction is expected to become an efficient tool for the synthesis of various butenolide derivatives, if enantio- and diastereoselectivities of the reaction are controlled by some means. Fukuyama *et al.* have reported that Michael addition reaction of 2-ethylthio-5-(trimethylsilyloxy)furan to chalcone derivative proceeds with high diastereoselectivity to give a key intermediate for the synthesis of mitomycins,[7b,c] while only moderate diastereoselectivity was observed in the



1a: R^1=H
1b: R^1=Me

2a: R^2=Me
2b: R^2=H

anti-**3a**: R^1=H, R^2=Me
anti-**3b**: R^1=Me, R^2=Me
3c: R^1=H, R^2=H

syn-**3a**: R^1=H, R^2=Me
syn-**3b**: R^1=Me, R^2=Me

Scheme 1

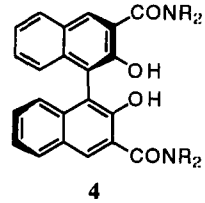
reaction of simple trimethylsilyloxyfurans and chalcones.[7a] Still, no enantioselective version of this type of reaction has been reported.[9] In order to clarify the scope of this useful reaction, we examined the Lewis acid promoted Michael addition reaction of 2-(trimethylsilyloxy)furans to oxazolidinone enoates (Scheme 1) using a chiral scandium(III) or a copper(II)-bis(oxazoline) complex as a catalyst.[10]

Initially, we examined the addition reaction of **1a** to **2a** in the presence of several Lewis acids and found that metal triflates such as $Sc(OTf)_3$[11] and $Cu(OTf)_2$ promoted the reaction to give *anti*-**3a** exclusively, though the yield of **3a** was only modest (Table 1, entries 1 and 2). The low yield was caused by the formation of an undesired Diels-Alder type adduct **7**, as discussed later (*vide infra*, Scheme 3). On the other hand, Kobayashi *et al.* have recently demonstrated that $Sc(OTf)_3$ or $Yb(OTf)_3$ modified with (*R*)-1,1'-bi-2-naphthol [(*R*)-BINOL] and a tertiary amine is an effective catalyst for asymmetric Diels-Alder reaction.[12] In this reaction, the axial

Table 1. Michael reaction of **1a** and **2a**[a)]

entry	catalyst	yield (%)[b)]	*anti*-**3a** : *syn*-**3a**[c)]	% ee[d)]
1	$Sc(OTf)_3$ (5 mol%)	36	>50 : 1	-
2	$Cu(OTf)_2$ (5 mol%)	38	>50 : 1	-
3[e)]	$Sc(OTf)_3$ (5 mol%) (*R*)-BINOL (6 mol%) Et_3N (7 mol%)	35	22 : 1	12
4[e)]	$Sc(OTf)_3$ (5 mol%) (*R*)-**4** (R= Et, 6 mol%)	48	>50 : 1	18

a) All reactions were carried out in dichloromethane at 0 °C.
b) Isolated yield of a mixture of *anti*- and *syn*-mixture.
c) Determined by ^1H NMR (270 MHz).
d) Determined by HPLC (Daicel Chiralpak AD; hexane/*i*-PrOH= 2:1).
e) Reaction was carried out in the presence of MS 4A.



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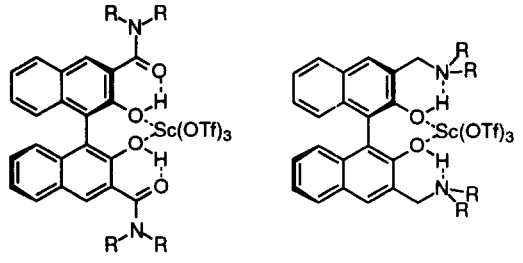
chirality of BINOL has been considered to be transmitted to the reaction site through the bulky tertiary amine which binds to BINOL by hydrogen-bond. Based on these reports, we next examined the reaction of **1a** and **2a** using a combination of $Sc(OTf)_3$, (*R*)-BINOL, and Et_3N as a catalyst but both the chemical yield and enantiomeric excess of the desired product were found to be only modest (entry 3). In the meantime, we have reported that optically active *N,N,N',N'*-tetraalkyl-BINOL-3,3'-dicarboxamides (**4**) are efficient chiral auxiliaries for asymmetric Simmons-Smith cyclopropanation of allylic alcohols[13] and for enantioselective diethylzinc addition to aldehydes.[13b,14] As an intramolecular hydrogen bond between phenolic hydrogen and carbonyl oxygen was considered to fix the conformation of the amide moiety in **4**, we expected that $Sc(OTf)_3$-**4** would serve as a chiral catalyst for the present reaction. Although *anti*-selectivity was high, both the chemical yield and enantioselectivity were again only modest (entry 4).

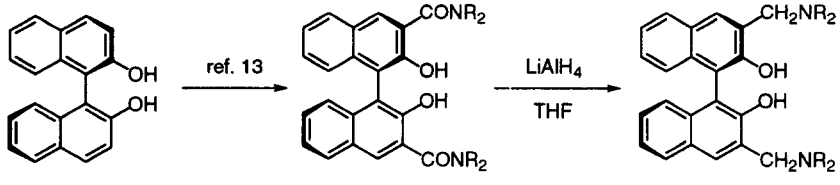
We reasoned that the amide alkyl groups of ligand **4** directing away from the reaction site could not induce asymmetry in the product effectively (Fig. 1). Led by this consideration and Kobayashi's reports,[12] we designed new BINOL-derived compound **5** bearing tertiary aminomethyl groups at 3,3'-carbons, expecting that the 3- and 3'-substituents would be fixed to direct their *N*-alkyl groups toward the reaction site by intramolecular hydrogen-bond formation. The ligands **5a-d** were prepared by reduction of the corresponding diamides **4a-d**



4-Sc(OTf)$_3$ **5**-Sc(OTf)$_3$

Fig. 1

with $LiAlH_4$ (Scheme 2). The optical purity of the resulting diamine **5** was verified (>99% ee) by HPLC analysis using chiral column (Daicel Chiralcel OD-R).



4a: R= Me, **4b**: R= Et
4c: R= Pr, **4d**: R= *i*-Pr

5a: R= Me, **5b**: R= Et
5c: R= Pr, **5d**: R= *i*-Pr

Scheme 2

With the new ligands obtained, we next examined the reaction of **1** and **2** under various reaction conditions (Table 2). When a Sc(OTf)3 (5 mol%) and **5b** (6 mol%) system was used as a chiral catalyst in CH_2Cl_2, the reaction of **1a** and **2a** proceeded with excellent diastereoselectivity (*anti*:*syn* = >50:1) and good enantioselectivity (73% ee, entry 1), but the chemical yield was still unsatisfactory. The major side product of this Lewis acid-catalyzed reaction was again a Diels-Alder type adduct **7** which was probably produced by Dieckmann condensation of the intermediary enolate **6** (Scheme 3). It was also observed that the enantioselectivity of the reaction dropped considerably without activated molecular sieves (MS) 4A,[15] but the reaction rate and the diastereoselectivity were not affected by the presence or absence of MS 4A (entry 2). To avoid the undesired side reaction, we carried out the reaction in the presence of 1 equiv. of an alcohol such as 2-propanol or *t*-butyl alcohol which was expected to accelerate the quenching of the enolate. However, addition of 1 equiv. of alcohols decreased enantioselectivity to some extent, though the chemical yield was improved as expected (entries 3 and 4). These results suggested that coordination of water or alcohol did not affect the catalytic activity of the Sc(OTf)3-**5b** system but caused some change in the coordination sphere of the Sc ion. Based on this analysis, we next used hexafluoroisopropyl alcohol (HFIP) which is more acidic but has poor coordinating ability, as an additive.[16] As expected, the reaction proceeded with high chemical yield and a similar level of stereoselectivity as compared with the reaction without alcohol (entries 5 and 6).

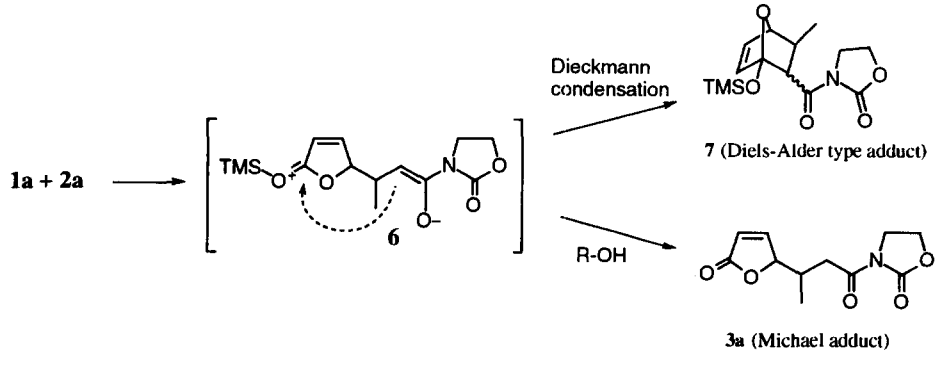
We next examined the solvent effect (entries 5 vs. 7-9) and the effect of aminoalkyl groups in ligand **5** (entries 5 vs. 10-12) on stereoselectivity under the above improved conditions. However, the reaction using diethylamino compound **5b** in dichloromethane was found to be the optimal conditions. Use of the other group III metal triflates or Yb(OTf)3 instead of Sc(OTf)3 decreased both enantio- and diastereoselectivity (entries 5 vs. 13-15). The reaction of 3-methyl-2-(trimethylsilyloxy)furan **1b** and **2a** under the optimized reaction conditions

Table 2. Michael reaction of **1** and **2** in the presence of $M(OTf)_3$-BINOL-derived diamine **5** complex[a)]

entry	substrate	ligand	metal	solvent	additive	yield(%)[b)]	*anti* : *syn*	% ee[c)]	confign.
1	**1a** + **2a**	**5b** (R= Et)	$Sc(OTf)_3$	CH_2Cl_2	-	44	>50 : 1	73	(*R*,*R*)
2[d)]	"	"	"	"	-	45	>50 : 1	37	(*R*,*R*)
3	"	"	"	"	*i*-PrOH	78	>50 : 1	49	(*R*,*R*)
4	"	"	"	"	*t*-BuOH	86	>50 : 1	50	(*R*,*R*)
5	"	"	"	"	HFIP	80	>50 : 1	65	(*R*,*R*)
6[e)]	"	"	"	"	"	86	>50 : 1	68	(*R*,*R*)
7	"	"	"	toluene	"	80	>50 : 1	55	(*R*,*R*)
8	"	"	"	Ph-Cl	"	87	>50 : 1	52	(*R*,*R*)
9	"	"	"	DCE[f)]	"	81	>50 : 1	48	(*R*,*R*)
10	"	**5a** (R= Me)	"	CH_2Cl_2	"	72	44 : 1	29	(*R*,*R*)
11	"	**5c** (R= Pr)	"	"	"	69	39 : 1	51	(*R*,*R*)
12	"	**5c** (R= *i*-Pr)	"	"	"	68	>50 : 1	34	(*R*,*R*)
13	"	**5b** (R= Et)	$Y(OTf)_3$	"	"	87	39 : 1	0	-
14	"	"	$La(OTf)_3$	"	"	62	1.6 : 1	28	(*R*,*R*)
15	"	"	$Yb(OTf)_3$	"	"	65	12 : 1	10	(*R*,*R*)
16	**1b** + **2a**	"	$Sc(OTf)_3$	"	-	64	41 : 1	60	(*R*,*R*)
17	"	"	"	"	HFIP	94	>50 : 1	56	(*R*,*R*)
18	**1a** + **2b**	"	"	"	"	59	-	41[g)]	(*R*)

a) All reactions were carried out at 0 °C in the presence of 5 mol% of metal triflate, 6 mol % of **5** and powdered MS 4A, unless otherwise mentioned.
b) The yield refers to the total yield of *syn*- and *anti*-isomers.
c) The value of % ee of *anti*-isomer. Determined by HPLC analysis (Daicel chiralpak AD; hexane/*i*-PrOH = 2:1), unless otherwise mentioned.
d) The reaction was carried out in the absence of MS 4A.
e) Ten mol% of $Sc(OTf)_3$ and 12 mol% of **5b** were used.
f) Dichloroethane
g) Determined by HPLC analysis (Daicel chiralpak AD; hexane/*i*-PrOH = 1:1).

also proceeded with high diastereo- and moderate enantioselectivity (entry 17). On the other hand, the reaction of **1a** and acryloyl derivative **2b** showed modest enantioselectivity (entry 18).



Scheme 3

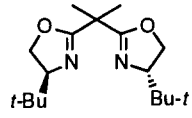
Since $Cu(OTf)_2$ showed high diastereoselectivity (*vide supra*), we also examined the reaction using a chirally modified $Cu(OTf)_2$ as a catalyst. It has already been reported that a combination of copper(II) triflate and bis(oxazoline) ligands constitutes excellent chiral catalysts for various asymmetric reactions,[17] including the Diels-Alder reaction of oxazolidinone enoates.[18] Thus, we were intrigued by the Michael reaction of **1** and

enoate **2** using a $Cu(OTf)_2$-bis(oxazoline) complex as the catalyst.[19] As shown in Table 3, excellent enantioselectivity (>90% ee) was observed in the reactions of crotonoyl derivative **2a**, although the diastereoselectivity was moderate to good. Again, addition of HFIP was found to be essential to achieve high chemical yield (*cf.* entries 1 and 2). The reaction with **2b** showed moderate enantioselectivity (entry 4).[20]

Table 3. Michael addition of **1** and **2** in the presence of $Cu(OTf)_2$ (5 mol%) and **8** (6 mol%)[a)]

entry	substrate	additive	yield(%)	*anti* : *syn*	% ee	confign.
1	**1a** + **2a**	-	37	10.5 : 1	92	(*S*,*S*)
2	"	HFIP	89	8.5 : 1	95	(*S*,*S*)
3	**1b** + **2a**	"	95	24 : 1	91	(*S*,*S*)
4	**1a** + **2b**	"	71	-	64	(*S*)

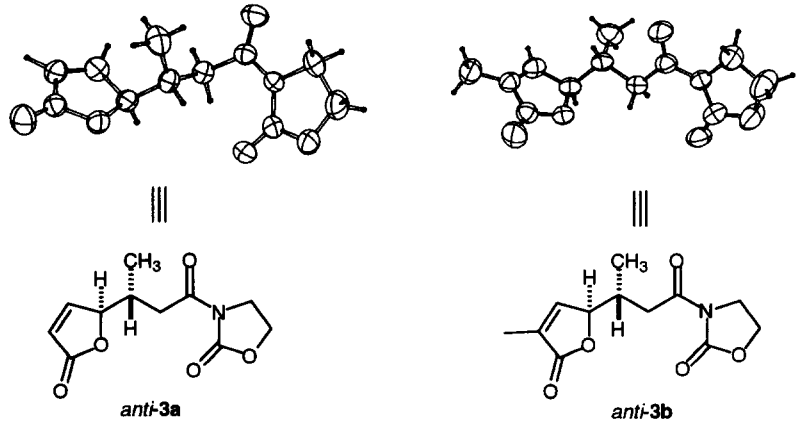
a) All reactions were carried out in dichloromethane at 0 °C in the presence of MS 4A.



(*S*,*S*) -**8**

Determination of the Stereochemistry of Michael Adducts (3a, 3b and 3c)

The stereochemistry of the major isomer of Michael adducts (**3a** and **3b**) was determined as follows. The major isomer of **3a** which was obtained by the reaction using $Sc(OTf)_3$-(*R*)-**5b**, crystallized out in an optically pure form upon recrystallization of the crude **3a** from ethyl acetate and hexane. The major isomer of **3b** (91% ee) which was obtained by the reaction using $Cu(OTf)_2$-(*S*,*S*)-**8**, also crystallized out as a single crystal. X-ray analysis of these single crystals of **3a** and **3b** revealed that both compounds possessed an *anti*-relationship between two stereogenic centers as shown in Figure 2.

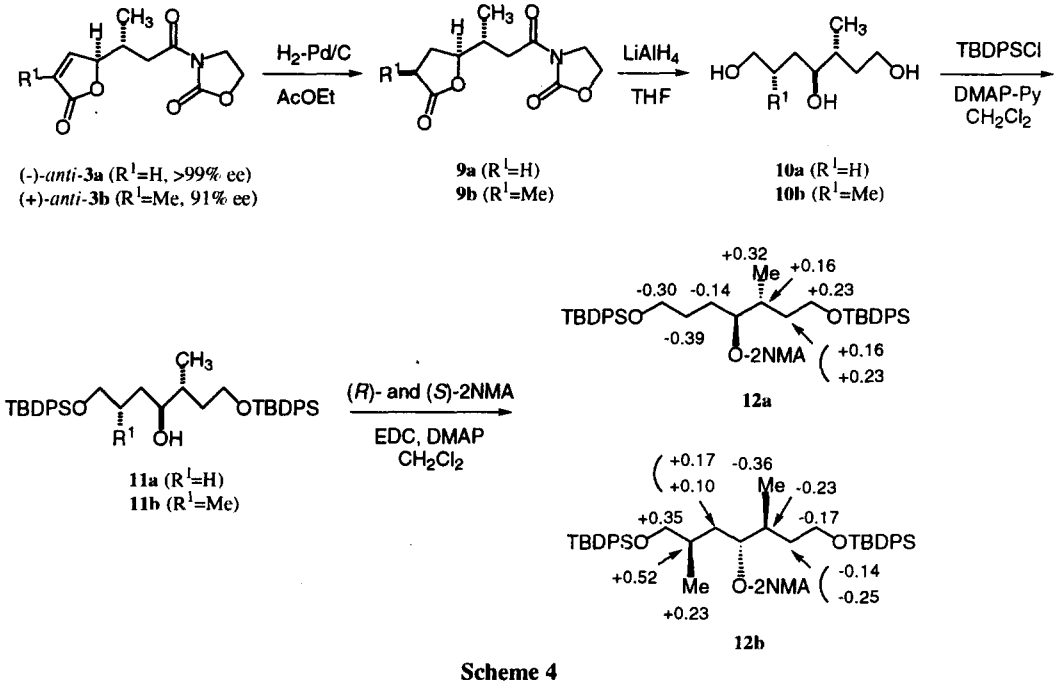


anti-**3a** *anti*-**3b**

Figure 2. X-Ray structures of *anti*-**3a** and *anti*-**3b**

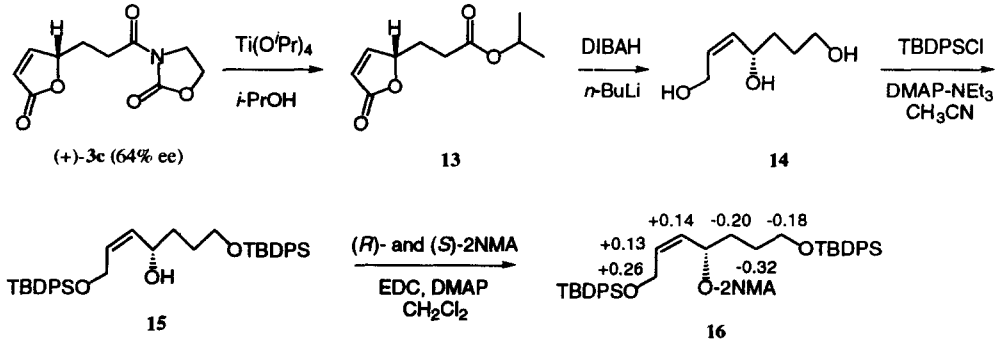
To determine the absolute configuration of (-)-*anti*-**3a** and (+)-*anti*-**3b**, both compounds were converted to the corresponding esters of (*R*)- and (*S*)-methoxy-(2-naphthyl)acetic acids (2NMA), which were known to be strong chiral anisotropic reagents.[21] Thus, the Michael adducts were initially hydrogenated using 10% Pd on carbon as catalyst in AcOEt to give butyrolactones **9a,b** (Scheme 4). Treatment of **9a,b** with $LiAlH_4$ in THF provided triols **10a,b**, the primary hydroxy groups of which were protected as *tert*-butyldiphenylsilylethers

using 4-*N,N*-dimethylaminopyridine (DMAP)-pyridine as bases in CH_2Cl_2 to afford alcohols **11a,b**. Condensation of 2NMA and alcohols **11a,b** was accomplished by using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC·HCl) and DMAP in CH_2Cl_2 to give the corresponding 2NMA esters **12a,b**. From the sign of δ (δ_R-δ_S) (ppm) values (see experimental section), the absolute configuration of the C4 carbon of **12a** was determined to be *S*.[21b] Thus, the configuration of (-)-*anti*-**3a** was proven to be *R,R*. In an identical manner, the configuration of (+)-*anti*-**3b** was determined to be *S,S*. That is, a $Sc(OTf)_3$-(*R*)-**5** system gave the (*R,R*)-isomer of **3a,b** preferentially and a $Cu(OTf)_2$-(*S,S*)-**8** system did the (*S,S*)-isomer.



Scheme 4

The absolute configuration of the (+)-**3c** was also determined according to the Kusumi's procedure[21b] (*vide supra*) after its conversion to the corresponding (*R*)- and (*S*)-2NMA esters. Thus, the Michael adducts (+)-**3c** was first treated with $Ti(O^iPr)_4$ in *i*-PrOH to give the corresponding isopropyl ester **13**. Reduction



Scheme 5

of ester **13** with diisobutylaluminium hydride (DIBAH) and *n*-butyllithium in toluene[22] gave triol **14**. The primary hydroxy groups in **14** were protected as *tert*-butyldiphenylsilylethers using DMAP and triethylamine as bases in acetonitrile to afford alcohol **15**. Alcohol **15** and 2NMA were condensed by using EDC·HCl and DMAP in CH_2Cl_2 to give the corresponding 2NMA ester **16**. From the sign of δ (δ_R-δ_S) (ppm) values (see experimental section), the absolute configuration of the C4 carbon of **16** was determined to be *S*.[21b] Thus, the configuration of (+)-**3c** was proven to be *S*.

The origin of high *anti*-selectivity observed in the reactions of **1** and **2a** is unclear at present. However, the sense of enantioface selection by the Cu(II)-bis(oxazoline) catalyst may be explained by using the structure proposed for the copper-bis(oxazoline) catalyst loaded with an oxazolidinone enoate (Fig. 3).[18] The approach of the substrate from the sterically less hindered bottom side leads to the expected product. On the other hand,

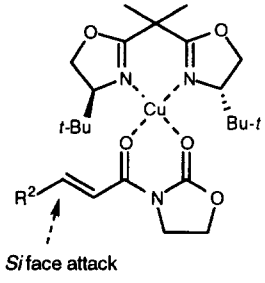


Figure 3

our knowledge on the structure of the scandium-BINOL diamide complex loaded with an oxazolidinone enoate is immature and it is too early to discuss the detailed mechanism of enantioface selection by the scandium complex. However, a 1:1 complex of $Sc(OTf)_3$ and **5** seems to be responsible for the present reaction, because the reaction was sluggish when two equivalents of chiral ligand to $Sc(OTf)_3$ were used.

In conclusion, we could demonstrate that two types of chiral Lewis acid catalysts promoted Michael addition of 2-(trimethylsilyloxy)furans to oxazolidinone enoates with good chemical yield and high stereoselectivity in the presence of HFIP which suppressed the undesired tandem Michael-Dieckmann condensation reaction by quenching the intermediary enolate. To the best of our knowledge, this is the first example of asymmetric and catalytic Michael addition reaction of 2-(trimethylsilyloxy)furans.

Experimental

All melting points are uncorrected. NMR spectra were recorded at 270 MHz on a JEOL EX-270 or at 400 MHz on a JEOL GX-400 instrument. Signals are expressed as ppm down field from tetramethylsilane used as an internal standard (δ value in $CDCl_3$) unless otherwise described. IR spectra were obtained with a SHIMADZU FTIR-8600 or JEOL JIR-6500W instrument. Optical rotation was measured with a JASCO DIP-360 automatic digital polarimeter. EI mass spectra were recorded on a JEOL JMX DX-300 instrument. High resolution mass (HRMS) spectra were recorded on a JOEL JMS-SX/SX 102A instrument. Column chromatography was conducted on Silica Gel BW-820-MH, 70-200 mesh ASTM, available from FUJI SILYSIA CHEMICAL LTD. Preparative thin layer chromatography was performed on 0.5 mm x 20 cm x 20 cm E. Merck silica gel plate (60 F-254). Solvents were dried and distilled shortly before use. Reactions were carried out under an atmosphere of nitrogen or argon if necessary. Compounds **4a-d** were prepared according to the reported procedure.[13b]

(*R*)-3,3'-Bis(*N*,*N*-dimethylaminomethyl)-2,2'-dihydroxy-1,1'-binaphthyl (5a)

To a solution of diamide **4a** (325 mg, 0.76 mmol) in THF (10 ml) was added $LiAlH_4$ (116 mg, 3.0 mmol) at 0 °C. After being refluxed for 4h, the mixture was cooled to 0 °C and quenched with saturated potassium fluoride solution (0.25 ml). Insoluble materials were filtered through a pad of Celite, and the filtrate was concentrated under reduced pressure. The residue was diluted with CH_2Cl_2 and washed with pH 7 phosphate buffer and brine, and the separated organic layer was dried over anhydrous $MgSO_4$ and concentrated. Silica gel chromatography of the residue ($CHCl_3$-MeOH = 25:1) and crystallization from MeOH gave **5a** (179 mg, 59%) as a white powder. Mp 250-251 °C (decomp.); MS *m/z* 400(M^+). $[\alpha]_D^{21}$ +11.8° (*c* 0.50, $CHCl_3$); ^1H NMR (270 MHz): δ 11.5 (bs, 2H), 7.78 (d, *J*= 7.9 Hz, 2H), 7.68 (s, 2H), 7.29-7.11 (m, 6H), 4.13 (d, *J*= 13.5 Hz, 2H), 3.85 (d, *J*= 13.5 Hz, 2H), 3.81 (s, 12H); IR (KBr): 3438, 2950, 2829, 1627, 1508, 1470, 1435, 1417, 1346, 1315, 1248, 889, 752. Found: C, 77.78; H, 7.01; N, 6.92%. Calcd for $C_{26}H_{28}N_2O_2$: C, 77.97; H, 7.05; N, 6.99%. The enantiomeric purity of **5a** (> 99% ee) was measured by HPLC [Daicel Chiralcel OD-R; 0.46 cm x 25 cm; CH_3CN: 0.5N $NaClO_4$ = 3:2, flow rate 0.5 ml min^{-1}; T_R 16.9 min for (*R*)-**5a**, 25.0 min for (*S*)-**5a**].

Compounds **5b-d** were prepared in the same manner as described above. Spectral data and physical properties of these compounds are as follows.

(*R*)-3,3'-Bis(*N,N*-diethylaminomethyl)-2,2'-dihydroxy-1,1'-binaphthyl (5b)

White crystals; yield 61%; Mp 138-139 °C; MS *m/z* 456(M^+). $[\alpha]_D^{21}$ +147° (*c* 0.50, $CHCl_3$); ^1H NMR (270 MHz): δ 11.8 (bs, 2H), 7.75 (d, *J*= 7.6 Hz, 2H), 7.60 (s, 2H), 7.24-7.15 (m, 6H), 4.17 (d, *J*= 12.9 Hz, 2H), 3.91 (d, *J*= 12.9 Hz, 2H), 2.76-2.56 (m, 8H), 1.08 (t, *J*= 7.3 Hz, 12H); IR (KBr): 2972, 2827, 1626, 1506, 1477, 1427, 1387, 1348, 1315, 1246, 1194, 1107, 881, 750. Found: C, 78.77; H, 7.99; N, 6.08%. Calcd for $C_{30}H_{36}N_2O_2$: C, 78.91; H, 7.95; N, 6.13%. The enantiomeric purity (> 99% ee) was measured by HPLC [Daicel Chiralcel OD-R; 0.46 cm x 25 cm; CH_3CN: 0.5N $NaClO_4$ = 3:2, flow rate 0.5 ml min^{-1}; T_R 47.0 min for (*R*)-**5b**, 54.4 min for (*S*)-**5b**].

(*R*)-3,3'-Bis(*N,N*-dipropylaminomethyl)-2,2'-dihydroxy-1,1'-binaphthyl (5c)

White crystals; yield 47%; Mp 165-166 °C; MS *m/z* 512(M^+). $[\alpha]_D^{21}$ +115° (*c* 0.50, $CHCl_3$); ^1H NMR (270 MHz): δ 11.5 (bs, 2H), 7.75 (d, *J*= 7.9 Hz, 2H), 7.60 (s, 2H), 7.25-7.15 (m, 6H), 4.17 (d, *J*= 14.2 Hz, 2H), 3.87 (d, *J*= 14.2 Hz, 2H), 2.58-2.47 (m, 8H), 1.65-1.55 (m, 8H), 0.87-0.82 (m, 12H); IR (KBr): 3436, 2960, 2933, 2873, 2823, 1466, 1429, 1257, 746. Found: C, 79.60; H, 8.70; N, 5.40%. Calcd for $C_{34}H_{44}N_2O_2$: C, 79.65; H, 8.65; N, 5.46%.

(*R*)-3,3'-Bis(*N,N*-diisopropylaminomethyl)-2,2'-dihydroxy-1,1'-binaphthyl (5d)

White crystals; yield 42%; Mp 214-215 °C; MS *m/z* 512(M^+). $[\alpha]_D^{21}$ +161° (*c* 0.57, $CHCl_3$); ^1H NMR (270 MHz): δ 11.8 (bs, 2H), 7.73 (d, *J*= 7.9 Hz, 2H), 7.61 (s, 2H), 7.24-7.10 (m, 6H), 4.18 (d, *J*= 14.5 Hz, 2H), 4.06 (d, *J*= 14.5 Hz, 2H), 3.26-3.17 (m, 4H), 1.14-1.11 (m, 24H); IR (KBr): 2962, 1462, 1427, 1369, 1250, 1170, 744. Found: C, 79.48; H, 8.61; N, 5.35%. Calcd for $C_{34}H_{44}N_2O_2$: C, 79.65; H, 8.65; N, 5.46%.

General Procedure for the Michael Addition Reaction of 2-(Trimethylsilyloxy)furans.

$Sc(OTf)_3$ (6.2 mg, 13 μmol) and diamine **5b** (6.8 mg, 15 μmol) were dissolved in 0.5 ml of CH_2Cl_2 in the presence of activated molecular sieves 4A (30 mg) and stirred for 30 min at 0 °C under nitrogen atmosphere. To the mixture were added a CH_2Cl_2 solution (0.5 ml) of **2a** (38.8 mg, 0.25 mmol), HFIP (26 μl, 0.25 mmol), and **1a** (50 μl, 0.3 mmol) and the whole mixture was stirred for 15 h at the temperature. The mixture was quenched with water and filtered through a pad of Celite to remove insoluble materials. The filtrate was diluted with CH_2Cl_2 and separated from the water layer. The organic layer was dried over anhydrous $MgSO_4$ and concentrated. The residue was chromatographed on silica gel (hexane-AcOEt = 3:7) to afford **3a** (48 mg, 80% yield) as a mixture of *anti*- and *syn*-isomers. The mixture was recrystallized twice from hexane-AcOEt to give *anti*-**3a** (27 mg, 45%) of >99% ee.

The reaction with $Cu(OTf)_2$-**8** complex was carried out in the same manner as described for the reaction with $Sc(OTf)_3$-**5b** complex, except that $Cu(OTf)_2$-**8** complex was used instead of $Sc(OTf)_3$-**5b** complex. Spectral data and physical properties of the Michael adducts are as follows.

(*R*,*R*)-3-(2',5'-Dihydro-5'-oxo-2'-furyl)butanoyl-1,3-oxazolidin-2-one (3a)

White crystals; Mp 88-89 °C; MS *m/z* 240(M^+). $[\alpha]_D^{21}$ -75.4° (*c* 1.0, $CHCl_3$); ^1H NMR (270 MHz): δ 7.53 (dd, *J*= 1.3 and 5.6 Hz, 1H), 6.16 (dd, *J*= 2.0 and 5.6 Hz, 1H), 5.02 (ddd, *J*= 1.3, 2.0 and 6.2 Hz, 1H), 4.48-4.41 (m, 2H), 4.07-4.01 (m, 2H), 3.16 (dd, *J*= 5.9 and 16.8 Hz, 1H), 2.86 (dd, *J*= 7.6 and 16.8 Hz, 1H), 2.59-2.44 (m, 1H), 1.10 (d, *J*= 6.6 Hz, 3H); IR (KBr): 1759, 1687, 1398, 1369, 1342, 1219, 1165, 1093, 1014, 758. Found: C, 55.18; H, 5.48; N, 5.79%. Calcd for $C_{11}H_{13}NO_5$: C, 55.23; H, 5.48; N, 5.85%. HPLC analysis [Daicel Chiralpak AD; 0.46 cm x 25 cm; hexane/*i*-PrOH= 2:1, flow rate 0.5 ml min^{-1}; T_R 42.5 min for (*R*,*R*)-form, 49.6 min for (*S*,*S*)-form].

Crystal data for *anti*-**3a**: Chemical formula $C_{11}H_{13}NO_5$, M = 239.23, monoclinic, space group $P2_1$, a = 9.490 (1) Å, b = 9.122 (1) Å, c = 6.587 (1) Å, β = 97.74 (1)°, V = 565.1 (2) $Å^3$, μ(Cu Kα) = 0.908 mm^{-1}, Dx = 1.405 $g{\cdot}cm^{-3}$, R = 0.034.

(*S*,*S*)-3-(2',5'-Dihydro-4'-methyl-5'-oxo-2'-furyl)butanoyl-1,3-oxazolidin-2-one (3b)

White crystals; Mp 100-101 °C; MS *m/z* 253 (M^+). $[\alpha]_D^{17}$ +38.9° (*c* 1.0, $CHCl_3$, 91% ee); ^1H NMR (270 MHz): δ 7.49 (dd, *J*= 1.3 and 1.7 Hz, 1H), 4.84 (ddd, *J*= 1.7, 2.0 and 6.6 Hz, 1H), 4.47-4.44 (m, 2H), 4.07-4.01 (m, 2H), 3.16 (dd, *J*= 5.6 and 16.5 Hz, 1H), 2.85 (dd, *J*= 7.6 and 16.5 Hz, 1H), 2.59-2.44 (m, 1H), 1.10 (d, *J*= 6.6 Hz, 3H); IR (KBr) 1794, 1745, 1695, 1390, 1335, 1279, 1211, 1153, 1082, 1053, 1016, 980, 760. Found: C, 56.62; H, 6.04; N, 5.48%. Calcd for $C_{12}H_{15}NO_5$: C, 56.91; H, 5.97; N, 5.53%. HPLC analysis [Daicel Chiralpak AD; 0.46 cm x 25 cm; hexane/*i*-PrOH= 2:1, flow rate 0.5 ml min^{-1}; T_R 33.8 min for (*R*,*R*)-form, 45.0 min for (*S*,*S*)-form].

Crystal data for *anti*-**3b**: Chemical formula $C_{12}H_{15}NO_5$, M = 253.25, monoclinic, space group $P2_1$, a = 12.417 (1) Å, b = 6.343 (1) Å, c = 8.112 (1) Å, β = 95.19 (1)°, V = 636.3 (2) $Å^3$, μ(Cu Kα) = 0.833 mm^{-1}, Dx = 1.321 $g{\cdot}cm^{-3}$, R = 0.038.

(+)-3-(2',5'-Dihydro-5'-oxo-2'-furyl)propanoyl-1,3-oxazolidin-2-one (3c)

White crystals; Mp 83-85 °C; MS *m/z* 225 (M^+). $[\alpha]_D^{21}$ +23.0° (*c* 3.09, $CHCl_3$, 64% ee); ^1H NMR (270 MHz): δ 7.49 (dd, *J*= 1.3 and 5.9 Hz, 1H), 6.13 (d, *J*= 2.0 and 5.9 Hz, 1H), 5.20-5.14 (m, 1H), 4.47-4.41 (m, 2H), 4.06-4.00 (m, 2H), 3.19-3.05 (m, 2H), 2.33-2.20 (m, 1H), 2.05-1.88 (m, 1H); IR (KBr): 1770, 1755, 1689, 1387, 1302, 1223, 1176, 1014. Found: C, 53.24; H, 4.93; N, 6.30%. Calcd for $C_{10}H_{11}NO_5$: C, 53.33; H, 4.92; N, 6.22%. HPLC analysis [Daicel Chiralpak AD; 0.46 cm x 25 cm; hexane/*i*-PrOH= 1:1, flow rate 0.5 ml min^{-1}; T_R 32.0 min for (*S*)-form, 43.6 min for (*R*)-form].

Determination of Absolute Configuration of Michael adduct 3a

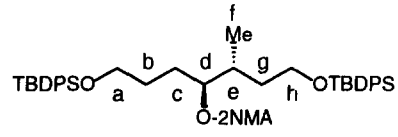
A solution of optically pure (-)-*anti*-**3a** (284 mg, 1.19 mmol) in AcOEt (15 ml) containing 10% Pd-C (50 mg) was stirred under H_2 (1 atm) at room temperature overnight. The catalyst was removed by filtration through a pad of Celite, and the filtrate was concentrated under reduced pressure to afford a solid, which was recrystallized from hexane-AcOEt to yield 240 mg (84 %) of 3-(5'-oxotetrahydro-2'-furyl)butanoyl-1,3-oxazolidin-2-one (**9a**) as white crystals. Mp 110-111 °C; MS *m/z* 241(M^+). $[\alpha]_D^{21}$ +31.5° (*c* 0.50, $CHCl_3$); ^1H NMR (270 MHz): δ 4.46-4.30 (m, 3H), 4.09-3.99 (m, 2H), 3.33 (d, *J*= 5.9 and 16.8 Hz, 1H), 2.85 (d, *J*= 7.3 and 16.8 Hz, 1H), 2.57-2.51 (m, 2H), 2.44-2.26 (m, 2H), 2.02-1.87 (m, 1H), 1.02 (d, *J*= 6.9 Hz, 3H); IR (KBr): 1786, 1759, 1686, 1389, 1282, 1194, 1128, 1016, 756. Found: C, 54.82; H, 6.41; N, 5.70%. Calcd for $C_{11}H_{15}NO_5$: C, 54.77; H, 6.27; N, 5.81%.

To a solution of **9a** (230 mg, 0.95 mmol) in THF (5 ml) was added $LiAlH_4$ (72 mg, 1.89 mmol) at 0 °C. After being stirred for 4 h at the temperature, the mixture was quenched with saturated potassium fluoride solution (0.2 ml). Insoluble materials were filtered through a pad of Celite, and the filtrate was concentrated under reduced pressure. Silica gel chromatography of the residue ($CHCl_3$-MeOH = 10:1) afforded 63 mg (41%) of 3-methyl-1,4,7-heptanetriol (**10a**) which was used for the next reaction without further purification.

To a solution of the above triol **10a** (30 mg, 0.19 mmol), DMAP (4.5 mg, 0.037 mmol), and pyridine (38 μl, 0.93 mmol) in CH_2Cl_2 (1 ml) and THF (0.5 ml) was added *tert*-butyldiphenylsilyl chloride (TBDPSCl) (96

μl, 0.37 mmol) at 0 °C. After being stirred overnight at room temperature, the mixture was diluted with CH_2Cl_2 and washed with water. The separated organic phase was dried over anhydrous $MgSO_4$ and concentrated. Silica gel chromatography of the residue (hexane-AcOEt = 10:1) afforded 83 mg (70%) of 1,7-bis(*tert*-butyldiphenylsilyloxy)-3-methyl-4-heptanol (**11a**) as a colorless oil. MS *m/z* 639 (M^+). $[\alpha]_D^{17}$ -2.5° (*c* 2.2, $CHCl_3$); ^1H NMR (270 MHz): δ 7.73–7.66 (m, 10H), 7.45–7.33 (m, 10H), 3.78-3.62 (m, 4H), 3.47-3.42 (m, 1H), 2.04 (bs, 1H), 1.74-1.42 (m, 7H), 1.05 (s, 9H), 1.04 (s, 9H), 0.87 (d, *J*= 6.6 Hz, 3H), IR (oil): 2958, 2931, 2858, 1427, 1113, 823, 739, 702, 505. Found: C, 75.00; H, 8.49%. Calcd for $C_{40}H_{54}O_3Si_2$: C, 75.18; H, 8.52%.

A small amount (5 mg) of **11a**, 2 equivs. of (*R*)- or (*S*)-methoxy-(2-naphthyl)acetic acid, 3 equivs. of EDC·HCl, and 0.2 equivs. of DMAP were dissolved in CH_2Cl_2 and allowed to stand overnight at room temperature. The mixture was directly loaded on preparative TLC and developed with hexane-AcOEt = 9:1. A zone containing the desired ester **12a** was collected and eluted with AcOEt. After evaporation, the residue was dissolved in $CDCl_3$. The (*R*)-2NMA ester: ^1H NMR (400 MHz) δ 7.87-7.30 (m, 27H), 4.88-4.82 (m, 2H), 3.73-3.58 (m, 2H), 3.43(s, 3H), 3.37-3.27 (m, 2H), 1.84-1.93 (m, 1H), 1.76-1.66 (m, 1H), 1.50-1.36 (m, 2H), 1.30-1.08 (m, 2H), 1.04-1.00 (m, 10H), 0.96 (s, 9H), 0.77 (d, *J*= 6.8 Hz, 3H). The (*S*)-2NMA ester: ^1H NMR (400 MHz) δ 7.87-7.30 (m, 27H), 4.88-4.82 (m, 2H), 3.73-3.58 (m, 2H), 3.53-3.36 (m, 5H), 1.77-1.67 (m, 1H), 1.63-1.43 (m, 5H), 1.04-1.00 (m, 10H), 0.96 (s, 9H), 0.45 (d, *J*= 6.8 Hz, 3H). The relevant ^1H NMR spectroscopic data of 2NMA esters **12a** were collected according to the Kusumi's procedure[21b] and described in Table 4. All the signals were reasonably assigned by analyzing the ^1H-^1H COSY spectra. From the sign of Δδ (δ_R-δ_S) (ppm) values, it was concluded that the absolute configuration of the C4-carbon in **12a** was *S*.



12a

Table 4. ^1H NMR data (chemical shifts and Δδ values) of **12a**

	δ*R* (ppm)	δ*S* (ppm)	Δδ (δ*R* -δ*S*)
a	3.32	3.62	-0.30
b	1.14	1.55	-0.39
c	1.45	1.59	-0.14
d	4.84	4.87	-0.03
e	1.88	1.72	+0.16
f	0.77	0.45	+0.32
g	1.72	1.56	+0.16
	1.26	1.03	+0.23
h	3.67	3.44	+0.23

Determination of Absolute Configuration of Michael adduct 3b

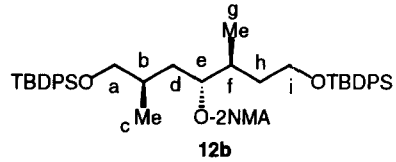
A solution of compound (+)-*anti*-**3b** (213 mg, 0.84 mmol, 91% ee) in AcOEt (8 ml) containing 10% Pd-C (40 mg) was stirred under H_2 (1 atm) at room temperature overnight. The catalyst was removed by filtration through a pad of Celite, and the filtrate was concentrated under reduced pressure to afford 213 mg (99 %) of 3-(4'-methyl-5'-oxo-tetrahydro-2'-furyl)butanoyl-1,3-oxazolidin-2-one (**9b**) as a solid. Mp 125-127 °C; MS *m/z* 255 (M^+). $[\alpha]_D^{17}$ -29.8° (*c* 0.50, $CHCl_3$); ^1H NMR (270 MHz): δ 4.45-4.39 (m, 1H), 4.20 (ddd, *J*= 5.3, 8.9 and 10.6 Hz, 1H), 4.06-4.00 (m, 2H), 3.25 (dd, *J*= 5.9 and 16.5 Hz, 1H), 2.89 (dd, *J*= 7.6 and 16.5 Hz, 1H), 2.71-2.61 (m, 1H), 2.49 (ddd, *J*= 5.3, 8.6 and 12.2 Hz, 1H), 2.38-2.27 (m, 2H), 1.93 (s, 3H), 1.55 (ddd, *J*= 10.6, 12.2 and 16.8 Hz, 1H), 1.26 (d, *J*= 7.9 Hz, 3H), 1.00 (d, *J*= 6.6 Hz, 3H); IR (KBr): 1790,

1759, 1697, 1387, 1196, 1157, 1014. Found: C, 56.28; H, 6.85; N, 5.45%. Calcd for $C_{12}H_{17}NO_5$: C, 56.46; H, 6.71; N, 5.49%.

To a solution of **9b** (168 mg, 0.66 mmol) in THF (3 ml) was added $LiAlH_4$ (50 mg, 1.33 mmol) at 0 °C. After being stirred for 4h at the temperature, the mixture was quenched with saturated potassium fluoride solution (0.1 ml). Insoluble materials were filtered through a pad of Celite, and the filtrate was concentrated under reduced pressure. Silica gel chromatography of the residue ($CHCl_3$-MeOH = 10:1) afforded 2,5-dimethyl-1,4,7-heptanetriol (**10b**, 65 mg, 56%), which was used for the next reaction without further purification.

To a solution of the above triol **10b** (65 mg, 0.37 mmol), DMAP (9.0 mg, 0.074 mmol), and pyridine (75 µl, 0.93 mmol) in CH_2Cl_2 (2 ml) was added TBDPSCl (0.20 ml, 0.75 mmol) at 0°C. After being stirred overnight at room temperature, the mixture was diluted with CH_2Cl_2 and washed with water. The organic phase was dried over anhydrous $MgSO_4$ and concentrated. Silica gel chromatography of the residue (hexane-AcOEt = 9:1) afforded 1,7-bis(*tert*-butyldiphenylsilyloxy)-2,5-dimethyl-4-heptanol (**11b**, 127 mg, 53%) as a colorless oil. MS *m/z* 653 (M^+), 595. $[\alpha]_D^{17}$ +3.8° (*c* 6.4, $CHCl_3$); ^1H NMR (270 MHz): δ 7.76–7.66 (m, 10H), 7.48–7.29 (m, 10H), 3.78-3.62 (m, 2H), 3.58-3.48 (m, 3H), 1.97-1.62 (m, 6H), 1.55-1.41 (m, 1H), 1.06 (s, 9H), 1.05 (s, 9H), 0.89 (d, *J*= 6.6 Hz, 3H), 0.87 (d, *J*= 6.6 Hz, 3H), IR (oil): 2958, 2931, 2858, 1471, 1427, 1113, 823, 739, 702, 613, 505. Found: C, 75.15; H, 8.54%. Calcd for $C_{41}H_{56}O_3Si_2$: C, 75.41; H, 8.64%.

A small amount (5 mg) of **11b**, 2 equivs. of (*R*)- or (*S*)-methoxy-(2-naphthyl)acetic acid, 3 equivs. of EDC·HCl, and 0.2 equivs. of DMAP were dissolved in CH_2Cl_2 and allowed to stand overnight at room temperature. The mixture was directly loaded on preparative TLC and developed with hexane-AcOEt = 9:1. A zone containing the desired ester **12b** was collected and eluted with AcOEt. After concentration under reduced pressure, the residue was dissolved in $CDCl_3$. The (*R*)-2NMA ester: ^1H NMR(270 MHz): δ 7.87-7.27 (m, 27H), 5.01-4.97 (m, 1H), 4.84 (s, 1H), 3.54-3.35 (m, 7H), 1.20-1.85 (m, 4H), 1.15-0.97 (m, 20H), 0.88 (d, *J*= 6.6 Hz, 3H), 0.45 (d, *J*= 6.9 Hz, 3H). The (*S*)-2NMA ester: ^1H NMR(270 MHz): δ 7.87-7.29 (m, 27H), 5.00-4.94 (m, 1H), 4.87 (s, 1H), 3.70-3.49 (m, 2H), 3.43 (s, 3H), 3.13 (d, *J*= 6.9 Hz, 2H), 2.05-1.50 (m, 3H), 1.31-1.00 (m, 12H), 0.97 (s, 9H), 0.78 (d, *J*= 6.8 Hz, 3H), 0.62 (d, *J*= 6.6 Hz, 3H). The relevant ^1H NMR spectroscopic data of 2NMA esters **12b** were collected according to the Kusumi's procedure[21b] and described in Table 5. All the signals were reasonably assigned by analyzing the ^1H-^1H COSY spectra. From the sign of Δδ (δ_R-δ_S) (ppm) values, it was concluded that the absolute configuration of the C4-carbon in **12b** was *R*.



12b

Table 5. ^1H NMR data (chemical shifts and Δδ values) of **12b**

	δ*R* (ppm)	δ*S* (ppm)	Δδ (δ*R* -δ*S*)
a	3.48	3.13	+0.35
b	1.65	1.13	+0.52
c	0.85	0.62	+0.23
d	1.80	1.63	+0.17
	1.12	1.02	+0.10
e	4.99	4.98	+0.01
f	1.67	1.90	-0.23
g	0.42	0.78	-0.36
h	1.54	1.68	-0.14
	1.00	1.25	-0.25
i	3.48	3.65	-0.17

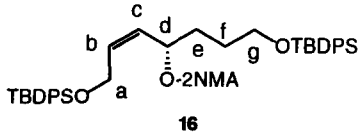
Determination of Absolute Configuration of Michael adduct 3c

To a solution of (+)-**3c** (96 mg, 0.43 mmol) in *i*-PrOH (2 ml) was added titanium tetraisopropoxide (0.26 ml, 0.86 mmol) at room temperature. After being refluxed for 7 h, the mixture was cooled to room temperature and quenched with 2*N* HCl (5 ml). After vigorous stirring for 1h, the mixture was extracted with ethyl acetate. The extract was dried over anhydrous $MgSO_4$ and evaporated. The residue was chromatographed on silica gel (hexane-AcOEt = 7:3) to afford **13** (75 mg, 89% yield) as a colorless oil. $[\alpha]_D^{25}$ +32.6° (*c* 0.88, $CHCl_3$); ^1H NMR (270 MHz): δ 7.46 (dd, *J*= 1.6 and 5.9 Hz, 1H), 6.13 (dd, *J*= 2.0 and 5.9 Hz, 1H), 5.18-5.11 (m, 1H), 5.01 (hept, *J*= 6.3 Hz, 1H), 2.47 (dt, *J*= 7.6 and 16.8 Hz, 1H), 2.43 (dt, *J*= 6.3 and 16.8 Hz, 1H), 2.21 (dddd, *J*= 4.3, 6.3, 7.6 and 14.2 Hz, 1H), 1.89 (ddt, *J*= 6.3, 7.6 and 14.2 Hz, 1H), 1.24 (d, *J*= 6.3 Hz, 3H), 1.23 (d, *J*= 6.3 Hz, 3H); IR (oil): 2981, 2937, 1755, 1728, 1375, 1165, 1109, 823. Found: C, 60.36; H, 7.11%. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12%.

n-Butyllithium (0.9 ml, 1.63 mol dm^{-3} in hexane) was added to a solution of diisobutylaluminium hydride (1.6 ml, 0.95 mol dm^{-3} in hexane) in toluene (2.6 ml) at 0 °C. After being stirred for 30 min, ester **13** (50 mg, 0.25 mmol) in toluene (1 ml) was added dropwise and allowed to gradually warm to room temperature. The mixture was quenched with MeOH (1 ml) and saturated aqueous potassium sodium tartrate (5 ml) was added. After vigorously stirred for 1 h, the organic layer was removed. The aqueous layer was extracted with $CHCl_3$-EtOH (3:1) and the combined organic extracts were dried over anhydrous $MgSO_4$ and concentrated. Silica gel chromatography of the residue ($CHCl_3$-MeOH = 10:1) afforded **14** (23 mg, 62%), which was used for the next reaction without further purification.

To a solution of the above triol **14** (23 mg, 0.16 mmol), DMAP (9.0 mg, 0.074 mmol), and triethylamine (100 µl, 0.79 mmol) in acetonitrile (5 ml) was added TBDPSCl (90 µl, 0.35 mmol) at room temperature. After being stirred overnight at the temperature, the mixture was diluted with ethyl acetate and washed with water. The organic phase was dried over anhydrous $MgSO_4$ and concentrated. Silica gel chromatography of the residue (hexane-AcOEt = 19:1~9:1) afforded 1,7-bis(*tert*-butyldiphenylsilyloxy)-2-hepten-4-ol (**15**, 48 mg, 49%) as a colorless oil. $[\alpha]_D^{25}$ -9.6° (*c* 0.55, $CHCl_3$); ^1H NMR (270 MHz): δ 7.74–7.62 (m, 10H), 7.46–7.31 (m, 10H), 5.67 (ddd, *J*= 5.6, 6.6 and 11.2 Hz, 1H), 5.43 (ddd, *J*= 1.6, 8.2 and 11.2 Hz, 1H), 4.31 (ddd, *J*= 1.6, 6.6 and 13.2 Hz, 1H), 4.21-4.12 (m, 1H), 4.20 (ddd, *J*= 1.6, 5.6 and 13.2 Hz, 1H), 3.61 (t, *J*= 5.6 Hz, 2H), 1.58-1.43 (m, 4H), 1.04 (s, 9H), 1.02 (s, 9H). IR (oil): 2957, 2932, 2858, 1472, 1427, 1113, 823, 740, 702, 613. Found: C, 75.08; H, 8.09%. Calcd for $C_{39}H_{50}O_3Si_2$: C, 75.19; H, 8.09%.

A small amount (5 mg) of **15**, 4 equivs. of (*R*)- or (*S*)-methoxy-(2-naphthyl)acetic acid, 6 equivs. of EDC·HCl, and 0.4 equivs. of DMAP were dissolved in CH_2Cl_2 and allowed to stand overnight at room temperature. The mixture was directly loaded on preparative TLC and developed with hexane-AcOEt = 8:2. A zone containing the desired ester **16** was collected and eluted with AcOEt. After concentration under reduced pressure, the residue was dissolved in $CDCl_3$. The (*R*)-2NMA ester: ^1H NMR (270 MHz): δ 7.90-7.26 (m, 27H), 5.74 (dt, *J*= 5.6 and 10.2 Hz, 1H), 5.42-5.28 (m, 2H), 4.81 (s, 1H), 4.34 (d, *J*= 5.6 Hz, 2H), 3.45-3.32 (m, 2H), 3.39 (s, 3H), 1.65-1.35 (m, 2H), 1.29-1.15 (m, 2H), 1.02 (s, 9H), 0.95 (s, 9H). The (*S*)-2NMA ester: ^1H NMR (270 MHz): δ 7.90–7.26 (m, 27H), 5.61 (dt, *J*= 5.9 and 11.2 Hz, 1H), 5.41-5.30 (m, 1H), 5.18 (ddt, *J*= 1.6, 9.2 and 11.2 Hz, 1H), 4.83 (s, 1H), 4.26 (dd, *J*= 1.6 and 5.9 Hz, 2H), 3.55 (t, *J*= 5.9 Hz, 2H), 3.40 (s, 3H), 1.65-1.51 (m, 2H), 1.48-1.30 (m, 2H), 1.01 (s, 9H), 1.00 (s, 9H). The relevant ^1H NMR spectroscopic data of 2NMA esters **16** were collected according to the Kusumi's procedure[21b] and described in Table 6. All the signals were reasonably assigned by analyzing the ^1H-^1H COSY spectra. From the sign of $\Delta\delta$ (δ_R-δ_S) (ppm) values, it was concluded that the absolute configuration of the C4-carbon in **16** was *S*.



16

Table 6. ^{1}H NMR data (chemical shifts and Δδ values) of **16**

	δ*R* (ppm)	δ*S* (ppm)	Δδ (δ*R* -δ*S*)
a	4.34	4.26	+0.26
b	5.74	5.61	+0.13
c	5.32	5.18	+0.14
d	5.35	5.35	0.00
e	1.37	1.57	-0.20
f	1.00	1.32	-0.32
g	3.37	3.55	-0.18

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