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# SYNTHESIS AND REACTION OF CHIRAL 4,5-DISUBSTITUTED 2-OXAZOLIDINONES FROM 3-ETHOXY-6-(*N*-ALKYL-*N*-*tert*-BUTOXYCARBONYL)AMINOHEXA-2,4-DIENOATES IN THE PRESENCE OF CONCENTRATED SULFURIC ACID SUPPORTED ON SILICA GEL

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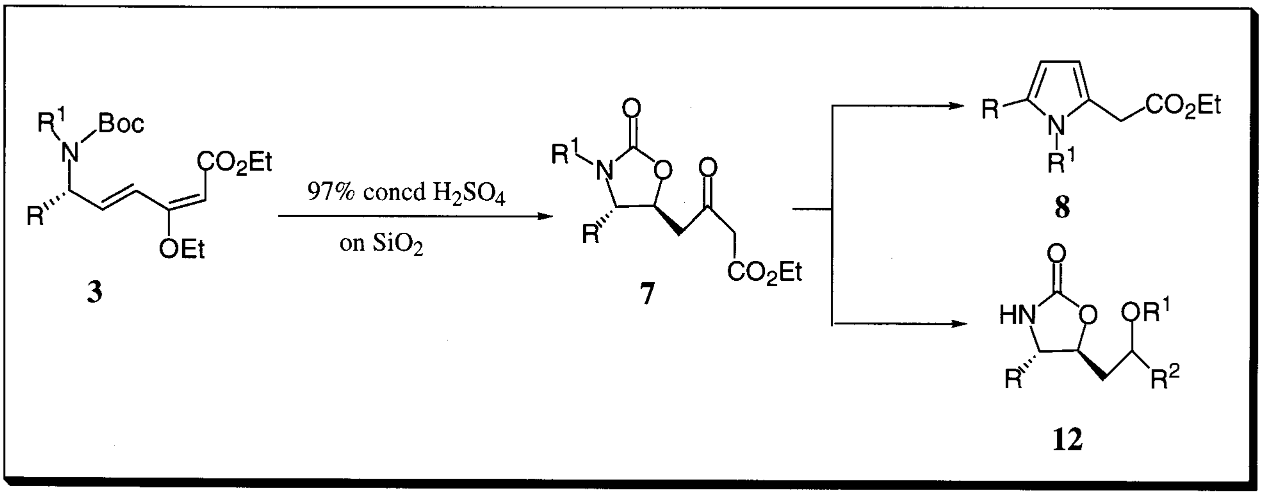
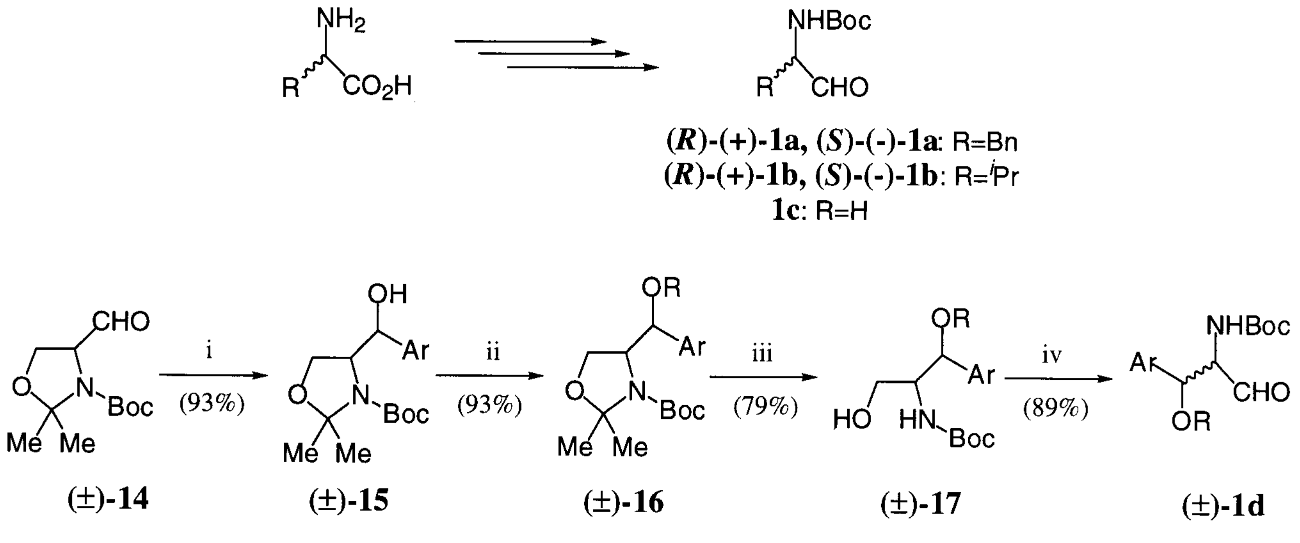
***Abstract*** – Reaction of chiral 3-ethoxy-6-(*N*-alkyl-*N*-*tert*-butoxycarbonyl)-amino-hexa-2,4-dienoates (**3**) and related compounds with 97% concentrated sulfuric acid supported on silica gel proceeded stereo- and regio-selectively to yield chiral 4,5-disubstituted *N*-alkyl-2-oxazolidinones (**7**). Under the limited conditions, **7** were converted into *N*-alkyl-2-pyrrolylacetates (**8**) and 2-oxazolidinone derivatives (**12**) which may serve as a chiral auxiliary.

Chiral 2-oxazolidinones are routinely employed in organic synthesis as chiral auxiliaries for asymmetric C-C bond formation.[1] The traditional method for the preparation of 2-oxazolidinones has been the transformation of amino alcohols to cyclic carbamates using various condensation reagents.[2] Recently, we have reported the ring-construction of dihydropyridones,[3] dihydropyrans,[3] furylacetates[4] and cyclopent-2-en-1-ones[5] by the use of 3-ethoxyhexa-2,4-dienoates bearing a functional group on the 6-position as synthetic synthons. In the preceding paper we reported the synthesis of 5-substituted *N*-*tert*-butoxycarbonyl-2-pyrrolylacetates from 3-ethoxy-6-(*N*-*tert*-butoxycarbonyl)aminohexa-2,4-dienoates (**2**).[6] In the course of our studies on the scope and limitations of this ring-construction, we have found that reaction of 3-ethoxy-6-(*N*-methyl-*N*-*tert*-butoxycarbonyl)aminohexa-2,4-dienoates with concentrated sulfuric acid supported on silica gel at 0 °C in dichloromethane proceeds stereo- and regio-selectively to give chiral *N*-methyl-2-oxazolidinones.[7] We report herein synthesis and reaction of chiral 4,5-disubstituted 2-oxazolidinones (**7**) which will be converted into 5-substituted *N*-alkyl-2-pyrrolylacetates (**8**) and **12** as a chiral auxiliary, from **3** and related compounds.



**Synthesis of ethyl (2*E*)-6-aminohexa-2,4-dienoates**. The starting materials, α-(*N*-*tert*-butoxycarbonyl)aminoacetaldehydes (**1a-d**) were synthesized by two routes (Scheme 1). Compounds (**1a-c**) were prepared from the corresponding α-amino acids according to the procedure described in the literature.[8] (*L*)-(-)- and (*D*)-(+)-α-Amino acids were converted into the corresponding (*S*)-(-)- and (*R*)-(+)-α-aminoacetaldehydes without racemization. Their configuration has been retained through all reactions studied in this series. Compound [(±)-**1d**] was prepared as a racemate in a total yield of 59% from the Garner aldehyde [(±)-**14**][9] in four steps as shown in Scheme 1.

**Scheme 1.**



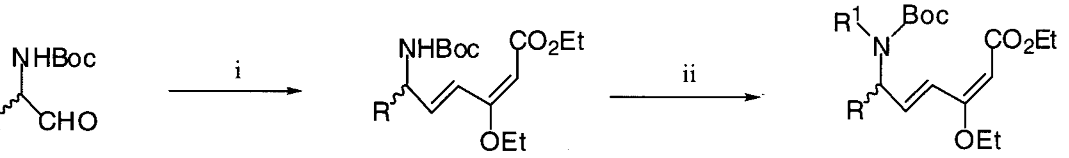
Ar=4-$MeC_6H_4$, R=$^t$Butyldiphenylsilyl (TBDPS)

Reagents and conditions: i) ArMgBr/THF, 0° C to rt; ii) TBDPS chloride, imidazole, catalytic amount of 4-dimethylaminopyridine/DMF, 60 °C; iii) 80% AcOH/THF, 35 °C; iv) Dess-Martin periodinane/$CH_2Cl_2$, rt.

Key intermediates (**3**, **5**, and **6**) were synthesized by the method shown in Scheme 2. (2*E*,4*E*)-6-(*N*-*tert*-Butoxycarbonyl)amino-3-ethoxyhexa-2,4-dienoate (**2a-d**) were synthesized by the Wittig reaction of **1a-d** with (*E*)-(2-ethoxy-3-ethoxycarbonylallylidene)triphenylphosphorane[10] in good yields. Key intermediates (**3a-d**, **5** and **6**) were synthesized as follows. Reaction of **2a-d** with methyl iodide in the presence of sodium hydride in dimethylformamide (DMF) gave **3a-d** in quantitative yields. Similarly, reaction of (*S*)-

**2a** with 4-methoxybenzyl (PMB) bromide gave **(*S*)-(-)-6** in 87% yield. Compound [**(±)-3d**] reacted with a mixture of tetrabutylammonium fluoride (15 equiv.) and acetic acid (15 equiv.) in tetrahydrofuran at 40 °C for nine days to give alcohol derivative [**(±)-4**] in 86% yield which was oxidized with the Dess-Martin reagent to give ketone derivative [**(±)-5**] along with **(±)-9d** which was prepared by enol ether-hydrolysis of **(±)-5**. The structure of **2-6** was determined on the basis of IR and NMR spectral data and elementary analyses. The double bonds at the 2- and 4-positions of these compounds were confirmed to be in (2*E*,4*E*)-configuration by comparing the data described in the literature.

**Scheme 2.**



**(*R*)-(+)-1a, (*S*)-(-)-1a**: R=Bn
**(*R*)-(+)-1b, (*S*)-(-)-1b**: R=$^i$Pr
**1c**: R=H
**(±)-1d**: R=ArCH(OR$^2$)

**(*R*)-(+)-2a, (*S*)-(-)-2a**: R=Bn
**(*R*)-(+)-2b, (*S*)-(-)-2b**: R=$^i$Pr
**2c**: R=H
**(±)-2d**: R=ArCH(OR$^2$)

**(*R*)-(+)-3a, (*S*)-(-)-3a**: R=Bn, R$^1$=Me
**(*R*)-(+)-3b, (*S*)-(-)-3b**: R=$^i$Pr, R$^1$=Me
**3c**: R=H, R$^1$=Me
**(±)-3d**: R=ArCH(OR$^2$), R$^1$=Me
iii
**(±)-4**: R=ArCH(OH), R$^1$=Me
iv
**(±)-5**: R=ArCO, R$^1$=Me
**(*S*)-(-)-6**: R=Bn, R$^1$=PMB

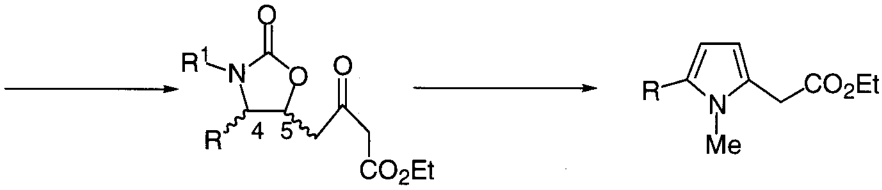
Ar=4-MeC$_6$H$_4$ , R$^2$=TBDPS

Reagents and conditions: i) (2-ethoxy-3-ethoxycarbonylallylidene)triphenylphosphorane/ THF, rt, 24 h; ii) MeI or PMBBr, NaH/DMF, 0 °C, 1.5 h; iii) TBAF (15 equiv.), AcOH (15 equiv.)/THF, 40 °C. 9 days; iv) Dess-Martin periodinane/CH$_2$Cl$_2$, rt, 1.5 h.

**Construction of the 2-oxazolidinone ring.** We first attempted conversion of **3a-c**, **5** and **6** to 2-oxazolidinones (**7**) according to the method described in the previous paper (Scheme 3, Table 1).[7] When **(*R*)-(+)-3a** was allowed to react with 1.0 equivalent of 97% concentrated $H_2SO_4$ supported on silica gel[11] [(97% concd $H_2SO_4$ (1.0 equiv.) on silica gel] in dichloromethane at 0 °C for 6 h, **(4*R*,5*R*)-(+)-7a** was obtained in 89% yield (Entry 1). The same treatment of **(*S*)-(-)-3a**, **(*R*)-(+)-3b** and **(*S*)-(-)-3b** gave the corresponding 2-oxazolidinones **(4*S*,5*S*)-(-)-7a**, **(4*R*,5*R*)-(+)-7b** and **(4*S*,5*S*)-(-)-7b)** in 87% to 91% yields (Entries 2, 3, 4). Two-hour treatment of **(*S*)-(-)-6** under the same acidic conditions gave **(4*S*,5*S*)-(-)-7e** in a good yield (Entry 7). Reaction of **3c** and racemate (**5**) with 97% concd $H_2SO_4$ (1.0 equiv.) on silica gel brought about different results (Entries 5, 6). Compound (**3c**) was allowed to react with 97% concd $H_2SO_4$(1.0 equiv.) on silica gel in dichloromethane at 0 °C until the compound disappeared on TLC (silica gel, solvent: $CHCl_3$:MeOH=10:1). After being quenched with saturated aqueous sodium bicarbonate solution, the reaction mixture was purified by silica gel column chromatography as an eluent of a (10:1) mixture of chloroform and methanol to give **9c** (15%) and **(±)-10c** (17%) along with a pyrrole derivative (**8c**; 13%) which will be prepared through **(±)-7c** (not isolated). On the other hand, **(±)-5** was allowed to react with 97% concentrated $H_2SO_4$ (1.0 equiv.) on silica gel in dichloromethane at 0 °C until the compound disappeared on TLC. Separation by silica gel column chromatography gave a pyrrole derivative (**8d**) in a good yield without the isolation of **(±)-7d**. Thus, **7c** and **(±)-7d**, which were unstable under the acidic reaction conditions, were shown to be easily converted into the pyrrole under the limited conditions.

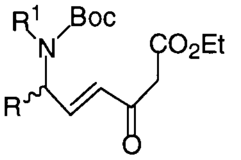
**Scheme 3.**

**(*R*)-(+)-3a, (*S*)-(-)-3a,**
**(*R*)-(+)-3b, (*S*)-(-)-3b,**
**3c, (±)-5, (*S*)-(-)-6**



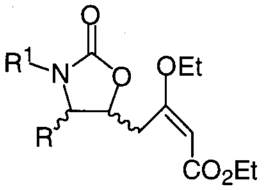
**(4*R*,5*R*)-(+)-7a, (4*S*,5*S*)-(-)-7a**: R=Bn, $R^1$=Me
**(4*R*,5*R*)-(+)-7b, (4*S*,5*S*)-(-)-7b**: R=$^i$Pr, $R^1$=Me
**(±)-7c**: R=H, $R^1$=Me (not isolated)
**(±)-7d**: R=ArCO, $R^1$=Me (not isolated)
**(4*S*,5*S*)-(-)-7e**: R=Bn, $R^1$=PMB

**8a**: R=Bn
**8b**: R=$^i$Pr
**8c**: R=H
**8d**: R=ArCO



**(*R*)-(+)-9a**: R=Bn, $R^1$=Me
**9c**: R=H, $R^1$=Me
**(±)-9d**: R=ArCO, $R^1$=Me

( **9b**: R=$^i$Pr, $R^1$=Me
**9e**: R=Bn, $R^1$=PMB )



**(4*S*,5*S*)-(-)-10a**: R=Bn, $R^1$=Me
**(4*S*,5*S*)-(-)-10b, (4*R*,5*R*)-(+)-10b**: R=$^i$Pr, $R^1$=Me
**(±)-10c**: R=H, $R^1$=Me

( **9d**: R=ArCO, $R^1$=Me
**9e**: R=Bn, $R^1$=PMB )

Table 1. 2-Oxazolidinones (**7**)

| Entry | Starting Compd No. | Conditions[a) ] Time | Product (Yield %)[b)] |
|---|---|---|---|
| 1 | **(*R*)-(+)-3a** | 6 h | **(4*R*,5*R*)-(+)-7a** (89) |
| 2 | **(*S*)-(-)-3a** | 6 h | **(4*S*,5*S*)-(-)-7a** (93) |
| 3 | **(*R*)-(+)-3b** | 6 h | **(4*R*,5*R*)-(+)-7b** (87) |
| 4 | **(*S*)-(-)-3b** | 6 h | **(4*S*,5*S*)-(-)-7b** (90) |
| 5 | **3c** | (20 min) | **7c**[c)] (0), **8c** (13),<br>**9c** (22), **10c**[c)] (17) |
| 6 | **(±)-5** | (20 min) | **7d**[c)] (0), **8d** (90) |
| 7 | **(*S*)-(-)-6** | 2 h | **(4*S*,5*S*)-(-)-7e** (91) |

a) Starting compounds (300 mM) were treated with 97% concd $H_2SO_4$ (1.0 equiv.) on silica gel (4.0 equiv.) in $CH_2Cl_2$ at 0 °C with vigorous stirring. b) Isolated yield. c) Racemate

The structure of the 2-oxazolidinones (**7** and **10**) was determined on the basis of IR and NMR spectral data and elementary analyses. The stereochemistry of their compound was confirmed by comparing with the data of **(4*R*,5*R*)-(+)-10a** described in the literature.[7] Two substituents at the 4- and 5-positions were shown to have a *trans* relationship. The configuration of the 4- and 5-positions was assigned to be the same that as the starting materials, chiral α-amino acids. The double bond of **9** and **10** was shown to be in (*E*)-configuration on the basis of $^1$H-NMR spectral data. Thus, the reaction was shown to proceed stereo- and regio-selectively, giving the 2-oxazolidinone ring.[7]

**Conversion of 2-oxazolidinones (7) into *N*-alkyl-2-pyrrolylacetates (8).** We next examined conversion of **7** into **8**. The results are summarized in Table 2.

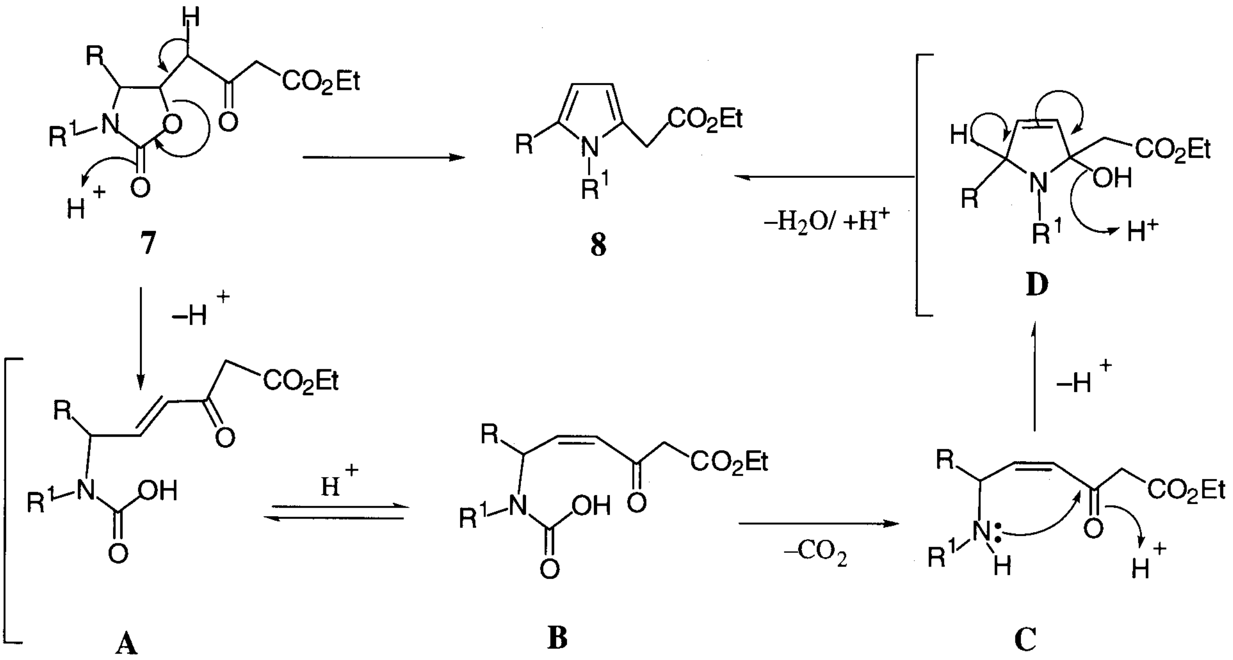
Table 2. Formation of the pyrrole ring

| Entry | Starting Compd No. | Conditions |  |  |  | Product (Yield %) |
|---|---|---|---|---|---|---|
|  |  | Reagent | Solvent | Temperature | Time |  |
| 1 | **(4*S*,5*S*)-(-)-7a** | *p*-TosOH/$H_2O$<br>(0.1 equiv.) | THF | reflux | 6 h | **8a** (13) |
| 2 | **(4*S*,5*S*)-(-)-7a** | *p*-TosOH/$H_2O$<br>(0.1 equiv.) | $C_6H_6$ | reflux | 17 h | **8a** (27) |
| 3 | **(4*S*,5*S*)-(-)-7a** | - | $C_6H_6$ | reflux | 17 h | **8a** (30) |
| 4 | **(4*S*,5*S*)-(-)-7a** | - | $C_6H_6$ | rt | 14 day | **8a** (23) |
| 5 | **(4*S*,5*S*)-(-)-7a** | - | - | rt | 5 day | **8a** (44) |
| 6 | **(4*R*,5*R*)-(+)-7b** | *p*-TosOH/$H_2O$<br>(0.1 equiv.) | THF | reflux | 19 h | **8b** (75) |
| 7 | **(4*R*,5*R*)-(+)-7b** | - | - | rt | 14 day | **8b** (73) |
| 8 | **3c** | 97% concd $H_2SO_4$<br>(1.0 equiv.) on $SiO_2$ | $CH_2Cl_2$ | 0 °C | 1 h | **8c** (26) |
| 9 | **(±)-5** | 97% concd $H_2SO_4$<br>(1.0 equiv.) on $SiO_2$ | $CH_2Cl_2$ | 0 °C to rt | 2 h | **8d** (69) |

As seen in Table 2, the conversion of **(4*S*,5*S*)-(-)-7a** into **8a** was achieved only in considerably low yields (Entries 1-4). Under the conditions examined, reaction of the oily product [**(4*S*,5*S*)-(-)-7a**] in neat was allowed to stand at room temperature for 5 days to give **8a** in the highest yield of 44% (Entry 5). On the other hand, **8b** was obtained in 75% on treatment of **(4*R*,5*R*)-(+)-7b** under the conditions of THF-refluxing for 19 h in the presence of *p*-toluenesulfonic acid monohydrate (0.1 equiv.) and in 73% yield when **(4*R*,5*R*)-(+)-7b** in neat was permitted to stand for 14 days at room temperature (Entries 6, 7). When **3c** was treated with 97% concd $H_2SO_4$ (1.0 equiv.) on silica gel at 0 °C for 1 h in dichloromethane, **8c** was obtained in a low yield of 26% (Entry 8). Compound [**(±)-5**], which was prepared by the Dess-Martin oxidation of **(±)-4**, was treated with 97% concd $H_2SO_4$ (1.0 equiv.) on silica gel to give **8d** in 69% yield (Entry 9) which was converted into a commercially available antiinflammatory agent, tolmetin®.

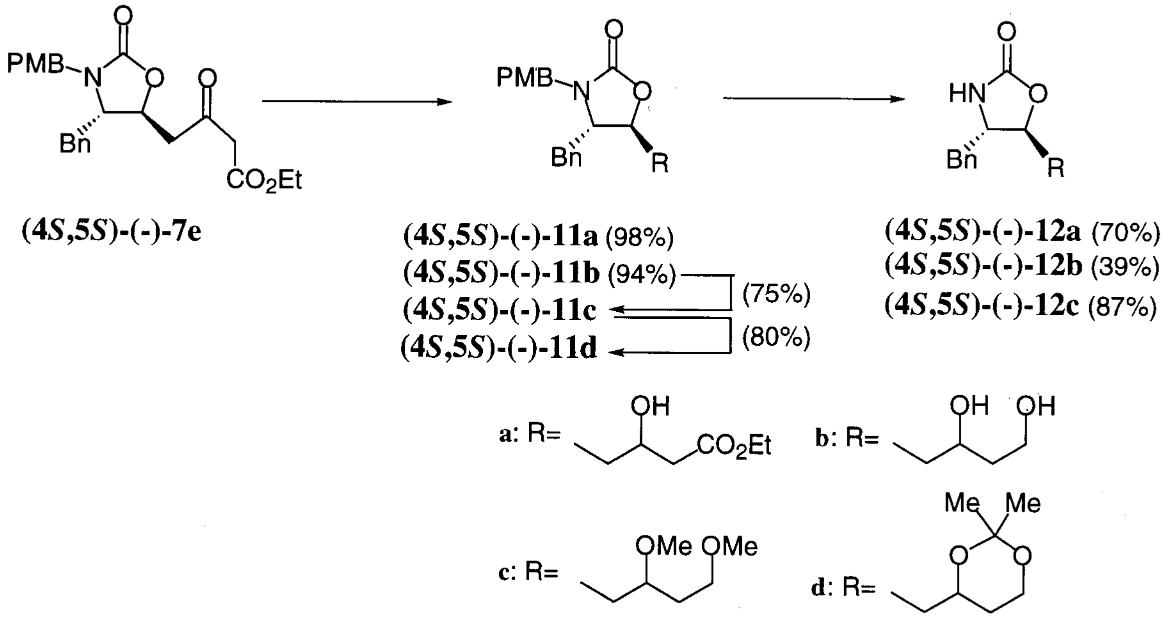
The mechanism of the conversion of **7** into **8** may be illustrated as follows (Scheme 4). 2-Oxazolidinone (**7**) undergoes ring-opening reaction in the presence of a proton dispersed on the silica gel surface to yield an intermediate (**A**) with *trans*configuration which will be isomerized to a *cis*-isomer (**B**). Decarboxylation of **B** gives a γ-amino-α,β-unsaturated ketone (**C**), followed by cyclodehydration to yield the pyrrole (**8**) through an intermediate (**D**).

**Scheme 4.**



**Deprotection of the PMB group of (4*S*,5*S*)-(-)-7e to (4*S*,5*S*)-(-)-12.** In order to remove the PMB group (Scheme 5), **(4*S*,5*S*)-(-)-7e** was oxidized with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in wet dichloromethane at room temperature to give only unchanged **(4*S*,5*S*)-(-)-7e** in a quantitative yield.

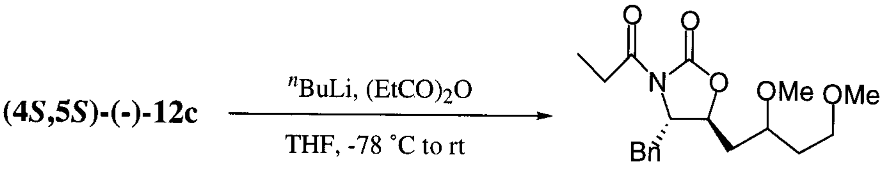
**Scheme 5.**



Compound [**(4*S*,5*S*)-(-)-7e**] was oxidized with ammonium cerium(IV) nitrate (CAN) in a (3:1) mixture of acetonitrile and water. The reaction was followed by TLC (silica gel; eluted with (3:1) hexane and ethyl acetate). At the point that the starting material [**(4*S*,5*S*)-(-)-7e**] disappeared, the reaction was stopped and the reaction mixture was worked up by silica gel column chromatographic separation to give 4-methoxybenzaldehyde in 18% yield along with a large amount of decomposition products, indicating deprotection of the PMB group. Then, we tried the deprotection of the PMB group of **(4*S*,5*S*)-(-)-11** which will be stabilized by changing a carbonyl group to an alcohol group (Scheme 5). Compounds [**(4*S*,5*S*)-(-)-11a-b** and **-11c**] were prepared in good yields by $NaBH_4$-reduction or $LiBH_4$-reduction of **(4*S*,5*S*)-(-)-7e**. Compound [**(4*S*,5*S*)-(-)-11c**] was prepared from **(4*S*,5*S*)-(-)-11b** and methyl iodide in the presence of sodium hydride in *N*,*N*-dimethylformamide. Compound [**(4*S*,5*S*)-(-)11b**] was also converted in 80% yield into **(4*S*,5*S*)-(-)-11d** on treatment with 2,2-dimethoxypropane in the presence of *p*-toluenesulfonic acid monohydrate for 4 days under benzene-refluxing. Compounds [**(4*S*,5*S*)-(-)-11a** and **-11c**] were oxidized with CAN in a (3:1) mixture of acetonitrile and water at room temperature for 10 to 15 min to give [**(4*S*,5*S*)-12a** and **-12c**] in 70% and 87% yields, respectively. Under the same conditions, **(4*S*,5*S*)-(-)-11d** gave **(4*S*,5*S*)-(-)-12b** in 39% yield. The low yield may result from oxidation of the primary hydroxyl group of **(4*S*, 5*S*)-(-)-12b**.

Acylation of **(4*S*,5*S*)-(-)-12c** according to the method described in the literature proceeded smoothly to give *N*-propionyl derivative [**(4*S*, 5*S*)-(-)-13**] in a quantitative yield.[12]

**Scheme 6.**



**(4*S*,5*S*)-(-)-13** (100%)

In conclusion, we have provided a new procedure for the preparation of chiral 2-oxazolidinones (**7** and **12**) from **3** and related compounds and for their conversion into the pyrrole ring. The usefulness of concentrated sulfuric acid supported on silica gel for the construction of the 2-oxazolidinones from 6-(*N*-alkyl-*N*-*tert*-butylcarbonyl)amino-3-ethoxyhexa-2,4-dienoates and conversion into the pyrrole ring lies in (a) simplicity of operations, (b) possibility of selective cyclization, and (c) good yields. Although we have not yet studied the scope and limitations of this method, it appears to have potential for application to the synthesis of a wide variety of 2-oxazolidinones and *N*-substituted pyrroles because of the ready availability of many amino acids and simple allylidenephosphoranes.

## EXPERIMENTAL

Melting points were determined on a Gallenkamp melting point apparatus and are uncorrected. NMR spectra were recorded on a JEOL JNM-LA400 spectrometer, operating at 400 MHz for $^1H$ NMR and 100 MHz for $^{13}C$ NMR. Chemical Shifts, in $CDCl_3$ solution, are reported downfield from TMS ($\delta$ = 0) for relative $^1H$ NMR. For $^{13}C$ NMR spectra, chemical shift in $CDCl_3$ are reported relative to the central $CDCl_3$ resonance ($\delta$ = 77.0). IR spectra were recorded on a Hitachi 260-30 infrared spectrophotometer. UV-visible spectra were recorded on a Hitachi U-3210 spectrophotometer. MS spectra were measured on JEOL JMS-600. Optical rotation was measured at 25 °C on Perkin Elmer 241 polarimeter. All reactions were carried out under argon atmosphere with dry, freshly distilled solvents under anhydrous conditions unless otherwise specified. Flash column chromatography was performed using Merck 60 silica gel, 240-400 mesh. Allylidenetriphenylphosphorane (**1**) was prepared according to our previous paper.[10] α-Aminoacetaldehydes (**1a-c**)[8] and the Garner aldehyde [(±)-**14**][9] were synthesized according to the method described in the literature.

**(±)-2-(*N*-*tert*-Butoxycarbonyl)amino-3-(*tert*-butyldiphenylsiloxy)-3-(4-methylphenyl)-1-propanal [(±)-1d]**. A solution of (±)-**17** (1.53 g, 2.94 mmol) in $CH_2Cl_2$ (15 mL) was mixed with a solution of the Dess-Martin reagent (3.11 g, 7.34 mmol) in $CH_2Cl_2$ (25 mL) at rt. The mixture was stirred for 1.5 h at ambient temperature and diluted with $Et_2O$ (200 mL). The resulting mixture was neutralized with saturated aqueous $NaHCO_3$ and stirred for 10 min and filtered on celite. The filtrate was washed with saturated aqueous $NaHCO_3$ and $H_2O$, successively and dried over $MgSO_4$. After removal of the solvent, the oily residue was purified by column chromatography using 10:1 hexane/AcOEt as an eluent to give pure (±)-**1d**. Yield: 1.77 g (87%) (a colorless foam). $^1$H-NMR (400 MHz, $CDCl_3$) δ: 9.73, 9.59 (2×s, 1H), 7.70-6.95 (m, 14H), 5.22 (d, 3/5H, *J* = 2.0 Hz), 5.18 (d, 2/5H, *J* = 4.9 Hz), 5.09 (d, 3/5H, *J* = 7.1 Hz), 5.00-4.80 (m, 2/5H), 4.49 (dd, 2/5H, *J* = 9.5, 5.1 Hz), 4.44 (dd, 3/5H, *J* = 7.3, 2.7 Hz), 4.30-4.10 (br d, 1/10H), 2.33, 2.30 (2×s, 3H), 1.37, 1.36 (2×s, 9H), 1.06, 1.05 (2×s, 9H). IR ($CHCl_3$) cm$^{-1}$: 3450, 3020, 2940, 2860, 1738, 1710, 1500. *Anal.* Calcd for $C_{31}H_{39}NO_4Si$: C, 71.92; H, 7.59; N, 2.71. Found: C, 71.68; H, 7.61; N, 2.65.

**Ethyl (*R*)-(+)-6-(*N*-*tert*-butoxycarbonyl)amino-3-ethoxy-7-phenylhepta-2,4-dienoate [(*R*)-(+)-2a]**. To a solution of (*R*)-(+)-**1a** (3.00 g, 12.0 mmol) in THF (150 mL) was added a solution of (2-ethoxy-3-ethoxycarbonylallylidene)triphenylphosphorane[10] (5.04 g, 12.0 mmol) in THF (150 mL) at rt and the mixture was stirred for overnight at rt. After removal of the solvent *in vacuo*, the residue was purified by column chromatography using 6:1 hexane/AcOEt as an eluent to give pure (*R*)-(+)-**2a**. Yield: 4.62 g (99%) (colorless solids). mp 73.4-73.9 °C (Hexane-$Et_2O$). $^1$H-NMR (400 MHz, $CDCl_3$) δ: 7.44 (dd, 1H, *J* = 1.3, 15.8 Hz ), 7.32-7.16 (m, 5H), 6.51 (br d, 1H), 5.03 (s, 1H), 4.75-4.26 (br s, 2H), 4.14 (q, 2H, *J* = 7.2 Hz), 3.86 (q, 2H, *J* = 7.0 Hz), 2.96 (dd, 1H, *J* = 6.0, 13.8 Hz), 2.90-2.74 (br, 1H), 1.44-1.33 (m, 12H), 1.27 (t, 3H, *J* = 7.1 Hz). IR ($CHCl_3$) cm$^{-1}$: 3360, 2990, 1700, 1655, 1585. FABMS (NBA): *m/z* 390 [(M+H)$^+$]. *Anal.* Calcd for $C_{22}H_{31}NO_5$: C, 67.84; H, 8.02; N, 3.60. Found: C, 68.10; H, 7.85; N, 3.33. $[\alpha]_D$: +2.5° (*c* 1.02, $CHCl_3$).

**Ethyl (*S*)-(-)-6-(*N*-*tert*-butoxycarbonyl)amino-3-ethoxy-7-phenylhepta-2,4-dienoate [(*S*)-(-)-2a]**. Yield: 4.62 g (99%) (colorless solids). (*S*)-(-)**2a** showed the same spectral data as those of (*R*)-(+)-**2a** except for the value of the optical rotation, $[\alpha]_D$: -1.4° (*c* 1.06, $CHCl_3$).

**Ethyl (*R*)-(+)-6-(*N*-*tert*-butoxycarbonyl)amino-3-ethoxy-7-methylocta-2,4-dienoate [(*R*)-(+)-2b]**. Yield: 4.01 g (98%) (a colorless foam). $^1$H-NMR (400 MHz, $CDCl_3$) δ: 7.41 (dd, 1H, *J* = 1.6, 15.7 Hz), 6.50-6.30 (br d, 1H), 5.03 (s, 1H), 4.70-4.55 (br s, 1H), 4.25-4,10 (m, 3H), 3.87 (q, 2H, *J* = 7.0 Hz), 1.95-1.75 (br s, 1H), 1.45 (s, 9H), 1.37 (t, 3H, *J* = 6.9 Hz), 1.28 (t, 3H, *J* = 7.2 Hz), 0.93 (d, 3H, *J* = 6.8 Hz), 0.91 (d, 3H, *J* = 6.8 Hz). IR (neat) cm$^{-1}$: 3350, 2960, 1700, 1660, 1590. *Anal.* Calcd for $C_{18}H_{31}NO_5 \cdot 1/4H_2O$: C, 62.49; H, 9.03; N, 4.05. Found: C, 62.75; H, 9.09; N, 3.88. EIMS: m/z 341 (M$^+$). HRMS (EI): Found: *m/z* 341.2179 (Calcd for $C_{18}H_{31}NO_5$ : 341.2203). $[\alpha]_D$: +4.6° (*c* 0.97, $CHCl_3$).

**Ethyl (*S*)-(-)-6-(*N*-*tert*-butoxycarbonyl)amino-3-ethoxy-7-methylocta-2,4-dienoate [(*S*)-(-)-2b]**. Yield: 3.97 g (97%) (a colorless foam). (*S*)-(-)-**2b** showed the same spectral data as those of

**(*R*)-(+)-2b** except for the value of the optical rotation, $[\alpha]_D$: -4.2° (*c* 0.88, $CHCl_3$).

**Ethyl 6-(*N*-*tert*-butoxycarbonyl)amino-3-ethoxyhexa-2,4-dienoate (2c)**. Yield: 1.87 g (52%) (a colorless oil). $^1$H-NMR (400 MHz, $CDCl_3$) δ: 7.44 (d, 1H, *J* = 15.6 Hz), 6.48 (td, 1H, *J* = 5.9, 16.1 Hz), 5.04 (s, 1H), 4.75-4.55 (br s, 1H), 4.14 (q, 2H, *J* = 7.1 Hz), 4.00-3.80 (m, 4H), 1.46 (s, 9H), 1.38 (t, 3H, *J* = 7.0 Hz), 1.28 (t, 3H, *J* = 7.1 Hz). IR (neat) cm$^{-1}$: 3360, 2980, 1700, 1635, 1590. *Anal.* Calcd for $C_{15}H_{25}NO_5$: C, 60.18; H, 8.42; N, 4.68. Found: C, 59.90; H, 8.22; N, 4.48. EIMS: *m/z* 299 ($M^+$). HRMS (EI): Found: *m/z* 299.1738 (Calcd for $C_{18}H_{31}NO_5$: 299.1733).

**Ethyl (±)-6-(*N*-*tert*-butoxycarbonyl)amino-3-ethoxy-7-(*tert*-butyldiphenylsiloxy)-7-(4-tolyl) hepta-2,4-dienoate [(±)-2d]**. Yield: 7.89 g (100%) (a colorless foam). $^1$H-NMR (400 MHz, $CDCl_3$) δ: 7.75-6.95 (m, 15H), 6.70-6.35 (2×d, 1H, *J* = 15.1, 15.1 Hz), 4.99 (s, 1H), 4.90-4.70 (br s and d, 1H), 4.70-4.20 (br, 2H), 4.11 (q, 2H, *J* = 7.1 Hz), 4.00-3.70 (m, 2H), 2.29, 2.28 (2×s, 3H), 1.37, 1.33 (2×s, 9H), 1.32-1.10 (m, 6H), 1.07, 1.03 (2×s; 9H). IR ($CHCl_3$) cm$^{-1}$: 3440, 3000, 2970, 2930, 2895, 2855, 1700, 1645, 1580. *Anal.* Calcd for $C_{39}H_{51}NO_6Si \cdot 1/2H_2O$: C, 70.23; H, 7.86; N, 2.10. Found: C, 70.50; H, 7.57; N, 2.05. FABMS (NBA): *m/z* 659 [$(M+H)^+$].

**Ethyl (*R*)-(+)-6-(*N*-*tert*-butoxycarbonyl-*N*-methyl)amino-3-ethoxy-7-phenylhepta-2,4-dienoate [(*R*)-(+)-3a]**. To a solution of **(*R*)-(+)-2a** (500 mg, 1.28 mmol) in DMF (5.0 mL) was added NaH (60% dispersion in mineral oil; 257 mg, 6.42 mmol) and $CH_3I$ (0.41 mL, 6.42 mmol) at 0 °C, successively. The mixture was stirred for 1.5 h at the same temperature, poured into saturated aqueous $NH_4Cl$ at 0 °C with care, keeping the pH 10 and then extracted with $Et_2O$. The extract was washed $H_2O$ and dried over $MgSO_4$. After removal of the solvent, the residue was purified by flash column chromatography using 20:1 hexane/AcOEt as an eluent to give **(*R*)-(+)-3a**. Yield: 517 mg (100%) (a colorless viscous oil). $^1$H-NMR (400 MHz, $CDCl_3$) δ: 7.50 (br d, 1H, *J* = 16.1 Hz ), 7.30-7.12 (m, 5H), 6.54 (dd, 1H, *J* = 15.9, 5.1 Hz), 5.28-5.12 (br s, 2/5H), 5.07 (s, 1H), 4.98-4.82 (br s, 3/5H), 4.16 (q, 2H, *J* = 7.1 Hz), 3.89 (br q, 2H, *J* = 6.7 Hz), 3.15-2.88 (br dd, 2H, *J* = 10.4, 13.8 Hz), 2.80-2.62 (br, 3H), 1.39 (br t, 3H, *J* = 6.7 Hz), 1.35-1.20 (br t, 12H, *J* = 7.1 Hz). IR (neat) cm$^{-1}$: 2960, 1690, 1650, 1585. FABMS (NBA): *m/z* 405 [$(M+H)^+$]. *Anal.* Calcd for $C_{23}H_{33}NO_5$: C, 68.46; H, 8.24; N, 3.47. Found: C, 68.13; H, 7.98; N, 3.72. $[\alpha]_D$: +36.6° (*c* 1.25, $CHCl_3$).

**Ethyl (*S*)-(-)-6-(*N*-*tert*-butoxycarbonyl-*N*-methyl)amino-3-ethoxy-7-phenylhepta-2,4-dienoate [(*S*)-(-)-3a]**. Yield: 512 mg (99%) (a colorless viscous oil). **(*S*)-(-)-3a** showed the same spectral data as those of **(*R*)-(+)-3a** except for the value of the optical rotation, $[\alpha]_D$: -44.0° (*c* 1.11, $CHCl_3$). *Anal.* Calcd for $C_{23}H_{33}NO_5$: C, 68.46; H, 8.24; N, 3.47. Found: C, 68.18; H, 8.44; N, 3.20.

**Ethyl (*R*)-(+)-6-(*N*-*tert*-butoxycarbonyl-*N*-methyl)amino-3-ethoxy-7-methylocta-2,4-dienoate [(*R*)-(+)-3b]**. Yield: 418 mg (92%) (a colorless oil). $^1$H-NMR (400 MHz, $CDCl_3$) δ: 7.40 (d, 1H, *J* = 15.6 Hz), 6.46 (dd, 1H, *J* = 7.4, 15.7 Hz), 5.04 (s, 1H), 4.45-4.20 (br, 2/5H), 4.15 (q, 2H, *J* = 7.1 Hz), 4.08-3.95 (br, 3/5H), 3.88 (q, 2H, *J* = 7.0 Hz), 2.74 (br s, 3H), 1.95 (d sept, 1H, *J* = 2.7, 5.9 Hz), 1.47 (s, 9H), 1.38 (t, 3H, *J* = 7.0 Hz), 1.28 (t, 3H, *J* = 7.1 Hz), 1.00-0.85 (br dd, 6H). IR (neat) cm$^{-1}$: 2960, 1700, 1685, 1650, 1585. *Anal.* Calcd for $C_{19}H_{33}NO_5$: C, 64.20; H, 9.36; N, 3.94. Found: C, 64.25; H, 9.20; N, 4.05. FABMS (NBA): *m/z* 356 [$(M+H)^+$]. $[\alpha]_D$: +8.4° (*c* 1.16, $CHCl_3$).

**Ethyl (*S*)-(-)-6-(*N*-*tert*-butoxycarbonyl-*N*-methyl)amino-3-ethoxy-7-methylocta-2,4-dienoate [(*S*)-(-)-3b]**. Yield:423 mg (93%) (a colorless oil). **(*S*)-(-)-3b** showed the same spectral data as those of **(*R*)-(+)-3b** except for the value of the optical rotation, $[\alpha]_D$: -9.2° (*c* 1.06, $CHCl_3$). *Anal.* Calcd for $C_{19}H_{33}NO_5$: C, 64.20; H, 9.36; N, 3.94. Found: C, 64.31; H, 9.38; N, 3.83.

**Ethyl 6-(*N*-*tert*-butoxycarbonyl-*N*-methyl)amino-3-ethoxyhexa-2,4-dienoate (3c)**. Yield: 329 mg (82%) (a pale yellow oil). $^1$H-NMR (400 MHz, $CDCl_3$) δ: 7.42 (td, 1H, *J* = 1.4, 15.7 Hz), 6.50-6.30 (br, 1H), 5.05 (s, 1H), 4.15 (q, 2H, *J* = 7.1 Hz), 4.08-3.85 (br, 2H), 3.88 (q, 2H, *J* = 7.0 Hz), 2.84 (s, 3H), 1.47 (s, 9H), 1.38 (t, 3H, *J* = 7.0 Hz), 1.28 (t, 3H, *J* = 7.2 Hz). IR (neat) cm$^{-1}$: 2980, 2940, 1700, 1652, 1583. *Anal.* Calcd for $C_{16}H_{27}NO_5$: C, 61.32; H, 8.68; N, 4.47. Found: C, 61.12; H, 8.43; N, 4.72. FABMS (NBA): *m/z* 314 [(M+H)$^+$].

**Ethyl (±)-6-(*N*-*tert*-butoxycarbonyl-*N*-methyl)amino-3-ethoxy-7-(*tert*-butyldiphenylsiloxy)7-(4-tolyl)hepta-2,4-dienoate [(±)-3d]**. Yield: 818 mg (95%) (a colorless foam). $^1$H-NMR (400 MHz, $CDCl_3$) δ: 7.57 (d, 2H, *J* = 7.3 Hz), 7.50-7.10 (m, 9H), 7.05-6.83 (m, 22/5H), 6.78 (dd, 2/5H, *J* = 6.8, 15.6 Hz), 6.49 (dd, 1/10H, *J* = 6.1, 15.6 Hz), 6.24 (d, 1/10H, *J* = 15.1 Hz), 5.20-4.85 (m, 7/5H), 4.85-4.65 (m, 6/5H), 4.55-4.35 (br s, 2/5H), 4.25-4.05 (m, 2H), 3.95-3.65 (m, 2H), 2.81, 2.73 (2×s, 4/5H), 2.44, 2.41 (2×s, 11/5H), 2.26, 2.25, 2.23 (3×s, 3H), 1.50-1.10 (m, 15H), 0.99, 0.96, 0.94 (3×s, 9H). IR ($CHCl_3$) cm$^{-1}$: 3000, 2975, 2935, 2900, 2860, 1685, 1655, 1588. *Anal.* Calcd for $C_{40}H_{53}NO_6Si$: C, 71.50; H, 7.95; N, 2.08. Found: C, 71.25; H, 7.73; N, 2.03. FABMS (NBA): *m/z* 673 [(M+H)$^+$].

**Ethyl (±)-6-(*N*-*tert*-butoxycarbonyl-*N*-methyl)amino-3-ethoxy-7-hydroxy-7-(4-tolyl)-hepta-2,4-dienoate [(±)-4]**. To a solution of **(±)-3d** (1.13 g, 1.69 mmol) in dry THF (25 mL) was added AcOH (1.45 mL, 25.4 mmol) and 1.0 M $N(Bu)_4F$ in THF (25.4 mL, 25.4 mmol) at -10 °C, successively. The mixture was allowed to stand for 1 h at rt and for additional 9 days at 40 °C with stirring. To the reaction mixture was added saturated aqueous $NH_4Cl$ (30.0 mL) and the mixture was extracted with AcOEt. The extract was washed brine and dried over $MgSO_4$. After removal of the solvent, the residue was purified by flash column chromatography with gradient elution changing the concentration of 20:1 hexane/AcOEt to 10:1 hexane/AcOEt as eluents to give **(±)-4** as two diastereomers. **A major diastereomer**. Yield: 50 mg (69%) (a colorless foam). $^1$H-NMR (400 MHz, $CDCl_3$) δ: 7.64 (br s, 1H), 7.32-7.20 (br, 2H), 7.14 (d, 2H, *J* = 8.1 Hz), 6.76 (dd, 1H, *J* = 6.6, 15.9 Hz), 5.07 (s, 1H), 5.04-4.78 (br, 1H), 4.52 (dd, 1H, *J* = 7.0, 7.0 Hz), 4.14 (q, 2H, *J* = 7.2 Hz), 3.90 (q, 2H, *J* = 6.9 Hz), 3.40-3.02 (br s, 1H), 2.64 (s, 3H), 2.33 (s, 3H), 1.40 (t, 3H, *J* = 6.9 Hz), 1.37 (s, 9H), 1.27 (t, 3H, *J* = 7.1 Hz). IR ($CHCl_3$) cm$^{-1}$: 3600, 2985, 2935, 1685, 1653, 1585. *Anal.* Calcd for $C_{24}H_{35}NO_6$: C, 66.49; H, 8.14; N, 3.23. Found: C, 66.65; H, 8.04; N, 3.21. FABMS: *m/z* 435 [(M+H)$^+$]. **A minor diastereomer.** Yield: 13 mg (17%) (a colorless viscous oil)]. $^1$H-NMR (400 MHz, $CDCl_3$) δ: 7.41 (br d, 1H, *J* = 15.6 Hz), 7.25 (d, 2H, *J* = 8.1 Hz), 7.14 (d, 2H, *J* = 8.1 Hz), 6.70-6.30 (br, 1H), 5.02 (s, 1H), 4.89 (dd, 1H, *J* = 6.2, 6.2 Hz), 4.75-4.25 (br, 1H), 4.13 (q, 2H, *J* = 7.2 Hz), 3.84 (q, 2H, *J* = 6.9 Hz), 3.00-2.60 (br, 3H), 2.33 (s, 3H), 1.68 (s, 1H), 1.50-1.30 (br s, 9H), 1.34 (t, 3H, *J* = 7.0 Hz), 1.26 (t, 3H, *J* = 7.2 Hz). IR ($CHCl_3$) cm$^{-1}$: 3600, 2985, 2935, 1685, 1653, 1585. FABMS (NBA): *m/z* 435 [(M+H)$^+$].

**Ethyl (±)-7-(4-tolyl)-7-oxo-6-(*N*-methyl-*N*-*tert*-butoxycarbonyl)amino-3-ethoxyhexa-2,4-dienoate [(±)-5] and Ethyl (±)-7-(4-tolyl)-3,7-dioxo-6-(*N*-methyl-*N*-*tert*-butoxycarbonyl)aminohexa-2,4-dienoate [(±)-9d]**. To a solution of **(±)-4** (75 mg, 0.17 mmol) in $CH_2Cl_2$ (1.0 mL) was added a solution of the Dess-Martin reagent (183 mg, 0.43 mmol) in $CH_2Cl_2$ (2.5 mL). The mixture was stirred for 25 min at rt and diluted with $Et_2O$. The resulting mixture was neutralized with saturated aqueous $NaHCO_3$ under ice-water cooling and filtered on celite. The filtrate was extracted with

$Et_2O$. The extract was washed with saturated aqueous $NaHCO_3$ and $H_2O$, successively and dried over $MgSO_4$. After removal of the solvent, the residue was purified by column chromatography with gradient elution changing the concentration of 4:1 hexane/AcOEt to 10:1 hexane/AcOEt to give a mixture of **(±)-5** and **(±)-9d** as a yellow oil.

**Ethyl (*S*)-(-)-6-(*N*-*tert*-butoxycarbonyl-*N*-4-methoxybenzyl)amino-3-ethoxy-7-phenylhepta-2,4-dienoate [(*S*)-(-)-6]**. This compound was prepared from **(*S*)-(-)-2a** (10.0 g, 0.026 mol), 4-methoxybenzyl bromide (25.8 g, 0.128 mol) and NaH (60% dispersion in mineral oil; 5.14 g, 0.128 mol) according to the method used for the preparation of **(*S*)-(-)-3a**. Yield: 11.5 g (87%) (a pale yellow viscous oil). $^1$H-NMR (400 MHz, $CDCl_3$) δ: 7.46-7.28 (br s, 1H), 7.28-6.98 (m, 7H), 6.75 (d, 2H, *J* = 8.5 Hz), 6.68-6.42 (br s, 1H), 5.00 (s, 1H), 4.88-4.65 (br s, 1/3H), 4.60-4.37 (br s, 1/3H), 4.36-4.00 (m and q, 13/3H, *J* = 7.1 Hz), 3.82 (dq, 2H, *J* = 1.0, 7.1 Hz), 3.77 (s, 3H), 3.22-2.86 (br, 2H), 1.55-1.20 (br s and 2×t, 15H, *J* = 7.0, 7.1 Hz). IR (neat) cm$^{-1}$: 2975, 2940, 1695, 1652, 1618, 1588, 1515. FABMS (NBA): *m/z* 511 [(M+H)$^+$]. *Anal.* Calcd for $C_{30}H_{39}NO_6 \cdot 1/2H_2O$: C, 69.47; H, 7.77; N, 2.70. Found: C, 69.17; H, 7.50; N, 2.47. $[\alpha]_D$: -44.2° (*c* 0.57, $CHCl_3$).

**(4*S*,5*S*)-(-)-4-Benzyl-5-(3-ethoxycarbonyl-2-oxo)propyl-3-*N*-(4-methoxybenzyl)-2-oxazolidinone [(4*S*,5*S*)-(-)-7e]**. To a $CH_2Cl_2$ (110 mL) solution containing 97% concd $H_2SO_4$ (2.24 g, 22.2 mmol) was added $SiO_2$ (5.33 g, 88.7 mmol). The mixture was stirred for 5 min at rt and cooled to 0 °C and **(*S*)-(-)-6** (11.3 g, 22.2 mmol) in $CH_2Cl_2$ (110 mL) was added. The resulting mixture was stirred for 2 h at 0 °C and filtered. The residue on the filter was washed with $CH_2Cl_2$. The filtrate and washing was combined and neutralized with 5% $NaHCO_3$. The organic and aqueous layers were separated and the aqueous layer was extracted with $CH_2Cl_2$. The organic layers were combined and washed with brine and dried over $MgSO_4$. After removal of the solvent below 20 °C *in vacuo*, the residue was purified by column chromatography with gradient elution changing the concentration of 4:1 hexane/AcOEt to 1:1 hexane/AcOEt to give **(4*S*,5*S*)-(-)-7e** as a mixture of keto and enol forms in the ratio of 5.5 : 1. Yield: 8.59 g (91%) (a pale yellow oil). $^1$H-NMR (400 MHz, $CDCl_3$) δ: 11.88-11.73 (br s, 1/5.5H), 7.33-7.22 (m, 3H), 7.16-7.02 (m, 4H), 6.92-6.84 (m, 2H), 4.81 (d, 1/6.5H, *J* = 14.9 Hz), 4.79 (d, 5.5/6.5H, *J* = 14.9 Hz), 4.78 (s, 1/6.5H), 4.60 (dt, 5.5/6.5H, *J* = 5.3, 5.8 Hz), 4.45 (dt, 1/6.5H, *J* = 4.8, 6.4 Hz), 4.20-4.08 (m, 2H), 3.96 (d, 1/6.5H, *J* = 14.9 Hz), 3.91 (d, 5.5/6.5H, *J* = 15.1 Hz), 3.82 (s, 3/6.5H), 3.81 (s, 16.5/6.5H), 3.47 (dt, 1/6.5H, *J* = 8.9, 4.5 Hz), 3.40 (dt, 5.5/6.5H, *J* = 7.2, 5.2 Hz), 3.30 (s, 11/6.5H), 3.05 (dd-like, 1H), 2.79 (dd, 5.5/6.5H, *J* = 7.3, 13.7 Hz), 2.71 (dd, 5.5/6.5H, *J* = 6.7, 17.4 Hz), 2.29 (dd-like, 1H), 2.20 (dd, 1/6.5H, *J* = 6.7, 14.5 Hz), 1.98 (dd, 1/6.5H, *J* = 6.0, 14.5 Hz), 1.28-1.20 (2×t, 3H, *J* = 7.2, 7.1 Hz). IR (neat) cm$^{-1}$: 2990, 2945, 1750, 1720, 1615, 1520. FABMS (NBA): *m/z* 426 [(M+H)$^+$]. *Anal.* Calcd for $C_{24}H_{27}NO_6 \cdot 1/2H_2O$: C, 66.35; H, 6.26; N, 3.22. Found: C, 66.06; H, 5.99; N, 3.27. $[\alpha]_D$: -39.5° (*c* 1.30, $CHCl_3$).

**(4*R*,5*R*)-(+)-5-(3-Ethoxycarbonyl-2-oxo)propyl-3-(*N*-methyl)-4-benzyl-2-oxazolidinone [(4*R*,5*R*)-(+)-7a]**. Yield: 6.30 g (89%) [a colorless oil as a (5.7:1.0) mixture of keto and enol forms]. $^1$H-NMR (400 MHz, $CDCl_3$) δ: 7.35-7.24 (m, 3H), 7.20-7.13 (m, 2H), 4.94 (s, 1/6.7H), 4.58 (dt, 5.7/6.7H, *J* = 5.6, 5.8 Hz), 4.45 (dt, 1/6.7H, *J* = 6.4, 5.0 Hz), 4.18 (q, 2H, *J* = 7.1 Hz), 3.67 (td, 1/6.7H, *J* = 7.1, 5.2 Hz), 3.63 (dt, 5.7/6.7H, *J* = 8.2, 5.0 Hz), 3.40 (d, 5.7/6.7H, *J* = 15.9 Hz), 3.35 (d, 5.7/6.7H, *J* = 15.9 Hz), 3.09 (dd, 5.7/6.7H, *J* = 5.4, 13.7 Hz), 2.90-2.78 (m, 32.5/6.7H), 2.74 (dd, 1/6.7H, *J* = 8.3, 13.7 Hz), 2.57 (dd, 5.7/6.7H, *J* = 6.0, 17.3 Hz), 2.38 (dd, 1/6.7H, *J* = 6.8, 14.4 Hz), 2.17 (dd, 1/6.7H, *J* = 6.1, 14.4 Hz), 1.26 (t, 3H; *J* = 7.1 Hz). IR (neat) cm$^{-1}$: 3500, 2995, 2945, 1760, 1740, 1720. FABMS (NBA): *m/z* 320 [(M+H)$^+$]. $[\alpha]_D$: +3.9° (*c* 1.05, $CHCl_3$).

**(4*S*,5*S*)-(-)-5-(3-Ethoxycarbonyl-2-oxo)propyl-3-(*N*-methyl)-4-benzyl-2-oxazolidinone [(4*S*, 5*S*)-(-)-7a]**. Yield: 6.58 g (93%) [colorless oil as a (5:1) mixture of keto and enol forms]. **(4*S*,5*S*)-(-)-7b** showed the same spectral data as those of **(*R*)-(+)-7a** except for the value of the optical rotation, $[\alpha]_D$: -2.1° (*c* 1.02, $CHCl_3$).

**(4*R*,5*R*)-(+)-5-(3-Ethoxycarbonyl-2-oxopropyl)-3-(*N*-methyl)-4-(1-methylethyl)-2-oxazolidinone [(4*R*,5*R*)-(+)-7b]**. Yield: 5.23 g (87%) (a colorless oil as a (5:1) mixture of keto and enol forms). $^1$H-NMR (400 MHz, $CDCl_3$) δ: 12.30-11.94 (br s, 1/6H), 5.10 (s, 1/6H), 4.63 (ddd, 5/6H, *J* = 4.1, 5.7, 6.6 Hz), 4.49 (ddd, 1/6H, *J* = 4.0, 6.5, 6.5 Hz), 4.20 (q, 5/3H, *J* = 7.2 Hz), 4.19 (q, 1/3H, *J* = 7.1 Hz), 3.51 (d, 5/6H, *J* = 15.9 Hz), 3.47 (d, 5/6H, *J* = 15.9 Hz), 3.34 (dd, 1/6H, *J* = 3.8, 3.8 Hz), 3.29 (dd, 5/6H, *J* = 3.7, 3.7 Hz), 3.01 (dd, 5/6H, *J* = 6.7, 17.2 Hz), 2.86 (s, 5/2H), 2.86 (s, 1/2H), 2.85 (dd, 5/6H, *J* = 5.5, 17.2 Hz), 2.59 (dd, 1/6H, *J* = 7.0, 14.3 Hz), 2.41 (dd, 1/6H, *J* = 6.1, 14.1 Hz), 2.08 (dsp, 1H, *J* = 3.4, 6.9 Hz), 1.29 (t, 1/2H, *J* = 7.1 Hz), 1.29 (t, 5/2H, *J* = 7.2 Hz), 0.96 (d, 5/2H, *J* = 7.1 Hz), 0.92 (d, 1/2H, *J* = 7.1 Hz), 0.91 (d, 5/2H, *J* = 7.1 Hz), 0.88 (d, 1/2H, *J* = 6.8 Hz). IR (neat) $cm^{-1}$: 2960, 1750, 1740, 1720. $[\alpha]_D$: +38.3° (*c* 1.04, $CHCl_3$).

**(4*S*,5*S*)-(-)-5-(3-Ethoxycarbonyl-2-oxopropyl)-3-(*N*-methyl)-4-(1-methylethyl)-2-oxazolidinone [(4*S*,5*S*)-(-)-7b]**. Yield: 5.41 g (90%) (a colorless oil as a mixture of keto and enol forms). **(4*S*,5*S*)-(-)-7b** showed the same spectral data as those of **(4*R*,5*R*)-(+)-7b** except for the value of the optical rotation, $[\alpha]_D$: -39.7° (*c* 1.11, $CHCl_3$). EIMS: *m/z* 271 ($M^+$). HRMS (EI): Found: *m/z* 271.1408 (Calcd for $C_{13}H_{21}NO_5$ : 271.1420).

**(±)-7c** and **(±)-7d** were not isolated under the conditions described above.

**Ethyl 1-(*N*-methyl)-5-benzyl-2-pyrrolylacetate (8a)**. **(4*S*,5*S*)-(-)-7a** (162 mg, 0.51 mmol) in a 50 mL flask was allowed to stand for 5 days at rt. The mixture was dissolved into $Et_2O$, washed with $H_2O$ and dried over $MgSO_4$. After removal of the solvent below 20 °C *in vacuo*, the residue was purified by flash column chromatography using 6:1 hexane/AcOEt as an eluent to give **8a**. Yield: 58 mg (44%) (pale yellow crystals). mp 71.9-72.9 °C (Hexane). $^1$H-NMR (400 MHz, $CDCl_3$) δ: 7.27 (dd-like, 2H), 7.19 (dd-like, 1H), 7.14 (d-like, 2H), 5.98 (d, 1H, *J* = 3.4 Hz), 5.84 (d, 1H, *J* = 3.4 Hz), 4.15 (q, 2H, *J* = 7.2 Hz), 3.94 (s, 2H), 3.60 (s, 2H), 3.32 (s, 3H), 1.24 (t, 3H, *J* = 7.1 Hz). IR (KBr) $cm^{-1}$: 3100, 3075, 3050, 3020, 2975, 2935, 2900, 2845, 1728, 1600, 1510. *Anal.* Calcd for $C_{16}H_{19}NO_2$: C, 74.68; H, 7.44; N, 5.44. Found: C, 74.75; H, 7.75; N, 5.63. EIMS: *m/z* 257 $(M)^+$.

**Ethyl 1-(*N*-methyl)-5-*iso*-propyl-2-pyrrolylacetate (8b)**. **(4*S*,5*S*)-(-)-7b** (167 mg, 0.75 mmol) in a 50 mL flask was allowed to stand for 14 days at rt. Work-up according to the method used for the preparation of **8a** gave **8b**. Yield: 78 mg (73%) (a pale yellow oil). $^1$H-NMR (400 MHz, $CDCl_3$) δ: 5.96 (d, 1H, *J* = 3.4 Hz), 5.84 (d, 1H, *J* = 3.7 Hz), 4.16 (q, 2H, *J* = 7.2 Hz), 3.61 (s, 2H), 3.47 (s, 3H), 2.88 (sept, 1H, *J* = 6.8 Hz), 1.26 (t, 3H, *J* = 7.1 Hz), 1.23 (d, 6H, *J* = 6.8 Hz). IR (neat) $cm^{-1}$: 2970, 2940, 2875, 1740. EIMS: *m/z* 209 ($M^+$). HRMS (EI) Found: *m/z* 209.1427 (Calcd for $C_{12}H_{19}NO_2$: 209.1417). This compound was too unstable to keep at rt.

**Ethyl 1-(*N*-methyl)-2-pyrrolylacetate (8c)**. **3c** (120 mg, 0.4 mmol) was reacted with 97% concd $H_2SO_4$ (1.0 equiv.) and $SiO_2$ (4.0 equiv.) in $CH_2Cl_2$ (6.0 mL) for 1 h at 0 °C to give **8c**.Yield: 22 mg (26%) (a colorless oil). $^1$H-NMR (400 MHz, $CDCl_3$) δ: 6.58 (dd, 1H, *J* = 2.2, 2.2 Hz), 6.06 (dd, 1H, *J* = 3.2, 3.2 Hz), 6.03 (dd, 1H, *J* = 1.8, 3.0 Hz), 4.16 (q, 2H, *J* = 7.2 Hz), 3.61 (s, 2H), 3.58 (s, 3H), 1.26

(t, 3H, $J = 7.1$ Hz).

**Ethyl 1-(*N*-methyl)-5-(4-toluoyl)-2-pyrrolylacetate (8d)**. A solution of (±)-**5** (48 mg, 0.17 mmol) in $CH_2Cl_2$ (1.0 mL)was mixed with 97% concd $H_2SO_4$ (17 mg, 0.17 mmol) on $SiO_2$ (40 mg, 0.67 mmol) in $CH_2Cl_2$ (1.0 mL) at 0 °C. The mixture was stirred for 1 h at 0 °C and for additional 1 h at rt, neutralized with saturated aqueous $NaHCO_3$ and extracted with AcOEt. The extract was washed with brine and dried over $MgSO_4$. After removal of the solvent below 20 °C *in vacuo*, the residue was purified by flash column chromatography using 6:1 hexane/AcOEt as an eluent to give **8d**. Yield: 33 mg (69%) (pale yellow crystals). mp 79.8-80.5 ℃ ($Et_2O$-Hexane). $^1H$-NMR (400 MHz, $CDCl_3$) δ: 7.71 (d-like, 2H), 7.24 (d, 2H, $J = 7.8$ Hz), 6.67 (d, 1H, $J = 3.9$ Hz), 6.11 (d, 1H, $J = 3.9$ Hz), 4.21 (q, 2H, $J = 7.2$ Hz), 3.95 (s, 3H), 3.70 (s, 2H), 1.29 (t, 3H, $J = 7.2$ Hz). $^{13}C$-NMR (100 MHz, $CDCl_3$) δ: 185.9, 169.3, 141.8, 137.4, 134.6, 131.4, 129.4, 128.7, 122.2, 109.4, 61.4, 33.2, 33.0, 21.5, 14.2. IR (KBr) $cm^{-1}$: 3110, 3100, 2990, 2960, 2940, 2900, 1740, 1620, 1565, 1510. *Anal.* Calcd for $C_{17}H_{19}NO_3$: C, 71.56; H, 6.71; N, 4.91. Found: C, 71.57; H, 6.73; N, 4.95. FABMS (NBA): *m/z* 286 [$(M+H)^+$].

**Ethyl (*R*)-(+)-6-(*N*-*tert*-butoxycarbonyl-*N*-methyl)amino-3-oxo-7-phenyl-4-heptenoate [(*R*)-(+)-9a] and (4*R*,5*R*)-(+)-5-(3-Ethoxycarbonyl-2-ethoxy-2-propenyl)-3-(*N*-methyl)-4-benzyl-2-oxazolidinone [(4*R*,5*R*)-(+)-10a]**. A mixture of 97% concd $H_2SO_4$ (20 mg, 0.20 mmol) and $SiO_2$ (241 mg, 4.01 mmol) in $CH_2Cl_2$ (5.0 mL) was stirred for 5 min at rt. **(*R*)-(+)-3a** (404 mg, 1.00 mmol) in $CH_2Cl_2$ (5.0 mL) was added to the mixture at 0 °C. The resulting mixture was stirred for 3 h at 0 °C and filtered. The residue on the filter was washed with $CH_2Cl_2$. The filtrate was neutralized with 5% saturated aqueous $NaHCO_3$ and extracted with $CH_2Cl_2$. The organic layers were combined and dried over $MgSO_4$. After removal of the solvent below 20 °C *in vacuo*, the residue was purified by flash column chromatography with gradient elution changing $CHCl_3$ to 100:1 $CHCl_3$/MeOH to give **(*R*)-(+)-9a** as a (2:3) mixture of keto and enol forms, and **(4*R*,5*R*)-(+)-10a** along with **(4*R*,5*R*)-(+)-7a** (57 mg; 18%). **(*R*)-(+)-9a**. Yield: 195 mg (52%) (a pale yellow oil)). $^1H$-NMR (400 MHz, $CDCl_3$) δ: 11.87 (s, 3/5H), 7.35-7.10 (m, 5H), 6.84 (dd, 2/5H, $J = 4.6$, 16.1 Hz), 6.62 (dd, 3/5H, $J = 5.1$, 15.6 Hz), 6.20 (d, 2/5H, $J = 15.6$ Hz), 5.83 (td, 3/5H, $J = 1.6$, 15.6 Hz), 5.30-4.84 (2×br, 1H), 5.03 (s, 3/5H), 4.30-4.14 (m, 2H), 3.58 (s, 4/5H), 3.04-2.84 (m, 2H), 2.84-2.60 (br, 3H), 1.45-1.20 (m, 12H). IR (neat) $cm^{-1}$: 2995, 2945, 1747, 1700, 1643, 1608. EIMS *m/z* : 375 ($M^+$). HRMS (EI) Found: *m/z* 375.2046 (Calcd for $C_{21}H_{25}NO_5$: 375.2047). $[\alpha]_D$: +41.7° (*c* 1.02, $CHCl_3$). **(4*R*,5*R*)-(+)-10a**. Yield: 66 mg (19%) (colorless prisms). mp 89.5-92.5 ℃ ($Et_2O$-Hexane). $^1H$-NMR (400 MHz, $CDCl_3$) δ: 7.40-7.20 (m, 3H), 7.13 (d, 2H, $J = 6.8$ Hz), 4.89 (s, 1H), 4.46 (ddd, 1H, $J = 4.1$, 6.3, 7.0 Hz), 4.12 (q, 2H, $J = 7.2$ Hz), 3.69 (ddd, 1H, $J = 4.1$, 4.9, 8.3 Hz), 3.62 (ddd, 1H, $J = 7.0$, 9.5, 14.1 Hz), 3.47 (ddd, 1H, $J = 7.0$, 9.5, 14.1 Hz), 3.10-2.95 (m, 3H), 2.87 (s, 3H), 2.70 (dd, 1H, $J = 8.3$, 13.7 Hz), 1.27 (t, 3H, $J = 7.2$ Hz), 1.23 (t, 3H, $J = 7.0$ Hz). $^{13}C$-NMR (100 MHz, $CDCl_3$) δ: 168.62, 167.35, 157.49, 135.79, 129.37, 128.72, 127.00, 93.63, 75.58, 63.99, 62.82, 59.63, 38.34, 36.52, 29.63, 14.38, 14.07. IR (KBr) $cm^{-1}$: 3000, 2950, 1755, 1710, 1635. *Anal.* Calcd for $C_{19}H_{25}NO_5$: C, 65.69; H, 7.25; N, 4.03. Found: C, 65.76; H, 7.12; N, 4.13. FABMS (NBA): *m/z* 348 [$(M+H)^+$]. $[\alpha]_D$: +22.6° (*c* 0.76, $CHCl_3$).

**(4*S*,5*S*)-(-)-5-(3-Ethoxycarbonyl-2-ethoxy-2-propenyl)-3-(*N*-methyl)-4-benzyl-2-oxazolidinone [(4*S*,5*S*)-(-)-10a]**. **(*S*)-(-)-3a** (156 mg, 0.4 mmol) was reacted with 97% concd $H_2SO_4$ (1.0 equiv.) on $SiO_2$ (4 equiv.) in $CH_2Cl_2$ (8.0 mL) for 3 h at 0 °C to give **(4*S*,5*S*)-(-)-10a** (11 mg; 8%) along with **(4*S*,5*S*)-(-)-7a** (109 mg; 85%). **(4*S*,5*S*)-(-)-10a** (colorless prisms). mp 89.5-92.5 °C ($Et_2O$-Hexane). **(4*S*,5*S*)-(-)-10a** showed the same spectral data as those of **(4*R*,5*R*)-(+)-10a** except for the value of the optical rotation, $[\alpha]_D$: -29.1° (*c* 0.78, $CHCl_3$). *Anal.* Calcd for $C_{19}H_{25}NO_5$: C, 65.69;

H, 7.25; N, 4.03. Found: C, 65.63; H, 7.13; N, 4.04.

**(4*R*, 5*R*)-(+)-5-(3-Ethoxycarbonyl-2-ethoxy-2-propenyl)-3-(*N*-methyl)-4-(1-methylethyl)-2-oxazolidinone [(4*R*,5*R*)-(+)-10b].** **(*R*)-(+)-3b** (140 mg, 0.41 mmol) reacted with 97% concd $H_2SO_4$ (1.0 equiv.) and $SiO_2$ (4 equiv.) in $CH_2Cl_2$ (7.0 mL) for 3 h at 0 °C to give **(4*R*,5*R*)-(+)-10b** (14 mg; 11%) along with **(4*R*,5*R*)-(+)-7b** (80 mg; 72%). **(4*R*,5*R*)-(+)-10b**: (a colorless oil). $^1$H-NMR (400 MHz, $CDCl_3$) δ: 5.11 (s, 1H), 4.50 (dt, 1H, *J* = 3.7, 6.7 Hz), 4.13 (q, 2H, *J* = 7.1 Hz), 3.82 (dq, 2H, *J* = 2.5, 7.2 Hz), 3.32 (t, 1H, *J* = 3.7 Hz), 3.17 (dd, 1H, *J* = 6.7, 13.5 Hz), 3.11 (dd, 1H, *J* = 7.0, 13.5 Hz), 2.02 (doublet of septets, 1H, *J* = 3.6, 7.0 Hz), 1.36 (t, 3H, *J* = 7.0 Hz), 1.27 (t, 3H, *J* = 7.2 Hz), 0.89 (d, 3H, *J* = 7.1 Hz), 0.86 (d, 3H, *J* = 6.8 Hz). IR (neat) cm$^{-1}$: 2960, 1750, 1705, 1620. FABMS (NBA): *m/z* 300 [$(M+H)^+$]. $[\alpha]_D$: +40.2° (*c* 0.86, $CHCl_3$).

**(4*S*, 5*S*)-(-)-5-(3-Ethoxycarbonyl-2-ethoxy-2-propenyl)-3-(*N*-methyl)-4-(1-methylethyl)-2-oxazolidinone [(4*S*,5*S*)-(-)-10b].** This compound was prepared from **(*S*)-(-)-3b** (140 mg, 0.41 mmol) according to the method used for the preparation of **(4*R*,5*R*)-(+)-10b**. Yield: 2.5 mg (2%) (a colorless oil). **(4*S*, 5*S*)-(-)-10b** showed the same spectral data as those of **(4*R*,5*R*)-10b** except for the value of the optical rotation, $[\alpha]_D$: -44.9° (*c* 1.05, $CHCl_3$).

**Ethyl 6-(*N*-*tert*-butoxycarbonyl-*N*-methyl)amino-3-oxo-4-hexenoate (9c) and (±)-5-(3-Ethoxycarbonyl-2-ethoxy-2-propenyl)-3-(*N*-methyl)-2-oxazolidinone [(±)-10c].** **3c** (120 mg, 0.4 mmol) was reacted with 97% concd $H_2SO_4$ (1.0 equiv.) and $SiO_2$ (4.0 equiv.) in $CH_2Cl_2$ (6.0 mL) for 20 min at 0 °C to give **9c** (30 mg; 22%) as a (7:10) mixture of keto and enol forms and **(±)-10c** (17 mg; 17%) along with **8c** (19 mg; 13%). **9c**: (a pale yellow oil). $^1$H-NMR (400 MHz, $CDCl_3$) δ: 11.87 (br s, 10/17H), 6.77 (td, 7/17H, *J* = 5.0, 16.1 Hz), 6.55 (td, 10/17H, *J* = 5.5, 15.4 Hz), 6.18 (td, 7/17H, *J* = 1.7, 15.9 Hz), 5.82 (br d, 10/17H), 5.03 (s, 10/17H), 4.30-4.17 (m, 2H), 4.10-3.90 (br, 2H), 3.60 (s, 14/17H), 2.86 (br s, 3H), 1.46 (s, 9H), 1.30 (t, 3H, *J* = 7.2 Hz), 1.28 (t, 3H, *J* = 7.1 Hz). **(±)-10c**: (a colorless oil). $^1$H-NMR (400 MHz, $CDCl_3$) δ: 4.51 (s, 1H), 4.10 (q+br, 3H, *J* = 7.1 Hz), 3.62-3.50 (m, 2H), 3.50-3.34 (m, 3H), 3.17 (dd, 1H, *J* = 6.6, 18.5 Hz), 2.80 (s, 3H), 1.25 (t, 3H, *J* = 7.1 Hz), 1.20 (t, 3H, *J* = 7.1 Hz).

**(4*S*, 5*S*)-(-)-4-Benzyl-5-(3-ethoxycarbonyl-2-hydroxypropyl)-3-*N*-(4-methoxybenzyl)-2-oxazolidinone [(4*S*,5*S*)-(-)-11a].** To a solution of **(4*S*,5*S*)-(-)-7e** (168 mg, 0.39 mmol) in dry EtOH (3.0 mL) at -78 °C was added $NaBH_4$ (30 mg, 0.79 mmol). The mixture was stirred for 1.5 h at -78 °C, neutralized with 10% aqueous citric acid and extracted with $CH_2Cl_2$. The extract was washed with brine and dried over $MgSO_4$. After removal of the solvent below 20 °C *in vacuo*, the residue was purified by flash column chromatography with gradient elution changing $CHCl_3$ to 100:1 $CHCl_3$/MeOH to give **(4*S*,5*S*)-(-)-11a** as a (1:1) mixture of C2' epimers. Yield: 158 mg (98%) (a colorless oil). $^1$H-NMR (400 MHz, $CDCl_3$) δ: 7.36-7.22 (m, 3H), 7.16-7.04 (m, 4H), 6.92-6.84 (m, 2H), 4.83 (d, 1/2H, *J* = 2.4 Hz), 4.79 (d, 1/2H, *J* = 2.2 Hz), 4.46 (dq, 1/2H, *J* = 5.5, 3.6, 9.5 Hz), 4.36 (dt, 1/2H, *J* = 7.1, 5.4 Hz), 4.11 (dq, 2H, *J* = 3.2, 7.2 Hz), 3.99 (d, 1/2H, *J* = 14.9 Hz), 3.94 (d, 1/2H, *J* = 15.1 Hz), 3.82 (s, 3/2H), 3.81 (s, 3/2H), 3.47 (dt, 1/2H, *J* = 8.5,4.9 Hz), 3.36 (dt, 1/2H, *J* = 7.9, 5.2 Hz), 3.12-2.98 (m, 3/2H), 2.76 (br d, 1/2H), 2.71 (dd, 1/2H, *J* = 7.8, 13.4 Hz), 2.66 (dd, 1/2H, *J* = 8.3, 13.4 Hz), 2.42-2.20 (m, 2H), 1.62 (td, 1/2H, *J* = 7.3, 14.5 Hz), 1.50-1.14 (m and t, 6H, *J* = 7.2 Hz), 0.96-0.84 (m, 1H).

**(4*S*, 5*S*)-(-)-4-Benzyl-5-(2,4-dihydroxybutyl)-3-(*N*-4-methoxybenzyl)-2-oxazolidinone [(4*S*, 5*S*)-(-)-11b].** To a solution of **(4*S*,5*S*)-(-)-7e** (0.60 g, 1.41 mmol) in dry THF (6.0 mL) was added $LiBH_4$ (0.37 g, 16.9 mmol) at 0 °C. To the mixture was added dry EtOH (6.0 mL) slowly. The resulting mixture was stirred for 24 h at ambient temperature and neutralized with 10% aqueous citric acid to pH 4.0. After removal the THF and EtOH *in vacuo*, the residue was dissolved into $CH_2Cl_2$. The $CH_2Cl_2$ layer was washed with $H_2O$ and dried over $MgSO_4$. After removal of the solvent below 20 °C *in vacuo*, the residue was purified by flash column chromatography with gradient elution changing $CHCl_3$ to 100:1 $CHCl_3$/MeOH to give **(4*S*,5*S*)-(-)-11b** as a (1:1) mixture of C2' epimers. Yield: 580 mg (94%) (a viscous colorless foam). $^1H$-NMR (400 MHz, $CDCl_3$) d: 7.35-7.20 (m, 3H), 7.20-7.02 (m, 4H), 6.94-6.83 (m, 2H), 4.82 (s, 1/2H), 4.78 (s, 1/2H), 4.54-4.41 (m, 1/2H), 4.32 (dt, 1/2H, *J* = 4.8 Hz), 4.10-3.60 (m, 7H), 3.56-3.25 (m, 1H), 3.18-2.96 (m, 1H), 2.85-2.77 (br s, 1/4H), 2.77-2.59 (m, 1H), 2.59-2.40 (br s, 1/2H), 1.77-1.38 (m, 3H), 1.36-1.02 (m, 1H). IR ($CHCl_3$) cm$^{-1}$: 3470, 3005, 2940, 1738, 1617, 1515. FABMS (NBA): *m/z* 386 [$(M+H)^+$]. $[\alpha]_D$: -41.° (*c* 1.08, $CHCl_3$).

**(4*S*,5*S*)-(-)-4-Benzyl-5-(2,4-dimethoxybutyl)-3-(*N*-4-methoxybenzyl)-2-oxazolidinone [(4*S*,5*S*)-(-)-11c]**. To a solution of **(4*S*, 5*S*)-(-)-11b** (305 mg, 0.79 mmol) in dry DMF (8.0 mL) was added dropwise in three portions NaH (60% dispersion in mineral oil; 285 mg, 7.12 mmol] and $CH_3I$ (0.46 mL, 7.12 mmol), successively, at 0 °C and the mixture was stirred for 1 h at the same temperature and for additional 24 h at rt and poured into saturated aqueous $NH_4Cl$ and ice. The resulting mixture was adjusted to pH 9 to 10 with saturated aqueous $NH_4Cl$ and extracted with AcOEt. The extract was washed with $H_2O$ and was dried over $MgSO_4$. After removal of the solvent below 20 °C *in vacuo*, the residue was purified by flash column chromatography with gradient elution changing the concentration of 4:1 hexane/AcOEt to 1:1 hexane/AcOEt to give **(4*S*,5*S*)-(-)-11c** as a (1:1) mixture of C2' epimers. Yield: 245 mg (75%) (a colorless viscous oil). $^1H$-NMR (400 MHz, $CDCl_3$) δ: 7.34-7.21 (m, 3H), 7.15 (d, 1H, *J* = 8.5 Hz), 7.13-7.03 (m, 3H), 6.87 (dd-like, 2H), 4.83 (d, 1/2H, *J* = 7.3 Hz), 4.79 (d, 1/2H, *J* = 7.3 Hz), 4.37 (ddd, 1/2H, *J* = 5.4, 3.4, 9.8 Hz), 4.28 (dt, 1/2H, *J* = 7.6, 5.1 Hz), 4.00 (d, 1/2H, *J* = 14.9 Hz), 3.92 (d, 1/2H, *J* = 15.1 Hz), 3.81 (2×s, 3H), 3.46-3.20 (m and 3×s, 8H), 3.16 (qn, 1/2H, *J* = 5.9 Hz), 3.08 (dd, 1/2H, *J* = 4.6, 13.4 Hz), 3.02 (dd, 1/2H, *J* = 5.4, 13.7 Hz), 2.97 (s, 3/2H), 2.70 (dd, 1/2H, *J* = 7.6, 13.7 Hz), 2.62 (dd, 1/2H, *J* = 8.8, 13.4 Hz), 1.71-1.43 (m, 3H), 1.32-1.14 (m, 1H). $^{13}C$-NMR (100 MHz, $CDCl_3$) δ: 159.31, 159.26, 157.71, 157.58, 135.78, 135.62, 129.51, 129.46, 129.27, 129.23, 128.86, 128.81, 127.87, 127.84, 127.12, 127.10, 114.16, 114.10, 76.07, 75.66, 74.54, 74.11, 68.72, 68.67, 60.78, 60.51, 58.53, 58.51, 57.21, 56.31, 55.24, 45.68, 45.61, 40.44, 38.76, 38.58, 38.30, 33.80, 33.03. IR (neat) cm$^{-1}$: 2935, 2847, 1750, 1617, 1518. FABMS (NBA): m/z 414 [$(M+H)^+$]. *Anal.* Calcd for $C_{24}H_{31}NO_5$: C, 69.71; H, 7.56; N, 3.39. Found: C, 69.51; H, 7.33; N, 3.30. $[\alpha]_D$: -50.4° (*c* 0.86, $CHCl_3$).

**(4*S*,5*S*)-(-)-4-Benzyl-5-(2,2-dimethyl-1,3-dioxan-4-ylmethyl)-3-*N*-(4-methoxybenzyl)-2-oxazolidinone [(4*S*,5*S*)-(-)-11d]**. A mixture of **(4*S*,5*S*)-(-)-11b** (127 mg, 0.33 mmol) in dry $C_6H_6$ (1.2 mL), 2,2-dimethoxypropane (0.3 mL, 2.55 mmol) and *p*-TosOH-$H_2O$ (6 mg, 0.03 mmol) was refluxed for 4 days, neutralized with 5% aqueous $NaHCO_3$ and concentrated *in vacuo* to remove volatile materials. The residue was extracted with AcOEt. The extract was washed with brine and dried over $MgSO_4$. After removal of the solvent, the residue was purified by flash column chromatography using 3:1 hexane/AcOEt as an eluent to give **(4*S*,5*S*)-(-)-11d** as a (1:1) mixture of C2' epimers. Yield: 113 mg (80%) (a colorless oil). $^1H$-NMR (400 MHz, $CDCl_3$) δ: 7.38-7.22 (m, 3H), 7.18-7.03 (m, 4H), 6.95-6.82 (m, 2H), 4.79 (2×d, 1H, *J* = 15.1, 14.9 Hz), 4.41 (ddd, 1/2H, *J* = 5.4, 3.7, 9.3 Hz), 4.26 (dt, 1/2H, *J* = 7.7, 5.2 Hz), 4.04-3.69 (m + 2×s, 7H), 3.48 (dt, 1/2H, *J* = 8.2, 5.3 Hz), 3.33 (dt, 1/2H, *J* = 7.6, 5.3 Hz), 3.05 (dd, 1/2H, *J* = 4.9, 13.4 Hz), 3.01 (dd, 1/2H, *J* = 5.1, 13.4 Hz), 2.71 (dd, 1/2H, *J* = 7.6, 13.7 Hz), 2.64 (dd, 1/2H, *J* = 8.3, 13.7 Hz), 1.62 (qn, 1/2H, *J* = 7.0 Hz), 1.51-1.12 (m and 3×s, 19/2H). IR

($CHCl_3$) $cm^{-1}$: 2995, 2945, 1740, 1612, 1512. FABMS (NBA): *m/z* 427 [$(M+H)^+$]. $[\alpha]_D$: -38.0° (*c* 0.79, $CHCl_3$).

**(4*S*,5*S*)-(-)-4-Benzyl-5-(3-ethoxycarbonyl-2-hydroxypropyl)-2-oxazolidinone [(4*S*,5*S*)-(-)-12a]**. To a solution of **(4*S*,5*S*)-(-)-11a** (115 mg, 0.27 mmol) in a mixed solvent of $CH_3CN$ (0.9 mL) and $H_2O$ (0.3 mL) was added ammonium cerium(IV) nitrate (369 mg, 0.67 mmol) at rt. The mixture was stirred for 30 min at ambient temperature and $H_2O$ (10 mL) was added to the reaction mixture. The resulting mixture was extracted with $CH_2Cl_2$. The extract was dried over $MgSO_4$. After removal of the solvent below 20 °C *in vacuo*, the residue was purified by flash column chromatography with gradient elution changing $CHCl_3$ to 100:1 $CHCl_3$/MeOH to give **(4*S*,5*S*)-(-)-12a** as a (1:1) mixture of C2' epimers. Yield: 58 mg (70%) (a colorless oil). $^1$H-NMR (400 MHz, $CDCl_3$) δ: 7.38-7.30 (m, 2H), 7.30-7.23 (m, 1H), 7.23-7.15 (m, 2H), 5.71 (s, 1/2H), 5.61 (s, 1/2H), 4.60 (ddd, 1/2H, *J* = 5.5, 3.8, 9.3 Hz), 4.54 (q, 1/2H, *J* = 6.1 Hz), 4.30-4.10 (m, 3H, *J* = 7.1, 7.2 Hz), 3.83 (dd, 1/2H, *J* = 6.0, 13.3 Hz), 3.72 (dt, 1/2H, *J* = 8.1, 5.4 Hz), 3.35 (dd, 1/2H, *J* = 0.9, 4.3 Hz), 3.19 (d, 3/2H, *J* = 3.7 Hz), 2.92 (dt, 1H, *J* = 5.4, 13.0 Hz), 2.83 (dt, 1H, *J* = 8.3, 13.9 Hz), 2.54-2.45 (m, 3/2H), 2.40 (dd, 1/2H, *J* = 8.8, 16.6 Hz), 1.93 (qn, 1/2H, *J* = 7.3 Hz), 1.87-1.60 (m, 3/2H), 1.27 (t, 3H, *J* = 7.2 Hz). $^{13}$C-NMR (100 MHz, $CDCl_3$) δ: 172.44, 158.37, 136.09, 135.96, 129.09, 129.03. 128.92, 127.21, 127.17, 78.98, 64.40, 64.36, 60.82, 59.49, 58.91, 41.39, 41.31, 41.24, 41.16, 40.87, 40.18, 14.10. IR ($CHCl_3$) $cm^{-1}$: 3460, 3020, 1752, 1720. FABMS (glycerin): *m/z* 308 [$(M+H)^+$]. *Anal.* Calcd for $C_{16}H_{21}NO_5$: C, 62.52; H, 6.89; N, 4.56. Found: C, 62.58; H, 6.82; N, 4.30. $[\alpha]_D$: -66.1° (*c* 0.57, $CHCl_3$).

**(4*S*,5*S*)-(-)-4-Benzyl-5-(2,4-dihydroxybutyl)-2-oxazolidinone [(4*S*,5*S*)-(-)-12b]**. This compound was prepared as a (1:1) mixture of C2' epimers from **(4*S*,5*S*)-(-)-11d** (78 mg, 0.18 mmol) and ammonium cerium(IV) nitrate (251 mg, 0.46 mmol) according to the method for the preparation of **(4*S*,5*S*)-(-)-12a**. Yield: 19 mg (39%) (a colorless oil). $^1$H-NMR (400 MHz, $CDCl_3$) δ: 7.38-7.23 (m, 3H), 7.23-7.14 (m, 2H), 5.68 (s, 1/2H), 5.54 (s, 1/2H), 4.60 (m, 1/2H), 4.50 (m, 1/2H), 4.20-3.97 (m , 1H), 3.97-3.69 (m, 3H), 3.69-3.50 (br s, 1/2H), 3.50-3.27 (br s, 1/2H), 3.00-2.70 (br, 1H), 2.92 (m, 1H), 2.81 (m, 1H), 2.10-1.85 (br + m, 3/2H), 1.85-1.75 (m, 1/2H), 1.73-1.61 (m, 3H). IR ($CHCl_3$) $cm^{-1}$: 2995, 2945, 1740, 1612, 1512. FABMS (NBA): *m/z* 266 [$(M+H)^+$]. $[\alpha]_D$: -38.0° (*c* 0.79, $CHCl_3$).

**(4*S*,5*S*)-(-)-4-Benzyl-5-(2,4-dimethoxybutyl)-2-oxazolidinone [4*S*,5*S*)-(-)-12c]**. To a solution of **(4*S*,5*S*)-(-)-11c** (0.70 g, 1.69 mmol) in $CH_3CN$ (6.0 mL) was added ammonium cerium(IV) nitrate (2.32 g, 4.23 mmol) at rt. The mixture was stirred for 10 min at ambient temperature and $H_2O$ (20 mL) was added to the reaction mixture. The resulting mixture was extracted with $CH_2Cl_2$. The extract was dried over $MgSO_4$. After removal of the solvent below 20 °C *in vacuo*, the residue was purified by flash column chromatography using $CHCl_3$ as an eluent to give **(4*S*,5*S*)-(-)-12c** as a (1:1) mixture of C2' epimers. Yield: 431 mg (87%) (pale yellow oil). $^1$H-NMR (400 MHz, $CDCl_3$) δ: 7.32 (t-like, 2H), 7.27 (t-like, 1H), 7.13-7.03 (d-like, 2H), 6.30 (s, 1/2H), 6.10 (s, 1/2H), 4.50 (ddd, 1/2H, *J* = 5.6, 3.7, 9.4 Hz), 4.43 (dt, 1/2H, *J* = 7.3, 5.5 Hz), 3.75 (dd, 1/2H, *J* = 6.6, 12.4 Hz), 3.69 (dd, 1/2H, *J* = 5.6, 13.2 Hz), 3.60-3.46 (m, 1/2H), 3.46-3.34 (m, 5/2H), 3.32 (s, 3/2H), 3.30 (s, 3/2H), 3.29 (s, 3/2H), 3.16 (s, 3/2H), 2.88 (dd, 1H, *J* = 6.2, 13.5 Hz), 2.82 (ddd, 1H, *J* = 2.4, 7.2, 13.5 Hz), 1.96-1.54 (m, 4H). IR (neat) $cm^{-1}$: 3270, 2920, 2875, 2820, 1752. FABMS (NBA): *m/z* 294 [$(M+H)^+$]. $[\alpha]_D$: -75.0° (*c* 1.00, $CHCl_3$).

**(4*S*,5*S*)-(-)-4-Benzyl-5-(2,4-dimethoxy)butyl-3-*N*-(1-oxopropyl)-2-oxazolidinone [(4*S*, 5*S*)-(-)-13]**. To a solution of **(4*S*,5*S*)-(-)-12c** (373 mg, 1.27 mmol) in dry THF (4.1 mL) was added slowly 1.6 M $^n$BuLi in hexane(0.90 mL, 1.40 mmol) at -78 °C and propionic anhydride (0.19 mL, 1.40

mmol), successively. The mixture was stirred for 30 min at -78 °C and for additional 1 h at ambient temperature and $H_2O$ (30 mL) was added. The mixture was evaporated *in vacuo* to the volume of 20 mL and extracted with $CH_2Cl_2$. The extract was washed with brine and dried over $MgSO_4$. After removal of the solvent below 20 °C *in vacuo*, the residue was purified by flash column chromatography using 4:1 hexane/AcOEt as an eluent to give **(4*S*, 5*S*)-(-)-13** as a (1:1) mixture of C2' epimers. Yield: 443 mg (100%) (a colorless oil). $^1$H-NMR (400 MHz, $CDCl_3$) δ: 7.38-7.29 (m, 2H), 7.29-7.16 (m, 3H), 4.58-4.44 (m, 1H), 4.39 (td, 1/2H, *J* = 2.8, 9.5 Hz), 4.37 (dt, 1/2H, *J* = 8.4, 2.8 Hz), 3.42-3.17 (m, 17/2H), 3.15-3.06 (m, 1/2H), 3.04-2.92 (m, 3/2H), 2.90 (s, 3/2H), 2.83 (dd, 1/2H, *J* = 9.0, 13.4 Hz), 2.72 (dd, 1H, *J* = 9.8, 13.2 Hz), 1.84-1.44 (m, 4H), 1.21 (t, 3/2H, *J* = 7.3 Hz), 1.21 (t, 3/2H, *J* = 7.3 Hz). IR (neat) $cm^{-1}$: 2985, 2940, 2885, 1780, 1702. FABMS (NBA): *m/z* 350 [$(M+H)^+$]. $[\alpha]_D$: -17.5° (*c* 0.93, $CHCl_3$).

**(±)-3-(*N*-*tert*-Butoxycarbonyl)-2,2-dimethyl-4-[(4-tolyl)hydroxymethyl]-1,3-oxazolidine [(±)-15]**. To a solution of 4-tolylmagnesium bromide, prepared from Mg (0.90 g, 36.9 mmol) and 4-bromotoluene (4.54 mL, 36.9 mmol) in THF (24 mL), was added dropwise to the Garner aldehyde **[(±)-14]** (4.21 g, 18.4 mmol) in THF (30 mL) at O °C. The mixture was stirred for 7 h at ambient temperature, poured into saturated aqueous $NH_4Cl$ and extracted with $Et_2O$. The extract was dried over $MgSO_4$. After removal of the solvent, the residue was purified by column chromatography using 10:1 hexane/AcOEt as an eluent to give **(±)-15**. Yield: 5.49 g (93%) (colorless crystals). mp 87.5-88.5 ℃ (Hexane). $^1$H-NMR (400 MHz, $CDCl_3$) δ: 7.26 (d, 2H, *J* = 8.1 Hz), 7.15 (d, 2H, *J* = 7.8 Hz), 5.25-4.65 (br m, 1H), 4.35-3.60 (br m, 3H), 2.33 (s, 3H), 1.60-1.40 (m, 15H), 1.30-1.20 (br s, 1H). IR (KBr) $cm^{-1}$: 3450, 3010, 2975, 2940, 2900, 1690. *Anal.* Calcd for $C_{18}H_{27}NO_4$: C, 67.26; H, 8.47; N, 4.36. Found: C, 67.31; H, 8.50; N, 4.38. FABMS (NBA): *m/z* 322 [$(M+H)^+$].

**(±)-3-*N*-*tert*-Butoxycarbonyl-2,2-dimethyl-4-[(4-methylphenyl)(*tert*-butyldiphenylsiloxy)methyl]-1,3-oxazolidine [(±)16]**. To a solution of **(±)-15** (5.10 g, 15.9 mmol) in DMF (60 mL) was added imidazole (9.69 g, 79.3 mmol), 4-dimethylaminopyridine (22 mg, 0.32 mmol) and TBDPS (6.2 mL, 23.8 mmol) at rt, successively. The mixture was stirred for 3 days at 60 °C, poured into 5% aqueous $KHSO_4$ and extracted with AcOEt. The extract was washed with $H_2O$, brine and dried over $MgSO_4$. After removal of the solvent, the oily residue was purified by column chromatography using 10:1 hexane/AcOEt as an eluent to give **(±)-16**. Yield: 8.28 g (93%) (a colorless foam). $^1$H-NMR (400 MHz, $CDCl_3$) δ: 7.70-6.80 (m, 14H), 5.40-4.90 (m, 1H), 4.65-3.70 (m, 3H), 2.30-2.20 (m, 3H), 1.60-1.20 (m, 15H), 1.03 (s, 9H). IR ($CDCl_3$) $cm^{-1}$: 3005, 2930, 2855, 1690. *Anal.* Calcd for $C_{34}H_{45}NO_4Si$: C, 72.95; H, 8.10; N, 2.50. Found: C, 73.07; H, 8.03; N, 2.40. FABMS (NBA): *m/z* 561 [$(M+H)^+$].

**(±)-2-(*N*-*tert*-Butoxycarbonyl)amino-3-(*tert*-butyldiphenylsiloxy)-3-(4-tolyl)-1-propanol [(±)17]**. A solution of **(±)-16** (4.45 g, 15.9 mmol) in THF (20 mL) was mixed with a mixed solvent of AcOH (192 mL) and $H_2O$ (50 mL) at rt. The mixture was stirred for 24 h at 35 °C, neutralized with saturated aqueous $NaHCO_3$ under ice-water cooling and extracted with AcOEt. The extract was washed with brine and dried over $MgSO_4$. After removal of the solvent, the oily residue was purified by column chromatography using 10:1 hexane/AcOEt as an eluent to give **(±)-17**. Yield: 6.53 g (79%) (a colorless foam). $^1$H-NMR (400 MHz, $CDCl_3$) δ: 7.69-7.64 (m, 2H), 7.45-7.00 (m, 12H), 5.10-4.51 (m, 2H), 3.90-3.30 (m, 3H), 2.40-2.32 (br d, 7/10H), 2.32, 2.30 (2×s, 3H), 1.85-1.75 (br s, 3/10H), 1.37, 1.34 (2×s, 9H), 1.06, 1.03 (2×s, 9H). IR ($CHCl_3$) $cm^{-1}$: 3450, 3005, 2960, 2930, 2900, 2865, 1700, 1500. *Anal.* Calcd for $C_{31}H_{41}NO_4Si$: C, 71.64; H, 7.95; N, 2.69. Found: C, 71.87; H, 8.05; N, 2.66. FABMS (NBA): *m/z* 521 [$(M+H)^+$].

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