Asymmetric Alkylation and Aldol Reactions of D-Mannitol-Derived Chiral Oxazolidin-2-one Derivatives

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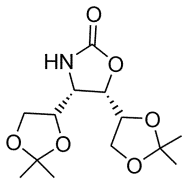
In the preceeding article, we have introduced a new chiral oxazolidin-2-one auxiliary (**1**) derived from a cheap D-mannitol, and demonstrated the chiral selectivity in alkylation, aldol reaction and β-lactam synthesis.[1] The present work began with a search for useful chiral directing groups with which to control the chiral selectivity. Because the rigidity of cyclic structures contributes significantly to control of chirality,[2] the 1,2:5,6-di-*O*-cyclohexylidene-D-mannitol (**2**) was used for the synthesis of oxazolidin-2-one chiral auxiliary (**3**) comparing the selectivity with the auxiliary (**1**) in alkylation and aldol reactions.



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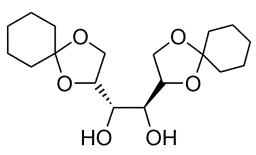

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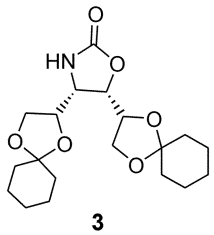

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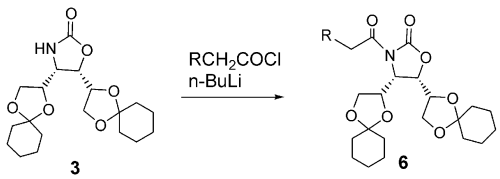
The 1,2:5,6-di-*O*-cyclohexylidene-D-mannitol (**2**), which was prepared from D-mannitol with cyclohexanone, boron trifluoride etherate and triethyl orthoformate in DMSO,[3] was converted into the cyclic sulfate **4** *via* cyclic sulfite methodology.[4] This cyclic sulfate is similar to epoxide in that they undergo nucleophilic displacement (S_N2) readily,[5] and produced 3-amino-3-deoxy-1,2:5,6-di-*O*-cyclohexylidene-D-altritol (**5**) *via* azide displacement, hydrolysis followed by reduction (Scheme 1). The altritol **5** was converted into the chiral auxiliary **3** in 95% yield by using diethyl carbonate with sodium methoxide.[6]

The *N*-acylated derivatives **6a-c** were easily prepared in high yield by reaction of auxiliary **3** with acyl chlorides **a-c** using n-butyllithium in THF at -60 °C (Table 1).

As we expected, LDA mediated asymmetric alkylations of N-acyl derivatives were obtained with high diastereomeric excess through *Z*-enolate and re-face selectivity (Table 2).[7]

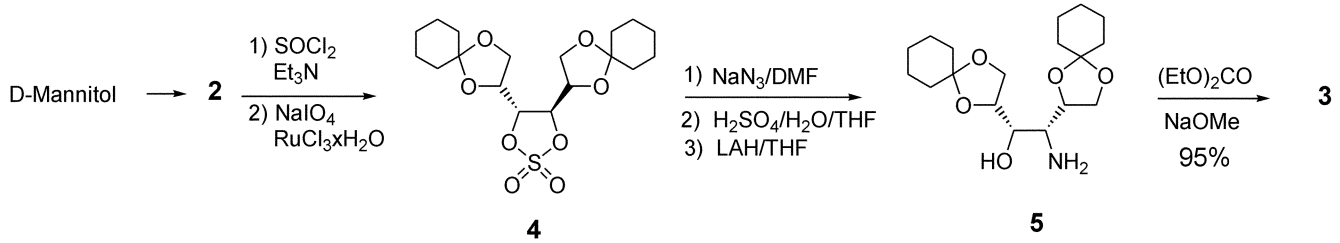
In most cases (entries a1-c1 except c2), the cyclohexylidene auxiliary **6** gave higher diastereomeric excess than the isopropylidene auxiliary derived from **1** (the %de in parenthesis indicates the %de from the isopropylidene auxiliary). The diasteromeric ratio was easily identified by the integration of benzyl (entries a1, b1, b2, c2) and allyl (entries a2, c1) protons in ^{1}H NMR chemical shift as we seen in previous results. Cyclohexylidene substituent in auxiliary

Table 1. N-Acylated derivatives **6a-c** from the chiral auxiliary **3**



3 **6**

Entry	R	Reaction time	Yield %	$[\alpha]_D^{25}$ (c, $CHCl_3$)
a	CH_3	30 min	92.2	+35.3 (0.6)
b	$PhCH_2$	30 min	95.6	+33.3 (1.2)
c	allyl	30 min	85.0	+32.9 (1.1)



4 **5**

Scheme 1

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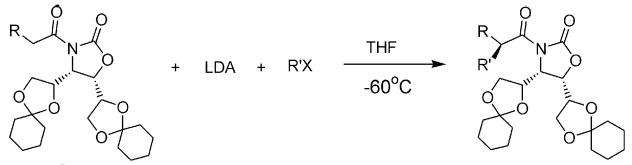
Table 2. Asymmetric alkylation of *N*-acyl derivatives **6**



6 **7**

Entry	R	R'X	Rxn (h)	% yield[a]	% de[b]	$[\alpha]_D$
a1	CH_3	$PhCH_2Br$	5	91.7	>99 (94.0)	-20.6 (c 1.1, $CHCl_3$)
a2	CH_3	allyl bromide	9	36.4	>99 (91.6)	-31.2 (c 1.7, $CHCl_3$)
b1	$PhCH_2$	MeI	9	45.6	96.9(92.6)	-53.8 (c 1.9, $CHCl_3$)
b2	$PhCH_2$	allyl bromide	6	55.6	96.8(91.6)	-75.4 (c=1.1, $CHCl_3$)
c1	allyl	MeI	20	46.3	97.1 (92.9)	-52.2 (c=0.9, $CHCl_3$)
c2	allyl	$PhCH_2Br$	20	52.1	89.4 (96.7)	-29.3 (c=1.1, $CHCl_3$)

[a]Isolated yield. [b]The %de in parenthesis indicates the yield from the isopropylidene auxiliary **1**.

shows bulkier and more ligid character in space than isopropylidene derivative, and gives better selectivity in alkylation.

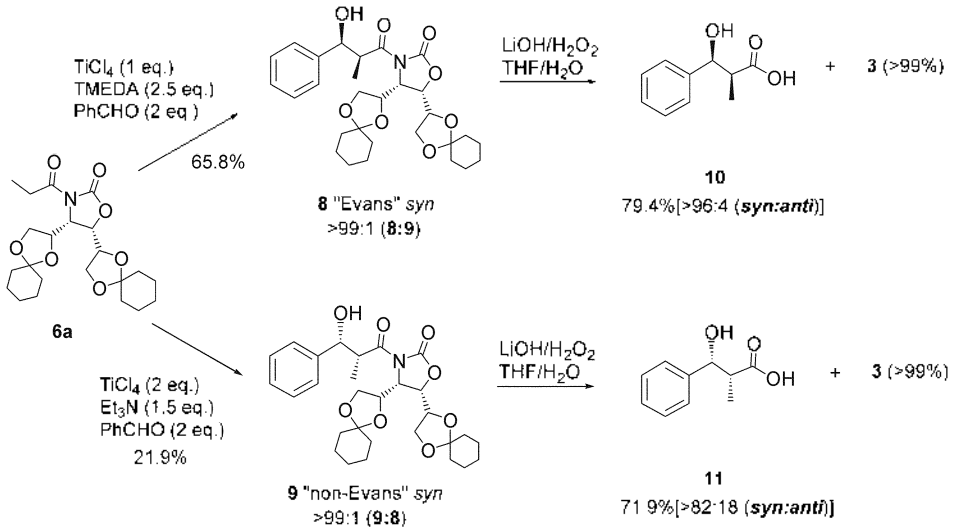
We also applied this cyclohexylidene auxiliary **6** to the aldol reaction with benzaldehyde. "Evans" *syn* product **8** was obtained by using 1 equiv of $TiCl_4$ *via* non-chelated *Z*-enolate, however, "non-Evans" *syn* aldol product **9** was produced by using 2 equiv of $TiCl_4$ *via* chelated *Z*-enolate (Scheme 2).[8] Selectivity employing 1 equiv of $TiCl_4$ was > 99 : 1 Evans *syn* **8** : non-Evans *syn* **9**. The absolute configuration of **8** and the selectivity of *syn:anti* ratio were determined after hydrolytic cleavage of **8** to **10** by using LiOOH.[9] The hydrolysis gave 79.4% yield of (2*S*,3*S*)-acid **10** $[[\alpha]_D^{25}$ = -24.4 (c=0.9, CH_2Cl_2), lit. $[\alpha]_D^{22}$ = -26.4 (c = 1.04, CH_2Cl_2)][10] with quantitative recovery (>99%) of auxiliary **3**. The ^1H NMR of the product **10** indicated the selectivity > 96 : 4 for *syn:anti* ratio similar to previous results.[1]

In the same way, we found that the selectivity for non-Evans *syn* **9** : Evans *syn* **8** employing 2 equiv of $TiCl_4$ was >99 : 1 and for *syn:anti* of **11** after hydrolysis was >82 : 18. No products from endocyclic cleavage in hydrolysis reaction were observed in both cases.[11]

In conclusion, the cyclohexylidene chiral auxiliary **3** derived from D-mannitol shows better selectivity in asymmetric alkylations and comparable selectivity in aldol reactions compare with the isopropylidene derivative **1**.

Experimental Section

All chemicals used were purchased from commercial sources and used as received unless otherwise stated. NMR spectra were recorded at Varian Gemini-400 MHz FT-NMR for ^1H and 100 MHz for ^{13}C, with the chemical shifts (δ) reported in parts per million (ppm) relative to TMS and the coupling constants (J) quoted in Hz. $CDCl_3$ was used as a solvent and an internal standard. Infrared spectra were recorded on a Shimadzu IR-435 spectrometer. GC-MS analyses were performed using a HP-5890/JMS-AM 150, JEOL. Flash chromatography was carried out using silica gel Merck 60 (230-400 mesh). Thin-layer chromatography (TLC) was performed on DC-Plastikfolien 60, F_{254} (Merck, layer thickness 0.2 mm) plastic-backed silica gel plates with visualization by UV light (254 nm) or by treatment with *p*-anisaldehyde. Melting points were measured on a MEL-TEMP II apparatus and were uncorrected.



Scheme 2

(4*S*,5*R*)-4,5-Bis-(2,2-dicyclohexyl-1,3-dioxolan-4-yl)-oxazolidin-2-one (3). To a solution of 3-amino-3-deoxy-1,2:5,6-di-*O*-isopropylidene-D-altritol (**5**) (0.63 g, 1.85 mmol) in diethyl carbonate (3.15 mL) under nitrogen atmosphere was added sodium methoxide (0.11 mL of 25% solution in MeOH, 0.46 mmol) and heated for 3 h at 70-80 °C. Diethyl carbonate was removed by evaporation and the residual solid was washed with hexane, recrystallized by MeOH to give the white solid **3** (0.64 g, 95%). R_f 0.47 (MeOH : $CHCl_3$ = 1 : 9); *mp* 170-172 °C; $[\alpha]_D^{20}$ -35.8 (*c* 1.0, $CHCl_3$); ν_{max} (film)/cm^{-1} 3288, 2933, 2850, 1757, 1738, 1094; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.40-1.66 (20H, m), 3.79 (1H, dd, *J* 9.3, 4.6 Hz), 3.83-3.88 (1H, m), 3.95-3.99 (1H, m), 4.13-4.19 (2H, m), 4.33-4.39 (2H, m), 4.40-4.46 (1H, m), 5.43 (1H, br s, NH); ^{13}C NMR (100 MHz, $CDCl_3$) 158.1, 111.2, 110.8, 78.1, 73.9, 71.9, 67.7, 67.1, 58.3, 36.9, 36.7, 34.9, 34.6, 25.4, 25.3, 24.4 (×2), 24.2, 24.1.

Typical Procedure for the Preparation of *N*-Acyloxazolidin-2-ones, 6a-c. To a solution of oxazolidinone **3** (1.00 g, 2.72 mmol) in THF (100 mL) under nitrogen atmosphere was added *n*-BuLi (2.55 mL of 1.6 M solution in Hexane, 4.08 mmol) at -60 °C and stirred for 30 min. Propionyl chloride (0.47 mL, 5.44 mmol) was added to this reaction mixture at -40 °C and stirred for 30 min. The reaction was quenched by the addition of water at 0 °C. The organic product was extracted with ethyl acetate, washed with brine, dried, concentrated and chromatographed (EtOAc : Hex = 1 : 4) to give the liquid **6a** (1.06 g, 92.2%).

(4*S*,5*R*)-3-(1-Oxopropyl)-4,5-bis-(2,2-dicyclohexyl-1,3-dioxolan-4-yl)-oxazolidin-2-one (6a). R_f 0.42 (EtOAc : Hex = 1 : 4); $[\alpha]_D^{20}$ +35.3 (*c* 0.6, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.18 (3H, t, *J* 7.3 Hz), 1.29-1.58 (20H, m), 3.92-4.06 (3H, m), 4.18 (1H, dd, *J* 9.2, 5.8 Hz), 4.31 (1H, dd, *J* 9.8, 7.0 Hz), 4.58-4.68 (2H, m), 4.73 (1H, d, *J* 6.7 Hz).

(4*S*,5*R*)-3-(3-Phenyl-1-oxopropyl)-4,5-bis-(2,2-dicyclohexyl-1,3-dioxolan-4-yl)-oxazolidin-2-one (6b). 95.6%; R_f 0.45 (EtOAc : Hex = 1 : 4); $[\alpha]_D^{20}$ +33.3 (*c* 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29-1.67 (20H, m), 2.94-3.11 (2H, m), 3.20-3.29 (2H, m), 3.87-4.05 (3H, m), 4.10-4.29 (2H, m), 4.56-4.65 (2H, m), 4.70 (1H, d, *J* 6.7 Hz), 7.15-7.32 (5H, m).

(4*S*,5*R*)-3-(1-Oxo-4-pentenyl)-4,5-bis-(2,2-dicyclohexyl-1,3-dioxolan-4-yl)-oxazolidin-2-one (6c). 85.0%; R_f 0.52 (EtOAc : Hex = 1 : 4); $[\alpha]_D^{20}$ +32.9 (*c* 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.39-1.72 (20H, m), 2.37-2.49 (2H, m), 2.96-3.07 (2H, m), 3.91-4.13 (3H, m), 4.18 (1H, dd, *J* 7.5, 3.4 Hz), 4.30 (1H, dd, *J* 9.8, 8.4 Hz), 4.58-4.69 (2H, m), 4.72 (1H, d, *J* 6.7 Hz), 4.99-5.14 (2H, m), 5.79-5.88 (1H, m).

Typical Procedure for the Preparation of Alkylated Products, 7a1-7c2. To a solution of diisopropyl amine (0.05 mL, 0.35 mmol) in THF (3 mL) at -20 °C under nitrogen atmosphere was added *n*-BuLi (0.22 mL of 1.6 M solution in Hexane, 0.35 mmol) and stirred for 30 min. *N*-Propionyl oxazolidinone **6a** (0.10 g, 0.24 mmol) in THF (2 mL) was added to this reaction mixture at -60 °C and stirred for 30 min. Benzyl bromide (0.11 mL, 0.94 mmol) was added to this reaction mixture at -40 °C and stirred for 2 h. The reaction was quenched by the addition of water at 0 °C. The organic product was extracted with ethyl acetate, washed with brine, dried, concentrated, and chromatographed (EtOAc : Hex = 1 : 4) to give the liquid **7a1** (0.11 g, 91.7%).

(4*S*,5*R*,2'*R*)-3-(2-Methyl-3-pheny-l-oxopropyl)-4,5-bis-(2,2-dicyclohexyl-1,3-dioxolan-4-yl)-oxazolidin-2-one (7a1). R_f 0.45 (EtOAc : Hex = 1 : 4); $[\alpha]_D^{20}$ +20.6 (*c* 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.10 (3H, d, *J* 6.8 Hz, α-methyl), 1.17-1.55 (20H, m), 2.50 (1H, dd, *J* 13.3, 8.4 Hz, benzyl proton), 3.18 (1H, dd, *J* 13.2, 6.2 Hz, benzyl proton), 3.47 (1H, dd, *J* 8.9, 7.3 Hz), 3.87 (1H, dd, *J* 9.0, 6.3 Hz), 3.91-3.98 (2H, m), 4.11 (1H, dd, *J* 9.1, 5.8 Hz), 4.25 (1H, dd, *J* 9.7, 6.9 Hz), 4.47 (1H, t, *J* 6.7 Hz), 4.57 (1H, m, α-proton), 4.66 (1H, d, *J* 7.0 Hz), 7.13 (1H, m), 7.19-7.21 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.5 (*C*=*O*), 151.9 (C=*O*), 138.2, 128.3 (x2), 127.3 (x2), 125.3, 109.8, 108.9, 76.1, 72.7, 71.3, 66.0, 64.5, 54.4, 28.6, 38.5, 35.9, 34.3, 34.0, 33.5, 24.0, 23.9, 23.0, 22.9, 22.8, 22.7, 15.4.

(4*S*,5*R*,2'*R*)-3-(2-Methyl-1-oxo-4-pentenyl)-4,5-bis-(2,2-dicyclohexyl-1,3-dioxolan-4-yl)-oxazolidin-2-one (7a2). 36.4%; R_f 0.48 (EtOAc : Hex = 1 : 4); $[\alpha]_D^{20}$ +31.2 (*c* 1.7, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.13 (3H, d, *J* 6.8 Hz, α-methyl), 1.37-1.63 (20H, m), 2.19 (1H, m, allyl proton), 2.59 (1H, m, allyl proton), 3.77 (1H, quintet, *J* 6.7 Hz), 3.84 (1H, dd, *J* 8.9, 6.7 Hz), 3.99-4.05 (2H, m), 4.18 (1H, dd, *J* 9.1, 5.9 Hz), 4.31 (1H, dd, *J* 9.7, 6.9 Hz), 4.60 (1H, t, *J* 6.6 Hz), 4.65 (1H, m), 4.73 (1H, d, *J* 6.9 Hz), 5.06 (1H, m, =CH *trans*), 5.12 (1H, s, =CH *cis*), 5.80 (1H, m, =CH *internal*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.7 (*C*=*O*), 152.9 (C=*O*), 135.3, 117.2 110.8, 110.1, 77.1, 73.8, 72.3, 67.1, 65.6, 55.8, 37.8, 37.1, 37.0, 35.5, 34.8, 34.6, 25.1, 25.0, 24.1, 23.9, 23.8 (x2), 16.4.

(4*S*,5*R*,2'*S*)-3-(2-Methyl-3-pheny-l-oxopropyl)-4,5-bis-(2,2-dicyclohexyl-1,3-dioxolan-4-yl)-oxazolidin-2-one (7b1). 45.6%; R_f 0.52 (EtOAc : Hex = 1 : 4); $[\alpha]_D^{20}$ +53.8 (*c* 1.9, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.27 (3H, d, *J* 6.8 Hz, α-methyl), 1.36-1.63 (20H, m), 2.72 (1H, dd, *J* 13.3, 7.0 Hz, benzyl proton), 2.93 (1H, dd, *J* 13.4, 8.2 Hz, benzyl proton), 3.87 (2H, dd, *J* 9.3, 6.5 Hz), 3.94 dd, *J* 9.0, 3.4 Hz), 4.00 (1H, dd, *J* 9.0, 6.4 Hz), 4.08-4.14 (2H, m), 4.52-4.57 (3H, m), 7.17-7.28 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.8 (*C*=*O*), 152.9 (C=*O*), 139.1, 129.1 (x2), 128.4 (x2), 126.4, 110.8, 110.1, 77.0, 73.8, 72.2, 67.0, 65.7, 55.8, 40.1, 38.9, 36.9, 35.4, 34.7, 34.5, 25.0, 24.9, 24.0, 23.9, 23.8 (x2), 17.6.

(4*S*,5*R*,2'*S*)-3-(2-Benzyl-l-oxo-4-pentenyl)-4,5-bis-(2,2-dicyclohexyl-1,3-dioxolan-4-yl)-oxazolidin-2-one (7b2). 55.6%; R_f 0.53 (EtOAc : Hex = 1 : 4); $[\alpha]_D^{20}$ +75.4 (*c* 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.42-1.60 (20H, m), 2.35 (1H, m, allyl proton), 2.60 (1H, m, allyl proton), 2.76 (1H, dd, *J* 13.0, 10.0 Hz, benzyl proton), 2.87 (1H, dd, *J* 13.0, 6.1 Hz, benzyl proton), 3.47 (1H, dd, *J* 9.8, 6.8 Hz), 3.76 (1H, br t, *J* 7.6 Hz), 3.85 (1H, dd, *J* 9.1, 3.4 Hz), 3.97 (1H, dd, *J* 8.9, 6.5 Hz), 4.08 (1H, dd, *J* 9.1, 5.9 Hz), 4.31 (2H, m), 4.46 (2H, m), 5.04 (1H, br d, *J* 10.3 Hz, =CH *trans*), 5.14 (1H, d, *J* 16.4 Hz, =CH *cis*), 5.84 (1H, m, =CH *internal*), 7.15 (2H, m), 7.19-7.27 (3H, m).

(4*S*,5*R*,2'*S*)-3-(2-Methyl-1-oxo-4-pentenyl)-4,5-bis-(2,2-dicyclohexyl-1,3-dioxolan-4-yl)-oxazolidin-2-one (7c1).

46.3%; R_f 0.59 (EtOAc : Hex = 1 : 4); $[\alpha]_D^{20}$ +52.2 (*c* 0.9, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25 (3H, d, *J* 6.6 Hz, α-methyl), 1.37-1.59 (20H, m), 2.17 (1H, m, allyl proton), 2.40 (1H, m, allyl proton), 3.79 (1H, m), 3.87 (1H, dd, *J* 9.0, 6.5 Hz), 4.03 (2H, m), 4.18 (1H, dd, *J* 9.2, 5.9 Hz), 4.28 (1H, dd, *J* 9.8, 6.9 Hz), 4.58-4.66 (2H, m), 4.73 (1H, d, *J* 6.9 Hz), 5.01 (1H, m, =CH *trans*), 5.07 (1H, s, =CH *cis*), 5.75 (1H, m, =CH *internal*).

(4*S*,5*R*,2'*R*)-3-(2-Benzyl-1-oxo-4-pentenyl)-4,5-bis-(2,2-dicyclohexyl-1,3-dioxolan-4-yl)-oxazolidin-2-one (7c2). 52.1%; R_f 0.56 (EtOAc : Hex = 1 : 4); $[\alpha]_D^{20}$ +29.3 (*c* 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.52-1.59 (20H, m), 2.24 (1H, m, allyl proton), 2.34 (1H, m, allyl proton), 2.71 (1H, dd, *J* 13.5, 7.2 Hz, benzyl proton), 3.16 (1H, dd, *J* 13.5, 7.5 Hz, benzyl proton), 3.43 (1H, dd, *J* 8.8, 7.8 Hz), 3.91 (1H, dd, *J* 9.0, 6.1 Hz), 4.02 (1H, dd, *J* 9.1, 3.5 Hz), 4.16 (1H, dd, *J* 9.1, 5.9 Hz), 4.20-4.25 (2H, m), 4.49 (1H, br t, *J* 7.2 Hz), 4.60 (1H, m), 4.67 (1H, dd, *J* 7.3, 0.9 Hz), 4.99 (1H, s, =CH *cis*), 5.03 (1H, d, *J* 5.9 Hz, =CH *trans*), 5.73 (1H, m, =CH *internal*), 7.18 (1H, m), 7.23-7.27 (4H, m).

(4*S*,5*R*,2'*S*,3'*S*)-3-(3-Hydroxy-2-methyl-3-pheny-l-oxopropyl)-4,5-bis-(2,2-dicyclohexyl-1,3-dioxolan-4-yl)-oxazolidin-2-one (8). To a solution of (4*S*,5*R*)-3-(1-oxopropyl)-4,5-bis-(2,2-dicyclohexyl-1,3-dioxolan-4-yl)-oxazolidin-2-one (**6a**) (0.15 g, 0.35 mmol) in CH_2Cl_2 (5 mL) under nitrogen atmosphere was added $TiCl_4$ (0.39 mL in 1.0 M solution in CH_2Cl_2, 0.39 mmol) at -60 °C and stirred for 5 min. TMEDA (0.13 mL, 0.89 mmol) was added to this reaction mixture at -60 °C and stirred for 30 min. Benzaldehyde (0.07 mL, 0.71 mmol) was added to this reaction mixture at -60 °C and stirred for 2 h. The reaction was quenched by the addition of 50% aqueous NH_4Cl at 0 °C. The organic product was extracted with ethyl acetate, washed with brine, dried and concentrated to give the product **8** (53 mg, 65.8%). R_f 0.31 (EtOAc : Hex = 1 : 2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.27 (3H, d, *J* 6.9 Hz, α-methyl), 1.34-1.57 (20H, m), 3.33 (1H, d, , *J* 3.0 Hz), 3.83-3.93 (3H, m), 4.01-4.14 (3H, m), 4.92 (1H, dd, *J* 5.0, 2.8 Hz), 7.24-7.32 (5H, m).

(4*S*,5*R*,2'*R*,3'*R*)-3-(3-Hydroxy-2-methyl-3-pheny-l-oxopropyl)-4,5-bis-(2,2-dicyclohexyl-1,3-dioxolan-4-yl)-oxazolidin-2-one (9). To a solution of (4*S*,5*R*)-3-(1-oxopropyl)-4,5-bis-(2,2-dimethyl-1,3-dioxolan-4-yl)-oxazolidin-2-one (**6a**) (0.15 g, 0.35 mmol) in CH_2Cl_2 (7 mL) under nitrogen atmosphere was added $TiCl_4$ (0.71 mL in 1.0 M solution in CH_2Cl_2, 0.71 mmol) at -60 °C and stirred for 5 min. Et_3N (0.07 mL, 0.53 mmol) was added to this reaction mixture at -60 °C and stirred for 30 min. Benzaldehyde (0.07 mL, 0.71 mmol) was added to this reaction mixture at -60 °C and stirred for 2 h. The reaction was quenched by the addition of water at 0 °C. The organic product was extracted with ethyl acetate, washed with brine, dried and concentrated to give the product **9** (41 mg, 21.9%). R_f 0.43 (EtOAc : Hex = 1 : 2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.96 (3H, d, *J* 6.9 Hz, α-methyl), 1.37-1.60 (20H, m), 3.51 (1H, d, *J* 4.7 Hz), 3.95-4.12 (4H, m), 4.15-4.21 (2H, m), 4.32-4.37 (1H, m), 4.67-4.70 (2H, m), 4.88 (1H, dd, *J* 7.1, 1.1 Hz), 7.24-7.37 (3H, m), 7.46 (2H, d, *J* 6.9 Hz).

***syn*-(2*S*,3*S*)- and *anti*-(2*R*,3*S*)-3-Hydroxy-2-methyl-3-phenylpropanoic acid (10).** To a solution of (4*S*,5*R*,2'*S*,3'*S*)-3-(3-hydroxy-2-methyl-3-pheny-l-oxopropyl)-4,5-bis-(2,2-dicyclohexyl-1,3-dioxolan-4-yl)-oxazolidin-2-one (**8**) (100 mg, 0.19 mmol) in THF (2.9 mL) and H_2O (0.95 mL) was added 30% H_2O_2 (1.07 g, 0.94 mmol) and $LiOH{\cdot}H_2O$ (16 mg, 0.38 mmol) at 0 °C and stirred for 30 min. Solid sodium sulfite and saturated $NaHCO_3$ solution were added to this reaction mixture until pH 10. THF in the reaction mixture was evaporated. The mixture was diluted with water (2.5 mL), extracted with CH_2Cl_2, washed with brine, dried and concentrated to give the auxiliary **3** (70 mg, 100%). The water layer was acidified with the addition of 3 N HCl solution until pH 2, and extracted with EtOAc, washed with brine, dried, concentrated and chromatographed to give the acids **10** (27 mg, 79.4%). R_f 0.19 (EtOAc : Hex = 1 : 2); $[\alpha]_D^{25}$ -24.4 (*c* 0.9, CH_2Cl_2); [lit.[10] $[\alpha]_D^{22}$ = -26.4 (*c* 1.04, CH_2Cl_2)]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.14 (3H, d, *J* 9.0 Hz, α-methyl), 2.83 (1H, m, α-H), 4.75 (0.01H, d, *J* 8.8 Hz, *anti* C*H*OH), 5.18 (0.99H, d, *J* 4.0 Hz, *syn* C*H*OH), 5.42 (2H, br s, OH and CO_2H), 7.35 (5H, s, aromatic). ^{1}H NMR integration afforded a ratio *syn*:*anti* = 96 : 4. The data were consistent with those reported in the literature.[10,12]

***syn*-(2*R*,3*R*)- and *anti*-(2*S*,3*R*)-3-Hydroxy-2-methyl-3-phenylpropanoic acid (11).** Prepared from **9** (41 mg, 0.08 mmol) as same as above procedure and gave the acids **11** (10 mg, 71.9%) and the auxiliary **3** (28 mg, 100%). R_f 0.19 (EtOAc : Hex = 1 : 2); $[\alpha]_D^{25}$ +26.5 (*c* 0.35, CH_2Cl_2); [lit.[10] $[\alpha]_D^{22}$ = -26.4 (*c* 1.04, CH_2Cl_2)] for the enantiomer **10**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.75 (0.04H, d, *J* 8.8 Hz, *anti* C*H*OH), 5.18 (0.96H, d, *J* 4.0 Hz, *syn* C*H*OH). ^{1}H NMR integration afforded a ratio *syn*:*anti* = 82 : 18.

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