Introduction of a New Chiral Oxazolidin-2-one Derived from D-Mannitol and Its Applications as a Chiral Auxiliary

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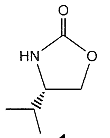
Chiral oxazolidin-2-one is easily prepared from D-mannitol and demonstrated to undergo highly diastereoselective alkylation reactions *via* lithium imide *Z*-enolates of its N-acyl derivatives to afford α-branched products. Evans *syn* and non-Evans *syn* aldol products were also selectively obtained using this new auxiliary in high diastereomeric purity by simply changing the stoichiometry of $TiCl_4$ and the nature of the amine base. Also, this new auxiliary is employed in diastereoselective Staudinger-type β-lactam syntheses. Using 2-chloro-1-methylpyridinium iodide as the dehydrating agent, the reaction of auxiliary tethered acetic acid with *trans* imines gave the desired β-lactams with *cis*-selectivity.

Keywords : Oxazolidin-2-one, D-Mannitol, Alkylation, Aldol reaction, β-Lactam.

Introduction

The use of enantiomerically pure oxazolidin-2-one derivative **1** as a chiral auxiliary in asymmetric aldol condensations was first reported by Evans *et al.* in 1981[1] and the enormous utility of this and related oxazolidinones has been amply demonstrated.[2]



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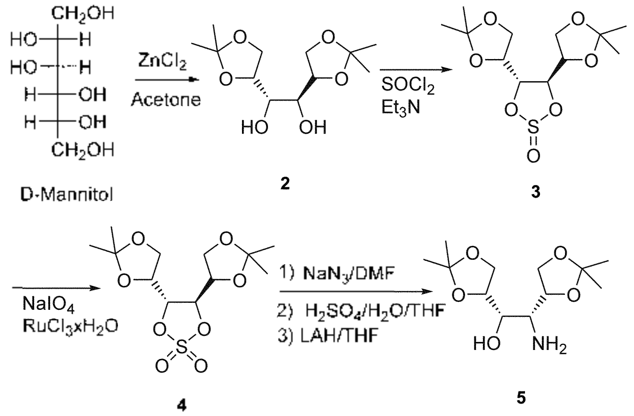
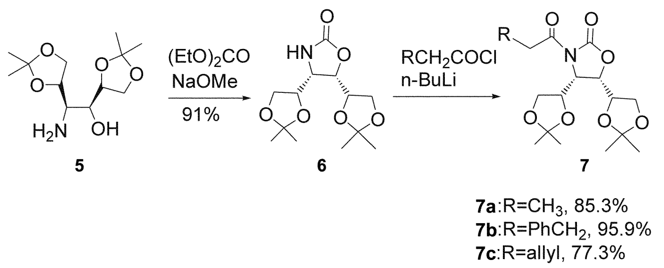
Alkylation, acylation, aldol reaction, Diels-Alder reaction, halogenation, amination, oxygenation, sulfenylation and β-lactam synthesis are the typical known applications of chiral oxazolidinone auxiliaries. Unfortunately, their broader application in asymmetric synthesis is seriously hampered by the lack of facile, safe and low-cost access to the chiral auxiliaries themselves. To circumvent this problem, many efforts have been made since the late 1980s.[3] Many sources for oxazolidin-2-one structure were known, however, preparative access to chiral auxiliary is quite difficult because enantiomerically pure amino alcohols are required.[4] D-Mannitol is a known source for chiral amino alcohol.[5] Sharpless *et al.*[6] reported the cyclic sulfates methodology for the improved synthesis of chiral amino alcohol, especially with acid-sensitive functionalities such as acetonide and silyloxy groups. 1,2:5,6-Di-*O*-isopropylidene-D-mannitol (**2**) was treated with thionyl chloride in the presence of triethyl amine for the quantitative formation of the cyclic sulfite (**3**), which was oxidized with catalytic RuO_4 to yield the cyclic sulfate (**4**). Subsequently nucleophilic opening of the cyclic sulfate with NaN_3, hydrolysis with sulfuric acid and reduction with $LiAlH_4$ produced 3-amino-3-deoxy-1,2:5,6-di-*O*-isopropylidene-D-altritol (**5**). We report herein the diastereoselective alkylation, aldol condensation and β-lactam synthesis using a new chiral oxazolidin-2-one derived from a cheap D-mannitol.



Results and Discussion

3-Amino-3-deoxy-1,2:5,6-di-*O*-isopropylidene-D-altritol (**5**) obtained from D-mannitol served as a chiral amino alcohol for the synthesis of (4*S*,5*R*)-4,5-bis-(2,2-dimethyl-1,3-dioxolan-4-yl)-oxazolidin-2-one (**6**). DMAP-catalyzed reaction[7] of amino alcohol **5** with di-*tert*-butyl dicarbonate, $(Boc)_2O$, for the oxazolidinone synthesis gave only 41.2% yield. The reaction yield was improved to 91% by using diethyl carbonate with sodium methoxide.[8] The *N*-acylated derivatives **7a-c** were easily prepared in high yield by reaction of auxiliary **6** with acyl chlorides **a-c** using *n*-butyllithium in THF at -60 °C (Scheme 1). The crystalline *N*-acylated substrates were recrystalized from hexane.

The lithium enolate of the *N*-acyl derivative **7a** was formed in THF by addition at -60 °C of lithium diisopropylamide, LDA, (1.5 equiv solution in THF). After benzyl bromide was added, the mixture was stirred for 2 h at -40 °C. The reaction was quenched by addition of water at -0 °C and the crude product **8A** was extracted with ethyl acetate. The non-crystalline product **8A** was purified by flash column chromato-



Scheme 1

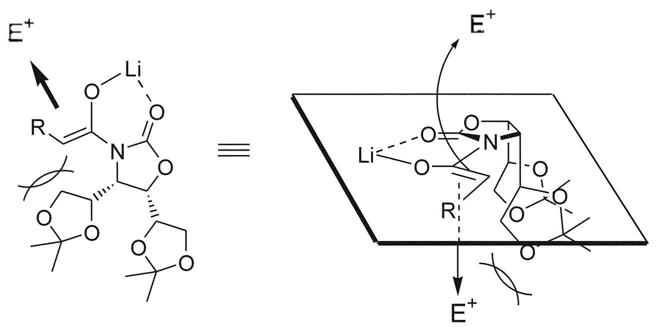
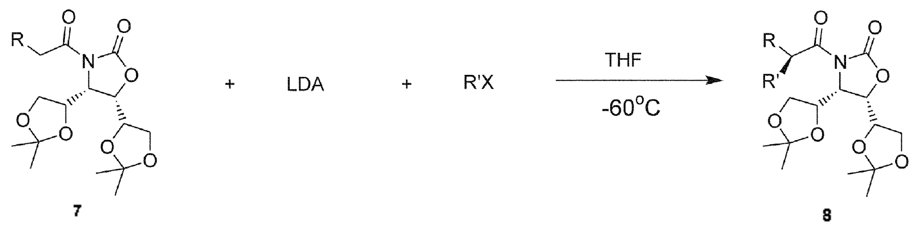


Figure 1

graphy on silica gel and obtained in 95.5% yield with a diastereomeric excess of 94.0% (Scheme 2). The absolute configuration of **8A** was determined by the reduction of **8A** to the known alcohol, as described below.

The enolization of imide **7** with LDA is known to generate a *Z*-enolate exclusively,[9] because the corresponding *E*-enolate would receive a severe nonbonded repulsion between R and the dioxolane moiety. The lithium enolate of **7** comprises two distinct π-faces (*re* and *si* face) because the lithium ion coordinates to both the *N*-acyl and the oxazolidinone carbonyl oxygens. The *si*-face is difficult to access for electrophiles because of the steric hindrance of the dioxolane substituent as shown in Figure 1. The result is well matched with this argument.

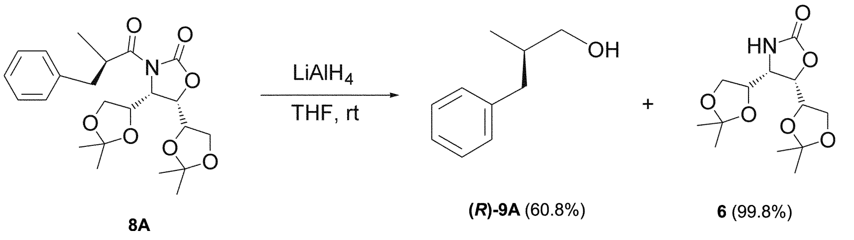
The reaction product of the lithium enolate of **7a** with benzyl bromide (entry A) showed the ^{1}H NMR chemical shift at 4.63 (1H, m, α-proton), 1.10 (3H, d, J = 6.7 Hz, α-methyl), 2.56 (1H, dd, J = 8.7 and 13.2 Hz, benzyl proton) and 3.28 (1H, dd, J = 5.8 and 13.2 Hz, benzyl proton). To ensure the diastereoselectivity of D-mannitol-based oxazolidinone, the methylation of the lithium enolate **7b** (entry B) was examined and showed the ^{1}H NMR chemical shift at 4.52 (1H, m, α-proton), 1.28 (3H, d, J = 6.7 Hz, α-methyl), 2.93 (1H, dd, J = 8.3 and 13.2 Hz, benzyl proton) and 2.73 (1H, dd, J = 7.0 and 13.3 Hz, benzyl proton). The diasteromeric ratio was easily identified by the integration of benzyl proton in ^{1}H NMR chemical shift. The integration of the product **8A** containing the trace amount of peaks at 2.93 and 2.73, which was compared with the peaks at 2.56 and 3.28, showed the diastereomeric excess of 94%. The absolute configuration of the stereogenic centers in **8A** was assigned after removal of the chiral auxiliary. Reduction of **8A** using $LiAlH_4$ in THF at rt generated 2-benzyl-1-propanol (**9A**) in 60.8% yield after column chromatography (Scheme 3). Comparison of the specific rotation $[\alpha]_D^{25}$ = +14.1 (c = 1.05, C_6H_6) of the alcohol **9A** thus obtained, with the literature value[10] for $[\alpha]_D^{25}$ = +11.1 (c = 1.25, C_6H_6) established its absolute configuration as (*R*). The chiral auxiliary **6** was recovered nearly quantitatively in this reduction (99.8%). The enantiomer **9B** was also obtained in same manner from **8B** and showed the absolute configuration as (*S*) [$[\alpha]_D^{25}$ = -12.1 (c = 1.05, C_6H_6), lit. $[\alpha]_D^{24}$ = -11.1 (c = 4.6, C_6H_6)].[11] The other examples (Entries C-D, E-F), also, easily showed the diastereomeric excess in same manner by using integration of ^{1}H NMR of structure **8** even without the reduction to **9**. These results indicate that the new chiral oxazolidin-2-one derived from D-mannitol showed to be a very effective chiral auxiliary in asymmetric alkylation reactions through



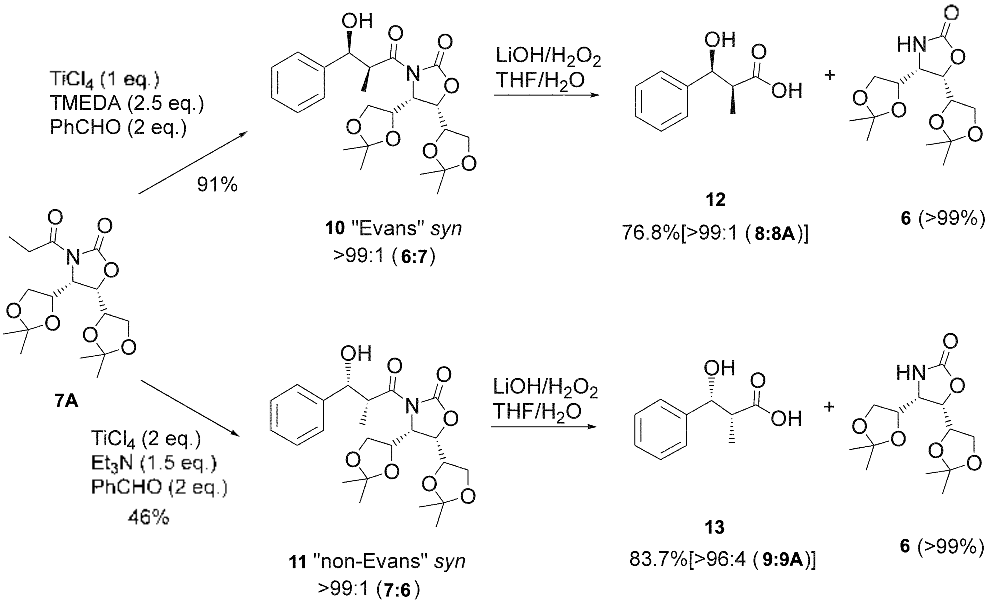
Entry	R	R'X	Rxn (h)	% yield[1]	% de[2]	[α]D
A	CH_3	$PhCH_2Br$	2	95.5	94.0	+24.3 (c=1.7, $CHCl_3$)
B	$PhCH_2$	MeI	4	79.5	92.6	+72.8 (c=1.4, $CHCl_3$)
C	CH_3	allyl bromide	2	89.5	91.6	+17.1 (c=0.9, $CHCl_3$)
D	allyl	MeI	4	86.9	92.9	+75.8 (c=0.4, $CHCl_3$)
E	$PhCH_2$	allyl bromide	20	63.9	91.6	+89.5 (c=1.8, $CHCl_3$)
F	allyl	$PhCH_2Br$	20	70.1	96.7	+35.6 (c=1.4, $CHCl_3$)

[1]Isolated yield. [2]Determined by 400MHz ^{1}H NMR.

Scheme 2



Scheme 3



Scheme 4

Z-enolate and *re*-face selectivity.

The chiral auxiliary **7a** was also employed in asymmetric aldol reaction as chlorotitanium enolate.[12] The use of titanium (IV) enolates of *N*-acyloxazolidinethions has been reported for the preparation of either the "Evans" or "non-Evans" *syn* aldol products in high diastereomeric purity by simply changing the stoichiometry of the Lewis acid and the nature of the amine base.[13] We first examined the titanium enolate of the Evans acyloxazolidinone by using $TiCl_4$ (1 equiv), TMEDA (2.5 equiv) and benzaldehyde (2 equiv), and found the Evans *syn* aldol product **10** *via* non-chelated *Z*-enolate **10A** in 91% yield (Scheme 4). Selectivity was > 99 : 1 Evans *syn* **10** : non-Evans *syn* **11**. The absolute configuration of **10** and the selectivity of *syn*:*anti* ratio were determined after hydrolytic cleavage of **10** to **12** by using LiOOH.[14] The hydrolysis gave 76.8% yield of (2*S*,3*S*)-acid **12** $[[\alpha]_D^{25}$ = -24.4 (c = 0.9, CH_2Cl_2), lit. $[\alpha]_D^{22}$ = -26.4 (c = 1.04, CH_2Cl_2)][15] with quantitative recovery (> 99%) of auxiliary **6**. The ^1H NMR of the product **12** indicated the selectivity > 99 : 1 for *syn* **12**:*anti* **12A** ratio (Fig. 2). The correlation between the vicinal coupling constant of the α and β protons at the *syn*/*anti* chiral centers of the aldol adducts, with relatively small α and β substituents, give small values of $^3J_{\alpha\beta}$ (3-5 Hz) for *syn* diastereomers and larger values (7-10 Hz) for *anti*, is well established.[16] The $^3J_{\alpha\beta}$ values are 4.0 Hz at 5.18 ppm and 8.8 Hz at 4.75 ppm for the diastereomers assigned as *syn* **12** (2*S*,3*S*) and *anti* **12A** (2*R*,3*S*), respectively.[17]

Experiment employing 2 equiv of $TiCl_4$ and 1.5 equiv of Et_3N gave also excellent selectivity for the non-Evans *syn* aldol product **11** *via* chelated *Z*-enolate **11A**. Selectivity is

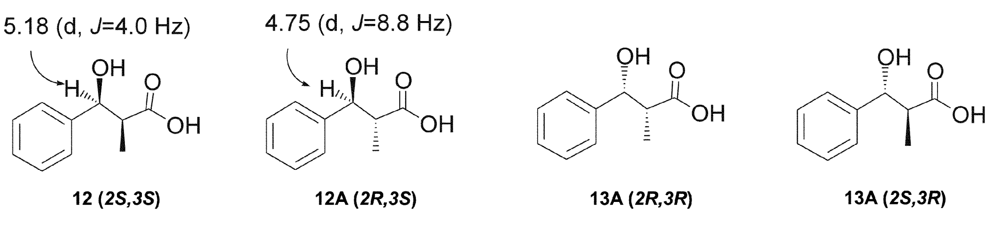
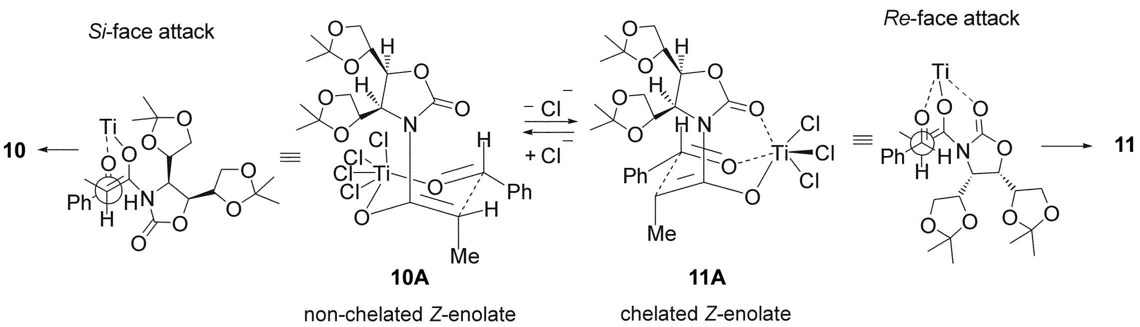
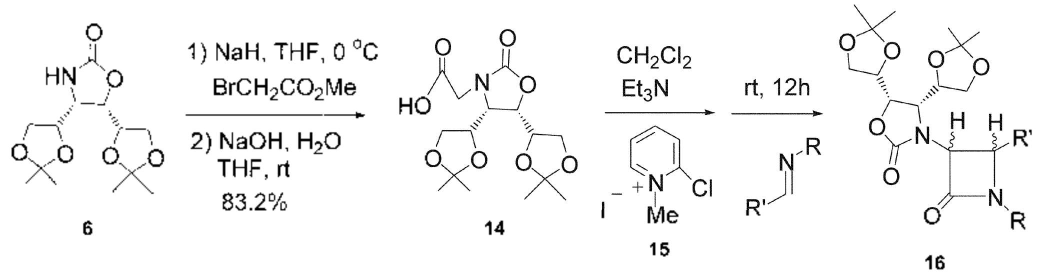


Figure 2



Scheme 5



Scheme 6

>96 : 4 for *syn* **13**:*anti* **13A** and >99 : 1 for non-Evans *syn*: Evans *syn*. No products from endocyclic cleavage in hydrolysis reaction were observed.[14] Crimmins[13] used oxazolidinethione auxiliary for the titanium enolate of asymmetric aldol reaction because the titanium prefers to coordinate to sulfur rather than oxygen.[18] Comparable high stereoselectivity was obtained in asymmetric aldol additions for non-Evans *syn* product using our new oxazolidinone auxiliary instead of oxazolidinethione. Non-Evans *syn* product was produced through *re*-face attack *via* chelated transition state **11A** resulting from abstraction of chloride ion by the second equivalent addition of $TiCl_4$, which enabled to coordinate the carbonyl oxygen of oxazolidinone ring with titanium (Scheme 5).[19]

In order to explore the utility of the new chiral oxazolidin-2-one derived from D-mannitol,[20] we applied the chiral auxiliary **6** in β-lactam ring preparation reaction. The [2+2] cycloaddition reaction of ketene to imines, known as the Staudinger reaction,[21] has acquired central importance for the asymmetric construction of the azetidinone ring, from both academic and industrial standpoints. One example is the cycloaddition reaction of Evans-Sjogren ketenes,[22] generated from chiral oxazolidinylacetic acid chlorides and triethyl amine, with achiral imines to form optically active β-lactams with high levels of asymmetric induction. Manhas[23] described that the readily available Mukaiyama reagent (2-chloro-N-methylpyridinium iodide)[24] can also function as an activating agent for the reaction between carboxylic acids and imines in the presence of triethylamine in refluxing dichloromethane to yield β-lactams in moderate yields of up to 55%.

Our new chiral auxiliary **6** was alkylated with ethyl bromoacetate using NaH in THF and hydrolyzed with NaOH in H_2O-THF to provide tethered acetic acid **14** in 83.2% yield (Scheme 6).[25] Then the acid **14** in dichloromethane was treated with Mukaiyama reagent **15** in the presence of triethyl amine at 0 °C. The resulting clear solution was subsequently allowed to react with *trans* imines at rt for 12h to give moderate yields of the desired β-lactams **16** (Table 1).

The stereochemistry of the monocyclic β-lactams **16** was identified from their ^{1}H-NMR spectra. The C-3 and C-4 protons appeared as an AB pattern in the region δ = 5-6 ppm. The coupling constant (J) of 1-2 Hz was known to

Table 1. Synthesis of β-lactams **16** by using Staudinger reaction of acid **14** with Mukaiyama reagent and trans imines

Imines	R	R'	% Yield (**16**)^a	$^ZJ_{3,4}$ (Hz)	$^EJ_{3,4}$ (Hz)	$^Z[\alpha]_D$ ($CHCl_3$)	Ratio (Z:E)
a	Ph	Ph	76.7	5.4	2.4	−38.3 (c 15.4)	1:1
b	p-MeOPh	Ph	57.7	5.2	2.1	−43.7 (c 1.00)	8:1
c	benzyl	Ph	33.3	4.6		−6.67 (c 0.35)	Z only
d	Ph	-C=CPh	32.2	5.2	2.1	+104.9 (c 0.55)	2.7:1
e	p-MeOPh	-C=CPh	42.1	5.2		+75.4 (c 1.00)	Z only
f	benzyl	-C=CPh	16.0	4.9		−35.2 (c 0.83)	Z only

^{a}Isolated yield.

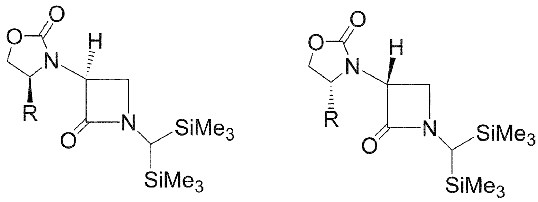


Figure 3

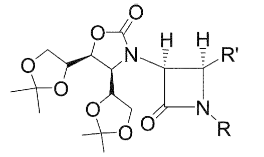


Figure 4

indicate *trans* disposition of these protons whereas a value of 5-6 Hz was an indication of their *cis* configuration.[26] The coupling constants ($J_{3,4}$) of major products in **16a-f** showed around 5 Hz and indicated the *cis* configuration, whereas the minor products showed around 2 Hz indicating *trans* isomer. This result matched with the previous reports that (*Z*)-imines lead to *trans*-azetidinones,[27] whereas (*E*)-imines favors *cis*-β-lactams.[28]

In most cases, the formation of *cis* β-lactams was favored. β-Lactams **16c, e, f** were obtained only as a *cis* isomer, however, β-lactam **16a** was obtained as 1 : 1 ratio of *cis*: *trans*. We do not exactly know the reason of this result, but the higher yield of **16a** indicates that the reaction with imine **a** possibly have the lower activation energy, which leads to the lower selectivity for the isomers. The steric difference between the imines **a** and **c** is not so big and seems not to be the reason for the selectivity.

The absolute configuration at C-3 was controlled by the orientation of the substituent in oxazolidinone group and determined by Palomo *et al.*[29] using the X-ray analysis. The stereochemistry of C-3 proton was favored from the opposite orientation of the substituent R group (Fig. 3). From this results by Palomo, the absolute structure of major products **16** was assumed as shown in Fig. 4.

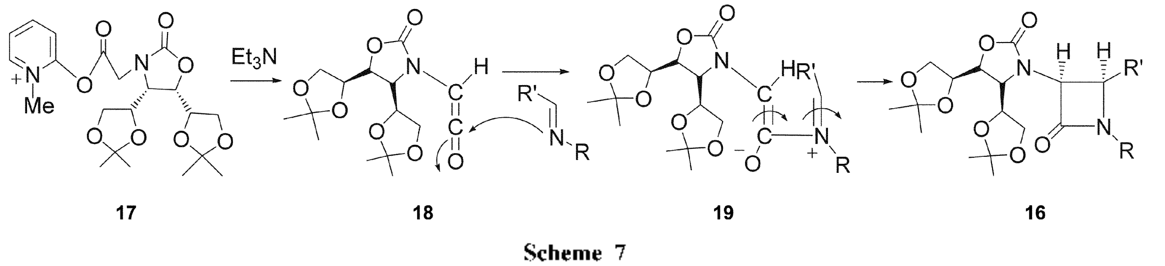
The mechanism for this Staudinger reaction can be explained as follow. Mukaiyama reagent **15** reacted with the acid **14** to give the ester **17** and served as a dehydrating agent for the *in situ* formation of the ketene **18** (Scheme 7). The non-concerted [2+2] cycloaddition[30] of ketene with *trans* imines assumed to form the zwitterionic intermediate **19** which undergoes a symmetry-allowed conrotation[31] leading to the major cycloadducts **16** in *cis* configuration.

In conclusion the results presented in this article show the chiral auxiliary (4*S*,5*R*)-4,5-bis-(2,2-dimethyl-1,3-dioxolan-4-yl)-oxazolidin-2-one (**6**) derived from D-mannitol to be a very effective chiral auxiliary in asymmetric alkylations and aldol reactions. In particular the reactions to remove the chiral auxiliary from the elaborated substrate occur very efficiently allowing effective recovery of the chiral auxiliary. Also, the auxiliary is utilized for the β-lactam synthesis and showed the *cis* selectivity in the reaction with the *trans* imines.

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 ^{1}H 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.

(4*S*,5*R*)-4,5-Bis-(2,2-dimethyl-1,3-dioxolan-4-yl)-oxazolidin-2-one (6). To a solution of 3-amino-3-deoxy-1,2:5,6-di-*O*-isopropylidene-D-altritol (**5**) (1.00 g, 3.83 mmol) in diethyl carbonate (15 mL) under nitrogen atmosphere was added sodium methoxide (0.21 mL of 25% solution in MeOH, 0.96 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 **6** (1.00 g, 91%). R_f 0.45 (MeOH : $CHCl_3$ = 1 : 9); mp 195-197 °C; $[\alpha]_D^{20}$ -24.2 (*c* 1.0, $CHCl_3$); ν_{max} (film)/cm^{-1} 3297, 2993, 1759, 1744; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.35 (6H, s, 2CH_3), 1.41 (3H, s, CH_3), 1.45 (3H, s, CH_3), 3.78 (1H, dd, J = 9.1, 4.7 Hz), 3.87 (1H, br t, J = 6.1 Hz), 4.02 (1H, dd, J = 8.8, 3.5 Hz), 4.15 (1H, dd, J = 9.1, 5.5 Hz), 4.18 (1H, m), 4.41-4.34 (2H, m), 4.44 (1H, dd, J = 11.2, 6.1 Hz), 5.67 (1H, br s, NH); ^{13}C NMR (100 MHz,



17 **18** **19** **16**

Scheme 7

$CDCl_3$) δ 158.70 (C=O), 110.63 (CMe_2), 110.46 (CMe_2), 78.15, 74.32, 72.54, 68.07, 67.41, 58.14, 27.31 (CH_3), 26.89 (CH_3), 25.53 (CH_3), 25.28(CH_3); MS (EI), m/e 288 (M^+), 272, 244, 230, 214, 172, 101 (base), 83, 73, 59, 43.

Typical Procedure for the Preparation of *N*-Acyloxazolidin-2-ones, 7a-c. To a solution of oxazolidinone **6** (1.50 g, 5.22 mmol) in THF (130 mL) under nitrogen atmosphere was added *n*-BuLi (4.90 mL of 1.6 M solution in Hexane, 7.83 mmol) at -60 °C and stirred for 30 min. Propionyl chloride (0.91 mL, 10.44 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 and concentrated to give the solid. The solid was washed with hexane to give the white solid **7a** (1.53 g, 85.3%).

(4*S*,5*R*)-3-(1-Oxopropyl)-4,5-bis-(2,2-dimethyl-1,3-dioxolan-4-yl)-oxazolidin-2-one (7a): R_f 0.32 (EtOAc : Hex = 1 : 4); mp 105-108 °C; $[\alpha]_D^{20}$ +44.37 (c 0.8, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 1.18 (3H, t, J = 7.3 Hz), 1.34 (3H, s, CH_3), 1.36 (3H, s, CH_3), 1.37 (3H, s, CH_3), 1.42 (3H, s, CH_3), 3.00-2.85 (2H, m), 4.08-3.99 (3H, m), 4.18 (1H, dd, J 9.3, 5.9 Hz), 4.30 (1H, dd, J = 9.9, 7.0 Hz), 4.64-4.58 (2H, m), 4.73 (1H, d, J = 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.28 (C=O), 153.33 (C=O), 110.27 (CMe_2), 109.72 (CMe_2), 77.15, 74.28, 72.62, 67.35, 66.15, 56.10, 28.86, 27.18, 25.78, 25.11, 25.09, 8.52;

(4*S*,5*R*)-3-(3-Phenyl-1-oxopropyl)-4,5-bis-(2,2-dimethyl-1,3-dioxolan-4-yl)-oxazolidin-2-one (7b): 85.3%; R_f 0.52 (EtOAc : Hex = 1 : 2); mp 98-100 °C; $[\alpha]_D^{20}$ +54.9 (c 1.1, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 1.33 (6H, s), 1.36 (3H, s), 1.41 (3H, s), 3.05-2.95 (2H, m), 3.29-3.21 (2H, m), 4.10-4.00 (3H, m), 4.28-4.14 (2H, m), 4.65-4.55 (2H, m), 4.71 (1H, d, J = 7.0 Hz), 7.29-7.19 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.53 (C=O), 152.22 (C=O), 139.34, 127.49 (x2), 127.44 (x2), 125.24, 109.25, 108.69, 76.11, 73.20, 71.55, 66.30, 65.09, 55.07, 35.70, 29.70, 26.14, 24.75, 24.09 (x2).

(4*S*,5*R*)-3-(1-Oxo-4-pentenyl)-4,5-bis-(2,2-dimethyl-1,3-dioxolan-4-yl)-oxazolidin-2-one (7c): 77.3%; R_f 0.58 (EtOAc : Hex = 1 : 2); mp 55-57 °C; $[\alpha]_D^{20}$ +53.2 (c 0.9, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 1.34 (3H, s, CH_3), 1.36 (3H, s, CH_3), 1.37 (3H, s, CH_3), 1.42 (3H, s, CH_3), 2.49-2.39 (2H, m), 3.11-2.93 (2H, m), 4.07-3.98 (3H, m), 4.18 (1H, dd, J = 9.2, 6.0 Hz), 4.29 (1H, dd, J = 9.8, 7.0 Hz), 4.63-4.58 (2H, m), 4.73 (1H, d, J = 7.0 Hz), 5.02 (1H, dd, J = 10.1, 1.3 Hz, =CH *trans*), 5.10 (1H, dd, J = 17.2, 1.3 Hz, =CH *cis*), 5.87 (1H, m, =CH *internal*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.72 (C=O), 153.30 (C=O), 136.65, 115.75, 110.31, 109.75, 77.18, 74.26, 72.62, 67.37, 66.16, 56.13, 34.47, 28.23, 27.20, 25.83, 25.13, 25.11.

Typical Procedure for the Preparation of Alkylated Products, 8A-8F. To a solution of diisopropyl amine (0.06 mL, 0.44 mmol) in THF (3 mL) at -20 °C under nitrogen atmosphere was added *n*-BuLi (0.27 mL of 1.6 M solution in Hexane, 0.44 mmol) and stirred for 30 min. *N*-Propionyl oxazolidinone **7a** (0.10 g, 0.29 mmol) in THF (2 mL) was added to this reaction mixture at -60 °C and stirred for 30 min. Benzyl bromide (0.14 mL, 1.16 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 **8A** (0.12 g, 95.5%).

(4*S*,5*R*,2'*R*)-3-(2-Methyl-3-pheny-l-oxopropyl)-4,5-bis-(2,2-dimethyl-1,3-dioxolan-4-yl)-oxazolidin-2-one (8A): R_f 0.48 (EtOAc : Hex = 1 : 3); $[\alpha]_D^{20}$ +24.3 (c 1.7, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 1.10 (3H, d, J = 6.7 Hz, α-methyl), 1.19 (3H, s, CH_3), 1.32 (3H, s, CH_3), 1.36 (3H, s, CH_3), 1.42 (3H, s, CH_3), 2.56 (1H, dd, J = 13.2, 8.7 Hz, benzyl proton), 3.28 (1H, dd, J = 13.2, 5.8 Hz, benzyl proton), 3.68 (1H, dd, J = 9.1, 6.6 Hz), 3.95 (1H, dd, J = 9.1, 6.6 Hz), 4.00 (1H, dd, J = 6.4, 2.1 Hz), 4.05 (1H, dd, J = 9.2, 3.4 Hz), 4.18 (1H, dd, J = 9.2, 5.9 Hz), 4.31 (1H, dd, J = 9.7, 6.9 Hz), 4.54 (1H, t, J = 6.6 Hz), 4.63 (1H, m, α-proton), 4.75 (1H, d, J = 6.4 Hz), 7.20 (1H, m), 7.28-7.25 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.0 (C=O), 153.3 (C=O), 139.6, 129.7 (x2), 128.7 (x2), 126.7, 110.6 (CMe_2), 109.8 (CMe_2), 77.4, 74.5, 72.9, 67.7, 66.2, 55.9, 40.0, 39.9, 27.5, 26.1, 25.7, 25.5, 16.6.

(4*S*,5*R*,2'*S*)-3-(2-Methyl-3-pheny-l-oxopropyl)-4,5-bis-(2,2-dimethyl-1,3-dioxolan-4-yl)-oxazolidin-2-one (8B): 79.5%; R_f 0.62 (EtOAc : Hex = 1 : 2); $[\alpha]_D^{20}$ +72.8 (c 1.4, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 1.28 (3H, d, J = 6.7 Hz, α-methyl), 1.33 (6H, s, 2CH_3), 1.34 (3H, s, CH_3), 1.40 (3H, s, CH_3), 2.73 (1H, dd, J = 13.3, 7.0 Hz, benzyl proton), 2.93 (1H, dd, J = 13.2, 8.3 Hz, benzyl proton), 3.85 (1H, dd, J = 9.8, 6.7 Hz), 4.01-3.92 (3H, m), 4.15-4.09 (2H, m), 4.52 (1H, m, α-proton), 4.55 (2H, m), 7.22-7.17 (3H, m), 7.28-7.24 (2H, 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, 110.2 (CMe_2), 109.5 (CMe_2), 76.9, 74.2, 72.5, 67.3, 66.0, 55.9, 40.1, 39.0, 27.1, 25.7, 25.2, 25.1, 17.6.

(4*S*,5*R*,2'*R*)-3-(2-Methyl-1-oxo-4-pentenyl)-4,5-bis-(2,2-dimethyl-1,3-dioxolan-4-yl)-oxazolidin-2-one (8C): 89.5 %; R_f 0.60 (EtOAc : Hex = 1 : 2); $[\alpha]_D^{20}$ +17.1 (c 0.9, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 1.14 (3H, d, J = 6.9 Hz, α-methyl), 1.34 (3H, s, CH_3), 1.35 (3H, s, CH_3), 1.37 (3H, s, CH_3), 1.42 (3H, s, CH_3), 2.19 (1H, m), 2.59 (1H, m), 3.78 (1H, sextet, J = 6.7 Hz), 3.91 (1H, dd, J = 9.0, 6.1 Hz), 4.00 (1H, dd, J = 9.1, 6.8 Hz), 4.06 (1H, dd, J = 9.2, 3.5 Hz), 4.12 (1H, q, J = 7.3 Hz), 4.19 (1H, dd, J = 9.2, 6.0 Hz), 4.31 (1H, dd, J = 9.8, 6.9 Hz), 4.63-4.58 (2H, m), 4.75 (1H, dd, J = 6.8, 1.0 Hz), 5.06 (1H, dd, J = 10.1, 1.5 Hz, =CH *trans*), 5.11 (1H, dd, J = 17.1, 1.5 Hz, =CH *cis*), 5.80 (1H, m, =CH *internal*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.0 (C=O), 153.3 (C=O), 135.6, 117.7 110.6 (CMe_2), 109.9 (CMe_2), 77.4, 74.5, 73.0, 67.7, 66.3, 56.2, 38.2, 37.5, 27.6, 26.2, 25.6, 25.5, 16.7.

(4*S*,5*R*,2'*S*)-3-(2-Methyl-1-oxo-4-pentenyl)-4,5-bis-(2,2-dimethyl-1,3-dioxolan-4-yl)-oxazolidin-2-one (8D): 86.9%; R_f 0.38 (EtOAc : Hex = 1 : 4); $[\alpha]_D^{20}$ +75.8 (c 0.4, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 1.26 (3H, d, J = 6.9 Hz, α-methyl), 1.31 (3H, s, CH_3), 1.36 (3H, s, CH_3), 1.37 (3H, s, CH_3), 1.42 (3H, s, CH_3), 2.18 (1H, quintet, J = 7.0 Hz), 2.42

(1H, quintet, J = 7.0 Hz), 3.81 (1H, sextet, J = 7.1 Hz), 3.94 (1H, dd, J = 9.1, 6.0 Hz), 4.01 (1H, dd, J = 9.1, 6.8 Hz), 4.05 (1H, dd, J = 9.2, 3.5 Hz), 4.18 (1H, dd, J = 7.2, 6.0 Hz), 4.26 (1H, dd, J = 9.1, 6.0 Hz), 4.64-4.56 (2H, m), 4.74 (1H, dd, J = 7.0, 0.8 Hz), 5.03 (1H, dd, J = 9.9, 1.5 Hz, =CH *trans*), 5.05 (1H, dd, J = 16.0, 1.5 Hz, =CH *cis*), 5.77 (1H, m, =CH *internal*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.8 (*C*=*O*), 152.9 (C=*O*), 135.5, 117.1 110.3 (*C*Me$_2$), 109.6 (*C*Me$_2$), 77.2, 74.2, 72.6, 67.4, 66.0, 55.8, 37.6, 37.2, 27.2, 27.8, 25.2, 25.1, 17.6.

(4*S*,5*R*,2'*S*)-3-(2-Benzyl-1-oxo-4-pentenyl)-4,5-bis-(2,2-dimethyl-1,3-dioxolan-4-yl)-oxazolidin-2-one (8E): 63.9%; R_f 0.70 (EtOAc : Hex = 1 : 2); $[\alpha]_D^{20}$ +89.5 (c 1.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28 (3H, s, CH_3), 1.31 (3H, s, CH_3), 1.33 (3H, s, CH_3), 1.38 (3H, s, CH_3), 2.36 (1H, m), 2.59 (1H, quintet, J = 7.1 Hz), 2.78 (1H, dd, J = 13.0, 10.0 Hz), 2.88 (1H, dd, J = 13.0, 6.1 Hz), 3.46 (1H, dd, J = 9.9, 6.8 Hz), 3.83 (1H, dd, J = 9.0, 7.0 Hz), 3.88 (1H, dd, J = 9.3, 3.4 Hz), 3.97 (1H, dd, J = 8.9, 6.5 Hz), 4.90 (1H, dd, J = 9.1, 5.9 Hz), 4.31 (1H, m), 4.33 (1H, dd, J = 6.6, 0.9 Hz), 4.49-4.41 (2H, m), 5.05 (1H, br d J = 10.9 Hz, =CH *trans*), 5.15 (1H, dd, J = 17.1, 1.5 Hz, =CH *cis*), 5.85 (1H, m, =CH *internal*), 7.20-7.15 (2H, m), 7.28-7.21 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.0 (*C*=*O*), 153.3 (C=*O*), 139.1, 135.4, 129.5 (x2), 128.8 (x2), 127.0, 117.9, 110.5 (*C*Me$_2$), 109.9 (*C*Me$_2$), 77.2, 74.4, 72.8, 67.7, 66.4, 56.2, 44.1, 39.7, 36.9, 27.6, 26.1, 25.9, 25.5.

(4*S*,5*R*,2'*R*)-3-(2-Benzyl-1-oxo-4-pentenyl)-4,5-bis-(2,2-dimethyl-1,3-dioxolan-4-yl)-oxazolidin-2-one (8F): 70.1%; R_f 0.70 (EtOAc : Hex = 1 : 2); $[\alpha]_D^{20}$ +35.6 (c 1.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.07 (3H, s, CH_3), 1.30 (3H, s, CH_3), 1.35 (3H, s, CH_3), 1.42 (3H, s, CH_3), 2.23 (1H, m), 2.35 (1H, m), 2.71 (1H, dd, J = 13.5, 7.6 Hz), 3.19 (1H, dd, J = 13.5, 7.2 Hz), 3.57 (1H, dd, J = 9.0, 7.1 Hz), 3.92 (1H, dd, J = 9.2, 6.9 Hz), 4.03 (1H, dd, J = 9.2, 3.5 Hz), 4.26-4.15 (3H, m), 4.49 (1H, br t, J = 6.9 Hz), 4.59 (1H, m), 4.69 (1H, dd, J = 6.9, 0.7 Hz), 5.02 (1H, br d, J = 10.1 Hz, =CH *trans*), 5.06 (1H, br d, J = 16.9 Hz, =CH *cis*), 5.75 (1H, m, =CH *internal*), 7.10 (1H, m), 7.27-7.21 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2 (*C*=*O*), 153.1 (C=*O*), 139.0, 135.3, 129.3 (x2), 128.5 (x2), 126.5, 117.3, 110.3 (*C*Me$_2$), 109.4 (*C*Me$_2$), 77.1, 74.1, 72.6, 67.4, 65.8, 55.6, 44.3, 37.9, 36.2, 27.2, 25.5 (x2), 25.1.

(*R*)-2-Benzyl-1-propanol (9A). To a solution of $LiAlH_4$ (35 mg, 0.92 mmol) in THF (2 mL) under nitrogen atmosphere in ice bath was added (4*S*,5*R*,2'*R*)-3-(2-methyl-3-phenyl-oxopropyl)-4,5-bis-(2,2-dimethyl-1,3-dioxolan-4-yl)-oxazolidin-2-one (**8A**) (0.10 g, 0.23 mmol) and stirred for 20 min at rt. The reaction was quenched by the addition of 1N NaOH aqueous solution (4 mL) and filtered. The filtrate was evaporated, diluted with EtOAc, dried, concentrated and chromatographed (EtOAc : Hex = 1 : 2) to give the alcohol **9A** (21 mg, 60.8%) and the auxiliary **6** (60 mg, 99.8%). R_f 0.40 (EtOAc : Hex = 1 : 2); $[\alpha]_D^{20}$ +14.1 (c 1.05, C_6H_6); [lit.[10] $[\alpha]_D^{25}$ = +11.1, (c 1.25, C_6H_6)]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (3H, d, J = 6.7 Hz, 2-methyl), 1.59 (1H, br s, OH), 1.94 (1H, m, C*H*Me), 2.41 (1H, dd, J = 13.4, 7.9 Hz, benzyl H), 2.75 (1H, dd, J = 13.4, 6.4 Hz, benzyl H), 3.50 (2H, m, CH_2OH), 7.20 (5H, m, aromatic). The data were consistent with those reported in the literature.[4e,9]

(*S*)-2-Benzyl-1-propanol (9B). Prepared from **8B** (0.04 g, 0.09 mmol) as same as above procedure and gave the alcohol **9B** (11 mg, 79.3%) and the auxiliary **6** (23 mg, 99.8%). R_f 0.40 (EtOAc : Hex = 1 : 2); $[\alpha]_D^{25}$ -12.1 (c 1.05, C_6H_6); [lit.[11] $[\alpha]_D^{25}$ = -11.1, (c 4.6, C_6H_6)].

(4*S*,5*R*,2'*S*,3'*S*)-3-(3-Hydroxy-2-methyl-3-phenyl-oxopropyl)-4,5-bis-(2,2-dimethyl-1,3-dioxolan-4-yl)-oxazolidin-2-one (10). 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 (**7a**) (42 mg, 0.12 mmol) in CH_2Cl_2 (2 mL) under nitrogen atmosphere was added $TiCl_4$ (0.14 mL in 1.0 M solution in CH_2Cl_2, 0.14 mmol) at -60 °C and stirred for 5 min. TMEDA (46 mg, 0.31 mmol) was added to this reaction mixture at -60 °C and stirred for 30 min. Benzaldehyde (0.03 mL, 0.24 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 **10** (50 mg, 91%). R_f 0.30 (EtOAc : Hex = 1 : 2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28 (3H, d, J = 6.9 Hz, α-methyl), 1.33 (6H, s, 2CH_3), 1.36 (3H, s, CH_3), 1.41 (3H, s, CH_3), 3.11 (1H, br s), 4.03-3.93 (4H, m), 4.08 (1H, m), 4.15 (1H, dd, J = 9.2, 6.0 Hz), 4.57 (3H, m), 4.98 (1H, br d, J = 3.4 Hz), 7.26 (2H, m), 7.40-7.30 (3H, m).

(4*S*,5*R*,2'*R*,3'*R*)-3-(3-Hydroxy-2-methyl-3-phenyl-oxopropyl)-4,5-bis-(2,2-dimethyl-1,3-dioxolan-4-yl)-oxazolidin-2-one (11). 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 (**7a**) (0.10 g, 0.29 mmol) in CH_2Cl_2 (5 mL) under nitrogen atmosphere was added $TiCl_4$ (0.58 mL in 1.0 M solution in CH_2Cl_2, 0.58 mmol) at -60 °C and stirred for 5 min. Et_3N (0.06 mL, 0.44 mmol) was added to this reaction mixture at -60 °C and stirred for 30 min. Benzaldehyde (0.06 mL, 0.58 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 **11** (60 mg, 46%). R_f 0.35 (EtOAc : Hex = 1 : 2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.97 (3H, d, J = 6.8 Hz, α-methyl), 1.33 (3H, s, CH_3), 1.38 (3H, s, CH_3), 1.43 (3H, s, CH_3), 1.44 (3H, s, CH_3), 3.37(1H, d, J = 4.5 Hz), 4.04-3.95 (3H, m), 4.08 (1H, m), 4.20 (2H, m), 4.34 (1H, dd, J = 9.8, 7.1 Hz), 4.66 (2H, m), 4.89 (1H, dd, J = 7.0, 0.9 Hz), 7.42-7.32 (3H, m), 7.49 (2H, d, J = 7.5 Hz).

***syn* (2*S*,3*S*)- and *anti* (2*R*,3*S*)-3-Hydroxy-2-methyl-3-phenylpropanoic acid (12 and 12A)**. To a solution of (4*S*,5*R*,2*S*,3*S*)-3-(3-hydroxy-2-methyl-3-phenyl-oxopropyl)-4,5-bis-(2,2-dimethyl-1,3-dioxolan-4-yl)-oxazolidin-2-one (**10**) (60 mg, 0.13 mmol) in THF (2 mL) and H_2O (0.65 mL) was added 30% H_2O_2 (0.76 g, 0.67 mmol) and $LiOH \cdot H_2O$ (11 mg, 0.27 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 mL), extracted with CH_2Cl_2, washed with brine, dried and concentrated to give the auxiliary **6** (34 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 **12** and **12A** (18 mg, 76.8%). R_f 0.19 (EtOAc : Hex = 1 : 2); $[\alpha]_D^{25}$ -24.4 (c 0.9, CH_2Cl_2); [lit.[15] $[\alpha]_D^{22}$ = -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* CHOH), 5.18 (0.99H, d, J = 4.0 Hz, *syn* CHOH), 5.42 (2H, br s, OH and CO_2H), 7.35 (5H, s, aromatic). ^{1}H NMR integration afforded a ratio **8** : **8A** = 99 : 1. The data were consistent with those reported in the literature.[15,17]

***syn* (2*R*,3*R*)- and *anti* (2*S*,3*R*)-3-Hydroxy-2-methyl-3-phenylpropanoic acid (13 and 13A)**. Prepared from **11** (24 mg, 0.05 mmol) as same as above procedure and gave the acids **13** and **13A** (8 mg, 83.7%) and the auxiliary **6** (15 mg, 100%). R_f 0.19 (EtOAc : Hex = 1 : 2); $[\alpha]_D^{25}$ +26.5 (c 0.35, CH_2Cl_2); [lit.[15] $[\alpha]_D^{22}$ = -26.4 (c 1.04, CH_2Cl_2)] for the enantiomer **12**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.75 (0.04H, d, J = 8.8 Hz, *anti* CHOH), 5.18 (0.96H, d, J = 4.0 Hz, *syn* CHOH). ^{1}H NMR integration afforded a ratio **13**:**13A** = 96:4.

[(4*S*,5*R*)-4,5-Bis-(2,2-dimethyl-1,3-dioxolan-4-yl)-2-oxo-3-oxazolidinyl]acetic acid (14). Ethyl bromoacetate (77 mL, 0.70 mmol) was added dropwise at 0 °C under a nitrogen atmosphere to a suspension of the oxazolidinone **6** (0.20 g, 0.70 mmol) and sodium hydride (20 mg, 0.84 mmol) in dry THF (20 mL). The resulting mixture was allowed to stir at room temperature for 24 h. Then, a aqueous solution of NaOH (0.16 g in 20 mL water) was added, and the mixture was allowed to stir at room temperature for 1 h. Finally the mixture was acidified with 6 N HCl and extracted with methylene chloride. The organic extracts were combined and dried over $MgSO_4$. Concentration in vacuo afforded the desired acid **14** (0.20 g, 83.2%), which was utilized in the next step without further purification. R_f 0.17 (MeOH : $CHCl_3$ = 1 : 9); ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.32 (3H, s, CH_3), 1.34 (3H, s, CH_3), 1.40 (3H, s, CH_3), 1.41 (3H, s, CH_3), 3.78 (1H, dd, J = 9.6, 4.7 Hz), 4.10-3.99 (4H, m), 4.29-4.16 (4H, m), 4.32 (2H, s, $COCH_2$), 4.50 (1H, m), 7.91 (1H, br s, OH).

General Procedure for the Preparation of β-Lactams, 16a-f. The acid **14** (0.15 g, 0.43 mmol) in dry methylene chloride (2.5 mL) was added at 0 °C to a solution of 2-chloro-1-methylpyridinium iodide (0.13 g, 0.52 mmol) in dry methylene chloride (2 mL) under nitrogen atmosphere. After the reaction mixture was clear, triethylamine (0.15 mL, 1.04 mmol) and the corresponding imine (0.52 mmol) in dry methylene chloride (3 mL) were added dropwise to the reaction mixture and stirred at 0 °C for 15 min and at room temperature for 12 h. The reaction was quenched by the addition of water and extracted with methylene chloride. The organic layer was washed with brine, dried, concentrated and chromatographed (EtOAc : Hex = 1 : 4) to give the solid.

[(4*S*,5*R*)-4,5-Bis-(2,2-dimethyl-1,3-dioxolan-4-yl)-2-oxo-3-oxazolidinyl]-1,4-diphenylazetidin-2-one (16a): 76.7%; ***cis*-(3S,4S)-16a**: 38.4%; R_f 0.43 (EtOAc : Hex = 1 : 1); mp 192-196 °C; $[\alpha]_D^{20}$ +38.3 (c 1.54, $CHCl_3$); ν_{max} (KBr)/cm^{-1} 3503, 3145, 3039, 1784, 1759, 1600, 1499, 1381, 1221, 844, 754; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.28 (3H, s, CH_3), 1.32 (3H, s, CH_3), 1.37 (3H, s, CH_3), 1.61 (3H, s, CH_3), 3.41 (1H, br t, J = 9.5 Hz), 3.51 (1H, br t, J = 9.5 Hz), 3.66 (1H, dd, J = 9.2, 5.2 Hz), 3.79 (1H, m), 4.20-4.00 (3H, m), 4.34 (1H, m), 5.27 (1H, d, J = 5.2 Hz, C-4 H), 5.49 (1H, d, J = 5.2, Hz, C-3H), 7.42-7.05 (10H, m). ***trans*-(3S,4R)-16a**: 38.3%; R_f 0.60 (EtOAc : Hex = 1 : 1); mp 146-149 °C; $[\alpha]_D^{20}$ +56.6 (c 0.98, $CHCl_3$); ν_{max} (KBr)/cm^{-1} 3497, 3134, 2990, 1777 (br), 1601, 1502, 1376, 1215, 1070, 844, 753; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.86 (3H, s, CH_3), 1.13 (3H, s, CH_3), 1.34 (3H, s, CH_3), 1.40 (3H, s, CH_3), 3.71 (1H, dd, J = 9.4, 6.4 Hz), 4.00 (1H, m), 4.31-4.10 (5H, m), 4.42 (1H, m), 5.13 (1H, d, J = 2.4 Hz, C-4 H), 5.20 (1H, d, J = 2.4, Hz, C-3 H), 7.36-7.05 (10H, m).

1-*p*-Methoxyphenyl-[(4*S*,5*R*)-4,5-bis-(2,2-dimethyl-1,3-dioxolan-4-yl)-2-oxo-3-oxazolidinyl]-4-phenylazetidin-2-one (16b): 57.7%; ***cis*-(3S,4S)-16b**: 51.3%; R_f 0.34 (EtOAc : Hex = 1 : 1); mp 225-228 °C; $[\alpha]_D^{20}$ +43.7 (c 1.00, $CHCl_3$); ν_{max} (KBr)/cm^{-1} 3477, 3141, 2989, 1776 (br), 1513, 1384, 1249, 1067, 837; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.28 (3H, s, CH_3), 1.32 (3H, s, CH_3), 1.37 (3H, s, CH_3), 1.60 (3H, s, CH_3), 3.38 (1H, br t, J = 8.2 Hz), 3.50 (1H, br t, J = 9.7 Hz), 3.67 (1H, dd, J = 9.5, 5.5 Hz), 3.76 (3H, s, MeO), 3.80 (1H, m), 4.20-4.00 (3H, m), 4.34 (1H, m), 5.23 (1H, d, J = 5.2 Hz, C-4 H), 5.47 (1H, d, J = 5.2 Hz, C-3 H), 6.81 (2H, d, J = 8.8 Hz), 7.44-7.31 (7H, m). ***trans*-(3S,4R)-16b**: 6.4%; R_f 0.50 (EtOAc : Hex = 1 : 1); ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.89 (3H, s, CH_3), 1.15 (3H, s, CH_3), 1.34 (3H, s, CH_3), 1.40 (3H, s, CH_3), 3.74 (3H, s, MeO), 3.99 (2H, m), 4.31-4.07 (4H, m), 4.49-4.38 (2H, m), 5.10 (1H, d, J = 2.1 Hz, C-4 H), 5.16 (1H, d, J = 2.1 Hz, C-3H), 6.78 (2H, d, J = 8.8 Hz), 7.25 (2H, d, J = 4.4 Hz), 7.35 (5H, s).

***cis*-(3S,4S)-1-Benzyl-[(4*S*,5*R*)--4,5-bis-(2,2-dimethyl-1,3-dioxolan-4-yl)-2-oxo-3-oxazolidinyl]-4-phenylazetidin-2-one (16c)**: 33.3%; R_f 0.23 (EtOAc : Hex = 1 : 1); mp 202-204 °C; $[\alpha]_D^{20}$ +6.67 (c 0.35, $CHCl_3$); ν_{max} (KBr)/cm^{-1} 3485, 3140, 3063, 1776 (br), 1496, 1421, 1382, 1219, 1146, 1068, 840, 700; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.26 (3H, s, CH_3), 1.28 (3H, s, CH_3), 1.33 (3H, s, CH_3), 1.51 (3H, s, CH_3), 3.12 (1H, br t, J = 8.2 Hz), 3.32 (1H, m), 3.59 (1H, dd, J = 9.5, 5.5 Hz), 3.76 (1H, m), 4.14-3.98 (4H, m), 4.30 (1H, m), 4.62 (1H, d, J = 4.6 Hz, C-4 H), 4.99 (1H, d, J = 14.6 Hz), 5.22 (1H, d, J = 4.6 Hz, C-3 H), 7.36-7.19 (10H, m).

[(4*S*,5*R*)-4,5-Bis-(2,2-dimethyl-1,3-dioxolan-4-yl)-2-oxo-3-oxazolidinyl]-1-phenyl-4-styrylazetidin-2-one (16d): 32.2 %; ***cis*-(3S,4S)-16d**: 23.6%; R_f 0.55 (EtOAc : Hex = 1 : 1); mp 213-214 °C; $[\alpha]_D^{20}$ +104.9 (c 0.55, $CHCl_3$); ν_{max} (KBr)/cm^{-1} 3443, 3051, 1763 (br), 1619, 1498, 1383, 1221, 1149, 1066, 846, 753; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.30 (3H, s, CH_3), 1.35 (3H, s, CH_3), 1.52 (3H, s, CH_3), 1.56 (3H, s, CH_3), 3.75 (1H, dd, J = 9.5, 5.2 Hz), 3.95 (1H, m), 4.27-4.04 (4H, m), 4.50 (1H, m), 4.89 (1H, dd, J = 8.7, 5.2 Hz, C-4H), 5.50 (1H, d, J = 5.2 Hz, C-3 H), 6.48 (1H, dd, J = 16.0, 8.7 Hz, =CH), 6.87 (1H, d, J = 16.0 Hz, =CHPh), 7.50-7.05

(10H. m). ***trans*-(3S,4R)-16d**: 8.6%; R_f 0.62 (EtOAc : Hex = 1 : 1); ^{1}H NMR (200 MHz. $CDCl_3$) δ 1.01 (3H, s. CH_3). 1.16 (3H. s. CH_3), 1.35 (3H, s, CH_3), 1.41 (3H, s. CH_3), 3.72 (1H, dd, J = 9.5. 6.4 Hz), 4.00 (1H. m), 4.39-4.10 (6H. m). 4.87 (1H, dd. J = 8.2, 2.1 Hz, C-4H), 5.13 (1H, d. J = 2.1 Hz. C-3H). 6.36 (1H, dd. J = 15.9. 8.2 Hz. =CH), 6.82 (1H, d. J = 15.9 Hz, =CHPh). 7.46-7.09 (10H. m).

***cis*-(3S,4S)-1-*p*-Methoxyphenyl-[(4*S*,5*R*)-4,5-bis-(2,2-dimethyl-1,3-dioxolan-4-yl)-2-oxo-3-oxazolidinyl]-4-styryl-azetidin-2-one (16e)**: 42.1%; R_f 0.43 (EtOAc : Hex = 1 : 1): mp 217-222 °C: $[\alpha]_D^{20}$ +75.4 (c 1.00. $CHCl_3$): ν_{max} (KBr)/cm^{-1} 3444. 2936, 1757, 1513, 1424, 1224. 1036. 834; ^{1}H NMR (200 MHz. $CDCl_3$) δ 1.30 (3H, s, CH_3). 1.35 (6H, s. 2CH_3), 1.51 (3H. s. CH_3). 3.75 (1H, m), 3.76 (3H. s, MeO). 3.94 (3H, m), 4.30-4.08 (4H. m), 4.51 (1H, m), 4.84 (1H. dd, J = 8.6. 5.2 Hz. C-4H). 5.47 (1H, d, J = 5.2 Hz. C-3H), 6.47 (1H, dd, J = 16.2. 8.6 Hz. =CH), 6.83 (2H, d, J = 8.9 Hz. aromatic) 6.86 (1H. d. J = 16.2 Hz. =CHPh). 7.44-7.31 (7H. m, aromatic).

***cis*-(3S,4S)-4-Benzyl-[(4*S*,5*R*)-4,5-bis-(2,2-dimethyl-1,3-dioxolan-4-yl)-2-oxo-3-oxazolidinyl]-1-strylazetidin-2-one (16f)**: 16.0%; R_f 0.33 (EtOAc : Hex = 1 : 1); mp 163-167 °C: $[\alpha]_D^{20}$ +35.2 (c 0.83, $CHCl_3$); ν_{max} (KBr)/cm^{-1} 3487, 2989. 1764, 1372. 1221. 1068, 847, 755; ^{1}H NMR (200 MHz. $CDCl_3$) δ 1.30 (3H. s. CH_3). 1.33 (3H. s. CH_3). 1.35 (3H. s. CH_3). 1.45 (3H, s. CH_3). 3.71 (1H, dd, J = 9.8. 4.9 Hz), 3.82 (1H, m). 3.91 (1H, dd. J = 9.2. 4.6 Hz). 4.19-4.08 (3H, m). 4.30-4.24 (2H, m), 4.53-4.42 (2H. m). 4.67 (1H, d. J = 15.0 Hz). 5.30 (1H, d, J = 4.9 Hz. C-3H). 6.23 (1H. dd, J = 16.0. 8.9 Hz. =CH), 6.56 (1H. d. J = 16.0 Hz, =CHPh). 7.33-7.27 (10H. m).

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