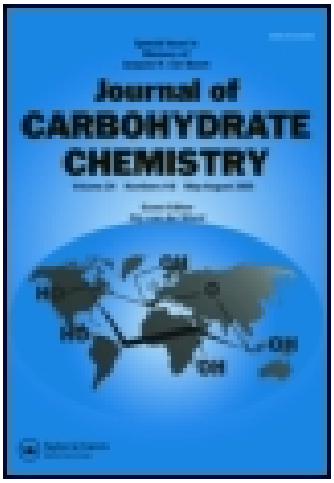

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2,3:4,5-DI-O-Isopropylidene-β-d-Fructopyranose as Chiral Auxiliary in Asymmetric α-Alkylation Of Ester Enolates

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2,3:4,5-DI-*O*-ISOPROPYLIDENE-β-D-FRUCTOPYRANOSE AS CHIRAL AUXILIARY IN ASYMMETRIC α-ALKYLATION OF ESTER ENOLATES

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ABSTRACT

The asymmetric α-alkylation of enolates of chiral esters derived from 2,3:4,5-di-*O*-isopropylidene-β-D-fructopyranose (**1**) was studied. The diastereoselectivities range from 1:1 to 7:3. The absolute stereochemistry of the major *S*-isomers were established by chemical correlation. The diastereoselectivities of the alkylated products were similar to those observed in the deprotonation steps. The stereochemical outcome can be interpreted by an intramolecular complexation of the lithium cation of the carbohydrate ester enolates.

INTRODUCTION

A number of natural products have been used as chiral auxiliaries in asymmetric synthesis.[1] Amino acids[2] and terpenoids[3] have been used most often for this purpose. In spite of the fact that carbohydrates have been extensively employed as starting materials for the construction of various natural products having one or more chiral centers,[4] their use as chiral auxiliaries is less extensive.

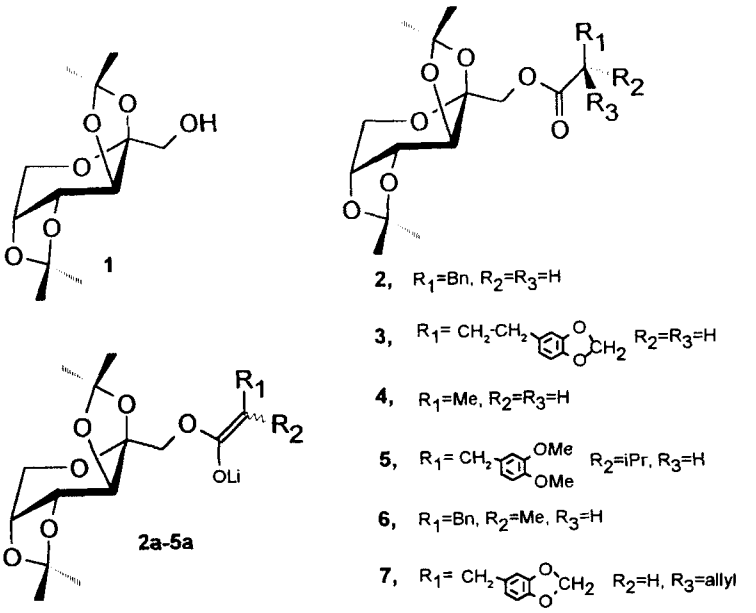
Among stereoselective reactions reported so far, the asymmetric α-alkylation of esters induced by chiral auxiliaries is one of the most studied.[5] Only a few examples of this reaction are found in the literature which use carbohydrates as chiral auxiliaries.[6] Herein we

report the first study of the asymmetric α-alkylation of esters **2-5** using 2,3:4,5-di-*O*-isopropylidene-β-D-fructopyranose (**1**) as the chiral auxiliary.

RESULTS AND DISCUSSION

2,3:4,5-Di-*O*-isopropylidene-β-D-fructopyranose (**1**) is an inexpensive chiral product easily obtained from the abundant carbohydrates sucrose or fructose by a simple acetonation reaction according to published procedures.[7] This sugar derivative has been only reported as a chiral auxiliary in aldol condensations.[8]

Reaction of the free hydroxy group of **1** with the appropriate acid chloride in the presence of triethylamine produced esters **2** and **4** in 70 and 67 % yield, respectively. Esters **3** and **5** were obtained directly from the corresponding acids by using DCC/DMAP in yields of 83 and 85 %, respectively.



SCHEME 1 : Reagents and diastereomeric alkylated products.

Kinetic alkylation of ester enolates **2-5** was conducted by stirring the ester (**2-5**) in THF with freshly prepared LDA (1.2 equiv.) at -78 ^{0}C under nitrogen for 45 min. Then the alkylating agent (1.05 equiv) was introduced and the mixture stirred for two hours at -78 ^{0}C. Workup gave crude mixtures which were purified by column chromatography. The

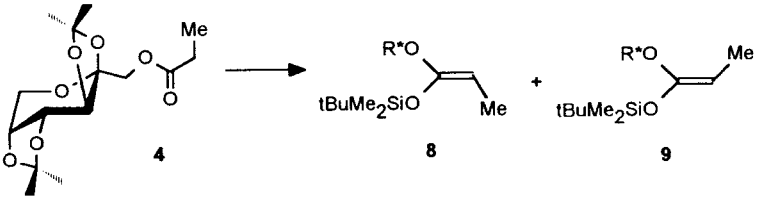
TABLE: Asymmetric α-alkylation of ester enolates **2a** - **5a**.

Entry	Enolate	conditions	Product	% yield	2-*S* /2-*R*
1	**2a**	LDA/THF/-78 ^{0}C	**6**	40	63:37
2	**3a**	LDA/THF/-78 ^{0}C	**7**	56	70:30
3	**4a**	LDA/THF/-78 ^{0}C	**6**	34	66:34
4	**4a**	LDA/THF/HMPA/-78 ^{0}C	**6**	40	50:50
5	**5a**	LDA/THF/-78 ^{0}C	N.R.	--	--

results shown in the table indicate that the esters studied led to mixtures of diastereomeric products with diastereoselectivities varying from 1:1 to 7:3.

As shown in the Table, benzylation of **4a** led to **6** as a mixture of diasteroisomers **6a/6b** in a 66:34 ratio (entry 3). The configuration of the new stereogenic center of the major product was proven to be *S* by reductively cleaving **6** to the known compound, 3-phenyl-1-hydroxy-2-methyl propane (**10**). The optical rotation of the product had the same sign as that of the known *S* enantiomer,[9] although its magnitude was somewhat smaller.

In order to determine the geometries of the enolates (**2a-5a**) generated under kinetic conditions, ester **4** was converted into the ketene silyl ketals **8** and **9** (Scheme 2).



4 **8** **9**

CONDITIONS		Ratio of **8** to **9**
1. LDA/THF, -78 ^{0}C	2. *t*-BuMe$_2$SiCl	23:77
1. LDA/THF/HMPA,-78 ^{0}C	2. *t*-BuMe$_2$SiCl	86:14

SCHEME 2: Kinetic formation of ketene-silyl-ketals **8** and **9**.

The *E* silyl enolate is favoured in THF alone but in the presence of HMPA the *Z* silyl enolate is favoured. Note that the nomenclature order is reversed in lithium enolates.

The diastereomeric results reported in entries 1-3 in the table, when compared with the ratio of ketene silyl ketals **8** and **9** suggest that the alkylation step of **4a** is

diastereoselective, i.e., the *E* enolate gave the *S*-ester preferentially and *Z* enolate favored the *R*-ester. However, this particular chiral auxiliary does not yield enolates with satisfactory *E*/*Z* selectivities.

The origin of the facial diastereoselectivity found in the enolate derived from **4a** probably is related to the pronounced complexing ability of cations by carbohydrates. We propose that the lithium cation complexes intramolecularly with the enolate oxygen atom and with *O*-2 and/or *O*-3 in the chiral auxiliary moiety. This enhances the rigidity of the transition state conformation blocking predominantly the *si* face. This hypothesis was investigated by performing the reaction in the presence of HMPA (entry 4), a reagent that decreases intramolecular complexation with the carbohydrate oxygen atoms. In this case, the *Z*-enolate predominates (Scheme 2). If chelation of the enolate was not important for diastereoselection, **2**-*R* would be obtained as the major diastereoisomer. The absence of diastereoselection in this reaction (Table) strongly suggests that intramolecular complexation is important for the topological differentiation of the π-faces of the enolates derived from **4a**.

Enolate **2a** reacts with methyl iodide to give ester **6** with the same configuration as found in the benzylation of **4a** (entry 1). To rationalize this unexpected result, we note that enolate **2a** was generated by LDA prepared from a *n*-butyl lithium solution in *n*-hexane while for **4a** a hexane-free LDA solution was employed. The difference in these stereochemical outcomes is probably due to the degree of aggregation of the reagents which influences the rate, regiochemistry and stereochemistry of the reactions.[10-12]

All attempts to alkylate enolate **5a** to prepare a chiral quaternary center failed. This low reactivity was attributed to the steric hindrance produced by the isopropyl group.

In conclusion, the chiral auxiliary described herein will be attractive if the stereochemistry of their enolates can be controlled. Asymmetric alkylation and other reactions involving sugar derivatives as chiral auxiliaries are under investigation in our laboratory.

EXPERIMENTAL

General Procedures. Melting points were determined with a Thomas-Hoover apparatus and are uncorrected. Optical rotations were recorded with a Perkin-Elmer 243-B polarimeter. Column chromatography was performed on silica gel 60 (Merck). TLC was

carried out on precoated silica gel plates (0.2 mm) F-254 (Merck). Infrared spectra were recorded with a Perkin-Elmer 783 spectrophotometer. NMR spectra were recorded with either a Varian VXR (300 MHz) or a Gemini (200 MHz) for solutions in $CDCl_3$. High (HRMS) and low resolution mass spectra (MS) were measured on an Autospec VG spectrometer.

2,3:4,5-Di-*O*-isopropylidene-β-D-fructopyranose (1). To a mixture of powdered sucrose (10 g) in dry acetone (200 mL) under nitrogen was added concd sulfuric acid (8 mL) at 0 ^{0}C. The ice bath was removed and the mixture vigorously stirred for 5-6 h at room temperature. The resulting yellow solution was neutralized with 50% aq NaOH, the precipitate removed by filtration and the filtrate stored over sodium carbonate. The acetone was removed under reduced pressure and the residual oil taken up in dichloromethane (200 mL). To this organic phase was added a solution of 0.5 M sulfuric acid (200 mL) and the mixture stirred for 2 h. The organic phase was separated, washed with a saturated solution of sodium carbonate (3 x 50 mL), then dried over anhydrous sodium sulfate. Evaporation of the solvent under reduced pressure gave an oil which crystallized (4.3 g, 65%) with hexane/EtOAc (19:1).

General procedure for preparation of 1-*O*-[3-phenylpropanoyl]-2,3:4,5-di-*O*-isopropylidene-β-D-fructopyranose (2) and 1-*O*-propanoyl-2,3;4,5-di-*O*-isopropylidene-β-D-fructopyranose (4). To a solution of **1** (1.2 mmol) in dry benzene (5 mL) and triethylamine (4.3 mmol, 0.6 mL) was slowly added 3-phenylpropanoyl chloride (2 mmol) at 0 ^{0}C. After being stirred for 24 h, the mixture was poured into water (20 mL). The organic layer was washed with solutions of 5% HCl (2 x 20 mL), and saturated sodium carbonate (2 x 20 mL) and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure and the residue purified by column chromatography on silica gel with hexane/EtOAc as eluent.

Compound **2** was obtained in 70% yield: IR (neat) 1753 (C=O), 1380 and 1387 (Me) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.35 (s, 6H, Me), 1.55 (s, 3H, Me), 1.60 (s, 3H, Me), 2.70 (t, J = 8 Hz, 2H, CH_2), 3.00 (t, J = 8 Hz, 2H, CH_2), 3.76 (dd, $J_{6',6}$ = 13 and $J_{6,5}$ = 1.9 Hz, 1H, H-6), 3.95 (dd, $J_{6',6}$ = 13 and $J_{6',5}$ = 0.8 Hz , 2H, H-6'), 4.05 (d, $J_{1,1'}$ = 11.7 Hz, 1H, H-1) , 4.25 (ddd, $J_{5,4}$ = 7.8, $J_{5,6}$ =1.9 and $J_{5,6'}$ = 0.8 Hz, 1H, H-5), 4.28 (d, $J_{3,4}$ = 2.7 Hz, 1H, H-3), 4.40 (d, $J_{1',1}$ = 11.7, 1H, H-1') 4.60 (dd, $J_{4,3}$ = 2.7 and $J_{4,5}$ = 7.8 Hz , 1H, H-4), 7.25 (m, 5H) ppm; ^{13}C NMR ($CDCl_3$, DEPT) δ 23.9, 25.0, 25.1, 25.8 (Me), 30.7 (C-

10), 35.7 (C-11), 61.1 (C-6), 65.0 (C-1), 69.8 (C-3), 70.0 (C-4), 70.6 (C-5), 101.3 (C-2), 108.5 (C-7), 108.6 (C-8), 126.2, 128.1, 128.2, 129.9, 138.9 (C-Ph) ppm; MS, *m/z* (relative intensity) 392 ($M^{+\cdot}$, 5), 377 (base), 193 (20), 83 (70); HRMS Calcd for $C_{21}H_{28}O_7$ (392.1835). Found: 392.1839.

Compound **4** was obtained in 67% yield: IR (neat) 1758 (C=O), 1382 and 1374 (Me) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.15 (t, 3H, J = 13.6 Hz, Me), 1.35 (s, 3H, Me), 1.40 (s, 3H, Me), 1.48 (s, 3H, Me), 1.55 (s, 3H, Me), 2.38 (q, 2H, J = 13.6 Hz, CH_2), 3.75 (dd, 1H, $J_{6,6'}$ = 13 Hz and $J_{6,5}$ = 1,6 Hz, H-6), 3.76 (d, 1H, $J_{1,1'}$ = 11.6 Hz, H-1), 3.95 (dd, 1H, $J_{6',6}$ = 13 and $J_{6,5}$ = 0.6 Hz, H-6), 4.03 (d, 1H, $J_{1',1}$ = 11.6 Hz, H-1'), 4.25 (ddd, 1H, $J_{5,4}$ = 8, $J_{5,6}$ = 1.6 and $J_{5,6'}$ = 0.6 Hz, H-5), 4.32 (d, 1H, $J_{3,4}$ = 2.6 Hz, H-3), 4.61 (dd, 1H, $J_{4,3}$ = 8 and $J_{4,5}$ = 2.6 Hz, H-4) ppm; ^{13}C NMR ($CDCl_3$, DEPT) δ 25.0, 25.8, 26.4 (Me), 23.9 (C-11), 27.3 (C-10), 61.0 (C-6), 65.1 (C-1), 69.9 (C-3), 70.4 (C-4), 70.6 (C-6), 101.5 (C-2), 108.6 (C-7), 109.0 (C-8), 127.6 (C-9) ppm; MS, *m/z* (relative intensity) 316 ($M^{+\cdot}$, 50), 301 (base), 83 (52), 57 (20); HRMS Calcd for $C_{15}H_{24}O_7$ (316.1522). Found: 316.1515)

General procedure for preparation of 1-*O*-[3-(3',4'-methylenedioxyphenyl)propanoyl]-2,3:4,5-di-*O*-isopropylidene-β-D-fructopyranose (3) and 1-*O*-[3-(3',4'-dimethoxyphenylmethyl)-3-methyl-(butanoyl)]-2,3:4,5-di-*O*-isopropylidene-β-D-fructopyranose (5). A mixture of 3-(3',4'-methylenedioxyphenyl)propanoic acid (1.1 mmol), compound **1** (1.0 mmol), dicyclohexylcarbodiimide (1.2 mmol) and 4-dimethylaminopyridine (0.2 mmol) in dry dichloromethane (5 mL) was stirred at room temperature under a nitrogen atmosphere for 48 h (for **3**) or 18 h (for **5**). The mixture was diluted with ethyl ether (10 mL) and filtered through silica gel. The filtrate was washed with 5% sodium bicarbonate, brine, dried over anhydrous sodium sulfate and the solution was concentrated. Flash chromatography on silica gel gave **3** or **5** as pale yellow oils.

Compound **3** was obtained in 83% yield: IR (neat) 1744 (C=O), 1610, 1502, 1442, 1160, 1074 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.31 (s, 3H), 1.33 (s, 3H), 1.44 (s, 3H), 1.50 (s, 3H), 2.59 (t, 2H, CH_2, J = 7.2 Hz), 2.85 (t, 2H, CH_2, J = 7.2 Hz), 3.72 (d, 1H, $J_{6,6'}$ = 12.9 and $J_{6,5}$ = 1.8 Hz, H-6), 3.83 (dd, 1H, $J_{6',6}$ = 12.9 and $J_{6',5}$ = 1.8 Hz, H-6'), 4.00 (d, 1H, $J_{1,1'}$ = 11.8 Hz, H-1), 4.19-4.21 (m, 2H), 4.35 (d, 1H, $J_{1',1}$ = 11.8 Hz,H-1'), 4.56 (dd, 1H, $J_{4,3}$ = 7.8 and $J_{4,5}$ = 2.6 Hz), 5.88 (s, 2H, O-CH_2-O), 6.58-6.71 (m, 3H, Ph) ppm; MS, *m/z* (relative intensity) 421 ($M^{+\cdot}$- 15, base) 83 (65), 57 (37); HRMS Calcd for $C_{21}H_{25}O_9$ (421.1498). Found: 421.1487.

Compound **5** was obtained in 85% yield: IR (KBr) 1730 (C=O), 1690, 1595, 1375, cm^{-1} ; ^1H NMR (200 MHz, $CDCl_3$) δ 073 (d, J = 1.21 Hz, Me), 0.76 (d, J = 1.2 Hz, Me), 1.25 (s,3H), 1.35 (s, 3H), 1.49 (s, 3H), 1.50 (Me, 3H), 2.22 - 2.42 (m, 1H, $CH(Me)_2$), 3.12 and 3.16 (d, J = 1.9 Hz, CH), 3.72 (s, 3H, OMe), 3.73 (s, 3H, OMe), 3.93 (dd, 1H, $J_{6,6'}$=11.2 and $J_{6,5}$ = 1,9 HZ, H-6), 4.10 (d, $J_{1,1'}$ = 12 Hz, H-1'), 4.12 (dd, $J_{6',6}$ = 11.3 and $J_{6',5}$ = 0.8 Hz, H-6'), 4.30 (ddd, $J_{5,4}$ = 8.6, $J_{5,6}$ = 1.9 and $J_{5,6'}$ = 0.8, H-5), 4.32 (dd, $J_{3,4}$ = 2.8 Hz, H-3), 4.50 (d, $J_{1',1}$ = 12 Hz, H-1'), 4.63 (dd, $J_{4,5}$ = 8.6 and $J_{4,3}$ = 2.8 Hz, H-4), 6.81 (d, J = 3.7 Hz, Ph) ppm; ^{13}C NMR ($CDCl_3$, DEPT) δ 21.0, 21.1, 22.5, 22.4, 25.0, 26.8, 26.3, 26.0, 27.4, 27.3, 33.3, 32.9, 60.2, 60.1, 62.1, 62.2, 65.9, 66.0, 71.9, 71.7, 71.6, 71.3, 71.1, 102.3, 102.2, 56.7, 109.6, 109.9, 110.0, 111.8, 111.7, 112.1, 111.9, 121.9, 131.5, 131.4, 149.8, 149.7, 149.1, 174.4, 174.3 ppm; MS, *m/z* (relative intensity) 480 ($M^{+\cdot}$, 19), 465 (5), 379 (5), 193 (46), 83 (base); HRMS Calcd for $C_{25}H_{36}O_9$ (438.1890). Found: 438.1893

General procedure for preparation of 1-*O*-(2-methyl-3-phenylpropanoyl)-2,3:4,5-di-*O*-isopropylidene-β-D-fructopyranose (6) and 1-*O*-[2-(3',4'-methylenedioxyphenylmethyl)-4-pentenoyl]-2,3:4,5-di-*O*-isopropylidene-β-D-fructopyranose (7). Solutions of esters **2-4** (1 equiv) in dry THF (1 mL) were added dropwise to cooled solutions (-78 ^0C) of LDA (1.1 equiv) in dry THF (or in the mixture of 30% HMPA-THF as stated in the table) and the mixtures were stirred at -78 ^0C under nitrogen atmophere for 45 min. To these solutions, 1.05 equiv of methyl iodide (for ester **2**) or allyl bromide (for ester **4**) were added and the mixtures were stirred for 2 h. The reactions were quenched by adding saturated solutions of ammonium chloride. The mixtures were extracted with ethyl acetate and washed with saturated solutions of sodium bicarbonate and brine, dried over anhydrous sodium sulfate and the solvents were removed under reduced pressure. The residues were purified by flash chromatography on silica gel using hexane and ethyl acetate (7:3) as eluent to yield **6** or **7** as colorless oils.

Compound **6** was obtained as a mixture of isomers 2*S* and 2*R* and the yields are shown in the Table: ^1H NMR (300 MHz, $CDCl_3$) δ 1.18 (d, 3H, J = 8.4 Hz, Me), 1.33 (s, 3H), 1.35 (s, 3H), 1.50 (s, 3H), 1.53 (s, 3H), 2.72 (m, 2H, CH_2), 3.06 (m, 1H, CH-Me), 3.76 (dd, 1H, $J_{6,6}$ = 12 and $J_{6,5}$ = 1.7 Hz, H-6), 3.90 (dd, 1H, $J_{6',6}$ = 12 and $J_{6',5}$ = 1.7 Hz, H-6'), 4.06 (d, 1H, $J_{1,1'}$= 12 Hz, H-1), 4.24 (dd, 1H, $J_{5,4}$ = 8.6 and $J_{5,6}$ = 1.7 Hz), 4.28 (d, 1H, J=2.55 Hz), 4.32 (d, 1H, $J_{1',1}$ = 12 Hz, H-1'), 4.56 (1H of isomer 2*R* , dd, $J_{4,5}$ = 8.6 and $J_{4,3}$ = 2.55 Hz), 4.62 (1H of isomer 2*S*, dd, $J_{4,5}$ = 8.6 and $J_{4,3}$ = 2.55 Hz), 7.20 (m, 5H)

ppm; ^{13}C NMR ($CDCl_3$, DEPT) δ 16.7, 24.0, 25.2, 25.3, 25.4, 39.5, 41.4, 61.2, 65.1, 70.0, 70.4, 101.5, 108.7, 109.1, 126.3, 128.4, 128.5, 128.9, 129.0, 139.0, 175.4 ppm; MS, *m/z* (relative intensity) 406 ($M^{+\cdot}$, 23), 391 (50%), 171 (21), 91 (base); HRMS Calcd for $C_{22}H_{30}O_7$ (406.1991). Found: 406.1980.

Compound **7** was obtained in a 56% yield as an isomeric mixture of *2S*/*2R* (70/30): IR (neat) 1742 (C=O), 1604, 1501, 1442, 1380 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.34 (s, 6H), 1.47 (s, 3H), 1.52 (s, 3H), 2.22-2.56 (m, 2H), 2.60-3.04 (m, 3H), 3.73 (1H of isomer **2***R*, d, $J_{6,6'}$ = 12.9 Hz), 3.75 (1H of isomer **2***S*, d, $J_{6,6'}$ = 12.9 Hz), 3.82-3.96 (m, 2H), 4.04 (d, 1H, $J_{1,1'}$ = 11.6 Hz), 4.13 (d, 1H, $J_{1',1}$ =11.6 Hz), 4.18-4.29 (m, 1H), 4.53 (1H of isomer **2***R*, dd, $J_{4,5}$ = 7.9 and $J_{4,3}$ = 2.2 Hz), 4.59 (1H, of isomer *2S*, dd, $J_{4,5}$ = 7.9 and $J_{4,3}$ = 2.2 Hz), 5.06-5.15 (m, 2H, allyl), 5.70-5.86 (m, 1H, allyl), 5.91 (s, 2H of isomer *2R*), 5.92 (s, 2H of isomer *2S*), 6.58-6.78 (m, 3H, Ph) ppm; ^{13}C NMR ($CDCl_3$, DEPT) δ 24.4, 25.6, 25.7, 26.2, 26.8, 26.9, 36.1, 36.2, 37.5, 38.1 47.8, 48.1, 61.5, 61.6, 65.4, 65.8, 70.3, 70.4, 70.5, 70.8, 71.2, 101.2, 101.7, 101.8, 108.5, 108.7, 109.0, 109.4, 109.5, 109.6, 109.7, 109.8, 117.7, 117.9, 122.2, 122.3, 132.9, 135.2, 135.3 146.1, 148.0, 174.4, 174.5 ppm.

Anal. Calcd for $C_{25}H_{32}O_9$ (476.52): C, 63.01; H, 4.61. Found: C, 63.13, H, 4.70.

General procedure for preparation of ketene silyl ketals (8) and (9). To a cooled solution (-78 ^0C) of LDA (2.2 equiv) in dry THF (or in the mixture of 30% HMPA-THF as stated in scheme 2) was added dropwise a solution of **4** (1 equiv) in dry THF (1 mL) and the mixture stirred at -78 ^0C under nitrogen atmosphere for 30 min. To this solution was added a solution of *tert*-butyldimethylsilyl chloride (TBDMS-Cl, 1.1 equiv) in 0.12 mL of HMPA (or in 0.16 mL of hexane). This solution was stirred for 30 min at the same temperature and allowed to reach room temperature. The mixture was partitioned between hexane and water. The organic layer was washed with saturated solutions of sodum bicarbonate and brine, dried over anhydrous sodium sulfate and the solvent was evaporated under reduced pressure to give crude mixtures of **8** or **9** as yellow coloured oils in quantitative yield.

Compounds **8** and **9** were obtained in the stereoselectivities as shown in Scheme 2: IR (neat) 1681 (C=C), 1388, 1379 (Me) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$, COSY) δ 0.05, 0.06, 0.08,0.09 (s, 3H, Me-Si), 0.19, 0.20 (s, 9H, *t*-Bu), 1.34 (s, 6H), 1.43 (s, 6H), 1.46 (s, 6H), 1.53 (s, 6H), 1.35-1.60 (4xd, 3H, Me cis and *trans*, J = 6.6 Hz), 3.70 (1H of **8**, d, $J_{1,1'}$ = 10.3), 3.71 (q, 1H, J = 6.6 Hz), 3.74 (d, 1H, $J_{6,6'}$ = 12.9 Hz), 3.83 (1H, of **9**, d, $J_{1,1'}$ =10.3

Hz), 3.89 (1H of **8**, d, $J_{1',1}$ = 10.3 Hz), 3.93 (1H of **9**, d, $J_{1',1}$ = 10.3 Hz), 3.94 (dd, 1H, $J_{6'6}$ = 12.9 and $J_{6',5}$ = 1.7 Hz), 4.24 (dd, 1H, $J_{5,4}$ = 7.9 and $J_{5,6}$ = 1.7 Hz), 4.40 (1H of **8**, d, $J_{3,4}$ = 2.6 Hz), 4.50 (1H of **9**, d, $J_{3,4}$ =2.6 Hz), 4.60 (dd, 1H, $J_{4,5}$ =7.9 and $J_{4,3}$ = 2.6 Hz) ppm.

(*S*)-3-Phenyl-1-hydroxy-2-methylpropane (10). To a solution of **6** (0.103 g, 0.25 mmol) in dry THF (7 mL) under nitrogen atmosphere was added lithium aluminum hydride (19.2 mg) portionwise and the mixture stirred at room temperature for 2 h. The reaction was quenched by addition of water (0.04 mL), a solution of 10% NaOH (0.03 mL) and ether (15 mL). The mixture was filtered, dried and the solvent removed under reduced pressure. The residue was chromatographed on a preparative TLC silica gel plate to yield a yellow colored oil (5.7 mg, 26%): $[\alpha]^{25}_D$ (*c* 2.02, $CHCl_3$) -8° (lit.[9] $[\alpha]^{25}_D$ -12.2°); ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.95 (3H, d, J = 7.0, Me), 1.45 (1H, OH), 1.97 (1H, m, H-2), 2.43 (1H, dd, J = 4.6 and 6.55 Hz, CH_2-Ph), 2.78 (1H, dd, J = 6.55 and 4.6 Hz, CH_2-Ph), 3.50 (2H, m, CH_2-OH), 7.22 (m, 5H) ppm.

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