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DIASTEREOSELECTIVE ADDITION OF ORGANOMETALLIC REAGENTS TO (*R*)-2,3-ISOPROPYLIDENEDIOXY-1-(2-FURYL)-1-PROPANONE YIELDING CHIRAL TERTIARY FURYL CARBINOLS†

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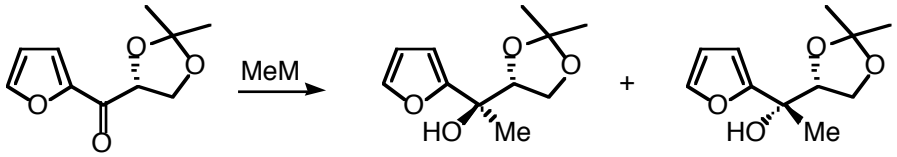
Abstract – The nucleophilic addition of either organolithium or Grignard reagents to (*R*)-2,3-isopropylidenedioxy-1-(2-furyl)-1-propanone (**1**) in Et_2O afforded the corresponding *anti* isomers predominantly, whereas addition of organolithium reagents in THF with HMPA as a co-solvent gave the *syn* isomers in moderate selectivities.

During the course of the enantioselective synthesis of malyngolide, we needed to prepare a chiral tertiary furyl carbinol by the nucleophilic addition of Grignard reagent (nonylmagnesium bromide) to α, β-isopropylidenedioxy 4-methylfuran-2-yl ketone.[1] Although 1,2-asymmetric induction based on the nucleophilic addition to 1,2-*O*-isopropylidenedioxy-D-glyceraldehyde or its enantiomer has been extensively studied,[2] the addition to the corresponding 1,2-*O*-isopropylidenedioxy ketones has been limited.[3] In general 1,2-*O*-isopropylidenedioxy ketones react with a considerably higher α-chelation controlled diastereoselectivities than 1,2-*O*-isopropylidenedioxy-D-glyceraldehyde due to the higher Lewis basicity of the ketone carbonyl group.[2, 3] Since furyl carbinols would be versatile starting materials for the synthesis of a wide variety of functionalized natural products,[4] we intended to investigate the preparation of chiral furyl carbinols employing the 1,2-asymmetric induction. There are many methods for preparation of chiral secondary furyl carbinols,[5] however, a few synthetic examples of chiral tertiary furyl carbinols have been reported.[1, 6] Here we describe the method for the diastereoselective synthesis of chiral tertiary furyl carbinols by the addition of organometallic reagents to (*R*)-2,3-isopropylidenedioxy-1-(2-furyl)-1-propanone (**1**).

We first examined the methylation of (*R*) -2,3-isopropylidenedioxy-1-(2-furyl)-1-propanone (**1**)[7] under various reaction conditions as shown in Table 1. Solvents used were hexane, toluene, CH_2Cl_2, Et_2O,

† This paper is dedicated to Prof. Shô Itô on the occasion of his 77th birthday.

Table1. Methylation of α,β - isopropylidenedioxy ketone (1)



1 **2** (*anti*) **3** (*syn*)

Entry	MeM	Solvent (Additive)	Temp (°C)	*anti* / *syn*		Yield (%)
1	MeLi	hexane	20	89	11	98
2		toluene	-78	95	5	90
3		CH_2Cl_2	-78	97	3	93
4		Et_2O	-10	***99***	***1***	92
5		THF	-78	64	36	86
6		THF+HMPA	-78	***33***	***67***	55
7		THF ($ZnBr_2$)	0	—	—	—
8	MeMgBr	hexane	20	72	28	92
9		toluene	-78	72	28	88
10		CH_2Cl_2	-78	72	28	78
11		Et_2O	-10	75	25	86
12		THF	-78	72	28	80
13		THF+HMPA	-78	***33***	***67***	58
14		THF ($ZnBr_2$)	0	—	—	—

and THF and 1.5 equiv. of organometallic reagents (MeLi and MeMgBr) were employed. Reactions were carried out at –78°C except the reactions in hexane and Et_2O used as solvents owing to the low solubility of **1** to them. Addition of MeLi to **1** proceeded with moderate to high (78 to 98% de) *anti* selectivities (Entries 1-4), especially in Et_2O (98% de). On the other hand, the diastereoselectivities dropped considerably (44 to 50% de) by the use of MeMgBr (Entries 8-12). The predominant formation of the *anti* diastereomer (**2**) might be attributed to the α-chelate **A** as shown in Figure 1. The lower diastereoselectivity found in the addition of MeMgBr can be explained by assuming β-chelate **B**. Thus chelation control may result in the formation of either *anti* or *syn* products depending on the relative

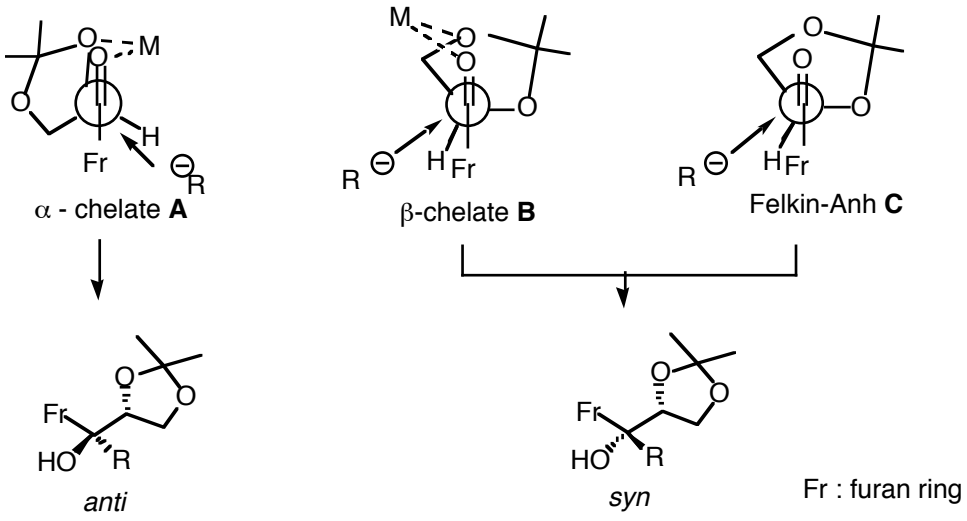
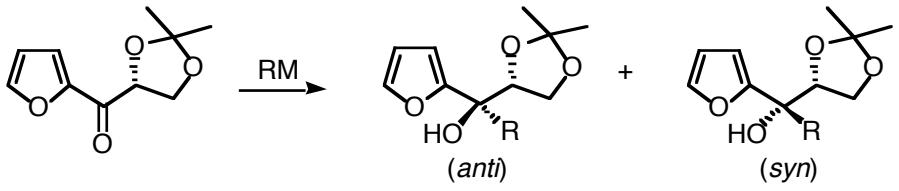


Figure 1

stabilities of respective α- and β-chelates. In the presence of HMPA (10 equiv.), both MeLi and MeMgBr showed slight preferences (34% de) for the *syn* diasteromeric addition product (**3**) (Entries 6, 13). The opposite stereochemistry could be rationalized by assuming the Felkin-Anh model **C**. Apparently, HMPA with chelating ability would compete with the α,β-dialkoxy ketone (**1**) for the lithium and magnesium cations, thus reducing the proportion of the α-chelaton-controlled *anti* isomer (**2**). Different from the glyceraldehyde, **1** did not react with both MeLi and MeMgBr when zinc bromide was additionally present (Entries 7, 14).[5d]

Table 2. Addition to α,β - isopropylidenedioxy ketone (1)



(*anti*) (*syn*)

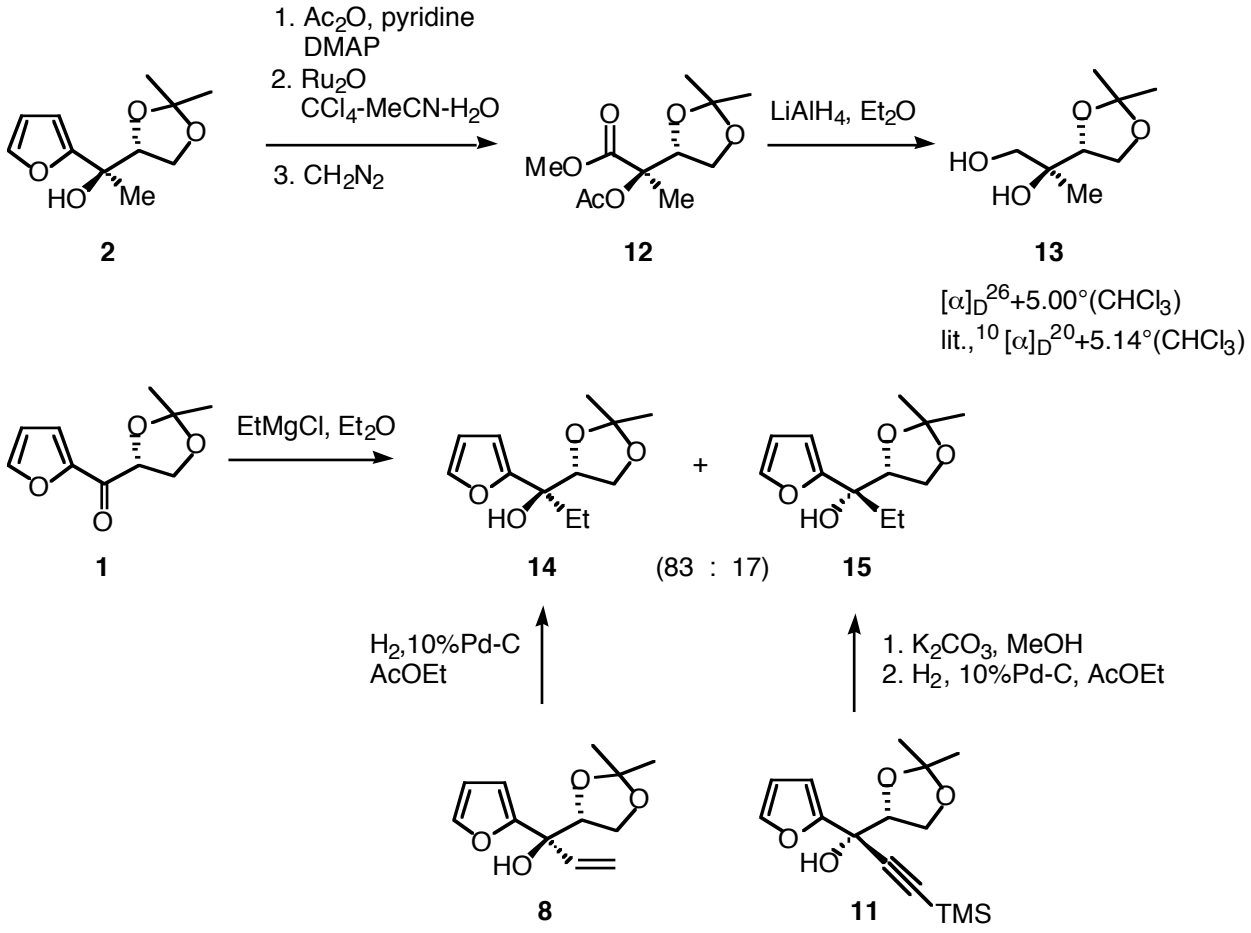
1

4 R=Bu **5 R=Bu**
6 R=Ph **7 R=Ph**
8 R= CH=CH$_2$ **9 R= CH=CH$_2$**
10 R= C≡CTMS **11 R= C≡CTMS**

Entry	RM	Solvent	Temp(°C)	*anti* / *syn*		Yield (%)
1	*n*-BuLi	Et_2O	-10	76	24	84
2		THF	-78	57	43	96
3		THF+HMPA	-78	9	91	51
4	*n*-BuMgCl	Et_2O	-10	***93***	***7***	86
5		THF	-78	84	16	76
6		THF+HMPA	-78	***4***	***96***	41
7	PhLi	Et_2O	-10	73	27	89
8		THF	-78	33	67	99
9		THF+HMPA	-78	***13***	***87***	80
10	PhMgBr	Et_2O	-10	76	24	94
11		THF	-78	***90***	***10***	98
12		THF+HMPA	-78	40	60	48
13	CH_2=CHLi	Et_2O	-10	61	39	81
14		THF	-78	33	67	97
15		THF+HMPA	-78	***11***	***89***	21
16	CH_2=CHMgBr	Et_2O	-10	67	33	91
17		THF	-78	***70***	***30***	79
18		THF+HMPA	-78	18	82	13
19	TMSC≡CLi	Et_2O	-10	***54***	***46***	92
20		THF	-78	42	58	99
21		THF+HMPA	-78	***2***	***98***	88
22	TMSC≡CMgCl	Et_2O	-10	17	83	97
23		THF	-78	50	50	55
24		THF+HMPA	-78	0	100	28

Addition of several organolithium and Grignard reagents in Et_2O and THF was investigated to gain the further insight. The results of butylation, phenylation, vinylation, and trimethylsilylethynylation were shown in Table 2. In contrast to the methylation, Grignard reagents showed higher α-chelation-controlled diastereoselectivities rather than organolithium reagents in butylation, phenylation, and

vinylation.[8] Reaction with Grignard reagents in Et_2O and THF gave moderate to good (34 to 86% de) *anti* selectivities (Entries 4, 5, 10, 11, 16, 17), whereas the use of organolithium reagents in Et_2O yielded low to moderate (8 to 52% de) *anti* selectivities (Entries 1, 2, 7, 13, 19). Interestingly, a reversal of the diastereoselectivities was observed when the addition of organolithium reagents was carried out in THF (Entries 8, 14, 20). The stronger donor solvent, such as THF, might afford a lower chelation control for the organolithium reagents. Unexpectedly, the addition of TMSC≡CMgCl in Et_2O proceeded with a moderate preference for the β-chelation-controlled product (**11**) (Entry 22). In analogy to the methylation, the presence of HMPA showed low to high (20 to 100% de) *syn* selectivities (Entries 3, 6, 9, 12, 15, 18, 21, 24).



Scheme 1

Although the stereochemistries of the addition products were deduced by ^1H NMR analysis according to the empirical rule,[9] several compounds were elucidated by their conversion to known compounds (Scheme 1). Furyl methyl carbinol (**2**) was transformed into the known erythritol (**13**)[10] by oxidation of a furan ring followed by reduction of the corresponding carboxylate (**12**). Hydrogenation of the furyl vinyl carbinol (**8**) gave the same *anti* product (**14**) prepared by addition of EtMgCl to **1**, while the furyl

trimethylsilylethnyl carbinol (**11**) was converted to the *syn* furyl ethyl carbinol (**15**).

In summary, we have prepared either *anti*- or *syn*- chiral tertiary furyl carbinols (**2-11**) depending on the combination of organometallic reagents and solvents. Since furyl carbinols are synthetically useful intermediates, the present method would be versatile in preparing a number of chiral tertiary furyl carbinols.

EXPERIMENTAL

Melting points were measured with a Yanagimoto MP apparatus and are uncorrected. IR spectra were obtained using a JASCO FT/IR-200 spectrophotometer. ^{1}H- and ^{13}C-NMR spectra were obtained on JEOL LAMBDA-270 (^{1}H-NMR: 270 MHz, ^{13}C-NMR: 67.8 MHz) instrument for solutions in $CDCl_3$, and chemical shifts are reported on the δ scale from internal TMS. MS spectra were measured with a JEOL JMS-D300 spectrometer. Optical rotations were taken with a JASCO DIP-360 polarimeter. Elemental analyses were performed on a Yanaco-MT5. Organolithium and Grignard reagents purchased were as follows: 1 mol/L MeLi in Et_2O solution, 3 mol/L MeMgBr in Et_2O solution, 2 mol/L EtMgCl in THF solution, 1.6 mol/L *n*-BuLi in *n*-hexane solution, 1 mol/L *n*-BuMgCl in THF solution, 1 mol/L PhLi in cyclohexane – Et_2O solution, 2 mol/L PhMgBr in THF solution, 1 mol/L CH_2=CHMgBr in THF solution. CH_2=CHLi, TMSC≡CLi, and TMSC≡CMgCl reagents were prepared.

General Procedure for Addition of Organometallics to Acylfuran

To a stirred solution of the ketone (**1**) (196 mg, 1 mmol) in solvent (5 mL) was added a solution of organometallic reagent in solvent (1.5 mmol) at an appropriate temperature. Stirring was continued at the same temperature until the ketone (**1**) was disappeared on TLC. After quenching with saturated aqueous NH_4Cl solution, the product was extracted with AcOEt. The organic layer was washed with brine and dried over anhydrous Na_2SO_4. Evaporation of the solvent afforded a residue, which was purified by column chromatography on silica gel eluting with hexane-AcOEt. The yields and ratios of *anti* to *syn* were shown in Tables 1 and 2.

(2*R*, 3*R*)-3-(2'-Furyl)-1,2-isopropylidenedioxy-3-butanol (2)

colorless oil, $[\alpha]_D^{24}$+22.3° (c 1.1, $CHCl_3$); IR νmax 3460 cm^{-1}; ^{1}H-NMR δ: 1.36 and 1.40 [each 3H, 2 x s, $C(CH_3)_2$], 1.58 (3H, s, 4-H), 2.59 (1H, s, OH), 3.84-3.98 (2H, m, 1-H), 4.29 (1H, t, *J* =6.7 Hz, 2-H), 6.28-6.34 (2H, m, 3', 4'-H) and 7.36 (1H, s, 5'-H); ^{13}C-NMR δ: 23.59, 24.72, 25.75, 64.73, 70.86, 80.17, 105.61, 109.27, 109.84, 141.42 and 156.40. HRMS Calcd for $C_{11}H_{16}O_4$ (M), 212.1052. Found (M^+), 212.1052.

(2*R*, 3*S*)-3-(2'-Furyl)-1,2-isopropylidenedioxy-3-butanol (3)

colorless needles, mp 76-78°C (from hexane), $[\alpha]_D^{24}$ -2.3° (c 1.0, $CHCl_3$); IR νmax 3455 cm^{-1}; ^{1}H-NMR

δ: 1.37 (3H, s, 4-H), 1.42 and 1.46 [each 3H, 2 x s, $C(CH_3)_2$], 2.66 (1H, s, OH), 3.89 (1H, t, *J* =7.3 Hz, 1-H), 4.00 (1H, t, *J* =6.7 Hz, 1-H), 4.44 (1H, dd, *J* =6.7 and 7.3 Hz, 2-H), 6.29-6.34 (2H, m, 3', 4'-H) and 7.34 (1H, s, 5'-H); ^{13}C NMR δ: 21.94, 25.13, 26.06, 64.95, 71.01, 80.15, 105.67, 109.72, 110.10, 141.77 and 157.36. HRMS Calcd for $C_{11}H_{16}O_4$ (M), 212.1045. Found (M^+), 212.1045. Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found C, 62.08; H, 7.60.

(2*R*, 3*R*)-3-(2'-Furyl)-1,2-isopropylidenedioxy-3-heptanol (4)

colorless oil, $[\alpha]_D^{30}$ +20.2° (c 0.8, $CHCl_3$); IR νmax 3490 cm^{-1}; ^{1}H-NMR δ: 0.86 (3H, t, *J* =7.3 Hz, 7-H), 1.05, 1.29, 1.62 and 1.88 (6H, 4 x m, 4, 5, 6-H), 1.38 and 1.40 [each 3H, 2 x s, $C(CH_3)_2$], 3.80 (2H, m, 1-H), 4.33 (1H, t, *J* = 6.9 Hz, 2-H), 6.31 (2H, m, 3', 4'-H) and 7.34 (1H, m, 5'-H); ^{13}C-NMR δ: 13.94, 22.80, 25.14, 25.38, 26.16, 38.00, 65.02, 74.21, 80.22, 106.55, 109.61, 110.08, 141.57 and 155.24. HRMS Calcd for $C_{14}H_{22}O_4$ (M), 254.1501. Found (M^+), 254.1502. Anal. Calcd for $C_{14}H_{22}O_4$: C, 66.11; H, 8.72. Found C, 65.83; H, 8.94.

(2*R*, 3*S*)-3-(2'-Furyl)-1,2-isopropylidenedioxy-3-heptanol (5)

colorless oil, $[\alpha]_D^{26}$ +4.3° (c 1.0, $CHCl_3$); IR νmax 3480 cm^{-1}; ^{1}H-NMR δ: 0.84 (3H, t, *J* =6.8 Hz, 7-H), 0.98 and 1.26 (6H, 2 x m, 4, 5, 6-H), 1.39 [6H, s, $C(CH_3)_2$], 2.50 (2H, m, 1-H), 4.43 (1H, t, *J* = 6.4 Hz, 2-H), 6.33 (2H, m, 3', 4'-H) and 7.38 (1H, m, 5-H); ^{13}C-NMR δ: 13.82, 22.78, 25.26, 25.34, 26.10, 29.58, 35.53, 64.45, 73.74, 79.72, 106.59, 109.33, 110.06, 141.54 and 156.49. HRMS Calcd for $C_{14}H_{22}O_4$ (M), 254.0151. Found (M^+), 254.1513. Anal. Calcd for $C_{14}H_{22}O_4$: C, 66.11; H, 8.72. Found C, 66.29; H, 8.88.

(1*R*, 2*R*)-1-(2'-Furyl)-2,3-isopropylidenedioxy-1-phenyl-1-propanal (6)

colorless oil, $[\alpha]_D^{25}$ +5.5° (c 0.9, $CHCl_3$); IR νmax 2940, 3440 cm^{-1}; ^{1}H-NMR δ: 1.48 [6H, s, $C(CH_3)_2$], 3.01 (1H, s, OH), 4.02 (2H, m, 3-H), 4.92 (1H, dd, *J* =6.8 and 13.5 Hz, 2-H), 6.30 (2H, m, 3', 4'-H), 7.32 (5H, m, Ph) and 7.54 (1H, m, 5'-H); ^{13}C-NMR δ: 25.04, 25.98, 65.41, 74.92, 79.30, 107.31, 109.88, 110.09, 126.43, 127.62, 127.92, 141.92, 142.17 and 155.71. HRMS Calcd for $C_{16}H_{18}O_4$ (M), 274.1172. Found (M^+), 274.1175. Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.05; H, 6.61. Found C, 69.13; H, 6.73.

(1*S*, 2*R*)-1-(2'-Furyl)-2,3-isopropylidenedioxy-1-phenyl-1-propanal (7)

colorless oil, $[\alpha]_D^{25}$ +65.3° (c1.0, $CHCl_3$); IR νmax 2922, 3550 cm-1; ^{1}H-NMR δ: 1.43 and 1.48 [each 3H, 2 x s, $C(CH_3)_2$], 3.17 (1H, s, OH), 3.59 (1H, dd, *J* =1.2 and 6.6 Hz, 3-H), 3.76 (1H, dd, *J* =1.2 and 7.8 Hz, 3-H), 4.89 (1H, dd, *J* =6.6 and 7.8 Hz, 2-H), 6.34 and 6.46 (1H, 2 x m, 3', 4'-H), 7.31 (5H, m, Ph) and 7.47 (1H, m, 5'-H); ^{13}C-NMR δ: 25.49, 26.23, 64.86, 73.59, 79.57, 107.04, 110.05, 110.40, 115.22, 125.11, 127.60, 128.27, 129.48, 140.02, 142.26 and 157.05. HRMS Calcd for $C_{16}H_{18}O_4$ (M), 274.1213. Found (M^+), 274.1212. Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.05; H, 6.61. Found C, 70.01; H, 6.63.

(2*R*, 3*R*)-3-(2'-Furyl)-1,2-isopropylidenedioxy-4-penten-3-ol (8)

colorless oil, $[\alpha]_D^{25}$ -26.3° (c 0.9, $CHCl_3$); IR νmax 3450 cm^{-1}; ^{1}H-NMR δ: 1.37 (3H, s, 1"-H), 1.42 and 1.46 [each 3H, 2 x s, $C(CH_3)_2$], 2.66 (1H, s, OH), 3.89 (1H, t, *J* =7.3 Hz, 3-H), 4.00 (1H, t, *J* =6.7 Hz, 3-H), 4.44 (1H, dd, *J* =6.7 and 7.3 Hz, 2-H), 6.29-6.34 (2H, m, 3', 4'-H) and 7.34 (1H, s, 5'-H); ^{13}C-NMR δ: 24.89, 26.05, 65.11, 73.84, 79.28, 107.13, 109.77, 110.22, 115.60, 138.03, 142.24 and 154.37. HRMS Calcd for $C_{12}H_{16}O_4$ (M), 224.1054. Found (M^+), 224.1053. Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found C, 64.05; H, 7.06.

(2*R*, 3*S*)-3-(2'-Furyl)-1,2-isopropylidenedioxy-4-penten-3-ol (9)

colorless oil, $[\alpha]_D^{26}$ +47.4° (c 0.9, $CHCl_3$); IR νmax 3450 cm^{-1}; ^{1}H-NMR δ: 1.38 and 1.44 [each 3H, 2 x s, $C(CH_3)_2$], 2.81 (1H, s, OH), 3.96 (2H, t, *J* =7.1 Hz, 1-H), 4.56 (1H, t, *J* =6.9 Hz, 2-H), 5.29 (1H, d, *J* = 10.7 Hz, 5-H), 5.48 (1H, d, *J* =17.3 Hz, 5-H), 6.00 (1H, dd, *J*= 10.7 and 17.3 Hz, 4-H), 6.35 (2H, s, 3', 4'-H) and 7.40 (1H, s, 5'-H); ^{13}C-NMR δ: 25.09, 26.10, 64.81, 73.65, 78.98, 106.69, 110.06, 110.19, 116.11, 136.07, 142.16 and 155.54. HRMS Calcd for $C_{12}H_{16}O_4$ (M), 224.1045. Found (M^+), 224.1045. Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found C, 64.35; H, 7.28.

(2*R*, 3*R*)-3-(2'-Furyl)-1,2-isopropylidenedioxy-5-trimethylsilyl-4-pentyn-3-ol (10)

colorless oil, $[\alpha]_D^{26}$+4.2° (c 1.1, $CHCl_3$); IR νmax 3400 cm^{-1}; ^{1}H-NMR δ: 0.21 (9H, s, TMS), 1.36 and 1.39 [each 3H, 2 x s, $C(CH_3)_2$], 2.85 (1H, s, OH), 4.12 (2H, dd, *J* =4.6 and 6.3 Hz, 1-H), 4.51 (1H, t, *J* =6.3 Hz, 2-H), 5.30-6.37 and 6.52-6.54 (1H, 2 x m, 3', 4'-H), and 7.41-7.42 (1H, m, 5'-H); ^{13}C-NMR δ: 25.72, 26.48, 29.96, 66.36, 69.86, 80.07, 91.50, 103.22, 109.11, 110.67, 110.82, 143.19 and 153.03. HRMS Calcd for $C_{15}H_{22}O_4Si$ (M), 276.1178. Found (M^+), 276.1178. Anal. Calcd for $C_{15}H_{22}O_4Si$: 61.19; H, 7.53. Found C, 61.29; H, 7.65.

(2*R*, 3*S*)-3-(2'-Furyl)-1,2-isopropylidenedioxy-5-trimethylsilyl-4-pentyn-3-ol (11)

colorless needles, mp 43°C (from hexane). $[\alpha]_D^{27}$ +21.4° (c 1.0, $CHCl_3$); IR νmax 3420 cm^{-1}; ^{1}H-NMR δ: 0.20 (9H, s, TMS), 1.40 and 1.51 [each 3H, 2 x s, $C(CH_3)_2$], 3.12 (1H, s, OH), 4.00 (2H, d, *J* = 6.8 Hz, 1-H), 4.57 (1H, t, *J* =6.8 Hz, 2-H), 6.34-6.36 and 6.49-6.50 (1H, 2 x m, 3', 4'-H), and 7.40-7.41 (1H, m, 5'-H); ^{13}C-NMR δ: 25.47, 26.18, 66.06, 69.74, 80.07, 91.27, 102.02, 108.27, 110.18, 110.71, 142.98 and 152.55. HRMS Calcd for $C_{15}H_{22}O_4Si$ (M), 276.1183. Found (M^+), 276.1183. Anal. Calcd for $C_{15}H_{22}O_4Si$: C, 61.19; H, 7.53. Found C, 60.89; H, 7.54.

2-*c*-Methyl-3,4-*O*-isopropylidenedioxy-D-erythritol (13)

A solution of alcohol (**2**) (470 mg, 2.2 mmol), a catalytic amount of DMAP, and acetic anhydride (1 mL, 13.3 mmol) in pyridine (5 mL) was heated at 40°C. The reaction mixture was poured into water and the

product was extracted with AcOEt. The organic layer was washed with aq. saturated NH_4Cl solution and dried over anhydrous Na_2SO_4. Evaporation of the solvent afforded a residue, which was purified by column chromatography on silica gel (hexane : AcOEt = 9 : 1) to give (2*R*, 3*R*)-3-(2'-furyl)-1,2-isopropylidenedioxy-3-butyl acetate (459 mg, 81.4%) as a colorless oil. $[\alpha]_D^{26}$ +9.1° (c 1.1, $CHCl_3$); IR νmax 1745 cm^{-1}; ^{1}H-NMR δ: 1.36 and 1.40 [each 3H, 2 x s, $C(CH_3)_2$], 1.84 (3H, s, 4-H), 2.03 (3H, s, CH_3CO), 4.06 (2H, m, 1-H), 4.40 (1H, t, *J* =6.8 Hz, 2-H), 6.34 (2H, m, 3', 4'-H) and 7.35 (1H, m, 5'-H); ^{13}C-NMR δ: 18.48, 21.79, 25.16, 25.89, 65.15, 78.44, 79.88, 107.80, 109.85, 110.38, 141.93, 153.19 and 169.26. HRMS Calcd for $C_{13}H_{18}O_5$ (M), 212.1045. Found (M^+), 254.1164. Anal. Calcd for $C_{13}H_{18}O_5$: C, 61.40; H, 7.14. Found C, 61.10; H, 7.08.

A suspension of RuO_2 (61 mg, 0.5 mmol) and $NaIO_4$ (488 mg, 2.2 mmol) in CCl_4/MeCN/H_2O {(2:3:2) 22 mL} was stirred for 20 min and a solution of $NaHCO_3$ (3.2 g, 37 mmol) in H_2O (2 mL) was added. After stirring for 5 min, a solution of the above acetate (94 mg, 0.4 mmol) in MeCN (1 mL) was added and then $NaIO_4$ (244 mg, 1.1 mmmol) was added. After addition of 2-propanol (5 mL), H_2O (5 mL) and AcOEt (20 mL) were added and the reaction mixture was filtered through celite pad. The filtrate was acidified with 4N HCl. The product was extracted with AcOEt. The organic layer was washed with brine and dried over anhydrous Na_2SO_4. Evaporation of the solvent afforded a residue (40 mg). To a solution of crude carboxylic acid in Et_2O (15 mL) was added a *ca.* 0.5 M Et_2O solution of diazomethane (1.5 mL, 0.75 mmol) and the reaction mixture was allowed to stand for 2h. Concentration of the solvent gave methyl (2*R*, 3*R*)-2-acetoxy-3-methyl-2,3-isopropylidenedioxy-butanoate (**12**) (40 mg). ^{1}H-NMR δ: 1.36 and 1.45 [each 3H, 2 x s, $C(CH_3)_2$], 1.61 (3H, s, 2-Me), 2.08 (3H, s, CH_3CO), 3.76 (3H, s, OCH_3), 3.99-4.16 (2H, m, 4-H), and 4.31 (1H, t, *J*=5.9, 3-H). This crude ester (**12**) was further used without any purification owing to its instability.

To a suspension of lithium aluminum hydride (84 mg, 2.2 mmmol) in Et_2O (15 mL) was added a solution of crude ester in Et_2O (2 mL) at 0°C and stirring was continued for 8 h at rt. After addition of 10% NaOH solution, the reaction mixture was stirred for 30 min. The reaction mixture was filtered through celite pad. The filtrate was extracted with AcOEt and the organic layer was washed with brine. The extract was dried over anhydrous Na_2SO_4. Evaporation of the solvent afforded a residue, which was purified by column chromatography on silica gel (hexane : AcOEt = 1 : 2) to give alcohol (**13**) (28 mg, 40%) as colorless prisms. mp 95-96°C (from hexane), lit.,[10] mp 100-101°C. $[\alpha]_D^{26}$ +5.00° (c 0.7, $CHCl_3$), lit.,[10] $[\alpha]_D^{20}$ +5.14° (c 1.07, $CHCl_3$) ; IR νmax 3340 cm^{-1}; ^{1}H-NMR δ: 1.17 and 1.36 [each 3H, 2 x s, $C(CH_3)_2$], 1.44 (3H, s, 2-Me), 2.32 (2H, br, OH), 3.43 and 3.64 (1H, 2 x d, *J* =11.4 Hz, 1-H), 3.92 (1H, dd, *J* =6.9 and 8.2 Hz, 2-H) and 4.06 (2H, m, 3-H); ^{13}C-NMR δ: 20.44, 24.97, 26.36, 65.10, 67.37, 72.38, 79.60 and 109.12. HRMS Calcd for $C_8H_{16}O_4$ (M), 276.11831. Found (M^+), 161.0812. Anal. Calcd for $C_8H_{16}O_4$: C, 54.53; H, 9.15. Found C, 54.37; H, 8.90.

(2*R*, 3*R*)-3-(2'-Furyl)-1,2-isopropylidenedioxy-3-pentanol (14)

A suspension of allylic alcohol (**8**) (42 mg, 0.2 mmol) and 10% Pd/C (18 mg) in AcOEt (15 mL) was stirred under hydrogen for 10 min. The catalyst was filtered and the filtrate was evaporated to give a residue, which was purified by column chromatography on silica gel (hexane : AcOEt = 9 : 1) to give alcohol (**14**) (30 mg, 71.8%) as colorless oil. $[\alpha]_D^{24}$+26.3° (c 1.0, $CHCl_3$); IR νmax 3480 cm^{-1}; ^{1}H-NMR δ: 0.81 (3H, t, *J* = 7.4 Hz, 5-H), 1.38 and 1.40 [each 3H, 2 x s, $C(CH_3)_2$], 1.92 (2H, t, *J* =7.4 Hz, 4-H), 2.36 (1H, s, OH), 3.82 (2H, m, 1-H), 4.34 (1H, t, *J* =6.9 Hz, 2-H), 6.31 (2H, m, 3', 4'-H), and 7.33 (1H, s, 5'-H); ^{13}C-NMR δ: 7.60, 25.16, 26.19, 31.02, 65.10, 74.56, 79.96, 106.82, 109.62, 110.10, 141.69 and 154.92. HRMS Calcd for $C_{12}H_{18}O_4$ (M), 226.1204. Found (M^+), 226.1204. Anal. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found C, 63.81; H, 7.94.

(2*R*, 3*S*)-3-(2'-Furyl)-1,2-isopropylidenedioxy-3-pentanol (15)

A mixture of ethynylsilane (**11**) (637 mg, 2.2 mmol), potassium carbonate (300 mg, 2.7 mmol), and MeOH (24m L) was stirred for 30 min. Concentration of the solvent gave a residue, which was extracted with AcOEt. The organic layer was washed with brine. The extract was dried over anhydrous Na_2SO_4. Evaporation of the solvent afforded a residue, which was purified by column chromatography on silica gel (hexane : AcOEt = 9 : 1) to give the corresponding ethyne (358 mg, 74.5%) as colorless prisms, mp 72-73°C (from hexane). $[\alpha]_D^{24}$ +9.4° (c 0.6, $CHCl_3$); IR νmax 3280 cm^{-1}; ^{1}H-NMR δ: 1.40 and 1.50 [each 3H, 2 x s, $C(CH_3)_2$], 2.63 (1H, s, OH), 3.11 (1H, s, 5-H), 4.06 (2H, d, *J* =6.6 Hz, 1-H), 4.59 (1H, t, *J* =6.6 Hz, 2-H), 6.37 and 6.53(1H, 2 x m, 3', 4'-H), and 7.42 (1H, m, 5'-H); ^{13}C-NMR δ: 25.29, 26.19, 65.93, 69.53, 74.61, 80.00, 81.09, 108.44, 110.45, 110.92, 143.14 and 152.29. HRMS Calcd for $C_{12}H_{14}O_4$ (M), 222.0902. Found (M^+), 222.0897. Anal. Calcd for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found C, 64.65; H, 6.39.

A suspension of ethyne (52.3 mg, 0.3 mmol) and 10% Pd/C (17 mg) in AcOEt (15 mL) was stirred for 15 min. The catalyst was filtered and the filtrate was evaporated to give a residue, which was purified by column chromatography on silica gel (hexane : AcOEt = 9 : 1) to give alcohol (**15**) (38.8 mg, 71.5%) as colorless oil. $[\alpha]_D^{25}$ +4.1° (c 0.9, $CHCl_3$); IR νmax 3460 cm^{-1}; ^{1}H-NMR δ: 0.78 (3H, t, *J* =7.6 Hz, 5-H), 1.36 and 1.39 [each 3H, 2 x s, $C(CH_3)_2$], 1.75 (2H, m, 4-H), 2.67 (1H, s, OH), 4.00 (2H, m, 1-H), 4.43 (1H, t, *J* =6.4 Hz, 2-H), 6.33 (2H, m, 3'- and 5'-H), and 7.38(1H, s, 4'-H); ^{13}C-NMR δ: 7.10, 24.98, 25.75, 28.24, 64.08, 73.73, 79.23, 106.51, 108.97, 109.70, 141.27 and 155.80. HRMS Calcd for $C_{12}H_{18}O_4$ (M), 226.1201. Found (M^+), 226.1201. Anal. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found C, 63.63; H, 8.01.

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