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Prins Cyclization to Tetrahydrofuran Units of Polyether Antibiotics: Remarkable Siloxy Effect for Stereocontrolled Cyclization

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Abstract: A novel route to substituted tetrahydrofurans is described, which is based on the Lewis acid-promoted Prins cyclization with side chain formation of carbon-carbon bond. Bishomoallylic silyl ethers, rather than the (chloro)benzyl ethers and esters, provide selectivity tetrahydrofurans, indicating the siloxy effect for facilitating the cyclization. Copyright © 1996 Elsevier Science Ltd

A substituted oxygen heterocycle bearing side chain chirality is a chracteristic feature of polyether antibiotics (Figure 1), and hence methods for assembling these structural units in stereocontrolled fashion have been developed in recent years.[1] During the course of our research project to develop the carbonyl-ene reaction,[2,3] as an efficient method for asymmetric synthesis, we made unanticipated observations: a substituted tetrahydrofuran was obtained in an attempted glyoxylate-ene reaction of bishomoallylic silyl ether, presumably via the Prins reaction[4] to form carbon-carbon bond followed by internal attack of the siloxy group into the cationic intermediate (Scheme 1).

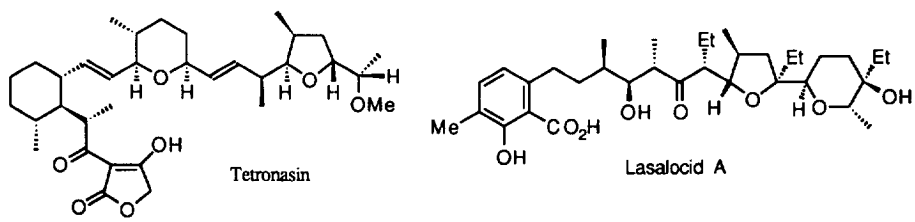
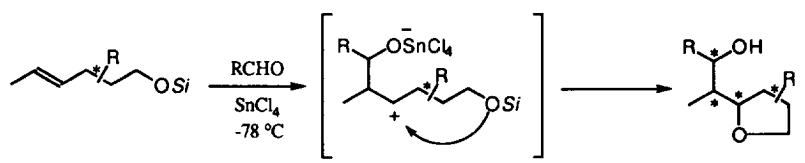


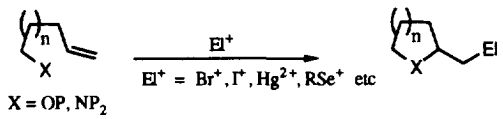
Figure 1



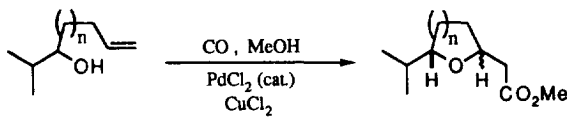
Scheme 1

So far, many precedent examples have been reported on heterocyclization with the side chain formation of carbon-heteroatom bonds initiated by the electrophilic attack of heteroatom electrophiles to olefins (eq. 1).[1] To the best of our knowledge, there is no example on the heterocyclization with side chain formation of carbon-carbon bond except for palladium-catalyzed alkoxycarbonylation (eq. 2).[5] Herein we report the Lewis acid-

promoted Prins cyclization with side chain formation of carbon-carbon bond as a stereocontrolled route to tetrahydrofuran units of polyether antibiotics.[6,7]



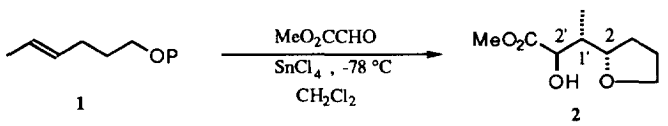
(1)



(2)

n = 1 *cis* / *trans* = 50 : 50
n = 2 *cis* / *trans* = 100 : 0

First, the reaction of dimethylthexylsilyl (*E*)-4-hexen-1-yl ether (**1a**) with methyl glyoxylate was found to give stereoselectively (>91%) the substituted tetrahydrofuran (**2**) in 48% isolated yield along with the glyoxylate-ene product **3a** (48% isolated yield) in the presence of $SnCl_4$ (1 equivalent) at -78 °C in CH_2Cl_2 (eq. 3, Table 1).



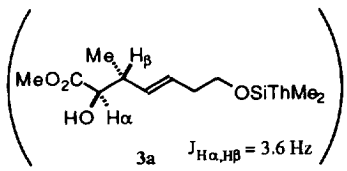
1 **2**

(3)

>91% stereoselective

Table 1. Prins cyclization of bishomoallylic silyl ether **1**

Entry	P	**2** (% Yield)
1a	Si ThMe$_2$	48
1b	Si ^{i}Pr$_3$	33
1c	Si ^{t}BuPh$_2$	18
1d	Si ^{i}PrMe$_2$	67
1e	Bn	32



3a $J_{H\alpha,H\beta}$ = 3.6 Hz

After screening the alcohol-protecting groups, the less bulky but relatively stable dimethyl-*iso*-propylsilyl group was found to be the best of choice. The 1',2'-*anti*-configuration of **2** was deduced by the similarlity in the ^{1}H NMR coupling constant of hydroxy methine proton ($J_{H2',H1'}$ = 3.9 Hz) to that of the corresponding *anti*-ene product **3a** ($J_{H\alpha,H\beta}$ = 3.6 Hz). The 2,1'-*syn* configuration of **2** was confirmed by further transformation through ^{1}H NMR comparison with the known *syn*- and *anti*-tetrahydrofuranyl acid **6** by the reduction-oxidation sequence; the major product with methyl protons at lower field was assigned to the *syn*-isomer (Scheme 2).[8] Thus, the internal siloxy group attacks a cationic intermediate (Figure A : R_1=Me, R_2=R_3=R_4=H) in an *anti*-fashion with an equatorial orientation of the glyoxylate-$SnCl_4$ complex. A similar reaction with dichloromethyl ether, which underwent vinylsilane-substitution reactions[9], gave only a trace amount of the cyclized aldehyde. The use of $TiCl_4$ or $MgBr_2$ was found to give only the desilylated form of the starting alcohol **1**. Solvent systems such as toluene or toluene-CH_2Cl_2 (1 : 1) lead to the complex mixture of the products.

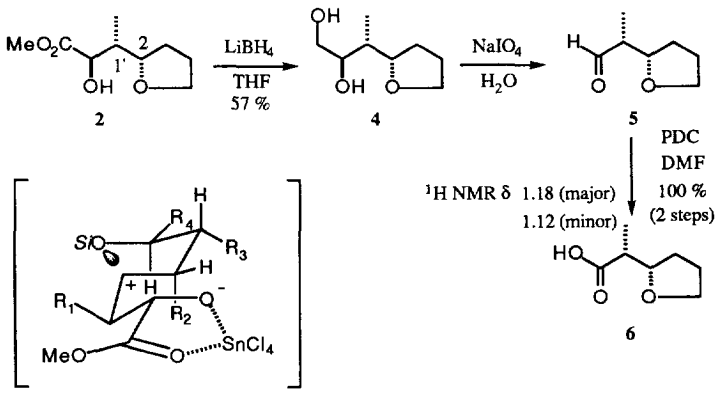
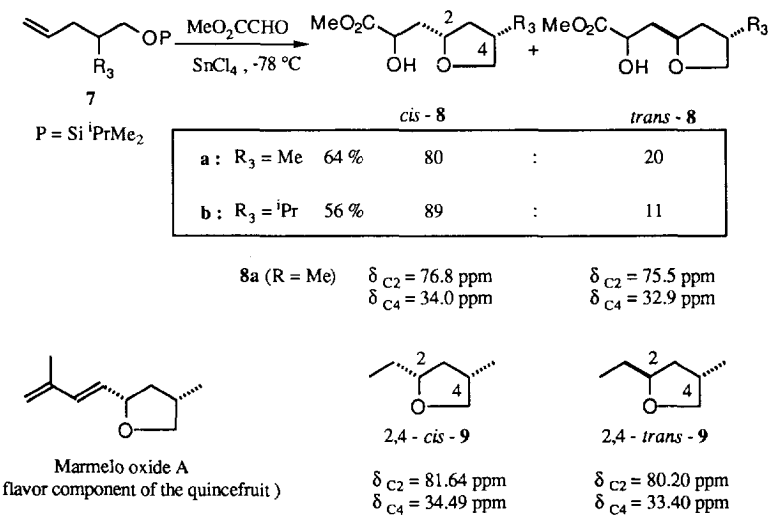


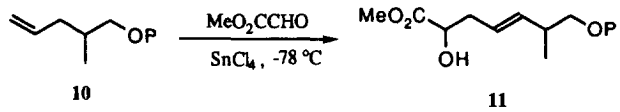
Figure A

Scheme 2

Next, the reaction of silyl ether **7a** (R_3 = Me) was examined, wherein the problem of the 1,3-remote relative[10] asymmetric induction arose (Scheme 4). 2,4-*cis* Product **8a** was obtained as the major diastereomer (80 % selective) determined by ^{13}C NMR spectral analysis through comparison with a similar 2,4-disubstituted tetrahydrofuran **9**.[11] 2,4-*cis* Product **8a** can be used as the key intermediate for the synthesis of marmelo oxide A, a flavor component of the quincefruit.[12] Furthermore, the silyl ether **7b** bearing sterically bulky *iso*-propyl group (R_3 = *i*-Pr) was found to provide the higher level of 2,4-*cis* selectivity than that obtained with the methyl group. Thus, 2,4-*cis* stereochemistry of **8** could be reasonably explained again by the Figure A with the alkyl group (R_3) at the pseudo-*equatorial* position. Interestingly, a similar reaction with 2,6-dichlorobenzyl ether **10**, which provided tetrahydrofuran in the iodocyclization reaction[13], gave the ene product **11** along with the lactone cyclized thereof, rather than the Prins cyclization product (eq. 4).



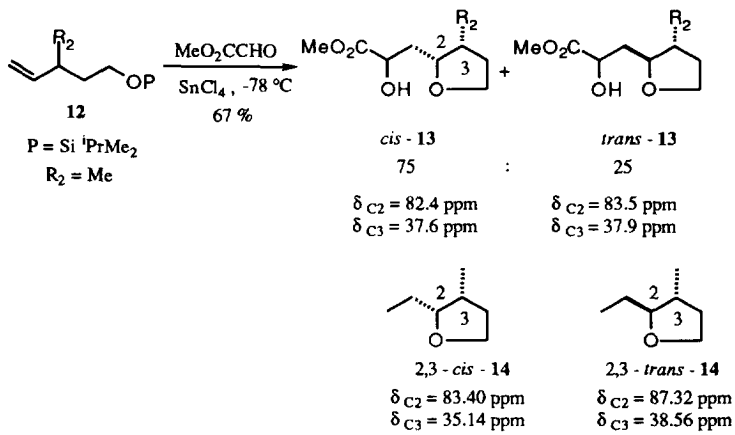
Scheme 3



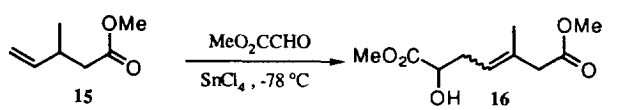
10 11 (4)

P = 2,6-dichlorobenzyl (DCB)

Furthermore, the 1,2-relative[10] asymmetric induction was examined using silyl ether **12** (Scheme 4) and the reaction was found to give 2,3-*cis* product **13** stereoselectively (75 %). 2,3-*cis* Stereochemistry of the cyclized product **13** was ascertained by ^{13}C NMR spectral analysis through comparison with a similar 2,3-disubstituted tetrahydrofuran **14**.[11] Quite interestingly, 2,3-*cis*-relationship implies the pseudo-*axial* orientation of the substituent, R_2 presumably because of the steric repulsion with the Lewis acid-glyoxylate complex (Figure A). By contrast, a similar reaction with ester **15**, which was successfully employed in the iodolactonization reaction, gave the ene product **16** predominantly (eq. 5). Thus, these results clearly indicate the remarkable siloxy effect for facilitating the Prins cyclization.



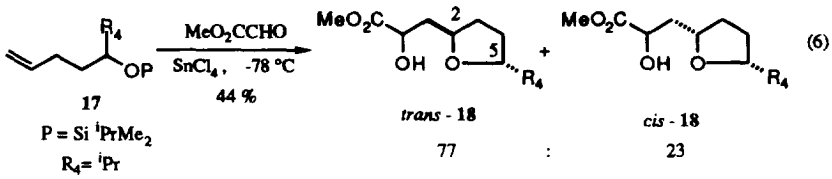
Scheme 4



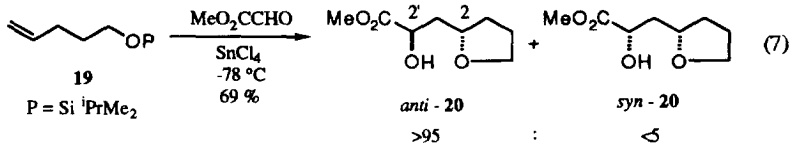
15 16 (5)

predominantly !

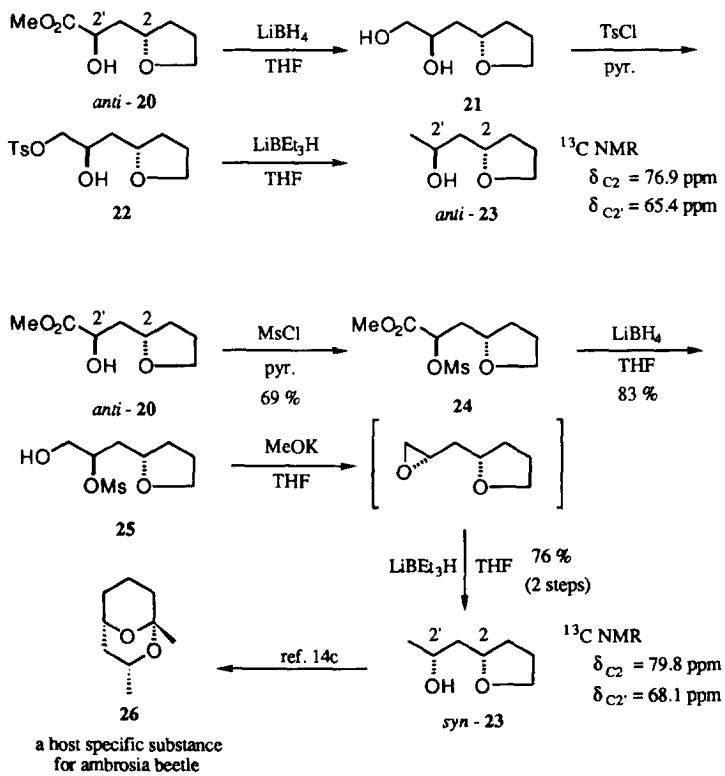
In the formation of 2,5-disubstituted tetrahydrofuran, commonly present structure in polyether antibiotics, the 1,4-relative asymmetric induction was examined using silyl ether **17** (eq. 6). 2,5-*trans* Stereochemistry of the cyclized product **18** was ascertained by ^{13}C NMR spectral analysis.[11] 2,5-*trans*-Relationship implies the pseudo-*equatorial* orientation of the alkyl substituent (Figure A; R_3=^{i}Pr). 2,5-*trans* Tetrahydrofuran units are found in the structural features of tetronomycin, lasalocid A, ionomycin, and tetronasin and so on.[1]



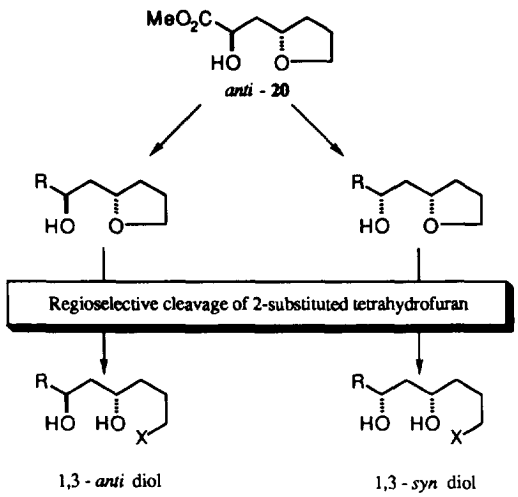
Finally, we found the extremely high level (>95%) of 1,3-internal[10] remote asymmetric induction in the reaction with simple silyl ether **19** to give **20** in 69 % isolated yield (eq. 7). 2,2'-*anti*-Stereochemistry could be deduced on the basis of the high levels of 2,1'-*syn*- and 1',2'-*anti*-selectivities which were found with (4*E*)-hexenyl ether **1** (eq. 3).



2,2'-*anti*-Configuration was further determined by the transformation to the known key intermediate with 2,2'-*syn* stereochemistry for a host specific substance to ambrosia beetle (**26**)[14] and their 2,2'-*anti*-isomer (Scheme 5). The 2,2'-*anti*- or -*syn*-stereochemical feature of tetrahydrofuran can be transferred to the acyclic units with 1,3-*anti*- or *syn*-configuration by the known ring opening reaction of oxygen heterocyles[15] (Scheme 6).



Scheme 5



Scheme 6

In conclusion, we have reported here the novel route to substituted tetrahydrofurans, based on the Lewis acid-promoted Prins cyclization with side chain formation of carbon-carbon bond. In a double or triple combination of relative and internal asymmetric induction, the present methodology for stereocontrolled cyclization to tetrahydrofurans would maximize the synthetic efficiency. We have further disclosed the remarkable siloxy effect for facilitating the Prins cyclization.

EXPERIMENTAL SECTION

General: ^{1}H and ^{13}C NMR spectra were measured on a Varian GEMINI 300 (300 MHz) spectrometers. Chemical shifts of ^{1}H NMR were expressed in parts per million downfield from tetramethylsilane as an internal standard (δ=0) in $CDCl_3$. Chemical shifts of ^{13}C NMR were expressed in parts per million in $CDCl_3$ as an internal standard (δ=77.1). IR spectra were measured on a JASCO FT/IR-5000 spectrometer. All experiments were carried out under nitrogen atomosphere. Dichloromethane was freshly distilled over calcium hydride before use.

General procedure for Prins cyclization reaction : To a 1 M solution of methyl glyoxylate (1 mmol, 1 mL) in CH_2Cl_2 was added olefine **1** (1 mmol) in CH_2Cl_2 (5 mL). To the mixture was then added a 1 M solution of $SnCl_4$ (1 mmol, 1 mL) in CH_2Cl_2 at -78 °C. After stirred for 0.5 ~ 2 h at that temperature, the mixture was quenched with a saturated aqueous solution of sodium bicarbonate. The aqueous layer was extracted with ethyl acetate (3 times) and the combined organic extract was washed with brine, dried over anhydrous magnesium sulfate. Removal of the organic solvent in vacuo gave the crude product. The crude product was purified by silica gel chromatography.

Methyl 2-hydroxy-3-(2-oxolane)-butanoate (2).
^{1}H NMR (300 MHz, $CDCl_3$) δ 0.96 (d, J=7.1 Hz, 3H), 1.56-1.88 (m, 4H), 2.02-2.12 (m, 1H), 2.40 (brs, 1H), 3.60-3.85 (m, 3H), 3.68 (s, 3H), 4.09 (d, J=3.9 Hz, 1H) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.5, 79.8, 74.7, 68.2, 51.9, 39.7, 28.7, 25.5, 11.3; IR (neat) 3412, 2958, 2880, 1734, 1439, 1388, 1212, 1064, 922, 835, 779 cm^{-1}.

(*E*)-Methyl 2-hydroxy-3-methyl-7-dimethylthexylsilyloxy-4-heptenoate (3a).
Isolated by flash column chromatography in 48 % yield as a single diastereomer. ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.04 (s, 6H), 0.80 (s, 6H), 0.84 (d, J=6.8 Hz, 6H), 1.09 (d, J=6.8 Hz, 3H), 1.49-1.65 (m, 1H), 2.16 (dt, J=6.6, 6.2 Hz, 2H), 2.49-2.69 (m, 2H), 3.54 (t, J=6.6 Hz, 2H), 3.73 (s, 3H), 4.05 (m, 1H), 5.34 (dd, J=15.5, 7.3 Hz, 1H), 5.48 (dt, J=15.5, 6.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.4, 131.4, 130.0, 75.2, 63.2, 52.7, 41.3, 36.5, 34.5, 25.4, 20.6, 18.8, 17.0, -3.2 ; IR (neat) 3446, 2962, 2870, 1742, 1464, 1441, 1381, 1253, 1220, 1098, 1017, 973, 938, 876, 832, 777 cm^{-1}.

3-(2-Oxolane)-butane-1,2-diol (4).
To a solution of methyl 2-hydroxy-3-(2-oxolane)-butanoate (0.590 g, 3.1 mmol) in THF (8 mL) was added 2 M THF solution of $LiBH_4$ (1.567 mL, 3.1 mmol) at 0 °C. After stirring for 2 h at room temperature, the mixture was quenched with water. The aqueous layer was extracted with ethyl acetate (3 times) and the combined organic phase was washed with brine. Removal of the organic solvent in vacuo followed by silica gel chromatography gave 3-(2-oxolane)-butane-1,2-diol (0.285 g, 57 %).
^{1}H NMR (300 MHz, $CDCl_3$) δ 0.84 (d, J=7.0 Hz, 3H), 1.60-2.09 (m, 5H), 3.48-4.05 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 82.0, 73.9, 68.1, 64.8, 37.1, 26.7, 25.6, 11.6; IR (neat) 3356, 2884, 2362, 1740, 1493, 1450, 1381, 1238, 1189, 1040, 922, 864, 665 cm^{-1}.

2-(2-Oxolane)-propanal (5).
To a solution of 3-(2-oxolane)-butane-1,2-diol (0.100 g, 0.62 mmol) in H_2O (3.0 mL) was added $NaIO_4$ (0.160 g, 1.2 eq.) at room temperature. After stirring for 30 min, the aqueous layer was extracted with methylene chloride (3 times). Removal of the organic solvent in vacuo gave the crude 2-(2-oxolane)-propanal which was used in the next step without further purification.
^{1}H NMR (300 MHz, $CDCl_3$) δ 0.93 (d, J=7.0 Hz, 3H), 1.51-1.63 (m, 1H), 1.83-1.92 (m, 1H), 1.94-2.06 (m, 1H), 2.51-2.61 (m, 1H), 3.67-3.74 (m, 1H), 3.78-3.85 (m, 1H), 4.04-4.11 (m, 1H), 9.72 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.0, 78.6, 68.1, 50.7, 28.8, 25.8, 9.3.

2-(2-Oxolane)-propionic acid (6).
The crude 2-(2-oxolane)-propanal was dissolved in DMF (2 mL) and to the solution was added pyridinium dichromate (0.466 g, 2 eq.) in one portion at room temperature. After stirring for 12 h, the reddish mixture was poured into water and the solution was acidified to pH = 4 by the addition of 2 N HCl. The aqueous layer was extracted with ether and the combined organic phase was washed with water and brine, dried over anhydrous magnesium sulfate. Removal of the organic solvent in vacuo gave 2-(2-oxalane)-propionic acid (0.089 g) quantitatively.
^{1}H NMR (300 MHz, $CDCl_3$) δ *syn* isomer : 1.18 (d, J=6.9 Hz, 3H), 1.55-1.66 (m, 1H), 1.80-2.04 (m, 3H), 2.44-2.55 (m, 1H), 3.67-3.84 (m, 2H), 3.92-3.99 (m, 1H), 8.87 (brs, 1H). *anti* isomer : 1.12 (d, J=7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.4, 80.0, 68.0, 44.1, 29.2, 25.6, 13.6.

Methyl 2-hydroxy-3-[2-(4-methyl)oxolane]-propanoate (8a).
Isolated by flash column chromatography in 64 % yield as an 80 : 20 mixture of diastereomers.

^{1}H NMR (300 MHz, $CDCl_3$) δ *cis* isomer : 1.01 (d, J=6.5 Hz, 3H), 1.58-2.01 (m, 3H), 2.11-2.35 (m, 2H), 3.30-3.35 (m, 2H), 3.74 (s, 3H), 3.84-3.89 (m, 1H), 4.00-4.10 (m, 1H), 4.35-4.39 (m, 1H). *trans* isomer : 0.99 (d, J=5.0 Hz, 3H), 3.23-3.28 (m, 2H), 3.94-3.99 (m, 2H), 4.10-4.20 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ *cis* isomer : 175.1, 76.8, 74.4, 69.2, 52.2, 41.0, 39.5, 34.0, 17.5. *trans* isomer : 175.1, 77.4, 74.9, 69.1, 52.2, 41.0, 39.8, 33.0, 17.8; IR (neat) 3412, 2962, 2932, 2876, 2334, 1744, 1439, 1381, 1276, 1214, 1139, 1100, 1046, 1017, 936, 903, 855, 820, 762 cm^{-1}.

Methyl 2-hydroxy-3-[2-(4-isopropyl)oxolane]-propanoate (8b).

Isolated by flash column chromatography in 56 % as an 89 : 11 mixture of diastereoisomers.
^{1}H NMR (300 MHz, $CDCl_3$) δ *cis* isomer : 0.83 (d, J=6.6 Hz, 3H), 0.88 (d, J=.6.6 Hz, 3H), 1.12-1.22 (m,1H), 1.35-1.49 (m, 1H), 1.83-2.14 (m, 4H), 3.32 (brs, 1H), 3.46 (dd, J=8.8, 8.5 Hz, 1H), 3.74 (s, 3H), 3.89 (dd, J=8.0, 8.0 Hz, 1H), 4.00-4.09 (m, 1H), 4.37 (dd, J=7.4, 3.6 Hz, 1H). *trans* isomer : 3.33 (dd, J=8.7, 8.6 Hz, 1H), 4.31 (dd, J=7.8, 4.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ *cis* isomer : 175.0, 76.9, 71.9, 69.2, 52.2, 47.3, 39.3, 37.7, 32.0, 21.5. *trans* isomer : 175.1, 76.0, 72.4, 69.0, 52.3, 46.2, 39.6, 36.3, 31.9, 21.4.

Methyl 2-hydroxy-3-[2-(3-methyl)oxolane]-propanoate (13).

Isolated by flash column chromatography in 67% yield as a 75 : 25 mixture of diastereomers.
^{1}H NMR (300 MHz, $CDCl_3$) δ *cis* isomer : 1.00 (d, J=6.8 Hz, 3H), 1.45-1.58 (m, 1H), 1.69-2.11 (m, 4H), 3.45-3.84 (m, 5H), 3.75 (s, 3H), 4.40 (m, 1H); *trans* isomer : 1.02 (d, J=6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ *cis* isomer : 175.1, 82.4, 69.2, 67.0, 52.3, 39.4, 37.6, 34.2, 16.5. *trans* isomer : 175.1, 83.5, 70.1, 67.1, 52.2, 39.6, 37.9, 34.1, 16.9.

Methyl 2-hydroxy-3-[2-(5-isopropyl)oxolane]-propanoate (18).

Isolated by flash column chromatography in 44 % yield as a 77 : 23 mixture of diastereomers.
^{1}H NMR (300 MHz, $CDCl_3$) *trans* isomer δ 0.82 (d, J=6.9 Hz, 3H), 0.91 (d, J=6.6 Hz, 3H), 1.45-1.68 (m, 3H), 1.83-2.00 (m, 4H), 3.28 (brs, 1H), 3.56-3.68 (m, 1H), 3.75 (s, 3H), 4.04-4.13 (m, 1H), 4.39 (dd, J=6.6, 3.8 Hz, 1H). *cis* isomer δ 1.96-2.09 (m, 4H), 3.50-3.58 (m, 1H), 4.00-4.04 (m, 1H), 4.39-4.42 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) *trans* isomer δ 175.1, 84.4, 75.9, 69.6, 52.0, 38.8, 32.9, 32.5, 29.0, 19.0, 18.1. *cis* isomer δ 175.1, 85.3, 76.0, 69.3, 52.0, 39.2, 33.0, 31.3, 28.0, 19.0, 18.3. IR (neat) 3420, 2960, 2876, 1742, 1468, 1441, 1388, 1367, 1265, 1212, 1137, 1079, 1017, 946, 905, 830, 764 cm^{-1}.

Methyl 2-hydroxy-3-(2-oxolane)-propanoate (20).

Isolated by flash column chromatography in 69 % yield.
^{1}H NMR (300 MHz, $CDCl_3$) δ 1.41-1.53 (m, 1H), 1.74-2.04 (m, 5H), 3.67-3.86 (m, 3H), 3.72 (s, 3H), 3.96-4.05 (m, 1H), 4.36 (dd, J=7.7, 3.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.1, 75.9, 69.1, 67.8, 52.2, 39.1, 31.6, 25.4. IR (neat) 3412, 2960, 2878, 2364, 2344, 1744, 1644, 1439, 1267, 1218, 1180, 1133, 1071, 1019, 926, 899, 870, 820 cm^{-1}.

3-(2-Oxolane)-propane-1,2-diol (21).

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.47 (m, 6H), 3.13 (brs, 2H), 3.48-4.11 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 76.5, 69.9, 67.8, 66.8, 37.9, 31.4, 25.6.

1-*p*-Toluenesulfonyloxy-2-hydroxy-3-(2-oxolane)-propane (22).

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.48-2.02 (m, 6H), 2.41 (s, 3H), 3.07 (brs, 1H), 3.63-4.08 (m, 6H), 7.31 (d,

J=8.0 Hz, 2H), 7.76 (d, J=10.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$)
δ 144.8, 132.6, 129.8, 127.8, 75.8, 73.1, 67.8, 67.0, 37.3, 31.4, 25.4, 21.5.

***anti*-1-(2-Oxolane)-propane-2-ol (*anti*-23).**
^1H NMR (300 MHz, $CDCl_3$) δ 1.22 (d, J=6.3 Hz, 3H), 1.50-1.78 (m, 3H), 1.83-2.06 (m, 3H), 3.56 (brs, 1H), 3.67-3.76 (m, 1H), 3.82-3.93 (m, 1H), 4.01-4.15 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 76.9, 67.9, 65.4, 42.5, 31.2, 25.6, 23.3.

Methyl 2-methanesulfonyloxy-3-(2-oxolane)-propanoate (24).
To a solution of methyl 2-hydroxy-3-(2-oxolane)-propanoate (0.453 g, 2.6 mmol) in CH_2Cl_2 (5 mL) was added methanesulfonyl chloride (0.221 mL, 2.86 mmol), triethylamine (0.544 mL, 3.9 mmol) in this order at 0 °C. After stirring for 2 h at room temperature, the mixture was diluted with ethyl acetate and washed with a saturated aqueous solution of sodium bicarbonate. The aqueous layer was extracted with ethyl acetate and the combined organic phase was dried over anhydrous magnesium sulfate. Removal of the organic solvent in vacuo followed by silica gel chromatography gave methyl 2-methanesulfonyloxy-3-(2-oxolane)-propanoate (0.449 g, 69 %).
^1H NMR (300 MHz, $CDCl_3$) δ 1.45-1.57 (m, 1H), 1.86-2.11 (m, 5H), 3.13 (s, 3H), 3.70-3.90 (m, 2H), 3.79 (s, 3H), 3.96-4.05 (m, 1H), 5.19 (dd, J=9.1, 4.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.8, 5.9, 73.8, 67.7, 52.8, 38.6, 37.8, 31.3, 25.7; IR (neat) 3104, 2962, 2878, 1756, 1634, 1441, 1361, 1294, 1241, 1176, 1125, 1054, 1019, 975, 944, 880, 799, 739 cm^{-1}.

2-Methanesulfonyloxy-3-(2-oxolane)-propane-1-ol (25).
To a solution of 2-methanesulfonyloxy-3-(2-oxolane)-propanoate (0.449 g, 1.77 mmol) in THF (10 mL) was added 2 M THF solution of lithium borohydride (0.889 mL, 1.77 mmol) at 0 °C. After stirring for 2 h at room temperature, the mixture was quenched with water and the aqueous layer was extracted with ethyl acetate (3 times). The combined organic phase was dried over anhydrous magnesium sulfate and was concentrated by rotary evaporatory. The residue was purified by silica gel chromatography to afford 2-methanesulfonyloxy-3-(2-oxolane)-propane-1-ol (0.304 g, 83 %).
^1H NMR (300 MHz, $CDCl_3$) δ 1.38-1.50 (m, 1H), 1.64-2.06 (m, 5H), 3.05 (s, 3H), 3.35 (brs, 1H), 3.61-3.93 (m, 5H), 4.73-4.80 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 82.2, 74.6, 67.6, 64.5, 37.9, 37.2, 31.5, 25.4; IR (neat) 3412, 3022, 2944, 2878, 2260, 1723, 1642, 1462, 1419, 1338, 1172, 1054, 977, 911, 793, 733 cm^{-1}.

***syn*-1-(2-Oxolane)-propane-2-ol (*syn*-23).**
To a suspension of MeOK (0.080 g, 1.15 mmol) in THF (3 mL) was added a solution of 2-methanesulfonyloxy-3-(2-oxolane)-propane-1-ol (0.052 g, 0.23 mmol) in THF (3 mL) at room temperature. After stirring for 2 h at room temperature, the flask was immersed in ice-water bath, again. To the reaction mixture was added 1 N THF solution of $LiBEt_3H$ (1 mL). After stirring for 1 h at that temperature, the water was added into the reaction flask. The aqueous layer was extracted with ethyl acetate and the combined organic phase was dried over anhydrous magnesium sulfate. Removal of the organic solvent in vacuo followed by silica gel chromatography gave 1-(2-oxolane)-propane-2-ol (0.022 g, 76 %).
^1H NMR (300 MHz, $CDCl_3$) δ 1.17 (d, J=6.2 Hz, 3H), 1.42-1.68 (m, 3H), 1.78-2.09 (m, 3H), 3.70 (brs, 1H), 3.71-3.79 (m, 1H), 3.85-3.92 (m, 1H), 3.95-4.07 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 79.8, 68.1, 67.9, 44.0, 32.2, 25.2, 23.4; IR (neat) 3372, 2974, 2876, 2246, 1729, 1462, 1377, 1321, 1224, 1183, 1077, 915, 808, 733, 646 cm^{-1}.

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