

HETEROCYCLES, Vol. 67, No. 2, 2006, pp. 731 - 748. © The Japan Institute of Heterocyclic Chemistry
 Received, 15th August, 2005, Accepted, 15th September, 2005, Published online, 16th September, 2005. COM-05-S(T)71

SYNTHESIS OF DIOXABICYCLO[3.2.1]OCTANE CORE OF THE ZARAGOZIC ACIDS

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Abstract – Synthesis of the bicyclic core of zaragozic acids employing chiral furylglycerol (**6**) is described. Key steps are stereoselective construction of the C4 to C6 carbon centers by *syn*-dihydroxylation of alkene followed by reduction of carbonyl group in pyranone (**8**), introduction of ethynyl moiety as a carboxylic acid synthon at C3 by nucleophilic addition of lithium trimethylsilylacetylide to aldehyde (**19**), and bicyclic formation of dihydroxy ketone by ketalization, providing the 2,8-dioxabicyclo[3.2.1]octane core of zaragozic acids.

INTRODUCTION

The zaragozic acids and squalostatins, (Figure 1) fungal metabolites isolated independently by three groups,¹⁻³ are potent inhibitors of squalene synthase (EC 2.5.1.21), that catalyzes the first committed enzyme of sterol biosynthesis. These compounds were shown to be not only inhibitors of mammalian squalene synthase,⁴ but also antifungal agents^{2a} and *ras*-farnesyl-protein transferase inhibitors.^{1,5} Since inhibition of squalene synthase would be ideal from a therapeutic point of view, they are the most promising lead compounds for the development of new cholesterol-lowering drugs. These acids possess unusual and characteristic 4,6,7-trihydroxy-2,8-dioxabicyclo[3.2.1]octane-3,4,5-tricarboxylic acid core with six contiguous stereogenic centers. The core system is common to all members of the family with the only differences arising at C1 alkyl and C6 fatty acid side chains. This combination of potent biological activity and the complexity of their structures has stimulated a large number of synthetic

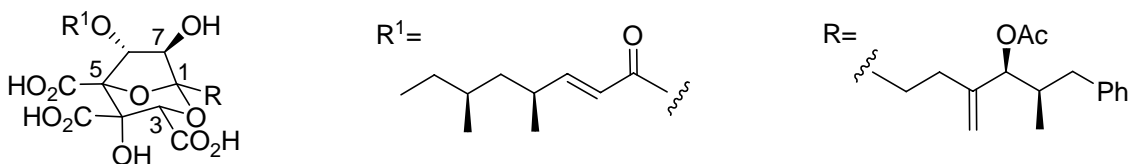
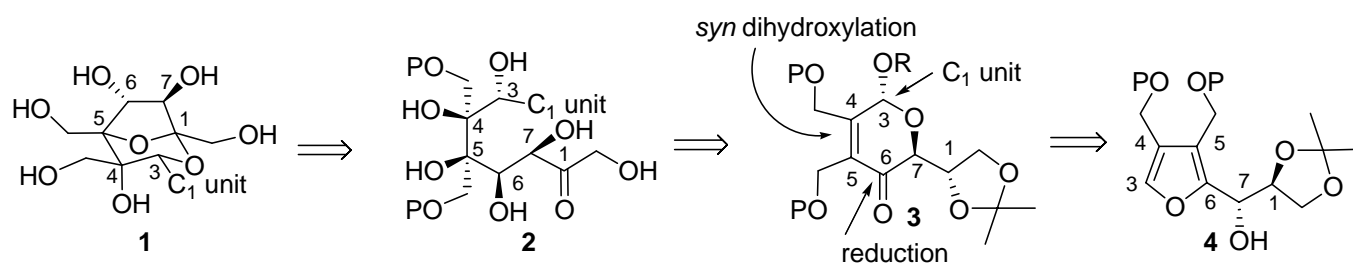


Figure 1. Zaragozic acid A (Squalestatin S1)

studies⁶ toward the core system and several total syntheses.⁷ As part of our continuing studies directed to the synthesis of physiologically active natural products using chiral furylcarbinols,⁸ we describe in detail a synthesis of the bicyclic core of zaragozic acids.⁹

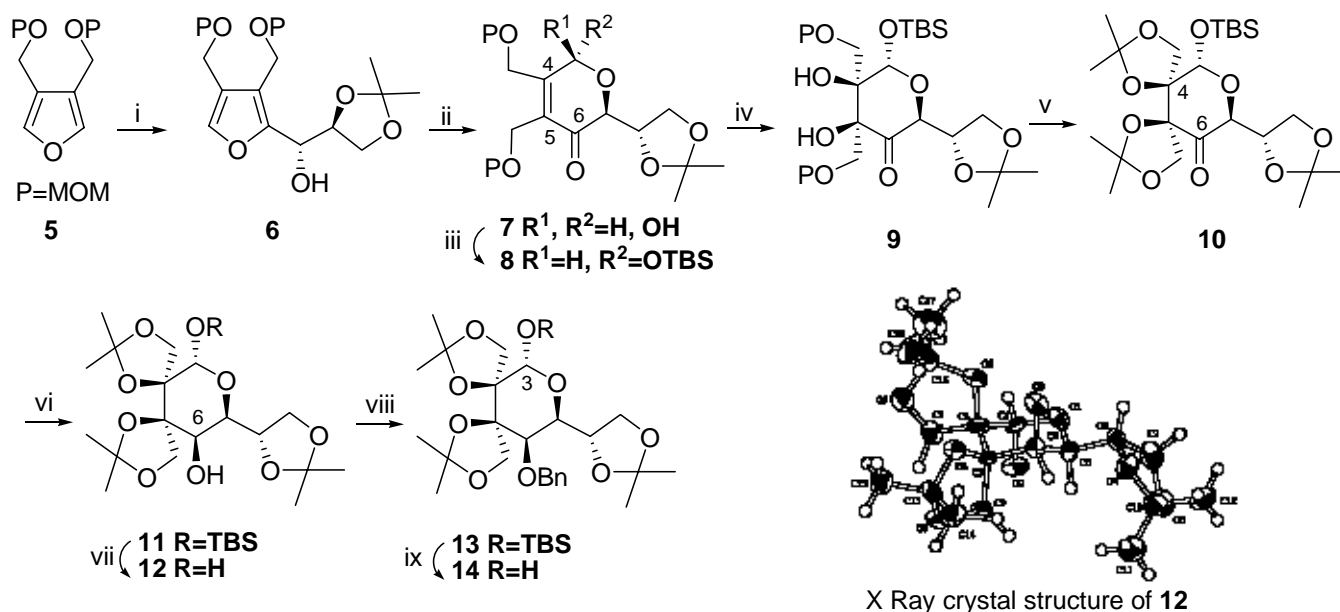
RESULTS AND DISCUSSION

The common core of zaragozic acids bears six contiguous stereogenic centers with citric acid unit, whose stereoselective construction seems to be a critical issue of the synthesis. The strategy for the synthesis of a model core (**1**) was envisaged to employ pyranone (**3**), readily accessible from chiral furyl glycerol (**4**) by oxidative transformation. (Scheme 1) *syn*-Dihydroxylation of **3** followed by reduction of ketone would occur from less hindered side to provide the corresponding 4,5,6-trihydroxypyran with the desired stereochemistries, and C₁ unit as carboxylic acid synthon can be introduced by stereoselective nucleophilic addition. Intramolecular ketalization of **2** would lead to the bicyclic core of zaragozic acids.



Scheme 1. Retrosynthetic analysis of zaragozic acid core system

Synthesis of the key intermediate, highly oxygenated pyran (**14**) was carried out as follows. (Scheme 2) Chelation controlled addition reaction¹⁰ of 2-lithio-3,4-bis(methoxymethoxymethyl)furan, prepared by treatment of **5** with BuLi, to (*S*)-2,3-*O*-isopropylidene-glyceraldehyde¹¹ in the presence of ZnBr₂ afforded a mixture of (2*S*, 3*S*)-glycerol (**6**) and its epimer in a ratio of 91:9, respectively. Ring enlargement of **6** by reaction with NBS¹² in aq. THF gave lactol (**7**), which was treated with TBSCl in the presence of Ag₂O to afford α -silyl ether (**8**) and β -ether in a ratio of 86:14, respectively. The stereochemistry at the anomeric position in **8** was deduced by the basis on our previous result.^{8b} Dihydroxylation of **8** with OsO₄ in the presence of pyridine occurred from the opposite side of adjacent silyl moiety to provide diol (**9**) quantitatively. Acid treatment of **9** in acetone brought about removal of MOM group followed by bis-ketalization to afford **10** in 63.9% yield. Reduction of ketone (**10**) at C6 (zaragozic acid numbering) with NaBH₄ in MeOH at -78 °C gave the desired (6*R*)-alcohol (**11**) and its epimer in 90.9 and 9.0% yields, respectively. Since the stereochemistries at C6 in both alcohols could not be deduced from their ¹H NMR spectral analyses, the stereostructure of **11** was unambiguously determined by the X-Ray crystallographic analysis of desilylated compound (**12**). Protection of alcohol (**11**) as benzyl ether gave **13**, which was

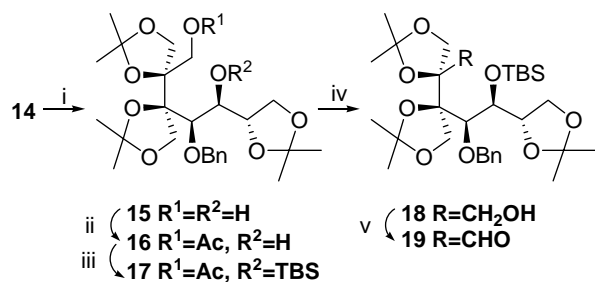


Scheme 2. i, *n*-BuLi, ZnBr₂, THF, (S)-2,3-O-isopropylidene-glyceraldehyde, 81.6 %; ii, NBS, aq. THF, 89.5 %; iii, TBSCl, Ag₂O, DMF, 73.7 %; iv, OsO₄, pyridine, Et₂O, 99.2 %; v, *p*-TsOH, acetone, 63.9 %; vi, NaBH₄, MeOH, 90.9 %; vii, TBAF, THF, 91.7 %; viii, NaH, BnBr, DMF, 93.8 %; ix, TBAF, THF, 84.7 %.

treated with TBAF to afford lactol (**14**). The observed stereoselectivity in the reduction of **10** at C6 position is rationalized that equatorial approach of hydride would favor over axial approach which generates the severe steric repulsion between hydride and bulky dioxolane ring at C4 position.

We first examined nucleophilic addition of C₁ equivalent synthon, such as vinylmagnesium halide, ethynylmagnesium halide, trimethylsilyl cyanide *etc.*, to lactol at C3 position in **14**. In most cases formation of unidentified polar products together with starting material was found probably due to the lower reactivity of lactol with quaternary carbon at α position. Therefore, introduction of C₁ unit to aldehyde followed by its transformation into the bicyclic core of zaragozic acids was devised as shown in Scheme 3. Lactol (**14**) was reduced with LiAlH₄ to the open-chain diol (**15**). Compound (**15**) was converted to aldehyde (**19**) by sequential acetylation of the primary hydroxyl group in **15**, silylation of the secondary hydroxyl group in **16**, hydrolysis of acetate in **17**, and oxidation of the primary hydroxyl group in **18** with Dess-Martin reagent¹³ in 75% overall yield.

Addition of C₁ synthon to aldehyde (**19**) was carried out using several reagents under various conditions, and the selected results are shown in Table 1. More than 5 equiv. of reagent was used for the reaction because a stoichiometric amount of reagent gave only the recovery of starting material. The addition of vinylmagnesium bromide and lithium acetylide·ethylenediamine complex to **19** gave a mixture of isomers in low yields with moderate selectivities (entries 1 and 3), whereas the reaction with ethynylmagnesium bromide and trimethylsilyl cyanide gave none of the desired adducts (entries 2 and 4). Pleasingly, the addition of lithium trimethylsilylacetylide gave a good yield of the adducts with moderate selectivity (entry 5). The best selectivity was recorded by lowering temperature. Highly diastereoselective



Scheme 3. i, LiAlH₄, THF, 93.6 %; ii, Ac₂O, DMAP, pyridine, CH₂Cl₂, 95.5 %; iii, TBSOTf, Et₃N, CH₂Cl₂, 92.6 %; iv, 1M LiOH, MeOH, 91.3 %; v, Dess-Martin oxid., 99.6 %.

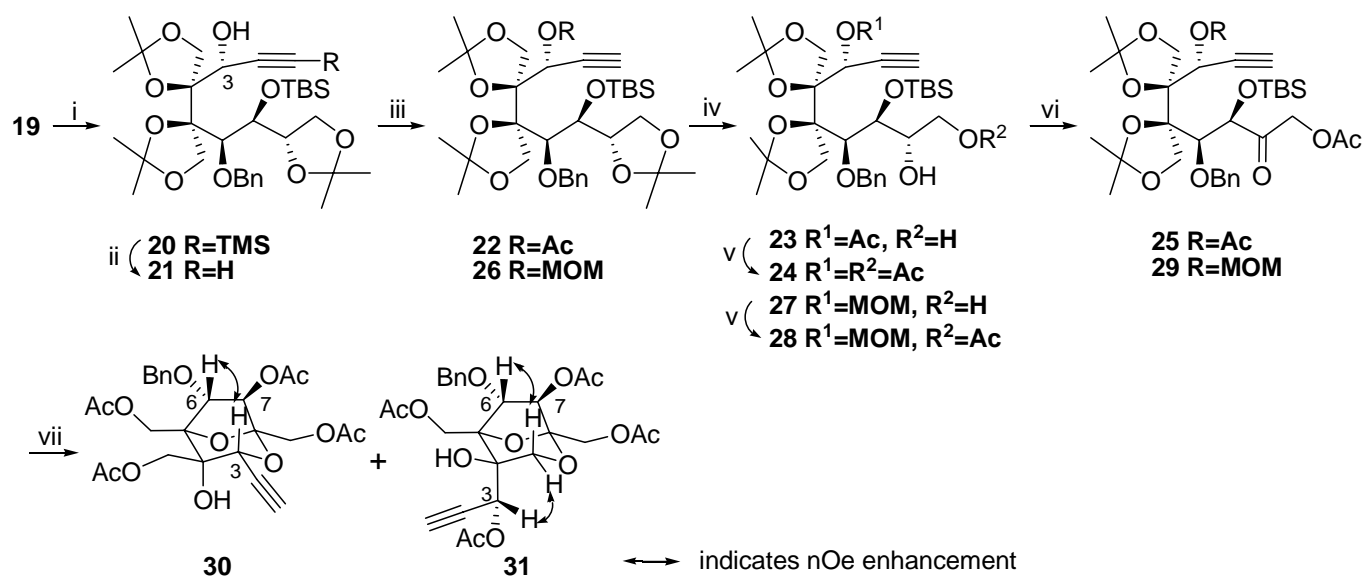
Table 1. Nucleophilic addition to aldehyde (**19**)

entry	reagent (equivalent)	condition	yield (%)	selectivity ^a
1	H ₂ C=CHMgBr (10)	THF, 0°C, 0.5 h	38.6	85:15
2	HC≡CMgBr (6)	THF, rt, 10 h	NR	-
3	HC≡CLi (10) H ₂ NCH ₂ CH ₂ NH ₂	THF, 0°C, 0.5 h	23.8 ^b	73:27
4	TMSCN (10) ^c	CH ₂ Cl ₂ , 0°C, 0.5 h	0	-
5	TMSC≡CLi (9)	THF, -10°C, 0.5 h	88.8	86:14
6	TMSC≡CLi (7)	THF, -78°C, 0.5 h	94.4	>99:1

^a The ratio of the (3*R*) to (3*S*) products was determined by 270 MHz ¹H NMR spectral analysis. ^b Together with the recovery of starting material. ^c A catalytic amount of ZnI₂ was also used.

addition of lithium trimethylsilylacetylide in THF at -78 °C proceeded to afford propargylic alcohol (**20**) as a sole product in 94.4% (entry 6). Usage of additives did not give any improvement of both yield and selectivity.

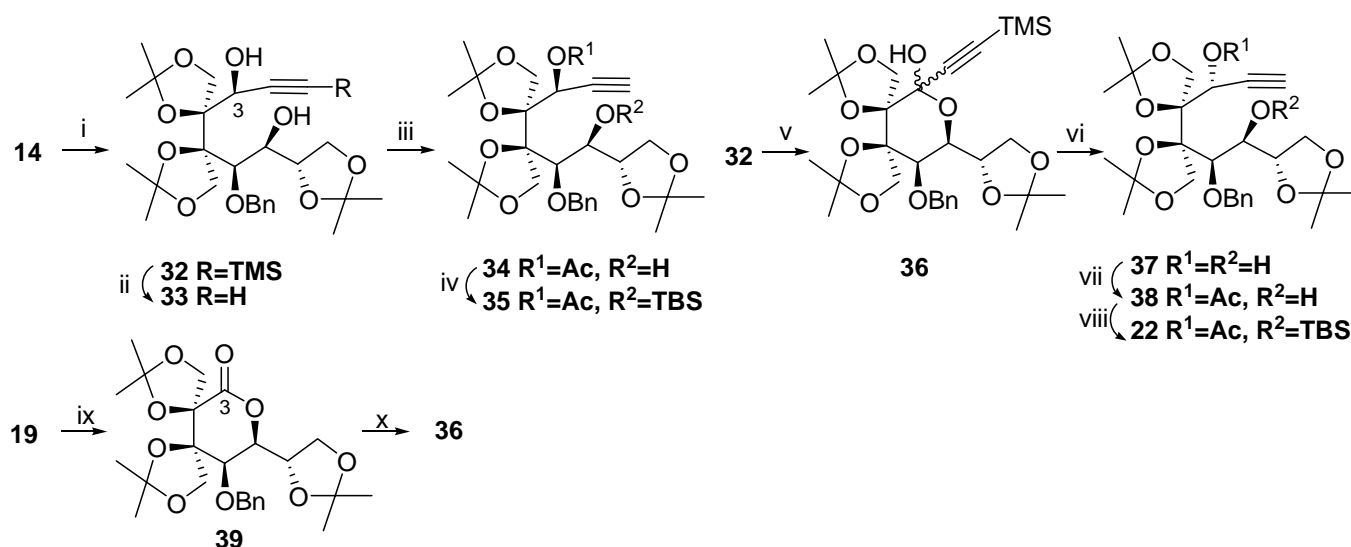
Although the stereochemistry at C3 position in **20** could not be determined at this stage, its conversion to the bicyclic core of zaragozic acids was carried out (Scheme 4). Desilylation of terminal silyl moiety in **20** with K₂CO₃ followed by acetylation of newly created alcohol in **21** gave acetate (**22**) quantitatively. Selective removal of less hindered acetonide in **22** with FeCl₃·SiO₂¹⁴ afforded diol (**23**), which was then converted into ketone (**25**) by sequential acetylation of the primary alcohol in **23** and Dess-Martin oxidation of the secondary alcohol in **24** in 54% overall yield. Alkaline hydrolysis of diacetate (**25**) disappointingly gave a trace amount of the corresponding dihydroxyketone. In this regard, protecting



Scheme 4. i, lithium trimethylsilylacetylide, THF, 94.4 %; ii, K₂CO₃, MeOH, 99.8 %; iii, Ac₂O, DMAP, pyridine, CH₂Cl₂, 99.4 % for **22**; MOMCl, *i*-Pr₂NEt, CH₂Cl₂, 97.4 % for **26**; iv, FeCl₃·SiO₂, CHCl₃, 86.1 % for **23**, 68.1 % for **27**; v, Ac₂O, DMAP, pyridine, CH₂Cl₂, 99.3 % for **24**, 96.7 % for **28**; vi, Dess-Martin oxid., 62.7 % for **25**, 75.4 % for **29**; vii, HCl, MeOH; then Ac₂O, DMAP, pyridine, CH₂Cl₂, 32.5 % for **30**, 20.7 % for **31** (2 steps).

group in **21** was changed from acetyl to methoxymethyl group, which could be readily removed by acid treatment. Methoxymethylation of alcohol (**21**) gave quantitatively **26**, which was further converted into **29** by the same sequences as above *via* diol (**27**) and monoacetate (**28**) in 50% overall yield. The stage was set for construction of the bicyclic core of zaragozic acids by ketalization. Although several bicyclic ketals could be formed upon acid cyclization of ketone (**29**), we hoped that acid-mediated cyclization would proceed under kinetic control to provide the desired 2,8-dioxabicyclo[3.2.1]octane system according to the useful observation by Myles.¹⁵ Treatment of **29** with a trace amount of conc. HCl in MeOH gave two unstable ketals in a ratio of *ca.* 3:2, which without purification were isolated by peracetylation to furnish the desired bicyclic compound (**30**) and its isomer (**31**) in 32.5 and 20.7% yields, respectively. The 3:2 ratio of the two ketal products did not change over 2 days time period. No other ketals were detected under this condition, even more prolonged reaction time. Assignment of the stereostructures of both bicyclic systems (**30**) and (**31**) was based on NMR experiments including HMQC, HMBC, and NOEDIFF. Diagnostic nOe enhancements for both **30** and **31** and also the coupling constants of $J_{6,7}=2.4\text{Hz}$ for **30** and $J_{6,7}=3.1\text{Hz}$ for **31** were observed, respectively. These NMR spectroscopic study provides strong evidence for the stereochemical confirmation and thus for the sense of diastereoselectivity of the nucleophilic addition process. Both bicyclic ketals (**30**) and (**31**) possess 2,8-dioxabicyclo[3.2.1]octane systems, however **31** has an incorrect substitution arrangement. The formation of product (**31**) is quite different from product distribution upon ketalization of similar polyoxy ketones reported by Myles¹⁵ and Armstrong.^{7g} We supposed that initial hydrolysis of the acetonide at C5 position followed by ring closure of the hydroxyl at C5 onto the carbonyl at C1 might lead to a five-membered intermediate, whose second acetonide at C4 may be removed and subsequently competitive ring closure of each the hydroxyl at C3 and the hydroxyl attached at C4 might result in the formation of **30** or **31** based on the informative results in acid-mediated ketalization by Hashimoto^{7f} and Armstrong.^{7g} Although this discrepancy in product distribution would not be rationally explained, the relatively higher nucleophilicity of hydroxyl attached at C4 than that of hydroxyl at C3 owing to the inductive effect of ethynyl moiety¹⁶ could play a significant role in the second ring closure.

For purposes of higher synthetic efficiency, introduction of C₁ unit to lactol (**14**) was reexamined. (Scheme 5) Treatment of 20 equiv. of lithium trimethylsilylacetylide in THF at rt for 10 h gave propargylic alcohol (**32**) in 32.3% together with the recovery of starting material. To our delight, addition of 40 equiv. of trimethylsilylethynylmagnesium chloride proceeded diastereoselectively to afford propargylic alcohol (**32**) in 84.5% yield and none of its epimer was found. The stereochemistry at C3 position in **32** was elucidated by comparison of the acetate (**22**) obtained above. Desilylation of silyl moiety in **32** gave diol (**33**), whose selective acetylation of alcohol at C3 position followed by silylation of alcohol in **34** afforded silyl ether (**35**). Since **35** was found to be an epimer of **22** at C3 position by



Scheme 5. i, trimethylsilylethynylmagnesium chloride, THF, 84.5 %; ii, K₂CO₃, MeOH, 65.3 %; iii, Ac₂O, DMAP, pyridine, CH₂Cl₂, 91.1 %; iv, TBSOTf, Et₃N, CH₂Cl₂, 62.5 %; v, Dess-Martin oxid., 97.0 %; vi, NaBH₄, aq. EtOH, THF, 31.4 %; vii, Ac₂O, DMAP, pyridine, CH₂Cl₂, 97.4 %; viii, TBSOTf, Et₃N, CH₂Cl₂, 88.9 %; ix, PCC, NaOAc, Celite, CH₂Cl₂, 71.5 %; x, lithium trimethylsilylacetylide, THF, 73.5 %.

their NMR spectral analyses, thus confirming that the stereostructure of **32** should be 3*S*. Inversion at C3 position in **32** was also carried out as follows. Attempts to directly invert the stereochemistry at C3 position by Mitsunobu reaction failed. Dess-Martin oxidation of **32** gave an inseparable mixture of hemiketals (**36**), in a ratio of 78:22, which was reduced with NaBH₄ to afford a mixture of the desired alcohol (**37**) and its epimer (**33**) in a ratio of 9:1 together with an unidentified product which might be deoxygenated compound. A mixture of **37** and **33** was converted into acetate (**22**) and its epimer (**35**) by the same procedure as above. Interestingly, hemiketals (**36**) was also prepared by the addition of lithium trimethylsilylacetylide (5 equiv.) to lactone (**39**), obtained by oxidation of lactol (**14**) with PCC, in THF at -78 °C in 73.5%.

The opposite diastereoselectivity observed in the nucleophilic addition reactions to aldehyde (**19**) and lactol (**14**) is of interest from a mechanistic point of view. Although several highly diastereoselective nucleophilic additions to open-chain α,β -dialkoxy aldehydes¹⁷ and higher carbohydrates¹⁸ are known, the stereochemical outcome of the reactions to polyalkoxy carbonyl compounds with quaternary carbons at α positions such as **19** and **14** is hardly predictable. These results can be explained by assuming an α -chelation transition state (**A**), which could be formed under relatively kinetic condition, in the addition to aldehyde (**19**) and either a δ -chelation¹⁹ transition state (**B**) or a Felkin-Anh transition state (**C**) in the addition to lactol (**14**). (Figure 2) The diastereoselectivity observed in the reduction of hemiketals (**36**) would be also rationalized by a Felkin-Anh transition state.

We have disclosed a new method for the construction of 2,8-dioxabicyclo[3.2.1]octane core of zaragozic acids employing the stereocontrolled modifications of chiral pyranone (**8**), accessible from (2*S*,3*S*)-

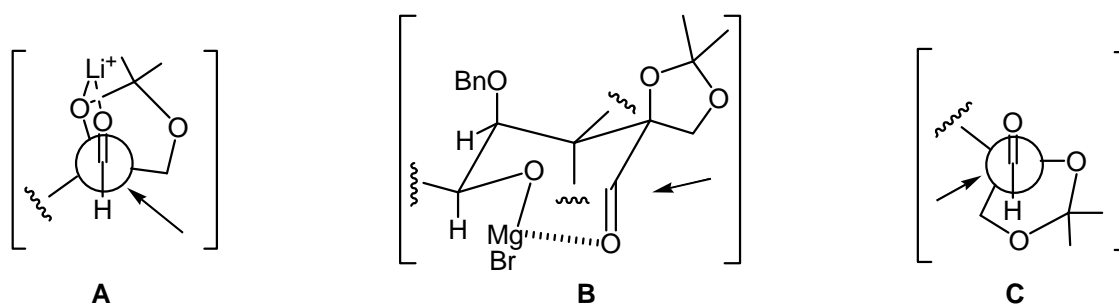


Figure 2.

furylglycerol (**6**), and the diastereoselective introduction of ethynyl moiety as a carboxylic acid synthon to aldehyde (**19**) as key steps. Acid treatment of ketone (**29**) followed by peracetylation led to the formation of bicyclic core (**30**) together with incorrect substituted isomer (**31**). Application of **30** to the natural product would be possible by oxidation of the core substituents and introduction of side chains.

EXPERIMENTAL

IR spectra were obtained using a JASCO FT/IR-200 spectrophotometer. ^1H and ^{13}C NMR spectra were obtained on a JEOL JNM-LA270 (^1H NMR: 270 MHz, ^{13}C -NMR: 67.8 MHz) for solutions in CDCl_3 , and chemical shifts are reported on the scale using TMS as an internal standard of 0.00 for ^1H NMR spectra and CDCl_3 as an internal standard of 77.00 for ^{13}C NMR spectra, respectively. JEOL JNM-LA500 (^1H NMR: 500 MHz, ^{13}C NMR: 125 MHz) instrument was used only for the measurement of compounds (**30**) and (**31**). 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. X-Ray measurement was carried out on a Rigaku AFC 7R diffractometer.

(2*S*,3*S*)-3-[2'-[3',4'-Bis(methoxymethyloxymethyl)furyl]]-1,2-*O*-isopropylidenglycerol (6**).** To a solution of 3,4-bis(methoxymethyloxymethyl)furan (**5**) (19.9 g, 92 mmol) in THF (300 mL) was added dropwise *n*-BuLi (1.69 M in hexane; 65.5 mL, 110 mmol) at -50°C . The reaction mixture was stirred for 1 h at 0°C , and ZnBr_2 (25 g, 110 mmol) was added portionwise. After being stirred for 30 min, a solution of (*S*)-2,3-*O*-isopropylidenglyceraldehyde (8.0 g, 61.5 mmol) in THF (50 mL) was added dropwise at 0°C . The reaction was allowed to warm to rt and stirred for 10 h. The reaction was carefully quenched with saturated aqueous NH_4Cl solution in ice bath. The reaction mixture was concentrated, and a residue was extracted with AcOEt, and the combined organic layer was washed with brine. The organic layer was dried over Na_2SO_4 and evaporated to give a residue, which was chromatographed on silica gel (hexane/AcOEt=3:2) to afford a mixture of (2*S*, 3*S*)-glycerol (**6**) and (2*S*, 3*R*)-glycerol (91:9) as a colorless oil (11.3 g, 81.6 %). A small sample of mixture was purified carefully to give pure (2*S*, 3*S*)-glycerol (**6**). IR cm^{-1} : 3450 (OH). ^1H NMR: 1.36 and 1.43 (each 3H, each s, CMe_2), 3.07 (1H, d, $J=3.7$ Hz, 3-OH), 3.38 and 3.40 (each 3H, each s, OMe), 4.12 and 4.20 (each 1H, each dd, $J=9.2$, 6.1 Hz, 1- H_2), 4.43 (1H, distorted q, $J=6.1$ Hz, 2-H), 4.48 (2H, s, 4'- CH_2), 4.54 and 4.61 (each 1H, each d, $J=12.2$ Hz, 3'- CH_2), 4.63 and 4.66 (each 2H, each s, OCH_2OMe), 4.83 (1H, dd, $J=6.1$, 3.7 Hz, 3-H), 7.39 (1H, s, 5'-H). HRMS m/z : Calcd for $\text{C}_{16}\text{H}_{26}\text{O}_8$ (M^+): 346.1627. Found: 346.1630. $[\alpha]_{\text{D}}^{25} +2.73^\circ$ ($c=1.01$, CHCl_3).

(2*S*)-6-Hydroxy-2-[(4'*S*)-2',2'-dimethyl-1',3'-dioxolan-4'-yl]-4,5-bis(methoxymethyloxymethyl)-6*H*-pyran-3(2*H*)-one (7**).** To a stirred solution of the above mixture of glycerol (6.0 g, 17.3 mmol) and sodium acetate (1.85 g, 22.5 mmol) in aqueous THF (150 mL, THF/ H_2O =4:1) was added portionwise NBS (4.0 g, 22.5 mmol) at 0°C , and the resulting mixture was stirred for 30 min at the same temperature. The reaction mixture was successively treated with an excess of 10% KI solution and with saturated

Na₂S₂O₃ solution. After removal of the solvent, the aqueous solution was extracted with AcOEt, and the combined organic layer was washed with brine. The organic layer was dried over Na₂SO₄ and evaporated to give a residue, which was chromatographed on silica gel (hexane/AcOEt=3:2) to afford lactol (**7**) (5.6 g, 89.5 %) as a colorless oil. IR cm^{-1} : 3400 (OH), 1690 (CO). ¹H NMR: 1.38 and 1.44 (each 3H, each s, CMe₂), 3.36 and 3.39 (each 3H, each s, OMe), 3.98 (2H, dt, $J=15.3, 6.7$ Hz, 5'-H₂), 4.28 and 4.37 (each 1H, each d, $J=11.0$ Hz, 4-CH₂), 4.39 and 4.57 (each 1H, each d, $J=14.0$ Hz, 5-CH₂), 4.45 (1H, d, $J=4.9$ Hz, 6-OH), 4.61 and 4.68 (each 2H, each s, OCH₂OMe), 4.71 (1H, ddd, $J=6.7, 6.7, 3.1$ Hz, 4'-H), 4.86 (1H, d, $J=3.1$ Hz, 2-H), 5.87 (1H, d, $J=4.9$ Hz, 6-H). HRMS m/z : Calcd for C₁₅H₂₃O₉ (M⁺-15): 347.1342. Found: 347.1342. Anal. Calcd for C₁₆H₂₆O₉: C, 53.03; H, 7.53. Found: C, 53.05; H, 7.33. $[\alpha]_{\text{D}}^{24} +4.66^{\circ}$ ($c=0.72$, CHCl₃).

(2S,6S)-6-tert-Butyldimethylsiloxy-2-[(4'S)-2',2'-dimethyl-1',3'-dioxolan-4'-yl]-4,5-bis(methoxymethyl)-6H-pyran-3(2H)-one (8). A mixture of lactol (**7**) (6.78 g, 18.8 mmol), Ag₂O (30.5 g, 131 mmol), and TBSCl (19.7 g, 131 mmol) in DMF (250 mL) was stirred for 2 days at -30 °C. After insoluble material was filtered off through a Celite pad, the filtrate was concentrated to leave a residue, which was chromatographed on silica gel (hexane/AcOEt=9:1) to afford α -silyl ether (**8**) and β -silyl ether (86:14) as a colorless oil (6.59 g, 73.7 %). A mixture was purified carefully to give pure α -silyl ether (**8**), however pure β -silyl ether could not be separated. α -Silyl ether (**8**): IR cm^{-1} : 1690 (CO). ¹H NMR: 0.19 and 0.20 (each 3H, each s, SiMe₂), 0.92 (9H, s, CMe₃), 1.37 and 1.43 (each 3H, each s, CMe₂), 3.35 and 3.38 (each 3H, each s, OMe), 3.97 (2H, m, 5'-H₂), 4.22 and 4.60 (each 1H, each d, $J=13.4$ Hz, 5-CH₂), 4.25 and 4.36 (each 1H, each d, $J=11.0$ Hz, 4-CH₂), 4.61 and 4.64 (each 2H, each s, 2 \times OCH₂OMe), 4.67-4.74 (2H, m, 2-H, 4'-H), 5.81 (1H, s, 6-H). HRMS m/z : Calcd for C₂₁H₃₇O₉Si (M⁺-15): 461.2207. Found: 461.2209. Anal. Calcd for C₂₂H₄₀O₉Si: C, 55.44; H, 8.46. Found: C, 55.30; H, 8.41. $[\alpha]_{\text{D}}^{29} +12.5^{\circ}$ ($c=1.0$, CHCl₃).

(2S,4S,5R,6S)-6-tert-Butyldimethylsiloxy-4,5-dihydroxy-4,5-bis(methoxymethyl)-2-[(4'S)-2',2'-dimethyl-1',3'-dioxolan-4'-yl]-3,4,5,6-tetrahydro-2H-pyran-3-one (9). To a stirred solution of enone (**8**) (3.2 g, 6.72 mmol) in Et₂O (150 mL) was added pyridine (2.2 mL, 26.9 mmol) and OsO₄ (2.2 g, 8.75 mmol) at 0 °C and the resulting mixture was further stirred for 12 h at rt. After removal of the solvent, the residue was dissolved in pyridine (100 mL). To this solution was added a solution of NaHSO₃ (9.1 g, 87.5 mmol) in H₂O (100 mL), and the mixture was stirred for 12 h at rt. Evaporation of the solvent gave a residue, which was chromatographed on silica gel (hexane/AcOEt=3:2) to afford diol (**9**) (3.4 g, 99.2 %) as a colorless oil. IR cm^{-1} : 1730 (CO), 3540 (OH). ¹H NMR: 0.19 and 0.26 (each 3H, each s, SiMe₂), 0.98 (9H, s, CMe₃), 1.38 and 1.39 (each 3H, each s, CMe₂), 3.30 and 3.38 (each 3H, each s, OMe), 3.30 and 4.21 (each 1H, each s, 4, 5-OH), 3.56 and 4.75 (each 1H, each d, $J=10.4$ Hz, 4-CH₂), 3.68 (2H, s, 5-CH₂), 4.01 (1H, dd, $J=8.6, 6.1$ Hz, 5'-HH), 4.13 (1H, dd, $J=8.6, 6.7$ Hz, 5'-HH), 4.53 and 4.58 (each 1H, each d, $J=6.7$ Hz, OCH₂OMe), 4.58 (1H, ddd, $J=6.7, 6.1, 4.3$ Hz, 4'-H), 4.62 and 4.66 (each 1H, each d, $J=6.7$ Hz, OCH₂OMe), 4.66 (1H, d, $J=4.3$ Hz, 2-H), 5.25 (1H, s, 6-H). HRMS m/z : Calcd for C₂₂H₄₂O₁₁Si (M⁺): 510.2494. Found: 510.2492. Anal. Calcd for C₂₂H₄₂O₁₁Si: C, 51.75; H, 8.29. Found: C, 51.67; H, 8.46. $[\alpha]_{\text{D}}^{22} -79.8^{\circ}$ ($c=1.03$, CHCl₃).

(2S,4S,5R,6S)-6-tert-Butyldimethylsiloxy-2-[(4'S)-2',2'-dimethyl-1',3'-dioxolan-4'-yl]-3,4,5,6-tetrahydro-2H-pyran-3-one-4,5-bis[spiro-4''-(2'',2''-dimethyl-1'',3''-dioxolane)] (10). A solution of diol (**9**) (1.0 g, 1.96 mmol) and *p*-TsOH·H₂O (1.86 g, 9.8 mmol) in acetone (50 mL) was refluxed for 5 h. To the mixture was added saturated NaHCO₃ solution in ice-bath. After removal of the solvent, the aqueous solution was extracted with hexane-Et₂O (1:1), and the combined organic layer was washed with brine. The organic layer was dried over Na₂SO₄ and evaporated to give a residue, which was chromatographed on silica gel (hexane/AcOEt=9:1) to afford triacetone (**10**) (629 mg, 63.9 %) as a colorless oil. IR cm^{-1} : 1740 (CO). ¹H NMR: 0.21 and 0.23 (each 3H, each s, SiMe₂), 0.96 (9H, s, CMe₃), 1.36 and 1.41 (each 3H, each s, CMe₂), 1.41 (6H, s, CMe₂), 1.47 and 1.55 (each 3H, each s, CMe₂), 3.98-4.15 (6H, m, 4, 5-CH₂, 5'-H₂), 4.52 (1H, d, $J=3.7$ Hz, 2-H), 4.67 (1H, m, 4'-H), 5.06 (1H, s, 6-H). HRMS m/z : Calcd for

$C_{24}H_{42}O_9Si$ (M^+): 502.2597. Found: 502.2597. Anal. Calcd for $C_{24}H_{42}O_9Si$: C, 57.35; H, 8.42. Found: C, 57.11; H, 8.36. $[\alpha]_D^{24}$ -85.4° ($c=1.27$, $CHCl_3$).

(2S,3R,4R,5R,6S)-6-tert-Butyldimethylsiloxy-3-hydroxy-2-[(4'S)-2',2'-dimethyl-1',3'-dioxolan-4'-yl]-3,4,5,6-tetrahydro-2H-pyran-4,5-bis[spiro-4''-(2'',2''-dimethyl-1'',3''-dioxolane)] (11). To a stirred solution of ketone (**10**) (629 mg, 1.25 mmol) in MeOH (30 mL) was added portionwise $NaBH_4$ (71 mg, 1.88 mmol) at $-78^\circ C$. The reaction mixture was allowed to warm to $0^\circ C$ over 3 h. To the mixture was added saturated NH_4Cl solution and the solvent was concentrated to give a residue, which was extracted with AcOEt. The combined organic layer was washed with brine. The organic layer was dried over Na_2SO_4 and evaporated to give a residue, which was chromatographed on silica gel (hexane/AcOEt=17:3) to afford (3R)-alcohol (**11**) (574 mg, 90.9 %) as a colorless oil. IR cm^{-1} : 3500 (OH). 1H NMR: 0.16 and 0.18 (each 3H, each s, $SiMe_2$), 0.93 (9H, s, CMe_3), 1.36 and 1.40 (each 3H, each s, CMe_2), 1.46 (6H, s, CMe_2), 1.47 and 1.51 (each 3H, each s, CMe_2), 3.48 (1H, d, $J=9.2$ Hz, 3-OH), 3.73 (1H, br d, $J=9.2$ Hz, 3-H), 3.74 (1H, br d, $J=6.1$ Hz, 2-H), 3.86 and 3.91 (each 1H, each d, $J=9.8$ Hz, 4 or 5- CH_2), 3.93 and 4.16 (each 1H, each d, $J=9.2$ Hz, 4 or 5- CH_2), 4.00 (1H, dd, $J=8.5$, 5.5 Hz, 5'-HH), 4.08 (1H, dd, $J=8.5$, 6.1 Hz, 5'-HH), 4.46 (1H, distorted q, $J=6.1$, 5.5 Hz, 4'-H), 4.94 (1H, s, 6-H). HRMS m/z : Calcd for $C_{23}H_{41}O_9Si$ (M^+-15): 489.2520. Found: 489.2521. $[\alpha]_D^{23}$ -49.7° ($c=0.84$, $CHCl_3$). Further elution gave (3S)-alcohol (57 mg, 9.0 %) as a colorless oil. IR cm^{-1} : 3530 (OH). 1H NMR: 0.16 and 0.17 (each 3H, each s, $SiMe_2$), 0.92 (9H, s, CMe_3), 1.46, 1.47 and 1.51 (18H, each s, CMe_2), 3.53 (1H, d, $J=9.2$ Hz, 3-OH), 3.76 (1H, br d, $J=9.2$ Hz, 3-H), 3.76 (1H, br d, $J=6.1$ Hz, 2-H), 3.86 and 3.91 (each 1H, each d, $J=9.6$ Hz, 4 or 5- CH_2), 3.94 and 4.16 (each 1H, each d, $J=9.2$ Hz, 4 or 5- CH_2), 3.96 and 3.98 (each 1H, each dd, $J=10.4$, 6.1 Hz, 5'- H_2), 4.40 (1H, distorted q, $J=6.1$ Hz, 4'-H), 5.00 (1H, s, 6-H). HRMS m/z : Calcd for $C_{23}H_{41}O_9Si$ (M^+-15): 489.2520. Found: 489.2521. $[\alpha]_D^{24}$ -49.5° ($c=1.08$, $CHCl_3$).

(2S,3R,4R,5R,6R)-3,6-Dihydroxy-2-[(4'S)-2',2'-dimethyl-1',3'-dioxolan-4'-yl]-3,4,5,6-tetrahydro-2H-pyran-4,5-bis[spiro-4''-(2'',2''-dimethyl-1'',3''-dioxolane)] (12). To a stirred solution of silyl ether (**11**) (46.5 mg, 0.092 mmol) in THF (2 mL) was added dropwise TBAF (1.0 M in hexane, 0.14 mL, 0.14 mmol) at $0^\circ C$ and the mixture was stirred for 1 h at the same temperature. After the mixture was quenched with saturated NH_4Cl solution, the solvent was removed to give a residue, which was extracted with AcOEt. The combined organic layer was washed with brine. The organic layer was dried over Na_2SO_4 and evaporated to give a residue, which was chromatographed on silica gel (hexane/AcOEt=7:3) to afford lactol (**12**) (33 mg, 91.7 %). Colorless prisms. mp $200-201^\circ C$ (Et_2O). IR cm^{-1} : 3500 (OH). 1H NMR: 1.36 and 1.43 (each 3H, each s, CMe_2), 1.45 and 1.47 (each 3H, each s, CMe_2), 1.48 and 1.51 (each 3H, each s, CMe_2), 2.82 (1H, d, $J=3.7$ Hz, 6-OH), 3.49 (1H, d, $J=8.5$ Hz, 3-OH), 3.76 (1H, br d, $J=8.5$ Hz, 3-H), 3.80 (1H, br d, $J=8.5$ Hz, 2-H), 3.87 and 3.97 (each 1H, each d, $J=9.8$ Hz, 4 or 5- CH_2), 3.96 and 4.10 (each 1H, each dd, $J=8.6$, 6.1 Hz, 5'- H_2), 4.12 and 4.19 (each 1H, each d, $J=9.2$ Hz, 5 or 6- CH_2), 4.46 (1H, distorted q, $J=6.1$ Hz, 4'-H), 5.07 (1H, d, $J=3.7$ Hz, 6-H). ^{13}C NMR: -5.9 , -4.6 , 17.7 , 25.2 , 25.5 , 26.1 , 55.4 , 55.5 , 64.7 , 67.8 , 69.0 , 69.9 , 73.0 , 80.9 , 81.5 , 94.7 , 96.7 , 97.2 , 109.1 , 203.8 . HRMS m/z : Calcd for $C_{18}H_{30}O_9$ (M^+): 390.1890. Found: 390.1890. Anal. Calcd for $C_{18}H_{30}O_9$: C, 55.37; H, 7.75. Found: C, 55.49; H, 7.84. $[\alpha]_D^{25}$ -43.6° ($c=1.15$, $CHCl_3$). **Crystal data of 12:** $C_{18}H_{30}O_9$, FW=390.43, orthorhombic, P 2 1_2 1 2_1 , $a=12.928(9)$ Å, $b=16.65(1)$ Å, $c=9.364(9)$ Å, $V=2016(2)$ Å³, $Z=4$, $\mu(CuK\alpha)=8.71$ cm^{-1} , $D(calc)=1.286$ g/cm^3 ; 1229 reflections with $2\theta_{max}=163.6^\circ$ were recorded on a Rigaku AFC7R diffractometer with graphite monochromated Cu-K α radiation. Of those, 1203 with $I>3.00\sigma(I)$ were judged as observed. The structure was solved using SHELXS-86. $R=0.088$, $R_w=0.090$.

(2S,3R,4R,5R,6S)-3-Benzyloxy-6-tert-butyldimethylsiloxy-2-[(4'S)-2',2'-dimethyl-1',3'-dioxolan-4'-yl]-3,4,5,6-tetrahydro-2H-pyran-4,5-bis[spiro-4''-(2'',2''-dimethyl-1'',3''-dioxolane)] (13). To a stirred solution of alcohol (**11**) (330 mg, 066 mmol) and benzyl bromide (0.16 mL, 1.31 mmol) in DMF (15 mL) was added portionwise NaH (ca. 60% purity, 52.3 mg, 1.31 mmol) at $0^\circ C$ and the reaction mixture was stirred for 30 min at the same temperature. After the mixture was quenched with saturated NH_4Cl solution, the solvent was removed to give a residue, which was extracted with hexane- Et_2O (1:1). The combined

organic layer was washed with brine. The organic layer was dried over Na_2SO_4 and evaporated to give a residue, which was chromatographed on silica gel (hexane/AcOEt=9:1) to afford benzyl ether (**13**) (365 mg, 93.8 %) as a colorless oil. ^1H NMR: δ 0.13 (6H, s, SiMe_2), 0.92 (9H, s, CMe_3), 1.41 (6H, s, CMe_2), 1.43 and 1.54 (each 3H, each s, CMe_2), 1.55 (6H, s, CMe_2), 3.59 (1H, br d, $J=8.5$ Hz, 2-H), 3.66 (1H, d, $J=1.2$ Hz, 3-H), 3.74 and 4.36 (each 1H, each d, $J=9.8$ Hz, 4- CH_2), 3.84 and 4.26 (each 1H, each d, $J=9.8$ Hz, 5- CH_2), 3.86 and 4.01 (each 1H, each dd, $J=8.5$, 6.1 Hz, 5'- H_2), 4.53 (1H, dt, $J=8.5$, 6.1 Hz, 4'-H), 4.80 and 5.05 (each 1H, each d, $J=11.6$ Hz, PhCH_2), 5.07 (1H, s, 6-H), 7.20-7.32 (3H, m, Ar-H), 7.43 (2H, dd, $J=7.9$, 1.8 Hz, m-Ar-H). ^{13}C NMR: δ -5.7, -4.6, 17.7, 25.5, 25.8, 26.2, 26.6, 26.8, 26.9, 66.9, 67.0, 69.9, 71.1, 72.9, 74.6, 79.8, 81.6, 83.4, 98.2, 108.9, 109.4, 111.2, 126.9, 127.7, 128.0, 139.1. HRMS m/z : Calcd for $\text{C}_{30}\text{H}_{47}\text{O}_9\text{Si}$ (M^+-15): 579.2989. Found: 579.2992. $[\alpha]_{\text{D}}^{26}$ -22.3° ($c=0.93$, CHCl_3).

(2S,3R,4R,5R,6R)-3-Benzoyloxy-6-hydroxy-2-[(4'S)-2',2'-dimethyl-1',3'-dioxolan-4'-yl]-3,4,5,6-tetrahydro-2H-pyran-4,5-bis[spiro-4''-(2'',2''-dimethyl-1'',3''-dioxolane)] (14). To a stirred solution of silyl ether (**13**) (760 mg, 1.28 mmol) in THF (20 mL) was added dropwise TBAF (1.0M in hexane, 1.92 mL, 1.92 mmol) at 0 °C and the mixture was stirred for 30 min at the same temperature. After the mixture was quenched with saturated NH_4Cl solution, the solvent was removed to give a residue, which was extracted with AcOEt. The combined organic layer was washed with brine. The organic layer was dried over Na_2SO_4 and evaporated to give a residue, which was chromatographed on silica gel (hexane/AcOEt=7:3) to afford lactol (**14**) (520 mg, 84.7 %) as a colorless oil. IR cm^{-1} : 3600 (OH). ^1H NMR: 1.36 and 1.41 (each 3H, each s, CMe_2), 1.42 (6H, s, CMe_2), 1.55 and 1.57 (each 3H, each s, CMe_2), 2.67 (1H, br s, 6-OH), 3.67 (1H, d, $J=8.5$ Hz, 2-H), 3.68 (1H, br s, 3-H), 3.73 and 4.37 (each 1H, each d, $J=9.8$ Hz, 4- CH_2), 3.83 and 4.04 (each 1H, each dd, $J=8.6$, 6.1 Hz, 5'- H_2), 4.01 and 4.31 (each 1H, each d, $J=9.2$ Hz, 5- CH_2), 4.54 (1H, dt, $J=8.5$, 6.1 Hz, 4'-H), 4.74 and 5.03 (each 1H, each d, $J=11.6$ Hz, PhCH_2), 5.15 (1H, br s, 6-H), 7.23-7.32 (3H, m, Ar-H), 7.44 (2H, dd, $J=7.9$, 1.8 Hz, m-Ar-H). HRMS m/z : Calcd for $\text{C}_{24}\text{H}_{33}\text{O}_9$ (M^+-15): 465.2122. Found: 465.2119. $[\alpha]_{\text{D}}^{26}$ -7.47° ($c=1.06$, CHCl_3).

(2R,3R,4R,5S,6S)-4-Benzoyloxy-6,7-O-isopropylidenedioxy-1,5-heptanediol-2,3-bis[spiro-4'-(2',2'-dimethyl-1',3'-dioxolane)] (15). To a stirred suspension of LiAlH_4 (79 mg, 2.08 mmol) in THF (5 mL) was added a solution of lactol (**14**) (200 mg, 2.08 mmol) in THF (2 mL) at 0 °C and the reaction mixture was stirred for 1 h at rt. After quenching with 30% NaOH, insoluble material was filtered off through a Celite pad. The filtrate was extracted with AcOEt and the combined organic layer was washed with brine. The organic layer was dried over Na_2SO_4 and evaporated to give a residue, which was chromatographed on silica gel (hexane/AcOEt=2:1) to afford diol (**15**) (188 mg, 93.6 %) as a colorless oil. IR cm^{-1} : 3500 (OH). ^1H NMR: 1.35 and 1.44 (each 3H, each s, CMe_2), 1.44 and 1.45 (each 3H, each s, CMe_2), 1.52 and 1.53 (each 3H, each s, CMe_2), 2.59 (1H, t, $J=5.5$ Hz, 1-OH), 3.48 (1H, d, $J=4.9$ Hz, 5-OH), 3.70 and 3.83 (each 1H, each dd, $J=11.6$, 5.5 Hz, 1- H_2), 3.86 and 4.00 (each 1H, each d, $J=9.2$ Hz, 2 or 3- CH_2), 3.96-4.17 (3H, m, 4, 5, 6-H), 4.06 and 4.25 (each 1H, each d, $J=9.2$ Hz, 2 or 3- CH_2), 4.73 and 4.83 (each 1H, each d, $J=11.6$ Hz, PhCH_2), 7.26-7.39 (5H, m, Ar-H). HRMS m/z : Calcd for $\text{C}_{24}\text{H}_{35}\text{O}_9$ (M^+-15): 467.2281. Found: 467.2283. Anal. Calcd for $\text{C}_{25}\text{H}_{38}\text{O}_9$: C, 62.22; H, 7.94. Found: C, 62.02; H, 7.95. $[\alpha]_{\text{D}}^{22}$ +6.55° ($c=1.08$, CHCl_3).

(2S,3R,4R,5S,6S)-1-Acetoxy-4-benzyloxy-6,7-O-isopropylidenedioxy-1,5-heptanol-2,3-bis[spiro-4'-(2',2'-dimethyl-1',3'-dioxolane)] (16). A solution of diol (**15**) (258 mg, 0.54 mmol), Ac_2O (0.2 mL, 2.14 mmol), a catalytic amount of DMAP, and pyridine (0.22 mL, 2.68 mmol) in CH_2Cl_2 (15 mL) was stirred for 1 h at rt. After quenching with saturated NH_4Cl solution, the mixture was extracted with AcOEt. The combined organic layer was washed with brine. The organic layer was dried over Na_2SO_4 and evaporated to give a residue, which was chromatographed on silica gel (hexane/AcOEt=3:1) to afford acetate (**16**) (268 mg, 95.5 %) as a colorless oil. IR cm^{-1} : 1740 (CO), 3500 (OH). ^1H NMR: 1.26 and 1.35 (each 3H, each s, CMe_2), 1.42 and 1.44 (each 3H, each s, CMe_2), 1.45 and 1.50 (each 3H, each s, CMe_2), 2.10 (3H, s, COCH_3), 3.50 (1H, d, $J=2.5$ Hz, 5-OH), 3.95-4.26 (11H, m), 4.70 and 4.85 (each 1H, each d, $J=11.6$ Hz, PhCH_2), 7.29-7.40 (5H, m, Ar-H). HRMS m/z : Calcd for $\text{C}_{26}\text{H}_{37}\text{O}_{10}$ (M^+-15): 509.2386.

Found: 509.2386. Anal. Calcd for C₂₇H₄₀O₁₀: C, 61.81; H, 7.69. Found: C, 61.52; H, 7.82. [α]_D²⁵ -6.54° (*c*=1.64, CHCl₃).

(2S,3R,4R,5S,6S)-1-Acetoxy-4-benzyloxy-5-tert-butyldimethylsiloxy-6,7-O-isopropylidenedioxy-heptane-2,3-bis[spiro-4'-(2',2'-dimethyl-1',3'-dioxolane)] (17). To a stirred solution of alcohol (**16**) (310 mg, 0.59 mmol) and Et₃N (0.49 mL, 3.55 mmol) in CH₂Cl₂ (15 mL) was added TBSOTf (0.54 mL, 2.37 mmol) at 0 °C and the mixture was stirred for 2 h at rt. After quenching with saturated NH₄Cl solution, the mixture was extracted with AcOEt. The combined organic layer was washed with brine. The organic layer was dried over Na₂SO₄ and evaporated to give a residue, which was chromatographed on silica gel (hexane/AcOEt=9:1) to afford silyl ether (**17**) (350 mg, 92.7 %) as a colorless oil. IR cm^{-1} : 1730 (CO). ¹H NMR: 0.09 and 0.15 (each 3H, each s, SiMe₂), 0.86 (9H, s, CMe₃), 1.32 and 1.39 (each 3H, each s, CMe₂), 1.44 and 1.45 (each 3H, each s, CMe₂), 1.49 (6H, s, CMe₂), 2.07 (3H, s, COCH₃), 3.61 (1H, d, *J*=7.3 Hz, 4-H), 3.72 and 3.78 (each 1H, each d, *J*=10.4 Hz, 2 or 3-CH₂), 3.98 (2H, d, *J*=7.3 Hz, 7-H₂), 4.21 and 4.40 (each 1H, each d, *J*=9.2 Hz, 2 or 3-CH₂), 4.23 (2H, br s, 1-H₂), 4.25 and 5.11 (each 1H, each d, *J*=11.6 Hz, PhCH₂), 4.30 (1H, dt, *J*=7.3, 2.4 Hz, 6-H), 4.53 (1H, dd, *J*=7.3, 2.4 Hz, 5-H), 7.23-7.34 (5H, m, Ar-H). HRMS *m/z*: Calcd for C₃₂H₅₁O₁₀Si (M⁺-15): 623.3252. Found: 623.3252. [α]_D²⁵ -20.4° (*c*=1.03, CHCl₃).

(2R,3R,4R,5S,6S)-4-Benzyloxy-5-tert-butyldimethylsiloxy-6,7-O-isopropylidenedioxy-1-heptanol-2,3-bis[spiro-4'-(2',2'-dimethyl-1',3'-dioxolane)] (18). To a stirred solution of acetate (**17**) (300 mg, 0.47 mmol) in MeOH (10 mL) was added dropwise 1M LiOH (1.0 mL, 0.94 mmol) at 0 °C and the mixture was stirred for 1 h at rt. After the mixture was neutralized with 1M HCl, the solvent was removed to give a residue, which was extracted with AcOEt. The combined organic layer was washed with brine. The organic layer was dried over Na₂SO₄ and evaporated to give a residue, which was chromatographed on silica gel (hexane/AcOEt=4:1) to afford lactol (**18**) (256 mg, 91.3 %) as a colorless oil. IR cm^{-1} : 3525 (OH). ¹H NMR: 0.12 and 0.16 (each 3H, each s, SiMe₂), 0.87 (9H, s, CMe₃), 1.33 and 1.41 (each 3H, each s, CMe₂), 1.43 and 1.46 (each 3H, each s, CMe₂), 1.52 (6H, s, CMe₂), 2.74 (1H, t, *J*=4.3 Hz, 1-OH), 3.45 and 3.67 (each 1H, each d, *J*=9.8 Hz, 2 or 3-CH₂), 3.67 (1H, d, *J*=6.1 Hz, 4-H), 3.67 and 3.76 (each 1H, each dd, *J*=11.6, 4.3 Hz, 1-H₂), 3.97 and 4.05 (each 1H, each dd, *J*=7.9, 6.1 Hz, 7-H₂), 4.21 and 4.39 (each 1H, each d, *J*=9.2 Hz, 2 or 3-CH₂), 4.21 and 5.09 (each 1H, each d, *J*=11.0 Hz, PhCH₂), 4.28 (1H, ddd, *J*=7.9, 6.1, 3.1 Hz, 6-H), 4.54 (1H, dd, *J*=6.1, 3.1 Hz, 5-H), 7.23-7.34 (5H, m, Ar-H). HRMS *m/z*: Calcd for C₃₀H₄₉O₉Si (M⁺-15): 581.3144. Found: 581.3144. [α]_D²⁵ -10.5° (*c*=1.39, CHCl₃).

(2R,3R,4R,5S,6S)-4-Benzyloxy-5-tert-butyldimethylsiloxy-6,7-O-isopropylidenedioxy-pentanal-2,3-bis[spiro-4'-(2',2'-dimethyl-1',3'-dioxolane)] (19). To a stirred solution of alcohol (**18**) (284 mg, 0.48 mmol) in CH₂Cl₂ (10 mL) was added portionwise Dess-Martin periodinane (1.62 g, 3.81 mmol) at 0 °C and the mixture was stirred for 1 h at rt. After dilution with Et₂O, insoluble material was filtered off. The filtrate was successively washed with saturated NaHCO₃ solution, saturated Na₂S₂O₃ solution, and brine. The organic layer was dried over Na₂SO₄ and evaporated to give a residue, which was chromatographed on silica gel (hexane/AcOEt=9:1) to afford aldehyde (**19**) (282 mg, 99.6 %) as a colorless oil. IR cm^{-1} : 1725 (CHO). ¹H NMR: 0.05 and 0.12 (each 3H, each s, SiMe₂), 0.83 (9H, s, CMe₃), 1.31 and 1.37 (each 3H, each s, CMe₂), 1.43 and 1.44 (each 3H, each s, CMe₂), 1.51 (6H, s, CMe₂), 3.52 (1H, d, *J*=6.7 Hz, 4-H), 3.85 and 4.20 (each 1H, each dd, *J*=9.8, 1.2 Hz, 2-CH₂), 3.92-4.01 (2H, m, 7-H₂), 4.09 and 4.35 (each 1H, each d, *J*=9.2 Hz, 3-CH₂), 4.20 (1H, m, 6-H), 4.33 and 5.04 (each 1H, each d, *J*=11.6 Hz, PhCH₂), 4.46 (1H, dd, *J*=6.7, 2.4 Hz, 5-H), 7.21-7.34 (5H, m, Ar-H), 9.49 (1H, d, *J*=1.2 Hz, CHO). ¹³C NMR: -4.4, -3.8, 18.1, 24.9, 25.6, 25.7, 25.9, 26.1, 26.2, 27.1, 63.8, 65.8, 67.7, 68.8, 74.1, 76.4, 76.5, 78.3, 86.0, 89.3, 108.5, 109.9, 111.4, 126.5, 127.0, 128.0, 137.4, 203.1. HRMS *m/z*: Calcd for C₃₀H₄₇O₉Si (M⁺-15): 579.2988. Found: 579.2993. [α]_D²² -7.37° (*c*=1.59, CHCl₃).

(2S,3S,4R,5R,6S,7R)-4-Benzyloxy-3-tert-butyldimethylsiloxy-1,2-O-isopropylidenedioxy-9-trimeth-

ylsilyl-8-nonyl-7-ol-5,6-bis[spiro-4'-(2',2'-dimethyl-1',3'-dioxolane)] (20). To a stirred solution of lithium trimethylsilylacetylide [prepared from trimethylsilylacetylene (0.55 mL, 3.91 mmol) and *n*-BuLi (1.56 M in hexane, 2.28 mL, 3.55 mmol) in THF (5 mL)] was added dropwise a solution of aldehyde (**19**) (290 mg, 0.488 mmol) in THF (2 mL) at -78 °C and the mixture was stirred for 30 min at the same temperature. After the mixture was quenched with saturated NH₄Cl solution, the solvent was removed to give a residue, which was extracted with AcOEt. The combined organic layer was washed with brine. The organic layer was dried over Na₂SO₄ and evaporated to give a residue, which was chromatographed on silica gel (hexane/AcOEt=9:1) to afford propargyl alcohol (**20**) (319 mg, 94.4 %) as a colorless oil. IR cm^{-1} : 3450 (OH). ¹H NMR: 0.02 and 0.14 (each 3H, each s, SiMe₂), 0.18 (9H, s, SiMe₃), 0.87 (9H, s, CMe₃), 1.32 and 1.46 (each 3H, each s, CMe₂), 1.51 (6H, s, CMe₂), 1.51 and 1.53 (each 3H, each s, CMe₂), 3.06 (1H, br s, 7-OH), 3.75 (1H, d, *J*=7.9 Hz, 4-H), 4.02 and 4.06 (each 1H, each d, *J*=10.4 Hz, 5 or 6-CH₂), 4.03 and 4.19 (each 1H, each d, *J*=8.5 Hz, 1-H₂), 4.32-4.41 (1H, m, 2-H), 4.37 and 5.09 (each 1H, each d, *J*=11.6 Hz, PhCH₂), 4.39 and 4.51 (each 1H, each d, *J*=9.8 Hz, 5 or 6-CH₂), 4.48 (1H, dd, *J*=7.9, 2.5 Hz, 3-H), 4.61 (1H, br s, 7-H), 7.22-7.35 (5H, m, Ar-H). ¹³C NMR: -4.4, -3.7, -0.4, 18.1, 24.8, 26.0, 26.1, 26.2, 26.3, 26.5, 26.6, 63.5, 63.8, 66.8, 67.8, 70.1, 73.6, 77.7, 77.8, 87.7, 92.1, 104.2, 108.5, 110.9, 111.3, 126.4, 127.1, 128.1, 137.8. HRMS *m/z*: Calcd for C₃₅H₅₇O₉Si₂ (M⁺-15): 677.3539. Found: 677.3534. $[\alpha]_{\text{D}}^{23}$ -14.1° (*c*=1.27, CHCl₃).

(2S,3S,4R,5R,6S,7R)-4-Benzoyloxy-3-tert-butyltrimethylsilyloxy-1,2-O-isopropylidenedioxy-8-nonyl-7-ol-5,6-bis[spiro-4'-(2',2'-dimethyl-1',3'-dioxolane)] (21). A mixture of trimethylsilylacetylene (**20**) (218 mg, 0.315 mmol) and K₂CO₃ (57 mg, 0.410 mmol) in MeOH (10 mL) was stirred for 2 h at rt. After insoluble material was filtered off, the filtrate was condensed to give a residue, which was chromatographed on silica gel (hexane/AcOEt=17:3) to afford acetylene (**21**) (195 mg, 99.8 %) as a colorless oil. IR cm^{-1} : 3300 (acetylene), 3500 (OH). ¹H NMR: 0.06 and 0.15 (each 3H, each s, SiMe₂), 0.87 (9H, s, CMe₃), 1.33 and 1.46 (each 3H, each s, CMe₂), 1.49 and 1.51 (each 3H, each s, CMe₂), 1.52 (6H, s, CMe₂), 2.51 (1H, d, *J*=1.8 Hz, 9-H), 3.18 (1H, d, *J*=3.1 Hz, 7-OH), 3.75 (1H, d, *J*=7.3 Hz, 4-H), 3.96-4.10 (2H, m, 1-H₂), 4.01 and 4.07 (each 1H, each d, *J*=9.8 Hz, 5 or 6-CH₂), 4.31 and 5.09 (each 1H, each d, *J*=11.6 Hz, PhCH₂), 4.28-4.35 (1H, m, 2-H), 4.39 and 4.44 (each 1H, each d, *J*=9.8 Hz, 5 or 6-CH₂), 4.49 (1H, dd, *J*=7.3, 2.4 Hz, 3-H), 4.66 (1H, dd, *J*=3.1, 1.8 Hz, 7-H), 7.25-7.35 (5H, m, Ar-H). HRMS *m/z*: Calcd for C₃₂H₄₉O₉Si (M⁺-15): 605.3144. Found: 605.3133. $[\alpha]_{\text{D}}^{20}$ -15.2° (*c*=1.36, CHCl₃).

(2S,3S,4R,5R,6S,7R)-7-Acetoxy-4-benzoyloxy-3-tert-butyltrimethylsilyloxy-1,2-O-isopropylidenedioxy-8-nonyne-5,6-bis[spiro-4'-(2',2'-dimethyl-1',3'-dioxolane)] (22). A solution of alcohol (**21**) (130 mg, 0.21 mmol), Ac₂O (79.3 μL, 0.84 mmol), a catalytic amount of DMAP, and pyridine (85 μL, 1.05 mmol) in CH₂Cl₂ (2.5 mL) was stirred for 12 h at rt. After quenching with saturated NH₄Cl solution, the mixture was extracted with AcOEt. The combined organic layer was washed with brine. The organic layer was dried over Na₂SO₄ and evaporated to give a residue, which was chromatographed on silica gel (hexane/AcOEt=9:1) to afford acetate (**22**) (138 mg, 99.4 %) as a colorless oil. IR cm^{-1} : 1750 (CO), 3300 (acetylene). ¹H NMR: 0.02 and 0.14 (each 3H, each s, SiMe₂), 0.87 (9H, s, CMe₃), 1.29 and 1.42 (each 3H, each s, CMe₂), 1.45 and 1.47 (each 3H, each s, CMe₂), 1.51 and 1.54 (each 3H, each s, CMe₂), 2.10 (3H, s, COCH₃), 2.47 (1H, d, *J*=2.5 Hz, 9-H), 3.75 (1H, d, *J*=8.6 Hz, 4-H), 3.96-4.07 (2H, m, 1-H₂), 4.08 and 4.38 (each 1H, each d, *J*=9.8 Hz, 5 or 6-CH₂), 4.36-4.45 (1H, m, 2-H), 4.40 and 4.62 (each 1H, each d, *J*=10.4 Hz, 5 or 6-CH₂), 4.50 (1H, dd, *J*=8.6, 1.2 Hz, 3-H), 4.54 and 5.23 (each 1H, each d, *J*=12.2 Hz, PhCH₂), 5.78 (1H, d, *J*=2.5 Hz, 7-H), 7.19-7.29 (5H, m, Ar-H). HRMS *m/z*: Calcd for C₃₄H₅₁O₁₀Si (M⁺-15): 647.3252. Found: 647.3252. $[\alpha]_{\text{D}}^{24}$ -33.5° (*c*=1.42, CHCl₃).

(2S,3S,4R,5R,6S,7R)-7-Acetoxy-4-benzoyloxy-3-tert-butyltrimethylsilyloxy-8-nonyl-1,2-diol-5,6-bis[spiro-4'-(2',2'-dimethyl-1',3'-dioxolane)] (23). A mixture of triacetone (**22**) (194 mg, 0.29 mmol) and FeCl₃-SiO₂ complex (20 mg) in CHCl₃ (10 mL) was stirred for 2 h at rt. After insoluble material was filtered off through a Celite pad, the filtrate was concentrated to leave a residue, which was

chromatographed on silica gel (hexane/AcOEt=7:3) to afford diol (**23**) (157 mg, 86.1 %) as a colorless oil. IR cm^{-1} : 1740 (CO), 3300 (acetylene), 3500 (OH). ^1H NMR: 0.03 and 0.18 (each 3H, each s, SiMe_2), 0.88 (9H, s, CMe_3), 1.43 and 1.45 (each 3H, each s, CMe_2), 1.54 and 1.55 (each 3H, each s, CMe_2), 2.11 (3H, s, COCH_3), 2.50-2.65 (2H, br s, 1, 2-OH), 2.50 (1H, d, $J=2.4$ Hz, 9-H), 3.86-4.97 (3H, m, 1-H₂, 2-H), 4.09 and 4.38 (each 1H, each d, $J=9.8$ Hz, 5 or 6-CH₂), 4.16 (1H, d, $J=8.6$ Hz, 4-H), 4.37 and 4.64 (each 1H, each d, $J=10.4$ Hz, 5 or 6-CH₂), 4.35 and 4.40 (1H, m, 3-H), 4.64 and 5.17 (each 1H, each d, $J=12.2$ Hz, PhCH_2), 5.83 (1H, d, $J=2.4$ Hz, 7-H), 7.25-7.34 (5H, m, Ar-H). HRMS m/z : Calcd for $\text{C}_{31}\text{H}_{47}\text{O}_{10}\text{Si}$ (M^+-15): 607.2937. Found: 607.2935. $[\alpha]_{\text{D}}^{24}$ -24.7° ($c=0.86$, CHCl_3).

(2S,3S,4R,5R,6S,7R)-1,7-Diacetoxy-4-benzyloxy-3-tert-butyltrimethylsilyloxy-8-nonyn-2-ol-5,6-bis[spiro-4'-(2',2'-dimethyl-1',3'-dioxolane)] (24). A solution of diol (**23**) (34 mg, 0.055 mmol), Ac_2O (7.7 μL , 0.082 mmol), a catalytic amount of DMAP, and pyridine (6.6 μL , 0.082 mmol) in CH_2Cl_2 (5 mL) was stirred for 1 h at rt. After quenching with saturated NH_4Cl solution, the mixture was extracted with AcOEt. The combined organic layer was washed with brine. The organic layer was dried over Na_2SO_4 and evaporated to give a residue, which was chromatographed on silica gel (hexane/AcOEt=4:1) to afford acetate (**24**) (36 mg, 99.3 %) as a colorless oil. IR cm^{-1} : 1740 (CO), 3300 (acetylene) 3500 (OH). ^1H NMR: 0.00 and 0.07 (each 3H, each s, SiMe_2), 0.86 (9H, s, CMe_3), 1.42 and 1.45 (each 3H, each s, CMe_2), 1.55 (6H, s, CMe_2), 2.10 (6H, s, 2 \times COCH_3), 2.45 (1H, br s, 2-OH), 2.51 (1H, d, $J=2.4$ Hz, 9-H), 4.03 (1H, m, 2-H), 4.10 (1H, d, $J=9.8$ Hz, 5 or 6-CHH), 4.14 (1H, d, $J=8.6$ Hz, 4-H), 4.25-4.44 (4H, m, 1-H₂, 3-H, 5 or 6-CHH), 4.35 and 4.63 (each 1H, each d, $J=9.8$ Hz, 5 or 6-CH₂), 4.59 and 5.19 (each 1H, each d, $J=12.2$ Hz, PhCH_2), 5.84 (1H, d, $J=2.4$ Hz, 7-H), 7.26-7.30 (5H, m, Ar-H). HRMS m/z : Calcd for $\text{C}_{33}\text{H}_{49}\text{O}_{11}\text{Si}$ (M^+-15): 649.3043. Found: 649.3012. $[\alpha]_{\text{D}}^{25}$ -28.8° ($c=0.75$, CHCl_3).

(3R,4R,5R,6S,7R)-1,7-Diacetoxy-4-benzyloxy-3-tert-butyltrimethylsilyloxy-8-nonyn-2-one-5,6-bis[spiro-4'-(2',2'-dimethyl-1',3'-dioxolane)] (25). A mixture of alcohol (**24**) (32 mg, 0.048 mmol) and Dess-Martin periodinane (102 mg, 0.241 mmol) in CH_2Cl_2 (2 mL) was stirred for 6 h at rt. After dilution with hexane- Et_2O (5 mL, 1/1), the mixture was filtered through a Celite pad. The filtrate was successively washed with saturated NaHCO_3 solution, saturated $\text{Na}_2\text{S}_2\text{O}_3$ solution, and brine. The organic layer was dried over Na_2SO_4 and evaporated to give a residue, which was chromatographed on silica gel (hexane/AcOEt=9:1) to afford ketone (**25**) (20 mg, 62.7 %) as a colorless oil. IR cm^{-1} : 1740 (CO), 3300 (acetylene). ^1H NMR: 0.06 and 0.11 (each 3H, each s, SiMe_2), 0.92 (9H, s, CMe_3), 1.41 and 1.44 (each 3H, each s, CMe_2), 1.50 and 1.51 (each 3H, each s, CMe_2), 2.13 and 2.17 (each 3H, each s, COCH_3), 2.44 (1H, d, $J=2.4$ Hz, 9-H), 4.10 and 4.30 (each 1H, each d, $J=9.8$ Hz, 1-H₂), 4.36 and 4.52 (each 1H, each d, $J=9.8$ Hz, 5 or 6-CH₂), 4.36 (1H, d, $J=6.1$ Hz, 4-H), 4.56 and 5.12 (each 1H, each d, $J=11.6$ Hz, 5 or 6-CH₂), 4.72 (1H, d, $J=6.1$ Hz, 3-H), 4.84 and 5.17 (each 1H, each d, $J=16.5$ Hz, PhCH_2), 5.83 (1H, d, $J=2.4$ Hz, 7-H), 7.24-7.31 (5H, m, Ar-H). HRMS m/z : Calcd for $\text{C}_{33}\text{H}_{47}\text{O}_{11}\text{Si}$ (M^+-15): 647.2886. Found: 647.2886. $[\alpha]_{\text{D}}^{21}$ -15.4° ($c=0.4$, CHCl_3).

(2S,3S,4R,5R,6S,7R)-4-Benzyloxy-3-tert-butyltrimethylsilyloxy-1,2-O-isopropylidenedioxy-7-methoxy-methoxy-8-nonyne-5,6-bis[spiro-4'-(2',2'-dimethyl-1',3'-dioxolane)] (26). A solution of alcohol (**21**) (252 mg, 0.41 mmol), MOMCl (0.46 mL, 6.1 mmol), and $i\text{-Pr}_2\text{NEt}$ (1.63 mL, 9.3 mmol) in CH_2Cl_2 (2.5 mL) was refluxed for 6 h. After quenching with saturated NH_4Cl solution, the mixture was extracted with AcOEt. The combined organic layer was washed with brine. The organic layer was dried over Na_2SO_4 and evaporated to give a residue, which was chromatographed on silica gel (hexane/AcOEt=9:1) to afford ether (**26**) (263 mg, 97.4 %) as a colorless oil. IR cm^{-1} : 3300 (acetylene). ^1H NMR: 0.04 and 0.15 (each 3H, each s, SiMe_2), 0.86 (9H, s, CMe_3), 1.31 and 1.44 (each 3H, each s, CMe_2), 1.45 (6H, s, CMe_2), 1.51 and 1.53 (each 3H, each s, CMe_2), 2.47 (1H, d, $J=2.5$ Hz, 9-H), 3.33 (3H, s, OCH_3), 3.95 (1H, d, $J=6.7$ Hz, 4-H), 3.93-4.10 (4H, m, 1-H₂, 5 or 6-CH₂), 4.31 and 5.14 (each 1H, each d, $J=12.2$ Hz, PhCH_2), 4.43 (2H, s, OCH_2O), 4.46-4.56 (3H, m, 2-H, 3-H, 7-H), 4.62 and 4.90 (each 1H, each d, $J=6.7$ Hz, 5 or 6-CH₂), 7.20-7.32 (5H, m, Ar-H). HRMS m/z : Calcd for $\text{C}_{34}\text{H}_{53}\text{O}_{10}\text{Si}$ (M^+-15): 649.3407. Found: 649.3407. $[\alpha]_{\text{D}}^{24}$ -33.9° ($c=1.28$, CHCl_3).

(2*S*,3*S*,4*R*,5*R*,6*S*,7*R*)-4-Benzoyloxy-3-*tert*-butyldimethylsiloxy-7-methoxymethoxy-8-nonyne-1,2-diol-5,6-bis[spiro-4'-(2',2'-dimethyl-1',3'-dioxolane)] (27). The same procedure as for the alcohol (22) was applied to compound (26) to afford diol (27) (68.1 %) as a colorless oil. IR cm^{-1} : 3310 (acetylene), 3490 (OH). $^1\text{H NMR}$: 0.05 and 0.18 (each 3H, each s, SiMe_2), 0.86 (9H, s, CMe_3), 1.43 and 1.46 (each 3H, each s, CMe_2), 1.56 (6H, s, CMe_2), 2.49 (1H, d, $J=1.8$ Hz, 9-H), 2.60 and 2.80 (each 3H, each br s, 1-OH, 2-OH), 3.33 (3H, s, OCH_3), 3.87-4.08 (5H, m, 1- H_2 , 2-H, 5 or 6- CH_2), 4.34-4.45 (5H, m, 3-H, 4-H, OCH_2O , PhCHH), 4.58 (1H, d, $J=1.8$ Hz, 7-H), 4.64 and 4.94 (each 1H, each d, $J=6.7$ Hz, 5 or 6- CH_2), 5.08 (1H, d, $J=12.2$ Hz, PhCHH), 7.23-7.34 (5H, m, Ar-H). $^{13}\text{C NMR}$: -4.7, -3.7, 18.1, 25.9, 26.0, 26.3, 26.7, 27.0, 55.9, 62.8, 66.5, 67.2, 68.0, 73.5, 74.0, 74.1, 76.4, 76.8, 80.6, 86.7, 87.5, 94.2, 110.3, 111.6, 126.2, 127.0, 128.0, 138.2. HRMS m/z : Calcd for $\text{C}_{31}\text{H}_{49}\text{O}_{10}\text{Si}$ (M^+-15): 609.3095. Found: 609.3097. $[\alpha]_{\text{D}}^{24}$ -24.7° ($c=0.86$, CHCl_3).

(2*S*,3*S*,4*R*,5*R*,6*S*,7*R*)-1-Acetoxy-4-benzoyloxy-3-*tert*-butyldimethylsiloxy-7-methoxymethoxy-8-nonyn-2-ol-5,6-bis[spiro-4'-(2',2'-dimethyl-1',3'-dioxolane)] (28). The same procedure as for the alcohol (23) was applied to compound (27) to afford acetate (28) (96.7 %) as a colorless oil. IR cm^{-1} : 1740 (CO), 3300 (acetylene) 3500 (OH). $^1\text{H NMR}$: 0.03 and 0.14 (each 3H, each s, SiMe_2), 0.85 (9H, s, CMe_3), 1.43 and 1.46 (each 3H, each s, CMe_2), 1.56 and 1.57 (each 3H, each s, CMe_2), 2.11 (3H, s, COCH_3), 2.50 (1H, d, $J=2.4$ Hz, 9-H), 2.66 (1H, br s, 2-OH), 3.32 (3H, s, OCH_3), 3.99-4.10 (3H, m, 2-H, 5 or 6- CHH), 4.23 (1H, dd, $J=11.6$, 7.9 Hz, 1- HH), 4.31-4.49 (6H, m, 1- HH , 3-H, 4-H, PhCHH , OCH_2O), 4.60 (1H, d, $J=2.4$ Hz, 7-H), 4.62 and 4.93 (each 1H, each d, $J=6.7$ Hz, 5 or 6- CH_2), 5.10 (1H, d, $J=11.6$ Hz, PhCHH), 7.23-7.34 (5H, m, Ar-H). HRMS m/z : Calcd for $\text{C}_{33}\text{H}_{51}\text{O}_{11}\text{Si}$ (M^+-15): 651.3196. Found: 651.3197. $[\alpha]_{\text{D}}^{22}$ -32.3° ($c=0.37$, CHCl_3).

(3*R*,4*R*,5*R*,6*S*,7*R*)-1-Acetoxy-4-benzoyloxy-3-*tert*-butyldimethylsiloxy-7-methoxymethoxy-8-nonyn-2-one-5,6-bis[spiro-4'-(2',2'-dimethyl-1',3'-dioxolane)] (29). The same procedure as for the alcohol (24) was applied to compound (28) to afford ketone (29) (75.4 %) as a colorless oil. IR cm^{-1} : 1740 (CO), 3280 (acetylene). $^1\text{H NMR}$: 0.05 and 0.11 (each 3H, each s, SiMe_2), 0.92 (9H, s, CMe_3), 1.39 and 1.46 (each 3H, each s, CMe_2), 1.53 (6H, s, CMe_2), 2.18 (3H, s, COCH_3), 2.48 (1H, d, $J=2.4$ Hz, 9-H), 3.36 (3H, s, OCH_3), 3.99 and 4.09 (each 1H, each d, $J=9.8$ Hz, 1- H_2), 4.30 and 4.38 (each 1H, each d, $J=9.2$ Hz, OCH_2O or 5- CH_2 or 6- CH_2), 4.32 and 4.93 (each 1H, each d, $J=11.0$ Hz, OCH_2O or 5- CH_2 or 6- CH_2), 4.50 (1H, d, $J=5.5$ Hz, 4-H), 4.61 (1H, d, $J=2.4$ Hz, 7-H), 4.64 and 4.95 (each 1H, each d, $J=6.7$ Hz, OCH_2O or 5- CH_2 or 6- CH_2), 4.81 (1H, d, $J=5.5$ Hz, 3-H), 4.85 and 5.12 (each 1H, each d, $J=16.5$ Hz, PhCH_2), 7.24-7.31 (5H, m, Ar-H). $^{13}\text{C NMR}$: -4.6, -4.5, 18.2, 20.5, 25.8, 25.9, 26.3, 26.9, 27.1, 56.0, 65.6, 66.9, 67.2, 68.2, 73.2, 75.4, 76.7, 77.7, 80.4, 86.8, 86.9, 94.2, 111.0, 127.2, 128.1, 138.0, 170.0, 201.7. HRMS m/z : Calcd for $\text{C}_{33}\text{H}_{49}\text{O}_{11}\text{Si}$ (M^+-15): 649.3042. Found: 649.3042. $[\alpha]_{\text{D}}^{23}$ -30.4° ($c=0.18$, CHCl_3).

Intramolecular ketalization of 29. A solution of ketone (29) (18 mg, 0.027 mmol) and a trace amount of conc. HCl in MeOH (2 mL) was heated at 50 °C for 2 days. After neutralization with saturated NaHCO_3 solution, the mixture was extracted with CHCl_3 . The organic layer was dried over Na_2SO_4 and evaporated to give a residue, which was used for the next reaction without any purification. A solution of the above crude product, Ac_2O (12.8 μL , 0.136 mmol), a catalytic amount of DMAP, and pyridine (13.2 μL , 0.163 mmol) in CH_2Cl_2 (2 mL) was stirred for 10 h at rt. After quenching with saturated NH_4Cl solution, the mixture was extracted with AcOEt. The combined organic layer was washed with brine. The organic layer was dried over Na_2SO_4 and evaporated to give a residue, which was chromatographed on silica gel ($\text{CH}_2\text{Cl}_2/\text{AcOEt}=9:1$) to afford **(4*R*,6*R*,7*R*)-7-acetoxy-4-(1*R*-1-acetoxypopynyl)-6-benzoyloxy-4-hydroxy-1,4,5-tris(acetoxymethyl)-2,8-dioxabicyclo[3.2.1]octane (31)** (3.0 mg, 20.7 %) as a colorless oil. IR cm^{-1} : 1750 (CO), 3280 (OH); $^1\text{H NMR}$ (500 MHz) 2.07, 2.08, 2.090 and 2.092 (each 3H, each s, 4 x CH_3CO), 2.59 (1H, d, $J=2.4$ Hz, $-\text{C}\equiv\text{CH}$), 3.21 (1H, br s, OH), 3.80 and 4.41 (each 1H, each d, $J=12.8$ Hz, 3- H_2), 4.07 and 4.17 (each 1H, each d, $J=12.2$ Hz, CH_2OAc), 4.18 and 4.52 (each 1H, each d, $J=11.3$ Hz, CH_2OAc), 4.51 (1H, d, $J=3.1$ Hz, H-6), 4.55 and 4.66 (each 1H, each d, $J=11.9$ Hz, PhCH_2),

5.44 (1H, d, $J=3.1$ Hz, H-7), 5.97 (1H, d, $J=2.4$ Hz, CHOAc), 7.23-7.38 (5H, m, ArH); ^{13}C NMR (125 MHz) 20.68, 20.70, 20.76, 22.82, 62.31, 63.07, 65.60, 66.35, 70.58, 72.50, 76.47, 77.73, 78.83, 81.76, 84.14, 102.82, 127.69, 128.07, 128.52, 137.13, 168.89, 169.06, 169.17, 170.05. HRMS m/z : Calcd for $\text{C}_{25}\text{H}_{27}\text{O}_{12}$ (M^+-15): 519.1500. Found: 519.1492. $[\alpha]_{\text{D}}^{28}$ -6.6° ($c=0.2$, CHCl_3). Further elution with $\text{CH}_2\text{Cl}_2/\text{AcOEt}$ (4/1) afforded **(3R,4S,6R,7R)-7-acetoxy-6-benzyloxy-3-ethynyl-4-hydroxy-1,4,5-tris-(acetoxymethyl)-2,8-dioxabicyclo[3.2.1]octane (30)** (4.7 mg, 32.5 %) as a colorless oil. IR cm^{-1} : 1750 (CO), 3280 (OH); ^1H NMR (500 MHz) 1.91, 1.98, 2.10 and 2.17 (each 3H, each s, 4 x CH_3CO), 2.61 (1H, d, $J=2.1$ Hz, $-\text{C}\equiv\text{CH}$), 3.42 (1H, s, OH), 4.13 and 4.30 (each 1H, each d, $J=12.2$ Hz, CH_2OAc), 4.14 and 4.44 (each 1H, each d, $J=12.2$ Hz, CH_2OAc), 4.35 (1H, d, $J=2.4$ Hz, H-6), 4.38 and 4.50 (each 1H, each d, $J=11.3$ Hz, CH_2OAc), 4.45 and 4.68 (each 1H, each d, $J=12.2$ Hz, PhCH_2), 4.87 (1H, d, $J=2.1$ Hz, H-3), 5.50 (1H, d, $J=2.4$ Hz, H-7), 7.25-7.38 (5H, m, ArH); ^{13}C NMR (125 MHz) 20.68, 20.71, 20.87, 22.70, 60.62, 63.08, 63.57, 67.97, 70.76, 71.93, 76.58, 76.83, 78.24, 82.00, 86.70, 103.17, 127.86, 128.34, 128.67, 136.69, 168.99, 169.37, 169.57, 169.95. EIMS m/z : 480 (M^+-54). $[\alpha]_{\text{D}}^{24}$ $+15.8^\circ$ ($c=0.1$, CHCl_3).

(2S,3S,4R,5R,6S,7S)-4-Benzyloxy-1,2-O-isopropylidenedioxy-9-trimethylsilyl-8-nonyn-3,7-diol-5,6-bis[spiro-4'-(2',2'-dimethyl-1',3'-dioxolane)] (32). To a stirred solution of trimethylsilylethynylmagnesium chloride [prepared from trimethylsilylacetylene (2.65 mL, 18.7 mmol) and EtMgCl (2 M in THF, 9.37 mL, 18.7 mmol) in THF (20 mL)] was added dropwise a solution of lactol (**14**) (222 mg, 0.46 mmol) in THF (6 mL) at 0°C and the mixture was stirred for 40 h at rt. After the mixture was quenched with saturated NH_4Cl solution, the solvent was removed to give a residue, which was extracted with AcOEt. The combined organic layer was washed with brine. The organic layer was dried over Na_2SO_4 and evaporated to give a residue, which was chromatographed on silica gel (hexane/AcOEt=7:1) to afford propargyl alcohol (**32**) (226 mg, 84.5 %) as a colorless oil. IR cm^{-1} : 3450 (OH). ^1H NMR: 0.19 (9H, s, SiMe_3), 1.33 and 1.50 (each 3H, each s, CMe_2), 1.45 (6H, s, CMe_2), 1.52 and 1.53 (each 3H, each s, CMe_2), 2.80 (1H, br s, 7-OH), 3.72 (1H, d, $J=3.1$ Hz, 3-OH), 3.97-4.36 (9H, m, 1-H₂, 2-H, 3-H, 4-H, 5-CH₂, 6-CH₂), 4.60 (1H, br s, 7-H), 4.78 and 4.83 (each 1H, each d, $J=11.6$ Hz, PhCH_2), 7.25-7.40 (5H, m, Ar-H). ^{13}C NMR: -0.4, 25.3, 26.0, 26.3, 26.7, 27.8, 66.5, 67.9, 68.1, 68.9, 74.0, 75.2, 75.7, 76.9, 87.3, 89.2, 93.4, 103.3, 109.1, 110.7, 111.8, 127.7, 128.3, 137.8. $[\alpha]_{\text{D}}^{26}$ -8.2° ($c=0.85$, CHCl_3). Further elution with hexane/AcOEt (6/4) gave the recovery of the starting material (**14**) (17.4 mg, 7.8%).

Conversion of 32 into (2S,3S,4R,5R,6S,7S)-7-acetoxy-4-benzyloxy-3-tert-butylidimethylsilyloxy-1,2-O-isopropylidenedioxy-8-nonyne-5,6-bis[spiro-4'-(2',2'-dimethyl-1',3'-dioxolane)] (35). The same procedure as for the trimethylsilylacetylene (**20**) was applied to compound (**32**) to afford **(2S,3S,4R,5R,6S,7S)-4-benzyloxy-1,2-O-isopropylidenedioxy-8-nonyn-3,7-diol-5,6-bis[spiro-4'-(2',2'-dimethyl-1',3'-dioxolane)] (33)** (65.3 %) as a colorless oil. ^1H NMR: 1.25 and 1.34 (each 3H, each s, CMe_2), 1.45 (6H, s, CMe_2), 1.52 and 1.53 (each 3H, each s, CMe_2), 2.61 (1H, d, $J=1.8$ Hz, 9-H), 2.80 (1H, br s, 7-OH), 3.70 (1H, d, $J=2.4$ Hz, 3-OH), 3.85-4.35 (9H, m, 1-H₂, 2-H, 3-H, 4-H, 5-CH₂, 6-CH₂), 4.60 (1H, br s, 7-H), 4.76 and 4.84 (each 1H, each d, $J=11.0$ Hz, PhCH_2), 7.26-7.42 (5H, m, Ar-H). The same procedure as for the above propargylic alcohol (**21**) was applied to compound (**33**) to afford **(2S,3S,4R,5R,6S,7S)-7-acetoxy-4-benzyloxy-1,2-O-isopropylidenedioxy-8-nonyn-3-ol-5,6-bis[spiro-4'-(2',2'-dimethyl-1',3'-dioxolane)] (34)** (91.1 %) as a colorless oil. ^1H NMR: 1.35 and 1.45 (each 3H, each s, CMe_2), 1.49 and 1.51 (each 3H, each s, CMe_2), 1.53 and 1.55 (each 3H, each s, CMe_2), 2.13 (3H, s, COCH_3), 2.51 (1H, d, $J=1.8$ Hz, 9-H), 2.80 (1H, br s, 7-OH), 3.69 (1H, d, $J=1.8$ Hz, 3-OH), 3.88-4.35 (9H, m, 1-H₂, 2-H, 3-H, 4-H, 5-CH₂, 6-CH₂), 4.67 and 4.84 (each 1H, each d, $J=11.0$ Hz, PhCH_2), 5.63 (1H, d, $J=2.4$ Hz, 7-H), 7.26-7.42 (5H, m, Ar-H). The same procedure as for the above alcohol (**16**) was applied to compound (**34**) to afford silyl ether (**35**) (62.5 %) as a colorless oil. IR cm^{-1} : 1750 (CO), 3300 (acetylene). ^1H NMR: 0.07 and 0.14 (each 3H, each s, SiMe_2), 0.85 (9H, s, CMe_3), 1.25 and 1.33 (each 3H, each s, CMe_2), 1.43 and 1.47 (each 3H, each s, CMe_2), 1.50 and 1.54 (each 3H, each s, CMe_2), 2.05 (3H, s, COCH_3), 2.49 (1H, d, $J=2.4$ Hz, 9-H), 3.78 (1H, d, $J=6.7$ Hz, 4-H), 3.87 (2H, br s, 5 or 6-CH₂), 3.98-4.07 (2H, m, 1-H₂), 4.25 and 4.37 (each 1H, each d, $J=9.8$ Hz, 5 or 6-CH₂), 4.35-4.45 (1H, m, 2-H), 4.42 and 5.12 (each 1H, each d, $J=11.6$ Hz, PhCH_2), 4.51 (1H, dd, $J=7.3$, 2.4 Hz, 3-H), 5.87 (1H, d,

$J=2.4$ Hz, 7-H), 7.22-7.29 (5H, m, Ar-H). HRMS m/z : Calcd for $C_{34}H_{51}O_{10}Si$ (M^+-15): 647.3252. Found: 647.3233.

(2*S*,3*S*,4*R*,5*R*,6*S*,7*R*)-4-Benzoyloxy-1,2-*O*-isopropylidenedioxy-8-nonyl-3,7-diol-5,6-bis[spiro-4'-(2',2'-dimethyl-1',3'-dioxolane)] (37). The same procedure as for the above propargylic alcohol (**18**) was applied to compound (**32**) to afford an inseparable diastereomixture (2:1) of **(2*S*,3*R*,4*R*,5*R*)-3-benzyloxy-6-hydroxy-2-[(4'*S*)-2',2'-dimethyl-1',3'-dioxolan-4'-yl]-6-trimethylsilylethynyl-3,4,5,6-tetrahydro-2*H*-pyran-4,5-bis[spiro-4'-(2'',2''-dimethyl-1'',3''-dioxolane)] (36)** (97.0 %) as a colorless oil. IR cm^{-1} : 3360 (OH). 1H NMR: 0.15 and 0.23 (total 9H, each s, $SiMe_3$), 1.26, 1.36, 1.37, 1.42, 1.49, 1.53, 1.58, 1.61, and 1.67 (total 18H, each s, $3 \times CMe_2$), 3.20 (1H, br s, OH), 3.40-5.05 (total 11H, m, 1-H, 2-H, $CHOCH_2$, $3 \times CH_2O$, $PhCH_2$), 7.23-7.32 (3H, m, Ar-H), 7.44 (2H, dd, $J=7.9, 1.8$ Hz, m-Ar-H). HRMS m/z : Calcd for $C_{29}H_{41}O_9Si$ (M^+-15): 561.2519. Found: 561.2519. To a stirred solution of lactol (**36**) (9 mg, 0.016 mmol) in 20% aqueous EtOH (1 mL) and THF (1 mL) was added portionwise $NaBH_4$ (2 mg, 0.053 mmol) at 0 °C. The reaction mixture was stirred for 4 h at rt. To the mixture was added saturated NH_4Cl solution and the solvent was concentrated to give a residue, which was extracted with AcOEt. The combined organic layer was washed with brine. The organic layer was dried over Na_2SO_4 and evaporated to give a residue, which was chromatographed on silica gel (hexane/AcOEt=7:3) to afford a mixture of alcohol (**37**) and its epimer (**33**) (9:1) as a colorless oil (2.5 mg, 31.4 %). For **37**: 1H NMR: 1.35 and 1.45 (each 3H, each s, CMe_2), 1.50 and 1.52 (each 3H, each s, CMe_2), 1.53 and 1.54 (each 3H, each s, CMe_2), 2.57 (1H, d, $J=2.3$ Hz, 9-H), 3.05 (1H, d, $J=3.9$ Hz, 7-OH), 3.47 (1H, d, $J=2.9$ Hz, 3-OH), 3.98-4.28 (9H, m, 1-H₂, 2-H, 3-H, 4-H, 5- CH_2 , 6- CH_2), 4.63 (1H, dd, $J=2.3, 3.9$ Hz, 7-H), 4.76 and 4.83 (each 1H, each d, $J=11.4$ Hz, $PhCH_2$), 7.26-7.42 (5H, m, Ar-H).

Conversion of 37 into 22. The same procedure as for the alcohol (**21**) was applied to compound (**37**) to afford a mixture of **(2*S*,3*S*,4*R*,5*R*,6*S*,7*R*)-7-acetoxy-4-benzyloxy-1,2-*O*-isopropylidenedioxy-8-nonyl-7-ol-5,6-bis[spiro-4'-(2',2'-dimethyl-1',3'-dioxolane)] (38)** and its epimer (9:1) as a colorless oil (97.4 %). For **38**: 1H NMR: 1.37 and 1.41 (each 3H, each s, CMe_2), 1.47 and 1.48 (each 3H, each s, CMe_2), 1.51 and 1.53 (each 3H, each s, CMe_2), 2.55 (1H, d, $J=2.3$ Hz, 9-H), 3.64 (1H, d, $J=2.0$ Hz, 3-OH), 3.96-4.42 (9H, m, 1-H₂, 2-H, 3-H, 4-H, 5- CH_2 , 6- CH_2), 4.72 and 4.91 (each 1H, each d, $J=11.4$ Hz, $PhCH_2$), 5.61 (1H, d, $J=2.3$ Hz, 7-H), 7.26-7.42 (5H, m, Ar-H). The same procedure as for the alcohol (**16**) was applied to compound (**38**) to afford a mixture of acetate (**22**) and its epimer (**35**) (9:1) as a colorless oil (88.9 %).

(2*S*,3*R*,4*R*,5*R*)-3-Benzoyloxy-2-[(4'*S*)-2',2'-dimethyl-1',3'-dioxolan-4'-yl]-3,4,5,6-tetrahydro-2*H*-pyran-6-one-4,5-bis[spiro-4'-(2'',2''-dimethyl-1'',3''-dioxolane)] (39). To a stirred suspension of PCC (112 mg, 0.52 mmol), anhydrous NaOAc (68 mg, 0.83 mmol), and Celite (112 mg) in CH_2Cl_2 (2 mL) was added a solution of lactol (**14**) (50 mg, 0.104 mmol) in CH_2Cl_2 (2 mL) at rt. The reaction mixture was stirred for 2 h at rt. After dilution with Et_2O , insoluble material was filtered off through a Celite pad. The filtrate was extracted with AcOEt. The combined organic layer was washed with brine. The organic layer was dried over Na_2SO_4 and evaporated to give a residue, which was chromatographed on silica gel (hexane/AcOEt=3:1) to afford lactone (**39**) (35.6 mg, 71.5 %) as a colorless oil. IR cm^{-1} : 1740 (CO). 1H NMR: 1.36, 1.39, 1.42, 1.52, 1.55, and 1.58 (each 3H, each s, $3 \times CMe_2$), 3.80 and 3.85 (each 1H, each d, $J=9.8$ Hz, 4- CH_2), 3.84 (1H, d, $J=2.4$ Hz, 3-H), 3.96 (1H, dd, $J=7.3, 2.4$ Hz, 2-H), 4.01 and 4.09 (each 1H, each dd, $J=9.2, 6.1$ Hz, 5'- H_2), 4.32 and 4.45 (each 1H, each d, $J=8.6$ Hz, 5- CH_2), 4.52 (1H, m, 4'-H), 4.72 and 5.04 (each 1H, each d, $J=11.6$ Hz, $PhCH_2$), 7.26-7.41 (5H, m, Ar-H). HRMS m/z : Calcd for $C_{25}H_{34}O_9$: 478.2201. Found: 478.2200. $[\alpha]_D^{24} +21.03^\circ$ ($c=0.71$, $CHCl_3$).

Addition of lithium trimethylsilylacetylide to 39. The same procedure as for the above aldehyde (**19**) was applied to compound (**39**) to afford an inseparable diastereomixture (2:1) of **36** (73.5 %) as a colorless oil.

ACKNOWLEDGEMENTS

This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology of Japan.

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