# Asymmetric Total Synthesis of (-)-Gymnasterkoreayne G 

Seung-Yong Seo, Chu Won Nho, ${ }^{\dagger}$ and Dongyun Shin ${ }^{\text {, }}{ }^{*}$<br>College of Pharmacy, Woosuk University, Wanju 565-701, Korea<br>${ }^{\dagger}$ Natural Products Research Center, KIST Gangneung Institute, Gangneung 210-340, Korea<br>${ }^{*}$ College of Pharmacy, Gachon University of Medicine and Science, Incheon 406-799, Korea. ${ }^{*}$ E-mail: dyshin21@gachon.ac.kr Received January 28, 2012, Accepted March 5, 2012

Key Words : Total synthesis, Asymmetric, Gymnasterkoreayne, Chemopreventive, Chiral resolution

Naturally occurring diynes are found as metabolites in a variety of fungi, higher plants, and marine sponges; their pharmacological properties, including cytotoxic, antimicrobial, and enzyme inhibitory activities, attract special attention in the realm of medicinal chemistry. ${ }^{1}$

Since Jung et al. reported the first isolation of gymnasterkoreaynes A-F from the roots of Gymnasterkoraiensis in 2002, gymnasterkoreayne G, a new compound, was isolated from the leaves of the same plant by the same group in 2005 (Figure 1). ${ }^{2,3}$ The gymnasterkoreayne family exhibits significant biological activities including inhibition of the NFAT (nuclear factor of activated T-cells) transcription factor and cytotoxicity. In particular, gymnasterkoreayne B showed the highest potency against the NFAT transcription factor $\left(\mathrm{IC}_{50}=1.44 \pm 0.59 \mu \mathrm{M}\right)$, while gymnasterkoreaynes E and G were mildly inhibitory $\left(\mathrm{IC}_{50}=\right.$ $7.24 \pm 0.42$ and $43.9 \pm 2.24 \mu \mathrm{M}$, respectively).
The structures of gymnasterkoreaynes B-G were elucidated as diyne natural products with linear ( $Z$ )-heptadeca-9,16-dien-4,6-diyn-8-ol skeletons using spectroscopic methods, while gymnasterkoreayne A is a C10 diyne. The absolute configuration of the C8 stereocenter of gymnasterkoreayne F was determined using the modified Mosher's Ester method, and was further confirmed through the total synthesis of (+)-gymnasterkoreayne F by Carpita et al. in 2005. ${ }^{4}$ However, the absolute stereochemistries of other gymnasterkoreaynes have not been solidly assigned, though those of gymnasterkoreayne B and gymnasterkoreayne C were assumed as $(10 S)$ and $(3 S, 8 S)$, respectively, by comparison of optical rotations and ${ }^{13} \mathrm{C}-\mathrm{NMR}$ data of structurally similar natural products.
Gymnasterkoreaynes G and E are the most structurally and stereochemically complex gymnasterkoreaynes. Both compounds are triols with three stereogenic centers ( $\mathrm{C} 2, \mathrm{C} 3$, and C8). According to the previous publication, the relative stereochemical relationship of C2 and C3 in gymnasterkoreayne E was reported to besyn (threo), while that of gymnasterkoreayne G is anti (erythro), which was predicted by comparisons of the coupling constants of $\mathrm{H}-2$ and $\mathrm{H}-3$ with those of other diols. ${ }^{2,3}$

Recently, in the course of the discovery of new cancer chemopreventive agents, we isolated gymnasterkoreaynes with significant chemopreventive activities from the root barks of Gymnasterkoraiensis, which include gymnasterkoreaynes B, D, E, and Fand reported preliminary structure-
activity relationship study. ${ }^{5}$ However, the limited quantity of the isolated compounds prevented further in vivo experiments. The interesting biological activity and the scarcity of the natural compounds, in addition to the necessity of stereochemical confirmation, prompted us to develop a general synthetic method for the gymnasterkoreayne natural products.

Herein, we disclose the first concise total synthesis of two enantiomerically pure $(2 S, 3 R, 8 R)$ - and $(2 R, 3 S, 8 R)$-hepta-deca- $9(Z), 16$-dien-4,6-diyne-2,3,8-triol(C2,C3-anti relationship), one of which is expected to be either natural ( + )gymnasterkoreayne $\mathrm{G}(\mathbf{1})$ or its enantiomer.

The retrosynthetic plan is outlined in Scheme 1. Considering the structural features, we envisioned that the rapid


Figure 1. The structures of gymnasterkoreaynes A-G.


Scheme 1. Restrosynthetic Plan.


Scheme 2. Reagents and Conditions: a. DMSO (3.0 equiv.), $\left(\mathrm{COCl}_{2}\right.$ (1.5 equiv.), $\mathrm{CH}_{2} \mathrm{Cl}_{2},-78^{\circ} \mathrm{C}$; then $\mathrm{Et}_{3} \mathrm{~N}$ ( 5.0 equiv.), $-78^{\circ} \mathrm{C}$ to rt b . $\mathrm{CBr}_{4}$ (1.2 equiv.), $\mathrm{PPh}_{3}$ (2.4 equiv.), $\mathrm{CH}_{2} \mathrm{Cl}_{2}, 0^{\circ} \mathrm{C}, 79 \%$ for two steps c. $n$-BuLi (2.0 equiv.), THF, $-78^{\circ} \mathrm{C}$ to $-20^{\circ} \mathrm{C}$; then DMF, $-78^{\circ} \mathrm{C}$ to $\mathrm{rt}, 87 \% \mathrm{~d}$. $\mathrm{Pd} / \mathrm{CaCO}_{3}$ ( $5.0 \mathrm{wt} \%, \mathrm{H}_{2}$ (Balloon), cyclohexene/ EtOAc (1:10), rt, 71\% e. 1,4-bis(trimethylsilyl)-buta-1,3-diyne (1.2 equiv.), $\mathrm{MeLi}-\mathrm{LiBr}$ ( 1.0 equiv. based on diacetylene), THF, $0^{\circ} \mathrm{C}, 2$ hrs; then aldehyde $\mathbf{8}, 10 \mathrm{~min}, 93 \%$.
assembly of three components, $\mathrm{C}_{10}$-cis-enal (8), $\mathrm{C}_{4}$-diyne (9), and $\mathrm{C}_{3}$-2-silyloxypropanals ( 6 or 7), ${ }^{6}$ would deliver the target compounds. Two addition reactions of diacetylenic anions to the corresponding aldehydes are the keystothis synthesis. The first addition of the diacetylenic anion from bis-(TMS)-diacetylene 9 to the enal $\mathbf{8}$ can furnish allyl propargylic carbinol 5, and the second addition of the resulting diacetylenic anion to the $\alpha$-alkoxyaldehyde can provide the desired diols 3 and 4 with defined stereochemistry.

The preparation of racemic alcohol 14 is presented in Scheme 2. Commercially available 7 -octen-1-ol (10) was oxidized under Swern oxidation conditions $\left((\mathrm{COCl})_{2}, \mathrm{DMSO}\right.$, $\mathrm{CH}_{2} \mathrm{Cl}_{2}$; then $\mathrm{Et}_{3} \mathrm{~N}$ ), and the resulting aldehyde $\mathbf{1 1}$ was converted to the gem-dibromide $\mathbf{1 2}$ by the Corey-Fuchs reaction $\left(\mathrm{CBr}_{4}, \mathrm{PPh}_{3}\right)$, with a yield of $79 \%$ over two steps. Generation of the alkynylanion from dibromide $\mathbf{1 2}$ with 2 equivalents of $n$-butyllithium and in situ capture with dimethylformamide delivered alkynal 13, the triple bond of which was reduced by partial hydrogenation ( Pd on $\mathrm{BaCO}_{3}$, $\mathrm{H}_{2}$ ) to give cis-enal $\mathbf{8}$ in $71 \%$ yield. Care is required in handling cis-enal $\mathbf{8}$, due to facile isomerization to the more stable trans-enal underany acidic or basic conditions. Thus, after rapid flash column chromatographic separation from the small amount of the trans-enal contaminant, the cis compound was readily reacted with the anion of buta-1,3diynyltrimethylsilane (obtained by reaction of 1,4-bis(tri-methylsilyl)-buta-1,3-diyne 9 with methyllithium-lithium bromide complex), to afford the desired racemic alcohol 14 in $93 \%$ yield. ${ }^{7}$
There are several methods for the resolution of racemic secondary alcohols, which include separation by chiralchromatography, chiral auxiliary assisted separation, kinetic resolution by enzyme or chemical reaction, and asymmetric reduction of the ketone derived from the racemic alcohol. After attempts with several different methods, enzymatic kinetic resolution was found to be very effective in our case. ${ }^{8}$ The reaction was carried out using Lipase "Amano" in hexanes at room temperature to give the chiral acetate $\mathbf{1 5}$ in


Scheme 3. Reagents and Conditions: a. Amano lipase AK (1.5 equiv. by mass of racemic alcohol), vinyl acetate ( 4.0 equiv.), $4 \AA$ molecular sieves ( 1.0 equiv. by mass of racemic alcohol), hexane, rt, 16 hrs, $43 \%$ b. LiOH ( 5.0 eq.), $\mathrm{H}_{2} \mathrm{O} / \mathrm{THF}(1: 3$ ), rt, $5 \mathrm{hrs}, 69 \% \mathrm{c}$. TBSCl (2.0 equiv.), imidazole (3.0 equiv.), $\mathrm{CH}_{2} \mathrm{Cl}_{2}, 0^{\circ} \mathrm{C}$ to $\mathrm{rt}, 1.5 \mathrm{hr}, 100 \%$.


Scheme 4. Synthesis of ( $8 R$ )- and (8S)-Mosher's esters.
$43 \%$ yield (enantiomeric ratio $>98: 2$ ), which was confirmed bychiral HPLC analysis (Chiracel OD-H column) by comparing with the racemic acetate (Scheme 3). Both trimethylsilyl and acetyl groups were removed by lithium hydroxide monohydrate in THF/ $\mathrm{H}_{2} \mathrm{O}$ (3:1) medium, followed by TBS protection ( TBSCl , imidazole, $\mathrm{CH}_{2} \mathrm{Cl}_{2}$ ) of the resulting alcohol 5 to afford the diyne 16 in a two-step yield of $78 \%$.

To confirm the absolute stereochemistry, the Mosher's Ester method was applied. ${ }^{9}$ The chiral secondary alcohol 5 was treated with $(S)$-1,1-methoxy trifluoromethyl phenylacetyl chloride ( $(S)$-MTPA-Cl) and $(R)$-1,1-methoxy trifluoromethyl phenylacetyl chloride $((R)-\mathrm{MTPA}-\mathrm{Cl})$ in the presence of pyridine in $\mathrm{CH}_{2} \mathrm{Cl}_{2}$ at room temperature, to deliver the corresponding $(8 R)$-Mosher's ester 17 and ( $8 S$ )Mosher's ester 18 respectively (Scheme 4). The chemical shifts of four protons $\mathrm{H}_{\mathrm{a}}, \mathrm{H}_{\mathrm{b}}, \mathrm{H}_{\mathrm{c}}$, and $\mathrm{H}_{\mathrm{d}}$ of the $(R)$-and $(S)$ Mosher's esters and their chemical shift differences are summarized in Table 1. Applying the subtraction protocol, the $\Delta \delta$ of the acetylenic proton $\mathrm{H}_{\mathrm{a}}$ exhibited a negative value and those of the other three protons positive ones, which implies that the absolute configuration ofthe chiral alcoholstereo center is $(S)$ according to the standard Mosher rule.
The completion of synthesis is shown in Scheme 5. The TBS-protected diyne $\mathbf{1 6}$ was deprotonated by EtMgBr , followed by treatment with (S)-2-(tert-butyldimethylsiloxy)propanal (6) or (R)-2-(tert-butyldimethylsiloxy)propanal (7)

Table 1. Calculation of chemical shift differences

|  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: |
| $\delta_{S}$ | 2.241 | 5.564 | 5.756 | 2.184 |
| $\delta_{R}$ | 2.257 | 5.460 | 5.716 | 2.157 |
| $\delta_{0}=\delta_{S}-\delta_{R}(\mathrm{~Hz})$ | -14.4 | 93.6 | 36 | 24.3 |







Scheme 5. Reagents and Conditions: a. EtMgBr (1.0 equiv.), THF, $0,30 \mathrm{~min}$; then aldehyde 6 or $7,68 \%$ and $73 \%$, respectively b. TBAF (3.0 equiv.), THF, rt, $10 \mathrm{~min}, 91 \%$, and $99 \%$, respectively.
at $-78^{\circ} \mathrm{C}$, respectively, to give anti-alcohols 19 and 20 predominantly (anti/syn ratio >90:10). Anti/syn-diastereomers were easily separated by $\mathrm{SiO}_{2}$ column chromatography. The stereoselectivity can be explained by the Felkin-Ahn model, and the relative stereochemistry was confirmed by NOE study of model compound ${ }^{10}$ and a reference article. ${ }^{11}$ Finally, deprotection of the two TBS groups in compounds $\mathbf{1 9}$ and 20 with TBAF in THF provided the desired 2,3-anti-diols 3 and 4 in quantitative yields, respectively.
The twotriols 3 and 4 gavevery similar spectral data, andthe coupling constant of $\mathrm{H} 2-\mathrm{H} 3$ of the two synthesized erythro- $(2 S, 3 R)$-diol $\mathbf{3}$ and erythro-( $2 R, 3 S$ )-diols 4 were 3.3 and 3.4 Hz , respectively, which are same with recently reported data of $(+)$-Gymnasterkoreayne $G$ in which the coupling constant of the erythro diol was also $3.3 \mathrm{~Hz} .{ }^{3,12}$ The authors of the 2002 and 2005 publications assigned the relative configuration of the 2,3-diol in gymnasterkoreayne E as threo (syn) and gymnasterkoreayne G as erythro (anti), based on the literature or empirical results, and our data confirmed that the relative stereochemistry of 2,3-diols in gymnasterkoreayne G is erythro (anti). Finally, Absolute configuration was determined by optical rotation, of which 3 and 4 were $-45.2^{\circ}\left(\mathrm{c}=0.03, \mathrm{CHCl}_{3}\right)$ and $-174.4^{\circ}(\mathrm{c}=0.03$, $\mathrm{CHCl}_{3}$ ), respectively, which showed that the optical rotations of $\mathbf{3}$ corresponds to the opposite value of the optical
rotations reported for ( + )-gymnasterkoreaynes $G\left[[\alpha]_{D}^{20}=\right.$ $\left.+40.0^{\circ}, \mathrm{c}=0.3, \mathrm{CHCl}_{3}\right]$.

In summary, we completed the asymmetric total synthesis of ( $2 S, 3 R, 8 R$ )-heptadeca- $9(Z)$, 16-dien-4,6-diyne-2,3,8-triol (3) and $(2 R, 3 S, 8 R)$-heptadeca- $9(Z)$, 16-dien-4,6-diyne-2,3,8triol (4) as a structural proof of gymnasterkoreayne G or its enantiomer. The syntheses were accomplished in 10 steps with $11 \%$ overall yields, starting from 7 -octen-1-ol (10). Racemic alcohol 14 was resolved by enzymatic kinetic resolution to enantiomerically enriched 5 using Lipase AK "Amano" and the stereochemistry of C3 was generated by a substrate-controlled, stereoselective addition reaction. Finally, $(2 S, 3 R, 8 R)$-heptadeca- $9(Z)$, 16-dien-4,6-diyne-2,3,8-triol (3) wasproved to bethe ( - )-gymnasterkoreayne $G$.

## Experimental Section

(Z)-1-(Trimethylsilyl)tetradeca-6,13-dien-1,3-diyn-5-ol
(14). $\mathrm{MeLi}-\mathrm{LiBr}(1.85 \mathrm{~mL}, 2.78 \mathrm{mmol})$ was added to a solution of 1,4-bis(trimethylsilyl)-buta-1,3-diyne ( 491 mg , $2.53 \mathrm{mmol})$ in THF $(10 \mathrm{~mL})$ at $0^{\circ} \mathrm{C}$. The reaction mixture was gradually warmed to room temperature and stirred for 2 h . After 2 h , the mixture was re-cooling to $0^{\circ} \mathrm{C}$ and aldehyde ( $316 \mathrm{mg}, 2.10 \mathrm{mmol}$ ) was added to the reaction mixture with stirring for 10 min . The reaction was quenched by addition of saturated aq. $\mathrm{NH}_{4} \mathrm{Cl}$. Layers were separated and the aqueous layer extracted with EtOAc. Combined organic extracts were washed with water and brine, dried by $\mathrm{Na}_{2} \mathrm{SO}_{4}$ and filtered. The filtrate was evaporated under reduced pressure. Silica gel chromatography (50:1 EtOAc/ hexanes) gave the desired compound ( $535 \mathrm{mg}, 93 \%$ ) ${ }^{1} \mathrm{H}-$ NMR ( $300 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta 5.78$ (ddt, $J=6.6,10.2,16.8 \mathrm{~Hz}$, $1 \mathrm{H}), 5.61-5.44(\mathrm{~m}, 2 \mathrm{H}), 5.15(\mathrm{~d}, J=7.8 \mathrm{~Hz}, 1 \mathrm{H}), 5.00-4.89$ $(\mathrm{m}, 2 \mathrm{H}), 2.11-1.98(\mathrm{~m}, 4 \mathrm{H}), 1.41-1.23(\mathrm{~m}, 6 \mathrm{H}), 0.17(\mathrm{~s}, 9 \mathrm{H})$; ${ }^{13} \mathrm{C}-\mathrm{NMR}\left(75 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 139.2,134.6,128.1,114.6$, 88.4, 87.5, 70.0, 58.8, 34.0, 29.4, 29.0, 28.9, 27.9, 16.9, -0.2; FT-IR (neat) $v_{\text {max }} 3394,2930,2857,2221,2106,1641,1252$, 996, 910, 846, 761, $638 \mathrm{~cm}^{-1}$; HRMS (ESI ${ }^{+}$): calcd for [ $\mathrm{C}_{17} \mathrm{H}_{27} \mathrm{OSi}^{+}$: 275.1831 , found: 275.1820 .
( $R, Z$ )-1-(Trimethylsilyl)tetradeca-6,13-dien-1,3-diyn-5yl acetate (15). The racemic alcohol $\mathbf{1 4}(595 \mathrm{mg}, 2.17$ mmol ) was mixed with Amano lipase AK ( $893 \mathrm{mg}, 1.5$ equiv. by mass of racemic alcohol), vinyl acetate ( 0.80 mL , 8.67 mmol ) and molecular sieves ( $595 \mathrm{mg}, 1.0$ equiv. by mass of racemic alcohol) in anhydrous hexane ( 12 mL ). The reaction mixture was stirred under nitrogen atmosphere for 16 hours at room temperature. After 16 hours, the mixture was filtered by paper and the residue was evaporated under reduced pressure. Silica gel chromatography ( $60: 1 \mathrm{EtOAc} /$ hexane) gave the desired acetate. ( $294 \mathrm{mg}, 43 \%$ ) $[\alpha]_{\mathrm{D}}^{20}=$ $-0.5\left(\mathrm{c}=0.09, \mathrm{CHCl}_{3}\right) ;{ }^{1} \mathrm{H}-\mathrm{NMR}\left(300 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) 6.10$ (d, $J=8.7 \mathrm{~Hz}, 1 \mathrm{H}), 5.78$ (ddt, $J=6.6,10.2,17.1 \mathrm{~Hz}, 1 \mathrm{H})$, $5.62(\mathrm{dt}, J=7.5,10.8,1 \mathrm{H}), 5.44(\mathrm{dd}, J=9.0,10.5 \mathrm{~Hz}, 1 \mathrm{H})$, 5.01-4.89 (m, 2H), 2.15-1.98 (m, 4H), $2.04(\mathrm{~s}, 3 \mathrm{H}), 1.40-$ $1.29(\mathrm{~m}, 6 \mathrm{H}), 0.17(\mathrm{~s}, 9 \mathrm{H}) ;{ }^{13} \mathrm{C}-\mathrm{NMR}\left(75 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta$ $169.4,139.0,136.2,124.3,114.6,88.4,87.4,74.2,70.5$, $60.2,33.9,29.2,28.9,28.8,28.0,21.0,0.1$; FT-IR (neat) $v_{\max }$

3435, 2934, 2860, 2281, 2202, 1671, 1138, 995, $912 \mathrm{~cm}^{-1}$; Calcd for $\left[\mathrm{C}_{19} \mathrm{H}_{28} \mathrm{OSi}^{+}: 316.1859\right.$, found: 316.1863.
( $\mathbf{2 S}, \mathbf{3 R}, 8 R, Z$ )-2,8-Bis(tert-butyldimethylsilyloxy)hepta-deca-9,16-dien-4,6-diyne-3-ol (19). EtMgBr ( $0.114 \mathrm{~mL}, 1$ M sol'n in THF), was added to a solution of diyne ( 36 mg , $0.114 \mathrm{mmmol})$ in anhydrous THF $(2 \mathrm{~mL})$ at $0^{\circ} \mathrm{C}$ and stirred for 30 min . After 30 min , the reaction mixture was gradually warmed to room temperature and stirred for 2 h . Then ( $S$ )-2-(tert-butyldimethylsilyloxy)propanal ( $32 \mathrm{mg}, 0.17 \mathrm{mmol}$ ) was added to the reaction mixture at $0{ }^{\circ} \mathrm{C}$ and reaction mixture was gradually warmed to room temperature. The mixture was stirred for 2 hr . The reaction was quenched by addition saturated aq. $\mathrm{NH}_{4} \mathrm{Cl}$. Layers were separated and the aqueous layer extracted with EtOAc. Combined organic extracts were washed with water and brine, dried by $\mathrm{Na}_{2} \mathrm{SO}_{4}$ and filtered. The filtrate was evaporated under reduced pressure. Silica gel chromatography (EtOAc/hexanes $=1: 80$ ) gave the desired alcohol as a colorless oil. ( $39 \mathrm{mg}, 68 \%$ ) $[\alpha]_{\mathrm{D}}^{20}=-82.1\left(\mathrm{c}=0.01, \mathrm{CHCl}_{3}\right) ;{ }^{1} \mathrm{H}-\mathrm{NMR}\left(300 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$ $\delta 5.78$ (ddt, $J=16.8,9.9,7.2 \mathrm{~Hz}, 1 \mathrm{H}), 5.50-5.40(\mathrm{~m}, 2 \mathrm{H})$, 5.15 (d, $J=6.9 \mathrm{~Hz}, 1 \mathrm{H}), 5.01-4.90(\mathrm{~m}, 2 \mathrm{H}), 4.27(\mathrm{dd}, J=$ $3.9,6.3 \mathrm{~Hz}, 1 \mathrm{H}), 3.89(\mathrm{dq}, J=3.3,6.3 \mathrm{~Hz}, 1 \mathrm{H}), 2.34(\mathrm{~d}, J=$ $6.3 \mathrm{~Hz}, 1 \mathrm{H}), 2.05-1.99(\mathrm{~m}, 4 \mathrm{H}), 1.41-1.28(\mathrm{~m}, 6 \mathrm{H}), 1.20(\mathrm{~d}, J$ $=6.3 \mathrm{~Hz}, 3 \mathrm{H}), 0.87(\mathrm{~s}, 18 \mathrm{H}), 0.11(\mathrm{~s}, 3 \mathrm{H}), 0.09(\mathrm{~s}, 1 \mathrm{H}), 0.07$ $(\mathrm{s}, 6 \mathrm{H}) ;{ }^{13} \mathrm{C}-\mathrm{NMR}\left(75 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 139.3,132.2,129.6$, 114.6, 79.9, 77.3, 71.2, 7068.6, 68.1, 59.7, 34.0, 30.0, 29.4, 29.03, 29.01, 28.0, 26.0, 18.8, 18.5, 18.3, 0.27, -4.15, -4.24, $-4.47,-4.57$; IR (neat) $v_{\max } 3437,2931,2859,1641,1464$, 1256, 1137, 1077, 939, 838, 778, $669 \mathrm{~cm}^{-1}$; HRMS (ESI ${ }^{+}$) Calcd for $\left[\mathrm{C}_{29} \mathrm{H}_{52} \mathrm{O}_{3} \mathrm{Si}_{2}\right]^{+}: 504.3455$, found: 504.3450.
(2R,3S,8R,Z)-2,8-Bis(tert-butyldimethylsilyloxy)hepta-deca-9,16-dien-4,6-diyne-3-ol (20). The experimental procedure was same as above, and $\mathrm{EtMgBr}(0.139 \mathrm{~mL}, 0.139$ mmol, 1 M sol' n in THF), diyne ( $44 \mathrm{mg}, 0.139 \mathrm{mmol}$ ), and ( $R$ )-2-(tert-butyldimethylsilyloxy)propanal $(42 \mathrm{mg}, 0.222$ $\mathrm{mmol})$ were used for this reaction. Yield: $73 \%,[\alpha]_{\mathrm{D}}^{20}=-21.7$ $\left(\mathrm{c}=0.02, \mathrm{CHCl}_{3}\right) ;{ }^{1} \mathrm{H}-\mathrm{NMR}\left(300 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 5.85-5.70$ $(\mathrm{m}, 1 \mathrm{H}), 5.50-5.43(\mathrm{~m}, 2 \mathrm{H}), 5.15(\mathrm{~d}, J=6.0 \mathrm{~Hz}, 1 \mathrm{H}), 4.97$, 4.92 (dd, 18.6, $12.6 \mathrm{~Hz}, 2 \mathrm{H}$ ), 2.77 (dd, $J=3.9,5.1,1 \mathrm{H}$ ), 3.90 (dq, $J=3.9,6.3 \mathrm{~Hz}, 1 \mathrm{H}), 2.33(\mathrm{~d}, J=5.1 \mathrm{~Hz}, 1 \mathrm{H}), 2.06-2.02$ (m, 4H), 1.39-1.22 (m, 6H), $1.20(\mathrm{~d}, J=6.3 \mathrm{~Hz}, 3 \mathrm{H}), 0.87(\mathrm{~s}$, $18 \mathrm{H}), 0.11(\mathrm{~s}, 3 \mathrm{H}), 0.09(\mathrm{~s}, 3 \mathrm{H}), 0.07(\mathrm{~s}, 6 \mathrm{H})$; FT-IR (neat) $v_{\text {max }} 3435,2934,2860,2281,2202,1671,1138,995,912$ $\mathrm{cm}^{-1}$; HRMS (ESI ${ }^{+}$) Calcd for $\left[\mathrm{C}_{29} \mathrm{H}_{52} \mathrm{O}_{3} \mathrm{Si}_{2}\right]^{+}: 504.3455$, found: 504.3452.
( $2 S, 3 R, 8 R, Z$ )-Heptadeca-9,16-dien-4,6-diyne-2,3,8-triol (3). TBAF ( $37 \mathrm{mg}, 0.14 \mathrm{mmol}$ ) was added to a solution of alcohol $19(24 \mathrm{mg}, 0.048 \mathrm{mmol})$ in THF $(0.2 \mathrm{~mL})$ at room temperature and stirred for 10 min . Then reaction mixture layers were separated and the aqueous layer extracted with EtOAc. Combined organic extracts were washed with water and brine, dried by $\mathrm{Na}_{2} \mathrm{SO}_{4}$ and filtered. The filtrate was evaporated under reduced pressure. Silica gel chromatography $(E t O A c /$ hexanes $=1: 2)$ gave the desired triol. $(12 \mathrm{mg}, 91 \%)$ : $[\alpha]_{\mathrm{D}}^{20}=-45.2\left(\mathrm{c}=0.03, \mathrm{CHCl}_{3}\right) ;{ }^{1} \mathrm{H}-\mathrm{NMR}\left(300 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$ $\delta 5.86(\mathrm{~m}, 1 \mathrm{H}), 5.69(\mathrm{~m}, 1 \mathrm{H}), 5.60(\mathrm{~m}, 1 \mathrm{H}), 5.24(\mathrm{~d}, J=7.8$, $1 \mathrm{H}), 5.03,4.98(\mathrm{~m}, 2 \mathrm{H}), 4.40(\mathrm{~d}, J=3.3,1 \mathrm{H}), 3.95(\mathrm{dq}, J=$
3.3, $6.3 \mathrm{~Hz}, 1 \mathrm{H}), 2.19-2.06(\mathrm{~m}, 4 \mathrm{H}), 1.44-1.30(\mathrm{~m}, 6 \mathrm{H}), 1.32$ (d, $J=6.2 \mathrm{~Hz}, 3 \mathrm{H}$ ); ${ }^{13} \mathrm{C}-\mathrm{NMR}\left(75 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 139.2$, 134.8, 128.0, 114.6, 79.7, 77.4, 70.9, 70.5, 69.0, 67.8, 58.9, 33.9, 29.4, 29.0, 28.9, 27.9, 18.6; FT-IR (neat) $v_{\max } 3400$, 1620, $1210 \mathrm{~cm}^{-1}$; HRMS (ESI $)$ Calcd for $\left[\mathrm{C}_{17} \mathrm{H}_{24} \mathrm{O}_{3}\right]^{+}$: 276.1725, found: 276.1722.
( $2 R, 3 S, 8 R, Z$ )-Heptadeca-9,16-dien-4,6-diyne-2,3,8-triol (4). The experimental procedure was same as above and TBAF ( $50 \mathrm{mg}, 0.19 \mathrm{mmol}$ ), alcohol 20 ( $32 \mathrm{mg}, 0.063 \mathrm{mmol}$ ) were used for this reaction. Yield: $99 \%,[\alpha]_{\mathrm{D}}^{20}=-174.4(\mathrm{c}=$ $0.03, \mathrm{CHCl}_{3}$ ); ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(300 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 5.78(\mathrm{~m}, 1 \mathrm{H})$, 5.63-5.46 (m, 2H), $5.17(\mathrm{~d}, J=8.1 \mathrm{~Hz}), 4.96,4.92(\mathrm{~m}, 2 \mathrm{H})$, $4.34(\mathrm{~d}, J=3.3 \mathrm{~Hz}, 1 \mathrm{H}), 3.89(\mathrm{dq}, J=3.3,6.3 \mathrm{~Hz}, 1 \mathrm{H}), 2.12-$ $1.99(\mathrm{~m}, 4 \mathrm{H}), 1.37-1.23(\mathrm{~m}, 6 \mathrm{H}), 1.24(\mathrm{~d}, J=6.2 \mathrm{~Hz}, 3 \mathrm{H})$; ${ }^{13} \mathrm{C}-\mathrm{NMR}\left(75 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 139.4,134.9,128.1,114.7$, 79.8, 77.5, 71.0, 70.6, 69.1, 67.8, 59.0, 34.1, 29.4, 28.9, 28.9, 28.0, 18.7; FT-IR (neat) $v_{\text {max }} 3390,1205 \mathrm{~cm}^{-1}$; HRMS (ESI ${ }^{+}$) Calcd for $\left[\mathrm{C}_{17} \mathrm{H}_{24} \mathrm{O}_{3}\right]^{+}: 276.1725$, found: 276.1727.

Acknowledgments. This work was supported by KISTGangneung Institute Intramural Grant (2Z03411).

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