Bioscience, Biotechnology, and Biochemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/tbbb20

Systematic Strategy for the Synthesis of Cyanobacterin and Its Stereoisomers. 1. Asymmetric Total Synthesis of Dechloro-cyanobacterin and Its Enantiomer

Yasushi HAGA[a], Momotoshi OKAZAKI[a] & Yoshihiro SHUTO[a]
[a] The United Graduate School of Agricultural Science, Ehime UniversityTarumi 3-5-7, Matsuyama 790-8566, Japan
Published online: 22 May 2014.

To cite this article: Yasushi HAGA, Momotoshi OKAZAKI & Yoshihiro SHUTO (2003) Systematic Strategy for the Synthesis of Cyanobacterin and Its Stereoisomers. 1. Asymmetric Total Synthesis of Dechloro-cyanobacterin and Its Enantiomer, Bioscience, Biotechnology, and Biochemistry, 67:10, 2183-2193, DOI: 10.1271/bbb.67.2183

To link to this article: http://dx.doi.org/10.1271/bbb.67.2183

Biosci. Biotechnol. Biochem., **67** (10), 2183–2193, 2003

Systematic Strategy for the Synthesis of Cyanobacterin and Its Stereoisomers. 1. Asymmetric Total Synthesis of Dechloro-cyanobacterin and Its Enantiomer

Yasushi HAGA,† Momotoshi OKAZAKI, and Yoshihiro SHUTO

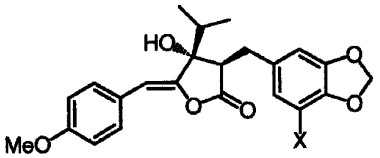
The United Graduate School of Agricultural Science, Ehime University, Tarumi 3-5-7, Matsuyama 790-8566, Japan

Received May 6, 2003; Accepted June 16, 2003

The stereocontrolled total synthesis of the non-chlorinated analog of cyanobacterin, a potent photosynthesis inhibitor, was achieved by 12 steps in a 10.0% overall yield. Its enantiomer was also synthesized from the same starting material. This synthetic strategy is expected to be applicable to prepare cyanobacterin and all its stereoisomers, together with other similar bioactive compounds.

Key words: cyanobacterin; photosynthesis inhibitor; β-hydroxy-γ-ylidene-γ-butyrolactone framework; enantiodivergent synthesis; Evans and non-Evans aldol reaction

Cyanobacterin **1** has been isolated as a secondary metabolite from the freshwater cyanobacterium, *Scytonema hofmanni*.[1] The structure of this compound was determined as a diaryl-substituted β-hydroxy-γ-ylidene-γ-butyrolactone framework with chlorine substituted on one of the aromatic rings,[2] and its absolute configuration at both asymmetric carbons is *R*[3] as shown in Fig. 1. It has been found in a biological investigation to inhibit the Hill reaction in isolated chloroplasts and showed high toxicity toward other cyanobacteria, green algae and higher plants.[4] A further investigation suggested that the site of action of this compound was photosystem II (PS II). The minimum concentration to inhibit the electron transport in PS II was lower than that of the typical PS II inhibitor, 3-(3,4-dichlorophenyl)-1,1-dimethylurea (DCMU). However further studies with the herbicide-resistant mutant showed that the binding site of **1** was different from that of DCMU[5,6] and suggested that **1** acted on another site in PS II. Synthesized racemic **1**[7] has been tested for its biological activity and found to need twice the minimum dose required of with natural compound.[8] This result implies that the unnatural isomer seemed to be inactive. In order to investigate the structure-activity relationship and mode of action in detail, it was necessary to prepare each enantiomer with high optical purity and to subject it to further biochemical research.



1 X=Cl, **2** X=H

Fig. 1. Structure of Cyanobacterin **1**.

However, the stereoselective synthesis of **1** has not previously been achieved.

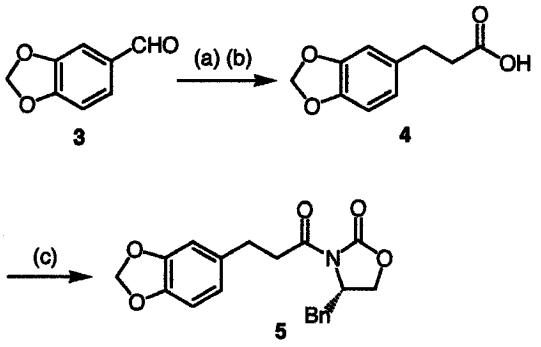
We are therefore studying the stereoselective synthesis of **1**, since it has a fascinating structure, significant bioactivity and an interesting mode of action. In this paper, we describe the total synthesis of both enantiomers of dechloro-cyanobacterin as a model compound of **1**.

Results and Discussion

The synthesis of both enantiomers of **2** started with the preparation of chiral imide **5**, which is a common starting material for our synthetic strategy as shown in Scheme 1. Condensation of commercially available piperonal **3** and malonic acid in the presence of piperidine[9] and subsequent catalytic reduction gave propionic acid derivative **4** in a 74.6% yield in 2 steps. After treating **4** with oxalyl chloride in CH_2Cl_2 to transform it to acyl chloride, imidation[10] to **5** was accomplished by condensation with the lithium salt of (4*S*)-4-benzyl-2-oxazolidinone, which had been readily prepared in 2 steps from L-phenylalanine.[11]

The diastereoselective aldol reaction between (*Z*)-boron-enolate, which had been derived from corresponding imide **5**, and 4-methoxyphenylpropynal **6** prepared from 4-anisaldehyde[12,13] in the presence of $TiCl_4$ (IV) afforded a mixture of two isomers, **7-a** and **7-b**, which are frequently called non-Evans aldol adducts,[14,15] in a combined yield of 72.4% as depicted in Scheme 2. Although the diastereomeric ratio of these adducts was determined as 79:21 by their ^{1}H-NMR spectra, it is not always necessary to separate

† To whom correspondence should be addressed. Fax: +81-89-943-5242; E-mail: haga@agr.ehime-u.ac.jp



Scheme 1. Synthesis of Imide **5**.

Reagents and conditions: (a) $CH_2(CO_2H)_2$, piperidine, pyridine, reflux, 81.9%; (b) H_2, 10% Pd–C, AcOH, reflux, 91.1%; (c) (1) $(COCl)_2$, CH_2Cl_2; (2) (4*S*)-4-benzyl-2-oxazolidinone, ^{n}BuLi, THF, −78°C–0°C, 99.2%.

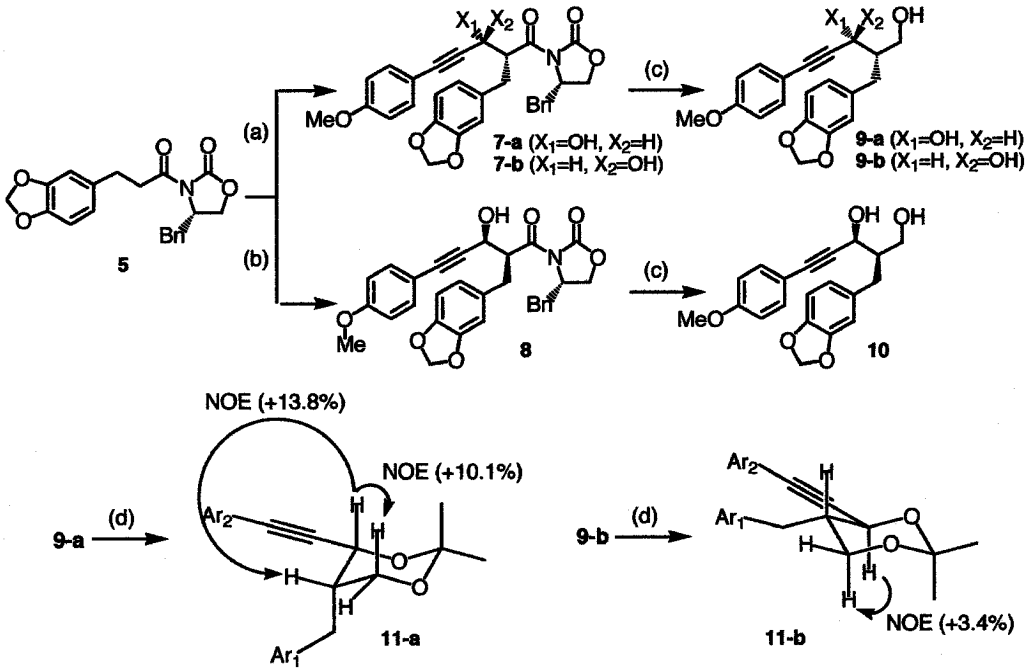
these isomers, since the epimeric secondary hydroxyl group was oxidized to a ketone in the subsequent step. The other Lewis acids such as two equivalents of $^n Bu_2BOTf$ and Et_2AlCl were examined in this reaction. However, in the case of the former reagent, the yield of **7-b** was 48.4%, but undesired (2*S*, 3*S*)-isomer **8** was also obtained in a 21.7% yield, and the latter case by-product was obtained instead of the objective aldol adducts. On the other hand, under the normal conditions for Evans aldol condensation,[16,17] which do not involve $TiCl_4$ (Ⅳ), the reaction proceeded simply and gave single product **8** in a 79.3% yield. According to the ^{1}H-NMR spectra of **7-a**, **7-b** and **8**, no peaks could be detected apart from the objective isomers. The stereochemistry of these compounds was next determined. After reductive removal of the chiral auxiliary in isolated **7-a** and **7-b** with $LiBH_4$ in aqueous Et_2O, resulting **9-a** and **9-b** were respectively transformed to acetonides **11-a** and **11-b** by treating with 2,2-dimethoxypropane and a catalytic amount of pyridinium *p*-toluenesulfonate (PPTS) in toluene. According to the analyses of these compounds by ^{1}H-NMR, all coupling constants (*J* values) supported the conformation of the isomers as shown in Scheme 2, and the observation of expected NOE further proved these structure. Thus, the relative stereochemistry at the C-2 and C-3 positions in **7-a** and **7-b** was confirmed. Similarly, **8** was reduced to **10**, and the physical properties of the three stereoisomers of the diol, **9-a**, **9-b** and **10**, were scanned. The result showed agreement between the data for **10** and those for **9-a**, which had been determined as a *syn* isomer as already stated, except for the opposite sign of specific rotation. It is difficult to think that the conditions for the non-Evans and Evans aldol reaction gave a product with the opposite stereo configuration to that in previous literatures.[14–17] It was therefore found that the absolute configuration of the C-2 and C-3 positions in **7-a**, **7-b** and **8** corresponded to (2*R*, 3*R*), (2*R*, 3*S*) and (2*S*, 3*S*), respectively. Thus, a pair of diols which completely controlled the stereochemistry at C-2 position were in hand.

Regioselective silylation of the primary hydroxyl group in **9** and **10** then proceeded efficiently with *tert*-butyldimethylsilyl chloride (TBS-Cl), imidazole and a catalytic amount of 4-(dimethylamino)pyridine (DMAP) in DMF (Scheme 3). Obtained **12** and **13** were subjected to oxidation with dimethyl sulfoxide (DMSO) and 1,3-dicyclohexylcarbodiimide (DCC) in the presence of pyridinium trifluoroacetate (TFA-pyr) to respectively provide silyloxy ketones **14** and **15**. Furthermore, acid-catalyzed cleavage of the silyl protection in **14** and **15** furnished β-hydroxy ketones **16** and **17** in 52.9% and 57.0% yields respectively, in 3 steps.

As shown in Scheme 4, a diastereoselective nucleophilic addition reaction of isopropylmagnesium bromide with **16** and **17** respectively gave 1,3-diols **18-a** and **19-a** in isolated yields of 66.6% and 56.2%, together with small amounts of undesired 3-epimers **18-b** and **19-b** in 4.2% and 3.0% yields. In this reaction, an excess of the Grignard reagent was required to give sufficient yield and selectivity compared with the conditions for the stoichiometric nucleophile with silyloxy ketones **14** and **15**. The relative stereochemistry of **18-a** was confirmed by NOEDIF spectra after cyclization to acetonide **20** by treating with 2,2-dimethoxypropane and a catalytic amount of PPTS in toluene (Scheme 5). NOE was observed between H_a and H_b in **20**, proving that they were situated in close proximity, this also being supported by the low *J* value (J_{ab} = 4.2 Hz). NOE was absent between H_a and H_c, as was expected, proving that they were in 1,2-diaxial proximity, this being further proved by high *J* value (J_{ac} = 11.7 Hz). NOE between H_a and H_d was also observed, proving that they too were situated in close proximity. Although deprotonation of the α-hydrogen by the Grignard reagent as a strong base can cause racemization, this reaction fortunately gave a single isomer of **18-a** with high optical purity (>99% enantiomeric excess) as observed by an HPLC analysis.

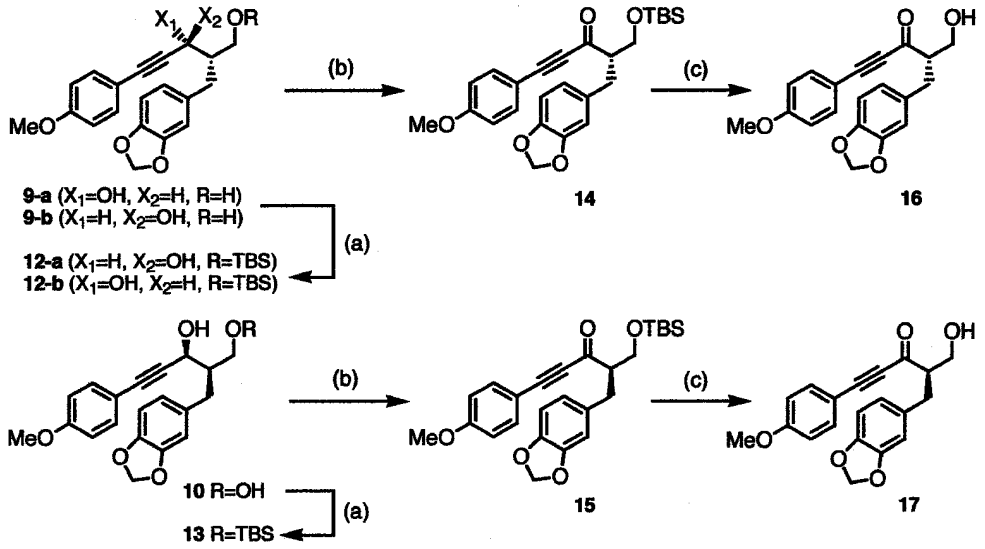
The direct oxidation of **18-a** and **19-a** to acids **21** and **22** was examined by the use of oxidizing reagents such as pyridinium dichromate (PDC) in DMF[18] and tetrapropylammonium perruthenate (TPAP) in aqueous CH_3CN.[19] However, the former resulted in decomposition and the latter proceeded slowly. Thus, the oxidation was carried out in 2 steps to achieve more suitable conditions; the reactions of **18-a** and **19-a** with a combination of TPAP and *N*-methylmorpholine-*N*-oxide (NMO) in CH_2Cl_2 provided intermediate aldehydes, and their further oxidation with sodium chlorite in the presence of 2-methyl-2-butene led to carboxylic acids **21** and **22** in respective 64.4% and 70.2% yields.

Finally, lactonization of **21** and **22** with silver ni-



Scheme 2. Synthesis and Identification of Diols **9** and **10**.

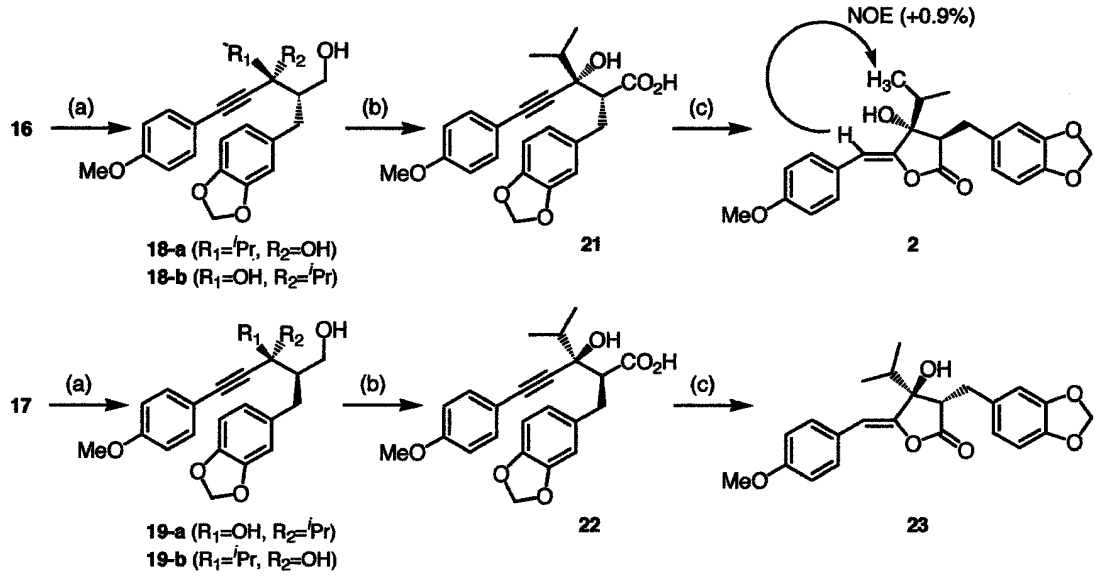
Reagents and conditions: (a) 4-methoxyphenylpropynal (**6**), $^{n}Bu_2BOTf$, $^{i}Pr_2NEt$, $TiCl_4$, CH_2Cl_2, $-78°C$–$0°C$, 72.4% (**7-a**:**7-b** = 79:21); (b) **6**, $^{n}Bu_2BOTf$, $^{i}Pr_2NEt$, CH_2Cl_2, $-78°C$, 79.3%; (c) $LiBH_4$, Et_2O, 100% (**9-a**), 100% (**9-b**), 100% (**10**); (d) $Me_2C(OMe)_2$, PPTS, toluene, 99.4% (**11-a**), 100% (**11-b**). *Abbreviations*: Ar_1, 3,4-methylenedioxyphenyl; Ar_2, 4-methoxyphenyl.



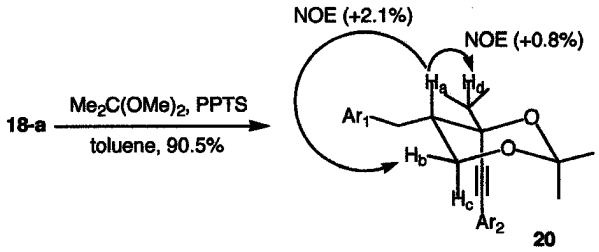
Scheme 3. Synthesis of β-Hydroxy Ketones **16** and **17**.

Reagents and conditions: (a) TBS-Cl, Et_3N, DMAP, DMF, 72.7% (**12-a**), 70.0% (**12-b**), 70.9% (**13**); (b) DMSO, DCC, TFA-pyr, toluene, 84.1% (**14**), 90.2% (**15**); (c) AcOH-THF-H_2O (2:1:1), 86.6% (**16**), 89.1% (**17**).

trate in CH_3OH[20] furnished desired products **2** and **23** in respective 81.9% and 67.1% yields. This step was conducted under the same conditions as those described by Jong *et al.*[7] for the synthesis of *dl*-**1**, and the reaction gave the desired *exo*-cyclic product in a good yield, as in their report. In addition to the relative stereochemistry at C-2 and C-3, the geometry of the exocyclic olefin in **2** was confirmed by NOEDIF experiments. When the C-2 hydrogen in **2** was irradiated, the signal of the methine hydrogen in the isopropyl group was not enhanced, while NOE was observed between the vinyl hydrogen and methyl hydrogen in the isopropyl group. Accordingly, it is obvious that the configuration of **2** was identical with that of **1**. Furthermore, the enantiomeric excess of **2** was evaluated to be >99% by an HPLC analysis, and the specific rotations of **2** and **23** showed approximately the same value but with opposite signs



Scheme 4. Synthesis of Dechloro-cyanobacterin **2** and Its Enantiomer **22**.
Reagents and conditions: (a) $Me_2CHMgBr$, THF, −78°C, 66.6% (**18-a**), (**18-a**:**18-b** = 94:6), 56.2% (**19-a**), (**19-a**:**19-b** = 95:5); (b) (1) TPAP, NMO, MS-4A, CH_2Cl_2; (2) $NaClO_2$, 2-methyl-2-butene, NaH_2PO_4, ^{t}BuOH-H_2O (4:1), 0°C, 64.4% (**21**), 70.2% (**22**); (c) $AgNO_3$, CH_3OH, 81.9% (**2**), 67.1% (**23**).



Scheme 5. NOEDIF Experiment on Acetonide **20**.

(+94.7 and −98.8, respectively). As a consequence of these analyses, both enantiomers were found to be in an optically pure form.

In summary, we accomplished the total synthesis of the non-chlorinated analog of cyanobacterin and its enantiomer in 12 steps in overall yields of 10.0% and 8.9%, respectively, with high optical purity (>99% enantiomeric excess) from the same starting material. The synthetic method described in this paper will be useful for the synthesis of **1** and other natural products with various biological activities possessing a similar framework.

Experimental

All melting point (mp) data are uncorrected. IR spectra were recorded by a Shimadzu FTIR-8100 spectrometer. ^{1}H- and ^{13}C-NMR spectra were measured with a JEOL JNM-EX400 spectrometer at 400 MHz and 100 MHz, respectively. Chemical shifts are reported relative to internal tetramethylsilane (TMS, 0.00 ppm) for ^{1}H and chloroform-d ($CDCl_3$, 77.0 ppm) for ^{13}C. Optical rotation values were determined with a Horiba SEPA-200 polarimeter. HPLC was performed with a Shimadzu LC-10AS liquid chromatograph equipped with an integrator (Shimadzu C-R6A Chromatopac) and UV-VIS detector (Shimadzu SPD-10A). Ten microliter of a sample were injected into the column and detected by its UV absorption at 254 nm. Details of the analytical conditions (*e.g.*, the column, solvent and flow rate) are shown in each subsequent section. Silica gel 60 (100–210 μm) was obtained from Kanto Chemical Co. TLC and preparative TLC were respectively carried out by using Merck silica gel 60 F_{254} precoated plastic plates of 0.2 mm in thickness and Merck silica gel 60 F_{254} precoated glass plates of 0.5 mm in thickness.

(3,4-Methylenedioxy)phenylpropionic acid (4). Malonic acid (20.85 g, 200.4 mmol) was added to a stirred solution of piperonal (15.18 g, 101.1 mmol) in pyridine (50 ml) at room temperature. After dissolving the acid, piperidine (1.50 ml, 15.2 mmol) was added to this solution. After refluxing for 8 h, the reaction mixture was poured into cold water (200 ml) and acidified with conc. HCl. The resulting precipitate was collected and recrystallized from acetic acid to afford white crystals (mp 238°C, 15.90 g, 81.9%).

This unsaturated acid (15.54 g, 80.87 mmol) was reduced with a catalytic amount of Pd–C in acetic acid (200 ml). After refluxing for 2 days under H_2 while vigorously stirring, Pd–C was removed from the reaction mixture, and the resulting light-brown solution was concentrated *in vacuo*. The residue was extracted with CH_2Cl_2 (30 ml) and EtOAc (2×

20 ml), and the combined organic layer was washed three times with 1 M-NaOH. The combined aqueous layer was acidified with conc. HCl, and then extracted with CH_2Cl_2 (20 ml) and EtOAc (2×20ml) again. The combined organic phase was washed with brine and dried over Na_2SO_4. After evaporating the solvent, the residue was recrystallized from petroleum ether-$CHCl_3$ (2:1) to give 14.31 g (91.1%) of acid **4** as white crystals, mp 85–86°C; ^{1}H-NMR ($CDCl_3$) δ: 2.62 (2H, t, J=7.6 Hz, CH_2–CO_2H), 2.87 (2H, t, J=7.6 Hz, Ar–CH_2), 5.92 (2H, s, O–CH_2–O), 6.64–6.74 (3H, m, Ar–H), 8.56 (1H, br, –CO_2H); ^{13}C-NMR ($CDCl_3$) δ: 30.38, 35.98, 100.85, 108.28, 108.76, 121.09, 133.99, 146.02, 147.67, 178.83; IR ν_{max} ($CHCl_3$) cm^{-1}: 1717, 1512, 1495, 1452, 1256, 1196, 1046, 944, 820. *Anal.* Found: C, 61.79; H, 5.22%. Calcd. for $C_{10}H_{10}O_4$: C, 61.85; H, 5.19%.

(4S)-4-Benzyl-2-[3-(3,4-methylenedioxyphenyl)propionyl]-2-oxazolidinone (5). To a stirred solution of **4** (13.86 g, 71.37 mmol) in CH_2Cl_2 (100 ml) was added oxalyl chloride (6.85 ml, 78.5 mmol) at 0°C. The reaction mixture was allowed to warm to room temperature and stirred for 12 h. The solvent was evaporated, and the residue was diluted with THF (30 ml). (4*S*)-4-Benzyl-2-oxazolidinone (12.65 g, 71.39 mmol) in THF (120 ml) in another flask was cooled to −78°C under an N_2 atmosphere, and then *n*-butyllithium (50.0 ml of a 1.57 M solution in hexane, 78.5 mmol) was added dropwise. After 40 min, to the reaction mixture was added the solution of the acyl chloride from **4**, and the mixture stirred for 1 h at the same temperature. The mixture was allowed to warm to 0°C, and then stirred for 2 h before being quenched by water (100 ml). The organic layer was separated, and the aqueous phase was extracted with EtOAc (20 ml). The combined organic layer was successively washed with 2 M-HCl, sat. $NaHCO_3$ and brine, before being dried over Na_2SO_4. After removing the solvent *in vacuo*, the residue was recrystallized from petroleum ether-$CHCl_3$ (1:1) to give **5** as white crystals. The mother liquor was concentrated, and the residue was purified by column chromatography on silica gel (hexane-EtOAc, 3:2) to give a second crop of **5** (combined yield of 25.01 g, 99.2%), mp 85–87°C, $[\alpha]_D^{25}$ +55.5° (*c* 2.29, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 2.76 (1H, dd, J=9.5, 13.4 Hz, Ph–CH_2), 2.93 (2H, t, J=7.3 Hz, ArCH_2–CH_2), 3.21 (2H, t, J=7.3 Hz, ArCH_2–CH_2), 3.27 (1H, dd, J=3.2, 13.4 Hz, Ph–CH_2), 4.17 (1H, dd, J=3.4, 7.9 Hz, CH–CH_2–O), 4.20 (1H, dd, J=6.6, 7.9 Hz, CH–CH_2–O), 4.64–4.70 (1H, m, N–CH–CH_2O), 5.92 (2H, s, O–CH_2–O), 6.73–6.77 (3H, m, Ar–H), 7.16–7.19 (2H, m, Ph–H), 7.27–7.35 (3H, m, Ph–H); ^{13}C-NMR ($CDCl_3$) δ: 29.92, 37.38, 37.74, 50.01, 66.12, 100.76, 108.15, 109.00, 121.29, 127.29, 128.87, 129.35, 134.20, 135.12, 145.87, 147.55, 153.33, 172.24; IR ν_{max} ($CHCl_3$) cm^{-1}: 2363, 1786, 1700, 1508, 1491, 1448, 1388, 1247, 1209, 1110, 1042, 940, 730. *Anal.* Found: C, 67.66; H, 5.58; N, 3.90%. Calcd. for $C_{20}H_{19}NO_5$: C, 67.98; H, 5.42; N, 3.96%.

(4S)-4-Benzyl-[(2R,3R/S)-3-hydroxy-5-(4-methoxyphenyl)-2-(3,4-methylenedioxybenzyl)-4-pentynoyl]-2-oxazolidinone (7). To a stirred solution of **5** (2.12 g, 6.00 mmol) in CH_2Cl_2 (20 ml) were added dibutylboron triflate (5.8 ml of a 1.0 M solution in CH_2Cl_2, 5.8 mmol) and *N*,*N*-diisopropylethylamine (1.18 ml, 6.57 mmol) at −20°C under an N_2 atmosphere. The reaction mixture was allowed to warm to 0°C and then stirred for 1.5 h, before being recooled to −78°C. In another flask, to a solution of $TiCl_4$ (IV) (1.34 ml, 12.2 mmol) in CH_2Cl_2 (50 ml) was added dropwise the solution of 4-methoxyphenylpropynal (**6**, 0.96 g, 6.05 mmol) in CH_2Cl_2 (2 ml) at −78°C under an N_2 atmosphere, and the mixture stirred for 15 min. To the reaction mixture was added foregoing solution of the boron enolate *via* a cannula under N_2 pressure. The resulting solution was stirred for 1 h at the same temperature, before being allowed to warm to 0°C, and then stirred more for 4 h. The reaction mixture was quenched by adding the mixed solvent of a phosphate buffer solution (pH 6.86, 25 ml) and MeOH (25 ml), and then 30%-H_2O_2 (25 ml) and MeOH (25 ml). After stirring vigorously for 1 h at 0°C, the organic layer was separated, and the aqueous layer was extracted with Et_2O (2×25 ml). The combined organic phase was successively washed with sat. $NaHCO_3$ and brine. After drying (Na_2SO_4) and concentrating, the residue was purified by column chromatography on silica gel (toluene-EtOAc, 20:1) to provide *syn*-adduct **7-a**, *anti*-adduct **7-b** and their mixture. **7-a** was recrystallized from hexane-EtOAc (2:1), while **7-b** was recrystallized from toluene. After combing their mother liquors and the mixture, the solvent was removed *in vacuo*, and the residue was purified by column chromatography on silica gel (hexane-EtOAc, 3:2) to provide **7** (combined yield of 2.23 g, 72.4%).

7-a: R_f 0.25 (toluene-EtOAc, 20:1), mp 114°C, $[\alpha]_D^{25}$ +32.8° (*c* 4.20, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 2.67 (1H, dd, J=9.8, 13.2 Hz, Ph–CH_2), 2.68 (1H, d, J=5.4 Hz, –OH), 3.12 (1H, dd, J=9.3, 13.4 Hz, Ar_1–CH_2–CHCO), 3.20 (1H, dd, J=5.6, 13.6 Hz, Ar_1–CH_2–CHCO), 3.27 (1H, dd, J=3.4, 13.2 Hz, Ph–CH_2), 3.81 (3H, s, –OCH_3), 3.95 (1H, dd, J=8.6, 9.4 Hz, CH–CH_2–O), 4.04 (1H, dd, J=2.4, 9.4 Hz, CH–CH_2–O), 4.52–4.60 (2H, m, Ar_1CH_2–CH–CO and N–CH–CH_2), 4.91 (1H, dd, J=5.4, 5.7 Hz, CHOH), 5.89 (2H, s, O–CH_2–O), 6.69–6.77 (3H, m, Ar_1–H), 6.84 (2H, dd, J=2.0, 6.8 Hz, Ar_2–H), 7.16 (2H, d, J=6.4 Hz, Ph–H), 7.24–7.36 (3H, m, Ph–H), 7.39 (2H, dd, J=2.0, 6.8 Hz, Ar_2–H); ^{13}C-NMR ($CDCl_3$) δ: 34.15, 37.74, 50.99, 55.29, 55.46, 63.95, 66.01, 85.72, 87.26,

100.85, 108.18, 109.64, 113.96, 114.29, 122.12, 127.31, 128.99, 129.41, 132.05, 133.37, 135.18, 146.50, 147.55, 152.95, 160.03, 172.87; IR ν_{max} ($CHCl_3$) cm^{-1}: 1782, 1705, 1615, 1517, 1449, 1393, 1256, 1200, 1046, 781, 760, 739.

7-b: R_f 0.27 (toluene-EtOAc, 20:1), mp 124.5–126°C, $[\alpha]_D^{25}$ +39.3° (*c* 1.22, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 2.74 (1H, dd, J=9.5, 13.7 Hz, Ph-CH_2), 3.00 (1H, dd, J=8.0, 12.6 Hz, Ar_1CH_2-CHCO), 3.08 (1H, dd, J=7.3, 12.6 Hz, Ar_1CH_2-CHCO), 3.30 (1H, dd, J=3.6, 13.7 Hz, Ph-CH_2), 3.45 (1H, d, J=10.0 Hz, -O*H*), 3.79 (3H, s, -OCH_3), 4.03 (1H, dd, J=8.4, 10.2 Hz, CH-CH_2-O), 4.10 (1H, dd, J=2.1, 10.2 Hz, CH-CH_2-O), 4.50 (1H, ddd, J=6.1, 7.3, 8.0 Hz, C*H*-CO), 4.56–4.62 (1H, m, N-C*H*-CH_2), 4.67 {1H, dd, J=6.1, 10.0 Hz, C*H*(OH)}, 5.91 (2H, s, O-CH_2-O), 6.71–6.78 (3H, m, Ar_1-*H*), 6.80 (2H, dd, J=2.0, 6.8 Hz, Ar_2-*H*), 7.18 (2H, dd, J=2.4, 7.6 Hz, Ph-*H*), 7.25–7.29 (3H, m, Ph-*H*), 7.34 (2H, dd, J=2.0, 6.8 Hz, Ar_2-*H*); ^{13}C-NMR ($CDCl_3$) δ: 34.84, 37.74, 50.90, 55.27, 55.37, 63.06, 65.99, 85.73, 86.99, 100.89, 108.22, 109.66, 113.95, 114.30, 122.30, 127.37, 128.94, 129.43, 131.35, 133.14, 134.99, 146.33, 147.50, 153.07, 159.78, 174.91; IR ν_{max} ($CHCl_3$) cm^{-1}: 1782, 1611, 1517, 1491, 1388, 1252, 1196, 1042, 760, 734. *Anal.* Found: C, 70.28; H, 5.49; N, 2.53%. Calcd. for $C_{30}H_{27}NO_7$: C, 70.16; H, 5.30; N, 2.73%.

(4S)-4-Benzyl-[(2S,3S)-3-hydroxy-5-(4-methoxyphenyl)-2-(3,4-methylenedioxybenzyl)-4-pentynoyl]-2-oxazolidinone (8). To a stirred solution of **5** (1.89 g, 5.38 mmol) in CH_2Cl_2 (50 ml) were added dibutylboron triflate (5.1 ml of a 1.0 M solution in CH_2Cl_2, 5.1 mmol) and *N*,*N*-diisopropylethylamine (1.05 ml, 5.80 mmol) at −20°C under an N_2 atmosphere. The reaction mixture was allowed to warm to 0°C and stirred for 1.5 h, before being recooled to −78°C. The solution of 4-methoxyphenylpropynal (**6**, 0.86 g, 5.34 mmol) in CH_2Cl_2 (5 ml) was added to this mixture, and the resulting solution was stirred for 2.5 h at the same temperature. The reaction mixture was quenched by adding a mixed solvent of a phosphate buffer solution (pH 6.86, 20 ml) and MeOH (20 ml), and then 30%-H_2O_2 (20 ml) and MeOH (20 ml). After stirring vigorously for 1 h at 0°C, the organic layer was separated, and the aqueous layer was extracted with Et_2O (2× 20 ml). The combined organic phase was successively washed with sat. $NaHCO_3$ and brine. After drying (Na_2SO_4) and concentrating, the residue was purified by column chromatography on silica gel (hexane-EtOAc, 2:1) to provide crude **8**. After removing the solvent *in vacuo*, the resulting yellow crystal was recrystallized from hexane-EtOAc (3:1) to give **8** as white crystals. The mother liquor was evaporated, and the residue was purified by column chromatography on silica gel (hexane-EtOAc, 2:1) to provide a second crop of **8** (combined yield of 2.19 g, 79.3%), R_f 0.20 (hexane-EtOAc, 2:1), mp 129.5–130°C, $[\alpha]_D^{25}$ +58.3° (*c* 1.55, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 2.50 (1H, d, J=5.4 Hz, -O*H*), 2.55 (1H, dd, J=9.0, 13.4 Hz, Ph-CH_2), 3.02 (1H, dd, J=3.4, 13.4 Hz, Ph-CH_2), 3.18 (1H, dd, J=8.6, 13.2 Hz, Ar_1CH_2-CH), 3.22 (1H, dd, J=6.1, 13.2 Hz, Ar_1CH_2-CH), 3.80 (3H, s, -OCH_3), 3.99 (1H, dd, J=7.8, 8.8 Hz, CH-CH_2-O), 4.03 (1H, dd, J=2.9, 8.8 Hz, CH-CH_2-O), 4.65–4.71 (2H, m, C*H*-CO and N-C*H*-CH_2), 4.81 (1H, dd, J=5.9, 6.4 Hz, C*H*OH), 5.86 (1H, d, J=1.5 Hz, O-CH_2-O), 5.91 (1H, d, J=1.5 Hz, O-CH_2-O), 6.73 {1H, d, J=8.3 Hz, Ar_1-*H*}, 6.80–6.86 {2H, m, Ar_1-*H*}, 6.82 (2H, d, J=8.8 Hz, Ar_2-*H*), 6.99 (2H, d, J=7.8 Hz, Ph-*H*), 7.25–7.26 (3H, m, Ph-*H*), 7.37 (2H, d, J=8.8 Hz, Ar_2-*H*); ^{13}C-NMR ($CDCl_3$) δ: 34.25, 37.36, 51.01, 54.93, 55.11, 63.87, 65.61, 85.78, 86.47, 100.68, 108.07, 109.76, 113.83, 114.03, 122.27, 127.14, 128.68, 129.26, 132.07, 133.17, 134.83, 146.05, 147.47, 153.24, 159.74, 172.53; IR ν_{max} ($CHCl_3$) cm^{-1}: 1782, 1705, 1615, 1546, 1517, 1495, 1393, 1256, 1200, 1115, 1046, 940, 764, 739. *Anal.* Found: C, 69.95; H, 5.72; N, 2.60%. Calcd. for $C_{30}H_{27}NO_7$: C, 70.16; H, 5.30; N, 2.73%.

*General procedure for preparing 5-(4-methoxyphenyl)-2-(3,4-methylenedioxyphenyl)methyl-4-pentyne-1,3-diol (**9-a**, **9-b** and **10**).* $LiBH_4$ (1.5 eq) was added to the solution of β-hydroxyimide **7** or **8** (1.0 eq) in Et_2O (15 ml/mmol) at 0°C. The reaction mixture was allowed to warm to room temperature and stirred for 6 h, before being slowly added to 2 M-HCl at 0°C. After decomposing the excess reducing agent, the ethereal layer was separated. The aqueous phase was extracted with EtOAc (2×10 ml), and the combined organic extract was successively washed with sat. $NaHCO_3$ and brine. After drying (Na_2SO_4) and concentrating, each product was purified.

The product from **7-a** was recrystallized from hexane-EtOAc (3:2) to give **9-a** as white crystals. The mother liquor was evaporated, and the residue was purified by column chromatography on silica gel (hexane-EtOAc, 2:1 to 1:1) to provide a second crop of **9-a** (total 100% yield), mp 126.5–128°C, $[\alpha]_D^{25}$ −144° (*c* 1.72, acetone); ^{1}H-NMR ($CDCl_3$) δ: 2.19 (1H, dd, J=4.9, 5.3 Hz, *prim*-O*H*), 2.25–2.33 (1H, m, C*H*-CH_2OH), 2.62 (1H, dd, J=7.8, 13.7 Hz, Ar-CH_2), 2.70 (1H, dd, J=7.3, 13.7 Hz, Ar-CH_2), 3.03 (1H, d, J=6.4 Hz, *sec*-O*H*), 3.79 (1H, dd, J=4.9, 10.9 Hz, CH_2OH), 3.82 (3H, s, OCH_3), 3.99 (1H, ddd, J=5.3, 8.7, 10.9 Hz, CH_2OH), 4.74 (1H, dd, J=4.0, 6.4 Hz, C*H*OH), 5.9 (2H, s, O-CH_2-O), 6.67–6.75 (3H, m, Ar_1-*H*), 6.86 (2H, d, J=8.3 Hz, Ar_2-*H*), 7.41 (2H, d, J=8.3 Hz, Ar_2-*H*); ^{13}C-NMR ($CDCl_3$) δ: 33.58, 47.50, 55.32, 64.13, 66.17, 86.18, 86.96, 100.86, 108.26, 109.37, 114.00, 114.48, 121.91, 133.14, 133.24, 146.01, 147.71, 159.85; IR

ν_{max} ($CHCl_3$) cm^{-1}: 3025, 2384, 1602, 1508, 1491, 1448, 1290, 1252, 1213, 1038, 940, 833, 773. *Anal.* Found: C, 70.31; H, 5.94%. Calcd. for $C_{20}H_{20}O_5$: C, 70.57; H, 5.92%.

The product from **7-b** was purified by column chromatography on silica gel (hexane-EtOAc, 2:1 to 1:1) to provide **9-b** as a colorless oil in a 100% yield, $[\alpha]_D^{25}$ −7.5° (*c* 1.06, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 2.02–2.10 (1H, m, C*H*–CH_2OH), 2.13 (1H, br, *prim*–O*H*), 2.72 (1H, dd, *J*=8.5, 13.9 Hz, Ar–CH_2), 2.83 (1H, d, *J*=4.9 Hz, *sec*–O*H*), 2.96 (1H, dd, *J*=6.6, 13.9 Hz, Ar–CH_2), 3.73 (1H, dd, *J*=5.4, 11.0 Hz, CH_2OH), 3.81 (3H, s, OCH_3), 4.10 (1H, dd, *J*=2.9, 11.0 Hz, CH_2OH), 4.69 (1H, dd, *J*=4.9, 5.4 Hz, C*H*OH), 5.93 (2H, s, O–CH_2–O), 6.69–6.75 (3H, m, Ar_1–*H*), 6.84 (2H, d, *J*=8.8 Hz, Ar_2–*H*), 7.38 (2H, d, *J*=8.8 Hz, Ar_2–*H*); ^{13}C-NMR ($CDCl_3$) δ: 33.86, 48.05, 55.28, 63.26, 65.46, 86.25, 87.63, 100.83, 108.23, 109.53, 113.96, 114.45, 122.06, 133.14, 133.48, 145.96, 147.69, 159.79; IR ν_{max} ($CHCl_3$) cm^{-1}: 2961, 2363, 1615, 1517, 1495, 1448, 1290, 1256, 1046, 940, 837, 773.

The product from **8** was recrystallized from hexane-EtOAc (3:2) to give **10** as white crystals. The mother liquor was evaporated, and the residue was purified by column chromatography on silica gel (hexane-EtOAc, 2:1 to 1:1) to provide a second crop of **10** (total 100% yield), mp 127–128.5°C, $[\alpha]_D^{25}$ +151° (*c* 1.26, acetone); ^{1}H-NMR ($CDCl_3$) δ: 2.24 (1H, dd, *J*=4.4, 5.1 Hz, *prim*–O*H*), 2.25–2.33 (1H, m, C*H*–CH_2OH), 2.60 (1H, dd, *J*=7.8, 13.9 Hz, Ar–CH_2), 2.70 (1H, dd, *J*=7.3, 13.9 Hz, Ar–CH_2), 3.07 (1H, d, *J*=5.9 Hz, *sec*–O*H*), 3.77–3.83 (4H, m, CH_2OH and OCH_3), 3.99 (1H, ddd, *J*=5.1, 8.3, 11.1 Hz, CH_2OH), 4.72 (1H, dd, *J*=3.9, 5.9 Hz, C*H*OH), 5.93 (2H, s, O–CH_2–O), 6.67–6.75 (3H, m, Ar_1–*H*), 6.86 (2H, d, *J*=8.8 Hz, Ar_2–*H*), 7.41 (2H, d, *J*=8.8 Hz, Ar_2–*H*); ^{13}C-NMR ($CDCl_3$) δ: 33.58, 47.49, 55.31, 64.12, 66.14, 86.20, 86.96, 100.86, 108.25, 109.37, 114.00, 114.50, 121.90, 133.14, 133.24, 146.02, 147.71, 159.85; IR ν_{max} ($CHCl_3$) cm^{-1}: 3047, 2392, 1602, 1517, 1487, 1448, 1290, 1247, 1217, 1038, 940, 837. *Anal.* Found: C, 70.13; H, 6.13%. Calcd. for $C_{20}H_{20}O_5$: C, 70.57; H, 5.92%.

*(4R/S, 5S)-2,2-Dimethyl-4-(4-methoxyphenyl)ethynyl-5-(3,4-methylenedioxybenzyl)-1,3-dioxolane (**11-a** and **11-b**).* To a stirred solution of **9-a** or **9-b** (1.0 eq) in toluene (20 ml/mmol) were added 2,2-dimethoxypropane (5.0 eq) and a catalytic amount of PPTS at room temperature under an N_2 atmosphere. After stirring for 12 h, the reaction mixture was poured into water (30 ml). The organic layer was separated, and the aqueous phase was extracted with Et_2O (10 ml). The combined organic layer was successively washed with sat. $NaHCO_3$ and brine. After drying (Na_2SO_4) and concentrating, the residue was recrystallized from $^iPr_2O$ to give **11-a** and **11-b** as white crystals, respectively. The mother liquors were each evaporated, and the residue was purified by column chromatography on silica gel (hexane-EtOAc, 4:1) to provide a second crop of **11-a** and **11-b**.

11-a: 99.4% yield, mp 105–106°C, $[\alpha]_D^{25}$ −127° (*c* 1.58, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 1.50 (3H, s, CH_3), 1.56 (3H, s, CH_3), 1.83–1.90 (1H, m, C*H*–CH_2O), 2.98 (1H, dd, *J*=10.3, 13.7 Hz, Ar–CH_2), 3.09 (1H, dd, *J*=4.4, 13.7 Hz, Ar–CH_2), 3.69 (1H, dd, *J*=3.4, 11.7 Hz, CH–CH_2O), 3.81 (3H, s, OCH_3), 3.86 (1H, dd, *J*=3.4, 12.2 Hz, CH–CH_2O), 5.09 (1H, d, *J*=3.4 Hz, C≡C–C*H*O), 5.92 (2H, s, O–CH_2–O), 6.72–6.75 (3H, m, Ar_1–*H*), 6.84 (2H, d, *J*=8.8 Hz, Ar_2–*H*), 7.42 (2H, d, *J*=8.8 Hz, Ar_2–*H*); ^{13}C-NMR ($CDCl_3$) δ: 21.09, 28.41, 31.81, 40.40, 55.28, 61.15, 64.94, 85.34, 86.81, 99.42, 100.78, 108.20, 109.64, 113.91, 114.55, 122.21, 133.35, 134.05, 145.83, 147.65, 159.95; IR ν_{max} ($CHCl_3$) cm^{-1}: 3025, 1611, 1512, 1491, 1444, 1380, 1290, 1252, 1217, 1196, 1128, 1042, 974, 935, 833, 773, 743, 760. *Anal.* Found: C, 72.51; H, 6.25%. Calcd. for $C_{23}H_{24}O_5$: C, 72.61; H, 6.36%.

11-b: 100% yield, mp 96–97°C, $[\alpha]_D^{25}$ −7.6° (*c* 1.32, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 1.47 (6H, s, CH_3 ×2), 2.17–2.27 (1H, m, C*H*–CH_2O), 2.36 (1H, dd, *J*=9.8, 14.2 Hz, Ar–CH_2), 2.98 (1H, dd, *J*=3.7, 14.2 Hz, Ar–CH_2), 3.62 (1H, dd, *J*=10.8, 12.2 Hz, CH–CH_2O), 3.73 (1H, dd, *J*=4.9, 12.2 Hz, CH–CH_2O), 3.81 (3H, s, –OCH_3), 4.62 (1H, d, *J*=10.3 Hz, C≡C–C*H*O), 5.91 (2H, s, O–CH_2–O), 6.61–6.73 (3H, m, Ar_1–*H*), 6.83 (2H, d, *J*=8.8 Hz, Ar_2–*H*), 7.41 (2H, d, *J*=8.8 Hz, Ar_2–*H*); ^{13}C-NMR ($CDCl_3$) δ: 19.42, 29.22, 34.83, 41.84, 55.27, 63.66, 65.96, 85.34, 86.07, 98.97, 100.87, 108.18, 109.29, 113.84, 114.25, 122.81, 131.99, 133.41, 146.05, 147.68, 159.80.

*General procedure for preparing 1-tert-butyldimethylsilyloxy-5-(4-methoxyphenyl)-2-(3,4-methylenedioxyphenyl)methyl-4-pentyn-3-ol (**12-a, 12-b** and **13**).* To a stirred solution of **9** or **10** (1.0 eq) in DMF (5 ml/mmol) were added Et_3N (2.5 eq), a catalytic amount of DMAP and TBS-Cl (1.0 eq) at −15°C. The reaction mixture was stirred for 4 h at the same temperature. After being quenched by sat. NH_4Cl (20 ml), the organic layer was separated, and the aqueous phase was extracted with Et_2O (2× 10 ml). The combined organic extract was successively washed with sat. $NaHCO_3$ and brine. After drying (Na_2SO_4) and concentrating, the residue was purified by column chromatography on silica gel (hexane-EtOAc, 9:1 to 7:1) to provide silyl ethers each as a colorless oil.

12-a: 72.7% yield, $[\alpha]_D^{25}$ −96.1° (*c* 1.81, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 0.09 (3H, s, Si–CH_3), 0.11 (3H, s, Si–CH_3), 0.92 {9H, s, C(CH_3)$_3$}, 2.27–2.34 (1H, m, C*H*–CH_2OSi), 2.55 (1H, dd, *J*=7.3, 14.2 Hz,

Ar-CH_2), 2.64 (1H, dd, J=7.8, 14.2 Hz, Ar-CH_2), 3.76 (1H, dd, J=4.2, 10.4 Hz, CH_2OSi), 3.81 (3H, s, -OCH_3), 3.97 (1H, dd, J=9.8, 10.4 Hz, CH_2OSi), 4.08 (1H, d, J=7.8 Hz, OH), 4.65 {1H, dd, J=3.4, 7.8 Hz, CH(OH)}, 5.92 (2H, s, O-CH_2-O), 6.65-6.74 (3H, m, Ar_1-H), 6.85 (2H, d, J=8.8 Hz, Ar_2-H), 7.41 (2H, d, J=8.8 Hz, Ar_2-H); ^{13}C-NMR ($CDCl_3$) δ: −5.66, −5.62, 18.09, 25.80, 33.51, 47.14, 55.24, 64.98, 66.10, 86.11, 86.64, 100.79, 108.16, 109.29, 113.88, 115.01, 121.82, 133.10, 133.15, 145.95, 147.66, 159.57; IR ν_{max} ($CHCl_3$) cm^{-1}: 2983, 2940, 2384, 1611, 1512, 1491, 1444, 1290, 1252, 1175, 1076, 1042, 940, 837, 816, 790. *Anal.* Found: C, 68.39; H, 7.57%. Calcd. for $C_{26}H_{34}O_5Si$: C, 68.69; H, 7.54%.

12-b: 70.0% yield, $[\alpha]_D^{25}$ −9.2° (*c* 5.07, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 0.08 (3H, s, Si-CH_3), 0.93 {9H, s, C(CH_3)$_3$}, 1.92-2.01 (1H, m, CHCH$_2$OSi), 2.74 (1H, dd, J=8.8, 13.7 Hz, Ar-CH_2), 2.97 (1H, dd, J=6.8, 13.7 Hz, Ar-CH_2), 3.61 (1H, d, J=7.8 Hz, -OH), 3.67 (1H, dd, J=4.3, 10.0 Hz, CH_2OSi), 3.80 (3H, s, OCH_3), 4.19 (1H, dd, J=3.5, 10.0 Hz, CH_2OSi), 4.63 {1H, dd, J=4.7, 7.8 Hz, CH(OH)}, 5.93 (2H, s, O-CH_2-O), 6.65-6.73 (3H, m, Ar_1-H), 6.83 (2H, d, J=8.3 Hz, Ar_2-H), 7.36 (2H, d, J=8.3 Hz, Ar_2-H); ^{13}C-NMR ($CDCl_3$) δ: −5.63, −5.60, 18.17, 25.84, 33.92, 47.46, 55.26, 63.66, 65.42, 85.45, 88.21, 100.80, 108.18, 109.54, 113.89, 114.98, 122.10, 133.78, 133.78, 145.87, 147.63, 159.57; IR ν_{max} ($CHCl_3$) cm^{-1}: 2983, 2940, 2384, 1615, 1517, 1495, 1444, 1294, 1256, 1175, 1102, 1042, 940, 841, 816. *Anal.* Found: C, 68.84; H, 7.51%. Calcd. for $C_{26}H_{34}O_5Si$: C, 68.69; H, 7.54%.

13: 70.9% yield, $[\alpha]_D^{25}$ +95.9° (*c* 0.74, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 0.08 (3H, s, Si-CH_3), 0.10 (3H, s, Si-CH_3), 0.91 {9H, s, C(CH_3)$_3$}, 2.27-2.34 (1H, m, CH-CH$_2$OSi), 2.53 (1H, dd, J=7.3, 13.7 Hz, Ar-CH_2), 2.63 (1H, dd, J=7.8, 13.7 Hz, Ar-CH_2), 3.76 (1H, dd, J=4.2, 10.0 Hz, CH_2OSi), 3.82 (3H, s, OCH_3), 3.98 (1H, dd, J=9.5, 10.0 Hz, CH_2OSi), 4.07 (1H, d, J=7.8 Hz, OH), 4.64 (1H, dd, J=3.9, 7.8 Hz, CHOH), 5.92 (2H, s, O-CH_2-O), 6.65-6.74 (3H, m, Ar_1-H), 6.85 (2H, d, J=8.8 Hz, Ar_2-H), 7.40 (2H, d, J=8.8 Hz, Ar_2-H); ^{13}C-NMR ($CDCl_3$) δ: −5.63, −5.59, 18.12, 25.82, 35.56, 47.13, 55.27, 65.05, 66.19, 86.14, 86.64, 100.83, 108.19, 109.32, 113.91, 115.05, 121.85, 133.13, 133.17, 145.97, 147.68, 159.60; IR ν_{max} ($CHCl_3$) cm^{-1}: 2983, 2940, 2384, 1615, 1517, 1495, 1452, 1290, 1256, 1175, 1076, 1042, 940, 837, 816. *Anal.* Found: C, 68.25; H, 7.34%. Calcd. for $C_{26}H_{34}O_5Si$: C, 68.69; H, 7.54%.

*General procedure for preparing (2R/S)-1-tert-butyldimethylsilyloxy-5-(4-methoxyphenyl)-2-(3,4-methylenedioxyphenyl)methyl-4-pentyn-3-one (**14** and **15**).* To a stirred solution of **12** or **13** (1.0 eq) in toluene (20 ml/mmol) were added DMSO (30 eq), DCC (3.0 eq) and TFA-pyridine (1.5 eq) at room temperature under an N_2 atmosphere. After 1 day, water (30 ml) was added to the reaction mixture while stirring for 5 min. The organic layer was separated, and the aqueous phase was extracted with Et_2O (15 ml). The combined organic layer was successively washed with sat. $NaHCO_3$ and brine, before being dried over Na_2SO_4. After removing the solvent *in vacuo*, the residue was purified by column chromatography on silica gel (hexane-EtOAc, 12:1) to provide a β-silyloxy ketone **14** or **15** as a colorless oil.

14: 84.1% yield, $[\alpha]_D^{25}$ −10.4° (*c* 2.90, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 0.037 (3H, s, Si-CH_3), 0.042 (3H, s, Si-CH_3), 0.88 {9H, s, (CH_3)×3}, 2.88 (1H, dd, J=5.8, 12.1 Hz, Ar-CH_2), 2.97-3.01 (1H, m, CHC=O), 3.03 (1H, dd, J=6.8, 12.1 Hz, Ar-CH_2), 3.84 (3H, s, OCH_3), 3.87 (1H, dd, J=5.8, 10.3 Hz, CH_2OSi), 3.93 (1H, dd, J=5.0, 10.3 Hz, CH_2OSi), 5.90 (2H, s, O-CH_2-O), 6.65-6.73 (3H, m, Ar_1-H), 6.89 (2H, d, J=8.8 Hz, Ar_2-H), 7.51 (2H, d, J=8.8 Hz, Ar_2-H); ^{13}C-NMR ($CDCl_3$) δ: −5.51, 18.20, 25.79, 32.97, 55.40, 58.55, 62.45, 87.54, 92.85, 100.79, 108.16, 109.48, 111.84, 114.34, 122.03, 132.71, 135.04, 145.98, 147.58, 161.62, 189.06; IR ν_{max} ($CHCl_3$) cm^{-1}: 2940, 2213, 1653, 1606, 1546, 1512, 1491, 1512, 1491, 1252, 1222, 1106, 1040, 935, 837, 739. *Anal.* Found: C, 68.92; H, 7.10%. Calcd. for $C_{26}H_{32}O_5Si$: C, 68.99; H, 7.13%.

15: 90.2% yield, $[\alpha]_D^{25}$ +10.8° (*c* 3.16, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 0.03 (3H, s, Si-CH_3), 0.04 (3H, s, Si-CH_3), 0.87 {9H, s, (CH_3)×3}, 2.87 (1H, dd, J=5.9, 12.2 Hz, Ar-CH_2), 2.96-3.01 (1H, m, CHC=O), 3.03 (1H, dd, J=6.8, 12.2 Hz, Ar-CH_2), 3.83 (3H, s, OCH_3), 3.87 (1H, dd, J=5.6, 10.1 Hz, CH_2OSi), 3.92 (1H, dd, J=4.9, 10.1 Hz, CH_2OSi), 5.89 (2H, s, O-CH_2-O), 6.65-6.72 (3H, m, Ar_1-H), 6.89 (2H, d, J=8.8 Hz, Ar_2-H), 7.50 (2H, d, J=8.8 Hz, Ar_2-H); ^{13}C-NMR ($CDCl_3$) δ: −5.57, −5.54, 18.16, 25.79, 32.92, 55.32, 58.51, 62.42, 87.50, 92.85, 100.76, 108.12, 109.47, 111.77, 114.29, 122.00, 132.66, 134.96, 145.96, 147.55, 161.59, 189.03; IR ν_{max} ($CHCl_3$) cm^{-1}: 2940, 2170, 1653, 1606, 1546, 1508, 1491, 1256, 1222, 1106, 1042, 940, 837, 747. *Anal.* Found: C, 68.77; H, 7.12%. Calcd. for $C_{26}H_{32}O_5Si$: C, 68.99; H, 7.13%.

*General procedure for preparing (2R/S)-1-hydroxy-5-(4-methoxyphenyl)-2-(3,4-methylenedioxyphenyl)methyl-4-pentyn-3-one (**16** and **17**).* Acetic acid (10.0 ml) was added to a stirred solution of **14** or **15** (0.50 g, 1.10 mmol) in THF (5.0 ml) and water (5.0 ml) at room temperature. After 15 h, water (10 ml) and EtOAc (10 ml) were added to the reaction mixture, and the organic layer was separated. The aqueous phase was extracted with EtOAc (10 ml), and the combined organic layer was successively washed with sat. $NaHCO_3$ and brine, before being dried over Na_2SO_4. After removing the solvent *in vacuo*, the residue was purified by column chro-

matography on silica gel (hexane-EtOAc, 2:1) to provide a hydroxyketone **16** or **17** as a colorless oil.

16: 86.6% yield, $[\alpha]_D^{25}$ −92.0° (*c* 1.71, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 2.01 (1H, dd, J=6.1, 6.7 Hz, -OH), 2.88 (1H, dd, J=8.0, 13.4 Hz, Ar-CH_2), 2.99–3.08 (1H, m, CHC=O), 3.16 (1H, dd, J=5.9, 13.2 Hz, Ar-CH_2), 3.81 (1H, dd, J=6.7, 11.8 Hz, CH_2OH), 3.83–3.91 (4H, m, OCH_3 and CH_2OH), 5.92 (2H, s, O-CH_2-O), 6.68–6.75 (3H, m, Ar_1-H), 6.90 (2H, dd, J=2.5, 6.8 Hz, Ar_2-H), 7.53 (2H, dd, J=2.5, 6.8 Hz, Ar_2-H); ^{13}C-NMR ($CDCl_3$) δ: 33.64, 55.45, 57.84, 61.49, 87.40, 92.24, 100.91, 108.31, 109.37, 111.37, 114.43, 122.03, 132.09, 135.28, 146.40, 147.74, 161.90, 189.85; IR ν_{max} ($CHCl_3$) cm^{-1}: 2213, 1735, 1653, 1607, 1508, 1491, 1444, 1252, 1110, 1042, 944, 837. *Anal.* Found: C, 70.62; H, 5.39%. Calcd. for $C_{20}H_{19}O_5$: C, 70.99; H, 5.36%.

17: 89.1% yield, $[\alpha]_D^{25}$ +87.9° (*c* 1.84, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 2.00 (1H, br, OH), 2.88 (1H, dd, J=8.4, 13.7 Hz, Ar-CH_2), 3.01–3.13 (1H, m, CHC=O), 3.15 (1H, dd, J=6.1, 13.7 Hz, Ar-CH_2), 3.83–3.90 (5H, m, OCH_3 and CH_2OH), 5.92 (2H, s, O-CH_2-O), 6.69–6.75 (3H, m, Ar_1-H), 6.90 (2H, dd, J=2.0, 6.8 Hz, Ar_2-H), 7.53 (2H, dd, J=2.0, 6.8 Hz, Ar_2-H); ^{13}C-NMR ($CDCl_3$) δ: 33.56, 55.36, 58.02, 61.46, 87.35, 94.15, 100.80, 108.22, 109.32, 111.35, 114.35, 121.96, 132.12, 135.19, 146.11, 147.65, 161.81, 189.84; IR ν_{max} ($CHCl_3$) cm^{-1}: 2213, 1735, 1653, 1606, 1508, 1491, 1444, 1252, 1110, 1042, 944, 837. *Anal.* Found: C, 70.60; H, 5.12%. Calcd. for $C_{20}H_{19}O_5$: C, 70.99; H: 5.36%.

*General procedure for preparing (2R/S,3R/S)-3-isopropyl-5-(4-methoxyphenyl)-2-(3,4-methylenedioxybenzyl)-4-pentyne-1,3-diol (**18** and **19**).* To a stirred solution of **16** or **17** (1.0 eq) in THF (60 ml/mmol) was added a solution of isopropyl magnesium bromide prepared from Mg (large excess) in THF (1.0 ml) and 2-bromopropane (3.0 eq). The reaction mixture was then diluted with THF (10 ml) at −78°C *via* a cannula under N_2 pressure. After 1 h, the reaction mixture was quenched by adding sat. NH_4Cl (60 ml) and allowed to warm to room temperature. The organic layer was separated, and the aqueous phase was extracted with Et_2O (2×20 ml). The combined organic layer was successively washed with sat. $NaHCO_3$ and brine, before being dried over Na_2SO_4. After concentrating the residue was purified by column chromatography on silica gel (hexane-EtOAc, 3:1) to provide the 1,3-diol as a mixture of diastereomers. Each isomer was separated by PTLC (hexane-EtOAc, 3:1) and **17** and **18** were obtained as colorless oils.

18-a (2*S*,3*R*): 66.6% yield, R_f 0.42 (hexane-EtOAc, 3:2), t_R 50.2 min {a CHIRALCEL OF column (4.6×250 mm, Daicel Chemical Industries) was used with hexane-2-propanol (9:1) as the mobile phase at a flow rate of 0.5 ml/min and column temperature of 25°C}, $[\alpha]_D^{25}$ −33.1° (*c* 0.97, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 1.13 (3H, d, J=6.4 Hz, CH_3), 1.15 (3H, d, J=6.8 Hz, CH_3), 2.10–2.15 (1H, m, Ar-CH_2-CH), 2.16–2.23 {1H, m, $(CH_3)_2$CH}, 2.65 (1H, dd, J=11.5, 14.1 Hz, Ar-CH_2), 2.83 (1H, s, OH), 3.04 (1H, dd, J=2.9, 14.1 Hz, Ar-CH_2), 3.36 (1H, br, OH), 3.75–3.84 (5H, m, OCH_3 and CH_2-OH), 5.93 (2H, s, O-CH_2-O), 6.68–6.76 (3H, m, Ar_1-H), 6.86 (2H, d, J=8.8 Hz, Ar_2-H), 7.41 (2H, d, J=8.8 Hz, Ar_2-H); ^{13}C-NMR ($CDCl_3$) δ: 16.42, 18.09, 33.15, 35.34, 47.47, 55.30, 61.96, 79.21, 86.29, 88.38, 100.80, 108.17, 109.45, 113.95, 114.73, 122.00, 133.18, 134.19, 145.84, 147.65, 159.71; IR ν_{max} ($CHCl_3$) cm^{-1}: 2983, 2363, 1715, 1615, 1546, 1517, 1495, 1448, 1279, 1256, 1179, 1110, 1046, 935, 841. *Anal.* Found: C, 72.15; H, 6.84%. Calcd. for $C_{23}H_{26}O_5$: C, 72.23; H, 6.85%.

18-b (2*S*,3*R*): 4.2% yield, R_f 0.48 (hexane-EtOAc, 3:2), $[\alpha]_D^{25}$ +15.9° (*c* 2.58, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 1.09 (1H, d, J=6.8 Hz, CH_3), 1.19 (1H, d, J=6.4 Hz, CH_3), 1.94–2.02 (1H, m, ArCH_2-CH), 2.20–2.32 {2H, m, $(CH_3)_2$CH and OH}, 2.86 (2H, d, J=9.8 Hz, Ar-CH_2), 3.66 (1H, dd, J=3.4, 11.0 Hz, CH_2OH), 3.78 (1H, s, OH), 3.81 (3H, s, OCH_3), 4.38 (1H, dd, J=2.0, 11.0 Hz, CH_2OH), 5.93 (2H, s, O-CH_2-O), 6.70–6.76 (3H, m, Ar_1-H), 6.83 (2H, d, J=8.8 Hz, Ar_2-H), 7.37 (2H, d, J=8.8 Hz, Ar_2-H); ^{13}C-NMR ($CDCl_3$) δ: 17.69, 18.46, 29.85, 34.98, 47.20, 55.75, 63.16, 79.55, 86.73, 88.93, 101.28, 108.72, 110.09, 114.35, 115.27, 122.48, 133.56, 134.64, 146.26, 148.11, 160.04.

19-a (2*R*,3*S*): 56.2% yield, R_f 0.43 (hexane-EtOAc, 3:2), t_R 55.7 min, $[\alpha]_D^{25}$ +28.7° (*c* 2.33, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 1.13 (3H, d, J=6.4 Hz, CH_3), 1.15 (3H, d, J=6.4 Hz, CH_3), 2.10–2.16 {1H, m, Ar-CH_2-CH}, 2.17–2.23 {1H, m, $(CH_3)_2$CH}, 2.65 (1H, dd, J=11.5, 14.0 Hz, Ar-CH_2), 2.81(1H, s, -OH), 3.05 (1H, dd, J=3.0, 14.0 Hz, Ar-CH_2), 3.34 (1H, br, OH), 3.78–3.87 (5H, m, OCH_3 and CH_2-OH), 5.92 (2H, s, O-CH_2-O), 6.67–6.74 (3H, m, Ar_1-H), 6.85 (2H, d, J=8.8 Hz, Ar_2-H), 7.40 (2H, d, J=8.8 Hz, Ar_2-H); ^{13}C-NMR ($CDCl_3$) δ: 16.41, 18.09, 33.15, 35.34, 47.47, 55.30, 61.97, 79.21, 86.30, 88.38, 100.80, 108.17, 109.45, 113.95, 114.73, 122.00, 133.17, 134.19, 145.84, 147.65, 159.71; IR ν_{max} ($CHCl_3$) cm^{-1}: 2983, 2363, 1715, 1615, 1546, 1508, 1495, 1448, 1287, 1247, 1179, 1110, 1038, 935, 841. *Anal.* Found: C, 72.04; H, 6.95%. Calcd. for $C_{23}H_{26}O_5$: C, 72.23; H, 6.85%.

19-b (2*R*,3*R*): 3.0% yield, R_f 0.48 (hexane-EtOAc, 3:2), $[\alpha]_D^{25}$ −10.7° (*c* 0.68, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 1.08 (1H, d, J=6.4 Hz, CH_3), 1.19 (1H, d, J=6.8 Hz, CH_3), 1.96–2.00 (1H, m, Ar-CH_2CH), 2.19–2.29 {1H, m, $(CH_3)_2$CH}, 2.35 (1H, br, -OH), 2.82–2.88 (2H, m, Ar-CH_2), 3.65 (1H, d, J=10.3 Hz, CH_2OH), 3.81 (4H, s, OCH_3 and -OH), 4.38 (1H, d, J=10.7 Hz, CH_2OH), 5.92 (2H, s,

O–CH_2–O), 6.70–6.75 (3H, m, Ar_1–H), 6.82 (2H, d, J=8.8 Hz, Ar_2–H), 7.36 (2H, d, J=8.8 Hz, Ar_2–H); ^{13}C-NMR ($CDCl_3$) δ: 17.22, 17.99, 29.44, 34.52, 46.81, 55.27, 62.98, 79.08, 86.27, 88.51, 100.79, 108.24, 109.55, 113.91, 114.85, 122.02, 133.09, 134.21, 145.81, 147.66, 159.61.

*(4R,5S)-2,2-Dimethyl-4-isopropyl-4-(4-methoxyphenyl)ethynyl-5-(3,4-methylenedioxybenzyl)-1,3-dioxolane (**20**).* To a stirred solution of **18-a** (0.14 g, 0.37 mmol) in toluene (10 ml) were added to 2,2-dimethoxypropane (0.27 ml, 2.20 mmol) and a catalytic amount of PPTS at room temperature under an N_2 atmosphere. After stirring for 18 h, the reaction mixture was poured into water (20 ml). The organic layer was separated, and the aqueous phase was extracted with Et_2O (2×5ml). The combined organic layer was successively washed with sat. $NaHCO_3$ and brine before being dried over Na_2SO_4. After concentrating, the residue was purified by column chromatography on silica gel (hexane-EtOAc, 9:1) to provide 0.14 g (90.5%) of **20** as a colorless oil, $[\alpha]_D^{25}$ +3.9° (*c* 2.29, $CHCl_3$); ^{1}H-NMR($CDCl_3$) δ: 1.04 (3H, d, J=6.6 Hz, CH_3), 1.18 (3H, d, J=6.6 Hz, CH_3), 1.32 (3H, s, CH_3), 1.75 (3H, s, CH_3), 2.01–2.10 {1H, m, $(CH_3)_2CH$}, 2.22–2.30 (1H, m, $ArCH_2$–CH), 2.35 (1H, dd, J=11.2, 13.7 Hz, Ar–CH_2), 2.79 (1H, dd, J=3.4, 13.7 Hz, Ar–CH_2), 3.55 (1H, d, J=4.2, 10.9 Hz, CH–CH_2O), 3.82 (3H, s, OCH_3), 3.90 (1H, dd, J=10.9, 11.7 Hz, CH–CH_2O), 5.91 (2H, s, O–CH_2–O), 6.59–6.72 (3H, m, Ar_1–H), 6.86 (2H, d, J=8.8 Hz, Ar_2–H), 7.39 (2H, d, J=8.8 Hz, Ar_2–H); ^{13}C-NMR ($CDCl_3$) δ: 14.11, 16.01, 17.86, 30.75, 33.5, 35.80, 55.34, 61.41, 76.29, 87.40, 89.67, 99.21, 100.84, 108.15, 109.29, 114.02, 115.35, 151.81, 132.74, 133.09, 145.90, 147.67, 159.59; IR ν_{max} ($CHCl_3$) cm^{-1}: 2961; 1611, 1517, 1495, 1462, 1388, 1290, 1256, 1179, 1115, 1046, 935, 837, 760. *Anal.* Found: C, 73.84; H, 7.41%. Calcd. for $C_{26}H_{30}O_5$: C, 73.91; H, 7.16%.

*General procedure for preparing (2R/S,3R/S)-3-hydroxy-3-isopropyl-5-(4-methoxyphenyl)-2-(3,4-methylenedioxybenzyl)-4-pentynoic acid (**21** and **22**).* To a stirred solution of 1,3-diol **18-a** or **19-a** (1.0 eq) in CH_2Cl_2 (10 ml/mmol) were added NMO (2.5 eq) and crushed 4A molecular sieves at room temperature under an N_2 atmosphere. After 5 min, a catalytic amount of TPAP was added to the reaction mixture which was stirred for 6 h. The solvent was removed *in vacuo*, and the residue was purified by column chromatography on silica gel (hexane-EtOAc, 3:1) to provide an aldehyde which was used in the next step without further purification.

To a stirred solution of this aldehyde (1.0 eq) in ^{t}BuOH and water (4:1) were added NaH_2PO_4 (2.7 eq) and 2-methyl-2-butene (10 eq) at room temperature. The reaction mixture was cooled to 0°C, before adding of $NaClO_2$ (80% purity, 1.1 eq). After 1 h at the same temperature, the resulting solution was diluted with EtOAc (5 ml) and water (5 ml). The organic layer was separated, and the aqueous phase was extracted with EtOAc (5 ml). The combined organic layer was washed with brine, before being dried over Na_2SO_4. After concentrating, the residue was purified by column chromatography on silica gel (hexane-EtOAc, 2:1 to 1:2) to provide **21** or **22**.

21: 64.4% yield, $[\alpha]_D^{25}$ −76.1° (*c* 1.86, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 1.12 (3H, d, J=6.4 Hz, CH_3), 1.19 (3H, d, J=6.4 Hz, CH_3), 1.26 (1H, s, –OH), 1.90–2.00 {1H, m, $(CH_3)_2CH$}, 3.08 (1H, d, J=9.4 Hz, Ar–CH_2), 3.15 (1H d, J=11.4 Hz, Ar–CH_2–CH), 3.38 (1H, dd, J=9.7, 10.4 Hz, Ar–CH_2), 3.82 (3H, s, –OCH_3), 5.92 (2H, s, O–CH_2–O), 6.65–6.74 (3H, m, Ar_1–H), 6.86 (2H, d, J=8.8 Hz, Ar_2–H), 7.41 (2H, d, J=8.8 Hz, Ar_2–H); ^{13}C-NMR ($CDCl_3$) δ: 17.59, 18.52, 35.20, 37.69, 55.01, 55.32, 77.08, 85.41, 86.96, 100.88, 108.30, 109.25, 113.98, 114.27, 121.82, 132.46, 133.32, 146.26, 147.70, 159.90, 177.86.

22: 70.2% yield, $[\alpha]_D^{25}$ +75.6° (*c* 3.33, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 1.12 (3H, d, J=6.4 Hz, CH_3), 1.19 (3H, d, J=6.4 Hz, CH_3), 1.25 (1H, s, OH), 1.87–1.97 {1H, m, $(CH_3)_2CH$}, 3.08 (1H, d, J=9.8 Hz, Ar–CH_2), 3.15 (1H, d, J=11.7 Hz, $ArCH_2CH$), 3.37 (1H, dd, J=10.0, 10.7 Hz, Ar–CH_2), 3.82 (3H, s, OCH_3), 5.90 (2H, s, O–CH_2–O), 6.65–6.72 (3H, m, Ar_1–H), 6.85 (2H, d, J=8.8 Hz, Ar_2–H), 7.40 (2H, d, J=8.8 Hz, Ar_2–H); ^{13}C-NMR ($CDCl_3$) δ: 17.57, 18.49, 35.16, 37.67, 54.99, 55.27, 77.06, 85.43, 86.79, 100.82, 108.23, 109.20, 113.93, 114.29, 121.77, 132.50, 133.25, 146.17, 147.63, 159.81, 178.77.

*General method for preparing (2R/S,3R/S,4Z)-3-hydroxy-3-isopropyl-5-(4-methoxyphenyl)-2-(3,4-methylenedioxybenzyl)-4-penten-4-olide (**2** and **23**).* To a stirred solution of acid **21** or **22** (1.0 eq) in CH_3OH (15.0 ml/mmol) was added 0.1 M aq. $AgNO_3$ (0.15 ml/mmol) at room temperature. After stirring for 2 days in the dark, the solvent was concentrated *in vacuo*, and the residue was purified by column chromatography on silica gel (CCl_4-EtOAc, 9:1). The obtained crystals were recrystalized from a mixed solvent of CH_2Cl_2-petroleum ether (1:3) to give the desired compound.

2: 81.9% yield, mp 140–141°C, t_R 33.1 min {a CHIRALCEL OD-H column (4.6×250 mm, Daicel Chemical Industries) was used with hexane-2-propanol (3:1) as the mobile phase at a flow rate of 0.5 ml/min and column temperature of 25°C}, $[\alpha]_D^{25}$ +94.7° (*c* 0.88, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 0.93 (3H, d, J=6.8 Hz, CH_3), 1.08 (3H, d, J=6.8 Hz, CH_3), 1.75 (1H, s, OH), 2.17–2.27 {1H, m, $(CH_3)_2CH$}, 2.91 (1H, dd, J=6.8, 14.2 Hz, Ar–CH_2), 3.17 (1H, dd, J=6.3, 6.8 Hz, CHC=O),

3.22 (1H, dd, J=6.3, 14.2 Hz, Ar–CH_2), 3.81 (3H, s, OCH_3), 5.70 (1H, s, Ar_2–CH), 5.94 (2H, s, O–CH_2–O), 6.75–6.84 (3H, m, Ar_1–H), 6.87 (2H, d, J=8.8 Hz, Ar_2–H), 7.53 (2H, d, J=8.8 Hz, Ar_2–H); ^{13}C-NMR ($CDCl_3$) δ: 15.69, 17.96, 29.05, 33.39, 53.16, 55.27, 82.36, 101.03, 105.69, 108.41, 109.20, 113.93, 121.72, 125.82, 130.14, 132.12, 146.35, 147.80, 148.28, 158.79, 173.05; IR ν_{max} ($CHCl_3$) cm^{-1}: 2363, 1807, 1692, 1615, 1517, 1499, 1452, 1287, 1256, 1187, 1042, 940, 841. *Anal.* Found: C, 69.35; H, 6.05%. Calcd. for $C_{23}H_{24}O_6$: C, 69.68; H, 6.10%.

23: 67.1% yield, mp 140–141 °C, t_R 23.9 min, $[\alpha]_D^{25}$ −98.8° (c 1.84, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) δ: 0.92 (3H, d, J=6.4 Hz, CH_3), 1.08 (3H, d, J=6.4 Hz, CH_3), 1.76 (1H, s, OH), 2.17–2.26 {1H, m, $(CH_3)_2$CH}, 2.90 (1H, dd, J=6.8, 14.2 Hz, Ar–CH_2), 3.17 (1H, dd, J=6.4, 6.8 Hz, CHC=O), 3.22 (1H, dd, J=6.4, 14.2 Hz, Ar–CH_2), 3.81 (3H, s, OCH_3), 5.70 (1H, s, Ar_2–CH), 5.94 (2H, s, O–CH_2–O), 6.75–6.84 (3H, m, Ar_1–H), 6.88 (2H, d, J=8.8 Hz, Ar_2–H), 7.54 (2H, d, J=8.8 Hz, Ar_2–H); ^{13}C-NMR ($CDCl_3$) δ: 15.67, 17.94, 29.02, 33.36, 53.13, 55.25, 82.32, 100.99, 105.65, 108.37, 109.21, 113.91, 121.71, 125.84, 130.13, 132.17, 146.32, 147.86, 148.34, 158.77, 173.09. *Anal.* Found: C, 69.38; H, 6.10%. Calcd. for $C_{23}H_{24}O_6$: C, 69.68; H, 6.10%.

References

1) Mason, C., Edwards, K., Carlson, R., Pignatello, J., Gleason, F., and Wood, J., Isolation of chlorine-containing antibiotic from the freshwater cyanobacterium *Scytonema hofmanni*. *Science*, **215**, 400–402 (1982).
2) Pignatello, J., Porwoll, J., Carlson, R., Xavier, A., Gleason, F., and Wood, J., Structure of the antibiotic cyanobacterin, a chlorine-containing γ-lactone from the freshwater cyanobacterium *Scytonema hofmanni*. *J. Org. Chem.*, **48**, 4035–4038 (1983).
3) Gleason, F., and Porwoll, J., X-ray structure determination of the naturally occurring isomer of cyanobacterin. *J. Org. Chem.*, **51**, 1615–1616 (1986).
4) Gleason, F., and Case, D., Activity of the natural algicide, cyanobacterin, on angiosperms. *Plant Physiol.*, **80**, 834–837 (1986).
5) Gleason, F., Case, D., Sipprell, K., and Magnuson, T., Effect of the natural algicide, cyanobacterin, on a herbicide-resistant mutant of *Anacystis nidulans* R2. *Plant Sci.*, **46**, 5–10 (1986).
6) Mallipudi, L., and Gleason, F., Characterization of a mutant of *Anacystis nidulants* R2 resistant to the natural herbicide, cyanobacterin. *Plant Sci.*, **60**, 149–154 (1989).
7) Jong, T., Williard, P., and Porwoll, J., Total synthesis and X-ray structure determination of cyanobacterin. *J. Org. Chem.*, **49**, 735–736 (1984).
8) Gleason, F., and Paulson, L., Site of action of the natural algicide, cyanobacterin, in the blue-green alga, *Synechococcus* sp. *Arch. Microbiol.*, **138**, 273–277 (1984).
9) Koo, J., Fish, M. S., Walker, G. N., and Balake, J., 2,3-Dimethoxycinnamic acid. *Org. Synth.*, Collect. Vol. **4**, 327–329 (1963).
10) Gage, J. R. and Evans, D. A., (*S*)-4-(Phenylmethyl)-2-oxazolidione. *Org. Synth.*, Collect. Vol. **8**, 528–531 (1993).
11) Gage, J. R., and Evans, D. A., Diastereoselective aldol condensation using a chiral oxazolidinone auxiliary: (2*S**, 3*S**)-3-hydroxy-3-phenyl-2-methylpropanoic acid. *Org. Synth.*, Collect. Vol. **8**, 339–343 (1993).
12) Corey, E. J., and Fuchs, P. L., A synthetic method for formyl→ethynyl conversion. *Tetrahedron Lett.*, 3769–3772 (1972).
13) Olah, G. A., and Arvanaghi, M., Aldehyde by formylation of Grignard or organolithium reagents with *N*-formylpiperidine. *Angew. Chem. Int. Ed. Engl.*, **20**, 878–879 (1981).
14) Danda, H., Hansen, M. M., and Heathcock, C. H., Reversal of stereochemistry in the aldol reactions of a chiral boron enolate. *J. Org. Chem.*, **55**, 173–181 (1990).
15) Walker, M. A., and Heathcock, C. H., Extending the scope of the Evans aldol reactions: preparation of *anti* and ''non-Evans'' *syn* aldols. *J. Org. Chem.*, **56**, 5747–5750 (1991).
16) Evans, D. A., Bartroli, J., and Shih, T. L., Enantioselective aldol condensations. 2. Erythro-selective chiral aldol condensation *via* boron enolates. *J. Am. Chem. Soc.*, **103**, 2127–2129 (1981).
17) Evans, D. A., Nelson, J. V., Vogel, E., and Taber, T. R., Stereoselective aldol condensation *via* boron enolates. *J. Am. Chem. Soc.*, **103**, 3099–3111 (1981).
18) Corey, E. J., and Schmidt, G., Useful procedures for the oxidation of alcohols involving pyridinium dichromate in aprotic media. *Tetrahedron Lett.*, 399–402 (1979).
19) Xu, Z., Johannes, C. W., Houri, A. F., La, D. S., Cogan, D. A., Hofilena, G. E., and Hoveyda, A. H., Applications of Zr-catalyzed carbomagnesation and Mo-catalyzed macrocyclic ring closing metathesis in asymmetric synthesis. Enantioselective total synthesis of Sch 38516 (Fluvirucin B_1). *J. Am. Chem. Soc.*, **119**, 10302–10316 (1997).
20) Belil, C., Pascual, J., and Serratosa, F., Intramolecular cyclization of alkylpropargylidenemalonic acids. *Tetrahedron*, **20**, 2701–2708 (1964).