

\$0040-4020(96)00296-7

Studies on Total Syntheses of Antitumor Styryllactones: Stereoselective Total Syntheses of (+)-Goniofufurone, (+)-Goniobutenolide A, and (-)-Goniobutenolide B

Chisato Mukai,*a Syuichi Hirai,^a In Jong Kim,^a Masaru Kido,^b and Miyoji Hanaoka*^a

 ^a Faculty of Pharmaceutical Sciences, Kanazawa University Takara-machi, Kanazawa 920 Japan
^b Medicinal Chemistry, 2nd Tokushima Institute of New Drug Research, Otsuka Pharmaceutical Co Ltd., Tokushima 771-01, Japan

Abstract: A highly stereoselective aldol reaction of the aldehyde 11, derived from (+)-tricarbonyl(η^{6} -2-trimethylsilylbenzaldehyde)chromium(0) complex (4), with 2-trimethysilyloxyfuran afforded the y-lactone derivative 13. The y-lactone 13 was subsequently converted into three antitumor styryllactones, (+)-goniobutenolide A, and (-)-goniobutenolide B. Copyright © 1996 Elsevier Science Ltd

Several styryllactones with unique structural features¹ have recently been isolated along with other bioactive compounds from the stem bark of *Goniothalamus giganteus* Hook. f., Thomas (Annonaceae) grown in Thailand. These styryllactones have been shown to possess significant cytotoxic activities¹ toward human tumor cells. Some of representative styryllactones are exhibited in Figure 1. They can be formally classified into two



1: (+)-Goniofufurone



2 : (+)-Goniobutenolide A (Z-isomer) 3 : (-)-Goniobutenolide B (E-isomer)



(+)-Goniotriol







(+)-Goniopypyrone



R = Me: (+)-Gonioheptolide A R = Et: (+)-Gonioheptolide B

Figure 1

groups by their structural features. The first group consists of styryllactones with the γ -lactone framework like goniofufurone (1) and goniobutenolide A and B (2 and 3). The second one is represented by goniotriol, goniofupyrone, and goniopypyrone having the δ -lactone skeleton. Furthermore isolation of two eight-membered lactones, gonioheptolide A and B,² has also been reported. Since the first publication on isolation¹ of such styryllactones, many efforts³ have so far been made on total syntheses of them because of their antitumor activities as well as their novel structures.



In the course of our program directed toward the development of highly stereoselective carbon-carbon bond formation reactions mediated by tricarbonyl(η^6 -arene)chromium(0) complexes and their application to total syntheses of bioactive compounds, we have completed (i) stereoselective preparation of the C-13 side chains of taxol and taxotère⁴ and (ii) highly stereoselective synthesis of the common amino residue of nikkomycin B and Bx⁵ based on a highly *anti*-selective aldol reaction of the optically active chromium(0)-complexed benzaldehyde derivative 4. By taking advantage of the chiral *anti*-aldol product 5, prepared from the reaction of 4 with *S-tert*butyl benzyloxyethanethioate in a highly stereoselective manner, we now focus our endeavor on development of highly stereoselective protocol for the synthesis of all kind of antitumor styryllactones. In this paper we describe efficient and stereoselective total syntheses of the γ -lactone derivatives, (+)-goniofufurone (1),⁶ (+)-goniobutenolide A (2), and (-)-goniobutenolide B (3) through the common synthetic intermediate.

Synthesis of (+)-Goniofufurone

Retrosynthetic analysis of the γ -lactones, goniofufurone (1)^{3a-k} and goniobutenolide A and B (2 and 3)^{3k-n} indicates that the γ -lactone 6 with suitable stereochemistry would become the key intermediate and be direct-



ly transformed into 1, 2, and 3. We envisioned, therefore, that stereoselective construction of the key intermediate 6 from the aldehyde 7 must be the most crucial point in this research. The γ -lactone 6 having the desirable stereochemistry will be selectively formed if the aldol reaction between the aldehyde 7 and 2-trimethylsilyloxyfuran (8)⁷ as a C₄-unit proceeds through the transition state like A.

Thus, as our point of departure, the aldol condition under the chelation-controlled circumstances leading to diastereoselective formation of 6 was searched by employing racemic compounds. The methyl ester 9,⁴ prepared from the thioester 5, was protected with *tert*-butyldimethylsilyl (TBS) group to give the TBS-protected ester 10 in 77% yield. Reduction of 10 with diisobutylaluminum hydride (DIBAL-H) in benzene was followed by the Swern oxidation to provide the labile aldehyde 11. Because of its instability 11 was immediately exposed to the aldol condition at -78°C in methylene chloride where 8 was used as a carbon nucleophile in the presence of SnCl4 affording the expected 12 together with its 4-epimer 13 in a ratio of *ca*. 1 to 1. It became apparent, however, that a main product is the γ -lactone derivative 14 resulting from carbon-carbon bond formation at C-3 position of 8, followed by double bond isomerization. Changing Lewis acid to TiCl4, ZrCl4, and Ti(OPrⁱ)₂Cl₂ brought about an interesting observation as indicated in Table 1. In all cases examined except for SnCl4, the unexpected γ -lactone 13 with the stereochemistry of *anti* (between C₄-H and C₁-H) and *syn* (between C₁-H and C₂-H) was found to be preferentially constructed. In particular, use of Ti(OPrⁱ)₂Cl₂ as a Lewis acid led to the exclusive formation of 13.



Preferential formation of 13 over 12 might be tentatively rationalized in terms of the transition state B instead of previously assumed transition state A. When 8 approaches to the aldehyde 11 being coordinated with a Lewis acid, the transition states A and B leading to 12 and 13, respectively could be assumed. In both transition states A and B, sterically less hindered hydrogen atom on the furan ring of 8 should be placed on the most sterically demanding position. There would be a dipole-dipole interaction between the oxygen atom of the furan ring and that of the aldehyde counterpart in the transition state A. Such an unfavorable interaction, however, might not be predicted in the transition state B. Therefore, 13 would become a major or exclusive product. Stereochemical assignment of 12 and 13 was made by careful consideration of coupling constant as well as comparison of them with the related compounds in the literature.^{3a,k,1} ¹H NMR spectrum of 12 disclosed that coupling constant between C₄-H and C₁-H has 4.3 Hz, while that of C₁-H with C₂-H is 2.0 Hz,

suggesting these consecutive stereogenic centers should be syn and syn. On the other hand, the preferentially formed 13 has 9.3 and 1.1 Hz for coupling constants between C₄-H and C₁'-H, and C₁'-H and C₂'-H, respectively. These values correspond to the stereochemistry of *anti* (C₄-C₁') and *syn* (C₁'-C₂'). In addition, relative stereochemistry of these two compounds was unambiguously established by X-ray crystallographic analysis⁸ of 13 as depicted in Figure 2. Thus relative stereochemistry of 13 should be assigned as 1'R*, 2'R*, 3'S*, 4S*, therefore, 12 has 1'R*, 2'R*, 3'S*, 4R* configuration.

Although 12 was not obtained in a selective fashion, we reached the idea that 13, the 4-epimer of 12, would be useful for our purpose if isomerization at C-4 stereogenic center is easily realized. Molecular model examination of 13 provided a very promising expectation. Direct Michael addition of C₂'-hydroxy group to the β -carbon of γ lactone moiety of 13 (after deprotection) would give rise to the formation of a dioxabicyclo[3.3.0]octanone derivative 15 with the stereochemistry depicted in Scheme 3. It would be expected to be severe nonbonding interaction of C3-benzylic appendage with C4hydroxy functionality since they are forced to be located in the concavity. The instability anticipated in the structure of 15 would force retro Michael reaction and result in isomerization to a suitable isomer 12 being able to cyclize to a dioxabicyclo[3.3.0]octanone with a desired stereochemistry. Based on the above consideration, we expected easy isomerization of 13 (in a deprotected form) to 12 (in a deprotected form), followed by cyclization to give goniofufurone under a suitable condition.



Figure 2



Scheme 3

TBS group of 13 was first removed with sodium iodide and $BF_3 \cdot OEt_2^9$ to afford 16 in 92% yield. Removal of benzyl group of 16 was troublesome under some standard conditions to give an intractable mixture. After screening several conditions, 1M-SnCl4 was found to be the most effective one in the case of 16 producing the triol 17 in 99% yield. Isomerization and cyclization of the triol 17 was examined in the presence of DBU in THF.^{3a,k} However, no reaction took place and the starting 17 was completely recovered. During conversion of 13 into 16 the partial isomerization at C-4 position of 16 had been detected when treated with tetra-*n*butylammonium fluoride (TBAF) in THF. This observation suggested that the fluoride anion might be useful for conversion of 17 into goniofufurone. Treatment of 17 with TBAF in THF at room temperature fortunately effected successive isomerization and cyclization to provide (±)-goniofufurone (1) in 87% yield. Thus we have developed an efficient and highly stereoselective way for a total synthesis of (±)-goniofufurone (1) by using racemic compounds.



Next phase of our program is faced to accomplishment of a total synthesis of natural (+)-goniofufurone (1) from optically active starting material according to the procedure described in a series of racemates. Reduction of optically active 10 (*anti* : syn = 95 : 5), ⁴ derived from optically active 9 (*anti* : syn = 95 : 5), with DIBAL-H and subsequent the Swern oxidation afforded the optically active 11 (*anti* : syn = 95 : 5). The aldehyde 11 was immediately exposed to 8 under the aldol condition with Ti(OPr^{*i*})₂Cl₂ to furnish, after chromatographic purification, (-)-13 in enantiomerically as well as diastereomerically pure form in 54% overall yield from 10. An alternative and more convenient method for getting (-)-13 was explored. Upon treatment with TBSOTf, optically active 5 (*anti* : syn = 95 : 5) yielded the TBS-protected 5 in 86% yield, which was reduced with DIBAL-H to afford the aldehyde 11 was then treated under the same aldol condition (94%) and debenzylation (96%) of (-)-13 produced the triol (+)-17 via (+)-16. Isomerization and spontaneous ring closure occurred on treatment with TBAF to give (+)-1 in 86% yield. Synthetic (+)-goniofufurone was identified with natural one¹⁰ by comparison of ¹H and ¹³C NMR spectra.

Synthesis of (+)-Goniobutenolide A and (-)-Goniobutenolide B

Shing *et al.*^{3k,1} have recently reported on conversion of 12 (in a deprotected form) into (+)-goniobutenolide A and B (2 and 3) *via* the corresponding acetate or trifluoroacetate derivatives, respectively. However, only moderate selectivity (2:3 = 2:1 or 2:3 = 1:3, respectively) could be realized. Two other groups^{3m,n} have also succeeded in preparation of goniobutenolide A and B in a nonselective fashion. With the useful intermediate 13 in hand, we next investigated selective as well as voluntary synthesis of goniobutenolide A and B from the common intermediate 13 *via* successive activation of C₁'-hydroxy group and elimination reaction.



The C_1 -hydroxy group of the compound 13 was first of all transformed into the activated forms (mesylate, acetate, and trifluoroacetate), which were subsequently exposed to elimination conditions. After screening various elimination conditions by combination of base and solvent along with reaction temperature,

we finally found two promising and convenient conditions. Mesylation of (-)-13, followed by treatment with diisopropylamine in methylene chloride at room temperature for 40 min afforded a mixture of (Z)- and (E)-18 in a ratio of 94 to 6 in 93% yield. Desilylation of the crude 18 effected under the standard condition (TBAF-HF) to give pure (Z)-19 in 73% overall yield from 13, which was converted into (+)-goniobutenolide A (2) by debenzylation with titanium tetrachloride in 95% yield. On the other hand, the mesylate derivative of (-)-13 was exposed to an aqueous potassium carbonate solution in THF at room temperature for 4 h to leave a mixture of (Z)- and (E)-18 (15 : 85) in 75% yield. According to the procedure that described for two step conversion of (Z)-18 to (+)-2, (-)-goniobutenolide B (3, 98%) was obtained from (E)-18 in a pure form through (E)-19 (62% from 13).

Thus, we could develop an efficient way for getting (+)-goniobutenolide A and B voluntarily from the same intermediate. It should be mentioned that both (Z)- and (E)-18 are stable enough under the elimination conditions employed. Indeed no isomerization could be observed and the starting (Z)- and (E)-18 were recovered intact when exposed independently to two elimination reactions (diisopropylamine / CH₂Cl₂ and aq. K₂CO₃ / THF) described above. However, it is still uncertain about the reason of selective formation of (+)-goniobutenolide A and (-)-goniobutenolide B by simply changing the reaction condition. Molecular model examination did not give us any clue for understanding the elimination mechanism (E₂, E₁cB, or E₁ elimination process). In any event we could succeed in highly stereoselective total synthesis of three antitumor styryl-lactones, (+)-goniofufurone, (+)-goniobutenolide A, and (-)-goniobutenolide B possessing γ -lactone skeleton as a common structural feature from the common synthetic intermediate 13.

Experimental Section

Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. Infrared spectra were measured with a JASCO-102 and Shimadzu IR-460 spectrometers in CHCl₃ unless otherwise stated, mass spectra with a Hitachi M-80 mass spectrometer, optical rotations with JASCO DIP-181 digital and Horiba SEPA-300 high sensitive polarimeters, ¹H NMR spectra with JEOL JNM-EX270, and JNM-GSX500 spectrometers in CDCl₃ using tetramethylsilane as an internal standard unless otherwise stated, and ¹³C NMR spectra with a JEOL JNM-EX270 and JNM-GSX500 spectrometers in CDCl₃ with CDCl₃ (77.00 ppm) as an internal reference unless otherwise stated. CH₂Cl₂ was freshly distilled from P₂O₅, and THF from sodium diphenylketyl prior to use. Aldol reactions were performed in oven-dried glassware under an inert atmosphere of nitrogen. Silica gel (silica gel 60, 230-400 mesh, Nacalai Tesque) was used for chromatography unless otherwise stated. Alumina (Aluminiumoxid 90, Aktivitätsstufe II-III, 70-230 mesh, Merck) was used for chromatography in a few cases. Organic extracts were dried over anhydrous Na₂SO₄.

Methyl $(2R^*, 3R^*)$ -2-Benzyloxy-3-tert-butyldimethylsilyloxy-3-phenylpropanoate [(±)-10]. TBSOTF (0.98 ml, 4.28 mmol) was added to a mixture of (±)-9 (613 mg, 2.14 mmol, anti : syn = 95 : 5) and DMAP (329 mg, 3.21 mmol) in dry CH₂Cl₂ (7 ml) at 0°C. The reaction mixture was stirred at rt for 30 min and quenched with MeOH (1 ml). The reaction mixture was taken into CH₂Cl₂ (20 ml) and washed with water, dried, and concentrated to dryness. Chromatography of the residue with hexane - acetone = 20 : 1 gave (±)-10

6553

(663 mg, 77%, *anti* : *syn* = 95 : 5) as a colorless oil; MS *m*/z 400 (M⁺, 0.05), 343 (24), 299 (26), 251 (42), 222 (100), 193 (38), 165 (32), 146 (46), 92 (38), 73 (83); IR 1730 (CO) cm⁻¹; ¹H NMR δ 7.36–7.29 (5H, m, Ar-H), 7.25–7.18 (3H, m, Ar-H), 6.99–6.96 (2H, m, Ar-H), 5.00 (0.05H, d, *J* =5.3 Hz, C₃-H), 4.85 (0.95H, d, *J* =7.9 Hz, C₃-H), 4.65 (0.05H, d, *J* =11.9 Hz, Bn-H), 4.44 (0.95H, d, *J* =12.2 Hz, Bn-H), 4.40 (0.05H, d, *J* =11.9 Hz, Bn-H), 4.22 (0.95H, d, *J* =12.2 Hz, Bn-H), 3.95 (0.05H, d, *J* =5.3 Hz, C₂-H), 3.92 (0.95H, d, *J* =7.9 Hz, C₂-H), 3.74 (2.85H, s, OCH₃), 3.55 (0.15H, s, OCH₃), 0.85 (0.45H, s, *t*-Bu), 0.81 (8.55H, s, *t*-Bu), 0.01 (0.15H, s, CH₃), -0.02 (2.85H, s, CH₃), -0.12 (0.15H, s, CH₃), -0.24 (2.85H, s, CH₃); ¹³C NMR δ (for *anti*-product) 171.72, 141.47, 136.93, 128.14, 127.94, 127.84, 127.75, 127.62, 127.33, 83.69, 75.40, 72.69, 51.79, 25.54, 17.94, -4.69, -5.44. *Anal.* Calcd for C₂₃H₃₂O₄Si: C, 68.96; H, 8.05. Found: C, 68.88; H, 8.08.

General Procedure for the Aldol Reaction of Aldehyde (±)-11 with 2-Trimethylsilyloxyfuran (8). To a solution of TBS-protected ester (\pm) -10 (1 eq.) in dry benzene (1.5 - 2 ml) was added dropwise a solution of DIBAL-H in toluene (1M solution; 2 eq.) at 0°C. The reaction mixture was stirred for 30 min, quenched with sat. sodium potassium tartrate aq., and diluted with ethyl acetate (30 ml). The organic solution was washed with water, dried, and concentrated to give the crude alcohol which was used for the following reaction. To a solution of oxalyl chloride (1.8 - 2.3 eq.) in CH₂Cl₂ (1 - 2 ml) was added dropwise a solution of DMSO (2.0 – 2.8 eq.) in CH₂Cl₂ (0.7 – 1.5 ml) at -78°C. The reaction mixture was stirred for 10 min, to which a solution of the crude alcohol (1 eq.) in CH_2Cl_2 (1 – 2 ml) was added dropwise. Stirring was continued for 15 min. Triethylamine (4 eq.) was added and the reaction mixture was stirred for 10 min and then allowed to warm to rt. The reaction mixture was diluted with diethyl ether (30 ml), washed with water and brine, dried and concentrated to dryness. The residue was passed through a alumina pad (hexane - acetone = 10:1), evaporated to give the aldehyde (\pm)-11. To a solution of aldehyde (\pm)-11 (1 eq.) in CH₂Cl₂ (0.7 – 1.5 ml) was added dropwise Lewis acid (1.0M CH₂Cl₂ solution; 1.2 - 2.5 eq.) (ZrCl₄ was directly added to the reaction mixture because of its insolubility to CH₂Cl₂) at -78°C. The reaction mixture was stirred for 15 min, and then a solution of 2-trimethylsilyloxyfuran (8) [3 eq., in CH₂Cl₂ (0.7 ml - 1.5 ml)] was added dropwise to the reaction mixture. The reaction mixture was stirred for an additional hour at -78°C, and quenched with water. The reaction mixture was taken into CH₂Cl₂ and washed with water and brine, dried and concentrated to dryness. Chromatography of the residue with hexane - ethyl acetate = 10:3 gave two fractions (F₁ consists of (±)-12 and (\pm) -13 and F₂ involves (\pm) -14). Additional chromatography of F₁ with benzene - ethyl acetate = 30 : 1 afforded pure (\pm) -12, (\pm) -13, and (\pm) -14. The yields and ratio of each compound are listed in Table 1.

SnCl₄-mediated Reaction: (\pm) -12 (2.4 mg, 5%), (\pm) -13 (2.2 mg, 4%), and (\pm) -14 (10.0 mg, 19%) were obtained from (\pm) -10 (45.5 mg, 0.11 mmol), 8 (44 mg, 0.28 mmol), and a solution of SnCl₄ in CH₂Cl₂ (1.0M solution; 0.11 ml, 0.11 mmol). TiCl₄-mediated Reaction: (\pm) -13 (21.9 mg, 41%) and (\pm) -14 (6.2 mg, 12%) were obtained from (\pm) -10 (46.9 mg, 0.12 mmol), 8 (39.0 mg, 0.25 mmol), and a solution of TiCl₄ in CH₂Cl₂ (1.0M solution; 0.10 ml, 0.10 mmol). ZrCl₄-mediated Reaction: (\pm) -12 (5.0 mg, 13%) and (\pm) -13 (13.2 mg, 35%) were obtained from (\pm) -10 (32.9 mg, 0.08 mmol), 8 (29.0 mg, 0.19 mmol), and ZrCl₄ (20.9 mg, 0.09 mmol). Ti(OPr^{*i*})₂Cl₂-mediated Reaction: (\pm) -13 (90.3 mg, 59%) was obtained from (\pm) -10 (136 mg, 0.34 mmol), 8 (97.3 mg, 0.62 mmol), and a solution of Ti(OPr^{*i*})₂Cl₂ in CH₂Cl₂ (1.0M solution; 0.50 mmol).

 $(1'R^*, 2'R^*, 3'S^*, 4R^*)-4-(2'-Benzyloxy-3'-tert-butyldimethylsilyloxy-1'-hydroxy-3'$ phenylpropyl)-2-buten-4-olide [(±)-12]: colorless needles. mp 89–91°C (hexane - MeOH); MS m/z 454(M⁺, 0.04), 397 (3), 289 (19), 264 (37), 222 (100), 207 (81), 198 (57), 165 (12), 91 (100), 73 (54); IR 1755 $(CO) cm⁻¹; ¹H NMR <math>\delta$ (CDCl₃ + D₂O) 7.41–7.32 (6H, m, Ar-H), 7.29 (1H, dd, J =1.5, 5.9 Hz, C₃-H), 7.28– 7.27 (2H, m, Ar-H), 7.09-7.07 (2H, m, Ar-H), 6.06 (1H, d, J =2.0, 5.9 Hz, C₂-H), 5.08 (1H, ddd, J =1.5, 2.0, 4.3 Hz, C₄-H), 4.87 (1H, d, J =7.3 Hz, C₃-H), 4.16 (1H, d, J =2.0, 4.3 Hz, C₁'-H), 4.06 (1H, d, J =10.7 Hz, Bn-H), 3.94 (1H, d, J =10.7 Hz, Bn-H), 3.47 (1H, dd, J =2.0, 7.3 Hz, C₂'-H), 0.87 (9H, s, t-Bu), 0.07 (3H, s, CH₃), -0.21 (3H, s, CH₃); ¹³C NMR δ 172.96, 154.41, 141.44, 136.96, 128.41, 128.37, 128.14, 128.07, 127.30, 121.47, 84.21, 80.94, 75.06, 73.05, 70.35, 25.73, 18.03, -4.51, -5.21. Anal. Calcd for C₂₆H₃₄O₅Si: C, 68.69; H, 7.54. Found: C, 68.56; H, 7.50.

 $(1^{R}, 2^{I}R^{*}, 3^{I}S^{*}, 4S^{*})$ -4- $(2^{I}$ -Benzyloxy-3^I-tert-butyldimethylsilyloxy-1^I-hydroxy-3^Iphenylpropyl)-2-buten-4-olide [(±)-13]: colorless orthorhombic crystals. mp 120-121°C (hexane -MeOH); MS *m*/z 455 (M⁺+1, 1), 397 (14), 296 (22), 264 (100), 223 (100), 198 (100), 149 (55), 117 (64), 91 (100), 73 (100); IR 1755 (CO) cm⁻¹; ¹H NMR δ 7.74 (1H, dd, *J* =1.5, 5.9 Hz, C₃-H), 7.41–7.28 (8H, m, Ar-H), 7.22–7.21 (2H, m, Ar-H), 6.10 (1H, dd, *J* =1.0, 5.9 Hz, C₂-H), 4.99 (1H, ddd, *J* =1.0, 1.5, 9.3 Hz, C₄-H), 4.93 (1H, d, *J* =5.9 Hz, C₃-H), 4.42 (1H, d, *J* =10.8 Hz, Bn-H), 4.24 (1H, d, *J* =10.8 Hz, Bn-H), 3.73 (1H, dd, *J* =1.1, 5.9 Hz, C₂-H), 3.65 (1H, dd, *J* =1.1, 9.3 Hz, C₁-H), 0.87 (9H, s, *t*-Bu), 0.05 (3H, s, CH₃), -0.16 (3H, s, CH₃); ¹³C NMR δ 172.90, 156.80, 140.93, 137.25, 128.43, 128.36, 128.09, 128.00, 126.79, 121.37, 82.01, 81.46, 75.15, 73.96, 72.29, 25.68, 18.03, -4.69, -5.25. Anal. Calcd for C₂₆H₃₄O₅Si: C, 68.69; H, 7.54. Found: C, 68.67; H, 7.59.

(1' R^* , 2' S^* , 3' R^*)-2-(2'-Benzyloxy-3'-*tert*-butyldimethylsilyloxy-1'-hydroxy-3'phenylpropyl)-2-buten-4-olide [(±)-14]: a colorless oil; MS *m*/*z* 397 (M⁺- *t*-Bu, 1), 341 (15), 285 (13), 257 (48), 222 (100), 187 (71), 115 (12), 73 (50); IR 1750 (CO) cm⁻¹; ¹H NMR δ 7.43–7.41 (2H, m, Ar-H), 7.37–7.34 (3H, m, Ar-H), 7.31–7.29 (1H, m, C₃-H), 7.28–7.24 (3H, m, Ar-H), 7.03–7.01 (2H, m, Ar-H), 4.92 (1H, d, *J* =6.4 Hz, C₃·-H), 4.82–4.77 (1H, m, C₁·-H), 4.71 (1H, br-d, *J* =18.1 Hz, C₄-H), 4.58 (1H, brd, *J* =18.1 Hz, C₄-H), 4.07 (1H, d, *J* =11.2 Hz, Bn-H), 3.95 (1H, d, *J* =11.2 Hz, Bn-H), 3.91 (1H, dd, *J* =1.5, 6.4 Hz, C₂·-H), 3.47 (1H, d, *J* =6.9 Hz, OH), 0.91 (9H, s, *t*-Bu), 0.09 (3H, s, CH₃), -0.15 (3H, s, CH₃); ¹³C NMR δ 171.99, 147.04, 141.53, 137.43, 135.09, 128.37, 128.25, 127.89, 127.82, 127.03, 82.07, 74.88, 73.89, 70.37, 66.96, 25.74, 18.06, -4.65, -5.21. Anal. Calcd for C₂₆H₃₄O₅Si: C, 68.69; H, 7.54. Found: C, 68.49; H, 7.58.

 $(1'R^*, 2'S^*, 3'S^*, 4S^*) - 4 - (2' - Benzyloxy - 1', 3' - dihydroxy - 3' - phenylpropyl) - 2 - buten - 4$ olide [(±)-16]. A solution of BF₃•OEt₂ in CH₃CN (1.0M solution; 0.23 ml, 0.23 mmol) was added dropwiseto a solution of (±)-13 (70.3 mg, 0.15 mmol) and NaI (50.8 mg, 0.34 mmol) in dry CH₃CN (4 ml) at 0°C. Thereaction mixture was stirred for 30 min and poured into cold water (10 ml). After a few drops of 15% Na₂S₂O₃aq. being added (for decolorization), the reaction mixture was diluted with CH₂Cl₂ (20 ml), washed with waterand brine, dried and concentrated to dryness. Chromatography of the residue with CH₂Cl₂ - MeOH = 40 : 1afforded (±)-16 (48.3 mg, 92%) as colorless crystals. mp 120.5–121.5°C (diisopropyl ether - acetone); MS*m/z* 340 (M⁺, 4), 249 (54), 216 (34), 190 (10), 143 (39), 127 (17), 107 (98), 91 (100), 73 (12); IR 3400 (OH), 1755 (CO) cm⁻¹; ¹H NMR δ (CDCl₃+ D₂O) 7.70 (1H, dd, *J* =1.5, 5.9 Hz, C₃-H), 7.39–7.35 (5H, m, Ar-H), 7.34–7.29 (3H, m, Ar-H), 7.26–7.23 (2H, m, Ar-H), 6.10 (1H, dd, *J* =2.0, 5.9 Hz, C₂-H), 5.08–5.00 (2H, m, C₄-H and C₃·-H), 4.52 (1H, d, *J* =10.7 Hz, Bn-H), 4.34 (1H, d, *J* =10.7 Hz, Bn-H), 3.86 (1H, dd, *J* =1.4, 5.8 Hz, C₂·-H) and 3.67 (1H, dd, *J* =1.4, 8.8 Hz, C₁·-H); ¹³C NMR δ 172.83, 156.42, 140.11, 137.05, 128.66, 128.54, 128.32, 128.23, 128.18, 126.24, 121.49, 82.01, 80.85, 73.84, 73.48, 72.15; *Anal.* Calcd for C₂₀H₂₀O₅: C, 70.58; H, 5.92. Found: C, 70.65; H, 5.96. High resolution mass calcd for C₂₀H₂₀O₅ 340.1310, found 340.1320.

 $(1^*R^*, 2^*S^*, 3^*S^*, 4S^*) - 4 - (1^*, 2^*, 3^* - Trihydroxy-3^* - phenylpropyl) - 2 - buten - 4 - olide [(±)-17]. To a solution of (±)-16 (55.2 mg, 0.16 mmol) in dry CH₂Cl₂ (2 ml) was added dropwise a solution of SnCl₄ in CH₂Cl₂ (1.0M solution; 0.32 ml, 0.32 mmol) at rt. After being stirred for 30 min, the reaction mixture was quenched by successive addition of MeOH (0.5 ml), sat. NaHCO₃ aq. (5 drops) and water (3 drops). The reaction mixture was then dried and concentrated to leave the crude triol. Chromatography of the residue with CH₂Cl₂ - MeOH = 30 : 1 provided (±)-17 (40.0 mg, 99%) as colorless crystals. mp 125.5–127.5 °C (hexane - ethyl acetate); MS$ *m* $/z 251 (M⁺+1, 1), 233 (5), 190 (11) 126 (28), 107 (100), 84 (30), 79 (32); IR (KBr) 3320 (OH), 1735 (CO) cm⁻¹; ¹H NMR <math>\delta$ [(CD₃)₂CO + D₂O] 7.88 (1H, dd, *J* =1.5, 5.9 Hz, C₃-H), 7.46–7.44 (2H, m, Ar-H), 7.34–7.31 (2H, m, Ar-H), 7.27–7.23 (1H, m, Ar-H), 6.15 (1H, dd, *J* =2.0, 5.9 Hz, C₂-H), 5.18 (1H, ddd, *J* =1.5, 2.0, 6.8 Hz, C₄-H), 4.77 (1H, d, *J* =7.8 Hz, C₃'-H), 4.00 (1H, dd, *J* =1.0, 6.8 Hz, C₁'-H) and 3.82 (1H, dd, *J* =1.0, 7.8 Hz, C₂'-H); ¹³C NMR δ [(CD₃)₂CO, internal reference; 30.3 ppm] 173.69, 158.13, 144.55, 129.24, 128.50, 128.36, 122.36, 84.76, 75.58, 72.73. Anal. Calcd for C₁₃H₁₄O₅: C, 62.39; H, 5.64.

(1R*,1'R*,3R*,4S*,5R*)-4-Hydroxy-3-(1'-hydroxy-1'-phenylmethyl)-2,6-

dioxabicyclo[3.3.0]octan-7-one [(±)-goniofufurone [(±)-1]]. To a solution of triol (±)-17 (28.9 mg, 0.12 mmol) was added dropwise TBAF (1.0M THF solution; 0.2 ml, 0.2 mmol) at rt. After being stirred for 30 min, the reaction mixture was quenched with sat. NH₄Cl aq. (3 drops) and EtOH (0.5 ml). The reaction mixture was then dried and concentrated to provide the crude material. Chromatography of the residue with CH₂Cl₂ - MeOH - hexane = 30 : 1 : 1 afforded (±)-1 (25.1 mg, 87%) as colorless plates. mp 142.5–144°C (hexane - acetone); MS *m*/z 250 (M⁺, 0.4), 232 (9), 126 (80), 107 (100), 82 (59), 79 (38); IR (KBr) 3400 (OH), 1755 (CO) cm⁻¹; ¹H NMR δ 7.44–7.33 (5H, m, Ar-H), 5.18 (1H, dd, *J* =2.9, 4.9 Hz, C₁·-H), 5.10 (1H, dd, *J* =3.9, 5.9 Hz, C₁-H), 4.86 (1H, dd, *J* =1.5, 3.9 Hz, C₅-H), 4.40 (1H, dt, *J* =1.5, 2.9 Hz, C₄-H), 4.22 (1H, d, *J* =2.9 Hz, C₄-OH), 4.09 (1H, dd, *J* =2.9, 4.9 Hz, C₃-H), 2.96 (1H, d, *J* =2.9 Hz, C₁·-OH), 2.74 (1H, dd, *J* =5.9, 18.6 Hz, C₈-H), 2.67 (1H, d, *J* =18.6 Hz, C₈-H); ¹³C NMR δ [(CD₃)₂CO] 176.57, 144.06, 129.27, 128.61, 128.16, 89.04, 85.48, 78.53, 75.28, 72.73, 36.97. *Anal.* Calcd for C₁₃H₁₄O₅: C, 62.39; H, 5.64. Found: C, 62.12; H, 5.94.

Methyl (2R,3R)-2-Benzyloxy-3-*tert*-butyldimethylsilyloxy-3-phenylpropanoate (10). According to the procedure that described for conversion of (\pm) -9 into (\pm) -10, optically active 10 (187 mg, 71%, *anti* : syn = 95 : 5) was obtained from optically active 9 (187 mg, 0.65 mmol, *anti* : syn = 95 : 5), TBSOTF (0.37 ml, 1.31 mmol), and DMAP (120 mg, 0.98 mmol). Optically active 10: a colorless oil; Anal. Calcd for C₂₃H₃₂O₄Si: C, 68.96; H, 8.05. Found: C, 69.11; H, 7.99.

(-)-(1'S,2'S,3'R,4R)-4-(2'-Benzyloxy-3'-*tert*-butyldimethylsilyloxy-1'-hydroxy-3'phenylpropyl)-2-buten-4-olide [(-)-13]. According to the procedure that described for conversion of (\pm)-11 into (\pm)-13, (-)-13 (116 mg, 54%) was obtained from optically active 10 (190 mg, 0.47 mmol), 8 (150 mg, 0.96 mmol). (-)-13: a colorless oil; $[\alpha]_D^{17}$ -3.9° (c 0.32, CHCl₃); Anal. Calcd for C₂₆H₃₄O₅Si: C, 68.69; H, 7.54. Found: C, 68.75; H, 7.58.

Conversion of Optically Active 5 into (-)-13. According to the procedure that described for conversion of (\pm) -9 into (\pm) -10, optically active 5 (120 mg, 0.35 mmol, anti : syn = 95 : 5) was treated with TBSOTf (0.2 ml, 0.87 mmol) and DMAP (85.0 mg, 0.70 mmol) to give the O-TBS derivative (138 mg, 86%, anti : syn = 95 : 5): a colorless oil; MS m/z 443 (M⁺-CH₃, 0.2), 401 (30), 352 (51), 285 (21), 239 (86), 222 (100), 193 (100), 91 (100), 57 (54); IR 1665 (CO); ¹H NMR δ 7.32–7.20 (8H, m, Ar-H), 7.05-7.03 (2H, m, Ar-H), 4.96 (0.05H, d, J = 4.9 Hz, C₃-H), 4.91 (0.95H, d, J = 6.4 Hz, C₃-H), 4.60 (0.95H, d, J = 12.2 Hz, Bn-H), 4.59 (0.05H, d, J =11.7 Hz, Bn-H), 4.36 (0.95H, d, J =12.2 Hz, Bn-H), 4.28 (0.05H, d, J =11.7 Hz, Bn-H), 3.86 (0.95H, d, J = 6.4 Hz, C₂-H), 3.80 (0.05H, d, J = 4.9 Hz, C₂-H), 1.47 (0.45H, s, t-Bu), 1.46 (8.55H, s, t-Bu), 0.85 (0.45H, s, t-Bu), 0.84 (8.55H, s, t-Bu), 0.01 (2.85H, s, CH₃), 0.00 (0.15H, s, CH₃), -0.17 (0.15H, s, CH₃), -0.23 (2.85H, s, CH₃); ¹³C NMR δ (for anti - product) 200.74, 141.03, 137.20, 128.12, 127.78, 127.74, 127.65, 127.56, 127.52, 88.97, 75.91, 73.10, 47.45, 27.79, 25.76, 18.07, -4.65, -5.15. Anal. Calcd for C₂₆H₃₈O₃SSi: C, 68.08; H, 8.35. Found: C, 68.19; H, 8.34. To a solution of the crude O-TBS derivative (138 mg, 0.30 mmol) in dry toluene (2 ml) was added dropwise a solution of DIBAL-H in toluene (1.0 M solution; 0.66 ml, 0.66 mmol) at 0°C. The reaction mixture was stirred for 30 min, quenched with sat. sodium potassium tartrate aq., passed through celite, and diluted with diethyl ether (20 ml). The organic layer was washed with water, dried, and concentrated to dryness. The residue was passed through an alumina pad (hexane - acetone = 10: 1) to give the optically active aldehyde 11 (87.6 mg, 0.24 mmol) which was immediately exposed to 8 (110 mg, 0.71 mmol) to provide (-)-13 (81.3 mg, 59%).

(+)-(1'S,2'R,3'R,4R)-4-(2'-Benzyloxy-1',3'-dihydroxy-3'-phenylpropyl)-2-buten-4olide [(+)-16]. According to the procedure that described for conversion of (±)-13 into (±)-16, (+)-16 (70.8 mg, 94%) was obtained from (-)-13 (101 mg, 0.22 mmol), NaI (73 mg, 0.49 mmol) and a solution of BF₃•OEt₂ in CH₃CN (1.0M solution; 0.33 ml, 0.33 mmol). (+)-16: colorless needles. mp 103-104°C (diisopropyl ether - acetone); $[\alpha]_D^{22}$ +25.5° (c 0.35, CHCl₃). Anal. Calcd for C₂₀H₂₀O₅: C, 70.58; H, 5.92. Found: C, 70.54; H, 5.92. High resolution mass calcd for C₂₀H₂₀O₅ 340.1310, found 340.1326.

(+)-(1'S,2'R,3'R,4R)-4-(1',2',3'-Trihydroxy-3'-phenylpropyl)-2-buten-4-olide [(+)-17]. According to the procedure that described for conversion of (±)-16 into (±)-17, (+)-17 (17.0 mg, 96%) was obtained from (+)-16 (24.0 mg, 0.07 mmol) and a solution of SnCl₄ in dry CH₂Cl₂ (1.0M solution; 0.14 ml, 0.14 mmol). (+)-17: colorless needles. mp 141–143°C (hexane - ethyl acetate); $[\alpha]_D^{24}$ +99.8° (*c* 0.30, EtOH). Anal. Calcd for C₁₃H₁₄O₅: C, 62.39; H, 5.64. Found: C, 62.24; H, 5.64. (+)-Goniofufurone [(+)-1]. According to the procedure that described for conversion of (±)-17 into (±)-goniofufurone [(±)-1], (+)-goniofufurone (10.0 mg, 86%) was obtained from (+)-triol 17 (11.6 mg, 0.04 mmol) and TBAF (1.0M THF solution; 0.07 ml, 0.07 mmol). (+)-goniofufurone: colorless crystals. mp 150–152°C (hexane - ethyl acetate) (lit.^{1c} mp 152–154 °C); $[\alpha]_D^{23}$ +8.9° (c 0.5, EtOH) [lit.^{1c} $[\alpha]_D^{22}$ +9.0° (c 0.5, EtOH)]. Anal. Calcd for C₁₃H₁₄O₅: C, 62.39; H, 5.64. Found: C, 62.29; H, 5.69.

(Z)-(2'S,3'R)-4-(2'-Benzyloxy-3'-tert-butyldimethylsilyloxy-3'-phenylpropylidene)-2buten-4-olide [(Z)-18]. To a solution of (-)-13 (45.3 mg, 0.10 mmol) in CH₂Cl₂ (1.5 ml) was added triethylamine (0.04 ml) and methanesulfonyl chloride (0.02 ml) at -60°C, and the mixture was stirred for 30 min at the same temperature. The reaction mixture was quenched by addition of sat. NH₄Cl aq. and extracted with CH₂Cl₂. The organic layer was washed with brine, dried, and concentrated to dryness. Diisopropylamine (81.3 mg, 0.80 mmol) was added to a solution of the crude mesylate in CH₂Cl₂ (3.0 ml) and the mixture was stirred for 40 min at rt. The reaction mixture was quenched by sat. NH₄Cl aq. and extracted with CH₂Cl₂. The organic layer was washed with brine, dried and concentrated to dryness. Chromatography of the residue with hexane ethyl acetate = 20 : 1 gave a mixture of (Z)- and (E)-18 (40.3 mg, 93%, Z : E = 94 : 6). (Z)-18: IR 1785, 1755(CO) cm⁻¹: ¹H NMR δ 7.33-7.22 (8H, m, Ar-H), 7.35 (1H, d, J =5.4 Hz, C₃-H), 7.12-7.11 (2H, m, Ar-H), 6.19 (1H, d, J =5.4 Hz, C₂-H), 5.37 (1H, d, J =9.8 Hz, C₁-H), 4.80 (1H, d, J =5.4 Hz, C₃-H), 4.56 (1H, dd, J =9.8, 5.4 Hz, C₂-H), 4.47 (1H, d, J =10.7 Hz, Bn-H), 4.33 (1H, d, J =10.7 Hz, Bn-H), 0.83 (9H, s, t-Bu), 0.02 (3H, s, CH₃), -0.15 (3H, s, CH₃); ¹³C NMR δ 169.45, 151.61, 143.23, 141.40, 137.97, 128.14, 127.85, 127.60, 127.51, 126.86, 120.52, 113.75, 78.65, 76.80, 71.72, 25.64, 18.10, -4.76, -4.92.

(+)-(Z)-(2'S,3'R)-4-(2'-Benzyloxy-3'-hydroxy-3'-phenylpropylidene)-2-buten-4-olide [(+)-(Z)-19]. A solution of TBAF - HF in THF (1.0M solution; 2.0 ml, 2.0 mmol) was added dropwise to a solution of a mixture of optically active (Z)- and (E)-18 (28.4 mg, 0.07 mmol, Z : E = 94 : 6) in THF (1.0 ml) at rt. After stirring for 19h, the reaction mixture was poured into water and extracted with ethyl acetate. The organic layer was washed with water and brine, dried and concentrated to dryness. Chromatography of the residue with hexane - ethyl acetate = 10 : 1 afforded (+)-(Z)-19 (16.7 mg, 73% overall yield from 13) as colorless crystals. mp 103-105°C (hexane - ethyl acetate); $[\alpha]_{D}^{25}$ +35.3° (*c* 0.46, CHCl₃); CIMS *m/z*: 323 (M⁺+1, 25), 305 (45), 259 (7), 217 (100), 199 (22), 107 (76), 91(43); IR 1780, 1755(CO) cm⁻¹; ¹H NMR δ 7.35-7.22 (11H, m, Ar-H and C₃-H), 6.16 (1H, d, J =5.4 Hz, C₂-H), 5.35 (1H, d, J =9.3 Hz, C₁-H), 5.02 (1H, d, J =3.9 Hz, C₃-H), 4.76 (1H, dd, J =9.3, 3.9 Hz, C₂-H), 4.60 (1H, d, J =11.2 Hz, Bn-H), 4.50 (1H, d, J =11.2 Hz, Bn-H), 2.70 (1H, brs, OH); ¹³C NMR δ 169.13, 151.93, 143.18, 138.99, 137.59, 128.45, 128.18, 127.92, 127.87, 127.82, 126.33, 120.83, 111.23, 77.16, 75.20, 71.65. Anal. Calcd for C₂₀H₁₈O₄: C, 74.52; H, 5.63. Found C, 74.57, H, 5.51.

(+)-(Z)-(2'S,3'R)-4-(2',3'-Dihydroxy-3'-phenylpropylidene)-2-buten-4-olide [(+)goniobutenolide A (2)]. To a solution of (+)-19 (11.6 mg, 0.04 mmol) in dry CH₂Cl₂ (1.0 ml) was added dropwise a solution of TiCl₄ in CH₂Cl₂ solution (1.0M solution; 0.1 ml, 0.1 mmol) at rt. After being stirred for 30 min, the reaction mixture was quenched by sat. NaHCO₃ aq. and extracted with CH₂Cl₂. The organic layer was washed with brine, dried and concentrated to dryness. Chromatography of the residue with hexane - ethyl acetate = 2 : 1 gave (+)-2 (goniobutenolide A) (7.9 mg, 95%) as a yellow oil; $[\alpha]_D^{25} + 183^\circ$ (c 0.17, CHCl₃) [lit.^{3k,1} [α]_D²⁷ +187° (*c* 0.4, CHCl₃)]; CIMS *m/z* 233 (M⁺+1, 43), 231 (30), 215 (100), 199 (20), 149 (5), 127 (87), 107 (60); IR 3400 (OH), 1780, 1755 (CO) cm⁻¹; ¹H NMR δ 7.38-7.27 (6H, m, Ar-H and C₃-H), 6.17 (1H, d, *J* =5.9 Hz, C₂-H), 5.30 (1H, d, *J* =8.3 Hz, C₁-H), 5.01 (1H, dd, *J* =8.3, 4.4 Hz, C₂-H), 4.95 (1H, d, *J* =4.4 Hz, C₃-H), 2.61 (2H, brs, OH); ¹³C NMR δ 169.25, 150.46, 143.63, 139.05, 128.32, 128.03, 126.42, 120.43, 112.97, 75.96, 70.62.

(*E*)-(2'*S*,3'*R*)-4-(2'-Benzyloxy-3'-*tert*-butyldimethylsilyloxy-3'-phenylpropylidene)-2buten-4-olide [(*E*)-18]. Mesylation of (-)-13 (38.8 mg, 0.09 mmol) under the similar condition described for the preparation of (*Z*)-18 provided the crude mesylate. To a solution of the crude mesylate in THF (3.0 ml) was added 10% K₂CO₃ aq. (1.5 ml) and the mixture was stirred at rt for 2 h. The reaction mixture was diluted with sat. NH₄Cl aq. and extracted with ethyl acetate. The organic layer was washed with brine, dried and concentrated to dryness. Chromatography of the residue with hexane - ethyl acetate = 20 : 1 gave (*Z*)- and (*E*)-18 (27.8 mg, 75%, *Z* : *E* = 15 : 85). (*E*)-18: IR 1790, 1760(CO) cm⁻¹; ¹H NMR δ 7.31-7.24 (8H, m, Ar-H), 7.22 (1H, dd, *J* =5.4, 1.0 Hz, C₃-H), 7.04-7.01 (2H, m, Ar-H), 6.11 (1H, dd, *J* =5.4, 2.0 Hz, C₂-H), 5.79 (1H, ddd, *J* =8.8, 2.0, 1.0 Hz, C₁-H), 4.78 (1H, d, *J* =5.9 Hz, C₃-H), 4.50 (1H, d, *J* =11.8 Hz, Bn-H), 4.27 (1H, d, *J* =11.8 Hz, Bn-H), 4.06 (1H, dd, *J* =8.8, 5.9 Hz, C₂-H), 0.82 (9H, s, *t*-Bu), 0.00 (3H, s, CH₃), -0.14 (3H, s, CH₃) ; ¹³C NMR δ 169.33, 152.13, 141.49, 140.47, 137.36, 128.34, 128.00, 127.71, 127.66, 127.60, 126.88, 120.85, 113.26, 79.59, 77.20, 71.02, 25.66, 18.08, -4.81, -4.92.

(-)-(*E*)-(2'S,3'*R*)-4-(2'-Benzyloxy-3'-hydroxy-3'-phenylpropylidene)-2-buten-4-olide [(-)-(*E*)-19]. According to the procedure that described for conversion of (*Z*)-18 into (*Z*)-19, a mixture of optically active (*Z*)- and (*E*)-18 (13.5 mg, 0.03 mmol, *Z* : *E* = 15 : 85) was treated with TBAF-HF to afford (-)-(*E*)-19 (8.3 mg, 62% overall yield from 13) as colorless crystals. mp 85-87°C (hexane - ethyl acetate); $[\alpha]_{D}^{25}$ -1.0° (*c* 0.27, CHCl₃); CIMS *m/z* 323 (M⁺+1, 25), 305 (29), 259 (11), 249 (5), 217 (100), 199 (13), 125 (10), 107 (34), 91 (34); IR 1790, 1760 (CO) cm⁻¹; ¹H NMR δ 7.36-7.20 (10H, m, Ar-H), 7.11 (1H, dd, *J* =5.4, 1.0 Hz, C₃-H), 6.09 (1H, dd, *J* =5.4, 2.0 Hz, C₂-H), 5.75 (1H, ddd, *J* =9.3, 2.0, 1.0 Hz, C₁-H), 5.00 (1H, dd, *J* =4.4, 2.9 Hz, C₃-H), 4.65 (1H, d, *J* =11.7 Hz, Bn-H), 4.42 (1H, d, *J* =11.7 Hz, Bn-H), 4.25 (1H, dd, *J* =9.3, 4.4 Hz, C₂-H), 2.59 (1H, d, *J* =2.9 Hz, OH); ¹³C NMR δ 169.06, 152.51, 139.75, 139.19, 137.00, 128.57, 128.30, 128.07, 127.96, 127.82, 126.49, 121.33, 110.94, 78.26, 75.83, 70.94. *Anal.* Calcd for C₂₀H₁₈O₄: C, 74.52; H, 5.63. Found C, 74.30, H, 5.63.

(-)-(*E*)-(2'*S*, 3'*R*)-4-(2',3'-Dihydroxy-3'-phenylpropylidene)-2-buten-4-olide [(-)goniobutenolide B (3)]. According to the procedure that described for conversion of (+)-(*Z*)-19 into (+)-2, (-)-(*E*)-19 (5.5 mg, 0.01 mmol) was treated with TiCl₄ to afford (-)-3 (goniobutenolide B) (3.9 mg, 98%) as colorless crystals. mp 146-148°C (hexane - ethyl acetate) (lit.^{3k,1} 148-149°C); $[\alpha]_D^{19}$ -109° (*c* 0.06, CHCl₃) [lit.^{3k,1} $[\alpha]_D^{27}$ -112° (*c* 0.2, CHCl₃)]; CIMS *m*/*z* 233 (M⁺+1, 93), 231 (21), 215 (84), 127 (100), 107 (55), 105 (9); IR 3450 (OH), 1790, 1755 (CO) cm⁻¹; ¹H NMR δ 7.50 (1H, d, *J* =5.4 Hz, C₃-H), 7.38-7.29 (5H, m, Ar-H), 6.12 (1H, dd, *J* =5.4, 2.0 Hz, C₂-H), 5.79 (1H, dd, *J* =7.3, 2.0 Hz, C₁-H), 4.88 (1H, d, *J* =4.4 Hz, C₃-H), 4.64 (1H, dd, *J* =7.3, 4.4 Hz, C₂-H), 2.59 (1H, brs, OH), 2.52 (1H, brs, OH); ¹³C NMR δ 169.27, 151.73, 140.68, 138.96, 128.62, 126.54, 121.11, 112.36, 77.20, 72.15; *Anal.* Calcd for C₁₃H₁₂O₄: C, 67.23; H, 5.21. Found C, 66.85, H, 5.35.

References and Notes

- (a) El-Zayat, A. A. E.; Ferrighi, N. R.; McKenzie, T. G.; Byrn, S. R.; Cassady, J. M.; Chang, C.-J.; McLaughlin, J. L. *Tetrahedron Lett.* 1985, 26, 955. (b) Alkofahi, A.; Ma, W.-W.; Mckenzie, A. T.; Byrn, S. R.; McLaughlin, J. L. J. Nat. Prod. 1989, 52, 1371. (c) Fang, X.-P.; Anderson, J. E.; Chang, C.-J.; Fanwick, P. E.; McLaughlin, J. L. J. Chem. Soc., Perkin Trans. 1 1990, 1655. (d) Fang, X.-P.; Anderson, J. E.; Chang, C.-J.; McLaughlin, J. L. Tetrahedron 1991, 47, 9751. (e) Fang, X.-P.; Anderson, J. E.; Chang, C.-J.; McLaughlin, J. L.; Fanwick, P. E. J. Nat. Prod. 1991, 54, 1034.(f) Wu, Y.-C.; Chang, F.-R.; Duh, C.-Y.; Wang, S.-K.; Wu, T.-S. Phytochem. 1992, 31, 2851.
- 2. Fang, X.-P.; Anderson, J. E.; Qiu, X.-X.; Kozlowski, J. F.; Chang, C.-J.; McLaughlin, J. L. *Tetrahedron* 1993, 49, 1563.
- 3. (a) Shing, T. K. M.; Tsui, H.-C. J. Chem. Soc., Chem. Commun. 1992, 432. Shing, T. K. M.; Tsui, H.-C.; Zhou, Z.-H. ibid 1992, 810. Idem. Tetrahedron 1992, 48, 8659. (b) Murphy, P. J. J. Chem. Soc., Chem. Commun. 1992, 1096. (c) Gracza, T.; Jäger, V. Synlett 1992, 191. (d) Saito, S.; Harunari, T.; Shimamura, N.; Asahara, M.; Morikawa, T. ibid 1992, 325. (e) Prakash, K. R. C.; Rao, S. P. Tetrahedron 1993, 49, 1505. (f) Tsubuki, M.; Kanai, K.; Honda, T. Synlett 1993, 653. (g) Ye, J.; Bhatt, R. K.; Falck, J. R. Tetrahedron Lett. 1993, 34, 8007. (h) Shing, T. K. M.; Tsui, H.-C. Tetrahedron : Asymmetry 1994, 5, 1269. (i) Gracza, T.; Jäger, V. Synthesis 1994, 1359. (j) Yang, Z.-C.; Zhou, W.-S. Tetrahedron 1995, 51, 1429. (k) Shing, T. K. M.; Tsui, H.-C.; Zhou, Z.-H. J. Org. Chem. 1995, 60, 3121. (i) Shing, T. K. M.; Tai, V. W.-F.; Tsui, H.-C. J. Chem. Soc., Chem. Commun. 1994, 1293. (m) Xu, D.; Sharpless, K. B. Tetrahedron Lett. 1994, 35, 4685. (n) Ko, S. Y.; Lerpiniere, J. ibid 1995, 36, 2101 (o) Gesson, J.-P.; Jacquesy, J.-C.; Mondon, M. ibid 1987, 28, 3949. Idem. ibid 1987, 28, 3945. Tadano, K.; Ueno, Y.; Ogawa, S. Chem. Lett. 1988, 111. Gillhouley, J. G.; Shing, T. K. M. J. Chem. Soc., Chem. Commun. 1988, 976. Gesson, J.-P.; Jacquesy, J.-C.; Mondon, M. Tetrahedron 1989, 45, 2627. Ueno, Y.; Tadano, K.; Ogawa, S.; McLaughlin, J. L.; Alkofahi, A. Bull. Chem. Soc. Jpn. 1989, 62, 2328. Kang, S.-H.; Kim, W.-J. Tetrahedron Lett. 1989, 30, 5915. Shing, T. K. M.; Zhou, Z.-H.; Mak, T. C. W. J. Chem. Soc., Perkin Trans. I 1992, 1907. Shing, T. K. M.; Zhou, Z.-H. Tetrahedron Lett. 1992, 33, 3333. Tsubuki, M.; Kanai, K.; Honda, T. J. Chem. Soc., Chem. Commun. 1992, 1640. Shing, T. K. M.; Tsui, H.-C.; Zhou, Z.-H. Tetrahedron Lett. 1993, 34, 691. Somfai, P. Tetrahedron 1994, 50, 11315. Friesen, R. W.; Bissada, S. Tetrahedron Lett. 1994, 35, 5615. Surivet, J.-P.; Goré, J.; Vatèle, J. M. Tetrahedron Lett. 1996, 37, 371.
- (a) Mukai, C.; Kim, I. J.; Hanaoka, M. Tetrahedron: Asymmetry 1992, 3, 1007. (b) Mukai, C.; Kim, I. J.; Furu, E.; Hanaoka, M. Tetrahedron 1993, 49, 8323.
- 5. Mukai, C.; Miyakawa, M.; Hanaoka, M. Synlett 1994, 165.
- 6. A part of this work on a total synthesis of (+)-1 was published in a preliminary communication: Mukai, C.; Kim, I. J.; Hanaoka, M. Tetrahedron Lett. 1993, 34, 6081.
- (a) Jefford, C. W.; Jaggi, D.; Boukouvalas, J. Tetrahedron Lett. 1987, 28, 4037. (b) Jefford, C. W.; Sledeski, A. W.; Boukouvalas, J. J. Chem. Soc., Chem. Commun. 1988, 364.

- 8. Crystal data: C₂₆H₃₄O₅Si, M= 454.64, orthorhombic, a= 20.9 (2) Å, b= 37.82 (9) Å, c= 6.63 (9) Å, V= 5242 Å³, Z= 8, Dc= 1.152 g/cm³, space group Pbca (#61), μ (MoKα) = 1.15 cm⁻¹. A colorless needle, ca. 0.2 x 0.2 x 0.5 mm, was mounted on a glass fiber. All measurements were made on a Rigaku AFC5S diffractometer. The cell dimensions and intensities were refined by the least-squares method, using 25 reflections on the diffractometer with Mo-Kα radiation with ω-scan mode for 2θ less than 45°. The structure was solved by direct method (MITHRIL method). The final cycle of full-matrix least-squares refinement was based on 3182 observed reflections. The final R value was 0.054.
- 9. Vankar, Y. D.; Rao, C. T. J. Chem. Res. Synop. 1985, 232.
- 10. The authors are grateful to Professor J. L. McLaughlin, Pudue University, for generous supply of the copies of ¹H-and ¹³C-NMR spectra of natural (+)-goniofufurone.

(Received in Japan 29 February 1996; accepted 15 March 1996)