Synthesis of an analog of (+)-goniopypyrone from 3-*O*-benzyl-1,2-*O*-isopropylidene-5-*C*-phenyl-α-*D*-gluco-pentofuranose

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8,9-Dimethoxy-7-epi-goniopypyrone, an analog of (+)-goniopypyrone, was synthesized from 3-*O*-benzyl-1, 2-*O*-isopropylidene-5-*C*-phenyl-α-*D*-gluco-pentofuranose (3).

Keywords Pyrans, styryl lactone, cytotoxicity

Introduction

Since they were isolated from *Goniothalamus giganteus*[1] and characterized by the Mclaughlin's group, the styryl lactones have been shown to possess marginally to significantly cytotoxic against human tumors.[2] A main structural feature of these natural products is that they all contain the polyol functionality fused into a γ- or δ-lactone moiety. Due to their bioactivity and interesting heterocyclic skeletons, much attention has been paid to the syntheses of these styryl lactones and its analogs.[3-5]

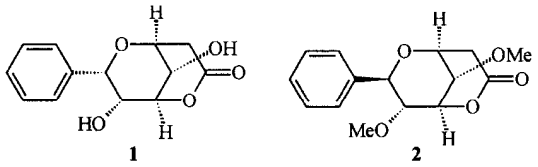

Fig. 1 Structures of (+)-goniopypyrone and 8,9-dimethoxy-7-epi-goniopypyrone.

Here we would like to report the synthesis of an analog of the most cytotoxic (+)-goniopypyrone in the styryl lactone family, 8, 9-dimethoxy-7-epi-goniopypyrone, starting from a derivative of (+)-glucose (**3**).[6,7]

Results and discussion

Based on the retrosynthetic analysis (Scheme 1) we planed to construct δ-lactone ring using an intramolecular Reformatsky reaction promoted by Cp_2TiCl_2 (cat.).[8] We found that 3-*O*-benzyl-1,2-*O*-isopropylidene-5-*C*-phenyl-α-*D*-gluco-pentafuranose (**3**) should be an appropriate starting material, which could be prepared from *D*-glucose[6,7] by known method because its three chiral carbons could fit into the target molecule without any configurational changes. The key of present work is how to open the furanose ring to release the aldehyde group and to choose proper protective groups for the polyols. In order to avoid potential troubles caused by unstable protective groups we chose to mask the hydroxyl in 8,9-diol in 7-epi-(+)-goniopypyrone (**1**) as methyl ethers.

The synthetic route is shown in Scheme 2. After the hydroxyl group of **3** was protected as allyl ether[2] compound **4** was reacted with 1,3-propanedithiol in the presence of $BF_3 \cdot Et_2O$ (cat.) in CH_2Cl_2 to give the 1, 3-dithian **5** in 65% yield.[9] Two newly formed hydroxyl groups were converted to dimethoxy product **6** in 66% yield.[10] The *S*, *S*-acetal of compound **6** was cleaved with HgO and $HgCl_2$[11] in aqueous acetone to form the aldehyde **7** which could be directly used in next step without purification.

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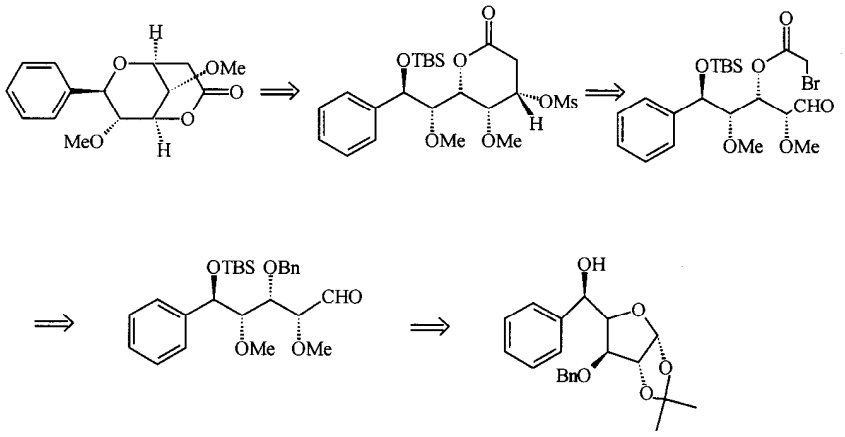
Scheme 1



We first tried to remove the benzyl protecting group of compound **7** by hydrogenation on Pd/C without masking of the aldehyde functionality, but the product was rather complicated. Therefore the aldehyde was then protected as dimethyl acetal[12] **8**. The yield of the two steps (from **6** to **8**) was 78%. Before debenzylation allyl group of **8** was cleaved by reaction of **8** with $Pd(PPh_3)_4$ and Bu_3SnH in the presence of $ZnCl_2$[13] in THF to give **9** in 96% yield. Treatment of **9** with *t*-butyldimethylsilyl chloride in the presence of imidazole in DMF provided **10** in 89% yield. Compound **3** could be protected as TBDMS ether too, but in this case the furan ring could not be opened by 1,3-propylenedithiol and $BF_3 \cdot Et_2O$, only a product of losing TBDMS (53%) was given.

Compound **10** was debenzylated by hydrogenation on Pd/C (10%, cat.) to give **11** in 90% yield. Reaction of **11** with α-bromoacetyl bromine in DMF at 0℃ gave **12** in 65% yield. After cleavage of the acetal, the cyclization precursor **13** underwent intramolecular Reformatsky reaction[8] mediated by Cp_2TiCl_2(cat.) in THF at room temperature to provide a pair of diastereoisomeric δ-lactones **14** (**a** + **b**) (when only Zn was used, the result of reaction was unsatisfactory). Compounds **14a** and **14b** were difficult to be separated from each other by chromatography at this stage. But the ratio of **a** to **b** was shown to be 2.5 to 1 by ^1H NMR (300 MHz). The mixture of **14a** and **14b** was mesylated to give **15**(**a** + **b**), which were easily separated by flash chromatography giving **15a** as the major product (in 65% yield). Treatment of **15a** with TBAF[14] in THF at room temperature provided the target molecule **1** in 84% yield. The structure of **1** was established by IR, ESIMS, ^1H NMR and NOESY.

Experimental

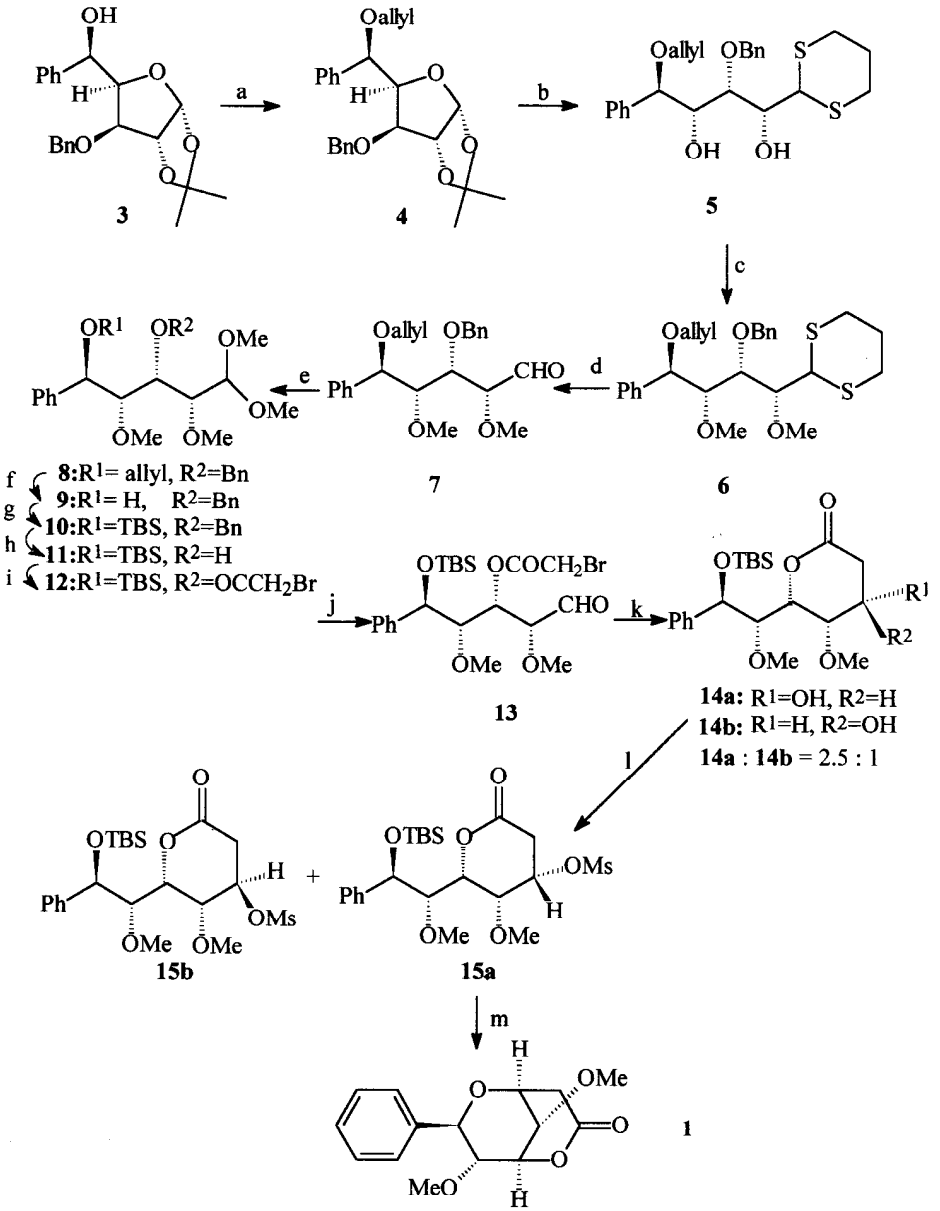
All solvents were purified before use according to the standard method. The commercially available reagents were used as received without further purification. IR spectra were measured in $CHCl_3$ on a Shimadzu IR-440 infrared spectrophotometer. ^1H NMR spectra were recorded on a Brucker AMX-300(300MHz) spectrometer in $CDCl_3$ and chemical shifts were reported in δ (TMS as internal standard). Elemental analyses were performed on Foss-Heraeus Vario EL instrument. Optical rotations were recorded with a Perkin-Elmer 241MC polarimeter at the sodium D line. Mass spectra were recorded using HP5984A mass spectrometer.

(1R,2R,3R,4R,5R)-5-O-Allyl-3-O-benzyl-5-C-phenyl-1,2-O-isopropylidene-α-D-gluco-pentofuranose (**4**)

To a stirred suspended NaH (80%, 246 mg, 8.2 mmol) in THF (20 mL) was added dropwise a solution of **3** (1.95 g, 5.47 mmol) in THF at 0℃. After the mixture was stirred at room temperature for 0.5 h, allyl bromine (0.7 mL, 8.2 mmol) was added dropwise and the solution was stirred at 70℃ for further 1 h. The reaction was quenched with CH_3OH (5 mL) and the mixture was filtered through Celite. Evaporation of filtrate gave a residue which was dissolved in EtOAc (20 mL) and washed with water and brine. Solvent removal followed by flash chromatography (EtOAc-petroleum ether, 1:5) gave **4** (1.36 g, 63%) as a colorless oil. $[\alpha]_D^{20}$ +37.0(*c* 1.13, MeOH). ν_{max}: 1648, 1497, 1455 cm^{-1}. δ_H: 1.32(s, 3H), 1.50(s, 3H), 3.78—3.98

(AB, J = 5.2 Hz, 2H), 4.30(d, J = 3.0 Hz, 1H), 4.38(dd, J = 3.0, 9.3 Hz, 1H), 4.65—4.83(m, 4H), 5.14—5.31(m, 2H), 5.80—5.90(m, 1H), 5.95(d, J = 3.6 Hz, 1H), 7.30—7.50(m, 10H). *m/z* (%): 396(M^+), 338($M^+ - Me_2CO$, 10.60), 305(M^+-$PhCH_2$, 5.89), 91($PhCH_2^+$, 100). Anal. $C_{24}H_{28}O_5$. Calcd: C, 72.70; H, 7.12; Found: C, 72.85; H, 7.18.

Scheme 2



Conditions and reagents: (a) allyl bromide, THF, NaH, 1 h, 63%; (b) $(HSCH_2)_2CH_2$, $BF_3 \cdot Et_2O$, CH_2Cl_2, overnight, 65%; (c) CH_3I, NaH, THF, overnight, 66%; (d) HgO, $HgCl_2$, acetone, 45℃, 3 h; (e) $HC(OCH_3)_3$, PTSA(cat.), MeOH, reflux, overnight, 78% from (c) to (e); (f) $Pd(PPh_3)_4$, Bu_3SnH, $ZnCl_2$, THF, r.t., 1 h, 96%; (g) TBDMSCl, imidazole, DMF, r.t., overnight, 89%; (h) Pd/C 10% (cat.), EtOAc, H_2, r.t., 2 h, 90%; (i) $BrCOCH_2Br$, DMF, 0℃, 2 h, 62%; (j) PTSA(cat.), acetone, r.t., overnight; (k) Cp_2TiCl_2(cat.), Zn(cat.), THF, 2 h, 44% from **12** to **14a**+**b**; (l) MsCl, pyridine, 0℃, 3 h, 65%; (m) TBAF, THF, r.t., 2 h, 84%.

(2R,3S,4R,5R)-5-O-Allyl-3-O-benzyl-2,4-dihydroxy-5-C-phenyl pentanal propanedithiol 1,3-acetal (**5**)

To a stirred solution of **4** (272 mg, 0.686 mmol) in dry CH_2Cl_2 (10 mL) were added 1,3-propanedithiol (0.15 mL, 1.5 mmol) and $BF_3 \cdot Et_2O$ (0.01 mL, cat.). The solution was stirred at room temperature overnight and washed with the saturated $NaHCO_3$ (10 mL). The organic layer was dried (Na_2SO_4) and filtered. Solvent removal followed by flash chromatography (EtOAc-petroleum ether, 1:2) afforded **5** (200 mg, 65%) as a colorless oil. $[\alpha]_D^{20}$ - 20.7 (*c* 1.08, MeOH). ν_{max}: 3456, 1647, 1496, 1454 cm^{-1}. δ_H: 1.90—2.01(m, 2H), 2.85—3.00(m, 4H), 3.68—3.98(AB, *J* = 5.8 Hz, 2H), 3.95—4.00(m, 3H), 4.35—4.40(m, 2H), 4.78(AB, *J* = 11.3 Hz, 1H), 4.92(AB, *J* = 11.3 Hz, 1H), 5.15—5.35(m, 1H), 7.30—7.50(m, 10H). *m/z* (%): 327 (M^+ - $C_4H_7S_2$), 251 ($C_{13}H_{15}OS_2^+$, 23.46), 119 ($C_4H_7S_2^+$, 5.19), 91 ($PhCH_2^+$, 100). Anal. $C_{24}H_{30}O_4S_2$. Calcd: C, 64.57; H, 6.37. Found: C, 64.68; H, 6.67.

(2R,3S,4R,5R)-5-O-Allyl-3-O-benzyl-2,4-dimethoxy-5-C-phenyl pentanal 1,3-propanedithiol acetal (**6**)

CH_3I (0.06 mL, 1 mmol) was added dropwise to a stirred mixture of **5** (200 mg, 0.45 mmol) and NaH (150 mg, 80%, 4.5 mmol) in THF (20 mL). Then the solution was stirred at room temperature overnight. A saturated solution of $Na_2S_2O_3$ (5 mL) and water (10 mL) were added and extracted with EtOAc (3 × 10 mL). The combined organic extracts were washed with brine and dried (Na_2SO_4). The mixture was filtered and solvent was removed *in vacuo*. The residue was purified by flash chromatography (EtOAc-petroleum ether, 1:5) to gave **6** (140 mg, 66%) as a colorless oil. $[\alpha]_D^{20}$ - 18.1 (*c* 1.62, MeOH). ν_{max}: 1647, 1496, 1454, 1452 cm^{-1}. δ_H: 2.00—2.01(m, 2H), 2.78—3.00(m, 4H), 2.88(s, 3H), 3.38(dd, *J* = 3.2, 8.3 Hz, 1H), 3.42(s, 3H), 3.52—3.85(m, 2H), 3.75(dd *J* = 3.8, 7.4 Hz, 1H), 4.13—4.13(m, 2H), 4.45(d, *J* = 7.4 Hz, 1H), 4.70(AB, *J* = 11.3 Hz, 1H), 4.88(AB, *J* = 11.3 Hz, 1H), 5.06—5.25(m, 2H), 5.78—5.89(m, 1H), 7.25—7.48(m, 10H). *m/z*(%): 473(M^+ - 1), 355($C_4H_7S_2^+$, 1.46), 251 ($C_{13}H_{15}OS_2^+$, 100), 119 ($C_4H_7S_2^+$, 42.38), 91 ($PhCH_2^+$, 96.30). Anal. $C_{26}H_{34}O_4S_2$. Calcd: C, 65.82; H, 7.17. Found: C, 66.00; H, 7.70.

(2R,3S,4R,5R)-5-O-Allyl-3-O-benzyl-2,4-dimethyoxy-5-C-phenyl pentanal (**7**)

To a solution of **6** (39 mg, 0.08 mmol) in acetone (5 mL) were added water (0.5 mL), HgO (35 mg, 0.16 mmol) and $HgCl_2$ (45 mg, 0.16 mmol). The mixture was stirred at 45℃ for 3 h and filtered through Celite. The filtrate was distilled under reduced pressure and the residue was dissolved in CH_2Cl_2 (50 mL). The solution was washed with a saturated solution of NaI (20 mL), water and brine and dried (Na_2SO_4). Concentration of the solution gave **7** as a yellow oil, which was used in the next reaction without further purification.

(2R,3S,4R,5R)-5-O-Allyl-3-O-benzyl-2,4-dimethoxy-5-phenyl pentanal dimethyl acetal (**8**)

To a stirred solution of **7** (134 mg, 0.35 mmol) in dry MeOH (10 mL) was added $HC(OCH_3)_3$ (0.2 mL) and PTSA (10 mg, cat.). The solution was stirred at reflux overnight and concentrated. The residue was dissolved with CH_2Cl_2 (20 mL) and washed with water and brine, the organic layer was dried (Na_2SO_4) and filtered. Concentration of filtrate followed by flash chromatography (EtOAc-petroleun ether, 1:5) afforded **8** (147 mg, 98%) as a syrup. $[\alpha]_D^{20}$ - 8.64 (*c* 0.49, MeOH). δ_H: 2.98, 3.32, 3.50, 3.55(4 × s, 12H), 3.45—3.55(m, 2H), 3.58—3.64(m, 1H), 3.82—3.92(m, 2H), 4.38—4.44(m, 2H), 4.73(s, 2H), 5.08—5.28(m, 2H), 5.78—5.90(m, 1H), 7.25—7.48(m, 10H). *m/z*(%): 429(M^+ - 1), 399(M^+ - OMe), 372(M^+ - Oallyl), 147 ($PhCHOCH_2CH=CH_2^+$, 93.70), 75($CH(OCH_3)_2^+$, 100). Anal. $C_{25}H_{34}O_6$. Calcd: C, 69.77; H, 7.91. Found: C, 69.75; H, 8.14.

(2R,3S,4R,5R)-3-O-Benzyl-2,4-dimethoxy-5-hydroxyl-5-C-phenyl pentanal dimethyl acetal (**9**)

To a stirred solution of **8** (80 mg, 0.19 mmol) in THF (5 mL) was added anhydrous $ZnCl_2$ (60 mg, 0.48 mmol). After stirring 15 min, $Pd(PPh_3)_4$ (40 mg, 0.04

mmol) and Bu_3SnH (0.2 mL) were added. The solution was stirred at room temperature for further 1 h and EtOAc (20 mL) was added. The mixture was washed with a 5% HCl aqueous (10 mL), water and brine and dried (Na_2SO_4). Filtration and concentration of solution followed by flash chromatography (EtOAc-petroleum ether, 1:5) provided **9** (70 mg, 96%) as a colorless oil. $[\alpha]_D^{20}$ + 13.9 (*c* 1.81, MeOH). ν_{max}: 3458, 1496, 1454 cm^{-1}. δ_H: 3.12, 3.52, 3.45, 3.54 (4 × s, 12H), 3.44—3.55 (m, 2H), 3.78—3.80 (m, 1H), 4.40 (d, J = 5.8 Hz, 1H), 4.68 (AB, J = 3.0 Hz, 2H), 4.82 (d, J = 5.8 Hz, 1H), 7.25—7.42 (m, 10H), *m/z* (%): 373 (M^+ H − H_2O, 13.26), 327 (M^+ − H − 2OMe, 11.66), 91 ($PhCH_2^+$, 94.18), 75 ($CH(OCH_3)_2^+$, 100). Anal. $C_{22}H_{30}O_6$. Calcd: C, 67.69; H, 7.69. Found: C, 67.28; H, 8.08.

(2R,3S,4R,5R)-O-Benzyl-2,4-dimethoxy-5-C-phenyl-5-O-t-butyldimethylsilyl-pentanaldimethylacetal (**10**)

A mixture of **9** (150 mg, 0.39 mmol), imidazole (40 mg, 0.59 mmol) and TBDMSCl (89 mg, 0.57 mmol) in dry DMF (5 mL) was stirred at room temperature overnight and then diluted with Et_2O (20 mL). The mixture was washed with water and brine then dried (Na_2SO_4). Concentration of the solution gave a residue which was purified by flash chromatography (EtOAc-petroleum ether, 1:10) to give **10** (172 mg, 89%) as a syrup. $[\alpha]_D^{20}$ − 2.16 (*c* 0.84, MeOH). δ_H: −0.18 (s, 3H), 0.08 (s, 3H), 0.90 (s, 9H), 3.18, 3.21, 3.28, 3.38 (4 × s, 12H), 3.12 (dd, J = 3.3, 6.3 Hz, 1H), 3.55 (dd, J = 4.8, 6.8 Hz, 1H), 3.70 (dd, J = 3.6, 6.3 Hz, 1H), 4.34 (d, J = 6.4 Hz, 1H), 4.50—4.78 (AB, J = 11.3 Hz, 2H), 4.80 (d, J = 4.9 Hz, 1H), 7.20—7.40 (m, 10H). *m/z* (%): 503 (M^+ − 1), 473 (M^+ − OMe, 0.84), 221 (PhCHOTBS$^+$, 100), 91 ($PhCH_2^+$, 42.99), 75 ($CH(OCH_3)_2^+$, 55.78). Anal. $C_{28}H_{44}O_6Si$. Calcd: C, 66.67; H, 8.73. Found: C, 66.54; H, 9.17.

(2R,3S,4R,5R)-2,4-Dimethoxy-3-hydroyl-5-C-phenyl-5-O-t-butyldimethylsilyl pentanal dimethyl acetal (**11**)

Pd/C (10%, 50mg) was added to a stirred solution of **10** (261 mg, 0.52 mmol) in EtOAc (10 mL). The mixture was hydrogenated at room temperature under atmospheric pressure for 2 h and filtered through Celite. Concentration of filtrate followed by flash chromatography (EtOAc-Petroleum ether, 1:3) gave **11** (194 mg, 90%) as a colorless oil. $[\alpha]_D^{20}$ − 26.7 (*c* 1.10, MeOH). ν_{max}: 3491 (OH), 1455, 1494 cm^{-1}. δ_H: −0.19 (s, 3H), 0.10 (s, 3H), 0.90 (s, 9H), 2.95, 3.42, 3.47, 3.50 (4 × s, 12H), 3.22 (dd, J = 3.6, 5.8 Hz, 1H), 3.28 (dd, J = 2.5, 6.5 Hz, 1H), 4.01—4.04 (m, 1H), 4.40 (d, J = 6.5 Hz, 1H), 4.78 (d, J = 7.1 Hz, 1H), 7.25—7.40 (m, 5H). *m/z* (%): 365 (M^+ − H_2O − OMe), 351 (M^+ − H_2O − Me − OMe). FAB (*m/z*): 415 (M^+ H). Anal. $C_{21}H_{38}O_6Si$. Calcd: C, 68.70; H, 9.18. Found: C, 69.02; H, 9.56.

(2R,3S,4R,5R)-3-O-(α-Bromoacetyl)-2,4-dimethoxy-5-C-phenyl-5-O-t-butyldimethylsilyl pentanal dimethyl acetal (**12**)

To a stirred solution of **11** (194 mg, 0.47 mmol) in dry DMF (5 mL) was added dropwise α-bromo acetyl bromide (0.2 mL) at 0℃. The solution was stirred at 0℃ for further 2 h and quenched with a diluted aqueous $NaHCO_3$ (5 mL). The organic layer was washed with water and brine then dried (Na_2SO_4). Filtration and concentration of solution followed by flash chromatography (EtOAc-Petroleum ether, 1:5) provided **12** (150 mg, 62%) as a colorless oil. $[\alpha]_D^{20}$ − 22.1 (*c* 0.88, MeOH). ν_{max}: 1744 (C = O), 1455, 1495 cm^{-1}. δ_H: −0.19 (s, 3H), 0.10 (s, 3H), 0.90 (s, 9H), 3.03, 3.47, 3.42, 3.50 (4 × s, 12H), 3.33 (dd, J = 3.6, 5.8 Hz, 1H), 3.45 (dd, J = 2.5, 6.5 Hz, 1H), 3.90—3.93 (m, 1H), 4.40 (d, J = 6.3 Hz, 1H), 4.78 (d, J = 7.1 Hz, 1H), 7.25—7.40 (m, 5H). *m/z* (%): 415 (M^+ + 2H − OCCH2Br), 221 (PhCHOTBS$^+$, 100), 75 ($CH(OCH_3)_2^+$, 78.70). Anal. $C_{23}H_{29}BrO_7Si$. Calcd: C, 51.59; H, 7.29. Found: C, 51.89; H, 7.63.

(2R,3S,4R,5R)-3-(α-Bromoacetyl)-2,4-dimethoxy-5-C-phenyl-5-O-t-butyldimethylsilyl pentanal (**13**)

A solution of **12** (819 mg, 1.53 mmol) and PTSA (20 mg, cat.) in acetone (20 mL) was stirred at room temperture overnight. The solution was washed with a saturated solution of $NaHCO_3$, water and brine then

dried (Na_2SO_4). Concentration of solution afforded **13** as colorless oil, which was used in next reaction without further purification.

(4R,5S,6S,7S,8S)-6-(7,8-Dihydro-7-methoxy-8-O-t-butyldimethylsilylstyryl)-3,4,5,6-tetrahydro-4-hydroxyl-5-methoxy-2H-pyran-2-one (**14a**) *and its diastereoisomer* (**14b**)

A solution of **13** and Cp_2TiCl_2 (78 mg, cat.) in THF (15 mL) was stirred at room temperature for 0.5 h, then the activated zinc powder (100 mg) was added and the mixture was stirred at room temperture for further 2 h. After being diluted with EtOAc (30 mL) and acidified with aqueous 5% HCl (15 mL), the mixture was extracted with EtOAc (3 × 20 mL). The extract was washed with water, brine and dried (Na_2SO_4). Evaporation of solvent gave a residue which was purified by flash chromatography (EtOAc-petroleum ether, 1:2) to afford diastereoisomeric δ-lactones **14(a + b)** (105 mg, two steps yield 44%) in a ratio of 2.5 to 1.

14a (major isomer) ν_{max}: 3444(OH), 1742 (C = O), 1495, 1472, 1455 cm^{-1}. δ_H: −0.22(s 3H), 0.08(s, 3H), 0.88(s, 9H), 2.68(s, 3H), 3.41(s, 3H), 2.44—3.06(AB, J = 8.3 Hz, 2H), 3.52—3.60(m, 2H), 4.04(q, J = 8.3 Hz, 1H), 4.70(d, J = 8.3 Hz, 1H), 4.88(dd, J = 1.2, 5.6 Hz, 1H), 7.24—7.40(m, 5H). FAB(m/z): 411(M + 1).

(4R,5S,6S,7S,8S)-6-(7,8-Dihydro-7-methoxy-8-O-t-butyldimethylsilylstyryl)-3,4,5,6-tetrahydro-5-methoxy-4-O-methylsulfonyl-2H-pyran-2-one (**15a**)

To a stirred solution of **14(a + b)** (75 mg, 0.18 mmol) in dry pyridine (5 mL) was added dropwise methylsulfonyl chloride (0.02 mL, 0.26 mmol) at 0℃. After being stirred for 3 h at 0℃ the solution was acidified with aqueous 5% HCl (5 mL) and extracted with EtOAc (3 × 10 mL). The extract was washed with water and brine, then dried (Na_2SO_4). Removal of solvent under reduced pressure followed by column chromatography (EtOAc-petroleum ether, 1:5) gave **15a** and **15b**. The first eluted fraction was the major product **15a** (58 mg, 65%) as a syrup. $[\alpha]_D^{20}$ −10.5 (c 1.17, MeOH). ν_{max}: 1724(C = O), 1496, 1455 cm^{-1}. δ_H: −0.22(s, 3H), 0.10(s, 3H), 0.90(s, 9H), 2.70 (s, 3H), 3.08(s, 3H), 3.45(s, 3H), 2.60—2.76 (AB, J = 11.5 Hz, 2H), 3.28(t, J = 4.1 Hz, 1H), 3.78(dd, J = 5.8, 9.3 Hz, 1H), 4.70(d, J = 8.5 Hz, 1H), 4.94(q, J = 9.3 Hz, 1H), 5.02(d, J = 5.8 Hz, 1H), 7.24—7.40(m, 5H). ESI(m/z): 511 ($M^+ + Na^+$). Anal. $C_{22}H_{36}O_8SSi$. Calcd: C, 54.10; H, 7.38. Found: C, 54.42; H, 7.61.

8,9-Dimetyoxy-7-epi-goniopypyrone (**1**)

To a stirred solution of **15a** (50 mg, 0.1 mmol) in dry THF (4 mL) was added dropwise a solution of TBAF (THF solution, 1 mol/L, 0.5 mL). The solution was stirred at room temperture for further 2 h and concentrated. The residue was purified by flash chromatography (EtOAc-petroleum ether, 1:3) to afford **1** (24 mg, 84%) as a colorless oil. $[\alpha]_D^{20}$ −67.2 (c 0.36, MeOH). ν_{max}: 1747(C = O), 1605, 1496, 1456 cm^{-1}. δ_H: 2.70, 3.05(AB, J = 11.3 Hz, 2H), 3.25(s, 3H), 3.55(s, 3H), 3.58(d, J = 11.5 Hz, 1H), 3.92(d, J = 4.1 Hz, 1H), 4.58(td, J = 2.3 Hz, 1H), 4.78(dd, J = 2.0, 4.1 Hz, 1H), 4.95(d, J = 9.3 Hz, 1H), 7.30—7.40(m, 5H). m/z(%): 279(M^+H, 0.12), 246(M^+ − MeOH, 3.20). ESI (m/z) 301 ($M^+ + Na^+$). HRMS: ($C_{15}H_{18}O_5$). Calcd: 278.1167; Found: 278.1155. Anal. $C_{15}H_{18}O_5$. Calcd: C, 64.75; H, 6.47. Found: C, 65.01; H, 6.78.

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