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Stereoselective Synthesis of (+)-Goniodiol, (+)-Goniotriol, (–)-Goniofupyrone, and (+)-Altholactone Using a Catalytic Asymmetric Hetero-Diels–Alder/Allylboration Approach

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The stereoselective total synthesis of several members of the styryllactone family was achieved efficiently from common intermediate **8**, prepared by a catalytic asymmetric inverse-electron-demand hetero-Diels–Alder/allylboration sequence. The transformation of **8** into α,β-unsaturated lactone led to the preparation of (+)-goniodiol (**1**) in a reduced number of steps. The epoxidation reaction was used to generate the remaining stereogenic centers on the lactone moiety of **8**, and these intermediates were then elaborated into (+)-goniotriol (**2**), (–)-goniofupyrone (**3**), and (+)-altholactone (**4**) by an isomerization or cyclization step.

Introduction

In the inventory of plants used in traditional medicine in Asia, the *Goniothalamus* species (Annonaceae) are well represented. Thus, extracts of seeds of *Goniothalamus amuyon* have been employed for the treatment of edema and rheumatism.[1] Other general applications include their use as painkillers[2] and mosquito repellents.[3] Taking into account their medicinal properties, these plants are considered a potential source of biologically active compounds. The phytochemical study of the genus *Goniothalamus* was intensified when, in 1972, Geran et al. showed that the ethanolic extract of stem bark of *Goniothalamus giganteus* Hook. f. & Thomas was very toxic to mice during a P-388 in vivo antileukemic screening.[4] Investigations of this extract, reported by McLaughlin and co-workers, led to the discovery of two major classes of compounds with biologically interesting properties that include annonaceous acetogenins[5] and styryllactones.[6] To date, more than 30 bioactive molecules belonging to the styryllactone family are listed from various *Goniothalamus* species.[7]

Styryllactones can be divided into two main groups according to the size of the lactone ring (γ- and δ-lactones). Owing to their significant cytotoxicity against several human tumor cell lines, styryllactones comprising a six-membered lactone moiety have attracted, in recent years, considerable attention from synthetic chemists.[8] Different approaches have been used for the formation of the 5,6-dihydropyran-2-one ring, including the two major routes reported to date for this class of compounds: Cyclization of substituted δ-hydroxy acid derivatives and ring-closing metathesis.[9] In addition, the stereochemical centers adjacent to the pyranyl ring system can be created by using chiral starting products[10] or by stoichiometric and catalytic asymmetric reactions.[11] Herein, we report a concise, stereoselective route to bioactive styryllactones, namely, (+)-goniodiol (**1**),[12] (+)-goniotriol (**2**), (–)-goniofupyrone (**3**), and (+)-altholactone (**4**) by using a tandem reaction suitable for the preparation of various stereoisomers and the design of analogues.[13]

In the course of our program directed towards the development of new multicomponent reactions involving an allylboration reaction,[14] we and others have simultaneously described a general approach for the asymmetric synthesis of α-hydroxyalkyldihydropyrans.[15] The first step of the sequence was the formation of cyclic allylboronate **7** obtained from ethyl vinyl ether and boroacrolein pinacolate by using a catalytic enantioselective inverse-electron-demand hetero-[4+2] cycloaddition reaction. Boronate **7** was then treated with an aldehyde in a second step (Figure 1). We have also shown that it was possible to create three contiguous asymmetric centers in a highly stereoselective manner when a chiral aldehyde is used in the allylboration step.[16] On the basis of these preliminary results, we envisioned that this strategy should be adaptable for the synthesis of several bioactive styryllactones by using common intermediate **8**, which can be prepared from a conveniently protected aldehyde derived from (*R*)-mandelic acid.

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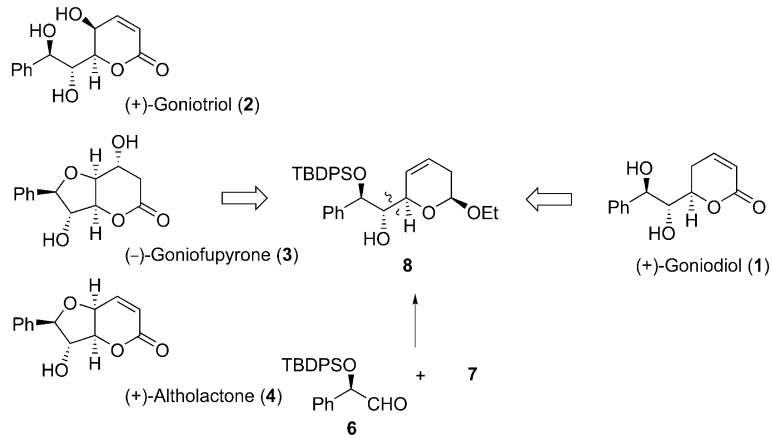


Scheme 1. IEDHDA/allylboration strategy applied to styryllactones synthesis.

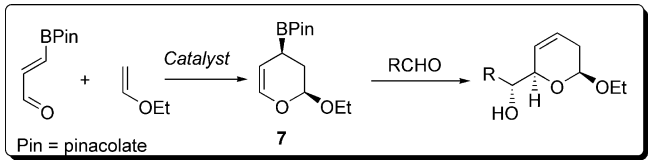


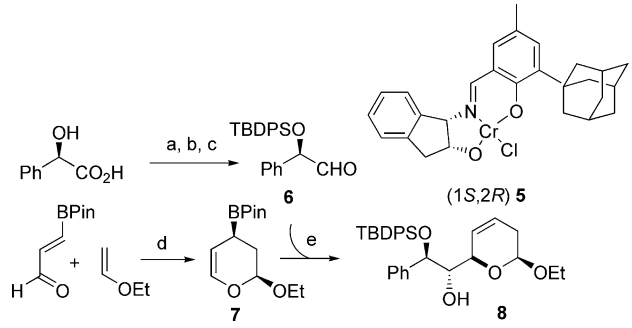
Figure 1. Catalytic inverse-electron-demand hetero-Diels–Alder (IEDHDA)/allylboration sequence.

Oxidation of ethyl lactol **8** followed by migration of the double bond would lead to the α,β-unsaturated δ-lactone skeleton of (+)-goniodiol (**1**), as depicted in Scheme 1. Concerning the elaboration of goniotriol (**2**), goniofupyrone (**3**), and altholactone (**4**), the installation of an additional hydroxy group with a definite configuration should be realized by exploiting the oxidation products of the endocyclic double bond of **8**.

Results and Discussion

Synthesis of the key building block **8** required the preparation of the (*R*)-(*tert*-butyldiphenylsilyloxy)phenylacetaldehyde (**6**) in three steps from (*R*)-mandelic acid.[17] After an esterification reaction followed by the protection of the hydroxy group with *tert*-butyldiphenylsilyl chloride, the resulting methyl mandelate was efficiently reduced with *i*Bu_2AlH at –78 °C to give expected aldehyde **6** in 77% overall yield (Scheme 2). Treatment of commercially available ethyl vinyl ether with 3-boronoacrolein pinacolate[18] in the presence of Jacobsen's tridentate [(Schiff base)chromium(III)] complex[19] **5** resulted in the formation of product **7** in good yield (85%) and high enantioselectivity (96%*ee*).

Allylation of **6** with cyclic allylboronate **7** was performed without solvent at 70 °C for 10 h to give dihydropyran **8** as a unique stereoisomer (>95%*dr*) in 65% yield,[20] which is acceptable taking into account the high stereoselectivity of this reaction.[21] Note that, to the best of our knowledge,



Scheme 2. Reagents and conditions: (a) MeOH, *p*-TsOH (0.01 equiv.), reflux, 3 h, quantitative yield; (b) *t*$BuPh_2SiCl$ (1.5 equiv.), imidazole (2 equiv.), DMAP (0.05 equiv.), CH_2Cl_2, room temp., 12 h, 93%; (c) *i*Bu_2AlH (1.1 equiv.), Et_2O, –78 °C, 0.5 h, 83%; (d) **5** (0.01 equiv.), 4 Å molecular sieves, room temp., 2 h, 85%; (e) **6** (1 equiv.), 70 °C, 10 h, 65%.

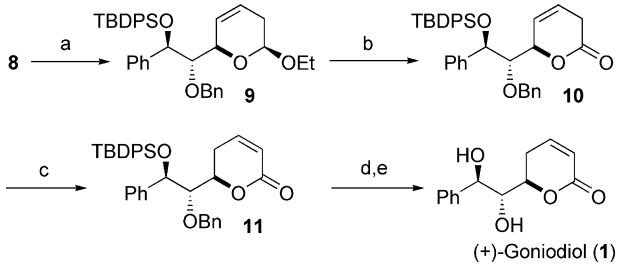
this is the first example of an allylboration reaction involving a chiral γ-alkoxyallylboronate and a functionalized α-chiral aldehyde to be reported in the literature.

Synthesis of (+)-Goniodiol (1)

(+)-Goniodiol (**1**) was first isolated from the leaves and twigs of *Goniothalamus sesquipedalis*[3] and was found to have a significant and selective cytotoxicity against human lung carcinoma cell line A-459 (ED_{50} = 0.122 μg mL^{-1})[6d] and P-388 murine leukemia cells (IC_{50} = 4.56 mg mL^{-1}).[10e] As mentioned earlier in our general synthetic plan, we envisioned that the synthesis of **1** could be feasible from **8** by using only a few synthetic transformations.

At first we considered the direct oxidation of ethyl lactol **8** in lactone. However, under the conditions described by Grieco et al.,[22] the expected product was not obtained, and only products resulting from a cyclization reaction due to the presence of the unprotected hydroxy group in the starting material, which acts as an internal nucleophile during the reaction, were obtained.[23] We thus decided to protect the alcohol function and compound **8** was converted into

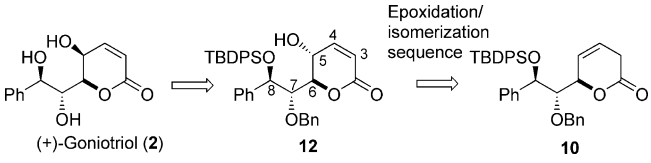
benzyl ether **9** in 84% yield by using standard conditions (Scheme 3). The one-pot conversion of **9** into the corresponding lactone **10** by using the *m*-CPBA/BF_3·OEt_2 system was effected very cleanly in 90% yield. No product arising from the epoxidation of the double bond was detected by ^{1}H NMR spectroscopy. Isomerization of the β,γ-unsaturated lactone **10** to the corresponding α,β-unsaturated lactone was achieved by using a catalytic amount of DBU at room temperature to afford **11** in 91% yield. Finally, successive deprotection of the different protecting groups present in **11**, TBDPS and benzyl ethers, delivered synthetic (+)-goniodiol (**1**) in 39% yield for the two-step sequence.



Scheme 3. Reagents and conditions: (a) NaH (1.3 equiv.), BnBr (1.5 equiv.), $Bu_4N^+I^-$ (0.1 equiv.), THF, room temp., 3 h, 84%; (b) *m*-CPBA (1.5 equiv.), BF_3·OEt_2 (1.5 equiv.), CH_2Cl_2, 0 °C to room temp., 14 h, 90%; (c) DBU (0.01 equiv.), THF, room temp., 18 h, 91%; (d) HF/pyridine, room temp., 48 h; (e) $TiCl_4$ (2 equiv.), CH_2Cl_2, room temp., 1 h, 39% from **11**.

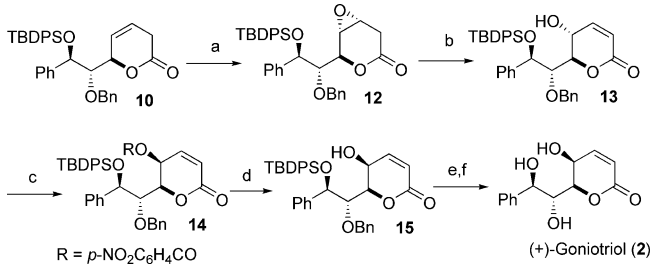
Synthesis of (+)-Goniotriol (2)

(+)-Goniotriol (**2**), a highly oxygenated styryllactone, has been, in particular, isolated from the stem bark of *Goniothalamus giganteus*, and it showed some activity in the brine shrimp lethality test (BST) and potato disc assay (PD) and mild activity towards human tumor cells.[6b] We planned to introduce the missing hydroxy group onto the lactone moiety of the advanced intermediate **10** by using an epoxidation/isomerization sequence followed by a reaction with inversion of configuration at C-5, as depicted in Scheme 4.



Scheme 4. Retrosynthesis of (+)-goniotriol **2**.

Accordingly, α,β-unsaturated lactone **10** was treated with *m*-CPBA in CH_2Cl_2 to afford the expected epoxide with complete conversion after 5 d. NMR spectroscopic analysis (^{1}H, ^{13}C) of the residue indicated the formation of a single diastereomer. Owing to the instability of **12** on silica gel, the stereochemistry of the epoxidation reaction could not be determined at this stage of the synthesis but was assigned after the following step on the basis of the stereochemistry of the isomerization product (Scheme 5). Treatment of **12** with DBU smoothly opened the epoxide ring to give allylic alcohol **13** in 60% overall yield from **10**. The assignment of the relative configuration of the two stereogenic centers in the δ-lactone ring of **13** was based on the coupling constant $J_{5,6}$ = 10.4 Hz, which indicates the equatorial nature of the hydroxy group.[24] Mitsunobu reaction of **13** with *p*-nitrobenzoic acid, triphenylphosphane, and diethyl azodicarboxylate (DEAD) furnished *p*-nitrobenzoate **14** in 76% yield, which was subsequently hydrolyzed with 1% aqueous potassium carbonate to provide **15** in 53% yield with an inverted stereochemistry at the allylic position ($J_{5,6}$ = 3.2 Hz). Desilylation of **15** with HF·pyridine followed by debenzylation with $TiCl_4$ led to (+)-goniotriol (**2**) in 65% yield for the last two steps.

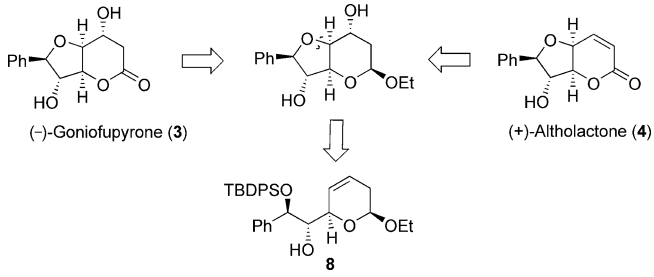


Scheme 5. Reagents and conditions: (a) *m*-CPBA (2.8 equiv.), CH_2Cl_2, room temp., 5 d; (b) DBU (2.9 equiv.), CH_2Cl_2, 0 °C to room temp., 36 h, 60% from **10**; (c) PPh_3 (3 equiv.), DEAD (3 equiv.), *p*-$NO_2C_6H_4CO_2H$ (3 equiv.), toluene, room temp., 18 h, 76%; (d) 1% K_2CO_3, MeOH, 0 °C to room temp., 12 h, 53%; (e) HF/pyridine, room temp., 48 h; (f) $TiCl_4$ (2 equiv.), CH_2Cl_2, room temp., 2 h, 65% from **15**.

Synthesis of (–)-Goniofupyrone (3) and (+)-Altholactone (4)

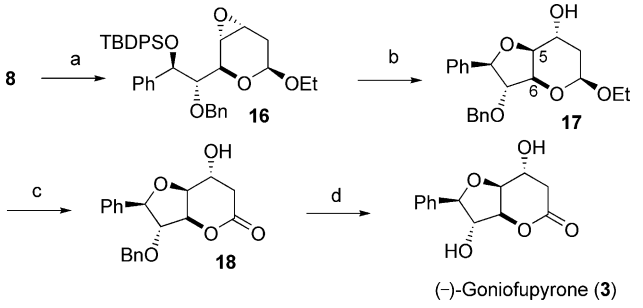
(–)-Goniofupyrone (**3**) and (+)-altholactone (**4**), which have in common a bicyclic skeleton, were first isolated from the stem bark of *Goniothalamus giganteus* [6e] and from the bark of an unnamed *Polyalthia* (Annonaceae) species, respectively.[25] (+)-Altholactone is known to possess antitumor activity against P-388 murine leukemia in vivo at 45 mg kg^{-1} as well as some cytotoxic activity (in vitro).[6a,10i] Owing to its biological importance, **4** has attracted the attention of several synthetic groups, in contrast to (–)-goniofupyrone (**3**).[26] Our strategy for the construction of the tetrahydrofuran ring with the desired four chiral centers present in these two natural products was based on an epoxidation reaction of the olefinic double bond of **8** followed by an intramolecular cyclization, as described in Scheme 6.

In the first step, the oxidation of **8** with *m*-CPBA in CH_2Cl_2 led to the formation of the expected epoxide **16** with a good level of diastereoselectivity (*dr* 9:1) and in 69% yield (Scheme 7). After separation of the two isomers by column chromatography, major epoxide **16** was subjected to treatment with *n*Bu_4NF at 50 °C for 24 h. Under these conditions, cyclized product **17**, which results from desilylation of **16** with concomitant ring closure, was obtained in 70% yield ($J_{5,6}$ = 2.8 Hz). Conversion of **17** into lactone



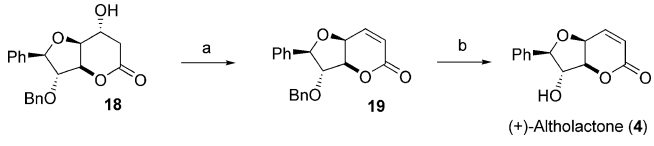
Scheme 6. Retrosynthesis of (–)-goniofupyrone (**3**) and (+)-altholactone (**4**).

18 was cleanly carried out with *m*-CPBA in the presence of $BF_3{\cdot}OEt_2$ in 90% yield. Finally, removal of the benzyl group with $SnCl_4$ provided (–)-goniofupyrone (**3**) in 80% yield.



Scheme 7. Reagents and conditions: (a) *m*-CPBA (2.3 equiv.), CH_2Cl_2, room temp., 12 h, 69%; (b) TBAF (1.5 equiv.), THF, 50 °C, 24 h, 70%; (c) *m*-CPBA (4 equiv.), $BF_3{\cdot}OEt_2$ (4 equiv.), CH_2Cl_2, 0 °C to room temp., 12 h, 90%; (d) $SnCl_4$ (2 equiv.), CH_2Cl_2, 40 °C, 10 h, 80%.

Concerning the synthesis of (+)-altholactone (**4**), the double bond was generated by a dehydration reaction of **18** (Scheme 8). By using a catalytic amount of *p*-toluenesulfonic acid (pTSA) in toluene at 85 °C for 5 h, α,β-unsaturated lactone **19** was obtained in 73% yield. The last step of the synthesis was the deprotection of the benzyl ether using $SnCl_4$, which gave the product in 78% yield. Synthetic altholactone (**4**) was identical to the natural compound by comparison with spectral and physical data.



Scheme 8. Reagents and conditions: (a) *p*-TsOH (0.3 equiv.), toluene, 85 °C, 5 h, 73%; (b) $SnCl_4$ (2 equiv.), CH_2Cl_2, 40 °C, 24 h, 78%.

Conclusions

In this paper we have demonstrated that the hetero-Diels–Alder/allylboration sequence is an appropriate strategy for the synthesis of several bioactive styryllactones. From common advanced intermediate **8**, (+)-goniodiol, (+)-goniotriol, (–)-goniofupyrone, and (+)-altholactone were prepared in 27, 12, 35, and 25% overall yields, respectively. This new approach successfully supplements the methodologies already described in the literature for the synthesis of this family of compounds. Moreover, by taking into account the availability of both isomers of mandelic acid and the chromium(III) complex, this strategy should be applicable to the synthesis of different stereoisomers. Application of this methodology to the preparation of other natural products is underway in the laboratory.

Experimental Section

General Remarks: The catalyst was prepared according to Jacobsen's procedure.[19] 3-Boroacrolein pinacolate was prepared according to the published procedure.[18] Reactions were performed in oven-dried glassware under an atmosphere of argon. Tetrahydrofuran (THF) was distilled from deep-blue solutions of sodium/benzophenone ketyl prior to use. CH_2Cl_2 was distilled from CaH_2. Unless otherwise stated, all reagents were used as received. Most reactions were monitored by TLC on precoated silica plates (Merck 60 F254, 0.25 mm). Silica gel 60F254 was used for column flash chromatography. Deactivated silica gel refers to silica gel washed with triethylamine prior to use. Melting points (uncorrected) were measured with a Kofler melting point apparatus. NMR spectra were recorded in $CDCl_3$ with a 300 MHz spectrometer operating in the Fourier transform mode. ^{1}H NMR spectroscopic data are presented as follows: chemical shift, multiplicity, coupling constant, integration. The following abbreviations are used: s, singlet; br. s, broad singlet; d, doublet; t, triplet; q, quartet; dq, doublet of quartets; dd, doublet of doublets; ddd, doublet of doublets of doublets; m, multiplet. ^{13}C NMR spectra were obtained with broadband proton decoupling. Chemical shifts were recorded relative to the internal tetramethylsilane (TMS) reference signal. Optical rotations were measured by using a 1-mL cell with a 1-dm path length at 23 °C with a Perkin-Elmer 341 digital polarimeter, and the concentration is expressed in g dL^{-1}. High-resolution mass spectra (HRMS) were recorded at the Centre Régional de Mesures Physiques de l'Ouest. Enantiomeric excesses were determined by gas chromatography performed by using a Varian CP3380 GC unit equipped with a capillary chiral column (Varian WCOT Fused Silica 25m × 0.25 mm coated CP Chirasil-dex CB DF = 0.25). Chromatography conditions: carrier gas, argon; injection temperature, 200 °C; detector temperature, 250 °C.

(1*S*,2*R*)-2-{[*tert*-Butyl(diphenyl)silyl]oxy}-1-[(2*R*,6*S*)-6-ethoxy-5,6-dihydro-2*H*-pyran-2-yl]-2-phenylethanol (8): Catalyst **5** (9.60 mg, 0.020 mmol) and powdered BaO (400 mg) were added to a mixture of boronoacrolein pinacolate (364 mg, 2.00 mmol) and ethyl vinyl ether (1.90 mL, 20.0 mmol) in an oven-dried round-bottomed flask (10 mL) containing a stirring bar. After stirring for 1.5 h at room temperature, the ethyl vinyl ether was evaporated in vacuo, and cycloadduct **7** was distilled by using a Kugelrohr apparatus (b.p. 90–95 °C/0.01 Torr, 430 mg, 85%, 96%*ee*). Allylboration with (*R*)-[(*tert*-butyldiphenylsilyl)oxy](phenyl)acetaldehyde (**6**; 637 mg, 1.7 mmol) was carried out at 70 °C for 10 h without solvent and then diluted with EtOAc. The solution was stirred for 30 min with an aqueous saturated solution of $NaHCO_3$. After this time, the organic layer was separated and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic extract was dried with $MgSO_4$ and concentrated. Purification by flash column chromatography (deactivated silica gel, cyclohexane/EtOAc, 95:5) led to pure product **8** (555 mg, 65%) as a white solid. M.p. 139–

141 °C. $[a]_D^{23}$ = +39.3 (*c* = 1.0, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.02 (s, 9 H), 1.18 (t, *J* = 7.1 Hz, 3 H), 2.13–2.24 (m, 2 H), 2.47 (d, *J* = 7.9 Hz, 1 H), 3.30 (dq, *J* = 9.5, 7.1 Hz, 1 H), 3.72 (dq, *J* = 9.5, 7.1 Hz, 1 H), 3.78 (dt, *J* = 7.8, 2.6 Hz, 1 H), 4.63 (dd, *J* = 6.1, 4.6 Hz, 1 H), 4.70–4.77 (m, 1 H), 4.82 (d, *J* = 7.6 Hz, 1 H), 5.58–5.70 (m, 1 H), 5.73–5.89 (m, 1 H), 7.12–7.50 (m, 13 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.5, 19.8, 27.4, 31.2, 64.6, 73.5, 76.3, 77.3, 98.4, 124.9, 127.6, 127.8, 127.9, 128.2, 128.4, 129.8, 133.7, 134.4, 136.4, 136.5, 141.7 ppm. HRMS (EI): calcd. for $C_{25}H_{23}O_3Si$ [M – HOC_2H_5 – *t*Bu]$^+$ 399.1417; found 399.1410.

({(1*R*,2*S*)-2-(Benzyloxy)-2-[(2*R*,6*S*)-6-ethoxy-5,6-dihydro-2*H*-pyran-2-yl]-1-phenylethyl}oxy)(*tert*-butyl)diphenylsilane (9): A solution of alcohol **8** (300 mg, 0.58 mmol) in THF (12 mL) was added to a suspension of NaH (60% dispersion in mineral oil, 46.4 mg, 1.16 mmol) in THF (18 mL) at 0 °C under an atmosphere of argon. After 15 min, benzyl bromide (86 μL, 0.70 mmol) and $Bu_4N^+I^-$ (22 mg, 0.058 mmol) were added to the solution. The mixture was stirred at room temperature for 3 h. After this period, water (6 mL) was added and the layers were separated. The aqueous layer was extracted with Et_2O (3 × 30 mL). The combined organic extract was dried with $MgSO_4$ and concentrated. Purification of the residue by deactivated silica gel chromatography (cyclohexane/EtOAc, 99:1) afforded **9** (288 mg, 84%) as a colorless oil. $[a]_D^{23}$ = +64.0 (*c* = 0.32, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.02 (s, 9 H), 1.15 (t, *J* = 7.0 Hz, 3 H), 2.09–2.19 (m, 2 H), 3.21 (dq, *J* = 9.1, 7.0 Hz, 1 H), 3.73 (dq, *J* = 9.1, 7.0 Hz, 1 H), 3.78 (m, 1 H), 4.24 (d, *J* = 11.1 Hz, 1 H), 4.35 (d, *J* = 11.1 Hz, 1 H), 4.53 (dd, *J* = 5.0, 3.3 Hz, 1 H), 4.56 (br. s, 1 H), 5.04 (d, *J* = 6.6 Hz, 1 H), 5.50 (d, *J* = 10.1 Hz, 1 H), 5.65 (m, 1 H), 7.02 (m, 2 H), 7.16–7.38 (m, 14 H), 7.46 (d, *J* = 7.9 Hz, 2 H), 7.62 (d, *J* = 7.9 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.1, 19.4, 27.1, 31.4, 63.8, 74.4, 74.6, 75.0, 84.9, 98.7, 124.4, 127.1, 127.2, 127.3, 127.4, 127.5, 127.7, 127.9, 128.1, 128.6, 129.4, 129.5, 133.3, 134.0, 136.0, 136.1, 138.5, 141.2 ppm. HRMS (ESI): calcd. for $C_{38}H_{44}O_4SiNa$ 615.2907; found 615.2902.

(6*R*)-6-[(1*S*,2*R*)-1-(Benzyloxy)-2-{[*tert*-butyl(diphenyl)silyl]oxy}-2-phenylethyl]-3,6-dihydro-2*H*-pyran-2-one (10): *m*-CPBA (45 mg, 0.26 mmol) followed by $BF_3{\cdot}OEt_2$ (25.1 μL, 0.20 mmol) were added to a stirred solution of ethyl lactol **9** (120 mg, 0.20 mmol) in CH_2Cl_2 (6 mL) at 0 °C under an atmosphere of argon. The resulting mixture was warmed to room temperature and stirred for 20 h. The mixture was quenched with saturated aqueous $Na_2S_2O_3$ solution (2 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layer was dried with $MgSO_4$ and concentrated. The residue was purified by silica gel chromatography (cyclohexane/EtOAc, 9:1) to afford lactone **10** (102 mg, 90%) as a colorless oil. $[a]_D^{23}$ = +100.0 (*c* = 0.34, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.05 (s, 9 H), 2.86–2.88 (m, 2 H), 3.57 (dd, *J* = 8.6, 1.2 Hz, 1 H), 3.61 (d, *J* = 10.2 Hz, 1 H), 3.96 (d, *J* = 10.2 Hz, 1 H), 4.97 (d, *J* = 8.6 Hz, 1 H), 5.40 (m, 1 H), 5.83–5.86 (m, 2 H), 6.83–6.85 (m, 2 H), 7.14–7.41 (m, 14 H), 7.45 (dd, *J* = 7.9, 1.4 Hz, 2 H), 7.62 (dd, *J* = 7.9, 1.4 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.5, 27.1, 30.8, 74.3, 75.2, 77.7, 85.1, 123.7, 124.1, 127.3, 127.5, 127.6, 127.7, 127.8, 127.9, 128.0, 128.1, 129.5, 129.6, 133.3, 133.4, 136.0, 136.1, 137.5, 141.4, 167.0 ppm. HRMS (ESI): calcd. for $C_{36}H_{38}O_4SiNa$ 585.2437; found 585.2433.

(6*R*)-6-[(1*S*,2*R*)-1-(Benzyloxy)-2-{[*tert*-butyl(diphenyl)silyl]oxy}-2-phenylethyl]-5,6-dihydro-2*H*-pyran-2-one (11): DBU (2 drops) was added dropwise to a solution of lactone **10** (90 mg, 0.16 mmol) in THF (10 mL) at 0 °C under an atmosphere of argon. The resulting solution was warmed to room temperature and stirred for 18 h. The mixture was quenched with a saturated aqueous NH_4Cl solution (2 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layer was dried with $MgSO_4$ and concentrated. Purification of the residue by silica gel chromatography (cyclohexane/EtOAc, 9:1) gave **11** (82 mg, 91%) as a colorless oil. $[a]_D^{23}$ = +45.9 (*c* = 1.82, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$): δ = 1.06 (s, 9 H), 2.00 (ddd, *J* = 18.1, 6.2, 3.7, 1 H), 2.42 (m, 1 H), 3.58 (dd, *J* = 7.8, 2.5 Hz, 1 H), 3.90 (d, *J* = 18.4 Hz, 1 H), 3.95 (d, *J* = 18.4 Hz, 1 H), 4.76 (dt, *J* = 12.6, 3.0 Hz, 1 H), 5.11 (d, *J* = 7.8 Hz, 1 H), 5.89 (dd, *J* = 9.8, 2.4 Hz, 1 H), 6.75 (ddd, *J* = 9.8, 6.2, 2.1 Hz, 1 H), 7.01 (m, 2 H), 7.19–7.68 (m, 18 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.4, 26.1, 27.1, 74.1, 74.5, 76.3, 83.9, 121.1, 127.3, 127.5, 127.6, 127.7, 127.8, 127.9, 128.0, 128.1, 128.2, 129.5, 129.7, 133.1, 133.5, 135.9, 136.0, 137.6, 141.3, 163.5 ppm. HRMS (ESI): calcd. for $C_{36}H_{38}O_4SiNa$ 585.2437; found 585.2434.

(6*R*)-6-[(1*R*,2*R*)-1,2-Dihydroxy-2-phenylethyl]-5,6-dihydro-2*H*-pyran-2-one [(+)-Goniodiol (1)]: The HF·pyridine complex (0.1 mL) was added to a room-temperature solution of silyl ether **11** (60 mg, 0.11 mmol) in CH_3CN (1 mL). After stirring for 2 d, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (1 mL) and extracted with EtOAc (3 × 5 mL). The combined organic layer was dried with $MgSO_4$ and concentrated. The residual oil was dissolved in CH_2Cl_2 (1 mL) and $TiCl_4$ (1.0 M CH_2Cl_2 solution; 0.22 mL, 0.22 mmol) was added to the solution. The reaction mixture was stirred at room temperature for 1 h, diluted with saturated aqueous $NaHCO_3$ solution, and extracted with CH_2Cl_2 (3 × 3 mL). The combined organic layer was washed with water and brine, dried with $MgSO_4$, and concentrated. The residue was purified by silica gel chromatography (cyclohexane/EtOAc, 1:1) to afford (+)-**1** (10 mg, 39%) as a colorless oil. $[a]_D^{23}$ = +74.1 (*c* = 0.20, $CHCl_3$) [ref.[6d] $[a]_D^{22}$ = +74.4 (*c* = 0.3, $CHCl_3$)]. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.22 (dddd, *J* = 18.4, 6.4, 3.8, 0.5 Hz, 1 H), 2.27 (br. s, 1 H), 2.55 (s, 1 H), 2.82 (dddd, *J* = 18.4, 12.8, 2.5, 2.0 Hz, 1 H), 3.71 (m, 1 H), 4.82 (ddd, *J* = 12.8, 3.8, 2.0 Hz, 1 H), 4.98 (d, *J* = 7.3 Hz, 1 H), 6.05 (ddd, *J* = 9.8, 2.9, 1.0 Hz, 1 H), 6.95 (ddd, *J* = 9.8, 6.4, 2.2 Hz, 1 H), 7.30–7.48 (m, 5 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.1, 73.8, 75.2, 77.2, 120.7, 126.4, 128.4, 128.8, 140.7, 146.0, 163.8 ppm. HRMS (ESI): calcd. for $C_{13}H_{14}O_4Na$ 257.0790; found 257.0795.

(5*R*,6*R*)-6-[(1*S*,2*R*)-1-(Benzyloxy)-2-{[*tert*-butyl(diphenyl)silyl]oxy}-2-phenylethyl]-5-hydroxy-5,6-dihydro-2*H*-pyran-2-one (13): *m*-CPBA (78 mg, 0.45 mmol) was added to a solution of lactone **10** (90 mg, 0.16 mmol) in CH_2Cl_2 (10 mL) at 0 °C under an atmosphere of argon. The resulting mixture was warmed to room temperature and stirred for 5 d. The mixture was washed with a saturated aqueous $NaHCO_3$ solution (3 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL) and the combined organic layer was dried with $MgSO_4$ and concentrated. Crude epoxide **12** was subjected to the next reaction without further purification. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.07 (s, 9 H), 2.66 (d, *J* = 18.2 Hz, 1 H), 2.83 (d, *J* = 18.2 Hz, 1 H), 3.17–3.19 (m, 2 H), 3.69 (d, *J* = 10.6 Hz, 1 H), 3.72 (d, *J* = 8.9 Hz, 1 H), 3.78 (d, *J* = 10.6 Hz, 1 H), 4.92 (d, *J* = 8.9 Hz, 1 H), 5.29 (m, 1 H), 6.87–6.88 (m, 2 H), 7.15–7.34 (m, 14 H), 7.50 (dd, *J* = 7.9, 1.4 Hz, 2 H), 7.60 (dd, *J* = 7.9, 1.4 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.5, 27.0, 31.9, 49.9, 50.7, 74.5, 74.6, 83.0, 127.3, 127.5, 127.8, 127.9, 128.0, 128.2, 128.3, 128.4, 129.5, 129.7, 132.9, 133.2, 136.0, 136.1, 136.7, 140.9, 166.3 ppm.

DBU (69 μL, 0.46 mmol) was added dropwise to a solution of the above epoxide in CH_2Cl_2 (4.5 mL) at 0 °C under an atmosphere of argon. The resulting solution was warmed to room temperature

and stirred for 24 h. The mixture was quenched with a saturated aqueous NH_4Cl solution (1 mL). The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 4 mL). The combined organic layer was dried with $MgSO_4$ and concentrated. Purification of the residue by silica gel chromatography (cyclohexane/EtOAc, 9:1) gave alcohol **13** (56 mg, 60% from **10**) as a colorless oil. $[\alpha]_D^{23}$ = –12.5 (*c* = 0.52, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.02 (s, 9 H), 2.06 (br. s, 1 H), 3.47 (d, *J* = 11.7 Hz, 1 H), 3.81 (dd, *J* = 8.4, 1.6 Hz, 1 H), 3.99 (d, *J* = 11.7 Hz, 1 H), 4.19 (m, 1 H), 4.46 (dd, *J* = 10.4, 1.6 Hz, 1 H), 5.10 (d, *J* = 8.4 Hz, 1 H), 5.73 (dd, *J* = 9.9, 2.2 Hz, 1 H), 6.59 (dd, *J* = 9.9, 1.7 Hz, 1 H), 7.07–7.10 (m, 2 H), 7.21–7.40 (m, 14 H), 7.48 (dd, *J* = 8.0, 1.3 Hz, 2 H), 7.62 (dd, *J* = 8.0, 1.4 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.4, 27.1, 62.5, 73.2, 73.7, 78.8, 80.0, 119.7, 127.3, 127.5, 127.9, 128.0, 128.1, 128.4, 128.6, 128.9, 129.5, 129.7, 135.9, 136.1, 137.4, 141.6, 149.5, 162.1 ppm. HRMS (ESI): calcd. for $C_{36}H_{38}O_5SiNa$ 601.2386; found 601.2389.

(5*S*,6*R*)-6-[(1*S*,2*R*)-1-(Benzyloxy)-2-{[*tert*-butyl(diphenyl)silyl]oxy}-2-phenylethyl]-5-[(*p*-nitrobenzoyl)oxy]-5,6-dihydro-2*H*-pyran-2-one (14): DEAD (33 μL, 0.21 mmol) was added to a solution of alcohol **13** (40 mg, 0.068 mmol), triphenylphosphane (55 mg, 0.21 mmol), and *p*-nitrobenzoic acid (35 mg, 0.21 mmol) in dry toluene (2 mL) under an atmosphere of argon. The resulting mixture was stirred for 15 h at room temperature. After addition of water (0.5 mL) and separation of the layers, the aqueous layer was extracted with EtOAc (3 × 4 mL). The combined organic layer was washed with a saturated aqueous $NaHCO_3$ solution (2 mL) and water (2 mL), dried with $MgSO_4$, and concentrated. The residue was purified by chromatography over silica gel (cyclohexane/EtOAc, 8:2) to furnish *p*-nitrobenzoate **14** (38.2 mg, 76%) as a colorless oil. $[\alpha]_D^{23}$ = +63.6 (*c* = 0.44, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.05 (s, 9 H), 4.16 (dd, *J* = 6.6, 3.8 Hz, 1 H), 4.58 (d, *J* = 11.2 Hz, 1 H), 4.70–4.72 (m, 2 H), 5.00 (d, *J* = 3.8 Hz, 1 H), 5.44 (dd, *J* = 5.8, 2.5 Hz, 1 H), 6.17 (d, *J* = 9.6 Hz, 1 H), 6.93–7.07 (m, 6 H), 7.20–7.39 (m, 13 H), 7.60 (d, *J* = 6.8 Hz, 2 H), 7.83 (d, *J* = 8.8 Hz, 2 H), 8.09 (d, *J* = 8.8 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.3, 27.0, 64.0, 74.7, 75.8, 78.6, 82.4, 123.3, 125.5, 127.1, 127.4, 127.6, 127.8, 128.0, 128.2, 129.8, 129.9, 130.7, 132.6, 133.0, 133.6, 135.9, 136.0, 137.9, 139.2, 139.7, 150.6, 162.0, 163.2 ppm. HRMS (ESI): calcd. for $C_{43}H_{41}NO_8SiNa$ 750.2499; found 750.2498.

(5*S*,6*R*)-6-[(1*S*,2*R*)-1-(Benzyloxy)-2-{[*tert*-butyl(diphenyl)silyl]oxy}-2-phenylethyl]-5-hydroxy-5,6-dihydro-2*H*-pyran-2-one (15): A 1% K_2CO_3 solution (1.54 mL) was added to a solution of *p*-nitrobenzoate **14** (30 mg, 0.04 mmol) in THF (2.6 mL) at 0 °C. The solution was stirred at room temperature for 12 h, diluted with water, and extracted with EtOAc (3 × 3 mL). The combined organic layer was dried with $MgSO_4$ and concentrated. Purification of the residue by silica gel chromatography (cyclohexane/EtOAc, 7:3) gave alcohol **15** (14 mg, 53%) as a colorless oil. $[\alpha]_D^{23}$ = +11.1 (*c* = 0.18, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.03 (s, 9 H), 2.91 (br. s, 1 H), 3.93, (d, *J* = 10.3 Hz, 1 H), 4.01 (dd, *J* = 6.8, 3.8 Hz, 1 H), 4.25 (m, 1 H), 4.33 (d, *J* = 10.3 Hz, 1 H), 4.50 (dd, *J* = 3.2, 3.2 Hz, 1 H), 5.11 (d, *J* = 6.8 Hz, 1 H), 5.96 (d, *J* = 9.6 Hz, 1 H), 6.81 (dd, *J* = 9.6, 5.7 Hz, 1 H), 7.03–7.06 (m, 2 H), 7.21–7.37 (m, 16 H), 7.63–7.66 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.4, 27.1, 62.5, 74.5, 74.7, 77.2, 83.7, 122.7, 127.4, 127.7, 127.8, 128.0, 128.1, 128.2, 128.3, 128.4, 129.7, 129.8, 135.9, 136.0, 137.2, 140.5, 143.5, 162.1 ppm. HRMS (ESI): calcd. for $C_{36}H_{38}O_5SiNa$ 601.2386; found 601.2389.

(5*S*,6*R*)-6-[(1*R*,2*R*)-1,2-Dihydroxy-2-phenylethyl]-5-hydroxy-5,6-dihydro-2*H*-pyran-2-one [(+)-Goniotriol (2)]: The HF·pyridine complex (0.17 mL) was added to a room-temperature solution of silyl ether **15** (25 mg, 0.043 mmol) in CH_3CN (2 mL). After stirring for 2 d, the reaction mixture was quenched with a saturated aqueous $NaHCO_3$ solution (1 mL) and extracted with EtOAc (3 × 5 mL). The combined organic layer was dried with $MgSO_4$ and concentrated. The residual oil was dissolved in CH_2Cl_2 (1 mL) and $TiCl_4$ (1.0 M CH_2Cl_2 solution; 86 μL, 0.086 mmol) was added to the solution. The reaction mixture was stirred at room temperature for 2 h, diluted with a saturated $NaHCO_3$ solution, and extracted with CH_2Cl_2 (3 × 3 mL). The combined organic layer was washed with water and brine, dried with $MgSO_4$, and concentrated. The residue was purified by silica gel chromatography (cyclohexane/EtOAc, 2:8) to afford (+)-**2** (7.2 mg, 65%) as a white solid. M.p. 168–170 °C. $[\alpha]_D^{23}$ = +117 (*c* = 0.10, MeOH) [ref.[6b] m.p. 170 °C, $[\alpha]_D^{25}$ = +121.0 (MeOH)]. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.18 (dd, *J* = 7.9, 3.9 Hz, 1 H), 4.43 (dd, *J* = 5.4, 2.7 Hz, 1 H), 4.59 (dd, *J* = 3.9, 2.7 Hz, 1 H), 4.73 (d, *J* = 7.9 Hz, 1 H), 6.08 (d, *J* = 9.9 Hz, 1 H), 7.02 (dd, *J* = 9.9, 5.4 Hz, 1 H), 7.22–7.50 (m, 5 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 63.5, 73.9, 75.5, 80.3, 123.0, 128.7, 128.9, 129.2, 143.3, 146.4, 166.0 ppm. HRMS (ESI): calcd. for $C_{13}H_{14}O_5Na$ 273.0739; found 273.0742.

Ethyl (7*R*)-3,4-Anhydro-6-*O*-benzyl-7-*O*-[*tert*-butyl(diphenyl)silyl]-2-deoxy-7-*C*-phenyl-α-D-*talo*-heptopyranoside (16): *m*-CPBA (97 mg, 0.56 mmol) was added to a solution of ethyl lactol **8** (150 mg, 0.25 mmol) in CH_2Cl_2 (5 mL) at 0 °C under an atmosphere of argon. The resulting mixture was warmed to room temperature and stirred for 12 h. The mixture was washed with a saturated aqueous $NaHCO_3$ solution (3 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL) and the combined organic layer was dried with $MgSO_4$ and concentrated. Purification of the residue by deactivated silica gel chromatography (cyclohexane/EtOAc, 9:1) afforded **16** (107 mg, 69%) as a colorless oil. $[\alpha]_D^{23}$ = +18.7 (*c* = 0.40, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.05 (s, 9 H), 1.13 (t, *J* = 7.0 Hz, 3 H), 1.73 (ddd, *J* = 14.2, 9.3, 1.7 Hz, 1 H), 2.14 (ddd, *J* = 14.2, 2.1, 2.1 Hz, 1 H), 2.57 (d, *J* = 4.4 Hz, 1 H), 2.93 (m, 1 H), 3.17 (dq, *J* = 9.4, 7.0 Hz, 1 H), 3.61 (dq, *J* = 9.4, 7.0 Hz, 1 H), 3.95 (dd, *J* = 4.9, 4.9 Hz, 1 H), 4.18 (d, *J* = 4.4 Hz, 1 H), 4.31 (d, *J* = 11.8 Hz, 1 H), 4.34 (dd, *J* = 9.3, 2.7 Hz, 1 H), 4.53 (d, *J* = 11.8 Hz, 1 H), 5.12 (d, *J* = 5.5 Hz, 1 H), 7.12–7.49 (m, 18 H), 7.66 (dd, *J* = 7.8, 1.4 Hz, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.1, 19.3, 26.9, 27.1, 31.3, 52.9, 53.5, 64.4, 73.9, 74.3, 74.9, 83.3, 96.9, 127.3, 127.4, 127.5, 127.6, 127.7, 127.8, 128.2, 128.9, 129.5, 129.6, 133.2, 133.9, 135.9, 136.0, 138.5, 140.6 ppm. HRMS (ESI): calcd. for $C_{38}H_{44}O_5SiNa$ 631.2856; found 631.2858.

Ethyl (7*R*)-4,7-Anhydro-6-*O*-benzyl-2-deoxy-7-phenyl-α-D-*ido*-heptopyranoside (17): A 1.0 M solution of TBAF (220 μL, 0.22 mmol) was added to a solution of epoxide **16** (90 mg, 0.15 mmol) in THF (4.5 mL) at 0 °C under an atmosphere of argon. The resulting solution was stirred at 50 °C for 24 h. The reaction was quenched with CH_2Cl_2 (10 mL) and a saturated aqueous NH_4Cl solution (10 mL). The phases were separated and the aqueous layer extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layer was dried with $MgSO_4$ and concentrated, and the crude product was purified by silica gel chromatography (cyclohexane/EtOAc, 8:2) to give **17** (37.8 mg, 70%) as a colorless oil. $[\alpha]_D^{23}$ = +85.3 (*c* = 0.34, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.25 (t, *J* = 7.0 Hz, 3 H), 1.70 (br. s, 1 H), 1.84–1.88 (m, 2 H), 3.56 (dq, *J* = 9.1, 7.0 Hz, 1 H), 3.87 (dd, *J* = 2.5, 2.5 Hz, 1 H), 3.94 (dq, *J* = 9.1, 7.0 Hz, 1 H), 4.02 (d, *J* = 3.7 Hz, 1 H), 4.37 (d, *J* = 2.5 Hz, 1 H), 4.42 (m, 1 H), 4.58 (d, *J* = 11.6 Hz, 1 H), 4.63 (d, *J* = 11.6 Hz, 1 H), 4.82 (d, *J* = 3.7 Hz, 1 H), 4.86 (d, *J* = 2.0 Hz, 1 H), 7.28–7.39 (m, 8 H), 7.45–7.49 (m, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.3, 34.6, 64.3, 66.4, 72.3, 78.0, 78.5, 86.8, 91.0, 96.7, 126.9, 127.7, 127.8,

127.9, 128.5, 137.6, 140.0 ppm. HRMS (ESI): calcd. for $C_{22}H_{26}O_5Na$ 393.1678; found 393.1677.

(1*S*,5*R*,6*S*,8*R*,9*R*)-9-(Benzyloxy)-5-hydroxy-8-phenyl-2,7-dioxabicyclo[4.3.0]nonan-3-one (18): *m*-CPBA (56 mg, 0.32 mmol) followed by $BF_3{\cdot}OEt_2$ (42 μL, 0.32 mmol) were added to a solution of ethyl lactol **17** (30 mg, 0.08 mmol) in CH_2Cl_2 (2.5 mL) at 0 °C under an atmosphere of argon. The resulting mixture was warmed to room temperature and stirred for 12 h. The mixture was washed with a saturated aqueous $NaHCO_3$ solution (1 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL) and the combined organic layer was dried with $MgSO_4$ and concentrated. The residue was purified by silica gel chromatography (cyclohexane/EtOAc, 6:4) to afford **18** (25 mg, 90%) as a colorless oil. $[\alpha]_D^{23}$ = +42.1 (*c* = 0.40, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.40 (br. s, 1 H), 2.70 (dd, *J* = 16.7, 5.3 Hz, 1 H), 2.94 (dd, *J* = 16.7, 3.6 Hz, 1 H), 4.11 (dd, *J* = 6.0, 1.7 Hz, 1 H), 4.34 (dd, *J* = 4.5, 4.5 Hz, 1 H), 4.48 (m, 1 H), 4.57 (d, *J* = 11.6 Hz, 1 H), 4.70 (d, *J* = 11.6 Hz, 1 H), 4.84 (d, *J* = 6.0 Hz, 1 H), 5.09 (dd, *J* = 4.5, 1.7 Hz, 1 H), 7.28–7.46 (m, 10 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 35.2, 65.8, 72.6, 84.3, 84.9, 86.6, 90.4, 126.1, 127.8, 128.1, 128.4, 128.5, 128.7, 136.8, 138.1, 168.6 ppm. HRMS (ESI): calcd. for $C_{20}H_{20}O_5Na$ 363.1208; found 363.1207.

(1*S*,5*R*,6*S*,8*R*,9*R*)-5,9-Dihydroxy-8-phenyl-2,7-dioxabicyclo[4.3.0]-nonan-3-one [(–)-Goniofupyrone (3)]: $SnCl_4$ (1.0 M CH_2Cl_2 solution, 0.12 mL, 0.12 mmol) was added to a solution of benzyl ether **18** (20 mg, 0.059 mmol) in CH_2Cl_2 (1.5 mL) at room temperature. The reaction mixture was heated at 40 °C for 10 h. After cooling, the reaction was quenched with a saturated aqueous $NaHCO_3$ solution. The aqueous layer was extracted with CH_2Cl_2 (3 × 3 mL) and the combined organic layer was washed with water, dried with $MgSO_4$, and concentrated to dryness. Chromatography of the residue (cyclohexane/EtOAc, 3:7) gave (–)-**3** (11.8 mg, 80%) as a colorless oil. $[\alpha]_D^{23}$ = –6.2 (*c* = 0.10, $CHCl_3$) [ref.[6e] $[\alpha]_D$ = –5.0 (*c* = 0.10, $CHCl_3$)]. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.65 (ddd, *J* = 16.6, 5.8, 1.0 Hz, 1 H), 2.78 (br. s, 1 H), 2.91 (dd, *J* = 16.6, 3.9 Hz, 1 H), 3.31 (br. s, 1 H), 4.29 (dd, *J* = 6.4, 2.4 Hz, 1 H), 4.36 (ddd, *J* = 5.4, 3.9, 1.0 Hz, 1 H), 4.44 (dt, *J* = 5.9, 3.9 Hz, 1 H), 4.70 (d, *J* = 6.4 Hz, 1 H), 4.96 (dd, *J* = 5.4, 2.4 Hz, 1 H), 7.28–7.36 (m, 5 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 35.1, 65.8, 76.4, 83.7, 85.7, 86.8, 126.0, 128.5, 128.7, 137.9, 169.3 ppm. HRMS (ESI): calcd. for $C_{13}H_{14}O_5Na$ 273.0739; found 273.0740.

(1*S*,6*S*,8*R*,9*R*)-9-(Benzyloxy)-8-phenyl-2,7-dioxabicyclo[4.3.0]non-4-en-3-one (19): *p*-$TsOH{\cdot}H_2O$ (4 mg, 0.02 mmol) was added to a solution of alcohol **18** (20 mg, 0.059 mmol) in toluene (2.5 mL). The reaction mixture was stirred at 85 °C for 5 h, neutralized with a saturated aqueous $NaHCO_3$ solution, and extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layer was dried with $MgSO_4$ and concentrated. The residue was purified by silica gel chromatography (cyclohexane/EtOAc, 6:4) to afford **19** (13.3 mg, 73%) as a colorless oil. $[\alpha]_D^{23}$ = +151.9 (*c* = 0.53, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 4.26 (dd, *J* = 5.3, 1.4 Hz, 1 H), 4.59 (d, *J* = 5.1 Hz, 1 H), 4.64 (d, *J* = 11.6 Hz, 1 H), 4.68 (d, *J* = 11.6 Hz, 1 H), 4.87 (dd, *J* = 5.3, 2.4 Hz, 1 H), 5.03 (dd, *J* = 4.7, 1.4 Hz, 1 H), 6.27 (d, *J* = 9.8 Hz, 1 H), 7.02 (dd, *J* = 9.8, 4.7 Hz, 1 H), 7.28–7.33 (m, 10 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 68.7, 72.8, 84.2, 85.3, 90.8, 124.3, 126.2, 127.8, 128.1, 128.3, 128.5, 128.6, 136.8, 138.2, 139.5, 160.9 ppm. HRMS (ESI): calcd. for $C_{20}H_{18}O_4Na$ 345.1103; found 345.1102.

(1*S*,6*S*,8*R*,9*R*)-9-Hydroxy-8-phenyl-2,7-dioxabicyclo[4.3.0]non-4-en-3-one [(+)-Altholactone (4)]: $SnCl_4$ (1.0 M CH_2Cl_2 solution, 62 μL, 0.062 mmol) was added to a solution of benzyl ether **19** (10 mg, 0.031 mmol) in CH_2Cl_2 (1 mL) at room temperature. The reaction mixture was heated at 40 °C for 24 h. After cooling, the reaction was quenched with a saturated aqueous $NaHCO_3$ solution. The aqueous layer was extracted with CH_2Cl_2 (3 × 2 mL) and the combined organic layer was washed with water, dried with $MgSO_4$, and concentrated to dryness. The residue was purified by silica gel chromatography (cyclohexane/EtOAc, 1:1) to afford (+)-**4** (5.6 mg, 78%) as a white solid. M.p. 108–110 °C. $[\alpha]_D^{23}$ = +181.4 (*c* = 0.10, EtOH) [lit.:[6a] m.p. 110 °C, $[\alpha]_D$ = +184.7 (EtOH)]. ^1H NMR (300 MHz, $CDCl_3$): δ = 2.48 (br. s, 1 H), 4.49 (dd, *J* = 5.6, 2.4 Hz, 1 H), 4.68 (dd, *J* = 5.1, 5.1 Hz, 1 H), 4.76 (d, *J* = 5.6 Hz, 1 H), 4.97 (dd, *J* = 5.4, 2.4 Hz, 1 H), 6.26 (d, *J* = 9.9 Hz, 1 H), 7.02 (dd, *J* = 9.9, 4.9 Hz, 1 H), 7.30–7.38 (m, 5 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 68.2, 83.7, 86.0, 86.2, 123.8, 126.1, 128.4, 128.7, 138.0, 140.2, 161.1 ppm. HRMS (ESI): calcd. for $C_{13}H_{12}O_4Na$ 255.0633; found 255.0634.

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[20] With an excess amount of aldehyde **6** (2 equiv.) the yield can be enhanced to 78% when the reaction is warmed in toluene at 70 °C for 48 h.

[21] A drop in the diastereoselectivity is observed (90% *dr*) under the same conditions by using the enantiomer of aldehyde **6**.

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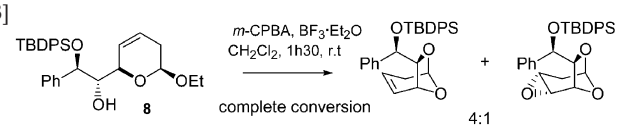
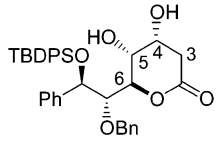


[24] The relative stereochemistry of the C-5 and C-6 atoms in **12** was also confirmed by the synthesis of the stable vicinal diol by using a catalytic amount of OsO_4 and *N*-methylmorpholine *N*-oxide as cooxidant. The reaction led to the formation of a single diastereomer with a coupling constant of 9.1 Hz between 5-H and 6-H, which indicates that the dihydroxylation, like the epoxidation, takes place from the sterically less-hindered face of alkene **10**.



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