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C-Glycosyl Juglone in Angucycline Synthesis: Total Synthesis of Galtamycinone, Common Aglycon of *C*-Glycosyl Naphthacenequinone-Type Angucyclines

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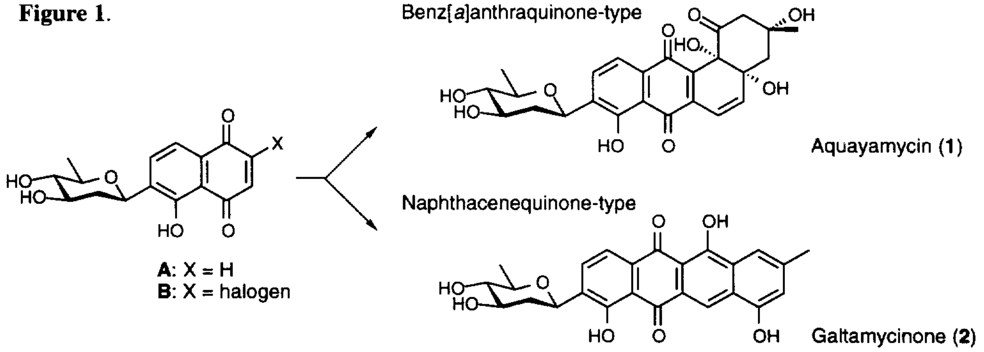
Abstract: A two-step access to *C*-glycosyl juglones, **16** and **17**, useful intermediates toward the angucyclines, either benz[*a*]anthraquinone-type or naphthacenequinone-type, has been developed based on (1) the *O*→*C*-glycoside rearrangement and (2) the regioselective cycloaddition of α-alkoxybenzyne and α-oxyfuran. The first total synthesis of galtamycinone (**2**), the common aglycon of naphthacenequinone-type angucyclines, has been achieved by utilizing **17** as the key intermediate.

Introduction

The angucyclines constitute the largest family of aryl *C*-glycoside antibiotics, attracting considerable synthetic interests due to the significant biological activities as well as the synthetically challenging structures.[1,2] The decaketide-derived curved (*angular*) tetracycle, from which the group name has stemmed, is represented in the structure of aquayamycin (**1**), the first member of aryl *C*-glycoside antibiotics.[3] However, a new class of congeners has begun to emerge, which are armed with a *linear* tetracycle as represented by galtamycinone (**2**).[4] These compounds are, despite the linear framework, also categorized as the angucyclines from the biogenetic standpoint,[1] and are attracting biological interests in structural relation to the anthracyclines, a clinically important class of antitumor agents.

Figure 1.

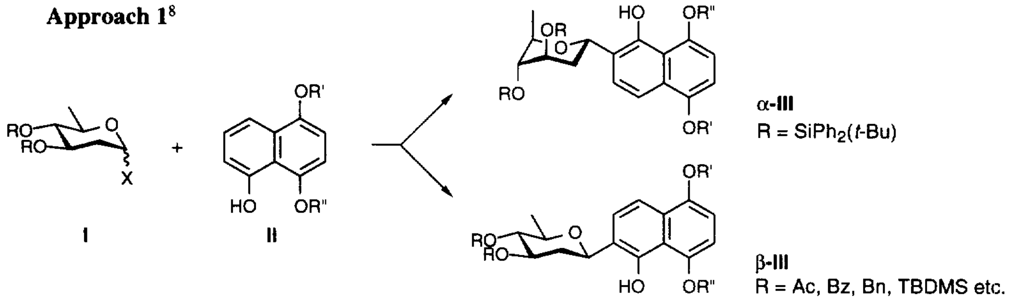


We reasoned that *C*-glycosylated juglone **A** or its halogenated congener **B** would serve as a general intermediate in the synthesis of both classes of the angucyclines, either angular (benz[*a*]anthraquinone-type) or linear (naphthacenequinone-type). The basis of the expectation is the wide availability of annulation procedures established for the parent juglones for constructing polyaromatic skeletons,[5,6] whether the angular or the linear derivatives are concerned.[6] Herein, we detail an easy access to the *C*-glycosylated juglones **A** and **B** (X = Cl). Also discussed is the synthetic utility of **B** in the context of the first total synthesis of galtamycinone (**2**), the common aglycon of the linear-type angucyclines.[7]

Results and Discussion

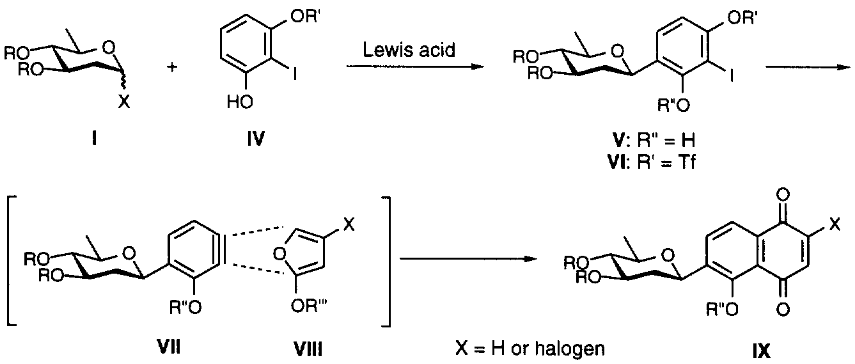
We previously showed a possible approach to such intermediates via the direct *C*-glycosylation of naphthalenetriol derivative **II** (Approach 1).[8] The *O*→*C*-glycoside rearrangement[9] effected the regioselective installation of the sugar at the ortho position to the free phenol. Furthermore, either the α- or β-*C*-glycoside of D-olivose, the sugar component typically included in the angucyclines, became accessible by suitable choice of the protecting groups of the sugar.[10]

Approach 1[8]



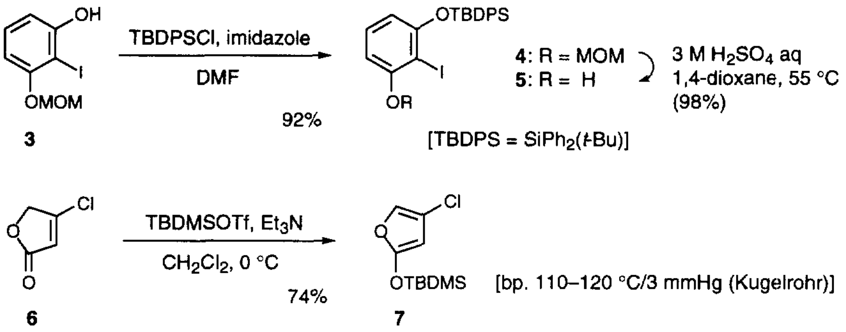
Although the above approach is attractive in its own right, a parallel study offered us an optional approach to *C*-glycosylated juglone derivatives with greater flexibility and efficiency as outlined below (Approach 2).[7,11,12] Firstly, mono-protected iodoresorcinol **IV** is *C*-glycosylated at the ortho position to the free phenol by the *O*→*C*-glycoside rearrangement.[9] Then, the oxygen functionality in **V** is selectively manipulated for the regioselective generation of benzyne **VII** that undergoes cycloaddition with α-oxyfuran **VIII** to form naphthoquinone skeleton.[13] If required, the *head-to-head* mode of cycloaddition, with respect to the two oxy-substituents,[9f,g,11,13] permits the site-selective installation of the halogen in **IX**, which serves as a regiocontrolling factor for further elaboration to the angucyclines.

Approach 2 (present report)[7]



Preparation of the starting materials: Scheme 1 shows the preparation of the starting materials, mono-protected 2-iodoresorcinol **5** and chlorofuran **7**, which are corresponding to **IV** and **VIII** in the above scheme, respectively.

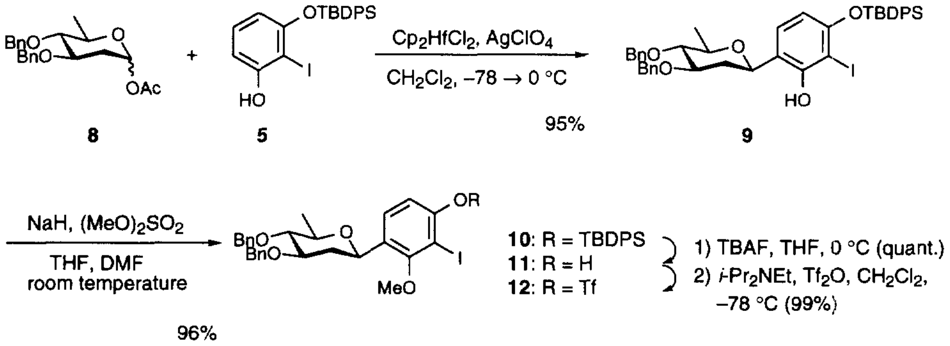
Scheme 1.



After silylation of the known phenol **3**,[9g] the MOM group was selectively removed under acidic conditions to give **5** in high overall yield. Chlorofuran **7** was prepared by the enolization–silylation of 4-chloro-2(5*H*)-furanone (**6**)[14] according to the procedure for the corresponding bromo congener.[15]

Aryl *C*-glycoside formation: Upon treatment of 3,4-di-*O*-benzyl-D-olivosyl acetate[16] (**8**, 1.0 equiv.) and resorcinol **5** (1.4 equiv.) with Cp_2HfCl_2 (1.5 equiv.) and $AgClO_4$ (3.0 equiv.) in CH_2Cl_2 at –78 °C, the phenol was rapidly converted to the *O*-glycoside. Subsequent warming to 0 °C effected conversion of the *O*-glycoside to the corresponding *C*-glycoside to give β-**9** as a sole product in 95% yield.[8,9b,d,11] Then, the two oxygen functionalities on the aromatic ring in **9** are elaborated in order to prepare the benzyne precursor **12**. Thus, methylation of the phenol in **9**, removal of the TBDPS group, and triflate formation afforded the benzyne precursor **12** in high overall yield.

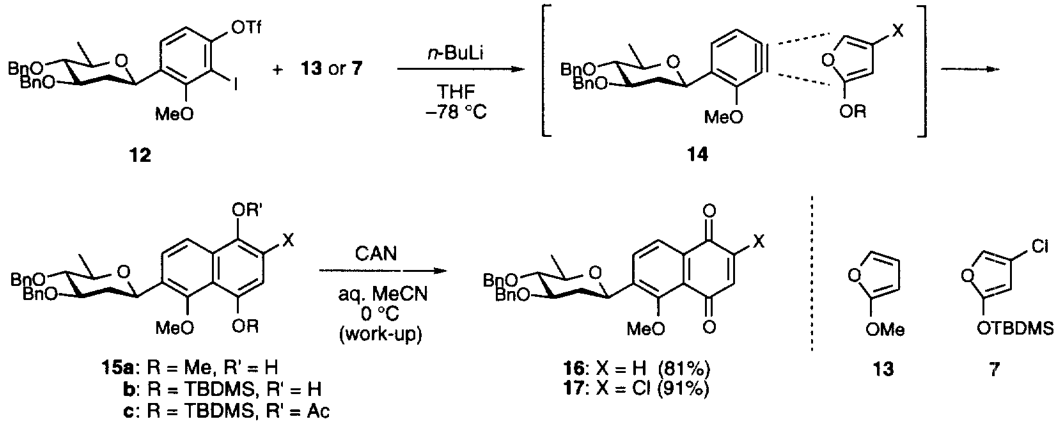
Scheme 2 *C*-Olivosylation of resorcinol derivative **5** by *O*→*C*-glycoside rearrangement.



Synthesis of non-halogenated juglone 16: Non-halogenated juglone **16** proved to be accessible by the cycloaddition of 2-methoxyfuran (**13**). Triflate **12** was treated with *n*-BuLi (1.6 equiv.) at –78 °C in the presence of **13** (3.0 equiv.). The benzyne **14**, thus generated, underwent clean cycloaddition with **13**, and the adduct underwent spontaneous aromatization at the temperature. Since it was found that the resulting naphthol **15a** is too unstable for isolation, we opted to work up the reaction mixture with ceric ammonium nitrate (CAN) to obtain quinone **16** in high yield.

Synthesis of chlorojuglone 17: We have collected a good deal of data that suggests this class of cycloaddition proceeds regioselectively (vide supra),[9f,g,11,13] which could be exploited for the selective synthesis of more elaborated juglones. Indeed, chlorofuran **7** underwent cycloaddition with benzyne **14** in a regioselective manner to give an excellent yield of 2-chlorojuglone **17** as a sole detectable product. It is fortunate that lithiation of chlorofuran **7** did not compete with the extremely rapid iodine–lithium exchange. The position of the chlorine atom was determined by the NOE experiment on acetate **15c** (see Experimental), which was prepared by the immediate acetylation of the crude cycloadduct **15b**. None of the 3-chloro congener was detected. The chlorine atom in **17** serves as a pivot for controlling the regioselectivity in further synthetic transformations.[5]

Scheme 3 Synthesis of *C*-olivosyl juglones via benzyne–furan cycloaddition.



Thus, a unified access has been established for the synthesis of the *C*-olivosyl juglones, **16** and **17**, which are potentially versatile intermediates for the synthesis of the angucyclines. In the following, we illustrate a part of their utility by the application of the first total synthesis of galtamycinone (**2**), the common aglycon of the linear-type angucyclines.

Total synthesis of galtamycinone: Figure 2 illustrates the naphthacenequinone-type angucyclines, recently isolated.[4] They are significant in the biogenetic study of the angucyclines,[1] and there are interests in their biological activities in lieu of the structural relation to the anthracyclines. The linear aromatic structure derives from the classical, benz[*a*]anthraquinone skeleton via enzymatic or non-enzymatic processes.[1]

Historically, galtamycinone (**2**), the common aglycon of this class of natural products, was obtained as the degradation product of aquayamycin prior to its discovery from natural sources.[3]

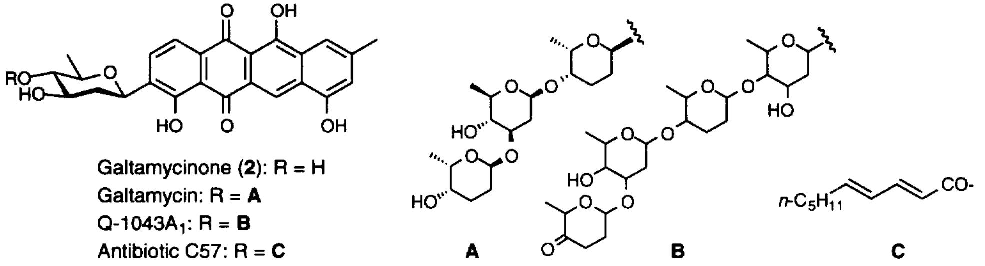
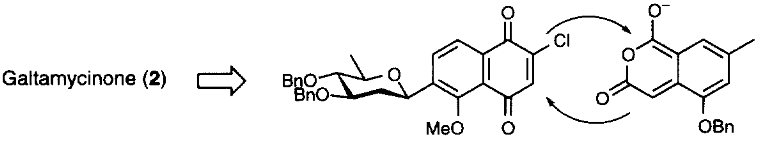


Figure 2 Naphthacenequinone-type angucyclines.

We envisaged that the *C*-glycosylated tetracycle of galtamycinone (**2**) would be directly accessible by applying the Kita–Tamura chemistry to chlorojuglone **17**, i.e., the base-induced cycloaddition with homophthalic anhydride (eq. 2).[17]

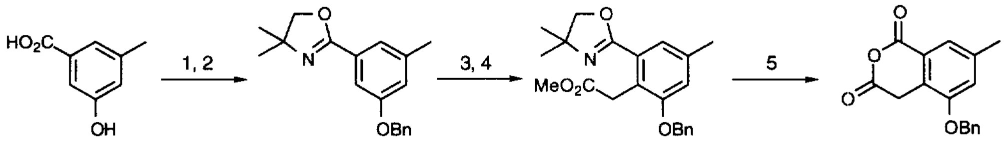


17

(2)

The coupling partner, homophthalic anhydride **21**, was prepared from the known benzoic acid **18**[18] via oxazoline-based chemistry[19] (Scheme 4). After protection of the hydroxyl group as a benzyl ether, acid **18** was converted to ester **20** via oxazoline **19** by repeated directed metallation;[19] (1) *ortho*-lithiation of **19** by using *n*-BuLi and methylation, and (2) the deprotonation of the newly introduced methyl (*benzylic*) followed by acylation with $ClCO_2Me$. For the next step, simultaneous hydrolysis of the oxazoline and the ester moieties in **20**, basic conditions were employed, since the attempted usual acid hydrolysis caused removal of the benzyl protective group.[20] Subsequent dehydration of the resulting diacid with acetyl chloride gave anhydride **21**.

Scheme 4 Preparation of homophthalic anhydride **21**.

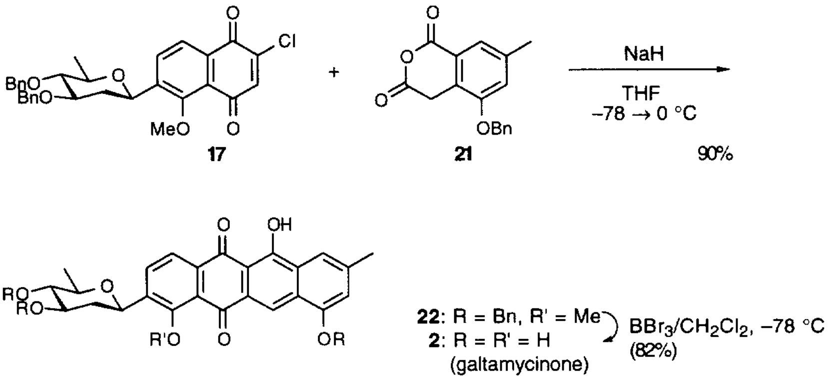


18 **19** **20** **21**

Keys: 1. (i) BnBr, K_2CO_3/acetone; (ii) aq. NaOH, MeOH (91%); 2. (i) $SOCl_2$; (ii) $H_2NC(Me)_2CH_2OH/CH_2Cl_2$; (iii) $SOCl_2$ (87%); 3. *n*-BuLi/THF, $-78 \rightarrow -45$ °C; then MeI (55%); 4. *n*-BuLi/THF, $-78 \rightarrow 0$ °C; then $ClCO_2Me$ (61%); 5. (i) $ClCO_2Bn$, aq. $NaHCO_3/CH_2Cl_2$; (ii) aq. NaOH, MeOH; (iii) MeCOCl/acetone (89%).

Treatment of anhydride **21** with NaH in THF at 0 °C generated a yellow solution of the corresponding anion, to which was added, after cooling to –78 °C, chloroquinone **17**. Upon gradual warming to 0 °C, the cycloaddition cleanly proceeded in highly regioselective manner as expected from literature precedents[5,17] to give, after spontaneous decarboxylation, naphthacenequinone **22** in 90% yield. Although the cycloaddition proceeds in a temperature range of ca. –30 to 0 °C as judged by TLC analysis, careful admixing of **17** and the anion of **21** at lower temperature is required to avoid concomitant formation of the isomeric adduct due to an increase in the internal temperature. The protecting groups in **22** were removed on exposure to BBr_3 at –78 °C, which completed the first synthesis of galtamycinone (**2**). The synthetic material was fully identical with an authentic sample by direct comparison (mp, $[\alpha]_D$, ^1H NMR, IR, and HRMS).[21]

Scheme 5 Total synthesis of galtamycinone.



	synthetic material	authentic sample
Mp	283.5–284.5 °C	282–283 °C
$[\alpha]_D$	+177 (*c* 0.13, 1,4-dioxane)	+176 (*c* 0.14, 1,4-dioxane)

Conclusion

A two-step access to *C*-glycosyl juglones is described, which would serve as valuable intermediates in the synthesis of the angucyclines of either benz[*a*]anthraquinone-type (angular) or naphthacenequinone-type (linear). The latter aspect was demonstrated by the application to the first total synthesis of galtamycinone (**2**). Further studies on the synthesis of the angular as well as linear angucyclines by applying these tactics are now in progress.

Acknowledgments. We are grateful to Dr. Shinichi Kondo, Institute of Microbial Chemistry, for providing us with valuable sample of aquayamycin. We thank also Prof. O. Vajna de Pava, Politecnico de Milano for kind information on the specific rotation of **2**. Partial financial support from the Ciba–Geigy Foundation (Japan) for the Promotion of Science is gratefully acknowledged.

Experimental Section

General procedures. All experiments dealing with air- and moisture-sensitive compounds were conducted under an atmosphere of argon. THF was distilled from benzophenone ketyl immediately before use. Dichloromethane was distilled successively from P_2O_5 and CaH_2 and stored over 4Å molecular sieves. For thin-layer chromatography (TLC) analysis, Merck precoated plates (silica gel 60 F254, Art 5715, 0.25 mm) were used. Silica gel 60 K070-WH (70–230 mesh) from Katayama Chemical was used for flash column chromatography. Silica gel preparative TLC (PTLC) was performed on Merck Kieselgel 60 PF254 (Art 7747). Melting point (mp) determinations were performed by using a Yanaco MP-S3 instrument and are uncorrected. ^{1}H (400 MHz) and ^{13}C NMR spectra (100 MHz) were measured on a JEOL JNM GX-400 spectrometer. Chemical shifts are expressed in parts per million downfield from internal tetramethylsilane (δ = 0). Infrared (IR) spectra were recorded on a Jasco IRA-202 spectrometer. Optical rotations ($[\alpha]_D$) were measured on Jasco DIP-360 polarimeter. High-resolution mass spectra under electron impact conditions (HRMS) were obtained with a Hitachi M-80 spectrometer.

3-(*tert*-Butyldiphenylsilyloxy)-2-iodo-1-(methoxymethoxy)benzene (4). A solution of 2-iodo-3-(methoxymethoxy)phenol[9g] (2.14 g, 7.64 mmol), imidazole (1.30 g, 19.1 mmol), and *tert*-butyldimethylsilyl chloride (5.25 g, 19.1 mmol) in DMF (16 mL) was stirred at room temperature for 30 min. The reaction was stopped by adding pH 7 phosphate buffer at 0 °C, and the products were extracted with Et_2O (x3). The combined organic extracts were washed successively with water, 2 M HCl, brine, saturated aqueous $NaHCO_3$, and dried over Na_2SO_4. Concentration in vacuo followed by purification by column chromatography (hexane/EtOAc = 92/8) gave silyl ether **4** as a colorless oil (3.63 g, 91.7%); ^{1}H NMR ($CDCl_3$) δ 1.16 (s, 9H), 3.54 (s, 3H), 5.24 (s, 2H), 6.08 (dd, 1H, J_1 = 8.2, J_2 = 1.0 Hz), 6.58 (dd, 1H, J_1 = 8.2, J_2 = 1.0 Hz), 6.78 (dd, 1H, J_1 = J_2 = 8.2 Hz), 7.33–7.48 (m, 6H), 7.70–7.77 (m, 4H); IR (NaCl) 2860, 1584, 1455, 1400, 1295, 1245, 1155, 1110, 1045 cm^{-1}.

3-(*tert*-Butyldiphenylsilyloxy)-2-iodophenol (5). A solution of silyl ether **4** (1.22 g, 2.35 mmol) and aqueous H_2SO_4 (3 M, 17 mL) in 1,4-dioxane (52 mL) was stirred at 55 °C for 5 h. After cooling, the mixture was diluted with EtOAc, washed with brine, and dried over Na_2SO_4. Concentration in vacuo followed by purification by column chromatography (hexane/EtOAc = 9/1) gave phenol **5** as a colorless solid (1.09 g, 97.6%); mp 125.5–126 °C; ^{1}H NMR ($CDCl_3$) δ 1.16 (s, 9H), 5.44 (s, 1H), 5.96 (dd, 1H, J_1 = 8.3, J_2 = 1.3 Hz), 6.53 (dd, 1H, J_1 = 8.3, J_2 = 1.3 Hz), 6.74 (dd, 1H, J_1 = J_2 = 8.3 Hz), 7.34–7.47 (m, 6H), 7.71–7.75 (m, 4H); IR (KBr) 3500, 2950, 1580, 1460, 1440, 1425, 1320, 1270, 1190, 1105, 1040 cm^{-1}; Anal. Calcd for $C_{22}H_{23}O_2SiI$: C, 55.70; H, 4.89. Found: C, 55.51; H, 5.01.

2-(*tert*-Butyldimethylsilyloxy)-4-chlorofuran (7).[15] To a chilled (0 °C) solution of 4-chloro-2(5*H*)-furanone (177 mg, 1.49 mmol)[14] and Et_3N (380 mg, 3.76 mmol) in CH_2Cl_2 was added TBDMSOTf (0.68 mL, 4.0 mmol). After stirring for 1 h, the reaction was stopped by adding 1% aqueous NaOH solution, and the products were extracted with Et_2O (x3). The combined organic extracts were washed with brine, and dried over Na_2SO_4. Concentration in vacuo followed by distillation [bp. 110–120 °C/3 mmHg (Kugelrohr, oven temp.)] gave furan **7** as a colorless oil (256 mg, 73.9%); ^{1}H NMR (C_6D_6) δ 0.02 (s, 6H), 0.85 (s, 9H), 5.15 (d, 1H, J = 1.0 Hz), 6.54 (d, 1H, J = 1.0 Hz).

6-(3,4-Di-*O*-benzyl-2,6-dideoxy-β-D-*arabino*-hexopyranosyl)-3-(*tert*-butyldiphenylsilyloxy)-2-iodophenol (9). To a suspension of Cp_2HfCl_2 (845 mg, 2.23 mmol), $AgClO_4$* (923 mg, 4.45 mmol), and powdered 4A molecular sieves (ca 1.20 g) in CH_2Cl_2 (5 mL) were added a solution of phenol **5** (841 mg, 1.77 mmol) in CH_2Cl_2 (20 mL) and D-olivosyl acetate **8** (549 mg, 1.48 mmol) in CH_2Cl_2 (10 mL) at –78 °C. The reaction mixture was gradually warmed to 0 °C during 40 min, and the stirring was continued for 15 min. After the reaction was stopped by adding pH 7 phosphate buffer, the mixture was acidified with 2 M HCl, and filtered through a Celite pad. The products were extracted with EtOAc (x3), and the combined organic extracts were washed with brine, and dried over Na_2SO_4. Concentration in vacuo followed by purification by flash column chromatography (hexane/acetone = 85/15) gave *C*-glycoside **9** as a white foam (1.10 g, 94.6%); mp 62–64 °C; ^{1}H NMR ($CDCl_3$) δ 1.15 (s, 9H), 1.35 (d, 3H, J = 6.1 Hz), 1.82 (ddd, 1H, J_1 = 13.2, J_2 = 11.7, J_3 = 11.2 Hz), 2.31 (ddd, 1H, J_1 = 13.2, J_2 = 4.9, J_3 = 2.0 Hz), 3.17 (dd, 1H, J_1 = 9.3, J_2 = 8.8 Hz), 3.51 (dq, 1H, J_1 = 9.3, J_2 = 6.1 Hz), 3.70 (ddd, 1H, J_1 = 11.2, J_2 = 8.8, J_3 = 4.9 Hz), 4.51 (dd, 1H, J_1 = 11.7, J_2 = 2.0 Hz), 4.58 (d, 1H, J = 11.4 Hz), 4.67 (d, 2H, J = 11.4 Hz), 4.97 (d, 1H, J = 10.4 Hz), 5.91 (d, 1H, J = 8.3 Hz), 6.54 (d, 1H, J = 8.3 Hz), 7.25–7.47 (m, 16H), 7.69–7.76 (m, 4H), 8.29 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 18.6, 19.7, 26.5, 37.1, 71.3, 75.4, 76.1, 76.8, 80.2, 82.0, 83.4, 110.3, 118.1, 126.5, 127.60, 127.64, 127.71, 127.79, 127.85, 127.87, 128.1, 128.4, 130.0, 132.0, 132.2, 135.4, 138.27, 138.29, 155.1, 155.5; IR (KBr) 3320, 2880, 1610, 1560, 1485, 1455, 1430, 1355, 1300, 1205, 1115, 1040 cm^{-1}; $[\alpha]^{20}_D$ –6.0 (*c* 1.4, $CHCl_3$); Anal. Calcd for $C_{42}H_{45}O_5SiI$: C, 64.28; H, 5.78. Found: C, 64.10; H, 6.00. **Caution*: $AgClO_4$ was purchased from Kojima Chemical Co. (99%) and used as such. Heating or drying should be avoided because $AgClO_4$ is potentially explosive.[22]

1-(3,4-Di-*O*-benzyl-2,6-dideoxy-β-D-*arabino*-hexopyranosyl)-4-(*tert*-butyldiphenylsilyloxy)-3-iodo-2-methoxybenzene (10). To a suspension of NaH (60 % in oil, 229 mg, 5.72 mmol) in THF (4 mL) was added a solution of *C*-glycoside **9** (898 mg, 1.15 mmol) in THF (20 mL) at 0 °C. The mixture was stirred for 10 min, to which were added $(MeO)_2SO_2$ (0.54 mL, 5.7 mmol) and

DMF (6 mL), and the stirring was continued at room temperature for 1 h. The reaction was stopped by adding Et_2NH (1.0 mL) followed by, after 10 min, pH 7 phosphate buffer at 0 °C. The products were extracted with Et_2O (x3), and the combined organic extracts were washed with 2 M HCl, brine, and dried over Na_2SO_4. Concentration in vacuo followed by purification by flash column chromatography (hexane/EtOAc = 19/1) gave methyl ether **10** as a colorless oil (874 mg, 95.6%); ^1H NMR ($CDCl_3$) δ 1.16 (s, 9H), 1.29 (d, 3H, J = 6.1 Hz), 1.64 (ddd, 1H, J_1 = 12.7, J_2 = J_3 = 11.2 Hz), 2.28 (ddd, 1H, J_1 = 12.7, J_2 = 4.9, J_3 = 1.5 Hz), 3.13 (dd, 1H, J_1 = 9.0, J_2 = 8.8 Hz), 3.50 (dq, 1H, J_1 = 9.0, J_2 = 6.1 Hz), 3.75 (ddd, 1H, J_1 = 11.2, J_2 = 8.8, J_3 = 4.9 Hz), 3.84 (s, 3H), 4.58 (d, 1H, J = 11.7 Hz), 4.61–4.69 (m, 3H), 4.97 (d, 1H, J = 11.0 Hz), 6.20 (d, 1H, J = 8.5 Hz), 6.97 (d, 1H, J = 8.5 Hz), 7.22–7.46 (m, 16H), 7.70–7.73 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 18.6, 19.7, 26.5, 37.7, 61.7, 71.2, 72.1, 75.2, 75.8, 80.9, 84.0, 87.8, 115.0, 127.3, 127.56, 127.60, 127.65, 127.74, 127.88, 127.91, 127.94, 128.3, 128.4, 130.06, 130.08, 131.88, 131.93, 135.41, 135.44, 138.4, 138.6, 155.6, 158.2; IR (NaCl) 2860, 1590, 1470, 1430, 1380, 1365, 1295, 1245, 1200, 1105, 1050 cm^{-1}; $[\alpha]^{20}_D$ −19.7 (*c* 1.20, $CHCl_3$); Anal. Calcd for $C_{43}H_{47}O_5SiI$: C, 64.65; H, 5.93. Found: C, 64.36; H, 5.78.

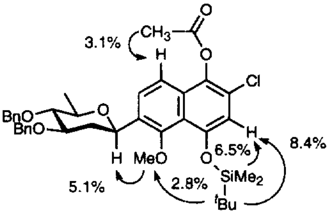
4-(3,4-Di-*O*-benzyl-2,6-dideoxy-β-D-*arabino*-hexopyranosyl)-2-iodo-3-methoxyphenol (11). To a solution silyl ether **10** (156 mg, 0.195 mmol) in THF (2.4 mL) was added TBAF (1.0 M in THF, 0.39 mL, 0.39 mmol) at 0 °C. After stirring for 20 min, 2 M HCl was added to the mixture, and the products were extracted with Et_2O (x3). The combined extracts were washed with 2 M HCl, brine, and dried over Na_2SO_4. Concentration in vacuo followed by purification by flash column chromatography (hexane/EtOAc = 4/1) gave phenol **11** as a colorless oil (109 mg, 99.6%); ^1H NMR ($CDCl_3$) δ 1.34 (d, 3H, J = 6.1 Hz), 1.77 (ddd, 1H, J_1 = 12.9, J_2 = 11.7, J_3 = 11.2 Hz), 2.30 (ddd, 1H, J_1 = 12.9, J_2 = 4.9, J_3 = 2.0 Hz), 3.21 (dd, 1H, J_1 = 9.0, J_2 = 8.8 Hz), 3.54 (dq, 1H, J_1 = 9.0, J_2 = 6.1 Hz), 3.79 (ddd, 1H, J_1 = 11.2, J_2 = 8.8, J_3 = 4.9 Hz), 3.80 (s, 3H), 4.62 (d, 1H, J = 11.7 Hz), 4.66 (dd, 1H, J_1 = 11.7, J_2 = 2.0 Hz), 4.70 (d, 1H, J = 11.7 Hz), 4.71 (d, 1H, J = 11.0 Hz), 5.00 (d, 1H, J = 11.0 Hz), 5.58 (s, 1H), 6.77 (d, 1H, J = 8.5 Hz), 7.23–7.37 (m, 11H); ^{13}C NMR ($CDCl_3$) δ 18.7, 37.8, 61.8, 71.3, 72.0, 75.3, 75.9, 81.0, 84.0, 84.1, 111.4, 127.4, 127.63, 127.68, 127.71, 128.0, 128.37, 128.41, 128.6, 138.4, 138.6, 155.8, 157.3; IR (NaCl) 3300, 2890, 1600, 1570, 1500, 1480, 1455, 1415, 1385, 1370, 1300, 1200, 1110, 1040 cm^{-1}; $[\alpha]^{20}_D$ +6.7 (*c* 1.3, $CHCl_3$); HRMS *m/z* 560.1067 (560.1059 calcd for $C_{27}H_{29}O_5I$, M^+).

4-(3,4-Di-*O*-benzyl-2,6-dideoxy-β-D-*arabino*-hexopyranosyl)-2-iodo-3-methoxyphenyl trifluoromethanesulfonate (12). To a chilled (−78 °C) solution of phenol **11** (380 mg, 0.679 mmol) and *i*-Pr_2NEt (175 mg, 1.36 mmol) in CH_2Cl_2 (35 mL) was added Tf_2O (574 mg, 2.03 mmol) in CH_2Cl_2 (10 mL). After stirring for 15 min, the reaction was stopped by adding saturated $NaHCO_3$ solution. The products were extracted with Et_2O (x3), and the combined organic extracts were washed with brine, and dried over Na_2SO_4. Concentration in vacuo followed by purification by flash column chromatography (hexane/EtOAc = 9/1) gave triflate **12** as a colorless oil (463 mg, 98.6%); ^1H NMR ($CDCl_3$) δ 1.36 (d, 3H, J = 6.1 Hz), 1.64 (ddd, 1H, J_1 = 12.9, J_2 = J_3 = 11.2 Hz), 2.39 (ddd, 1H, J_1 = 12.9, J_2 = 4.9, J_3 = 2.0 Hz), 3.21 (dd, 1H, J_1 = 9.0, J_2 = 8.8 Hz), 3.54 (dq, 1H, J_1 = 9.0, J_2 = 6.1 Hz), 3.80 (ddd, 1H, J_1 = 11.2, J_2 = 8.8, J_3 = 4.9 Hz), 3.84 (s, 3H), 4.63 (d, 1H, J = 11.5 Hz), 4.66–4.72 (m, 1H), 4.70 (d, 1H, J = 11.5 Hz), 4.71 (d, 1H, J = 11.0 Hz), 5.01 (d, 1H, J = 11.0 Hz), 7.13 (d, 1H, J = 8.8 Hz), 7.24–7.37 (m, 10H), 7.56 (d, 1H, J = 8.8 Hz); ^{13}C NMR ($CDCl_3$) δ 18.6, 38.1, 62.0, 71.4, 72.0, 75.3, 76.0, 80.7, 83.8, 88.6, 118.2, 118.7, 127.69, 127.72, 128.0, 128.4, 128.6, 136.0, 138.3, 138.5, 150.3, 158.6; IR (NaCl) 1590, 1500, 1465, 1430, 1390, 1370, 1220, 1140, 1115, 1020 cm^{-1}; $[\alpha]^{21}_D$ +17.2 (*c* 2.51, $CHCl_3$); HRMS *m/z* 692.0530 (692.0551 calcd for $C_{28}H_{28}O_7F_3SI$, M^+).

6-(3,4-Di-*O*-benzyl-2,6-dideoxy-β-D-*arabino*-hexopyranosyl)-5-methoxy-1,4-naphthoquinone (16). To a mixture of freshly distilled 2-methoxyfuran (70.9 mg, 0.723 mmol) and triflate **12** (100 mg, 0.145 mmol) in THF (10 mL) was added *n*-BuLi (1.75 M/hexane, 0.15 mL, 0.26 mmol) at −78 °C. After 10 min, TLC indicated the complete consumption of the starting material and a new spot appeared, which most probably corresponds to the naphthol. To this solution was added MeCN (8 mL) and aqueous solution of CAN (1.0 M, 1.45 mL, 1.45 mmol) at 0 °C. After stirring for 30 min, water was added, and the products were extracted with $CHCl_3$ (x3). The combined organic extracts were washed with water, and dried over Na_2SO_4. Concentration in vacuo followed by purification by flash column chromatography (CCl_4/acetone = 92/8) gave juglone **16** as a yellow oil (58.5 mg, 81.3%); ^1H NMR ($CDCl_3$) δ 1.39 (d, 3H, J = 6.1 Hz), 1.51 (ddd, 1H, J_1 = 12.7, J_2 = J_3 = 11.2 Hz), 2.52 (ddd, 1H, J_1 = 12.7, J_2 = 4.9, J_3 = 2.0 Hz), 3.22 (dd, 1H, J_1 = 9.0, J_2 = 8.8 Hz), 3.57 (dq, 1H, J_1 = 9.0, J_2 = 6.1 Hz), 3.83 (ddd, 1H, J_1 = 11.2, J_2 = 8.8, J_3 = 4.9 Hz), 3.87 (s, 3H), 4.62 (d, 1H, J = 11.5 Hz), 4.70 (d, 1H, J = 11.5 Hz), 4.72 (d, 1H, J = 11.0 Hz), 4.80 (dd, 1H, J_1 = 11.2, J_2 = 2.0 Hz), 5.01 (d, 1H, J = 11.0 Hz), 6.88 (d, 1H, J = 10.3 Hz), 6.91 (d, 1H, J = 10.3 Hz), 7.27–7.37 (m, 10H), 7.93 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 18.6, 38.2, 62.4, 71.4, 71.6, 75.3, 75.9, 80.8, 83.8, 123.3, 123.5, 127.65, 127.69, 127.71, 128.0, 128.39, 128.43, 132.5, 133.1, 136.9, 138.4, 138.6, 140.3, 143.7, 156.6, 184.4, 184.7; IR (NaCl) 1670, 1615, 1585, 1575, 1500, 1450, 1365, 1330, 1290, 1105, 1090, 1020 cm^{-1}; $[\alpha]^{20}_D$ −51.6 (*c* 1.39, $CHCl_3$); HRMS *m/z* 498.2040 (498.2026 calcd for $C_{31}H_{30}O_6$, M^+).

2-Chloro-6-(3,4-di-*O*-benzyl-2,6-dideoxy-β-D-*arabino*-hexopyranosyl)-5-methoxy-1,4-naphthoquinone (17). To a mixture of chlorofuran **7** (106 mg, 0.455 mmol) and triflate **12** (105 mg, 0.152 mmol) in THF (4 mL) was added *n*-BuLi (1.75 M/hexane, 0.17 mL, 0.30 mmol) at –78 °C. After 10 min, TLC indicated the complete consumption of the starting material and a new spot appeared, which most probably corresponds to the naphthol. To this solution was added MeCN (4 mL) and aqueous solution of CAN (1.0 M, 1.52 mL, 1.52 mmol) at 0 °C. After 30 min, water was added, and the products were extracted with $CHCl_3$ (x3). The combined organic extracts were washed with water, and dried over Na_2SO_4. Concentration in vacuo followed by purification by flash column chromatography (CCl_4/acetone = 97/3) gave chlorojuglone **17** as a yellow oil (74.0 mg, 91.4%); ^{1}H NMR ($CDCl_3$) δ 1.39 (d, 3H, J = 6.1 Hz), 1.49 (ddd, 1H, J_1 = 12.7, J_2 = J_3 = 11.2 Hz), 2.51 (ddd, 1H, J_1 = 12.7, J_2 = 4.9, J_3 = 1.7 Hz), 3.22 (dd, 1H, J_1 = 9.3, J_2 = 8.5 Hz), 3.57 (dq, 1H, J_1 = 9.3, J_2 = 6.1 Hz), 3.83 (ddd, 1H, J_1 = 11.2, J_2 = 8.5, J_3 = 4.9 Hz), 3.87 (s, 3H), 4.63 (d, 1H, J = 11.5 Hz), 4.70 (d, 1H, J = 11.5 Hz), 4.72 (d, 1H, J = 11.0 Hz), 4.78 (dd, 1H, J_1 = 11.2, J_2 = 1.7 Hz), 5.01 (d, 1H, J = 11.0 Hz), 7.12 (s, 1H,), 7.25–7.38 (m, 10H), 7.93 (d, 1H, J = 8.1 Hz), 8.02 (d, 1H, J = 8.1 Hz); ^{13}C NMR ($CDCl_3$) δ 18.6, 38.1, 62.5, 71.4, 71.6, 75.3, 75.9, 80.7, 83.7, 123.3, 124.4, 127.66, 127.71, 128.0, 128.39, 128.42, 132.4, 132.6, 137.4, 138.3, 138.5, 144.5, 144.6, 156.9, 177.9, 181.8; IR (NaCl) 2880, 1680, 1660, 1610, 1580, 1450, 1385, 1365, 1330, 1240, 1110, 1080 cm^{-1}; $[\alpha]^{20}_D$ –56.7 (*c* 1.22, $CHCl_3$); HRMS *m/z* 532.1647 (532.1650 calcd for $C_{31}H_{29}O_6Cl$, M^+).

Acetate 15c: ^{1}H NMR ($CDCl_3$) δ 0.22 (s, 3H), 0.24, (s, 3H), 1.04 (s, 9H), 1.37 (d, 3H, J = 6.1 Hz), 1.71 (ddd, 1H, J_1 = 12.7, J_2 = J_3 = 11.5 Hz), 2.34 (ddd, 1H, J_1 = 12.7, J_2 = 4.9, J_3 = 1.5 Hz), 2.47 (s, 3H), 3.25 (dd, 1H, J_1 = 9.3, J_2 = 8.8 Hz), 3.58 (dq, 1H, J_1 = 9.3, J_2 = 6.1 Hz), 3.73 (s, 3H), 3.85 (ddd, 1H, J_1 = 11.5, J_2 = 8.8, J_3 = 4.9 Hz), 4.66 (d, 1H, J = 10.7 Hz), 4.70 (d, 1H, J = 10.7 Hz), 4.73 (d, 1H, J = 10.7 Hz), 4.91 (dd, 1H, J_1 = 11.5, J_2 = 1.5 Hz), 5.02 (d, 1H, J = 10.7 Hz), 6.87 (s, 1H), 7.27–7.39 (m, 10H), 7.50 (d, 1H, J = 8.9 Hz), 7.63 (d, 1H, J = 8.9 Hz); IR (NaCl) 2900, 2850, 1780, 1580, 1470, 1405, 1370, 1320, 1270, 1200, 1120, 1040 cm^{-1}.



(⟶ NOE) **15c**

3-Benzyloxy-5-methylbenzoic acid. A suspension of carboxylic acid **18**[18] (3.22 g, 21.2 mmol), K_2CO_3 (5.86 g, 42.4 mmol), and benzyl bromide (5.0 mL, 42 mmol) in acetone (100 mL) was refluxed for 4.5 h. After cooling to 0 °C, Et_2NH (7 mL) was added to the mixture, which was stirred for 10 min. The reaction was quenched with 2 M HCl, and the products were extracted with CH_2Cl_2 (x3). The combined extracts were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was dissolved in MeOH (60 mL), to which was added aqueous NaOH (4 M, 20 mL) at room temperature, and the mixture was stirred for 12 h. After washing with Et_2O, the aqueous layer was acidified (pH 1) with 4 M HCl, and extracted with Et_2O (x3). The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated in vacuo to give the title compound (4.65 g, 90.7%). Recrystallization from MeOH–H_2O gave colorless needles (3.53 g, 68.7%); mp 129–130 °C; ^{1}H NMR ($CDCl_3$) δ 2.38 (s, 3H), 5.10 (s, 2H), 7.06 (s, 1H), 7.30–7.47 (m, 5H), 7.52 (s, 1H), 7.56 (s, 1H); IR (KBr) 2850, 1690, 1590, 1420, 1330, 1300, 1245, 1160, 1050 cm^{-1}; Anal. Calcd for $C_{15}H_{14}O_3$: C, 74.36; H, 5.83. Found: C, 74.76; H, 5.80.

2-(3-Benzyloxy-5-methylphenyl)-4,4-dimethyl-2-oxazoline (19). The mixture of thionyl chloride (2.95 mL, 40.4 mmol) and 3-(benzyloxy)-5-methylbenzoic acid (3.26 g, 13.5 mmol) was refluxed for 2 h, and the excess thionyl chloride was distilled off at reduced pressure. The remaining dark oil was dissolved in CH_2Cl_2 (25 mL), to which was slowly added a solution of 2-amino-2-methyl-1-propanol (6.00 g, 67.3 mmol) in CH_2Cl_2 (15 mL) at 0 °C. After stirring at room temperature for 12 h, the mixture was filtered through a Celite pad, and concentrated in vacuo to give a quantitative yield of the *N*-(1,1-dimethyl-2-hydroxyethyl)benzamide as a brown oil. After thionyl chloride (5.90 mL, 80.8 mmol) was added dropwise to the brown oil at 0 °C, the mixture was stirred at room temperature for 2 h, and then poured into 20% aqueous NaOH. The products were extracted with Et_2O (x3), and the combined extracts were washed with brine, and dried over Na_2SO_4. Concentration in vacuo followed by purification by column chromatography (hexane/EtOAc = 85/15) gave oxazoline **19** as a colorless oil (3.45 g, 86.8%); ^{1}H NMR ($CDCl_3$) δ 1.39 (s, 6H), 2.34 (s, 3H), 4.11 (s, 2H), 5.09 (s, 2H), 6.92 (s, 1H), 7.29–7.46 (m, 7H); IR (NaCl) 2960, 1645, 1590, 1450, 1355, 1335, 1250, 1200, 1160, 1050 cm^{-1}; HRMS *m/z* 295.1579 (295.1571 calcd for $C_{19}H_{21}O_2N$, M^+).

2-(3-Benzyloxy-2,5-dimethylphenyl)-4,4-dimethyl-2-oxazoline. To a stirred solution of oxazoline **19** (4.09 g, 13.9 mmol) in THF (80 mL) was added *n*-BuLi (1.66 M/hexane, 15.0 mL, 24.9 mmol) at –78 °C over 10 min. After stirring for 2 h, the temperature was gradually raised to –40 °C during 1 h. After stirring for 1 h, a solution of methyl iodide (5.90 g, 41.5 mmol) in THF (20 mL) was added to the mixture dropwise over 10 min, and the stirring was continued for another 30 min. The reaction was quenched with pH 7 phosphate buffer, and the products were extracted with Et_2O (x3). The combined extracts were washed with brine, and dried over Na_2SO_4. Concentration in vacuo followed by purification by column chromatography (hexane/EtOAc = 85/15) gave the title compound as a white solid (2.35 g, 54.9%); mp 74–75

°C; ^{1}H NMR ($CDCl_3$) δ 1.39 (s, 6H), 2.30 (s, 3H), 2.40 (s, 3H), 4.07 (s, 2H), 5.06 (s, 2H), 6.80 (s, 1H), 7.13 (s, 1H), 7.28–7.46 (m, 5H); IR (KBr) 2875, 1630, 1600, 1580, 1450, 1330, 1280, 1190, 1140, 1030 cm^{-1}; Anal. Calcd for $C_{20}H_{23}O_2N$: C, 77.64; H, 7.49; N, 4.53. Found: C, 77.88; H, 7.38; N, 4.70.

2-(3-Benzyloxy-2-carbomethoxymethyl-5-methylphenyl)-4,4-dimethyl-2-oxazoline (20). To a stirred solution of 2-(3-benzyloxy-2,5-dimethylphenyl)-4,4-dimethyl-2-oxazoline (782 mg, 2.53 mmol) in THF (10 mL) was added *n*-BuLi (1.66 M/hexane, 1.87 mL, 3.10 mmol) at –78 °C over 10 min. The mixture was gradually warmed to 0 °C during 1 h, and further stirred for 2 h. A solution of methyl chloroformate (731 mg, 7.74 mmol) in THF (5 mL) was added dropwise to the mixture over 10 min. After stirring for 1 h, the reaction was quenched with pH 7 phosphate buffer, and the mixture was extracted with Et_2O (x3). The combined organic extracts were washed with brine, and dried over Na_2SO_4. Concentration in vacuo followed by purification by column chromatography (hexane/EtOAc = 85/15) gave methyl ester **20** as a yellow oil (565 mg, 60.8%); ^{1}H NMR ($CDCl_3$) δ 1.34 (s, 6H), 2.33 (s, 3H), 3.61 (s, 3H), 4.03 (s, 2H), 4.17 (s, 2H), 5.07 (s, 2H), 6.86 (s, 1H), 7.26 (s, 1H), 7.31–7.41 (m, 5H); IR (NaCl) 2970, 1740, 1640, 1610, 1580, 1455, 1355, 1335, 1260, 1170, 1040 cm^{-1}; HRMS *m/z* 367.1770 (367.1781 calcd for $C_{22}H_{25}O_4N$, M^+).

5-Benzyloxy-7-methylisochroman-1,3-dione (21). To a solution of methyl ester **20** (491 mg, 1.34 mmol) and $NaHCO_3$ (788 mg, 9.38 mmol) in a mixture of CH_2Cl_2 (2 mL) and water (2 mL) was added benzyl chloroformate (0.67 mL, 4.7 mmol) at room temperature. After stirring for 12 h at 40 °C, the products were extracted with CH_2Cl_2 (x3). The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was dissolved in MeOH (30 mL), to which was added aqueous NaOH (4 M, 10 mL) at room temperature, and the mixture was stirred for 3 h. After washing with Et_2O, the aqueous layer was acidified (pH 1) with 4 M HCl, and extracted with Et_2O (x3). The combined organic extracts were dried over Na_2SO_4, and concentrated in vacuo. The residue was dissolved in acetone (10 mL), to which was added acetyl chloride (2 mL, 7 mmol). After stirring at room temperature for 2 h, the mixture was concentrated in vacuo to give anhydride **21** as a colorless solid (334 mg, 88.5%). Recrystallization from Et_2O gave **20** as needles; mp 119–120 °C; ^{1}H NMR ($CDCl_3$) δ 2.43 (s, 3H), 4.03 (s, 2H), 5.13 (s, 2H), 7.07 (s, 1H), 7.35–7.46 (m, 5H), 7.64 (s, 1H); IR (KBr) 2940, 1795, 1745, 1610, 1505, 1460, 1320, 1290, 1200, 1105, 1045 cm^{-1}; Anal. Calcd for $C_{17}H_{14}O_4$: C, 72.33; H, 5.00. Found: C, 72.06; H, 5.06.

2-(3,4-Di-*O*-benzyl-2,6-dideoxy-β-D-*arabino*-hexopyranosyl)-10-benzyloxy-6-hydroxy-1-methoxy-8-methylnaphthacene-5,12-dione (22). To a suspension of NaH (60% in oil, 16 mg, 0.41 mmol) in THF (5 mL) was added a solution of anhydride **21** (104 mg, 0.369 mmol) in THF (7 mL) at 0 °C. The yellow reaction mixture was stirred for 30 min at room temperature, to which were slowly added a solution of chloro juglone **17** (72.3 mg, 0.138 mmol) in THF (9 mL) at –78 °C. The mixture was gradually warmed to 0 °C during 1.5 h. The solution turned red in a temperature range between –30 and –10 °C. The reaction was quenched by saturated aqueous NH_4Cl, and the mixture was acidified with 10% HCl. The products were extracted with CH_2Cl_2 (x3), and the combined organic extracts were washed with brine, and dried over Na_2SO_4. Concentration in vacuo followed by purification by column chromatography ($CHCl_3$/MeOH = 49/1) gave naphthacenequinone **22** as a red solid (89.3 mg, 89.6%); mp 139.5–140 °C; ^{1}H NMR ($CDCl_3$) δ 1.41 (d, 3H, J = 6.0 Hz), 1.54 (ddd, 1H, $J_1 = J_2 = 11.1$, $J_3 = 13.2$ Hz), 2.53 (s, 3H), 2.57 (ddd, 1H, $J_1 = 13.2$, $J_2 = 5.1$, $J_3 = 1.7$ Hz), 3.24 (dd, 1H, $J_1 = J_2 = 9.0$ Hz), 3.59 (dq, 1H, $J_1 = 9.0$, $J_2 = 6.0$ Hz), 3.86 (ddd, 1H, $J_1 = 11.1$, $J_2 = 9.0$, $J_3 = 5.1$ Hz), 3.95 (s, 3H), 4.64 (d, 1H, J = 11.5 Hz), 4.72 (d, 1H, J = 11.5 Hz), 4.73 (d, 1H, J = 11.1 Hz), 4.85 (dd, 1H, $J_1 = 11.1$, $J_2 = 1.7$ Hz), 5.02 (d, 1H, J = 11.1 Hz), 5.28 (s, 2H), 6.96 (s, 1H), 7.25–7.47 (m, 13H), 7.52–7.55 (m, 2H), 7.86 (s, 1H), 7.96 (d, 1H, J = 8.1 Hz), 8.23 (d, 1H, J = 8.1 Hz), 8.71 (s, 1H), 14.34 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 18.7, 22.6, 38.2, 62.5, 70.6, 71.3, 71.8, 75.3, 75.9, 80.9, 83.9, 109.7, 113.0, 116.1, 116.3, 123.5, 126.6, 126.8, 127.4, 127.62, 127.67, 127.71, 128.0, 128.2, 128.38, 128.41, 128.5, 128.76, 128.80, 132.2, 135.3, 136.3, 138.5, 138.7, 140.1, 143.9, 156.2, 157.7, 162.4, 181.8, 187.5; IR (KBr) 3500, 2940, 1670, 1620, 1570, 1390, 1370, 1285, 1260, 1110, 1030 cm^{-1}; $[\alpha]^{20}_D$ –15 (*c* 0.72, $CHCl_3$); HRMS *m/z* 734.2882 (734.2877 calcd for $C_{47}H_{42}O_8$, M^+). Admixing of **17** and the anion of **21** at higher temperature rather than –78 °C caused formation of the minor isomer of **22**, which could be removed after acetylation by silica-gel PTLC (CCl_4/EtOAc = 85/15). Data for acetate derivative of the major isomer **22**: ^{1}H NMR ($CDCl_3$) δ 1.40 (d, 3H, J = 6.2 Hz), 1.48–1.58 (m, 1H), 2.52 (s, 3H), 2.52–2.58 (m, 1H), 2.64 (s, 3H), 3.23 (dd, 1H, $J_1 = J_2 = 8.8$ Hz), 3.59 (dq, 1H, $J_1 = 8.8$, $J_2 = 6.2$ Hz), 3.85 (ddd, 1H, $J_1 = 11.0$, $J_2 = 8.8$, $J_3 = 4.8$ Hz), 3.95 (s, 3H), 4.63 (d, 1H, J = 11.7 Hz), 4.71 (d, 1H, J = 11.7 Hz), 4.72 (d, 1H, J = 11.0 Hz), 4.84 (br d, 1H, J = 11 Hz), 5.02 (d, 1H, J = 11.0 Hz), 5.30 (s, 2H), 6.90 (s, 1H), 7.24–7.46 (m, 14H), 7.52–7.55 (m, 2H), 7.93 (d, 1H, J = 8.4 Hz), 8.12 (d, 1H, J = 8.4 Hz), 9.20 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 18.6, 21.3, 22.9, 38.2, 62.5, 70.6, 71.3, 71.7, 75.3, 75.9, 80.9, 83.9, 111.5, 114.6, 119.6, 122.3, 123.9, 125.8, 126.8, 127.4, 127.59, 127.65, 127.7, 127.97, 128.02, 128.2, 128.36, 128.39, 128.8, 129.8, 131.4, 132.3, 136.2, 136.5, 138.5, 138.7, 141.3, 143.1, 146.8, 156.0, 157.1, 169.3, 181.9; IR (NaCl) 2890, 1780, 1680, 1625, 1575, 1510, 1455, 1420, 1390, 1370, 1330, 1275, 1255, 1195, 1110, 1030 cm^{-1}; $[\alpha]^{22}_D$ –19.6 (*c* 1.66, $CHCl_3$); HRMS *m/z* 776.2986 (776.2982 calcd for $C_{49}H_{44}O_9$). Data for acetate derivative of the minor isomer of **22**: ^{1}H NMR ($CDCl_3$) δ 1.40 (d, 3H, J = 6.1 Hz), 1.46–1.60 (m, 1H), 2.54 (s, 3H), 2.53–2.62

(m, 1H), 2.65 (s, 3H), 3.23 (dd, 1H, J_1 = 9.2, J_2 = 8.7 Hz), 3.58 (dq, 1H, J_1 = 9.2, J_2 = 6.1 Hz), 3.85 (ddd, 1H, J_1 = 11.3, J_2 = 8.7, J_3 = 4.9 Hz), 3.89 (s, 3H), 4.62 (d, 1H, J = 11.5 Hz), 4.71 (d, 1H, J = 11.5 Hz), 4.72 (d, 1H, J = 11.0 Hz), 4.84 (dd, 1H, J_1 = 11.3, J_2 = 1.2 Hz), 5.02 (d, 1H, J = 11.0 Hz), 5.30 (s, 2H), 6.91 (s, 1H), 7.26–7.57 (m, 16H), 7.93 (d, 1H, J = 8.1 Hz), 8.15 (d, 1H, J = 8.1 Hz), 9.17 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 18.7, 21.4, 23.0, 38.2, 62.6, 70.6, 71.3, 71.8, 75.3, 75.8, 80.9, 83.8, 111.3, 114.6, 121.5, 122.1, 123.4, 126.5, 127.1, 127.4, 127.6, 127.7, 127.99, 128.04, 128.3, 128.39, 128.42, 128.8, 131.9, 132.1, 135.0, 136.1, 138.5, 138.6, 141.6, 143.2, 146.5, 156.1, 157.1, 169.6, 182.3, 182.7; IR (NaCl) 2950, 1780, 1740, 1680, 1625, 1570, 1505, 1455, 1420, 1335, 1260, 1200, 1110, 1105, 1080, 1050 cm^{-1}; $[\alpha]^{21}_{D}$ +17.7 (*c* 0.965, $CHCl_3$).

Galtamycinone (2) To a solution of naphthacenequinone **22** (34.0 mg, 0.046.5 mmol) in CH_2Cl_2 (6 mL) was added a solution of BBr_3 (582 mg, 2.32 mmol) in CH_2Cl_2 (3 mL) at –78 °C. After 1.5 h, the solution was poured into saturated aqueous $NaHCO_3$ at 0 °C. After stirring at 0 °C for 10 min, the mixture was acidified with 2 M HCl, and the products were extracted with CH_2Cl_2 (x3). The combined extracts were washed with brine, and dried over Na_2SO_4. Concentration in vacuo followed by purification by chromatography ($CHCl_3$/MeOH = 9/1) gave galtamycinone (**2**) as a red solid (17.2 mg, 82.2%); mp 283.5–284.5 °C [authentic sample;[3,21] 282–283 °C]; ^{1}H NMR (DMSO) δ 1.24–1.33 (m, 1H), 1.29 (d, 3H, J = 6.4 Hz), 2.28 (ddd, 1H, J_1 = 12.8, J_2 = 5.1, J_3 = 1.8 Hz), 2.39 (s, 3H), 2.90 (ddd, 1H, J_1 = J_2 = 8.7, J_3 = 5.0 Hz), 3.33–3.41 (m, 1H), 3.50–3.58 (m, 1H), 4.75 (dr d, 1H, J = 10 Hz), 4.96 (d, 1H, J = 4.1 Hz), 5.06 (d, 1H, J = 5.0 Hz), 6.92 (br s, 1H), 7.48 (br s, 1H), 7.72 (d, 1H, J = 7.8 Hz), 7.81 (d, 1H, J = 7.8 Hz), 8.36 (s, 1H), 10.89 (s, 1H), 13.39 (s, 1H), 14.41 (s, 1H); IR (KBr) 3430, 1615, 1580, 1435, 1390, 1285, 1260, 1185 cm^{-1}; $[\alpha]^{20}_{D}$ +177 (*c* 0.13, 1,4-dioxane) [authentic sample;[3,21] $[\alpha]^{22}_{D}$ +176 (*c* 0.14, 1,4-dioxane); HRMS *m/z* 450.1295 (450.1312 calcd for $C_{25}H_{22}O_8$, M^+); Anal. Calcd for $C_{25}H_{22}O_8 \cdot CH_3OH$: C, 64.72; H, 5.43. Found: C, 64.66; H, 5.12.

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