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Total Synthesis of Antibiotic C104: Benzyne–Furan Cycloaddition Approach to the Angucyclines

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Abstract: First total synthesis of antibiotic C104 (**1**), a prototypical member of the angucyclines, was accomplished. Highly regioselective cycloaddition of α-alkoxybenzyne **12** with angularly fused α-siloxyfuran **10** enabled the straightforward construction of the characteristic benz[*a*]anthraquinone framework. The D-olivosyl *C*-glycoside was introduced via the *O*→*C*-glycoside rearrangement in a regio- and stereoselective manner.

Introduction

The angucyclines constitute a growing class of antibiotics, which are defined as the derivatives of benz[*a*]anthraquinone.[1] The group name came from the characteristically curved (*angular*) tetracyclic framework of decaketide origin,[2] which stands in good contrast to the linear tetracycles of the anthracyclines, clinically important antitumor agents. In addition to such a skeletal contrast, the *C*-glycoside structure is uniquely involved in some members of this class. Such structural features as well as the diverse biological activities have stimulated the synthetic studies on these compounds.[3] The advance, however, remains at an early stage, in particular, for the synthesis of *C*-glycosylated congeners, and the ingenious synthesis of (–)-urdamycinone B by Yamaguchi is the only successful achievement of the total synthesis of the full structure of *C*-glycosyl angucycline.[3a]

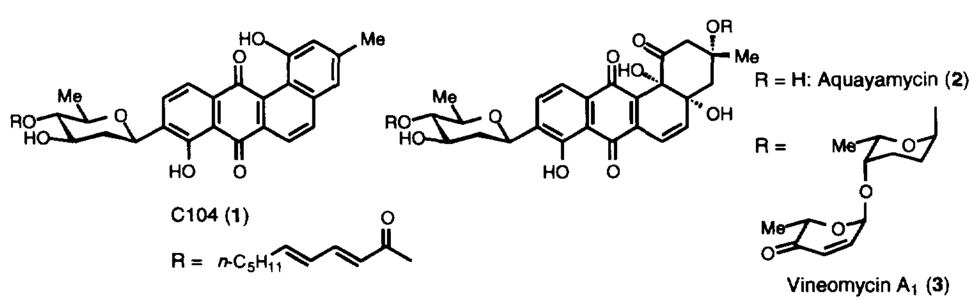


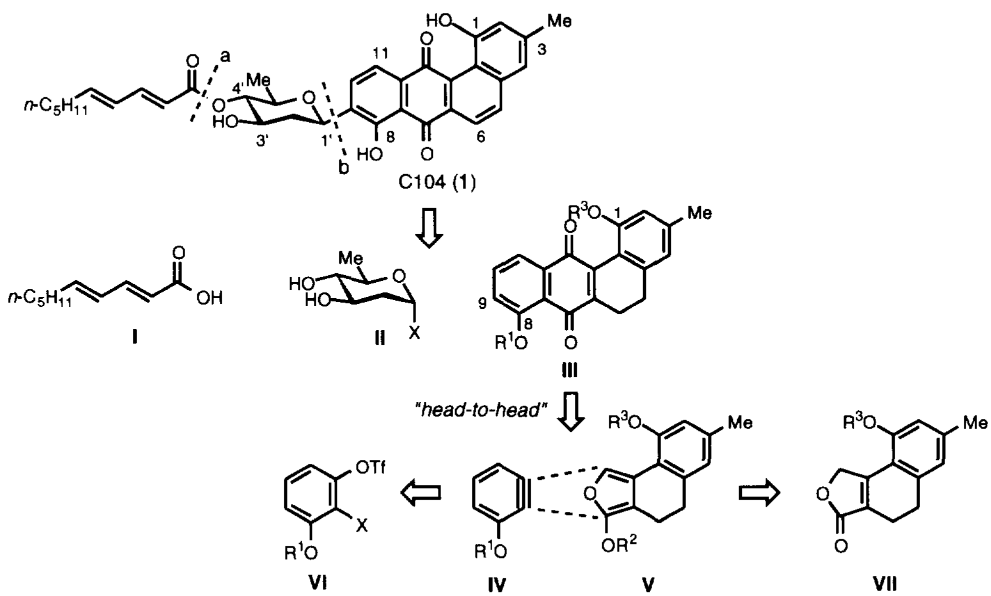
Figure 1. Angucycline-type antibiotics

Antibiotic C104 (**1**), an antifungal compound isolated by Arnone et al.,[4] involves essential problems associated with the synthesis of *C*-glycosyl angucyclines, i.e., the selective construction of the benz[*a*]anthraquinone framework and the regio- and stereochemical control in the *C*-glycosylation of the tetracyclic skeleton. Specifically, the issue is the β selective introduction of D-olivose, which is a typical sugar installed in the angucyclines. Herein, we describe the first total synthesis of this compound by exploiting two new methodologies for the selective construction of the chromophore portion and for the *C*-glycoside formation.[5]

Synthetic Plan

Scheme 1 shows the retrosynthesis that divides the target into three moieties: the dienoic acid **I**, the sugar **II**, and the tetracyclic skeleton **III**. Two regiochemical issues must be faced with for assembly of these units, i.e., (1) esterificaion of the C(4') hydroxyl (bond a) leaving the C(3') hydroxyl intact, and (2) the *C*-glycoside formation at the C(9) position (bond b). We expected that the former issue would be solved by exploiting the steric difference of the two hydroxyl groups, while the latter by "the ortho selectivity" of the $O \rightarrow C$-rearrangement[6,7] by utilizing the C(8) hydroxyl group as the director.

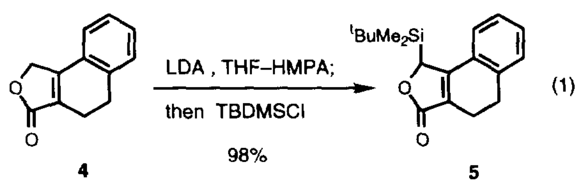
Scheme 1 Synthetic strategy based on the benzyne–furan cycloaddition.



Then, the main focus could be centered on the construction of the angular tetracyclic skeleton **III** that possesses a hydroxyl group at C(8). We envisaged that this structural motif would be directly accessible via the regioselective benzyne–furan cycloaddition (**IV** + **V** → **III**).[8,9] The question was whether the head-to-head mode of the cycloaddition, which is induced electronically by two alkoxyl groups and has been established for simpler cases,[9] is valid also for such an elaborated system or not. In reducing this strategy into practice, we utilized *siloxyfuran* **V** ($R_2 = SiR_3$),[10] rather than an *alkoxyfuran*, because the former is more readily accessible by the enolization–silylation of angular butenolide **VII**.[10]

Results and Discussion

Benzyne–siloxyfuran cycloaddition: Initial experiments by using model butenolide **4** revealed several problems in the generation and the use of α-siloxyfurans.[10]



(1)

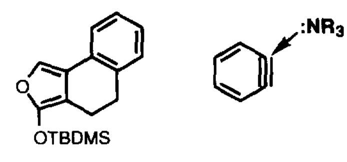
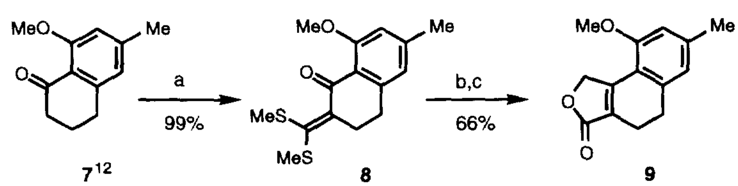


Figure 2

Treatment of **4** with LDA in THF(–HMPA) followed by TMSCl or TBDMSCl led exclusively to *C*-silylation (Eq 1).[10b,f] Silylation by using tertiary amine as the base (Et_3N or $^iPr_2NEt/CH_2Cl_2$) produced the desired siloxyfuran **6**,[10a,d] which, however, was too moisture sensitive for isolation. At this stage, we decided to generate the siloxyfuran in situ and directly use it for the subsequent cycloaddition chemistry. This decision excluded the use of tertiary amine (vide supra) because it causes side reaction with benzyne as shown in Figure 2.[11] After considerable experimentation, we were able to establish a protocol for the in situ-cycloaddition strategy that makes the use of NaH as the base. The essential point is that enolization–silylation gives rise to *sodium chloride* as the only side product that does not interfere with the subsequent benzyne cycloaddition reaction.

Scheme 2 Preparation of butenolide **9**.[13]

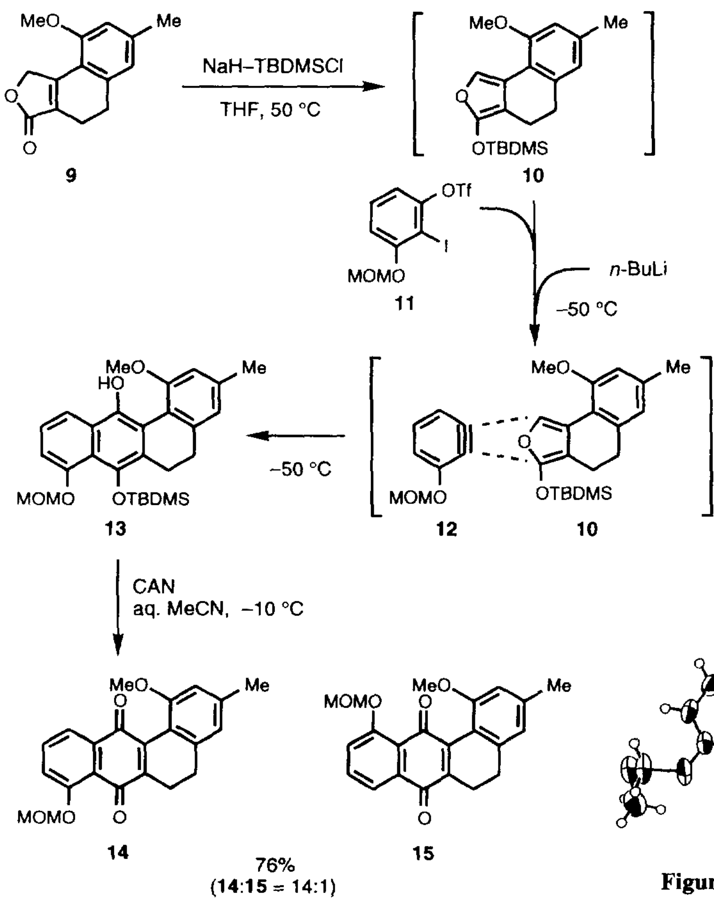


(a) lithium 2,6-di-*tert*-butyl-4-methylphenoxide, CS_2 / THF then MeI; (b) NaH, $Me_3S^+I^-$ / DMSO; (c) 4 N HCl / MeOH.

Now the stage was set to start the total synthesis, and the precursor to the requisite siloxyfuran, butenolide **9**, was prepared from tetralone **7**[12] by the Okazaki's method (Scheme 2).[13] By treatment with NaH in the presence of TBDMSCl in THF at 50 °C, betenolide **9** was cleanly converted to α-siloxyfuran **10** (tlc assay).[14] Without quenching, the mixture was cooled to –50 °C, to which was added triflate **11**.[9c] Upon careful addition of *n*-BuLi to this mixture, the generated benzyne species **12** underwent quick cycloaddition with siloxyfuran **10** to give rise to unstable adduct **13** and its regioisomer. These products were oxidatively worked up ($CAN/CH_3CN–H_2O$, –10 °C), where the regioisomeric quinones **14** and **15** were obtained in 76% yield, and to our delight, in a ratio as high as 14 / 1. The minor isomer **15** was removed chromatographically and/or by recrystallization,[15] and the structure of **14** was unambiguously confirmed by an X-ray structural analysis (Figure 3).

Synthesis of tetrangulol: Quinone **14** was readily converted to tetrangulol (**17**), the first member of the angucyclines (Scheme 4).[16] Dehydrogenation at C(5)–C(6) was cleanly effected by heating **14** in refluxing 1,4-dioxane in the presence of DBU followed by exposure to air.[3c] The protecting groups of the phenolic hydroxyls were removed by treatment with BBr_3 at low temperature to give tetrangulol (**17**), mp 201–202 °C (EtOAc) [*lit.*[16a] mp 198–200 °C, *lit.*[16b] mp 201–203 °C].

Scheme 3 Benzyne–siloxyfuran cycloaddition.



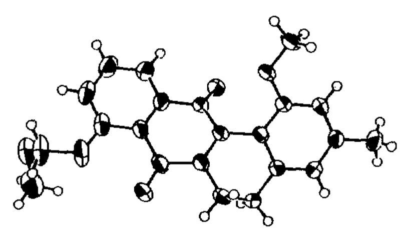
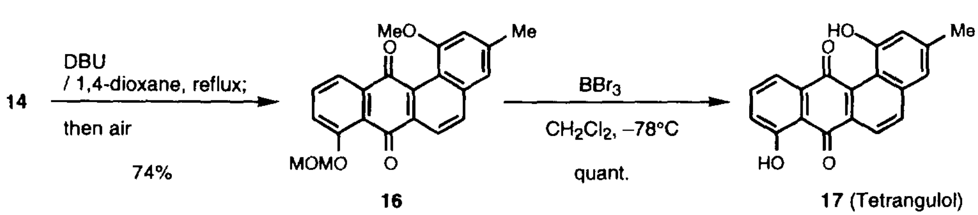


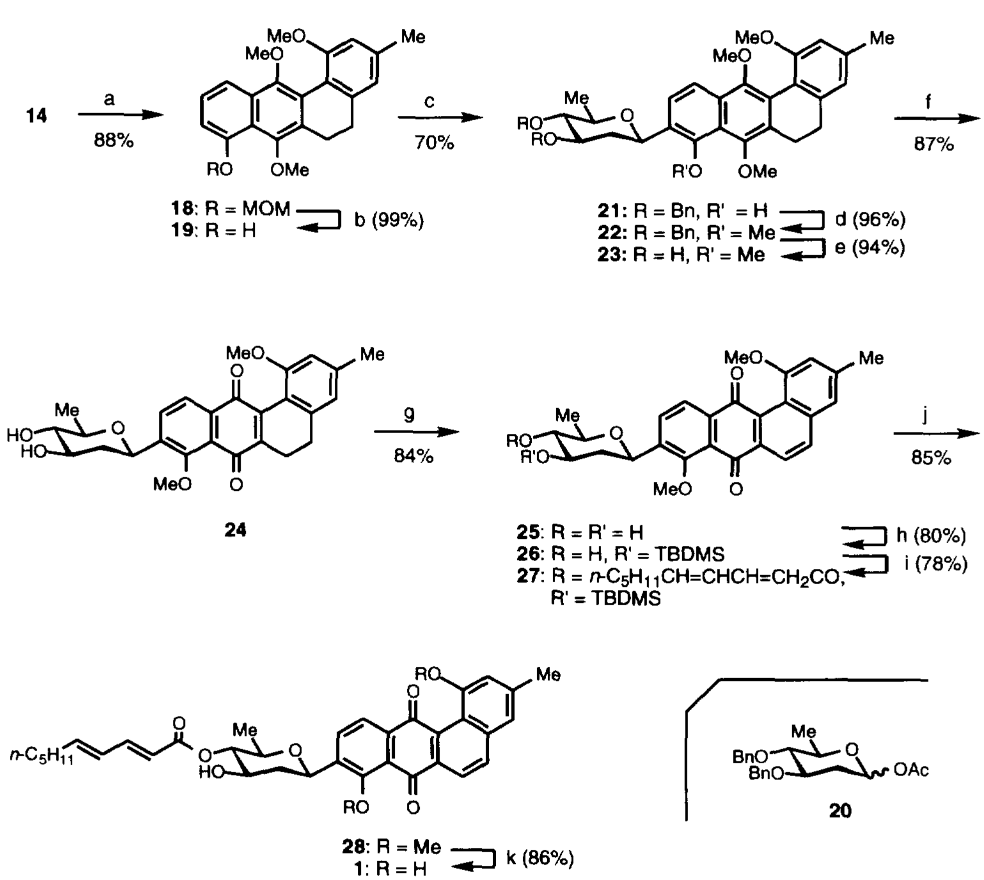
Figure 3 ORTEP drawing of **14**.

Scheme 4 Synthesis of tetrangulol (**17**).



Total synthesis of antibiotic C104 (1): With the tetracyclic skeleton in hand, now the stage was set for the *C*-glycosylation.[6,7] Toward this end, substrate **19** was so desinged as to be sufficiently electron rich and armed with the C(8) hydroxyl for the regiocontrolled *C*-glycoside formation. Thus, quinone **14** was reductively bis-methylated by catalytic hydrogenation followed by treatment with NaH and $(MeO)_2SO_2$ in one pot to give **18** in 88% yield. The MOM group was selectively removed by treatment with $BF_3{\bullet}OEt_2$ and EtSH to give phenol **19** in 99% yield.

Scheme 5 Total synthesis of antibiotic C104 (**1**).



(a) H_2, 10% Pd–C / DMF, room temperature; then NaH, $(MeO)_2SO_2$; (b) EtSH, $BF_3{\bullet}OEt_2$ / CH_2Cl_2, −78→−40 °C; (c) **20** Cp_2HfCl_2, $AgClO_4$ / CH_2Cl_2, −78 °C; (d) NaH, $(MeO)_2SO_2$ /THF–DMF, 40 °C; (e) H_2, Pd–C / EtOAc–MeOH, room temperature; (f) CAN / $MeCN–H_2O$, 0 °C; (g) DBU / 1,4-dioxane, reflux; then air; (h) TBDMS-Cl, imidazole / DMF, room temperature; (i) 2,4,6-$Cl_3C_6H_2COCl$, (*E*,*E*)-*n*-$C_5H_{11}(CH{=}CH)_2COOH$,[22] Et_3N / THF; then filtration, evaporation, and dissolved in toluene, **26**, DMAP, room temperature; (j) aq. HF / MeCN, room temperature; (k) BBr_3 / CH_2Cl_2, −78 °C.

Upon reaction with D-olivosyl acetate **20**[17,18] in the presence of Cp_2HfCl_2–$AgClO_4$,[7,19] phenol **19** was quickly converted to *C*-glycoside **21** at –78 °C in regio- and stereoselective manner. The β-configuration was evident from the ^{1}H NMR ($J_{1',2'ax}$ = 11.4, $J_{1',2'eq}$ = 1.8 Hz).[20] None of the α-isomer was detected.

The C(8) hydroxyl was then methylated, and the benzyl protecting groups were detached to give diol **23** without affecting the anomeric stereochemistry,[20] and oxidation with CAN (MeCN–H_2O, 0 °C) followed by dehydrogenation at C(5)–C(6) (vide supra) to give fully conjugated **25** in 84% yield.

For the selective introduction of the dienoyl moiety to the C(4') hydroxyl, the less hindered C(3') hydroxyl was selectively silylated to give **26** (TBDMSCl, imidazole, DMF). Esterification of the C(4') hydroxyl was effected by the Yamaguchi's method[21] in 78% yield. To our delight, this esterification proceeded without accompanied by two side reactions of our prior concern; (1) the *O*(3')→*O*(4') silyl migration, and (2) the *E/Z* isomerization of the dienoyl moiety.[23] The silyl group was removed by treatment with hydrogen fluoride in aqueous acetonitrile. Use of hydrogen fluoride is important because desilylation with *n*-Bu_4NF in THF was accompanied by the acyl migration to the C(3') hydroxyl. The final demethylation was effected by BBr_3 at low temperature to accomplish the total synthesis of antibiotic C104 (**1**). The synthetic material was fully identical with an authentic sample kindly provided from Prof. O. Vajna de Pava, mp 173–175 °C, $[\alpha]^{21}_D$ +82° (*c* 0.12, $CHCl_3$) [*lit.*[4] mp 175 °C, $[\alpha]_D$ +83.05° (*c* 1.18, $CHCl_3$)]. The optical rotation coincided with that of the natural product, thereby establishing the absolute stereochemistry of this compound.

Conclusion

In summary, the first total synthesis of antibiotic C104 was achieved. The present approach would provide useful entries to a variety of benz[*a*]anthraquinones including more complex members of the angucyclines.

Experimental Section

General procedures. All experiments dealing with air- and moisture-sensitive compounds were conducted under atmosphere of dry argon. THF was distilled from benzophenone ketyl immediately before use. Dichloromethane was distilled succesively 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 F_{254}, 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.

8-Methoxy-6-methyl-2-bis(methylthio)methylene-1-oxo-1,2,3,4-tetrahydronaphthalene (8). To a solution of 2,6-di-*tert*-butyl-4-methylphenol (8.02 g, 36.5 mmol) in THF (30 mL) was added *n*-BuLi (1.61 M hexane solution, 22.5 mL, 36.2 mmol) at 0 °C over 10 min. After 10 min, the ice bath was removed, and the mixture was stirred at room temperature for 1 h. To this solution were added a solution of tetralone **7**[12] (3.03 g, 15.9 mmol) in THF (10 mL) and carbon disulfide (4.80 mL, 79.8 mmol). After the mixture was stirred for 4 h, methyl iodide (2.50 mL, 40.2 mmol) was added. After 4 h, water was added at 0 °C, and the product was extracted with EtOAc. The combined extracts were washed with brine and dried over Na_2SO_4. The solvents were removed in vacuo and the crude product was purified by chromatography (hexane/EtOAc = 7:3) to afford dithiomethylene ketone **8** (4.62 g, 98.5%) as a yellow oil which solidified on standing in a refrigerator: mp 76–77 °C; ^{1}H NMR ($CDCl_3$) δ 2.34 (s, 3H), 2.36 (s, 3H), 2.45 (s, 3H), 2.79–2.83 (m, 2H), 3.09–3.13 (m, 2H), 3.88 (s, 3H), 6.61 (s, 1H), 6.64 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 18.5, 19.1, 22.0, 29.9, 31.6, 55.9, 111.1, 120.4, 121.6, 137.7, 144.1, 145.0, 150.0, 160.3, 185.2; IR (NaCl) ν_{max} 2930, 1640, 1610, 1570, 1480, 1460, 1430, 1350, 1320, 1295, 1270, 1240, 1215, 1100 cm^{-1}; HRMS *m/z* 294.0740 (294.0746 calcd for $C_{15}H_{18}O_2S_2$, M^+).

3,4-Dihydro-8-methoxy-6-methylnaphtho[1,2-*c*]furan-2(5*H*)-one (9). To a solution of dimethylsulfonium methylide in DMSO (60 mL) and THF (60 mL), prepared according to the Corey's procedure[24] from NaH (60% in oil, 530 mg, 13.3 mmol) and trimethylsulfonium iodide (3.14 g, 15.4 mmol), was added dithiomethylene ketone **8** (1.50 g, 5.09 mmol) in THF (30 mL) at 0 °C. After the mixture was stirred at room temperature for 6 h, the reaction was stopped by adding pH 7 phosphate buffer, and the product was extracted with EtOAc. The combined extracts were washed with water and 4 N HCl, and dried over Na_2SO_4. The solvents were removed in vacuo, and the crude product was dissolved in MeOH (150 mL). To this solution was added 2 N HCl (18 mL), and the mixture was stirred under reflux for 12 h. To the mixture, cooled to 0 °C, were added benzene (200 mL) and water (200 mL), and the methanol was azeotropically removed. The products were extracted with EtOAc, and the combined extracts were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. Purification by chromatography (hexane/EtOAc = 7:3) gave butenolide **9** as crystalline solids (773 mg, 66.0%). Recrystallization from MeOH–EtOH gave **9** as pale yellow needles: mp 175–176 °C; ^{1}H NMR ($CDCl_3$) δ 2.36 (s, 3H), 2.53 (tt, 2H, J_1 = 8.3, J_2 = 2.2 Hz), 2.92 (t, 2H, J = 8.3 Hz), 3.85 (s, 3H), 5.21 (t, 2H, J = 2.2 Hz), 6.60 (s, 1H), 6.71 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 18.1, 22.1, 28.5, 55.5, 72.2, 110.2, 115.0, 122.1, 122.3, 139.3, 142.7, 155.3, 156.7, 174.0; IR (KBr) ν_{max} 2950, 1740, 1640, 1610, 1570, 1465, 1320, 1295, 1090 cm^{-1}; Anal. Calcd for $C_{14}H_{14}O_3$: C, 73.03; H, 6.13. Found: C, 72.77; H, 6.17.

1-Methoxy-8-methoxymethoxy-3-methyl-5,6-dihydrobenz[*a*]anthracene-7,12-dinone (14) and 1-methoxy-11-methoxymethoxy-3-methyl-5,6-dihydrobenz[*a*]anthracene-7,12-dinone (15). To a suspension of NaH (60% in oil, 175 mg, 4.38 mmol) in THF (3 mL) was added a solution of butenolide **9** (227 mg, 0.987 mmol) in THF (16 mL), and the mixture was stirred at 50 °C for 1 h. To the mixture, cooled to –50 °C, were successively added a solution of triflate **11**[9c] (944 mg, 2.29 mmol) in THF (10 mL) and *n*-BuLi (1.67 M hexane solution, 1.36 mL, 2.27 mmol). After 20 min, the reaction was stopped by adding pH 7 phosphate buffer, and the products were extracted with Et_2O. The combined extracts were washed with saturated $NaHCO_3$ solution and brine, and dried over K_2CO_3. The solvents were removed in vacuo, and the residue was dissolved in MeCN (15 mL). To this solution was added aqueous solution of CAN (1.0 M, 2.2 mL, 2.2 mmol) at –15 °C. Brine was added after 15 min, and the products were extracted with Et_2O. The combined organic extracts were washed with saturated $NaHCO_3$ solution and brine, and dried over K_2CO_3. Concentration in vacuo followed by purification by chromatography (hexane/EtOAc = 4:1) gave a mixture of quinone **14** and a minor amount of the isomer **15** (273 mg, 76.0%). Further purification of the mixture by chromatography (benzene/acetone = 95:5) or by recrystallization (EtOAc/hexane) gave pure **14** as yellow needles: mp 144–145 °C; ^{1}H NMR ($CDCl_3$) δ 2.37 (s, 3H), 2.65–2.85 (br, 4H), 3.55 (s, 3H), 3.80 (s, 3H), 5.35 (s, 2H), 6.70 (s, 1H), 6.72 (s, 1H), 7.45 (dd, 1H, J_1 = 8.3, J_2 = 1.2 Hz), 7.61 (dd, 1H, J_1 = 8.3, J_2 = 7.6 Hz), 7.75 (dd, 1H, J_1 = 7.6, J_2 = 1.2 Hz); ^{13}C NMR ($CDCl_3$) δ 20.5, 21.9, 28.4, 56.0, 56.6, 95.3, 111.6, 117.0, 120.3, 121.07, 121.12, 121.4, 134.1, 136.6, 141.1, 141.83, 141.87, 144.3, 156.7, 157.4, 182.7, 183.5; IR (KBr) ν_{max} 2940, 1670, 1650, 1605, 1585, 1565, 1470, 1450, 1370, 1335, 1305, 1260, 1205, 1150, 1120, 1095, 1040, 1020 cm^{-1}; Anal. Calcd for $C_{22}H_{20}O_5$: C, 72.51; H, 5.53. Found: C, 72.25; H, 5.65. Minor isomer **15**: mp 109–110.5 °C; ^{1}H NMR ($CDCl_3$) δ 2.37 (s, 3H), 2.6–2.8 (br, 4H), 3.58 (s, 3H), 3.81 (s, 3H), 5.36 (s, 2H), 6.69 (s, 1H), 6.73 (s, 1H), 7.44 (dd, 1H, J_1 = 8.3, J_2 = 1.2 Hz), 7.57 (dd, 1H, J_1 = 8.3, J_2 = 7.9 Hz), 7.79 (dd, 1H, J_1 = 7.9, J_2 = 1.2 Hz); ^{13}C NMR ($CDCl_3$) δ 20.0, 21.9, 28.2, 56.1, 56.4, 95.4, 111.6, 117.7, 120.3, 121.3, 122.0, 124.4, 133.2, 134.4, 139.7, 141.3, 142.3, 145.8, 155.4, 157.2, 183.4, 184.0; IR

(KBr) ν_{max} 2940, 1665, 1640, 1600, 1580, 1560, 1460, 1365, 1335, 1295, 1255, 1235, 1220, 1150, 1030 cm^{-1}; HRMS *m/z* 364.1306 (364.1309 calcd for $C_{22}H_{20}O_5$, M^+). Crystal data for **14**: triclinic, space group $P\bar{1}$, a = 12.469(3), b = 9.713(3), c = 7.825(1)Å, α = 96.90(2), β = 103.67(1), γ = 74.26(2)°, V = 884.8(3)$Å^3$, Z = 2, Dc = 1.368 g/cm^3. R = 0.054, Rw = 0.059 for 2809 reflections with I > 3σ(I) and 324 variables. Diffraction data were collected on a Rigaku AFC5S diffractomater with Mo Kα radiation (3° < 2θ < 160°). The solution was obtained and refined employing the TEXSAN software.

1-Methoxy-8-methoxymethoxy-3-methylbenz[*a*]anthracene-7,12-dinone (16). A solution of quinone **14** (24.7 mg, 0.0679 mmol) and DBU (143 mg, 0.940 mmol) in 1,4-dioxane (3 mL) was heated under reflux for 10 h. After the solution was cooled to 0 °C, 2 N HCl (10 mL) was added, and the product was extracted with CH_2Cl_2. The combined extracts were washed with brine, and dried over Na_2SO_4. Concentration in vacuo followed by purification by chromatography (hexane/EtOAc = 3:2) gave benz[*a*]anthraquinone **16** as a yellow solid (18.1 mg, 73.7%). Recrystallization from hexane/EtOAc gave yellow needles: mp 150–151 °C; ^{1}H NMR ($CDCl_3$) δ 2.53 (s, 3H), 3.57 (s, 3H), 3.98 (s, 3H), 5.40 (s, 2H), 6.89 (s, 1H), 7.26 (s, 1H), 7.48 (dd, 1H, J_1 = 8.3, J_2 = 1.3 Hz), 7.65 (dd, 1H, J_1 = 8.3, J_2 = 7.6 Hz), 7.74 (dd, 1H, J_1 = 7.6, J_2 = 1.3 Hz), 7.92 (d, 1H, J = 8.6 Hz), 8.20 (d, 1H, J = 8.6 Hz); IR (KBr) ν_{max} 2940, 1680, 1665, 1620, 1590, 1565, 1495, 1470, 1445, 1280, 1260, 1165, 1145, 1080, 1040 cm^{-1}; Anal. Calcd for $C_{22}H_{18}O_5$: C, 72.92; H, 5.01. Found: C, 72.78; H, 5.02.

Tetrangulol (17). To a solution of **16** (34.7 mg, 0.0959 mmol) in CH_2Cl_2 (3 mL) was added a solution of BBr_3 (185 mg, 0.739 mmol) in CH_2Cl_2 (1.5 mL) at –78 °C. After 30 min, saturated $NaHCO_3$ solution was added. The mixture was stirred at 0 °C for 30 min, acidified with 2 N HCl, and the products were extracted with CH_2Cl_2. The combined extracts were washed with brine, and dried over Na_2SO_4. Concentration in vacuo followed by purification by chromatography (CCl_4/EtOAc = 4:1) gave tetrangulol (**17**) (29.0 mg, 99.5 %). Recrystallization from EtOAc gave **17** as dark red needles; mp 201–202 °C: ^{1}H NMR ($CDCl_3$) δ 2.49 (s, 3H), 7.13 (d, 1H, J = 1.8 Hz), 7.24 (br s, 1H), 7.32 (dd, 1H, J_1 = 8.1, J_2 = 1.1 Hz), 7.68 (dd, 1H, J_1 = 8.1, J_2 = 7.3 Hz), 7.85 (dd, 1H, J_1 = 7.3, J_2 = 1.1 Hz), 8.12 (d, 1H, J = 8.4 Hz), 8.30 (d, 1H, J = 8.4 Hz), 11.3 (s, 1H), 12.2 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 21.3, 114.7, 120.0, 120.2, 121.2, 121.3, 121.9, 124.7, 132.4, 134.8, 136.9, 137.7, 139.1, 142.0, 155.3, 161.7, 187.8, 189.6; IR (KBr) ν_{max} 1635, 1620, 1585, 1545, 1500, 1480, 1450, 1415, 1375, 1295, 1250, 1160 cm^{-1}; Anal. Calcd for $C_{19}H_{12}O_4$: C, 74.99; H, 3.97. Found: C, 74.70; H, 4.10.

1,7,12-Trimethoxy-8-methoxymethoxy-3-methyl-5,6-dihydrobenz[*a*]anthracene (18). A suspension of quinone **14**, containing a minor amount of the isomeric quinone **15**, (225 mg, 0.618 mmol) in DMF (15 mL) was stirred under H_2 (1 atm) in the presence of 10% Pd–C (100 mg) at room temperature for 1 h. After changing the atmosphere to Ar, NaH (60% in oil, 165 mg, 4.13 mmol) was added to the mixture. After 10 min, $(MeO)_2SO_2$ (0.35 mL, 3.7 mmol) was added, and the stirring was continued for 30 min. The reaction was stopped by adding Et_2NH (0.4 mL), Et_2O (15 mL), and then pH 7 phosphate buffer at 0 °C. The mixture was filtered through a Celite pad, and the product was extracted with Et_2O. The combined extracts were washed with saturated $NaHCO_3$ solution and brine, and dried over Na_2SO_4. Concentration in vacuo followed by purification by chromatography (hexane/EtOAc = 4:1) gave trimethyl ether **18** as a colorless oil (202 mg, 82.9%) and its isomer **18'** (1,7,12-trimethoxy-11-methoxymethoxy-3-methyl-5,6-dihydrobenz[*a*]anthracene) as amorphous solids (14.0 mg, 5.7%). Major isomer **18**: ^{1}H NMR ($CDCl_3$, 50 °C) δ 2.39 (s, 3H), 2.4–2.9 (br, 4H), 3.47 (s, 3H), 3.59 (s, 3H), 3.82 (s, 3H), 3.85 (s, 3H), 5.30 (s, 2H), 6.74 (s, 1H), 6.75 (s, 1H), 7.12 (d, 1H, J = 7.6 Hz), 7.32 (dd, 1H, J_1 = 7.6, J_2 = 8.1 Hz), 7.98 (d, 1H, J = 8.1 Hz); ^{13}C NMR ($CDCl_3$) δ 21.6, 23.7, 30.7, 56.1, 56.4, 60.8, 61.8, 96.5, 111.1, 112.8, 117.5, 119.5, 120.3, 120.6, 121.0, 125.1, 130.9, 131.1, 138.6, 141.9, 146.9, 150.6, 153.0, 157.2; IR (NaCl) ν_{max} 2940, 1610, 1590, 1570, 1490, 1460, 1440, 1360, 1340, 1310, 1290, 1260, 1230, 1210, 1150, 1050 cm^{-1}; HRMS *m/z* 394.1771 (394.1778 calcd for $C_{24}H_{26}O_5$, M^+). Minor isomer **18'**: mp 152–153 °C; ^{1}H NMR ($CDCl_3$) δ 2.3–2.45 (br m, 1H), 2.40 (s, 3H), 2.5–2.65 (br m, 1H), 2.75–2.85 (br m, 1H), 3.3–3.4 (br m, 1H), 3.40 (s, 3H), 3.63 (s, 3H), 3.87 (s, 3H), 3.88 (s, 3H), 5.32 (d, 1H, J = 13.9 Hz), 5.34 (d, 1H, J = 13.9 Hz), 6.76 (s, 2H), 7.11 (dd, 1H, J_1 = 7.6, J_2 = 1.2 Hz), 7.37 (dd, 1H, J_1 = 8.5, J_2 = 7.6 Hz), 7.84 (dd, 1H, J_1 = 8.5, J_2 = 1.2 Hz); ^{13}C

NMR ($CDCl_3$) δ 21.6, 24.1, 30.6, 56.2, 56.5, 61.7, 61.8, 97.7, 111.7, 115.0, 117.2, 119.7, 120.4, 120.9, 123.2, 125.8, 130.0, 130.7, 138.2, 141.8, 147.5, 150.8, 153.6, 157.4; IR (KBr) ν_{max} 2940, 1595, 1565, 1460, 1370, 1355, 1340, 1305, 1255, 1230, 1160, 1070, 1030 cm^{-1}; HRMS *m/z* 394.1778 (394.1778 calcd for $C_{24}H_{26}O_5$, M^+).

1,7,12-Trimethoxy-3-methyl-5,6-dihydrobenz[*a*]anthracene-8-ol (19). To a solution of trimethyl ether **18** (170 mg, 0.431 mmol) in CH_2Cl_2 (5 mL) were added a solution of EtSH (241 mg, 3.88 mmol) in CH_2Cl_2 (3 mL) and $BF_3{\bullet}OEt_2$ (320 mg, 2.25 mmol) in CH_2Cl_2 (3.5 mL) at –78 °C. The reaction mixture was gradually warmed to –40 °C during 1.5 h. The reaction was stopped by adding pH 7 phosphate buffer, and the product was extracted with EtOAc. The combined extracts were washed with brine, and dried over Na_2SO_4. Concentration in vacuo, followed by purification by chromatography (hexane/EtOAc = 7:3) gave phenol **19** as a colorless solid (150 mg, 99.3%). Recrystallization from hexane–EtOAc gave **19** as pellets; mp 172–173°C; ^1H NMR ($CDCl_3$) δ 2.40 (s, 3H), 2.4–3.4 (br, 4H), 3.47 (s, 3H), 3.89 (s, 3H), 3.92 (s, 3H), 6.76 (s, 2H), 6.90 (dd, 1H, J_1 = 7.7, J_2 = 1.1 Hz), 7.34 (dd, 1H, J_1 = 7.7, J_2 = 8.4 Hz), 7.78 (dd, 1H, J_1 = 8.4, J_2 = 1.1 Hz), 9.64 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 21.6, 24.2, 30.6, 56.0, 60.8, 62.6, 110.8, 111.2, 114.3, 116.7, 119.1, 120.3, 120.9, 126.6, 128.3, 130.2, 138.7, 141.5, 147.3, 151.2, 153.5, 157.3; IR (KBr) ν_{max} 3300, 2940, 1630, 1605, 1580, 1500, 1455, 1435, 1360, 1200, 1040, 1025 cm^{-1}; HRMS *m/z* 350.1508 (350.1516 calcd for $C_{22}H_{22}O_4$, M^+); Anal. Calcd for $C_{22}H_{22}O_4$: C, 75.41; H, 6.33. Found: C, 75.21; H, 6.44.

9-(3',4'-di-*O*-benzyl-2',6'-dideoxy-β-D-*arabino*-hexopyranosyl)-8-hydroxy-1,7,12-trimethoxy-3-methyl-5,6-dihydrobenz[*a*]anthracene (21). To a suspension of Cp_2HfCl_2 (263 mg, 0.693 mmol), $AgClO_4$ (288 mg, 1.39 mmol), and powdered 4A molecular sieves (ca. 600 mg) in CH_2Cl_2 (5 mL) were added a solution of phenol **19** (162 mg, 0.463 mmol) in CH_2Cl_2 (8 mL) and D-olivosyl acetate **20** (343 mg, 0.927 mmol) in CH_2Cl_2 (9 mL) at –78 °C. After the mixture was stirred for 15 min, the reaction was stopped by adding pH 7 phosphate buffer. The mixture was acidified by 2 N HCl, filtered through a Celite pad, and the products were extracted with EtOAc. The combined extracts were washed with brine, and dried over Na_2SO_4. Concentration in vacuo followed by purification by chromatography (hexane/EtOAc = 4:1 and then CCl_4/EtOAc = 86:14) gave *C*-glycoside **21** as a foam (214 mg, 70.1%); mp 87–88 °C; ^1H NMR ($CDCl_3$, 50 °C) δ 1.40 (d, 3H, J = 6.2 Hz), 1.68 (ddd, 1H, J_1 = J_2 = 11.4, J_3 = 12.8 Hz), 2.40 (s, 3H), 2.54 (ddd, 1H, J_1 = 12.8, J_2 = 3.7, J_3 = 1.8 Hz), 1.8–3.2 (br, 4H), 3.26 (dd, 1H, J_1 = J_2 = 9.2 Hz), 3.45 (s, 3H), 3.60 (dq, 1H, J_1 = 9.2, J_2 = 6.2 Hz), 3.83–3.90 (m, 1H), 3.86 (s, 3H), 3.91 (s, 3H), 4.64 (d, 1H, J = 11.7 Hz), 4.72 (d, 1H, J = 11.7 Hz), 4.73 (d, 1H, J = 11.0 Hz), 5.01 (d, 1H, J = 11.0 Hz), 5.03 (dd, 1H, J_1 = 11.4, J_2 = 1.8 Hz), 6.75 (s, 2H), 7.22–7.38 (m, 10H), 7.56 (d, 1H, J = 8.8 Hz), 7.78 (d, 1H, J = 8.8 Hz), 9.88 (s, 1H); ^{13}C NMR ($CDCl_3$, 50 °C) δ 18.8, 21.6, 24.2, 30.6, 37.8, 56.1, 60.8, 62.7, 71.3, 75.3, 75.7, 81.4, 84.3, 111.3, 114.5, 116.2, 119.1, 120.2, 120.8, 123.2, 124.2, 127.5, 127.6, 127.7, 128.1, 128.4, 128.5, 129.4, 138.7, 138.8, 141.5, 147.4, 148.9, 151.2, 157.3; IR (NaCl) ν_{max} 3330, 2950, 1635, 1610, 1580, 1500, 1450, 1360, 1300, 1260, 1110, 1045 cm^{-1}; $[\alpha]^{21}{}_D$ +40.1° (*c* 1.17, $CHCl_3$); HRMS *m/z* 660.3076 (660.3084 calcd for $C_{42}H_{44}O_7$, M^+); Anal. Calcd for $C_{42}H_{44}O_7$: C, 76.34; H, 6.71. Found: C, 75.98; H, 6.89.

9-(3',4'-di-*O*-benzyl-2',6'-dideoxy-β-D-*arabino*-hexopyranosyl)-1,7,8,12-tetramethoxy-3-methyl-5,6-dihydrobenz[*a*]anthracene (22). To a suspension of NaH (60% in oil, 76.3 mg, 1.91 mmol) in THF (3 mL) was added a solution of *C*-glycoside **21** (210 mg, 0.318 mmol) in THF (12 mL) at 0 °C. The mixture was stirred for 10 min, to which were added $(MeO)_2SO_2$ (0.12 mL, 1.3 mmol) and DMF (3 mL). The mixture was stirred at 40 °C for 40 min, and the reaction was stopped by adding Et_2NH (0.2 mL) and then pH 7 phosphate buffer at 0 °C. The product was extracted with Et_2O, and the combined extracts were washed with 2 N HCl and brine, and dried over Na_2SO_4. Concentration in vacuo followed by purification by chromatography (hexane/EtOAc = 85:15) gave tetramethyl ether **22** as a foam (205 mg, 95.7%); mp 86–87 °C; ^1H NMR ($CDCl_3$, 50 °C) δ 1.39 (d, 3H, J = 6.1 Hz), 1.83 (ddd, 1H, J_1 = J_2 = 11.2, J_3 = 12.9 Hz), 2.3–2.4 (br, 1H), 2.39 (s, 3H), 2.5–3.0 (br, 4H), 3.27 (dd, 1H, J_1 = 9.0, J_2 = 8.8 Hz), 3.46 (s, 3H), 3.61 (dq, 1H, J_1 = 9.0, J_2 = 6.1 Hz), 3.79 (s, 3H), 3.8–3.9 (m, 1H), 3.84 (s, 3H), 3.85 (s, 3H), 4.65 (d, 1H, J = 11.5 Hz), 4.71 (d, 1H, J = 11.5 Hz), 4.74 (d, 1H, J = 11.5 Hz), 5.0–5.05 (m, 2H), 6.73 (s, 1H), 6.75 (s, 1H), 7.22–7.39 (m, 10H), 7.56 (d, 1H, J = 8.8 Hz), 8.09 (d, 1H, J = 8.8 Hz); ^{13}C NMR ($CDCl_3$) δ 18.8, 21.6, 23.8, 30.7, 38.7, 56.0, 60.8, 61.8, 63.1, 71.5, 71.6, 75.3, 75.9, 81.4, 84.3, 111.1, 119.4, 119.9, 120.3, 120.9, 121.8, 123.5, 127.56, 127.60, 127.7, 128.1, 128.4, 130.5, 131.5, 131.6, 138.58, 138.68, 138.74, 141.8, 146.3, 150.8, 151.1, 157.2; IR (KBr) ν_{max} 2950, 1610, 1595, 1575, 1500, 1455, 1360, 1335, 1305, 1260, 1235, 1115, 1055, 1010 cm^{-1}; $[\alpha]^{22}_D$ +20.4° (*c* 2.55, $CHCl_3$); HRMS *m/z* 674.3231 (674.3240 calcd for $C_{43}H_{46}O_7$, M^+); Anal. Calcd for $C_{43}H_{46}O_7$: C, 76.53; H, 6.87. Found: C, 76.44; H, 6.94.

9-(2',6'-dideoxy-β-D-*arabino*-hexopyranosyl)-1,7,8,12-tetramethoxy-3-methyl-5,6-dihydrobenz[*a*]anthracene (23). A suspension of tetramethyl ether **22** (119 mg, 0.177 mmol) in EtOAc (8 mL) and MeOH (16 mL) was stirred under H_2 (1 atm) in the presence of 10% Pd–C (50 mg) at room temperature for 1 h. After changing the atmosphere to Ar, the mixture was filtered through a Celite pad and concentrated in vacuo. The crude product was purified by chromatography ($CHCl_3$/MeOH = 9:1) to give diol **23** as amorphous solids (82.1 mg, 94.1%); mp 114–116 °C; ^1H NMR ($CDCl_3$, 55 °C) δ 1.39 (d, 3H, J = 6.4 Hz), 1.82 (br ddd, 1H, $J_1 = J_2 = J_3$ = 12 Hz), 2.0–2.35 (br, 3H), 2.39 (s, 3H), 2.4–2.9 (br, 4H), 3.21 (br dd, 1H, $J_1 = J_2$ = 9 Hz), 3.45–3.55 (m, 1H), 3.47 (s, 3H), 3.79 (s, 3H), 3.8–3.9 (m, 1H), 3.84 (s, 3H), 3.88 (s, 3H), 5.09 (br d, 1H, J = 12 Hz), 6.73 (s, 1H), 6.75 (s, 1H), 7.54 (d, 1H, J = 8.8 Hz), 8.09 (d, 1H, J = 8.8 Hz); ^{13}C NMR ($CDCl_3$, 55 °C) δ 18.3, 21.6, 24.0, 30.9, 41.3, 56.1, 60.7, 61.8, 63.1, 72.2, 73.6, 76.7, 78.3, 111.4, 119.7, 119.8, 120.4, 121.0, 121.8, 123.5, 130.7, 131.5, 131.6, 138.6, 141.9, 146.5, 151.0, 152.0, 157.5; IR (NaCl) ν_{max} 3450, 2950, 1610, 1600, 1575, 1450, 1360, 1340, 1090, 1060 cm^{-1}; $[\alpha]^{21}_D$ +23.3° (*c* 1.93, $CHCl_3$); HRMS *m/z* 494.2280 (494.2302 calcd for $C_{29}H_{34}O_7$, M^+).

9-(2',6'-dideoxy-β-D-*arabino*-hexopyranosyl)-1,8-dimethoxy-3-methyl-5,6-dihydrobenz[*a*]anthracene-7,12-dione (24). To a solution of diol **23** (24.7 mg, 50.0 μmol) in MeCN (5 mL) was added aqueous solution of CAN (0.10 M, 1.25 mL, 0.125 mmol) at 0 °C. After the mixture was stirred for 30 min, brine was added, and the product was extracted with EtOAc. The combined extracts were washed with brine, and dried over Na_2SO_4. Concentration in vacuo followed by purification by chromatography ($CHCl_3$/MeOH = 92:8) gave quinone **24** as amorphous solids (20.1 mg, 86.6%); mp 115–116 °C; ^1H NMR ($CDCl_3$, 55 °C) δ 1.39 (d, 3H, J = 6.1 Hz), 1.58 (ddd, 1H, $J_1 = J_2$ = 11.2, J_3 = 12.5 Hz), 2.1–2.4 (br, 2H), 2.32 (ddd, 1H, J_1 =12.5, J_2 = 4.9, J_3 = 2.0 Hz), 2.36 (s, 3H), 2.6–2.8 (br, 4H), 3.19 (dd, 1H, $J_1 = J_2$ = 9.0 Hz), 3.50 (dq, 1H, J_1 = 9.0, J_2 = 6.1 Hz), 3.79 (s, 3H), 3.75–3.9 (m, 1H), 3.91 (s, 3H), 4.89 (dd, 1H, J_1 = 11.2, J_2 = 2.0 Hz), 6.69 (s, 1H), 6.71 (s, 1H), 7.83 (d, 1H, J = 8.1 Hz), 7.87 (d, 1H, J = 8.1 Hz); ^{13}C NMR ($CDCl_3$) δ 18.2, 20.8, 21.8, 28.5, 40.6, 56.1, 62.5, 71.9, 73.5, 76.2, 78.3, 111.9, 117.2, 121.2, 122.7, 124.0, 131.9, 135.8, 141.2, 141.9, 142.0, 142.3, 144.2, 156.6, 157.7, 182.8, 183.1; IR (KBr) ν_{max} 3450, 2950, 1710, 1670, 1650, 1610, 1585, 1565, 1460, 1365, 1330, 1295, 1255, 1115, 1085, 1025 cm^{-1}; $[\alpha]^{22}_D$ –46.3° (*c* 0.53, $CHCl_3$); HRMS *m/z* 464.1824 (464.1832 calcd for $C_{27}H_{28}O_7$, M^+).

9-(2',6'-dideoxy-β-D-*arabino*-hexopyranosyl)-1,8-dimethoxy-3-methylbenz[*a*]anthracene-7,12-dione (25). A solution of quinone **24** (62.1 mg, 0.134 mmol) and DBU (221 mg, 1.45 mmol) in 1,4-dioxane (7 mL) was heated under reflux for 5 h. After the solution was cooled to 0 °C, 2 N HCl (10 mL) was added, and the product was extracted with CH_2Cl_2. The combined extracts were washed with brine, and dried over Na_2SO_4. Concentration in vacuo followed by purification by chromatography (CCl_4/acetone = 3:2) gave benz[*a*]anthraquinone **25** as a yellow solid (51.6 mg, 83.5%); mp 110–111 °C; ^1H NMR ($CDCl_3$) δ 1.40 (d, 3H, J = 6.1 Hz), 1.59 (ddd, 1H, $J_1 = J_2$ = 11.5, J_3 = 12.7 Hz), 2.34 (ddd, 1H, J_1 = 12.7, J_2 = 4.9, J_3 = 2.0 Hz), 2.45–2.55 (br, 1H), 2.53 (s, 3H), 2.55–2.65 (br, 1H), 3.21 (ddd, 1H, $J_1 = J_2$ = 9.0, J_3 = 2.7 Hz), 3.52 (dq, 1H, J_1 = 9.0, J_2 = 6.1 Hz), 3.8–3.9 (m, 1H), 3.96 (s, 3H), 3.97 (s, 3H), 4.92 (dd, 1H, J_1 = 11.2, J_2 = 2.0 Hz), 6.90 (s, 1H), 7.26 (s, 1H), 7.88 (d, 1H, J = 8.3 Hz), 7.90 (d, 1H, J = 8.3 Hz), 7.93 (d, 1H, J = 8.5 Hz), 8.20 (d, 1H, J = 8.5 Hz); ^{13}C NMR ($CDCl_3$) δ 18.2, 22.1, 40.4, 56.1, 62.6, 71.7, 73.3, 76.0, 78.1, 111.3, 119.2, 120.1, 122.3, 122.5, 124.4, 132.5, 132.6, 133.7, 135.5, 137.9, 138.1, 140.6, 141.4, 156.6, 157.1, 182.2, 185.7; IR (KBr) ν_{max} 3460, 2950, 1670, 1620, 1590, 1450, 1410, 1370, 1285, 1265, 1145, 1085, 1050, 1020 cm^{-1}; $[\alpha]^{22}_D$ –29.3° (*c* 0.95, $CHCl_3$); HRMS *m/z* 462.1673 (462.1676 calcd for $C_{27}H_{26}O_7$, M^+).

9-[2',6'-dideoxy-3'-*O*-(*tert*-butyldimethylsilyl)-β-D-*arabino*-hexopyranosyl]-1,8-dimethoxy-3-methylbenz[*a*]anthracene-7,12-dione (26). A solution of benz[*a*]anthraquinone **25** (26.3 mg, 0.0569 mmol), imidazole (19.4 mg, 0.285 mmol), and *tert*-butyldimethylsilyl chloride (25.7 mg, 0.171 mmol) in DMF (0.8 mL) was stirred at room temperature for 2 h. The reaction was stopped by adding pH 7 phosphate buffer at 0 °C, and the product was extracted with Et_2O. The combined extracts were washed with water, saturated $NaHCO_3$ solution, and brine, and dried over Na_2SO_4. Concentration in vacuo followed by purification by chromatography (hexane/EtOAc = 7:3) gave silyl ether **26** as a yellow oil (26.3 mg, 80.2%): ^1H NMR ($CDCl_3$) δ 0.09 (s, 3H), 0.14 (s, 3H), 0.89 (s, 9H), 1.41 (d, 3H, J = 6.1 Hz), 1.60 (ddd, 1H, $J_1 = J_2$ = 11.2, J_3 = 12.7 Hz), 2.21 (ddd, 1H, J_1 = 12.7, J_2 = 4.9, J_3 = 2.0 Hz), 2.3–2.35 (br, 1H), 2.53 (s, 3H), 3.21 (ddd, 1H, J_1 = 9.3, J_2 = 8.6, J_3 = 1.0 Hz), 3.55 (dq, 1H, J_1 = 9.3, J_2 = 6.1 Hz), 3.80 (ddd, 1H, J_1 = 11.2, J_2 = 8.6, J_3 = 4.9 Hz), 3.966 (s, 3H), 3.974 (s, 3H), 4.91 (dd, 1H, J_1 = 11.2, J_2 = 2.0 Hz), 6.89 (d, 1H, J = 1.2 Hz), 7.26 (d, 1H, J = 1.2 Hz), 7.88 (d, 1H, J = 7.8 Hz), 7.91 (d, 1H, J = 7.8 Hz), 7.93 (d, 1H, J = 8.6 Hz), 8.21 (d, 1H, J = 8.6 Hz); ^{13}C NMR ($CDCl_3$) δ –4.6, –4.1, 18.0, 18.4, 22.1, 25.8, 41.4, 56.0, 62.5, 71.6, 74.6, 75.8, 77.9, 111.3, 119.2, 120.1, 122.4, 122.5, 124.5, 132.5, 132.6, 133.7, 135.5, 137.9, 138.1, 140.6, 141.6, 156.5, 157.2, 182.3, 185.7; IR (NaCl) ν_{max} 3540, 2950, 1670, 1620, 1585, 1495, 1460, 1405, 1365, 1280, 1260, 1140, 1120, 1080, 1050 cm^{-1}; $[\alpha]^{22}_D$ –43.4° (*c* 1.30, $CHCl_3$); HRMS *m/z* 576.2555 (576.2541 calcd for $C_{33}H_{40}O_7Si$, M^+).

9-[2',6'-dideoxy-3-*O*-(*tert*-butyldimethylsilyl)-4-*O*-[(*E,E*)-2",4"-decadienoyl]-β-D-*arabino*-hexopyranosyl]-1,8-dimethoxy-3-methylbenz[*a*]anthracene-7,12-dione (27). To a solution of 2,4,6-trichlorobenzoyl chloride (203 mg, 0.832 mmol) and triethylamine (90.3 mg, 0.894 mmol) in THF (3 mL) was added (*E,E*)-2,4-decadienoic acid[22] (101 mg, 0.601 mmol) in THF (1 mL) at room temperature, and the solution was stirred for 20 min. After removal of triethylamine hydrochloride by filtration, the filtrate was concentrated, and the residue was dissolved in toluene (1 mL). A half volume of this solution of the mixed anhydride was added to the flask containing alcohol **26** (32.0 mg, 0.0556 mmol) at 0 °C followed by DMAP (33.9 mg, 0.278 mmol). (To carry out the reaction in proper concentration this procedure was adopted.) Immediately the ice bath was removed, and the reaction mixture was stirred for 1.5 h at room temperature. After the mixture was cooled to 0 °C, water was added, and the solution was extracted with Et_2O. The combined extracts were washed successively with 2 N HCl, brine, saturated $NaHCO_3$ solution, and brine, and dried over Na_2SO_4. Concentration in vacuo followed by purification by chromatography (hexane/EtOAc = 8:2) gave ester **27** (31.4 mg, 77.9%) as yellow solids: mp 72–75 °C; ^1H NMR ($CDCl_3$) δ 0.02 (s, 3H), 0.04 (s, 3H), 0.81 (s, 9H), 0.90 (t, 3H, J = 7.1 Hz), 1.27 (d, 3H, J = 6.1 Hz), 1.27–1.37 (m, 4H), 1.45 (tt, 2H, $J_1 = J_2$ = 7.1 Hz), 1.72 (ddd, 1H, $J_1 = J_2$ = 11.5, J_3 = 12.9 Hz), 2.18 (dt, 2H, J_1 = 6.4, J_2 = 7.1 Hz), 2.25 (ddd, 1H, J_1 = 12.9, J_2 = 4.9, J_3 = 2.0 Hz), 2.53 (s, 3H), 3.64 (dq, 1H, J_1 = 9.5, J_2 = 6.1 Hz), 3.95–4.03 (m, 1H), 3.97 (s, 3H), 3.98 (s, 3H), 4.84 (ddd, 1H, J_1 = 9.5, J_2 = 9.3 Hz) 4.93 (dd, 1H, J_1 = 11.5, J_2 = 2.0 Hz), 5.82 (d, 1H, J = 15.4 Hz), 6.15 (dt, 1H, J_1 = 15.1, J_2 = 6.4 Hz), 6.21 (dd, 1H, J_1 = 15.1, J_2 = 9.5 Hz), 6.90 (s, 1H), 7.27 (s, 1H), 7.31 (dd, 1H, J_1 = 15.4, J_2 = 9.5 Hz), 7.88–7.95 (m, 3H), 8.21 (d, 1H, J = 8.6 Hz); ^{13}C NMR ($CDCl_3$) δ –4.8, –4.5, 14.0, 17.8, 18.1, 22.1, 22.5, 25.6, 28.4, 31.4, 33.0, 42.0, 56.0, 62.6, 71.6, 74.8, 111.3, 118.9, 119.2, 120.0, 122.45, 122.48, 124.4, 128.3, 132.5, 132.6, 133.7, 135.6, 137.9, 138.1, 140.6, 141.4, 145.2, 145.8, 156.5, 157.2, 166.5, 182.3, 185.7; IR (KBr) ν_{max} 2940, 1720, 1670, 1640, 1620, 1590, 1495, 1460, 1360, 1280, 1260, 1140, 1080 cm^{-1}; $[\alpha]^{19}_D$ –30.0° (*c* 1.69, $CHCl_3$); HRMS *m/z* 726.3589 (726.3584 calcd for $C_{43}H_{54}O_8Si$, M^+); Anal. Calcd for $C_{43}H_{54}O_8Si$: C, 71.04; H, 7.49. Found: C, 70.74; H, 7.43.

9-[2',6'-dideoxy-4-*O*-[(*E,E*)-2",4"-decadienoyl]-β-D-*arabino*-hexopyranosyl]-1,8-dimethoxy-3-methylbenz[*a*]anthracene-7,12-dione (28). A solution of **27** (33.8 mg, 0.0466 mmol) in MeCN (2 mL) and 46% aqueous solution of HF (0.1 ml) was stirred at room temperature for 1.5 h. To this solution was added water, and the mixture was extracted with CH_2Cl_2. The combined extracts were washed with brine, and dried over Na_2SO_4. Concentration in vacuo followed by purification by chromatography (hexane/EtOAc = 6:4) gave alcohol **28** (24.3 mg, 85.3%) as a yellow oil: ^1H NMR ($CDCl_3$) δ 0.90 (t, 3H, J = 7.0 Hz), 1.25–1.35 (m, 4H), 1.31 (d, 3H, J = 6.1 Hz), 1.41–1.49 (m, 2H), 1.70 (ddd, 1H, $J_1 = J_2$ = 11.5, J_3 = 12.9 Hz), 2.16–2.22 (m, 2H), 2.44 (ddd, 1H, J_1 = 12.9, J_2 = 5.1, J_3 = 1.7 Hz), 2.54 (s, 3H), 2.65–2.75 (br d, 1H), 3.70 (dq, 1H, J_1 = 9.3, J_2 = 6.1 Hz), 3.95–4.05 (m, 1H), 3.972 (s, 3H), 3.974 (s, 3H), 4.67 (ddd, 1H, J_1 = J_2 = 9.3 Hz) 4.94 (dd, 1H, J_1 = 11.5, J_2 = 1.7 Hz), 5.86 (d, 1H, J = 15.1 Hz), 6.15–6.25 (m, 2H), 6.90 (s, 1H), 7.27 (s, 1H), 7.31–7.39 (m, 1H), 7.90 (d, 1H, J = 8.3 Hz), 7.92 (d, 1H, J = 8.3 Hz), 7.93 (d, 1H, J = 8.5 Hz), 8.20 (d, 1H, J = 8.5 Hz); ^{13}C NMR ($CDCl_3$) δ 14.0, 18.2, 22.2, 22.5, 28.3, 31.4, 33.0, 41.0, 56.1, 62.6, 71.6, 71.7, 74.4, 79.0, 111.3, 118.0, 119.2, 120.1, 122.4, 122.5, 124.4, 128.2, 132.4, 132.6, 133.7, 135.5, 137.9, 138.2, 140.6, 141.0, 146.2, 146.9, 156.7, 157.1, 168.2, 182.2, 185.7; IR (NaCl) ν_{max} 3480, 2940, 1715, 1670, 1640, 1615, 1585, 1450, 1365, 1280, 1260, 1140, 1050 cm^{-1}; $[\alpha]^{20}_D$ +26° (*c* 0.71, $CHCl_3$); HRMS *m/z* 612.2732 (612.2721 calcd for $C_{37}H_{40}O_8$, M^+).

Antibiotic C104 (1). To a solution of **28** (26.1 mg, 0.0426 mmol) in CH_2Cl_2 (5 mL) was added a solution of BBr_3 (92.1 mg, 0.368 mmol) in CH_2Cl_2 (2 mL) at –78 °C. After 40 min, saturated $NaHCO_3$ solution was added. The mixture was stirred for 30 min, acidified with 2 N HCl, and the products were extracted with CH_2Cl_2. The combined extracts were washed with brine, and dried over Na_2SO_4. Concentration in vacuo followed by purification by chromatography (benzene/EtOAc/MeOH = 88:10:2) to give C104 (**1**) (21.3 mg, 85.5 %) as a dark red crystals; mp 173–175 °C; ^1H NMR ($CDCl_3$) δ 0.90 (t, 3H, J = 6.8 Hz), 1.27–1.36 (m, 4H), 1.34 (d, 3H, J = 6.0 Hz), 1.45 (tt, 2H, J_1 = J_2 = 7.3 Hz), 1.53–1.63 (m, 1H), 2.17–2.23 (m, 2H), 2.50 (s, 3H), 2.64 (ddd, 1H, J_1 = 13.0, J_2 = 5.1, J_3 = 1.7 Hz), 2.69 (d, 1H, J = 4.7 Hz), 3.71 (dq, 1H, J_1 = 9.4, J_2 = 6.0 Hz), 3.98–4.06 (m, 1H), 4.67 (dd, 1H, J_1 = 9.4, J_2 = 9.0 Hz) 4.95 (dd, 1H, J_1 = 11.5, J_2 = 1.7 Hz), 5.87 (d, 1H, J = 15.4 Hz), 6.17–6.26 (m, 2H), 7.15 (d, 1H, J = 1.3 Hz), 7.26 (br s, 1H), 7.32–7.39 (m, 1H), 7.89 (d, 1H, J = 8.1 Hz), 7.93 (d, 1H, J = 8.1 Hz), 8.14 (d, 1H, J = 8.5 Hz), 8.32 (d, 1H, J = 8.5 Hz); 11.4 (s, 1H); 12.7 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 14.0, 18.2, 21.3, 22.5, 28.3, 31.4, 33.1, 39.9, 71.2, 71.6, 74.3, 78.9, 114.0, 118.0, 120.05, 120.10, 121.2, 121.4, 121.8, 128.2, 132.4, 133.5, 134.8, 137.5, 137.6, 137.8, 139.1, 140.2, 146.3, 146.9, 155.3, 157.9, 168.2, 188.2, 189.4; IR (NaCl) ν_{max} 3470, 2940, 1715, 1700, 1630, 1590, 1500, 1435, 1370, 1310, 1260, 1145, 1075, 1045 cm^{-1}; $[\alpha]^{21}_D$ +82° (*c* 0.12, $CHCl_3$); HRMS *m/z* 584.2410 (584.2408 calcd for $C_{35}H_{36}O_8$, M^+); Anal. Calcd for $C_{35}H_{36}O_8 \cdot 1/2H_2O$: C, 70.68; H, 6.14. Found: C, 70.81; H, 6.28.

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References and Notes

1 Rohr, J; Thiericke, R. *Nat. Prod. Rep.* **1992**, 103–137.

2 Drautz, H.; Zähner, H.; Rohr, J.; Zeeck, A. *J. Antibiot.* **1986**, *39*, 1657.

3 (a) Yamaguchi, M.; Okuma, T.; Horiguchi, A.; Ikeura, C.; Minami, T. *J. Org. Chem.* **1992**, *57*, 1647–1649. (b) Kim, K.; Reibenspies, J.; Sulikowski, G. *Ibid.* **1992**, *57*, 5557–5559. (c) Gordon, D. M.; Danishefsky, S. J.; Schulte, G. K. *Ibid.* **1992**, *57*, 7052–7055. (d) Larsen, D. S.; O'Shea, M. D. *Tetrahedron Lett.* **1993**, *34*, 1373–1376. (e) Krohn, K.; Khanbabaee, K. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 99–100. (f) Krohn, K.; Khanbabaee, K.; Florke, U.; Jones, P. G.; Chrapkowski, A. *Liebigs Ann. Chem.* **1994**, 471–477.

4 Arnone, A.; Nasini, G.; Vajna de Pava, O. *Gazz. Chim. Ital.* **1988**, *118*, 749–751.

5 A preliminary report of this work has appeared: Matsumoto, T; Sohma, T.; Yamaguchi, H.; Kurata, S.; Suzuki, K. *Synlett* **1995**, 263–266.

6 For reviews on the synthesis of aryl *C*-glycoside compounds, see: (a) Hacksell, U.; Daves, G. D., Jr. *Prog. Med. Chem.* **1985**, *22*, 1–65. (b) Postema, M. H. D. *Tetrahedron* **1992**, *48*, 8545–8599. (c)

Suzuki, K.; Matsumoto, T. In *Recent Progress in the Chemical Synthesis of Antibiotics and Related Microbial Products*; Lukacs, G., Ed; Vol. 2, pp 353–404; Springer: Berlin, 1993.

7 For the *O→C*-glycoside rearrangement, see: (a) Matsumoto, T.; Katsuki, M.; Suzuki, K. *Tetrahedron Lett.* **1988**, *29* 6935–6938. (b) Matsumoto, T; Katsuki, M.; Jona, H.; Suzuki, K. *Ibid.* **1989**, *30*, 6185–6188. (c) Matsumoto, T; Hosoya, T.; Suzuki, K. *Ibid.* **1990**, *31*, 4629–4632. (d) Matsumoto, T; Katsuki, M.; Jona, H.; Suzuki, K. *J. Am. Chem. Soc.* **1991**, *113*, 6982–6992. (e) Matsumoto, T; Hosoya, T.; Suzuki, K. *Synlett* **1991**, 709–711. Also see, ref. 9b, c.

8 For a leading review on benzynes, see: Hoffmann, R. W. *Dehydrobenzene and Cycloalkynes*; Academic: New York, 1967.

9 For the bezyne–furan cycloaddition reaction, see: (a) Matsumoto, T.; Hosoya, T.; Katsuki, M.; Suzuki, K. *Tetrahedron Lett.* **1991**, *32*, 6735–6736. (b) Matsumoto, T; Hosoya, T.; Suzuki, K. *J. Am. Chem. Soc.* **1992**, *114*, 3568–3570. (c) Hosoya, T.; Takashiro, E.; Matsumoto, T.; Suzuki, K. *Ibid.* **1994**, *116*, 1004–1015. See also: (d) Giles, R. G. F.; Sargent, M. V.; Sianipar, H. *J. Chem. Soc., Perkin Trans. 1* **1991**, 1571–1579. (e) Giles, R. G. F.; Hughes, A. B.; Sargent, M. V. *Ibid.* **1991**, 1581–1587.

10 For the generation and reaction of α-siloxyfuran, see: (a) Asaoka, M.; Miyake, K.; Takei, H. *Chem. Lett.* **1977**, 167–170. (b) Garver, L. C.; van Tamelen, E. E. *J. Am. Chem. Soc.* **1982**, *104*, 867–869. (c) Ramage, R.; Owen, O. J. R.; Southwell, I. A. *Tetrahedron Lett.* **1983**, *24*, 4487–4490. (d) Jefford, C. W.; Sledeski, A. W.; Rossier, J.-C.; Boukouvalas, J. *Ibid.* **1990**, *31*, 5741–5744. (e) Yoshii, E.; Koizumi, T.; Kitatsuji, E.; Kawazoe, T.; Kaneko, T. *Heterocycles* **1976**, *4*, 1663–1667. (f) Sánchez, A. J.; Konopelski, J. P. *J. Org. Chem.* **1994**, *59*, 5445–5452.

11 For the reaction of amine with benzyne, see: Kessar, S. V. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Vol. 4, Chapter 2.3; Pergamon: Oxford, 1991. Also see ref. 8.

12 Tarnchompoo, B.; Thebtaranonth, C.; Thebtaranonth, Y. *Synthesis* **1986**, 785–786.

13 Okazaki, R.; Negishi, Y.; Inamoto, N. *J. Org. Chem.* **1984**, *49*, 3819–3824.

14 Although some α-(*tert*-butyldimethylsiloxy)furan derivatives are reportedly inert to moisture, furan **10** turned out to be too labile to be isolated. See ref. 10d, f.

15 In practice, the isomers were separable more easily at the stage of compound **18** (silica-gel chromatography).

16 (a) Kuntsmann, M. P.; Mitscher, L. A. *J. Org. Chem.* **1966**, *31*, 2920–2925. (b) Brown, P. M.; Thomson, R. H. *J. Chem. Soc., Perkin Trans. 1* **1976**, 997–1000. (c) Katsuura, K.; Snieckus, V. *Can. J. Chem.* **1987**, *65*, 124–130.

17 (a) Fraser–Reid, B.; Kelly, D. R.; Tulshian, D. B.; Ravi, P. S. *J. Carbohydr. Chem.* **1983**, *2*, 105–114. (b) Beau, J.–M.; Jaurand, G.; Esnault, J.; Sinaÿ, P. *Tetrahedron Lett.* **1987**, *28*, 1105–1108.

18 Bolitt, V.; Mioskowski, C.; Lee, S.–G.; Falck, J. R. *J. Org. Chem.* **1990**, *55*, 5812–5813.

19 Suzuki, K. *Pure Appl. Chem.* **1994**, *66*, 1557–1564.

20 As evidenced by the careful NMR analyses of the intermediates, all the steps, from **21** to the target **1**, were proven to be free from epimerization of the anomeric stereochemistry.

21 Inanaga, J.; Hirata, K.; Saeki, H.; Katsuki, T.; Yamaguchi, M.; *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1989–1993.

22 Bari, S. S.; Sattar, M. A.; Vig, R.; Kumar, A.; Vasisht, N. *J. Indian Chem. Soc.* **1990**, *67*, 995–996.

23 Bartlett, P. A.; Green, F. R., III *J. Am. Chem. Soc.* **1978**, *100*, 4858–4865. Shoda, S.; Mukaiyama, T. *Chem. Lett.* **1980**, 391–392. Roush, W. R.; Blizzard, T. A. *J. Org. Chem.* **1984**, *49*, 1772–1783.

24 Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1353.

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