Convergent Total Synthesis of Vineomycinone B_2 Methyl Ester and Its C(12)-Epimer

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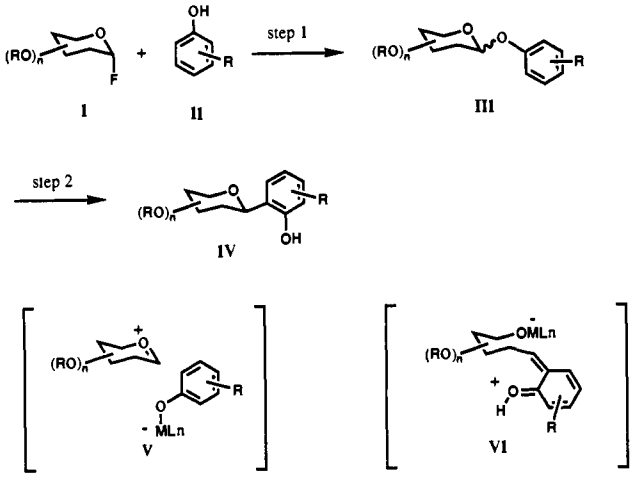
Abstract: Total syntheses of vineomycinone B_2 methyl ester (**7**) and its C(12)-epimer (*epi*-**7**) have been completed. The key reaction for construction of the aryl *C*-glycoside linkage is the *O*→*C*-glycoside rearrangement starting from D-olivosyl fluoride derivative **11** and anthrol derivative **21**, which provides the regio- and stereocontrolled formation of the aryl *C*-glycoside sector of the target. The combination of Cp_2HfCl_2–$AgClO_4$ serves as a particularly efficient promoter for this reaction. An extensive model study for attaching the side chain is presented. The Lochmann–Schlosser base cleanly effects ortho metalation of anthracene derivatives **19** and **20**. The metalated species can be trapped as stannyl derivatives, from which the corresponding aryllithium species are generated by using *n*-BuLi or preferably MeLi in toluene. These specific reaction conditions are necessary to suppress the abnormal reaction of RLi reagents at the C(9)/C(10)-positions of the anthracenes. Coupling of the side chain moiety was efficiently carried out by such metalation of anthracene derivative **25** followed by reaction with chiral aldehyde (*S*)-**29**. The chiral aldehyde was derived from enantiomerically pure acid (*S*)-**37** obtained by enzymatic kinetic resolution. Deoxygenation of the benzylic alcohol function followed by several steps allowed the total synthesis of **7**. Starting from (*R*)-aldehyde **29**, the same sequence of reactions accomplished the total synthesis of *epi*-**7**. The epi series of intermediates provided firm evidence for the stereochemical homogeneity of synthetic **7**.

Introduction

The unique structures of aryl *C*-glycosides are embodied in various biologically important natural products recently isolated. Figure 1 shows some of the examples: Aquayamycin (**1**),[1a] medermycin (**2**),[1b] ravidomycin (**3**),[1c] and hedamycin (**4**)[1d] possess structures in which the sugars are directly bound by a C–C bond to naphthoquinone and anthraquinone derivatives. The aryl *C*-glycoside bonds are quite often located ortho to a phenolic hydroxyl group as in **1** and **2**, although *p*- as in **3** or both *o*- and *p*-*C*-glycoside bonds as in **4** are also seen. These compounds exhibit diverse biological activities, such as antibacterial activity, enzyme inhibitory effects, inhibition of platelet aggregation and, more significantly, antitumor activities.[2]

These aryl *C*-glycoside antibiotics are challenging synthetic targets,[3] which provide impetus for development of new methodology. One of the essential problems is to find an efficient method for the construction of the aryl *C*-glycosidic linkage in a regio- and stereoselective manner under mild conditions.[4]

Scheme I



We recently exploited a new synthetic reaction that provides an efficient solution to this problem. Scheme I illustrates its key features: In the presence of a Lewis acid, the O-glycosidation of phenol II with glycosyl fluoride I proceeds at low temperature (step 1). By raising the reaction temperature, *O*-glycoside III is converted in situ to *C*-glycoside IV (step 2). This "*O*→*C*-glycoside rearrangement" occurs via ion pair V, generated from *O*-glycoside III, which undergoes an irreversible Friedel–Crafts coupling *regioselectively at the ortho position to the phenolic hydroxyl group.* This "ortho selectivity" of the aryl *C*-glycoside bond formation is the most notable feature of the reaction. Another important point is the anomeric stereocontrol of *C*-glycoside IV. The α/β-selectivity is determined not only kinetically but also by a possible contribution of an *ortho*-quinone methide (VI).[5,6] Group IV metallocene complexes Cp_2MCl_2 (M = Zr, Hf), in combination with $AgClO_4$, serve as particularly efficient promoters in this reaction.[7] The cationic complex $Cp_2MCl^+ClO_4^-$, postulated as the key species, has a number of special reactivities different from

(1) (a) Sezaki, M.; Kondo, S.; Maeda, K.; Umezawa, H.; Ohno, M. *Tetrahedron* **1970**, *26*, 5171. (b) Takano, S.; Hasuda, K.; Ito, A.; Koide, Y.; Ishii, F.; Haneda, I.; Chihara, S.; Koyama, Y. *J. Antibiot.* **1976**, *29*, 765. (c) Sehgal, S. N.; Czerkawski, H.; Kudelski, A.; Pandev, K.; Saucier, R.; Vezina, C. *Ibid.* **1983**, *36*, 355. Findlay, J. A.; Liu, J.-S.; Radics, L.; Rakhit, S. *Can. J. Chem.* **1981**, *59*, 3018. (d) Zehnder, M.; Séquin, U.; Nadig, H. *Helv. Chim. Acta* **1979**, *62*, 2525.

(2) For further examples, see the following. Urdamycins: Drautz, H.; Zähner, H.; Rohr, J.; Zeeck, A. *J. Antibiot.* **1986**, *39*, 1657. Saquayamycins: Uchida, T.; Imoto, M.; Watanabe, Y.; Miura, K.; Dobashi, T.; Matsuda, N.; Sawa, T.; Naganawa, H.; Hamada, M.; Takeuchi, T.; Umezawa, H. *Ibid.* **1985**, *38*, 1171. Benzanthrins: Rasmussen, R. R.; Nuss, M. E.; Scherr, M. H.; Mueller, S. L.; McAlpine, J. B.; Mitscher, L. A. *Ibid.* **1986**, *39*, 1515. Pluramycin: Séquin, U.; Nadig, H. *Helv. Chim. Acta* **1987**, *70*, 1217. For the compounds with platelet aggregation inhibitory effects, see the following. OM-4842 (aggreticin): Ōmura, S.; Nakagawa, A.; Fukamachi, N.; Miura, S.; Takahashi, Y.; Komiyama, K.; Kobayashi, B. *J. Antibiot.* **1988**, *41*, 812. PI-083: Kawashima, A.; Yoshimura, Y.; Gotō, J.; Nakaike, S.; Mizutani, T.; Hanada, K.; Ōmura, S. *Ibid.* **1988**, *41*, 1913. For the enzyme inhibitor, see the following. P-1894B: Ohta, K.; Mizuta, E.; Okazaki, H.; Kishi, T. *Chem. Pharm. Bull.* **1984**, *32*, 4350.

(3) For examples of the total synthesis, see the following. (a) Nogalamycin: Kawasaki, M.; Matsuda, F.; Terashima, S. *Tetrahedron Lett.* **1986**, *27*, 2145; *Ibid.* **1988**, *29*, 791. (b) Medermycin: Tatsuta, K.; Ozeki, H.; Yamaguchi, M.; Tanaka, M.; Okui, T. *Tetrahedron Lett.* **1990**, *31*, 5495. (c) Gilvocarcin: Patten, A. D.; Nguyen, N. H.; Danishefsky, S. J. *J. Org. Chem.* **1988**, *53*, 1003.

(4) For other synthetic methods to aryl *C*-glycoside, see: (a) Outten, R. A.; Daves, G. D., Jr. *J. Org. Chem.* **1987**, *52*, 5064. (b) Casiraghi, G.; Cornia, M.; Rassu, G.; Zetta, L.; Fava, G. G.; Belicchi, M. F. *Tetrahedron Lett.* **1988**, *29*, 3323. (c) Czernecki, S.; Dechavanne, V. *Can. J. Chem.* **1983**, *61*, 533. (d) Schmidt, R. R.; Hoffmann, M. *Tetrahedron Lett.* **1982**, *23*, 409. (e) Williams, R. M.; Stewart, A. O. *Tetrahedron Lett.* **1983**, *24*, 2715. (f) Ohrui, H.; Kuzuhara, H.; Emoto, S. *Agric. Biol. Chem.* **1972**, *36*, 1651. (g) Kraus, G. A.; Molina, M. T. *J. Org. Chem.* **1988**, *53*, 752.

(5) (a) Matsumoto, T.; Katsuki, M.; Suzuki, K. *Tetrahedron Lett.* **1988**, *29*, 6935. (b) Matsumoto, T.; Hosoya, T.; Suzuki, K. *Ibid.* **1990**, *31*, 4629. For the BF_3·OEt_2-promoted reaction, also see: (c) Kometani, T.; Kondo, H.; Fujimori, Y. *Synthesis* **1988**, 1005. For a Friedel–Crafts approach, see: (d) Matsumoto, T.; Katsuki, M.; Suzuki, K. *Tetrahedron Lett.* **1989**, *30*, 833.

(6) A preliminary report of this work has appeared: Matsumoto, T.; Katsuki, M.; Jona, H.; Suzuki, K. *Tetrahedron Lett.* **1989**, *30*, 6185.

(7) For the use of Cp_2MCl_2–$AgClO_4$ in *O*-glycoside synthesis, see: (a) Matsumoto, T.; Maeta, H.; Suzuki, K.; Tsuchihashi, G. *Tetrahedron Lett.* **1988**, *29*, 3567, 3571, 3575. (b) Suzuki, K.; Maeta, H.; Matsumoto, T. *Ibid.* **1989**, *30*, 4853.

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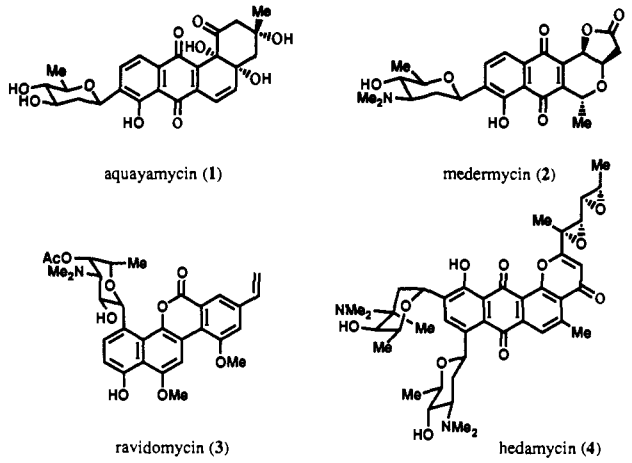


Figure 1. Naturally occurring aryl *C*-glycosides.

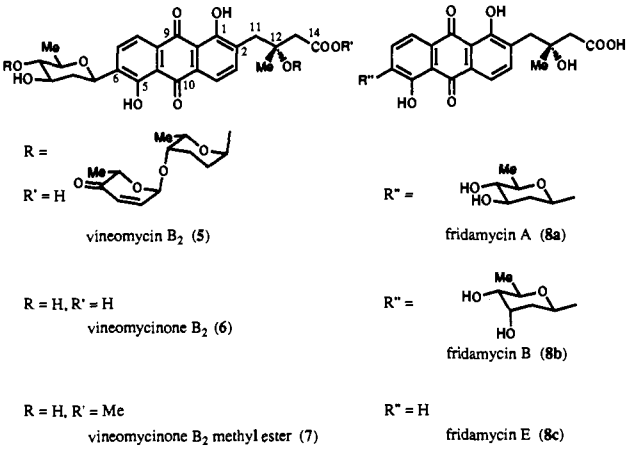


Figure 2. Vineomycin–fridamycin-type antibiotics.

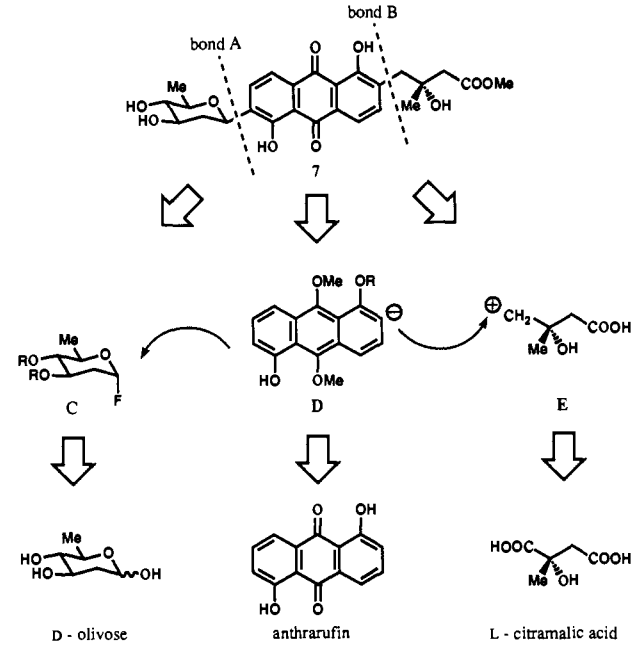
typical Lewis acids such as $BF_3{\cdot}OEt_2$.[7b]

We were attracted to the total synthesis of the vineomycin–fridamycin class of aryl *C*-glycoside antibiotics (vide infra) not only to demonstrate the synthetic potential of the *O*→*C*-glycoside rearrangement but also to open an efficient route to more complex series of related natural products.

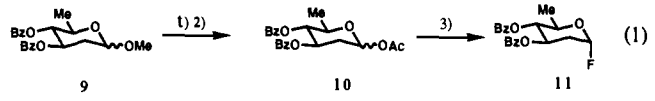
The vineomycins constitute a class of aryl *C*-glycoside antibiotics isolated from the culture broth of *Streptomyces matensis vineus* by Ōmura.[8] They are active against Gram-positive bacteria and also exhibit antitumor activity on Sarcoma 180 solid tumor on mice. Vineomycin B_2 (**5**, Figure 2) manifests the characteristic structural feature of this class of antibiotics, a β-linked D-olivoside moiety directly bound via a C–C bond to the 1,5-dihydroxy-9,10-anthraquinone chromophore. The other sector of the molecule is composed of a characteristic aliphatic side chain that is biologically derived via the D-ring cleavage of vineomycin A_1, a member of this class of antibiotics with an aquayamycin-type isotetracenone skeleton.[8d] A series of new antibiotics with closely related structures was subsequently isolated from the culture broth of *Streptomyces parvulus* and named as fridamycins (**8a–c**).[9] Note that the major component of the fridamycin antibiotics, fridamycin A (**8a**), is identical with vineomycinone B_2 (**6**), the aglycon portion of **5**.

In the following discussion, our successful approach to the total syntheses of the methyl ester of vineomycinone B_2 (**7**) and its

Scheme II



Scheme III[a]



(1)

[a] Key: 1, HCl(aq), AcOH/DME, 90 °C, 16 h, 86%; 2, Ac_2O, catalytic DMAP/pyridine, room temperature, 1 h, quantitative; 3, HF–pyridine/CH_2Cl_2, −20 → 0 °C, 25 min, 99%.

Synthetic Plan

C(12)-epimer will be presented.[6,10,11]

Scheme II shows the retrosynthesis of vineomycinone B_2 methyl ester (**7**). The target structure is divided into three moieties: the anthraquinone ring, the sugar, and the aliphatic side chain. If viable, the regio- and stereocontrolled formation of two C–C bonds onto the anthracene derivative, derived from commercially available 1,5-dihydroxy-9,10-anthraquinone (anthrarufin), would open a convergent and flexible approach to this class of antibiotics.

The aryl *C*-glycoside linkage (bond A) would be formed by employing the aforementioned *O*→*C*-glycoside rearrangement. The regiochemistry of the *C*-glycoside bond formation could be controlled by the ortho selectivity of the reaction. The precursor of the carbohydrate moiety is D-olivosyl fluoride C. The major problem would be stereocontrol of the *C*-glycoside formation since a 2-deoxy sugar is concerned.

For bond formation between the anthracene derivative D and the side chain (bond B), we envisaged the use of directed ortho metalation followed by reaction with the electrophilic side chain synthon E derived from chiral L-citramalic acid.

Results and Discussion

Aryl *C*-Glycoside Synthesis. Methyl D-olivoside derivative **9**[12] was hydrolyzed under acidic conditions to the corresponding lactol, which was acetylated to give the acetate **10** as a mixture of anomers. Subsequent fluorination according to the Noyori procedure[13] gave the α-fluoride **11** in 99% yield after silica-gel flash chromatography (Scheme III).[14]

(8) Isolation: (a) Ōmura, S.; Tanaka, H.; Ōiwa, R.; Awaya, J.; Masuma, R.; Tanaka, K. *J. Antibiot.* **1977**, *30*, 908. Structure determination: (b) Imamura, N.; Kakinuma, K.; Ikekawa, N.; Tanaka, H.; Ōmura, S. *Ibid.* **1981**, *34*, 1517. (c) Idem. *Chem. Pharm. Bull.* **1981**, *29*, 1788. Biosynthetic studies: (d) Idem. *J. Antibiot.* **1982**, *35*, 602.

(9) Zeeck, A.; Kricke, P. Unpublished results. Kricke, P. Ph.D. Dissertation, Universität Göttingen, 1984.

(10) (a) Total synthesis: Danishefsky, S. J.; Uang, B. J.; Quallich, G. *J. Am. Chem. Soc.* **1985**, *107*, 1285. Synthetic approaches: (b) Tius, M. A.; Gomez-Galeno, J.; Zaidi, J. H. *Tetrahedron Lett.* **1988**, *29*, 6909. (c) Krohn, K.; Baltus, W. *Tetrahedron* **1988**, *44*, 49.

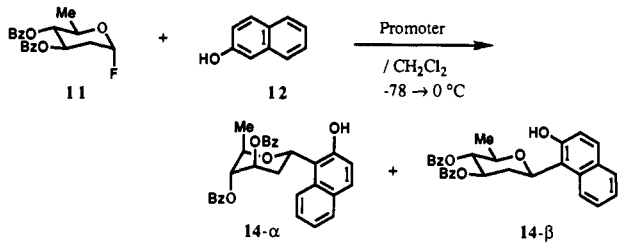
(11) After completion of this work, an independent total synthesis of this compound appeared: Tius, M. A.; Gu, X.-Q.; Gomez-Galeno, J. *J. Am. Chem. Soc.* **1990**, *112*, 8188. We thank Prof. Tius for this information prior to publication.

(12) Staněk, J. Jr.; Marek, M.; Jarý, J. *Carbohydr. Res.* **1978**, *64*, 315.

(13) Hayashi, M.; Hashimoto, S.; Noyori, R. *Chem. Lett.* **1984**, 1747.

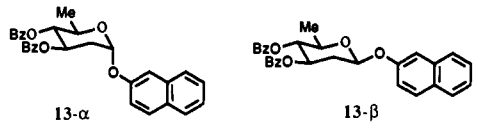
(14) Although some glycosyl fluorides derived from 2-deoxy sugars are unstable, fluoride **11** is stable enough to allow normal manipulation and also prolonged storage at 0 °C.

Table I. *O*→*C*-Glycoside Rearrangement with **11** and **12**



promoter	yield (%)	α/β
Cp_2HfCl_2–$AgClO_4$	98	β only
BF_3·OEt_2	70[a]	3.4/1

[a] The corresponding *O*-glycoside **13** was also isolated in 28% yield (α/β = 4.6/1).



Glycosidation of 2-deoxy sugars is often troublesome in terms of side reactions and poor α/β-selectivity. However, promising results were obtained in a preliminary study of aryl *C*-glycoside formation with fluoride **11**. The choice of reaction promoter is crucial, which is best illustrated by the results shown in Table I.

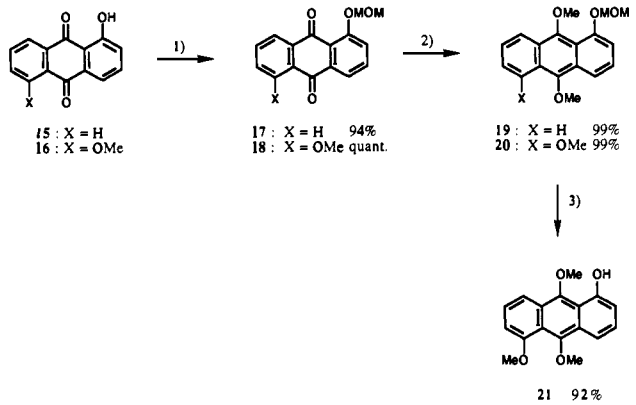
Treatment of fluoride **11** and 2-naphthol (**12**), a model aromatic compound, with BF_3·OEt_2 (CH_2Cl_2, −78 °C) led to formation of *O*-glycoside **13** in 30 min.[15] Conversion of the *O*-glycoside to *C*-glycoside took place during gradual warming. At the final temperature of 0 °C, *C*-glycoside **14** was obtained in 70% yield together with the unrearranged *O*-glycoside **13** in 28% yield. C–C bond formation occurred exclusively at the C(1)-position, and no positional isomers were detected. Notably high α-selectivity was observed for the *C*-glycoside **14**, although this is the undesired stereochemical outcome for the total synthesis.

In contrast, use of Cp_2HfCl_2–$AgClO_4$ gave an excellent yield and stereochemical outcome. Under the same reaction conditions as above (−78 → 0 °C), the reaction proceeded rapidly to afford the desired *C*-glycoside in 98% yield *as the sole isolable product*. *O*-Glycoside **13** was not detected at 0 °C. Furthermore, the anomeric stereochemistry was impressively reversed, with the desired β-anomer of **14** being obtained as the only product.

This marked β-selectivity deserves some comments. Since the anomeric effect does not play a major role for *C*-glycosides,[16] the β-anomer **14** is the more stable isomer. Relevant model studies[5] suggested existence of an anomerization process that converts an initially formed α/β mixture to the more stable β-anomer (cf. Scheme I). Actually, such anomerization was observed by the treatment of **14**-α with Cp_2HfCl_2–$AgClO_4$.[17] Moreover, low-temperature quenching showed that the *C*-glycoside **14** is rich in the β-anomer already in the early stage of the reaction with Cp_2HfCl_2–$AgClO_4$,[18] whereas BF_3·OEt_2 showed a preference for the α-anomer.

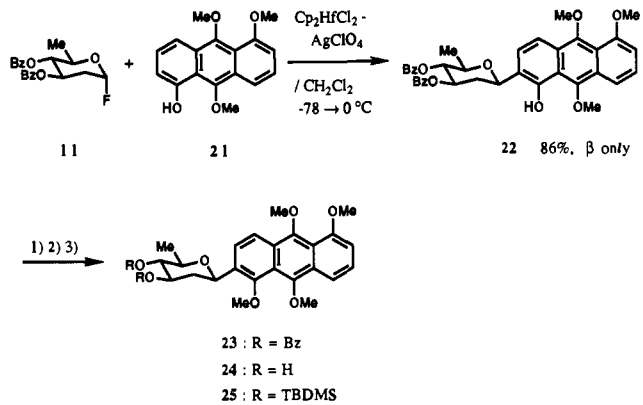
We next turned attention to the aromatic portion of the molecule. Preliminary attempts to effect aryl *C*-glycoside formation with anthrarufin itself were fruitless due to the electron deficiency of the aromatic system. Strong hydrogen bonding of the phenol to the quinone carbonyl seemed to inhibit even the initial O-glycosidation. These considerations led us to seek "an anthrarufin equivalent" that is electron rich and has an "unarrested OH" for performing the *O*→*C*-glycoside rearrangement reaction. The anthracene derivative **21** seemed ideally suited for such a purpose, and was readily prepared by the reductive dimethylation protocol (Scheme IV).

Scheme IV[a]



[a] Key: 1, MOMCl, $(i\text{-Pr})_2NEt/CH_2Cl_2$, room temperature; 2, H_2, 10% Pd–C/DMF, room temperature and then NaH, Me_2SO_4; 3, EtSH, BF_3·OEt_2/CH_2Cl_2, −78 → −20 °C.

Scheme V[a]



[a] Key: 1, NaH, Me_2SO_4/THF, room temperature, 2 h, quantitative; 2, NaOH/MeOH–H_2O, room temperature, overnight, 96%; 3, TBDMSOTf, 2,6-lutidine/CH_2Cl_2, room temperature, 2 h, 96%.

Anthraquinone **17** was hydrogenated in DMF in the presence of 10% Pd/C for 15 min. To this reaction mixture were directly added NaH and Me_2SO_4 to give anthracene derivative **19** in 99% yield.[19] Similarly, the known phenol **16**, derived from anthrarufin in two steps,[20] was protected as the methoxymethyl ether, which was then reductively dimethylated to afford **20**. These MOM ethers (**19** and **20**) were utilized in the model study on the side chain synthesis as discussed later. Treatment of **20** with BF_3·OEt_2 and ethanethiol led to the clean and selective deprotection of the MOM group to afford anthrol derivative **21** in 92% yield.

With anthrol **21** in hand, synthesis of the *C*-glycoside sector of the target was carried out (Scheme V). Reaction of anthrol **21** with fluoro sugar **11** was conducted at −78 °C in the presence of Cp_2HfCl_2–$AgClO_4$, followed by gradual warming of the mixture to 0 °C, to afford the *C*-glycoside **22** in 86% yield. The O→O-rearrangement proceeded quite fast, and no *O*-glycoside was observed. The anomeric stereochemistry was solely β, and the aromatic substitution took place regioselectively at the C(2)-position. Thus, a regio- and stereocontrolled route to the *C*-glycoside sector of the target was established.[21]

(15) The reaction, stopped at this stage, afforded only the α-anomer **13** in 90% yield. Also see: Matsumoto, T.; Katsuki, M.; Suzuki, K. *Chem. Lett.* **1989**, 437.

(16) It is interesting to note that the **14**-α anomer prefers the flipped $^1C_4$(D) conformation as depicted, disposing the C(1)-aryl group in the equatorial position.

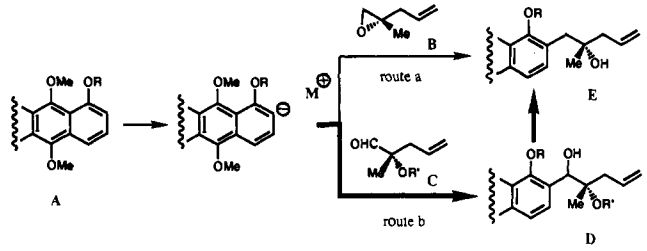
(17) Treatment of **14**-α with Cp_2HfCl_2–$AgClO_4$ (CH_2Cl_2, −78 → 0 °C) gave β-rich **14** (α/β = 1/2.2).

(18) The reaction, quenched at −50 °C, afforded mainly *O*-glycoside (71% yield, α/β = 27/1). A minor amount of *C*-glycoside, obtained in 28% yield, was already highly rich in β-anomer (α/β = 1/14).

(19) This experimental procedure is crucial for the high-yield reductive dimethylation, since the reduced products, hydroquinones, are highly oxygen sensitive. See ref 3a. We thank Dr. S. Terashima (Sagami Central Research Institute) and Dr. F. Matsuda (Hokkaido University) for their kind suggestion on this procedure and encouragement.

(20) Preston, P. N.; Winwick, T.; Morley, J. O. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1439.

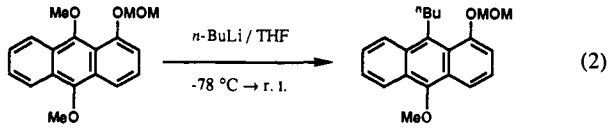
Scheme VI



For further elaboration, the phenolic hydroxyl group of **22** was protected as a methyl ether by treatment with NaH followed by Me_2SO_4 in THF (30 °C, 2 h) to give tetramethyl ether **23** in quantitative yield. The two benzoyl groups were deprotected under basic conditions to give diol **24** in 96% yield. Both of the liberated 3′- and 4′-hydroxyl groups in **24** were then silylated with *tert*-butyldimethylsilyl triflate and 2,6-lutidine in CH_2Cl_2 to give anthracene **25** as an amorphous solid. This compound served as the key intermediate in the total synthesis for introduction of the side chain portion.

Side Chain Synthesis (Model Study). In designing a route for the side chain synthesis, our original plan was to use the ortho metalation[22] of anthracene derivatives A followed by ring opening of chiral epoxide B as shown in route a (Scheme VI). However, preliminary experiments showed that the epoxide is extremely resistant to ring opening due to the high steric hindrance around the electrophilic center. Alternatively, an indirect route (b, Scheme VI) was examined: coupling with aldehyde C followed by benzylic deoxygenation. The synthetic intermediate D would also provide opportunities for synthesis of oxidized congeners of vineomycin antibiotics of clinical interest. In the following, the model study to substantiate this strategy will be described.[23]

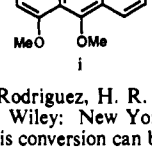
In order to check the feasibility of the ortho metalation, lithiation of a model substrate (**19**) was examined. This proved not to be an easy task due to the unexpectedly facile attack of the alkyl anion at C(9) and/or C(10) of the anthracene ring. For example, reaction of **19** with *n*-BuLi (−78 °C to room temperature; eq 2) led to complete decomposition of the starting material and



(2)

to formation of the product **26**, resulting from the nucleophilic substitution of *n*-butyl anion at the C(9)-position (49% yield).[24]

(21) In sharp contrast, attempted *C*-glycoside formation with the fully protected anthracene i gave a mixture of regioisomeric products in low yield.

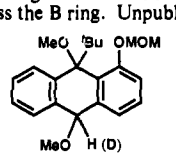


i

(22) Gschwend, H. W.; Rodriguez, H. R. In *Organic Reactions* (*New York*); Dauben, W. G., Ed.; Wiley: New York, 1979; Vol. 26, pp 1–360.

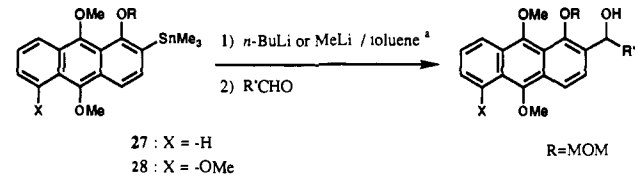
(23) In a formal sense, this conversion can be carried out in a single step by the use of the Marshalk reaction (Marshalk, C.; Koenig, F.; Ouroussoff, N. *Bull. Soc. Chim. Fr.* **1936**, *3*, 1545). 1-Hydroxy-9,10-anthraquinone (rather than the 1,4-dihydroxy derivative) is a poor substrate for this reaction: Krohn, K. *Tetrahedron* **1990**, *46*, 291. See also ref 10c.

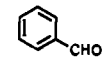
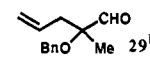
(24) Reaction of **19** with *t*-BuLi gave the addition product ii rather than the substitution product. D_2O quenching gave ii fully deuterated at the C(10)-position, clearly suggesting that the side reaction proceeds via 1,4-addition–(1,4-elimination) across the B ring. Unpublished results of H. Kakigi.



ii

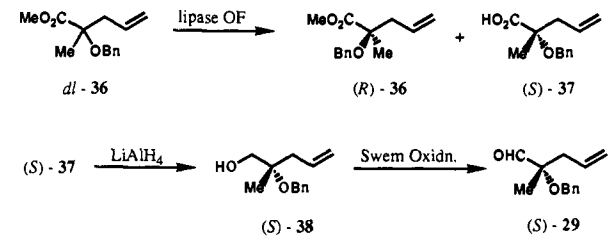
Table II. Coupling of Arylstannanes **27** and **28**



run	R′CHO	X	product	yield (%)
1		-H	**30**	97
2		-OMe	**31**	97
3	n-$C_9H_{19}CHO$	-H	**32**	89
4		-OMe	**33**	79
5		-H	**34**	88
6		-OMe	**35**	77

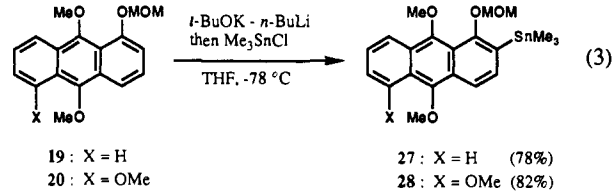
[a] *n*-BuLi was used for **27**; MeLi was used for **28** (see text). [b] *dl* form was used.

Scheme VII



Changing the alkyllithium species, solvent, and/or cosolvent did not solve the problem and C(9)/C(10) attack was uniformly the major pathway.[25]

Fortunately, the Lochmann–Schlosser base[26] enabled us to carry out the desired ortho metalation at low temperature (eq 3). Treatment of **19** with *t*-BuOK–*n*-BuLi (2.0 equiv of each) in THF at −78 °C followed by quenching with D_2O led to clean recovery of **19** with >95% deuterium incorporation. Side products derived



from C(9)/C(10) attack were not detected. Direct reaction with the aldehyde partner seemed impractical since excess base is required to complete the metalation. Therefore, the metalation reaction was quenched with Me_3SnCl to afford arylstannane **27** in 78% yield. Similarly, arylstannane **28** was obtained in 82% yield.[27] It is worth noting that the metalation proceeds quickly at low temperature (−78 °C), which is of particular significance in the total synthesis as discussed later.

Upon successful completion of the above experiments, tin–lithium exchange[28] followed by aldehyde addition was attempted (Table II). Again, the standard procedure (*n*-BuLi/THF) was incompatible with these particular substrates (**27** and **28**), owing to the competing attack of the *n*-butyl anion at the C(9)- and/or C(10)-position. However, this side reaction can be nicely suppressed by *using toluene as the reaction medium*. Treatment of

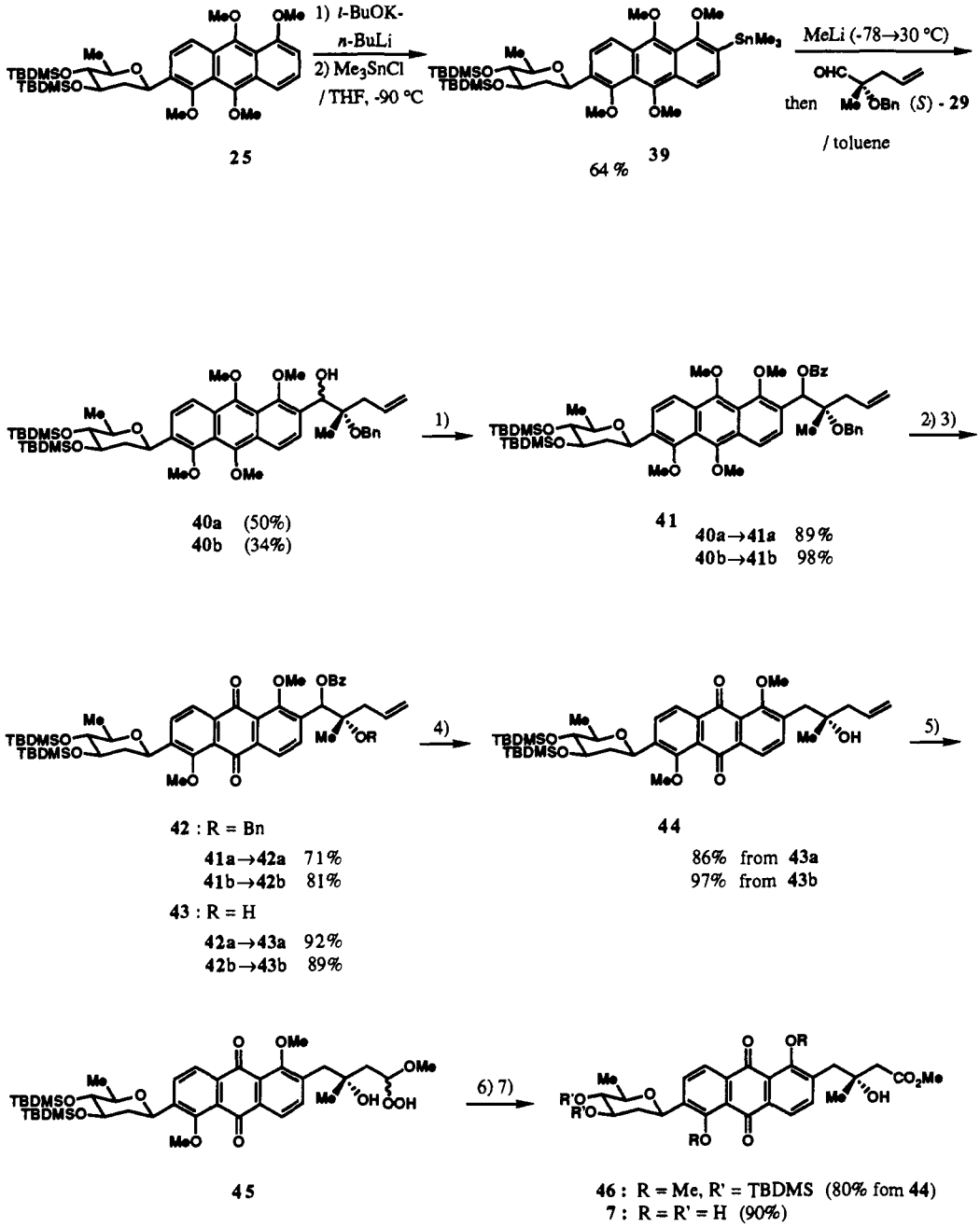
(25) Nucleophilic attack of benzyllithium on anthracene is known: Fox, M. A.; Ranade, A. C.; Madany, I. *J. Organomet. Chem.* **1982**, *239*, 269.

(26) Lochmann, L.; Pospíšil, J.; Lím, D. *Tetrahedron Lett.* **1966**, 257. Schlosser, M. *J. Organomet. Chem.* **1967**, *8*, 9. Schlosser, M. *Pure Appl. Chem.* **1988**, *60*, 1627.

(27) These arylstannanes were sensitive to acid including silica gel; therefore, the purification was carried out on basic-alumina chromatography.

(28) Pereyre, M.; Quintard, J.-P.; Rahm, A. *Tin in Organic Synthesis*; Butterworths: London, 1987; see also references cited therein.

Scheme VIII[a]



[a] Key: 1, benzoyl chloride, catalytic DMAP/pyridine, room temperature, overnight; 2, CAN/MeCN-H_2O, -17 °C, 15 min; 3, DDQ/CH_2Cl_2-pH 8.0 buffer, room temperature, 8 h; 4, $Na_2S_2O_4$, 1 N NaOH/1,4-dioxane-H_2O, room temperature, 45 min; 5, O_3/MeOH, -78 °C; 6, Ac_2O, Et_3N/CH_2Cl_2, 0 °C, 25 min; 7, BBr_3/CH_2Cl_2, -78 °C, 25 min.

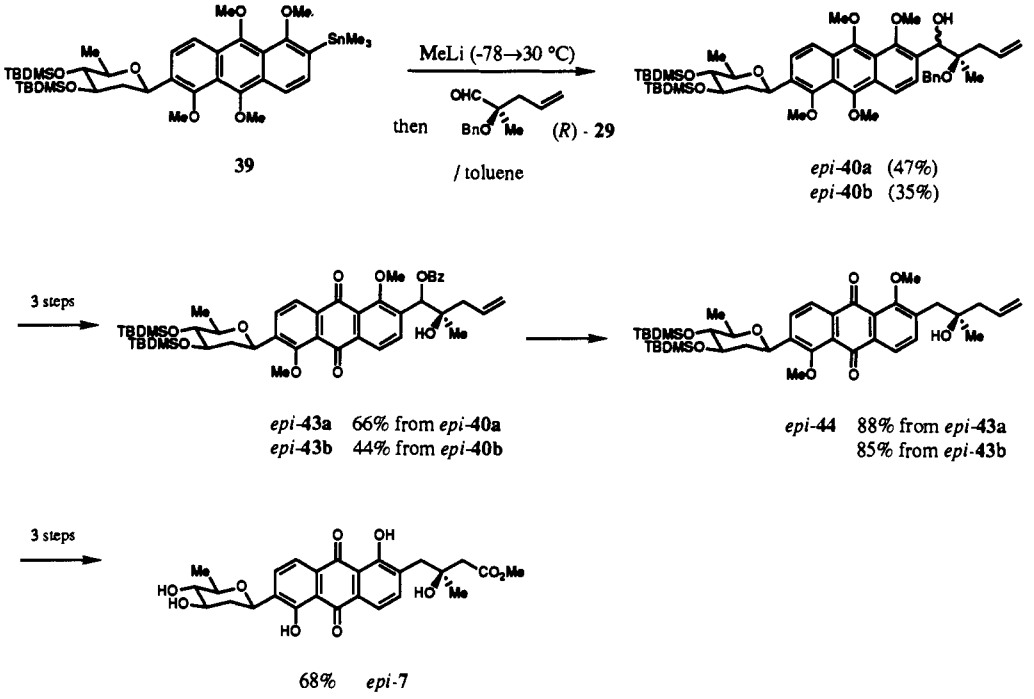
27 with *n*-BuLi (-78 → -15 °C) in toluene followed by the addition of aldehydes furnished the products **30**, **32**, and **34** in high yields. For the transmetalation of **28**, containing a 5-methoxy substituent, MeLi gave superior results to *n*-BuLi since the latter reagent competitively attacks the C(9)/C(10)-carbons even in toluene solution. Thus, *MeLi in toluene* (-78 → 0 °C) was shown to be the reagent of choice to effect lithiation of **28**, which produced the adducts **31**, **33**, and **35** after reactions with aldehydes. The results of the reaction with the aldehyde **29** (runs 5 and 6) gave us confidence in the validity of this strategy. With this reliable method for the C-C bond formation in hand, we proceeded to the final stage of the total synthesis.

Total Synthesis of Vineomycinone B_2 Methyl Ester. For preparation of the enantiomerically pure side chain, we decided to employ the chiral citramalic acid equivalent **37** (Scheme VII), available in both enantiomeric forms via the enzymatic asymmetric hydrolysis of *dl*-ester **36** as reported by Ohta et al.[29] The (*S*)-acid **37** (>99% ee) was reduced with $LiAlH_4$ to give alcohol **38**, and subsequent Swern oxidation afforded (*S*)-**29** in 96% yield after Kugelrohr distillation; bp 105-110 °C (2 mmHg, oven temperature), $[\alpha]^{25}_D$ -33° (*c* 0.97, $CHCl_3$). A similar reduction-oxidation sequence of the antipodal ester (*R*)-**36** (>99% ee) afforded the enantiomeric aldehyde (*R*)-**29**, $[\alpha]^{23}_D$ +34° (*c* 1.5, $CHCl_3$), which was employed in the synthesis of the C(12)-epimer of vineomycinone B_2 methyl ester.

Scheme VIII shows the synthetic route to vineomycinone B_2 methyl ester (**7**). Anthracene **25** was metalated with *t*-BuOK (5.0 equiv) and *n*-BuLi (5.0 equiv) in THF (-90 °C, 5 min) to generate the arylmetal species, which was quenched with excess Me_3SnCl to give stannane **39** in 64% yield after purification.[27] The success of this stannylation is notable on two counts: (1) the reaction

(29) Sugai, T.; Kakeya, H.; Ohta, H. *J. Org. Chem.* **1990**, *55*, 4643. See also: Sugai, T.; Kakeya, H.; Ohta, H. *Tetrahedron* **1990**, *46*, 3463.

Scheme IX



proceeded efficiently and regioselectively at the ortho position to the C(1)-methoxyl group, even though this is a relatively weak ortho metalation director, and (2) there was no indication of competing abstraction of the anomeric proton of the sugar moiety, even though it is located at the benzylic position. Stannane **39** was then lithiated with MeLi in toluene (−78 → +30 °C), and subsequent reaction with (*S*)-aldehyde **29** gave the adduct **40** as a 3/2 mixture of diastereomers in 84% yield. The diastereomers were easily separated by silica-gel chromatography to give the less polar isomer **40a** (R_f = 0.40, hexane/AcOEt = 85/15) and the more polar isomer **40b** (R_f = 0.33). The configuration of these diastereomers has not been assigned.[30]

The next task was selective deoxygenation of the benzylic hydroxyl group without affecting the pyranoside ring. This was carried out by converting the anthracene to the corresponding anthraquinone followed by treatment with $Na_2S_2O_4$ to generate the transient hydroquinone, which expels the benzylic oxygen functionality.[31,32] A model study showed that two precautions are necessary: (1) the benzylic C(11)-hydroxyl group should be converted to a better leaving group, such as a benzoyloxy,[33] since the parent alcohol undergoes reduction only slowly, and (2) the deoxygenation proceeds more readily if the adjacent tertiary hydroxyl group is liberated.[34]

Thus, adduct **40a** was benzoylated (BzCl/pyridine, 4-DMAP) to give benzoate **41a** in 89% yield, and this was treated with cerium(IV) ammonium nitrate in acetonitrile (−17 °C, 10 min) to give anthraquinone **42a** as a yellow solid in 71% yield. Treatment of **42a** with buffered (pH 8) DDQ in CH_2Cl_2 effected a clean detachment of the benzyl group to give **43a** in 92% yield. The same conversion of **40b** gave the isomeric anthraquinone **43b** (70% yield in three steps) ready for the deoxygenation reaction. Benzoate **43a** was then treated with 3.0 equiv of $Na_2S_2O_4$ in dioxane/H_2O solution under slightly basic conditions,[35] which effected a clean deoxygenation to give **44** in 86% yield. The isomer **43b** underwent the deoxygenation in a similar manner to afford **44** in 97% yield. It should be noted that *the pyranoside ring underwent no reductive cleavage under these conditions.* Although we carried out the synthesis for the separated isomers of **40a** and **40b**, the transformation of **40** to **44** can be conveniently carried out without separating the isomers.

The final stage of the synthesis is fission of the double bond and deprotection. Oxidative cleavage of the double bond was cleanly achieved via a two-step procedure.[36] Ozonolysis of **44** was carried out in MeOH at −78 °C to give a diasteromeric mixture of hydroperoxides **45**. Treatment of **45** with Ac_2O–Et_3N in CH_2Cl_2 at 0 °C afforded methyl ester **46** in 80% yield. Finally, methyl ester **46** was treated with BBr_3 in CH_2Cl_2 at −78 °C for 25 min to simultaneously remove the two methyl and two *tert*-butyldimethylsilyl protecting groups. Vineomycinone B_2 methyl ester (**7**) was obtained as an orange solid, which was recrystallized from chloroform and hexane to give a pure sample of **7** as orange needles. The melting point and the optical rotation were in accordance with those of the reported values: mp 186–187 °C ($CHCl_3$–hexane) [lit.[1a] mp 184–185 °C], $[\alpha]^{29}_D$ +118° (*c* 1.05, dioxane) [lit.[9] $[\alpha]^{21}_D$ +119° (*c* 0.83, dioxane)]. The synthetic material was fully identical with an authentic sample[37] by direct comparison (^{1}H NMR, IR, and TLC behavior in several different solvent systems).

Starting from the enantiomeric aldehyde, (*R*)-**29**, total synthesis of the C(12)-epimer of vineomycinone B_2 methyl ester (*epi*-**7**) was achieved (Scheme IX). The rates and yields of the reactions were similar to those in the "vineo" series. The final product *epi*-**7**, mp 193–194 °C ($CHCl_3$–hexane), $[\alpha]^{28}_D$ +111° (*c* 0.45, dioxane), showed a ^{1}H NMR spectrum in accordance with the data reported by Danishefsky et al.[10a,38] Careful comparison of intermediates

(30) For compounds **41**, **42**, and **43**, the suffix **a** or **b** designates that the compound is derived from **40a** or **40b**.

(31) This reaction corresponds to the last stage of the Marshalk reaction. See ref 23. It is known that the ester of 2-(hydroxymethyl)anthraquinone undergoes facile specific cleavage with $Na_2S_2O_4$, which was applied in a protecting group: Kemp, D. S.; Reczek, J. *Tetrahedron Lett.* **1977**, 1031.

(32) Related studies in the redox process of daunomycins were reported by Koch et al. and Fischer et al.: Bird, D. M.; Gaudiano, G.; Koch, T. H. *J. Am. Chem. Soc.* **1991**, *113*, 308 and references cited therein. Brand, D. J.; Fischer, J. F. *J. Org. Chem.* **1990**, *55*, 2518 and references cited therein.

(33) Acetate was less satisfactory than benzoate because it undergoes competing hydrolysis under the reaction conditions to give the less reactive parent alcohol.

(34) This may be due to anchimeric assistance by the hydroxyl group, which facilitates the departure of the benzoyloxy leaving group.

(35) Periodic addition of 1 N NaOH was performed in order to neutralize the acids formed (see Experimental Section).

(36) Schreiber, S. L.; Claus, R. E.; Reagan, J. *Tetrahedron Lett.* **1982**, *23*, 3867. Claus, R. E.; Schreiber, S. L. In *Organic Synthesis*; Kende, A. S., Ed.; Wiley: New York, 1985; Vol. 64, pp 150–156.

(37) Prepared by the degradation of aquayamycin (ref 1a), which was kindly provided by Dr. S. Kondo, Institute of Microbial Chemistry.

(38) As reported in ref 10a, the ^{1}H NMR spectrum of *epi*-**7** was similar to that of **7**, but clearly distinguishable at the C(11)-benzylic methylene protons. Interestingly, the ^{13}C NMR spectra of **7** and *epi*-**7** fully coincided for all 26 lines.

in the vineo and the epi series of synthetic sequences showed stereochemical homogeneity of the synthetic materials. Particularly, at the stage of anthraquinone **43**, all of the four diastereomers (**43a**, **43b**, *epi*-**43a**, and *epi*-**43b**) can be easily distinguished by silica-gel TLC,[39] which showed no cross contamination of the isomeric pairs.

Conclusions

Total syntheses of vineomycinone B_2 methyl ester and its C-(12)-epimer have been accomplished. This synthesis clearly shows the promising aspect of the *O*→*C*-glycoside rearrangement in the synthesis of aryl *C*-glycoside antibiotics. The synthetic methods developed in this study should allow the synthesis of many analogues and also more complex members of this class of antibiotics.

Experimental Section[40]

3,4-Di-*O*-benzoyl-2,6-dideoxy-α-D-arabinopyranosyl Fluoride (11). To a mixture of 68% HF–pyridine (1.5 mL) and CH_2Cl_2 (8 mL) was added a solution of glycosyl acetate **10** (471 mg, 1.18 mmol) in CH_2Cl_2 (5 mL) at −20 °C. After being stirred at that temperature for 20 min and then at 0 °C for 5 min, the mixture was poured into ice-cold water and extracted with $CHCl_3$ (3×). The combined organic layer was washed successively with saturated $NaHCO_3$ and brine and dried over Na_2SO_4. Removal of solvent followed by purification by flash chromatography (hexane/EtOAc = 93/7) afforded the fluoride **11** (419 mg, 98.8%) as a colorless oil: R_f = 0.51 (hexane/EtOAc = 8/2); ^{1}H NMR ($CDCl_3$) δ 7.91–8.00 (m, 4 H), 7.47–7.55 (m, 2 H), 7.34–7.42 (m, 4 H), 5.79 (ddd, 1 H, $J_{1\text{-}F}$ = 51.3, $J_{1\text{-}2ax}$ = 2.9, $J_{1\text{-}2eq}$ = 1.5 Hz), 5.64 (ddd, 1 H, J_1 = 11.7, J_2 = 9.8, J_3 = 5.9 Hz), 5.30 (dd, 1 H, J_1 = J_2 = 9.8 Hz), 4.30 (dq, 1 H, J_1 = 9.8, J_2 = 5.9 Hz), 2.73 (dddd, 1 H, J_1 = 13.6, J_2 = 1.5, J_3 = J_4 = 5.9 Hz), 2.00 (dddd, 1 H, J_1 = 38.6, J_2 = 13.6, J_3 = 11.7, J_4 = 2.9 Hz), 1.33 (d, 3 H, J = 5.9 Hz); IR (KBr) 2990, 1720, 1600, 1585, 1490, 1450, 1400, 1370, 1345, 1310, 1250, 1210, 1175, 1155, 1130, 1105, 1090, 1065, 1025, 965, 855, 765, 710 cm^{-1}; $[\alpha]^{29}_D$ −54° (*c* 2.2, $CHCl_3$); HRMS *m*/*z* 358.1188 (358.1215 calcd for $C_{20}H_{19}FO_5$, M^+).

Model Study for Aryl C-Glycosidation of Glycosyl Fluoride 11: General Procedure for *O*→*C*-Glycoside Rearrangement. To a stirred mixture of Cp_2HfCl_2 (56.9 mg, 150 μmol), $AgClO_4$ (31.1 mg, 150 μmol), 2-naphthol (**12**) (21.6 mg, 150 μmol), and powdered molecular sieves 4A (ca. 350 mg) in CH_2Cl_2 (0.5 mL) was added fluoride **11** (17.9 mg, 50.0 μmol) in CH_2Cl_2 (2 mL) at −78 °C. The temperature was gradually raised to 0 °C during 2 h, and the reaction was quenched with saturated $NaHCO_3$. The mixture was filtered through Celite and extracted with EtOAc (2×), and the combined organic layer was washed with brine and dried over Na_2SO_4. Removal of solvent in vacuo and purification by PTLC (CCl_4/Et_2O = 9/1) afforded the *C*-glycoside **14**-β (R_f = 0.41; 23.6 mg, 97.9%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 8.71 (s, 1 H), 8.00–8.03 (m, 2 H), 7.89–7.92 (m, 2 H), 7.69–7.78 (m, 3 H), 7.31–7.57 (m, 8 H), 7.14 (d, 1 H, J = 8.8 Hz), 5.73 (dd, 1 H, J_1 = 11.7, J_2 = 2.0 Hz), 5.65 (ddd, 1 H, J_1 = 11.7, J_2 = 9.3, J_3 = 4.9 Hz), 5.47 (dd, 1 H, J_1 = J_2 = 9.3 Hz), 4.06 (dq, 1 H, J_1 = 9.3, J_2 = 6.4 Hz), 2.74 (ddd, 1 H, J_1 = 13.2, J_2 = 4.9, J_3 = 2.0 Hz), 2.31 (ddd, 1 H, J_1 = 13.2, J_2 = J_3 = 11.7 Hz), 1.48 (d, 3 H, J = 6.4 Hz); IR (neat) 3360, 2980, 1720, 1620, 1600, 1520, 1465, 1450, 1410, 1275, 1120, 1025, 910, 820, 710 cm^{-1}; $[\alpha]^{28}_D$ −3.6° (*c* 1.2, $CHCl_3$); HRMS *m*/*z* 482.1705 (482.1727 calcd for $C_{30}H_{26}O_6$, M^+).

14-α: a colorless oil; R_f = 0.50 (CCl_4/Et_2O = 9/1); ^{1}H NMR ($CDCl_3$) δ 9.17 (s, 1 H), 8.14–8.22 (m, 4 H), 7.50–7.80 (m, 9 H), 7.37–7.42 (m, 1 H), 7.28–7.33 (m, 1 H), 7.18 (d, 1 H, J = 8.8 Hz), 6.20 (dd, 1 H, J_1 = 12.2, J_2 = 2.0 Hz), 5.54–5.57 (m, 1 H), 5.26–5.29 (m, 1 H), 4.66 (q, 1 H, J = 7.3 Hz), 2.71 (ddd, 1 H, J_1 = 15.6, J_2 = 12.2, J_3 = 2.9 Hz), 2.23–2.30 (m, 1 H), 1.81 (d, 3 H, J = 7.3 Hz); IR (neat) 3330, 2940, 1725, 1625, 1600, 1590, 1530, 1470, 1455, 1415, 1315, 1260, 1095, 955, 820, 715 cm^{-1}; $[\alpha]^{27}_D$ +44° (*c* 1.2, $CHCl_3$); HRMS *m*/*z* 482.1725 (482.1727 calcd for $C_{30}H_{26}O_6$, M^+).

1-(Methoxymethoxy)-5,9,10-trimethoxyanthracene (20). A suspension of quinone **18** (1.00 g, 3.36 mmol) and 10% Pd/C (100 mg) in DMF (25 mL) was stirred under H_2 (1 atm) at room temperature for 15 min. After the atmosphere was changed to argon, NaH (60% in oil, 81 mg, 20 mmol) was added in two portions at 0 °C and the mixture was stirred at room temperature for 15 min. Me_2SO_4 (1.91 mL, 20.1 mmol) was added dropwise to the mixture at 0 °C. After being stirred at room temperature for 20 min, the mixture was poured into ice-cold water. The mixture was filtered through Celite and extracted with Et_2O, and the organic layer was washed with water and brine and then dried (Na_2SO_4). The solvent was removed in vacuo, and the residue was purified by flash chromatography (hexane/EtOAc = 85/15) to afford the trimethyl ether **20** (1.08 g, 98.5%) as a yellow solid: mp 74–77 °C; R_f = 0.45 (hexane/EtOAc = 7/3); ^{1}H NMR ($CDCl_3$) δ 8.09 (dd, 1 H, J_1 = 8.8, J_2 = 1.0 Hz), 7.98 (dd, 1 H, J_1 = 8.8, J_2 = 1.0 Hz), 7.36 (dd, 1 H, J_1 = 8.8, J_2 = 7.3 Hz), 7.34 (dd, 1 H, J_1 = 8.8, J_2 = 7.3 Hz), 7.11 (dd, 1 H, J_1 = 7.3, J_2 = 1.0 Hz), 6.80 (dd, 1 H, J_1 = 7.3, J_2 = 1.0 Hz), 5.41 (s, 2 H), 4.07 (s 3 H), 4.01 (s, 3 H), 3.99 (s, 3 H), 3.64 (s, 3 H); IR (KBr) 2940, 1620, 1540, 1455, 1440, 1360, 1250, 1215, 1170, 1150, 1095, 1060, 1035, 980, 930, 780, 740, 700 cm^{-1}; HRMS *m*/*z* 329.1403 (329.1387 calcd for $C_{19}H_{21}O_5$, M^+ + 1). Anal. Calcd for $C_{19}H_{20}O_5$: C, 69.50; H, 6.14. Found: C, 69.72; H, 6.33.

In the same manner, **19** was obtained from **17** in 99.2% yield as bright yellow plates: mp 114–115 °C (hexane); R_f = 0.43 (hexane/EtOAc = 8/2); ^{1}H NMR ($CDCl_3$) δ 8.35–8.40 (m, 1 H), 8.23–8.28 (m, 1 H), 7.99 (dd, 1 H, J_1 = 8.8, J_2 = 1.0 Hz), 7.46–7.54 (m, 2 H), 7.36 (dd, 1 H, J_1 = 8.8, J_2 = 7.6 Hz), 7.08 (dd, 1 H, J_1 = 7.6, J_2 = 1.0 Hz), 5.42 (s, 2 H), 4.09 (s, 3 H), 4.05 (s, 3 H), 3.65 (s, 3 H); IR (KBr) 2950, 1615, 1560, 1530, 1450, 1360, 1250, 1230, 1150, 1090, 1070, 1025, 1010, 975, 785, 755 cm^{-1}. Anal. Calcd for $C_{18}H_{18}O_4$: C, 72.47; H, 6.08. Found: C, 72.44; H, 6.09.

1-Hydroxy-5,9,10-trimethoxyanthracene (21). To a solution of methoxymethyl ether **20** (683 mg, 2.08 mmol) and EtSH (3.10 mL, 41.9 mmol) in CH_2Cl_2 (25 mL) was added BF_3·OEt_2 (2.58 mL, 21.0 mmol) at −78 °C. The mixture was stirred for 20 min at −78 °C, then gradually warmed to −20 °C during 30 min, and then quenched with pH 7 phosphate buffer. The mixture was extracted with EtOAc (3×), and the combined organic layer was washed successively with saturated $NaHCO_3$ and brine and then dried (Na_2SO_4), filtered, and evaporated. Purification of the residue by flash chromatography (CCl_4/hexane/Et_2O = 5/4/1) afforded anthrol **21** (546 mg, 92.3%). Recrystallization from $CHCl_3$–ether gave **21** as yellow plates: mp 145 °C; R_f = 0.30 (hexane/CH_2Cl_2 = 7/3); ^{1}H NMR ($CDCl_3$) δ 9.79 (s, 1 H), 7.90 (dd, 1 H, J_1 = 8.8, J_2 = 0.9 Hz), 7.77 (dd, 1 H, J_1 = 8.8, J_2 = 0.9 Hz), 7.38 (dd, 1 H, J_1 = 8.8, J_2 = 7.3 Hz), 7.37 (dd, 1 H, J_1 = 8.8, J_2 = 7.3 Hz), 6.90 (dd, 1 H, J_1 = 7.3, J_2 = 0.9 Hz), 6.79 (dd, 1 H, J_1 = 7.3, J_2 = 0.9 Hz), 4.09 (s, 3 H), 4.08 (s, 3 H), 4.00 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 156.5, 153.1, 149.8, 147.1, 127.8, 126.4, 125.9, 125.6, 118.5, 116.7, 114.3, 113.9, 108.8, 103.8, 64.0, 63.3, 56.1; IR (KBr) 3320, 2920, 1615, 1535, 1450, 1420, 1355, 1220, 1110, 1080, 1040, 1020, 950, 780, 700 cm^{-1}; HRMS *m*/*z* 284.1055 (284.1048 calcd for $C_{17}H_{16}O_4$, M^+). Anal. Calcd for $C_{17}H_{16}O_4$: C, 71.82; H, 5.67. Found: C, 71.75; H, 5.82.

***C*-Glycoside 22.** To a stirred mixture of Cp_2HfCl_2 (76.0 mg, 200 μmol), $AgClO_4$ (41.5 mg, 200 μmol), anthrol **21** (57.0 mg, 200 μmol), and powdered molecular sieves 4A (ca. 500 mg) in CH_2Cl_2 (1 mL) was added the fluoride **11** (23.9 mg, 66.8 μmol) in CH_2Cl_2 (1.5 mL) at −78 °C. The temperature was gradually raised to 0 °C during 50 min, and the reaction was quenched with saturated $NaHCO_3$. The mixture was filtered through Celite and extracted with EtOAc (2×), and the combined organic layer was washed with brine, dried (Na_2SO_4), and filtered. The solvent was removed in vacuo, and the residue was purified by flash chromatography (hexane/EtOAc = 8/2) to afford the *C*-glycoside **22** (35.5 mg, 85.5%) as a yellow oil: R_f = 0.24 (hexane/EtOAc = 8/2); ^{1}H NMR ($CDCl_3$) δ 10.11 (s, 1 H), 7.92–8.04 (m, 5 H), 7.76 (d, 1 H, J = 8.8 Hz), 7.63 (d, 1 H, J = 8.8 Hz), 7.33–7.56 (m, 7 H), 6.78 (d, 1 H, J = 7.3 Hz), 5.62 (ddd, 1 H, J_1 = 11.2, J_2 = 9.8, J_3 = 5.4 Hz), 5.40 (dd, 1 H, J_1 = 11.7, J_2 = 2.0 Hz), 5.40 (dd, 1 H, J_1 = J_2 = 9.8 Hz), 4.08 (s, 3 H), 4.07 (s, 3 H), 3.95–4.03 (m, 1 H), 3.98 (s, 3 H), 2.73 (ddd, 1 H, J_1 = 12.7, J_2 = 5.4, J_3 = 2.0 Hz), 2.07 (ddd, 1 H, J_1 = 12.7, J_2 = 11.7, J_3 = 11.2 Hz), 1.41 (d, 3 H, J = 6.4 Hz); IR (KBr) 3340, 2950, 1725, 1620, 1600, 1535, 1450, 1360, 1280, 1255, 1120, 1060, 1030, 760, 710 cm^{-1}; $[\alpha]^{29}_D$ +35° (*c* 1.5, $CHCl_3$); HRMS *m*/*z* 623.2279 (623.2279 calcd for $C_{37}H_{35}O_9$, M^+ + 1). Anal. Calcd for $C_{37}H_{34}O_9$: C, 71.37; H, 5.50. Found: C, 71.34; H, 5.62.

Tetramethyl Ether 23. To a suspension of NaH (60% in oil, 242 mg, 6.05 mmol) in THF (3 mL) at 0 °C were added a THF (5 mL) solution

(39) $CHCl_3$/Et_2O = 95/5, R_f: **43a**, 0.35; **43b**, 0.47; *epi*-**43a**, 0.27; *epi*-**43b**, 0.53.

(40) Infrared (IR) spectra were recorded on a Jasco A-202 spectrometer. ^{1}H NMR spectra (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). Splitting patterns are indicated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad peak. Melting point determinations were performed by using a Yanaco MP-S3 instrument and are uncorrected. Mass spectra (MS) were obtained with a Hitachi M-80 spectrometer. All experiments dealing with air- and moisture-sensitive compounds were carried out under an atmosphere of dry argon. For thin-layer chromatography (TLC) analysis, Merck precoated plates (silica gel 60 GF_{254}, 0.25 mm) were used. Silica gel 60 K070-WH (70–230 mesh) of Katayama Chemical Co. was used for flash column chromatography. Preparative TLC was performed on Merck Kieselgel 60 PF_{254} (Art 7747). For preparative TLC on Al_2O_3, Merck Aluminiumoxid 60 PF_{254} (Typ E) was used. Ethereal solvents were distilled from benzophenone ketyl immediately before use. Methylene chloride was distilled successively from P_2O_5 and CaH_2 and stored over molecular sieves 4A.

of *C*-glycoside **22** (188 mg, 0.302 mmol) and then Me_2SO_4 (0.372 mL, 3.93 mmol). The mixture was stirred for 2 h at room temperature and quenched by adding Et_2NH (1.5 mL) and then pH 7 phosphate buffer at 0 °C. The resulting mixture was extracted with Et_2O (2×), and the combined organic layers were washed with 1 N HCl, saturated $NaHCO_3$, and brine and then dried (Na_2SO_4), filtered and evaporated. Flash chromatography of the residue (hexane/EtOAc = 85/15) afforded the tetramethyl ether **23** (192 mg, quantitative) as a yellow oil: R_f = 0.50 (hexane/EtOAc = 7/3); ^{1}H NMR ($CDCl_3$) δ 8.25 (d, 1 H, J = 9.3 Hz), 8.01–8.04 (m, 2 H), 8.00 (d, 1 H, J = 8.8 Hz), 7.94–7.97 (m, 2 H), 7.62 (d, 1 H, J = 9.3 Hz), 7.33–7.56 (m, 7 H), 6.81 (d, 1 H, J = 7.3 Hz), 5.64 (ddd, 1 H, J_1 = 11.2, J_2 = 9.8, J_3 = 5.4 Hz), 5.42 (dd, 1 H, J_1 = J_2 = 9.8 Hz), 5.41 (dd, 1 H, J_1 = 11.2, J_2 = 1.5 Hz), 4.07 (s, 3 H), 3.98–4.06 (m, 1 H), 3.983 (s, 3 H), 3.978 (s, 3 H), 3.97 (s, 3 H), 2.64 (ddd, 1 H, J_1 = 12.2, J_2 = 5.4, J_3 = 1.5 Hz), 2.19 (ddd, 1 H, J_1 = J_2 = 11.2, J_3 = 12.2 Hz), 1.41 (d, 3 H, J = 6.4 Hz); ^{13}C NMR ($CDCl_3$) δ 166.02, 165.99, 156.2, 151.6, 149.1, 147.5, 133.2, 133.1, 129.74, 129.71, 129.65, 129.62, 129.4, 128.7, 128.4, 128.3, 128.1, 125.4, 123.1, 120.3, 119.7, 118.5, 115.3, 104.1, 75.0, 74.8, 73.3, 71.6, 63.42, 63.36, 63.2, 56.1, 38.2, 18.3; IR (KBr) 2940, 1730, 1620, 1530, 1450, 1365, 1280, 1260, 1120, 1070, 1045, 860, 755, 715 cm^{-1}; $[\alpha]^{27}_D$ **+26°** (*c* 0.93, $CHCl_3$); HRMS *m/z* 636.2323 (636.2356 calcd for $C_{38}H_{36}O_9$, M^+).

Diol 24. To a solution of benzoate **23** (124 mg, 0.195 mmol) in MeOH (12 mL) was added 3 N aqueous NaOH (2 mL), and the mixture was stirred overnight at room temperature. The reaction was terminated with pH 7 phosphate buffer, and benzene was added. After removal of solvent in vacuo, the resulting mixture was extracted with Et_2O (3×), and the combined organic layers were washed with brine and then dried (Na_2SO_4), filtered, and concentrated in vacuo. Purification of the residue by flash chromatography (hexane/EtOAc = 2/8) afforded diol **24** (80.3 mg, 96.2%) as a yellow oil: R_f = 0.35 (hexane/EtOAc = 1/9); ^{1}H NMR ($CDCl_3$) δ 8.21 (d, 1 H, J = 8.8 Hz), 7.98 (d, 1 H, J = 8.8 Hz), 7.55 (d, 1 H, J = 8.8 Hz), 7.37 (dd, 1 H, J_1 = 7.3, J_2 = 8.8 Hz), 6.80 (d, 1 H, J = 7.3 Hz), 5.18 (dd, 1 H, J_1 = 11.2, J_2 = 1.5 Hz), 4.07 (s, 3 H), 3.97 (s, 3 H), 3.95 (s, 3 H), 3.90 (s, 3 H), 3.87–3.94 (m, 1 H), 3.58 (dq, 1 H, J_1 = 8.8, J_2 = 6.4 Hz), 3.28 (dd, 1 H, J_1 = J_2 = 8.8 Hz), 2.7–3.1 (br, 2 H), 2.27 (ddd, 1 H, J_1 = 12.7, J_2 = 4.9, J_3 = 1.5 Hz), 1.91 (ddd, 1 H, J_1 = J_2 = 11.2, J_3 = 12.7 Hz), 1.41 (d, 3 H, J = 6.4 Hz); ^{13}C NMR ($CDCl_3$) δ 156.1, 151.4, 149.0, 147.4, 130.1, 128.6, 128.1, 125.4, 123.4, 120.2, 119.8, 118.4, 115.3, 104.1, 78.2, 76.0, 73.5, 71.6, 63.4, 63.3, 63.1, 56.1, 40.5, 18.3; IR (neat) 3440, 2950, 1625, 1565, 1530, 1450, 1370, 1260, 1070, 760 cm^{-1}; $[\alpha]^{28}_D$ +24° (*c* 1.2, $CHCl_3$); HRMS *m/z* 428.1850 (428.1833 calcd for $C_{24}H_{28}O_7$, M^+).

Bis(silyl ether) 25. To a solution of diol **24** (72.4 mg, 0.169 mmol) and 2,6-lutidine (145 mg, 1.35 mmol) in CH_2Cl_2 (8 mL) was added TBDMSOTf (0.136 mL, 0.677 mmol), and the mixture was stirred for 2 h at room temperature. Phosphate buffer (pH 7) was added, and the mixture was extracted with EtOAc. The organic layer was washed successively with 1 N HCl, saturated $NaHCO_3$, and brine, and then dried (Na_2SO_4) and filtered. Removal of the solvent in vacuo and purification of the residue by flash chromatography (hexane/EtOAc = 95/5) afforded bis(silyl ether) **25** (107 mg, 96.4%) as a foam: R_f = 0.57 (hexane/EtOAc = 8/2); ^{1}H NMR ($CDCl_3$) δ 8.21 (d, 1 H, J = 9.3 Hz), 7.99 (d, 1 H, J = 8.8 Hz), 7.57 (d, 1 H, J = 9.3 Hz), 7.37 (dd, 1 H, J_1 = 7.3, J_2 = 8.8 Hz), 6.80 (d, 1 H, J = 7.3 Hz), 5.14 (dd, 1 H, J_1 = 11.7, J_2 = 2.0 Hz), 4.07 (s, 3 H), 3.98 (s, 3 H), 3.96 (s, 3 H), 3.89 (s, 3 H), 3.87–3.95 (m, 1 H), 3.52 (dq, 1 H, J_1 = 8.8, J_2 = 6.4 Hz), 3.31 (dd, 1 H, J_1 = J_2 = 8.8 Hz), 2.21 (ddd, 1 H, J_1 = 12.7, J_2 = 4.4, J_3 = 2.0 Hz), 1.87 (ddd, 1 H, J_1 = J_2 = 11.7, J_3 = 12.7 Hz), 1.34 (d, 3 H, J = 6.4 Hz), 0.94 (s, 9 H), 0.91 (s, 9 H), 0.17 (s, 3 H), 0.15 (s, 3 H), 0.13 (s, 3 H), 0.11 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 156.2, 151.3, 149.1, 147.4, 130.7, 128.6, 128.1, 125.3, 123.5, 120.1, 119.9, 118.4, 115.3, 104.0, 78.5, 77.4, 75.0, 71.3, 63.4, 63.3, 62.9, 56.1, 42.5, 26.4, 26.2, 19.3, 18.4, 18.2, −2.5, −2.9, −3.8, −4.1; IR (neat) 2940, 1620, 1560, 1530, 1460, 1365, 1255, 1110, 1070, 1050, 1000, 835, 780 cm^{-1}; $[\alpha]^{26}_D$ +34° (*c* 1.2, $CHCl_3$); HRMS *m/z* 657.3619 (657.3639 calcd for $C_{36}H_{57}O_7Si_2$, $M^+ + 1$). Anal. Calcd for $C_{36}H_{56}O_7Si_2$: C, 65.81; H, 8.59. Found: C, 65.88; H, 8.36.

Arylstannane 27. To a suspension of *t*-BuOK (83 mg, 0.74 mmol) in THF (10 mL) was added dropwise *n*-BuLi (1.45 M in hexane, 0.51 mL, 0.74 mmol) at −78 °C, and the mixture was stirred for 10 min. A solution of anthracene **19** (110 mg, 0.369 mmol) in THF (2.5 mL) was then added. After 15 min, a solution of Me_3SnCl (440 mg, 2.21 mmol) in THF (1 mL) was added in one portion. The mixture was stirred for 10 min and quenched with pH 7 phosphate buffer. The resulting mixture was extracted with Et_2O, washed with water, dried (Na_2SO_4), and filtered. The solvent was removed in vacuo, and the product was purified by PTLC (basic Al_2O_3, hexane/Et_2O = 95/5) to afford stannane **27** (132 mg, 77.8%) as a yellow oil: R_f = 0.61 (hexane/EtOAc = 85/15); ^{1}H NMR ($CDCl_3$) δ 8.36–8.41 (m, 1 H), 8.23–8.28 (m, 1 H), 8.10 [1 H, d, J = 8.6 Hz (J^{117}_{Sn-H}, $J^{119}_{Sn-H} \approx 9$ Hz)], 7.48 [1 H, d, J = 8.6 Hz (J^{117}_{Sn-H}, J^{119}_{Sn-H} = 39.2, 39.7 Hz)], 7.47–7.55 (m, 2 H), 5.13 (s, 2 H), 4.10 (s, 3 H), 3.98 (s, 3 H), 3.52 (s, 3 H), 0.43 [9 H, s (J^{117}_{Sn-H} = 53.7, J^{119}_{Sn-H} = 56.2 Hz)]; IR (neat) 2940, 1620, 1595, 1555, 1515, 1450, 1440, 1360, 1320, 1170, 1085, 1030, 1010, 970, 930, 770 cm^{-1}; HRMS *m/z* 460.0867 (460.0846 calcd for $C_{21}H_{26}O_4Sn$, M^+).

In the same manner, **28** was obtained from **20** in 82.4% yield as a yellow oil: R_f = 0.58 (hexane/EtOAc = 8/2); ^{1}H NMR ($CDCl_3$) δ 8.19 [1 H, d, J = 8.6 Hz (J^{117}_{Sn-H}, $J^{119}_{Sn-H} \approx 9$ Hz)], 7.99 (dd, 1 H, J_1 = 8.8, J_2 = 1.0 Hz), 7.47 [1 H, d, J = 8.6 Hz (J^{117}_{Sn-H} = J^{119}_{Sn-H} = 39.0 Hz)], 7.37 (dd, 1 H, J_1 = 8.8, J_2 = 7.6 Hz), 6.80 (d, 1 H, J = 7.6 Hz), 5.11 (s, 2 H), 4.07 (s, 3 H), 3.99 (s, 3 H), 3.95 (s, 3 H), 3.51 (s, 3 H), 0.42 [9 H, s (J^{117}_{Sn-H} = 53.7, J^{119}_{Sn-H} = 56.2 Hz)] IR (neat) 2940, 1620, 1595, 1555, 1515, 1450, 1360, 1310, 1260, 1155, 1070, 1025, 985, 970, 935, 805, 780, 760, 710 cm^{-1}; HRMS *m/z* 490.0949 (490.0950 calcd for $C_{22}H_{28}O_5Sn$, M^+).

32: General Procedure for the Coupling Reaction Using Stannane 27. To a solution of the stannane **27** (103 mg, 0.223 mmol) in toluene (3 mL) was added *n*-BuLi (1.53 M in hexane, 0.292 mL, 0.446 mmol) at −78 °C, and the mixture was warmed to −15 °C during 30 min. Decanal (139 mg, 0.892 mmol) in toluene (1.5 mL) was added, and after 10 min, the reaction was quenched with pH 7 phosphate buffer. The mixture was extracted with Et_2O (3×), washed with brine, dried (Na_2SO_4), and filtered. The solvent was removed in vacuo, and the residue was purified by PTLC (hexane/Et_2O = 1/1) to afford **32** 90.5 mg, 89.3%) as a yellow crystalline solid: mp 81–82 °C; R_f = 0.39 (hexane/Et_2O = 1/1); ^{1}H NMR ($CDCl_3$) δ 8.32–8.37 (m, 1 H), 8.23–8.28 (m, 1 H), 8.13 (d, 1 H, J = 8.8 Hz), 7.55 (d, 1 H, J = 8.8 Hz), 7.48–7.54 (m, 2 H), 5.39 (t, 1 H, J = 6.8 Hz), 5.21 (d, 1 H, J = 6.8 Hz), 5.09 (d, 1 H, J = 6.8 Hz), 4.09 (s, 3 H), 3.97 (s, 3 H), 3.63 (s, 3 H), 3.0–3.1 (br, 1 H), 2.00–2.10 (m, 1 H), 1.82–1.92 (m, 1 H), 1.49–1.61 (m, 1 H), 1.20–1.47 (m, 13 H), 0.86 (t, 3 H, J = 6.8 Hz); IR (KBr) 3450, 2940, 1620, 1555, 1520, 1450, 1365, 1330, 1155, 1090, 1070, 1030, 970, 935, 825, 770, 700 cm^{-1}; HRMS *m/z* 454.2726 (454.2717 calcd for $C_{28}H_{38}O_5$, M^+). Anal. Calcd for $C_{28}H_{38}O_5$: C, 73.98; H, 8.43. Found: C, 74.08; H, 8.32.

Aldehyde 29. To a solution of oxalyl chloride (550 mg, 4.33 mmol) in CH_2Cl_2 (3 mL) was added a solution of DMSO (675 mg, 8.66 mmol) in CH_2Cl_2 (1 mL) at −78 °C. After 10 min, a solution of the alcohol **38**[29] (223 mg, 1.08 mmol) in CH_2Cl_2 (4 mL) was added, and the mixture was stirred for another 10 min. A solution of Et_3N (1.09 g, 10.8 mmol) in CH_2Cl_2 (4 mL) was added, and the mixture was allowed to warm to 0 °C during 30 min. The reaction was quenched with pH 7 phosphate buffer, and the products were extracted with Et_2O (2×). The combined organic layer was washed successively with water and brine and then dried (Na_2SO_4) and filtered. Removal of solvent, and flash chromatography of the residue (hexane/EtOAc = 95/5), followed by bulb-to-bulb distillation afforded aldehyde **29** (211 mg, 95.7%) as a colorless oil: bp 105–110 °C (2 mmHg, oven temperature); R_f = 0.25 (hexane/EtOAc = 95/5); ^{1}H NMR ($CDCl_3$) δ 9.66 (s, 1 H), 7.27–7.39 (m, 5 H), 5.77–5.88 (m, 1 H), 5.11–5.18 (m, 2 H), 4.52 (d, 1 H, J = 11.0 Hz), 4.48 (d, 1 H, J = 11.0 Hz), 2.55 (dddd, 1 H, J_1 = 14.7, J_2 = 7.3, J_3 = J_4 = 1.0 Hz), 2.45 (dddd, 1 H, J_1 = 14.7, J_2 = 7.3, J_3 = J_4 = 1.0 Hz), 1.34 (s, 3 H); IR (neat) 2940, 1735, 1640, 1500, 1450, 1385, 1210, 1160, 1120, 1085, 1065, 1025, 1000, 920, 740, 700 cm^{-1}; HRMS *m/z* 175.1107 (175.1122 calcd for $C_{12}H_{15}O_1$, M^+ − CHO). *S* form: $[\alpha]^{25}_D$ −33° (*c* 0.97, $CHCl_3$). *R* form: $[\alpha]^{23}_D$ +34° (*c* 1.5, $CHCl_3$).

Stannane 39. To a suspension of *t*-BuOK (54.0 mg, 0.482 mmol) and anthracene **25** (63.3 mg, 0.0965 mmol) in THF (10 mL) was added dropwise *n*-BuLi (1.51 M in hexane, 0.319 mL, 0.482 mmol) at −90 °C. After 5 min, a solution of Me_3SnCl (386 mg, 1.93 mmol) in THF (1 mL) was added to the reaction in one portion. The mixture was stirred for 10 min, and quenched with pH 7 phosphate buffer. The mixture was extracted with Et_2O (2×), wash with water, and then dried (Na_2SO_4) and filtered. Removal of solvent in vacuo and purification of the product by PTLC (basic Al_2O_3, hexane/Et_2O = 94/6) afforded stannane **39** (50.6 mg, 64.0%) as a yellow glass: R_f = 0.29 (hexane/Et_2O = 95/5); ^{1}H NMR ($CDCl_3$) δ 8.23 (d, 1 H), J = 9.3 Hz), 8.17 [1 H, d, J = 8.6 Hz (J^{117}_{Sn-H}, $J^{119}_{Sn-H} \approx 9$ Hz)], 7.59 (d, 1 H, J = 9.3 Hz), 7.48 [1 H, d, J = 8.6 Hz (J^{117}_{Sn-H} = J^{118}_{Sn-H} = 40.3 Hz)], 5.15 (dd, 1 H, J_1 = 11.5, J_2 = 1.7 Hz), 3.97 (s, 3 H), 3.95 (s, 3 H), 3.89 (s, 3 H), 3.87 (s, 3 H), 3.87–3.95 (m, 1 H), 3.52 (dq, 1 H, J_1 = 8.6, J_2 = 6.3 Hz), 3.31 (dd, 1 H, J_1 = J_2 = 8.6 Hz), 2.20 (ddd, 1 H, J_1 = 12.9, J_2 = 4.6, J_3 = 1.7 Hz), 1.86 (ddd, 1 H, J_1 = J_2 = 11.5, J_3 = 12.9 Hz), 1.34 (d, 3 H, J = 6.3 Hz), 0.94 (s, 9 H), 0.90 (s, 9 H), 0.40 [9 H, s (J^{117}_{Sn-H} = 53.5, J^{119}_{Sn-H} = 55.9 Hz)], 0.17 (s, 3 H), 0.16 (s, 3 H), 0.12 (s, 3 H), 0.11 (s, 3 H); IR (neat) 2940, 1620, 1590, 1510, 1460, 1350, 1250, 1110, 1050, 830, 775 cm^{-1}; $[\alpha]^{26}_D$ +29° (*c* 1.3, $CHCl_3$).

Coupling of Stannane 39 and Aldehyde (*S*)-29. To a solution of stannane **39** (76.4 mg, 0.0933 mmol) in toluene (4 mL) was added MeLi (1.09 M in Et_2O, 0.428 mL, 0.467 mmol) at −78 °C. The mixture was gradually warmed to 30 °C during 30 min and stirred for 1 h. A solution

of optically pure aldehyde (*S*)-**29** (133 mg, 0.652 mmol) in toluene (1.5 mL) was added, and the reaction was quenched with pH 7 phosphate buffer after 5 min. The resulting mixture was extracted with EtOAc (3×), washed with brine, and then dried (Na_2SO_4) and filtered. Removal of solvent in vacuo and purification of the residue by PTLC (hexane/EtOAc = 85/15) afforded two diastereomers (the less polar isomer **40a**, R_f = 0.40, 40.2 mg, 50.1%; the more polar isomer **40b**, R_f = 0.33, 27.0 mg, 33.6%) as pale yellow oils.

40a: ^{1}H NMR ($CDCl_3$) δ 8.23 (d, 1 H, J = 9.3 Hz), 8.16 (d, 1 H, J = 9.3 Hz), 7.73 (d, 1 H, J = 9.3 Hz), 7.61 (d, 1 H, J = 9.3 Hz), 7.36–7.44 (m, 4 H), 7.29–7.34 (m, 1 H), 6.00 (dddd, 1 H, J_1 = 17.1, J_2 = 10.3, J_3 = 7.3, J_4 = 6.8 Hz), 5.49 (d, 1 H, J = 2.4 Hz), 5.16 (dd, 1 H, J_1 = 11.7, J_2 = 1.5 Hz), 5.04 (dd, 1 H, J_1 = 10.3, J_2 = 1.5 Hz), 5.01 (dd, 1 H, J_1 = 17.1, J_2 = 1.5 Hz), 4.69 (d, 1 H, J = 9.3 Hz), 4.67 (d, 1 H, J = 9.3 Hz), 3.98 (s, 3 H), 3.91 (s, 3 H), 3.90 (s, 3 H), 3.87 (s, 3 H), 3.84–3.97 (m, 1 H), 3.53 (dq, 1 H, J_1 = 8.8, J_2 = 6.4 Hz), 3.32 (dd, 1 H, J_1 = J_2 = 8.8 Hz), 3.19 (d, 1 H, J = 2.4 Hz), 2.69 (dd, 1 H, J_1 = 14.2, J_2 = 6.8 Hz), 2.19 (ddd, 1 H, J_1 = 12.7, J_2 = 4.4, J_3 = 1.5 Hz), 2.13 (dd, 1 H, J_1 = 14.2, J_2 = 7.3 Hz), 1.84 (ddd, 1 H, J_1 = 12.7, J_2 = J_3 = 11.7 Hz), 1.41 (s, 3 H), 1.36 (d, 3 H, J = 6.4 Hz), 0.95 (s, 9 H), 0.90 (s, 9 H), 0.17 (s, 3 H), 0.16 (s, 3 H), 0.12 (s, 3 H), 0.10 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 152.6, 151.4, 148.0, 147.9, 139.1, 134.4, 130.7, 128.9, 128.45, 128.38, 128.3, 127.5, 127.4, 125.7, 123.9, 119.84, 119.78, 119.2, 118.7, 117.6, 81.3, 78.5, 77.4, 75.0, 71.5, 71.3, 64.5, 63.47, 63.46, 62.9, 62.4, 42.8, 39.4, 26.3, 26.2, 19.4, 19.3, 18.4, 18.2, –2.6, –2.9, –3.8, –4.1; IR (neat) 3570, 2940, 1640, 1620, 1525, 1450, 1385, 1360, 1250, 1110, 1055, 995, 835, 760 cm^{-1}; $[\alpha]^{27}_D$ +28° (*c* 1.6, $CHCl_3$); HRMS *m/z* 860.4712 (860.4711 calcd for $C_{49}H_{72}O_9Si_2$, M^+). Anal. Calcd for $C_{49}H_{72}O_9Si_2$: C, 68.33; H, 8.43. Found: C, 68.27; H, 8.08.

40b: ^{1}H NMR ($CDCl_3$) δ 8.21 (d, 1 H, J = 9.3 Hz), 8.15 (d, 1 H, J = 9.3 Hz), 7.68 (d, 1 H, J = 9.3 Hz), 7.59 (d, 1 H, J = 9.3 Hz), 7.30–7.43 (m, 5 H), 6.04 (dddd, 1 H, J_1 = 17.1, J_2 = 10.2, J_3 = 7.8, J_4 = 6.8 Hz), 5.45 (d, 1 H, J = 2.4 Hz), 5.09–5.22 (m, 3 H), 4.64 (d, 1 H, J = 10.7 Hz), 4.57 (d, 1 H, J = 10.7 Hz), 3.98 (s, 3 H), 3.95 (s, 3 H), 3.90 (s, 3 H), 3.89 (s, 3 H), 3.83–3.95 (m, 1 H), 3.52 (dq, 1 H, J_1 = 8.8, J_2 = 6.4 Hz), 3.31 (dd, 1 H, J_1 = J_2 = 8.8 Hz), 3.28–3.33 (br, 1 H), 2.74 (dd, 1 H, J_1 = 14.7, J_2 = 6.8 Hz), 2.51 (dd, 1 H, J_1 = 14.7, J_2 = 7.8 Hz), 2.23 (ddd, 1 H, J_1 = 12.7, J_2 = 4.4, J_3 = 1.5 Hz), 1.85 (ddd, 1 H, J_1 = 12.7, J_2 = J_3 = 11.2 Hz), 1.34 (d, 3 H, J = 6.4 Hz), 1.20 (s, 3 H), 0.95 (s, 9 H), 0.91 (s, 9 H), 0.17 (s, 3 H), 0.15 (s, 3 H), 0.13 (s, 3 H), 0.11 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 152.5, 151.4, 147.91, 147.88, 138.8, 134.0, 130.7, 129.3, 128.5, 128.3, 127.7, 127.6, 125.7, 123.9, 119.73, 119.70, 119.2, 118.6, 118.1, 81.0, 78.5, 77.4, 75.0, 71.3, 70.4, 64.1, 63.44, 63.39, 62.8, 62.4, 42.6, 39.8, 26.4, 26.2, 19.3, 18.9, 18.4, 18.2, –2.6, –2.9, –3.8, –4.1; IR (neat) 3570, 2940, 1640, 1620, 1525, 1450, 1385, 1360, 1255, 1110, 1050, 1000, 840, 760, 670 cm^{-1}; $[\alpha]^{27}_D$ +14° (*c* 1.7, $CHCl_3$); HRMS *m/z* 845.4486 (845.4477 calcd for $C_{48}H_{69}O_9Si_2$, $M^+ - CH_3$).

Benzoates 41a and 41b. A solution of the less polar isomer **40a** (35.2 mg, 0.0409 mmol) BzCl (28.8 mg, 0.205 mmol) and a catalytic amount of 4-(dimethylamino)pyridine in pyridine (2 mL) was stirred overnight at room temperature. The mixture was diluted with EtOAc, then successively washed with saturated $CuSO_4$ and saturated Na_2SO_4, and then dried (Na_2SO_4) and filtered. Removal of solvent in vacuo and purification of the residue by PTLC (hexane/EtOAc = 88/12) afforded benzoate **41a** (34.9 mg, 88.5%) as a yellow oil: R_f = 0.58 (hexane/EtOAc = 85/15); ^{1}H NMR ($CDCl_3$) δ 8.23 (d, 1 H, J = 9.3 Hz), 8.13–8.17 (m, 2 H), 8.11 (d, 1 H, J = 9.3 Hz), 7.65 (d, 1 H, J = 9.3 Hz), 7.61 (d, 1 H, J = 9.3 Hz), 7.56–7.62 (m, 1 H), 7.46–7.50 (m, 2 H), 7.33–7.36 (m, 2 H), 7.20–7.29 (m, 3 H), 6.95 (s, 1 H), 6.07 (dddd, 1 H, J_1 = 17.1, J_2 = 10.3, J_3 = 7.3, J_4 = 6.8 Hz), 5.15 (dd, 1 H, J_1 = 11.2, J_2 = 1.5 Hz), 5.10 (d, 1 H, J = 10.3 Hz), 5.09 (d, 1 H, J = 17.1 Hz), 4.80 (d, 1 H, J = 11.7 Hz), 4.73 (d, 1 H, J = 11.7 Hz), 4.07 (s, 3 H), 3.94 (s, 3 H), 3.90–3.94 (m, 1 H), 3.89 (s, 3 H), 3.87 (s, 3 H), 3.53 (dq, 1 H, J_1 = 8.8, J_2 = 6.4 Hz), 3.32 (dd, 1 H, J_1 = J_2 = 8.8 Hz), 2.78 (dd, 1 H, J_1 = 14.2, J_2 = 6.8 Hz), 2.45 (dd, 1 H, J_1 = 14.2, J_2 = 7.3 Hz), 2.18 (ddd, 1 H, J_1 = 12.7, J_2 = 4.4, J_3 = 1.5 Hz), 1.85 (ddd, 1 H, J_1 = 12.7, J_2 = J_3 = 11.2 Hz), 1.45 (s, 3 H), 1.35 (d, 3 H, J = 6.4 Hz), 0.94 (s, 9 H), 0.90 (s, 9 H), 0.164 (s, 3 H), 0.156 (s, 3 H), 0.11 (s, 3 H), 0.10 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 165.7, 153.2, 151.4, 148.2, 147.9, 139.5, 134.3, 133.1, 130.7, 130.4, 129.7, 128.50, 128.46, 128.4, 128.1, 127.1, 127.0, 126.3, 125.4, 123.9, 119.94, 119.86, 119.1, 118.7, 117.7, 80.0, 78.5, 77.4, 75.0, 73.7, 71.2, 64.8, 63.6, 63.4, 62.9, 62.3, 42.7, 40.8, 26.4, 26.2, 19.6, 19.3, 18.4, 18.2, –2.6, –2.9, –3.8, –4.1; IR (KBr) 2950, 1730, 1640, 1625, 1610, 1590, 1530, 1450, 1385, 1365, 1270, 1255, 1105, 1055, 995, 835, 780 cm^{-1}; $[\alpha]^{27}_D$ +136° (*c* 1.1, $CHCl_3$). Anal. Calcd for $C_{56}H_{76}O_{10}Si_2$: C, 69.67; H, 7.93. Found: C, 69.71; H, 7.64.

In the same manner, benzoate **41b** was obtained from **40b** as a yellow oil (97.6%): R_f = 0.54 (hexane/EtOAc = 85/15); ^{1}H NMR ($CDCl_3$) δ 8.22 (d, 1 H, J = 9.3 Hz), 8.14–8.17 (m, 2 H), 8.09 (d, 1 H, J = 9.3 Hz), 7.65 (d, 1 H, J = 9.3 Hz), 7.56–7.61 (m, 2 H), 7.45–7.50 (m, 2 H), 7.35–7.38 (m, 2 H), 7.22–7.31 (m, 3 H), 6.85 (s, 1 H), 5.89–6.02 (m, 1 H), 5.05–5.12 (m, 3 H), 4.78 (d, 1 H, J = 11.7 Hz), 4.67 (d, 1 H, J = 11.7 Hz), 4.10 (s, 3 H), 3.95 (s, 3 H), 3.94 (s, 3 H), 3.86 (s, 3 H), 3.85–3.94 (m, 1 H), 3.51 (dq, 1 H, J_1 = 8.8, J_2 = 6.4 Hz), 3.31 (dd, 1 H, J_1 = J_2 = 8.8 Hz), 2.88 (dd, 1 H, J_1 = 14.2, J_2 = 6.8 Hz), 2.47 (dd, 1 H, J_1 = 14.2, J_2 = 7.8 Hz), 2.23 (ddd, 1 H, J_1 = 12.7, J_2 = 4.4, J_3 = 1.5 Hz), 1.85 (ddd, 1 H, J_1 = 12.7, J_2 = J_3 = 11.7 Hz), 1.43 (s, 3 H), 1.34 (d, 3 H, J = 6.4 Hz), 0.94 (s, 9 H), 0.91 (s, 9 H), 0.16 (s, 3 H), 0.15 (s, 3 H), 0.13 (s, 3 H), 0.11 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 165.7, 152.9, 151.4, 148.2, 147.9, 139.5, 133.6, 133.1, 130.8, 130.5, 129.7, 128.5, 128.45, 128.36, 128.2, 127.2, 127.14, 127.09, 126.5, 125.5, 123.9, 119.8, 119.1, 118.7, 118.3, 80.0, 78.5, 77.4, 75.0, 73.6, 71.3, 64.5, 63.5, 63.3, 62.8, 62.2, 42.6, 39.8, 26.4, 26.2, 20.0, 19.3, 18.4, 18.2, –2.6, –2.9, –3.8, –4.1; IR (KBr) 2950, 1730, 1640, 1620, 1610, 1590, 1525, 1450, 1370, 1355, 1270, 1255, 1110, 1055, 995, 835, 780 cm^{-1}; $[\alpha]^{27}_D$ –100° (*c* 1.4, $CHCl_3$). Anal. Calcd for $C_{56}H_{76}O_{10}Si_2$: C, 69.67; H, 7.93. Found: C, 69.94; H, 7.64.

Oxidation of 41a and 41b to the 9,10-Anthraquinones 42a and 42b. To a solution of benzoate **41a** (42.4 mg, 0.0440 mmol) in MeCN (8 mL) and H_2O (0.7 mL) was added CAN (1.2 M aqueous solution, 0.092 mL, 0.11 mmol) at –17 °C, and the mixture was stirred for 15 min. The mixture was diluted with EtOAc, washed with water, and then dried (Na_2SO_4) and filtered. Removal of solvent and purification of the residue by PTLC (hexane/EtOAc = 85/15) afforded the anthraquinone **42a** (29.1 mg, 70.8%) as a yellow glass: R_f = 0.46 (hexane/EtOAc = 85/15); ^{1}H NMR ($CDCl_3$) δ 8.13 (d, 1 H, J = 8.3 Hz), 8.07–8.11 (m, 2 H), 8.03 (d, 1 H, J = 8.3 Hz), 7.94 (d, 1 H, J = 8.3 Hz), 7.93 (d, 1 H, J = 8.3 Hz), 7.58–7.63 (m, 1 H), 7.48 (dd, 2 H, J_1 = J_2 = 7.8 Hz), 7.22–7.33 (m, 5 H), 6.66 (s, 1 H), 5.96 (dddd, 1 H, J_1 = 17.1, J_2 = 10.2, J_3 = 7.3, J_4 = 6.8 Hz), 5.09 (dd, 1 H, J_1 = 10.2, J_2 = 2.0 Hz), 5.07 (dd, 1 H, J_1 = 17.1, J_2 = 2.0 Hz), 4.88 (dd, 1 H, J_1 = 11.2, J_2 = 1.5 Hz), 4.75 (d, 1 H, J = 11.7 Hz), 4.68 (d, 1 H, J = 11.7 Hz), 4.12 (s, 3 H), 3.91 (s, 3 H), 3.85 (ddd, 1 H, J_1 = 11.2, J_2 = 8.3, J_3 = 4.8 Hz), 3.47 (dq, 1 H, J_1 = 8.8, J_2 = 6.4 Hz), 3.25 (dd, 1 H, J_1 = 8.8, J_2 = 8.3 Hz), 2.57 (dd, 1 H, J_1 = 14.2, J_2 = 6.8 Hz), 2.37 (dd, 1 H, J_1 = 14.2, J_2 = 7.3 Hz), 2.27 (ddd, 1 H, J_1 = 12.7, J_2 = 4.8, J_3 = 1.5 Hz), 1.54 (ddd, 1 H, J_1 = 12.7, J_2 = J_3 = 11.2 Hz), 1.42 (s, 3 H), 1.33 (d, 3 H, J = 6.4 Hz), 0.93 (s, 9 H), 0.88 (s, 9 H), 0.14 (s, 3 H), 0.13 (s, 3 H), 0.11 (s, 3 H), 0.09 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 182.4, 182.0, 165.6, 158.5, 156.8, 143.0, 139.1, 138.9, 136.7, 136.0, 134.8, 133.6, 133.4, 132.8, 129.9, 129.7, 128.6, 128.3, 127.2, 127.1, 124.64, 124.55, 123.9, 122.8, 118.2, 79.3, 78.3, ca.77 (concealed in solvent peaks), 74.7, 73.5, 71.4, 65.1, 62.4, 62.2, 42.3, 40.8, 26.3, 26.2, 19.6, 19.2, 18.3, 18.1, –2.6, –2.9, –3.8, –4.1; IR (KBr) 2940, 1725, 1675, 1630, 1580, 1570, 1460, 1450, 1385, 1315, 1250, 1105, 1070, 835, 780 cm^{-1}; $[\alpha]^{27}_D$ +180° (*c* 1.1, $CHCl_3$); HRMS *m/z* 827.4026 (827.4007 calcd for $C_{47}H_{63}O_9Si_2$, M^+ – OBn).

In the same manner, anthraquinone **42b** was obtained from **41b** as a yellow glass (80.9%): R_f = 0.46 (hexane/EtOAc = 85/15); ^{1}H NMR ($CDCl_3$) δ 8.09–8.14 (m, 3 H), 8.00 (d, 1 H, J = 8.3 Hz), 7.97 (d, 1 H, J = 8.3 Hz), 7.94 (d, 1 H, J = 8.3 Hz), 7.58–7.63 (m, 1 H), 7.48 (dd, 2 H, J_1 = J_2 = 7.8 Hz), 7.24–7.32 (m, 5 H), 6.53 (s, 1 H), 5.90 (dddd, 1 H, J_1 = 17.1, J_2 = 10.2, J_3 = 8.3, J_4 = 6.4 Hz), 5.12 (dd, 1 H, J_1 = 10.2, J_2 = 1.5 Hz), 5.07 (dd, 1 H, J_1 = 17.1, J_2 = 1.5 Hz), 4.87 (dd, 1 H, J_1 = 11.2, J_2 = 1.5 Hz), 4.68 (d, 1 H, J = 11.2 Hz), 4.55 (d, 1 H, J = 11.2 Hz), 4.18 (s, 3 H), 3.92 (s, 3 H), 3.85 (ddd, 1 H, J_1 = 11.2, J_2 = 8.3, J_3 = 4.8 Hz), 3.47 (dq, 1 H, J_1 = 8.3, J_2 = 6.4 Hz), 3.25 (dd, 1 H, J_1 = J_2 = 8.3 Hz), 2.80 (dd, 1 H, J_1 = 14.2, J_2 = 6.4 Hz), 2.49 (dd, 1 H, J_1 = 14.2, J_2 = 8.3 Hz), 2.27 (ddd, 1 H, J_1 = 12.7, J_2 = 4.8, J_3 = 1.5 Hz), 1.53 (ddd, 1 H, J_1 = 12.7, J_2 = J_3 = 11.2 Hz), 1.34 (d, 3 H, J = 6.4 Hz), 1.31 (s, 3 H), 0.93 (s, 9 H), 0.88 (s, 9 H), 0.14 (s, 3 H), 0.13 (s, 3 H), 0.11 (s, 3 H), 0.09 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 182.4, 182.2, 165.6, 158.0, 156.8, 143.0, 139.1, 139.0, 136.8, 136.1, 135.5, 133.3, 133.0, 132.7, 129.9, 129.7, 128.6, 128.3, 127.3, 127.2, 124.68, 124.66, 123.8, 122.9, 118.8, 79.3, 78.3, 77.4, 74.7, 73.0, 71.4, 64.5, 62.3, 42.3, 40.1, 26.3, 26.2, 19.7, 19.2, 18.3, 18.1, –2.6, –2.9, –3.8, –4.1; IR (KBr) 2940, 1725, 1670, 1640, 1580, 1565, 1460, 1450, 1385, 1315, 1250, 1105, 1070, 835, 775 cm^{-1}; $[\alpha]^{26}_D$ –194° (*c* 1.3, $CHCl_3$); HRMS *m/z* 903.4339 (903.4320 calcd for $C_{53}H_{67}O_9Si_2$, M^+ – OMe). Anal. Calcd for $C_{54}H_{70}O_{10}Si_2$: C, 69.35; H, 7.54. Found: C, 69.05; H, 7.23.

Tertiary Alcohols 43a and 43b. To a two-phase mixture of anthraquinone **42a** (38.9 mg, 0.0416 mmol), CH_2Cl_2 (3 mL), and pH 8.04 phosphate buffer (5 mL) was added DDQ (472 mg, 2.08 mmol), and the mixture was stirred for 8 h at room temperature. After dilution with EtOAc, the mixture was washed successively with saturated $NaHCO_3$ and brine and dried (Na_2SO_4). Removal of solvent and purification by PTLC (hexane/EtOAc = 75/25) afforded alcohol **43a** (32.4 mg, 92.2%) as a yellow glass: R_f = 0.61 (hexane/EtOAc = 7/3), R_f = 0.35 ($CHCl_3/Et_2O$ = 95/5); ^{1}H NMR ($CDCl_3$) δ 8.12 (d, 1 H, J = 8.3 Hz), 8.09–8.12 (m, 2 H), 8.08 (d, 1 H, J = 8.3 Hz), 7.94 (d, 1 H, J = 8.3 Hz), 7.85 (d, 1 H, J = 8.3 Hz), 7.61–7.66 (m, 1 H), 7.48–7.53 (m, 2 H), 6.41

(s, 1 H), 5.97 (ddt, 1 H, J_1 = 17.1, J_2 = 9.8, J_3 = 7.3 Hz), 5.23 (dd, 1 H, J_1 = 9.8, J_2 = 1.5 Hz), 5.13 (dd, 1 H, J_1 = 17.1, J_2 = 1.5 Hz), 4.88 (dd, 1 H, J_1 = 11.2, J_2 = 1.5 Hz), 4.14 (s, 3 H), 3.91 (s, 3 H), 3.85 (ddd, 1 H, J_1 = 11.2, J_2 = 8.8, J_3 = 4.9 Hz), 3.47 (dq, 1 H, J_1 = 8.8 Hz, J_2 = 6.3 Hz), 3.25 (dd, 1 H, J_1 = J_2 = 8.8 Hz), 2.50–2.54 (br, 1 H), 2.40 (d, 2 H, J = 7.3 Hz), 2.27 (ddd, 1 H, J_1 = 12.7, J_2 = 4.9, J_3 = 1.5 Hz), 1.54 (ddd, 1 H, J_1 = 12.7, J_2 = J_3 = 11.2 Hz), 1.34 (s, 3 H), 1.33 (d, 3 H, J = 6.3 Hz), 0.93 (s, 9 H), 0.89 (s, 9 H), 0.14 (s, 3 H), 0.13 (s, 3 H), 0.11 (s, 3 H), 0.09 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 182.2, 182.0, 165.3, 157.9, 156.9, 143.2, 138.7, 136.7, 135.9, 133.5, 132.8, 132.5, 129.7, 129.5, 128.7, 124.8, 124.5, 123.9, 123.4, 120.0, 78.2, 77.4, 74.7, 74.3, 73.6, 71.4, 62.2, 62.0, 43.6, 42.3, 26.3, 26.2, 22.7, 19.2, 18.3, 18.1, −2.6, −2.9, −3.8, −4.1; IR (neat) 3540, 2950, 1730, 1675, 1580, 1570, 1465, 1450, 1390, 1360, 1315, 1250, 1180, 1110, 1075, 1015, 830, 760, 665 cm^{-1}; $[\alpha]^{26}_D$ +215° (*c* 1.5, $CHCl_3$); HRMS *m/z* 844.4037 (844.4035 calcd for $C_{47}H_{64}O_{10}Si_2$, M^+). Anal. Calcd for $C_{47}H_{64}O_{10}Si_2$: C, 66.79; H, 7.63. Found: C, 66.41; H, 7.41.

In the same manner, alcohol **43b** was obtained from **42b** as a yellow glass (88.8%): R_f = 0.61 (hexane/EtOAc = 7/3), R_f = 0.47 ($CHCl_3$/Et_2O = 95/5); ^{1}H NMR ($CDCl_3$) δ 8.12 (d, 1 H, J = 8.3 Hz), 8.09–8.13 (m, 2 H), 8.06 (d, 1 H, J = 8.3 Hz), 7.94 (d, 1 H, J = 8.3 Hz), 7.93 (d, 1 H, J = 8.3 Hz), 7.60–7.65 (m, 1 H), 7.47–7.52 (m, 2 H), 6.37 (s, 1 H), 5.92 (dddd, 1 H, J_1 = 17.1, J_2 = 10.6, J_3 = 8.3, J_4 = 6.8 Hz), 5.18 (dd, 1 H, J_1 = 10.6, J_2 = 1.5 Hz), 5.13 (dd, 1 H, J_1 = 17.1, J_2 = 1.5 Hz), 4.87 (dd, 1 H, J_1 = 11.2, J_2 = 1.5 Hz), 4.15 (s, 3 H), 3.92 (s, 3 H), 3.85 (ddd, 1 H, J_1 = 8.3, J_2 = 4.8, J_3 = 11.2 Hz), 3.47 (dq, 1 H, J_1 = 8.3, J_2 = 6.4 Hz), 3.24 (dd, 1 H, J_1 = J_2 = 8.3 Hz), 2.55 (dd, 1 H, J_1 = 13.7, J_2 = 6.8 Hz), 2.45 (dd, 1 H, J_1 = 13.7, J_2 = 8.3 Hz), 2.27 (ddd, 1 H, J_1 = 12.7, J_2 = 4.8, J_3 = 1.5 Hz), 2.03–2.13 (br, 1 H), 1.53 (ddd, 1 H, J_1 = 12.7, J_2 = J_3 = 11.2 Hz), 1.33 (d, 3 H, J = 6.4 Hz), 1.18 (s, 3 H), 0.93 (s, 9 H), 0.88 (s, 9 H), 0.14 (s, 3 H), 0.13 (s, 3 H), 0.11 (s, 3 H), 0.10 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 182.3, 182.1, 165.4, 158.0, 156.8, 143.1, 138.6, 136.9, 136.0, 134.3, 133.5, 132.9, 132.8, 129.7, 128.7, 124.8, 124.6, 123.8, 123.2, 119.4, 78.3, 77.4, 74.7, 74.5, 74.2, 71.4, 62.29, 62.28, 43.9, 42.2, 26.3, 26.1, 23.2, 19.2, 18.3, 18.1, −2.6, −2.9, −3.8, −4.1; IR (neat) 3540, 2940, 1725, 1675, 1580, 1570, 1465, 1450, 1390, 1360, 1315, 1250, 1180, 1105, 1075, 1015, 830, 760, 665 cm^{-1}; $[\alpha]^{26}_D$ −200° (*c* 1.3, $CHCl_3$); HRMS *m/z* 787.3320 (787.3330 calcd for $C_{43}H_{55}O_{10}Si_2$, $M^+ - {}^t$Bu). Anal. Calcd for $C_{47}H_{64}O_{10}Si_2$: C, 66.79; H, 7.63. Found: C, 66.51; H, 7.34.

epi-**43a**: a yellow glass; R_f = 0.54 (hexane/EtOAc = 7/3), R_f = 0.27 ($CHCl_3$/Et_2O = 95/5); ^{1}H NMR ($CDCl_3$) δ 8.12 (d, 1 H, J = 8.1 Hz), 8.09–8.13 (m, 2 H), 8.07 (d, 1 H, J = 8.1 Hz), 7.94 (d, 1 H, J = 8.1 Hz), 7.93 (d, 1 H, J = 8.1 Hz), 7.60–7.65 (m, 1 H), 7.47–7.53 (m, 2 H), 6.37 (s, 1 H), 5.93 (dddd, 1 H, J_1 = 17.1, J_2 = 10.6, J_3 = 8.3, J_4 = 6.8 Hz), 5.18 (dd, 1 H, J_1 = 10.6, J_2 = 1.7 Hz), 5.13 (dd, 1 H, J_1 = 17.1, J_2 = 1.7 Hz), 4.88 (dd, 1 H, J_1 = 11.2, J_2 = 1.7 Hz), 4.14 (s, 3 H), 3.91 (s, 3 H), 3.85 (ddd, 1 H, J_1 = 11.2, J_2 = 8.3, J_3 = 4.4 Hz), 3.47 (dq, 1 H, J_1 = 8.5, J_2 = 6.4 Hz), 3.25 (dd, 1 H, J_1 = 8.5, J_2 = 8.3 Hz), 2.55 (dd, 1 H, J_1 = 13.7, J_2 = 6.8 Hz), 2.45 (dd, 1 H, J_1 = 13.7, J_2 = 8.3 Hz), 2.27 (ddd, 1 H, J_1 = 12.7, J_2 = 4.4, J_3 = 1.7 Hz), 2.00–2.14 (br, 1 H), 1.57 (ddd, 1 H, J_1 = 12.7, J_2 = J_3 = 11.2 Hz), 1.33 (d, 3 H, J = 6.4 Hz), 1.19 (s, 3 H), 0.93 (s, 9 H), 0.88 (s, 9 H), 0.14 (s, 3 H), 0.13 (s, 3 H), 0.11 (s, 3 H), 0.09 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 182.2, 182.0, 165.4, 158.1, 156.9, 143.1, 138.6, 136.8, 136.0, 134.4, 133.5, 132.9, 132.8, 129.68, 129.67, 128.7, 124.8, 124.5, 123.9, 123.2, 119.4, 78.2, ca.77 (concealed in solvent peaks), 74.7, 74.5, 74.2, 71.4, 62.2, 43.9, 42.3, 26.3, 26.1, 23.3, 19.2, 18.3, 18.1, −2.6, −2.9, −3.8, −4.1; IR (neat) 3540, 2950, 1730, 1675, 1580, 1565, 1465, 1450, 1390, 1360, 1315, 1250, 1180, 1110, 1075, 1015, 835, 760, 665 cm^{-1}; $[\alpha]^{24}_D$ +221° (*c* 0.93, $CHCl_3$). Anal. Calcd for $C_{47}H_{64}O_{10}Si_2$: C, 66.79; H, 7.63. Found: C, 66.83; H, 7.53.

epi-**43b**: a yellow glass; R_f = 0.67 (hexane/EtOAc = 7/3), R_f = 0.53 ($CHCl_3$/Et_2O = 95/5); ^{1}H NMR ($CDCl_3$) δ 8.11 (d, 1 H, J = 8.1 Hz), 8.09–8.12 (m, 2 H), 8.07 (d, 1 H, J = 8.1 Hz), 7.94 (d, 1 H, J = 8.1 Hz), 7.84 (d, 1 H, J = 8.1 Hz), 7.61–7.66 (m, 1 H), 7.48–7.53 (m, 2 H), 6.39 (s, 1 H), 5.97 (ddt, 1 H, J_1 = 17.1, J_2 = 10.6, J_3 = 7.3 Hz), 5.23 (dd, 1 H, J_1 = 10.6, J_2 = 2.0 Hz), 5.12 (dd, 1 H, J_1 = 17.1, J_2 = 2.0 Hz), 4.87 (dd, 1 H, J_1 = 11.2, J_2 = 1.7 Hz), 4.15 (s, 3 H), 3.92 (s, 3 H), 3.85 (ddd, 1 H, J_1 = 11.2, J_2 = 8.3, J_3 = 4.6 Hz), 3.47 (dq, 1 H, J_1 = 8.5, J_2 = 6.4 Hz), 3.25 (dd, 1 H, J_1 = 8.5, J_2 = 8.3 Hz), 2.50–2.57 (br, 1 H), 2.39 (d, 2 H, J = 7.3 Hz), 2.26 (ddd, 1 H, J_1 = 12.9, J_2 = 4.6, J_3 = 1.7 Hz), 1.53 (ddd, 1 H, J_1 = 12.9, J_2 = J_3 = 11.2 Hz), 1.33 (d, 3 H, J = 6.4 Hz), 1.33 (s, 3 H), 0.92 (s, 9 H), 0.89 (s, 9 H), 0.14 (s, 3 H), 0.13 (s, 3 H), 0.11 (s, 3 H), 0.09 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 182.2, 182.1, 165.4, 157.9, 156.9, 143.1, 138.7, 136.8, 136.0, 133.6, 133.5, 132.8, 132.5, 129.7, 129.5, 128.7, 124.9, 124.6, 123.9, 123.4, 120.0, 78.3, 77.4, 74.7, 74.3, 73.6, 71.4, 62.3, 62.1, 43.6, 42.2, 26.3, 26.1, 22.7, 19.2, 18.3, 18.1, −2.6, −2.9, −3.8, −4.1; IR (neat) 3540, 2940, 1725, 1675, 1580, 1570, 1465, 1450, 1390, 1360, 1315, 1250, 1180, 1110, 1075, 1015, 830, 750, 665 cm^{-1}; $[\alpha]^{28}_D$ −208° (*c* 0.92, $CHCl_3$). Anal. Calcd for $C_{47}H_{64}O_{10}Si_2$: C, 66.79; H, 7.63. Found: C, 67.06; H, 7.55.

Benzylic Deoxygenation of 43 To Give 44. To a mixture of the tertiary alcohol **43a** (32.4 mg, 0.0384 mmol) and $Na_2S_2O_4$ (20.0 mg, 0.115 mmol) in 1,4-dioxane (6 mL)–H_2O (2 mL) was added 1 N aqueous NaOH (three drops; ca. 0.075 mL) four times at intervals of 15 min. The mixture was neutralized by the addition of 1 N HCl at 0 °C. After dilution with EtOAc, the mixture was washed with water and then dried (Na_2SO_4) and filtered. The solvent was removed, and the residue was purified by PTLC (hexane/EtOAc = 7/3) to afford **44** (23.8 mg, 85.6%) as a yellow oil.

In the same manner, **44** was obtained from **43b** (97.4%): R_f = 0.57 (hexane/EtOAc = 7/3), R_f = 0.35 ($CHCl_3$/Et_2O = 95/5); ^{1}H NMR ($CDCl_3$) δ 8.10 (d, 1 H, J = 8.1 Hz), 8.05 (d, 1 H, J = 8.1 Hz), 7.93 (d, 1 H, J = 8.1 Hz), 7.68 (d, 1 H, J = 8.1 Hz), 5.95 (ddt, 1 H, J_1 = 17.1, J_2 = 10.3, J_3 = 7.3 Hz), 5.19 (dd, 1 H, J_1 = 10.3, J_2 = 2.0 Hz), 5.15 (dd, 1 H, J_1 = 17.1, J_2 = 2.0 Hz), 4.88 (dd, 1 H, J_1 = 11.2, J_2 = 1.5 Hz), 3.94 (s, 6 H), 3.85 (ddd, 1 H, J_1 = 11.2, J_2 = 8.3, J_3 = 4.6 Hz), 3.47 (dq, 1 H, J_1 = 8.5, J_2 = 6.4 Hz), 3.25 (dd, 1 H, J_1 = 8.5, J_2 = 8.3 Hz), 3.02 (d, 1 H, J = 13.4 Hz), 2.89 (d, 1 H, J = 13.4 Hz), 2.56 (s, 1 H), 2.25–2.36 (m, 3 H), 1.54 (ddd, 1 H, J_1 = J_2 = 11.2, J_3 = 12.9 Hz), 1.33 (d, 3 H, J = 6.4 Hz), 1.15 (s, 3 H), 0.93 (s, 9 H), 0.89 (s, 9 H), 0.14 (s, 3 H), 0.13 (s, 3 H), 0.12 (s, 3 H), 0.09 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 182.42, 182.38, 158.6, 156.8, 143.1, 139.4, 138.2, 136.1, 136.0, 133.9, 132.7, 125.0, 124.7, 123.8, 123.2, 119.0, 78.3, 77.4, 74.7, 72.8, 71.4, 62.3, 61.9, 47.2, 42.3, 41.6, 26.8, 26.3, 26.2, 19.2, 18.3, 18.1, −2.6, −2.9, −3.8, −4.1; IR (neat) 3540, 2940, 1670, 1580, 1570, 1465, 1390, 1325, 1260, 1110, 1010, 840, 780, 760 cm^{-1}; $[\alpha]^{26}_D$ +16° (*c* 1.6, $CHCl_3$); HRMS *m/z* 725.3937 (725.3902 calcd for $C_{40}H_{61}O_8Si_2$, $M^+ + 1$). Anal. Calcd for $C_{40}H_{60}O_8Si_2$: C, 66.26; H, 8.34. Found: C, 66.02; H, 8.22.

epi-**44**: a yellow oil; R_f = 0.57 (hexane/ EtOAc = 7/3), R_f = 0.35 ($CHCl_3$/Et_2O = 95/5); ^{1}H NMR ($CDCl_3$) δ 8.10 (d, 1 H, J = 8.1 Hz), 8.05 (d, 1 H, J = 8.1 Hz), 7.93 (d, 1 H, J = 8.1 Hz), 7.67 (d, 1 H, J = 8.1 Hz), 5.95 (ddt, 1 H, J_1 = 17.1, J_2 = 10.3, J_3 = 7.3 Hz), 5.19 (dd, 1 H, J_1 = 10.3, J_2 = 2.2 Hz), 5.14 (dd, 1 H, J_1 = 17.1, J_2 = 2.2 Hz), 4.88 (dd, 1 H, J_1 = 11.5, J_2 = 1.7 Hz), 3.941 (s, 3 H), 3.939 (s, 3 H), 3.85 (ddd, 1 H, J_1 = 11.5, J_2 = 8.3, J_3 = 4.6 Hz), 3.47 (dq, 1 H, J_1 = 8.5, J_2 = 6.4 Hz), 3.25 (dd, 1 H, J_1 = 8.5, J_2 = 8.3 Hz), 3.02 (d, 1 H, J = 13.4 Hz), 2.88 (d, 1 H, J = 13.4 Hz), 2.50–2.57 (br, 1 H), 2.24–2.36 (m, 3 H), 1.54 (ddd, 1 H, J_1 = J_2 = 11.5, J_3 = 12.9 Hz), 1.33 (d, 3 H, J = 6.4 Hz), 1.15 (s, 3 H), 0.93 (s, 9 H), 0.89 (s, 9 H), 0.14 (s, 3 H), 0.13 (s, 3 H), 0.12 (s, 3 H), 0.09 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 182.44, 182.38, 158.6, 156.8, 143.0, 139.4, 138.2, 136.1, 136.0, 133.9, 132.7, 125.0, 124.7, 123.8, 123.2, 119.0, 78.3, ca.77 (concealed in solvent peaks), 74.7, 72.8, 71.4, 62.3, 62.0, 47.2, 42.3, 41.6, 26.8, 26.3, 26.2, 19.2, 18.3, 18.1, −2.6, −2.9, −3.8, −4.1; IR (neat) 3540, 2940, 1675, 1580, 1570, 1465, 1390, 1325, 1260, 1110, 1010, 840, 780, 760 cm^{-1}; $[\alpha]^{27}_D$ −23° (*c* 1.1, $CHCl_3$). Anal. Calcd for $C_{40}H_{60}O_8Si_2$: C, 66.26; H, 8.34. Found: C, 66.34; H, 8.14.

Methyl Ester 46. O_3 (ca. 2% in O_2) was bubbled (50 mL/h) into a solution of **44** (44.9 mg, 0.0620 mmol) in MeOH (10 mL) at −78 °C. Excess ozone was purged by bubbling N_2, and the mixture was concentrated in vacuo. Purification by PTLC (hexane/EtOAc = 1/1) afforded a diasteromeric mixture of hydroperoxide **45** (44.3 mg, 92.3%) as a yellow oil, which was used in the next step without purification: R_f = 0.15 (hexane/EtOAc = 7/3); ^{1}H NMR ($CDCl_3$) δ {9.48 (br s), 9.21 (br s), 1 H}, {8.098 (d, J = 8.1 Hz), 8.096 (d, J = 8.1 Hz), 1 H}, 8.06 (d, 1 H, J = 8.1 Hz), 7.94 (d, 1 H, J = 8.1 Hz), {7.70 (d, J = 8.1 Hz), 7.64 (d, J = 8.1 Hz), 1 H}, {5.02 (t, J = 6.1 Hz), 4.95 (dd, J_1 = 7.3, J_2 = 4.9 Hz), 1 H}, 4.86–4.91 (br d, 1 H), {3.97 (s), 3.95 (s), 3.94 (s), 6 H}, 3.82–3.97 (m, 2 H), {3.54 (s), 3.49 (s), 3 H}, 3.47 (dq, 1 H, J_1 = 8.5, J_2 = 6.4 Hz), 3.25 (dd, 1 H, J_1 = 8.5, J_2 = 8.2 Hz), {3.24 (d, J = 13.4 Hz), 3.01 (s), 2.85 (d, J = 13.4 Hz), 2 H}, 2.28 (ddd, 1 H, J_1 = 12.8, J_2 = 4.6, J_3 = 1.8 Hz), {2.13 (dd, J_1 = 15.0, J_2 = 6.1 Hz), 2.05 (dd, J_1 = 15.0, J_2 = 7.3 Hz), 1.91 (dd, J_1 = 15.0, J_2 = 6.1 Hz), 1.86 (dd, J_1 = 15.0, J_2 = 4.9 Hz), 2 H}, 1.48–1.59 (m, 1 H), {1.31–1.35 (m), 1.19 (s), 6 H}, 0.93 (s, 9 H), 0.89 (s, 9 H), 0.14 (s, 3 H), 0.13 (s, 3 H), 0.12 (s, 3 H), 0.09 (s, 3 H); IR (neat) 3430, 2950, 1670, 1580, 1570, 1470, 1390, 1325, 1260, 1110, 1010, 840, 780, 760 cm^{-1}.

To a solution of hydroperoxide **45** (24.4 mg, 0.0315 mmol) in CH_2Cl_2 (3 mL) were successively added Ac_2O (13.5 mg, 0.132 mmol) and Et_3N (11.0 mg, 0.109 mmol) at 0 °C, and the mixture was stirred for 25 min. The reaction was diluted with EtOAc, and the mixture was washed successfully with 15% aqueous NaOH, 0.1 N HCl, and water and then dried (Na_2SO_4) and filtered. Removal of solvent and purification of the product by PTLC (hexane/EtOAc = 7/3) gave methyl ester **46** (20.7 mg, 86.9%) as a yellow oil: R_f = 0.33 (hexane/EtOAc = 7/3); ^{1}H NMR ($CDCl_3$) δ 8.10 (d, 1 H, J = 8.1 Hz), 8.04 (d, 1 H, J = 8.1 Hz), 7.93 (d, 1 H, J = 8.1 Hz), 7.75 (d, 1 H, J = 8.1 Hz), 4.88 (dd, 1 H, J_1 = 11.2, J_2 = 1.7 Hz), 3.93 (s, 3 H), 3.91 (s, 3 H), 3.85 (ddd, 1 H, J_1 = 11.2, J_2 = 8.5, J_3 = 4.6 Hz), 3.71 (s, 3 H), 3.47 (dq, 1 H, J_1 = 8.5, J_2 = 6.3 Hz),

3.25 (dd, 1 H, $J_1 = J_2 = 8.5$ Hz), 3.10 (d, 1 H, $J = 13.2$ Hz), 3.02 (d, 1 H, $J = 13.2$ Hz), 2.52 (s, 2 H), 2.27 (ddd, 1 H, $J_1 = 12.7$, $J_2 = 4.6$, $J_3 = 1.7$ Hz), 1.53 (ddd, 1 H, $J_1 = J_2 = 11.2$, $J_3 = 12.7$ Hz), 1.33 (d, 3 H, $J = 6.3$ Hz), 1.26 (s, 3 H), 0.93 (s, 9 H), 0.89 (s, 9 H), 0.14 (s, 3 H), 0.13 (s, 3 H), 0.12 (s, 3 H), 0.09 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 182.44, 182.38, 173.3, 158.7, 156.8, 143.0, 138.8, 138.4, 136.1, 132.7, 125.0, 124.7, 123.8, 123.1, 78.3, ca. 77 (concealed in solvent peaks), 74.7, 71.7, 71.4, 62.3, 62.0, 51.7, 44.4, 42.3, 41.1, 27.3, 26.3, 26.2, 19.2, 18.3, 18.1, -2.6, -2.9, -3.8, -4.1; IR (neat) 3530, 2950, 1730, 1675, 1580, 1570, 1470, 1445, 1390, 1325, 1250, 1110, 1010, 835, 780, 760 cm^{-1}; $[\alpha]^{27}_D$ -3° (c 1.2, $CHCl_3$); HRMS m/z 756.3750 (756.3722 calcd for $C_{40}H_{60}O_{10}Si_2$, M^+).

Vineomycinone B_2 Methyl Ester (7). To a solution of **46** (34.1 mg, 0.0451 mmol) in CH_2Cl_2 (6 mL) was added a solution of BBr_3 (303 mg, 1.21 mmol) in CH_2Cl_2 (1 mL) at -78 °C. After 25 min, saturated $NaHCO_3$ was added. The mixture was stirred for 5 min, acidified with 1 N HCl, and extracted with $CHCl_3$. The extract was washed with brine, dried (Na_2SO_4), and concentrated in vacuo. Purification of the product by PTLC (hexane/EtOAc = 1/9) afforded vineomycinone B_2 methyl ester (7) (20.3 mg, 90.0%). Recrystallization from $CHCl_3$-hexane gave **7** as orange needles: mp 186-187 °C; $R_f = 0.52$ (EtOAc); ^{1}H NMR ($CDCl_3$) δ 13.2 (s, 1 H), 13.1 (s, 1 H), 7.91 (d, 1 H, $J = 7.9$ Hz), 7.85 (d, 1 H, $J = 7.9$ Hz), 7.80 (d, 1 H, $J = 7.9$ Hz), 7.69 (d, 1 H, $J = 7.9$ Hz), 4.94 (dd, 1 H, $J_1 = 11.2$, $J_2 = 1.8$ Hz), 3.86 (ddd, 1 H, $J_1 = 11.2$, $J_2 = 9.0$, $J_3 = 4.9$ Hz), 3.73 (s, 3 H), 3.53 (dq, 1 H, $J_1 = 9.0$, $J_2 = 6.2$ Hz), 3.22 (dd, 1 H, $J_1 = J_2 = 9.0$ Hz), 3.11 (d, 1 H, $J = 13.6$ Hz), 3.02 (d, 1 H, $J = 13.6$ Hz), 2.59 (d, 1 H, $J = 15.8$ Hz), 2.55 (d, 1 H, $J = 15.8$ Hz), 2.54 (ddd, 1 H, $J_1 = 12.8$, $J_2 = 4.9$, $J_3 = 1.8$ Hz), 1.48 (ddd, 1 H, $J_1 = 12.8$, $J_2 = J_3 = 11.2$ Hz), 1.42 (d, 3 H, $J = 6.2$ Hz), 1.31 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 188.2, 188.1, 173.3, 161.3, 159.0, 139.6, 138.3, 134.7, 133.3, 131.84, 131.78, 119.4, 118.9, 115.6, 115.5, 78.0, 75.9, 73.1, 71.8, 71.3, 51.8, 44.4, 40.5, 39.4, 27.3, 18.1; IR (neat) 3400, 2930, 1725, 1625, 1580, 1430, 1255, 1090, 1070, 790, 760 cm^{-1}; $[\alpha]^{29}_D$ +118° (c 1.05, dioxane); HRMS m/z 485.1438 (485.1446 calcd for $C_{25}H_{25}O_{10}$, $M^+ - CH_3$). Anal. Calcd for $C_{26}H_{28}O_{10}$: C, 62.39; H, 5.64. Found: C, 62.57; H, 5.54.

12-*epi*-Vineomycinone B_2 Methyl Ester (*epi*-7): orange needles; mp 193-194 °C ($CHCl_3$-hexane); $R_f = 0.52$ (EtOAc); ^{1}H NMR ($CDCl_3$) δ 13.2 (s, 1 H), 13.1 (s, 1 H), 7.92 (d, 1 H, $J = 7.8$ Hz), 7.85 (d, 1 H, $J = 7.8$ Hz), 7.80 (d, 1 H, $J = 7.8$ Hz), 7.69 (d, 1 H, $J = 7.8$ Hz), 4.94 (dd, 1 H, $J_1 = 11.2$, $J_2 = 1.5$ Hz), 3.86 (ddd, 1 H, $J_1 = 11.2$, $J_2 = 9.0$, $J_3 = 4.9$ Hz), 3.73 (s, 3 H), 3.54 (dq, 1 H, $J_1 = 9.0$, $J_2 = 5.9$ Hz), 3.22 (dd, 1 H, $J_1 = J_2 = 9.0$ Hz), 3.09 (d, 1 H, $J = 13.7$ Hz), 3.04 (d, 1 H, $J = 13.7$ Hz), 2.57 (s, 2 H), 2.54 (ddd, 1 H, $J_1 = 12.7$, $J_2 = 4.9$, $J_3 = 1.5$ Hz), 1.48 (ddd, 1 H, $J_1 = 12.7$, $J_2 = J_3 = 11.2$ Hz), 1.43 (d, 3 H, $J = 5.9$ Hz), 1.31 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 188.2, 188.1, 173.3, 161.3, 159.0, 139.6, 138.3, 134.7, 133.3, 131.84, 131.78, 119.4, 118.9, 115.6, 115.5, 78.0, 75.9, 73.1, 71.8, 71.3, 51.8, 44.4, 40.5, 39.4, 27.2, 18.1; IR (neat) 3300, 2930, 1720, 1620, 1580, 1430, 1255, 1090, 1065, 790, 755 cm^{-1}; $[\alpha]^{28}_D$ +111° (c 0.45, dioxane); HRMS m/z 469.1505 (469.1497 calcd for $C_{25}H_{25}O_9$, $M^+ - OCH_3$). Anal. Calcd for $C_{26}H_{28}O_{10}$: C, 62.39; H, 5.64. Found: C, 62.18; H, 5.51.

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Supplementary Material Available: Physical properties for compounds **10**, **13**, **17**, **18**, **26**, **30**, **31**, **33**, **34**, **35**, *epi*-**40a-42a**, *epi*-**40b-42b**, *epi*-**45**, and *epi*-**46** (8 pages). Ordering information is given on any current masthead page.

Preparation of Chiral Cyanohydrins by an Oxynitrilase-Mediated Transcyanation

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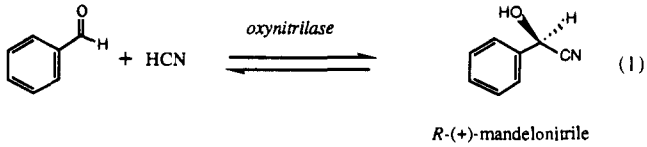
Abstract: The transcyanation of aromatic and aliphatic aldehydes **1** (RCHO) with acetone cyanohydrin is catalyzed by the enzyme D-oxynitrilase to afford (*R*)-cyanohydrins **2** (RCH(OH)CN). The biocatalytic method using acetone cyanohydrin gives products of high enantiomeric purity with better consistency than similar conditions using hydrogen cyanide as the cyanide source. The use of an ether-buffer biphasic solvent system is essential for producing products of optimum optical purity, but the solubility properties of the substrate have a pronounced effect on the enantiomeric purity of the final product. A discussion relating the solubility partition coefficient (log *P*) of a substrate to the enantiomeric purity of the product as a guide for predicting the outcome with new substrates is presented. Application of the method to the preparation of the following cyanohydrins is reported (R, ee): **a**, C_6H_5, 92% ee; **b**, 3,4-$(CH_2O_2)C_6H_3$, 90% ee; **c**, 2-$(CH_3O)C_6H_4$, 96% ee; **d**, $C_6H_5CH_2$, 88% ee; **e**, $CH_3SCH_2CH_2$, 92% ee; **f**, $CH_3(CH_2)_5CH_2$, 92% ee; **g**, $(CH_3)_3C$, 92% ee; **h**, c-C_6H_{11}, 96% ee; **i**, $CH_3O_2C(CH_2)_6CH_2$, 97% ee; **j**, (*E*,*E*)-$CH_3CH{=}CHCH{=}CH$, 96% ee; **k**, $(CH_3)_2C{=}CHCH_2CH_2C(CH_3){=}CH$, 99% ee.

The flavoprotein D-oxynitrilase (mandelonitrile-benzaldehyde lyase (EC 4.1.2.10)) catalyzes the reversible condensation of benzaldehyde with hydrogen cyanide to form (*R*)-(+)-mandelonitrile[1,2] (eq 1). Since its original isolation and purification, attempts have been made to use this enzyme as a biocatalyst for preparing chiral cyanohydrins.[3,4] Early work on the



(1)

R-(+)-mandelonitrile

oxynitrilase-mediated condensation of unnatural substrates with hydrogen cyanide met with varying degrees of success. For example, achieving high enantioselectivity in aqueous media was often difficult due to a competing nonenzymic reaction of the substrate with cyanide.[5] Also, the enantiomeric purity of the

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