Allylation of 2-Alkanoyl 1,4-Quinones with Allylsilanes and Allylstannanes. Efficient Synthesis of Pyranonaphthoquinone Antibiotics[1]

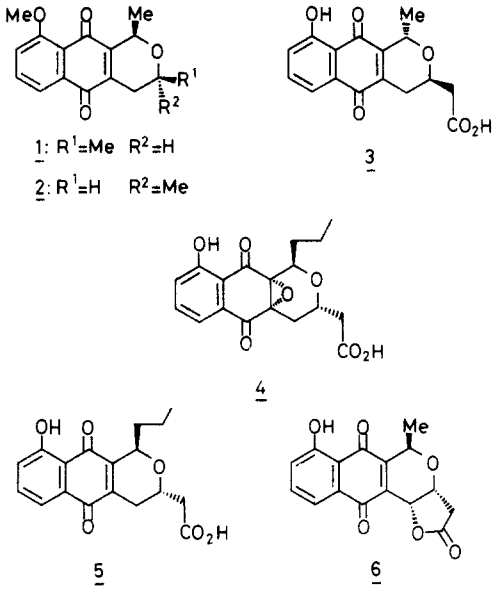
Hidemitsu Uno[†]

Department of Chemistry, Faculty of Science, Kyoto University, Sakyo-ku, Kyoto 606, Japan

Received April 29, 1985

Total syntheses of pyranonaphthoquinone antibiotics eleutherin, isoeleutherin, nanaomycin A, and deoxyfrenolicin are described. The crucial step in the route is a regioselective allylation of alkanoyl quinones with allylsilanes and allylstannanes. The allylated products are easily converted to pyranonaphthoquinones by either intramolecular Michael addition or oxymercuration or phenylseleno etherification.

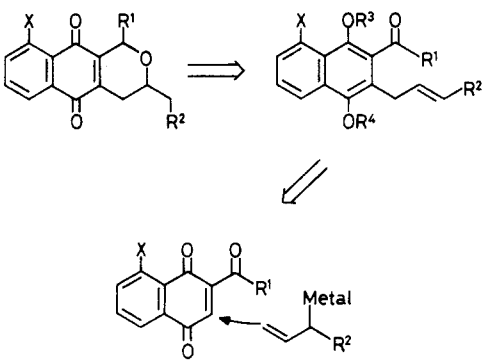
Pyranonaphthoquinones show characteristic biological activities. For example, nanaomycin A (**3**),[2] frenolicin (**4**),[3] and kalafungin (**6**)[4] have been shown to be extremely active



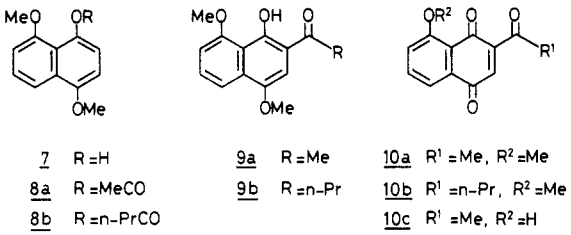
against Gram-positive bacteria, fungi, and mycoplasmas. Their benzoisochromanquinone skeleton plays an important role in the appearance of bioactivity, and it has been suggested that in vivo reduction causes a transformation to an active hydroquinone form which functions as bisalkylating agent. Moore[5] has suggested that these pyranonaphthoquinones may exhibit antitumor activity since the proposed mechanism of action resembles that of alkylating antibiotics such as mitomycins. Many synthetic routes[6-14] to these pyranonaphthoquinones have been reported. We have also established an efficient synthetic route to a series of these pyranonaphthoquinone antibiotics.

Our retrosynthetic route was designed as follows (Scheme I). Construction of the pyran ring system could be achieved by intramolecular Michael addition or etherification (for example, oxymercuration or phenylseleno etherification). The required carbon chains could be prepared by the reaction of alkanoylnaphthoquinone with simple or modified allylmetals. The success of this route requires the addition of an allyl group or a 3-(methoxycarbonyl)allyl group at the vicinal position of 2-alkanoyl 1,4-quinones.[15] In our preliminary reports,[16] we described the total syntheses of eleutherin (**1**),[17] isoeleutherin (**2**),[17] nanaomycin A (**3**), and deoxyfrenolicin (**5**) via the above

Scheme I



Scheme II



7 R=H
8a R=MeCO
8b R=n-PrCO
9a R=Me
9b R=n-Pr
10a R1=Me, R2=Me
10b R1=n-Pr, R2=Me
10c R1=Me, R2=H

route. In this paper we describe further details of this method.

[†] Present address: Advanced Instrumentation Center for Chemical Analysis, Ehime University, Bunkyo-cho, Matsuyama 790, Japan.

(1) Synthesis of Naturally Occurring Quinones. 17. Part 16: Uno, H.; Naruta, Y.; Maruyama, K. *Tetrahedron* **1984**, *40*, 4725.
(2) (a) Omura, S.; Tanaka, H.; Koyama, Y.; Katagiri, M. *J. Antibiot.* **1974**, *27*, 363. (b) Tanaka, H.; Koyama, Y.; Marumo, H.; Oiwa, R.; Katagiri, M.; Nagai, T.; Omura, S. *Ibid.* **1975**, *28*, 860. (c) Tanaka, H.; Koyama, Y.; Nagai, T.; Omura, S. *Ibid.* **1975**, *28*, 868.
(3) (a) van Meter, J. C.; Dann, M.; Bohonos, N. "Antibacterial Agents Annual–1960"; Prenum Press: New York, 1961; p 77. (b) Ellestad, G. A.; Kunstmann, M. P.; Whaley, H. A.; Patterson, E. L. *J. Am. Chem. Soc.* **1968**, *90*, 1325. (c) Iwai, Y.; Kora, A.; Takahashi, Y.; Hayashi, T.; Awaya, H.; Masuma, R.; Oiwa, R.; Omura, S. *J. Antibiot.* **1978**, *31*, 959.
(4) (a) Bergy, M. E. *J. Antibiot.* **1968**, *21*, 454. (b) Hoeksema, H.; Kruger, W. C. *Ibid.* **1976**, *29*, 704.
(5) Moore, H. W. *Science (Washington, D.C.)* **1977**, *197*, 527.
(6) Eisenhuth, W.; Schmid, H. *Helv. Chim. Acta* **1958**, *41*, 2021.
(7) Pyrek, J. St.; Achmatowicz, O., Jr.; Zamojski, A. *Tetrahedron* **1977**, *33*, 673.
(8) Li, T.-T.; Ellison, R. H. *J. Am. Chem. Soc.* **1978**, *100*, 6263.
(9) Kraus, G. A.; Roth, B. *J. Org. Chem.* **1978**, *43*, 4923.
(10) Ichihara, A.; Ubukata, M.; Oikawa, H.; Murakami, K.; Sakamura, S. *Tetrahedron Lett.* **1980**, *21*, 4469.
(11) (a) Kometani, T.; Yoshii, E. *J. Chem. Soc., Perkin Trans. 1* **1981**, 1191. (b) Kometani, T.; Yoshii, E. *J. Chem. Soc., Perkin Trans. 1* **1981**, 1197. (c) Kometani, T.; Takeuchi, Y.; Yoshii, E. *J. Org. Chem.* **1983**, *48*, 2631.
(12) Kraus, G. A.; Cho, H.; Crouley, S.; Roth, B.; Sugimoto, H.; Prugh, S. *J. Org. Chem.* **1983**, *48*, 3439.
(13) (a) Semmelhack, M. F.; Zark, A. *J. Am. Chem. Soc.* **1983**, *105*, 2034. (b) Semmelhack, M. F.; Bodurow, C.; Baum, M. *Tetrahedron Lett.* **1984**, *25*, 3171.
(14) South, M. S.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1984**, *106*, 4181.
(15) Naruta, Y.; Uno, H.; Maruyama, K. *Tetrahedron Lett.* **1981**, *22*, 5221.

0022-3263/86/1951-0350$01.50/0

Results and Discussion

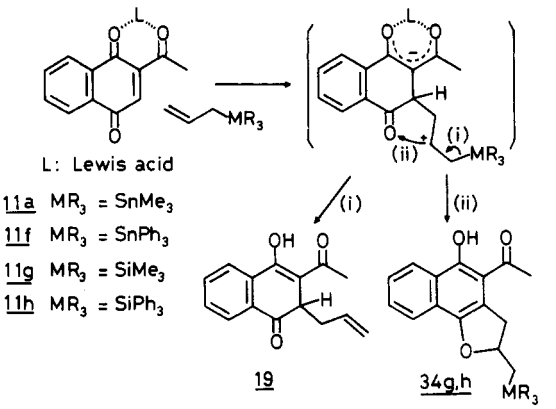
Preparation of 3-Alkanoyl Quinones. In our synthetic approach to pyranonaphthoquinone antibiotics, 3-alkanoyl-5-methoxy-1,4-naphthoquinones were chosen as starting quinones. However the reported procedures[18] for these quinones were unsatisfactory because large quantities of the starting materials were required. A new route to the quinones was developed as follows (Scheme II).

Acetylation of 1,5-dimethoxy-4-naphthol (**7**)[19] with acetic anhydride and pyridine gave the corresponding acetate **8a** in 94% yield after recrystallization from benzene–hexane. Fries rearrangement of acetate **8a** with BF_3·OEt_2 (neat or in dry xylene) at ca. 120 °C afforded a yellow fluorescent acetylnaphthol (**9a**) as fine yellow needles in 87% yield. Friedel–Crafts acetylation of the naphthol **7**, however, resulted in the formation of an inseparable mixture of **9a** and partially demethylated products. Oxidative demethylation of the acetylnaphthol **9a** with ceric(IV) ammonium nitrate (CAN) gave the desired quinone **10a** in 77% yield (63% overall yield from **7**). Exhaustive demethylation of **9a** with BBr_3 (2.2 equiv) followed by oxidation with an excess of Ag_2O afforded 3-acetyljuglone (**10c**) in 78% yield. In a similar manner butanoylquinone **10b** was obtained in 59% overall yield from naphthol **7** and butanoic anhydride.

Allylation of Alkanoyl Quinones with Allylmetals. Recent studies[20] have revealed that allyl derivatives of group IVa metals are one of the most efficient reagents for allylation of quinones in the presence of a Lewis acid. As a result of the mechanistic study, it was established that the allylation of alkyl and alkoxy quinones proceeds via 1,2-addition followed by allylic migration to give allylhydroquinones.[21] The Lewis acid employed plays two roles: activator of a quinone carbonyl group and acid catalyst for allylic migration. In the case of alkanoyl quinones, however, it turned out that allyl groups were directly introduced to the 3-position of the quinones.

In the absence of a Lewis acid the reaction of 2-acetyl-1,4-naphthoquinone (**18**) with the soft nucleophile allyltrimethylstannane (**11a**) gave a complex mixture, although the 3-position of the quinone **18** possessed strong electrophilic character and was easily attacked by anionic species.[12] On the other hand, the presence of a catalytic amount (0.1 equiv of the quinone) of Lewis acid (BF_3·OEt_2) in the reaction mixture led to instantaneous formation of conjugate adduct **19** in quantitative yield even at −78 °C (Table I, entry 4). Aromatization of the conjugate adduct **19** was suppressed by the steric interaction between the introduced allyl group and the vicinal acetyl group. Since the conjugate adduct **19** was rather unstable and aromatized during chromatographic separation on silica gel, the reaction mixture was treated with acetic anhydride and pyridine to obtain the diacetate and then chromatographed. Various combinations of alkanoyl quinones and allylstannanes were examined and the results are summarized in Table I.

Scheme III



Predominant formation of conjugate γ-addition products in the reaction with crotyl- and prenylstannanes (entries 2, 5, 7, 10, and 14) and isolation of the primary adducts support our direct addition mechanism. If we assume that 1,2 addition followed by allylic migration would be the main reaction pathway, crotyl and prenyl groups should be introduced at a less hindered position to minimize the steric interaction with the vicinal alkanoyl group.[20] Isomerization to the corresponding hydroquinone was observed even after immediate quenching in entries 1, 12, and 13, while in entries 2 and 11 primary 1,4-adducts were isolated by fractional crystallization. In the case of cinnamyltrimethylstannane (**11e**) (entry 8), partial retro-Claisen rearrangement led to a mixture of 1,4-adduct **24** (40%) and cinnamyl ether **25** (30%). During recrystallization of the mixture from benzene, however, the rearrangement was completed to afford **25** in 64% yield. In the reaction of *trans*-2-butenyltrimethylstannane (**11b**) (entry 2, 5, 10, and 14), formation of diastereomeric 1,4 adducts would be expected. In fact, when acetylnaphthoquinones were employed as substrates, two diastereomeric isomers of unknown stereochemistry were produced (entries 5 and 10). Interestingly, only one of the expected diastereomers could be obtained when benzoquinone derivatives were used (entries 2 and 14). The reason for this remarkable stereoselectivity remains unclear.

Other quinones substituted with formyl or methoxycarbonyl were also effectively allylated (entries 12, 13, and 14). In the former case, it is interesting to note that the conjugate addition occurred in preference to attack of the reactive formyl group.

While in the case of allylstannanes only allylation of the quinones was observed, allyltriphenylsilane (**11h**) afforded an interesting product, to which was assigned dihydrofuran structure **34h** (Table II). Use of the stronger Lewis acid ($AlCl_3$) and higher temperature were required to obtain good yield because of the low reactivity of silane **11h**. This dihydrofuran ring formation could be explained in terms of the metal effect as described below. After the conjugate addition of allylmetal to quinone, the resulting cation stabilized by the σ–π conjugation with silicon would react via two competing pathways: (i) elimination of the metal group or (ii) intramolecular electrophilic attack on the carbonyl oxygen atom (Scheme III). Since in acidic media the dissociation rate decreases in the order of R_3SnC < Me_3SiC < Ph_3SiC, the triphenylsilyl group would prefer

(16) (a) Naruta, Y.; Uno, H.; Maruyama, K. *J. Chem. Soc., Chem. Commun.* **1981**, 1277. (b) Naruta, Y.; Uno, H.; Maruyama, K. *Chem. Lett.* **1982**, 609.

(17) (a) Schmid, H.; Ebnother, A. Meijer, Th. M. *Helv. Chim. Acta* **1950**, *33*, 1751. (b) Schmid, H.; Ebnother, A. *Ibid.* **1951**, *34*, 561. (c) Cameron, D. W.; Kingston, D. G. I.; Sheppard, N.; Todd, R. *J. Chem. Soc.* **1964**, 98.

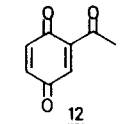
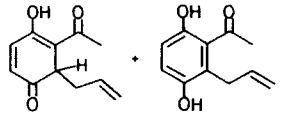
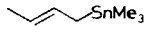
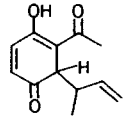
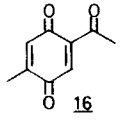
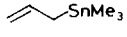
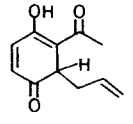
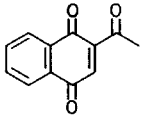
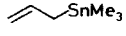
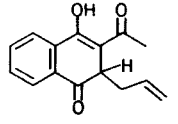
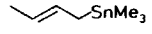
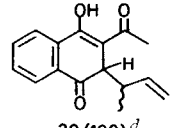
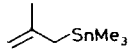
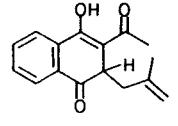
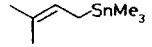
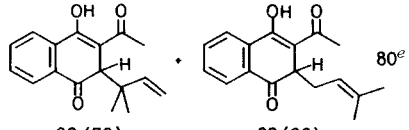
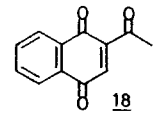
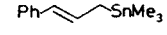
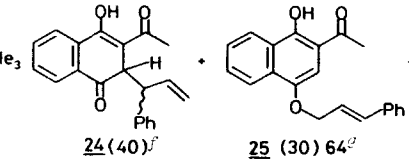
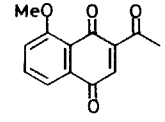
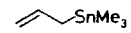
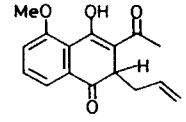
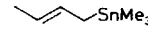
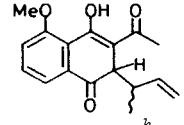
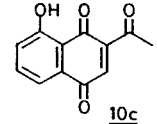
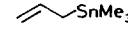
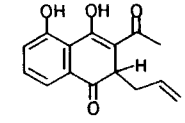
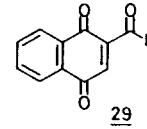
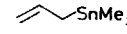
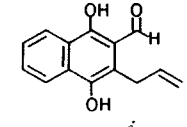
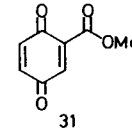
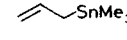
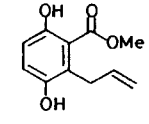
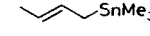
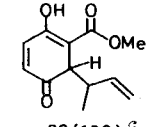
(18) (a) Nenchi, M.; Schmidt, W. *J. Pract. Chem.* **1981**, *23*, 546. (b) Klotzel, M. C.; Daiton, R. P.; Ababier, B. Y. *J. Org. Chem.* **1955**, *20*, 38. (c) Kurosawa, E. *Bull. Chem. Soc. Jpn.* **1964**, *34*, 300. (d) Hardegger, E.; Widmer, E.; Steiner, K.; Pfiffner, A. *Helv. Chim. Acta* **1964**, *47*, 2027. (e) Bosshard, P.; Fumagalli, S.; Good, R.; Treub, W.; Philipsborn, W.; Eugster, C. H. *Ibid.* **1964**, *47*, 769.

(19) Hannan, R. L.; Barber, R. B.; Rapoport, H. *J. Org. Chem.* **1979**, *44*, 2153.

(20) (a) Naruta, Y. *J. Am. Chem. Soc.* **1980**, *102*, 3774. (b) Naruta, Y. *J. Org. Chem.* **1980**, *45*, 4097. (c) Maruyama, K.; Takuwa, A.; Naruta, Y.; Satao, K.; Soga, O. *Chem. Lett.* **1981**, 47.

(21) It was also established that quinols were intermediates to allylhydroquinones in the reaction of (π-allyl)nickel bromide with quinones, see: Hegedus, L. S.; Evans, B. R. *J. Am. Chem. Soc.* **1978**, *100*, 3461.

Table I. Allylation of Alkanoyl Quinone

Entry	Quinone	Stannane	Products NMR Yield/%[a]	Isol. Yield/%[b]
1	 12	 11a	 13(64) + 14(18)	61
2		 11b	 15(100)[c]	91
3	 16	 11a	 17(100)	64
4	 18	 11a	 19(100)	95
5		 11b	 20(100)[d]	84
6		 11c	 21(100)	84
7		 11d	 22(70) + 23(30)	80[e]
8	 18	 11e	 24(40)[f] + 25(30) 64[d]	-
9	 10a	 11a	 26(100)	-
10		 11b	 27(100)[h]	74
11	 10c	 11a	 28(100)	-
12	 29	 11a	 30 39[i]	-
13	 31	 11a	 32(100)	71[j]
14		 11b	 33(100)[e]	80

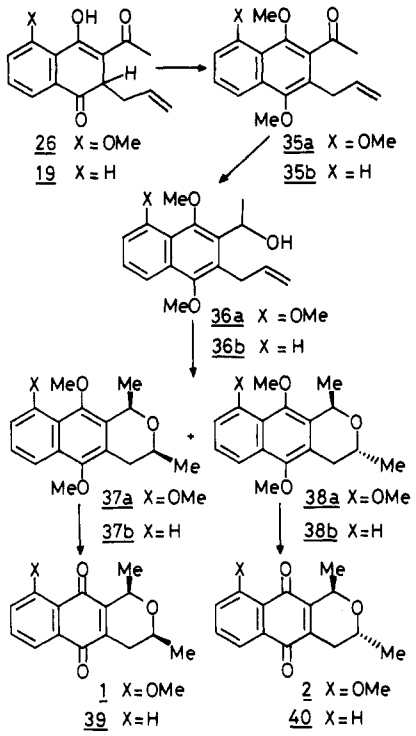
[a] Yields were estimated by ^{1}H NMR using *cis*-dichloroethylene as an internal standard. [b] Isolated yield of the corresponding diacetate otherwise noted. [c] Only one diastereomer whose configuration was not assigned. [d] Diastereomeric mixture (68:32). [e] A mixture of two regioisomers ($\gamma:\alpha$ = 88:12) after purification by column chromatography. [f] The diastereomeric ratio could not be determined. [g] Isolated yield by recrystallization from benzene. [h] Diastereomeric mixture (54:46). [i] Isolated yield by column chromatography. [j] Isolated yield of the corresponding quinone after treatment with Ag_2O in ether.

Table II. Reaction of Acetylnaphthoquinone with Allylmetals

entry	allyl-MR_3	conditions	yield,[a] % 19	34
4	**11a**, allyl-$SnMe_3$	BF_3-OEt_2, −78 °C, 1 h	(100)	
15	**11f**, allyl-$SnPh_3$	BF_3-OEt_2, −78 °C, 1 h	(47)	
16	**11g**, allyl-$SiMe_3$	BF_3-OEt_2, −50 °C, 1 h	(39)	(30)
17	**11h**, allyl-$SiPh_3$	$AlCl_3$, 0 °C, 0.5 h	trace	61[b]

[a] Yields were determined by ^1H NMR using *cis*-dichloroethylene as an internal standard. [b] Isolated yield.

Scheme IV



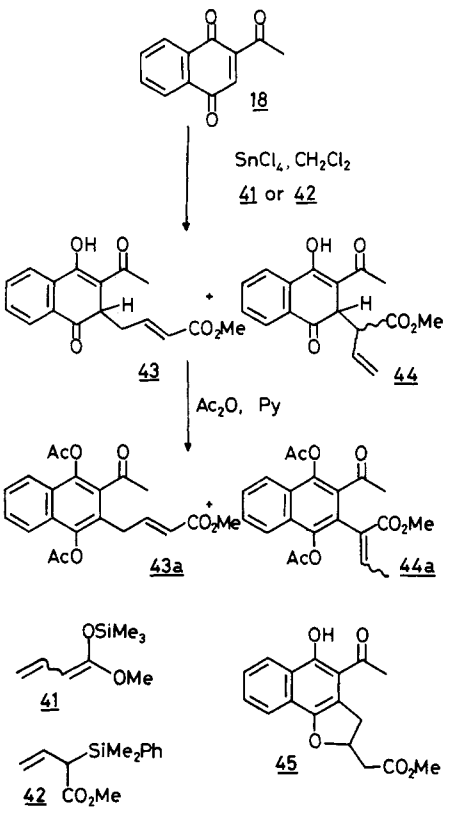
the latter pathway (ii). Thus, stannyl groups were completely eliminated to afford the allylation product, while two products were obtained in comparable yields when allyltrimethylsilane was used. Results are summarized in Table II.

Synthesis of (±)-Eleutherin, (±)-Isoeleutherin, and Their Demethoxy Analogues. We attempted to synthesize these quinones using the allylated alkanoyl quinones successfully prepared by the method described above (Scheme IV).

Allylated product **26** was directly converted to the corresponding trimethoxynaphthalene **35a** in 92% yield by treatment with MeI and K_2CO_3 in acetone. Reduction of **35a** with $LiAlH_4$ produced alcohol **36a** in 98% yield. Intramolecular oxymercuration[11,22] and subsequent reduction with $NaBH_4$ gave a mixture of two diastereomeric naphthopyrans (**37a**:**38a** = ca. 1:1, combined yield was 93%). Separation by column chromatography (silica gel, 10–20% ether–hexane as eluent) gave the pure cis and trans isomers **37a** (42%) and **38a** (47%). Each isomer (**37a** or **38a**) was separately oxidized by CAN[10] to afford (±)-eleutherin (**1**) (90%) and (±)-isoeleutherin (**2**) (89%). Overall yields of (±)-eleutherin and (±)-isoeleutherin were 38% and 34%, respectively, and conversion of the starting quinone **10a** was 73%.

Similarly, the demethoxy analogues were synthesized from **19**. Direct methylation (MeI, K_2CO_3) of **19** gave **35b** (87%), which was reduced with $LiAlH_4$ to give alcohol **36b** (68%). Phenylseleno etherification with PhSeBr[23] followed by reductive elimination (Raney nickel) gave a diastereomeric mixture of naphthopyrans (**37b**:**38b** = ca. 2:1, combined yield was 51%), which on oxidation with CAN gave a mixture of (±)-demethoxyeleutherin (**39**) and (±)-demethoxyisoeleutherin (**40**) (combined yield, 98%), which were isolated by preparative TLC (**39**, 54%; **40**, 26%).

Scheme V



Synthesis of (±)-Nanaomycin A and (±)-Deoxyfrenolicin. For the synthesis of the antibiotics, we needed a synthon for the 3-(methoxycarbonyl)allyl anion with soft nucleophilic character in order to prevent further reactions.[24] A dienol silyl ether seemed to be a potential candidate for such a synthon according to Fleming and his co-workers' work.[25] However, reaction of acetylnaphthoquinone (**18**) with dienol silyl ether **41** gave a mixture of γ- and α-addition products, which was immediately treated with Ac_2O and pyridine. By ^1H NMR analysis, the reaction mixture was determined to consist of γ-adduct **43a** (35%) and α-adduct **44a** (65%). In the course of acetylation the double bond of the latter compound had migrated to the position conjugated to the aromatic ring (Scheme V). On the other hand, methyl 2-(dimethylphenylsilyl)-3-butenoate (**42**), whose preparation and application have already been reported,[1,16b,26] reacted only at the γ-position. In addition, the silicon–carbon bond of the reagent is so polarized and so weakened by the geminal methoxycarbonyl group that desilylation occurred to give **43** quantitatively. Under basic conditions,

(22) Brown, H. C.; Rei, M.-H. *J. Am. Chem. Soc.* **1969**, *91*, 5646.

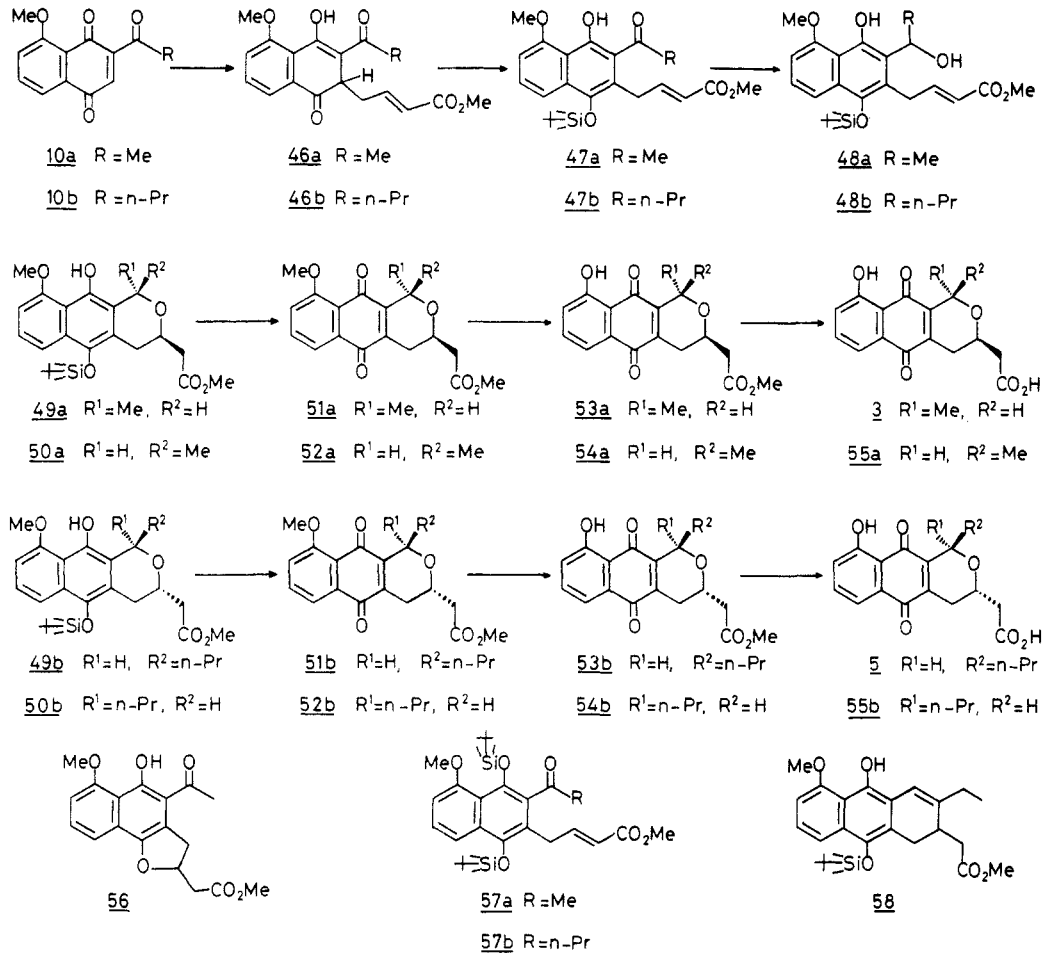
(23) Nicolaou, K. C.; Magolda, R. L.; Sipio, W. J.; Barnette, W. E.; Lysenko, Z.; Joullie, M. M. *J. Am. Chem. Soc.* **1980**, *102*, 3784.

(24) Rieck, A. J.; Grunwell, R. J. *J. Org. Chem.* **1980**, *45*, 3512.

(25) Fleming, I.; Goldhill, J.; Paterson, I. *Tetrahedron Lett.* **1979**, 3205, 3209, and references cited therein.

(26) (a) Naruta, Y.; Uno, H.; Maruyama, K. *Chem. Lett.* **1982**, 961. Also see: (b) Albaugh-Robertson, P.; Katzenellenbogen, J. A. *Tetrahedron Lett.* **1982**, *23*, 723. (c) Albaugh-Robertson, P.; Katzenellenbogen, J. A. *J. Org. Chem.* **1983**, *48*, 5288. (d) Morizawa, Y.; Kanemoto, S.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1982**, *23*, 2953.

Scheme VI



43 spontaneously isomerized to dihydrofuran derivative **45**.

Having settled on a reaction to introduce a (methoxycarbonyl)allyl group, we set about synthesizing the antibiotics (Scheme VI). Reaction of the acetyljuglone derivative **10a** with butenoate **42** using $SnCl_4$ as catalyst afforded the conjugate adduct **46a** in quantitative yield (88% isolated yield after crystallization from ether). Once **46a** aromatized to the corresponding hydroquinone, intramolecular cyclization occurred to give undesired dihydrofuran derivative **56**. To avoid this side reaction, **46a** was treated with *t*-$BuMe_2SiCl$ and imidazole in DMF[27] for 3 h afforded the corresponding monosilyl ether **47a** (80%) selectively. A prolonged reaction time, however, caused the production of the disilyl ether **57a**, which was found to be inert toward reduction with $NaBH_4$ probably because of its steric hindrance. Reaction of **47a** with an excess of $NaBH_4$ in methanol followed by base-catalyzed intramolecular Michael addition (NaOMe, MeOH, room temperature, 1 h) gave a mixture of two diastereomers (**49a**:**50a** = ca. 1:1, 89% yield from **47a**). The isomer ratio was determined by the phenolic proton signals in the ^1H NMR spectrum of the mixture (**49a**, δ = 9.22 ppm; **50a**, δ = 9.32 ppm). Chromatographic separation of the two diastereomers (silica gel, hexane–CH_2Cl_2 as eluent) afforded pure **49a** and **50a**. Desilylative oxidation of **49a** and **50a** with CAN gave quinones **51a** (73%) and **52a** (91%), respectively. Each of them was demethylated with $AlCl_3$[7] to give (±)-nanaomycin A methyl ester (**53a**) (94%) and its (±) epimer (**54a**) (98%). Acid-catalyzed isomerization[7] (concentrated H_2SO_4) of **54a** afforded an equilibrium mixture (**53a**:**54a** = ca. 2:1 determined by NMR). Saponification[9] (0.1 N KOH) of the trans isomer **53a** afforded (±)-nanaomycin A (**3**) in 94% yield. All spectroscopic data (NMR, IR, and MS) and melting points are identical with those of natural or synthetic products. (±)-Epinanaomycin A (**55a**) was also obtained from the cis isomer **54a** in 67% yield.

In a similar manner, (±)-deoxyfrenolicin (**5**) was synthesized from the 3-butanoylquinone **10b**. Lewis acid mediated reaction of **10b** with **42** gave **46b** (94% isolated yield by crystallization from ether), which was silylated to give **47b** (82%). When **47b** was treated with an excess of $NaBH_4$ in dioxane at room temperature, reduction of the keto group and subsequent intramolecular Michael addition occurred to give an isomeric mixture of **49b** and **50b** (**49b**:**50b** = ca. 2:5, 85% yield) accompanied by small amounts of **48b** and **58**. Formation of **58** could be understood as follows: Enolate anion of **47b** generated by base cyclized to give a tetrahydroanthracene derivative, which was reduced and dehydrated to produce **58**. In absolute dioxane, the main product was benzylic alcohol **48b** which could be converted to **49b** and **50b** by base treatment. A trace amount of water present in dioxane might have promoted the cyclization. Chromatographic separation of the diasteromeric mixture afforded pure **49b** and **50b** which, on oxidation with CAN and subsequent demethylation with $AlCl_3$, gave **53b** (73%) and **54b** (88%), respectively. Acid-catalyzed epimerization[7] of **54b** (concentrated H_2SO_4) gave mainly the desired **53b** (**53b**:**54b** = ca. 5.3:1, determined by NMR). Hydrolysis of *trans*-**53b** gave (±)-deoxyfrenolicin (**5**) in 85% yield, and (±)-epideoxyfrenolicin (**55b**) was similarly obtained from *cis*-**54b**

(27) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190.

in 85% yield. Their spectroscopic data and melting points are identical with the reported ones.

Thus we have established a synthetic route to (±)-nanaomycin A and (±)-deoxyfrenolicin via seven steps from the starting alkanoyl quinones in respective overall yields of 38% and 43%.

Experimental Section

General Methods. Melting points were measured with a Yanagimoto micromelting point apparatus and are uncorrected. Proton nuclear magnetic resonance spectra were observed with JEOL PS-100, JNM-MH-100, and JEOL-GX-400 spectrometers with tetramethylsilane as an internal standard, and chemical shifts are reported in δ values. Infrared spectra were measured with a JASCO IRA-1 spectrometer. Mass spectra were measured with Hitachi M-52 and JEOL JMS-DX 300 mass spectrometers. Column chromatography was performed on Wako-gel C-200. Microanalyses were performed by the Microanalytical Laboratory of Kyoto University. All solvents were freshly distilled and stored under a nitrogen atmosphere. Dichloromethane was distilled from calcium hydride. Ether and THF were distilled from benzophenone ketyl and stored over sodium wire. Dioxane was distilled from sodium. Unless otherwise noted, other solvents were used after simple distillation. Allylstannanes **11a–e** were prepared by the reported method.[20] Commercially available Lewis acids, $TiCl_4$, $AlCl_3$, $SnCl_4$, and $BF_3{\cdot}OEt_2$, were used without further purification.

2-Formyl-1,4-naphthoquinone (29). To 1,4-dimethoxynaphthalene (3.76 g, 20 mmol) in 40 mL of $CHCl_3$ was added Br_2 (3.2 g) in $CHCl_3$ (6 mL) in the presence of iron powder followed by the usual workup to afford 2-bromo-1,4-dimethoxynaphthalene (5.11 g, 96%): colorless plates; mp 54–55 °C; NMR ($CDCl_3$) δ 3.90 (s, 6 H), 6.77 (s, 1 H), 7.20 (m, 2 H), 8.04 (m, 2 H). The bromide (5.34 g, 20 mmol) in 20 mL of THF was added dropwise to a suspension of magnesium (0.51 g) in 50 mL of THF followed by addition of DMF (10 mL). The reaction mixture was quenched with aqueous ammonium chloride solution and extracted with ether. The ethereal phase was washed with water and brine and then dried over Na_2SO_4. After evaporation and isolation by column chromatography on silica gel (benzene–ether as eluent), 2-formyl-1,4-dimethoxynaphthalene (2.57 g, 60%) was obtained as pale yellow needles: mp 118–119 °C; NMR ($CDCl_3$) δ 4.03 (s, 3 H), 4.11 (s, 3 H), 7.14 (s, 1 H), 7.64 (m, 2 H), 8.27 (m, 2 H), 10.61 (s, 1 H). Demethylative oxidation was carried out by following the method of Rapoport et al.[28] To a suspension of 2-formyl-1,4-dimethoxynaphthalene (648 mg, 3 mmol) and AgO (1.5 g) in dioxane (30 mL) was added 6 N HNO_3 (3 mL). When AgO was consumed, the reaction was terminated by addition of $CHCl_3/H_2O$ (120 mL/30 mL). The organic layer was washed with water and evaporated in vacuo to afford **29** as yellow crystals: NMR ($CDCl_3$) δ 7.28 (s, 1 H), 7.60–8.32 (m, 4 H), 10.52 (s, 1 H). The quinone was immediately used without further purification because of its instability.

4-Acetoxy-1,5-dimethoxynaphthalene (8a). 1,5-Dimethoxy-4-naphthol (**7**)[19] (4.08 g, 20 mmol) was dissolved into a mixture of pyridine (30 mL) and acetic anhydride (20 mL) by external heating. The mixture was stirred for 12 h at room temperature and then poured into 500 mL of water. After the resulting suspension was stirred for additional 30 min, the precipitate was filtered and washed with water for several times. Recrystallization of the precipitate from benzene–hexane gave 4.62 g (18.8 mmol, 94%) of **8a** as colorless plates: mp 119–121 °C; NMR ($CDCl_3$) δ 2.31 (s, 3 H), 3.85 (s, 3 H), 3.90 (s, 3 H), 6.64–7.00 (m, 3 H), 7.30 (t, 1 H, J = 8 Hz), 7.81 (d, 1 H, J = 8 Hz); IR (KBr) 1750 cm^{-1} (vs). Anal. Calcd for $C_{14}H_{14}O_4$: C, 68.28; H, 5.73. Found: C, 68.20; H, 5.80.

3-Acetyl-1,5-dimethoxy-4-naphthol (9a). The flask containing **8a** (4.404 g, 17.9 mmol) was heated at ca. 120 °C, and then 2.56 mL of $BF_3{\cdot}OEt_2$ was added by a syringe. Vigorous evolution of ether occurred to afford dark red solids. After 5 min, the solids were decomposed by addition of water (200 mL) and CH_2Cl_2 (100 mL). The aqueous layer was extracted with CH_2Cl_2, the combined organic phase was washed with water and brine and dried over Na_2SO_4, and the solvent was evaporated to give a crude material, which was chromatographed through a short silica gel column (CH_2Cl_2 as eluent) and recrystallized from benzene–hexane to give 3.84 g (15.8 mmol, 87%) of **9a** as fine yellow needles: yellow fluorescent in solution; mp 133–135 °C; NMR ($CDCl_3$) δ 2.76 (s, 3 H), 3.93 (s, 3 H), 4.04 (s, 3 H), 6.08–6.96 (m, 2 H), 7.44 (t, 1 H, J = 8 Hz), 7.72 (d, 1 H, J = 8 Hz), 13.28 (s, 1 H); IR (KBr) 3335 (s), 1605 cm^{-1} (vs). Anal. Calcd for $C_{14}H_{14}O_4$: C, 68.28; H, 5.73. Found: C, 67.98; H, 5.83.

3-Acetyl-5-methoxy-1,4-naphthoquinone (10a). A solution of CAN (2.72 g) in water (15 mL) was added to an acetonitrile solution (35 mL) of **9a** (492 mg, 2 mmol). The mixture was stirred for 5 min and then poured into water–CH_2Cl_2. The aqueous phase was extracted with CH_2Cl_2. The combined organic phase was washed with water and brine and dried over Na_2SO_4, and the solvent was evaporated to give 423 mg (1.84 mmol, 92%) of **10a**. Recrystallization from ether–hexane gave 353 mg (1.54 mmol, 77%) of the quinone **10a** as long yellow needles: mp 101–105 °C dec; NMR ($CDCl_3$) δ 2.59 (s, 3 H), 4.01 (s, 3 H), 6.93 (s, 1 H), 7.36 (dd, 1 H, J = 8, 3 Hz), 7.55–7.80 (m, 2 H); IR (KBr) 1685 (vs), 1655 cm^{-1} (vs). Anal. Calcd for $C_{13}H_{10}O_4$: C, 67.82; H, 4.38. Found: C, 67.99; H, 4.47.

3-Acetyl-5-hydroxy-1,4-naphthoquinone (10c) (3-Acetyljuglone). To a solution of **9a** (442 mg, 1.8 mmol) in CH_2Cl_2 (40 mL) was added dropwise BBr_3 (0.38 mL in 8 mL of CH_2Cl_2) at −78 °C with stirring. The mixture was gradually warmed to room temperature and stirred for an additional 3 h. The reaction mixture was quenched with 50 mL of water and extracted with ether. The ethereal phase was washed with water and brine and dried over $MgSO_4$, and the solvent was evaporated to give 379 mg (1.74 mmol, 97%) of crude 3-acetyl-1,4,5-trihydroxynaphthalene: NMR (acetone-d_6) δ 2.69 (s, 3 H), 6.98 (dd, 1 H, aromatic H, J = 8, 2 Hz), 7.06 (s, 1 H, Ar H), 7.40–7.70 (m, 2 H, Ar H), 8.96 (s, 1 H, 1-phenolic H), 9.90 (s, 1 H, 5-phenolic H), 15.63 (s, 1 H, 4-phenolic H). The crude hydroxynaphthalene was dissolved in ether and then Ag_2O (1.27 g) and $MgSO_4$ (5 g) were added. The suspension was stirred overnight and filtered through a $MgSO_4$ column, which was washed with ether, and the combined ethereal solution was evaporated to give 304 mg (1.41 mmol, 78% from **9a**) of 3-acetyljuglone (**10c**): orange needles recrystallized from ether–hexane; mp 98 °C dec; NMR ($CDCl_3$) δ 2.60 (s, 3 H), 7.07 (s, 1 H, ring H), 7.20–7.70 (m, 3 H, Ar H), 11.71 (s, 1 H, phenolic H); IR (KBr) 3040 (w), 1695 (vs), 1660 (vs), 1630 cm^{-1} (vs). Anal. Calcd for $C_{12}H_8O_4$: C, 66.67; H, 3.73. Found: C, 66.57; H, 3.92.

Reaction of Allyltrimethylstannanes with Alkanoyl Quinones. General Procedure. The reactions of alkanoyl quinones and allyltrimethylstannanes were carried out by a standard procedure. The quinone (1 mmol) was placed in a two-necked, 50-mL flask fitted with a stopcock and a rubber serum cap. The vessel was filled with nitrogen. After addition of CH_2Cl_2 (30 mL), $BF_3{\cdot}OEt_2$ (0.13 mL, 1 mmol) was added at −78 °C with stirring. The stannane reagent (1.2 mmol) was slowly added by syringe. The mixture was stirred at −78 °C for 1 h after the addition was complete. The reaction mixture was quenched with water and extracted with CH_2Cl_2 or ether. The organic phase was washed with water and brine and then dried by being passed through a $MgSO_4$ column. After evaporation of solvent *cis*-dichloroethylene (ca. 0.5 mmol) was added to the residue and the ^1H NMR spectra was run. The residue was dissolved into a mixture of pyridine and acetic anhydride (1 mL/1 mL) and stirred at room temperature overnight. Water and ether (20 mL/20 mL) was added to the solution, and the mixture was stirred for additional 0.5 h. The aqueous phase was extracted with ether or CH_2Cl_2, the combined organic phase was washed with water and brine and dried over $MgSO_4$, and the solvent was evaporated. The products were purified by column chromatography on silica gel (hexane–ether or benzene–ether as eluent) and/or by recrystallization from ether–hexane.

3-Acetyl-2-allyl-1,4,5-trimethoxynaphthalene (35a). According to the general procedure, **26** was prepared by the reaction of **10a** (1.15 g, 5 mmol) with **11a** (1.23 g, 6 mmol). **26**: NMR ($CDCl_3$) δ 2.25 (s, 3 H), 2.39 (m, 2 H, allylic H), 3.59 (dd, 1 H, ring H, J = 8, 6 Hz), 4.00 (s, 3 H), 4.8–5.2 (m, 2 H, —CH=CH_2), 5.67 (ddt, 1 H, —CH=CH_2, J = 17, 11, 7 Hz), 7.2–7.4 (m, 1 H, Ar H), 16.92 (s, 1 H, hydroxylic H). A vessel containing **26** was purged with nitrogen, and dry acetone (150 mL), MeI (5 mL), and

(28) Snider, C. D.; Rapoport, H. *J. Am. Chem. Soc.* **1972**, *94*, 227.

K_2CO_3 (15 g) were added to it. The mixture was refluxed overnight under nitrogen. The reaction was quenched by addition of water and ether. The aqueous phase was extracted with ether, the combined organic phase was washed with water and brine and dried over $MgSO_4$, and the solvent was evaporated. Column chromatography on silica gel (CH_2Cl_2 as eluent) gave 1.376 g (4.59 mmol, 92%) of **35a**: a pale yellow viscous oil; NMR ($CDCl_3$) δ 2.58 (s, 3 H), 3.55 (d, 2 H, J = 6 Hz), 3.77 (s, 3 H), 3.86 (s, 3 H), 3.99 (s, 3 H), 4.84–5.12 (m, 2 H), 5.95 (ddt, 1 H, J = 17.5, 10.5, 6 Hz), 6.87 (d, 1 H, J = 8 Hz), 7.41 (t, 1 H, J = 8 Hz), 7.67 (d, 1 H, J = 8 Hz); IR (NaCl) 2930 (m), 1700 (vs), 1570 (vs), 1370 (vs), 1265 (vs), 1070 cm^{-1} (vs); MS, m/e 300 (M^+, 51), 285 (100), 270 (42), 255 (27).

2-Allyl-3-(1-hydroxyethyl)-1,4,5-trimethoxynaphthalene (36a). To a solution of the ketone **35a** (600 mg, 2 mmol) in dry ether (30 mL) was added 3 mL of 0.74 M ethereal $LiAlH_4$ solution (2.22 mmol) with stirring at 0 °C. After being stirred for 1 h, the reaction mixture was poured into water and acidified with 0.5 N HCl. The organic phase was separated and the aqueous phase was extracted with ether. The combined organic phase was washed sequentially with water, aqueous $NaHCO_3$, water, and brine and dried over $MgSO_4$. After evaporation, the residue was chromatographed on silica gel (CH_2Cl_2 as eluent) to give 296 mg (1.96 mmol, 98%) of **36a**:[11b] a colorless viscous oil; NMR ($CDCl_3$) δ 1.63 (d, 3 H, J = 7 Hz), 3.67 (m, 2 H), 3.84 (s, 3 H), 3.90 (s, 3 H), 3.99 (s, 3 H), 4.83–5.18 (m, 2 H), 5.22 (m, 1 H), 6.06 (ddt, 1 H, J = 17, 11, 7 Hz), 6.47 (d, 1 H, J = 8 Hz), 7.38 (t, 1 H, J = 8 Hz), 7.68 (d, 1 H, J = 8 Hz); IR (NaCl) 3460 (m), 2920 (s), 1570 (vs), 1370 (vs), 1360 (vs), 1260 (vs), 1070 cm^{-1} (vs).

***cis*- and *trans*-5,9,10-Trimethoxy-1,3-dimethyl-3,4-dihydro-1*H*-naphtho[2,3-*c*]pyran (37a and 38a).** A mixture of **36a** (604 mg, 2 mmol) and mercury(II) acetate (653 mg, 2.05 mmol) in THF (5 mL) and water (5 mL) was stirred for 1 h and then 3 N aqueous NaOH (2.05 mL) was added. The mixture was stirred for 1 h, and $NaBH_4$ (3 M solution in 3 N aqueous NaOH; 10 mL, 30 mmol) was added. The mixture was stirred at room temperature for 30 min, diluted with water, and extracted with ether. The ethereal phase was washed with water and brine and dried over $MgSO_4$. The solvent was evaporated to give a mixture of naphthopyrans as a pale yellow oil (560 mg, 93%). The ratio of cis and trans isomers was estimated to be ca. 10:9 by NMR spectroscopy on the basis of the integral ratio of the two 1-H signals (**37a** (cis isomer) 5.10 ppm, **38a** (trans isomer) 5.15 ppm) upon irradiating at 1-CH_3 (1.52 ppm). Column chromatography on silica gel (hexane–ether as eluent) gave pure **37a** and **38a**. **37a** (cis isomer, 282 mg, 47%, first eluted): colorless needles recrystallized from ether–hexane; mp 106–107 °C; NMR (CCl_4) δ 1.33 (d, 3 H, 3-CH_3, J = 6 Hz), 1.53 (d, 3 H, 1-CH_3, J = 7 Hz), 2.48 (dd, 1 H, 4-pseudoaxial H, J = 16, 11 Hz), 2.96 (dd, 1 H, 4-pseudoequatorial H, J = 16, 2 Hz), 3.6 (m, 1 H, 3-H), 3.68 (s, 3 H), 3.81 (s, 3 H), 3.92 (s, 3 H), 5.10 (quartet, 1 H, 1-H, J = 6 Hz), 6.70 (d, 1 H, Ar H, J = 8 Hz), 7.22 (t, 1 H, Ar H, J = 8 Hz), 7.56 (d, 1 H, Ar H, J = 8 Hz); IR (KBr) 2960 (m), 2830 (m), 1565 (s), 1370 (vs), 1330 (s), 1260 (s), 1070 cm^{-1} (vs). Anal. Calcd for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33. Found: C, 71.79; H, 7.22. **38a** (trans isomer, 253 mg, 42%, secondarily eluted): colorless needles recrystallized from ether–hexane; mp 95.5–96.5 °C; NMR (CCl_4) δ 1.31 (d, 3 H, 3-CH_3, J = 6 Hz), 1.51 (d, 3 H, 1-CH_3, J = 7 Hz), 2.47 (dd, 1 H, 4-pseudoaxial H, J = 16, 1 Hz), 2.96 (dd, 1 H, 4-pseudoequatorial H, J = 16, 3 Hz), 3.72 (s, 3 H), 3.77 (s, 3 H), 3.91 (s, 3 H), 3.80–4.05 (m, 1 H, 3-H), 5.15 (quartet, 1 H, 1-H, J = 7 Hz), 6.69 (d, 1 H, Ar H, J = 8 Hz), 7.18 (t, 1 H, Ar H, J = 8 Hz), 7.52 (d, 1 H, Ar H, J = 8 Hz); IR (KBr) 2960 (m), 2820 (m), 1570 (s), 1370 (s), 1335 (s), 1060 cm^{-1} (vs). Anal. Calcd for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33. Found: C, 71.41; H, 7.41.

(±)-Eleutherin (1). A solution of CAN (664 mg) in water (5 mL) was added to an acetonitrile solution (10 mL) of the *cis*-naphthopyran **37a** (150 mg, 0.497 mmol) at room temperature. After usual workup, the reaction mixture was chromatographed on silica gel (CH_2Cl_2–hexane as eluent) to give 121 mg (0.445 mmol, 90%) of pure (±)-eleutherin (1): yellow needles recrystallized from EtOH; mp 158–160 °C (lit. mp 155.5–156.5[6] and 155–156 °C[11b]); NMR ($CDCl_3$) δ 1.34 (d, 3 H, J = 6 Hz), 1.51 (d, 3 H, J = 7 Hz), 2.20 (ddd, 1 H, J = 18, 10, 3.5 Hz), 2.73 (dt, 1 H, J = 18, 2.5 Hz), 3.58 (m, 1 H), 3.98 (s, 3 H), 4.84 (m, 1 H), 7.26 (m, 1 H), 7.5–7.8 (m, 2 H); IR (KBr) 1645 (vs), 1590 cm^{-1} (vs). Anal. Calcd for $C_{16}H_{16}O_4$: C, 70.58; H, 5.92. Found: C, 70.28; H, 5.87.

(±)-Isoeleutherin (2). Oxidation of the *trans*-naphthopyran **38a** (100 mg, 0.331 mmol) in acetonitrile (7 mL) with CAN (443 mg) dissolved in water (3 mL) was performed in the similar manner as 1 to afford 80 mg (0.294 mmol, 89%) of pure (±)-isoeleutherin (2): yellow needles recrystallized from EtOH; mp 149–151 °C (lit. mp 154–155[6] and 154–155 °C[11b]); NMR ($CDCl_3$) δ 1.33 (d, 3 H, J = 6 Hz), 1.52 (d, 3 H, J = 7 Hz), 2.23 (ddd, 1 H, J = 19, 10, 2 Hz), 2.67 (dd, 1 H, J = 19.4, 4 Hz), 3.85 (m, 1 H), 3.99 (s, 3 H), 4.99 (quartet, 1 H, J = 7 Hz), 7.26 (m, 1 H), 7.5–7.8 (m, 2 H); IR (KBr) 1645 (vs), 1580 cm^{-1} (vs). Anal. Calcd for $C_{16}H_{16}O_4$: C, 70.58; H, 5.92. Found: C, 70.32; H, 5.91.

(±)-Demethoxyeleutherin (39) and (±)-Demethoxyisoeleutherin (40). Oxidation of the diastereomeric naphthopyrans (95 mg, 0.35 mmol, **37b**:**38b** = ca. 2:1) with CAN (465 mg) was performed in the similar manner as described above to give 83 mg (0.34 mmol, 98%) of a diastereomeric mixture of the title quinones (**39**:**40** = ca. 3:2). The two quinones were separated by preparative thin layer chromatography developed with CH_2Cl_2. The upper band contained 46 mg (0.19 mmol, 54%) of (±)-demethoxyeleutherin (**39**): yellow needles recrystallized from EtOH; mp 143.5–145 °C (lit.[11a] mp 122–125 °C): NMR ($CDCl_3$) δ 1.36 (d, 3 H, J = 7 Hz), 1.55 (d, 3 H, J = 7 Hz), 2.26 (ddd, 1 H, J = 18.9, 3.5 Hz), 2.78 (dt, 1 H, J = 18, 2.5 Hz), 3.60 (m, 1 H), 4.83 (m, 1 H), 7.6–7.8 (m, 2 H), 7.95–8.00 (m, 2 H); IR (KBr) 1655 (vs), 1615 (m), 1590 (s), 1390 (s), 1330 (s), 1300 cm^{-1} (vs); MS, m/e 242 (M^+, 100), 227 (100), 224 (51), 213 (41). Anal. Calcd for $C_{15}H_{14}O_3$: C, 74.37; H, 5.82. Found: C, 73.72; H, 5.71. The lower band contained 22 mg (0.091, 26%) of (±)-demethoxyisoeleutherin (**40**): yellow needles recrystallized from EtOH; mp 150.5–151.5 °C (lit.[10] mp 146–148 °C); NMR ($CDCl_3$) δ 1.35 (d, 3 H, J = 7 Hz), 1.53 (d, 3 H, J = 7 Hz), 2.35 (ddd, 1 H, J = 19, 10, 2 Hz), 2.74 (dd, 1 H, J = 19, 4 Hz), 4.00 (m, 1 H), 5.01 (qd, 1 H, J = 7, 2 Hz), 7.6–7.8 (m, 2 H), 7.95–8.10 (m, 2 H); IR (KBr) 1655 (vs), 1620 (m), 1590 (vs), 1390 (s), 1330 (vs), 1305 (s), 1295 cm^{-1} (vs); MS, m/e 242 (M^+, 84), 227 (100), 224 (19), 213 (16). Anal. Calcd for $C_{15}H_{14}O_3$: C, 74.37; H, 5.82. Found: C, 74.24; H, 6.01.

Reaction of Acetylnaphthoquinone with Dienol Silyl Ether 41.[24] Tin(IV) tetrachloride (0.14 mL) and **41** (190 mg, 1.1 mmol) were successively added to a CH_2Cl_2 solution (30 mL) of **18** (200 mg, 1 mmol) at −78 °C under a N_2 atmosphere. The mixture was stirred and gradually warmed up to 0 °C during 2 h. Water was added and the resulted mixture was extracted with CH_2Cl_2. The organic phase was washed with water and brine, and the solvent was evaporated. Although in the ^1H NMR spectrum of the residue the presence of **43** and diastereomeric **44** was strongly suggested by three kinds of hydroxylic protons which firmly chelated to carbonyl groups (δ = 16.32, 16.22, and 16.19 ppm), detailed assignment was difficult. After acetylation according to the usual manner, the reaction mixture was chromatographed on silica gel (CH_2Cl_2 as eluent) to give 230 mg of γ-adduct **43a** (35%) and α-adduct **44a** (65%). **43a**: colorless needles recrystallized from benzene–hexane; mp 118.5–119.5 °C; NMR ($CDCl_3$) δ 2.36 (s, 3 H), 2.40 (s, 3 H), 2.48 (s, 3 H), 3.52 (dd, 2 H, allylic H, J = 6, 1.5 Hz), 3.65 (s, 3 H), 5.73 (dt, 1 H, =$CHCO_2$, J = 16, 1.5 Hz), 6.94 (dt, 1 H, CH_2CH=, J = 16, 6 Hz), 7.4–7.8 (m, 4 H); IR (KBr) 1760 (vs), 1735 (vs), 1690 (m), 1640 cm^{-1} (m); MS, m/e 384 (M^+, 1), 342 (16), 301 (20), 300 (100), 282 (14), 268 (19), 240 (13), 227 (20), 226 (65), 225 (27), 223 (25); high-resolution MS, calcd for $C_{21}H_{20}O_7$ 384.1209, found 384.1208. **44a**: stereoisomeric mixture (13:8); pale yellow viscous oil; NMR ($CDCl_3$) δ 1.61 (d, 3 H, major CH_3CH=, J = 7 Hz), 2.14 (d, 3 H, minor CH_3CH=, J = 7 Hz), 2.15–2.50 (m, 9 H, acetyl CH_3), 3.71 (s, 3 H), 6.17 (quartet, 1 H, minor CH_3CH=, J = 7 Hz), 7.23 (quartet, 1 H, major CH_3CH=, J = 7 Hz), 7.4–7.9 (m, 4 H).

Reaction of Acetylnaphthoquinone with 2-Silylbutenoate 42.[26a] According to the procedure described in the previous reaction, **18** (200 mg, 1 mmol) was treated with the butenoate **42** (257 mg, 1.1 mmol) and $SnCl_4$ (0.14 mL) to give the γ-adduct **43** quantitatively: NMR ($CDCl_3$) 2.20 (s, 3 H), 2.3–2.6 (m, 2 H), 3.60 (s, 3 H), 3.62 (m, 1 H), 5.65 (d, 1 H, J = 16 Hz), 6.70 (dt, 1 H, J = 16, 8 Hz), 7.2–8.2 (m, 4H), 16.32 (s, 1 H). After acetylation, 308 mg of **43a** was obtained by column chromatography on silica gel (CH_2Cl_2 as eluent).

(*E*)-Methyl 4-[3-Acetyl-1-[(*tert*-butyldimethylsilyl)oxy]-4-hydroxy-5-methoxynaphth-2-yl]-2-butenoate (47a).

To a solution of **10a** (460 mg, 2 mmol) and **42** (562 mg, 2 mmol) was added $SnCl_4$ (0.28 mL, 2 mmol) at −78 °C. The solution immediately turned to deep purple. After addition was complete, the reaction mixture was allowed to warm to room temperature (over 30 min) and stirred for an additional 30 min. In the course of the reaction, the mixture turned from a deep purple solution to a yellowish brown suspension. The reaction mixture was quenched with water and extracted with CH_2Cl_2. The organic phase was washed with brine and dried through a $MgSO_4$ column. After evaporation in vacuo at room temperature, ether (5 mL) was added to the yellow residue, and then the mixture was stored in a freezer overnight. The crystals were filtered and washed with hexane to afford 584 mg (1.77 mmol, 88%) of (*E*)-methyl 4-(3-acetyl-4-hydroxy-5-methoxy-1-oxo-1,2-dihydronaphth-2-yl)-2-butenoate (**46a**): yellow crystals; mp >85 °C dec; NMR ($CDCl_3$) δ 2.25 (s, 3 H, acetyl CH_3), 2.48 (t, 2 H, allylic H, J = 8 Hz), 3.65 (s, 3 H, CO_2CH_3, and t, 1 H, ring H, J = 7 Hz), 3.96 (s, 3 H, OCH_3), 5.59 (d, 1 H, $=CHCO_2$, J = 16 Hz), 6.65 (dt, 1 H, $CH_2CH=$, J = 16, 8 Hz), 7.22 (dd, 1 H, Ar H, J = 8, 2 Hz), 7.45 (m, 2 H, Ar H), 17.19 (s, 1 H, hydroxylic H); IR (KBr) 1720 (vs), 1690 (vs), 1650 cm^{-1} (s); MS, m/e 330 (M^+, 83), 328 (56), 326 (17), 310 (22), 296 (22), 295 (22), 269 (100), 267 (61); high-resolution MS, calcd for $C_{18}H_{18}O_6$ 330.1104, found 330.1106. For preparative purpose, satisfactory yields were obtained in the next reaction without purification of **46a**. A DMF solution (2 mL) of the crude product, *t*-$BuMe_2SiCl$ (484 mg, 3.2 mmol), and imidazole (476 mg, 7 mmol) was stirred for 3 h at room temperature under nitrogen. The reaction was quenched with water, and the mixture was extracted with ether. The ethereal phase was washed with water and brine and dried over $MgSO_4$, and the solvent was evaporated. Isolation by column chromatography on silica gel (hexane–CH_2Cl_2 as eluent) gave 713 mg (1.6 mmol, 80%) of **47a**: pale yellow crystals recrystallized from ether–hexane; mp 107–109 °C; NMR ($CDCl_3$) δ 0.16 (s, 6 H, $SiCH_3$), 1.10 (s, 9 H, *t*-Bu), 2.58 (s, 3 H, acetyl CH_3), 3.68 (s, 3 H, CO_2CH_3), 3.72 (d, 2 H, benzylic H, J = 6 Hz), 4.02 (s, 3 H, OCH_3), 5.68 (d, 1 H, $=CHCO_2$, J = 16 Hz), 6.80 (d, 1 H, Ar H, J = 8 Hz), 6.93 (dt, 1 H, $CH_2CH=$, J = 16, 6 Hz), 7.32 (t, 1 H, Ar H, J = 8 Hz), 7.62 (d, 1 H, Ar H), 9.45 (s, 1 H, phenolic H); IR (KBr) 3390 (s), 1715 (vs), 1675 (vs), 1645 (m), 1390 cm^{-1} (vs); MS, m/e 444 (M^+, 37), 426 (9), 402 (9), 387 (9), 370 (70), 366 (100). Anal. Calcd for $C_{24}H_{32}O_6Si$: C, 64.84; H, 7.25. Found: C, 64.78; H, 7.46.

In this reaction, neither dihydrofuran **56** nor disilylated product **57a** was produced in a detectable amount. **57a**: colorless needles; mp 80–83 °C; NMR ($CDCl_3$) δ −0.05 (s, 6 H), 0.15 (s, 6 H), 0.97 (s, 9 H), 1.05 (s, 9 H), 2.53 (s, 3 H, acetyl CH_3), 3.64 (s, 3 H, CO_2CH_3), 3.72 (d, 2 H, benzylic H, J = 6 Hz), 3.89 (s, 3 H, OCH_3), 5.57 (d, 1 H, $=CHCO_2$, J = 16 Hz), 6.77 (d, 1 H, Ar H, J = 8 Hz), 6.85 (dt, 1 H, $CH_2CH=$, J = 16, 6 Hz), 7.32 (t, 1 H, Ar H, J = 8 Hz), 7.60 (d, 1 H, Ar H, J = 8 Hz).

(*E*)-Methyl 4-[1-[(*tert*-Butyldimethylsilyl)oxy]-4-hydroxy-3-(1-hydroxyethyl)-5-methoxynaphth-2-yl]-2-butenoate (48a). The ketone **47a** (127 mg, 0.27 mmol) and $NaBH_4$ (38 mg) were dissolved in methanol (10 mL) and stirred for 1 h at room temperature. The reaction mixture was quenched with saturated aqueous ammonium chloride and extracted with ether. The organic phase was washed with water and brine and dried over $MgSO_4$. After evaporating the solvent, purification by column chromatography on silica gel (CH_2Cl_2 as eluent) gave 120 mg (0.269 mmol, 94%) of **48a**: NMR ($CDCl_3$) δ 0.12 (s, 3 H, diastereotopic $SiCH_3$), 0.15 (s, 3 H, diastereotopic $SiCH_3$), 1.08 (s, 9 H, *t*-Bu), 1.62 (d, 3 H, $CHCH_3$, J = 7 Hz), 3.68 (s, 3 H, CO_2CH_3), 3.75 (d, 2 H, benzylic H, J = 6 Hz), 4.06 (s, 3 H, OCH_3), 4.44 (br, 1 H, OH), 4.97 (m, 1 H, CHOH), 5.70 (d, 1 H, $=CHCO_2$, J = 16 Hz), 6.82 (d, 1 H, Ar H, J = 8 Hz), 7.08 (dt, 1 H, $CH_2CH=$, J = 16, 6 Hz), 7.27 (t, 1 H, Ar H, J = 8 Hz), 7.65 (d, 1 H, Ar H, J = 8 Hz), 9.75 (s, 1 H, phenolic H); IR (CCl_4) 3380 (s), 1740 cm^{-1} (vs).

***trans*- and *cis*-Methyl [5-[(*tert*-Butyldimethylsilyl)oxy]-10-hydroxy-9-methoxy-1-methyl-3,4-dihydro-1*H*-naphtho[2,3-*c*]pyran-3-yl]acetate (49a and 50a).** Sodium methoxide (26%, in methanol; 0.1 mmol) was added dropwise to a solution of **48a** (60 mg, 0.135 mmol) in methanol (10 mL) at room temperature. After being stirred for 1 h, the reaction mixture was quenched with saturated ammonium chloride solution and extracted with ether. After the usual workup, simple purification by short column chromatography (silica gel, CH_2Cl_2 as eluent) gave 57 mg (94%) of diastereomers. The isomer ratio was determined to be **49a**:**50a** = ca. 1:1 by NMR. A careful chromatographic separation (hexane–CH_2Cl_2 as eluent) gave pure cis isomer **50a** (first eluted) as colorless needles recrystallized from ether–hexane [mp 85.5–86.5 °C; NMR ($CDCl_3$) δ 0.13 (s, 3 H, diastereotopic $SiCH_3$), 0.19 s, 3 H, diastereotopic, $SiCH_3$), 1.08 (s, 9 H, *t*-Bu), 1.61 (d, 3 H, 1-CH_3, J = 7 Hz), 2.53 (dd, 1 H, 4-pseudoaxial H, J = 16, 10 Hz), 2.46 (dd, 1 H, one of CH_2CO_2, J = 15, 7 Hz), 2.74 (dd, 1 H, another CH_2CO_2, J = 15, 7 Hz), 3.06 (dd, 1 H, 4-pseudoequatorial H, J = 16, 1.5 Hz), 3.69 (s, 3 H, CO_2CH_3), 3.75–3.95 (m, 1 H, 1-H), 3.99 (s, 3 H, OCH_3), 5.23 (quartet, 1 H, 1-H, J = 7 Hz), 6.70 (d, 1 H, Ar H, J = 8 Hz), 7.19 (t, 1 H, Ar H, J = 8 Hz), 7.58 (d, 1 H, Ar H, J = 8 Hz), 9.32 (s, 1 H, phenolic H); IR (KBr) 3375 (s), 2925 (s), 1740 (vs), 1620 (m), 1605 (s), 1390 (vs), 1360 (s), 1070 cm^{-1} (s); MS, m/e 446 (M^+, 100), 431 (84), 408 (10); high-resolution MS, calcd for $C_{24}H_{34}O_6Si$ 446.2124, found 446.2124.] and pure trans isomer **49a** as a colorless viscous oil [NMR ($CDCl_3$) δ 0.14 (s, 3 H, diastereotopic $SiCH_3$), 0.17 (s, 3 H, diastereotopic $SiCH_3$), 1.08 (s, 9 H, *t*-Bu), 1.59 (d, 3 H, 1-CH_3, J = 7 Hz), 2.55 (dd, 1 H, 4-pseudoaxial H, J = 16, 11 Hz), 2.67 (m, 2 H, CH_2CO_2), 3.02 (dd, 1 H, 4-pseudoequatorial H, J = 16, 3.5 Hz), 3.72 (s, 3 H, CO_2CH_3), 4.00 (s, 3 H, OCH_3), 4.36 (m, 1 H, 3-H), 5.27 (quartet, 1 H, 1-H, J = 7 Hz), 6.70 (d, 1 H, Ar H, J = 8 Hz), 7.20 (t, 1 H, Ar H, J = 8 Hz), 7.58 (d, 1 H, Ar H, J = 8 Hz), 9.20 (s, 1 H, phenolic H).].

***trans*-Methyl [9-Methoxy-1-methyl-5,10-dioxo-3,4,5,10-tetrahydro-1*H*-naphtho[2,3-*c*]pyran-3-yl]acetate (51a).** Ceric(IV) ammonium nitrate (326 mg) in water (3 mL) was added to a solution of the *trans*-naphthopyran **49a** (105 mg, 0.269 mmol) in CH_3CN (15 mL). After being stirred for 30 min, the reaction mixture was poured into water and extracted with ether. After the usual workup, the reaction mixture was simply chromatographed on silica gel (CH_2Cl_2 as eluent) to give 68 mg (0.207 mmol, 77%) of **51a**: yellow needles recrystallized from CH_2Cl_2–hexane: mp >138 °C dec; NMR ($CDCl_3$) δ 1.54 (d, 3 H, 1-CH_3, J = 7 Hz), 2.32 (ddd, 1 H, 4-pseudoaxial H, J = 19, 11, 2 Hz), 2.65 (d, 2 H, CH_2CO_2, J = 7 Hz), 2.76 (dd, 1 H, 4-pseudoequatorial H, J = 19, 3 Hz), 3.73 (s, 3 H, CO_2CH_3), 4.00 (s, 3 H, OCH_3), 4.30 (m, 1 H, 3-H), 5.00 (m, 1 H, 1-H), 7.27 (m, 1 H, Ar H), 7.65 (m, 2 H, Ar H); IR (KBr) 1730 (vs), 1655 (vs), 1635 (m), 1590 (s), 1290 (vs), 1275 (vs), 1260 cm^{-1} (s); MS, m/e 330 (M^+, 80), 298 (40), 270 (37), 257 (100), 256 (85), 241 (43); high-resolution MS, calcd for $C_{18}H_{18}O_6$ 330.1104, found 330.1107.

***trans*-Methyl [9-Hydroxy-1-methyl-5,10-dioxo-3,4,5,10-tetrahydro-1*H*-naphtho[2,3-*c*]pyran-3-yl]acetate (53a) (Nanaomycin A Methyl Ester).** Anhydrous aluminum trichloride (42 mg) was added to a solution of **51a** (22 mg, 0.067 mmol) in CH_2Cl_2 (5 mL) at room temperature. During the reaction, the color of the solution turned from yellow to purple gradually. After being stirred for 1 h, the reaction mixture was quenched with water and extracted with CH_2Cl_2. After the usual workup, purification by short column chromatography on silica gel (CH_2Cl_2 as eluent) gave 20 mg (0.063 mmol, 94%) of pure **53a**: yellow needles recrystallized from CH_2Cl_2–hexane; mp 132–136 °C dec (lit. mp 118–120[10] and 133–135 °C[11b]); NMR ($CDCl_3$) δ 1.58 (d, 3 H, 1-CH_3, J = 7 Hz), 2.33 (ddd, 1 H, 4-pseudoaxial H, J = 18.5, 10, 1.5 Hz), 2.65 (d, 2 H, CH_2CO_2, J = 6 Hz), 2.81 (dd, 1 H, 4-pseudoequatorial H, J = 18.5, 4 Hz), 3.74 (s, 3 H, CO_2CH_3), 4.28 (m, 1 H, 3-H), 4.94 (m, 1 H, 1-H), 7.20 (m, 1 H, Ar H), 7.56 (m, 2 H, Ar H), 11.93 (s, 1 H, phenolic H); IR (KBr) 3160 (w), 1740 (vs), 1660 (m), 1640 cm^{-1} (vs); MS, m/e 316 (M^+, 21), 298 (10), 284 (56), 243 (40), 242 (100), 214 (65); high-resolution MS, calcd for $C_{17}H_{16}O_6$ 316.0946, found 316.0942.

(±)-Nanaomycin A (3). An aqueous KOH solution (0.1 N, 20 mL) was added to a solution of **53a** (12 mg, 0.039 mmol) in EtOH (5 mL) at room temperature. The color of the solution turned to reddish purple. After being stirred for 1 h, the reaction mixture was acidified with 2 N aqueous HCl. The resulted suspension was extracted with CH_2Cl_2. The organic phase was washed with water and brine and dried over $MgSO_4$, and the solvent was evaporated to give 11 mg (0.036 mmol, 94%) of (±)-nanaomycin A (**3**). Recrystallization from CH_2Cl_2–hexane gave 10 mg of **3** as yellow needles: mp 166–171 °C dec (lit. mp 171–174,[8] 171–173,[11b] 177–181,[10] and 171–172 °C[14]); NMR ($CDCl_3$) δ 1.60 (d, 3 H, 1-CH_3, J = 6 Hz), 2.37 (ddd, 1 H, 4-pseudoaxial H, J = 18.4, 10.2, 1.5 Hz), 2.73 (d, 2 H, CH_2CO_2, J = 10 Hz), 2.85

(dd, 1 H, 4-pseudoequatorial H, J = 18.4, 3.9 Hz), 4.29 (m, 1 H, 3-H), 5.02 (m, 1 H, 1-H), 7.2-7.7 (m, 3 H, Ar H), 9.5 (br, 1 H), 11.98 (s, 1 H); IR (KBr) 2980 (br m), 1715 (vs), 1655 (s), 1635 (vs), 1615 cm^{-1} (vs); MS, m/e 300 (M^+, 9), 298 (48), 282 (61), 257 (57), 255 (57), 248 (87), 214 (100); high-resolution MS, calcd for $C_{16}H_{14}O_6$ 302.0789, found 302.0788.

(±)-Epinanaomycin A (55a). Hydrolysis of **54a** (cis isomer, 26 mg, 0.082 mmol) was carried out in a similar manner to afford (±)-epinanaomycin A (**55a**) (17 mg, 0.058 mmol, 68%). Recrystallization from CH_2Cl_2 afforded 15 mg of **55a** as yellow needles: mp 175-187 °C dec (lit.[14] mp 168-170 °C); NMR ($CDCl_3$) δ 1.58 (d, 3 H, 1-CH_3, J = 6 Hz), 2.36 (dd, 1 H, 4-pseudoaxial H, J = 18.6, 10.3, 3.9 Hz), 2.73 (m, 2 H, CH_2CO_2), 2.85 (dt, 1 H, 4-pseudoequatorial H, J = 18.6, 2.5 Hz), 3.92 (m, 1 H, 3-H), 5.14 (m, 1 H, 1-H), 7.2-7.7 (m, 3 H, Ar H), 9.5 (br, 1 H), 11.95 (s, 1 H); IR ($CDCl_3$) 2980 (br m), 1710 (vs), 1660 (s), 1640 cm^{-1} (vs); MS, m/e 302 (M^+, 34), 287 (15), 285 (18), 284 (97), 272 (16), 256 (26), 255 (24), 243 (48), 242 (100); high-resolution MS, calcd for $C_{16}H_{14}O_6$ 302.0789, found 302.0789.

(±)-Deoxyfrenolicin (5). Hydrolysis of **53b** (16 mg, 0.047 mmol) was carried out in a similar manner to the preparation of **3**. Recrystallization from CH_2Cl_2-hexane gave 13 mg (0.039 mmol, 85%) of (±)-deoxyfrenolicin (**5**) as yellow needles: mp 210-219 °C dec (lit. mp 179-181[3b] and 214-214.5 °C[13a]); 400-MHz NMR ($CDCl_3$) δ 1.01 (t, 3 H, J = 7.3 Hz), 1.57 (m, 1 H), 1.67 (m, 1 H), 1.80 (m, 2 H), 1.36 (ddd, 1 H, J = 19.2, 10.7, 1.7 Hz), 2.72 (d, 2 H, J = 6.4 Hz), 2.86 (dd, 1 H, J = 19.2, 3.4 Hz), 4.30 (m, 1 H), 4.86 (m, 1 H), 7.24 (m, 1 H), 7.62 (m, 2 H), 9.0-10.0 (br, 1 H), 12.00 (s, 1 H); IR (KBr) 3060 (br m), 2950 (s), 1710 (vs), 1655 (vs), 1640 (vs), 1615 cm^{-1} (vs); MS, m/e 330 (M^+, 30), 328 (25), 312 (32), 287 (65), 282 (49), 242 (54), 241 (100), 227 (65); high-resolution MS, calcd for $C_{18}H_{18}O_6$ 330.1103, found 330.1105.

(±)-Epideoxyfrenolicin (55b). Hydrolysis of the *cis*-quinone **54b** (22 mg, 0.064 mmol) was carried out in a similar way as described above. Recrystallization from CH_2Cl_2-hexane gave 18 mg (0.055 mmol, 85%) of (±)-epideoxyfrenolicin (**55b**) as orange prisms: mp 167-183 °C dec; NMR ($CDCl_3$) δ 0.91 (t, 3 H, J = 7 Hz), 1.1-2.1 (m, 4 H), 2.32 (ddd, 1 H, J = 18, 10, 4 Hz), 2.73 (d, 2 H, J = 7 Hz), 2.88 (dt, 1 H, J = 18, 2.5 Hz), 3.88 (m, 1 H), 4.80 (m, 1 H), 7.1-7.3 (m, 1 H), 7.44-7.66 (m, 2 H), 9.60 (br, 1 H), 11.92 (s, 1 H); IR (KBr) 3040 (br m), 2960 (m), 1710 (vs), 1660 (vs), 1635 (vs), 1610 cm^{-1} (vs); MS, m/e 330 (M^+, 34), 328 (6), 312 (39), 287 (100), 242 (50), 241 (72), 227 (56), 213 (40); high-resolution MS, calcd for $C_{18}H_{18}O_6$ 330.1103, found 330.1102.

Acknowledgment. The author thanks Prof. Kazuhiro Maruyama (Kyoto Univ.) and Dr. Yoshinori Naruta (Kyoto Univ.) for their guidance and valuable suggestions throughout this work. The author also thanks Mr. H. Furuta and Mr. S. Kawabata for the measurement of 400-MHz NMR and high-resolution mass spectra. Gifts of organosilicon compounds from Shin-etsu Chemical Co. are greatly appreciated.

Registry No. **1**, 64869-73-4; **2**, 64869-74-5; **3**, 73804-47-4; **5**, 73804-49-6; **7**, 3843-55-8; **8a**, 73705-44-9; **8b**, 81644-26-0; **9a**, 81418-41-9; **9b**, 81644-27-1; **10a**, 81418-42-0; **10b**, 81644-28-2; **10c**, 99668-76-5; **11a**, 762-73-2; **11b**, 3200-73-5; **11c**, 55562-82-8; **11d**, 17314-40-8; **11e**, 63522-99-6; **11f**, 76-63-1; **11g**, 962-72-1; **11h**, 18752-21-1; **12**, 1125-55-9; **13**, 81665-21-6; **14**, 40815-79-0; **15**, 81665-20-5; **16**, 63076-94-8; **17**, 81665-21-6; **18**, 5813-57-0; **19**, 81665-24-9; **20**, 99668-84-5; **21**, 81665-25-0; **22**, 81665-26-1; **23**, 99668-87-8; **24**, 99668-90-3; **25**, 99668-91-4; **26**, 81418-44-2; **27**, 99668-92-5; **28**, 99668-94-7; **29**, 76916-86-4; **30**, 99668-95-8; **31**, 3958-79-0; **32**, 79950-44-0; **33**, 99668-97-0; **34g**, 99668-99-2; **34h**, 81665-29-4; **35a**, 81418-43-1; **35b**, 81418-45-3; **36a**, 78284-31-8; **36b**, 81418-46-4; **37a**, 78284-33-0; **37b**, 81418-47-5; **37b** (3-CH_2SePh), 99669-00-8; **38a**, 78284-34-1; **38b**, 81418-48-6; **38b** (3-CH_2SePh), 99705-83-6; **39**, 78591-52-3; **40**, 78572-94-8; **41**, 85636-50-6; **42**, 82654-01-1; **43**, 83039-90-1; **43a**, 99668-77-6; **44a**, 99668-78-7; **45**, 99669-01-9; **46a**, 83039-90-1; **46b**, 99669-02-0; **47a**, 99668-79-8; **47b**, 99669-03-1; **48a**, 99745-09-2; **48b**, 99669-04-2; **49a**, 82654-03-3; **49b**, 81644-31-7; **50a**, 82654-04-4; **50b**, 81644-32-8; **51a**, 78340-69-9; **51b**, 81702-89-8; **52a**, 78340-68-8; **52b**, 81702-90-1; **53a**, 73804-46-3; **53b**, 73804-48-5; **54a**, 78340-70-2; **54b**, 82690-99-1; **55a**, 90761-55-0; **55b**, 99745-10-5; **57a**, 99668-80-1; **58**, 99669-05-3; 1,4-dimethoxynaphthalene, 10075-62-4; 2-bromo-1,4-dimethoxynaphthalene, 64648-81-3; 3-acetyl-1,4,5-trihydroxynaphthalene, 99668-75-4; 1,4-diacetoxy-2-acetyl-3-allylbenzene, 99668-81-2; 1,4-diacetoxy-2-acetyl-3-(1-methyl-2-propenyl)benzene, 99668-82-3; 1,4-diacetoxy-2-acetyl-3-allylnaphthalene, 99668-83-4; 1,4-diacetoxy-2-acetyl-3-(1-methyl-2-propenyl)naphthalene, 99668-85-6; 1,4-diacetoxy-2-acetyl-3-(2-methyl-2-propenyl)naphthalene, 99668-86-7; 1,4-diacetoxy-2-acetyl-3-(1,1-dimethyl-2-propenyl)-naphthalene, 99668-88-9; 1,4-diacetoxy-2-acetyl-3-(3-methyl-2-butenyl)naphthalene, 99668-89-0; 1,4-diacetoxy-3-acetyl-5-methoxy-2-(1-methyl-2-propenyl)-1,4-naphthalene, 99668-93-6; 3-allyl-2-methoxycarbonyl-1,4-benzoquinone, 99668-96-9; methyl 1,4-diacetoxy-3-(1-methyl-2-propenyl)-2-benzoate, 99668-98-1; 1,4-diacetoxy-2-acetyl-3-allyl-5-methylbenzene, 99669-06-4; 2-formyl-1,4-dimethoxynaphthalene, 75965-83-2.

Supplementary Material Available: Additional experimental information for other compounds in this paper (15 pages). Ordering information is given on any current masthead page.

Effects of Electron-Donating Substituents on the Bond Alternations in Pentalene and Heptalene

M. Kataoka, T. Ohmae, and T. Nakajima*

Department of Chemistry, Faculty of Science, Tohoku University, Sendai 980, Japan

Received October 9, 1985

On the basis of the second-order Jahn-Teller effect, the index (I_r) for predicting the existence of bond alternation in substituted conjugated hydrocarbons is defined. The possible relation between I_r and the number of the excess electrons (ΔN_r) transferred from an electron-donating substituent and the dependence of I_r on the substituted position (r) in pentalene and heptalene are examined by using the perturbation theory. It is revealed that the substitutions with an electron-donating group at the 1-, 3-, 4-, or 6-position in pentalene and at the 2-, 4-, 7-, or 9-position in heptalene bring about a large ΔN_r and a smaller I_r and result in the relaxation of the bond alternation. On the other hand, the substitutions at other positions in both molecules are anomalous in the sense that they bring about a very small ΔN_r and a larger I_r and result in the reinforcement of the bond alternation. The above predictions are confirmed by the model calculations made by using the Pariser-Parr-Pople-type SCF MO CI method in conjunction with the variable bond-length technique.

The prediction of the geometrical structures with respect to C-C bond lengths of pentalene and heptalene has long been an important subject in theoretical organic chemistry. All the molecular orbital (MO) calculations[1-9] have agreed

0022-3263/86/1951-0358$01.50/0