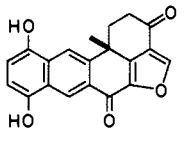
Total Synthesis of (+)-Halenaquinol and (+)-Halenaquinone. Experimental Proof of Their Absolute Stereostructures Theoretically Determined

Nobuyuki Harada,*[1a] Tatsuo Sugioka,[1a,b] Yusuke Ando,[1a] Hisashi Uda,[1a] and Takeo Kuriki[1b]

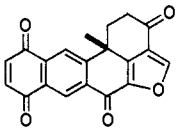
Contribution from the Chemical Research Institute of Nonaqueous Solutions, Tohoku University, 2-1-1 Katahira, Sendai 980, Japan, and Pharma Research Laboratory, Hoechst Japan Ltd., 1-3-2 Minamidai, Kawagoe, Saitama 350, Japan. *Received April 1, 1988. Revised Manuscript Received July 29, 1988*

Abstract: Theory and theoretically obtained results themselves naturally want to be proved in an experimental way. Recently, Kitagawa and we have theoretically determined the absolute configuration of a series of novel pentacyclic polyketides, halenaquinol (**1**) and halenaquinone (**2**), isolated from tropical marine sponges, to be 12b*S* by the application of the π-electron SCF–CI–dipole velocity MO method to the calculation of CD spectra. Here, we report the experimental proof of their absolute stereostructures theoretically determined, by describing the first total synthesis of (+)-halenaquinol **1** and (+)-halenaquinone **2** with the novel pentacyclic polyketide skeleton. Optically pure (8a*R*)-(−) Wieland–Miescher ketone (**4**) was converted to enone (+)-(**12**) via the reactions of nine steps. The Diels–Alder reaction of 3,6-dimethoxybenzocyclobutene (**18**) and (+)-**12** gave compound (+)-(**19**) of a tetracyclic skeleton, which was converted to halenaquinol dimethyl ether (12b*S*)-(+)-(**3**) by the reactions of four steps. All of the spectroscopic data of the synthetic sample of **3**, including the chiroptical data of $[\alpha]_D$ and CD spectra, were completely identical with those of the authentic sample derived from natural halenaquinol, as expected from the theoretical determination: synthetic, $[\alpha]^{25}_D$ +150.3°; natural, $[\alpha]^{23}_D$ +150.1°. Dimethyl ether (12b*S*)-(+)-**3** was converted to halenaquinone (12b*S*)-**2** and finally to halenaquinol (12b*S*)-**1** of the natural enantiomeric form. We have thus succeeded in the first total synthesis of halenaquinol **1** and halenaquinone **2** and also in the experimental verification of their absolute configurations theoretically determined. The present results have established the reliability of the π-electron SCF–CI–DV MO method, which is useful for the theoretical determination of the absolute stereochemistry of twisted π-electron systems.

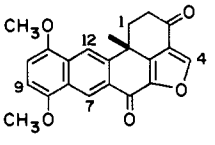
Theory and theoretically obtained results themselves naturally want to be proved in an experimental way. In the field of absolute configurational studies, the absolute stereostructure of a twisted π-electron system can be theoretically determined by the application of the π-electron SCF–CI–dipole velocity MO method[2,3] to the calculation of CD spectra. In fact, we have recently reported the theoretical determination of the absolute stereostructures of (+)-1,8a-dihydro-3,8-dimethylazulene, a labile biosynthetic intermediate for 1,4-dimethylazulene[4] and of chiral troponoid spiro compounds.[5] Moreover, Kitagawa and we have recently theoretically determined the absolute configurations of a series of novel pentacyclic polyketides, halenaquinol (**1**)[6] and halenaquinone (**2**),[6,7] isolated from tropical marine sponges, on the basis of the calcu-



(12bS)-(+)-1

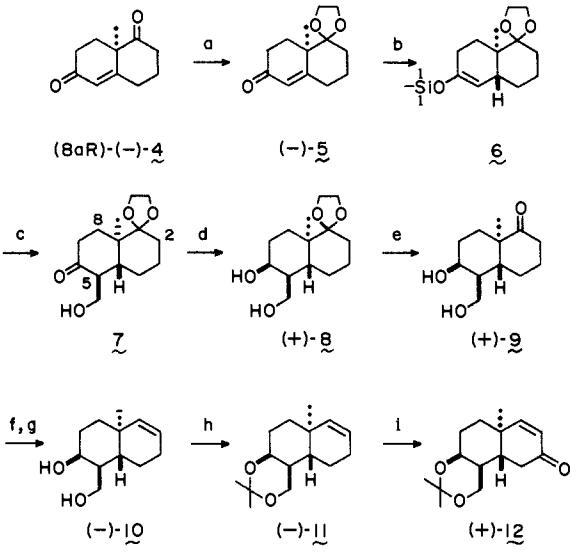


(12bS)-(+)-2



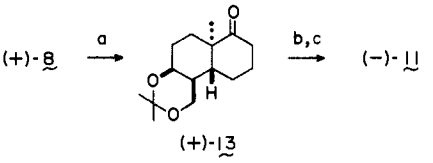
(12bS)-(+)-3

Scheme I[a]



[a] (a) 2-Ethyl-2-methyl-1,3-dioxolane, *p*-toluenesulfonic acid (*p*-TsOH); (b) Li, NH_3, tetrahydrofuran (THF), and then $(CH_3)_3SiCl$, $(CH_3CH_2)_3N$; (c) CH_3Li, THF, and then CH_2O; (d) Li(*sec*-Bu)$_3$BH, THF; (e) water, *p*-TsOH; (f) *p*-toluenesulfonhydrazide, EtOH; (g) CH_3Li, THF; (h) acetone, *p*-TsOH; (i) CrO_3, 3,5-dimethylpyrazole, CH_2Cl_2.

Scheme II[a]



[a] (a) Acetone, dichloromethane, *p*-TsOH; (b) *p*-toluenesulfonhydrazide, EtOH; (c) CH_3Li, THF.

lation of the CD spectrum of a pertinent derivative.[8] These two novel marine natural products and a related compound, xesto-

(1) (a) Tohoku University. (b) Hoechst Japan Ltd.
(2) (a) Moscowitz, A. *Tetrahedron*, **1961**, *13*, 48. (b) Kemp, C.; Mason, S. F. *Tetrahedron* **1966**, *22*, 629. Brown, A.; Kemp, C.; Mason, S. F. *J. Chem. Soc. A* **1971**, 751.
(3) Harada, N.; Nakanishi, K. *Circular Dichroic Spectroscopy—Exciton Coupling in Organic Stereochemistry*; University Science Books: Mill Valley, CA, 1983.
(4) Harada, N.; Kohori, J.; Uda, H.; Nakanishi, K.; Takeda, R. *J. Am. Chem. Soc.* **1985**, *107*, 423.
(5) Harada, N.; Uda, H.; Nozoe, T.; Okamoto, Y.; Wakabayashi, H.; Ishikawa, S. *J. Am. Chem. Soc.* **1987**, *109*, 1661.
(6) Kobayashi, M.; Shimizu, N.; Kyogoku, Y.; Kitagawa, I. *Chem. Pharm. Bull.* **1985**, *33*, 1305.

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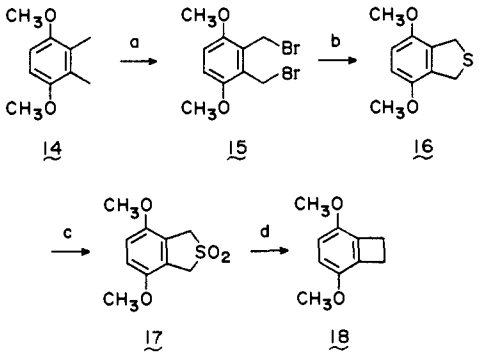
Scheme III[a]



[a] (a) *N*-Bromosuccinimide (NBS), α,α'-azobisisobutyronitrile (AIBN), CCl_4; (b) Na_2S, EtOH; (c) *m*-chloroperbenzoic acid, CH_2Cl_2; (d) 305–310 °C.

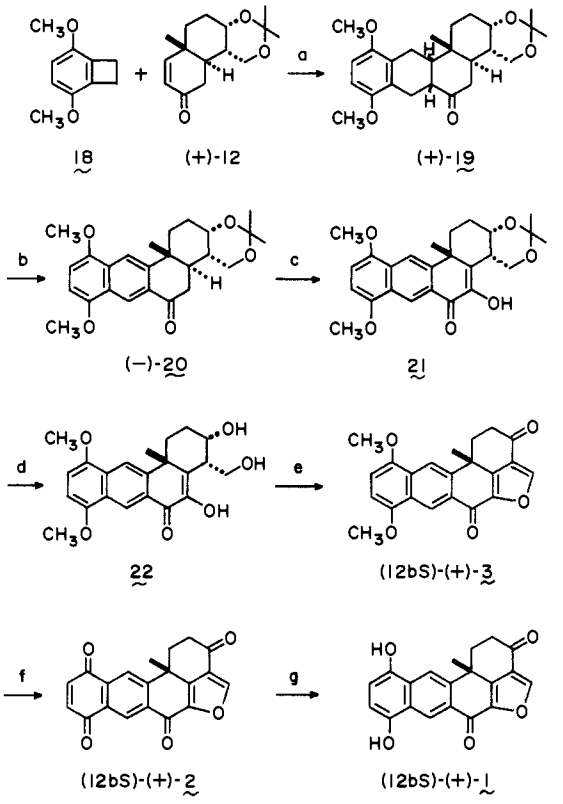
quinone,[9] have attracted much attention because of their interesting antibiotic and cardiotonic activities. Here, we report the experimental proof of their absolute stereostructures theoretically determined, by describing the first total synthesis of (+)-halenaquinol **1** and (+)-halenaquinone **2** with the novel pentacyclic polyketide skeleton.

Results and Discussion

Retrosynthesis. As a synthetic strategy, we adopted the route shown in Schemes I, III, and IV, where halenaquinol **1** can be obtained by the reduction of halenaquinone **2**. The naphthoquinone moiety of **2** is obtainable by the oxidative cleavage of the hydroquinone dimethyl ether (**3**), and the furan ring of **3** is cyclized by the oxidation of triol (**22**). The diosphenol moiety of **21** would be obtained by the air oxidation of ketone **20**, and the tetracyclic skeleton of **19** is constructed by the Diels–Alder reaction of 3,6-dimethoxybenzocyclobutene (**18**) and enone **12**. The dienophile **12** is derived starting from the Wieland–Miescher ketone (**4**) as shown in Scheme I, where the extra one-carbon unit is introduced as the hydroxymethyl group at the C-5 position of compound **7** by the application of the Stork's reductive hydroxymethylation method.[10] In the present synthetic route, the absolute configuration of the bridgehead methyl group of the optically active Wieland–Miescher ketone is retained as that of the corresponding methyl group of the final products. So, since the absolute configuration of halenaquinol and halenaquinone has been theoretically determined to be 12b*S*, it indicates that we should start from the (8a*R*)-(−) enantiomer of the Wieland–Miescher ketone (**4**).

Total Synthesis of (+)-Halenaquinol and (+)-Halenaquinone. The carbonyl group of the optically pure (8a*R*)-(−) Wieland–Miescher ketone (**4**), $[\alpha]^{25}_D$ −98.96° (*c* 1.039, benzene), was selectively protected to give monoacetal (−)-(**5**),[11] which was then reductively hydroxymethylated according to the procedure of Stork[10,12] (Scheme I); enone **5** was reduced with lithium in liquid ammonia, and the resultant enolate was trapped as trimethylsilyl ether (**6**). Regeneration of the enolate by treatment of **6** with methyllithium and then addition of gaseous formaldehyde gave keto alcohol **7** as a sole stereoisomer in 82% overall yield from **5**.[13] Keto alcohol **7** was reduced with lithium tri-*sec*-butylborohydride (L-Selectride), yielding glycol (+)-**8** in 92% yield,

Scheme IV[a]



[a] (a) Benzene, 210–215 °C, 20 h; (b) 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), benzene; (c) potassium *tert*-butoxide, *tert*-butyl alcohol, O_2; (d) 60% aqueous acetic acid; (e) dimethyl sulfoxide (DMSO), 1,3-dicyclohexylcarbodiimide (DCC), benzene, trifluoroacetic acid, pyridine; (f) cerium(IV) ammonium nitrate (CAN), aqueous methanol; (g) aqueous sodium hydrosulfite ($Na_2S_2O_4$), acetone.

which was then converted to keto glycol (+)-**9** in 98% yield by treatment with *p*-toluenesulfonic acid in water. The stereochemistries of 6(ax)-hydroxyl and 5(eq)-hydroxymethyl groups of compounds **8** and **9** were secured by the ^1H NMR coupling constant data of keto acetonide (+)-**13** (Scheme II): ^1H NMR (300.15 MHz, $CDCl_3$) δ 3.884 (1 H, dd, J = 12.2, 1.1 Hz), 3.961 (1 H, dd, J = 12.2, 2.6 Hz), 4.068 (1 H, ddd, J = 2.6, 2.6, 2.6 Hz). Formation of the *p*-toluenesulfonhydrazone of **9**, followed by treatment with methyllithium, gave olefin (−)-**10** in a quantitative yield. Next, the glycol moiety of **10** was protected as an acetonide to give acetonide olefin (−)-**11**.[14] At first we adopted the shortcut path of the conversion of ketal glycol **8** to olefin acetonide **11** via keto acetonide **13** (Scheme II). However, the acetonide moiety of **13** was found to be unstable toward the tosylhydrazone formation reaction, and the yield of **11** was low. Finally, the allylic position of acetonide olefin (−)-**11** was oxidized with the reagent of CrO_3/3,5-dimethylpyrazole,[15] affording conjugated enone (+)-**12** in 63% yield, which was next used as a dienophile of the Diels–Alder reaction with 3,6-dimethoxybenzocyclobutene (**18**).

Dimethoxybenzocyclobutene **18** was synthesized by the pyrolysis of sulfone **17**, which was prepared starting from 2,3-dimethyl-1,4-dimethoxybenzene (**14**)[16] as shown in Scheme III.[17] Bro-

(7) Roll, D. M.; Scheuer, P. J.; Matsumoto, G. K.; Clardy, J. *J. Am. Chem. Soc.* **1983**, *105*, 6177.

(8) Kobayashi, M.; Shimizu, N.; Kitagawa, I.; Kyogoku, Y.; Harada, N.; Uda, H. *Tetrahedron Lett.* **1985**, *26*, 3833.

(9) Nakamura, H.; Kobayashi, J.; Kobayashi, M.; Ohizumi, Y.; Hirata, Y. *Chem. Lett.* **1985**, 713.

(10) Stork, G.; D'Angelo, J. *J. Am. Chem. Soc.* **1974**, *96*, 7114.

(11) Bauduin, G.; Pietrasanta, Y. *Tetrahedron* **1973**, *29*, 4225. See also: McMurry, J. E. *J. Am. Chem. Soc.* **1968**, *90*, 6821.

(12) Trost, B. M.; Nishimura, Y.; Yamamoto, K.; McElvain, S. *J. Am. Chem. Soc.* **1979**, *101*, 1328. McMurry, J. E.; Andrus, A.; Ksander, G. M.; Musser, J. H.; Johnson, M. A. *J. Am. Chem. Soc.* **1979**, *101*, 1330.

(13) All of the new compounds have been characterized by spectroscopic methods including high-resolution mass spectrometry.

(14) In the case of the mass spectra of acetonides **11–13**, the molecular ion peaks were not obtained by the usual electron ionization procedure. The base peaks observed were M − CH_3 peaks, respectively. So, their molecular compositions were secured by the high-resolution analysis of M + H peaks, which were obtained by the chemical ionization procedure with 2-methylpropane.

(15) Salmond, W. G.; Barta, M. A.; Havens, J. L. *J. Org. Chem.* **1978**, *43*, 2057.

(16) McHale, D.; Mamalis, P.; Marcinkiewicz, S.; Green, J. *J. Chem. Soc.* **1959**, 3358. See also: Nilsson, J. G.; Sievertsson, H.; Selander, H. *Acta Pharm. Suec.* **1968**, *5*, 215. Smith, L. I.; Austin, F. L. *J. Am. Chem. Soc.* **1942**, *64*, 528.

mination of **14** with *N*-bromosuccinimide (NBS), followed by treatment of the resulting dibromide **15** with sodium sulfide in aqueous ethanol, gave sulfide **16** in 70% yield. Oxidation of **16** with *m*-chloroperbenzoic acid in dichloromethane afforded sulfone **17** in 89% yield. For the next thermal elimination reaction of sulfur dioxide, various reaction conditions were examined, and the direct heating method of the solid material of sulfone **17** without any solvents was finally found to afford the desired 3,6-dimethoxybenzocyclobutene (**18**) in a moderate yield. The crystals of **17** were pyrolyzed at 305–310 °C in a muffle furnace under a stream of nitrogen to give **18** in 48% yield.

The Diels–Alder reaction of compounds **18** and (+)-**12** was achieved by heating a benzene solution in a sealed tube at 210–215 °C for 20 h, giving a tetrahydronaphthalene derivative (+)-**19** in 33% yield (Scheme IV). The ^{13}C NMR spectrum of **19** indicated that the product was composed of a single stereoisomer. However, the relative stereochemistry of the chiral centers newly formed was not investigated further because they vanish at the next dehydrogenation reaction. A benzene solution of **19** was refluxed with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) to afford a naphthalene derivative (−)-**20** in 89% yield, which was then subjected to the following air oxidation in the presence of a base. Oxygen gas was bubbled through a solution of **20** and potassium *tert*-butoxide in *tert*-butyl alcohol for 5 h, and the mixture was worked up with aqueous ammonium chloride to give diosphenol **21** in 90% yield. The structure of **21** was secured by the ^1H NMR (the sharp singlet at δ 7.60 disappeared when adding D_2O), UV (a red shift and a hyperchromic effect of the UV absorption band at the longer wavelength region when adding aqueous NaOH), and HRMS data. Deprotection of the acetonide group of **21** by treatment with 60% aqueous acetic acid yielded triol **22**, which was subjected to the next reaction without purification. The oxidation reaction of the primary and secondary hydroxyl groups of **22** and successive cyclization to form a furan ring were accomplished by treatment with dimethyl sulfoxide (DMSO) and 1,3-dicyclohexylcarbodiimide (DCC) in benzene in the presence of trifluoroacetic acid and pyridine, giving the desired compound (12b*S*)-(+)-**3** of the furan–diketone system in 44% overall yield from **20**.

All of the spectroscopic data (see Experimental Section) of the synthetic sample of halenaquinol dimethyl ether (+)-**3**, including the chiroptical data of $[\alpha]_D$ and CD spectra, were completely identical with those of the authentic sample of (+)-**3**[18] derived from natural halenaquinol, as expected from the theoretical determination: (synthetic) $[\alpha]^{25}_D$ +150.3° (*c* 1.042, CH_2Cl_2), CD (EtOH) λ_{ext} 413 nm ($\Delta\epsilon$ +1.8), 383 (+1.4), 363 (+1.6), 347 (+2.6), 303 (−5.4), 244 (+4.7), 232 (−9.1); (natural) $[\alpha]^{23}_D$ +150.1° (*c* 1.124, CH_2Cl_2), CD (EtOH) λ_{ext} 413 nm ($\Delta\epsilon$ +1.8), 383 (+1.4), 363 (+1.7), 347 (+2.8), 303 (−5.5), 244 (+4.6), 232 (−8.9). Since the absolute configuration of the angular methyl group is retained throughout the reactions discussed above, the present results lead to the experimental and unambiguous determination that the absolute configuration of (+)-halenaquinol and (+)-halenaquinone is 12b*S*.

The hydroquinone dimethyl ether moiety of (12b*S*)-(+)-**3** was next deprotected by the oxidative cleavage with cerium(IV) ammonium nitrate (CAN) in aqueous methanol affording halenaquinone (12b*S*)-**2** of pale yellow color in 45% yield. The ^1H NMR and UV spectra of the synthetic sample agreed with those of natural halenaquinone. Finally, halenaquinone (12b*S*)-**2** was reduced with aqueous sodium hydrosulfite in acetone to give halenaquinol (12b*S*)-**1** of yellow color in an almost quantitative yield. As discussed by Kitagawa and co-workers in their paper of the isolation of natural halenaquinol,[6] compound **1** was very sensitive to light, heat, and air. So, the reaction was carried out in a dark room. The ^1H NMR spectrum of halenaquinol (12b*S*)-**1** in DMSO-d_6 exhibited two broad singlets at δ 9.6 and 9.8 due to the phenolic hydroxyl groups, which disappeared when adding D_2O. The remaining ^1H NMR peaks and UV spectrum curve were in a good agreement with those of the natural sample, respectively. The hydroquinone structure of **1** was also secured by the mass spectrum;[19] although the usual measurement procedure of mass spectra afforded only the signals due to the quinone form **2**, the peaks due to the hydroquinone form **1** were exclusively obtained by the application of the direct injection method of the solid sample. The first total synthesis of (+)-halenaquinol and (+)-halenaquinone with a novel polyketide skeleton has been thus accomplished.

Concluding Remarks

We have succeeded in the first total synthesis of (+)-halenaquinol **1** and (+)-halenaquinone **2** by starting from the (8a*R*)-(−) Wieland–Miescher ketone (**4**) and also have experimentally determined their absolute configurations to be 12b*S*. The conclusions on the absolute configuration are in agreement with those derived from the theoretical calculation of CD spectrum, which was previously reported by Kitagawa and us. So, the present total synthesis of (+)-halenaquinol and (+)-halenaquinone provides the experimental proof of the absolute stereostructures theoretically determined. We have thus established the reliability of the π-electron SCF–CI–DV MO method, which is useful for the determination of the absolute stereochemistry of twisted π-electron systems.

Experimental Section

(8a*R*)-(−)-3,4,8,8a-Tetrahydro-8a-methyl-1,6(2*H*,7*H*)-naphthalenedione (4). Following the literature procedure,[20] optically active (8a*R*)-(−)-3,4,8,8a-tetrahydro-8a-methyl-1,6(2*H*,7*H*)-naphthalenedione (**4**) was prepared by using unnatural (*R*)-D-(+)-proline as a chiral catalyst: mp 50.5–51.0 °C, $[\alpha]^{25}_D$ −98.96° (*c* 1.039, benzene) [lit.[20] for (8a*S*)-(+) enantiomer, mp 50–51 °C, $[\alpha]_D$ +100° (*c* 1.1, benzene)].

(4a*R*,8a*R*)-3,4,4a,7,8,8a-Hexahydro-8a-methyl-6-(trimethylsiloxy)-1(2*H*)-naphthalenone 1-Ethylene Acetal (6). To a blue solution of lithium metal (2.81 g, 405 mmol) in liquid ammonia (600 mL) cooled at −78 °C was gradually added a solution of the enone (−)-**5** (15.0 g, 67.6 mmol) and *tert*-butyl alcohol (10.0 g, 135 mmol) in dry tetrahydrofuran (THF; 100 mL) over 10 min. At the final stage of the addition, the mixture became too viscous to stir the content magnetically. After being kept at that temperature for 20 min, the mixture was treated with isoprene (18.4 g, 270 mmol) until the blue color disappeared. Ammonia was evaporated, and then the remaining mixture was stirred at room temperature for 1 h, in order to remove ammonia completely. After addition of dry THF (100 mL), the flask was placed in an ice bath. A turbid mixture of chlorotrimethylsilane (44.0 g, 405 mmol), triethylamine (41.0 g, 405 mmol), and dry THF (100 mL) was added all at once. After being vigorously stirred for 20 min, the reaction mixture was poured into a mixture of diethyl ether, ice, and aqueous $NaHCO_3$ solution and then extracted with diethyl ether. The organic layer was concentrated and distilled in vacuo with a short-path distillation apparatus, giving silyl enol ether **6** (18.4 g, 92%): ^1H NMR (89.55 MHz, $CDCl_3$) δ 0.174 (9 H, s, $Si(CH_3)_3$), 0.936 (3 H, s, CH_3), 1.07–2.76 (11 H, m), 3.903 (4 H, m, acetal), 4.521 (1 H, br s, H-5).

(4a*R*,5*S*,8a*R*)-3,4,4a,5,8,8a-Hexahydro-5-(hydroxymethyl)-8a-methyl-1,6(2*H*,7*H*)-naphthalenedione 1-Ethylene Acetal (7). To a solution of silyl enol ether **6** (2.00 g, 6.76 mmol) in dry THF (100 mL) was added a methyllithium solution in diethyl ether (1.6 M solution, 5.10 mL, 8.16 mmol). The mixture was stirred at room temperature for 30 min and then cooled to −78 °C. The formaldehyde gas of excess amount, which was generated by heating paraformaldehyde at 150 °C, was blown into the reaction mixture with a stream of nitrogen. After blowing for 60 min, the mixture was poured into ice water and extracted with diethyl ether. The organic layer was washed with brine, evaporated to dryness, and then subjected to a column chromatography on silica gel ($CHCl_3$/diethyl ether 1:1), giving hydroxymethyl ketone **7** (1.53 g, 89%) as a syrup: ^1H NMR (89.55 MHz, $CDCl_3/D_2O$) δ 1.24 (3 H, s, 8a-CH_3),

(17) Compound **18** had been previously synthesized by the method of photocycloaddition. Oda, M.; Kanao, Y. *Chem. Lett.* **1981**, 37.

(18) Reinvestigation of the $[\alpha]_D$ value of **3** derived from natural halenaquinol gave the larger value than that reported in ref 8 (the private communication from Prof. M. Kobayashi).

(19) All of the mass spectra of halenaquinol **1**, halenaquinone **2**, and halenaquinol dimethyl ether **3** show the M − CH_3 peaks as base peaks, respectively. For example, halenaquinol **1** exhibits *m/z* 319 as a base peak. (High-resolution mass spectrum calcd for $C_{20}H_{14}O_5$ − CH_3: 319.06064. Found: 319.06161.) These results indicate that the halenaquinol and halenaquinone skeletons easily lose the angular methyl groups, respectively.

(20) Gutzwiller, J.; Buchschacher, P.; Furst, A. *Synthesis* **1977**, 167.

1.3–2.5 (12 H, m), 3.62 (1 H, dd, J = 12.6, 5.4 Hz, 9-H), 3.82 (1 H, m, 9-H), 3.90 (4 H, m, acetal); MS m/z 254 (parent, relative intensity 90%), 99 (100%).

(4a*R*,5*S*,6*S*,8a*R*)-(+)-3,4,4a,5,6,7,8,8a-Octahydro-6-hydroxy-5-(hydroxymethyl)-8a-methyl-1(2*H*)-naphthalenone 1-Ethylene Acetal (8). To a solution of ketone **7** (12.4 g, 48.8 mmol) in dry THF (300 mL) cooled to 0 °C was added a solution of lithium tri-*sec*-butylborohydride (L-Selectride) in THF (1.0 M solution, 59.0 mL, 59.0 mmol), and the reaction mixture was stirred at that temperature for 20 min. An aqueous sodium hydroxide solution (1.0 M, 100 mL) and an aqueous hydrogen peroxide solution (35%, 100 mL) were added under ice cooling. After it was stirred for a further 20 min, the reaction mixture was poured into ice water and extracted with ethyl acetate. The organic layers were washed with brine and then evaporated to dryness. The residue was subjected to a short column chromatography on silica gel (hexane/ethyl acetate 1:1), giving diol (+)-**8** (11.5 g, 92%) as crystals: mp 136 °C (ethyl acetate); IR (KBr) ν_{max} 3350, 2910, 2850, 1425, 1175, 1120, 1070, 1025, 940, 900 cm^{-1}; ^{1}H NMR (300.15 MHz, $CDCl_3$) δ 0.998 (3 H, s, CH_3), 1.220 (1 H, dt, J = 12.9, 3.3 Hz), 1.418 (1 H, dm, J = 12.1 Hz), 1.5–1.8 (8 H, m), 1.910 (1 H, td, J = 12.8, 5.7 Hz), 2.188 (1 H, td, J = 12.2, 2.9 Hz), 2.355 (1 H, br s, OH), 2.620 (1 H, br s, OH), 3.8–4.0 (6 H, m), 4.135 (1 H, br s, 6-H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 13.760 (Q), 22.753, 23.078, 23.674, 28.875 (T), 30.229 (T), 34.996 (D), 41.551 (D), 42.526 (S), 64.142, 64.955, 65.171, 70.751, 112.899 (S); $[\alpha]_D$ +33.6° (c 1.058, $CHCl_3$); MS m/z 256 (parent, 10%), 238 (17%), 194 (22%), 99 (100%). High-resolution mass spectrum calcd for $C_{14}H_{24}O_4$: 256.16744. Found: 256.16741.

(4a*R*,5*S*,6*S*,8a*R*)-(+)-3,4,4a,5,6,7,8,8a-Octahydro-6-hydroxy-5-(hydroxymethyl)-8a-methyl-1(2*H*)-naphthalenone (9). A mixture of acetal (+)-**8** (8.0 g, 31.3 mmol), p-toluenesulfonic acid monohydrate (0.40 g, 2.1 mmol), and water (300 mL) was stirred at room temperature for 3 h, during which time the starting material gradually dissolved to give a clear solution. The reaction mixture was extracted with ethyl acetate. The water layer separated was saturated with solid sodium chloride and was subjected to the extraction again. The combined organic layers were washed with brine and evaporated to dryness, giving ketone (+)-**9** (6.5 g, 98%) as crystals: mp 129 °C (ethyl acetate/petroleum ether); IR (KBr) ν_{max} 3250, 2940, 2890, 2860, 1695, 1440, 1325, 1250, 1100, 1060, 995, 955, 920 cm^{-1}; ^{1}H NMR (89.55 MHz, $CDCl_3$) δ 1.115 (3 H, s), 1.2–2.9 (12 H, m), 2.95 (1 H, br s, disappeared in D_2O), 3.27 (1 H, br s, disappeared in D_2O), 3.847 (2 H, br s, d in D_2O, J = 3.5 Hz), 4.15 (1 H, br s, m in D_2O); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 15.764, 22.887, 25.787, 26.228, 28.820, 37.272, 38.843, 41.118, 48.215, 64.305, 70.914, 216.102; $[\alpha]_D$ +79.8° (c 1.027, $CHCl_3$); MS m/z 212 (parent, 73%), 194 (64%), 179 (38%), 93 (100%). High-resolution mass spectrum calcd for $C_{12}H_{20}O_3$: 212.14123. Found: 212.14123.

(4a*R*,5*S*,6*S*,8a*R*)-(+)-3,4,4a,5,6,7,8,8a-Octahydro-6-hydroxy-5-(hydroxymethyl)-8a-methyl-1(2*H*)-naphthalenone Acetonide (13). A mixture of diol acetal (+)-**8** (1.0 g, 3.91 mmol), p-toluenesulfonic acid (0.050 g, 0.29 mmol), acetone (25 mL), and dichloromethane (25 mL) was stirred at room temperature for 20 h. The reaction mixture was poured into ice water and extracted with dichloromethane. The organic layer was washed with an aqueous sodium bicarbonate solution and then evaporated to dryness. The residue was chromatographed on silica gel (hexane/EtOAc 1:1), giving keto acetonide (+)-**13** (0.61 g, 62%) as a solid material: mp 96 °C; IR (KBr) ν_{max} 2980, 2930, 2860, 1700, 1445, 1380, 1265, 1235, 1190, 1155, 1085, 980, 845 cm^{-1}; ^{1}H NMR (300.15 MHz, $CDCl_3$) δ 1.106 (3 H, s, 8a-CH_3), 1.363 (3 H, s, acetonide), 1.434 (3 H, s, acetonide), 1.32–1.93 (8 H, m), 2.071 (1 H, m), 2.285 (2 H, m), 2.651 (1 H, td, J = 14.0, 6.8 Hz), 3.884 (1 H, dd, J = 12.2, 1.1 Hz), 3.961 (1 H, dd, J = 12.2, 2.6 Hz), 4.068 (1 H, ddd, J = 2.6, 2.6, 2.6 Hz); ^{13}C NMR (75.48 MHz, $CDCl_3$) δ 15.904, 19.022, 22.676, 25.512, 26.585, 26.633, 29.671, 35.916, 37.201, 38.726, 47.875, 61.454, 66.786, 98.441, 215.756; $[\alpha]_D$ +72.0° (c 1.043, $CHCl_3$); MS (direct injection and chemical ionization with 2-methylpropane) m/z 253 (M + H, 40%), 237 (100%), 177 (28%). High-resolution mass spectrum calcd for $C_{15}H_{24}O_3$ + H: 253.18036. Found: 253.18034.

(1*S*,2*S*,4a*S*,8a*R*)-(−)-1,2,3,4,4a,7,8,8a-Octahydro-1-(hydroxymethyl)-4a-methyl-2-naphthalenol (10). A solution of keto diol (+)-**9** (6.5 g, 30.7 mmol) and p-toluenesulfonhydrazide (6.8 g, 36.5 mmol) in dry ethanol (500 mL) was refluxed for 4 h, during which time ethanol was gradually distilled. The reaction mixture was evaporated in vacuo to dryness, and the residue was dissolved in ethyl acetate. The solution was treated with active charcoal and then evaporated, giving tosylhydrazone (13.0 g).

To a solution of tosylhydrazone (13.0 g) in dry THF (250 mL) cooled at 0 °C was added a methyllithium solution in diethyl ether (1.4 M, 98 mL, 137 mmol) under nitrogen. After it was stirred at room temperature for 1 h, the reaction mixture was poured into ice water and extracted with ethyl acetate. The organic layer was washed with brine and evaporated to dryness, giving olefin (−)-**10** (6.0 g) in a quantitative yield: mp 141 °C (ethyl acetate); IR (KBr) ν_{max} 3270, 3000, 2930, 1055, 1005, 970 cm^{-1}; ^{1}H NMR (89.55 MHz, $CDCl_3$) δ 0.899 (3 H, s), 1.1–2.2 (10 H, m), 2.63 (1 H, br s, disappeared in D_2O), 2.88 (1 H, br s, disappeared in D_2O), 3.866 (2 H, br s, d in D_2O, J = 3.3 Hz), 4.198 (1 H, br s, m in D_2O), 5.478 (2 H, s); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 18.852, 20.315, 26.057, 29.579, 32.938, 34.671, 35.863, 41.226, 64.305, 71.943, 124.167, 139.065; $[\alpha]_D$ −41.7° (c 1.006, $CHCl_3$); MS m/z 196 (parent, 8%), 178 (48%), 163 (45%), 147 (100%), 145 (83%). High-resolution mass spectrum calcd for $C_{12}H_{20}O_2$: 196.14632. Found: 196.14639.

(1*S*,2*S*,4a*S*,8a*R*)-(−)-1,2,3,4,4a,7,8,8a-Octahydro-1-(hydroxymethyl)-4a-methyl-2-naphthalenol Acetonide (11). A mixture of diol (−)-**10** (6.0 g, 30.6 mmol), p-toluenesulfonic acid (0.20 g, 1.2 mmol), and acetone (200 mL) was stirred at room temperature for 4 h. After addition of triethylamine (1.0 mL), the mixture was evaporated to dryness, and the residue was chromatographed on silica gel (hexane/EtOAc 1:1), giving acetonide (−)-**11** (6.2 g, 86%) as a syrup: IR ($CHCl_3$) ν_{max} 2900, 1430, 1370, 1080, 980, 840 cm^{-1}; ^{1}H NMR (89.55 MHz, $CDCl_3$) δ 0.89 (3 H, s, 4a-CH_3), 1.1–2.3 (10 H, m), 1.38 (3 H, s, acetonide), 1.44 (3 H, s, acetonide), 3.94 (2 H, d, J = 2.6 Hz, 5-H), 4.14 (1 H, ddd, J = 2.8, 2.8, 2.8 Hz, 2-H), 5.48 (2 H, br s, 5-H and 6-H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 18.961, 19.177, 20.152, 26.166, 27.303, 29.687, 33.479, 34.292, 35.863, 36.026, 61.000, 67.609, 98.272, 124.113, 139.282; $[\alpha]_D$ −20.0° (c 1.745, $CHCl_3$); MS (direct injection and chemical ionization with 2-methylpropane) m/z 237 (M + H, 65%), 221 (100%), 179 (32%), 161 (57%). High-resolution mass spectrum calcd for $C_{15}H_{24}O_2$ + H: 237.18544. Found: 237.18524.

(4a*S*,7*S*,8*S*,8a*R*)-(+)-4a,5,6,7,8,8a-Hexahydro-7-hydroxy-8-(hydroxymethyl)-4a-methyl-2(1*H*)-naphthalenone Acetonide (12). To a suspension of chromium(VI) oxide (CrO_3, 25.4 g, 254 mmol) in dichloromethane (125 mL) cooled at −25 °C was added 3,5-dimethylpyrazole (24.4 g, 254 mmol) in one portion, and the mixture was stirred at that temperature for 20 min. A solution of olefin acetonide (−)-**11** (3.0 g, 12.7 mmol) in dichloromethane (125 mL) was added, and the reaction mixture was stirred at −20 °C for 2.5 h. After an aqueous sodium hydroxide solution (5 M, 100 mL) was added, the mixture was stirred at 0 °C for 1 h, poured into water, filtered with Celite, and extracted with dichloromethane. The organic layer was washed with 1 M hydrochloric acid and brine and then evaporated to dryness. The residue was chromatographed on silica gel (hexane/EtOAc 1:1) to yield enone (+)-**12** (2.0 g, 63%) as a syrup: IR ($CHCl_3$) ν_{max} 2900, 1655, 1370, 1080, 980, 945, 900 cm^{-1}; ^{1}H NMR (89.55 MHz, $CDCl_3$) δ 1.054 (3 H, s, 4a-CH_3), 1.356 (3 H, s, acetonide), 1.436 (3 H, s, acetonide), 1.2–1.8 (5 H, m), 2.05 (1 H, dd, J = 17.0, 14.0 Hz), 2.4–2.9 (2 H, m), 3.81 (1 H, dd, J = 12.6, 1.5 Hz, 10-H), 3.97 (1 H, dd, J = 12.6, 2.8 Hz, 10-H), 4.12 (1 H, m, 7-H), 5.872 (1 H, d, J = 9.9 Hz, 3-H), 6.767 (1 H, d, J = 9.9 Hz, 4-H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 16.582, 18.989, 26.857, 29.719, 31.865, 35.637, 35.897, 36.872, 60.283, 66.396, 98.457, 126.948, 161.407, 199.860, where the peak due to a quarternary carbon was not found because of the overlap with other peaks; $[\alpha]_D$ +46.7° (c 1.113, $CHCl_3$); MS (direct injection and chemical ionization with 2-methylpropane) m/z 251 (M + H, 59%), 235 (100%), 193 (20%), 175 (24%). High-resolution mass spectrum calcd for $C_{15}H_{22}O_3$ + H: 251.16471. Found: 251.16475.

3,6-Dimethoxybenzocyclobutene (18). In a glass-made muffle furnace heated at 305–310 °C were placed by portions the crystals of sulfone **17** (1.383 g, 6.07 mmol). A slightly yellow syrup formed was collected by washing the vessel with dichloromethane, and the solution was evaporated to dryness. The residue was chromatographed on silica gel (hexane/EtOAc 10:1), giving benzocyclobutene **18** (0.480 g, 48%) as crystals: mp 52–53 °C; IR (KBr) ν_{max} 2935, 2835, 1590, 1485, 1430, 1250, 1045, 1000, 810, 735 cm^{-1}; ^{1}H NMR (100 MHz, $CDCl_3$) δ 3.27 (4 H, s), 3.80 (6 H, s), 6.62 (2 H, s); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 29.308 (T), 56.395 (Q), 113.983 (D), 130.235 (S), 148.221 (S); MS m/z 164 (parent, 100%), 149 (87%). High-resolution mass spectrum calcd for $C_{10}H_{12}O_2$: 164.08372. Found: 164.08363. From the polar fractions of the chromatography, the starting material of sulfone **17** (0.218 g, 16%) was recovered.

(3*S*,4*S*,4a*R*,6aξ,12aξ,12b*S*)-(+)-1,2,3,4,4a,6a,7,12,12a,12b-Decahydro-3-hydroxy-4-(hydroxymethyl)-8,11-dimethoxy-12b-methyl-6(5*H*)-benzo[*a*]anthracenone Acetonide (19). A mixture of enone (+)-**12** (0.150 g, 0.60 mmol) and benzocyclobutene **18** (0.450 g, 2.74 mmol) in benzene (0.5 mL) in a sealed tube was heated at 210–215 °C for 20 h. The reaction mixture was dissolved in a small amount of chloroform, which was subjected to HPLC on silica gel (hexane/EtOAc 1:1), giving the Diels–Alder adduct (+)-**19** (0.083 g, 33%) as colorless crystals: mp 225 °C (ethyl acetate/diethyl ether); IR (KBr) ν_{max} 2925, 1700, 1475, 1375, 1250, 1225, 1190, 1155, 1075 cm^{-1}; ^{1}H NMR (89.55 MHz, $CDCl_3$) δ 1.282 (3 H, s), 1.392 (3 H, s), 1.434 (3 H, s), 1.6–3.8 (15 H, m), 3.717 (3 H, s), 3.781 (3 H, s), 3.89 (1 H, dd, J = 12.8, 2.6 Hz), 4.11 (1 H, ddd, J = 2.6, 2.6, 2.6 Hz, 3_{eq}-H), 6.547 (2 H, s, 9-H and 10-H);

^{13}C NMR (22.5 MHz, $CDCl_3$) δ 18.310, 19.123, 21.073, 22.211, 27.412, 29.416, 29.687, 33.208, 36.459, 37.380, 40.685, 44.260, 46.860, 55.474, 55.583, 60.675, 66.742, 96.159, 98.543, 106.669, 106.886, 124.818, 125.197, 151.309, 209.980; $[\alpha]_D$ +115.9° (*c* 1.010, $CHCl_3$); MS *m/z* 414 (parent, 100%). High-resolution mass spectrum calcd for $C_{25}H_{34}O_5$: 414.24061. Found: 414.24086.

(3*S*,4*S*,4a*R*,12b*R*)-(−)-1,2,3,4,4a,12b-Hexahydro-3-hydroxy-4-(hydroxymethyl)-8,11-dimethoxy-12b-methyl-6(5*H*)-benzo[*a*]anthracenone Acetonide (20). A solution of adduct (+)-**19** (0.083 g, 0.20 mmol) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ; 0.096 g, 0.42 mmol) in benzene (10 mL) was refluxed under nitrogen for 3.5 h. After it was cooled to room temperature, the reaction mixture was subjected to short column chromatography on basic alumina (hexane/EtOAc 1:1) to remove hydroquinone formed and excess DDQ. The crude product obtained was further purified by HPLC on silica gel (hexane/EtOAc 1:1), giving yellow crystals of naphthalene ketone (−)-**20** (0.073 g, 89%): mp 224 °C (diethyl ether); IR (KBr) ν_{max} 2920, 1670, 1620, 1580, 1455, 1375, 1325, 1260, 1215, 1185, 1155, 1100, 1080, 840, 800, 715 cm^{-1}; ^1H NMR (300.15 MHz, $CDCl_3$) δ 1.222 (3 H, s), 1.295 (3 H, s), 1.409 (1 H, m), 1.462 (3 H, s), 1.938 (2 H, m), 2.171 (1 H, ddd, *J* = 13.1, 10.3, 7.0 Hz, 1_{ax}-H), 2.286 (1 H, ddd, *J* = 13.1, 3.6, 3.6 Hz, 1_{eq}-H), 2.427 (1 H, dd, *J* = 18.1, 13.2 Hz, 5_{ax}-H), 2.874 (1 H, ddd, *J* = 13.2, 11.2, 4.5 Hz, 4_{ax}-H), 2.970 (1 H, dd, *J* = 18.1, 4.5 Hz, 5_{eq}-H), 3.891 (1 H, d, *J* = 12.1 Hz), 3.954 (3 H, s), 3.965 (3 H, s), 4.032 (1 H, dd, *J* = 12.1, 2.7 Hz), 4.205 (1 H, ddd, *J* = 2.7, 2.7, 2.7 Hz, 3_{eq}-H), 6.657 (1 H, d, *J* = 8.1 Hz, 9-H or 10-H), 6.788 (1 H, d, *J* = 8.1 Hz, 10-H or 9-H), 8.210 (1 H, s, 12-H), 8.968 (1 H, s, 7-H); ^{13}C NMR (75.48 MHz, $CDCl_3$) δ 19.051, 21.676, 27.264, 29.647, 30.832, 34.416, 36.672, 36.888, 38.583, 55.701, 55.794, 60.839, 66.479, 98.512, 103.074, 106.172, 116.494, 123.755, 124.451, 128.785, 129.560, 148.984, 149.534, 151.026, 198.347; $[\alpha]_D$ −11.5° (*c* 1.055, $CHCl_3$). High-resolution mass spectrum calcd for $C_{25}H_{30}O_5$: 410.20931. Found: 410.20924.

(3*S*,4*S*,12b*S*)-1,2,3,4-Tetrahydro-3,5-dihydroxy-4-(hydroxymethyl)-8,11-dimethoxy-12b-methyl-6(12b*H*)-benzo[*a*]anthracenone Acetonide (21). Into a solution of ketone (−)-**20** (0.070 g, 0.17 mmol) and potassium *tert*-butoxide (0.096 g, 0.86 mmol) in *tert*-butyl alcohol (10 mL) was bubbled oxygen gas for 4 h at room temperature. The reaction mixture was acidified with an aqueous ammonium chloride solution and extracted with chloroform. The organic layer was washed with brine and evaporated to dryness, giving diosphenol **21** (0.065 g, 90%): ^1H NMR (300.15 MHz, $CDCl_3$) δ 1.907 (1 H, dddd, *J* = 13.3, 2.7, 2.7, 2.7 Hz, 2_{eq}-H), 2.022 (1 H, ddd, *J* = 13.3, 13.2, 2.7 Hz, 1_{ax}-H), 2.209 (1 H, dddd, *J* = 13.3, 13.3, 2.7, 2.7 Hz, 2_{ax}-H), 2.383 (1 H, ddd, *J* = 13.2, 2.7, 2.7 Hz, 1_{eq}-H), 2.663 (1 H, ddd, *J* = 3.0, 2.7, 1.9 Hz, 4_{ax}-H), 4.170 (1 H, dd, *J* = 12.0, 3.0 Hz, 14_{ax}-H), 4.308 (1 H, ddd, *J* = 2.7, 2.7, 2.7 Hz, 3_{eq}-H), 5.070 (1 H, dd, *J* = 12.0, 1.9 Hz, 14_{eq}-H), 6.676 (1 H, d, *J* = 8.1 Hz, 9-H or 10-H), 6.788 (1 H, d, *J* = 8.1 Hz, 10-H or 9-H), 7.603 (1 H, s, hydrogen-bonded OH, disappeared in D_2O), 8.414 (1 H, s, 12-H), 9.191 (1 H, s, 7-H); UV (EtOH) λ_{max} 399 nm (ε 2600), 328 (sh) (4800), 280 (15000), 220 (26000); UV (EtOH/aqueous NaOH) λ_{max} 408 nm (ε 4100), 274 (11600), 256 (13700). High-resolution mass spectra calcd for $C_{25}H_{28}O_6$: 424.18857. Found: 424.18849. Trimethylsilyl ether for $C_{25}H_{27}O_6(CH_3)_3Si$. Calcd: 496.2281. Found: 496.2262.

(3*S*,4*S*,12b*S*)-1,2,3,4-Tetrahydro-3,5-dihydroxy-4-(hydroxymethyl)-8,11-dimethoxy-12b-methyl-6(12b*H*)-benzo[*a*]anthracenone (22). A mixture of acetonide **21** (0.065 g, 0.15 mmol) and 60% aqueous acetic acid (10 mL) was stirred at room temperature for 30 min. The reaction mixture was poured into water and extracted with chloroform. The organic layer was washed with brine and evaporated to dryness, giving a solid material of orange color (0.071 g). Since triol **22** was unstable, the crude product was subjected to the next oxidation reaction without purification.

(12b*S*)-(+)-8,11-Dimethoxy-12b-methyl-1*H*-benzo[6,7]phenanthro[10,1-*bc*]furan-3,6(2*H*,12b*H*)-dione (3). To a solution of triol **22** (crude sample, 0.071 g) in benzene (12 mL) was added a solution of pyridine (0.098 g, 1.24 mmol) and trifluoroacetic acid (0.074 g, 0.66 mmol) in dimethyl sulfoxide (DMSO; 12 mL), and then 1,3-dicyclohexylcarbodiimide (DCC; 0.288 g, 1.40 mmol) was added. The reaction mixture was stirred at room temperature for 20 h, poured into ice water, and extracted with ethyl acetate. The organic layer was washed with brine and evaporated to dryness, giving a yellow material. The crude product was chromatographed on silica gel (hexane/EtOAc 1:1), affording halenaquinol dimethyl ether (+)-**3** (0.027 g, 44% overall yield from ketone (−)-**20**) as yellow crystals: mp 245 °C; IR (KBr) ν_{max} 1665, 1624, 1462, 1337, 1262, 1237, 1148, 1115, 1086, 1040, and 963 cm^{-1}; ^1H NMR (399.8 MHz, $CDCl_3$) δ 1.678 (3 H, s, 12b-CH_3), 2.336 (1 H, ddd, *J* = 13.3, 13.3, 4.8 Hz, 1_{ax}-H), 2.828 (1 H, ddd, *J* = 18.6, 4.8, 1.8 Hz, 2_{eq}-H), 2.918 (1 H, ddd, *J* = 13.3, 5.2, 1.8 Hz, 1_{eq}-H), 3.026 (1 H, ddd, *J* = 18.6, 13.3, 5.2 Hz, 2_{ax}-H), 3.992 (3 H, s, OCH_3), 3.995 (3 H, s, OCH_3), 6.738 (1 H, d, *J* = 8.5 Hz, 9-H or 10-H), 6.850 (1 H, d, *J* = 8.5 Hz, 10-H or 9-H), 8.218 (1 H, s, 4-H), 8.312 (1 H, s, 12-H), and 9.300 (1 H, s, 7-H); difference NOE, between 12-H at δ 8.312 and 1_{eq}-H at δ 2.918, 12b-CH_3 at δ 1.681 and 2_{ax}-H at δ 3.026, 12b-CH_3 at δ 1.681 and 1_{eq}-H at δ 2.918; ^{13}C NMR (100.5 MHz, $CDCl_3$) δ 31.76, 34.21, 35.78, 36.82, 55.74, 103.79, 106.56, 118.49, 122.56, 124.74, 124.82, 127.61, 130.45, 144.44, 145.72, 147.01, 148.25, 148.68, 150.82, 172.74, 192.17; $[\alpha]^{25}_D$ +150.3° (*c* 1.042, CH_2Cl_2) [natural],[18] $[\alpha]^{23}_D$ +150.1° (*c* 1.124, CH_2Cl_2)]; UV (EtOH) λ_{max} 408 nm (ε 4500), 298 (25900), 282 (sh) (20000), and 226 (41200); CD (EtOH) λ_{ext} 410 nm (Δε +1.8), 362 (+1.6), 347 (+2.6), 303 (−5.6), 244 (+4.5), 232 (−9.4); MS *m/z* 362 (parent, 95%), 347 (100%), 332 (20%), 317 (30%). High-resolution mass spectrum calcd for $C_{22}H_{18}O_5$: 362.11541. Found: 362.11598.

(12b*S*)-(+)-12b-Methyl-1*H*-benzo[6,7]phenanthro[10,1-*bc*]furan-3,6,8,11(2*H*,12b*H*)-tetrone (2). To a mixture of dimethyl ether (12b*S*)-(+)-**3** (0.013 g, 0.036 mmol), methanol (8 mL), and water (4 mL) was added cerium(IV) ammonium nitrate (CAN; 0.100 g, 0.182 mmol) under ice cooling. After it was stirred for 2 h in an ice bath and for 1 h at room temperature, the reaction mixture of pale yellow color was poured into water and extracted with chloroform. The organic layer was washed with brine and evaporated to dryness. The residue was subjected to HPLC on silica gel (hexane/EtOAc 1:1), giving halenaquinone (12b*S*)-**2** (0.0054 g, 45%): thin-layer chromatography on silica gel (TLC) R_f 0.42 (hexane/EtOAc 1:1); ^1H NMR (89.55 MHz, dimethyl sulfoxide-d_6 (DMSO-d_6)) δ 1.659 (3 H, s), 2.1–2.4 (1 H, m), 2.6–3.2 (3 H, m), 7.187 (2 H, s), 8.329 (1 H, s), 8.718 (1 H, s), 8.887 (1 H, s); UV (acetonitrile) λ_{max} 326 (sh) nm (ε 5700), 278 (15200), 260 (sh) (20200), 253 (21600); MS *m/z* 332 (parent, 30%), 317 (100%). High-resolution mass spectrum calcd for $C_{20}H_{12}O_5$: 332.06847. Found: 332.06872.

(12b*S*)-(+)-8,11-Dihydroxy-12b-methyl-1*H*-benzo[6,7]phenanthro[10,1-*bc*]furan-3,6(2*H*,12b*H*)-dione (1). To a solution of halenaquinone (12b*S*)-**2** (0.0046 g, 0.014 mmol) in acetone (4 mL) was added aqueous sodium hydrosulfite ($Na_2S_2O_4$; 0.57 M, 0.5 mL, 0.285 mmol), and the mixture was stirred for 30 min. The reaction mixture with bright yellow color was diluted with dichloromethane (4 mL), and the organic layer was separated, dried over anhydrous sodium sulfate, and evaporated in vacuo, giving halenaquinol (12b*S*)-**1** in an almost quantitative yield: TLC R_f 0.20 (hexane/EtOAc 1:1); ^1H NMR (89.55 MHz, DMSO-d_6) δ 1.649 (3 H, s), 2.2–2.4 (1 H, m), 2.6–3.3 (3 H, m), 6.802 (1 H, d, *J* = 8.1 Hz), 6.857 (1 H, d, *J* = 8.1 Hz), 8.278 (1 H, s), 8.819 (1 H, s), 9.022 (1 H, s), 9.6 (1 H, br s, disappeared in D_2O/DMSO-d_6), 9.8 (1 H, br s, disappeared in D_2O/DMSO-d_6); UV (methanol) λ_{max} 430 nm (ε 3500), 302 (23000), 282 (sh) (18500), 228 (36200), where the ε values are corrected so that the ε value of the peak at 302 nm agrees with that of the natural sample; MS (direct injection) *m/z* 334 (parent, 65%), 319 (100%). High-resolution mass spectrum calcd for $C_{20}H_{14}O_5$: 334.08411. Found: 334.08429.

Acknowledgment. We thank Professors Isao Kitagawa and Motomasa Kobayashi, Osaka University, for a generous gift of an authentic sample and spectroscopic data. This work was supported in part by grants from the Ministry of Education, Science, and Culture, Japan (No. 59430005 to N.H.) and the Suntory Institute for Bioorganic Research (to N.H.). N.H. is grateful to the Central Research and Development Department, Experimental Station, E. I. du Pont de Nemours and Co., for measurements of some spectral data during his stay as a visiting research scientist.

Supplementary Material Available: Details of the synthesis of intermediates not described in the Experimental Section (3 pages). Ordering information is given on any current masthead page.