Special Issue Article

Photoracemization of Blestriarene C and Its Analogs

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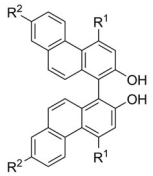
ABSTRACT Two analogs of blestriarene C (4,4'-dimethoxy-1,1'-biphenanthrene-2,2',7,7'-tetraol) bearing no 7,7'-dihydroxy (**3**) and 4,4'-dimethoxy groups **4** were prepared. Unlike blestriarene C (**1**), compounds **3** and **4**, as well as 1,1'-biphenanthrene-2,2'-diol (**5**), do not racemize under fluorescent lamp illumination. Cyclic voltammetry analysis reveals that compound **1** has a lower half-wave potential ($E_{1/2}$) than compounds **3–5**, suggesting that a redox cycle is involved in the racemization. Compound **1** racemizes by absorbing UV light corresponding to the ^1L_b band. During the reaction, no side products are observed. The racemization is significantly inhibited under nitrogen. Based on these observations, we propose a feasible mechanism for the easy racemization of compound **1**, which is mediated by a cation radical generated in situ by a reversible photo-induced oxygen oxidation. *Chirality 27:479–486, 2015*. © 2015 Wiley Periodicals, Inc.

KEY WORDS: biaryl synthesis; photoreaction; racemization; atropisomerism; photooxidation

Blestriarene C (**1**)[1–3] is one of the naturally occurring 1,1'-biphenanthrenes mainly isolated from orchids.[4] The compound is active against Gram-positive bacteria, *Staphylococcus aureus* and *Streptococcus mutans*.[1] Previously, we synthesized compound **1** for the first time and determined the absolute stereochemistry.[5] During the study, we found that the compound, as well as its synthetic precursor **2**, racemizes under ambient light exposure. It is known that some atropisomeric biaryls undergo photoracemization with different reaction mechanisms.[6–15] For example, 1,1'-binaphthalene racemizes through the triplet state,[7] while 6*H*-dibenzo[*b*,*d*]pyrans through biaryl quinone methides.[8,9] Excited-state proton transfer participates in the racemization of 1,1'-binaphthalene-2,2'-diol.[10–12] However, the extreme tendency of compound **1** toward photoracemization cannot be explained by any of these reaction mechanisms. As compound **1** is susceptible to oxidation, we supposed that a cation radical generated in situ by photo-induced oxidation mediates the racemization. On the basis of this assumption, we prepared blestriarene C analogs **3** and **4**, which are expected to be less susceptible to oxidation, and investigated the relationship between the photoracemization activity and half-wave potential of compounds **1–5**. We also investigated the photoracemization of compound **1** in detail.



1 R^1 = OMe, R^2 = OH
2 R^1 = OMe, R^2 = O^{i}Pr
3 R^1 = OMe, R^2 = H
4 R^1 = H, R^2 = OH
5 R^1 = H, R^2 = H

MATERIALS AND METHODS

Melting points were taken using a Mitamura Riken MP-P apparatus. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX-400 or DRX-500 spectrometer using tetramethylsilane as an internal standard. IR and UV-Vis spectra were recorded on Shimadzu FTIR-8300 and UV-2500 spectrophotometers, respectively. Microanalyses were carried out in the Microanalytical Laboratory of the Institute of Multidisciplinary Research for Advanced Materials, Tohoku University. HRMS spectra were measured using a JEOL JMS-700 in the Technical Division, School of Engineering, Tohoku University. Cyclic voltammograms were recorded on a Hokuto Denko HSV-100 potentiostat. Photo-irradiation was conducted using a Hitachi FL20SS N/18-B 18 W fluorescent lamp, an Ushio USH-500SC ultrahigh-pressure mercury lamp, or a Hitachi F-4500 fluorescence spectrophotometer. Merck silica gel 60 (63–200 μm) was used for column chromatography. Dry THF and benzene were of commercial grade. Dichloromethane, DMF, HMPA, and triethylamine were distilled from CaH_2. Acetone and methanol were distilled from $CaSO_4$ and Mg turnings, respectively. Compounds **1**,[5] **2**,[5] **5**,[16] **6**,[5] and **8**[17] were prepared as described previously.

Synthesis of Compound 3

2-Bromo-5-isopropoxy-1-methoxy-3-methylbenzene (7). A mixture of phenol **6** (3.00 g, 13.8 mmol), dry acetone (150 ml), and K_2CO_3 (3.81 g, 27.6 mmol) was stirred at room temperature for 1 h. To the mixture was added 2-bromopropane (*d* 1.31; 7.77 ml, 82.8 mmol), and the mixture was refluxed for 48 h. After cooling, the reaction was quenched with water, and the mixture was extracted with diethyl ether. The extract was washed with water, dried over $MgSO_4$, and evaporated. The residue was purified by column chromatography with hexane–ethyl acetate (7:1) as an eluent to give ether **7** (3.40 g, 95%) as an oil, ^{1}H NMR (400 MHz, $CDCl_3$,

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Received for publication 7 January 2015; Accepted 14 March 2015
DOI: 10.1002/chir.22447
Published online 05 May 2015 in Wiley Online Library (wileyonlinelibrary.com).

δ): 1.30 [d, J = 6.0 Hz, 6H, OCH(CH_3)$_2$], 2.36 (s, 3H, ArCH_3), 3.81 (s, 3H, OCH_3), 4.49 [sept, J = 6.0 Hz, 1H, OCH(CH$_3$)$_2$], 6.32 (d, J = 2.7 Hz, 1H, ArH), 6.41 (d, J = 2.7 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 21.8, 23.3, 55.9, 69.8, 98.7, 104.5, 109.0, 139.4, 156.4, 157.3. Anal. calcd. for $C_{11}H_{15}BrO_2$: C 50.98, H 5.83, Br 30.83; found: C 50.94, H 5.45, Br 30.68.

2,6-Di-*tert*-butyl-4-methoxyphenyl 4'-isopropoxy-2'-methoxy-6'-methyl-1,1'-biphenyl-2-carboxylate (9). Magnesium turnings (1.03 g, 42.4 mmol) was activated with 1,2-dibromoethane (30 μl) in dry THF (10 ml) under ultrasonic irradiation (53 W, 41 kHz) for 10 min. To the suspension was added dropwise a mixed solution of compound **7** (5.50 g, 21.2 mmol) and 1,2-dibromoethane (50 μl) in dry THF (40 ml) over a period of 1 h, and the mixture was irradiated for a further 1 h. The solvent was evaporated under reduced pressure to leave a residue, which was dried in vacuo for 2 h and then dissolved by the addition of dry benzene (50 ml) under ultrasonic irradiation to give a Grignard solution of compound **7**. The Grignard solution was added dropwise to a solution of compound **8** (5.24 g, 14.2 mmol) in dry benzene (50 ml) over a period of 30 min, and the mixture was refluxed for 2 h. After cooling, the mixture was quenched with saturated aqueous NH_4Cl, and the resulting mixture was extracted with diethyl ether. The extract was washed successively with water and saturated aqueous NH_4Cl, dried over $MgSO_4$, and evaporated. The residue was purified by column chromatography with hexane–ethyl acetate (20:1) as an eluent to give biphenyl **9** (7.25 g, 99%) as a colorless powder, mp 154–155 °C; ^{1}H NMR (400 MHz, $CDCl_3$, δ): 1.28 [s, 9H, C(CH_3)$_3$], 1.29 [s, 9H, C(CH_3)$_3$], 1.31 [d, J = 6.0 Hz, 3H, OCH(CH_3)$_2$], 1.32 [d, J = 6.0 Hz, 3H, OCH(CH_3)$_2$], 1.86 (s, 3H, ArCH_3), 3.52 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 4.50[(sept, J = 6.0 Hz, 1H, OCH(CH$_3$)$_2$], 6.23 (d, J = 2.0 Hz, 1H, ArH), 6.30 (d, J = 2.0 Hz, 1H, ArH), 6.81 (d, J = 3.0 Hz, 1H, ArH), 6.82 (d, J = 3.0 Hz, 1H, ArH), 7.23 (d, J = 7.5 Hz, 1H, ArH), 7.53 (t, J = 7.5 Hz, 1H, ArH), 7.65 (t, J = 7.5 Hz, 1H, ArH), 8.51 (d, J = 7.5 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 20.4, 22.3, 22.4, 31.4, 31.5, 35.6, 35.7, 55.3, 55.3, 69.4, 96.9, 107.2, 111.6, 111.7, 123.0, 127.5, 129.3, 131.6, 132.8, 133.0, 136.6, 141.8, 142.4, 143.6, 143.9, 156.2, 157.3, 157.8, 165.1; IR (KBr): ν = 2946, 1745 cm^{-1}. Anal. calcd. for $C_{33}H_{42}O_5$: C 76.42, H 8.16; found: C 76.17, H 8.06.

2-Isopropoxy-4-methoxyphenanthren-9-ol (10). To an ice-cold solution of diethylamine (d 0.707; 6.37 ml, 61.6 mmol) in dry THF (40 ml) was added dropwise butyllithium (1.59 M in hexane; 35.4 ml, 56.0 mmol), and the solution was stirred for 1 h. The solution was added dropwise over a period of 40 min to an ice-cold solution of biphenyl **9** (7.24 g, 14.0 mmol) in THF–HMPA (2:1 v/v; 60 ml). After stirring at 0 °C for 1 h, the mixture was quenched with water and acidified by the addition of 2 M HCl. The resulting mixture was extracted with diethyl ether, and the extract was washed successively with water and brine, dried over $MgSO_4$, and evaporated. The residue was purified by column chromatography with hexane–ethyl acetate (4:1) as an eluent to give phenanthrol **10** as a foam (3.29 g, 84%), ^{1}H NMR (400 MHz, $CDCl_3$, δ): 1.40 [d, J = 6.0 Hz, 6H, OCH(CH_3)$_2$], 4.06 (s, 3H, OCH_3), 4.69 [sept, J = 6.0 Hz, 1H, OCH(CH$_3$)$_2$], 5.86 (s, 1H, ArOH), 6.61 (d, J = 2.4 Hz, 1H, ArH), 6.67 (d, J = 2.4 Hz, 1H, ArH), 6.85 (s, 1H, ArH), 7.52 (ddd, J = 8.1, 6.9, 1.2 Hz, 1H, ArH), 7.63 (ddd, J = 8.6, 6.9, 1.6 Hz, 1H, ArH), 8.29 (dd, J = 8.1, 1.6 Hz, 1H, ArH), 9.53 (dd, J = 8.6, 1.2 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 22.2, 31.1, 55.7, 69.9, 98.5, 102.1, 106.5, 121.7, 124.7, 124.8, 127.2, 127.6, 131.9, 136.2, 150.4, 156.6, 160.1; IR (KBr): ν = 3371, 1596 cm^{-1}.

2-Isopropoxy-4-methoxyphenanthren-9-yl trifluoromethanesulfonate (11). To a mixed solution of phenanthrol **10** (3.29 g, 11.7 mmol) and dry triethylamine (d 0.726; 4.87 ml, 35.1 mmol) in dry dichloromethane (50 ml) was added dropwise trifluoromethanesulfonic anhydride (d = 1.677; 2.94 ml, 17.6 mmol) at –78 °C, and the mixture was stirred at this temperature for 3.5 h. The mixture was quenched with water, and acidified by the addition of 2 M HCl. The resulting mixture was extracted with diethyl ether, and the extract was washed successively with water and brine, dried over $MgSO_4$, and evaporated. The residue was purified by column chromatography with hexane–ethyl acetate (7:1) as an eluent to give ester **11** (4.96 g, 98%) as crystals, mp 84.8–86.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$, δ): 1.44 [d, J = 6.0 Hz, 6H, OCH(CH_3)$_2$], 4.10 (s, 3H, OCH_3), 4.75 [sept, J = 6.0 Hz, 1H, OCH(CH$_3$)$_2$], 6.81 (d, J = 2.4 Hz, 1H, ArH), 6.90 (d, J = 2.4 Hz, 1H, ArH), 7.60 (s, 1H, ArH), 7.63 (ddd, J = 7.6, 7.1, 1.1 Hz, 1H, ArH), 7.70 (ddd, J = 8.3, 7.1, 1.5 Hz, 1H, ArH), 8.10 (dd, J = 8.3, 1.1 Hz, 1H, ArH), 9.60 (d, J = 7.6 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 22.0, 55.8, 70.1, 101.8, 103.6, 114.7, 117.0, 117.7, 120.8, 124.4, 125.9, 127.9, 128.0, 132.2, 133.8, 145.1, 157.2, 159.9; IR (KBr): ν = 3651, 1610 cm^{-1}. Anal. calcd. for $C_{19}H_{17}F_3O_5S$: C 55.07, H 4.13; found: C 55.04, H 4.04.

2-Isopropoxy-4-methoxyphenanthrene (12). A mixture of ester **11** (4.14 g, 9.98 mmol), palladium acetate (45.0 mg, 0.20 mmol), triphenylphosphine (130 mg, 0.50 mmol), dry triethylamine (d 0.726; 4.17 ml, 29.9 mmol), and dry DMF (35 ml) was stirred at room temperature for 10 min. To it was added formic acid (d 1.22; 840 μl, 22.3 mmol), and the mixture was stirred at 65 °C for 2 h. The mixture was quenched with water and acidified by the addition of 2 M HCl. The resulting mixture was extracted with ethyl acetate, and the extract was washed successively with water and brine, dried over $MgSO_4$, and evaporated. The residue was purified by column chromatography with hexane–ethyl acetate (20:1) as an eluent to give phenanthrene **12** (2.61 g, 98%) as crystals, mp 64.5–65.8 °C; ^{1}H NMR (400 MHz, CD_2Cl_2, δ): 1.43 [d, J = 6.0 Hz, 6H, OCH(CH_3)$_2$], 4.09 (s, 3H, OCH_3), 4.75 [sept, J = 6.0 Hz, 1H, OCH(CH$_3$)$_2$], 6.76 (d, J = 2.4 Hz, 1H, ArH), 6.89 (d, J = 2.4 Hz, 1H, ArH), 7.50 (ddd, J = 7.5, 7.4, 1.1 Hz, 1H, ArH), 7.58 (ddd, J = 8.0, 7.5, 1.5 Hz, 1H, ArH), 7.58 (d, J = 8.7 Hz, 1H, ArH), 7.70 (d, J = 8.7 Hz, 1H, ArH), 7.83 (dd, J = 8.0, 1.1 Hz, 1H, ArH), 9.52 (dd, J = 7.4 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 22.1, 55.7, 69.8, 100.6, 103.4, 115.4, 124.8, 126.4, 126.8, 127.6, 128.2, 128.3, 130.5, 131.7, 135.5, 156.4, 160.1; IR (KBr): ν = 1589 cm^{-1}. Anal. calcd. for $C_{18}H_{18}O_2$: C 81.17, H 6.81; found: C 81.15, H 6.91.

4-Methoxyphenanthren-2-ol (13). To an ice-cold solution of compound **12** (120 mg, 0.45 mmol) in dry dichloromethane (5 ml) was added dropwise BCl_3 (1.0 M in heptane; 2.25 ml, 2.25 mmol), and the mixture was stirred at room temperature for 4.5 h. The mixture was quenched by slowly adding water in an ice-water bath and the resulting mixture was extracted with ethyl acetate. The extract was washed successively with water and brine, dried over $MgSO_4$, and evaporated. The residue was purified by column chromatography with hexane–ethyl acetate (2:1) as an eluent to give phenanthrol **13** (82.4 mg, 81%) as crystals, mp 123.9–125.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$, δ): 4.10 (s, 3H, OCH_3), 5.03 (s, 1H, ArH), 6.75 (d, J = 2.0 Hz, 1H, ArH), 6.87 (d, J = 2.0 Hz, 1H, ArH), 7.51 (ddd, J = 6.3, 5.6, 0.9 Hz, 1H, ArH), 7.54 (d, J = 7.0 Hz, 1H, ArH), 7.60 (ddd, J = 6.9, 5.6, 1.3 Hz, 1H, ArH), 7.69 (d, J = 7.0 Hz, 1H, ArH), 7.83 (dd, J = 6.3, 1.3 Hz, 1H, ArH), 9.52 (d, J = 6.9 Hz, 1H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 55.6, 98.8, 104.8, 115.3, 125.0, 126.3, 126.5, 127.5, 128.3, 128.6, 130.4, 131.6, 135.5, 154.0, 160.2; IR (KBr): ν = 3323, 1616 cm^{-1}. Anal. calcd. for $C_{15}H_{12}O_2$: C 80.34, H 5.39; found: C 80.14, H 5.56.

4,4'-Dimethoxy-1,1'-biphenanthrene-2,2'-diol (3). A mixture of $Cu(NO_3)_2 \cdot 3H_2O$ (620 mg, 2.57 mmol), 1-phenylethylamine (d 0.94; 1.19 ml, 9.23 mmol), and dry methanol (10 ml) was stirred at room temperature for 1 h. To the mixture was added dropwise a solution of phenanthrol **13** (287 mg, 1.28 mmol) in dry methanol (10 ml) over a period of 30 min, and the mixture was stirred for 4 h. After most of the methanol was evaporated under reduced pressure, the mixture was quenched with water in an ice-water bath. The resulting mixture was extracted with ethyl acetate, and the extract was washed successively with water and brine, dried over $MgSO_4$, and evaporated. The residue was purified by column chromatography with hexane–ethyl acetate (4:1) as an eluent to give biphenanthrol **3** (285 mg, 99%) as crystals, α = 2.06, R_s = 2.20 [Daicel CHIRALPAK AD (250 mm × 4.6 mm i.d.), hexane–ethanol (1:1)]; mp 326.0–327.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$, δ): 4.23 (s, 6H, OCH_3), 5.15 (s, 2H, ArOH), 7.07 (s, 2H, ArH), 7.12 (d, J = 9.0 Hz, 2H, ArH), 7.54 (ddd, J = 9.3, 7.2, 1.1 Hz, 2H, ArH), 7.57 (d, J = 9.0 Hz, 2H, ArH), 7.66 (ddd, J = 9.2, 7.2, 1.5 Hz, 2H, ArH), 7.80 (dd, J = 9.2, 1.1 Hz, 2H, ArH), 9.45 (d, J = 9.3 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 55.9, 98.4, 105.6, 116.4, 123.3, 125.4, 126.9,

127.8, 128.4, 129.8, 130.6, 131.5, 134.9, 154.0, 161.3; IR (KBr): ν = 3471, 1585 cm^{-1}; HRMS (EI) calcd for $C_{30}H_{22}O_4$ M^+ 446.1518, found 446.1517. Compound **3** was optically resolved by preparative HPLC on a Daicel CHIRALPAK AD column (250 mm × 20 mm i.d.) with hexane–2-propanol (5:4) as an eluent. The faster running enantiomer exhibited dextrorotation, $[\alpha]_D^{16}$ + 147 (*c* 0.136, ethanol).

Synthesis of Compound 4

1-Bromo-4-methoxymethoxy-2-methylbenzene (15). A mixture of phenol **14** (4.98 g, 26.6 mmol), K_2CO_3 (9.20 g, 66.6 mmol), and dry acetone (40 ml) was stirred at room temperature for 10 min. To it was added chloromethyl methyl ether (*d* 1.06; 4.05 ml, 53.3 mmol), and the mixture was refluxed for 5 h. After cooling, the reaction was quenched with water, and the mixture was extracted with diethyl ether. The extract was washed successively with water and brine, dried over $MgSO_4$, and evaporated. The residue was purified by column chromatography with hexane–ethyl acetate (15:1) as an eluent to give ether **15** (5.66 g, 92%) as an oil, ^{1}H NMR (400 MHz, $CDCl_3$, δ): 2.36 (s, 3H, ArC*H*$_3$), 3.46 (s, 3H, OC*H*$_3$), 5.13 (s, 2H, OC*H*$_2$OCH$_3$), 6.75 (dd, *J* = 8.7, 2.9 Hz, 1H, Ar*H*), 6.93 (d, *J* = 2.9 Hz, 1H, Ar*H*), 7.39 (d, *J* = 8.7 Hz, 1H, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 23.1, 56.0, 94.4, 115.3, 116.7, 118.6, 132.8, 138.9, 156.3. Anal. calcd. for $C_9H_{11}BrO_2$: C 46.78, H 4.80, Br 34.58; found: C 46.41, H 4.52, Br 34.51.

Methyl 2,5-dimethoxybenzoate (17). To an ice-cold solution of dihydroxy acid **16** (25.0 g, 162 mmol) in dry DMF (350 ml) was added NaH (60% dispersion in mineral oil; 30.2 g, 754 mmol), and the mixture was stirred at this temperature for 1 h. To the cold mixture was added dropwise iodomethane (*d* 2.28; 61.0 ml, 980 mmol) over a period of 1 h, and the resulting mixture was stirred at room temperature for 2 h. The reaction was quenched by acidifying the mixture with 2 M HCl, and the resulting mixture was extracted with diethyl ether. The extract was washed successively with water and brine, dried over $MgSO_4$, and evaporated. The residue was purified by column chromatography with hexane–ethyl acetate (4:1) as an eluent to give dimethoxy ester **17** (30.6 g, 96%) as an oil, ^{1}H NMR (400 MHz, $CDCl_3$, δ): 3.84 (s, 3H, CO_2CH_3), 3.86 (s, 3H, OC*H*$_3$), 3.89 (s, 3H, OC*H*$_3$), 6.91 (d, *J* = 8.9 Hz, 1H, Ar*H*), 7.00 (dd, *J* = 8.9, 3.2 Hz, 1H, Ar*H*), 7.33 (d, *J* = 3.2 Hz, 1H, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 51.7, 55.4, 56.3, 113.5, 115.6, 119.1, 120.1, 152.7, 153.1, 166.1. Anal. calcd. for $C_{10}H_{12}O_4$: C 61.22, H 6.16; found: C 60.84, H 6.07.

2,5-Dimethoxybenzoic acid (18). A mixture of ester **17** (28.1 g, 143 mmol), KOH (28.4 g, 436 mmol), ethanol (250 ml), and water (50 ml) was refluxed for 1 h. After cooling, most of the ethanol was evaporated and the mixture was acidified with 2 M HCl. The resulting mixture was extracted with diethyl ether, and the extract was washed successively with water and brine, dried over $MgSO_4$, and evaporated to give acid **18** (22.2 g, 85%). The product was spectrometrically pure enough to use in the following step without purification, mp 76.0–79.7 °C; ^{1}H NMR (400 MHz, CD_3OD, δ): 3.78 (s, 3H, OC*H*$_3$), 3.87 (s, 3H, OC*H*$_3$), 7.06–7.12 (m, 2H, Ar*H*), 7.37 (d, *J* = 3.0 Hz, 1H, Ar*H*); ^{13}C NMR (100 MHz, CD_3OD, δ): 56.2, 57.1, 114.9, 117.3, 120.8, 121.2, 154.6, 154.7, 169.2; IR (KBr): ν = 3161, 1730 cm^{-1}. Anal. calcd. for $C_9H_{10}O_4$: C 59.34, H 5.53; found: C 59.33, H 5.58.

2,6-Di-*tert*-butyl-4-methoxyphenyl 2,5-dimethoxybenzoate (19). To a mixture of acid **18** (20.5 g, 113 mmol), 2,6-di-*tert*-butyl-4-methoxyphenol (26.6 g, 113 mmol), and dry benzene (100 ml) was added trifluoroacetic anhydride (*d* 1.487; 31.8 ml, 225 mmol), and the mixture was stirred at room temperature. After 6 h, an additional trifluoroacetic anhydride (15.9 ml, 113 mmol) was added to the mixture, and the resulting mixture was stirred for a further 1.5 h. The reaction was quenched by carefully adding 2 M NaOH in an ice-water bath, and the resulting mixture was extracted with diethyl ether. The extract was washed successively with 2 M NaOH, water, and brine, dried over $MgSO_4$, and evaporated. The residue was crystallized from ethanol to give ester **19** (35.6 g). The mother liquid was evaporated and the residue was purified by column chromatography with hexane–ethyl acetate (9:1) as an eluent to give an additional crop (5.95 g) for a total yield of 41.6 g (92%) as crystals, mp 93.7–94.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$, δ): 1.33 (s, 18H, C(C*H*$_3$)$_3$), 3.82 (s, 3H, OC*H*$_3$), 3.83 (s, 3H, OC*H*$_3$), 3.87 (s, 3H, OC*H*$_3$), 6.90 (s, 2H, Ar*H*), 6.99 (d, *J* = 9.1 Hz, 1H, Ar*H*), 7.11 (dd, *J* = 9.1, 3.2 Hz, 1H, Ar*H*), 7.66 (d, *J* = 3.2 Hz, 1H, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 31.3, 35.6, 55.2, 55.8, 56.5, 111.5, 114.3, 117.2, 120.0, 120.4, 141.9, 143.6, 153.0, 154.6, 156.1, 166.1; IR (KBr): ν = 1710 cm^{-1}. Anal. calcd. for $C_{24}H_{32}O_5$: C 71.97, H 8.05; found: C 71.89, H 8.00.

2,6-Di-*tert*-butyl-4-methoxyphenyl 4-methoxy-4'-methoxymethoxy-2'-methyl-1,1'-biphenyl-2-carboxylate (20). This compound was prepared by essentially the same procedure as mentioned for the preparation of compound **9**. Magnesium turnings (1.15 g, 47.4 mmol) was activated with 1,2-dibromoethane (30 μl) in THF (35 ml). To the suspension was added a solution of compound **15** (5.45 g, 23.6 mmol) and 1,2-dibromoethane (50 μl) in THF (10 ml) over a period of 1 h under ultrasonic irradiation, and the mixture was irradiated for a further 2 h. After the solvent was evaporated, the residue was dried in vacuo for 3 h and dissolved with benzene (50 ml) to give a Grignard solution of compound **15**, which was added to a solution of compound **19** (6.33 g, 15.8 mmol) in benzene (50 ml) over a period of 30 min, and the mixture was refluxed for 4 h. After the workup, the residue was purified by column chromatography with hexane–ethyl acetate (9:1) as an eluent to give biphenyl **20** (7.77 g, 95%) as crystals, mp 114.2–117.5 °C; ^{1}H NMR (400 MHz $CDCl_3$, δ): 1.24 [s, 9H, C(C*H*$_3$)$_3$], 1.32 [s, 9H, C(C*H*$_3$)$_3$], 1.96 (s, 3H, ArC*H*$_3$), 3.47 (s, 3H, OC*H*$_3$), 3.75 (s, 3H, OC*H*$_3$), 3.94 (s, 3H, OC*H*$_3$), 5.11–5.15 (m, 2H, OC*H*$_2$OCH$_3$), 6.74 (dd, *J* = 8.4, 2.7 Hz, 1H, Ar*H*), 6.79–6.84 (m, 4H, Ar*H*), 7.17 (s, 2H, Ar*H*), 7.96 (t, *J* = 2.7 Hz, 1H, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 20.4, 31.5, 31.5, 35.6, 35.7, 55.3, 55.6, 56.0, 94.5, 111.6, 111.7, 112.4, 116.3, 116.9, 118.2, 129.4, 129.7, 133.2, 134.9, 137.6, 137.8, 141.6, 143.5, 143.7, 156.3, 158.6, 165.2; IR (KBr): ν = 2960, 1745 cm^{-1}. Anal. calcd. for $C_{32}H_{40}O_6$: C 73.82, H 7.74; found: C 73.77, H 7.95.

7-Methoxy-2-(methoxymethoxy)phenanthren-9-ol (21). This compound was prepared by essentially the same procedure as mentioned for the preparation of compound **10**. A solution of lithium diethylamide, which was prepared from diethylamine (*d* 0.707; 6.37 ml, 61.6 mmol) and butyllithium (1.59 M in hexane; 35.4 ml, 56.2 mmol) in THF (35 ml), was added to an ice-cold solution of biphenyl **20** (7.28 g, 14.0 mmol) in THF–HMPA (7:4 v/v; 55 ml) over a period of 90 min, and the mixture was stirring at 0 °C for 3 h. After the workup, the residue was purified by column chromatography with hexane–ethyl acetate (5:2) as an eluent to give phenanthrol **21** (3.28 g, 83%) as crystals, mp 115–118 °C; ^{1}H NMR (400 MHz, $CDCl_3$, δ): 3.54 (s, 3H, OC*H*$_3$), 3.96 (s, 3H, OC*H*$_3$), 5.30 (s, 2H, OC*H*$_2$OCH$_3$), 5.74 (s, 1H, ArO*H*), 6.92 (s, 1H, Ar*H*), 7.19 (dd, *J* = 8.9, 2.5 Hz, 1H, Ar*H*), 7.29 (d, *J* = 8.9 Hz, 1H, Ar*H*), 7.30 (d, *J* = 8.9 Hz, 1H, Ar*H*), 7.65 (d, *J* = 2.5 Hz, 1H, Ar*H*), 8.39 (d, *J* = 8.9 Hz, 1H, Ar*H*), 8.45 (d, *J* = 8.9 Hz, 1H, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 55.4, 56.0, 94.2, 94.5, 102.6, 106.3, 110.5, 115.4, 118.0, 122.0, 123.6, 123.9, 125.9, 132.7, 149.7, 155.3, 157.7; IR (KBr): ν = 3315 cm^{-1}.

7-Methoxy-2-(methoxymethoxy)phenanthren-9-yl trifluoromethanesulfonate (22). This compound was prepared by the same procedure as mentioned for the preparation of compound **11**. Treatment of phenanthrol **21** (2.99 g, 10.5 mmol) with trifluoromethanesulfonic anhydride (*d* = 1.677; 2.66 ml, 15.8 mmol) in the presence of triethylamine (*d* 0.726; 4.40 ml, 31.6 mmol) in dichloromethane (50 ml) gave, after chromatographic purification with hexane–ethyl acetate (8:1) as an eluent, ester **22** (4.03 g, 92%) as crystals, mp 77–79 °C; ^{1}H NMR (400 MHz, $CDCl_3$, δ): 3.54 (s, 3H, OC*H*$_3$), 3.98 (s, 3H, OC*H*$_3$), 5.32 (s, 2H, OC*H*$_2$OCH$_3$), 7.35 (dd, *J* = 9.2, 2.4 Hz, 1H, Ar*H*), 7.39 (dd, *J* = 9.2, 2.4 Hz, 1H, Ar*H*), 7.45 (d, *J* = 2.4 Hz, 1H, Ar*H*), 7.49 (d, *J* = 2.4 Hz, 1H, Ar*H*), 7.68 (s, 1H, Ar*H*), 8.49 (d, *J* = 9.2 Hz, 1H, Ar*H*), 8.51 (d, *J* = 9.2 Hz, 1H, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 55.4, 56.1, 94.6, 101.6, 112.5, 118.1, 119.1, 119.4, 120.3, 123.8, 124.3, 124.8, 125.7, 126.2, 130.6, 144.4, 155.8, 158.5; IR (KBr): ν = 2939, 1622 cm^{-1}. Anal. calcd. for $C_{18}H_{15}F_3O_6S$: C 51.92, H 3.63; found: C 51.90, H 3.77.

2-Methoxy-7-(methoxymethoxy)phenanthrene (23). This compound was prepared by essentially the same procedure as mentioned

for the preparation of compound **12**. Ester **22** (2.77 g, 6.65 mmol) was treated with formic acid (*d* 1.22; 500 µl, 13.3 mmol) in DMF (35 ml) in the presence of palladium acetate (29.8 mg, 0.133 mmol), triphenylphosphine (87.2 mg, 0.332 mmol), and triethylamine (*d* 0.726; 2.78 ml, 20.0 mmol) at 65 °C for 4 h. The reaction mixture was worked up, using diethyl ether as an extraction solvent, and purified by column chromatography with hexane–ethyl acetate (9:1) as an eluent to give phenanthrene **23** (1.78 g, 99%) as crystals, mp 80–82 °C; ^{1}H NMR (400 MHz, CD_2Cl_2, δ): 3.54 (s, 3H, OC*H*$_3$), 3.95 (s, 3H, OC*H*$_3$), 5.32 (s, 2H, OC*H*$_2$OCH$_3$), 7.23–7.28 (m, 2H, Ar*H*), 7.33 (dd, *J* = 9.0, 2.6 Hz, 1H, Ar*H*), 7.46 (d, *J* = 2.6 Hz, 1H, Ar*H*), 7.65 (s, 2H, Ar*H*), 8.48 (d, *J* = 9.0 Hz, 1H, Ar*H*), 8.49 (d, *J* = 9.0 Hz, 1H, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 55.4, 56.1, 94.6, 108.5, 112.3, 117.2, 117.9, 123.7, 123.8, 124.7, 125.7, 127.1, 127.1, 132.2, 132.5, 155.1, 157.7; IR (KBr): ν = 1616 cm^{-1}. Anal. calcd. for $C_{17}H_{16}O_3$: C 76.10, H 6.01; found: C 76.01, H 6.12.

7-Methoxyphenanthren-2-ol (24). A mixture of compound **23** (1.65 g, 6.14 mmol), 2 M HCl (3.69 ml, 7.37 mmol), methanol (40 ml), and THF (8 ml) was refluxed for 3 h. After cooling, most of the organic solvents were evaporated and the residue was dissolved by the addition of water and diethyl ether. The aqueous layer was extracted with diethyl ether, and the combined organic layer was washed successively with water and brine, dried over $MgSO_4$, and evaporated. The residue was purified by column chromatography with hexane–ethyl acetate (3:1) as an eluent to give phenanthrol **24** (1.37 g, 99%) as crystals, mp 171–174 °C; ^{1}H NMR (400 MHz, CD_2Cl_2, δ): 3.95 (s, 3H, OC*H*$_3$), 4.97 (s, 1H, ArO*H*), 7.17-7.27 (m, 4H, Ar*H*), 7.58-7.65 (m, 2H, Ar*H*), 8.45–8.47 (m, 2H, Ar*H*); ^{13}C NMR (100 MHz, CD_2Cl_2, δ): 55.1, 109.1, 112.1, 117.4, 117.8, 124.2, 124.6, 125.2, 125.3, 127.2, 127.8, 132.9, 133.0, 154.2, 158.3; IR (KBr): ν = 3386 cm^{-1}. Anal. calcd. for $C_{15}H_{12}O_2$: C 80.34, H 5.39; found: C 80.29, H 5.54.

7,7'-Dimethoxy-1,1'-biphenanthrene-2,2'-diol (25). This compound was prepared by the same procedure as mentioned for the preparation of compound **3**. A mixture of $Cu(NO_3)_2 \cdot 3H_2O$ (1.60 g, 6.62 mmol), 1-phenylethylamine (*d* 0.94; 2.06 ml, 16.0 mmol), and dry methanol (15 ml) was stirred at room temperature for 1 h. To the mixture was added dropwise a solution of phenanthrol **24** (991 mg, 4.42 mmol) in dry methanol (35 ml) over a period of 30 min, and the mixture was stirred at room temperature. After 21 h, additional $Cu(NO_3)_2 \cdot 3H_2O$ (1.07 g, 4.43 mmol), 1-phenylethylamine (1.37 ml, 10.6 mmol), and methanol (10 ml) were added to the mixture, and the resulting mixture was stirred for a further 16 h. After most of the methanol was evaporated under reduced pressure, the mixture was acidified by the addition of 2 M HCl in an ice-water bath, and the resulting mixture was extracted with ethyl acetate. The extract was washed successively with water and brine, dried over $MgSO_4$, and evaporated. The residue was purified by column chromatography with hexane–ethyl acetate (3:2) as an eluent to give biphenanthrol **25** (776 mg, 79%) as crystals, mp 290–291 °C; ^{1}H NMR (500 MHz, $(CD_3)_2CO$, δ): 3.93 (s, 6H, OC*H*$_3$), 7.09 (d, *J* = 9.1 Hz, 2H, Ar*H*), 7.30 (dd, *J* = 9.0, 2.6 Hz, 2H, Ar*H*), 7.33 (d, *J* = 2.6 Hz, 2H, Ar*H*), 7.46 (d, *J* = 9.0 Hz, 2H, Ar*H*), 7.51 (d, *J* = 9.1 Hz, 2H, Ar*H*), 7.96 (s, 2H, ArO*H*), 8.71 (d, *J* = 9.0 Hz, 2H, Ar*H*), 8.75 (d, *J* = 9.0 Hz, 2H, Ar*H*); ^{13}C NMR (125 MHz, $(CD_3)_2CO$, δ): 56.0, 109.4, 118.1, 118.5, 118.8, 125.0, 125.1, 125.9, 126.0, 126.5, 128.1, 133.3, 133.4, 155.0, 158.9; IR (KBr): ν = 3436 cm^{-1}; HRMS (EI) calcd for $C_{30}H_{22}O_4$ M^+ 446.1518, found 446.1516.

1,1'-Biphenanthrene-2,2',7,7'-tetraol (4). To an ice-cold solution of biphenanthrol **25** (209 mg, 0.468 mmol) in dry dichloromethane (10 ml) was added dropwise BBr_3 (1.0 M in dichloromethane; 2.81 ml, 2.81 mmol), and the mixture was stirred at this temperature for 2 h. To the mixture water was carefully added, and the resulting mixture was allowed to warm to room temperature. The mixture was extracted with ethyl acetate, and the extract was washed successively with water and brine, dried over $MgSO_4$, and evaporated. The residue was purified by column chromatography with hexane–ethyl acetate (1:1) as an eluent to give tetraol **4** (141 mg, 72%), α = 2.18, R_s = 1.96 [Daicel CHIRALPAK AD (250 mm × 4.6 mm i.d.), hexane–ethanol (1:1)]; mp 338–340 °C; ^{1}H NMR (400 MHz, CD_3OD, δ): 6.99 (d, *J* = 9.2 Hz, 2H, Ar*H*), 7.08 (d, *J* = 2.6 Hz, 2H, Ar*H*), 7.17 (dd, *J* = 9.0, 2.6 Hz, 2H, Ar*H*), 7.32 (d, *J* = 9.2 Hz, 2H, Ar*H*), 7.37 (d, *J* = 9.0 Hz, 2H, Ar*H*), 8.57 (d, *J* = 9.0 Hz, 2H, Ar*H*), 8.65 (d, *J* = 9.0 Hz, 2H, Ar*H*); ^{13}C NMR (100 MHz, $CDCl_3$, δ): 112.1, 118.0, 119.0, 124.4, 124.8, 125.8, 127.5, 133.1, 133.6, 154.2, 156.3, 166.4, 170.7, 171.5; IR (KBr): ν = 3186, 1616, 1581 cm^{-1}; HRMS (FAB) calcd for $C_{28}H_{18}O_4$ M^+ 418.1205, found 418.1206. Compound **4** was optically resolved by preparative HPLC on a Daicel CHIRALPAK AD (250 mm × 20 mm i.d.) with hexane–2-propanol (5:4) as an eluent. The faster running enantiomer exhibited dextrorotation, $[\alpha]_D^{16}$ + 15.9 (*c* 0.506, ethyl acetate).

General Procedure for Photoracemization

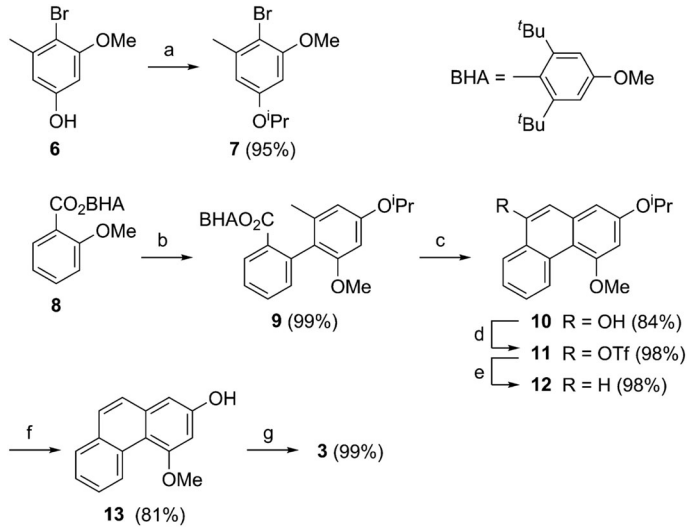
A biphenanthrene (1.5 mg) was dissolved in ethanol (25 ml) and the solution was poured into a quartz cuvette (10 × 10 mm). The cuvette was placed 15 cm behind an 18 W fluorescent lamp or a 500 W mercury lamp, and a decrease in enantiopurity was monitored by HPLC on a Daicel CHIRALPAK AD column (250 mm × 4.6 mm i.d.), eluting with hexane–ethanol (1:1) for compounds **1–4** or hexane–2-propanol (1:1) for compound **5**. The light of the mercury lamp was passed through a pinhole plate (4 mm i.d.) and a glass filter (HOYA UV-36) in order to reduce the intensity and remove UV light with wavelengths shorter than about 360 nm.

Cyclic Voltammetry Analysis

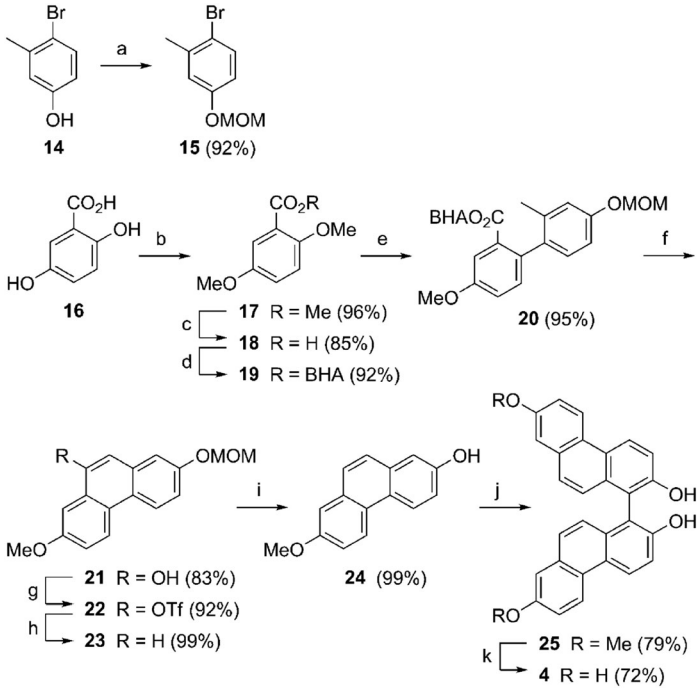
A 1 mM solution of each biphenanthrene was prepared by dissolving the compound in a 1:1 (v/v) mixture of ethanol and a 0.1 M aqueous solution of phosphoric acid. The cyclic voltammogram of the sample was recorded using a glassy carbon working electrode and a reference electrode of Ag/AgCl with a platinum wire counter electrode at a scan rate of 50 mV s^{-1}.

RESULTS AND DISCUSSION

It is not an easy task to regioselectively synthesize multisubstituted fused aromatic compounds. We previously succeeded in preparing the phenanthrene half of blestriarene C by connecting the two terminal benzene rings bearing appropriate substituents, followed by constructing the mid ring by cyclization.[5] For the biaryl coupling, we employed an ester-mediated nucleophilic aromatic substitution (S_NAr) reaction of a 2-methoxybenzoate ester with an aryl Grignard reagent, which was developed in our laboratory.[18] The mid-ring was constructed by modifying the Snieckus' cyclization of *N*,*N*-diethyl-2'-methylbiphenyl-2-carboxamide to phenanthrene-9-ol with LDA.[19] These methods were successfully applied to the synthesis of biphenanthrols **3** and **4**. Thus, *p*-bromophenol **6**,[5] after protection of the hydroxy group as an isopropyl ether (**7**), was converted into the Grignard reagent by treating with magnesium turnings in THF (Scheme 1). The Grignard reagent was allowed to react with ester **8**,[17] the carboxy group of which was protected from the nucleophilic attack of the Grignard reagent as a bulky 2,6-di-*tert*-butyl-4-methoxyphenyl (BHA) ester,[18] to give biphenyl **9** in almost quantitative yield; benzene was employed as a solvent to facilitate the reaction as reported previously.[5] Biphenyl **9** was treated with lithium diethylamide in THF–HMPA gave phenanthrol **10** in an 84% yield. Reductive removal of the 9-hydroxy group of phenanthrol **10**,[20] followed by selective deprotection of the 2-isopropoxy group of the resulting phenanthrene **12** with BCl_3, gave 2-phenanthrol **13**. Oxidative coupling of phenanthrol **13**, using a copper (II)–1-phenylethylamine complex,[21] furnished the desired biphenanthrol **3** in a total yield of 64% starting from ester **8**. On the other hand, a Grignard reagent was prepared from bromide **15**, which had been prepared by etherification of commercially available *p*-bromophenol **14** with chloromethyl methyl ether (MOMCl) (Scheme 2). The coupling partner **19**



Scheme 1. Synthesis of compound **3**. Reagents: (a) ^{i}PrBr, K_2CO_3, acetone; (b) Grignard reagent prepared from **7**, benzene; (c) $LiNEt_2$, THF, HMPA; (d) Tf_2O, NEt_3, CH_2Cl_2; (e) $Pd(OAc)_2$, PPh_3, HCO_2H, NEt_3, DMF; (f) BCl_3, CH_2Cl_2; (g) $Cu(NO_3)_2 \cdot 3H_2O$, 1-phenylethylamine, MeOH.



Scheme 2. Reagents: (a) MOMCl, K_2CO_3, acetone; (b) MeI, NaH, DMF; (c) KOH, EtOH, H_2O; (d) BHAOH, Tf_2O; (e) Grignard reagent prepared from **15**, THF, benzene; (f) $LiNEt_2$, THF, HMPA; (g) Tf_2O, NEt_3, CH_2Cl_2; (h) $Pd(OAc)_2$, PPh_3, HCO_2H, NEt_3, DMF (i) 2 M HCl, MeOH; (j) $Cu(NO_3)_2 \cdot 3H_2O$, 1-phenylethylamine, MeOH; (k) BBr_3, CH_2Cl_2.

was prepared by simultaneous etherification and esterification of 2,5-dihydroxybenzoic acid (**16**) with iodomethane, followed by alkaline hydrolysis of the resulting dimethoxy ester **17**, and subsequent esterification of acid **18** with BHAOH. They were treated by the same procedure to that employed for the preparation of biphenanthrol **3** to give biphenanthrol **4** in a total yield of 30% starting from acid **16**, after deprotection of the 7,7'-dimethoxy groups with BBr_3. Racemic biphenanthrols **3** and **4** were optically resolved by HPLC using a cellulose-derived chiral column (see the experimental section).

Racemization activities of biphenanthrols **1–5** were tested using an 18 W fluorescent lamp. An ethanol solution of each biphenanthrol was placed in a quartz cuvette and irradiated for 4 h with the fluorescent lamp installed 15 cm behind the sample. Figure 1 shows the time course of the change in enantiopurity as monitored by HPLC analysis. Compound **1** completely racemized within 4 h, while compound **2** slightly racemized, decreasing the enantiopurity by 3% (from 96% ee to 93% ee). These results are in reasonable agreement with those reported previously.[5] On the other hand, no racemization was observed for compounds **3–5**. A racemization experiment of compounds **1–5** was then conducted using a 500 W mercury lamp equipped with a pinhole plate (4 mm i.d.) and a cut-off glass filter ($\lambda > 360$ nm) (Figure 2). On exposure to the UV light for 4 h, compounds **2–5** racemized by 74% (from 97%

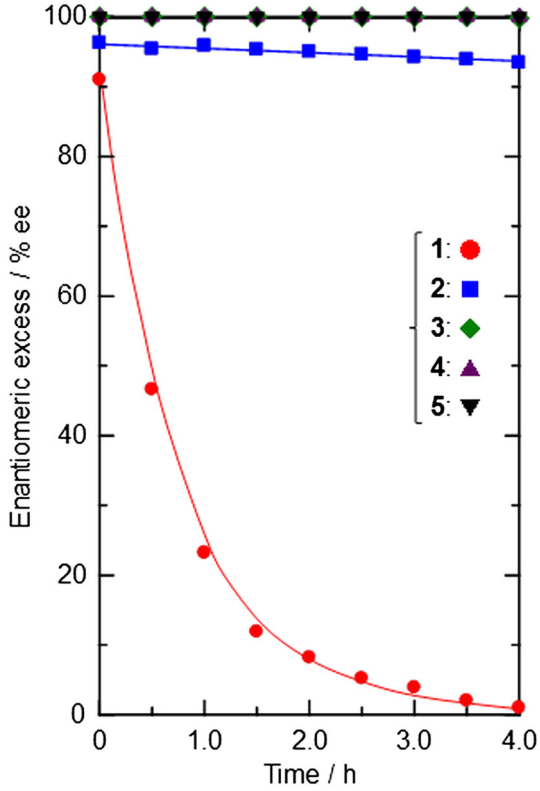


Fig. 1. Racemization of compounds **1–5** under fluorescent lamp illumination. Conditions: concentration, 0.1–0.2 mM in ethanol; light source, 18 W fluorescent lamp ($\lambda > 300$ nm).

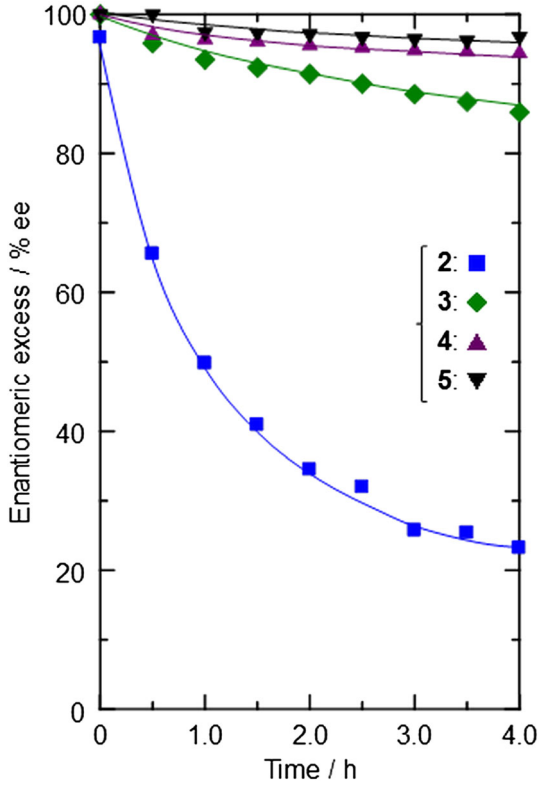


Fig. 2. Racemization of compounds **2–5** under mercury lamp illumination. Conditions: concentration, 0.1–0.2 mM in ethanol; light source, 500 W superpressure mercury lamp equipped with a pinhole plate (4 mm i.d.) and a cut-off filter ($\lambda > 360$ nm).

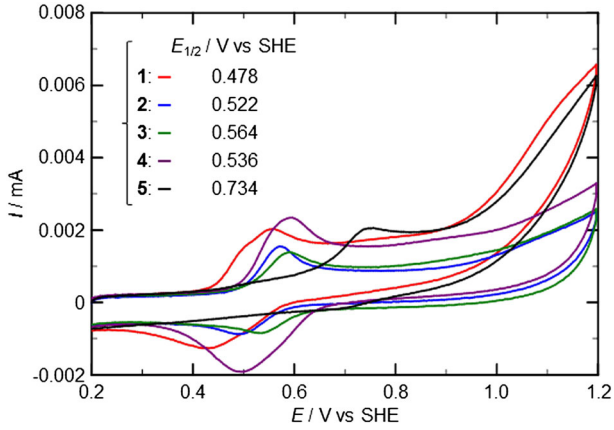


Fig. 3. Cyclic voltammograms of compounds **1–5**. Conditions: concentration, 1.0 mM in in ethanol–0.1 M H_3PO_4 (1:1, v/v); scan rate, 50 mV s^{-1}.

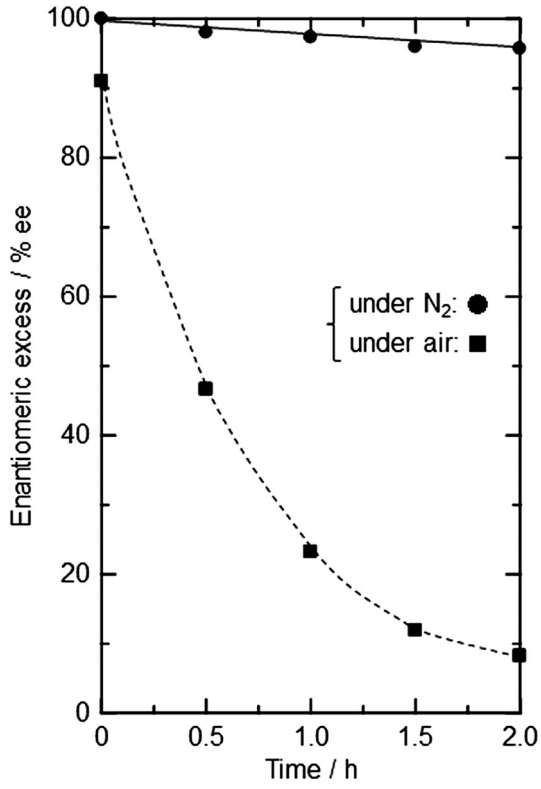


Fig. 4. Racemization of compound **1** under nitrogen and under air (data from Figure 1). Conditions: concentration, 0.1 mM in ethanol, light source, 18 W fluorescent lamp ($\lambda > 300$ nm).

ee to 23% ee), 14% (from 100% ee to 86% ee), 6% (100% ee to 94% ee), and 3% (100% ee to 97% ee), respectively; the racemization of compound **1** was too fast to follow the time course by HPLC but a sample of 92% ee was completely racemized within 30 min under the conditions. The extreme tendency of compound **1** toward racemization strongly suggests that a distinctive mechanism operates in its racemization. The half-wave potentials ($E_{1/2}$) determined by cyclic voltammetry (CV) increase in the order of **1** < **2** < **4** < **3** < **5**, indicating that compound **1** is easier to be oxidized than compounds **2–5** (Figure 3). This suggests that a redox cycle is involved in the racemization of compound **1**. We then investigated the racemization of compound **1** in detail. Figure 4 shows

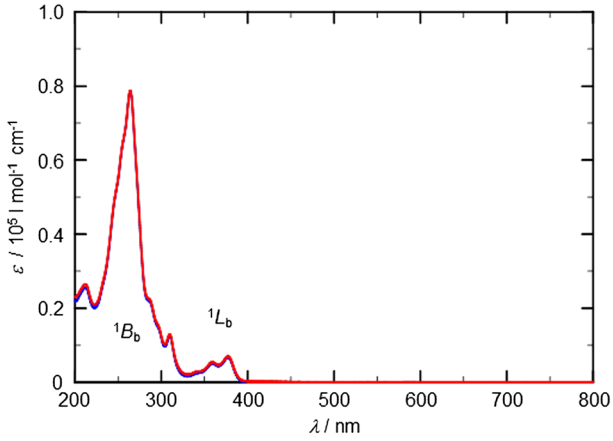


Fig. 5. UV-Vis spectra of compound **1** before (blue) and after (red) irradiation with a fluorescent lamp. Conditions: sample, a 0.1 mM solution of racemic compound **1** in ethanol; light source, 18 W fluorescent lamp;irradiation time, 4 h.

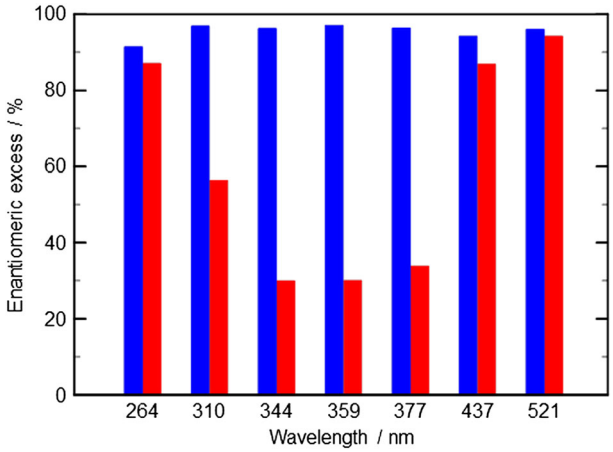
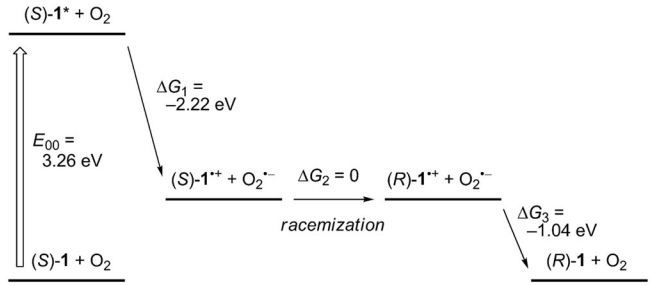


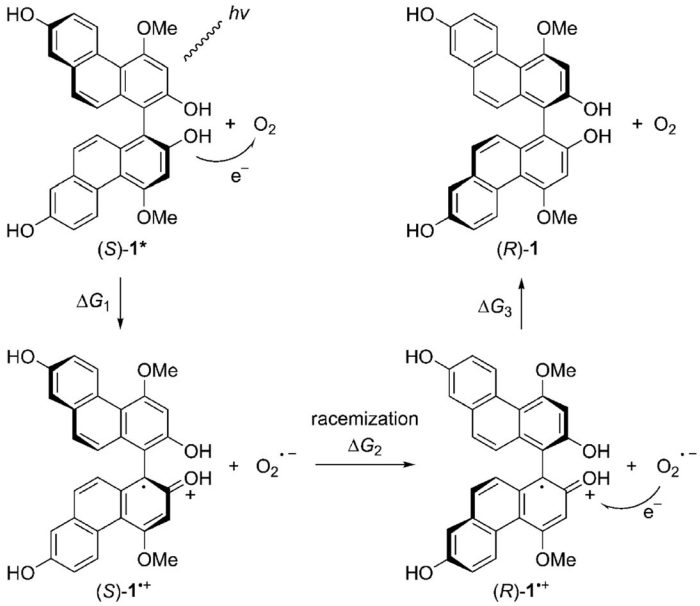
Fig. 6. Enantiopurity of compound **1** before (blue) and after (red) irradiation of UV light. Solutions of compound **1** in ethanol (0.1 mM) were irradiated with monochromatic UV light of different wavelengths (light source, 150 W xenon lamp; bandwidth, 10 nm) for 30 min.



Scheme 4. Energy diagram for the photoracemization of compound **1**.

the effect of oxygen on the racemization of compound **1**; as compound **1** is easily oxidized under atmospheric conditions, it was purified by HPLC under nitrogen just before use to remove oxidized impurities. As can be seen in Figure 4, racemization was significantly inhibited under nitrogen, suggesting the intermediary of oxygen. During the reaction using the fluorescent lamp under air, no oxidized products were detected, as shown by a comparison between the UV-Vis spectra of compound **1** measured before and after irradiation (Figure 5); on the contrary, substantial decomposition was observed in the reaction using the mercury lamp. Figure 6 shows the enantiopurity of compound **1** measured before and after the irradiation of monochromatic UV light with different wave lengths. Compound **1** significantly racemized at the wavelengths 344, 359, and 377 nm, which correspond to the ^1L_b absorption (HOMO–LUMO transition) band.

Based on these observations, a feasible mechanism for the photoracemization of compound **1** is depicted in Scheme 3. First, a photoexcited biphenanthrene is oxidized with oxygen to give a cation radical. The species easily racemizes due to the partial double-bond character of the axis connecting the two phenanthrene halves. The resulting cation radical receives an electron from its counter ion, superoxide anion radical, to give a racemized biphenanthrene. It is readily conceivable that a biphenanthrene with a small $E_{1/2}$ value



Scheme 3. Feasible mechanism for the photoracemization of compound **1**.

has a strong tendency toward racemization as it easily forms a cation radical. Scheme 4 shows the energy diagram for the proposed mechanism. The energy difference between the ground and excited states at the zero vibrational levels (E_{00}) was calculated to be 3.26 eV from the UV and fluorescence spectra of compound **1**. On the other hand, the free-energy change for the third step (ΔG_3) was calculated to be −1.04 eV from the $E_{1/2}$ value and the standard electrode potential for $O_2/O_2^{\bullet -}$ (−0.563 V vs. SHE). The free-energy change for the first step (ΔG_1) was determined to be −2.22 eV by using the E_{00} and ΔG_3 values. Scheme 4 shows that once compound **1** is excited, the reaction proceeds spontaneously. However, it should be noted that this is not the sole mechanism operating in the photoracemization of compound **1**, as compound **1** gradually racemized even under nitrogen (Figure 4).

CONCLUSION

We investigated the photoracemization of compounds **1–5**, from which a possible reaction mechanism mediated by a cation radical was derived for compound **1**. Although the redox mechanism seems to be involved also in the racemization of the other compounds, to a small or large extent depending on the easiness of oxidation, further studies are necessary for full understanding of the reaction mechanisms.

LITERATURE CITED

1. Yamaki M, Bai L, Inoue K, Takagi S. Biphenanthrenes from Bletilla striata. Phytochemistry 1989; 28: 3503–3505.
2. Majumder PL, Pal A, Joardar M. Cirrhopetalanthrin, a dimeric phenanthrene derivative from the orchid Cirrhopetalum maculosum. Phytochemistry 1990; 29: 271–274.
3. Morikawa T, Xie H, Matsuda H, Wang T, Yoshikawa M. Bioactive constituents from Chinese natural medicines. XVII. Constituents with radical scavenging effect and new glucosyloxybenzyl 2-isobutylmalates from Gymnadenia conopsea. Chem Pharm Bull 2006; 54: 506–513.
4. Kovács A, Vasas A, Hohmann J. Natural phenanthrenes and their biological activity. Phytochemistry 2008; 69: 1084–1110.
5. Hattori T, Shimazumi Y, Goto H, Yamabe O, Morohashi N, Kawai W, Miyano S. Synthesis, resolution, and absolute stereochemistry of (–)-blestriarene C. J Org Chem 2003; 68: 2099–2108.
6. Zimmerman HE, Crumrine DS. Duality of mechanism in photoracemization of optically active biphenyls. Mechanistic and exploratory organic photochemistry. LXV. J Am Chem Soc 1972; 94: 498–506.
7. Irie M, Yoshida K, Hayashi K. Laser photolysis study of the photoracemization of 1,1'-binaphthyl. J Phys Chem 1977; 81: 969–972.
8. Shi Y, Wan P. Photocyclization of a 1,1'-bisnaphthalene: planarization of a highly twisted biaryl system after excited state ArOH dissociation. Chem Commun 1997; 273–274.
9. Burnham KS, Schuster GB. A search for chiral photochromic optical triggers for liquid crystals: Photoracemization of 1,1'-binaphthylpyran through a transient biaryl quinone methide intermediate. J Am Chem Soc 1998; 120: 12619–12625.
10. Cavazza M, Zandomeneghi M, Ouchi A, Koga Y. Photochromism in 1,1'-bi-2-naphthols. J Am Chem Soc 1996; 118: 9990–9991.
11. Flegel M, Lukeman M, Wan P. Photochemistry of 1,1'-bi-2-naphthol (BINOL)–ESIPT is responsible for photoracemization and photocyclization. Can J Chem 2008; 86: 161–169.
12. Solntsev KM, Bartolo EA, Pan G, Muller G, Bommireddy S, Huppert D, Tolbert LM. Excited-state proton transfer in chiral environments: Photoracemization of BINOLs. Isr J Chem 2009; 49: 227–233.
13. Deracemization with circular polarized light has also been reported. See refs. 14 and 15.
14. Hayashi K, Irie M. Jpn. Kokai Tokkyo Koho JP7818549, 2 Feb 1978 (Chemical Abstr. 1978:406151).
15. Zhang M, Schuster GB. Photoracemization of optically active 1,1'-binaphthyl derivatives: Light-initiated conversion of cholesteric to compensated nematic liquid crystals. J Phys Chem 1992; 96: 3063–3067.
16. Hattori T, Sakurai K, Koike N, Miyano S, Goto H, Ishiya F, Harada N. Is the CD exciton chirality method applicable to chiral 1,1'-biphenanthryl compounds? J Am Chem Soc 1998; 120: 9086–9087.
17. Hattori T, Satoh T, Miyano S. Convenient synthesis of triarylamines via ester-mediated nucleophilic aromatic substitution. Synthesis 1996; 514–518.
18. Hattori T, Suzuki T, Hayashizaka N, Koike N, Miyano S. Convenient synthesis of biphenyl-2-carboxylic acids via the nucleophilic aromatic substitution reaction of 2-methoxybenzoates by aryl Grignard reagents. Bull Chem Soc Jpn 1993; 66: 3034–3040.
19. Fu JM, Sharp MJ, Snieckus V. The directed ortho metalation connection to aryl-aryl cross coupling. A general regiospecific synthesis of phenanthrols. Tetrahedron Lett 1988; 29: 5459–5462.
20. Cacchi S, Ciattini PG, Morera E, Ortar G. Palladium-catalyzed triethylammonium formate reduction of aryl triflates. A selective method for the deoxygenation of phenols. Tetrahedron Lett 1986; 27: 5541–5544.
21. Feringa B, Wynberg H. Oxidative phenol coupling with cupric-amine complexes. Tetrahedron Lett 1977; 18: 4447–4450.