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# Synthesis, Resolution, and Absolute Stereochemistry of (−)-Blestriarene C

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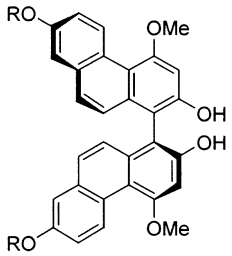
A naturally occurring 1,1′-biphenanthrene, blestriarene C (**1**), was prepared in 13 steps and 30% overall yield. The key steps are the ester-mediated nucleophilic aromatic substitution on 2,6-di-*tert*-butyl-4-methoxyphenyl 5-isopropoxy-2-methoxybenzoate (**4**) by 2-methoxy-4-methoxymethoxy-6-methylphenylmagnesium bromide (**5**) and a novel intramolecular cyclization of the resulting 4-isopropoxy-2′-methoxy-4′-methoxymethoxy-6′-methylbiphenyl-2-carboxylic ester **14** to 7-isopropoxy-4-methoxy-2-(methoxymethoxy)phenanthren-9-ol (**15**). The racemic blestriarene C was optically resolved by chiral HPLC on a preparative scale to give several 10-mg yields of both the enantiomers in up to 95% ee. The absolute stereochemistry was determined to be $S_a$-(−) by the axial chirality recognition method, which was based on the stereospecific formation of a 12-membered cyclic diester containing two biaryl-*o*,*o*′-diyl unites joined by ester $-CO_2-$ linkages. The validity of the method was confirmed by an X-ray crystallographic analysis and ab initio conformational analyses of such 12-membered cyclic diesters. It was found that blestriarene C and its 7,7′-diisopropyl ether **2** underwent rapid photoracemization even under ambient light exposure.

## Introduction

There are a certain number of 1,1′-biphenanthrene compounds, e.g. (−)-blestriarene C (cirrhopetalanthrin, **1**),[1] isolated from orchids along with analogues having 9,10-dihydro- and 9,9′,10,10′-tetrahydro-1,1′-biphenanthrene frameworks.[1a,c,d,2] These compounds generally possess at least three hydroxy and/or methoxy groups in total on each phenanthrene half, two being at the 2,2′-positions. Therefore, they may exist as nonracemic substances, as is often the case with the isolated ones.[1a,d,2g] However, no studies have ever tried to determine their absolute stereochemistries, not to mention their single-enantiomer preparations. In this connection, we have recently reported that the CD exciton chirality method is not suitable for determining the axial chirality of 1,1′-biphenanthrenes,[3] although it is a well-known nonempirical method often applied to biaryl compounds.[4] Here, we report a synthesis and optical resolutions of such a biphenanthrene, (−)-blestriarene C (**1**),[5,6] which was




($S_a$)-(−)-**1** R = H
($S_a$)-(−)-**2** R = *i*-Pr

isolated from *Bletilla striata* by Yamaki and co-workers[1a] and from *Cirrhopetalum maculosum* by Majumder et al.[1b] The compound was reported to be active against gram-positive bacteria, *Staphylococcus aureus* and *Streptococ-*

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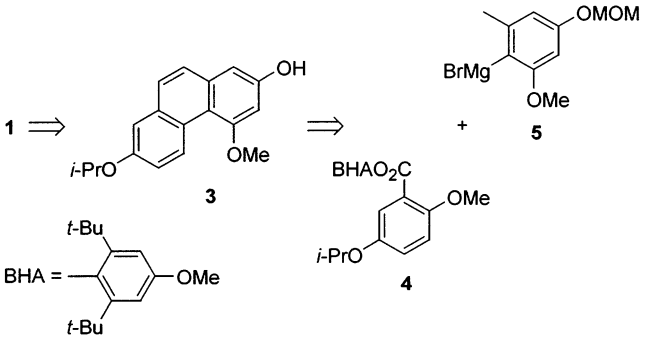
**SCHEME 1**

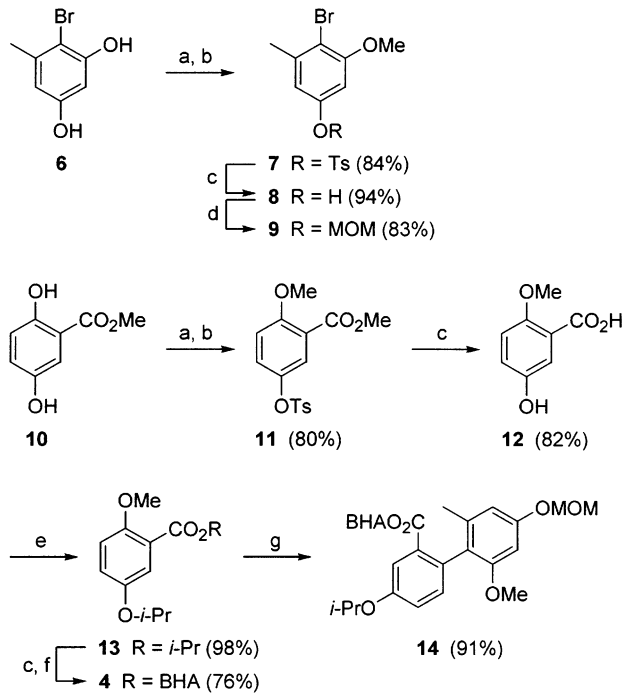



*cus mutans*.[1a] During the study, we have found that tetraol **1** undergoes rapid photoracemization even under ambient light exposure and thus the compound isolated from nature cannot be optically pure. Also reported is its absolute stereochemistry determined by *the axial chirality recognition method*, which is based on the stereospecific formation of a 12-membered cyclic diester containing two biaryl-*o*,*o*′-diyl unites joined by ester $-CO_2-$ linkages, e.g. compound **21**.[7] The validity of the method was confirmed by an X-ray crystallographic analysis and ab initio conformational analyses of such 12-membered cyclic diesters.

## Results and Discussion

**Synthesis of Racemic Tetraol 1.** Our synthetic strategy for racemic tetraol **1** was focused on regioselective synthesis of properly protected phenanthrenetriol **3**, since **1** should be readily prepared from **3** by oxidative phenol coupling reaction (Scheme 1). In previous papers,[8] we reported that ester function substantially activates an *o*-alkoxy group for nucleophilic aromatic substitution

**SCHEME 2**[a]




[a] Reagents: (a) $K_2CO_3$, TsCl, acetone; (b) MeI; (c) KOH, aq EtOH; (d) $K_2CO_3$, MOMCl, acetone; (e) $K_2CO_3$, *i*-PrBr, KI, DMF; (f) BHAOH, TFAA; (g) **5**, PhH.

($S_NAr$) reaction by various nucleophiles, which provides a convenient substitute for the oxazoline-mediated *o*-alkoxy displacement from aryloxazolines (the Meyers reaction).[9,10] We intended to employ the ester-mediated $S_NAr$ protocol for the coupling reaction between ester **4** and Grignard reagent **5** to biphenyl **14**, which was expected to serve as a convenient precursor of phenanthrol **3** (vide infra).

Prerequisite ester **4** and bromide **9** were prepared as follows (Scheme 2). Regioselective tosylation of benzenediol **6** at the 1-position, followed by methylation of the 3-hydroxy group in a one-pot fashion, as demonstrated by Wulff and co-workers for 4-bromobenzene-1,3-diol,[11] gave methoxy sulfonate **7**. It was hydrolyzed to phenol **8** and the hydroxy group was reprotected with MOMCl to give bromide **9**. On the other hand, regioselective func-

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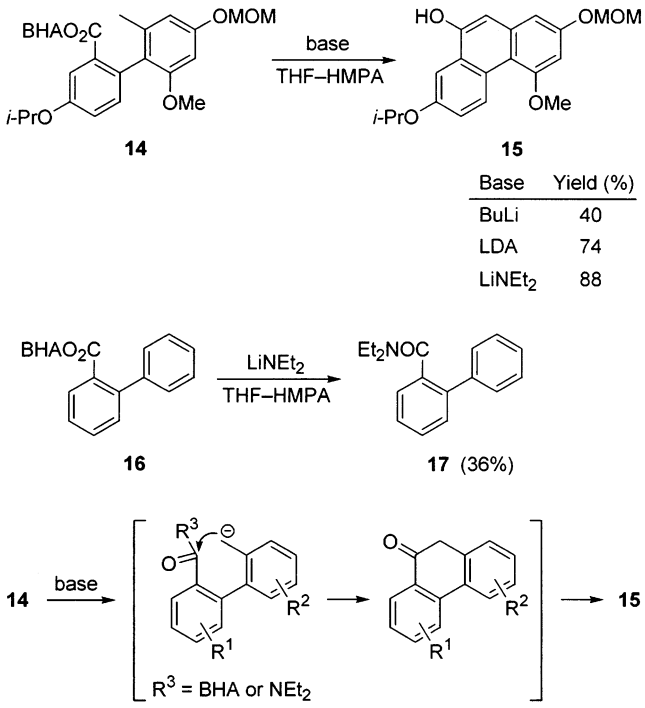
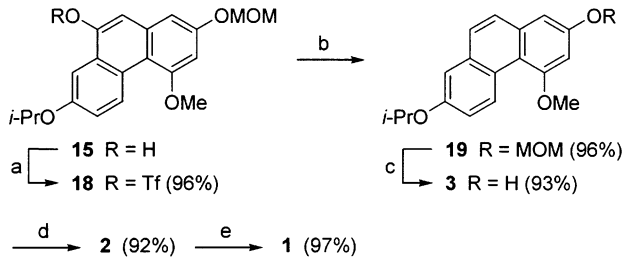
**SCHEME 3**




tionalization of 2,5-dihydroxybenzoate **10** by the same procedure as used for compound **6** gave methoxy sulfonate **11**, which was hydrolyzed to give hydroxy acid **12**. The 5-hydroxy group was converted into an isopropoxy group by treatment with 2-bromopropane in the presence of $K_2CO_3$ and KI to ester **13**, followed by its alkaline hydrolysis. The resulting acid was esterified with 2,6-di-*tert*-butyl-4-methoxyphenol (BHAOH) to give ester **4**. The $S_NAr$ reaction was first conducted by adding the Grignard reagent **5**, which had been prepared from bromide **9** and magnesium turnings in THF, to a benzene solution of ester **4** and then heating the mixture at reflux for 24 h to give biphenyl **14** in 55% yield with recovery of the starting ester (37%). However, the product yield was improved to 91% by replacing the THF with benzene (see Experimental Section), which may indicate the importance of the chelation between the substrate and the Grignard reagent to further the $S_NAr$ reaction.[8n,12]

As the desired biphenyl was in hand, its transformation into phenanthrol **15** was investigated (Scheme 3). Previously, Snieckus and co-workers reported that *N*,*N*-diethyl-2′-methylbiphenyl-2-carboxamide on treatment with LDA in THF gave the benzyl anion, which attacked intramolecularly to the carbonyl carbon to afford phenanthren-9-ol after enolization of the resulting ketone.[13,14] The method was extended to the cyclization of ester **14**, by conducting the cyclization in THF with 4.0 equiv of LDA at room temperature according to the reported procedure to give phenanthrol **15** in only 12% yield. However, utilization of HMPA as a cosolvent significantly increased the product yield (74%) even at lower temperature (0 °C) (Scheme 3). It is of interest to note that lithium diethylamide was more effective than LDA as a base, while butyllithium was less effective, giving unidentified byproducts. A control reaction of ester **16** with lithium diethylamide gave a substantial amount of acid amide **17** (36%) (Scheme 3). Therefore, although direct attack of the benzyl anion of ester **14** to the ester carbonyl group should be the main path to phenanthrol **15**, an alternative path via the intermediary acid amide generated in situ from ester **14** with lithium diethylamide may contribute to improving the product yield, to some extent, in the case of the lithium amide (Scheme 3).

**SCHEME 4**[a]




[a] Reagents: (a) $Tf_2O$, $NEt_3$, $CH_2Cl_2$; (b) $HCO_2H$, $NEt_3$, $Pd(OAc)_2$, $PPh_3$, DMF; (c) 1.5 M HCl, MeOH; (d) 1-phenylethylamine, $Cu(NO_3)_2{\cdot}3H_2O$, MeOH; (e) $BCl_3$, $CH_2Cl_2$.

Reductive removal of the 9-hydroxy moiety of phenanthrol **15** (Scheme 4),[15] followed by deprotection of the 2-hydroxy moiety of the resulting phenanthrene **19**, gave the desired phenanthrol **3**, which was oxidatively coupled in the presence of a copper(II) complex to give biphenanthrol **2**.[16] Deprotection of the 7,7′-dihydroxy groups of the biphenanthrol gave racemic tetraol **1** in a total of 30% yield based on the starting ester **10**.

**Optical Resolution of Tetraol 1 and Its Photoracemization.** It has been reported that optically pure 1,1′-binaphthalene-2,2′-diol (BINOL) is obtained by the enantioselective oxidative coupling of naphthalen-2-ol with the aid of a complex of $CuCl_2$ and (−)-sparteine.[17] Deracemizations of BINOL by use of this complex[17] and cyclohexane-1,2-diamine[18] are also fascinating procedures for the single-enantiomer preparation. These methods were applied to biphenanthrol **2** and a little success was achieved in the deracemization with the copper complex, recovering (−)-**2** of 30% ee from precipitate. Eventually, an optical resolution method based on the formation of diastereomeric thiophosphoramides was applied to **2** (Scheme 5).[19,20] Thus, racemic **2** was converted into a diastereomeric mixture of thiophosphoramides **20**. Crystallization of the mixture from hexane−benzene−acetonitrile resulted in the formation of prismatic crystals, which were composed of equimolar amounts of the diastereomers. Several variations of the crystallization

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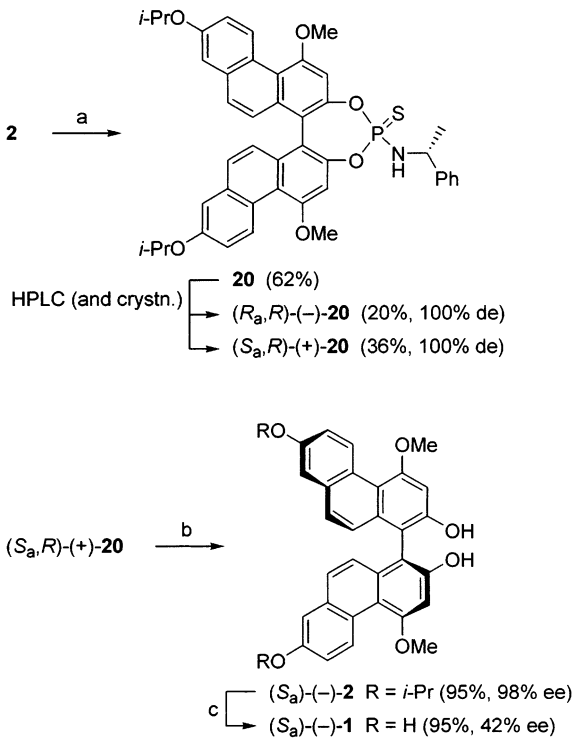
(20) See also: Gong, B.; Chen, W.; Hu, B. *J. Org. Chem.* **1991**, *56*, 423.

**SCHEME 5**[a]




[a] Reagents: (a) (*R*)-(+)-1-phenylethylamine, $PSCl_3$, pyridine; (b) $LiAlH_4$, THF; (c) $BCl_3$, $CH_2Cl_2$.

conditions including change of the solvent, crystallization temperature, and the like did not alter the diastereomeric composition. However, it could be separated into diastereomerically pure (−)-**20** and (+)-enriched **20** by preparative scale HPLC on a silica gel column. The latter was crystallized from hexane−benzene−ethanol to give (+)-**20** of 100% de. Reduction of (+)-**20** with $LiAlH_4$ gave biphenanthrol (−)-**2** with a slight loss of the axial integrity (98% ee), which was ascribed to a tendency for biphenanthrol **2** to racemize under ambient light exposure (vide infra). To our surprise, tetraol **1** was found to undergo far more rapid photoracemization. Thus, deprotection of biphenanthrol (−)-**2** of 98% ee with $BCl_3$ gave the desired (−)-**1** but its optical purity was only 42% ee although considerable care was taken not to expose these photosensitive compounds to light during the manipulations. On the other hand, baseline resolution of racemic **1** could be achieved by HPLC on a preparative scale by using a cellulose-derived chiral column (Daicel Chiralpak AD), which gave several 10-mg yields of both the enantiomers in up to 95% ee. It should be noted that a sample of (−)-**1** showed an $[\alpha]_D$ value of −101.6° in methanol, while its optical purity was estimated to be 95−92% ee by HPLC analyses conducted before and after the rotation measurement. Therefore, naturally occurring (−)-blestriarene C, the specific rotation of which was reported to be −16.7°,[1a] seems to have partially racemized during the isolation from the plant.

Figure 1 shows a decrease in the optical purity of tetraol **1** under fluorescent lamp illumination. The reaction followed first-order kinetics, the apparent rate constant $k_{rac}$ under the conditions being $1.90 \times 10^{-4}$ s$^{-1}$. No side products were detected by HPLC and the

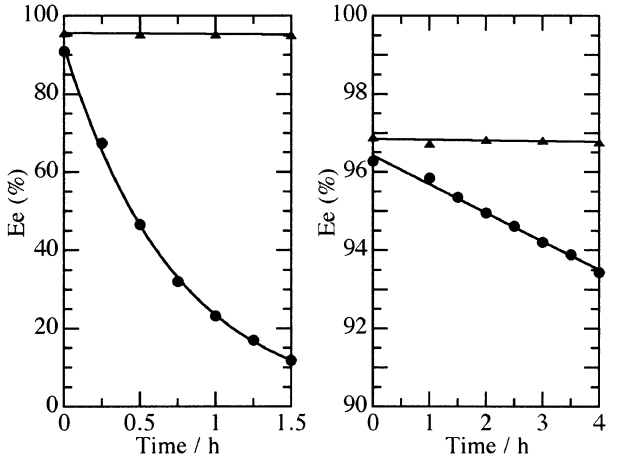



**FIGURE 1.** Racemization of (−)-blestriarene C (**1**) (left) and its diether (−)-**2** (right) under fluorescent lamp illumination (circle) or dark (triangle).

racemization was completely suppressed under dark. Diisopropyl ether **2** also had a tendency toward the racemization ($k_{rac} = 1.07 \times 10^{-6}$ s$^{-1}$) (Figure 1), while 1,1′-biphenanthrene-2,2′-diol did not in itself. There are several precedents in which biaryl compounds racemized under strong UV irradiation. For example, 1,1′-binaphthalene reportedly racemized through its triplet excited state where the rotation barrier of the biaryl axis was diminished compared to that in its ground state.[21] 6*H*-Dibenzo[*b*,*d*]pyrans racemized through biaryl quinone methides,[22] 1,1′-binaphthalene-2,2′-diol under the conditions where a photoproduct was formed by intramolecular addition of the 2′-hydroxy group to the $C_2-C_3$ bond,[23] and so on.[24] However, these mechanisms seem not to explain the marked tendency of the present compounds toward racemization. Although the reaction mechanism is not clear at present, a photoexcited quinone-type species might mediate the reaction.[25]

**Determination of the Absolute Stereochemistry of (−)-Blestriarene C.** The axial chirality recognition method predicts that two biaryl-*o*,*o*′-diyl units should have the same axial twist to form a 12-membered cyclic diester, e.g. compound **21**, because of the steric requirements imposed by the bulky and rigid components.[7,26] This provides a convenient method for recognizing axial chirality of a biaryl half of unknown stereochemistry by forming a cyclic diester with the other biaryl half of known axial chirality. This method was applied to determine the absolute stereochemistry of (−)-blestriarene C (Scheme 6). Thus, treatment of racemic bi-

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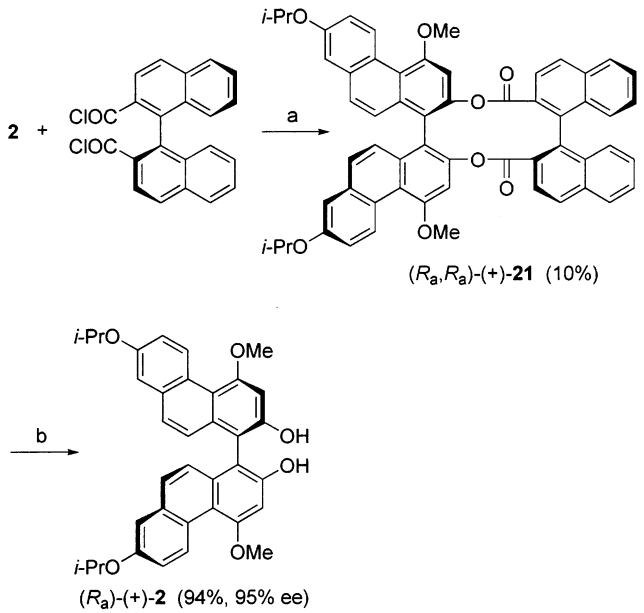
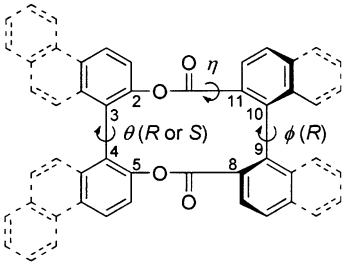
**SCHEME 6**[a]




[a] Reagents: (a) DMAP, $NEt_3$, PhH; (b) $LiAlH_4$, THF.

phenanthrol **2** with 1.0 equiv of ($R_a$)-1,1′-binaphthalene-2,2′-dicarbonyl chloride in refluxing benzene−triethylamine in the presence of DMAP picked up only one enantiomer ($R_a$)-**2** among the racemate to allow cyclization to give diastereomerically pure cyclic diester **21**, which should be $R_a$,$R_a$ configuration. Reductive cleavage of diester **21** with $LiAlH_4$ gave dextrorotatory biphenanthrol **2** of 95% ee. The incomplete preservation of enantiomeric integrity should be ascribed to the photoracemization (vide supra). Thus, the absolute stereochemistry of biphenanthrol **2** was unambiguously assigned to be $R_a$-(+). This, combined with the fact that deprotection of (−)-**2** gave (−)-**1** (vide supra), determined the absolute stereochemistry of naturally occurring (−)-blestriarene C to be $S_a$. This assignment was unambiguously confirmed by an X-ray crystallographic analysis of cyclic diester **21**. The ORTEP drawing of diester **21** clearly showed the *R* chirality of the biphenanthrene axis, referring to the *R* axis of the binaphthalene moiety (see Figure S1 in Supporting Information).

**Mechanistic Consideration of the Cyclic Diester Formation Method.** The asymmetric intramolecular coupling of two aryl halves held together by a chiral tether is an efficient way to obtain nonracemic biaryl compounds.[27] An alternative method to this is the kinetic resolution of racemic biaryls by cyclization with such a bifunctional chiral tether molecule.[28] These methods have been employed for the synthesis of natural products, taking advantage of an inherent chiral tether found in the target molecule.[29] Synthesis of biaryl-type chirality-recognizing elements by using an artificial tether has also been studied,[30] since the axial chirality recognition method had been developed in this laboratory.[7,26] In these reactions, it has often been claimed that the thermodynamically less stable diastereomer preferentially forms under kinetic control.[29b−d,g,i] In this respect, it is of interest to note the diastereoselectivity in the cyclic diester formation between a substituted diphenic acid and the 2,3-dihydroxy groups of a properly protected α-$_D$-glucopyranose, which was studied in connection with the synthesis of ellagitannins. Intramolecular Ullmann coupling of two substituted benzoyl halves linked together with the glucopyranose resulted in exclusive formation of a cyclic diester of $S_a$ chirality,[29h] while kinetic resolution of the racemic diphenic acid by esterification with the glucopyranose gave the ($R_a$)-cyclic diester as a single diastereomer.[29g] In our axial chirality recognition method, both the intramolecular Ullmann coupling and the kinetic esterification give a cyclic diester of the same absolute stereochemistry,[7,26] which qualifies the method as a convenient and reliable way to determine the axial chirality. Now that the X-ray crystal structure of such a cyclic diester was obtained for the first time, conformational analyses of this kind of cyclic diesters **22**−**24** were carried out by the ab initio molecular orbital method to deduce the origin of the stereospecificity.




| | alcohol unit | acid unit |
|---|---|---|
| **22** | biphenanthryl | binaphthyl |
| **23** | binaphthyl | binaphthyl |
| **24** | biphenyl | biphenyl |

The X-ray crystal structure of ($R_a$,$R_a$)-**21** showed that the two Aryl−$CO_2$−Aryl moieties adopt a double-helix-like conformation, a $C_2$ symmetry axis passing through the midpoints of the biaryl axes (Figure S1). Conformational analysis of diester ($R_a$,$R_a$)-**22** at the HF/6-31G* level by using Gaussian 98[31] revealed that there are two stable conformations in the same energy level (Figure 2). Thus, one has a $C_2$-symmetric structure similar to the X-ray structure of ($R_a$,$R_a$)-**21**, except that the carbonyl groups are a little more distorted out of the 12-membered ring than those of ($R_a$,$R_a$)-**21**, as shown by comparison of the dihedral angle η between the two (Table 1). The other has an asymmetric structure, tilting the one carbonyl

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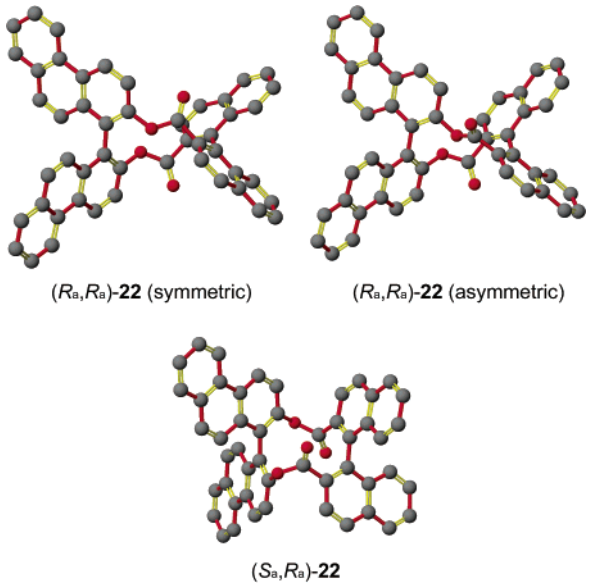


**FIGURE 2.** Geometries of cyclic diesters ($R_a$,$R_a$)- and ($S_a$,$R_a$)-**22** optimized at the HF/6-31G* level. Hydrogen atoms are omitted for clarity.

**TABLE 1. Dihedral Angles for Optimized 22−24**

| | | ($R_a$,$R_a$)-isomer | | | ($S_a$,$R_a$)-isomer | | |
|---|---|---|---|---|---|---|---|
| compd | conformation index | $\theta^a$ (deg) | $\phi^b$ (deg) | $\eta^c$ (deg) | $\theta^a$ (deg) | $\phi^b$ (deg) | $\eta^c$ (deg) |
| **21**[d] | sym | −76.8 | −65.7 | −43.1 | | | |
| **22** | sym | −76.7 | −70.5 | −52.7 | 110.7 | −86.1 | −52.9 |
| | asym | −68.3 | −84.4 | −44.5 | | | |
| | | | | −138.8 | | | |
| **23** | sym | −76.3 | −70.1 | −51.7 | 112.3 | −86.3 | −52.7 |
| | asym | −67.6 | −84.3 | −44.1 | | | |
| | | | | −140.6 | | | |
| **24** | sym | −62.9 | −57.9 | −49.3 | 130.7 | −97.4 | −58.8 |
| | asym | −57.3 | −74.1 | −42.9 | | | |
| | | | | −150.5 | | | |

[a] Dihedral angle between $C_2$−$C_3$ and $C_4$−$C_5$ bonds. [b] Dihedral angle between $C_8$−$C_9$ and $C_{10}$−$C_{11}$ bonds. [c] Dihedral angle between $C_7$═O ($C_{12}$═O) and $C_8$−$C_9$ ($C_{10}$−$C_{11}$) bonds. [d] X-ray data.

group toward the pseudoequatorial orientation of the 12-membered ring. The preference of the symmetric structure in crystals may be attributed to some packing forces. On the other hand, a similar calculation of the ($S_a$,$R_a$)-counterpart gave a unique structure, where the two aromatic planes of each Aryl−$CO_2$−Aryl moiety bent to form a v-shape and the two v-shape moieties were arranged upside down as shown in Figure 2. A $C_2$ symmetry axis passed through the midpoints of the biaryl axes in the same way as the symmetric ($R_a$,$R_a$)-isomer. The symmetric and asymmetric ($R_a$,$R_a$)-isomers lay 13.98 and 16.38 kcal mol$^{-1}$ lower in energy than the ($S_a$,$R_a$)-counterpart, respectively (Table 2). The same tendency was observed in the relative energies between two diastereomers of diesters **23** and **24** estimated by the same theoretical level calculations.[32] Therefore, it will be concluded that a thermodynamically stable diastereomer preferentially forms in the axial chirality recognition method.

**TABLE 2. Total and Relative Energies for Optimized 22−24**[a]

| compd | conformation Index | $E$($R_a$,$R_a$) | $E$($S_a$,$R_a$) | $\Delta E^b$ |
|---|---|---|---|---|
| **22** | sym | −1 386 347.11 | −1 386 333.13 | 13.98 |
| | asym | −1 386 349.51 | | 16.38 |
| **23** | sym | −1 194 763.49 | −1 194 749.57 | 13.92 |
| | asym | −1 194 765.79 | | 16.22 |
| **24** | sym | −811 610.37 | −811 596.64 | 13.73 |
| | asym | −811 613.31 | | 16.67 |

[a] Units: kcal mol$^{-1}$. [b] Relative energy given by $E$($S_a$,$R_a$) − $E$($R_a$,$R_a$).

## Conclusion

Racemic blestriarene C (**1**) was synthesized and optically resolved by chiral HPLC or via diastereomeric thiophosphoramides. Compound **1** and its 7,7′-diisopropyl ether **2** were found to undergo unprecedentedly rapid photoracemization even under ambient light exposure. The axial chirality recognition method could be advantageously utilized for the determination of the absolute stereochemistries of these easily racemizing biaryls. Further studies on the photoracemization mechanism are in progress.

## Experimental Section

**General.** Melting points were taken on a micro melting point apparatus and are uncorrected. Specific rotations are given in units of $10^{-1}$ deg cm$^2$ g$^{-1}$. Microanalyses were carried out in the Microanalytical Laboratory of the Institute of Multidisciplinary Research for Advanced Materials, Tohoku University. $^1$H and $^{13}$C NMR spectra were measured with tetramethylsilane as an internal standard and $CDCl_3$ as a solvent, unless otherwise noted. Silica gel (63−200 $\mu$m) was used for analytical and preparative TLC (PLC) and for column chromatography. Water- and air-sensitive reactions were routinely carried out under nitrogen. Diethyl ether, THF, and benzene were distilled from sodium diphenyl ketyl just before use. Other solvents for experiments requiring anhydrous conditions were purified by the usual methods. 4-Bromo-5-methylbenzene-1,3-diol (**6**) was prepared according to the literature procedure.[34]

**4-Bromo-3-methoxy-5-methylphenyl Toluene-*p*-sulfonate (7).** A mixture of dihydroxybenzene **6** (5.74 g, 28.3 mmol), $K_2CO_3$ (25.4 g, 184 mmol), and dry acetone (420 mL) was stirred at room temperature for 30 min. To the mixture was added TsCl (5.40 g, 28.3 mmol) and the mixture was heated under reflux. After 23 h, iodomethane (10.9 g, 76.8

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(32) Conformational analyses of cyclic diesters **22**−**24** by MOPAC2000 (ref 33) with use of AM1 and PM3 Hamiltonians gave similar optimized geometries to those obtained by the ab initio calculations. However, the relative energies between the two diastereomers estimated by these Hamiltonians were opposite to each other in every diester (see Supporting Information).

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mmol) was added and the mixture was refluxed for a further 28 h. After cooling, the resulting precipitate was filtered off on a kieselguhr plug and the filtrate was evaporated. The residue was chromatographed on silica gel with hexane−ethyl acetate (30:1) as the eluent to give tosylate **7** (8.86 g, 84%) as crystals, mp 72.9−74.6 °C; IR (KBr) 1604 $cm^{-1}$; $^1H$ NMR (500 MHz) $\delta$ 2.32 (3H, s), 2.46 (3H, s), 3.74 (3H, s), 6.37 (1H, d, $J$ = 2.5 Hz), 6.52 (1H, d, $J$ = 2.5 Hz), 7.33 (2H, d, $J$ = 8.3 Hz), 7.73 (2H, d, $J$ = 8.3 Hz); $^{13}C$ NMR (125 MHz) $\delta$ 21.7, 23.3, 56.4, 103.9, 112.4, 116.2, 128.6, 129.7, 132.2, 140.4, 145.5, 148.8, 156.4. Anal. Calcd for $C_{15}H_{15}BrO_4S$: C, 48.53; H, 4.07; Br, 21.52; S, 8.64. Found: C, 48.26; H, 4.02; Br, 21.77; S, 8.78.

**4-Bromo-3-methoxy-5-methylphenol (8).** Tosylate **7** (8.85 g, 23.8 mmol) was boiled with KOH (3.00 g) in a mixture of ethanol (150 mL) and water (150 mL) for 2 h. After the ethanol had been evaporated, the aqueous solution was neutralized with acetic acid and the resulting mixture was extracted with diethyl ether. The organic layer was washed with 1 M $NaHCO_3$ and extracted with 5% aqueous KOH. The extract was acidified with 6 M HCl and the liberated phenol was extracted with diethyl ether. The extract was washed with brine, dried over $MgSO_4$, and evaporated. The residue was purified by column chromatography on silica gel with hexane−ethyl acetate (4:1) as the eluent to give phenol **8** (4.88 g, 94%) as crystals, mp 119−121 °C; IR (KBr) 3288 $cm^{-1}$; $^1H$ NMR (400 MHz) $\delta$ 2.34 (3H, s), 3.84 (3H, s), 4.97 (1H, s), 6.30 (1H, d, $J$ = 2.7 Hz), 6.36 (1H, d, $J$ = 2.7 Hz); $^{13}C$ NMR (100 MHz) $\delta$ 23.2, 56.3, 97.8, 104.9, 109.7, 140.1, 155.1, 156.7. Anal. Calcd for $C_8H_9BrO_2$: C, 44.27; H, 4.18; Br, 36.81. Found: C, 44.11; H, 4.15; Br, 36.77.

**2-Bromo-1-methoxy-5-methoxymethoxy-3-methylbenzene (9).** A mixture of phenol **8** (8.68 g, 40.0 mmol), $K_2CO_3$ (13.8 g, 99.9 mmol), and dry acetone was stirred at room temperature for 20 min. To the mixture was added chloro(methoxy)methane (6.44 g, 80.0 mmol) and the mixture was refluxed for 17 h. The mixture was passed through a kieselguhr plug and the solvent was evaporated. The residue was dissolved by the addition of water and diethyl ether, and the two layers were separated. The aqueous layer was extracted with diethyl ether and the combined organic layer was washed with water, dried over $MgSO_4$, and evaporated. The residue was chromatographed on silica gel with hexane−ethyl acetate (12:1) as the eluent to give MOM ether **9** (8.64 g, 83%) as crystals, mp 33.4−35.1 °C; $^1H$ NMR (250 MHz) $\delta$ 2.38 (3H, s), 3.48, (3H, s), 3.86 (3H, s), 5.15 (2H, s), 6.48 (1H, d, $J$ = 2.7 Hz), 6.59 (1H, d, $J$ = 2.7 Hz); $^{13}C$ NMR (100 MHz) $\delta$ 23.4, 56.0, 56.2, 94.5, 98.8, 106.3, 110.0, 139.9, 156.6, 156.9. Anal. Calcd for $C_{10}H_{13}BrO_3$: C, 46.00; H, 5.02; Br, 30.60. Found: C, 45.71; H, 4.85; Br, 30.75.

**Methyl 2-Methoxy-5-(tolunene-*p*-sulfonyloxy)benzoate (11).** A mixture of dihydroxybenzoate **10** (16.0 g, 95.2 mmol), $K_2CO_3$ (79.8 g, 577 mmol), and dry acetone (1.0 L) was stirred at room temperature for 30 min. To the mixture was added TsCl (18.3 g, 96.0 mmol) portionwise over a period of 2 h and the mixture was refluxed for 19 h. To this mixture was added iodomethane (36.5 g, 257 mmol) and the resulting mixture was refluxed for a further 20 h. After cooling, the resulting precipitate was filtered off on a kieselguhr plug and the filtrate was evaporated. The residue was chromatographed on silica gel with hexane−ethyl acetate (2:1) as the eluent to give ester **11** (25.6 g, 80%) as crystals, mp 80.9−82.1 °C; IR (KBr) 1722 $cm^{-1}$; $^1H$ NMR (250 MHz) $\delta$ 2.45 (3H, s), 3.84 (3H, s), 3.87 (3H, s), 6.86 (1H, d, $J$ = 9.0 Hz), 7.10 (1H, dd, $J$ = 9.0, 3.0 Hz), 7.31 (2H, d, $J$ = 7.2 Hz), 7.39 (1H, d, $J$ = 3.0 Hz), 7.71 (2H, d, $J$ = 7.2 Hz); $^{13}C$ NMR (125 MHz) $\delta$ 21.6, 52.1, 56.3, 112.7, 120.5, 125.5, 127.2, 128.4, 129.7, 131.8, 142.0, 145.5, 157.7, 165.0. Anal. Calcd for $C_{16}H_{16}O_6S$: C, 57.13; H, 4.79; S, 9.53. Found: C, 57.10; H, 4.91; S, 9.48.

**5-Hydroxy-2-methoxybenzoic Acid (12).** Ester **11** (23.1 g, 68.7 mmol) was boiled with KOH (23.1 g) in a mixture of ethanol (135 mL) and water (30 mL) for 4 h. After the ethanol had been evaporated, the aqueous solution was washed with diethyl ether and then acidified with concentrated HCl. The mixture was extracted with diethyl ether and the extract was washed with brine, dried over $MgSO_4$, and evaporated. The residue was crystallized from ethyl acetate to give acid **12** (9.47 g, 82%) as crystals, mp 171−173 °C; IR (KBr) 3435, 1674 $cm^{-1}$; $^1H$ NMR (400 MHz, acetone-$d_6$) $\delta$ 3.99 (3H, s), 7.07 (1H, dd, $J$ = 8.9, 3.0 Hz), 7.11 (1H, d, $J$ = 8.9 Hz), 7.43 (1H, d, $J$ = 3.0 Hz), 8.41 (1H, s), 11.05 (1H, br); $^{13}C$ NMR (100 MHz) $\delta$ 57.2, 115.0, 118.8, 121.0, 121.9, 152.2, 153.8, 169.2. Anal. Calcd for $C_8H_8O_4$: C, 57.14; H, 4.80. Found: C, 57.02; H, 4.91.

**Isopropyl 5-Isopropoxy-2-methoxybenzoate (13).** A mixture of acid **12** (6.21 g, 36.9 mmol), $K_2CO_3$ (20.4 g, 148 mmol), and dry DMF (175 mL) was stirred at room temperature for 15 min. To the mixture was added 2-bromopropane (18.2 g, 148 mmol) and the resulting mixture was refluxed for 27 h. To the cooled mixture was added KI (610 mg, 3.67 mmol) and the mixture was stirred at room temperature for 20 h to complete the reaction. The mixture was cooled in an ice bath and quenched with 2 M HCl. The resulting mixture was extracted with diethyl ether and the extract was washed successively with 2 M $Na_2CO_3$ and water, dried over $MgSO_4$, and evaporated. The residue was chromatographed on silica gel with hexane−ethyl acetate (5:1) as the eluent to give isopropyl ester **13** (9.14 g, 98%) as an oil, IR (neat) 1728 $cm^{-1}$; $^1H$ NMR (250 MHz) $\delta$ 1.31 (6H, d, $J$ = 6.1 Hz), 1.35 (6H, d, $J$ = 6.3 Hz), 3.84 (3H, s), 4.46 (1H, sept, $J$ = 6.1 Hz), 5.24 (1H, sept, $J$ = 6.3 Hz), 6.88 (1H, d, $J$ = 9.1 Hz), 6.99 (1H, dd, $J$ = 9.1, 3.1 Hz), 7.31 (1H, d, $J$ = 3.1 Hz); $^{13}C$ NMR (100 MHz) $\delta$ 21.9, 22.0, 56.8, 68.1, 71.0, 113.8, 119.0, 120.9, 121.7, 151.1, 153.4, 165.5. Anal. Calcd for $C_{14}H_{20}O_4$: C, 66.65; H, 7.99. Found: C, 66.37; H, 7.93.

**2,6-Di-*tert*-butyl-4-methoxyphenyl 5-Isopropoxy-2-methoxybenzoate (4).** Ester **13** (9.05 g, 35.9 mmol) was hydrolyzed by boiling with KOH (6.01 g) in a mixture of ethanol (100 mL) and water (20 mL) for 3 h. After the ethanol had been evaporated, the aqueous solution was washed with diethyl ether and acidified with 2 M HCl to liberate the free acid, which was extracted with diethyl ether. The extract was washed with brine, dried over $MgSO_4$, and evaporated to give 5-isopropoxy-2-methoxybenzoic acid[35] as an oil (7.47 g), IR (neat) 3261, 1734 $cm^{-1}$; $^1H$ NMR (400 MHz) $\delta$ 1.32 (6H, d, $J$ = 6.0 Hz), 4.04 (3H, s), 4.53 (1H, sept, $J$ = 6.0 Hz), 6.99 (1H, d, $J$ = 9.0 Hz), 7.10 (1H, dd, $J$ = 9.0, 3.2 Hz), 7.68 (1H, d, $J$ = 3.2 Hz), 11.02 (1H, br); $^{13}C$ NMR (100 MHz) $\delta$ 21.8, 57.1, 70.9, 113.1, 117.9, 118.9, 123.8, 152.1, 152.5, 165.4. The acid (1.03 g) was treated with BHAOH (1.17 g, 4.95 mmol) in TFAA (4.2 mL) at room temperature for 2 d. The mixture was cooled in an ice bath, made basic with 2 M NaOH, and then extracted with diethyl ether. The extract was washed successively with 2 M NaOH and water, dried over $MgSO_4$, and evaporated. The residue was purified by column chromatography on silica gel with hexane−ethyl acetate (5:1 to 7:1) as the eluent to give BHA ester **4** (1.61 g, 76%) as crystals, mp 121−123 °C; IR (KBr) 1743 $cm^{-1}$; $^1H$ NMR (500 MHz) $\delta$ 1.33 (18H, s), 1.34 (6H, d, $J$ = 6.1 Hz), 3.81 (3H, s), 3.86 (3H, s), 4.49 (1H, sept, $J$ = 6.1 Hz), 6.89 (2H, s), 6.98 (1H, d, $J$ = 9.1 Hz), 7.11 (1H, dd, $J$ = 9.1, 3.2 Hz), 7.66 (1H, d, $J$ = 3.2 Hz); $^{13}C$ NMR (125 MHz) $\delta$ 22.0, 31.3, 35.6, 55.3, 56.5, 71.0, 111.5, 114.2, 119.7, 120.0, 123.0, 141.9, 143.7, 151.1, 154.6, 156.2, 166.1. Anal. Calcd for $C_{26}H_{36}O_5$: C, 72.87; H, 8.47. Found: C, 72.63; H, 8.45.

**2,6-Di-*tert*-butyl-4-methoxyphenyl 4-Isopropoxy-2′-methoxy-4′-methoxymethoxy-6′-methylbiphenyl-2-carboxylate (14).** The Grignard reagent **5** was prepared from bromide **9** (3.27 g, 12.5 mmol) and magnesium turnings (607 mg, 25.0 mmol) in THF (25 mL) as usual.[8b] The solvent was removed under reduced pressure and the residue was dissolved by addition of benzene (20 mL). The Grignard solution was added dropwise to a solution of ester **4** (2.98 g, 6.95 mmol) in benzene (25 mL) over a period of 30 min and the mixture was

(35) Hughes, A. B.; Sargent, M. V. *J. Chem. Soc., Perkin Trans. 1* **1989**, 1787.

refluxed for 24 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 with water, dried over $MgSO_4$, and evaporated. The residue was chromatographed on silica gel with hexane−ethyl acetate (6:1) as the eluent to give biphenyl **14** (3.65 g, 91%) as crystals, mp 151−153 °C; IR (KBr) 1749 $cm^{-1}$; $^1H$ NMR (400 MHz) $\delta$ 1.28 (9H, s), 1.30 (9H, s), 1.43 (6H, d, $J$ = 6.1 Hz), 1.87 (3H, s), 3.48 (3H, s), 3.54 (3H, s), 3.74 (3H, s), 4.65 (1H, sept, $J$ = 6.1 Hz), 5.11−5.15 (2H, m), 6.36 (1H, d, $J$ = 2.2 Hz), 6.46 (1H, d, $J$ = 2.2 Hz), 6.80−6.82 (2H, m), 7.09 (1H, d, $J$ = 8.4 Hz), 7.18 (1H, dd, $J$ = 8.4, 2.7 Hz), 8.00 (1H, d, $J$ = 2.7 Hz); $^{13}C$ NMR (100 MHz) $\delta$ 20.3, 22.0, 31.4, 31.5, 35.5, 35.6, 55.2, 55.2, 56.0, 70.1, 94.5, 96.9, 108.3, 111.5, 111.7, 117.6, 121.0, 124.0, 129.7, 133.4, 133.9, 137.3, 141.6, 143.5, 143.7, 156.2, 156.9, 157.1, 157.4, 164.9. Anal. Calcd for $C_{35}H_{46}O_7$: C, 72.64; H, 8.01. Found: C, 72.44; H, 8.06.

**7-Isopropoxy-4-methoxy-2-(methoxymethoxy)phenanthren-9-ol (15).** To an ice-cold solution of biphenyl **14** (3.00 g, 5.18 mmol) in a mixture of THF (20 mL) and dry HMPA (20 mL) was added dropwise lithium diethylamide, which had been prepared from diethylamine (1.70 g, 23.2 mmol) and butyllithium (1.59 M in hexane; 13.4 mL, 21.3 mmol) in THF (12 mL). After being stirred at 0 °C for 2 h, the mixture was quenched by successive addition of water and 1 M HCl. The resulting mixture was extracted with diethyl ether and the extract was washed with water, dried over $MgSO_4$, and evaporated. The residue was chromatographed on silica gel with hexane−ethyl acetate (3:1) as the eluent to give phenanthrol **15** (1.56 g, 88%) as an amorphous solid, IR (KBr) 3332 $cm^{-1}$; $^1H$ NMR (400 MHz) $\delta$ 1.42 (6H, d, $J$ = 6.1 Hz), 3.56, (3H, s), 4.06 (3H, s), 4.79 (1H, sept, $J$ = 6.1 Hz), 5.29 (2H, s), 5.74 (1H, s), 6.70 (1H, d, $J$ = 2.4 Hz), 6.84 (1H, s), 6.90 (1H, d, $J$ = 2.4 Hz), 7.24 (1H, dd, $J$ = 9.4, 2.9 Hz), 7.72 (1H, d, $J$ = 2.9 Hz), 9.44 (1H, d, $J$ = 9.4 Hz); $^{13}C$ NMR (125 MHz) $\delta$ 22.1, 55.6, 56.1, 70.0, 94.4, 97.9, 103.2, 105.2, 106.8, 112.7, 118.3, 126.0, 126.5, 129.4, 134.7, 149.9, 155.0, 155.1, 159.2.

**2,6-Di-*tert*-butyl-4-methoxyphenyl Biphenyl-2-carboxylate (16).** This compound was prepared by the same procedure as used for the preparation of similar biphenyls before.[8c] 2,6-Di-*tert*-butyl-4-methoxyphenyl 2-methoxybenzoate[8l] (372 mg, 1.00 mmol) was treated with 2.5 equiv of phenylmagnesium bromide in a mixture of diethyl ether (3.5 mL) and benzene (7.0 mL) at room temperature for 24 h. After the usual workup, the crude product was purified by PLC with hexane−ethyl acetate (9:1) as the developer to give biphenyl **16** (414 mg, 99%) as crystals, mp 193−194 °C; IR (KBr) 1745 $cm^{-1}$; $^1H$ NMR (400 MHz) $\delta$ 1.30 (18H, s), 3.75 (3H, s), 6.82 (2H, s), 7.21−7.31 (5H, m), 7.35 (1H, dd, $J$ = 7.6, 1.2 Hz), 7.56 (1H, td, $J$ = 7.6, 1.2 Hz), 7.63 (1H, td, $J$ = 7.6, 1.2 Hz), 8.45 (1H, dd, $J$ = 7.6, 1.2 Hz); $^{13}C$ NMR (100 MHz) $\delta$ 31.5, 35.6, 55.2, 111.6, 119.6, 126.8, 127.3, 127.6, 128.6, 131.4, 132.2, 132.3, 141.6, 141.7, 143.6, 146.2, 156.2, 165.5. Anal. Calcd for $C_{28}H_{32}O_3$: C, 80.73; H, 7.74. Found: C, 80.80; H, 7.68.

***N,N*-Diethylbiphenyl-2-carboxamide (17).** This compound was prepared by a similar procedure to that used for the preparation of phenanthrol **15**. Biphenyl **16** (212 mg, 509 $\mu$mol) was treated with 4.0 equiv of lithium diethylamide in a mixture of THF (3.0 mL) and HMPA (1.5 mL) at 0 °C for 2 h. After the workup, the crude product was chromatographed on silica gel with hexane−ethyl acetate (5:1) as the eluent to give amide **17** (46.4 mg, 36%) as an oil, IR (neat) 1627 $cm^{-1}$; $^1H$ NMR (400 MHz) $\delta$ 0.73 (3H, t, $J$ = 7.2 Hz), 0.89 (3H, t, $J$ = 7.2 Hz), 2.61−2.68 (1H, m), 2.91−3.02 (2H, m), 3.69−3.79 (1H, m), 7.32−7.48 (9H, m); $^{13}C$ NMR (100 MHz) $\delta$ 11.9, 13.3, 38.4, 42.2, 127.0, 127.5, 127.5, 128.2, 128.8, 128.9, 129.4, 136.4, 138.4, 139.8, 170.4. Anal. Calcd for $C_{17}H_{19}NO$: C, 80.60; H, 7.56; N, 5.53. Found: C, 80.33; H, 7.57; N, 5.38.

**7-Isopropoxy-4-methoxy-2-(methoxymethoxy)phenanthren-9-yl Trifluoromethanesulfonate (18).** To a mixture of phenanthrol **15** (1.54 g, 4.50 mmol), triethylamine (1.37 g, 13.5 mmol), and dichloromethane (15 mL) was added dropwise $Tf_2O$ (1.90 g, 6.73 mmol) at −78 °C and the mixture was stirred at this temperature for 1.5 h. The reaction was quenched by successive addition of water and 1 M HCl and the mixture was extracted with diethyl ether. The extract was washed with water, dried over $MgSO_4$, and evaporated. The residue was chromatographed on silica gel with hexane−ethyl acetate (6:1) as the eluent to give triflate **18** (2.04 g, 96%) as crystals, mp 83.6−85.0 °C; IR (KBr) 1620 $cm^{-1}$; $^1H$ NMR (400 MHz) $\delta$ 1.44 (6H, d, $J$ = 6.1 Hz), 3.55, (3H, s), 4.10 (3H, s), 4.76 (1H, sept, $J$ = 6.1 Hz), 5.31 (2H, s), 6.88 (1H, d, $J$ = 2.4 Hz), 7.11 (1H, d, $J$ = 2.4 Hz), 7.29 (1H, dd, $J$ = 9.5, 2.8 Hz), 7.46 (1H, d, $J$ = 2.8 Hz), 7.61 (1H, s), 9.50 (1H, d, $J$ = 9.5 Hz); $^{13}C$ NMR (100 MHz) $\delta$ 21.9, 55.8, 56.2, 70.1, 94.6, 101.2, 103.4, 105.1, 115.9, 117.1, 118.3, 119.0, 126.2, 126.3, 129.9, 132.4, 144.7, 155.6, 155.9, 159.0. Anal. Calcd for $C_{21}H_{21}F_3O_7S$: C, 53.16; H, 4.46; S, 6.76. Found: C, 53.04; H, 4.64; S, 6.59.

**7-Isopropoxy-4-methoxy-2-(methoxymethoxy)phenanthrene (19).** A mixture of triflate **18** (2.07 g, 4.36 mmol), triethylamine (1.37 g, 13.5 mmol), palladium acetate (19.6 mg, 87.3 $\mu$mol), triphenylphosphine (57.2 mg, 218 $\mu$mol), and dry DMF (70 mL) was stirred at room temperature for 10 min. To the mixture was added formic acid (385 mg, 8.36 mmol) and the resulting mixture was heated at 65 °C for 16.5 h. After being cooled in an ice bath, the mixture was quenched by successive addition of water and 2 M HCl. The mixture was extracted with diethyl ether and the extract was washed with water, dried over $MgSO_4$, and evaporated. The residue was chromatographed on silica gel with hexane−ethyl acetate (10:1) as the eluent to give phenanthrene **19** (1.36 g, 96%) as crystals, mp 50.1−52.7 °C; $^1H$ NMR (400 MHz) $\delta$ 1.42 (6H, d, $J$ = 6.1 Hz), 3.55 (3H, s), 4.10 (3H, s), 4.73 (1H, sept, $J$ = 6.1 Hz), 5.31 (2H, s), 6.85 (1H, d, $J$ = 2.4 Hz), 7.09 (1H, d, $J$ = 2.4 Hz), 7.21 (1H, dd, $J$ = 9.2, 2.8 Hz), 7.24 (1H, d, $J$ = 2.8 Hz), 7.58 (1H, d, $J$ = 8.9 Hz), 7.61 (1H, d, $J$ = 8.9 Hz), 9.44 (1H, d, $J$ = 9.2 Hz); $^{13}C$ NMR (100 MHz) $\delta$ 22.1, 55.6, 56.1, 69.8, 94.6, 100.0, 104.9, 111.2, 116.5, 117.6, 124.6, 127.3, 127.9, 129.3, 133.5, 134.2, 154.9, 155.0, 159.2. Anal. Calcd for $C_{20}H_{22}O_4$: C, 73.60; H, 6.79. Found: C, 73.63; H, 6.79.

**7-Isopropoxy-4-methoxyphenanthren-2-ol (3).** A mixture of phenanthrene **19** (2.92 g, 8.95 mmol), 1.5 M HCl (5.97 mL, 8.96 mmol), and methanol (70 mL) was heated at 60 °C for 7 h. After the methanol had been evaporated, 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 with water, dried over $MgSO_4$, and evaporated. The residue was purified by column chromatography on silica gel with hexane−ethyl acetate (2:1) as the eluent to give phenanthrol **3** (2.36 g, 93%) as crystals, mp 112−114 °C; IR (KBr) 3350 $cm^{-1}$; $^1H$ NMR (400 MHz, $CD_2Cl_2$) $\delta$ 1.40 (6H, d, $J$ = 6.1 Hz), 4.08 (3H, s), 4.73 (1H, sept, $J$ = 6.1 Hz), 5.17 (1H, s), 6.74 (1H, d, $J$ = 2.5 Hz), 6.86 (1H, d, $J$ = 2.5 Hz), 7.18 (1H, dd, $J$ = 9.4, 2.8 Hz), 7.23 (1H, d, $J$ = 2.8 Hz), 7.52 (1H, d, $J$ = 8.8 Hz), 7.60 (1H, d, $J$ = 8.8 Hz), 9.41 (1H, d, $J$ = 9.4 Hz); $^{13}C$ NMR (100 MHz) $\delta$ 22.1, 55.6, 70.2, 99.0, 104.8, 111.7, 115.5, 117.7, 124.8, 126.8, 128.0, 129.2, 133.2, 134.4, 153.3, 154.7, 159.5. Anal. Calcd for $C_{18}H_{18}O_3$: C, 76.57; H, 6.43. Found: C, 76.49; H, 6.52.

**7,7′-Diisopropoxy-4,4′-dimethoxy-1,1′-biphenanthrene-2,2′-diol (2).** A mixture of $Cu(NO_3)_2 \cdot 3H_2O$ (2.72 g, 11.3 mmol), 1-phenylethylamine (4.08 g, 33.7 mmol), and dry methanol (35 mL) was stirred at room temperature for 1 h. To the mixture was added dropwise a solution of phenanthrol **3** (2.12 g, 7.51 mmol) in methanol (55 mL) over a period of 2 h and the resulting mixture was stirred for a further 2 h. The mixture was cooled in an ice bath and quenched with 2 M HCl. The resulting mixture was extracted with ethyl acetate and the extract was washed with water, dried over $MgSO_4$, and evaporated. The residue was crystallized from ethanol to give biphenanthrol **2** (1.95 g, 92%) as crystals, mp 141−143 °C; IR (KBr) 3519 $cm^{-1}$; $^1H$ NMR (400 MHz) $\delta$ 1.39 (6H, d, $J$ = 6.1 Hz), 1.41 (6H, d, $J$ = 6.1 Hz), 4.22 (6H, s), 4.73 (2H, sept, $J$ = 6.1 Hz), 5.08 (2H, s), 7.04 (2H, s), 7.09 (2H, d, $J$ = 9.1 Hz),

7.19 (2H, d, $J$ = 2.8 Hz), 7.27 (2H, dd, $J$ = 9.4, 2.8 Hz), 7.46 (2H, d, $J$ = 9.1 Hz), 9.55 (2H, d, $J$ = 9.4 Hz); $^{13}$C NMR (100 MHz) $\delta$ 22.1, 22.1, 55.9, 69.9, 98.5, 105.8, 111.3, 116.7, 118.3, 123.8, 124.9, 129.2, 129.5, 133.2, 133.8, 153.2, 155.2, 160.6. Anal. Calcd for $C_{36}H_{34}O_6$: C, 76.85; H, 6.09. Found: C, 76.57; H, 6.10.

**4,4′-Dimethoxy-1,1′-biphenanthrene-2,2′,7,7′-tetraol (1).** To an ice-cold solution of biphenanthrol **2** (84.4 mg, 150 $\mu$mol) in dichloromethane (10 mL) was added dropwise $BCl_3$ (1.0 M in pentane; 750 $\mu$L, 750 $\mu$mol) and the mixture was stirred at 0 °C for 2 h. The reaction was quenched with water and the mixture was extracted with ethyl acetate. The extract was washed with water, dried over $MgSO_4$, and evaporated. The residue was purified by column chromatography on silica gel with hexane−ethyl acetate (1:2) as the eluent to give tetraol **1** (69.7 mg, 97%) as crystals. Spectral data of the sample were identical with those of blestriarene C reported in the literature.[1a]

**($R_a$,*R*)-(−)- and ($S_a$,*R*)-(+)-*N*-(1-Phenylethyl)-7,7′-diisopropoxy-4,4′-dimethoxy-1,1′-biphenanthrene-2,2′-diylthiophosphoramide (20).** To an ice-cold solution of thiophosphoryl chloride (115 mg, 679 $\mu$mol) in dry pyridine (6.0 mL) was added (*R*)-(+)-1-phenylethylamine (164 mg, 679 $\mu$mol) and the solution was allowed to warm to room temperature. To the solution was added biphenanthrol **2** (322 mg, 572 $\mu$mol) and the mixture was refluxed for 6 h. The reaction was quenched with 10% $H_2SO_4$ and the mixture was extracted with ethyl acetate. The extract was washed successively with 10% $H_2SO_4$ and water, dried over $MgSO_4$, and evaporated. The residue was chromatographed on silica gel with hexane−ethyl acetate (4:1) as the eluent to give diastereomeric phosphoramides **20** (265 mg, 62%) as crystals. Anal. Calcd for $C_{44}H_{42}NO_6PS$: C, 71.05; H, 5.69; N, 1.88; S, 4.31. Found: C, 71.04; H, 5.88; N, 1.88; S, 4.29. The diastereomeric mixture of **20** (190 mg) was separated into diastereomerically pure (−)-**20** (37.9 mg, 20%) and (+)-enriched **20** (152 mg) by preparative HPLC on a YMC silica gel column (S-5 120A SIL; 250 mm × 20 mm i.d.) with hexane−ethyl acetate (9:1) as the eluent. The latter was crystallized from a mixture of hexane (5.0 mL), benzene (1.2 mL), and ethanol (1.2 mL) to give diastereomerically pure (+)-**20** (68.3 mg, 36%).

**(−)-20:** mp 162−164 °C; $[\alpha]^{28}_D$ −192 (*c* 0.69, $CHCl_3$); IR (KBr) 3393, 1015 cm$^{-1}$; $^1$H NMR (400 MHz) $\delta$ 1.40−1.43 (12H, m), 1.50 (3H, d, $J$ = 6.8 Hz), 3.78 (1H, dd, $J$ = 11.7, 10.6 Hz), 3.81 (3H, s), 4.24 (3H, s), 4.36−4.47 (1H, m), 4.73 (1H, sept, $J$ = 6.2 Hz), 4.74 (1H, sept, $J$ = 6.2 Hz), 6.81 (1H, s), 7.06−7.30 (12H, m), 7.36 (1H, d, $J$ = 9.1 Hz), 7.42 (1H, d, $J$ = 9.1 Hz), 9.56 (1H, d, $J$ = 9.5 Hz), 9.61 (1H, d, $J$ = 9.5 Hz); $^{13}$C NMR (100 MHz) $\delta$ 22.1, 22.2, 22.2, 26.2, 26.2, 53.2, 55.7, 56.3, 69.9, 69.9, 102.6, 103.3, 110.8, 115.8, 115.8, 118.1, 118.2, 119.3, 119.7, 119.9, 124.3, 124.5, 125.7, 125.9, 126.1, 127.3, 128.1, 128.3, 128.6, 130.2, 130.3, 132.7, 133.9, 133.9, 144.0, 144.0, 146.2, 146.3, 147.5, 147.7, 155.9, 156.0, 159.0, 159.4.

**(+)-20:** mp 166−170 °C; $[\alpha]^{28}_D$ +226 (*c* 0.89, $CHCl_3$); IR (KBr) 3366, 1015 cm$^{-1}$; $^1$H NMR (400 MHz) $\delta$ 1.41 (6H, d, $J$ = 6.1 Hz), 1.41 (6H, d, $J$ = 6.1 Hz), 1.55 (3H, d, $J$ = 6.9 Hz), 3.58 (1H, dd, $J$ = 10.3, 6.4 Hz), 3.85 (3H, s), 4.23 (3H, s), 4.72 (1H, sept, $J$ = 6.1 Hz), 4.73 (1H, sept, $J$ = 6.1 Hz), 4.88−4.99 (1H, m), 6.56 (1H, s), 7.14−7.18 (3H, m), 7.22−7.28 (4H, m), 7.30−7.42 (7H, m), 9.53 (1H, d, $J$ = 9.5 Hz), 9.59 (1H, d, $J$ = 9.5 Hz); $^{13}$C NMR (100 MHz) $\delta$ 22.1, 22.1, 22.2, 24.2, 24.3, 52.7, 56.0, 56.2, 69.9, 70.0, 102.7, 103.3, 110.8, 110.9, 115.9, 116.4, 118.1, 118.2, 119.3, 119.8, 124.2, 124.5, 125.9, 126.0, 126.4, 127.6, 128.1, 128.3, 128.8, 130.1, 130.3, 132.7, 133.8, 133.9, 144.5, 144.5, 146.1, 146.1, 147.1, 147.2, 155.9, 155.9, 159.1, 159.4.

**($S_a$)-(−)-7,7′-Diisopropoxy-4,4′-dimethoxy-1,1′-biphenanthrene-2,2′-diol (2).** To an ice-cold solution of (+)-**20** (29.7 mg, 39.9 $\mu$mol) in THF (3.0 mL) was added $LiAlH_4$ (15.2 mg, 400 $\mu$mol) and the mixture was stirred at 0 °C for 10 min. The mixture was allowed to warm to room temperature and stirred for a further 3 h. The reaction was quenched by successive addition of water and 2 M HCl at 0 °C, and the mixture was extracted with ethyl acetate. The extract was washed successively with 0.5 M HCl and water, dried over $MgSO_4$, and evaporated. The residue was purified by column chromatography on silica gel with hexane−ethyl acetate (1:1) as the eluent to give levorotatory biphenanthrol **2** (21.3 mg, 95%) as crystals, $[\alpha]^{30}_D$ −5.22 (*c* 3.95, $CHCl_3$). The spectral data of the sample were identical with those of the racemate (vide supra). The optical purity of the sample was determined to be 98% ee by HPLC on a Daicel Chiralpak AD with hexane−ethanol (1:1) as the eluent.

**($S_a$)-(−)-4,4′-Dimethoxy-1,1′-biphenanthrene-2,2′,7,7′-tetraol (1).** Nonracemic tetraol (−)-**1** was obtained from biphenanthrol (−)-**2** of 98% ee by the same procedure as used for the preparation of racemic **1**. Thus, biphenanthrol (−)-**2** (25.1 mg, 44.6 $\mu$mol) was treated with $BCl_3$ (1.0 M in pentane; 233 $\mu$L, 233 $\mu$mol) in dichloromethane (2.0 mL) at 0 °C for 2 h. After workup, the crude product was purified by PLC with hexane−ethyl acetate (2:3) as the developer to give tetraol (−)-**1** (20.3 mg, 95%) as crystals, the spectral data of which were identical with those of the racemate. The optical purity of the sample was determined to be 42% ee by HPLC on a Daicel Chiralpak AD with hexane−ethanol (1:1) as the eluent.

**Chiral HPLC Separation of 1.** Racemic tetraol **1** (151 mg) was dissolved in ethanol (20 mL) and a 14th part each of the solution was injected into the preparative HPLC apparatus equipped with a Daicel Chiralpak AD column (250 mm × 20 mm i.d.) with hexane−ethanol (1:1) as the eluent. Because of the rapid photoracemization, the optical purity of the sample used for the optical rotation measurement was estimated by HPLC analyses conducted before and after the rotation measurement.

**($R_a$)-(+)-1**: as the first-eluted fraction in total yield of 68.3 mg (94% ee), $[\alpha]^{29}_D$ +98.3 (*c* 0.565, MeOH) for the sample of 94−92% ee.

**($S_a$)-(−)-1:** as the second-eluted fraction in total yield of 66.7 mg (95% ee), $[\alpha]^{28}_D$ −101.6 (*c* 0.525, MeOH) for the sample of 95−92% ee {lit.[1a] $[\alpha]^{20}_D$ −16.7}.

**Measurement of Photoracemization of Biphenanthrenes 1 and 2.** A solution of a nonracemic biphenanthrene (120 $\mu$M in ethanol) in a quartz cuvette (10 × 10 mm) was placed 15 cm behind a 18 W fluorescent lamp (Hitachi, FL20SS N/18-B) at 22 °C under air and a decrease in the enantiomeric purity of the sample was monitored by HPLC.

**($R_a$,$R_a$)-(+)-3,10-Diisopropoxy-13,32-dimethoxydinaphtho[2,1-*h*:1′,2′-*j*]diphenanthro[2,1-*b*:1′,2′-*d*][1,6]-dioxacyclododecin-16,29-dione (21).** ($R_a$)-1,1′-Binaphthalene-2,2′-dicarboxylic acid[36] (343 mg, 1.00 mmol) was boiled in thionyl dichloride (10 mL) for 4 h and then volatiles were removed under reduced pressure to give the acid chloride, which was dissolved in benzene (50 mL). Also prepared was a solution of racemic biphenanthrol **2** (563 mg, 1.00 mmol) in benzene (50 mL). The two solutions were added dropwise at the same rate over a period of 3 h to a boiled mixture of DMAP (244 mg, 2.00 mmol), triethylamine (5 mL), and benzene (150 mL). After the addition had been completed, the mixture was refluxed for a further 3 h. After cooling, the mixture was quenched with 2 M HCl and the resulting mixture was extracted with diethyl ether. The extract was washed with water, dried over $MgSO_4$, and evaporated. The residue was chromatographed on silica gel with benzene as the eluent to give cyclic diester ($R_a$,$R_a$)-(+)-**21** (89.0 mg, 10%) as crystals, mp 267−270 °C; $[\alpha]^{32}_D$ +357 (*c* 1.12, $CHCl_3$); IR (KBr) 1757 cm$^{-1}$; $^1$H NMR (400 MHz) $\delta$ 1.39 (6H, d, $J$ = 6.1 Hz), 1.39 (6H, d, $J$ = 6.1 Hz), 3.90 (6H, s), 4.71 (2H, sept, $J$ = 6.1 Hz), 6.87 (2H, s), 6.94 (2H, d, $J$ = 9.2 Hz), 7.13−7.17 (4H, m), 7.22 (2H, dd, $J$ = 9.5, 2.7 Hz), 7.29−7.34 (4H, m), 7.51−7.55 (2H, m), 7.80 (2H, d, $J$ = 8.6 Hz), 7.89−7.92 (4H, m), 9.51 (2H, d, $J$ = 9.5 Hz); $^{13}$C NMR (100 MHz) $\delta$ 22.0, 22.1, 55.6, 69.8, 103.4,

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110.8, 115.7, 117.9, 119.3, 124.3, 124.7, 125.7, 127.2, 127.5, 127.6, 127.9, 128.1, 128.6, 130.1, 130.1, 133.0, 133.7, 133.9, 134.3, 137.1, 147.0, 155.7, 158.0, 167.2. Anal. Calcd for $C_{58}H_{44}O_8$: C, 80.17; H, 5.10. Found: C, 79.85; H, 5.34.

**X-ray Crystallographic Analysis of Cyclic Diester ($R_a$,$R_a$)-(+)-21.** Vapor diffusion of hexane into a solution of diester **21** in acetone at room temperature gave prismatic crystals, one of which was subjected to X-ray crystallographic analysis. Data were collected on a CCD diffractometer with graphite-monochromated Mo Kα radiation. The structure was solved by direct methods (SIR92[37]) and expanded by using Fourier techniques (DIRDIF94[38]). A total of 21216 reflections were measured and 2876 were unique ($R_{int}$ = 0.028). Crystal data and refinement statistics are as follows: $C_{58}H_{44}O_8$, $M$ = 868.98, orthorhombic, $a$ = 14.090(2) Å, $b$ = 28.820(4) Å, $c$ = 11.160(2) Å, $V$ = 4531(1) Å$^3$, $T$ = 173 K, space group $C222_1$ (no. 20), $Z$ = 4, $\mu$(Mo Kα) = 0.84 cm$^{-1}$, $R(F)$ = 0.047, $wR(F)$ = 0.048, GOF = 1.42. The absolute stereochemistry of the biphenanthrene moiety was assigned to be $R_a$ by using the *R*-binaphthalene axis as an internal reference. See Figure S1 for the ORTEP drawing.

**($R_a$)-(+)-7,7′-Diisopropoxy-4,4′-dimethoxy-1,1′-biphenanthrene-2,2′-diol (2).** To an ice-cold solution of diester ($R_a$,$R_a$)-(+)-**21** (43.6 mg, 50.2 μmol) in THF (5.0 mL) was added $LiAlH_4$ (47.4 mg, 1.25 mmol) portionwise and the mixture was stirred at 0 °C for 15 min. The resulting mixture was allowed to warm to room temperature and stirred for a further 3 h. After being cooled in an ice bath, the mixture was quenched by successive addition of water and 2 M HCl. The mixture was extracted with ethyl acetate and the extract was washed with water, dried over $MgSO_4$, and evaporated. The residue was purified by PLC with hexane−ethyl acetate as the developer to give biphenanthrol ($R_a$)-**2** (26.6 mg, 94%) as crystals, $[\alpha]^{29}_D$ +0.72 (*c* 3.75, $CHCl_3$). Spectral data of the sample were identical with those of racemic **2**. The optical purity was determined to be 95% ee by HPLC on a Daicel Chiralpak AD with hexane−ethanol (1:1) as the eluent.

The positive sign of the specific rotation indicated that the absolute stereochemistry of diol **2** is $R_a$-(+). This, combined with the fact that (−)-**2** gave (−)-**1** (vide supra), determined the axial chirality of naturally occurring (−)-blestriarene C to be *S*.

**Computational Method.** Gaussian98[31] and MOPAC2000[33] were used for Hatree−Fock level calculations of cyclic diesters **22**−**24**, using AM1/PM3 Hamiltonians and 6-31G* basis set, respectively. Standard default criteria of each package were applied for the SCF convergence and the gradient geometry optimization. In both the MOPAC and Gaussian calculations, vibrational analyses and the imaginary frequency criterion were used to identify energy minima.

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**Supporting Information Available:** ORTEP drawing and detailed X-ray data for ($R_a$,$R_a$)-**21**, tables of dihedral angles and heats of formation for AM1 and PM3 geometries of **22**−**24**, Cartesian coordinates for calculated structures of **22**−**24**, and a $^1$H NMR spectrum of **15**. This material is available free of charge via the Internet at http://pubs.acs.org.

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