Synthesis of 8,8′-Disubstituted 1,1′-Binaphthyls Stable to Atropisomerization: 2,2′-Dimethyl-1,1′-binaphthalene-8,8′-diol and 2,2′-Dimethyl-8,8′-bis(4-*tert*-butyloxazolyl)-1,1′-binaphthyl

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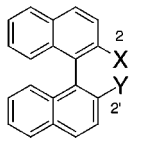
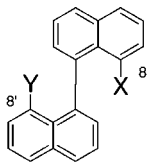
Axially chiral binaphthyls **3a** and **3b** were synthesized taking, advantage of Ullman coupling of **4a** and **4b**, respectively. The binaphthyls were shown to be stable to atropisomerization. Binaphthol **3b** was resolved with (−)-(1*S*)-menthyl chloroformate (**11**). *R*-axis diastereomer of bisoxazoline **3b** was used for enantioselective cyclopropanation of styrene with ethyl diazoacetate.

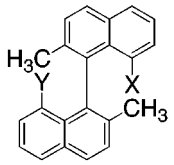
The axially chiral C_2-symmetrical 1,1′-binaphthyl scaffold has seen extensive use in organic synthesis in the design of nonracemic ligands and chiral auxiliaries. The most widely used compounds based on the 1,1′-binaphthyl framework are the chiral ligands 1,1′-bi-2-naphthol (**1a**),[1] (*S*,*S*)-2,2′-bis(4-alkyloxazolyl)-1,1′-binaphthyl (**1b**),[2] 2-diphenylphosphino-2′-methoxy-1,1′-binaphthyl (**1c**),[3] and 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl (**1d**).[4] Binaphthol **1a** has also been used as a chiral auxiliary. A common feature of **1a**−**d** is that their functional groups capable of chelating a metal ion attached in the 2,2′ position of the rigid binaphthyl skeleton also raise the barrier to atropisomerization, making it slow even at elevated temperature.[5]

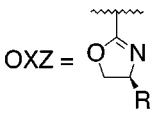


1a X=Y=OH,
1b X=Y=OXZ
1c X=OMe, Y=PPh_2,
1d X=Y=PPh_2



2a X=Y=OH
2b X=Y=OXZ
2c X=OMe, Y=PPh_2





3a X=Y=OH
3b X=Y=OXZ

The isomeric derivatives **2a**−**c** wherein the functional groups are placed in the 8,8′ position of the 1,1′ binaphthyl scaffold have also been reported. Binaphthol **2a** was found to be a superior chiral auxiliary to binaphthol **1a** in a tandem conjugate addition of Me_2CuLi and *n*-Bu_2CuLi to a tethered monocinnamate ester.[6a] Further uses of binaphthol **2a** as a chiral auxiliary included an enantioselective protonation of enolates,[6b] a Diels−Alder reaction,[6c] and synthesis of a novel monophosphine ligand **2c**.[6d] Diastereomeric *R*-axis (a-*R*,*S*,*S*) and *S*-axis (a-*S*,*S*,*S*) bisoxazoline **2b** (R = *t*-Bu) was accessed by Ullman coupling. A complex of (a-*R*,*S*,*S*)**2b** (R = *t*-Bu) ligated to CuOTf was reported to catalyze an enantioselective cyclopropanation of styrene with ethyl diazoacetate.[7]

A distinct feature of the **2a**−**c** as typical examples of 8,8′-disubstituted 1,1′-binaphthyls is that they are stable at room temperature but are prone to atropisomerization at elevated temperature.[8a] For example, the barrier to atropisomerization for **2a** and **2c** was reported to be 30.0

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(4) (a) Noyori, R.; Takaya, H. *Acc. Chem. Res.* **1990**, *23*, 345−350. (b) Takaya, H.; Ohta, T.; Mashima, K. *Adv. Chem. Ser.* **1992**, 230 (*Homogen. Transition Met. Catal. React.*), 123−142; *Chem. Abstr.* **1993**, *118*, 21717. (c) Akutagawa, S. *Appl. Catal.*, **1995**, *128*, 171−217; *Chem. Abstr.* **1995**, *123*, 255801. (d) Kumobayashi, H.; Sayo, N.; Akutagawa, S.; Sakaguchi, T.; Tsuruta, H. *Nippon Kagaku Kaishi*, **1997**, 835−846; *Chem. Abstr.* **1998**, *128*, 36303.

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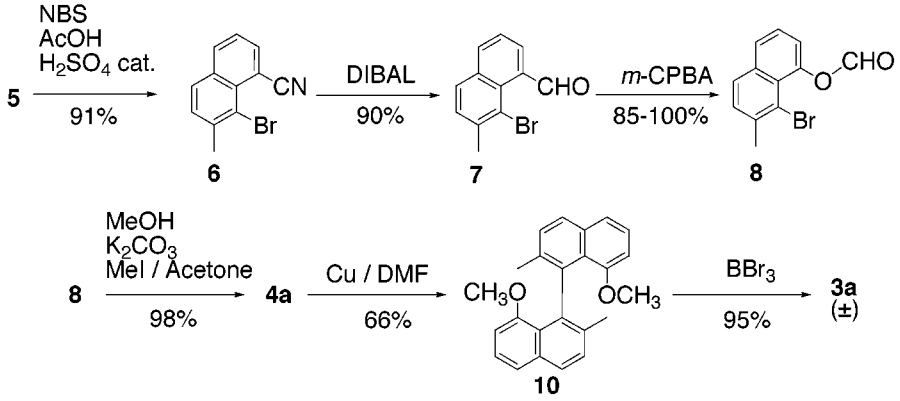
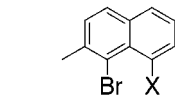
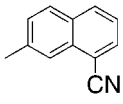
Scheme 1



and 30.2 kcal/mol, which translates into a half-life of 4.8 and 5.7 h at 100 °C, respectively.[8b] Therefore, additional sp^3 hybridized anchoring groups are needed in the 2,2′ positions of **2a**−**c** to slow the atropisomerization of these systems.[8a] The resulting dimethyl substituted axially chiral ligand and auxiliary **3b** and **3a** can be used at a temperature where their corresponding desmethyl counterparts **2a** and **2b** would atropisomerize.[8a] This paper presents a synthesis of binaphthyls **3a** and **3b**, their absolute configuration, proof of their conformational stability, and some preliminary results of enantioselective cyclopropanation catalyzed by CuOTf ligated to **3b**.



4a X=OMe
4b X=OXZ



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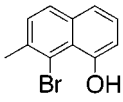

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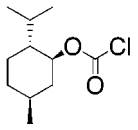

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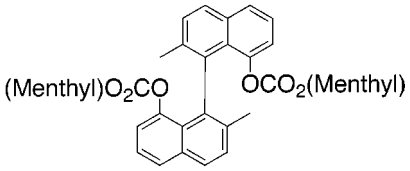

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The binaphthyl core of both **3a** and **3b** was constructed making use of an Ullman coupling[9] of the corresponding functionalized naphthalene bromides **4a** and **4b,** which were both derived from nitrile **5** (Scheme 1). Bromination of **5** with NBS under ionic conditions[10] in a mixture of acetic and trifluoroacetic acids catalyzed by sulfuric acid afforded **6** in 91% yield. Reduction of **6** with DIBAL gave the corresponding aldehyde **7** in 90% yield. Bayer−Villiger oxidation[11] of **7** was carried out with an excess of *m*-CPBA to afford **8** in 85−100% yield, which partially hydrolyzed to naphthol **9** upon aqueous workup [saturated $NaHCO_3$(aq)]. To obviate isolation and purification of the easily oxidizable **9**, formate **8** was directly converted into methoxynaphthalene **4a**, which was air and shelf stable. Coupling of **4a** under Ullman conditions with copper bronze yielded racemic methoxy protected binaphthol **10** in 66% yield. Deprotection of **10** with boron tribromide smoothly afforded **3a** in nearly quantitative yield.

Resolution of **3a** was achieved using (−)-(1*S*)- menthyl chloroformate (**11**). As reported by De Lucchi and coworkers,[12] both **1a** and **2a** form diastereomeric dicarbonates with **11**, which differ in crystallinity and can be separated by simple crystallization from hexane. The same result was obtained with the pair of diastereomeric dicarbonates **12a** and **12b** obtained from **3a** and **11**. However, on a smaller scale, the separation of **12a** and **12b** can also be achieved using thin-layer preparative radial chromatography (Chromatotron) or gravity column chromatography eluting with nonpolar system of solvents. X-ray crystal analysis showed that the more crystalline dicarbonate **12b** with lower R_f had the *S*-stereogenic axis.[28] Removing the menthyl auxiliary from **12a**,**b** with lithium aluminum hydride[12] afforded pure individual enantiomers of binaphthol **3a**. The optical

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(19) Huang-Minlon, *J. Am. Chem. Soc*. **1946**, *68*, 2487−2488.

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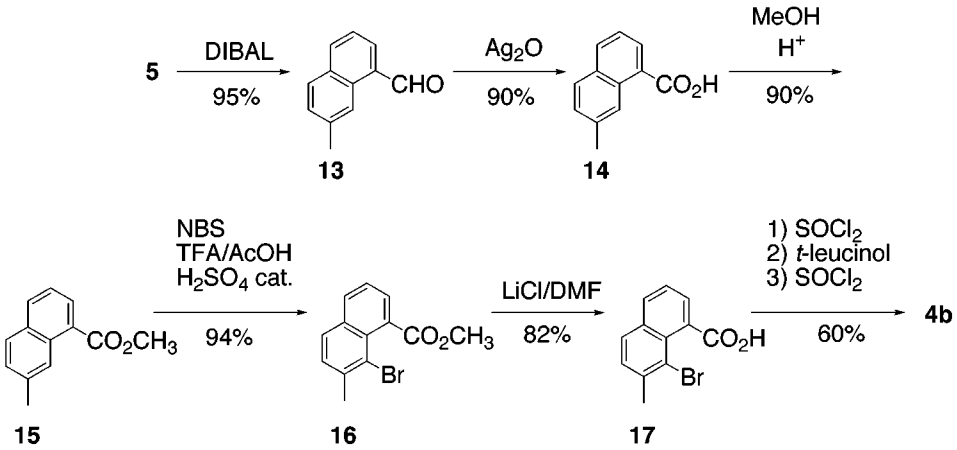
Scheme 2



purity of **3a** was verified with chiral HPLC. As expected, heating either of the pure enantiomers of **3a** at 180 °C in the melt for 30 min did not lead to any atropisomerization as evidenced by HPLC.

For the synthesis of bisoxazoline **3b** (Scheme 2), nitrile **5** was reduced with DIBAL to aldehyde **13** in 95% yield, which was oxidized with silver(I) oxide to acid **14** in 90% yield.[13] Sulfuric-acid-catalyzed Fischer esterification of acid **14** with methanol afforded ester **15** in 90%, which was regioselectively brominated with NBS under ionic conditions[10] in 94% yield. It was further found that **7** could be obtained by bromination of **13** under identical conditions. However, the 8-bromo substituent makes aldehyde **7** less reactive than **13** possibly due to steric hindrance. Therefore, it was not surprising that **7** could not be oxidized with silver(I) oxide to acid **17**. Likewise, bromoester **16** is also hindered and proved to be inert to hydrolysis (LiOH/ethanol). Ester **16** was converted to acid **17** in 82% yield with lithium chloride in refluxing DMF taking advantage of the S_N2 dealkylation.[14] Acid **17** was then converted to the oxazoline **4b** under standard conditions in 60% yield.[2a] Coupling of **4b**, under Ullman conditions, both in DMF and pyridine, was found to be solvent dependent and provided both diastereomers of **3b** in fair chemical yield and good diastereoselectivity (Figure 2). Some debrominated material **18** (16−18%) was also isolated. To assign the absolute stereochemistry about the chiral axis, the X-ray crystal structure of (a-*S*,*S*,*S*)**3b** was determined.[27]

Our current rationale for the observed diastereoselectivity in the Ullman coupling of **4b** is based upon the different nature of the solvents used (Figure 2). In pyridine, the copper(I) bromide formed during the reaction will be easily complexed by the huge excess of pyridine allowing the oxazolines to position themselves such that both the nitrogens and the *tert*-butyl groups are at maximum distance from each other as shown for copper(III) intermediate (A). This minimizes steric repulsion of *tert*-butyl groups and the lone pair repulsion of the oxazoline nitrogens. However, in the less coordinating DMF (B), the copper(I) ion will readily coordinate to the two oxazoline nitrogens forming the Cu(III) intermediate B (Figure 2), which will reductively eliminate to yield the observed biaryl with (a-*R*,*S*,*S*) configuration. Thus, pyridine leads mainly to the (a-*S*,*S*,*S*) biaryl configuration whereas DMF allows formation of the diastereomeric (a-*R*,*S*,*S*)**3b**. Support for this mechanistic rational can be obtained by the fact that the bisoxazoline **3b** formed in DMF still contains the copper(I) ion complexed in the product. The copper is removed by washing with aqueous ammonia leaving the (a-*R*,*S*,*S*) diastereomer of **3b**.

As an alternative approach to the formation of the binaphthyl skeleton of **3b**, we utilized Lipshutz's conditions which rely on the oxidative dimerization of higher order cyanocuprates with molecular oxygen.[15] The cyanocuprates are formed by transmetalation of the corresponding organolithium compounds with 0.5 equiv of CuCN. A metalation study demonstrated that **4b** can be readily lithiated, and the resulting carbanion was protonated with methanol to afford 87% of **18**. Following Lipshutz protocol, lithiated **4b** was treated with CuCN and oxidized to **3b**. This coupling procedure afforded 24% of (a-*S*,*S*,*S*)**3b**, 10% of (a-*R*,*S*,*S*)**3b**, and 11% of **18**. As evidenced by ^{1}H NMR, no incorporation of deuterium into **18** was detected when the reaction mixture was quenched with methanol-*d* prior to aqueous workup. This result suggests formation of **18** during the reaction and not during the aqueous workup.[15]

To demonstrate high barrier to atropisomerization for **3b**, its two diastereomers were heated at reflux in mesitylene (bp 165 °C) for several hours, at which time no atropisomerization was detected by TLC and ^{1}H NMR. In fact, heating the diastereomers of **3b** in the melt slightly above their melting point (>200 °C) for 5 min did not result in atropisomerization. Because of the high

(25) For ^{1}H NMR assignment of the phenylcyclopryl esters, see Nakamura, A.; Konishi, A.; Tsujitani, R.; Kudo, M.-a.; Otsuka, S. *J. Am. Chem. Soc.* **1978**, *100*, 3449−3461.

(26) Dewar, M. J. S.; Grisdale, P. J. *J. Am. Chem. Soc.* **1962**, *84*, 3541−3546.

(27) Crystal structure analysis of (a-*S*,*S*,*S*)**3b**: $C_{36}H_{40}N_2O_2$, M_r 532.70, colorless prizms, 0.42 × 0.38 × 0.09 mm, monoclinic, $P2_1$, a = 11.3187(5) Å, b = 10.1020(4) Å, c = 13.6236(6) Å, $\alpha = \gamma = 90°$, β = 106.2210(10)°, V = 1495.71(11) Å^3, Z = 2, ρ_{calc}= 1.183 g/cm^{-3}, MoKα (λ = 0.710 73 Å), T = 158(2) K; μ = 0.073 mm^{-1}. Area detector data collected on a Siemens SMART CCD diffractomerer. A total of 9912 reflections were collected (1.56 < Θ < 28.42°); independent reflections 6030 (R_{int} = 0.0188). Structure solved by direct methods (SHELXTL) and refined by full-matrix least-squares on $|F|^2$. Final R indices [$I > 2\sigma(I)$]: $R1$ = 0.0372, w$R2$ = 0.1177. GOF = 0.563. Residual electron density (e Å^{-3}) 0.193/−0.156.

(28) Crystal structure analysis of (a-*S*,*S*,*S*)**12b**: $C_{44}H_{54}O_6$, M_r 678.87, colorless prizms, 0.20 × 0.40 × 0.40 mm, orthorhombic, $P2_12_12_1$, a = 11.52710(10) Å, b = 17.4108(2) Å, c = 19.16840(10) Å, $\alpha = \beta = \gamma$ = 90°, V = 3847.02(6) Å^3, Z = 4, ρ_{calc}= 1.172 g/cm^{-3}, MoKα (λ = 0.710 73 Å), T = 158(2) K; μ = 0.076 mm^{-1}. Area detector data collected on a Siemens SMART CCD diffractometer. A total of 25507 reflections were collected (1.58 < Θ < 28.29°); independent reflections 9206 (R_{int} = 0.0458). Structure solved by direct methods (SHELXTL) and refined by full-matrix least-squares on $|F|^2$. Final R indices [$I > 2\sigma(I)$]: $R1$ = 0.0568, w$R2$ = 0.1044. GOF = 1.065. Residual electron density (e Å^{-3}) 0.165/−0.205.

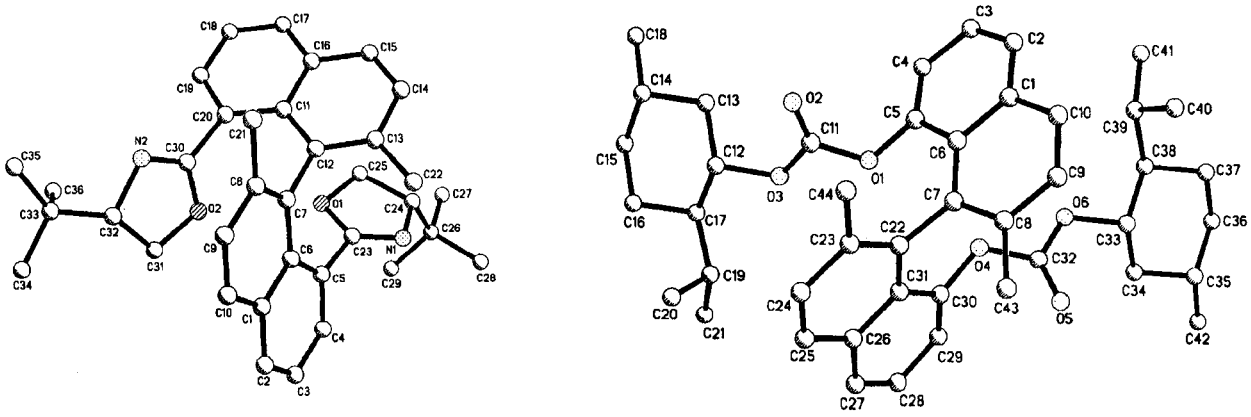


Figure 1. Crystal structures of (a-*S*,*S*,*S*)**3b** and (a-*S*,*S*,*S*)**12b**, respectively. The hydrogen atoms have been omitted for clarity.

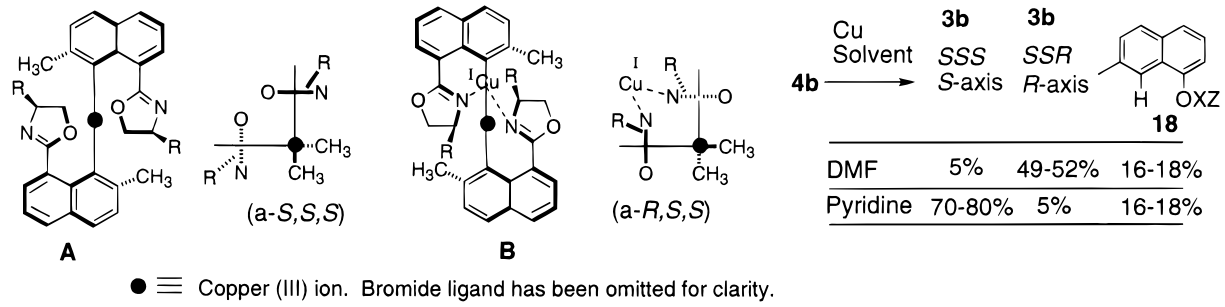
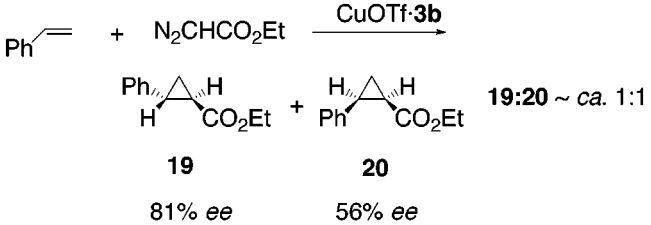


Figure 2. Proposed copper(III) intermediates of the Ullman coupling of **4b** in pyridine (A) and DMF (B).

barrier to atropisomerization, addition of copper(I) bromide to a refluxing solution of (a-*S*,*S*,*S*) **3b** in DMF did not promote the atropisomerization either.[9d] Indeed, the reported barrier to atropisomerization of 2,2′-dimethy-1,1′-binaphthyl is 50 kcal/mol.[5a]

It was earlier reported from these laboratories that only heterochiral (a-*R*,*S*,*S*) bisoxazoline **2b** could serve as a ligand for CuOTf to catalyze enantioselective cyclopropanation[16] of styrene with ethyl diazoacetate.[7b] Interestingly, Hayashi and co-workers observed opposite behavior for the corresponding homochiral and heterochiral **1b**.[2d] Therefore, a heterochiral (a-*R*,*S*,*S*)**3b** in which nitrogen atoms can chelate a metal copper ion without forcing the *tert*-butyl groups of the oxazolines into each other was chosen as a ligand to examine this process further. In dichloromethane, 81% *ee* for the trans-cyclopropane ester **19** and 56% *ee* for the cis isomer **20** were achieved. It is not entirely clear what eroded the enantioselectivity of the cyclopropanation reaction catalyzed by **3b** as compared to **2b**.[7b] Perhaps less rigidity of **2b** may account for subtle changes in the energy of the diastereomeric transition states for the cyclopropanation process.



In conclusion, C_2-symmetrical axially chiral 2,2′-dimethyl-8,8′-bi-2-naphthol (**3a**) and (a-*S*,*S*,*S*)- and (a-*R*,*S*,*S*)-2,2′ dimethyl-8,8′-bis(4-*tert*-butyloxazolyl)-1,1′-binaphthyls (**3b**) were prepared. Resolution of **3a** was achieved with (−)-(1*S*)- menthyl chloroformate (**11**). As predicted, both **3a** and **3b** are stable to atropisomerization. A complex of heterochiral (a-*R*,*S*,*S*)bisoxazoline **3b** and CuOTf catalyzed cyclopropanation of styrene with ethyl diazoacetate with moderate enantioselectivity.

Experimental Section

General. All reactions were run with magnetic stirring under an atmosphere of dry nitrogen unless otherwise noted. The drying agent Na_2SO_4 refers to anhydrous sodium sulfate. All solvents and reagents were of reagent quality, purchased commercially, and used without further purification, except as noted below. Dry triethylamine, dichloromethane, and toluene were freshly distilled from calcium hydride prior to use. Dry THF and 2-Me-THF were freshly distilled from sodium and benzophenone. DMF was stirred with CaH_2 at 60 °C overnight, filtered, fractionally distilled, and stored over 4 Å molecular sieves. *N*,*N*,*N*′*N*′-Tetramethylethylenediamine was distilled from and stored over strips of sodium metal. Dry pyridine was refluxed over CaH_2 overnight and distilled from CaH_2 and a small amount of lithium aluminum hydride. Oxygen was dried by passing it through a column filled with P_2O_5/Dryrite and cooled by passing it through a thin copper tube immersed into acetone/dry ice bath. *N*-Bromosuccinimide was recrystallized from water.

Analytical thin-layer chromatography (TLC) was performed on 0.2 mm silica gel coated plastic sheets (Merck) with F_{254} indicator. Flash chromatography was performed on Scientific Adsorbents Inc. 40 μm silica gel. Preparative thin-layer radial chromatography was performed on silica gel coated plates (silica gel 60 PF_{254} containing gypsum, EM Science) using a Chromatotron (Harrison Research). HPLC was performed on a Chiracel OJ (analysis of **3a**) and Chiracel OB (cyclopropanation products) columns (l = 25 cm, id = 4.6 mm) at 1 mL/min in (20% 2-propanol/hexanes) and (1% EtOAc/hexanes), respectively, with UV detection at 264 nm. Melting points are uncorrected.

Nuclear magnetic resonance (NMR) spectra were recorded in chloroform-*d* ($CDCl_3$) unless otherwise stated. When chloroform-*d* was used as a solvent chemical shifts were measured relative to the residual chloroform peak (7.26 ppm for ^{1}H NMR) and the center of $CDCl_3$ multiplet (77 ppm for ^{13}C NMR). When dimethyl sulfoxide-d_6 (DMSO-d_6) was used, chemical shifts were measured relative to the center of residual DMSO multiplet (2.49 ppm for ^{1}H NMR) and the center of DMSO-d_6 multiplet (39.7 ppm for ^{13}C NMR). Coupling constants are reported in hertz (Hz). When other deuterated solvents were used, chemical shifts were measured relative to the center of residual solvent peaks. GS-MS was performed on a HP Gas Chromatograph 5890 (Series II) coupled to an HP 5970 series MSD mass selective detector. Elemental analyses were performed at Atlantic Microlab, INC, Norcross, Georgia.

Nitrile **5**[17] was synthesized by the following reaction sequence. Neat toluene was acylated with succinic anhydride in the presence of anhydrous aluminum trichloride.[18] The resulting ketoacid was reduced using Huang−Minlon modification[19,21] of the Wolf−Kishner reaction conditions[20] with hydrazine hydrate, and the γ-*p*-tolylbutyric acid was cyclized in neat polyphosphoric acid (PPA) to afford 7-methyl tetralone.[21] The tetralone was treated with TMSCN using either zinc diiodide[22a] or boron trifluoride etherate[22b] as catalysts. Aromatization of dihydro derivative of **5** was affected by DDQ in refluxing 1,4-dioxane. *tert*-Leucinol was obtained by I_2/$NaBH_4$ reduction of commercially available *tert*-leucine.[23] Copper bronze used in Ullman coupling was freshly activated with iodine/acetone/HCl (concentrated aq.).[24]

2,2′-Dimethyl-8,8′-dihydroxy-1,1′-binaphthyl (3a). To a clear solution of 750 mg (2.2 mmol) of **10** in 8 mL of dry CH_2Cl_2 cooled to 0 °C (ice/water) was added dropwise 5 mL (5 mmol) of solution of BBr_3 (1 M/CH_2Cl_2). The resulting brownish red solution was stirred at room temperature for several hours until TLC of an aliquot partitioned between CH_2Cl_2 and saturated $NaHCO_3$(aq) showed the reaction to be complete. The brownish solution was poured into a mixture of crushed ice, saturated aq. $NaHCO_3$ and CH_2Cl_2 (**CAUTION: gas evolution!**). The collected organic layer was dried (Na_2SO_4) and decanted. The solvent was rotoevaporated. The brown residue was chromatographed over silica gel (40% CH_2Cl_2/hexanes). The material was further purified by preparative thin-layer radial chromatography (1% EtOAc/hexanes to 10% EtOAc/hexanes) to afford 650 mg (95%) of **3a** as an off-white solid. Later a better elution system was found to be a gradient of CH_2Cl_2 in hexanes starting with (5% CH_2Cl_2/hexanes). Note: the material was loaded as a solution in minimal amount of CH_2Cl_2 onto a dry plate. The lid of the Chromatotron was removed to let the solvent evaporate followed by elution. An analytically pure sample of **3a** was obtained by recrystallization from a small amount of peroxide-free di(*iso*-propyl)ether or EtOAc in bulk hexane: mp 172−173 °C; ^{1}H NMR δ 7.90 (1H, d, J = 8.4), 7.49 (1H, dd, J = 8.1, J = 1.1), 7.46 (1H, d, J = 8.4), 7.37 (1H, t, J = 7.7), 6.84 (1H, dd, J = 7.7, J = 1.1), 5.67 (1H, s br), 2.00 (3H, s); ^{13}C NMR δ 153.2, 135.3, 134.6, 130.5, 130.1, 128.6, 126.9, 121.6, 121.1, 112.5, 19.8. Anal. Calcd for $C_{22}H_{18}O_2$: C, 84.05; H, 5.77; O, 10.18. Found: C, 83.82; H, 5.90.

General Procedure for the Ullman Coupling. (a-*R,S,S*)-2,2′-Dimethyl-8.8′-bis(4-*tert*-butyloxazolyl)-1,1′-binaphthyl (3b). A mixture of 500 mg (7.8 mmol) of freshly activated copper bronze and 200 mg (0.6 mmol) of **4b** in 4 mL of dry DMF was deoxygenated using a freeze−pump−thaw cycle twice, and the resulting suspension was heated at ca. 100 °C overnight. A small aliquot was withdrawn. The solvent was removed under high vacuum. The dark residue was partitioned between CH_2Cl_2 and saturated NH_3(aq). The solvent from the collected organic layer was removed under high vacuum. TLC of the aliquot indicated the reaction to be complete. The bulk dark suspension was cooled to room temperature, diluted with DMF, and filtered through a plug of Celite. DMF was removed using short-path Kugelrohr distillation. The resulting dark residue was partitioned between CH_2Cl_2 and saturated NH_3(aq). The solvent from the collected organic layer was rotoevaporated. The dark residue was chromatographed over silica gel (30% EtOAc/CH_2Cl_2 to 50% EtOAc/CH_2Cl_2 to 5% MeOH in 30% EtOAc/CH_2Cl_2) to afford 25 mg (16%) of **18** as an oil, 8.0 mg (5%) of (a-*S,S,S*)**3b** as a tan solid and 75 mg (49%) of (a-*R,S,S*)-**3b** as a tan solid. Analytically pure sample of (a-*R,S,S*)**3b** was obtained by thin-layer preparative radial chromatography (10% EtOAc/CH_2Cl_2 to 15% EtOAc/CH_2Cl_2): mp 220−221 °C; ^{1}H NMR δ 7.97 (1H, dd, J = 6.0, J = 2.6), 7.87 (1H, d, J = 8.5), 7.55 (1H, d, J = 8.4), 7.41−7.37 (2H, m), 3.64 (1H, m), 3.36 (1H, m), 2.63 (br, H_2O), 2.47 (1H, m), 2.11 (3H, s), 0.66 (9H, s); ^{13}C NMR δ 165.4, 138.0, 134.1, 133.0, 131.0, 130.4, 128.7, 128.6, 126.9, 124.0, 75.5, 68.0, 33.2, 25.8, 21.0. Anal. Calcd for $C_{36}H_{40}N_2O_2\cdot H_2O$: C, 78.51; H, 7.69; N, 5.09; O, 8.72. Found: C, 78.50; H, 7.64; N, 5.05. $[\alpha]_D$ = −380° (c, 1.4, CH_2Cl_2).

(a-*S,S,S*)-2,2′-Dimethyl-8.8′-bis(4-*tert*-butyloxazolyl)-1,1′-binaphthyl (3b). Using a procedure analogous to that for coupling of **4b** in DMF, 200 mg (0.6 mmol) of **4b** and 500 mg (7.8 mmol) of copper bronze in 4 mL of dry pyridine were refluxed for 36 h to afford 10 mg (6%) of **18** as an oil, 130 mg (85%) of (a-*S,S,S*)**3b**, and 8 mg (5%) of (a-*R,S,S*)**3b**. An analytically pure sample of (a-*S,S,S*)**3b** was obtained by thin-layer preparative radial chromatography (5% EtOAc/CH_2Cl_2): mp 206−208 °C; ^{1}H NMR δ 7.98 (1H, dd, J = 7.3, J = 2.6), 7.83 (1H, d, J = 8.4), 7.5−7.4 (3H, m), 3.42 (1H, m), 3.15 (1H, m), 2.23 (1H, m), 1.92 (3H, s), 0.79 (9H, s); ^{13}C NMR δ 166.2, 138.2, 134.0, 132.6, 130.8, 130.4, 129.2, 128.5, 127.3, 123.9, 75.4, 68.2, 33.6, 25.8, 21.1 Anal. Calcd for $C_{36}H_{40}N_2O_2$: C,81.17; H, 7.52; N, 5.26; O, 6.01. Found: C, 81.01; H, 7.61; N, 5.19. $[\alpha]_D$ = −241°(c 1.3, CH_2Cl_2).

Typical Procedure for Lipshutz Coupling. To a clear solution of 692 mg (2 mmol) of **4b** in 15 mL of dry 2-Me-THF cooled to −120 °C (pentane/dry ice/L N_2) was added 1.6 mL (2.4 mmol) of *tert*-BuLi (1.5 M/pentane) dropwise with a syringe. The resulting red solution was stirred for 45 min and allowed to warm to −78 °C. To this solution was added 90 mg (1 mmol) of dry copper cyanide with an addition funnel having a large bore stopcock by rinsing CuCN down with 1 mL of dry 2-Me-THF followed by 1 mL of dry TMEDA. The resulting red suspension was stirred at −40 °C for 1.5 h to give a clear olive solution. The solution was cooled to −78 °C, and dry oxygen precooled to −78 °C was bubbled through the solution for 1 h at −78 °C and 1 h at room temperature. The resulting dark solution was quenched with 3 mL of methanol, rotoevaporated, and partitioned between CH_2Cl_2 and saturated NH_3(aq). The collected organic layer was washed with water, collected, dried (Na_2SO_4), and decanted. The solvent was rotoevaporated, and the dark residue was chromatographed over silica gel (30% EtOAc/CH_2Cl_2 to 50% EtOAc/CH_2Cl_2 to 5% MeOH in 30% EtOAc/CH_2Cl_2) to afford 60 mg (11%) of **18**, 130 mg (24%) of (a-*S,S,S*)**3b**, and 50 (10%) mg of (a-*R,S,S*)**3b**. On occasion, (a-*R,S,S* **3b** was further chromatographed over neutral alumina (20% EtOAc/CH_2Cl_2 to 50% EtOAc/CH_2Cl_2).

8-Bromo-7-methyl-1-methoxy-naphthalene (4a). To a yellowish solution of 1.83 g of **8**, 2 g (62 mmol) of methanol, 5 g (35 mmol) of methyl iodide, and 68 mg of 18-crown-6 in 14 g of reagent grade acetone was added 3.18 g (23 mmol) of potassium carbonate, and the greenish suspension was refluxed overnight at which time TLC showed the reaction to be complete. The resulting reddish suspension was cooled to room temperature, diluted with CH_2Cl_2, and filtered through a plug of Celite. The solvent was rotoevaporated and the brown residue was chromatographed over silica gel (30% CH_2Cl_2/hexanes) to afford 1.7 g (98%) of **4a** as a white solid. An analytically pure sample of **4a** was obtained by recrystallization from methanol: mp 66−68 °C; ^{1}H NMR (benzene-d_6) δ 7.37 (1H, d, J = 8.4), 7.23 (1H, dd, J = 8.0, J = 1.1), 7.10 (1H, t, J = 8.0), 6.96 (1H, d, J = 8.0), 6.53 (1H, d, J = 8.0), 3.44 (3H, s), 2.45 (3H, s); ^{13}C NMR δ 155.7, 137.5, 135.5, 129.0, 127.4, 125.5, 124.3, 121.2, 118.1, 107.9, 55.8, 25.6. MS 250, 252. Anal. Calcd for $C_{12}H_{11}OBr$: C, 57.40; H, 4.41; Br, 31.82; O, 6.37. Found: C, 57.30; H, 4.46; Br, 31.93. In a separate experiment the crude **4a** was purified by Kugelrohr distillation followed by recrystallization from methanol.

8-Bromo-7-methyl-1-(4-*tert*-butyloxazolinyl) naphthalene (4b). A suspension of 14.3 g (54 mmol) of **17**, 50 mL of

neat thionyl chloride, and several drops of DMF was refluxed for several hours until all **17** dissolved. Excess of $SOCl_2$ was removed by distillation at normal pressure using a still head. Residual $SOCl_2$ was removed by an aseotropic distillation with 250 mL of benzene. The resulting brownish residue was pumped under high vacuum and dissolved in 50 mL of dry CH_2Cl_2. The brownish solution was added to a solution of 7 g (60 mmol) of *tert*-leucinol and 9 mL (70 mmol) of NEt_3 in 100 mL of dry CH_2Cl_2 kept at 0 °C. After the addition of the acid chloride was complete, the reaction mixture was stirred at room temperature for several hours, washed with 5% HCl(aq), saturated $NaHCO_3$(aq), collected, dried (Na_2SO_4), and decanted. The solvent was rotoevaporated, and the resulting off-white oil was pumped under high vacuum at which time it crystallized. The solid was dissolved in 200 mL of dry CH_2Cl_2 and reacted with 8.6 mL (120 mmol) of neat $SOCl_2$ which was added dropwise. The resulting solution was stirred for 1 h at room temperature, at which time TLC of an aliquot partitioned between saturated $NaHCO_3$(aq) and CH_2Cl_2 indicated the reaction to be complete. The solvent from the bulk reaction was rotoevaporated. The residue was dissolved in 150 mL of CH_2Cl_2 and stirred in a 1 L beaker with excess of saturated $NaHCO_3$(aq) until no further gas evolution was observed and pH(aq) = 8 (**CAUTION: gas evolution!**). The collected organic layer was dried (Na_2SO_4) and decanted. The solvent was rotoevaporated and the yellowish solid was chromatographed over silica gel (0.5% methanol/CH_2Cl_2 to 2% methanol/CH_2Cl_2) followed by chromatography over neutral alumina (50% CH_2Cl_2/hexanes) to afford 11.3 g (60% from **17**) of **4b** as an off-white solid after crystallization from hexane/several drops EtOAc. An analytically pure sample of **4b** was obtained by thin-layer preparative radial chromatography (20% CH_2Cl_2/hexanes to CH_2Cl_2 to 1% EtOAc/CH_2Cl_2): mp 106−108 °C; ^{1}H NMR δ 7.89 (1H, dd, J = 8.0, J = 1.1), 7.79−7.74 (2H, m), 7.44−7.38 (2H, m), 4.51 (1H, m), 4.34 (1H, m), 4.13 (1H, m), 2.63 (3H, s), 1.08 (9H, s); ^{13}C NMR δ 138.9, 134.3, 131.6, 131.4, 130.7, 129.8, 128.3, 127.1, 124.6, 121.3, 76.8, 69.2, 34.3, 26.5, 25.4. MS 330, 332. Anal. Calcd for $C_{18}H_{20}NOBr$: C, 62.44; H, 5.82; N, 4.05; Br, 23.08; O, 4.62. Found: C, 62.34; H, 5.84; N, 4.01; Br, 22.97. $[\alpha]_D = -72°$ (c 1.5, CH_2Cl_2).

8-Bromo-1-cyano-7-methylnaphthalene (6). Using a procedure analogous to that used for **16**, 4.4 g (26.3 mmol) of **5** was reacted with 6.5 g (36.5 mmol) of NBS in a mixture of 10 mL of AcOH and 10 mL of TFA catalyzed by 5 mL of concentrated H_2SO_4. The only exception was that no sodium acetate was used during the workup. There was obtained 5.9 g (91%) of **6** as a creamy solid after recrystallization from ethanol: mp 102−104 °C; ^{1}H NMR (benzene-d_6) δ 7.48 (1H, dd, J = 7.3, J = 1.5), 7.23 (1H, dd, J = 8.0, J = 1.1), 7.07 (1H, d, J = 8.2), 6.77 (1H, d, J = 8.4), 6.63 (1H, m), 2.17 (3H, s); ^{13}C NMR ($CDCl_3$) δ 140.4, 138.6, 134.0, 133.6, 130.4, 130.0, 128.5, 124.4, 121.0, 120.1, 109.5, 25.2. MS 245, 247.

8-Bromo-7-methyl-1-naphthalenecarboxaldehyde (7). Using a procedure analogous to that used for **16**, 0.6 g (3.5 mmol) of **13** was reacted with 0.96 g (5.4 mmol) of NBS in a mixture of 2 mL of AcOH and 2 mL of TFA catalyzed by 10 drops of concentrated H_2SO_4. The only exception was that no sodium acetate was used during the workup. The product was subjected to thin-layer preparative radial chromatography (10% CH_2Cl_2/hexanes to 30% CH_2Cl_2/hexanes). There was obtained 0.62 g (71%) of **7** as a creamy solid after recrystallization from ethanol. There was also recovered 120 mg (20%) of unreacted **13**. The spectral characteristics and the melting point of the material were identical to those of **7** obtained by the reduction of **6** with DIBAL.

8-Bromo-7-methyl-1-naphthalenecarboxaldehyde (7). Using a procedure analogous to that for **13**, 5.25 g (21 mmol) of **6** was reacted with 4.6 mL (26 mmol) of DIBAL in 40 mL of toluene. In this case, the yellow solid resulting from the initial reaction mixture after the quench with EtOAc and absolute ethanol followed by removal of the solvent was partitioned between $CHCl_3$ and 20% HCl(aq). The resulting yellow biphasic mixture was reflux for 1 h and cooled to room temperature. The organic layer was collected, washed with water, collected, dried (Na_2SO_4), and decanted. The solvent was rotoevaporated, and the resulting yellow solid was chromatographed over silica gel (50% CH_2Cl_2/hexanes to 70% CH_2Cl_2/hexanes) to afford 4.7 g (90%) of **7** as an off-white solid after recrystallization from methanol: mp 86−88 °C; ^{1}H NMR δ 11.29 (1H, s), 7.90 (1H, dd, J = 8.5, J = 1.5), 7.78 (1H, dd, J = 8.3, J = 1.5), 7.73 (1H, d, J = 8.4), 7.45 (1H, m), 7.38 (1H, d, J = 8.4), 2.58 (3H, s); ^{13}C NMR δ 192.61, 138.9, 136.3, 134.1, 133.0, 131.4, 129.6, 129.4, 128.9, 124.9, 120.1, 24.9. MS 248, 250. Analytically pure sample of **7** was obtained by recrystallization from methanol. Anal. Calcd for $C_{12}H_9OBr$: C, 57.86; H, 3.64; Br, 32.08; O, 6.42. Found: C, 57.72; H,3.73; Br, 32.19.

8-Bromo-7-methyl-1-formyloxy-naphthalene (8). To a clear solution of 4 g (16 mmol) of **7** in 80 mL of CH_2Cl_2 was added 16 g of solid *m*-CPBA (57−85%) at once. The clear solution was stirred overnight, at which time it became yellow and a white precipitate formed. TLC showed complete consumption of **7**. The suspension was diluted with CH_2Cl_2 and filtered through a plug of Celite. The solution was washed with saturated $NaHCO_3$(aq), at which time the solution became brown because of the partial deprotection of the formate ester and oxidation of the phenol **9**. The organic layer was quickly collected and washed with 5% HCl(aq). The collected organic layer was dried (Na_2SO_4) and decanted. The solvent was rotoevaporated. The brown residue was chromatographed over silica gel (50% CH_2Cl_2/hexanes to 60% CH_2Cl_2/hexanes) to afford 3.7 g (87%) as a mixture of 8 (MS 264, 266) and phenol 9 (MS 236, 238) (11:2 by GC/MS) as a tan solid: mp 50−52 °C.

On a smaller scale of 0.73 g (~3 mmol) of 7 and 2.45 g (8.5−12 mmol) of m-CPBA (57−85%) in 10 mL of CH_2Cl_2 after the reaction was complete by TLC, the yellow suspension was diluted with 15 mL of hexanes and filtered. The filtrate was mixed with 20 mL of silica gel and rotoevaporated. The products, thus preloaded on silica gel, were put onto silica gel column (50 mL of silica gel) packed in (40% CH_2Cl_2/hexanes) and eluted with the same solvent mixture to afford 0.7 g (95%) of pure **8** as a white solid: ^{1}H NMR δ 8.46 (1H, s), 7.78 (1H, dd, J = 8.5, J = 1.5), 7.75 (1H, dd, J = 8.4), 7.45 (1H, m), 7.39 (1H, d, J = 8.0), 7.23 (1H, dd, J = 7.3, J = 1.1), 2.61 (3H, s); ^{13}C NMR δ 160.4, 144.6, 139.1, 135.4, 129.4, 127.9, 127.8, 125.1, 125.1, 121.5, 116.8, 25.2.

2,2′-Dimethyl-8,8′-dimethoxy-1,1′-binaphthyl (10). Using a procedure analogous to that for **4b,** 1.10 g (4.4 mmol) of **4a** was reacted with 1.16 g (18 mmol) of copper bronze in 10 mL of DMF. The wash of the residue from the reaction mixture with saturated NH_3(aq) was omitted. Instead, the solid products from the reaction mixture were chromatographed directly after dilution with additional DMF, filtration, and removal of DMF using short-path Kugelrohr distillation. Column chromatography of the dark residue over silica gel (30% CH_2Cl_2/hexanes) was followed by thin-layer preparative radial chromatography (0.5% EtOAc/hexanes) to afford 497 mg (66%) of **10** as a white solid: mp 155−157 °C; ^{1}H NMR δ 7.73 (1H, d, J = 8.0), 7.50 (1H, dd, J = 8.0, J = 0.8), 7.42 (1H, d, J = 8.0), 7.31 (1H, t, J = 8.0), 6.67 (1H, dd, J = 8.0, J = 0.8), 3.11 (3H, s), 1.96 (3H, s); ^{13}C NMR δ 157.3, 138.4, 134.0, 131.8, 128.7, 125.7, 124.7, 124.3, 121.0, 106.0, 55.9, 20.4. MS 342. Anal. Calcd for $C_{24}H_{22}O_2$: C, 84.18; H, 6.48; O, 9.34. Found: C, 83.90; H, 6.60. There was also obtained 180 mg (24%) of 1-methoxy-7-methylnaphthalene: ^{1}H NMR (benzene-d_6) δ 8.33 (1H, s), 7.59 (1H, d J = 8.0), 7.36 (1H, d, J = 8.0), 7.19 (1H, t, J = 8.0), 7.13 (1H, d, J = 8.0), 6.45 (1H, d, J = 7.7), 3.44 (3H, s), 2.276 (3H, s). MS 172.

Resolution of 3a. A general procedure[12] with several exceptions was followed. Thus, to a solution of 0.7 g (2.3 mmol) of racemic **3a** in a mixture of 7 mL of dry CH_2Cl_2 and 2 mL (14.3 mmol) of dry triethylamine cooled with an ice/water bath was added dropwise with a syringe 1.3 mmol (6 mmol) of (−)-(1*S*)-menthyl chloroformate, at which time a white precipitate formed. The suspension was refluxed for 3 h, at which time no starting **3a** was detected by TLC. [Note: (a-*S*,*S*,*S*)**12a** has an R_f value identical to that of starting **3a**. However, once exposed to atmospheric oxygen, the TLC spot of **3a** stains yellow while that of the dicarbonate does not.] The resulting slightly brownish solution was cooled to room temperature,

diluted with CH_2Cl_2, and washed with saturated aqueous solution of $NaHCO_3$. The collected organic layer was dried ($NaSO_4$) and decanted. The solvent was rotoevaporated. The resulting brownish oil was gravity chromatographed over 160 mL of silica gel (25% CH_2Cl_2/hexanes to 30% CH_2Cl_2/hexanes) to afford 590 mg (39%) of (a-*R*,*S*,*S*)**12a** with a higher R_f as a foamy white solid, 600 mg (40%) of (a-*S*,*S*,*S*)**12b** with lower R_f as a crystalline off-white solid, and 300 mg (20%) of mixed fractions of **12a**,**b** as a foamy white solid. Eluting the column further with 10%EtOAc/CH_2Cl_2 afforded 280 mg of *N*,*N*-diethyl (−)-(1*R*)-menthyl carbamate as a brownish oil identified by its molecular ion (M^+ 255) and ^{1}H NMR.

A mixture of 400 mg of pure (a-*R*,*S*,*S*)**12a** and 400 mg of pure (a-*S*,*S*,*S*)**12b** was dissolved in 20 mL of hexanes, and the solvent was allowed to evaporate overnight to afford a mixture of white crystals and an oil. To this mixture was added 7 mL of hexanes, at which time all the oil dissolved. The liquid was removed with a pipet. The crystals were rinsed with 1 mL of hexanes and recrystallized from hexanes to afford 280 mg (70%) of (a-*S*,*S*,*S*)**12b** (97.5% *de* as determined by specific rotation).

The mixed fractions collected at all stages of the resolution were combined and purified by preparative thin-layer radial chromatography (5% CH_2Cl_2/hexanes to 30% CH_2Cl_2/hexanes) to afford 530 mg of (a-*R*,*S*,*S*)**12a** and 350 mg of (a-*S*,*S*,*S*)**12b**.

If a sample of (a-*R*,*S*,*S*)**12a** as an oil is evacuated under high vacuum, it forms a white foamy sold. However, if a solution of **12a** in hexanes is rotoevaporated and the resulting oil is allowed to crystallize at room temperature and normal pressure, it produces a crystalline off-white solid: mp 77−79 °C, ^{1}H NMR δ 7.76 (1H, d, J = 7.4), 7.75 (1H, d, J = 8.4), 7.40 (1H, t, J = 7.7), 7.37 (1H, d, J = 8.4), 7.06 (1H, dd, J = 7.7, J = 1.1), 4.14 (1H, dt, J = 10.4, J = 4.4), 1.81 (3H, s), 1.75−0.65 (8H, series of m), 0.96 (3H, d, J = 6.6), 0.76 (3H, d, J = 7.0), 0.63 (3H, d, J = 7.0), 0.56 (1H, t, J = 11.3); ^{13}C NMR δ 153.1, 147.5, 135.0, 134.4, 134.2, 129.6, 127.3, 126.3, 126.1, 124.4, 119.6, 78.3, 46.8, 40.1, 33.9, 31.1, 25.6, 22.9, 22.0, 20.7, 20.1, 16.0. $[\alpha]_D$ = +252.6 (*c* 1.5, CH_2Cl_2).

(a-*S*,*S*,*S*)**12b**: mp 173−175 °C, ^{1}H NMR δ 7.73 (1H, d, J = 7.5), 7.69 (1H, d, J = 8.0, J = 1.1), 7.37 (1H, d, J = 8.4), 7.33 (1H, t, J = 7.5), 7.03 (1H, dd, J = 7.5, J = 1.1), 4.06 (1H, dt, J = 10.9, J = 4.4), 1.85 (3H, s), 1.65−0.65 (8H, series of m), 0.87 (3H, d, J = 7.0), 0.85 (3H, d, J = 6.2), 0.70 (3H, d, J = 7.0), 0.43 (1H, *AB*q); ^{13}C NMR δ 152.7, 147.7, 134.9, 134.4, 129.2, 127.0, 126.3, 125.3, 124.3, 119.2, 78.4, 46.46, 39.5, 34.0, 31.1, 25.1, 22.8, 21.9, 20.9, 20.4, 16.1. $[\alpha]_D$ = −166.0 (c 1.1, CH_2Cl_2).

To a solution of 237 mg (0.355 mmol) of (a-*R*,*S*,*S*)**12a** in 8 g of dry THF was added 135 mg (3.55 mmol) of LAH, and the suspension was refluxed for 2 h, at which time TLC showed all the starting **12a** to be consumed. The gray suspension was cooled with ice/water, and excess LAH was quenched with 2 mL of EtOAc followed by 1 mL of 10% HCl(aq). The solvent was rotoevaporated. The residue was partitioned between 10% HCl(aq) and CH_2Cl_2. The collected organic layer was washed with saturated $NaHCO_3$(aq), collected, dried (Na_2SO_4), and decanted. The solvent was rotoevaporated. The brownish oil was chromatographed over silica gel (25% CH_2Cl_2/hexanes) to afford 96 mg (88%) of (a-*R*)**3a** as white short needles as a single enantiomer as evidenced by chiral HPLC: mp 184−186 °C, $[\alpha]_D$ = −69.2 (c 1.1, CH_2Cl_2).

Following analogous procedure, 200 mg (0.3 mmol) of (a-*S*,*S*,*S*)**12b** was reacted with 80 mg (2.1 mmol) of LAH to afford 94 mg (97%) of (a-*S*)**3a** as short white needles as a single enantiomer as evidenced by chiral HPLC: mp 184−186 °C, $[\alpha]_D$ = +71.8 (c 0.94, CH_2Cl_2).

General Procedure for the Reduction of 5 and 6 with DIBAL. 7-Methyl-1-naphthalenecarboxaldehyde (13). To a clear solution of 25.3 g (149 mmol) of **5** in 250 mL of toluene cooled to 0 °C (ice/water) was added dropwise 30 mL (168 mmol) of neat DIBAL. After the addition of DIBAL was complete, the resulting yellow solution was stirred for 30 min at 0 °C and overnight at room temperature. TLC of an aliquot partitioned between 10% HCl(aq) and CH_2Cl_2 indicated complete consumption of **5**. The bulk yellow solution was cooled to 0 °C (ice/water) and excess DIBAL was quenched by dropwise addition of 10 mL of EtOAc, followed by 10 mL of absolute ethanol (**CAUTION!**). The solvent from the resulting yellow solution was rotoevaporated to as much as possible. The yellow residue was reacted with 150 mL of water followed by portionwise addition of 150 mL of 10% HCl(aq) and 20 mL concentrated HCl(aq), while keeping the flask in an ice/water cooling bath. (**CAUTION! Exothermic!**). The canary yellow emulsion was mixed with 300 mL of CH_2Cl_2 and stirred at room temperature for 2 h. The collected organic layer was washed with water, dried (Na_2SO_4), and decanted. The solvent was rotoevaporated, and the yellowish residue was subjected to short-path Kugelrohr distillation to afford 24 g (95%) of **13** as a colorless oil that crystallized upon standing. A more pure sample of **13** was obtained by crystallization from hexane: mp 42−44 °C; ^{1}H NMR δ 10.37 (1H, s), 9.08 (1H, s), 8.03 (1H, d, J = 8.0), 7.93 (1H, dd, J = 7.0, J = 1.1), 7.80 (1H, d, J = 8.1), 7.54 (1H, t, J = 7.2), 7.43 (1H, dd, J = 8.4, J = 0.8), 2.59 (3H, s); ^{13}C NMR δ 193.6, 139.3, 136.8, 135.0, 131.9, 130.7, 130.6, 129.0, 128.2, 123.8, 22.2. MS 170.

7-Methyl-1-naphthalenecarboxylic Acid (14). To a solution of 46 g (270 mmol) of $AgNO_3$ in 160 mL of water was added a solution of 23 g (575 mmol) of NaOH in 140 mL of water, at which time a brown precipitate formed. To the mechanically stirred suspension of Ag_2O prepared as above was added a solution of 22.3 g (131.2 mmol) of **13** in a mixture of 90 mL of 1,4-dioxane and 80 mL of ethanol. The resulting suspension was heated to 75 °C (internal), at which time the solid changed color from brown to gray. The suspension was stirred at 75 °C for 30 min, diluted with 300 mL of warm water, and filtered. The filtrate was rotoevaporated to remove ethanol and dioxane to about a half of its original volume, diluted to 1 L with water, and acidified to pH 1 with concentrated HCl(aq). A creamy solid formed. The solid was filtered and recrystallized from ethanol/water to afford 22 g (90%) of **14** as a creamy solid: mp 146−148 °C (lit mp: 146−147).[26]

Methyl 7-methyl-1-naphthalenecarboxylate (15). To 80 mL of methanol cooled to 0 °C (ice/water) was added dropwise 25 mL of concentrated H_2SO_4. To the resulting clear solution was added at once 21 g (112 mmol) of the **14**, and the mixture was refluxed for 3 h, at which time TLC indicated the reaction to be complete. The resulting yellowish emulsion was cooled to room temperature, and the solvent was evaporated as much as possible. The residue was partitioned between CH_2Cl_2 and water. The collected organic layer was washed with saturated $NaHCO_3$(aq), collected, dried (Na_2SO_4) and decanted. The solvent was rotoevaporated and the resulting brownish oil was subjected to short-path Kugelrohr distillation to afford 20 g (90%) of **15** as a yellowish oil: ^{1}H NMR δ 8.71 (1H, s), 8.15 (1H, dd, J = 7.3, J = 1.5), 7.97 (1H, d, J = 8.0), 7.78 (1H, d, J = 8.0), 7.40 (2H, m), 4.00 (3H, s), 2.57 (3H, s). MS 200.

8-Bromo-1-carbomethoxy-7-methylnaphthalene (16). To a clear solution of 18.3 g (91.5 mmol) of **15** in a mixture of 40 mL of glacial acetic and 40 mL of trifluoroacetic acid cooled with ice/water was added 19.5 g (110 mmol) of NBS at once. To the resulting clear suspension was added 12 mL of concentrated H_2SO_4 dropwise, at which time all NBS dissolved. The olive solution was stirred for 30 min, and an additional 3 g (17 mmol) of NBS was added. After the olive solution was stirred for additional 30 min, TLC indicated complete consumption of **15**. The olive solution was mixed with 20 g (244 mmol) of solid sodium acetate, and the resulting suspension was partitioned between CH_2Cl_2 and water. The collected organic layer was washed with saturated $NaHCO_3$(aq) until pH(aq) 8, and no gas evolution was observed. The collected organic layer was dried (Na_2SO_4) and decanted, and the solvent was rotoevaporated to afford an olive oil which was chromatographed over silica gel (30% CH_2Cl_2/hexanes to 60% CH_2Cl_2/hexanes). The desired **16** as a slightly olive oil was distilled using short-path Kugelrohr distillation to afford 24 g (94%) of **16** as an off-white solid. A more pure sample of **16** was obtained by preparative thin-layer chromatography (20% CH_2Cl_2/hexanes) followed by recrystallization from heptane/EtOAc: mp 70−72 °C; ^{1}H NMR δ 7.89 (1H, dd, J = 8.4, J = 1.5), 7.76 (1H, d, J = 8.4), 7.65 (1H, dd, J = 7.3, J = 0.7), 7.45

(1H, dd, $J = 7.4$, $J = 0.7$), 7.42 (1H, d, $J = 8.0$), 4.00 (3H, s), 2.64 (3H, s); ^{13}C NMR δ 171.5, 138.7, 134.2, 132.0, 131.1, 129.4, 128.7, 128.2, 124.5, 121.1, 52.9, 25.1. MS 278, 280.

8-Bromo-7-methyl-1-naphthalenecarboxylic Acid (17). A mixture of 18.2 g (65 mmol) of **16** and 25 g (590 mmol) of lithium chloride in 60 mL of DMF was refluxed overnight, at which time TLC showed the reaction to be complete. The resulting olive solution was diluted with 80 mL of DMF, transferred to a 1 L round-bottom flask, and the solvent was removed by short-path Kugelrohr distillation. The resulting greenish residue was dissolved in 500 mL of water, filtered through a plug of Celite, and acidified to pH 1 with concentrated HCl(aq), at which time an off-white precipitated formed. The solid was filtered and recrystallized from ethanol/water to afford 14.3 g (82%) of **17** as a creamy solid: mp 162−163 °C; ^{1}H NMR (DMSO-d_6) δ 13.18 (1H, s), 8.05 (1H, dd, $J = 8.4$, $J = 1.4$), 7.96 (1H, d, $J = 8.4$), 7.64 (1H, dd, $J = 7.3$, $J = 1.4$), 7.58 (1H, d, $J = 8.4$), 7.53 (1H, m), 2.58 (3H, s); ^{13}C NMR (DMSO-d_6) δ 171.3, 138.2, 133.7, 133.4, 130.4, 129.4, 128.3, 128.0, 124.8, 120.6, 24.5.

7-Methyl-1-(4-*tert*-butyloxazolinyl) Naphthalene (18). To a clear solution of 200 mg (0.58 mmol) of **4b** in 5 mL of dry THF cooled to −78 °C (acetone/dry ice) was added 2 mL (3 mmol) of *tert*-BuLi (1.5 M/pentane) dropwise. The resulting orange solution was stirred at 30 min and quenched by the addition of 1 mL (26 mmol) of methanol. The resulting clear solution was stirred at room temperature for 10 min. The solvent was rotoevaporated. The residue was partitioned between water and CH_2Cl_2. The collected organic layer was dried (Na_2SO_4) and decanted. The solvent was rotoevaporated. The residue was purified by thin-layer preparative radial chromatography (1% EtOAc/hexanes to 2% EtOAc/hexanes) to afford 135 mg (87%) of **18** as a colorless oil: ^{1}H NMR δ 8.96 (1H, d, $J = 0.7$), 8.06 (1H, dd, $J = 7.3$, $J = 0.7$), 7.93 (1H, d, $J = 8.4$), 7.80 (1H, d, $J = 8.4$), 7.45 (1H, m), 7.40 (1H, dd, $J = 8.4$, $J = 1.5$), 4.5−4.2 (3H, m), 2.61 (3H, s), 1.11 (9H, s); ^{13}C NMR δ 163.1, 136.9, 131.4, 131.4, 131.3, 128.8, 128.2, 128.1, 125.4, 124.0, 123.6, 77.0, 67.6, 34.0, 26.0, 22.3. MS 267. $[\alpha]_D = -51$ (c 2.1, CH_2Cl_2).

Typical Procedure for Cyclopropanation of Styrene with Ethyl Diazoacetate. A nylon syringe filter (0.2 μm) was dried under high vacuum at 65 °C to constant weight and tared. A mixture of 26 mg of $(CuOTf)_2$·PhH and 82 mg (0.154 mmol) of (a-*R*,*S*,*S*)**3b** was mixed in 4 mL of CH_2Cl_2, and the suspension was stirred at room temperature for 2 h. The resulting brownish suspension was filtered through the tared nylon syringe filter into a 50 mL round-bottom flask. The nylon filter was washed with CH_2Cl_2, dried under high vacuum at 65 °C to constant weight and tared. The weight increase totaled 10 mg of solid material. Therefore, 16 mg of $(CuOTf)_2$·PhH formed the catalyst (0.06 mmol of Cu; 0.75 mol %). To the resulting filtered olive solution of the catalyst was added 2.7 g (26 mmol) of styrene passed through a plug of basic alumina and 900 mg (7.9 mmol) of ethyl diazoacetate. The brownish solution was stirred at room temperature for 4 h, at which time TLC indicated complete consumption of ethyl diazoacetate. The solvent was rotoevaporated. The residue was subjected to Kugelrohr distillation with slight heating to remove excess of styrene. (Note: the recovered styrene did not contain any cyclopropanation products as evidenced by ^{1}H NMR.) The receiver was changed and all volatile products were collected, heating the pot to higher temperature. The resulting colorless oil was subjected to preparative thin-layer radial chromatography (0.5% EtOAc/hexanes to 2% EtOAc/hexanes). There were recovered 160 mg (11%) of 1*R*- (*trans*)-1-carbethoxy-2-phenylcyclopropane **19** of 76% *ee*, 130 mg (9%) of 1*R*-(*cis*)-1-carbethoxy-2-phenylcyclopropane **20** of 60% *ee*, and 150 mg (10%) of a 1:1 mixture of the two.[25] The enantiomeric excesses of the products were determined by chiral HPLC over Chirocel OB and by specific rotation.

In a separate experiment starting with 5 g (48 mmol) of styrene, 0.955 g (8.4 mmol) of ethyl diazoacetate, and 65 mg (0.122 mmol) of (a-*R*,*S*,*S*)**3b** in the presence of 16 mg (0.06 mmol; 0.71mol %) of solubilized $(CuOTf)_2$·PhH in 4 mL of CH_2Cl_2, there were recovered 320 mg of (20%) of 1*R*-(*trans*)-1-carbethoxy-2-phenylcyclopropane **19** of 76% *ee*, 300 mg (19%) of 1*R*-(*cis*)-1-carbethoxy-2-phenylcyclopropane **20** of 55% *ee*. In this experiment the enantiomeric excesses were determined by specific rotation of pure diastereomers.

In another experiment, 240 mg (0.45 mmol) of (a-*R*,*S*,*S*)**3b** and 80 mg (0.3 mmol; 2.3 mol %) of $(CuOTf)_2$·PhH solubilized in 5 g (48 mmol) of neat styrene were diluted with 3.5 g (33.6 mmol) of styrene and allowed to react with 1.44 g (12.6 mmol) of ethyl diazoacetate added portionwise over 6 h. The styrene solution of the catalyst was kept in an ice/water bath. These conditions afforded 320 mg (13.3%) of 1*R*-(*trans*)-1-carbethoxy-2-phenylcyclopropane **19** of 81% *ee*, 340 mg (14.2%) of 1*R*-(*cis*)-1-carbethoxy-2-phenylcyclopropane **20** of 56% *ee*, and 510 mg (21.3%) of a 1:1 mixture of the two diastereomers as estimated by ^{1}H NMR.

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Supporting Information Available: X-ray tables for compounds **3b** and **12b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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