Studies in Stereochemistry. 47. Asymmetric Induction by Leaving Group in Nucleophilic Aromatic Substitution[1,2]

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We report here the first examples of transfer of asymmetry from a leaving group to a biaryl product in nucleophilic, aromatic substitution reactions. Chiral products 2-[2-(1,1′-binaphthylyl)]-4,4-dimethyl-Δ^2-oxazoline (**6**), 2-[2-(2′-methoxy-1,1′-binaphthylyl)]-4,4-dimethyl-Δ^2-oxazoline (**8**), and 2-[2-(3′-methoxy-1,2′-binaphthylyl)]-4,4-dimethyl-Δ^2-oxazoline (**11**) were produced in high to medium optical yields by aryl–aryl coupling reactions in which 1-naphthyllithium, 3-methoxy-2-naphthyllithium, or 2-methoxy-1-naphthylmagnesium bromide was treated with 2-[2-(1-alkoxynaphthyl)]-4,4-dimethyl-Δ^2-oxazolines **15–19**. The alkoxy leaving groups of the naphthyloxazolines were derived from the naturally occurring alcohols *l*-menthol, quinine, quinidine, α-fenchol, and borneol. The oxazoline group activates the aromatic nucleus toward nucleophilic aromatic substitution by stabilizing the transition states leading to and from σ-complex intermediates. These reaction intermediates are diastereomeric and are therefore of unequal free energy. Thus one enantiomeric product is formed faster than the other. The configurations of starting materials and products (with the exception of **11**) were established by converting them to compounds of established absolute configuration. The optical yields in the 14 reactions examined ranged from $\gtrsim$95% to 8% and the chemical yields from 88% to 7%. The *l*-menthoxy leaving group gave the highest chiral transfer efficiencies (% chemical yield × % optical yield), which ranged from 65% to 41%. The more spherical, least dissymmetric α-fenchoxy and bornoxy groups gave the lowest optical yields (77–8% ee) but rather good chemical yields (88–65%). The quininoxy and quinidinoxy group produced the most consistently high optical yields (94–80% ee) but the lowest chemical yields (7–27%). These two leaving groups gave products of opposite configurations in the three systems examined. The highest value observed for the difference in free energy of the diastereomeric transition states was $\Delta(\Delta G^{\ddagger}) = 2.4$ kcal mol^{-1} and involved 2-methoxy-1-naphthylmagnesium bromide as nucleophile, quininoxy as leaving group, and **8** as product. Unlike most covalently bound chiral auxilliary units used for asymmetric induction in organic synthesis, those of the current study are displaced during the reaction. The direction of the configurational biases is interpreted in terms of the superposition of steric effects on the tendency of the lithium and magnesium ions to be ligated internally in the σ-complex intermediates.

The 1,1′-binaphthyl unit has enjoyed extensive use in the design and synthesis of chiral hosts for resolving amino acids by complexation,[3] of chiral catalysts for making carbon–carbon[4] or carbon–hydrogen bonds,[5] and of chiral reagents for reducing ketones to optically active alcohols.[6] The degrees of chiral recognition and asymmetric induction observed for these binaphthyl compounds have been among the highest reported and have been attributed to the freedom from conformational ambiguity of this axially dissymmetric unit. In many cases, the direction of the configurational bias has been rationalized on stereoelectronic grounds.[3-6]

These facts have stimulated several searches for methods of generating enantiomers of binaphthyl derivatives by methods other than those of classical resolution of racemic material. Wynberg et al.[7] reported that oxidative coupling of β-naphthol to give 2,2′-dihydroxy-1,1′-binaphthyl provided 16% ee when carried out in the presence of optically active amines. Kumada et al.[8] reported that coupling 1-bromo-2-methylnaphthalene with its corresponding Grignard reagent in the presence of a chiral binaphthylnickel species gave 2,2′-dimethyl-1,1′-binaphthyl with 14% ee. Miyano et al.[9] described an intramolecular Ullman reaction of the diester of optically pure 2,2′-dihydroxy-1,1′-binaphthyl and 1-bromo-2-naphthoic acid which, after reduction of the cyclic diester intermediate, gave 2,2′-bis(hydroxymethyl)-1,1′-binaphthyl in 100% ee. Meyers et al.[10] have reported that nucleophilic aromatic substitution of a methoxyl group ortho to a chiral oxazoline group substituted on a naphthalene ring gives 1,1′-binaphthyl derivatives in 70–90% ee optical yields.

We report here the syntheses of substituted binaphthyl compounds in high to medium optical yields through nucleophilic aromatic substitution reactions in which the leaving groups are asymmetric alkoxy moieties derived from naturally occurring alcohols. Asymmetric induction by chiral leaving groups in nucleophilic substitution reactions at elements other than carbon (e.g., at tin) have long been known.[11a] Duggan and Murphy[11b] observed 19–13% ee in electrophilic aromatic substitution reactions (cyclizations) with a chiral leaving group ((+)-camphor-10-sulfonate). Since the results of our work were communicated, McManus et al.[11c] reported small differences in solvolysis rates of diastereomeric 2-octyl and 1-cholesteryl camphor-10-sulfonates in which the leaving groups were chiral.

We selected as the activating substituent for the aromatic substitution reactions the 4,4-dimethyl-Δ^2-oxazoline group for a number of reasons. (1) This group has been

(1) We warmly thank the National Science Foundation for Grant NSF CHE 81-09532 for support of this research.

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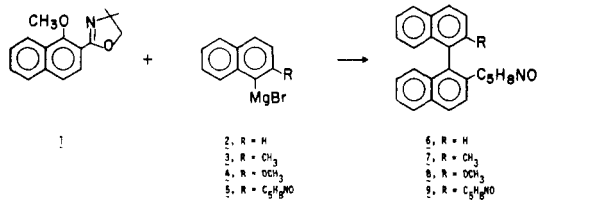
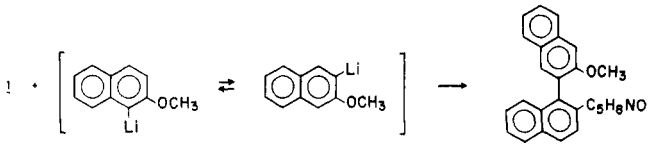
developed very successfully by Meyers[12] as a substituent which activates ortho fluorine or methoxyl groups toward aromatic substitution reactions with organometallic reagents as nucleophiles. (2) The oxazoline group is readily converted to a carboxyl group,[12] which in turn is the starting point for generating other functional groups. (3) We judged there was a good chance that the oxazoline group would activate conversions of ArBr or $ArOCH_3$ to ArOR*, compounds which were needed as starting materials in our study.[13]

Results

Feasibility. To establish feasibility for synthesizing binaphthyl compounds by nucleophilic aromatic substitutions, model reactions of 1 with several naphthyl organometallic reagents were studied. Compound 1 was

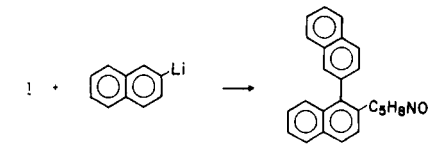


1 2, R = H; 3, R = CH_3; 4, R = OCH_3; 5, R = C_5H_8NO 6, R = H; 7, R = CH_3; 8, R = OCH_3; 9, R = C_5H_8NO



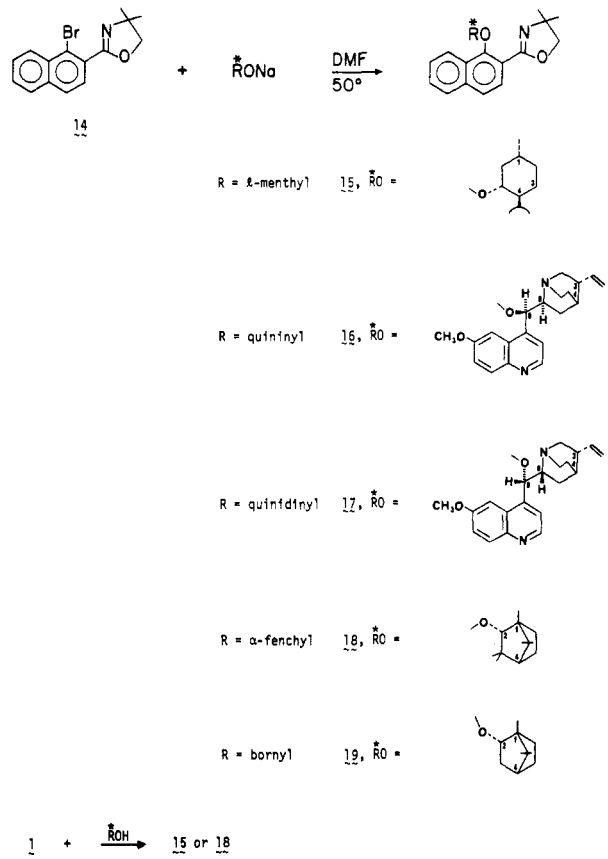
10a 10b 11

prepared by standard procedures[13b,14] from 1-methoxy-2-naphthoic acid.[15] When treated with **2** or **3** in benzene at 80 °C in the presence of $Ni(Ph_3P)_2Cl_2$ catalyst,[16] **6** (96%) and **7** (80%) were formed, respectively. Under the same conditions, 1 with **4** gave **8** (95%). In the absence of catalyst in benzene at 80 °C and in THF at 65 °C, **8** was also produced (54% and 65%, respectively). In the absence of catalyst in Et_2O at 36 °C, **5** reacted with **1** to give a trace of **9**, the main reaction being the demethylation of **1** to give the corresponding phenol. When **1** was treated with either **10a** or **10b** (prepared by reaction of *sec*-BuLi with the respective bromides at −78 °C) in THF at −30 to −42 °C, **11** was produced in 71% and 79% yields, respectively. This result indicates that **10a** and **10b** equilibrate under the conditions of their formation and that the less hindered **10b** reacts faster with **1** than does **10a**. In a control experiment, 1-bromo-2-methoxynaphthalene[17] was metalated at −30 °C in THF with *sec*-BuLi and carbonated. The product (78%) was a 1:6 mixture of 2-methoxy-1-naphthoic and 3-methoxy-2-naphthoic acids, respectively. Possibly **10a** and **10b** equilibrate through a chain reaction in which traces of 2-methoxynaphthalene are produced and metalated reversibly. Similar rearrangements have been observed previously.[18] Similarly in THF at −42 °C, **1** reacted with **12** to give **13** in 98% yield. These results demonstrated the viability of the kinds of reactions whose stereochemical course we wished to examine.



12 13

Preparation of Chiral Ethers. Treatment of 1-bromo-2-naphthoyl chloride[19] with 2-amino-2-methyl-1-propanol[12] gave oxazoline **14** (74%). The bromine of **14** was displaced in DMF at 50 °C by sodium *l*-menthoxide, quininoxide, quinidinoxide, *d*-α-fenchoxide, and *l*-bornoxide to produce chiral ethers **15** (87%), **16** (67%), **17** (45%), **18** (83%), and **19** (73%), respectively. These



14

1 + *ROH → 15 or 18

compounds were recrystallized to maximum rotations. The reactions were carried out under dry, oxygen-free conditions to minimize possible ketone and base-catalyzed epimerizations.[20] In the synthesis of **19**, the excess borneol isolated from the reaction mixture was shown to contain less than 1% isoborneol. Thus it appears unlikely that epimerizations occurred, and to the extent they did, the traces of diastereomers produced were removed by crystallization. Compounds **15** and **18** were also produced (70% and 88% yields, respectively) by trans etherification reactions in which **1** was heated with an *ROH–*RONa mixture. The properties of **15** and **18** made by the two

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Table I. Asymmetric Induction by Chiral Leaving Groups in Aromatic Nucleophilic Substitutions

run	reactant: compd	reactant: leaving group	nucleophile	reactn condns: solvent	reactn condns: temp, °C	reactn condns: time, h	product: struct	product: yield, %	product: opt yield,[a] %	product: confign	$\Delta\Delta G^{\ddagger}$,[b] kcal mol^{-1}	
1	15	*l*-menthoxy	2	THF	−42	1	6	80	67	*S*	0.7	
2	16	quininoxy	2	THF	−42	1	6		12	80 *S*		1.0
3	17	quinidinoxy	2	THF	−42	0.75	6	15	81	*R*	1.0	
4	18	α-fenchoxy	2	THF	−42	5	6	78	45	*S*	0.4	
5	19	bornoxy	2	THF	−42	1	6	83	10	*R*	0.09	
6	15	*l*-menthoxy	4	C_6H_6	80	2	8	53	82	*S*	1.6	
7	16	quininoxy	4	C_6H_6	80	0.8	8	7	94	*R*	2.4	
8	17	quinidinoxy	4	C_6H_6	80	0.8	8	27	84	*S*	1.7	
9	18	α-fenchoxy	4	C_6H_6	80	9	8	65	48	*S*	0.8	
10	15	*l*-menthoxy	9	THF	−20	9.5	11	68	>95	(+)	>1.8	
11	16	quininoxy	9	THF	−20	4	11	20	87	(+)	1.3	
12	17	quinidinoxy	9	THF	−20	1.25	11	22	84	(−)	1.2	
13	18	α-fenchoxy	9	THF	−20	9.5	11	88	77	(+)	1.0	
14	19	bornoxy	9	THF	−20	10	11	67	8	(+)	0.08	

[a] % ee. [b] Differences in the activation free energies.

methods were the same. Attempts to prepare **16** and **17** by the same kind of reaction failed.

Substitutions of Chiral Leaving Groups by Organometallics. Conditions for maximizing optical and chemical yields in the production of **6** from **15** were found with 1-naphthyllithium in THF (−42 °C and 1 h) and gave **6** in 80% yield and an optical yield of 67% ee. With α-naphthylmagnesium bromide at 65 °C, **6** was produced in 57% yield and gave an optical yield of 52% ee. Accordingly, **16–19** were submitted to substitution with 1-naphthyllithium under the above conditions to produce **6**, whose yield, optical purity, and absolute configuration were determined (see next section). Care was taken not to fractionate racemate and enantiomer during isolation. Table I records the results.

Reaction conditions for optimization of chemical and optical yields of binaphthyl compound **8** were carried out with the α-fenchyl ether **18** and 2-methoxy-1-naphthylmagnesium bromide. In THF, only traces of **8** were produced from −20 to 60 °C. In 1:1 ether/benzene from −20 °C to 36 °C (4.5 days), 48% of **8** was produced of 57% ee along with 20% of 2-(1-hydroxynaphthyl)-4,4-dimethyl-Δ^2-oxazoline, the phenol produced by ether cleavage of **18**. In benzene at 25 °C for 48 h, the chemical yield of **8** was <20%, but at 80 °C for 9 h, the chemical yield was 65% and the optical yield was 48%. These conditions were then applied to the reaction of **4** with **15–17**. Table I records the results.

The best reaction conditions for the study of asymmetric induction in the conversion **15–19** with **10a** ⇄ **10b** into **11** were found to involve THF at −20 °C, the reaction being too slow at −40 °C. The equilibrating mixture of **10a** and **10b** was formed by treating *sec*-BuLi with 1-bromo-2-methoxynaphthalene. The results are shown in Table I. When 3-bromo-2-methoxynaphthalene was metalated with *sec*-BuLi and the resulting organometallic was used as a nucleophile with menthyl system **15** as reactant, a higher chemical yield of **11** (92%) was obtained than when 1-bromo-2-methoxynaphthalene was employed, although the optical yields of **11** were both 92% ee from the different starting bromides. Apparently 2-methoxy-3-naphthyllithium reacts with **15–19** at a rate much greater than that with 2-methoxy-1-naphthyllithium, probably for steric reasons.

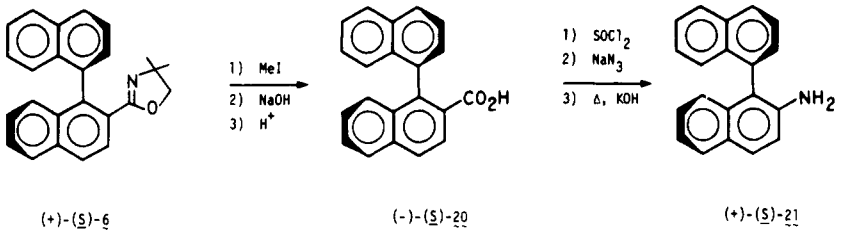
Treatment of quininoxy ether **16** with 2-naphthyllithium (**12**) gave binaphthyl compound **13**, which as expected, exhibited no optical activity. The barrier to rotation with respect to one another of the two naphthalenes is too low in this compound to provide enantiomers at working temperatures.

Determination of the Enantiomeric Purities and Maximum Rotations. The enantiomeric purities of the samples of **6**, **8**, and **11** produced in the nucleophilic aromatic substitution reactions were determined with tris-[3-[(trifluoromethyl)hydroxymethylene]-*d*-camphorato]-europium[21] ($Eu(tfc)_3$) as a chiral shift reagent with ^1H NMR spectral techniques (Bruker 200-MHz instrument). The samples were purified by chromatography, care being taken not to enantiomerically fractionate them. For runs 1–5 of Table I with **6** as product, $CDCl_3$ was used as solvent. The oxazoline methyl singlets originally at δ 1.009 and 1.039 were shifted downfield for (±)-**6**/$Eu(tfc)_3$ = 1.5 (mol/mol) and split into signals at δ 1.091, 1.125, and 1.171, of 2:1:1 relative intensity, respectively. The more intense signal at 1.091 ppm was the superposition of two signals, one for each diastereomer of **6**·$Eu(tfc)_3$. Depending on the leaving group used in the generation of **6**, different enantiomers were formed in excess. The establishment of the absolute configuration of (+)-(*S*)-**6** (see next section) allowed assignment of the peaks to the enantiomers producing them. The signals of the greatest and least chemical shift correspond to the diastereomeric methyls of (*S*)-**6**·$Eu(tfc)_3$, whereas the two upfield signals arise from the diastereomeric methyls of (*R*)-**6**·$Eu(tfc)_3$.

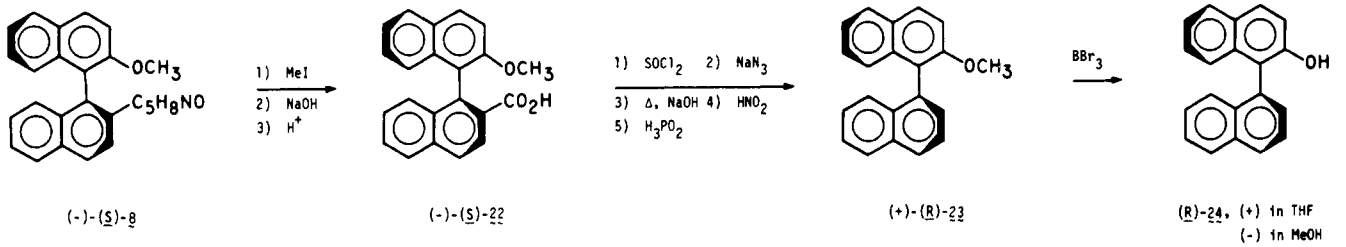
To determine the optical yields of binaphthyl compound **8** produced in runs 6–9 of Table I, $Eu(tfc)_3$ was added to solutions of **8** in C_6D_{12}. In **8** itself, the diastereotopic oxazoline methyl signals are at δ 0.695 and 0.867 and the $ArOCH_3$ signal is at δ 3.550. With **8**/$Eu(tfc)_3$ = 16 (mol/mol), the diastereomeric oxazoline methyls of (±)-**8**·$Eu(tfc)_3$ gave four signals of equal intensities at δ 0.801, 0.823, 1.041, and 1.055. The diastereomeric $ArOCH_3$ methyls gave two signals of equal intensities at δ 3.675 and 3.726. The more shifted signals associated with $(CH_3)_2C$ and CH_3OAr of **8** in the diastereomeric complexes are due to the (−)-(*S*)-**8** enantiomer (see next section for absolute configurational assignments).

The optical yields of binaphthyl product **11** of runs 10–14 of Table I were determined with $Eu(tfc)_3$ in $CDCl_3$. Compound **11** itself gave δ 1.134 and 1.159 for its $(CH_3)_2C$ signals, which in (±)-**11**·$Eu(tfc)_3$ (at **11**/$Eu(tfc)_3$ = 3 (mol/mol)) moved to δ 1.237, 1.252, and 1.325 of relative intensity of 1:2:1, respectively. The lower intensity signals correspond to the methyls of (−)-**11**·$Eu(tfc)_3$ and the higher intensity singlet to the methyls of (+)-**11**·$Eu(tfc)_3$. The methoxy signal of (±)-**11** was also shifted in (±)-**11**·$Eu(tfc)_3$, but overlapping methylene signals prohibited its use for

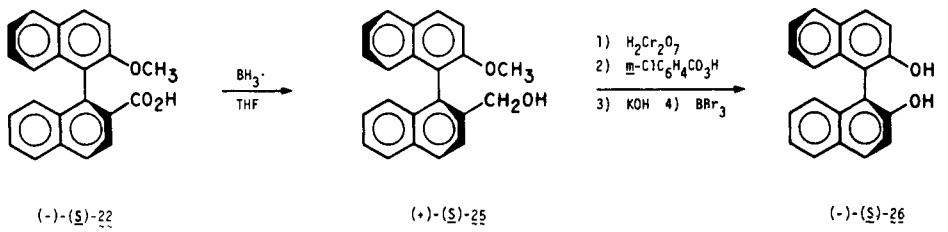
(21) Aldrich, used without purification.



(+)-(S)-6 (-)-(S)-20 (+)-(S)-21



(-)-(S)-8 (-)-(S)-22 (+)-(R)-23 (R)-24, (+) in THF (-) in MeOH



(-)-(S)-22 (+)-(S)-25 (-)-(S)-26

analytical purposes. The absolute configuration of **11** was not determined, although a hypothetical configuration is suggested.

The measurements of optical purity for **6**, **8**, and **11** using $Eu(tfc)_3$ were reproducible with ±1.5% ee, and the optical rotations were within ±1%. The maximum rotations of the enantiomers of **6**, **8**, and **11** were estimated from the optical rotations and enantiomeric purities of a variety of samples of each compound produced from **15**–**18** (rotations produced from **19** were too low to be included). The averaged value of $[\alpha]^{25}_{578}$ ±118.5 (±3.4°) (*c* 2.6, THF) was calculated for **6**, of $[\alpha]^{25}_{578}$ ±124 (±0.8°) (*c* 2.0, THF was calculated for **8**, and of $[\alpha]^{25}_{578}$ ±36.1 (±0.5°) (*c* 3.2, THF) was calculated for **11**.

Absolute Configurations of 6 and 8. The absolute configurations of binaphthyl compounds **6** and **8** were determined by conversions of enantiomerically enriched samples to compounds of established configurations. The procedures were developed with racemic material and then applied to enantiomerically enriched samples. Thus (+)-(*S*)-**6** was hydrolyzed to acid (-)-(*S*)-**20** which when submitted to a Curtius rearrangement gave (+)-(*S*)-**21** whose configuration has been determined.[22] Similarly (-)-(*S*)-**8** was hydrolyzed to (-)-(*S*)-**22** which was submitted to the Curtius rearrangement to give 2-amino-2′-methoxy-1,1′-binaphthyl. This material was diazotized and reduced to (+)-(*R*)-**23**. This compound was demethylated to give (*R*)-**24** whose rotation in THF is (+) and in CH_3OH is (-) at λ 589 nm. Since the absolute configurations of the enantiomers of **24** were a matter of controversy,[22,23] we reduced the acid–ether (-)-(*S*)-**22** to the alcohol–ether (+)-(*S*)-**25**, which was oxidized to the corresponding aldehyde–ether. This aldehyde when subjected to the Baeyer–Villiger rearrangement gave ester which was hydrolyzed and demethylated to produce (-)-(*S*)-**26** of established configuration.[24] The procedure used in the conversion **22** to **26** was kindly provided to us by Meyers and Lutomski in advance of publication.[10] These interconversions firmly establish the absolute configurations of (-)-(*S*)-**8**, (-)-(*S*)-**22**, (+)-(*R*)-**23**, (*R*)-**24**, and (+)-(*S*)-**25** confirm the configurational assigments of Meyers and Lutomski[10] for (-)-(*S*)-**22** and (+)-(*S*)-**25** and that of Meyers and Yamaguchi[22b] for (*R*)-**24**.

To check the estimate of the maximum rotation of the enantiomers of (±)-**8**, a sample of (-)-(*S*)-**8** of rotation $[\alpha]^{25}_{578}$ -100.7° (*c* 2.22, THF) was hydrolyzed to (-)-(*S*)-**22** of $[\alpha]^{25}_{578}$ -23.0° (*c* 1.20, THF), care being taken not to enantiomerically fractionate the sample. This material was brought to optical purity by repeated recrystallizations of its quinidine salt to give (-)-(*S*)-**22**, $[\alpha]^{25}_{578}$ -28.28° (*c* 1.22, THF). Calculation of the maximum rotation of the enantiomers of (±)-**8** based on these values gives $[\alpha]^{25}_{578}$ ±123.8°, which compares with the value of ±124 (±0.8°) based on chemical shift analysis and rotations of samples produced from **15**–**18** (see above).

Other Attempted Conversions. Attempts were made to synthesize from **15** enantiomerically enriched binaphthyl compounds convertible to 1,1′-binaphthyl-2,2′-dicarboxylic acid. Treatment of **15** with either 2-methyl-1-naphthyl-

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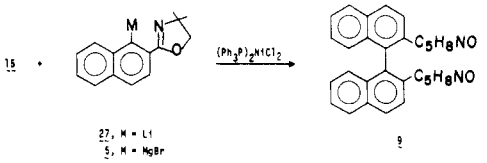
(23) Berson, J. A.; Greenbaum, M. A. *J. Am. Chem. Soc.* **1958**, *80*, 653–656.

(24) (a) Akimoto, H.; Iitaka, Y. *Acta Crystallogr., Sect. B* **1969**, *25*, 1491–1500. (b) Hanazaki, I.; Akimoto, H. *J. Am. Chem. Soc.* **1972**, *94*, 4102–4106.

lithium or 2-methyl-1-naphthylmagnesium bromide (3) gave chromatographically pure samples of 7, but their ^1H NMR spectra indicated them to contain extraneous signals. Possibly, all samples of 1-bromo-2-methylnaphthalene contained small amounts of isomeric impurities.[19a] In other experiments, attempts were made to convert 15 to 9 by treatment with either 27 or 5. With 27 as nucleophile,



27, M = Li
5, M = MgBr

only 15 was recovered, whereas 5 only cleaved 15 to its corresponding phenol. When the reaction of 15 with 5 was carried out in the presence of $[Ph_3P]_2NiCl_2$ catalyst in either benzene or Et_2O at 25 °C, 67% and 61% yields, respectively, of racemic 9 were obtained. This catalyzed reaction appears to go by a mechanism other than that observed for the conversions to binaphthyl products that occur in the absence of catalyst, possibly by a radical coupling reaction.

Discussion

The enantiomeric yields and differences in activation free energy for the transition states leading to the different enantiomers vary markedly as the leaving groups are changed. In runs 1–5 in THF with 1-naphthyllithium as nucleophile, the optical yields decreased with the following order of leaving group: quinidinoxy (81% ee) ~ quininoxy (80% ee) > *l*-menthoxy (67% ee) > α-fenchoxy (45% ee) > bornoxy (10% ee). The corresponding $\Delta(\Delta G^{\ddagger})$ values ranged from 1.0 to 0.09 kcal mol^{-1}. Nearly the same order was observed for runs 6–9 in benzene with 2-methoxy-1-naphthylmagnesium bromide as nucleophile: quininoxy (94% ee) > quinidinoxy (84% ee) > *l*-menthoxy (82% ee) > α-fenchoxy (48% ee). The $\Delta(\Delta G^{\ddagger})$ values for these runs ranged from 2.4 to 0.8 kcal mol^{-1}. A small variation in order is found for runs 10–14 in THF with 2-methoxy-3-naphthyllithium as nucleophile: *l*-menthoxy (≳95% ee) > quininoxy (87% ee) > quinidinoxy (84% ee) > α-fenchoxy (77% ee) > bornoxy (8% ee). The corresponding $\Delta(\Delta G^{\circ})$ values run from ≳1.8 to 0.08 kcal mol^{-1}. Thus quininoxy and quinidinoxy leaving groups generally provide the highest enantiomeric yields followed closely by that of the *l*-menthoxy group. The chemical yields with the quininoxy and quinidinoxy leaving groups with the three nucleophiles range only from 7% to 27%, whereas those for *l*-menthoxy are between 53% and 80%. Thus the *l*-menthoxy substituent provided the maximum *chiral transfer efficiency*, defined by eq 1. This leaving group provided values of 54%, 41%, and 65% in runs 1, 6, and 10, respectively.

$$\text{chiral transfer efficiency} = (\%\ \text{chemical yield} \times \%\ \text{ee})/100 \quad (1)$$

Others have observed in studies of asymmetric induction in other reactions that the menthyl is more effective than the bornyl group.[25] Quinine and quinidine have served as chiral basic catalysts[26] in a number of studies. As in our study, they provided opposite configurational biases in a given reaction. In run 2 quininoxy gave (*S*)-6, whereas in run 3 quinidinoxy gave (*R*)-6; in run 7, quininoxy gave (*R*)-8, whereas in run 8 quinidinoxy gave (*S*)-8; in run 11, quininoxy gave (+)-11, whereas in run 12, quinidinoxy gave (−)-11. Quinine and quinidine are diastereomers whose configurations at the 8- and 9-positions are opposite but at the 3-positions are the same. The vinyl group at the 3-position is nonbinding to Li^+ or Mg^{2+}, whereas both the oxygen at the 9-position and the nitrogen at the 1-position are excellent ligands. Furthermore, the 3-position is remote in molecular models from the seat of reaction and appears to play only a minor stereochemical role. Thus the quininoxy and quinidinoxy groups nearly behave as if they were enantiomerically related.

Interesting questions arise about whether the direction of the configurational bias is controlled solely by the configuration of the leaving group or whether the character of the nucleophile can play a determining role. Runs 1 and 6 in which *l*-menthoxy was a leaving group provided products whose dominant enantiomers belonged to dissimilar families of configurations. The fact that the dominant enantiomer produced has the same configurational symbol (L-6 and L-8) is an artifact of the notation.[27] The same conclusion applies to runs 4 and 9 with α-fenchoxy leaving groups. In these runs the direction of the configurational bias did depend on the nucleophile. However, a comparison of runs 2 and 7 with quininoxy and of runs 3 and 8 with quinidinoxy as leaving groups indicates that the direction of the configurational bias was independent of the nucleophile and was controlled solely by the configuration of the leaving group.

We assume that the general Meyers mechanism applies to these reactions.[10] This mechanism involves formation of an organometallic σ intermediate involving either a lithium or magnesium amide bond. Examinations of CPK molecular models of the possible σ intermediates provide rationalizations for the directions of the chiral bias for different combinations of the *l*-menthoxy, α-fenchoxy, quininoxy, and quinidinoxy leaving groups and the 1-naphthyllithium and 2-methoxy-1-naphthylmagnesium bromide (4) nucleophiles. From the conclusions emerges a pattern of correlations which provides a basis for provisionally assigning configurations to the enantiomers of 11. The very low asymmetric induction observed when the bornoxy leaving group was involved (runs 5 and 14) justifies it being disregarded in the discussion.

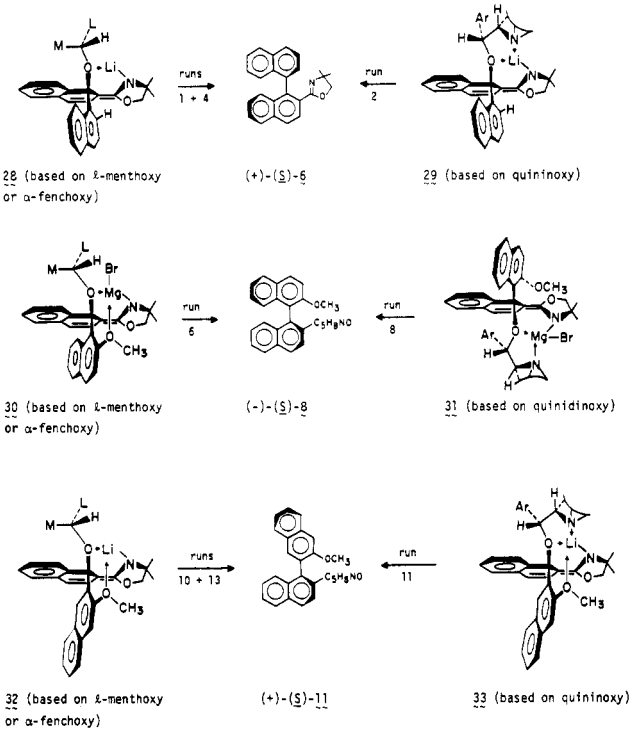
Four features appear to govern the structures of these σ intermediates and the configurations of the products. (1) The lithium or magnesium amides formed tend to maximize their coordination to structurally compatible heteroatoms in the σ intermediates. These heteroatoms are located in either the leaving group or the nucleophile, or both. (2) The face of the oxazoline–ether which is attacked controls the configuration of the new "σ" asymmetric center. (3) The orientation of the attacking nucleophile governs the configuration of the asymmetric element growing out of the two different conformations of the two aryl residues relative to one another in the σ intermediate. (4) Superimposed on these effects is the minimization of nonbonded repulsions.

In Scheme I are visualized the structures of minimal free energy derived from molecular model examination. In 28–33, the metal ions all have the oxazoline nitrogen and the leaving group oxygen as ligands. These are the only heteroatoms available for metal ion coordination in 28. In

(25) Morrison, J. D.; Mosher, H. S. "Asymmetric Organic Reactions"; Prentice Hall, Inc.: Englewood Cliffs, NJ, 1971.
(26) (a) Langstrom, B.; Bergson, G. *Acta Chem. Scand.* **1973**, *27*, 3118–3119. (b) Hermann, K.; Wynberg, H. *J. Org. Chem.* **1979**, *44*, 2238–2244. (c) Lyle, G. G.; Keefer, L. K. *Tetrahedron* **1967**, *23*, 3253–3263.

(27) The Cahn–Ingold–Prelog notation admirably denotes individual configurational names but fails to provide family names to different compounds of similar configurations.

Scheme I



29 the quinuclidine nitrogen is also available. In **30**, the methoxy oxygen of the nucleophile and bromide also coordinate with the magnesium ion. In **31**, the quinuclidine nitrogen and bromide additionally coordinate the magnesium ion. In **32**, methoxy oxygen is the sole additional ligand for the lithium ion. In **33**, the quinuclidine nitrogen and the methoxy oxygen serve as additional ligands for the lithium. Thus in all σ complexes except **28** at least three internal heteroatoms ligate the metal ions.

The configurations of the σ carbons are similar in **28**, **29**, **30**, **32**, and **33** and are controlled by steric effects growing out of the configurations and ligating properties of the leaving groups. The diastereoisomers formulated are the least compressed of the two alternatives. Since the quinidinoxy group is pseudoenantiomeric to the quininoxy group, the configurations at the σ carbons of their complexes should be pseudoenantiomeric as well (compare **29** with **31**). In **28**, **30**, and **32**, L stands for the large and M for the medium sized moieties in the *l*-menthoxy or α-fenchoxy groups, in the same sense these symbols were used in formulating Cram's rule.[28]

The conformations of the nucleophiles in σ complexes **28**, **29**, and **31** are those which avoid compression between the peri hydrogen of the nucleophile and the face of the naphthalene ring undergoing substitution. They account for the configurational biases observed in runs 1, 2, 4, 6, and 8. A similar conformation is found in the pseudoenantiomer of **29** based on the quinidinoxy leaving group whose structure accounts for the configurational bias of run 3 leading to (−)-(*R*)-**6** (not formulated). A similar conformation is found in the pseudoenantiomer of **31** (based on the quininoxy leaving group) whose structure explains the configurational bias of run 7 leading to (+)-(*R*)-**8** (not formulated). The strong tendency of the divalent magnesium ion to ligate the methoxy oxygen overrides this peri-hydrogen-to-aryl compression in run 6 to provide **30** which leads to (−)-(*S*)-**8**. The presence of the quinuclidine nitrogen ligand in run 8 reduces the driving force of the methoxy oxygen to coordinate magnesium, leaving the less hindered **31** to dominate the reaction coordinate. In runs 10–14 involving 3-methoxy-2-naphthyllithium as nucleophile, the peri-hydrogen compression is absent from the σ complexes. Therefore, the methoxy oxygen ligates the lithium and controls the conformation, as is shown in **32** and **33**. A similar conformation is found in the pseudoenantiomer of **33** (based on the quinidinoxy leaving group) which rationalizes the configurational bias of run 12 leading to (−)-(*R*)-**11** (not formulated).

In this interpretation, the configuration of (+)-**11** has been presumed to be *S*, as is drawn in Scheme I. This assignment extrapolates to the results of runs 10–14 the patterns of facts and mechanistic arguments that rationalize runs 1–8. An independent determination of the configuration of (+)- or (−)-**11** is highly desirable but is beyond the scope of the present investigation.

Models of σ complexes **28**–**31** are particularly crowded and difficult to assemble compared to **32** and **33**. These observations correlate with the fact that of the equilibrating mixture of 1-methoxy-2-naphthyllithium (**10a**) and 3-methoxy-2-naphthyllithium (**10b**), only the latter leads to detectable product **11**. Molecular model examination also indicates why no reaction occurs when **15** is treated with **5** or **27** in the absence of catalyst. The simultaneous accumulation of a menthoxy and two oxazoline groups around the σ carbon of a σ intermediate is sterically impossible. The fact that this reaction is catalyzed by $[Ph_3P]_2NiCl_2$ to give racemic product **29** suggests the mechanism involves a radical coupling stage.

Experimental Section

General Methods. Reactions involving alkoxides, organometallic reagents, and Lewis acids were conducted under dry nitrogen. Diethyl ether and benzene were freshly distilled from $LiAlH_4$, tetrahydrofuran (THF) was distilled from benzophenone ketyl, and dimethylformamide (DMF) was distilled from CaH_2. Benzene and DMF were stored over 4-Å molecular sieves in a nitrogen atmosphere. Medium pressure chromatography (120 psi at ca. 10 mL/min) was conducted on either a 250 mm × 25 mm (column A) or, where not otherwise designated, a 1000 mm × 50 mm Altex column. When solvent gradients were used, they are indicated as starting and ending solvent composition, with an arrow (→) indicating the direction of the gradient. Medium pressure columns were packed with silica gel 60 (E. Merck, particle size 40–63 μm) or alumina (Woelm Pharma, particle size 32–63 μm). Gravity and filtration columns were packed with silica gel 60 (E. Merck, particle size 63–200 μm). Melting points below 200 °C were measured on a Thomas-Hoover melting point apparatus and those above 200 °C were measured on a Mel-Temp apparatus. Melting points and boiling points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 297 grating infrared spectrophotometer. Optical rotations were recorded on a Perkin-Elmer 241 MC polarimeter in 1-mL cells with a light path of 1 dm. Proton NMR spectra were recorded on either a Varian T-60 (60 MHz) or, where not otherwise indicated, on a Bruker WP-200 (200 MHz) instrument. Carbon-13 NMR spectra were recorded on a JOEL FX-90 (90 MHz) instrument. Spectral assignments are based on analogy to previously characterized systems. The chemical shifts are expressed in parts per million downfield from internal tetramethylsilane (Me_4Si). Coupling constants (J) are given in hertz, with splitting patterns designated as s (singlet), d (doublet), t (triplet), m (multiplet), and br (broad). Mass spectra were obtained on an AEI model MS-9 double-focusing spectrometer.

2-[2-(1-Methoxynaphthyl)]-4,4-dimethyl-Δ²-oxazoline (1). Procedure 1. To a stirred mixture of 37.4 mL (0.52 mol) of $SOCl_2$ and 0.5 mL of DMF was added slowly 33.0 g (0.16 mol) of 1-methoxy-2-naphthoic acid.[15] The mixture was refluxed for 4 h and concentrated under reduced pressure, and the residual oil

(28) (a) Cram, D. J.; Elhafez, F. A. A. *J. Am. Chem. Soc.* **1952**, *74*, 5828–5835. (b) Cram, D. J.; Kopecky, K. R. *J. Am. Chem. Soc.* **1959**, *81*, 2748–2755.

was distilled at 70 °C (0.065 mm) to give 29.2 g (0.14 mol, 87%) of 1-methoxy-2-naphthoyl chloride, mp 69–73 °C. A solution of this material in 40 mL of CH_2Cl_2 (reagent grade) was added with stirring at 0 °C to a solution of 29.2 g (0.348 mol) of 2-amino-2-methyl-1-propanol in 40 mL of CH_2Cl_2 under dry conditions. The mixture was stirred at 25 °C for 24 h and concentrated, and the residue was partitioned between water and CH_2Cl_2. The organic layer was washed with 10% HCl in water and then with water, dried ($MgSO_4$), and concentrated to give the hydroxy amide. To a stirred solution of this material in 80 mL of benzene held at 0 °C was added 40 mL (0.56 mol) of $SOCl_2$ over a period of 25 min. The mixture was stirred for 2 h at 25 °C and poured into 300 mL of Et_2O. the precipitate that separated was collected and washed with Et_2O. the solid was dissolved in water, the aqueous solution was made basic with NaOH to pH 13, and the solution was washed with two 200-mL portions of Et_2O. The combined ether fractions were washed with brine and dried and evaporated to give **1** (32.5 g, 81%) suitable for use in the next steps. Crystallization of a sample from cyclohexane gave pure **1**: mp 75–78 °C; MS, *m/e* 255 (M^+); IR (KBr) 1640 cm^{-1} (C=N); ^1H NMR ($CDCl_3$) δ 1.436 (s, 6 H, CH_3), 4.001 (s, 3 H, OCH_3), 4.170 (s, 2 H, CH_2), 7.486–8.277 (m, 6 H, Ar H). Anal. Calcd for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71; N, 5.49. Found: C, 75.30; H, 6.70; N, 5.40.

2-[2-(1-Bromonaphthyl)]-4,4-dimethyl-Δ²-oxazoline (14). Application of procedure 1 to 11.5 g (0.046 mol) of 1-bromo-2-naphthoic acid[19] gave 1-bromo-2-naphthoyl chloride which was sublimed at 95 °C (0.2 mm) to give product of mp 82–84 °C; IR (KBr) 1780 cm^{-1} (C=O). From this was obtained 13.2 g (0.041 mol) of the corresponding benzamide which, as a solution in 150 mL of 2:1 (v/v) benzene/CH_2Cl_2, was cyclized at 0 °C with $SOCl_2$ to give a yellow solid. Sublimation (80 °C (0.08 mm)) of the product gave **14** (10.4 g, 74%). Crystallization of the product from hexane gave an analytically pure sample of **14**: mp 102–106 °C; MS, *m/e* 303 (M^+); IR (KBr) 1667 cm^{-1} (C=N); ^1H NMR ($CDCl_3$) δ 1.464 (s, 6 H, CH_3), 4.201 (s, 2 H, CH_2), 7.556–8.429 (m, 6 H, Ar H). Anal. Calcd for $C_{15}H_{14}BrNO$: C, 59.23; H, 4.63; N, 4.60; Br, 26.27. Found: C, 59.22; H, 4.60; N, 4.52; Br, 26.24.

Racemic 2-[2-(2′-Methoxy-1,1′-binaphthylyl)]-4,4-dimethyl-Δ²-oxazoline (8) by Procedure 2 (Involving Catalyst). A solution of 3.5 g (0.015 mol) of 1-bromo-2-methoxynaphthalene[17] (mp 83–84 °C) in 10 mL of dry THF was added with stirring over 30 min to 0.38 g (16 mmol) of Mg ribbon under 25 mL of dry THF. The mixture was refluxed for 2.5 h, and the solvent was removed under a stream of dry nitrogen. To the resulting solid was added 20 mL of dry benzene, 1.0 g (3.9 mmol) of **1**, and 0.25 g (0.39 mol) of dichlorobis(triphenylphosphine) nickel.[29] [**NOTE**: Either the catalyst should be added to the solution containing Grignard reagent and reactant at ambient temperature or lower and in small portions or the catalyst should be added to the Grignard reagent before addition of the substrate in order to avoid a very vigorous reaction.] The dark mixture was refluxed for 30 min, cooled to 25 °C, and poured into a saturated aqueous solution of NH_4Cl. The resulting mixture was washed with Et_2O. The ethereal extract was washed (saturated aqueous NH_4Cl, water, and brine), dried ($MgSO_4$), and concentrated. Chromatography (100 g of SiO_2, toluene → 1:1 toluene/acetonitrile) of the residue gave **6** (1.40 g, 95%) as a light yellow oil. Crystallization of this oil from Et_2O gave light yellow needles of analytically pure **8**: mp 153–155 °C, molecular distillation 175 °C (0.2 mm); MS, *m/e* 381 (M^+); IR (KBr) 1620 cm^{-1} (C=N), 1260 cm^{-1} ($COCH_3$); ^1H NMR ($CDCl_3$) δ 0.883 (s, 3 H, CCH_3), 1.022 (s, 3 H, CCH_3), 3.225 (1 H, A of AB, *J* = 8.0 Hz, CH_2), 3.521 (1 H, B of AB, *J* = 8.0 Hz, CH_2), 3.755 (s, 3 H, OCH_3), 7.240–7.968 (m, 12 H, Ar H); ^1H NMR (C_6D_{12}) δ 0.695 (s, 3 H, CCH_3), 0.867 (s, 3 H, CCH_3), 3.278 (1 H, A of AB, *J* = 7.6 Hz, CH_2), 3.410 (1 H, B of AB, *J* = 7.6 Hz, CH_2), 3.550 (s, 3 H, OCH_3), 6.986–8.011 (m, 12 H, Ar H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 27.899 (CH_3), 56.720 (OCH_3), 66.986 ($C(CH_3)_2$), 79.176 (CH_2), 113.658–154.722 (Ar), 163.688 (OC=N). Anal. Calcd for $C_{26}H_{23}NO_2$: C, 81.87; H, 6.07; N, 3.67. Found: C, 81.93; H, 6.31; N, 3.74.

Racemic 2-[2-(2′-Methoxy-1,1′-binaphthylyl)]-4,4-dimethyl-Δ²-oxazoline (8) by Procedure 3 (No Catalyst, Benzene as Solvent). To 4.23 g (0.17 mol) of magnesium just covered by dry Et_2O was added over 30 min a solution of 39.0 g (0.18 mol) of 1-bromo-2-methoxynaphthalene as a solution in 100 mL of 1:1 ether/benzene. After being refluxed overnight, the mixture was gently heated under a stream of N_2 to remove the Et_2O, leaving approximately 40 mL of solution in benzene. To this hot solution was added 15.0 g (59 mmol) of **1**, and the mixture was refluxed for 30 min. The resulting solution, cooled to 25 °C, was poured into 100 mL of a saturated aqueous solution of NH_4Cl, and the mixture was extracted with three portions of Et_2O. The combined organic fractions were washed (water, brine), dried ($MgSO_4$), and concentrated. Chromotography of the residual oil (150 g of SiO_2, hexane → CH_2Cl_2) gave impure **6** as a dark oil which did not crystallize. Filtration chromatography of the oil (10 g of alumina, CH_2Cl_2) gave a light yellow oil which upon crystallization from Et_2O gave **8** (12.2 g, 54%): mp 152–155 °C; ^1H NMR and TLC behavior identical with **8** produced by procedure 2.

2-[2-(2′-Methoxy-1,1′-binaphthylyl)]-4,4-dimethyl-Δ²-oxazoline (8). Procedure 4 (No Catalyst, THF as Solvent). The Grignard reagent was prepared from 0.52 g (21 mmol) of Mg ribbon, 6.0 g (27 mmol) of 1-bromo-2-methoxynaphthalene, and 25 mL of dry THF after 45 min of reflux. To the resulting warm solution was added 2.0 g (7.8 mmol) of **1**, and the solution was refluxed for 3.5 h. The mixture was cooled to ambient temperature overnight, and to it was added 20 mL of a saturated aqueous solution of NH_4Cl and 20 mL of Et_2O. The organic layer was separated, washed (water, brine), dried ($MgSO_4$), and concentrated to give a yellow oil. Chromatography (150 g of silica gel, hexane → CH_2Cl_2) of this oil gave **8** (1.93 g, 65%) which exhibited the same ^1H NMR and TLC behavior as the sample of **8** prepared by procedure 2.

Racemic 2-[2-(1,1′-Binaphthylyl)]-4,4-dimethyl-Δ²-oxazoline (6). Procedure 2 was applied to 0.38 g (26 mmol) of Mg, 2.8 mL (20 mmol) of 1-bromonaphthalene, 1.50 g (10 mmol) of **1**, and 0.25 g (0.76 mmol) of dichlorobis(triphenylphosphine)nickel, except that the Grignard reagent was generated in dry Et_2O instead of THF. As described previously, the ether was replaced by benzene. The catalyst and oxazoline substrate were added and the mixture was refluxed for 5 min. The cooled mixture was poured into a saturated aqueous NH_4Cl solution. Crude product was isolated by extraction as a yellow oil. Chromatography (100 g of silica gel, CH_2Cl_2 → Et_2O) of this material gave **6** (1.75 g, 75%), pure by analytical thin layer chromatography and ^1H NMR. Molecular distillation of the product (250–280 °C (0.2 mm)) gave an analytically pure sample of **6** as a light yellow glass: MS, *m/e* 351 (M^+); IR (KBr) 1621 cm^{-1} (C=N); ^1H NMR ($CDCl_3$) δ 1.009 (s, 3 H, CCH_3), 1.049 (s, 3 H, CCH_3), 3.359 (1 H, A of AB, *J* = 8.5 Hz, CH_2), 3.469 (1 H, B of AB, *J* = 8.5 Hz, CH_2), 7.258–7.987 (m, 13 H, Ar H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 27.764 (CH_3), 67.040 ($C(CH_3)_2$), 79.067 (CH_2) 124.953–138.280 (Ar), 163.471 (OC=N). Anal. Calcd for $C_{25}H_{21}NO$: C, 85.44; H, 6.02; N, 3.99. Found: C, 85.30; H, 5.90; N, 3.83.

Racemic 2-[2-(3′-Methoxy-1,2′-binaphthylyl)]-4,4-dimethyl-Δ²-oxazoline (11) from 1-Bromo-2-methoxynaphthalene. Procedure 5. A solution of 9.20 g (39 mmol) of 1-bromo-2-methoxynaphthalene in 37 mL of dry THF was cooled to −78 °C. As the mixture reached this temperature the bromide precipitated. To this heterogeneous mixture was added, over 10 min, 30 mL (39 mmol) of a 1.31 M solution of *sec*-BuLi in cyclohexane, and the mixture was stirred for 45 min. The mixture was warmed to −42 °C over a 10-min period, and to this solution was added a solution of 2.0 g (8.0 mmol) of **1** in 10 mL of dry THF. The amber solution was stirred at −42 ± 2 °C for 5.25 h; then to it was added 50 mL of a saturated aqueous solution of NH_4Cl. The mixture was warmed to ambient temperature. The aqueous portion was neutralized with 10% HCl and washed with Et_2O. The organic fractions were combined, washed (water, brine), dried ($MgSO_4$), and concentrated to give an oil. Chromatography (100 g of silica gel, CH_2Cl_2 → Et_2O) of this material gave an oil which when crystallized from Et_2O gave **11** (2.06 g, 71%, mp 146–153 °C). Recrystallization of this material from cyclohexane gave a sample of analytically pure **11**: mp 154–157 °C; MS, *m/e* 350 (M^+ − 31); IR (KBr) 1650 cm^{-1} (C=N), 1250 ($COCH_3$); ^1H NMR ($CDCl_3$) δ 1.134 (s, 3 H, CCH_3), 1.159 (s, 3 H, CCH_3), 3.465 (1 H, A of AB, *J* = 8.0 Hz, CH_2), 3.697 (1 H, B of AB, *J* = 8.0 Hz, CH_2), 3.789 (s, 3 H, OCH_3), 7.249–7.910 (m, 12 H, Ar H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 28.116 (CH_3), 55.555 (OCH_3), 67.257 ($C(CH_3)_2$),

(29) Cotton, F. A.; Faut, O. D.; Goodgame, D. M. L. *J. Am. Chem. Soc.* **1961**, *83*, 344–351.

79.338 (CH_2), 105.017–156.699 (Ar), 163.877 (OC=N). Anal. Calcd for $C_{26}H_{23}NO_2$: C, 81.86; H, 6.08; N, 3.67. Found: C, 82.00; H, 6.10; N, 3.51.

Racemic 3′-Methoxy-1,1′-binaphthyl-2-carboxylic Acid. Hydrolysis[12a] of racemic 11 gave the title compound (93%) as crystals, mp 168–170 °C. Recrystallization of this material from benzene gave white needles: mp 171–173 °C; IR (KBr) 1683 cm^{-1} (C=O); MS, *m/e* 328 (M^+); ^1H NMR ($CDCl_3$) δ 3.712 (s, 3 H, OCH_3), 7.085–8.201 (m, 12 H, Ar H). Anal. Calcd for $C_{22}H_{16}O_3$: C, 80.48; H, 4.91. Found: C, 80.42; H, 5.17.

Racemic 2-[2-(3′-Methoxy-1,2′-binaphthylyl)]-4,4-dimethyl-Δ²-oxazoline (11) from 2-Bromo-3-methoxynaphthalene. The 2-bromo-3-methoxynaphthalene used was prepared by the literature method:[30a] mp 69–71 °C;[30b] ^1H NMR ($CDCl_3$) δ 4.001 (s, 3 H, OCH_3), 7.155 (s, 1 H, Ar H), 7.351–7.499 (m, 2 H, Ar H), 7.671–7.742 (2 H, d of d, *J* = 7.1 and *J* = 7.1, Ar H), 8.059 (s, 1 H, Ar H). A solution of 6.30 g (26.6 mmol) of this compound in 27 mL of THF was cooled to −78 °C over a 20-min period. To the resulting heterogeneous mixture was added 14.0 mL (20 mmol) of a 1.39 M solution of *sec*-BuLi in cyclohexane, and the mixture was stirred for 1 h. The reaction temperature was raised to −30 °C, and 1.0 g (3.9 mmol) of 1 was added. The solution was stirred at −30 °C for 1 h, after which time 20 mL of an aqueous saturated NH_4Cl solution was added. The mixture was washed with Et_2O. The organic layers were combined, washed (water, brine), dried (Na_2SO_4), and concentrated. Flash chromatography (100 g of alumina, hexane → ether) of the residual oil gave 11 (1.20 g, 79%, mp 143–145 °C) as light yellow crystals. Recrystallization of this material from cyclohexane gave an analytically pure sample of 11: mmp with authentic material, 154–156 °C; ^1H NMR ($CDCl_3$) δ 1.135 (s, 3 H, CH_3), 1.160 (s, 3 H, CH_3), 3.581 (center of AB, 2 H, CH_2), 3.789 (s, 3 H, OCH_3), 7.249–7.910 (m, 12 H, Ar H); analytical thin layer chromatographic behavior of this sample was identical with that of authentic material.

2-[2-(1,2′-Binaphthylyl)]-4,4-dimethyl-Δ²-oxazoline (13). To a solution of 4.0 g (15 mol) of 2-bromonaphthalene in 35 mL of THF at −78 °C was added 11.0 mL (15 mmol) of a 1.49 M solution of *sec*-BuLi in cyclohexane, and the resulting heterogeneous mixture was stirred at −78 °C for 45 min. The mixture was warmed over a 10-min period to −42 °C when 0.90 g (3.50 mmol) of 1 was added in one portion. The light yellow solution was stirred at −42 ± 2 °C for 1 h. To this was added 20 mL of a saturated aqueous solution of NH_4Cl, and the mixture was warmed to 25 °C. The aqueous fraction was removed, neutralized with 10% aqueous HCl, and washed with Et_2O. The combined organic fractions were washed (water, brine), dried ($MgSO_4$), and concentrated. Steam distillation of the residual oil removed naphthalene. The residue from the distillation was recovered by extraction with Et_2O, followed by drying ($MgSO_4$), and concentration to give 13, 1.20 g, 98%, as a light yellow oil, pure by ^1H NMR and analytical thin layer chromatography. An analytically pure sample of 13 was prepared by thick layer chromatography (silica gel, CH_2Cl_2): MS, *m/e* 351 (M^+); IR (KBr) 1650 (C=N); ^1H NMR ($CDCl_3$) δ 1.130 (s, 3 H, CH_3), 1.143 (s, 3 H, CH_3), 3.533 (1 H, A of AB, *J* = 7.9 Hz, CH_2), 3.655 (1 H, B of AB, *J* = 7.9 Hz, CH_2), 7.246–7.938 (m, 13 H, Ar H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 28.062 (CH_3), 67.447 ($C(CH_3)_2$), 79.392 (CH_2), 126.009–140.013 (Ar), 163.850 (OC=N). Anal. Calcd for $C_{25}H_{21}NO$: C, 85.44; H, 6.02; N, 3.99. Found: C, 85.19; H, 6.12; N, 3.71.

As further structure proof, a sample of 13 was hydrolyzed[12a] to give 1,2′-binaphthyl-2-carboxylic acid (89%) as a white powder. Crystallization of the product from glacial acetic acid gave the following: mp 202–204 °C (lit.[31] 204–205 °C); ^1H NMR ($CDCl_3$) δ 7.324–8.035 (m, Ar H); IR (KBr) 1680 cm^{-1} (C=O). The ^1H NMR and IR spectra of this acid were similar but not identical with that of 1,1′-binaphthyl-2-carboxylic acid (see below).

Racemic 2-[2-(2′-Methyl-1,1′-binaphthylyl)]-4,4-dimethyl-Δ²-oxazoline (7). The Grignard reagent of 1-bromo-2-methylnaphthalene[19a] was prepared by the usual method from 1.20 mL (7.70 mmol) of bromide, 0.18 g (7.80 mmol) of Mg, and 4 mL of Et_2O. A heavy precipitate formed due to the insolubility of this Grignard reagent in Et_2O. When the mixture was diluted with 2 mL of 1:1 Et_2O/THF, the precipitate dissolved. The mixture was refluxed until Mg metal was no longer visible. The solvent was removed under an N_2 stream and was replaced by 8 mL of dry benzene. To the resulting refluxing solution was added 0.13 g (0.2 mmol) of dichlorobis(triphenylphosphine)nickel and 0.50 g (2.0 mmol) of 1, and the mixture was stirred for 3 h. The mixture was cooled and poured into water. The product was extracted as usual to give an oil. Column chromatography (100 g of silica gel, toluene → 1:1 $CH_3CN/C_6H_5CH_3$) of this material gave 7 as a yellow oil. Crystallization of the oil from hexane gave analytically pure 7 (0.57 g, 80%): mp 166–168 °C; MS *m/e* 365 (M^+); IR (KBr) 1635 cm^{-1} (C=N); ^1H NMR ($CDCl_3$) δ 0.898 (s, 3 H, CCH_3), 1.028 (s, 3 H, CCH_3); 2.075 (s, 3 H, Ar CH_3) 3.295 (1 H, A of AB, *J* = 7.9 Hz, CH_2), 3.439 (1 H, B of AB, *J* = 7.9 Hz, CH_2), 7.045–7.959 (m, 12 H, Ar H). Anal. Calcd for $C_{26}H_{23}NO$: C, 85.45; H, 6.34; N, 3.83. Found: C, 85.66; H, 6.26; N, 3.81.

Hydrolysis of 7 under basic conditions[12a] gave 2′-methyl-1,1′-binaphthyl-2-carboxylic acid (89%), which was recrystallized: mp 182–184 °C; MS, *m/e* 312 (M^+); ^1H NMR ($CDCl_3$) δ 2.011 (s, 3 H, Ar CH_3), 6.906–8.179 (m, 12 H, Ar H); IR (KBr) 1680 cm^{-1} (C=O); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 122.732–140.907 (Ar), 171.110 (CO_2H); exact mass 312.1146 (calcd for $C_{22}H_{16}O_2$, 312.1150).

Lithiation and Carbonation of 1-Bromo-2-methoxynaphthalene. To 1.0 g (4.2 mmol) of 1-bromo-2-methoxynaphthalene was added 4 mL of dry THF, and the solution was cooled to −78 °C. To the heterogeneous mixture was added 3.0 mL (3.9 mmol) of a 1.31 M *sec*-BuLi solution in cyclohexane, and the heterogeneous mixture was stirred for 1.25 h. The reaction temperature was raised to −30 °C and the solution was stirred for 2 h. Dry CO_2 was bubbled through the solution for ca. 5 min and the heterogeneous mixture was warmed to 25 °C. The mixture was partitioned between 20 mL of Et_2O and 20 mL of water. The ethereal fraction was washed (water, brine), dried ($MgSO_4$), and concentrated to give an oily solid which was dissolved in $CHCl_3$. This solution was washed with three portions of concentrated aqueous NH_4OH. The combined basic solutions were washed twice with $CHCl_3$ and then acidified by addition of concentrated aqueous HCl. The cloudy mixture was cooled and washed with three portions of Et_2O. The ethereal extracts were washed (water, brine), dried ($MgSO_4$), and concentrated to give a white solid (0.66 g) whose ^1H NMR (60 MHz) spectrum showed the presence of two methoxy signals in a ratio of 6:1. The major fraction corresponded to 2-methoxy-3-naphthoic acid, as determined by signal enhancement upon addition of authentic material. The minor fraction corresponded to 2-methoxy-1-naphthoic acid, as determined by the same criterion.

Authentic 2-methoxy-3-naphthoic acid was prepared by lithiation of 1.0 g (6.3 mmol) of 2-methoxynaphthalene as described by others,[30] followed by treatment with CO_2. Extractive treatment gave 0.64 g of acid product, showing a single methoxy signal in the product ^1H NMR (60 MHz) spectrum. Crystallization of the product from benzene gave 3-methoxy-2-naphthoic acid, mp 130–132 °C (lit.[32] mp 133–136 °C).

Preparation of 2-methoxy-1-naphthoic acid was accomplished as follows. A mixture of 0.10 g (4.2 mmol) of magnesium ribbon, 1.0 g (4.2 mmol) of 1-bromo-2-methoxynaphthalene, 2 drops of dibromomethane, and 5 mL of dry Et_2O was refluxed for 1 h. To the heterogeneous mixture was added 6 mL of dry benzene to dissolve the Grignard reagent, and the mixture was refluxed for 1 h. The Et_2O was removed by gently heating the mixture under a stream of nitrogen, and the amber solution was refluxed for 2 h. To this was added dry CO_2 (bubbled through for 10 min), and the mixture was cooled to 25 °C and diluted with 20 mL of Et_2O. Extractive treatment as described previously gave 2-methoxy-1-naphthoic acid (82%, mp 152–155 °C) as the only acid product seen in the ^1H NMR (60 MHz) spectrum. Two recrystallizations of the product from benzene gave white needles, mp 175–176.5 °C (lit.[32] mp 176 °C).

(−)-2-[2-(1-(1*R*,3*R*,4*S*)-Menthoxynaphthyl)]-4,4-dimethyl-Δ²-oxazoline (15). Procedure 6. A mixture of 1.79 g (37 mmol) of NaH washed free of oil with pentane, 16 mL of DMF,

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(31) Swain, G.; Todd, A. R. *J. Chem. Soc.* **1941**, 674–679.
(32) Sunthankar, S. V.; Bilman, H. *J. Org. Chem.* **1951**, *16*, 8–16.

and 6 g (0.038 mol) of *l*-menthol was stirred until no more H_2 was evolved (25 min). The mixture was warmed to 50 °C over 1 h and was then stirred for 2 h at 50 °C. To the light yellow solution at 50 °C was added to solution of 3.05 g (10 mmol) of **14** in 10 mL of dry DMF. The mixture was stirred for 5 h and poured into 50 mL of water. The aqueous suspension was neutralized with 10% HCl and washed with three portions of Et_2O. The combined ether fractions were washed (water, brine), dried ($MgSO_4$), and concentrated to give a light yellow oil. Medium pressure chromatography (alumina, 80% cyclohexane/toluene → toluene) of the material gave **16** (3.30 g, 87%) as a clear oil which crystallized upon standing. Crystallization of the material from cyclohexane gave an analytically pure sample of **16**: mp 71–73 °C; IR (KBr) 1625 cm^{-1} (C=N); MS, *m/e* 379 (M^+); ^1H NMR ($CDCl_3$) δ 0.715–1.783 (m, 13 H), 2.615–2.626 (1 H, m), 4.130 (1 H, A of AB, J = 7.9 Hz); 4.158 (1 H, B of AB, J = 7.8 Hz), 4.257–4.363 (1 H, m), 7.258–8.312 (6 H, m);$[\alpha]^{25}_{589}$ −63.89°, $[\alpha]^{25}_{578}$ −66.77°, $[\alpha]^{25}_{546}$ −76.51°, $[\alpha]^{25}_{435}$ −141.26°, (*c* 5.01, $CHCl_3$). Anal. Calcd for $C_{25}H_{33}NO_2$: C, 79.12; H, 8.76; N, 3.69. Found: C, 79.11; H, 8.71; N, 3.60.

This menthyl ether (**15**) was also prepared by procedure 7 (see below) from 115 g (0.74 mol) of *l*-menthol, 14.0 g (0.29 mol) of oil-free NaH, and 15.25 g (60 mmol) of **1**. After 3 h of reaction at 90 ± 5 °C, extraction, and steam distillation, a yellow solid was produced. This material was triturated with cold hexane to give a white solid which was recrystallized from cyclohexane to give 16 g (70%) of **15**: mp 71–72.5 °C; $[\alpha]^{25}_{578}$ −66.65° (*c* 4.98, $CHCl_3$).

(+)-2-[2-(1-(1*R*,2*S*,4*S*)-α-Fenchoxynaphthyl)]-4,4-dimethyl-Δ²-oxazoline (18) by Procedure 6. Reduction of (−)-fenchone (Aldrich), $[\alpha]^{25}_D$ −50.6° (neat), was accomplished by either Li/NH_3 or $LiAlH_4$ reduction, as described previously.[33] Low temperature crystallization from pentane of the product obtained gave pure α-fenchol (as indicated by ^1H NMR (60 MHz)), in approximately 50% isolated yield. Procedure 6 was applied to 0.96 g (0.02 mol) of NaH, 3.20 g (21 mmol) of α-fenchol, and 1.40 g (5.0 mmol) of **14**. After 18 h of reaction at 48 °C, the cooled mixture was poured into water. Extractive treatment and medium pressure chromatography gave a colorless oil which crystallized upon standing. Recrystallization of the product from hexane gave **18** (1.57 g, 83%): mp 80–83.5 °C; IR (KBr) 1626 cm^{-1} (C=N); MS, *m/e* 377 (M^+); ^1H NMR ($CDCl_3$) δ 0.857–1.900 (22 H, m), 4.130 (1 H, A of AB, J = 7.9 Hz), 4.192 (1 H, B of AB, J = 7.9 Hz), 4.358 (s, 1 H), 7.423–8.442 (m, 6 H); $[\alpha]^{25}_{589}$ +36.51°, $[\alpha]^{25}_{578}$ +38.55°, $[\alpha]^{25}_{546}$ +46.12°, $[\alpha]^{25}_{455}$ +105.95° (*c* 5.05, THF). Anal. Calcd for $C_{25}H_{31}NO_2$: C, 79.54; H, 8.27; N, 3.71. Found: C, 79.61; H, 8.23; N, 3.66.

By Procedure 7. To a dried 250-mL Schlenk flask fitted with an N_2 inlet and a drying tube (silica gel as the dessicant) was added 11.0 g (0.23 mol) of NaH as a 50% NaH/mineral oil suspension, and the suspension was washed with pentane. To this at 25 °C was added 68.0 g (0.44 mol) of *d*-α-fenchol[33] in several portions. The flask was heated to ca. 50 °C in order to melt the alcohol, and vigorous evolution of gas was observed. The mixture was stirred at 25 °C for 1 h and then heated and stirred at 90 ± 5 °C for 10 h. To the slightly heterogeneous mixture was added 13.0 g (15 mmol) of **1**. After 7 h, the mixture was cooled to 25 °C over 30 min and poured into a saturated aqueous solution of NH_4Cl. The aqueous mixture was extracted with three portions of Et_2O. The combined organic fractions were washed (10% NaOH, water, saturated aqueous $NaHCO_3$), dried ($MgSO_4$), and concentrated to give a yellow oil. Steam distillation removed the remaining fenchol after distillation of 1 L of water. The residue was washed with Et_2O. The ethereal extract was washed (water, brine), dried ($MgSO_4$), and concentrated to an oil. Column chromatography (alumina, cyclohexane → diethyl ether) of the residue gave a colorless oil. Crystallization of this material from cyclohexane gave **18** (17 g, 88%): mp 80–82 °C; ^1H NMR and TLC behavior were indistinguishable from **18** made from **14**: $[\alpha]^{25}_{589}$ +36.48°, $[\alpha]^{25}_{578}$ +38.50°, $[\alpha]^{25}_{546}$ +46.02°, $[\alpha]^{25}_{435}$ +105.83° (*c* 4.93, THF).

(−)-2-[2-(1-(1*S*,2*R*,4*S*)-Bornoxynaphthyl)]-4,4-dimethyl-Δ²-oxazoline (19). Procedure 6 was applied to 0.60 g (12.5 mmol) of a NaH dispersion in mineral oil, 1.29 g (8.35 mmol) of *l*-borneol (Matheson, Coleman, Bell), and 0.53 g (1.72 mmol) of **14**. After 3 h of reaction at 51 °C, the mixture was poured into a saturated aqueous solution of NH_4Cl. Thin layer chromatography of this reaction mixture showed the absence of detectable amounts of isoborneol, with which its behavior was compared. Extractive treatment and medium pressure chromatography gave a colorless oil. Crystallization of this material from hexane gave **19** (0.54 g, 83%, mp 96–99 °C). Recrystallization from cyclohexane gave a sample of analytically pure **19**: mp 99–102 °C; MS, *m/e* 377 (M^+); IR (KBr) 1623 cm^{-1} (C=N); ^1H NMR ($CDCl_3$) δ 0.793 (s, 3 H), 0.881 (s, 3 H), 1.008 (s, 3 H), 1.66–1.945 (m, 12 H), 2.557–2.686 (m, 1 H), 4.150 (s, 2 H), 4.575–4.621 (m, 1 H), 7.241–8.399 (m, 6 H); $[\alpha]^{25}_{589}$ −45.59°, $[\alpha]^{25}_{578}$ −47.98°, $[\alpha]^{25}_{546}$ −56.53, $[\alpha]^{25}_{435}$ −122.3° (*c* 4.9, THF). Anal. Calcd for $C_{25}H_{31}NO_2$: C, 79.54; H, 8.27; N, 3.71. Found: C, 79.65; H, 8.20; N, 3.65.

(+)-2-[2-(1-(3*R*,4*R*,8*S*,9*R*)-Quininoxynaphthyl)]-4,4-dimethyl-Δ²-oxazoline (16). Procedure 8. To 1.85 g (38 mmol) of oil-free NaH mixed with 65 mL of dry DMF was added in several portions 20.0 g (62 mmol) of anhydrous quinine (Aldrich). As the mixture stirred at 25 °C for 4 h, the color of the mixture darkened from yellow to dark brown. The temperature was adjusted to 60 °C, and the solution was stirred for 24 h at 60 ± 2 °C. To this was added 4.0 g (13 mmol) of **14**, and the dark mixture was stirred 12 h. The cooled mixture was partitioned between 100-mL portions of water and Et_2O. The aqueous layer was removed and washed with Et_2O. The combined organic fractions were washed (water, brine), dried ($MgSO_4$), and concentrated. Chromatography (150 g of SiO_2, Et_2O → THF) of the residue afforded impure **16**. Further chromatography (150 g of neutral alumina, diethyl ether → THF) gave **16** (4.8 g, 67%) as an oil. This was crystallized from acetone to give **16**·$(CH_3)_2CO$ (1:1 adduct): mp 98–100 °C; IR (KBr) 1620 cm^{-1} (C=N), 1705 (C=O); MS, *m/e* 547 (M^+); exact mass 547.2846 (calcd for $C_{35}H_{37}N_3O_3$, 547.2835); ^1H NMR ($CDCl_3$) δ 1.439 (s, 3 H), 1.474 (s, 3 H), 1.593–3.011 (m, 16 H), 3.500–3.794 (m, 4 H), 4.018 (1 H, A of AB, J = 8.0 Hz), 4.999–5.063 (m, 2 H), 5.862–6.063 (m, 1 H), 6.417–6.453 (d, 1 H), 7.17–8.601 (m, 11 H); $[\alpha]^{25}_{589}$ +48.58°, $[\alpha]^{25}_{578}$ +50.50°, $[\alpha]^{25}_{546}$ +56.99°, $[\alpha]^{25}_{435}$ +82.16° (*c* 5.00, THF). Anal. Calcd for $C_{35}H_{37}N_3O_3 \cdot C_3H_6O$: C, 75.35 H, 7.16; N, 6.94. Found: C, 75.32; H, 7.02; N, 6.95.

(−)-2-[2-(1-(3*R*,4*R*,8*R*,9*S*)-Quinidinoxynaphthyl)]-4,4-dimethyl-Δ²-oxazoline (17). Procedure 8 was applied to 0.90 g (10 mmol) of NaH (pentane washed), 20 mL of dry DMF, 8.0 g (25 mmol) of quinidine (Aldrich), and 2.0 g (6.60 mmol) of **14**. After being stirred for 18 h at 56 ± 2 °C, the mixture was cooled and partitioned between a saturated aqueous solution of NH_4Cl (50 mL) and CH_2Cl_2 (100 mL). The aqueous fraction was removed, neutralized with 10% aqueous HCl, and washed with CH_2Cl_2. The combined organic fractions were washed (water, brine), dried ($MgSO_4$), and concentrated to an oily solid. Chromatography (200 g of alumina, CH_2Cl_2 → diethyl ether) of this material gave an oil, crystallization of which from cyclohexane gave **17** (1.6 g, 45%). A sample of analytically pure **17** was prepared by recrystallization from cyclohexane: mp 135–137 °C; MS, *m/e* 547 (M^+); exact mass 547.2818 (calcd for $C_{35}H_{37}N_3O_3$, 547.2835); IR (KBr) 1620 cm^{-1} (C=N); ^1H NMR ($CDCl_3$) δ 1.261–1.825 (m, 10 H), 2.162–2.264 (m, 2 H), 2.625–2.855 (m, 4 H), 3.496–3.574 (m, 1 H), 3.740 (s, 3 H), 3.953 (1 H, A of AB, J = 8.3 Hz), 4.099 (1 H, B of AB, J = 8.3 Hz), 4.899–5.011 (m, 2 H), 5.813–6.004 (m, 1 H), 6.319–6.351 (d, 1 H), 7.222–8.642 (m, 11 H); $[\alpha]^{25}_{589}$ −92.08°, $[\alpha]^{25}_{578}$ −97.11°, $[\alpha]^{25}_{546}$ −116.5°, $[\alpha]^{25}_{435}$ −268.4° (*c* 4.23, THF). Anal. Calcd for $C_{35}H_{37}N_3O_3$: C, 76.76; H, 6.80; N, 7.67. Found: C, 76.62; H, 6.76; N, 7.66.

Optically Active 2-[2-(1,1′-Binaphthyl)]-4,4-dimethyl-Δ²-oxazoline (6). Procedure 9. A solution of 0.70 mL (5.0 mmol) of 1-bromonaphthalene in 2 mL of dry THF was cooled to −78 °C, and to it was added 3.8 mL (5.0 mmol) of a 1.31 M solution of *sec*-BuLi in cyclohexane. The yellow heterogeneous mixture was stirred for 1 h at −78 °C and then was warmed to −42 °C. To the yellow solution was added a solution of 0.105 g (0.28 mmol) of **15** in 4 mL of dry THF, and the solution was stirred at −42 ± 2 °C for 1 h. To this was added 5 mL of a saturated aqueous NH_4Cl solution, and the mixture was warmed to 25 °C. The aqueous phase was neutralized with 10% HCl and washed with Et_2O. The ethereal portions were combined, washed (water, brine), dried ($MgSO_4$), and concentrated. Thick layer chromatography (silica gel, 2% pentane in CH_2Cl_2) of the product gave **6** (84 mg,

(33) Coulombeau, A.; Rossat, A. *Mem. Pres. Soc. Chim.* **1965**, 3338.

80%): ^{1}H NMR ($CDCl_3$) identical with that obtained for racemic **6** (see above); $[\alpha]^{25}_{589}$ +88.42°, $[\alpha]^{25}_{578}$ +93.06°, $[\alpha]^{25}_{546}$ +109.9°, $[\alpha]^{25}_{435}$ +238.5° (*c* 3.30, THF).

The synthesis was also carried out at −60 °C as follows. To a solution of 0.22 mL (1.57 mmol) of 1-bromonaphthalene at −78 °C was added dropwise 0.68 mL (1.5 mmol) of a solution of 2.2 M *n*-BuLi in hexane. The mixture became yellow and was stirred at −78 °C for 15 min. The mixture was warmed to −63 °C over 15 min, and to this solution was added a solution of 0.20 g (0.52 mmol) of **15** in 5 mL of THF. The solution was stirred at −63 ± 3 °C for 5.5 h. Analytical thin layer chromatography indicated no further change in the reaction at this time. The mixture was cannulated into an aqueous saturated solution of NH_4Cl. The neutralized aqueous layer was washed with Et_2O, and the combined organic fractions were washed (water, brine), dried ($MgSO_4$), and concentrated to give a mixture of equal portions of starting material **15** and product **6** (as determined by ^{1}H NMR (60 MHz) and thin layer chromatography). Thick layer chromatography of the product (silica gel, 15% CH_3CN in toluene) gave **6** (50 mg, 26%): ^{1}H NMR (60 MHz) and TLC both indicated the sample to be pure, and both were identical with those of an analytical sample of racemic **6**; $[\alpha]^{25}_{589}$ +97.26°, $[\alpha]^{25}_{578}$ +102.02°, $[\alpha]^{25}_{546}$ +119.60°, $[\alpha]^{25}_{435}$ +250.58° (*c* 5.0, $CHCl_3$).

The synthesis was also carried out at −20 °C. Procedure **9** was followed except for the reaction temperature difference. Product **6** was obtained as a light yellow oil (76%) whose ^{1}H NMR and TLC were identical with those of racemic **6**: $[\alpha]^{25}_{589}$ +60.21°, $[\alpha]^{25}_{578}$ +68.24°, $[\alpha]^{25}_{546}$ +79.93°, (*c* 3.27, THF).

Run 1, Table I. Procedure 9 was applied to 0.75 mL (5.4 mmol) of purified 1-bromonaphthalene,[34] 3.6 mL (5.0 mmol) of a solution of 1.39 M *sec*-BuLi in cyclohexane, and a solution of 0.40 g (1.06 mmol) of **13** in 2 mL of dry THF. After 1 h of reaction at −42 ± 2 °C, 20 mL of a saturated aqueous NH_4Cl solution was added and the mixture warmed to 25 °C. Extractive treatment as described above, followed by medium pressure chromatography (column A, silica gel, CH_2Cl_2 → diethyl ether), gave a yellow oil. Thick layer chromatography (alumina, toluene) gave **6** (0.29 g, 80%) as a colorless foam: ^{1}H NMR and TLC were identical with those obtained for an analytically pure sample of racemic **6**. Chiral shift ^{1}H NMR analysis (mol of **6**/mol of Eu(Tfc)$_3$ = 4.2) gave 67% ee: $[\alpha]^{25}_{589}$ +78.30°, $[\alpha]^{25}_{578}$ +82.55°, $[\alpha]^{25}_{546}$ +97.10°, $[\alpha]^{25}_{435}$ +211.0° (*c* 2.59, THF). Anal. Calcd for $C_{25}H_{21}NO$: C, 85.44; H, 6.02; N, 3.99. Found: C, 85.64; H, 6.22; N, 3.71.

Run 2, Table I. Procedure 9 was applied to a solution of 1.30 mL (9.3 mmol) of purified 1-bromonaphthalene, 6.5 mL (9.04 mmol) of a 1.39 M solution of *sec*-BuLi in cyclohexane, and a solution of 0.90 g (1.64 mmol) of **16** in 3.5 mL of dry THF. The dark solution was stirred for 1 h at −40 ± 2 °C and was quenched and extracted as described previously. The dark oil obtained was chromatographed (50 g SiO_2, CH_2Cl_2 → 20% ether/CH_2Cl_2) to give a yellow oil. Medium pressure chromatography (alumina, Column A, 1:1 hexane/toluene → toluene) gave **6** (56 mg, 10%) as a yellow foam: ^{1}H NMR ($CDCl_3$) identical with racemic **6**. Chiral shift analysis (mol of **6**/mol of Eu(tfc)$_3$ = 4.1) gave 92% ee: $[\alpha]^{25}_{589}$ +89.43°, $[\alpha]^{25}_{578}$ +94.26°, $[\alpha]^{25}_{546}$ +111.0°, $[\alpha]^{25}_{435}$ +240.9° (*c* 2.63, THF). Anal. Calcd for $C_{25}H_{21}NO$: C, 85.44; H, 6.02; N, 3.99. Found: C, 85.68; H, 6.27; N, 3.68.

Run 3, Table I. Procedure 9 was applied to a solution of 0.70 mL (5 mmol) of purified 1-bromonaphthalene, 3.30 mL (4.6 mmol) of a 1.39 M solution of *sec*-BuLi in cyclohexane, and a solution of 0.50 g (0.91 mmol) of **17** in 2 mL of dry THF. After being stirred at −42 ± 2 °C for 1 h, the reaction was quenched and extracted to give a solid. Thick layer chromatography (silica gel, 10% Et_2O/CH_2Cl_2) of the product gave a yellow oil of impure **6**. A second thick layer chromatogram (alumina, CH_2Cl_2) of this product gave **6** (52 mg, 16%) as a light yellow foam; ^{1}H NMR and thin layer chromatographic behavior were identical with that of racemic **6**. Chiral shift analysis (mol of **6**/mol of Eu(tfc)$_3$ = 3.9) indicated 81% ee; $[\alpha]^{25}_{589}$ −90.60°, $[\alpha]^{25}_{578}$ −95.70°, $[\alpha]^{25}_{546}$ −100.5°, $[\alpha]^{25}_{435}$ −174.8° (*c* 2.98, THF).

Run 4, Table I. Procedure 9 was applied to a solution of 0.75 mL (5.36 mmol) of purified 1-bromonaphthalene in 12 mL of dry THF, 3.6 mL (5.0 mmol) of a 1.39 M solution of *sec*-BuLi in cyclohexane, and a solution of 0.30 g (1.06 mmol) of **18** in 3 mL of dry THF. After 5.5 h of reaction time at −42 ± 2 °C, starting material had been consumed (TLC, 10% Et_2O/CH_2Cl_2). Quench and extractive treatment gave a yellow oil. Medium pressure chromatographic purification (alumina, 1:1 toluene/hexane → toluene) of the product gave a light yellow oil. Thick layer chromatography gave **6** (0.31 g, 78%) as a colorless foam pure to ^{1}H NMR and TLC as indicated by comparison with analytically pure racemic **6**. Chiral shift analysis (mol of **19**/mol of Eu(tfc)$_3$ = 2.7) indicated 45% ee: $[\alpha]^{25}_{589}$ +47.86°, $[\alpha]^{25}_{578}$ +50.40°, $[\alpha]^{25}_{546}$ +59.1°, $[\alpha]^{25}_{435}$ +128.4°, (*c* 2.52, THF).

Run 5, Table I. Procedure 9 was applied to a solution of 1.13 mL (8.08 mmol) of 1-bromonaphthalene in 20 mL of dry THF, 5.70 mL (7.47 mmol) of a 1.31 M solution of *sec*-BuLi in cyclohexane, and a solution of 0.60 g (1.58 mmol) of **19** in 5 mL of dry THF. After 1 h of reaction at −42 ± 2 °C, the yellow solution was quenched and extracted to give a yellow oil. Flash chromatography of this oil (75 g of alumina, hexane → CH_2Cl_2) gave **6** (0.46 g, 83%) as a light yellow oil which when submitted to HPLC (μ-Bondapak C-18, 30% MeOH/H_2O) gave a small sample of **6** pure to ^{1}H NMR and TLC as compared to an analytically pure sample of racemic **6**. Chiral shift analysis (mol of **19**/mol of Eu(tfc)$_3$ = 3.8) indicated 10% ee; $[\alpha]^{25}_{589}$ −8.92°, $[\alpha]^{25}_{578}$ −9.17°, $[\alpha]^{25}_{546}$ −10.72°, $[\alpha]^{25}_{435}$ −23.34° (*c* 2.78, THF).

Optically Active 2-[2-(2′-Methoxy-1,1′-binaphthylyl)]-4,4-dimethyl-Δ^2-oxazoline (8). Procedure 10. Run 9, Table I. To 0.3 g (12.5 mmol) of Mg ribbon was added 2 mL of dry Et_2O/benzene (1:1) and a small portion of 2.25 g (10 mmol) of 1-bromo-2-methoxynaphthalene. When the Grignard reaction started, the remaining bromide and 35 mL of dry Et_2O/benzene (1:1) were added, and the mixture was refluxed for 2 h. In more concentrated solutions, the Grignard reagent precipitated. The mixture (slightly heterogeneous) was heated under a stream of N_2 to remove the Et_2O present, until the reaction volume was approximately 20 mL, and the reaction temperature was at least 50 °C. The solution was filtered through dried Celite under N_2 into a solution of 0.40 g (1.1 mmol) of **18** in 6 mL of dry benzene. After 9 h at reflux temperature, the solution was cooled, and to it was added 10 mL of a saturated aqueous NH_4Cl solution. The aqueous fraction was neutralized and washed with Et_2O. The combined organic fractions were washed (water, brine), dried ($MgSO_4$), and concentrated to give an oil. Medium pressure chromatography, (column A, silica gel, hexane → CH_2Cl_2 → 10% Et_2O/CH_2Cl_2) gave 2-(1-hydroxyphenyl)-4,4-dimethyl-Δ^2-oxazoline and **8** as pink oils identified by TLC and ^{1}H NMR spectra. Thick layer chromatography of the binaphthyl product (alumina, toluene) gave **8** (0.27 g, 65%): ^{1}H NMR (C_6D_{12}) identical with an analytically pure sample of racemic **8**. Chiral shift analysis (mol of **8**/mol of Eu(tfc)$_3$ = 15) indicates 47% ee (downfield methyl signal) and 48% ee (methoxy signal): $[\alpha]^{25}_{589}$ −55.60°; $[\alpha]^{25}_{578}$ −58.41°; $[\alpha]^{25}_{546}$ −69.31°, $[\alpha]^{25}_{435}$ −152.9° (*c* 2.32, THF).

Run 6. Procedure 11. To 1.2 g (50 mmol) of Mg ribbon was added 10 mL of dry Et_2O and part of 10 g (42 mmol) of 1-bromo-2-methoxynaphthalene. The mixture was heated with a few drops of dibromoethane until the Grignard reaction started. To this was added the remaining bromide as a solution in 40 mL of dry benzene, and the mixture was refluxed overnight. The slightly heterogeneous Grignard reagent was filtered through dry Celite into a refluxing solution of 4.0 g (10.6 mmol) of **15**. During this addition, the reaction flask was open under a stream of nitrogen to allow evaporation of the Et_2O used during the Grignard formation. The resulting solution was refluxed for 3.25 h and then cooled to 25 °C. To this solution was added a saturated aqueous solution of NH_4Cl and 50 mL of diethyl ether. The aqueous portion was removed, neutralized, and washed with Et_2O. The combined ethereal extracts were washed (water, brine), dried ($MgSO_4$), and concentrated. Column chromatography (500 g of alumina, cyclohexane → CH_2Cl_2 → Et_2O) of the residue gave an oil (2.37 g) containing **8** as determined by ^{1}H NMR and TLC. Medium pressure chromatography (silica gel, column C, 10% Et_2O/CH_2Cl_2) of this oil gave **8** (2.09 g, 52%) as a white foam: ^{1}H NMR (C_6D_{12}) identical with an analytically pure sample of racemic **8**. Chiral shift analysis (mol of **8**/mol of Eu(tfc)$_3$ = 13) gave 82% ee (downfield methyl signal) and 82% ee (methoxy signal): $[\alpha]^{25}_{589}$ −95.81°, $[\alpha]^{25}_{578}$ −100.7°, $[\alpha]^{25}_{546}$ −119.7°, $[\alpha]^{25}_{435}$ −264.6° (*c* 2.22, THF).

(34) Suyver, J. F.; Wibaut, J. P. *Recl. Trav. Chim. Pays-Bas* **1945**, 65–79.

Run 8. Procedure 11 was applied to 0.19 g (8.0 mmol) of Mg ribbon, 5 mL of dry Et_2O, a solution of 1.65 g (7.0 mmol) of 1-bromo-2-methoxynaphthalene in 10 mL of dry benzene, and a solution of 1.0 g (1.83 mmol) of **17** in 15 mL of refluxing benzene. A precipitate formed immediately in the reaction mixture. After 45 min of reflux, the cooled mixture was quenched and put through the extractive treatment to give an oil. Column chromatography (50 g of alumina, $CH_2Cl_2 \rightarrow$ diethyl ether, followed by silica gel, 2% diethyl ether/CH_2Cl_2) of the oil gave **8** (120 mg, 27%) as a foam: ^1H NMR (C_6D_{12}) identical with an analytically pure sample of racemic **8**. Chiral shift analysis (mol of **8**/mol of $Eu(tfc)_3$ = 18) indicates 84% ee, determined from relative integrations of the methoxy signals: $[\alpha]^{25}_{589}$ −99.75°, $[\alpha]^{25}_{578}$ −105.7°, $[\alpha]^{25}_{546}$ −124.6°, $[\alpha]^{25}_{435}$ −273.9° (*c* 2.03, THF).

Run 7. Procedure 11 was applied to 0.19 g (8.0 mmol) of Mg ribbon, 1.65 g (7.0 mmol) of 1-bromo-2-methoxynaphthalene, 2.5 mL of dry Et_2O, and 10 mL of dry benzene. The Grignard mixture was filtered into a refluxing solution of 1.0 g (1.03 mmol) of **16** in 15 mL of dry benzene. A precipitate formed immediately. After 45 min of reflux (disappearance of starting ether **16** was determined by TLC, alumina, Et_2O), the mixture was cooled to 25 °C, and to it was added 10 mL of a saturated aqueous NH_4Cl solution and 20 mL of Et_2O. The aqueous fraction was neutralized and washed with Et_2O. The combined organic portions were washed (water, brine), dried ($MgSO_4$), and concentrated to give a brown oil. Column chromatography (50 g of alumina, $CH_2Cl_2 \rightarrow$ diethyl ether) of this material gave 2-(1-hydroxyphenyl)-4,4-dimethyl-Δ^2-oxazoline) (0.12 g, 27%) and an oil containing **8**. Thick layer chromatography (silica gel, 2% Et_2O/CH_2Cl_2) of this oil gave **8** (0.05 g, 7%) as a colorless foam; ^1H NMR (C_6D_{12}) identical with an analytically pure sample of racemic **8**. Chiral shift analysis (mol of **8**/mol of $Eu(tfc)_3$ = 17) showed only one peak for the methoxy signal and one peak for each of the diastereotopic methyl signals: $[\alpha]^{25}_{589}$ +110.76°, $[\alpha]^{25}_{578}$ +115.94°, $[\alpha]^{25}_{546}$ +136.91°, $[\alpha]^{25}_{435}$ +301.84° (*c* 2.07, THF). If one assumes the rotation of optically pure **8** is $[\alpha]^{25}_{578} = \pm 124°$ (*c* 2.0, THF), this material is 94% ee.

Attempted Synthesis of Optically Active 2-[2-(1,2′-Binaphthylyl)]-4,4-dimethyl-Δ^2-oxazoline (13). To a solution of 1.05 g (5.0 mmol) of 2-bromonaphthalene (Eastman Kodak) at −78 °C in 10 mL of dry THF was added 3.5 mL (4.6 mmol) of a 1.31 M solution of *sec*-BuLi in cyclohexane, and the mixture was stirred for 45 min. To this was added a solution of 0.40 g (0.73 mmol) of **16** in 5 mL of dry THF, and the mixture was stirred at −42 ± 1 °C for 35 min. All of the starting material was consumed as determined by TLC. To this mixture was added 20 mL of a saturated aqueous solution of NH_4Cl, and the mixture was warmed to 25 °C. The neutralized, aqueous fraction was removed and washed with Et_2O. The combined ethereal fractions were washed (water, brine), dried ($MgSO_4$), and concentrated. Filtration chromatography (75 g of alumina, hexane → CH_2Cl_2) of the residual oil gave **13** (0.21 g, 82%). A sample of analytically pure **13** was prepared by thick layer chromatography (silica gel, CH_2Cl_2) to give material whose ^1H NMR and TLC behavior were identical with that of authentic racemic **13** (see above): observed rotations were α_{589} −0.004°, α_{578} +0.002°, α_{546} +0.006° (*c* 2.94, THF), which are all within experimental error of zero. Addition of $Eu(tfc)_3$ chiral shift reagent to a sample of **13** produced here failed to show splitting of the oxazoline methyl signals in the ^1H NMR spectrum. In all solvent systems investigated, this sample shows TLC behavior identical with that of racemic **6**.

Synthesis of Optically Active 2-[2-(3′-Methoxy-1,2′-binaphthylyl)]-4,4-dimethyl-Δ^2-oxazoline (11). Procedure 12. Run 10, Table I. To a solution of 2.5 g (11 mmol) of 1-bromo-2-methoxynaphthalene[17] in 10 mL of dry THF stirred at −78 °C was added over 5 min 8.00 mL (10 mmol) of a 1.31 M solution of *sec*-BuLi in cyclohexane. The heterogeneous mixture was stirred at −78 °C for 1.5 h and was then warmed to −20 °C over 10 min. To the dark green solution was added a solution of 0.80 g (2.11 mmol) of **15** in 4.5 mL of dry THF, and the dark solution was stirred at −20 ± 2 °C for 9.5 h. To this was added 10 mL of a saturated aqueous solution of NH_4Cl, and the mixture was warmed with stirring to 25 °C. The neutralized aqueous fraction was washed with Et_2O. The combined ethereal portions were washed (water, brine), dried ($MgSO_4$), and concentrated. Chromatography of the residue (100 g of alumina, toluene) gave an oil, thick layer chromatography of which (silica gel, 5% ether/CH_2Cl_2) gave **11** (0.40 g, 49%) and **15** (0.23 g, 29%) identified by its ^1H NMR and TLC behavior. This sample of **11** gave ^1H NMR and TLC behavior which was identical with that of an analytically pure sample of racemic **11**. Chiral shift analysis (mol of **11**/mol of $Eu(tfc)_3$ = 3.2) gave only a single, unsplit methyl signal: $[\alpha]^{25}_{589}$ +33.65°, $[\alpha]^{25}_{578}$ +35.40°, $[\alpha]^{25}_{546}$ +40.25°, $[\alpha]^{25}_{435}$ +60.80° (*c* 3.26, THF). Anal. Calcd for $C_{26}H_{23}NO_2$: C, 81.86; H, 6.08; N, 3.67. Found: C, 81.61; H, 6.15; N, 3.54.

Repetition of the above procedure gave, after 8 h of reaction at −20 ± 2 °C, **11** (0.41 g, 51%) and **15** (0.26 g, 32%). The ^1H NMR and TLC behavior of this sample was identical with that of pure, authentic racemic **11**. Chiral shift analysis (mol of **11**/mol of $Eu(tfc)_3$ = 1.5) indicates 95% ee: $[\alpha]^{25}_{589}$ +32.82°, $[\alpha]^{25}_{578}$ +34.19°, $[\alpha]^{25}_{546}$ +39.24°, $[\alpha]^{25}_{435}$ +57.87° (*c* 2.91, THF).

Run 11. Procedure 12 was applied to a solution of 2.2 g (9.32 mmol) of 1-bromo-2-methoxynaphthalene in 10 mL of dry THF, 6.70 mL (8.78 mmol) of a 1.31 M solution of *sec*-BuLi in cyclohexane, and a solution of 1.0 g (1.83 mmol) of **16** in 4.5 mL of dry THF. The dark solution stirred at −20 ± 2 °C for 4 h (no remaining **16** by TLC, diethyl ether/alumina). Quench and extractive treatment gave an oil which solidified upon standing. Flash chromatography (100 g of alumina, $CH_2Cl_2 \rightarrow$ THF) of the product followed by thick layer chromatography (silica gel, CH_2Cl_2) gave **11** (0.14 g, 20%): ^1H NMR spectrum was identical with that of authentic racemic **11**. Chiral shift analysis (mol of **11**/mol of $Eu(tfc)_3$ = 3.7) indicated 87% ee: $[\alpha]^{25}_{589}$ +29.56°, $[\alpha]^{25}_{578}$ +31.25°, $[\alpha]^{25}_{546}$ +35.45°, $[\alpha]^{25}_{435}$ +52.42° (*c* 2.97, THF).

In a similar run, 2-bromo-3-methoxynaphthalene was substituted for the 1-bromo-2-methoxynaphthalene of run **11** as follows. To a mixture of 1.60 g (7.24 mmol) of 2-bromo-3-methoxynaphthalene in 8 mL of dry THF at −78 °C was added 4.80 mL (7.15 mmol) of a 1.49 M solution of *sec*-BuLi in hexane. The light yellow solution was stirred at −78 °C for 1 h and then warmed to −21 °C over 15 min. To this was added a solution of 0.48 g (1.2 mmol) of **16** in 2 mL of dry THF, and the solution stirred at −21 ± 2 °C for 50 min. The reaction mixture was quenched and the crude product was isolated as in procedure 12. Flash chromatography (200 g of silica gel, $CH_2Cl_2 \rightarrow$ 1:3 Et_2O/CH_2Cl_2) of this material gave **11** (0.42 g, 92%) as an oil, pure by ^1H NMR. An analytical sample of **11** was obtained by medium pressure chromatography (column A, alumina, 1:1 cyclohexane/$CH_2Cl_2 \rightarrow$ CH_2Cl_2) to give an ^1H NMR spectrum identical with that of pure racemic **11**. Chiral shift analysis (mol of **11**/mol of $Eu(tfc)_3$ = 1.5) gave 92% ee: $[\alpha]^{25}_{589}$ +32.13°, $[\alpha]^{25}_{578}$ +33.32°, $[\alpha]^{25}_{546}$ +38.22°, $[\alpha]^{25}_{435}$ +56.48° (*c* 2.02, THF). Anal. Calcd for $C_{26}H_{23}NO_2$: C, 81.86; H, 6.08; N, 3.67. Found: C, 81.56; H, 6.07; N, 3.49.

Run 12. Procedure 12 was applied to a solution of 2.20 g (9.32 mmol) of 1-bromo-2-methoxynaphthalene in 10 mL of dry THF, 6.30 mL (8.76 mmol) of a 1.39 M solution of *sec*-BuLi in cyclohexane, and a solution of 1.0 g (1.83 mmol) of **17** in 5 mL of dry THF. After 1.25 h the mixture contained no more **17** (analytical TLC). It was quenched, and crude product was isolated. Chromatography of this oil (50 g of silica gel, $CH_2Cl_2 \rightarrow$ 10% Et_2O/CH_2Cl_2) gave **11** (0.15 g, 22%): ^1H NMR and TLC identical with those for an analytical sample of racemic **11**. Chiral shift analysis (mol of **11**/mol of $Eu(tfc)_3$ = 1.9) indicates 84% ee: $[\alpha]^{25}_{589}$ −29.27°, $[\alpha]^{25}_{578}$ −30.38°, $[\alpha]^{25}_{546}$ −34.61°, $[\alpha]^{25}_{435}$ −41.69° (*c* 3.43, THF). Anal. Calcd for $C_{26}H_{23}NO_2$: C, 81.86; H, 6.08; N, 3.67. Found: C, 81.84; H, 6.19; N, 3.56.

Run 13. Procedure 12 was applied to a solution of 2.5 g (10.5 mmol) of 1-bromo-2-methoxynaphthalene in 10 mL of dry THF, 8.0 mL (10.5 mmol) of a 1.31 M solution of *sec*-BuLi in cyclohexane, and a solution of 0.80 g (2.12 mol) of **18** in 4.5 mL of dry THF. After 9.5 h at −22 ± 3 °C, the reaction was quenched and crude product isolated. Filtration chromatography (100 g of silica gel, $CH_2Cl_2 \rightarrow$ 10% Et_2O/CH_2Cl_2) of this material gave an oil composed of **18** and **11**. Medium pressure chromatography (column A, alumina, 1:1 hexane/toluene → toluene) gave **18** (0.54 g, 67%, identified by an ^1H NMR and TLC match with authentic material) and **11** (0.23 g, 28%). The ^1H NMR and TLC behavior of this sample of **11** was identical with that of authentic racemic **11**. Chiral shift analysis (mol of **11**/mol of $Eu(tfc)_3$ = 3.9) indicates 77% ee: $[\alpha]^{25}_{589}$ +27.71°, $[\alpha]^{25}_{578}$ +28.76°, $[\alpha]^{25}_{546}$ +33.01° (*c* 2.49, THF).

Run 14. Procedure 12 was applied to a solution of 1.30 g (5.50 mmol) of 1-bromo-2-methoxynaphthalene in 15 mL of dry THF, 3.80 mL (4.98 mmol) of a 1.31 M solution of *sec*-BuLi in cyclohexane, and a solution of 0.40 g (1.05 mmol) of **19** in 3 mL of dry THF. After 10 h at −18 ± 2 °C, the solution was quenched. The product was isolated as in run 13 to give **19** (0.14 g, 35%, identified by a TLC match with an authentic sample of **19**) and **11** (0.18 g, 45%). The sample of **11** gave ^{1}H NMR and TLC identical with pure racemic **11**. Chiral shift analysis (mol of **11**/mol of Eu(tfc)$_3$ = 1.8) indicates 8% ee. Upon standing, the sample crystallized. Some of these crystals were used to seed crystallization of racemic material. Because of that, fractionation of the sample was possible. Crude rotation on the fractionated sample indicated a predominance of the (+) enantiomer.

2,2′-Bis[2-(4,4-dimethyl-Δ^2-oxazolinyl)]-1,1′-binaphthyl (9). To 60 mg (2.3 mmol) of Mg filings was added a solution of 0.50 g (1.64 mmol) of **14** in 1.5 mL of dry Et$_2$O containing a few drops of 1,2-dibromoethane. When the Grignard reaction started (cloudy ethereal solution, and shiny Mg surface), 1 mL of dry Et$_2$O was added and the mixture refluxed for 1.5 h. The ether was removed by gently heating the mixture under a stream of nitrogen. To the oil containing traces of Mg was added 2 mL of dry benzene, 20 mg (0.05 mmol) of dichlorobis(triphenylphosphine)nickel, and 0.16 g (0.42 mmol) of **15**. The resulting solution was refluxed for 40 min. To the cooled solution was added 5 mL of water. The aqueous phase was acidified by the addition of aqueous 10% HCl, and the two-phase mixture was stirred for 15 min. The aqueous layer was removed, neutralized (NaHCO$_3$), and washed with Et$_2$O. The combined organic fractions were washed (water, brine), dried (MgSO$_4$), and concentrated. Thick layer chromatography (silica gel, 10% CH$_3$CN/toluene) of the residue gave a yellow oil containing **9**. An additional thick layer chromatograph (alumina, 60% hexane/CH$_2$Cl$_2$) of this oil gave **9** (15 mg, 17%): ^{1}H NMR spectrum and TLC match those of an analytical sample of racemic **9** (see below); observed rotations, α_{589} +0.007°, α_{578} +0.006°, α_{546} +0.010°, α_{435} +0.012° (*c* 1.48, THF).

The same reaction was run at 25 °C and involved 0.12 g (0.6 mmol) of Mg, 1.0 g (3.28 mmol) of **14**, and 5 mL of Et$_2$O. After the Et$_2$O had been removed, 60 mg (0.09 mmol) of dichlorobis(triphenylphosphine)nickel and 0.32 g (0.82 mmol) of **15** in 5 mL of dry benzene were added to the Grignard reagent. The mixture was stirred at 25 °C for 53 h. The oil isolated (see above) after extractive procedure was subjected to medium pressure chromatography (silica gel, 10% CH$_3$CN/toluene → 50% CH$_3$CN/toluene). The fraction containing **9** was further treated by thick layer chromatography (alumin, 1:1 CH$_2$Cl$_2$/pentane) to give **9**, 0.12 g (67%): ^{1}H NMR spectrum and TLC both indicate the sample to be pure; observed rotation, α_{589} +0.008°, α_{578} +0.005°, α_{546} +0.011°, α_{435} +0.022° (*c* 4.07, THF). Crystallization of the sample from CHCl$_3$ gave an analytically pure sample of **9**: mp 159–161 °C; ^{1}H NMR (CDCl$_3$) δ 0.948 (s, 3 H, CH$_3$), 1.119 (s, 3 H, CH$_3$), 3.243 (A of AB, *J* = 7.9 Hz, 1 H, CH$_2$), 3.499 (B of AB, *J* = 7.9 Hz, 1 H, CH$_2$), 7.289–8.040 (m, 12 H, Ar H); MS, *m/e* 448 (M$^+$); IR (KBr) 1680 cm^{-1} (C=N). Anal. Calcd for C$_{30}$H$_{28}$N$_2$O$_2$: C, 80.33; H, 6.29; N, 6.25. Found: C, 80.48; H, 6.53; N, 6.25.

A sample of **9** was hydrolyzed to 1,1′-binaphthyl-2,2′-dicarboxylic acid (4 N HCl at reflux for 24 h) to give product (75%) of mp 265–269 °C, observed rotations, α_{589} +0.007°, α_{578} +0.004°, α_{546} +0.002°, and α_{435} 0.000° (*c* 1.14, 0.14 N NaOH in H$_2$O, 25 °C). Synthesis of this diacid by other means[35] gave mp 266–270 °C. The compound has been fully characterized. Optically pure (−)-**9** gave as maximum rotations $[\alpha]^{25}_{589}$ −102.4°, $[\alpha]^{25}_{578}$ −108.6°, $[\alpha]^{25}_{546}$ −126.4°, $[\alpha]^{25}_{435}$ − 250.8° (*c* 0.94, 0.1 N NaOH in H$_2$O).[35]

Conversion of (+)-(*S*)-2-[2-(1,1′-Binaphthylyl)]-4,4-dimethyl-Δ^2-oxazoline (6) via (−)-(*S*)-1,1′-Binaphthyl-2-carboxylic Acid (20) to (+)-(*S*)-2-Amino-1,1′-binaphthyl (21). The procedure was developed with racemic **6**. A solution of 0.30 g (0.85 mmol) of racemic **6** and 0.6 mL (9.64 mmol) of CH$_3$I was stirred for 24 h under N$_2$. The excess CH$_3$I was removed by evaporation under a stream of N$_2$, and the residue was dissolved in 35 mL of MeOH. Aqueous 20% NaOH was added (35 mL), and the suspension was refluxed under N$_2$ overnight. The cooled solution was poured slowly into concentrated (40%) aqueous HCl. The resulting suspension was cooled to 20 °C and filtered. The filtercake was washed (water), air-dried, and crystallized from benzene to give **20** as fine white crystals: mp 200–201 °C (lit.[36] mp 199–200 °C); IR (KBr) 1680 cm^{-1} (C=O). This acid was refluxed for 30 min under N$_2$ in 5 mL of SOCl$_2$ containing 2 drops of DMF. The excess SOCl$_2$ was removed under vacuum to give an oil. Addition and then removal by rotary evaporation of three 15-mL portions of benzene served to azeotropically remove residual SOCl$_2$. The resulting oil was dissolved in 9 mL of reagent acetone. To this stirred solution was added, dropwise, a solution of 0.2 g (3.1 mmol) of NaN$_3$ in 0.5 mL of water.[22a,c] The heterogeneous mixture was stirred for 15 min at 25 °C and cooled to 0 °C in an ice bath, and 18 mL of water was slowly added. The mixture was washed with two 20-mL portions of reagent benzene. The combined organic fractions were dried (MgSO$_4$) and refluxed for 1 h. To the solution was added 20 mL of an aqueous solution of 50% NaOH, and the mixture was stirred at reflux for 1 h. The basic layer was removed and to the benzene solution was added 40 mL of aqueous 6 N HCl. The mixture was refluxed for 15 min and cooled to 25 °C. The aqueous layer was removed and filtered through paper in 100 mL of aqueous 20% NaOH. The cooled, basic mixture was washed with three 20-mL portions of CHCl$_3$. The combined organic extracts were washed (water, brine), dried (MgSO$_4$), and concentrated to an oil which crystallized upon standing. Recrystallization of this solid from methanol/water gave brown crystals (mp 168–181 °C). Sublimation of the solid gave white crystals of **14** (0.11 g, 50% from **6**): mp 175–178 °C; MS, *m/e* 269 (M$^+$).

This procedure was used to convert (+)-(*S*)-**6** to (+)-(*S*)-**21**. The sample of (+)-(*S*)-**6** used was 0.80 g (2.28 mmol): $[\alpha]^{25}_{589}$ +30.5°, $[\alpha]^{25}_{578}$ +31.8°, $[\alpha]^{25}_{546}$ +37.60°, $[\alpha]^{25}_{435}$ +81.7 (*c* 3.40, THF). It gave acid (−)-(*S*)-**20**: 0.45 g; mp 174–181 °C; $[\alpha]^{25}_{589}$ −11.68°, $[\alpha]^{25}_{578}$ −11.76°, $[\alpha]^{25}_{546}$ −12.80°, $[\alpha]^{25}_{435}$ −6.74° (*c* 2.77, benzene). It gave crude amine as an oil, thick layer chromatography (alumina, toluene) of which gave an orange solid. Crystallization of this material from CH$_3$OH gave crystals (mp 180–205 °C). The solid was dissolved in 95% ethanol and passed through 10 g of Norit A. The charcoal pad was washed with 100 mL of 95% EtOH. The colorless alcohol solution was diluted with 100 mL of water and 50 mL of saturated aqueous NaHCO$_3$ solution and washed with three portions of Et$_2$O. The combined ethereal fractions were washed (water, brine), dried (Na$_2$SO$_4$), and concentrated to give a white solid. Crystallization of this material from methanol/water gave (+)-(*S*)-**21** (0.19 g, 53% from **20**): mp 187–189 °C; MS, *m/e* 269 (M$^+$); TLC identical with that of racemic **21**: $[\alpha]^{25}_{589}$ +12.6°, $[\alpha]^{25}_{578}$ +13.8°, $[\alpha]^{25}_{435}$ +86.0° (*c* 1.08, THF). Anal. Calcd for C$_{20}$H$_{15}$N: C, 89.19; H, 5.61; N, 5.20. Found: C, 88.95; H, 5.66; N, 5.02.

Conversion of (−)-(*S*)-2-[2-(2-Methoxy-1,1′-binaphthylyl)]-4,4-dimethyl-Δ^2-oxazoline ((−)-(*S*)-8) via (−)-(*S*)-2′-Methoxy-1,1′-binaphthyl-2-carboxylic Acid ((−)-(*S*)-22) via (+)-(*R*)-2-Methoxy-1,1′-binaphthyl ((+)-(*R*)-23) to (*R*)-2-Hydroxy-1,1′-binaphthyl ((*R*)-24). The procedure was developed with racemic **8** as follows. A solution of racemic **8** (2.80 g, 7.35 mmol) in 20 mL (0.32 mol) of CH$_3$I was stirred under N$_2$ for 9 h. Residual CH$_3$I was evaporated under reduced pressure and the residue was refluxed for 40 h in 125 mL of CH$_3$OH and 125 mL of 20% aqueous NaOH. The mixture was cooled to 25 °C, washed with Et$_2$O, and filtered into 250 mL of 40% aqueous HCl. The solid obtained was filtered, washed with water, and dissolved in benzene. Concentration of the benzene solution to 10 mL and cooling of the solution gave acid **22** as colorless needles. This material was refluxed in 20 mL of SOCl$_2$ containing 2 drops of DMF for 30 min under N$_2$. The excess SOCl$_2$ was removed under vacuum. Addition and then removal by rotary evaporation of three 25-mL portions of benzene removal residual SOCl$_2$ to give a yellow solid which was warmed into solution in 20 mL of acetone. To this solution was added a solution of 0.40 g (6.2 mmol) of NaN$_3$ in 1 mL of water. The mixture was stirred at 25 °C for 30 min and cooled to 0 °C, and 20 mL of water at 0 °C was added. The mixture was extracted with three 15-mL portions of benzene. The combined organic layers were washed (cold water, then cold

(35) Brown, S. B.; Mazaleyrat, J.-P.; Cram, D. J., unpublished results.

(36) Martin, R. H. *J. Chem. Soc.* **1941**, 679–685.

brine), dried ($MgSO_4$), and filtered. The resulting solution was refluxed under N_2 for 2 h. An aqueous solution of 50% KOH in water was added, and the mixture was refluxed for 1 h. The mixture was cooled to 25 °C and the aqueous phase was removed. The organic portion was washed with water saturated with $NaHCO_3$, dried ($MgSO_4$), and concentrated to give amine as a foam: MS, m/e 299 (M^+); ^1H NMR ($CDCl_3$, 60 MHz) δ 3.48 (br s, 2 H), 3.65 (s, 3 H), 6.9–8.1 (m, 12 H). To 0.20 g of this amine was added 25 mL of aqueous 5 N HCl. The heterogeneous suspension was cooled and stirred at 0 °C. To this mixture was added a solution of 0.20 g (3.3 mmol) of $NaNO_2$ in 2 mL of water over 1 min. The mixture remained heterogeneous, but turned red. As the mixture stirred for 20 min at 0 °C, it became homogeneous, and was then slowly added with stirring to 75 mL of H_3PO_2 at 4 °C. Gas was evolved and a yellow precipitate formed. The mixture was stirred at 4 °C for 45 min and then was left in the refrigerator at 4 °C for 5 h. The mixture had turned light yellow, indicating disappearance of the diazonium salt. The mixture was washed with three portions of Et_2O. The combined organic fractions were washed (1 N NaOH, 10% HCl, water), dried ($MgSO_4$), and concentrated. Chromatography (alumina, CH_2Cl_2) of the residual oil gave a yellow oil which turned orange when exposed to light and air. The material was sublimed (125 °C (0.5 mm)) to give a white solid. Crystallization of this material from methanol–water gave 0.10 g of 2-methoxy-1,1′-binaphthyl (**23**): mp 108–109 °C (lit.[23] mp 110.5–111 °C); ^1H NMR ($CDCl_3$, 60 MHz) δ 3.70 (s, 3 H, OCH_3), 7.15–8.20 (m, 13 H, Ar H). To a solution of 0.35 g (1.23 mmol) of **23** in 5 mL of CH_2Cl_2 at −78 °C was added 0.12 mL (1.26 mmol) of BBr_3. The solution was stirred at −78 °C for 1 h. The solution was warmed to 25 °C over 1 h and stirred for 3 h. To this was slowly added 4 mL of water (very vigorous reaction of water with excess BBr_3), and the organic fraction was separated. The aqueous portion was washed with CH_2Cl_2. The combined organic fractions were washed (water saturated with $NaHCO_3$, water, brine), dried ($MgSO_4$), and concentrated to give a white foam. Crystallization of the product from aqueous methanol gave **24** (0.31 g, 87%): mp 84–86 °C (lit.[37] mp 87–89 °C (nearly racemic), lit.[22a] mp 88–89 °C (racemic)); ^1H NMR ($CDCl_3$) δ 4.892 (s, 1 H, OH), 7.078–8.057 (m, 13 H, Ar H).

The above procedure was applied to the conversion of (−)-(*S*)-**8** to (*R*)-**24**. Thus 1.15 g (3.02 mmol) of (−)-(*S*)-**8** ($[\alpha]^{25}_{589}$ −80.70°, $[\alpha]^{25}_{578}$ −84.65°, $[\alpha]^{25}_{546}$ −100.6°, $[\alpha]^{25}_{435}$ −222.0° (*c* 2.30, THF)), was transformed into (−)-(*S*)-**22** (0.84 g, 85%; mp 188–235 °C; $[\alpha]^{25}_{589}$ −17.85°, $[\alpha]^{25}_{578}$ −19.59°, $[\alpha]^{25}_{546}$ −25.87°, $[\alpha]^{25}_{435}$ −100.3°, (*c* 1.21, THF)). A sample of 0.78 g (2.38 mmol) of this material was converted to its acid chloride which in turn gave crude (+)-(*R*)-**23** as an oil, which was subjected to thick layer chromatography (silica gel, 5% CH_2Cl_2/pentane). The product was (+)-(*R*)-**23** (0.50 g; $[\alpha]^{25}_{589}$ −31.44°, $[\alpha]^{25}_{578}$ −33.24°, $[\alpha]^{25}_{546}$ −41.33°, $[\alpha]^{25}_{435}$ −130.1° (*c* 2.10, THF)) isolated as a white foam. A 0.48-g (1.7 mmol) sample of this material was converted to crude (*R*)-**24**, which was purified by thick layer chromatography (silica gel, CH_2Cl_2) to give a white foam ($[\alpha]^{25}_{589}$ +13.33°, $[\alpha]^{25}_{578}$ +13.10°, $[\alpha]^{25}_{546}$ +12.38°, $[\alpha]^{25}_{435}$ −27.38° (*c* 0.84, THF); $[\alpha]^{25}_{589}$ −1.20°, $[\alpha]^{25}_{578}$ −1.96°, $[\alpha]^{25}_{546}$ −5.02°, $[\alpha]^{25}_{435}$ −59.47° (*c* 2.25, MeOH)). Crystallization of this foam from methanol gave material enriched in racemate: mp 121–145 °C (lit.[23] (optically pure **24**) mp 197–199 °C); MS, m/e 270 (M^+); ^1H NMR and TLC behavior were identical with those of racemic **24**; exact mass 270.1037 (calcd for $C_{20}H_{14}O$, 270.1045); $[\alpha]^{25}_{589}$ +6.7°, $[\alpha]^{25}_{578}$ +6.5°, $[\alpha]^{25}_{546}$ +5.9°, $[\alpha]^{25}_{435}$ −21.1° (*c* 1.00, THF); $[\alpha]^{25}_{589}$ −0.95°, $[\alpha]^{25}_{578}$ −1.2°, $[\alpha]^{25}_{546}$ −2.3°, $[\alpha]^{25}_{435}$ −35° (*c* 2, MeOH).

Conversion of (−)-(*S*)-2′-Methoxy-1,1′-binaphthyl-2-carboxylic Acid ((−)-(*S*)-22) via 2′-Hydroxy-2-(hydroxymethyl)-1,1′-binaphthyl ((+)-(*S*)-25) to (−)-(*S*)-2,2′-Dihydroxy-1,1′-binaphthyl ((−)-(*S*)-26). To a solution of 0.25 g (0.77 mmol) of **22** ($[\alpha]^{25}_{589}$ −14.72°, $[\alpha]^{25}_{578}$ −15.94°, $[\alpha]^{25}_{546}$ −21.04°, $[\alpha]^{25}_{435}$ −81.79° (*c* 1.06, THF)) in 5 mL of dry THF was added at 0 °C over 5 min 2 mL (2 mmol) of a 1 M solution of BH_3·THF in THF. The solution bubbled and became yellow. After 5 min at 0 °C, the solution was warmed to 25 °C and stirred for 1 h. To the colorless solution at 0 °C was slowly added 4 mL of aqueous THF (2:1 THF/H_2O), and the mixture was stirred at 25 °C for 15 min. The aqueous layer was washed with Et_2O. The combined organic layers were washed with K_2CO_3–saturated water, dried ($MgSO_4$), and concentrated. Thick layer chromatography (silica gel, CH_2Cl_2) of the residue gave 2′-hydroxy-2-(hydroxymethyl)-1,1′-binaphthyl ((+)-(*S*)-**25**) as a white foam: ^1H NMR ($CDCl_3$) δ 2.004 (t, J = 6.1 Hz, 1 H, OH), 3.727 (s, 3 H, OCH_3), 4.346 (d, J = 6.1 Hz, 2 H, Ar CH_2), 6.895–8.015 (m, 12 H); MS, m/e 314 (M^+); $[\alpha]^{25}_{589}$ +21.90°, $[\alpha]^{25}_{578}$ +22.86°, $[\alpha]^{25}_{546}$ + 24.76°, $[\alpha]^{25}_{435}$ +28.57° (*c* 0.21, $CHCl_3$). Anal. Calcd for $C_{22}H_{18}O_2$: C, 84.05; H, 5.77. Found: C, 83.83; H, 5.71.

This material was dissolved in 18 mL of reagent acetone and to the solution was added a solution of 8 N Jones reagent in 18 mL of reagent acetone until the orange color persisted. To this was added reagent isopropyl alcohol until the green color returned. The mixture was diluted with 10 mL of water and was washed with two portions of Et_2O. The combined ethereal extracts were washed (water, $NaHCO_3$–saturated water, brine), dried ($MgSO_4$), and concentrated to an oily solid, pure by analytical TLC. This product was dissolved in 35 mL of reagent CH_2Cl_2, and to the solution was added 1.0 g (5.8 mmol) of *m*-chloroperbenzoic acid and 0.50 g (5.0 mmol) of $NaHCO_3$. The heterogeneous mixture was refluxed for 20 h, by which time starting material had been consumed (TLC, silica gel, CH_2Cl_2). The mixture was washed (1 N aqueous KOH, water, 10% HCl in water, brine), dried ($MgSO_4$), and concentrated to give a solid. The solid was heated on a steam bath with 50 mL of an aqueous solution of 20% KOH for 2 h. The cooled heterogeneous mixture was washed twice with Et_2O. The organic fractions were combined, washed (10% aqueous HCl, water, brine), dried ($MgSO_4$), and concentrated to give part of the 2′-methoxy-2-hydroxy-1,1′-binaphthyl. The original basic fraction was acidified with concentrated aqueous HCl, cooled, and washed with two portions of Et_2O. The organic layers from the extractions were combined, washed (water, brine), dried ($MgSO_4$), and concentrated to an oil which was submitted to flash chromatography (20 g of SiO_2, CH_2Cl_2) to give 2′-methoxy-2-hydroxy-1,1′-binaphthyl. This material was combined with that obtained from the neutral portions (^1H NMR ($CDCl_3$) δ 3.75 (s, 3 H, OCH_3), 5.23 (br s, 1 H, OH), 7.05–8.15 (m, 12 H, Ar H)). This product, as a solution in 5 mL of CH_2Cl_2 at −78 °C was demethylated by the addition of 0.15 mL (14 mmol) of BBr_3. After 0.5 h at −78 °C, the dark solution was warmed to 25 °C and stirred for an additional 1.5 h. The solution was then slowly poured into 20 mL of water and was extracted with CH_2Cl_2. The combined organic fractions were washed (water, water saturated with $NaHCO_3$), dried ($MgSO_4$), and concentrated. Thick layer chromatography (silica gel, 10% Et_2O/CH_2Cl_2) of the residual oil gave diol **26** (25 mg, 12%). Crystallization of this product from methanol gave (−)-(*S*)-**26**: mp 197–211 °C (lit.[38] mp 207–208 °C); ^1H NMR ($CDCl_3$) δ 5.030 (br s, 2 H, OH), 7.126–7.404 (m, 8 H), 7.867–7.998 (m, 4 H); TLC behavior identical with that of an authentic sample of racemic **26**; $[\alpha]^{25}_{589}$ −15.05°, $[\alpha]^{25}_{578}$ −16.81°, $[\alpha]^{25}_{546}$ −22.97° (*c* 0.91, THF).

Conversion of Enantiomerically Enriched (−)-(*S*)-2-[2-(2′-Methoxy-1,1′-binaphthylyl)]-4,4-dimethyl-Δ²-oxazoline ((−)-(*S*)-8) to 2′-Methoxy-1,1′-binaphthyl-2-carboxylic Acid ((−)-(*S*)-22) of Maximum Rotation. A sample of (−)-(*S*)-8 of 82% ee (chiral shift analysis), which gave $[\alpha]^{25}_{578}$ −100.68% (*c* 2.22, THF), served as starting material (1.66 g, 4.3 mmol). It was dissolved in 10 mL of CH_3I and stirred under N_2 at 25 °C for 12 h. Methanol (20 mL) was added, and the solution was evaporated under reduced pressure. To the residual oil was added 100 mL of methanol and 100 mL of an aqueous 20% NaOH solution. The mixture was refluxed for 24 h. The cooled solution was washed with Et_2O, and the ether layer was washed with three portions of aqueous 20% KOH. The combined basic fractions were filtered through filter paper into 500 mL of an aqueous solution of 20% aqueous HCl. The resulting suspension was cooled to ca. 15 °C and filtered. The filtercake was washed (water) and dried (65 °C (0.5 mm)) to give (−)-(*S*)-**22** (1.18 g, 84%): mp 150–180 °C; ^1H NMR ($CDCl_3$) identical with authentic racemic **22**; $[\alpha]^{25}_{589}$ −21.25°, $[\alpha]^{25}_{578}$ −23.00°, $[\alpha]^{25}_{546}$ −30.33°, $[\alpha]^{25}_{435}$ −186.67° (*c* 1.20, THF). Crystallization of 1.0 g of this acid from benzene gave

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microcrystalline **22**: 0.46 g; mp 183–230 °C; $[\alpha]^{25}_{589}$ −15.95°, $[\alpha]^{25}_{578}$ −17.66°, $[\alpha]^{25}_{546}$ −23.33°, $[\alpha]^{25}_{435}$ −90.81° (*c* 1.11, THF). Anal. Calcd for $C_{22}H_{16}O_3$: C, 80.48; H, 4.91. Found: C, 80.54; H, 5.09). A second crystallization of these crystals from benzene gave microcrystalline **22**: 0.14 g; mp 250–257 °C; $[\alpha]^{25}_{589}$ −4.02°, $[\alpha]^{25}_{578}$ −4.57°, $[\alpha]^{25}_{546}$ −5.91°, $[\alpha]^{25}_{435}$ −22.44° (*c* 1.27, THF). A final crystallization of the product obtained from benzene gave microcrystalline **22**: 80 mg; mp 252–258 °C; $[\alpha]^{25}_{589}$ −2.02°, $[\alpha]^{25}_{578}$ −2.09°, $[\alpha]^{25}_{546}$ −2.71°, $[\alpha]^{25}_{435}$ −10.54° (*c* 1.29, THF). Concentration to 7 mL of the benzene filtrate obtained from the first crystallization described above gave light yellow crystals of **22** upon standing: 0.40 g; mp 190–192 °C; $[\alpha]^{25}_{589}$ −24.41°, $[\alpha]^{25}_{578}$ −26.31°, $[\alpha]^{25}_{546}$ −34.95°, $[\alpha]^{25}_{435}$ −136.31° (*c* 1.11, THF). Anal. Calcd for $C_{22}H_{16}O_3$: C, 80.48; H, 4.91. Found: C, 80.58; H, 5.02. Recrystallization of this material from benzene gave **22**: 0.30 g; mp 191–193 °C; ()$\alpha]^{25}_{589}$ −23.98°, $[\alpha]^{25}_{578}$ −26.10°, $[\alpha]^{25}_{546}$ −34.39°, $[\alpha]^{25}_{435}$ −134.63° (*c* 1.23, THF). A third crystallization of this product from benzene gave **22**: 0.20 g; mp 191–193 °C; $[\alpha]^{25}_{589}$ −23.71°, $[\alpha]^{25}_{578}$ −25.93°, $[\alpha]^{25}_{546}$ −34.07°, $[\alpha]^{25}_{435}$ −133.43° (*c* 1.08, THF).

The combined crystals and filtrates of **22** (.70 g) from the optically enriched samples described above were dissolved in 25 mL of refluxing absolute ethanol. To this hot solution was added a hot solution of 0.70 *q* of quinidine in 25 mL of absolute ethanol. The resulting solution was concentrated to 20 mL. Three recrystallizations from absolute ethanol of the crystals that separated gave a salt of constant melting point and specific rotation: mp 200–206 °C; $[\alpha]^{25}_{589}$ +63.21°, $[\alpha]^{25}_{578}$ +64.90°, $[\alpha]^{25}_{546}$ +71.94°, $[\alpha]^{25}_{435}$ +91.03° (*c* 1.23, THF). Decomposition of this salt was accomplished by washing a solution of it in 30 mL of 1:1 Et_2O/benzene with five portions of aqueous 10% HCl and one portion of aqueous $NaHCO_3$. The organic layer was dried ($MgSO_4$) and concentrated to give a foam which crystallized when dissolved in 5 mL of benzene. The white crystals obtained were dried (56 °C (0.5 mm) 36 h) to give (−)-(*S*)-**22**: mp 190–193 °C; $[\alpha]^{25}_{589}$ −25.98°, $[\alpha]^{25}_{578}$ −28.28°, $[\alpha]^{25}_{546}$ −37.21°, $[\alpha]^{25}_{435}$ −145.3° (*c* 1.22, THF). Anal. Calcd for $C_{22}H_{16}O_3$: C, 80.48; H, 4.91. Found: C, 80.71; H, 5.31.

Chair–Twist Equilibria in Some *tert*-Butyl Octalones

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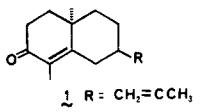
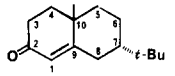
The solution conformations of four bicyclic enones, 7α-*tert*-butyl-10β-methyl-$\Delta^{1,9}$-octalone (**3**), its 7β-epimer (**4**), and the isomeric 6β- (**5**) and 6α-*tert*-butyloctalones (**6**), have been examined with ^{13}C and high-field ^1H NMR in conjunction with molecular mechanics calculations. Enones **4** and **6** were chosen as references in which ring B exists as a normal chair with an equatorial substituent. Enone **5** was used as a model in which ring B exists in a twist conformation with a ψ-equatorial *tert*-butyl group. Enone **3** is conformationally heterogeneous, with a significant contribution from the chair conformer bearing an axial *tert*-butyl group.

During an investigation of the conformation of epi-α-cyperone (**1**), we prepared enone **2**, a *tert*-butyl analogue of this well-known intermediate for sesquiterpene synthesis. Although it was assumed that enone **2** would exist



1 R = CH_2=CCH_3
2 R = *t*-Bu
10 R = *i*-Pr



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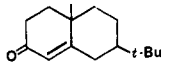

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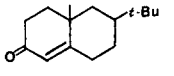

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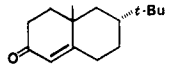

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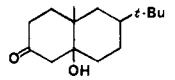

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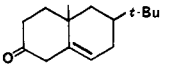

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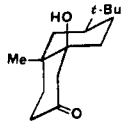
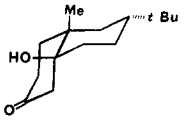


7a



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predominently if not exclusively, with the ring bearing the *tert*-butyl group in a twist conformation, experimental data concerning the conformation were contradictory. Neither CD nor lanthanide shift ^1H NMR data for **2**, when compared to those of **1** and various derivatives of **1**, were particularly informative. The ^{13}C NMR spectrum of **2** seemed to indicate that the preferred conformation was that with an axial *tert*-butyl appended to a chair (or deformed chair) cyclohexane ring while the crystal structure of the oxime of enone **2** indicated a twist conformation with a ψ-equatorial *tert*-butyl group. High-field ^1H NMR spectra were best interpreted in terms of an equilibrium mixture containing greater than 50% of a nonchair conformer.[1] The study of the conformation of enone **2** was complicated somewhat by the lack of availability of the stereoisomer bearing an equatorial *tert*-butyl group and suitable model compounds in which ring B could be safely assumed to be in a twist conformation.

For many years it was considered that a cyclohexane ring would invariably adopt a twist conformation in preference to a chair bearing an axial *tert*-butyl substituent;[2] however, recent work has provided a number of examples in which conformationally mobile cyclohexane derivatives exist either partially or completely in a chair conformation with an axial *tert*-butyl group.[3] Enone **2** and related compounds appeared to be suitable substrates for an investigation into steric effects governing the chair–twist equilibrium in bicyclic systems bearing a potential axial

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