removal of **9** so it may be cleaved to the ketones. Further work on these interesting enamidines is in progress.

Acknowledgment. We are grateful to the National Science Foundation and the National Institutes of Health for financial support of this work.

Registry No. 1, 23314-06-9; **2**, 80376-66-5; **3** (R_1 = Ph; R_2 = H), 80376-67-6; **3** (R_1R_2 = Ph), 80376-68-7; **3** (R_1R_2 = α-tetralin), 80376-69-8; **3** (R_1 = 3,4-$(MeO)_2C_6H_3$; R_2 = H), 80376-70-1; **3** (R_1 = PhCH-(CH_3); R_2 = H), 80376-71-2; **3** (R_1 = PhCH=CH; R_2 = H), 80376-72-3; **3** (R_1 = 2-pyridyl; R_2 = Me), 80376-73-4; **3** (R_1 = 5-norbornen-2-yl; R_2 = H), 80376-74-5; **4** (R_1 = Ph; R_2 = H), 80376-75-6; **4** (R_1, R_2 = Ph), 80376-76-7; **4** (R_1R_2 = α-tetralin), 80376-77-8; **4** (R_1 = 3,4-$(MeO)C_6H_3$; R_2 = H), 80376-78-9; **4** (R_1 = PhCH(CH_3); R_2 = H), 80376-79-0; **4** (R_1 = PhCH=CH; R_2 = H), 80376-80-3; **4** (R_1 = 2-pyridyl; R_2 = Me), 80376-81-4; **5** (R_1 = Ph; R_2 = H), 589-08-2; **5** (R_1 = Ph; R_2 = H) HCl, 4104-43-2; **5** (R_1, R_2 = Ph), 80376-82-5; **5** (R_1, R_2 = Ph) HCl, 80376-83-6; **5** (R_1, R_2 = α-tetralin), 80376-84-7; **5** (R_1, R_2 = α-tetralin) HCl, 80376-85-8; **5** (R_1 = 3,4-$(MeO)_2C_6H_3$; R_2 = H), 3490-06-0; **5** (R_1 = 3,4-$(MeO)_2C_6H_3$; R_2 = H) HCl, 13078-76-7; **5** (R_1 = PhCH(CH_3); R_2 = H), 40192-26-5; **5** (R_1 = PhCH(CH_3); R_2 = H) HCl, 80376-86-9; **5** (R_1 = PhCH=CH; R_2 = H), 24316-73-2; **5** (R_1 = PhCH=CH; R_2 = H) HCl, 80376-87-0; **5** (R_1 = 2-pyridyl; R_2 = Me), 26832-29-1; **6** (R_1 = 3,4-$(MeO)_2C_6H_3$; R_2 = H), 5703-21-9; **6** (R_1 = 5-norbornen-2-yl; R_2 = H), 80376-88-1; **6** (R_1, R_2 = α-tetralin), 18278-24-5; **6** (R_1, R_2 = Ph), 947-91-1; **6** (R_1, R_2 = $(CH_2)_5$), 2043-61-0; **7**, 80376-89-2; **7a**, 80376-90-5; **8** (R_1 = Bu; R_2 = H), 80376-91-6; **8** (R_1, R_2 = $(CH_2)_5$), 80376-92-7; **8** (R_1 = 5-norbornen-2-yl; R_2 = H), 80376-93-8; **8** (R_1, R_2 = Ph), 80376-94-9; **9** (R_1, E = Bu; R_2 = H), 80376-95-0; **9** (E = Bu; R_1, R_2 = $(CH_2)_5$), 80376-96-1; **9** (E = Bu; R_1 = 5-norbornen-2-yl; R_2 = H), 80376-97-2; **9** (E = CH_3CH_2CHOH; R_1, R_2 = $(CH_2)_5$), 80376-98-3; **9** (E = Bu; R_1, R_2 = Ph), 80376-99-4; **10** (E = $CH_3(CH_2)_4$; R_1 = Pr; R_2 = H), 820-29-1; **10** (E = c-C_6H_{11}; R_1 = Pr; R_2 = H), 5445-35-2; **10** (E = 5-norbornen-2-ylmethyl; R_1 = Pr; R_2 = H), 80377-00-0; **10** (E = c-C_6H_{11}; R_1 = OH; R_2 = Et), 80377-01-1; **10** (E = $(Ph)_2CH$; R_1 = Pr; R_2 = H), 22117-90-4; *i*, 80377-02-2; benzaldehyde, 100-52-7; benzophenone, 119-61-9; α-tetralone, 529-34-0; veratraldehyde, 120-14-9; α-methylphenylacetaldehyde, 93-53-8; cinnamaldehyde, 104-55-2; α-acetylpyridine, 1122-62-9; 5-norbornene-2-carboxaldehyde, 5453-80-5; cyclohexanone, 108-94-1; valeraldehyde, 110-62-3; *N*-methyl-*N*-pentyl-*N'-tert*-butylformamidine, 80377-03-3; *N*-pentyl-*N*-phenylethenyl-*N'-tert*-butylformamidine, 80377-04-4; *N*-methyl-*N*-butylformamidine, 80377-05-5.

Enantioselective Synthesis of Binaphthyls via Nucleophilic Aromatic Substitution on Chiral Oxazolines

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Received September 30, 1981

The extraordinary chiral recognition properties of axially dissymmetric binaphthyl derivatives has opened exciting new routes to enantiomerically enriched organic compounds. The elegant studies by Cram[1] using crown-type ethers containing chiral binaphthyl moieties has resulted in complete separation of racemic amino acids via selective complexation of one enantiomer. Transition metals, complexed with ligands derived from chiral binaphthyls, have catalyzed hydrogenations[2] and isomerizations[3] of prochiral olefins in high enantiomeric excess, whereas binaphthyl

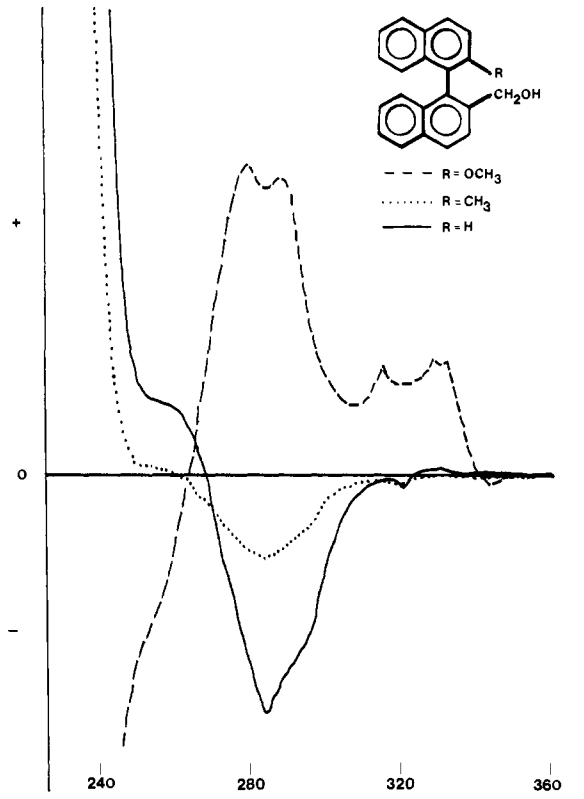

Figure 1. CD spectra in dioxane.

hydride[4] and binaphthyllithium[5] reagents have led to chiral alcohols by enantioselective reactions on carbonyl compounds. In spite of these highly useful properties, there is no viable synthetic route to chiral binaphthyls, and their acquisition relies only on resolution of racemic materials. Kumada[6] described the cross coupling of 1-bromo-2-methylnaphthalene via the Grignard reagent, catalyzed, ironically, by a chiral binaphthylnickel species, to give 2,2'-dimethyl-1,1'-binaphthyl in 12.5% ee. Wynberg[7] reports an oxidative binaphthyl coupling catalyzed by chiral amines in 16% ee. The best method to date is that of Miyano,[8] which involves an intramolecular Ullmann coupling of a bis(bromonaphthoic) ester derived from optically active, 1,1'-binaphthol. The latter route, which led to ~100% ee of binaphthoic ester, also required an optically pure binaphthyl as the starting material.

We now introduce a synthetic route to chiral binaphthyls **7** using nucleophilic aromatic displacement of an *o*-methoxy group[9] activated by chiral oxazoline **4**, furnishing these interesting substances in 87–96% ee.[10] The process is based on the addition of the Grignard reagent of 1-bromo-2-substituted naphthalenes to the 2-methoxy-1-oxazolinylnaphthalene **4** to afford the binaphthyl system **5** in 68–80% yields. The requisite chiral (methoxynaphthyl)oxazoline **4** was prepared from 2-methoxy-1-naphthoic acid[11] after conversion to its amide **2** (oxalyl chloride, NH_4OH, 83%, mp 155–158 °C) and treatment with (+)-1-methoxy-2-amino-3-phenyl-3-hydroxypropane[12] via its imidinium salt **3**.[13]

(1) Peacock, S. C.; Walba, D. M.; Gaeta, F. C. A.; Helgeson, R. C.; Cram, D. J. *J. Am. Chem. Soc.* **1980**, *102*, 2043. Lingenfelter, D. S.; Helgeson, R. C.; Cram, D. J. *J. Org. Chem.* **1981**, *46*, 393.

(2) Miyashita, A.; Yasuda, A.; Takaya, H.; Toriumi, K.; Ito, T.; Souchi, T.; Noyori, R. *J. Am. Chem. Soc.* **1980**, *102*, 7935 and references cited therein.

(3) Tani, K.; Yamagata, T.; Otsuka, S.; Takaya, H.; Miyashita, A.; Noyori, R. Lecture presented at the U.S.–Japan Seminar on Asymmetric Processes, Stanford University, July 1981; to be soon published as an ACS Monograph.

(4) Noyori, R.; Tomino, I.; Tanimoto, Y. *J. Am. Chem. Soc.* **1979**, *101*, 3129. Nishizawa, M.; Yamada, M.; Noyori, R. *Tetrahedron Lett.* **1981**, 247.

(5) Mazaleyrat, J.-P.; Cram, D. J. *J. Am. Chem. Soc.* **1981**, *103*, 4585.

(6) Tamao, K.; Yamamoto, H.; Matsumoto, H.; Miyake, N.; Hayashi, T.; Kumada, M. *Tetrahedron Lett.* **1977**, 1389.

(7) Feringa, B.; Wynberg, H. *Bioorg. Chem.* **1978**, *7*, 397.

(8) Miyano, S.; Tobita, M.; Nawa, M.; Sato, S.; Hashimoto, H. *J. Chem. Soc., Chem. Commun.* **1980**, 1233.

(9) Nucleophilic substitution on *o*-MeO or *o*-F aryloxazolines have been reported for simple achiral oxazolines: Meyers, A. I.; Gabel, R.; Mihelich, E. D. *J. Org. Chem.* **1978**, *43*, 1372. Meyers, A. I.; Williams, B. E. *Tetrahedron Lett.* **1978**, 223.

(10) An interesting alternative route to axially dissymmetric binaphthyls wherein a *chiral* alkoxy group is displaced from an *achiral* aryloxazoline has been performed by Cram (cf. accompanying communication).

(11) Shirley, D. A.; Cheng, C. F. *J. Organomet. Chem.* **1969**, *20*, 251.

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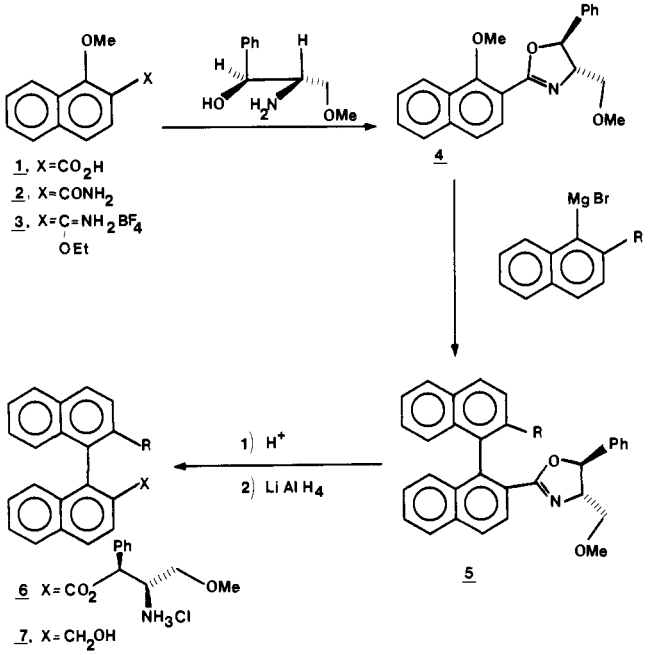
Table I. Chiral Binaphthyls from 4 and Naphthalene Grignard Reagents[a]

	5		7			
R	% yield	diastereomeric ratio[b]	% yield	mp,[c] °C	$[\alpha]_D$ ($CHCl_3$), deg	% ee (config)
H	80	87.0:13.0	56	151-152	+67.3 (c 0.04)	90 (R)[e]
Me	68	76.2:23.8	43	127.5	+4.33 (c 0.2)[d]	87.4 (R)
MeO	71	91.9:8.9	65	129-131	−71.4 (c 0.15)	96.0 (R)[e]

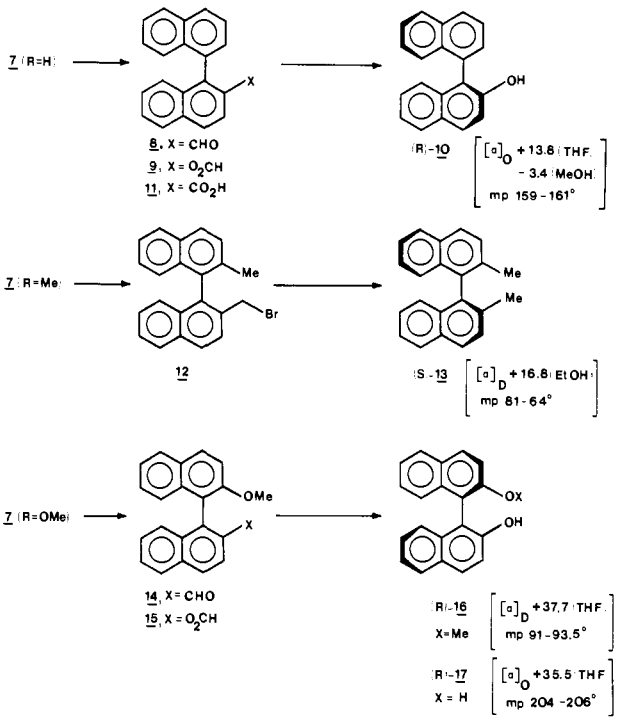
[a] Reactions were run in THF by using 2.0 equiv of Grignard reagent. [b] Determined by 100-MHz ^1H NMR Spectroscopy using the 5-H benzylic doublet (J = 7 Hz) at δ 4.80-5.00. [c] All compounds gave satisfactory elemental analyses. [d] Rotation changes to −8.0° in ethanol (c 0.03). [e] Determined by chiral shift reagent (tris[3-(heptafluoropropylhydroxymethylene)-d-camphorato]europium(III)) at 100 mHz.

Three different naphthalene Grignard reagents were attempted and gave the binaphthyl adduct **5**. Acidic hydrolysis (ethanolic HCl, reflux) produced the amino ester, salt **6**, which was not characterized as pure material but was directly reduced with excess lithium aluminum hydride (THF, 25 °C, 6 h) to the (hydroxymethyl)binaphthyls **7**. Diastereomeric ratios for the initial adducts



5 and enantiomeric purity for the chiral binaphthyls **7** are given in Table I. In order to assess the absolute configurations of the newly formed biaryls **7**, they were transformed into known derivatives. Furthermore, comparisons with known compounds should also provide information regarding their optical purity. The diastereomeric ratios given in Table I should also indicate the enantiomeric excess present in **7**; however, unavoidable enantiomeric enrichment during the hydrolysis and hydride reduction steps (**5** → **6** → **7**) was observed. This was due to 10–15% of the corresponding rearranged hydroxy amide, derived from **6**, which could be detected (NMR) in the crude reaction product containing **7**.

The binaphthyl alcohol **7** (R = H) was oxidized to the aldehyde **8** (Jones procedure) and taken directly to the formate **9** (MCPBA, CH_2Cl_2, reflux, 18 h) which was then saponified (10% KOH–MeOH, 50 °C, 1 h) to the binaphthol **10**. The *R* configuration was assigned by comparison with the carboxy derivative **11** obtained via another route by Cram[14] and consistent Cotton curves with other binaphthyls of known configuration (see below).



The binaphthyl **7** (R = Me) had its absolute configuration determined by transformation to the bromide **12** (PBr_3, benzene, 25 °C, 3 h) in quantitative yield and without purification was reduced (excess $LiAlH_4$, ether, reflux, 30 min) to the dimethyl compound **13** (79%). Comparison with authentic material reported by Mislow[15] confirmed that the (+) enantiomer had the *S* configuration (87.4% ee). Although the diastereomeric ratio (Table I) for **5** (R = Me) was assessed to be 52.4%, the hydrolysis and reduction resulted in enantiomeric enrichment to greater than 87%. The absolute configuration of **7** (R = MeO) was correlated to the known (*S*)(−)-diol **17** reported by Cram.[16] This was done by oxidation (Jones) to **14** ($[\alpha]_D$ −59.7°, mp 152–153 °C) followed by Baeyer–Villiger oxidation (MCPBA, CH_2Cl_2, $NaHCO_3$, reflux 21 h) to the formate ester **15** which was saponified (17% KOH–

(12) Meyers, A. I.; Knaus, G.; Kamata, K.; Ford, M. E. *J. Am. Chem. Soc.* **1976**, *98*, 567.

(13) Preparation of **4** [oil; $[\alpha]_D$ 97.0° (c 0.4, $CHCl_3$); NMR ($CDCl_3$) δ 3.49 (s, 3 H), 3.78 (m, 2 H), 4.07 (s, 3 H), 4.44 (m, 1 H), 4.61 (d, 1 H), 7.26–8.45 (m, 11 H)]. Amide **2** (26 g) in 400 mL of 1,2-dichloroethane was treated with triethyloxonium fluoroborate (28. 9 g) in 40 mL of the same solvent at room temperature. The cloudy solution became clear (~20 min), deposited a precipitate after several hours, and was stored for 30 h at ambient temperature. The (+)-methoxyamino alcohol (30.3 g) was added neat and the mixture heated at reflux for 48 h after whch the cooled mixture was poured into saturated bicarbonate, the layers separated, dried, and concentrated to give 53 g of crude **4**. Chromatography (silica gel, 30% ethyl acetate–hexane) produced a colorless clear oil, 75% yield.

(14) Cram, D. J.; Wilson, J. *J. Am. Chem. Soc.*, following paper in this issue. We thank Professor Cram and Ms. Wilson for assisting us in making this correlation. It should be noted that the absolute configuration for (−)-**10** was concluded to be *S* by Berson (Berson, J. A.; Greenbaum, M. A. *J. Am. Chem. Soc.* **1958**, *80*, 653) and Yamada (Akimoto, H.; Yamada, S. *Tetrahedron* **1971**, *27*, 5999) on the basis of studies of a different kind. However, the configurations assigned by these authors now should be changed to *R*(−) in methanol and *R*(+) in THF. A recent report by Yamaguchi (*Tetrahedron Lett.* **1981**, 659) also notes that the original assignment is in error but gives no details.

(15) Fitts, D. D.; Siegal, M.; Mislow, K. *J. Am. Chem. Soc.* **1958**, *80*, 480. We are grateful to Professor Mislow for supplying us with a sample of the enantiometrically pure 2,2′-bis(bromomethyl)-1,1′-binaphthyl from which we were able to prepare (*S*)(+)-**13**.

(16) Kyba, E. P.; Gokel, G. W.; deJong, F.; Koga, K.; Sousa, L. R.; Siegal, M. G.; Kaplan, L.; Sogah, G. D. Y.; Cram, D. J. *J. Org. Chem.* **1977**, *42*, 4173. We thank Professor Cram for an authentic sample of (*S*)(−)-**17** for CD comparison purposes.

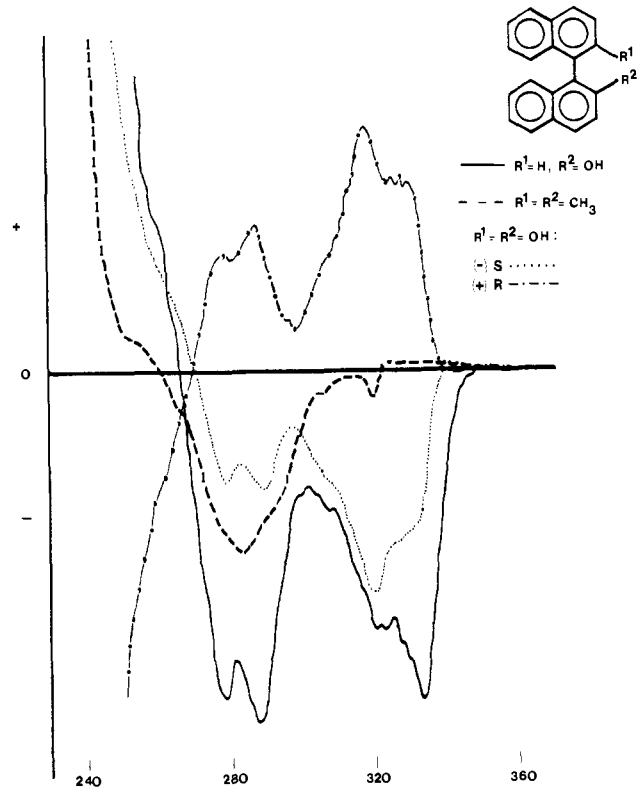


Figure 2. CD spectra in dioxane.

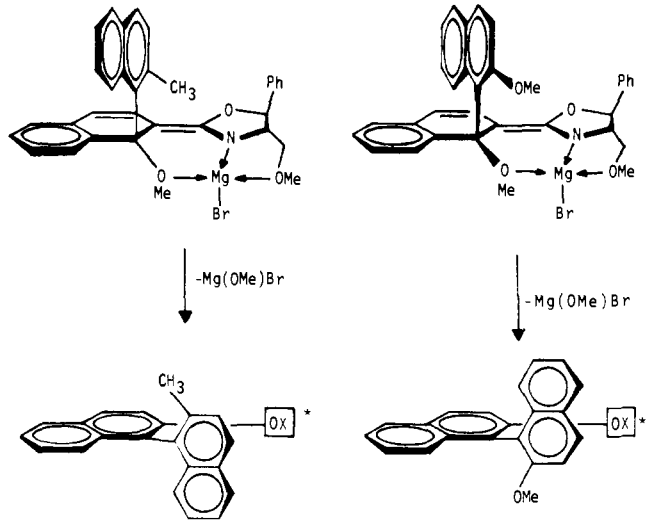


Figure 3.

MeOH) to the hydroxy ether **16**.[17] Cleavage, using boron tribromide (−78 °C, CH_2Cl_2), gave the (*R*)(+)-diol **17** which exhibited virtually mirror image Cotton curves with the (*S*)(−) enantiomer (Figure 2). The optical rotation of (+)-**17**, when compared to the known rotation of (−)-**17**, indicated ~100% ee, once again the result of enantiomeric enrichment in going from **5** (R = MeO) to **7** (R = MeO) (Table I). The absolute configurations of **7** (R = H, Me, MeO) and **13** were further substantiated from their CD spectra (Figure 1).

A preliminary rationalization of the sense of asymmetric coupling (**4** → **5**) can be advanced by examining the initially formed adducts (Figure 3), which after loss of Mg(OMe)Br leads to the observed chiral binaphthyls **5**. For the H and Me substituted systems, the approach of the naphthalene Grignard reagent will be most accessible with the unsubstituted ring at the maximum distance from the 5-phenyl substituent in the oxazoline. For the methoxy-substituted naphthalene, chelation with the magnesium appears to override the steric effect and leads to the observed opposite configuration. Further experiments will need to be performed in order to gain additional insight into this process.

Acknowledgment. Financial assistance by the Army Research Office and the National Science Foundation is gratefully acknowledged.

Registry No. 1, 883-21-6; **2**, 80409-51-4; **3**, 80409-53-6; **4**, 80409-54-7; **5** (R = H) isomer 1, 80409-55-8; **5** (R = H) isomer 2, 80409-56-9; **5** (R = Me) isomer 1, 80409-57-0; **5** (R = Me) isomer 2, 80409-58-1; **5** (R = MeO) isomer 1, 80409-59-2; **5** (R = MeO) isomer 2, 80409-60-5; **6** (R = H) isomer 1, 80409-61-6; **6** (R =H) isomer 2, 80446-25-9; **6** (R = Me) isomer 1, 80409-62-7; **6** (R = Me) isomer 2, 80446-26-0; **6** (R = MeO) isomer 1, 80409-63-8; **6** (R = MeO) isomer 2, 80446-27-1; **7** (R = H), 80409-64-9; **7** (R = Me), 80409-65-0; **7** (R = MeO), 80409-66-1; **8**, 80409-67-2; **9**, 80409-68-3; **10**, 35216-79-6; **11**, 80317-68-6; **12**, 80409-69-4; **13**, 32587-64-7; **14**, 80409-70-7; **15**, 80409-71-8; **16**, 79547-82-3; **17**, 18531-94-7; (+)-1-methoxy-2-amino-3-phenyl-3-hydroxypropane, 51594-34-4.

(17) Jacques and Fouquey, (Jacques, J.; Fouquey, C. *Tetrahedron Lett.* **1971**, 4617) report that (−)-**16** possesses the *S* configuration.

Chiral Leaving Groups Induce Asymmetry in Syntheses of Binaphthyls in Nucleophilic Aromatic Substitution Reactions[1]

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The binaphthyl unit has enjoyed extensive use in the design and syntheses of chiral hosts for resolving amino acids by complexation[2], of chiral catalysts for organic carbon–carbon[3] or carbon–hydrogen[4] bond-making reactions, and of chiral reagents for reducing ketones to optically active alcohols.[5] The degrees of chiral recognition, induction, and transfer observed for these binaphthyl compounds have been among the highest reported and have been attributed to the rigidity and freedom from conformational ambiguity in the complexes or transition states involved.[2-5] In some cases, the direction of the configurational bias has been rationalizable on stereoelectronic grounds.[2-5] These facts stimulated our search for methods of synthesizing optically active substituted binaphthyl compounds that avoid classical resolution methods. 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. The results provide the first examples of asymmetric induction by chiral leaving groups in nucleophilic substitution reactions at carbon.[6]

The 4,4-dimethyl-Δ^2-oxazoline (a masked carboxyl group that Meyers has developed so successfully)[7] was selected as the ac-

(1) (a) This paper is dedicated to the memory of Professor F. Sörme for his contributions and devotion to chemical science. (b) The authors warmly thank the National Science Foundation for Grant NSF 80-00044, which supported this research.

(2) (a) Peacock, S. C.; Walba, D. M.; Gaeta, F. C. A.; Helgeson, R. C.; Cram, D. J. *J. Am. Chem. Soc.* **1980**, *102*, 2043–2052. (b) Lingenfelter, D. S.; Helgeson, R. C.; Cram, D. J. *J. Org. Chem.* **1981**, *46*, 393–406.

(3) (a) Cram, D. J.; Sogah, G. D. Y. *J. Chem. Soc., Chem. Commun.* **1981**, 625–628. (b) Mazaleyrat, J.-P.; Cram, D. J. *J. Am. Chem. Soc.* **1981**, *103*, 4585–4586.

(4) (a) Miyashita, A.; Yasuda, A.; Takaya, H.; Toriumi, K.; Ito, T.; Souchi, T.; Noyori, R. *J. Am. Chem. Soc.* **1980**, *102*, 7932–7934. (b) Miyano, S.; Nawa, M.; Hashimoto, H. *Chem. Lett.* **1980**, 729–730.

(5) Noyori, R.; Tomino, I.; Tanimoto, Y. *J. Am. Chem. Soc.* **1979**, *101*, 3129–3133.

(6) Asymmetric induction by chiral leaving groups in nucleophilic substitution reactions at elements other than carbon have been reported. For example, for nucleophilic substitution reactions on tin, see: (a) Folli, U.; Iarossi, D.; Taddei, F. *J. Chem. Soc., Perkin Trans. 2* **1973**, 638–642. (b) Lequan, R. M.; Lequan, M. *Tetrahedron Lett.* **1981**, 1323–1326.

(7) (a) Meyers, A. I.; Gable, R.; Mihelich, E. D. *J. Org. Chem.* **1978**, *43*, 1372–1379. (b) Meyers, A. I.; Williams, B. E. *Tetrahedron Lett.* **1978**, 223–226.

0002-7863/82/1504-0881$01.25/0