Nucleophilic Aromatic Substitution on 1-Alkoxy-2-naphthoates with 1-Naphthyl Grignard Reagents. A Practical and Convenient Asymmetric Synthesis of 1,1′-Binaphthyl-2-carboxylates

Tetsutaro HATTORI, Hiroki HOTTA, Takatsugu SUZUKI, and Sotaro MIYANO*
Department of Biochemistry and Engineering, Faculty of Engineering, Tohoku University, Aramaki-Aoba, Aoba-ku, Sendai 980

(Received September 29, 1992)

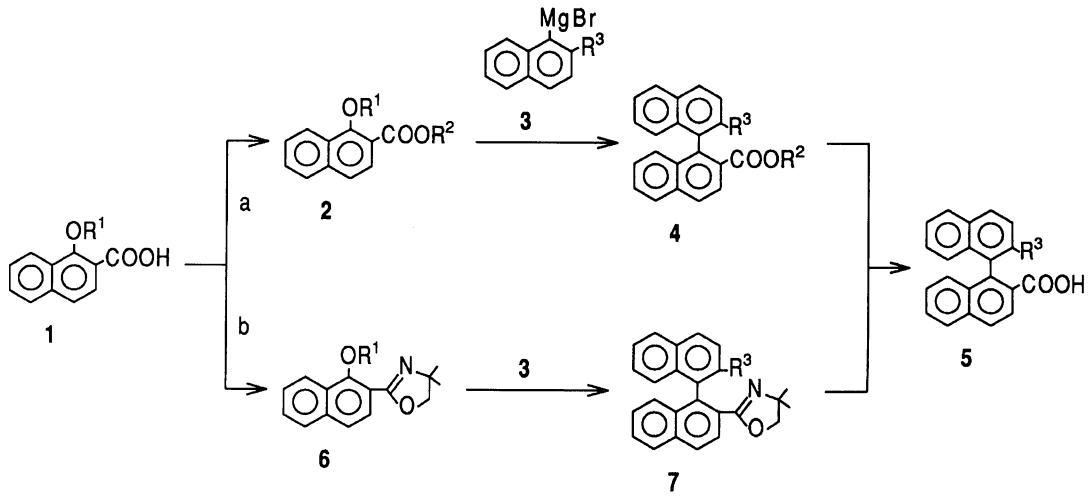
1-Naphthyl Grignard reagents efficiently displace the 1-alkoxyl group of 1-alkoxy-2-naphthoic esters to provide an easy access to the corresponding 1,1′-binaphthyl-2-carboxylates in excellent yields; isopropyl ester is bulky enough to prevent the Grignard addition to the ester carbonyl function. High levels of asymmetric induction (up to 98% optical yield) have been achieved in the joining of the two naphthalene rings by using 1-(*l*-*p*-menth-3-yloxy)-2-naphthoates, while the reaction of chiral alkyl esters of 1-methoxy-2-naphthoic acid proceeded with appreciable to moderate stereoselectivity. The probable reaction mechanisms are discussed for the binaphthyl coupling and the asymmetric induction.

There has been considerable recent interest in the use of atropisomeric 1,1′-binaphthyl skeleton as the chirality-recognizing element for a wide range of asymmetric reactions and chiral recognitions.[1,2] Consequently, obtainment of the prerequisite optically active 1,1′-binaphthyl derivatives has been the objective of many research laboratories.[3,4] We have mentioned the importance of 1,1′-binaphthyl-2-carboxylic acids as the starting material for elaboration of various atropisomeric 1,1′-binaphthyls.[5] In 1982, Meyers and Lutomski,[6] and Wilson and Cram[7] reported an elegant method for the construction of 1,1′-binaphthyl structure via the nucleophilic substitution on 2-oxazoline-activated 1-alkoxynaphthalenes, e.g. **6**, by a naphthyl Grignard (**3**) or lithium reagent to give 2-(1,1′-binaphthyl-2-yl)oxazolines **7**, which are latent binaphthyl-2-carboxylic acids **5** (the Meyers reaction) (Scheme 1, path b). The 2-oxazolinyl substituent serves activation of the 1-alkoxyl group to the nucleophilic aromatic substitution (S_NAr) as well as protection of the carboxylic function from the nucleophilic attack of the organometallic species. Asymmetric induction in the binaphthyl coupling is realized by the use of a chiral oxazolinyl moiety[6] or chiral leaving alkoxyl group.[7] However, both transformation of the starting 1-alkoxy-2-naphthoic acid **1** into the oxazoline **6** and regeneration of the carboxylic acid **5** from the sterically congested binaphthylyloxazoline **7** require rather troublesome manipulations.

In the course of our continuing efforts to exploit convenient routes for construction of axially dissymmetric binaphthyl framework,[5,8] we found that 1-alkoxy-2-naphthoates **2** smoothly react with 1-naphthyl Grignard reagents **3** to give the 1,1′-binaphthyl-2-carboxylates **4** in excellent yields (Scheme 1, path a).[9] This means that the oxazolinyl functionality in the Meyers reaction can be replaced by trivial ester group, which is far more easily prepared and hydrolyzed than the former. Furthermore, it has been found that *C*-centro-chirality of the 1-alkoxyl or the 2-alkoxycarbonyl group of the 2-naphthoate substrates **2** induces asymmetric coupling of the two naphthalene rings with up to 98% optical yield. Herein, we report the details of the convenient synthesis of 1,1′-binaphthyl-2-carboxylates and present plausible mechanisms for the binaphthyl coupling and asymmetric induction.

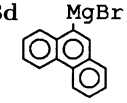
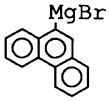
Results and Discussion

Synthesis of 1,1′-Binaphthyl-2-carboxylates. It is well known that the reaction of a Grignard reagent with esters is one of the most established routes to tertiary alcohols.[10,11] Thus, it was at first an unexpected result when we obtained methyl 1,1′-binaphthyl-2-carboxylate **4b** as the major product from the reaction of methyl 1-methoxy-2-naphthoate **2a** with an excess amount of 1-naphthylmagnesium bromide **3b** (Table 1, Run 3). As obviously the reaction was of potential importance for the construction of 1,1′-binaphthyl framework, we investigated in some detail the reaction variables to promote the binaphthyl coupling (Table 1). The reaction of the methyl ester **2a** with **3** of varying steric bulk is indicative: Sterically crowded Grignard reagents (**3c** and **3d**) gave the desired products **4** in good yields (Runs 4 and 5). On the other hand, treatment of **2a** with **3a** and **3b** afforded **4** in moderate yields, but accompanied the formation of appreciable amounts of binaphthyl naphthyl ketones **9** (Chart 1). The formation of **9** can be rationalized by the initial addition of **3** to the ester carbonyl of **2** to form a 1-methoxy-2-naphthyl 1-naphthyl ketone **8**, which in turn undergoes the S_NAr reaction to **9**.[12] It is interesting that coordination of the *ortho*-methoxyl group of **3a** to the magnesium center seems to expel part of the solvating ethyl ether to reduce the apparent bulk of the carbanion species to facilitate the carbonyl attack (Run 1).[13,14] Addition of a catalytic amount of bis(triphenylphosphine)nickel dichloride did not improve the reaction of **3a** with **2a** to give the coupling product **4a** (Run 2), though Grignard cross coupling with aryl halides in the presence of nickel-phosphine complexes is well documented (the Kumada-Tamao reaction).[4,15]



Scheme 1.

Table 1. Synthesis of 1,1′-Binaphthyl-2-carboxylates **4**[a]

Run	2 R^2	3 R^3	4 Yield/%[b]
1	**2a** CH_3	**3a** OCH_3	**4a** 50
2			47[c]
3		**3b** H	**4b** 52
4		**3c** CH_3	**4c** 90[d]
5		**3d** 	**4d** 85
6	**2b** Pr^i	**3a** OCH_3	**4e** 87
7		**3b** H	**4f** 93
8		**3c** CH_3	**4g** 82
9		**3d** 	**4h** 91

a) Reaction conditions: **2**, ca. 1.8 mmol; **3**/**2** = 1.8 (mol/mol). Reactions were carried out in Et_2O (10—15 ml)–PhH (15 ml) at ambient temp (3 h) and then heated at reflux (2 h). b) Isolated yield. c) $NiCl_2(PPh_3)_2$ (3 mol%) was added. d) Contains about 15% of **9** ($R^3 = CH_3$) (see Experimental).

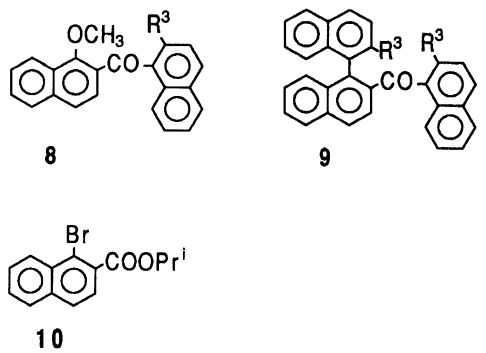


Chart 1.

It can be seen that isopropyl ester **2b** is bulky enough to almost completely prevent the ester carbonyl attack by the 1-naphthyl carbanion species **3**, giving the coupling products in excellent yields (Runs 6—9). It should be noted that isopropyl 1-bromo-2-naphthoate **10** remained intact by treatment with **3a** (vide infra), though halides should be better leaving group than alkoxides in common nucleophilic substitution reactions.

Close scrutiny of the literature revealed that Fuson and Wassmundt reported the prototype of the Grignard coupling reaction in as early as 1956 in which phenyl 2-methoxy-1-naphthoate reacted with aryl Grignard reagents to give the corresponding phenyl 2-aryl-1-naphthoates.[16] In spite of the potential importance of the reaction not only as an aryl-aryl coupling methodology but also as an unusual Grignard reaction, the Fuson's reaction has only rarely appeared in scattered papers.[17]

Asymmetric Induction in the Binaphthyl Coupling by the Use of Chiral Alkoxycarbonyl Moiety. Before describing the results of the asymmetric binaphthyl coupling, we would like to define *p* and *m* designation as depicted in Fig. 1 just for sake of convenience to clearly show the direction of the twist of the two naphthalene rings, because it varies in terms of the conventional a*R* and a*S* designation depending on the substituents on the rings.[18]

Table 2 lists the results of the reaction of enantiomeric *l*-*p*-menth-3-yl (**2c**) or (*S*)-1-phenylethyl 1-methoxy-2-naphthoate **2d** with 1-naphthyl Grignard reagents **3**; both of the esters afforded the coupling products **4** in excellent yields. Although the chiral center is lo-

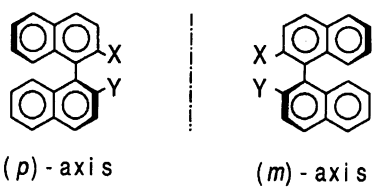
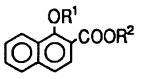
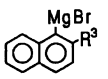
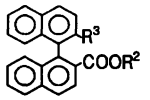
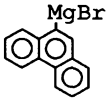
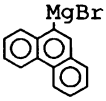
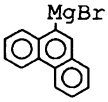


Fig. 1. Designation of (*p*)- and (*m*)-axis.

Table 2. Asymmetric Synthesis of 1,1′-Binaphthyl-2-carboxylates **4**[a)]

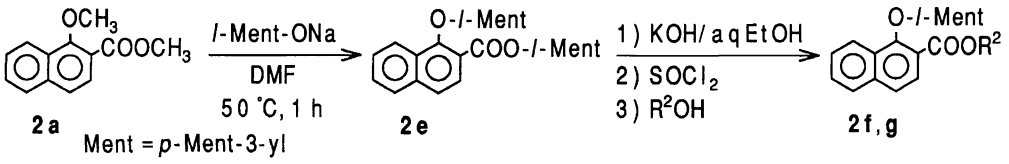
	 **2**[b)]			 **3**		 **4**			
Run		R^1	R^2		R^3		Yield[c)] %	Opt.Yield[d)] %	Config. of axis
10	**2c**	CH_3	*l*-Ment	**3a**	OCH_3	**4i**	88	10	a*R*(*m*)
11				**3b**	H	**4j**	86	4	a*R*(*p*)
12				**3c**	CH_3	**4k**	99	9	a*S*(*m*)
13				**3d** 		**4l**	91	5	a*S*(*m*)
14	**2d**	CH_3	(*S*)-Phen	**3a**	OCH_3	**4m**	92	51	a*R*(*m*)
15							74	56[e)]	a*R*(*m*)
16				**3b**	H	**4n**	96	28	a*R*(*p*)
17				**3c**	CH_3	**4o**	93	20	a*R*(*p*)
18				**3d** 		**4p**	95	49	a*R*(*p*)
19	**2e**	*l*-Ment	*l*-Ment	**3a**	OCH_3	**4i**	81	98	a*S*(*p*)
20				**3b**	H	**4j**	93	76	a*S*(*m*)
21				**3d** 		**4l**	78	59	a*S*(*m*)
22	**2f**	*l*-Ment	Pr^i	**3a**	OCH_3	**4e**	92	97	a*S*(*p*)
23				**3b**	H	**4f**	95	80	a*S*(*m*)
24				**3d** 		**4h**	55	65	a*S*(*m*)
25	**2g**	*d*-Ment	(*S*)-Phen	**3a**	OCH_3	**4m**	85	91	a*R*(*m*)
26				**3b**	H	**4n**	74	91	a*R*(*p*)
27	**2h**	*l*-Born	*l*-Born	**3a**	OCH_3	**4q**	71	10	a*R*(*m*)

a) Reaction conditions are similar to those in Table 1. b) Ment = *p*-Menth-3-yl; Phen = 1-Phenylethyl; Born = 2-Bornyl. c) Isolated yield. d) As for determination of the optical yield and absolute configuration, see Experimental. e) Reaction was carried out at 0°C for 12 h.

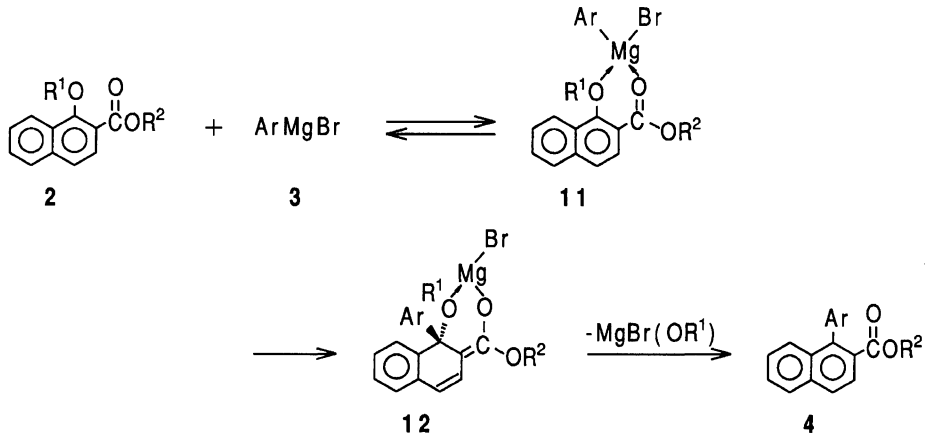
cated rather remote from the reaction site, chiral alkoxycarbonyl moiety of **2d** induced appreciable to moderate bias in the formation of atropisomeric binaphthyl axis with up to 56% optical yield.[19)] Absolute stereochemistry of the binaphthylcarboxylic acids except 1-(9-phenanthryl)-2-naphthoic acid **5a** has already been reported in the literature.[7)] The absolute configuration of **5a** was first assigned as (a*S*)-(−) based on the ^{1}H NMR study of the 1-phenylethyl ester,[9b)] but it should be revised herein as (a*R*)-(−) by an X-ray crystallographic analysis carried on a single crystal of the amide prepared from (−)-**5a** and (−)-2,10-camphorsultam ([3a*S*-(3aα,6α,7aβ)]-hexahydro-8,8-dimethyl-3*H*-3a,6-methano-2,1-benzisothiazole-2,2-dioxide).[20)]

It is seen that the chirality of the ester alkyl moiety does not solely determine the direction of the preferentially induced binaphthyl axis: The reaction of **3a** with *l*-*p*-menth-3-yl ester **2c**, which had (*R*)-chirality at the C_1 center, induced (*m*)-axis (Run 10), while the reaction with **2d**, which had (*S*)-C_1 center, also preferred (*m*)-axis (Run 14). Moreover, attacking Grignard reagent also affected the direction of the binaphthyl axis as is seen by comparing the reactions of **3a** and **3b** with **2d** (Runs 14 and 16) (vide infra).

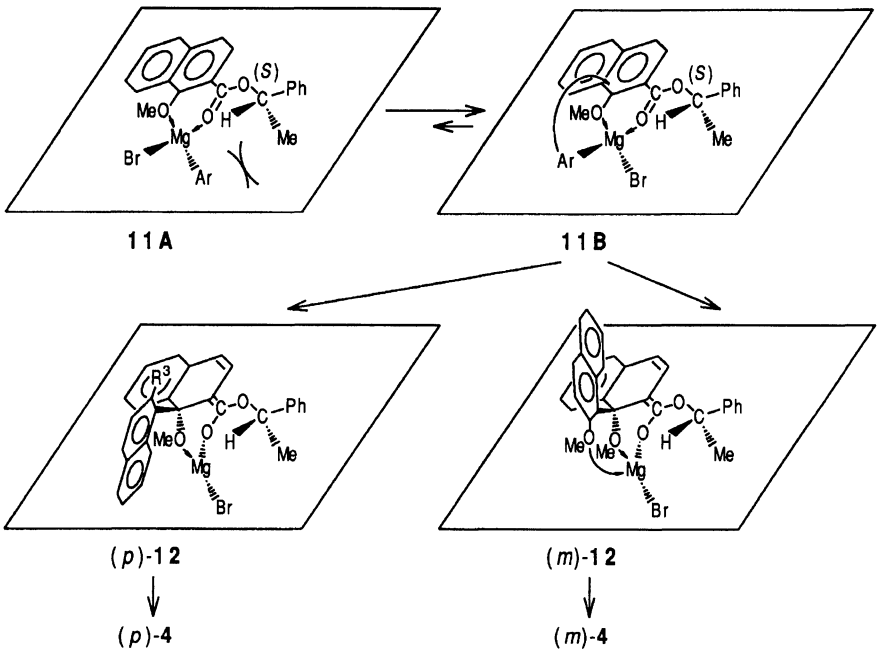
Preparation and Reaction of 1-(Chiral Alkoxy)-2-naphthoates 2e—2h. It is not an easy task to introduce enantiomerically pure alkoxyl group into an aromatic nucleus.[7)] The binaphthyl coupling disclosed above (Scheme 1, path a) corresponds to a nucleophilic substitution on **2** with naphthyl carbanion species. It is of quite interest whether other nucleophiles than naphthyl Grignards can enter into the S_NAr reaction to displace the 1-methoxyl group from **2**, a process without precedent.[21,22)] To our pleasure, treatment of



Scheme 2.



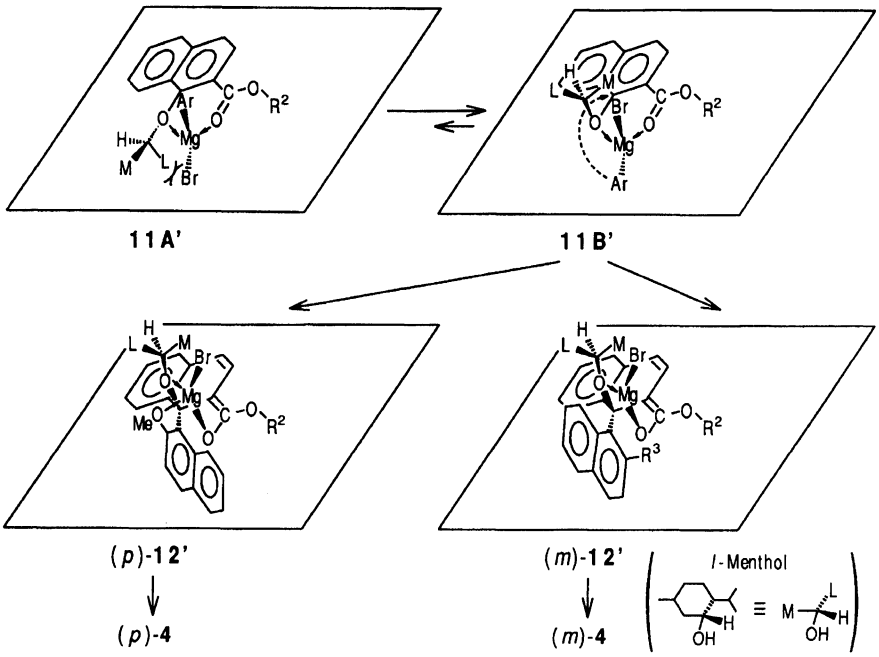
Scheme 3.



Scheme 4.

sodium *l*-*p*-menthoxide in dimethylformamide (DMF) with **2a** under rather mild conditions readily induced not only transesterification but also displacement of the 1-methoxyl group to give *l*-*p*-menth-3-yl 1-(*l*-*p*-menth-3-yloxy)-2-naphthoate **2e** in good yield (Scheme 2). Conversion of **2e** into other alkyl naphthoates is simple and straightforward. Similar treatment of **2a** with *l*-2-bornoxide gave *l*-2-bornyl 1-(*l*-2-bornyloxy)-2-naphthoate **2h**.

Table 2 also contains the results of the reaction of 1-(chiral alkoxy)-2-naphthoates **2e**—**2h** with **3**. Good to excellent asymmetric induction was achieved by the use of 1-*l*-*p*-menth-3-yloxyl as the leaving group, while the reaction of 1-(*l*-2-bornyloxy)-2-naphthoate **2h** gave poor stereoselectivity (Run 27). It should be noted that the reaction of *l*-*p*-menth-3-yl 1-(*l*-*p*-menth-3-yloxy)-2-naphthoate **2e** with 2-methoxy-1-naphthylmagnesium bromide **3a**, which can readily be carried out in practically preparative scale, proceeded with high stereoselectivity of 98% optical yield to give **4i** (Run 19), and that alkaline hydrolysis followed by a single crystalliza-



Scheme 5.

tion from ethanol gave practically enantiomerically pure (a*S*)-2′-methoxy-1,1′-binaphthyl-2-carboxylic acid **5b** as judged by HPLC on a chiral column. The utility of **5b** as a chiral derivatizing agent[23] or a starting material for elaboration of axially dissymmetric binaphthyls[24] has been demonstrated.

It can be seen that the 1-(*l-p*-menth-3-yloxyl) leaving group mainly determines the axial bias rather than the 2-alkoxycarbonyl substituent (compare Run 19 with Run 22). Here again, the effect of the stereochemistry of the 1-alkoxyl as well as the 2-alkoxycarbonyl group was not uniform to induce the axial bias. Thus, the effect of 2-[(*S*)-1-phenylethoxycarbonyl] group (cf., Run 16) and 1-(*d-p*-menth -3-yloxyl) moiety (cf., Run 23) to promote the (*p*)-axis coupling was advantageously tuned up to improve the optical yield (Run 26), but the result of the reaction of **2g** with **3a** was somewhat disappointing (compare Run 25 with Run 22).

Mechanistic Consideration of the Binaphthyl Coupling and Asymmetric Induction. Scheme 3 illustrates a probable mechanism for the binaphthyl coupling, which is deduced from the Meyers reaction[6,7b] by replacing oxazoline for alkoxycarbonyl function as the activating group for the S_NAr process. The importance of ligation of the 1-alkoxyl leaving group to the magnesium center is evident from the fact that **10** does not react with **3a**. Sterically crowded Grignard reagent **3c** did not react with isopropyl 1-(*l-p*-menth-3-yloxy)-2-naphthoate **2f**, showing that the steric balance among R^1, R^2, and attacking carbanion species **3** is also important for the coupling to occur.

The moderate to excellent optical yields in the coupling of 1-phenylethyl 1-methoxy-2-naphthoate **2d** and 1-(*l-p*-menth-3-yloxy)-2-naphthoates with **3** may deserve to consider steric models for the asymmetric induction. The Prelog generalization[25] suggests that the naphthyl Grignard carbanion will preferentially approach to (*S*)-**2d** from the upper side of the relevant naphthalene plane as depicted in Scheme 4. Then, steric repulsion between the two naphthalene rings will lead to the crucial intermediate (*p*)-**12** for the reagents **3b**, **3c**, and **3d**. In case of **3a**, however, ligation of the 2-methoxyl group to magnesium will override the steric repulsion between the naphthalene rings to prefer the intermediate (*m*)-**12**. The intermediate (*p*)- and (*m*)-**12** will lead to the (*p*)- and (*m*)-axis of the coupling products **4**, respectively. At the present time, however, no meaningful correlational models can be drawn from the reaction of *p*-menth-3-yl ester **2c** with **3** because of the poor optical yields and too many conformational alternatives of the 2-(*l-p*-menth-3-yloxycarbonyl) auxiliary (Run 10—13).

CPK molecular models indicate that the *l-p*-menthyl moiety of 1-(*l-p*-menth-3-yloxy)naphthoates locates either upper or lower side of the naphthalene plane to avoid the steric repulsion. Scheme 5 illustrates that the naphthyl Grignard carbanion will approach from the lower side of the naphthalene plane of a 1-(*l-p*-menth-3-yloxy)-2-naphthoate **2** to avoid the steric repulsion between the *l-p*-menthyloxyl group and **3**. Here again, paths to the crucial intermediates **12′** will be determined by the steric repulsion between the two naphthalene rings or by the ligation of the 2-methoxyl group of **3** to magnesium as above. The presence of the chiral center in the close vicinity of the reaction site in the rather tightly packed transient complex **11** may explain the high asymmetric induction. On the other hand, bornyl group is rather spherical, and seems not to provide effective dissymmetry to the substrate 2-naphthoate **2h**.

In conclusion, we have shown here highly efficient method for the construction of 1,1′-binaphthyl structure by the reaction of readily available 1-alkoxy-2-naphthoates with 1-naphthyl Grignard reagents, and its application for the asymmetric synthesis of the atropisomeric binaphthyls. The present method rivals well the Meyers oxazoline route considering the simplicity of the reaction procedure, excellent yield, and high levels of stereoselectivity.

Experimental

Measurements. IR spectra were measured on a Shimadzu IR-430 grating spectrophotometer. ^{1}H NMR spectra were recorded on a JEOL JNM-FX60 instrument using tetramethylsilane as internal standard. Mass spectra were recorded on a JEOL JMS-D300 double focusing mass spectrometer with direct sample injection. Optical rotations were recorded on a Union PM-101 automatic digital polarimeter in a 1-cm cell or a Perkin–Elmer 241 electronic polarimeter in a 10-cm cell. HPLC was carried out on a Shimadzu LC-5A with UV detection at 254 nm. Stainless-steel columns (0.46 cm i.d.×25 cm) were packed with Hitachi Gel 3056 for the silica-gel column and with 3-aminopropylsilanized silica modified with (*R*)-*N*-(3,5-dinitrobenzoyl)-phenylglycine for the chiral column (Pirkle column). Microanalyses were carried out in the Microanalytical Laboratory of the Institute for Chemical Reaction Science, Tohoku University. Melting points were measured on a Yamato MP-21 apparatus and were uncorrected.

Materials. Merck silica gel 60GF$_{254}$ was used for analytical and preparative TLC. Silica-gel columns were prepared by use of Nacalai silica gel 60 (70—230 mesh). Ethyl ether and benzene were distilled from sodium diphenylketyl just before use. Other solvents for experiments requiring anhydrous conditions were purified by usual methods. Commercial materials were used as purchased unless otherwise noted. Sodium hydride (60 wt% in mineral oil) was washed free of oil with hexane before use. 1-Bromo-2-methylnaphthalene was purified according to the literature (bp 120—126°C/1.3 mmHg #).[4] 1-Bromonaphthalene and 9-bromophenanthrene were stored in a silica-gel desiccator. 1-Bromo-2-methoxynaphthalene was synthesized according to the literature procedure.[26] Water- and air-sensitive reactions were routinely carried out under a nitrogen atmosphere.

Preparation of 1-Alkoxy-2-naphthoates 2. Methyl 1-Methoxy-2-naphthoate (2a): To a vigorously stirred suspension of NaH (21.4 g, 0.892 mol) in DMF (400 ml) was added a solution of 1-hydroxy-2-naphthoic acid (70.0 g, 0.372 mol) in DMF (400 ml) by portions. After the addition was complete, methyl iodide (152 g, 1.07 mol) was added and the mixture was heated at 60°C, and the reaction was monitored by TLC. After 3 h, additional NaH (4.03 g, 0.168 mol) and methyl iodide (79.6 g, 0.561 mol) were added and the resulting mixture was heated for further 1 h. The cooled mixture was poured into 400 ml of 2 M ## HCl and extracted several times with ethyl ether. The combined ether extracts were washed successively with 2 M HCl, 2 M Na_2SO_3, 2 M Na_2CO_3, and water and dried over $MgSO_4$. After the solvent was evaporated, the residue was distilled under reduced pressure (bp 107—112°C/0.4 mmHg (lit,[27] 193—195°C/17 mmHg)) to give 71.3 g of **2a** as a pale yellow oil (89%); IR (liq. film) 1721 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=3.96 (3H, s, $COOCH_3$), 4.05 (3H, s, OCH_3), and 7.20—8.38 (6H, m, Ar-H).

Isopropyl 1-Methoxy-2-naphthoate (2b): **2a** (20.5 g, 94.8 mmol) was boiled with KOH (12.0 g) in ethanol (100 ml) and water (10 ml) for 1 h. After most of the ethanol was removed under reduced pressure, the residue was dissolved in water and washed with ethyl ether. The aqueous layer was acidified by addition of concd HCl to liberate the free acid as a white precipitate. It was collected by filtration, washed with water, and then dried in vacuo to give 17.1 g of 1-methoxy-2-naphthoic acid **13a** (89%); mp 126—128°C (lit,[27] 126—127°C); IR (KBr) 2930 and 1688 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=4.16 (3H, s, OCH_3) and 7.22—8.27 (6H, m, Ar-H).

Then, 17.1 g of **13a** (84.6 mmol) was heated under reflux for 3 h in thionyl chloride (40 ml) and volatiles were removed under reduced pressure. The acid chloride was dissolved in dry benzene (100 ml) and added to a mixture of 2-propanol (65 ml, 853 mmol), 4-dimethylaminopyridine (DMAP) (3.00 g), benzene (30 ml), and pyridine (10 ml). Then the mixture was heated under reflux for 3 h. To the cooled mixture was added 0.1 ml of 3-(dimethylamino)propylamine. The mixture was washed successively with 2 M HCl, 2 M Na_2CO_3, and water and dried over $MgSO_4$. After volatiles were evaporated, the residue was distilled under reduced pressure to give 17.7 g of **2b** as a pale yellow oil (86%); bp 138—139°C/0.4 mmHg; IR (liq. film) 1715 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.42 (6H, d, J=6.15 Hz, CH_3), 4.06 (3H, s, OCH_3), 5.34 (1H, sept, J=6.15 Hz, COOCH), and 7.30—8.80 (6H, m, Ar-H). Found: C, 73.44; H, 6.60%. Calcd for $C_{15}H_{16}O_3$: C, 73.75; H, 6.60%.

***l*-*p*-Menth-3-yl 1-Methoxy-2-naphthoate (2c):** 1-Methoxy-2-naphthoyl chloride prepared from 13.3 g of **13a** (65.8 mmol) was treated with *l*-menthol (20.5 g, 131 mmol) in benzene–pyridine in the presence of 8.00 g of DMAP. Chromatography on a silica-gel column with benzene as the eluent gave 21.7 g of **2c** as a pale yellow oil (97%); $[\alpha]_D^{16}$ −59° (*c* 1.08, $CHCl_3$); IR (liq. film) 1720 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.50—2.40 (18H, m, menthyl-H), 4.05 (3H, s, OCH_3), 4.63—5.28 (1H, m, COOCH), and 7.20—8.37 (6H, m, Ar-H). Found: C, 77.98; H, 8.31%. Calcd for $C_{22}H_{28}O_3$: C, 77.61; H, 8.29%.

(*S*)-l-Phenylethyl 1-Methoxy-2-naphthoate (2d): **2d** was prepared by a similar procedure to that used for **2b**. 1-Methoxy-2-naphthoyl chloride prepared from 5.46 g of **13a** (27.0 mmol) was treated with (*S*)-(−)-1-phenylethanol (2.82 g, 23.1 mmol) in benzene–pyridine in the presence of 3.00 g of DMAP under reflux for 6 h and worked up as above. Distillation gave 6.13 g of **2d** as a pale yellow oil (87% based on 1-phenylethanol); bp 160—161°C/0.02 mmHg; $[\alpha]_D^{25}$ +41° (*c* 1.18, $CHCl_3$); IR (liq. film) 1722 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.71 (3H, d, J=6.60 Hz, CH_3), 3.99 (3H, s, OCH_3), 6.20 (1H, q, J=6.60 Hz, COOCH), and 7.22—8.32 (11H, m, Ar-H). Found: C, 78.52; H, 5.82%. Calcd for $C_{20}H_{18}O_3$: C, 78.41; H, 5.92%.

***l*-*p*-Menth-3-yl 1-(*l*-*p*-Menth-3-yloxy)-2-naphthoate (2e):** A mixture of NaH (10.3 g, 429 mmol) and *l*-menthol (78.0 g, 499 mmol) was heated at 65°C under

1 mmHg =133.322 Pa.
1 M=1 mol dm^{-3}.

nitrogen; gradual dissolution of the menthol and evolution of hydrogen indicated the formation of sodium menthoxide. During the time course, the mixture solidified, which was melted by warming to 90°C, and the reaction was continued until hydrogen evolution ceased. The mixture was cooled to 50°C and 65 ml of dry DMF was added with stirring to form a suspension, to which was added **2a** (30.8 g, 142 mmol) and stirring was continued for 1 h at 50°C. The cooled mixture was poured into 250 ml of 2 M HCl and extracted several times with ethyl ether. The combined ether extracts were washed successively with 2 M HCl, 2 M Na_2CO_3, and water and dried over $MgSO_4$. After the solvent was evaporated, the excess menthol was distilled out under reduced pressure (up to 200°C/0.2 mmHg). The residue was recrystallized from ethanol to give 51.3 g of **2e** as colorless crystals (78%); mp 103—104°C; $[\alpha]_D^{24}$ −97° (*c* 1.03, $CHCl_3$); IR (KBr) 1719 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.70—2.92 (36H, m, menthyl-H), 4.13—4.54 (1H, m, OCH), 4.83—5.25 (1H, m, COOCH), and 7.35—8.40 (6H, m, Ar-H). Found: C, 80.11; H, 9.53%. Calcd for $C_{31}H_{44}O_3$: C, 80.13; H, 9.54%.

Isopropyl 1-(*l*-*p*-Menth-3-yloxy)-2-naphthoate (2f): **2e** (10.9 g, 23.5 mmol) was boiled with KOH (11.8 g) in ethanol (100 ml)–water (10 ml) for 10 h. After volatiles were evaporated, the residue was dissolved in water (100ml) – ethyl ether (100 ml) and two layers were separated. The aqueous layer was washed with ethyl ether and acidified by adding concd HCl. It was extracted several times with ethyl ether. The combined extracts were washed with water and dried over $MgSO_4$. After the solvent was evaporated, the residue was recrystallized from acetonitrile to give 6.04 g of 1-(*l*-*p*-menth-3-yloxy)-2-naphthoic acid (**13b**) as colorless crystals (79%); mp 116—117°C; $[\alpha]_D^{15}$ −54° (*c* 1.03, $CHCl_3$); IR (KBr) 2930 and 1693 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.78—2.86 (18H, m, menthyl-H), 4.28—4.88 (1H, m, OCH), 7.51—8.20 (6H, m, Ar-H), and 11.62 (1H, br, COOH). Found: C, 77.30; H, 8.06%. Calcd for $C_{21}H_{26}O_3$: C, 77.27; H, 8.03%.

Esterification of **13b** was performed by a similar procedure used for **13a**. 1-(*l*-*p*-Menth-3-yloxy)-2-naphthoyl chloride prepared from 1.38 g of **13b** (4.23 mmol) was treated with 2-propanol (3.3 ml, 43.3 mmol) in benzene–pyridine in the presence of 0.51 g of DMAP. Chromatography on a silica-gel column eluting with benzene–hexane (1/1) gave 1.23 g of **2f** as a pale yellow oil (79%); $[\alpha]_D^{23}$ −55° (*c* 0.945, $CHCl_3$); IR (liq. film) 1721 cm^{-1}; ^1H NMR ($CDCl_3$) δ= 0.71—2.91 (18H, m, menthyl-H), 1.41 (6H, d, *J*=6.17 Hz, CH_3), 4.13—4.53 (1H, m, OCH), 5.31 (1H, sept, *J*=6.17 Hz, COOCH), and 7.42—8.38 (6H, m, Ar-H). Found: C, 78.15; H, 8.71%. Calcd for $C_{24}H_{32}O_3$: C, 78.22; H, 8.75%.

(*S*)-1-Phenylethyl 1-(*d*-*p*-Menth-3-yloxy)-2-naphthoate (2g): The antipode of **2e**, i.e. *d*-*p*-menth-3-yl 1-(*d*-*p*-menth-3-yloxy)-2-naphthoate was obtained as above by the reaction of **2a** with *d*-menthoxide, and hydrolyzed to give 1-(*d*-*p*-menth-3-yloxy)-2-naphthoic acid. After the acid (1.46 g, 4.47 mmol) was converted to the acid chloride, it was treated with (*S*)-1-phenylethanol (0.51 g, 4.17 mmol) in benzene–pyridine in the presence of 0.50 g of DMAP. Chromatography on a silica-gel column eluting with hexane–benzene (1/1) gave 1.40 g of **2g** as a pale yellow oil (78% based on 1-phenylethanol); $[\alpha]_D^{24}$ +27° (*c* 0.935, $CHCl_3$); IR (liq. film) 1727 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.68—2.83 (18H, menthyl-H), 1.70 (3H, d, *J*=6.60 Hz, CH_3), 3.80—4.28 (1H, m, OCH), 6.19 (1H, q, *J*=6.60 Hz, COOCH), and 7.25—8.36 (11H, m, Ar-H). Found: C, 81.08; H, 8.03%. Calcd for $C_{29}H_{34}O_3$: C, 80.89; H, 7.96%.

***l*-2-Bornyl 1-(*l*-2-Bornyloxy)-2-naphthoate (2h):** To a suspension of NaH (1.55 g, 64.6 mmol) in dry DMF (30 ml) was added *l*-borneol (10.0 g, 64.8 mmol) by portions and stirred at ambient temperature until no hydrogen gas evolved. Then it was heated at 50°C for 1 h, to which was added 4.71 g of **2a** (21.8 mmol). The resulting mixture was heated at 50°C for further 1.5 h. After being cooled to ambient temperature, the mixture was poured into 100 ml of 2 M HCl and extracted several times with ethyl ether. The combined extracts were worked up as usual. After the solvent was evaporated, the residue was chromatographed on a silica-gel column eluting with benzene–hexane (1/1) and recrystallized from ethanol to give 6.16 g of **2h** as colorless crystals (61%); mp 132—133 °C; $[\alpha]_D^{15}$ −52° (*c* 1.08, $CHCl_3$); IR (KBr) 1723 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.80—2.79 (32H, m, bornyl-H), 4.44—4.67 (1H, m, OCH), 5.06—5.30 (1H, m, OCH), and 7.38—8.46 (6H, m, Ar-H). Found: C, 81.09; H, 8.76%. Calcd for $C_{31}H_{40}O_3$: C, 80.83; H, 8.75%.

Synthesis of 1,1′-Binaphthyl-2-carboxylates 4. General procedure for the synthesis of **4** is illustrated by the reaction of **2d** with **3a** to give **4m** as follows.

Asymmetric Synthesis of (*S*)-1-Phenylethyl 2′-Methoxy-1,1′-binaphthyl-2-carboxylate (4m) (Run 14): To 0.12 g of magnesium turnings and 2 ml of dry ethyl ether was added several drops of ethyl iodide under nitrogen and the mixture was irradiated with ultrasound (53 W, 41 kHz) for 10 min. Then the solvent was removed with a syringe and the residue was washed with small portions of ethyl ether. To the activated magnesium was added dropwise a solution of 1-bromo-2-methoxynaphthalene (0.75 g, 3.16 mmol) in ethyl ether (10 ml) over 10 min under ultrasonic irradiation and the mixture was irradiated under gentle reflux for 2 h to give **3a** as a slurry. It was dissolved by addition of 10 ml of dry benzene. The cooled solution was added dropwise to **2d** (0.540 g, 1.76 mmol) in benzene (5 ml) over 5 min. The mixture was stirred at ambient temperature for 3 h and then heated under reflux for 2 h. To the cooled mixture was added 30 ml of 2 M HCl and two layers were separated. After the organic layer was diluted with ethyl ether, it was washed successively with 2 M HCl, 2 M Na_2CO_3, and water and dried over $MgSO_4$. Then volatiles were evaporated and the residue was dried in vacuo to give an oil (947 mg), which was purified by preparative TLC with hexane–ethyl acetate (6/1) as the eluent to give 703 mg of **4m** as an oil[23a] (92%); IR (liq. film) 1702 cm^{-1}; ^1H NMR (C_6D_6) δ=0.68, 0.86 (3H: d, *J*=6.45 Hz, CH_3 (a*R*); d, *J*=6.45 Hz, CH_3 (a*S*)), 3.16, 3.20 (3H: s, OCH_3 (a*R*); s, OCH_3 (a*S*)), 5.79, 5.85 (1H: q, *J*=6.45 Hz, COOCH (a*R*); q, *J*=6.45 Hz, COOCH (a*S*)), and 6.42—8.44 (17H, m, Ar-H); MS (70 eV) *m*/*z* (rel intensity) 432 (M^+; 83), 328 (76), 327 (87), 295 (19), 283 (40), 268 (100), 239 (21), and 105 (26). ^1H NMR in C_6D_6 in the presence of Eu(fod)$_3$ indicated the sample to be 51%de (a*R* rich).[23b] Alkaline hydrolysis of **4m** with KOH in aqueous ethanol gave 2′-methoxy-1,1′-binaphthyl-2-carboxylic acid **5b**, which showed the same IR and ^1H NMR spectra with those of the authentic sample.[5]

Similar reactions gave the following binaphthyls **4**; preparative TLC was used for purification of the products using indicated eluent unless otherwise noted. See Tables 1

and 2 for the yield and stereochemistry of **4**. Binaphthyl esters were substantiated after hydrolysis to the free acids by comparison of IR and ^{1}H NMR spectra with those of authentic samples.[5)]

Racemic 4a (Runs 1 and 2): Benzene as the eluent; mp 121—124°C; IR (KBr) 1720 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=3.46 (3H, s, $COOCH_3$), 3.72 (3H, s, OCH_3), and 6.74—8.22 (12H, m, Ar-H); MS (70 eV) *m/z* (rel intensity) 342 (M^+; 100), 268 (25), 239 (13), and 199 (33).

Racemic 4b (Run 3): Benzene as the eluent; oil; IR (liq. film) 1724 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=3.36 (3H, s, $COOCH_3$) and 6.96—8.14 (13H, m, Ar-H); MS (70 eV) *m/z* (rel intensity) 312 (M^+; 100), 281 (39), 253 (31), 252 (49), 250 (13), 126 (18), and 125 (11).

Racemic 4c (Run 4): The reaction mixture was purified by TLC using hexane–benzene (1/1) as the eluent to give **4c** as an oil (90%), which was accompanied by hardly separable **9** (R^3=CH_3) (ca. 15% by ^{1}H NMR). Spectral data of the mixture: IR (liq. film) 1739 and 1651 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.75 (s, CH_3 (**9**)), 1.95 (s, CH_3 (**9**)), 2.02 (s, CH_3 (**4c**)), 3.41 (s, $COOCH_3$), and 6.76—8.18 (m, Ar-H).

Racemic 4d (Run 5): Benzene as the eluent; glass; IR (KBr) 1716 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=3.31 (3H, s, $COOCH_3$) and 6.72—8.70 (15H, m, Ar-H); MS (70 eV) *m/z* (rel intensity) 362 (M^+; 100), 331 (28), 303 (23), 302 (36), 300 (13), 151 (17), and 150 (17).

Racemic 4e (Run 6): Hexane–ethyl acetate (4/1) as the eluent; mp 104—114°C; IR (KBr) 1700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.50 (3H, d, J=6.15 Hz, CH_3), 0.72 (3H, d, J=6.15 Hz, CH_3), 3.69 (3H, s, OCH_3), 4.77 (1H, sept, J=6.15 Hz, COOCH), and 6.74—8.20 (12H, m, Ar-H); MS (70 eV) *m/z* (rel intensity) 370 (M^+; 100), 328 (42), 269 (13), 268 (24), 239 (15), and 185 (25).

Optically Active 4e (Run 22): Hexane–ethyl acetate (4/1) as the eluent; $[\alpha]_D^{24}$ −48° (*c* 1.12, $CHCl_3$); IR and ^{1}H NMR spectra were identical with those of the racemate. Transesterification of **4e** with excess sodium methoxide in dry methanol under reflux afforded optically active **4a**. Optical yield and absolute configuration of the **4a** were determined by HPLC on the Pirkle column eluting with hexane–2-propanol (2%).[23b)]

Racemic 4f (Run 7): Benzene–hexane (2/1) as the eluent; oil; IR (liq. film) 1701 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.51 (3H, d, J=6.15 Hz, CH_3), 0.55 (3H, d, J=6.15 Hz, CH_3), 4.73 (1H, sept, J=6.15 Hz, COOCH), and 6.96—8.31 (13H, m, Ar-H); MS (70 eV) *m/z* (rel intensity) 340 (M^+; 100), 298 (69), 281 (21), 253 (45), 252 (61), 250 (13), and 126 (15).

Optically Active 4f (Run 23): Benzene–hexane (2/1) as the eluent; $[\alpha]_D^{23}$ −6.8° (*c* 1.03, $CHCl_3$); IR and ^{1}H NMR spectra were identical with those of the racemate. Optical yield and absolute configuration were determined by the same method as mentioned for **4n** (vide infra).

Racemic 4g (Run 8): Hexane–ethyl acetate (8/1) as the eluent; oil; IR (liq. film) 1701 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.46 (3H, d, J=6.15 Hz, CH_3), 0.67 (3H, d, J=6.15Hz, CH_3), 2.02 (3H, s, Ar-CH_3), 4.75 (1H, sept, J=6.15 Hz, COOCH), and 6.85—8.40 (12H, m, Ar-H); MS (70 eV) *m/z* (rel intensity) 354 (M^+; 100), 312 (51), 295 (15), 294 (22), 293 (25), 267 (23), 266 (19), 265 (29), and 252 (18).

Racemic 4h (Run 9): Benzene–hexane (2/1) as the eluent; oil; IR (liq. film) 1703 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.36 (3H, d, J=6.15 Hz, CH_3), 0.49 (3H, d, J=6.15 Hz, CH_3), 4.71 (1H, sept, J=6.15 Hz, COOCH), and 7.10—9.20 (15H, m, Ar-H); MS (70 eV) *m/z* (rel intensity) 390 (M^+; 100), 348 (48), 331 (16), 303 (27), 302 (38), 300 (13), 151 (12), and 150 (10).

Optically Active 4h (Run 24): Hexane–benzene (2/1) as the eluent; $[\alpha]_D^{24}$ +27° (*c* 0.985, $CHCl_3$); IR and ^{1}H NMR spectra were identical with those of the racemate. Alkaline hydrolysis of the optically active **4h** afforded (a*S*)-(+)-1-(9-phenanthryl)-2-naphthoic acid **5a**;[20)] $[\alpha]_D^{24}$ +30° (*c* 1.05,THF); IR (KBr) 3045 and 1696 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ=7.08—8.96 (15H, m, Ar-H) and 12.26 (1H, s, COOH). Optical yield was determined to be 65%ee by HPLC on the Pirkle column as the methyl ester of the acid eluting with hexane–2-propanol (1%).

Optically Active 4i (Runs 10 and 19): Benzene–hexane (3/1) as the eluent; IR (KBr) 1687 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.30—2.04 (18H, m, menthyl-H), 3.70, 3.72 (3H: s, OCH_3 (a*R*); s, OCH_3 (a*S*)), 4.14—4.73 (1H, m, COOCH), and 6.68—8.23 (12H, m, Ar-H); MS (70 eV) *m/z* (rel intensity) 466 (M^+; 40), 328 (100), and 185 (12). Optical yields and absolute configurations were determined by HPLC on the silica-gel column eluting with hexane–ethyl acetate (2.5%).[23a)]

Optically Active 4j (Runs 11 and 20): Benzene–hexane (2/1) as the eluent; IR (KBr) 1691 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.32—1.84 (18H, m, menthyl-H), 4.00—4.82 (1H, m, COOCH), and 7.03—8.17 (13H, m, Ar-H); MS (70 eV) *m/z* (rel intensity) 436 (M^+; 21), 298 (100), 281 (11), 253 (15), and 252 (22). Optical yields and absolute configurations were determined by the same method as mentioned for **4n** (vide infra).

Optically Active 4k (Run 12): Benzene as the eluent; IR (KBr) 1696 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.35—1.73 (18H, m, menthyl-H), 2.00, 2.04 (3H: s, CH_3), 4.20—4.73 (1H, m, COOCH), and 6.77—8.20 (12H, m, Ar-H); MS (70 eV) *m/z* (rel intensity) 450 (M^+; 33), 312 (100), 265 (11), and 44 (46). Optical yield was determined by ^{1}H NMR by using Eu(fod)$_3$ in C_6D_6. Reduction of **4k** with $LiAlH_4$ afforded (a*S*)-(+)-2-hydroxymethyl-2′-methyl-1,1′-binaphthyl[6a)] (50%); $[\alpha]_D^{25}$ +1.3° (*c* 1.38, CH_3OH, 10-cm cell); IR (liq. film) 3325 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.57 (1H, s, OH), 2.02 (3H, s, CH_3), 4.31 (2H, s, CH_2), and 6.90—8.02 (12H, m, Ar-H).

Optically Active 4l (Runs 13 and 21): Hexane–benzene (2/1) as the eluent; IR (KBr) 1702 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.10—1.64 (18H, m, menthyl-H), 4.12—4.69 (1H, m, COOCH), and 7.00—8.85 (15H, m, Ar-H); MS (70 eV) *m/z* (rel intensity) 486 (M^+; 36), 348 (100), 331 (11), 303 (18), 302 (24), and 44 (19). Optical yields and absolute configurations were determined by the same method as mentioned for **4h**.

Optically Active 4m (Runs 14, 15, and 25): **4m** was obtained from **2d** and **3a** as mentioned in the typical procedure (Run 14). Similar reaction was carried out at 0°C for 12 h to give **4m** in somewhat reduced yield (Run 15). It was also obtained by the reaction of **2g** with **3a** (Run 25). Hexane–ethyl acetate (5/1) was used as the eluent.

Optically Active 4n (Runs 16 and 26): Benzene–hexane (3/2) as the eluent; oil; IR (liq. film) 1703 cm^{-1}; ^{1}H NMR (C_6D_6) δ=0.66, 0.68 (3H: d, J_1=6.76 Hz, CH_3 (a*S*); d, J_2=6.46 Hz, CH_3 (a*R*)), 5.58—5.97 (1H, m, COOCH),

and 6.43—8.38 (18H, m, Ar-H); MS (70 eV) *m/z* (rel intensity) 402 (M^+; 26), 298 (100), 253 (21), 252 (29), and 105 (33). Reduction of the optically active **4n** obtained from Run 16 with $LiAlH_4$ afforded (a*R*)-(+)-2-hydroxymethyl-1,1′-binaphthyl[6a] (85%); $[\alpha]_D^{25}$ +13° (*c* 1.17, CH_3OH); IR (KBr) 3305 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.93 (1H, s, OH), 4.30 (2H, s, CH_2), and 7.08—7.92 (13H, m, Ar-H). As the Mosher's MTPA did not work well as the chiral derivatizing agent, the alcohol was converted into the corresponding pair of diastereomeric esters of (a*S*)-2′-methoxy-1,1′-binaphthyl-2-carboxylic acid.[23b] ^1H NMR analysis of the sample in C_6D_6 in the presence of Eu(fod)$_3$ differentiated well the methoxyl protons of (a*S*, a*S*)- and (a*R*, a*S*)-ester (Table 2, Run 16).

Optically Active 4o (Run 17): Benzene–hexane (2/1) as the eluent; IR (liq. film) 1708 cm^{-1}; ^1H NMR (C_6D_6) δ=0.60, 0.76 (3H: d, J_1=6.76 Hz, CH_3 (a*S*); d, J_2=6.46 Hz, CH_3 (a*R*)), 1.94, 1.99 (3H: s, Ar-CH_3 (a*S*); s, Ar-CH_3 (a*R*)), 5.58—5.95 (1H, m, COOCH), and 6.37—8.37 (17H, m, Ar-H). Reduction of **4o** with $LiAlH_4$ afforded (a*R*)-(−)-2-hydroxymethyl-2′-methyl-1,1′-binaphthyl, the IR and ^1H NMR spectra of which were identical with those of the sample from **4k** (vide supra); $[\alpha]_D^{25}$ −3.4° (*c* 0.893, CH_3OH). Optical yield was determined by the same method as mentioned for **4k**.

Optically Active 4p (Run 18): Benzene–hexane (3/1) as the eluent; oil; IR (liq. film) 1707 cm^{-1}; ^1H NMR (C_6D_6) δ=0.46, 0.58 (3H: d, J=6.60 Hz, CH_3 (a*R*); d, J=6.60 Hz, CH_3 (a*S*)), 5.58—5.90 (1H, m, COOCH), and 6.37—8.62 (20H, m, Ar-H); MS (70 eV) *m/z* (rel intensity) 452 (M^+; 35), 348 (100), 303 (21), 302 (28), and 105 (25). Absolute configuration was determined by the same method as mentioned for **4h**. Optical yield was determined by HPLC on the silica-gel column eluting with hexane–1,2-dichloroethane (25%).

Optically Active 4q (Run 27): Hexane–dichloromethane (3/2) as the eluent on silica-gel column; IR (KBr) 1694 cm^{-1}; ^1H NMR (C_6D_6) δ=0.17—2.34 (16H, m, bornyl-H), 3.26, 3.28 (3H: s, OCH_3 (a*R*); s, OCH_3 (a*S*)), 4.98—5.28 (1H, m,COOCH), and 6.79—8.48 (12H, m, Ar-H); MS (70 eV) *m/z* (rel intensity) 464 (M^+; 93), 328 (100), 311 (59), 296 (11), and 295 (13). Optical yield was determined by ^1H NMR by using Eu(fod)$_3$ in C_6D_6.[23b]

Preparative Scale Synthesis of Enantiomerically Pure (a*S*)-2′-Methoxy-1,1′-binaphthyl-2-carboxylic Acid (5b). To 3.77 g of magnesium turnings and 20 ml of dry ethyl ether was added 70 μl of 1,2-dibromoethane under nitrogen and the mixture was irradiated with ultrasound for 20 min. To the activated magnesium was added a solution of 1-bromo-2-methoxynaphthalene (9.19 g, 38.8 mmol) in ethyl ether (120 ml) over 20 min under ultrasonic irradiation and the mixture was irradiated under gentle reflux for 4 h to form a white slurry, which was dissolved by addition of 140 ml of dry benzene. To the solution was added 30 μl of 1,2-dibromoethane and the reaction was continued for further 2 h to give **3a** as a solution with gray precipitates. After being cooled to ambient temperature, it was added dropwise to a solution of **2e** (10.0 g, 21.5 mmol) in benzene (140 ml) over 2 h. The mixture was stirred at ambient temperature for 8 h and then heated under reflux for 2 h. After the same workup as mentioned for **4m**, volatiles were distilled out under reduced pressure (up to 170°C/0.1 mmHg). The residue was distilled by Kugelrohr's method (170°C/0.05 mmHg) and recrystallized from ethanol to give 8.45 g of **4i** as colorless crystals (84%); mp 154—155 °C; $[\alpha]_D^{21}$ −157° (*c* 1.00, $CHCl_3$); IR (KBr) 1688 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.43—1.73 (18H, m, menthyl-H), 3.72 (3H, s, OCH_3), 4.28—4.70 (1H, m, COOCH), and 6.85—8.23 (12H, m, Ar-H). Found: C, 82.28; H, 7.34%. Calcd for $C_{32}H_{34}O_3$: C, 82.37; H, 7.34%. Optical yield was determined to be 99%de by HPLC on the silica-gel column.

Then, 6.50 g of **4i** (13.9 mmol) was boiled with KOH (61.2 g) in ethanol (520 ml) and water (20 ml) for 12 h. The cooled mixture was worked up by the same method as mentioned for **13b**. After the solvent was evaporated, the residue was recrystallized from ethanol to give 3.73 g of **5b** as colorless needles (82%); mp 193—194 °C (lit,[7b] mp 190—193°C); $[\alpha]_D^{21}$ −26.9° (*c* 0.998, THF) (lit,[7b] $[\alpha]_D^{25}$ −26.0° (*c* 1.22, THF)); IR (KBr) 3055 and 1691 cm^{-1}; ^1H NMR (DMSO-d_6) δ=3.68 (3H, s, OCH_3), 6.69—8.14 (12H, m, Ar-H), and 12.33 (1H, br, COOH). Optical yield was determined to be virtually 100%ee by HPLC as mentioned for **4e**.

This work was supported by a Grant-in-Aid for Scientific Research No. 02555177 from the Ministry of Education, Science and Culture.

References

1) Review: S. Miyano and H. Hashimoto, *Yuki Gosei Kagaku Kyokai Shi*, **44**, 713 (1986).

2) Recent examples: Y. Uozumi and T. Hayashi, *J. Am. Chem. Soc.*, **113**, 9887 (1991); K. Yamamoto, K. Ueno, and K. Naemura, *J. Chem. Soc., Perkin Trans. 1*, **1991**, 2607; Y. Yamamoto, A. Sakamoto, T. Nishioka, J. Oda, and Y. Fukazawa, *J. Org. Chem.*, **56**, 1112 (1991); G. Delogu, O. De Lucchi, P. Maglioli, and G. Valle, *J. Org. Chem.*, **56**, 4467 (1991); S. H. Wilen, J. Z. Qi, and P. G. Williard, *J. Org. Chem.*, **56**, 763 (1991); M. Terada, K. Mikami, and T. Nakai, *Tetrahedron Lett.*, **32**, 935 (1991).

3) Review: G. Bringmann, R. Walter, and R. Weirich, *Angew. Chem., Int. Ed. Engl.*, **29**, 977 (1990).

4) T. Hayashi, K. Hayashizaki, T. Kiyoi, and Y. Ito, *J. Am. Chem. Soc.*, **110**, 8153 (1988), and literatures cited therein.

5) S. Miyano, S. Okada, T. Suzuki, S. Handa, and H. Hashimoto, *Bull. Chem. Soc. Jpn.*, **59**, 2044 (1986).

6) a) A. I. Meyers and K. A. Lutomski, *J. Am. Chem. Soc.*, **104**, 879 (1982); b) A. I. Meyers and K. A. Lutomski, *Synthesis*, **1983**, 105.

7) a) J. M. Wilson and D. J. Cram, *J. Am. Chem. Soc.*, **104**, 881 (1982); b) J. M. Wilson and D. J. Cram, *J. Org. Chem.*, **49**, 4930 (1984).

8) S. Miyano, S. Handa, M. Tobita, and H. Hashimoto, *Bull. Chem. Soc. Jpn.*, **59**, 235 (1986).

9) Preliminary communications: a) H. Hotta, T. Suzuki, and S. Miyano, *Chem. Lett.*, **1990**, 143; b) T. Suzuki, H. Hotta,T. Hattori, and S. Miyano, *Chem. Lett.*, **1990**, 807.

10) M. S. Kharash and O. Reinmuth, "Grignard Reactions of Nonmetallic Substances," Prentice-Hall, New York (1954).

11) W. E. Bachmann and H. P. Hetzner, *Org. Synth.*, Col. Vol. 3, 839 (1955).

12) R. C. Fuson, *Adv. Organomet. Chem.*, **3**, 221 (1965).
13) M. Hirota, H. Satonaka, and T. Hagiwara, *Tetrahedron Lett.*, **19**, 1785 (1967).
14) Cf.: T. Hattori, T. Suzuki, and S. Miyano, *J. Chem. Soc., Chem. Commun.*, **1991**, 1375.
15) M. Kumada, K. Tamao, and K. Sumitani, *Org. Synth.*, Col. Vol. 6, 407 (1988); Cf.: R. A. W. Johnstone and W. N. McLean, *Tetrahedron Lett.*, **29**, 5553 (1988).
16) R. C. Fuson and F. W. Wassmundt, *J. Am. Chem. Soc.*, **78**, 5409 (1956).
17) For example, see: J. E. Rice, H.-C. Shih, N. Hussain, and E. J. LaVoie, *J. Org. Chem.*, **52**, 849 (1987); J. E. Rice and Z.-M. He, *J. Org. Chem.*, **55**, 5490 (1990).
18) In this paper, axial chirality is denoted by prefix "a" as in a*S* or a*R* for discrimination from *C*-centro-chirality.
19) Cf.: S. Miyano, M. Tobita, S. Suzuki, Y. Nishikawa, and H. Hashimoto, *Chem. Lett.*, **1980**, 1027.
20) N. Harada, T. Hattori, T. Suzuki, A. Okamura, H. Ono, S. Miyano, and H. Uda, "Preprint of the 63rd Annual Meeting of the Chemical Society of Japan, 2B118," Osaka, March 1992. The details of the X-ray analysis will be published elsewhere.
21) For general overview of S_NAr reaction, see: J. Miller, "Aromatic Nucleophilic Substitution," Elsevier, New York (1968).
22) Cf.: M. Hojo, R. Masuda, and E. Okada, *Tetrahedron Lett.*, **28**, 6199 (1987).
23) a) S. Miyano, S. Okada, H. Hotta, M. Takeda, C. Kabuto, and H. Hashimoto, *Bull. Chem. Soc. Jpn.*, **62**, 1528 (1989); b) S. Miyano, S. Okada, H. Hotta, M. Takeda, T. Suzuki, C. Kabuto, and F. Yasuhara, *Bull. Chem. Soc. Jpn.*, **62**, 3886 (1989).
24) T. Hattori, M. Shijo, S. Kumagai, and S. Miyano, *Chem. Express*, **6**, 335 (1991).
25) J. D. Morrison and H. S. Mosher, "Asymmetric Organic Reaction," Prentice-Hall, New Jersey (1971).
26) R. C. Fuson and D. H. Chadwick, *J. Org. Chem.*, **13**, 484 (1948).
27) E. Bretscher, H. G. Rule, and J. Spence, *J. Chem. Soc.*, **1928**, 1493.