Asymmetric Reduction with C_1- and C_2-Symmetric NADH Model Compounds Containing Chiral 1,1′-Binaphthyls

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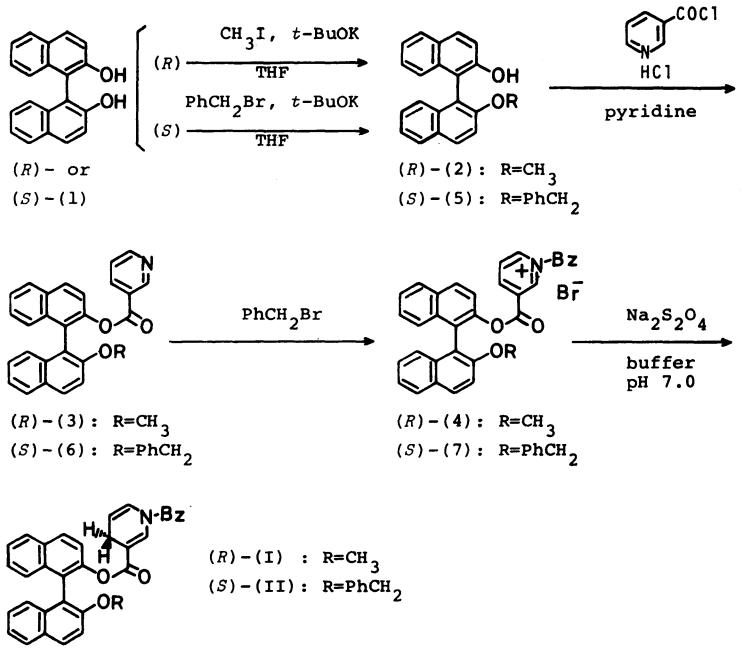
The present study deals with Mg-catalyzed asymmetric reduction of ethyl benzoylformate by the use of C_2-symmetric NADH model compounds in which axial dissymmetry(chiral 1,1′-binaphthyl derivatives) was introduced as a chiral source for the first time and the results were compared with those obtained by the corresponding C_1-symmetric models bearing the same chiral center. Better e.e.'s of the reduction product were obtained by the use of NADH models having C_2-symmetry than does the corresponding C_1-symmetric ones. Further, the kind of bonding as well as the distance between chiral binaphthyl and the reaction center affected the stereochemical course of hydrogen transfer.

Recently some intriguing works have been reported concerning salient effect of C_2-symmetry on the asymmetric synthesis for improving stereoselectivity. The study includes alkylation of enamines,[1] asymmetric reduction of prochiral carbonyl substrates by the use of lithium aluminium hydride modified with chiral 1,1′-binaphthyl,[2] borane–amine complexes modified with optically pure 1,1′-binaphthyl[3] and bis(NADH) model compound,[4] and Michael addition reactions catalyzed by C_2-symmetric chiral crown complexes.[5] However, at present, it is a question that what structure of the chiral reactant(s) is necessary for manifestation of the C_2-symmetry effect in general.

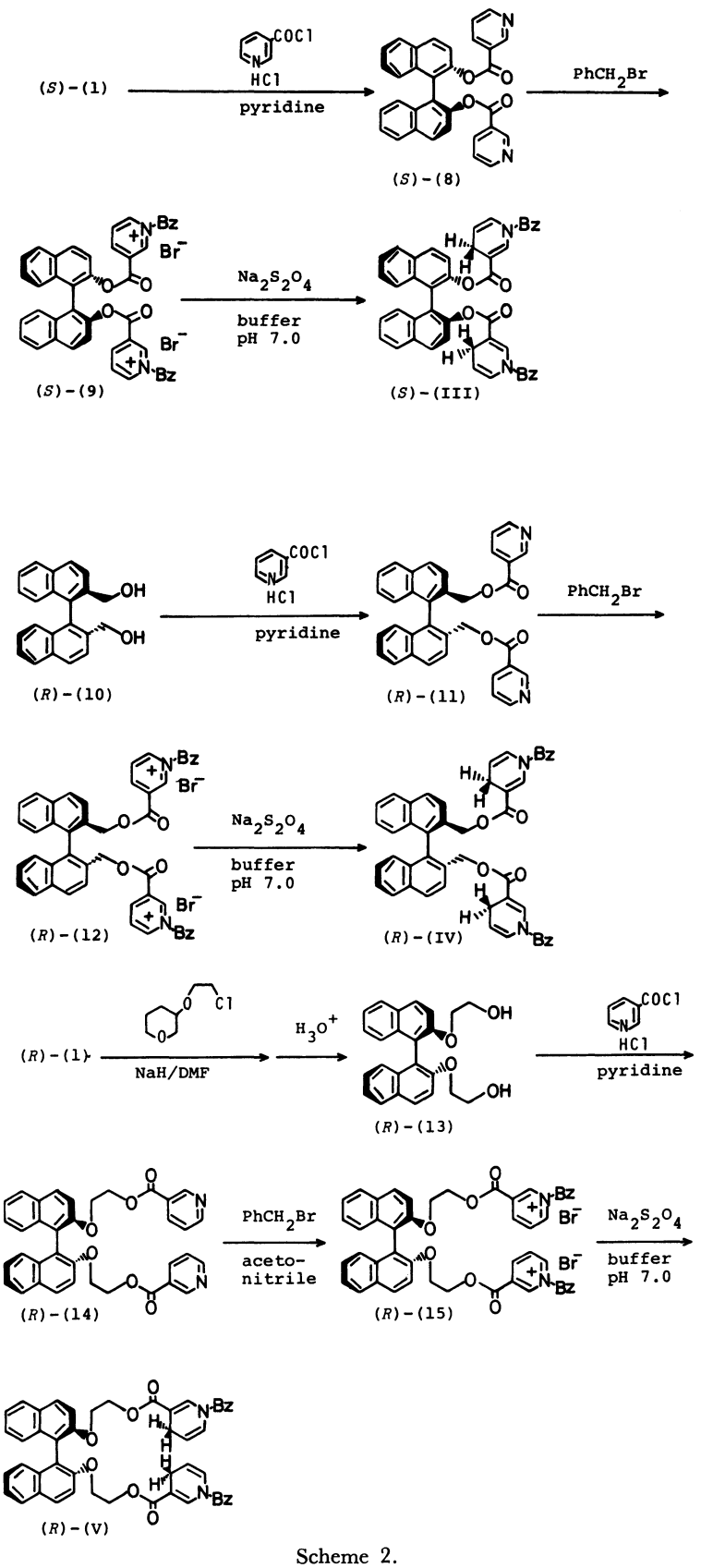
In the present study, we intended to design C_2-dissymmetric[6] NADH model compounds which have a C_2-axis passing through the center of the molecule and have diastereotopic hydrogens at the reaction center. For this purpose, a class of chiral 1,4-dihydropyridines were prepared in which axially dissymmetric binaphthyls were introduced for the first time as a chiral moiety instead of centro-asymmetry, and asymmetric reduction of ethyl benzoylformate was conducted therewith. The results were compared with those obtained by the use of the corresponding C_1-symmetric NADH models bearing the same chirality and the effect of C_2-symmetry was assessed. In addition, influence of polar functional groups, bonding mode of dihydropyridine and chiral binaphthyls as well as the distance between the reaction center and the binaphthyl moiety on the stereoselectivity were discussed.

Results and Discussion

Synthesis of C_1- and C_2-Symmetric NADH Model Compounds (NAH) with Chiral Binaphthyls. In the molecular design for constructing the axially dissymmetric NADH model compounds, enantiomeric 1,1′-bi-2-naphthols, 1,1′-bi-2-naphthylamines and 2,2′-bis-(hydroxymethyl)-1,1′-binaphthyls were introduced as the chiral center of choice. These chiral sources were prepared from 2-naphthol and 2-methylnaphthalene according to the literature.[7-9] The synthetic route for final 1,4-dihydropyridines were shown in Scheme 1 for (*R*)-(**I**) and (*S*)-(**II**), Scheme 2 for (*S*)-(**III**), (*R*)-

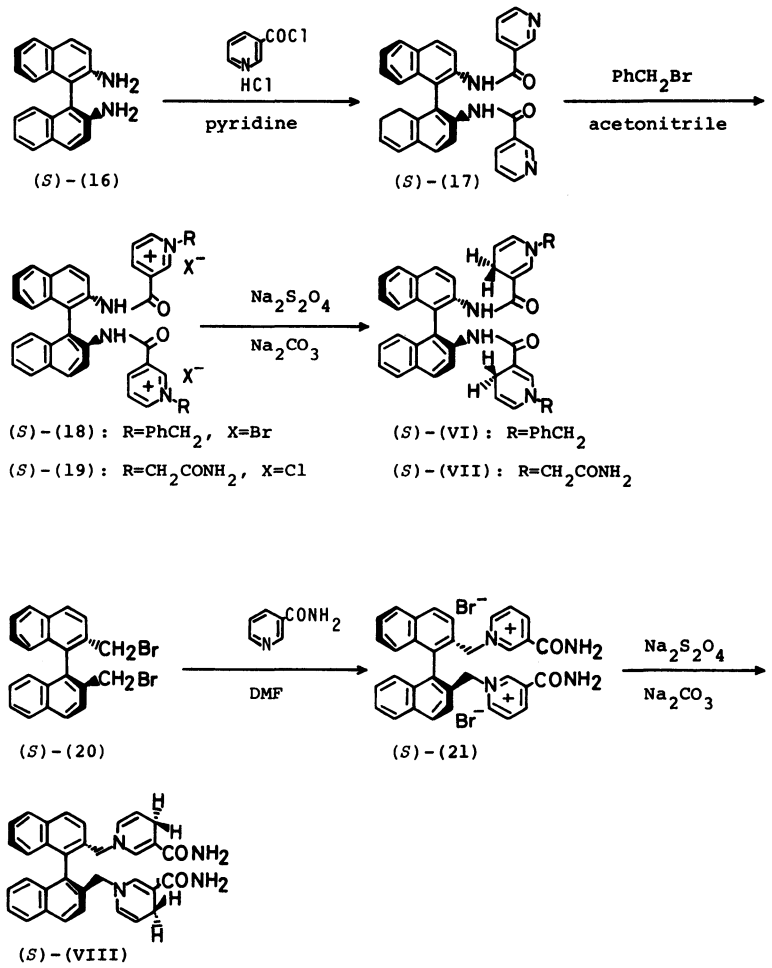


Scheme 1.



Scheme 2.

(**IV**), and (*R*)-(**V**), Scheme 3 for (*S*)-(**VI**), (*S*)-(**VII**), and (*S*)-(**VIII**). In particular, in the last step of synthesis of NADH models (**I**—**V**) possessing ester bonding, the sodium dithionite reductions were carried out in a phosphate buffer adjusted at pH 7.0 to avoid ester hydrolysis under the conventional basic conditions. All the C_1- and C_2-symmetric NADH models thus prepared were featured by their fluorescence on tlc and also



Scheme 3.

TABLE. 1. ASYMMETRIC REDUCTION OF ETHYL BENZOYLFORMATE WITH C_1- AND C_2-SYMMETRIC NADH MODEL COMPOUNDS BEARING CHIRAL BINAPHTHYLS

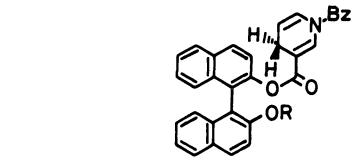
Run	NAH			Ethyl mandelate		
	Model	Configuration	Symmetry	Chem. yield / %	e.e. / %	Configuration
1	(**I**)	*R*	C_1	50.5	10.0	*S*
2	(**II**)	*S*	C_1	55.6	9.1	*R*
3	(**III**)	*S*	C_2	24.8	43.2	*R*
4	(**IV**)	*R*	C_2	36.0	8.8[a)]	*S*
5	(**V**)	*R*	C_2	56.1	5.7	*R*
6	(**VI**)	*S*	C_2	14.3	45.6	*R*
7	(**VII**)	*S*	C_2	66.1	11.4	*R*
8	(**VIII**)	*S*	C_2	26.0	43.5[a)]	*S*

a) Corrected for the optical purity of the models(**IV**) and (**VIII**) used.

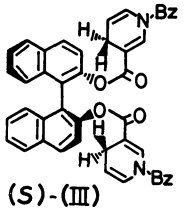
fully substantiated by their NMR and UV spectra.

Asymmetric Reduction of Ethyl Benzoylformate with Present NADH Models. In the present study, the magnesium perchlorate-catalyzed asymmetric reduction of ethyl benzoylformate was preferred as the model system of choice since considerable amount of informations have already been accumulated from both mechanistic and stereochemical aspects,[10] which would make the analysis of the experimental results easier. The results from the asymmetric reductions of ethyl benzoylformate at the ratio of $Mg(ClO_4)_2$: NAH=1 : 2 (mol : mol) by the use of the NADH models (**I**—**VIII**) were listed in Table 1.

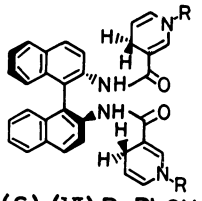
The reductions of ethyl benzoylformate by the use of (*R*)-(**I**) and (*S*)-(**II**), both of C_1-symmetry, gave the reduction products (*R*)- and (*S*)-ethyl mandelate in 10 and 9% e.e. respectively (runs 1 and 2). The rather moderate optical yield may partially be ascribed to the ester function as pointed out by Ohno in the system involving chiral 1,4-dihydropyridine with *l*-menthyl group linked by the amide, ester or carbonylmethylene group.[11] The free rotation about the ester bond could



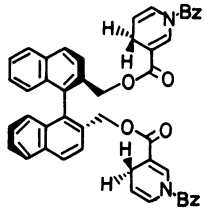
(*R*)-(I) R=CH_3
(*S*)-(II) R=$PhCH_2$



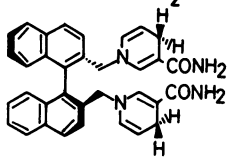
(*S*)-(III)



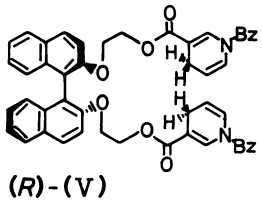
(*S*)-(VI) R=$PhCH_2$
(*S*)-(VII) R=CH_2CONH_2



(*R*)-(IV)



(*S*)-(VIII)



(*R*)-(V)

also be responsible for the low stereoselectivity. On the other hand, the model reaction using C_2-symmetric (*S*)-(**III**) even with the same ester bondings gave (*R*)-mandelate in much higher e.e. (43.2%) clearly suggesting that individual dihydropyridines hinder the free rotations around the ester bonds each other rendering a decrease of the number of conformations at the stereochemical determining stage. As will be shown later in this section, the interaction of dihydropyridylcarbonyloxy group with magnesium ion seems to be little as judged from UV spectrometry. So that, the augmentation of the optical yield caused by introducing a C_2-symmetry axis could possibly be ascribed to the enhanced access of the substrate to one specific face of dihydropyridine moiety by steric requirement, as were demonstrated by Whitesell in the enamine alkylation[1] and Inouye in the bis (NADH) model reaction.[4] In the model (*S*)-(**III**), the two dihydropyridine nuclei disposed in C_2-symmetry on the chiral binaphthyl may expose the specific one of their faces toward outside, permitting the access of substrate from the outside to the faces predominantly. However, when dihydropyridine moieties are removed from the chiral binaphthyls, as the cases with (*R*)-(**V**) the steric effect of chiral binaphthyls on the dihydropyridines may be diminished. Actually, observed e.e. by the use of (*R*)-(**IV**) and (*R*)-(**V**) steeply decreased giving 8.8%-(*S*) and 5.7%-(*R*) product respectively. It is also noteworthy that both the reductant (*S*)-(**III**) and (*R*)-(**V**) gave the same (*R*)-mandelate. Thus, the product stereochemistry was reversed by removing the reaction center from the binaphthyl moiety.

The model (*S*)-(**VI**) differs from (*S*)-(**VIII**) in that the binaphthyl was linked at 3-position of the dihydropyridine for the former whereas at N_1-position for the latter. Interesting is a result from this difference that product configuration was dramatically reversed from (*R*)-45.6% to (*S*)-43.5%.

Stereochemical behavior of (*S*)-(**III**) and (*S*)-(**VI**) reductants in the asymmetric reductions were further examined in detail. The reduction of ethyl benzoylformate by the use of these two models were conducted in the presence of varying amounts of magnesium perchlorate and the optical yields were plotted against the catalyst amount. As shown in Fig. A-1 and B-1, with the reductant (*S*)-(**III**), the e.e.'s remained constant in contrast to the case with (*S*)-(**VI**) where the e.e.'s changed greatly by variation of the catalyst amount with a maximum optical yield (45.6%) at $Mg(ClO_4)_2$/(**VI**)=0.5. However, the maximum values with the both reductants were very similar. Furthermore, the reduction with (*S*)-(**VI**) showed a dependence of e.e. on the reaction conversion as shown in Fig. B-2, whereas such was not the case with (*S*)-(**III**) (Fig. A-2). The two markedly different stereochemical behaviors between these models should obviously be ascribed to the difference in electronic nature of the ester and the amide functions. In fact, as revealed by UV spectroscopy, the reductant (*S*)-(**VI**) showed a spectral change with varying amounts of magnesium perchlorate (Fig. B-3), while no change was observed for (*S*)-(**III**) indicating that the amide functions interact to some extent with magnesium ion[12] in contrast to the ester functions (Fig. A-3). Accordingly, the chelative properties of the amide group must be responsible for the dependence of e.e. on the catalyst amount and on the reaction conversion observed in the asymmetric reduction with the model (*S*)-(**VI**). From this view, the C_2-symmetric diester reductant (*S*)-(**III**) could be regarded as a reasonable model to demonstrate unequivocally the importance of C_2-symmetry for the stereoselectivity since the electronic factor involving chelative interaction of the model (*S*)-(**III**) with magnesium ion seems to be negligible for the stereochemical course of the hydrogen transfer as described above.

In the present study, axial chirality was transferred successfully for the first time to centro-chirality of the reduction product in NADH model systems and the importance of C_2-symmetry for stereospecificity was unambiguously demonstrated by the use of the model (*S*)-(**III**) derived from optically active binaphthyl. In the diamide model (*S*)-(**VI**), the chelative interaction with magnesium ion was found to be significant and responsible for the dependence of e.e. on the catalyst amount as well as the reaction conversion.

Also, of interest was a finding that the product stereochemistry including configurational reversal was found to be greatly dependent on the bonding site of the dihydropyridine (N_1-position in **VIII** and 3-position in **I**—**VII**) to chiral moiety and also on the distance between the binaphthyls and the reaction center.

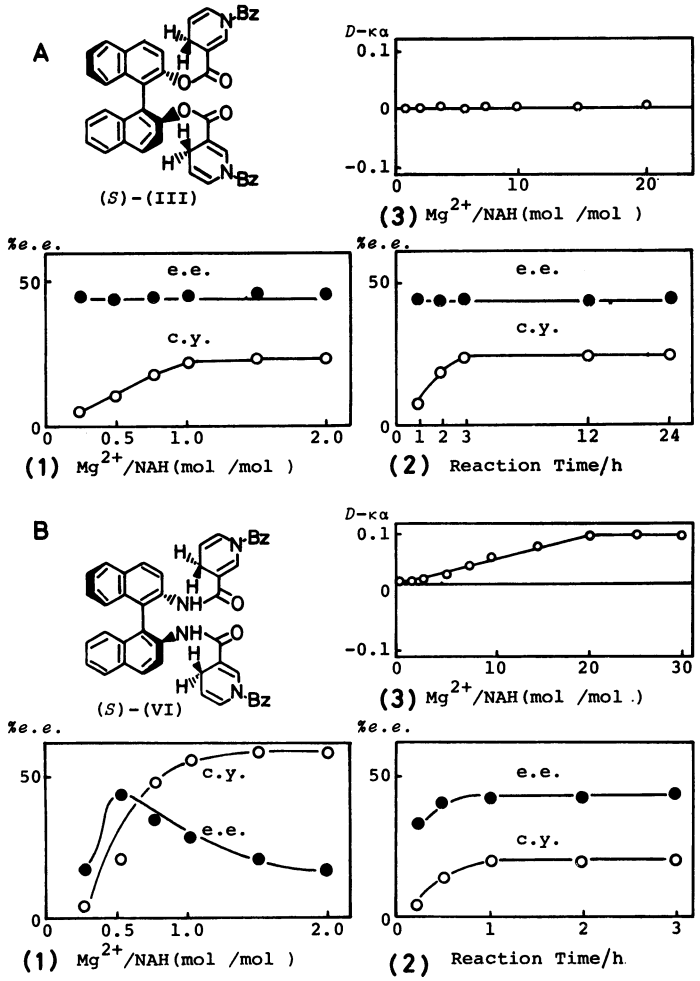


Fig. 1. Dependence of e.e. on the catalyst amount and the reaction conversion in the asymmetric reductions of ethyl benzoylformate with (*S*)-(**III**) and (*S*)-(**VI**), and determination of the mole ratio in the complexes of these models with magnesium perchlorate by UV spectroscopy.

Experimental

General. IR spectra were recorded with a Hitachi 215 spectrometer, ^{1}H-NMR spectra with a Varian EM-360 spectrometer with tetramethylsilane as internal standard. UV spectra were recorded on a Hitachi 340 spectrometer. Optical rotations were measured with a Perkin-Elmer 241 polarimeter. VPC analyses were performed on a Shimadzu GC-4CM instrument with 15% polyethylene glycol succinate(PEGS) on Chromosorb W at 180 °C. Preparative VPC analyses were on Varian Aerograph Model 920 with alminum column (3 m) packed with 15% Apiezone L at 190 °C.

Ethyl benzoylformate from commercial source was purified by chromatography (Kieselgel 60, 70—230 mesh) eluted by benzene, followed by distillation. Anhydrous magnesium perchlorate was kept in a vacuum desiccator over phosphorus pentoxide. Acetonitrile was distilled over phosphorus pentoxide. Ethanol was distilled over calcium hydride.

General Procedure for Asymmetric Reduction. A mixture of ethyl benzoylformate, NADH model compound (NAH) and magnesium perchlorate in dry acetonitrile (10 ml/1.0 mmol) was stirred at room temperature under nitrogen atmosphere in the dark, after which water (1 ml) was added to the reaction mixture. The mixture was stirred for 5 min at room temperature, and extracted with dichloromethane. The organic phase was evaporated *in vacuo*. The residue was chromatographed on TLC (Kieselgel G nach Stahl, Type 60) with benzene. The purity of the alcohol obtained was confirmed by VPC and ^{1}H-NMR.

Chemical yields were determined by VPC. Optical yields were calculated from optical rotations of the isolated ethyl mandelate based on the reported maximum rotation of enantiomerically pure ethyl mandelate, $[\alpha]_D^{25}$ $\pm$104.4° in ethanol.[13]

(R)-2-Hydroxy-2'-methoxy-1,1'-binaphthyl (R)-(2): A mixture of (*R*)-1,1'-bi-2-naphthol (**1**) (3.0 g, 10.5 mmol, $[\alpha]_D^{25}$ +31.5°, *c* 1.03, THF) and *t*-BuOK (1.8 g, 10.5 mmol) in 200 ml of dry THF was stirred under nitrogen atmosphere and methyl iodide (1.49 g, 10.5 mmol) in 50 ml of dry THF was added dropwise. The mixture was heated under reflux for 15 h, cooled and concentrated under reduced pressure. The residue was partitioned between dichloromethane and saturated sodium carbonate solution. The organic layer was washed with brine, dried and the solution was evaporated under reduced pressure to give an oil which was purified by silica-gel column chromatography with benzene elution; yield 1.94 g (61.6%), $[\alpha]_D^{25}$ +38.59° (*c* 0.99, THF), ^{1}H-NMR (chloroform-d_1): δ=3.86 (3H, s, $-CH_3$), 5.03 (1H, s, -OH), 7.15—8.30 (12H, m, aromatic protons).

(R)-2-Methoxy-2'-(3-pyridylcarbonyloxy)-1,1'-binaphthyl (R)-(3): To a solution of nicotinoyl chloride hydrochloride (1.8 g, 10.1 mmol) in pyridine (50 ml), (*R*)-(**2**) (2.0 g, 6.7 mmol) was added and the mixture was stirred at room temperature overnight, followed by reflux for 2 h. After cooling, evaporation under reduced pressure gave a residue, which was partitioned betweed dichloromethane and saturated sodium carbonate solution. The aqueous layer was extracted with dichloromethane. The organic layer was washed with brine, dried and chromatographed on silica-gel column chromatography with dichloromethane solution; yield 2.5 g (92.5%), $[\alpha]_D^{25}$ +29.10° (*c* 1.00, THF), ^{1}H-NMR (chloroform-d_1): δ= 3.73 (3H, s, $-CH_3$), 7.00—8.20 (14H, m, aromatic and pyridine protons), 8.40—8.80 (2H, m, pyridine).

(S)-2-Benzyloxy-2'-hydroxy-1,1'-binaphthyl (S)-(5): Benzyl ether (*S*)-(**5**) was prepared in the same manner with (*S*)-(**2**) from (*S*)-1,1'-bi-2-naphthol (3.0 g, 10.5 mmol) and benzyl bromide (1.80 g, 10.5 mmol); yield 2.6 g (66.0%), $[\alpha]_D^{25}$ −58.61° (*c* 1.034, THF), mp 93 °C, ^{1}H-NMR (chloroform-d_1): δ=4.96 (1H, s, -OH), 5.10 (2H, s, $-CH_2-$), 6.90—8.20 (17H, m, aromatic protons).

(S)-2-Benzyloxy-2'-(3-pyridylcarbonyloxy)-1,1'-binaphthyl (S)-(6): (*S*)-(**6**) was prepared in the same manner with (*R*)-(**3**) from (*S*)-(**5**) (2.4 g, 6.4 mmol) and nicotinoyl chloride hydrochloride (1.7 g, 9.5 mmol); yield 3.1 g (100%), $[\alpha]_D^{25}$ −44.73° (*c* 2.28, ethanol), ^{1}H-NMR (chloroform-d_1): δ=5.10 (2H, s, $-CH_2-$), 7.00—8.30 (14H, m, aromatic and pyridine protons), 8.60—8.80 (2H, m, pyridine).

(S)-2,2'-Bis(3-pyridylcarbonyloxy)-1,1'-binaphthyl (S)-(8): To a mixture of nicotinoyl chloride hydrochloride (22 g, 124 mmol) in a solution of triethylamine (25 g) in dichloromethane (200 ml), was added a dichloromethane solution (200 ml) of (*S*)-1,1'-bi-2-naphthol (**1**) (15 g, 52 mmol) and refluxed for 1 h, cooled and washed with saturated sodium carbonate solution and brine, dried over anhydrous sodium sulfate, followed by concentration under reduced pressure. The residue was chromatographed on silica-gel column with ethyl acetate as eluent to give pure (*S*)-(**8**); yield 21.0 g (81%), $[\alpha]_D^{25}$ −79.5° (*c* 1.00, ethanol), ^{1}H-NMR (chloroform-d_1): δ=7.05—8.20 (16H, m, aromatic and pyridine protons), 8.60—8.90 (4H, m, pyridine).

(R)-2,2'-Bis(3-pyridylcarbonyloxymethyl)-1,1'-binaphthyl (R)-(11): Binaphthyl derivative (*R*)-(**11**) was prepared in the same manner with (*S*)-(**8**) from (*R*)-2,2'-bis(hydroxymethyl)-1,1'-binaphthyl (**10**)[9] (1.1 g, 3.5 mmol) and nicotinoyl chloride hydrochloride (1.45 g, 8.4 mmol); yield 1.1 g (66.0%). In the preparation of this compound, the diol[optical purity 81%, $[\alpha]_D^{25}$ +68.0° (*c* 0.98, acetone)] was used. $[\alpha]_D^{25}$ +9.28° (*c* 1.00, chloroform), ^{1}H-NMR (chloroform-d_1): δ=5.27 (2H, s, $-CH_2-$), 7.17—8.20 (16H, m, aromatic and pyridine protons), 8.50—9.20 (4H, m, pyridine).

(R)-2,2'-Bis(2-hydroxyethoxy)-1,1'-binaphthyl (R)-(13): To a solution of (*R*)-1,1'-bi-2-naphthol (**1**) (1.0 g, 3.5 mmol: $[\alpha]_D^{25}$ +31.9° (*c* 1.00, THF) in DMF (20 ml) was added NaH (390 mg, 8.13 mmol, 50% oil emulsion). The mixture was heated to 70 °C with stirring under nitrogen atmosphere. After 1 h, 2-chloroethyl tetrahydro-3-pyranyl ether (1.32 g, 8.02 mmol) was added. The reaction mixture was stirred at 70 °C for 48 h in a nitrogen stream, cooled and shaken with 100 ml of water. The mixture was extracted with dichloromethane, and the combined organic layer was washed with water, dried, and concentrated. To the residue, dichloromethane (50 ml), methanol (25 ml) and 7 drops of concd hydrochloric acid was added and stirred for 1 h at room temperature. The reaction mixture was neutralized with saturated sodium hydrogencarbonate solution, washed with water, dried over anhydrous sodium sulfate and concentrated. The residue was crystallized from benzene–hexane; yield 920 mg (70%), $[\alpha]_D^{25}$ −21.6°[7] (*c* 1.01, THF), ^{1}H NMR (chloroform-d_1): δ=2.30 (2H, br, -OH), 3.60 (4H, m, $-CH_2O-$), 4.13 (4H, m, $-OCH_2-$), 6.80—8.20 (12H, m, aromatic protons), MS *m/e* (M^+) 374.

(R)-2,2'-Bis[2-(3-pyridylcarbonyloxy)ethoxy]-1,1'-binaphthyl (R)-(14): (*R*)-(**14**) was prepared in a similar procedure to the preparation of (*S*)-(**8**) from (*R*)-(**13**) (2.74 g, 7.32 mmol) and nicotinoyl chloride hydrochloride (5.48 g, 30.8 mmol); yield 4.1 g (96.0%), $[\alpha]_D^{25}$ −50.58° (*c* 1.02, THF), ^{1}H-NMR (chloroform-d_1): δ=4.30 (8H, s, $-CH_2CH_2-$), 7.10—8.05 (16H, m, aromatic and pyridine protons), 8.66—9.00 (4H, m, pyridine), MS *m/e* (M^+) 584.

(S)-2,2'-Bis(3-pyridylcarbonylamino)-1,1'-binaphthyl (S)-(17): To a solution of nicotinoyl chloride hydrochloride (7.0 g, 39.3 mmol) in pyridine (100 ml), (*S*)-1,1'-bi-2-naphthylamine (**16**)[8] (4.85 g, 17.1 mmol) was added and heated at 80 °C for 1 h. After the period, the mixture was cooled, followed by addition of saturated sodium hydrogencarbonate solution. The mixture was extracted with chloroform and the organic layer was washed with brine, dried over anhydrous sodium sulfate, concentrated and the residue was crystallized from ethyl acetate–benzene to give pure (*S*)-(**17**); yield 6.20 g (73.5%), $[\alpha]_D^{25}$ −127.08° (*c* 1.008, chloroform), IR ν (cm^{-1}, KBr): 3300—3500 ν (N–H), 1680 ν (C=O), 680—820 δ (aromatic C–H), ^{1}H-NMR (chloroform-d_1): δ=7.0—8.7 (22H, m, aromatic and pyridine protons and NH).

The Preparation of Oxidized Forms (R)-(4), (S)-(7), (S)-(9), (R)-(12), (R)-(15), (S)-(18), (S)-(19), and (S)-(21). The bromides (*R*)-(**4**), (*S*)-(**7**), (*S*)-(**9**), (*R*)-(**12**), and (*R*)-(**15**) were prepared by the use of stoichiometric amount of benzyl bromide without solvent to avoid cleavage of ester linkage by solvolysis. The salt, (*S*)-(**18**) was prepared by heating with benzyl bromide in acetonitrile. These quaternized salts were submitted as such to the sodium dithionite reduction without further purification. The amide, (*S*)-(**17**) was quaternized with chloroacetamide by heating in acetonitrile for 30 min. The residue, (*S*)-(**19**) obtained by the distillation of the solvent was submitted as such to the reduction with sodium dithionite. The salt, (*S*)-(**21**), was prepared by heating a solution of (*S*)-2,2'-bis(bromomethyl)-1,1'-binaphthyl (**20**)[9] (1.1 g, 2.5 mmol) and nicotinamide (555 mg, 4.6 mmol) in DMF (20 ml) at 70 °C overnight. The reaction mixture was added dropwise into ethanol (100 ml) to give colorless precipitate which was washed with ether over phosphorus pentoxide; yield 1.69 g (93.6%).

General Preparation of 1,4-Dihydropyridines by the Reduction with Sodium Dithionite. i) Preparation of (R)-(1), (S)-(II), (S)-(III), (R)-(IV), and (R)-(V): The quaternized salt (6.0 mmol) was dissolved in DMF (10 ml) and the solution was added to 0.25 M (1 M = 1 mol dm^{-3}) sodium phosphate buffer (1 l, pH 7.0) containing sodium dithionite (147 mmol) and stirred at room temperature under nitrogen atmosphere. After 15 min, the flocculent material separated out of the solution was filtered, washed with water. The reductant was purified by silica-gel column chromatography with dichloromethane elution.

(R)-2-Methoxy-2'-(1-benzyl-1,4-dihydro-3-pyridylcarbonyloxy)-1,1'-binaphthyl (R)-(I); Yield 61.1% $[\alpha]_D^{25}$ +69.3° (*c* 1.03, acetonitrile), UV λ_{max} (acetonitrile): 360—361 nm (ε_{max} 8696), IR ν (cm^{-1}, KBr): 1700 ν (C=O), 680—820 δ (aromatic C–H), ^{1}H-NMR (chloroform-d_1): δ=2.90 (2H, m, pyr–C_4–2H), 3.80 (3H, s, $-OCH_3$), 4.03 (2H, s, $-CH_2Ph$), 4.76 (1H, m, pyr–C_5–H), 5.66 (1H, br, pyr–C_6–H), 6.50 (1H, m, pyr–C_2–H), 7.10—8.33 (22H, m, aromatic protons).

(S)-2-Benzyloxy-2'-(1-benzyl-1,4-dihydro-3-pyridylcarbonyloxy)-1,1'-binaphthyl (S)-(II); Yield 88.9%, $[\alpha]_D^{25}$ −67.4° (*c* 1.005, acetonitrile), UV λ_{max} (acetonitrile): 361 nm (ε_{max} 8584), IR ν (cm^{-1}, KBr): 1700 ν (C=O), 1600 ν (C=C), 1150 ν (C–O–C).

680—820 δ (aromatic C–H), ^{1}H-NMR (chloroform-d_1): δ= 2.86 (2H, m, pyr–C_4–2H), 3.85 (2H, s, –NCH_2Ph), 4.65 (1H, m, pyr–C_5–H), 5.00 (2H, s, –OCH_2Ph), 5.50 (1H, m, pyr–C_6–H), 6.30 (1H, m, pyr–C_2–H), 6.80—8.20 (22H, m, aromatic protons).

(S)-2, 2'-Bis(1-benzyl-1, 4-dihydro-3-pyridylcarbonyloxy)-1, 1'-binaphthyl(S)-(III); Yield 42.0%, $[\alpha]_D^{25}$ −9.6° (*c* 1.05, ethanol), UV λ_{max} (ethanol): 362 nm (ε_{max} 17167), IR ν (cm^{-1}, KBr): 1740 ν (C=O), 1595 ν (C=C), 660—890 δ (aromatic C–H), ^{1}H-NMR (chloroform-d_1): δ=2.73 (4H, m, pyr–C_2–2H), 3.96 (4H, s, –CH_2Ph), 4.63 (2H, m, pyr–C_5–H), 5.50 (2H, m, pyr–C_6–H), 6.50 (2H, m, pyr–C_2–H), 6.90—9.10 (22H, m, aromatic protons).

(R)-2, 2'-Bis(1-benzyl-1, 4-dihydro-3-pyridylcarbonyloxymethyl)-1, 1'-binaphthyl(R)-(IV); Yield 17.1%, $[\alpha]_D^{25}$ +42.54° (*c* 0.992, ethyl acetate), UV λ_{max} (ethyl acetate): 357 nm (ε_{max} 13570), ^{1}H-NMR (chloroform-d_1): δ=3.03 (4H, m, pyr–C_4–2H), 4.24 (4H, s, –CH_2Ph), 4.90 (4H, s, CH_2O–), 4.50—5.20 (2H, m, pyr–C_5–H), 5.67 (2H, m, pyr–C_6–H), 6.93 (2H, m, pyr–C_2–H), 7.00—8.20 (22H, m, aromatic protons).

(R)-Bis[2-(1-benzyl-1, 4-dihydro-3-pyridylcarbonyloxy)ethoxy]-1, 1'-binaphthyl (R)-(V); Yield 60.0%, $[\alpha]_D^{25}$ +56.4° (*c* 1.08, acetonitrile), UV λ_{max} (acetonitrile): 355 nm (ε_{max} 12530), IR ν (cm^{-1}, KBr): 1680 ν (C=O), 1600 ν (C=C), 700—840 δ (arc-matic C–H), ^{1}H-NMR (chloroform-d_1): δ=3.00 (4H, m, pyr–C_4–2H), 4.20 (8H, d, J=2 Hz, –CH_2CH_2–), 4.80 (2H, m, pyr–C_5–H), 5.73 (2H, m, pyr–C_6–H), 6.70 (2H, m, pyr–C_2–H), 7.10—8.10 (22H, m, aromatic protons).

ii) Preparation of (S)-(VI), (S)-(VII), and (S)-(VIII): To a solution of sodium hydrogencarbonate (230 ml) in water (634 ml) saturated with carbon dioxide up to pH 8.0, sodium dithionite (72.8 mmol) and the quaternized salt (3.79 mmol) in methanol (238 ml) were added and kept in the dark overnight. After the period, the solid separated material was filtered and dried over phosphorous pentoxide.

(S)-2, 2'-Bis(1-benzyl-1, 4-dihydro-3-pyridylcarbonylamino)-1, 1'-binaphthyl (S)-(VI); Yield 91.7%, $[\alpha]_D^{25}$ +112.2° (*c* 0.50, acetonitrile), UV λ_{max} (acetonitrile): 363 nm (ε_{max} 21162), ^{1}H-NMR (chloroform-d_1): δ=2.26 (4H, m, pyr–C_4–2H), 4.13 (4H, s, –CH_2Ph), 4.40 (2H, m, pyr–C_5–H), 5.53 (2H, m, pyr–C_6–H), 6.83 (2H, m, pyr–C_2–H), 6.90—8.15 (22H, m, aromatic protons).

(S)-2, 2'-Bis(1-carbamoylmethyl-1, 4-dihydro-3-pyridylcarbonylamino)-1, 1'-binaphthyl (S)-(VII); Yield 23.7%, $[\alpha]_D^{25}$ +74.73° (*c* 0.182, chloroform), UV λ_{max} (chloroform): 362 nm (ε_{max} 20370), ^{1}H-NMR (chloroform-d_1): δ=2.33 (4H, m, pyr–C_4–2H), 3.66 (4H, s, –CH_2–), 4.53 (2H, m, pyr–C_5–H), 5.65 (2H, m, pyr–C_6–H), 6.83 (2H, s, pyr–C_2–H), 7.20—8.50 (22H, m, aromatic protons).

(S)-2, 2'-Bis(3-carbamoyl-1, 4-dihydro-1-pyridylmethyl)-1, 1'-binaphthyl (S)-(VIII); Yield 55.9%, $[\alpha]_D^{25}$ −197.5° (*c* 0.99, dichloromethane), UV λ_{max} (dichloromethane): 356 nm (ε_{max} 12000), ^{1}H-NMR (chloroform-d_1): δ=2.27 (4H, m, pyr–C_4–2H), 3.97 (4H, s, –CH_2N), 4.60 (2H, m, pyr–C_5–H), 5.53 (2H, m, pyr–C_6–H), 5.60 (4H, s, NH_2), 6.67 (2H, d, J=2 Hz, pyr–C_2–H), 6.90—8.20 (12H, m, aromatic protons).

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