Asymmetric Construction of Binaphthyl by the Chiral Diether-Mediated Conjugate Addition of Naphthyllithium to Naphthalenecarboxylic Acid 2,6-Di-i-butyl-4-methoxyphenyl Ester

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Two ways for the synthesis of binaphthyl were examined based on a chiral ligand-mediated asymmetric conjugate addition of 1-naphthyllithium to naphthalene-2-carboxylic acid 2,6-di-i-butyl-4-methoxyphenyl esters. The one-pot method by conjugate addition-elimination gave a relatively higher enantioselectivity than the two-step synthesis based on addition and subsequent oxidative aromatization.

Key words axial chirality; central chirality; asymmetric addition; chiral ligand

Asymmetric construction of axial chirality represented by biaryl has been the continuing interest of organic chemistry.1) Coupling of two naphthyl groups is the fundamental strategy for the formation of chiral biaryl bond by using chiral partner(s) or chiral mediator. Practical level of asymmetric oxidative coupling of naphthols to chiral binaphthol has been demonstrated by Nakajima et al.2,3) Transition metal-catalyzed formation of axial chirality has been proven to be in the reasonably high level of efficiency.4,5) Other interesting way is the application of conjugate addition of naphthylmetals to chiral naphthyl acceptors and subsequent elimination process as has been demonstrated by Meyers and Lutomski,6) Wilson and Cram,7) and Miyano and colleagues.8) We have also developed an efficient asymmetric conjugate addition-elimination of 1-naphthyllithium 3 and fluoronaphthylamine 2 giving chiral binaphthyls 4 and 5 with 91% ee by setting the external chiral diether ligand 19,10) (5 mol%)-catalyzed methodology as shown in Chart 1.1) As part of the continuing approach toward conjugate addition-elimination protocol, we selected a naphthyl ester as a directing group in place of imine.12) We describe herein the comparison of two approaches to axial chirality of binaphthyl by using asymmetric conjugate addition of 1-naphthyllithium 3 to naphthalenecarboxylic acid BHA (2,6-di-i-butyl-4-methoxyphenyl) ester 6 under the steric control of chiral diether 1.

Asymmetric conjugate addition reaction of 3 to 6 is controlled by a chiral diether 1-chelated complex to give addition intermediate 7 as an initial product. Protonation would give us a chiral addition product 8 if X (=H) is not a leaving group (Chart 2). Subsequent oxidative aromatization of 8 is the way to binaphthyl to give target 9. Another way is the asymmetric conjugate addition and subsequent elimination of a leaving group X from 7 to give the target 9 in a one pot. It is important to point out that the central chirality in 7 and 8 should be transferred or converted to axial chirality of 9 in both of two approaches.

Asymmetric Conjugate Addition and Subsequent Oxidative Aromatization to Binaphthyl We began our studies with two-step procedure, that is, asymmetric conjugate addition and subsequent oxidative aromatization to binaphthyl. The reaction of 3 eq of 3 with naphthalenecarboxylic acid BHA ester (6a) in the presence of 3.3 eq of diether ligand 1 in a mixture of toluene and diethyl ether at −45 °C for 5 h gave, after protonation of an intermediate enolate 7a (X=H) with trifluoroacetic acid, a 1:1 olefin isomeric mixture of addition products 8 in 66% yield (Chart 3). Since the subsequent in situ treatment of an enolate 7a successively with super-hydride, methyl iodide, and finally sodium borohydride has been confirmed to give an alcohol 10 with 95% enantiomeric excess (ee) in 40% yield,13) the adducts 8 should have 95% enantiomeric purity. The central chirality in 8 was then transferred by treating with 2,3-dichloro-5,6-dicyano-p-benzoquinone (DDQ) in refluxing tetrahydrofuran (THF) for 1.5 h into axial chirality in (+)-(S)-9 in 92% chemical yield. Enantiomeric purity of (+)-(S)-9 was, however, disappointingly low, 24% ee.

The referential binaphthyl ester (−)-(R)-9 with established absolute configuration and specific rotation was synthesized from the corresponding aldehyde (R)-511) that was obtained

![Chart 1](image1)

![Chart 2](image2)
Discussions

Oxidative aromatization of dihydrophenanthroline compound bearing central chirality is the efficient process to binaphthyl. However, transfer of central chirality to axial chirality involves loss of enantiomeric selectivity in a large extent. Addition-elimination sequence is a more efficient way for the transfer of central chirality to axial chirality as well as for aromatization. It is quite interesting to note that the two ways gave the antipode each other.

Experimental

All melting points are uncorrected. Silica gel column chromatography was used for purification. NMR was measured in CDCl3, unless otherwise noted, and chemical shifts and coupling constants are presented in ppm relative to tetramethylsilane and Hz, respectively. Abbreviations are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. The wave numbers of maximum absorption peaks of IR spectroscopy are presented in cm⁻¹.

Synthesis of 2,6-Di-t-butyl-4-methoxyphenyl (S)-1,1'-binaphthalene-2-carboxylic acid ((+)-9) with 24% ee by Two Step Procedure

To a solution of 1-bromonaphthalene (0.42 ml, 3.0 mmol) and t-butyl-lithium (1.85 M, 1.62 ml, 3.0 mmol) in hexane at −78 °C, was added via cannula at −78 °C to a solution of 2-naphthoic acid BHA ester (391 mg, 1.0 mmol) and 1 (800 mg, 3.3 mmol) in toluene (25 ml). The orange solution was stirred at −45 °C for 6 h, and then was quenched with trifluoroacetic acid (0.77 ml). The mixture was diluted with ether (50 ml), washed with saturated sodium bicarbonate, brine, and then dried over magnesium sulfate. Concentration and chromatography (hexane/ether = 100:1—5/1) gave a 1:1 mixture of 1,2-dihydro- and 1,4-dihyro isomers **8** (344 mg, 66%) as a colorless amorphous and recovered 1 (0.76 g, 95%). ¹H-NMR, IR, and TLC of **8** were identical with those of authentic sample.¹⁻¹⁴)

A mixture of **8** (164 mg, 0.32 mmol) and 2,3-dichloro-5,6-dicyano-1,4-benzocoumarone (90 mg, 0.38 mmol) in THF (5 ml) was refluxed for 1.5 h. The brown mixture was diluted with ether (50 ml) and washed with 15% NaOH (50 ml) and then dried over magnesium sulfate. Concentration and chromatography (hexane/ether = 15/1) gave (+)-(S)-9 (150 mg, 92%) as colorless solids of mp 190—205 °C and [α]D²⁵ = +18.4 (c = 1.24, CHCl₃). Optical purity was 24% (vide infra).

Chart 3

Fig. 1

Chart 4

Asymmetric Conjugate Addition-Elimination to Binaphthyl in One Pot

The attempted reaction of **3** with isopropyl 1-methoxynaphthalene-2-carboxylate, in place of BHA ester, in THF gave 1,2-addition product without formation of conjugate addition product. BHA ester **6b** was the appropriate acceptor of conjugate addition in THF at −78 °C for 1.5 h and further at −45 °C for 1 h giving addition-elimination product **9** in 91% yield (Chart 4).

The chiral diether ligand 1-mediated asymmetric reaction proceeded much more smoothly in toluene at −78 °C for 0.5 h to give binaphthyl (−)-(R)-**9** with 52% ee in 93% yield. The absolute configuration was determined to be **R** by the comparison of specific rotation.
yellow solution above at −78 °C and the pale green solution was stirred at 
−78 °C for 0.5 h. The mixture was added with saturated ammonium chloride 
(20 ml) and extracted with ether (25 ml×3). The combined extracts were 
washed with brine and dried over magnesium sulfate. Concentration and 
chromatography (hexane/ether=15:1) gave (R)-9 with 52% ee (0.48 g, 93%) 
as colorless solids of mp 218—221 °C and [α]D25 −40.0 (c=1.08, CHCl3).

(R)-1,1’-Binaphthalene-2-carboxylic Acid BHA Ester (((−)-(R)-9 with 
62% ee) A mixture of above 1,1’-binaphthalene-2-carboxylic acid (83.9 
mg, 0.28 mmol), pyridine (1 drop), and thionyl chloride (2 ml) was refluxed 
for 1.5 h, and then concentrated to afford acid chloride (0.11 g) as a yellow 
solution above at 754 °C and the pale green solution was stirred at 
78 °C for 0.5 h. The mixture was added with saturated ammonium chloride 
(15 ml×3). Then optically pure ((−)-(R)-9) was added under reflux a solu-
tion of potassium permanganate (0.50 g, 3.17 mmol) in hot water (4 ml).
After reflux for 1.5 h, the mixture was treated with 10% HCl (2 ml) and 
then dried over magnesium sulfate. Concentration and chromatography 
(hexane/ether=10:1) gave an acid (92.2 mg, 59%) as a powder of mp 177—
184 °C and [α]D25 +19.0 (c=2.74, benzene). 1H-NMR (DMSO-d6) δ: 7.0—
8.3 (13H, m), 12.44 (1H, s). IR (KBr): 1780. Spectroscopic data were super-
imposable with those reported.16)

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