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Highly Stereospecific Conversion of Planar Chirality of a Cyclophane into Axial Chirality of Binaphthyls

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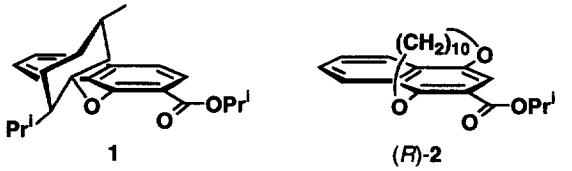
Abstract: Reaction of oxanaphthalenophane (*R*)-**2** with 1-naphthyl Grignard reagents **3** affords 1,1'-binaphthyls **4** of high enantiomeric purity, providing the first example of an asymmetric ring-opening of the cyclophane class of compounds. Because the stereoselectivity of the reaction coincides very well with that of the reaction of (–)-menthyl ether **1** with **3**, which we reported previously, it is supposed that the steric effect of the (–)-menthoxy moiety of **1** is equivalent to that of the ansa chain of (*R*)-**2** in these reactions.

Although the optical isomerism of cyclophanes arising from restricted rotation of the aromatic ring about single bonds has been the subject of much interest for decades,[1,2] research on asymmetric reactions of this class of planer chiral molecules themselves and/or their use as chiral inducers has been limited.[3] We have reported the applications of chiral cyclophanes to a chiral stationary phase for HPLC or to a chiral derivatizing agent for the discrimination of enantiomers.[4,5] Only recently, Antonov *et al.* have utilized a [2.2]paracyclophane as chiral inducer for the synthesis of α-amino acids.[6] Herein, we report the first example of an asymmetric ring-opening of a facially chiral naphthalenophane **2** to axially chiral binaphthyls by reaction with naphthyl Grignard reagents **3** (Fig. 1 and Scheme 1).

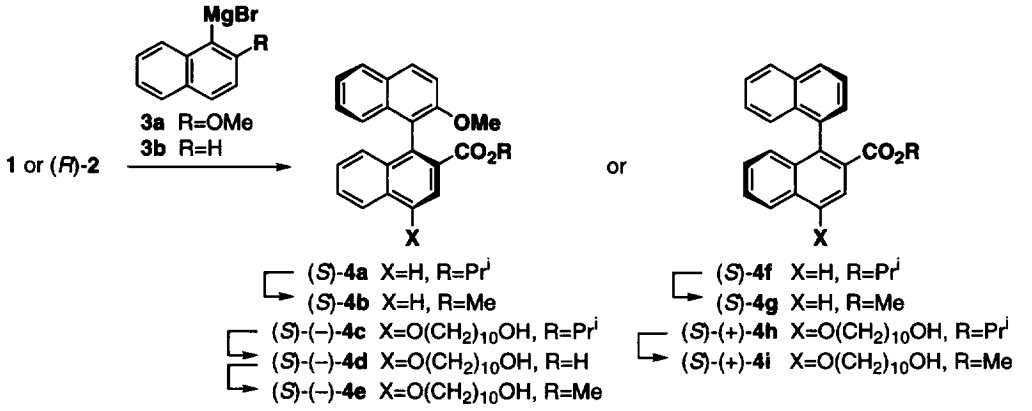
Some time ago we reported an effective asymmetric synthesis of axially chiral 1,1'-binaphthyl-2-carboxylic esters **4** by nucleophilic aromatic displacement of 1-(–)-menthoxy-2-naphthoates (*e.g.* **1**) with 1-naphthyl Grignard reagents **3**.[7,8] Although investigation of CPK and dreiding molecular models suggested substantial flexibility of the conformation of the substrate **1**, the origin of the high stereoselectivity was deduced from the seemingly most stable conformation of the naphthoate **1**, in which the bulky (–)-menthyl auxiliary resides in the out-of-the-plane of the naphthoxy moiety because of steric congestion, thus tilting toward the upper face of the naphthalene ring (Fig. 1). Therefore, the attacking naphthyl Grignard reagents **3** will be forced to approach mainly from the underside of the naphthalene plane, which plays a crucial role in determining the absolute configuration of the binaphthyl linkage.[7,9,10]

However, for a better mechanistic understanding of the efficient transfer of *C*-centrochirality of the leaving (–)-menthoxy group into axial chirality of the resulting 1,1'-binaphthyls, it was highly desired to investigate the reaction of a conformationally non-fluxional chiral 1-alkoxy-2-naphthoate with 1-naphthyl



1 (*R*)-**2**

Fig. 1 Schematic views of (–)-menthyl ether **1** and oxanaphthalenophane (*R*)-**2**



Scheme 1

Grignard reagents **3**. As we had recently been able to prepare both enantiomers of facially chiral naphthalenophane, 1,12-dioxa[12](1,4)naphthalenophane-14-carboxylic acid, and had determined its absolute configuration,[5] it occurred to us that its isopropyl ester **2** should be one of the best candidates to examine the mechanism by reacting with Grignard reagents **3** because the ansa chain effectively shields the upper face of the naphthalene ring as the (–)-menthoxy group supposedly does in the naphthoate **1** (Fig. 1).

The oxacyclophane (*R*)-**2** was treated with an excess of Grignard reagent **3a** (*ca.* 2 equiv.) in ether/benzene solution at room temperature for 3 h. After usual work-up of the reaction, chromatography on silica gel with hexane/AcOEt (4/1 v/v) as eluent gave the 1,1'-binaphthyl-2-carboxylic ester **4c** in 82% yield as a pale yellow solid; $[\alpha]_D^{26}$ –55.0 (*c* 1.19, $CHCl_3$). The binaphthyl product (–)-**4c** was hydrolyzed to acid (–)-**4d**, and its enantiomeric purity was determined to be more than 99% ee by HPLC on CHIRALPAK AD eluting with 2-propanol (20%) and trifluoroacetic acid (0.1 %) in hexane. The *S* absolute configuration was established by comparison of the CD spectrum of its methyl ester (–)-**4e** with that of methyl (*S*)-2'-methoxy-1,1'-binaphthyl-2-carboxylate **4b** (Fig. 2). This result coincides very well with that of the reaction of naphthoate **1** with Grignard reagent **3a** to give the binaphthyl coupling product (*S*)-**4a** of high atropisomeric purity (97% ee).[7]

The reaction of cyclophane (*R*)-**2** with Grignard reagent **3b** also proceeded smoothly to give the coupling product (+)-**4h** in good yield (85%) but in somewhat reduced atropisomeric purity (91% ee). However, the sense of the induced axial twist of the binaphthyl linkage was proved to be opposite to that of **4c** as evidenced by comparison of the CD spectrum of the methyl ester (+)-**4i** with that of methyl (*S*)-1,1'-binaphthyl-2-carboxylate **4g** (Fig. 3). This indicates that the direction of the induced axis depends on the nucleophile. Here again, the result is quite similar to that of the reaction of naphthoate **1** with naphthyl Grignard **3b** to give binaphthyl-2-carboxylate (*S*)-**4f** of 80% ee.[7]

The stereochemical course of the conversion of facial chirality of the cyclophane **2** into axial chirality of the binaphthyl products **4c**, **h** can be visualized as in Scheme 2. It may be obvious that migration of the naphthyl nucleus from the chelated magnesium complex **5** to the *ipso* position of the ansa chain is allowed only from the underside of the naphthalenophane ring to produce enolate intermediate **6**. This step is crucial to determine the sense of the axial twist of the binaphthyl product. For the reaction of 1-naphthyl Grignard

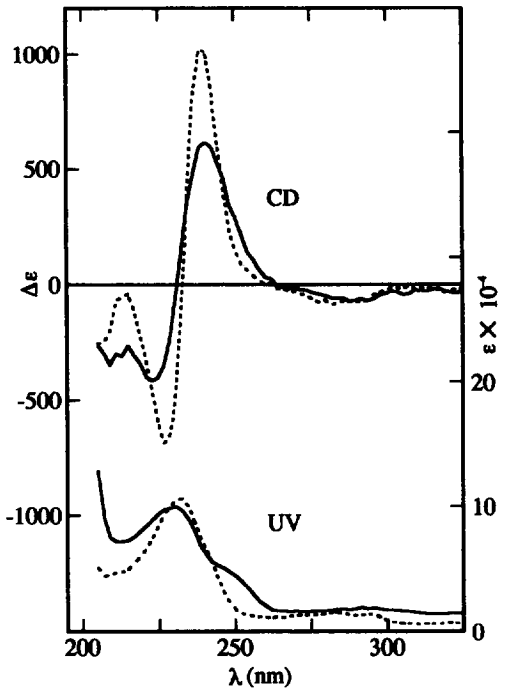


Fig. 2 CD and UV spectra of (–)-**4e** (solid lines) and authentic (*S*)-**4b** (broken lines) in dioxane/EtOH (1/9)

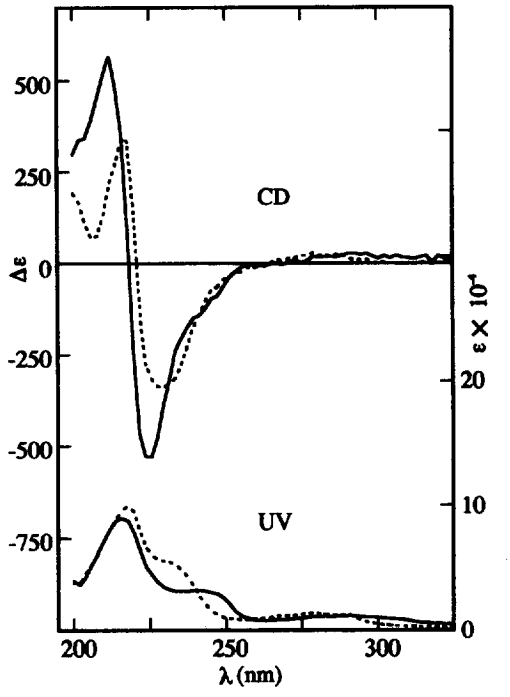
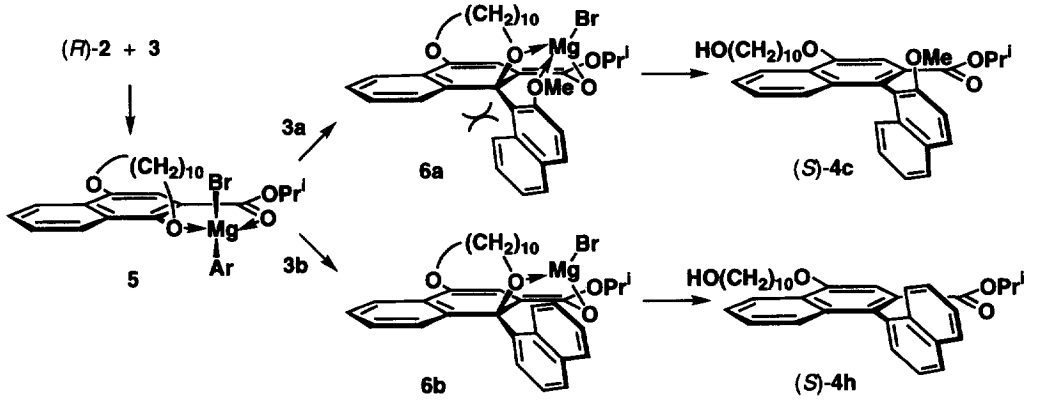


Fig. 3 CD and UV spectra of (+)-**4i** (solid lines) and authentic (*S*)-**4g** (66%ee) (broken lines) in dioxane/EtOH (1/9)

reagent **3b**, steric repulsion on approach of the naphthalene nucleophile to the naphthalenophane ring will dispose the peri hydrogen of the former as far as possible from the face of the latter to give the enolate intermediate **6b**, which then loses the alkoxymagnesium moiety to form the final binaphthyl product (*S*)-**4h** after aqueous work-up. For the 2-methoxy-1-naphthyl Grignard **3a**, however, strong co-ordination of the 2-



Scheme 2

methoxy substituent to the magnesium center will override the steric repulsion caused by the peri hydrogen and the naphthalenophane ring to give enolate **6a**, and then to binaphthyl product (*S*)-**4c**.

Although the stereochemical course stated above is mostly indebted to those previously proposed by Meyers[9] and Cram[10] for the oxazoline-mediated binaphthyl coupling reaction (the Meyers reaction), it should be noted that the mechanisms mostly are deduced from CPK molecular model considerations, which leave many other alternative possibilities in view of the conformational mobility of the substrates. We should like to say that the reaction of the cyclophane **2** with Grignard reagents **3** not only presents the first example of the transfer of a facial chirality of cyclophane into an axial chirality of the binaphthyl products with very high stereospecificity, but also substantiates the proposed mechanisms for the chiral induction of the ester-[7] or oxazoline-mediated[9,10] binaphthyl coupling reactions. It should also be noted that the development of novel methodologies for the construction of axially chiral 1,1'-binaphthyl linkage in an asymmetric manner is of potential importance and highly desired[11] because of the excellent chiral recognition ability provided by this class of atropisomeric binaphthyls.[12]

References

1. Mitchell, R. H. in *Cyclophanes Vol. 1;* Keehn, P. M.; Rosenfeld, S. M. Eds.; Academic: New York, 1983; p. 240.
2. Chan, T.-L.; Hung, C.-W.; Man, T.-O.; Leung, M. *J. Chem. Soc., Chem. Commun.*, **1994,** 1971 and references cited therein.
3. Cf., Schögl, K. *Top. Curr. Chem.*, **1984**, *125*, 27.
4. Oi, S.; Miyano, S. *Chem. Lett.*, **1992**, 987.
5. Hattori, T.; Harada, N.; Oi, S.; Abe, H.; Miyano, S. *Tetrahedron: Asymmetry*, **1995**, *6*, 1043.
6. Antonov, D. Y.; Belokon, Y. N.; Ikonnikov, N. S.; Orlova, S. A.; Pisarevsky, A. P.; Raevski, N. I.; Rozenberg, V. I.; Sergeeva, E. V.; Struchkov, Y. T.; Tararov, V. I.; Vorontsov, E. V. *J. Chem. Soc., Perkin Trans. 1*, **1995**, 1873.
7. Suzuki, T.; Hotta, H.; Hattori T.; Miyano, S. *Chem. Lett.*, **1990**, 807; Hattori, T.; Hotta, H.; Suzuki T.; Miyano, S. *Bull. Chem. Soc. Jpn.*, **1993**, *66*, 613.
8. See also: Hattori, T.; Koike, N.; Miyano, S. *J. Chem. Soc., Perkin Trans. 1*, **1994**, 2273; Hattori, T.; Tanaka, H.; Okaishi, Y.; Miyano, S. *J. Chem. Soc., Perkin Trans. 1*, **1995**, 235.
9. Meyers, A. I.; Lutomski, K. A. *J. Am. Chem. Soc.*, **1982**, *104*, 879.
10. Wilson, J. M.; Cram, D. J. *J. Am. Chem. Soc.*, **1982**, *104*, 881; Wilson, J. M.; Cram, D. J. *J. Org. Chem.* **1984**, *49*, 4930.
11. Recent examples: Hayashi, T.; Niizuma, S.; Kamikawa, T.; Suzuki, N.; Uozumi, Y. *J. Am. Chem. Soc.*, **1995**, *117*, 9101; Uemura, M.; Daimon, A.; Hayashi, Y. *J. Chem. Soc., Chem. Commun.*, **1995**, 1943; Bringmann, G.; Vitt, D. *J. Org. Chem.*, **1995**, *60*, 7674.
12. Recent examples: Kitayama, K.; Uozumi, Y.; Hayashi, T. *J. Chem. Soc., Chem. Commun.*, **1995**, 1533; Anderson, S.; Neidlein, U.; Gramlich, V.; Diederich, F. *Angew. Chem., Int. Ed. Engl.*, **1995**, *34*, 1596; Bandarage, U. K.; Painter, G. F.; Smith, R. A. *Tetrahedron: Asymmetry*, **1995**, *6*, 295; Carreira, E. M.; Lee, W.; Singer, R. A. *J. Am. Chem. Soc.*, **1995**, *117*, 3649; Maruoka, K.; Saito, S.; Yamamoto, H.; *J. Am. Chem. Soc.*, **1995**, *117*, 1165; Kuroki, T.; Hamada, T.; Katsuki, T. *Chem. Lett.*, **1995**, 339.

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