Pergamon

Tetrahedron Letters 42 (2001) 8035–8038

TETRAHEDRON LETTERS

Highly stereospecific conversion of *C*-centrochirality of a 3,4-dihydro-2*H*-1,1′-binaphthalen-1-ol into axial chirality of a 3,4-dihydro-1,1′-binaphthalene

Tetsutaro Hattori,[a,*] Masamitsu Date,[a] Kenta Sakurai,[a] Naoya Morohashi,[a] Hiroshi Kosugi[b] and Sotaro Miyano[a,*]

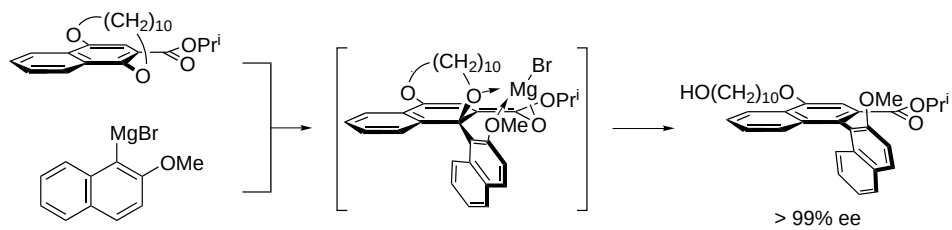
[a]*Department of Biomolecular Engineering, Graduate School of Engineering, Tohoku University, Aramaki-Aoba 07, Aoba-ku, Sendai 980-8579, Japan*

[b]*College of Medical Sciences, Tohoku University, Seiryo 2-1, Aoba-ku, Sendai 980-8575, Japan*

Received 1 June 2001; revised 5 September 2001; accepted 7 September 2001

Abstract—*C*-Centrochirality of 3,4-dihydro-2′-methoxy-2-methyl-2*H*-1,1′-binaphthalen-1-ol (*R*,*R*)-**3e**, which had been prepared by diastereoselective 1,2-addition of a 2-methoxy-1-naphthylytterbium reagent to 2-methyl-1-tetralone (*R*)-**1b**, was stereospecifically converted into axial chirality of 3,4-dihydro-2′-methoxy-2-methyl-1,1′-binaphthalene (a*R*)-**4** with up to 95% ee by dehydration with trifluoroacetic anhydride. DDQ aromatization of (a*R*)-**4** gave 2′-methoxy-2-methyl-1,1′-binaphthalene (a*R*)-**5** without appreciable loss of the axial integrity. The net process provides a potential access to nonracemic 1,1′-binaphthalenes.

Atropisomeric biaryls are not only structural units of biologically active natural products, but also prominent chiral discriminators in a variety of asymmetric reactions, as well as molecular recognition.[1] Thus, development of a new method for induction of axial chirality into the biaryl linkage has attracted much interest.[2,3] As a part of our study in this area, we reported previously that planner chirality of an oxanaphthalenophane could be highly stereospecifically converted into axial chirality of 1,1′-binaphthalenes by nucleophilic aromatic substitution with 1-naphthyl Grignard reagents (Scheme 1).[4] The stereochemical course of the reaction was rationalized by initial induction of *C*-centrochirality at the 1-position of the naphthoate ring by addition of the Grignard reagent with complete stereoselectivity because of the steric requirement of the ansa chain of the cyclophane, followed by highly stereospecific conversion of the *C*-centrochirality of the enolate intermediate into the axial chirality of the binaphthalene on leaving the alkoxymagnesium moiety. We have been seeking a system to which these chiral-element transfer principles can be applied. Here, we report such a new process, where *C*-centrochirality is induced by the diastereoselective 1,2-addition of 1-naphthyl anion to chiral 2-methyl-1-tetralone **1b** and the *C*-centrochirality of the resulting carbinol **3** is transformed into axial chirality of 1-aryl-substituted 3,4-dihydronaphthalene **4** by dehydration.[5] Although the protocol is known as a classical method for the preparation of biaryl compounds,[6] the asymmetric version has yet to be explored.



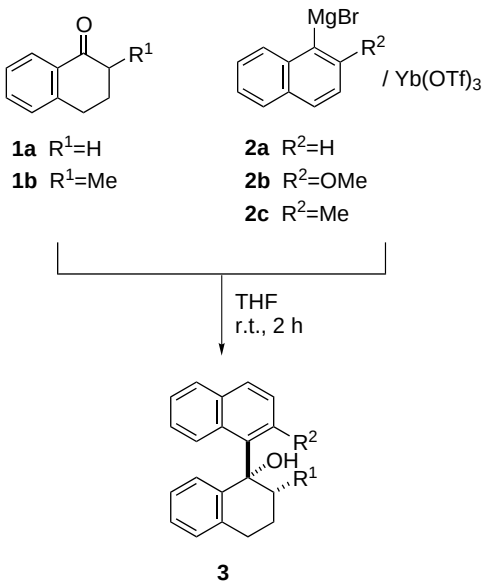
Scheme 1.

* Corresponding authors. Tel.: +81-22-217-7263; fax: +81-22-217-7293; e-mail: hattori@orgsynth.che.tohoku.ac.jp; miyano@orgsynth.che.tohoku.ac.jp

0040-4039/01/$ - see front matter
PII: S0040-4039(01)01708-7

First, 1,2-addition of 1-naphthyl anions to 1-tetralones **1a**, **b** was examined (Scheme 2, Table 1). The reaction of 1-tetralone **1a** with 1-naphthyl Grignard reagents **2a–c** resulted in failure, giving the corresponding carbinols **3** only in unsatisfactory yields (entries 1, 3 and 5). The competitive abstraction of an α-proton of the carbonyl group by the nucleophiles would be a plausible explanation of the low yields. This prompted us to test organolanthanide reagents, which have been reported to be efficient for the 1,2-addition to highly enolizable carbonyl compounds.[7,8] Thus, tetralone **1a** was treated with an organoytterbium reagent, which was prepared by simply stirring a mixture of the Grignard reagent **2** and $Yb(OTf)_3$ in THF at room temperature for 10 min. Although reaction variables were not optimized, carbinol **3** was obtained in good yield when the organoytterbium reagent having a Yb/**2** ratio of about 1:2 was employed (entries 2, 4 and 6). The reaction of 2-methyl-1-tetralone **1b** with the 2-methoxy-1-naphthylytterbium reagent resulted in exclusive formation of a single diastereoisomer (entry 9), whose relative configuration was determined to be *cis* (**3e**) by an X-ray crystallographic analysis (vide infra).[9] The stereochemical course of the reaction can be rationalized by the attack of the nucleophile to the carbonyl carbon from the opposite face to the 2-methyl group to avoid steric repulsion. The yield of carbinol **3e** was improved by increasing the ratio of the ytterbium reagent to the substrate (entry 10). The 1-naphthylytterbium reagent afforded two diastereoisomers in a ratio of 15:1 (entry 7). The relative configuration of the major diastereoisomer is expected to be *cis* (**3d**), considering the stereochemistry of the addition of **2b** to **1b**. In contrast to these ytterbium reagents, the bulkier 2-methyl-1-naphthylytterbium reagent did not afford the corresponding carbinol in a significant yield under the same reaction conditions. Enolization of the substrate seems to be predominant in this case.

A control reaction of (*R*)-**1b** with the 2-methoxy-1-naphthylytterbium reagent gave enantiomerically pure **3e** (entry 11),[10] the absolute stereochemistry of which was assigned to be (*R*,*R*) by the X-ray crystallographic



Scheme 2.

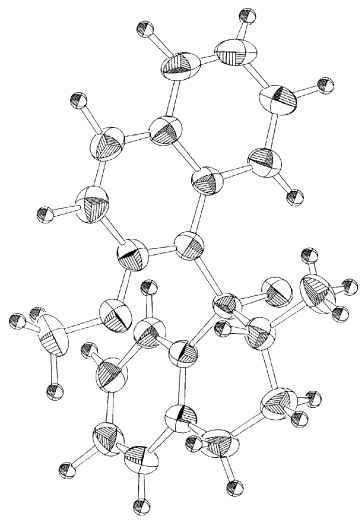


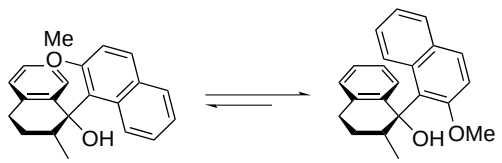
Figure 1. ORTEP drawing of carbinol (*R*,*R*)-**3e**.

Table 1. Reaction of tetralones **1** with Grignard reagents **2** in the presence or absence of $Yb(OTf)_3$

Entry	1		2			$Yb(OTf)_3$	3	
		R^1		R^2	Equiv.	Equiv.		Yield (%)[a]
1	**1a**	H	**2a**	H	1.0	0	**3a**	6
2			**2a**	H	2.3	1.0	**3a**	59
3			**2b**	OMe	2.0	0	**3b**	16
4			**2b**	OMe	2.0	1.0	**3b**	63
5			**2c**	Me	2.0	0	**3c**	6
6			**2c**	Me	2.0	1.0	**3c**	63
7	*rac*-**1b**	Me	**2a**	H	2.7	1.5	**3d**	90[b]
8			**2b**	OMe	1.1	1.1	**3e**	0
9			**2b**	OMe	2.0	1.1	**3e**	64
10			**2b**	OMe	2.7	1.5	**3e**	90
11	(*R*)-**1b**	Me	**2b**	OMe	2.7	1.5	(*R*,*R*)-**3e**	92

[a] Isolated yield after TLC on silica gel with hexane–dichloromethane or hexane–ethyl acetate as the developer.
[b] *trans* Isomer was also isolated in 6% yield.

analysis (Fig. 1). The ^{1}H NMR spectrum of carbinol (*R*,*R*)-**3e** revealed that it was in an equilibrium state between two conformational isomers, the ratio being 1:5.7 in $CDCl_3$. This is assumed to originate from restricted rotation around the 1-naphthyl–COH bond (Scheme 3). Similar atropisomerism was reported by Casarini et al. for hindered 1-naphthylcarbinols.[12] They found that each conformation of the two atropisomers can be assigned to *syn*- or *anti*-periplanar structure by taking advantage of the H-8 chemical shift of the naphthalene ring, which is greatly different between the two atropisomers. For example, in the case of 2,2,4,4-tetramethyl-3-(1-naphthyl)pentan-3-ol, the H-8 signal of the *syn*-periplanar atropisomer, which corresponds to structure **a** in the present case, appears at a much lower field (9.50 ppm in $CDCl_3$) than that of the *anti*-periplanar atropisomer (8.60 ppm), which corresponds to structure **b**, because of an interaction between the hydroxy group and the H-8 atom. The H-8 signal of the major atropisomer of (*R*,*R*)-**3e** appeared at 7.69 ppm in $CDCl_3$, while the minor appeared at 9.51 ppm. This should assign the conformation of the major atropisomer to be structure **b**. The ratio of the two atropisomers, which was determined by relative integration of the 2-Me signals, varied from 1:1 to 1:6.3 depending on the nature of the solvent (Table 2). It should be noted that the atropisomer obtained as crystals (Fig. 1) is the minor one in solution (i.e. conformation **a**). This might be attributed to the difference in the lattice energy between the two atropisomers.



a **b**

Scheme 3.

Table 2. Solvent dependence of the equilibrium between the two atropisomers of (*R*,*R*)-**3e**

Solvent	Chemical shift (δ/ppm) of the Me group		**a**:**b**
	Conformer **a**	Conformer **b**	
CD_2Cl_2	1.05	0.95	1:6.3
$CDCl_3$	1.09	0.96	1:5.7
Benzene-d_6	1.21	1.07	1:1.9
Acetone-d_6	1.06	0.94	1:1
CD_3OD	1.03	0.96	1:1.9

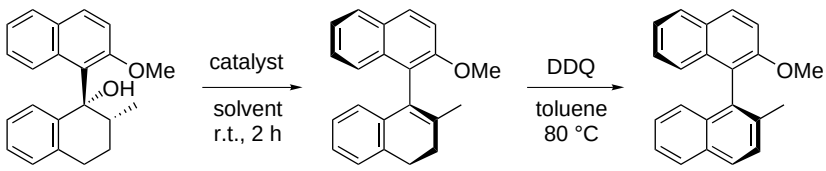
Dehydration of carbinol (*R*,*R*)-**3e** was examined in several dry solvents at room temperature by using 2.0 equiv. of toluene-*p*-sulfonic acid as the catalyst, giving dihydrobinaphthalene (–)-**4** (Scheme 4, Table 3).[13] The stereoselectivity of the reaction varied depending on the solvent employed (entries 1–6). This would be attributed to the difference in proportion of the two atropisomers in each solvent because the two atropisomers should induce axial chirality opposite to each other. It should be noted, however, that the enantiomeric excess (ee) values of dihydrobinaphthalene **4** were higher than those expected from the equilibrium. The stereoselectivity was improved up to 95% by using trifluoroacetic anhydride as the dehydrator at lower temperature (entry 10). Aromatization of dihydrobinaphthalene (–)-**4** of 84% ee with 3.0 equiv. of DDQ in toluene at 80°C, proceeded without appreciable loss of the axial integrity, giving binaphthalene (+)-**5** of 83% ee in 86% yield.[14] The absolute configuration of (+)-**5** was determined to be (a*R*) by comparison of the sign of specific rotation with that in the literature.[15] Therefore, it may be concluded that the dehydration occurs preferentially from the structure **b** to induce clockwise twist on the axis of **4**.

In conclusion, we have shown here that 1,2-addition of the 2-methoxy-1-naphthylytterbium reagent to chiral tetralone (*R*)-**1b** induced *C*-centrochirality at the car-

Table 3. Dehydration of carbinol (*R*,*R*)-**3e** to dihydrobinaphthalene (a*R*)-**4**

Entry	Catalyst	Solvent	Yield[a] (%)	Ee[b] (%)
1	*p*-TsOH	CH_2Cl_2	84	84
2		$CHCl_3$	85	78
3		Benzene	93	82
4		Toluene	84	80
5		Et_2O	93	70
6		Acetone	92	58
7		None[c]	92	50
8	$(CF_3CO)_2O$	Benzene	82	82
9		CH_2Cl_2	96	93
10[d]		CH_2Cl_2	94	95

[a] Isolated yield after TLC on silica gel with hexane–dichloromethane (2:1) as the developer.
[b] Determined by HPLC analysis on a Daicel Chiralcel OD-H with 0.3% propan-2-ol in hexane.
[c] Reaction was performed in solid phase.
[d] The reaction temperature was gradually raised from –60 to –20°C.



(*R*,*R*)-**3e** (a*R*)-(–)-**4** (a*R*)-(+)-**5**

Scheme 4.

bonyl carbon with complete stereoselectivity, giving carbinol (*R*,*R*)-**3e**. Although the carbinol existed as an equilibrium mixture of two conformational isomers, the *C*-centrochirality was highly stereospecifically converted into the axial chirality of dihydrobinaphthalene (a*R*)-**4** by the preferential dehydration of conformer **b**. Dihydrobinaphthalene (a*R*)-**4** was aromatized to binaphthalene (a*R*)-**5** without appreciable loss of the axial integrity. The present procedure, combined with an efficient method for the preparation of enantiomerically pure 2-substituted 1-tetralones,[16] will open a potential access to nonracemic 1,1′-binaphthalenes.

Acknowledgements

We are grateful to Dr. Masataka Watanabe of our university for helpful discussions. We thank the Ministry of Education, Culture, Sports, Science and Technology, Japan for financial support (Grants-in-Aid for Scientific Research No. 08405058 and 10208202).

References

1. Reviews: (a) Rosini, C.; Franzini, L.; Raffaelli, A.; Salvadori, P. *Synthesis* **1992**, 503; (b) Pu, L. *Chem. Rev.* **1998**, *98*, 2405.
2. Reviews: (a) Bringmann, G.; Walter, R.; Weirich, R. *Angew. Chem., Int. Ed.* **1990**, *29*, 977; (b) Putala, M. *Enantiomer* **1999**, *4*, 243. See also Ref. 1a.
3. Recent examples: (a) Saito, S.; Kano, T.; Muto, H.; Nakadai, M.; Yamamoto, H. *J. Am. Chem. Soc.* **1999**, *121*, 8943; (b) Cammidge, A. N.; Crépy, K. V. L. *Chem. Commun.* **2000**, 1723; (c) Yin, J.; Buchwald, S. L. *J. Am. Chem. Soc.* **2000**, *122*, 12051.
4. Hattori, T.; Koike, N.; Okaishi, Y.; Miyano, S. *Tetrahedron Lett.* **1996**, *37*, 2057.
5. For the related procedure, see: Myers, A. I.; Wettlaufer, D. G. *J. Am. Chem. Soc.* **1984**, *106*, 1135.
6. (a) Weiss, R. *Org. Synth. Coll. Vol. 3* **1955**, 729; (b) Berson, J. A.; Greenbaum, M. A. *J. Am. Chem. Soc.* **1958**, 653.
7. (a) Imamoto, T. *Lanthanides in Organic Synthesis*; Academic Press: London, 1994; (b) Molander, G. A. *Chem. Rev.* **1992**, *92*, 29.
8. For diastereoselective 1,2-addition of organoytterbium reagents to 2-methylcyclohexanone, see: Molander, G. A.; Burkhardt, E. R.; Weinig, P. *J. Org. Chem.* **1990**, *55*, 4990.
9. Similar high diastereoselectivity has been achieved in related reactions: (a) Gilchrist, T. L.; Stanford, J. E. *J. Chem. Soc., Perkin Trans. 1* **1987**, 225; (b) Draper, R. W.; Hou, D.; Iyer, R.; Lee, G. M.; Liang, J. T.; Mas, J. L.; Vater, E. J. *Org. Process Res. Dev.* **1998**, *2*, 186; (c) Mölm, D.; Flörke, U.; Risch, N. *Eur. J. Org. Chem.* **1998**, 2185. See also Ref. 8.
10. Tetralone (*R*)-**1b** of >98% ee was prepared by asymmetric protonation of the lithium enolate of **1b** with a chiral protonating agent, (*S*,*R*s)-1,1,1-trifluoro-3-[(4-methylphenyl)sulfinyl]propan-2-ol,[11] followed by optical resolution of the resulting **1b** of 90% ee by HPLC on a Daicel Chiralpak AD with 1% propan-2-ol in hexane as the eluent.
11. Kosugi, H.; Hoshino, K.; Uda, H. *Tetrahedron Lett.* **1997**, *38*, 6861.
12. Casarini, D.; Lunazzi, L.; Mazzanti, A. *J. Org. Chem.* **1997**, *62*, 3315.
13. (a*R*)-(−)-**4** of 84% ee, $[\alpha]_D^{23}$ −75.7 (*c* 0.99, $CHCl_3$).
14. The enantiomeric excess was determined by HPLC analysis on a Daicel Chiralpak AD with 3% ethanol in hexane as the eluent. (a*R*)-(+)-**5** of 83% ee, $[\alpha]_D^{22}$ +11.2 (*c* 0.63, $CHCl_3$) {lit.[15] $[\alpha]_D$ +10.8 (*c* 1.39, $CHCl_3$) for (a*R*)-**5**}.
15. Tamai, Y.; Nakano, T.; Miyano, S. *J. Chem. Soc., Perkin Trans. 1* **1994**, 439.
16. See, for example: McClure, D. E.; Lumma, P. K.; Arison, B. H.; Jones, J. H.; Baldwin, J. J. *J. Org. Chem.* **1983**, *48*, 2675.