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1,1'-Binaphthalene-8,8'-diol as an Efficient Chiral Controller: Highly Enantioselective Synthesis of Optically Active Ketones

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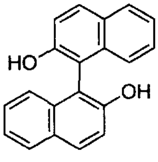
Abstract: Half esters (*R*)-**5** of 1,1'-binaphthalene-8,8'-diol undergo 1,4-addition of lithium dialkyl cuprates followed by formal 1,2-addition to give β-substituted ketones (*S*)-**6** or (*S*)-**7** with high enantioselectivity (96 ~ 100% ee). A brief discussion of the mechanism is presented.

Optically active 1,1'-binaphthalene-2,2'-diol (**1**) has been extensively used to provide a chiral environment in asymmetric syntheses[1,2] and in molecular recognitions.[3] However, the corresponding 8,8'-diol **2** has received little attention.[4] Recently, we reported a one-step synthesis of the optically active ketone (*R*)-**3** through successive 1,4- and 1,2-addition of Me$_2$CuLi to the (*S*)-binaphthyl ester **4**.[5] Although we were able to obtain an 84% yield at 87% ee, this is still inadequate from a preparative point of view. We report here that the replacement of a chiral auxiliary from 1,1'-binaphthalene-2,2'-diol (**1**) to 1,1'-binaphthalene-8,8'-diol (**2**) remarkably increases the ee.



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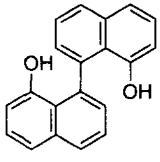

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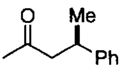
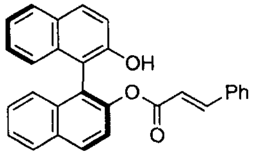


(*R*)-**3**



(*S*)-**4**

α,β-Unsaturated esters (*R*)-**5** were easily prepared by the condensation of (*R*)-1,1'-binaphthalene-8,8'-diol (**2**)[6] with the corresponding acids in the presence of 1-ethyl-3-[3-(dimethylamino)propyl]carbodiimide hydrochloride and a catalytic amount of DMAP. Conjugate addition of Me$_2$CuLi to the ester (*R*)-**5a** gave (*S*)-**6a** in

Scheme 1.

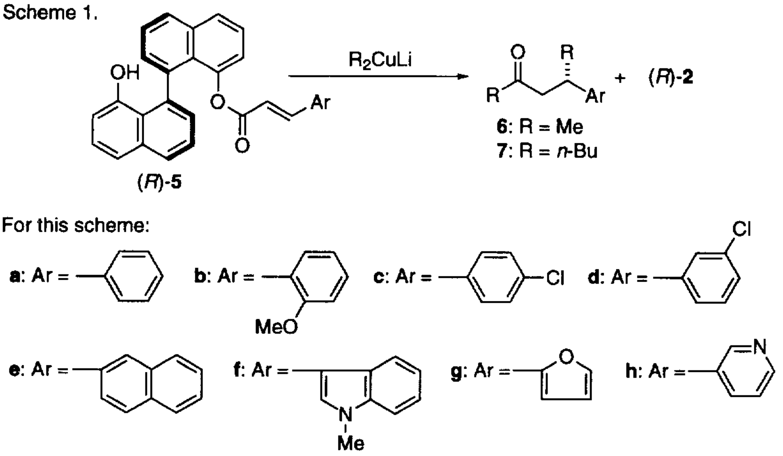


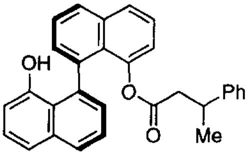
Table 1. Preparation of Ketones **6** and **7** from **5**.

ester[a]	reaction conditions			product[a]	yield, %[b]	% ee[c]
	reagent	temp, °C	time, h			
5a	Me_2CuLi	-20 → r.t.	3.5	**6a**[d]	85	98
5b	Me_2CuLi	-20 → r.t.	3	**6b**	82	97
5c	Me_2CuLi	-20 → r.t.	4	**6c**[e]	72	97
5d	Me_2CuLi	-20 → r.t.	3	**6d**[f]	86	100[g]
5e	Me_2CuLi	-20 → r.t.	3.5	**6e**	91	98
5f	Me_2CuLi	-20 → r.t.	3	**6f**	80	97[h]
5g	Me_2CuLi	-20 → r.t.	3	**6g**[i]	83	100[g]
5h	Me_2CuLi	-20 → r.t.	8	**6h**[j]	73	100[g,h]
5a	*n*-Bu_2CuLi	-78 → r.t.	2.5	**7a**[k]	69	97
5b	*n*-Bu_2CuLi	-78 → r.t.	8.5	**7b**	54	99
5c	*n*-Bu_2CuLi	-78 → r.t.	3	**7c**	68	96

[a] All new compounds gave satisfactory spectral data and elementary analysis and/or high resolution mass spectrum. [b] Isolated yield. [c] Determined by HPLC using a chiral column (Daicel Chiralcel OJ). [d] Ref. 8. [e] Ref. 9. [f] Cho, C. S.; Tanabe, K.; Uemura, S. *Tetrahedron Lett.* **1994**, *35*, 1275. [g] Another enantiomer was not detected. [h] Daicel Chiralcel OD was used. [i] Poirier, J.-M.; Dujardin, G. *Heterocycles* **1987**, *25*, 399. [j] Tamaru, Y.; Yamada, Y.; Yoshida, Z. *J. Org. Chem.* **1978**, *43* 3396. [k] Jensen, S. R.; Kristiansen, A.-M.; Petersen, J. M. *Acta Chem. Scand.* **1970**, *24*, 2641.

85% yield and 98% ee (Scheme 1).[7] Results for other esters **5** are listed in Table 1. The absolute configuration of **6a** was based on a comparison with the previously reported value[8] for the specific rotation. The CD spectra of **6a** and **7a** indicated that they had the same absolute configuration. We assume an *S*-configuration for other products **6** and **7**, since these Michael additions should proceed *via* the same type of mechanism.[9]

Extremely high ee of greater than 96% was obtained in every case examined. A lower chemical yield was observed for the addition of *n*-Bu_2CuLi, but a high ee was retained. Temperature control was crucial for successive 1,4- and 1,2-addition of the reagent. Unreacted (*R*)-**5a** was recovered quantitatively at -78 °C and the 1,4-addition product **8** was obtained in 68% yield along with a small amount of (*S*)-**6a** at -20 °C. This indicates that elimination of the 1,1-binaphthalene-8,8'-diol moiety from intermediate **9** to give another intermediate **10** (Scheme 2) starts at around -20 °C. Increasing the reaction temperature from -20 °C to room temperature over several hours generally gave satisfactory results.



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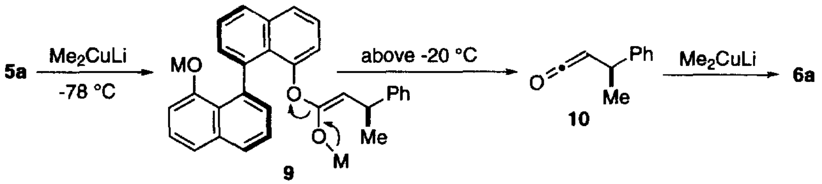
Scheme 2.



It is generally accepted that the most stable conformation for an enoate is *s-cis* with respect to the carbonyl group and the double bond.[10] Molecular mechanics calculations[11] indicated that **5a** also takes the *s-cis* form, as shown in Figure 1. Parallel alignment of the α,β-unsaturated group and another naphthyl ring is quite reasonable considering steric interaction and π-stacking. This model clearly shows that the *re*-face of the β-carbon to the carbonyl group is completely blocked by another naphthyl ring at the *peri*-position. Interestingly, the alkyl group must transfer from the highly hindered *re*-face of the β-carbon, assuming that the original *s*-cis conformation of **5a** is retained throughout the reaction to yield (*S*)-ketones **6** and **7**. A transition model is proposed to explain this intriguing result (Figure 2). Complexation of the reagent with the oxyanion at the 8'-position is crucial for the intramolecular delivery of the alkyl group to the β-carbon.[5] Cuprate-π-complexation of the enoate

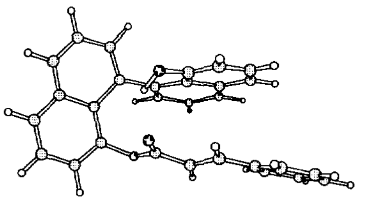


Figure 1. The most stable conformation of **5a** calculated by MacroModel/AMBER*.

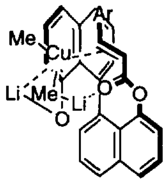


Figure 2. Chelation model for the intramolecular transfer of methyl group affording (*S*)-**6a**.

to the copper center is reportedly the first event in the addition of Me_2CuLi to methyl *trans*-cinnamate, according to NMR studies.[12] These results provide an efficient method for syntheses of ketones with an aromatic substituent at the β-position with high enantiomeric purity. Studies of the detailed mechanism, including the function of the 8'-hydroxy group, and extension of this method to aliphatic enoates are under way.

Acknowledgment. This study was financially supported by a Grant in Aid for Scientific Research from the Ministry of Education, Science and Culture of Japan .

References and Notes

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(4) (a) In an isolated example, Cram *et al.* used racemic **2** as a building block for the synthesis of a crown ether.[3] (b) Fuji, K.; Kawabata, T.; Kuroda, A.; Taga, T. *J. Org. Chem.* **1995**, *60*, 1914. (c) Fukushi, Y.; Shigematsu, K.; Mizutani, J.; Tahara, S. *Tetrahedron Lett.* **1996**, *32*, 4737.

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(6) For optical resolution of **2**, see: Ref. 4b and Fabbri, D.; Delogu, G.; Lucchi, O. D. *J. Org. Chem.* **1995**, *60*, 6599.

(7) Typical procedure for (*S*)-**6a**: To a stirred solution of CuI (183 mg, 0.96 mmol) in Et_2O (3 ml) was added 1.15 mol hexane solution of MeLi (1.9 ml, 1.96 mmol) under the atmosphere of argon at -20 °C. After being stirred for 30 min, this solution was added at -20 °C to the solution of (*R*)-**5a** (40 mg, 0.096 mmol) in Et_2O (3 ml). The temperature was gradually raised to room temperature in 2.5 h and the mixture was stirred for another 1 h at room temperature. After adding saturated NH_4Cl solution, the mixture was extracted with Et_2O and the ethereal layer was washed successively with NH_4Cl solution, water, and brine, dried over Mg_2SO_4, filtered, and evaporated under reduced pressure to give crude material, which was purified by PTLC (hexane : AcOEt = 10 : 1) to afford (*S*)-**6a** (13.2 mg, 85%), $[\alpha]_D^{20}$ +34.8 (c 0.7, $CHCl_3$); lit.[8] $[\alpha]_D^{25}$ -5.3 (neat) for the (*R*)-isomer of 15.6% ee.

(8) Hayashi, T.; Yamamoto, K.; Kumada, T. *Tetrahedron Lett.* **1975,** 3.

(9) Although optically active **6c** appeared in the literature, no $[\alpha]_D$ value was reported. See: van Klaveren, M.; Lambert, F.; Eijkelkamp, J. F. M.; Grove, D. M.; van Koten, G. *Tetrahedron Lett.* **1994**, *35*, 6135.

(10) Shida, N.; Kabuto, C.; Niwa, T.; Ebata, T.; Yamamoto, Y. *J. Org. Chem.* **1994,** *59*, 4068.

(11) The MacroModel / AMBER* (version 4.5) force field was used.

(12) Ullenius, C.; Christenson, B. *Pure Appl. Chem.* **1988,** *60*, 57.

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