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Practical synthetic protocols of enantiopure 1,1′-binaphthyl-2,2′-dicarboxylic acid and 2,2′-dicyano-1,1′-binaphthyl starting from optically active dibromide precursor

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Abstract—Dilithiation of optically active 2,2′-dibromo-1,1′-binaphthyl **2** with *t*-BuLi followed by carboxylation of the resulting dilithio-intermediate **3** with CO_2 gave optically active 1,1′-binaphthyl-2,2′-dicarboxylic acid **1**, which was further transformed to its dicyano derivative **4**. Both of these transformations were carried out in a one-pot operation and the products were obtained in excellent yields with no observable racemization.

Enantiopure 1,1′-binaphthyl-2,2′-dicarboxylic acid **1** has received much attention as a versatile synthetic intermediate in the preparation of a variety of chiral catalysts and ligands in enantioselective processes.[1] Since its first preparation by Kuhn and Albrecht,[2] several practical synthetic routes have been reported: (1) Optical resolution of racemate (±)-**1** or its precursors.[3] (2) Inter- or intramolecular diastereoselective Ullmann coupling of optically active 2-halonaphthalene derivatives.[4] (3) Palladium-catalyzed methoxycarbonylation of enantiopure 2,2′-bis(triflate)-1,1′-binaphthyl.[5] However, the optical resolution and Ullmann coupling protocols require multi-pot operations starting from the key intermediates. Though methoxycarbonylation directly affords the dimethyl ester of **1** in high yield, highly toxic CO gas must be handled with care in the laboratory. Because it is well precedented that carboxylation of organometallic reagents with CO_2 directly affords carboxylic acids without any toxic reagents,[6] we report herein a novel practical synthesis of enantiopure **1** via a one-pot operation of the dilithiation followed by carboxylation of optically active 2,2′-dibromo-1,1′-binaphtyl **2**, which is easily available according to our recently reported procedure.[7] We also describe a one-pot, quantitative and racemization-free transformation from **1** to 2,2′-dicyano-1,1′-binaphthyl **4** as a novel synthetic application of enantiopure **1**.

The synthetic studies of optically active (*R*)-**1** are summarized in Table 1. Initially, we chose *n*-BuLi as dilithiation reagent. Dilithiation of optically active (*R*)-**2** (97% ee) with 2.4 equiv of *n*-BuLi was complete in less than 30 min at −72 °C under N_2. After the atmosphere was exchanged from N_2 to CO_2, carboxylation of the resulting dilithio-intermediate (*R*)-**3** with atmospheric CO_2 was carried out at this temperature for 17 h to afford (*R*)-**1** in 65% yield and 86% ee (entry 1). The chemical yield was at a satisfactory level. However, decrease in enantiopurity, which was repeatedly observed in this reaction condition (entry 2), suggested that racemization of the axial chirality slowly but surely occurred during the transformation. Incorporation of sterically demanding substituents into 2,2′-positions of optically active binaphthyl compounds is a well-recognized strategy for restricting racemization of its axial chirality. Then, we investigated the chelating effect of TMEDA (*N*,*N*,*N*′,*N*′-tetramethylethylenediamine) and PMDTA (*N*,*N*,*N*′,*N*″,*N*″-pentamethyldiethylenetriamine) with the expectation that their chelating effects would increase steric bulk of the lithium substituents of nucleophilic binaphthyl intermediates.[8] However, no detectable improvement of the retention of the axial chirality was observed when 2.4 equiv of TMEDA was added to the reaction mixture (entry 3). Though the

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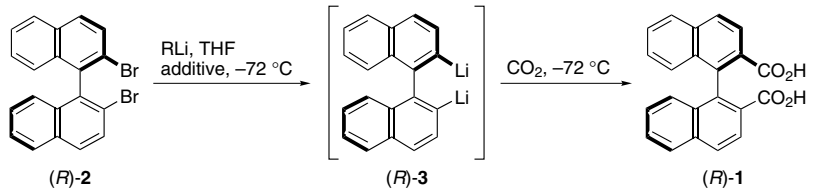
Table 1. Synthetic study of (*R*)-**1** via dilithiation followed by carboxylation of (*R*)-**2**[a,b]



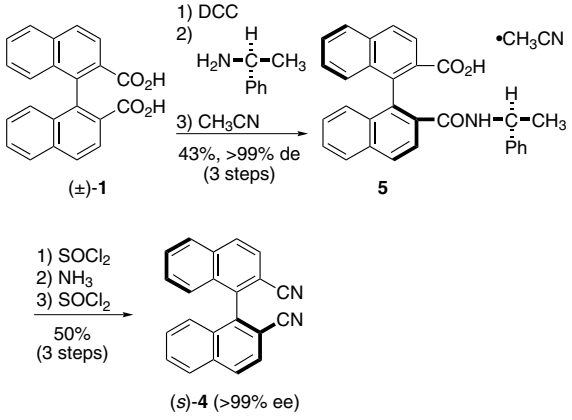
(*R*)-**2** (*R*)-**3** (*R*)-**1**

Entry	ee of (*R*)-**2**[f] (%)	RLi (equiv)	Additive (equiv)	ee of (*R*)-**1**[g] (%)	Yield of (*R*)-**1** (%)
1[c]	97	*n*-BuLi (2.4)	—	86	65
2[d]	94	*n*-BuLi (2.4)	—	82	61
3[d]	94	*n*-BuLi (2.4)	TMEDA (2.4)	81	70
4[d]	94	*n*-BuLi (2.4)	TMEDA (20)	90	21
5[d]	94	*n*-BuLi (2.4)	PMDTA (2.4)	85	65
6[c,e]	92	*t*-BuLi (4.8)	—	91	90
7[c]	92	*n*-BuLi (2.7)	LiBr (2.8)	89	43

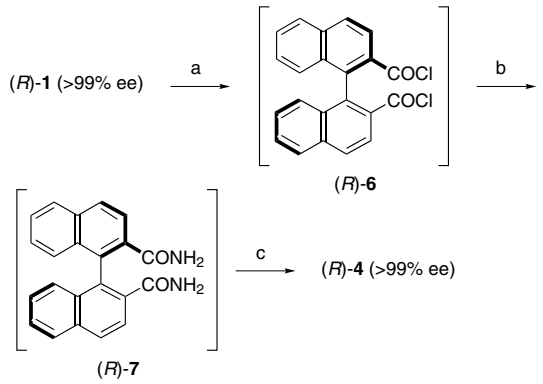
[a] The reaction scales were in the range from 0.60 to 7.3 mmol.
[b] The reaction times of carboxylation were in the range from 17 to 24 h.
[c] The dilithiation reaction was carried out for 30 min.
[d] The dilithiation reaction was carried out for 1 h.
[e] Average of two runs.
[f] The enantiopurity of (*R*)-**2** was estimated based on the specific rotation value (Ref. 10).
[g] The enantiopurity of (*R*)-**1** was determined by HPLC using a Daicel Chiralcel OD-H (Ref. 9).

retention of enantiopurity was gradually improved as the amount of TMEDA was increased, the complete retention of enantiopurity was not realized even through the use of 20 equiv of TMEDA and the chemical yield was significantly decreased (entry 4). The tridentate chelating agent PMDTA was also ineffective for the complete retention of the axial chirality (entry 5). Fortunately, in contrast to *n*-BuLi, *t*-BuLi was found to be sufficient to effect the transformation from (*R*)-**2** to (*R*)-**1** (entry 6). Actually, the complete retention of the axial chirality was reproductively achieved through the use of *t*-BuLi. Though no explanation for this excellent result can be offered at this time, we felt that it was reasonable to assume that the LiBr byproduct may play an important role in the retention of the axial chirality. In fact, the improvement of the retention of the axial chirality was also observed when *n*-BuLi was used in the presence of LiBr (entry 7). In addition, it is noteworthy that not only the enantiopurity but also the chemical yield of (*R*)-**1** were remarkably improved when *t*-BuLi was used as the dilithiation reagent. Since the racemate (±)-**1** crystallized preferentially from an ether solution,[3d] the contamination of the minor enantiomer (*S*)-**1** could be removed by recrystallization followed by filtration of the resulting nearly racemic precipitates to afford enantiopure (*R*)-**1** confirmed by HPLC analysis.[9]

Enantiopure 2,2′-dicyano-1,1′-binaphthyl **4** would be a prospective candidate for a versatile synthetic intermediate of chiral ligands because the cyano group is convertible into not only a variety of other functional groups but also heterocycles containing nitrogen as the ligating donor in transition metal complexes.[11,12] To the best of our knowledge, only one effective synthetic protocol of enantiopure **4** has been reported by Vondenhof and Mattay (Scheme 1).[11a] However, their synthetic protocol requires multi-pot operations starting from racemate (±)-**1** and the chemical yield derived from the enantiopure intermediate **5** is moderate. Thus, in order to find a convenient synthetic protocol for enantiopure **4** and a novel synthetic application of enantiopure **1**, we investigated the synthesis of enantiopure (*R*)-**4** starting from enantiopure (*R*)-**1** with the expectation that the axial chirality would be completely retained during the transformation (Scheme 2). Because the transformation from a carboxylic acid to a nitrile consists of three steps in which an acyl chloride and an amide are consecutively produced as intermediates, we carried out a one-pot operation without isolation of the two intermediates (*R*)-**6** and (*R*)-**7** in order to simplify this protocol. A solution of enantiopure (*R*)-**1** in $SOCl_2$ was heated to reflux for 10 min. After evaporation of residual $SOCl_2$, THF and NH_3 were sequentially added



Scheme 1.



Scheme 2. Reagents and conditions: (a) $SOCl_2$ (excess), reflux, 10 min; (b) NH_3 (excess), THF, 0 °C, 15 min; (c) NEt_3 (excess), Tf_2O (excess), 0 °C, 40 min, 97% (three steps).

to the crude product at 0 °C. Then, the reaction mixture was stirred at this temperature for 15 min. After evaporation of THF and excess NH_3, the residue was diluted with CH_2Cl_2 and then reacted with large excess of Et_3N and Tf_2O at 0 °C for 40 min. Concentration of the reaction mixture and subsequent purification by chromatography on silica gel afforded the desired enantiopure (*R*)-**4** in 97% overall yield with no observable racemization confirmed by HPLC analysis.[13]

In conclusion, our present study demonstrated novel practical protocols for the synthesis of enantiopure 1,1′-binaphthyl-2,2′-dicarboxylic acid (*R*)-**1** and its dicyano derivative (*R*)-**4** starting from optically active dibromide precursor (*R*)-**2**. We also found that the employment of *t*-BuLi as dilithiation reagent is crucial for the retention of the axial chirality during the transformation from (*R*)-**2** to (*R*)-**1**. Synthetic application of these enantiopure functional binaphthyl compounds to the preparation of chiral catalysts and ligands is under way in our laboratory.

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References and notes

1. (a) Ooi, T.; Uematsu, Y.; Maruoka, K. *J. Org. Chem.* **2003**, *68*, 4576–4578, and references cited therein; (b) Yang, D.; Wong, M.-K.; Yip, Y.-C.; Wang, X.-C.; Tang, M.-W.; Zheng, J.-H.; Cheung, K.-K. *J. Am. Chem. Soc.* **1998**, *120*, 5943–5952, and references cited therein; (c) Trost, B. M.; Lee, D. C.; Rise, F. *Tetrahedron Lett.* **1989**, *30*, 651–654; (d) Groves, J. T.; Myers, R. S. *J. Am. Chem. Soc.* **1983**, *105*, 5791–5796; (e) Mazaleyrat, J.-P.; Cram, D. J. *J. Am. Chem. Soc.* **1981**, *103*, 4585–4586.
2. Kuhn, R.; Albrecht, O. *Justus Liebigs Ann. Chem.* **1928**, *465*, 282–287.
3. (a) Seki, M.; Yamada, S.-I.; Kuroda, T.; Imashiro, R.; Shimizu, T. *Synthesis* **2000**, 1677–1680; (b) Furutani, T.; Hatsuda, M.; Imashiro, R.; Seki, M. *Tetrahedron: Asymmetry* **1999**, *10*, 4763–4768; (c) Oi, S.; Matsuzaka, Y.; Yamashita, J.; Miyano, S. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 956–957; (d) Kanoh, S.; Hongoh, Y.; Motoi, M.; Suda, H. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 1032–1034; (e) Colter, A. K.; Clemens, L. M. *J. Am. Chem. Soc.* **1965**, *87*, 847–852; (f) Hall, D. M.; Turner, E. E. *J. Chem. Soc.* **1955**, 1242–1251.
4. (a) Nelson, T. D.; Meyers, A. I. *J. Org. Chem.* **1994**, *59*, 2655–2658; (b) Miyano, S.; Shimizu, K.; Sato, S.; Hashimoto, H. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 1345–1346; (c) Miyano, S.; Tobita, M.; Hashimoto, H. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 3522–3526.
5. Ohta, T.; Ito, M.; Inagaki, K.; Takaya, H. *Tetrahedron Lett.* **1993**, *34*, 1615–1616.
6. Hattori, T.; Suzuki, Y.; Miyano, S. *Chem. Lett.* **2003**, *32*, 454–455, and references cited therein.
7. Hoshi, T.; Shionoiri, H.; Suzuki, T.; Ando, M.; Hagiwara, H. *Chem. Lett.* **1999**, *28*, 1245–1246.
8. For chelating effects of TMEDA and PMDTA with an aryllithium, see: Reich, H. J.; Goldenberg, W. S.; Sanders, A. W.; Jantzi, K. L.; Tzchucke, C. C. *J. Am. Chem. Soc.* **2003**, *125*, 3509–3521, and references cited therein.
9. Daicel Chiralcel OD-H (0.46 cm $\phi \times 25$ cm), hexane/EtOH/TFA = 90:10:0.1, wavelength: 254 nm, flow rate: 1.0 mL/min, retention time: 7.8 min (*R*), 11.8 min (*S*).
10. Brown, K. J.; Berry, M. S.; Waterman, K. C.; Lingenfelter, D.; Murdoch, J. R. *J. Am. Chem. Soc.* **1984**, *106*, 4717–4723.
11. For the preparation of enantiopure **4**, see: (a) Vondenhof, M.; Mattay, J. *Chem. Ber.* **1990**, *123*, 2457–2459; (b) Kurz, L.; Lee, G.; Morgans, D., Jr.; Waldyke, M. J.; Ward, T. *Tetrahedron Lett.* **1990**, *31*, 6321–6324.
12. For the preparation of optically active **4**, see: (a) Karák, P.; Putala, M. *Collect. Czech. Chem. Commun.* **2000**, *65*, 729–740; (b) Hoshi, T.; Katano, M.; Nozawa, E.; Suzuki, T.; Hagiwara, H. *Tetrahedron Lett.* 2004, 45 following paper. doi: 10.1016/j.tetlet.2004.02.156.
13. Daicel Chiralcel OD-H (0.46 cm $\phi \times 25$ cm), hexane/*i*-PrOH = 3:1, wavelength: 254 nm, flow rate: 0.2 mL/min, retention time: 34.8 min (*R*), 38.7 min (*S*).