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The Ullmann Coupling Reaction of Axially Chiral (*S*)-2,2′-Bis(1-iodo-2-naphthyloxycarbonyl)-1,1′-binaphthyl

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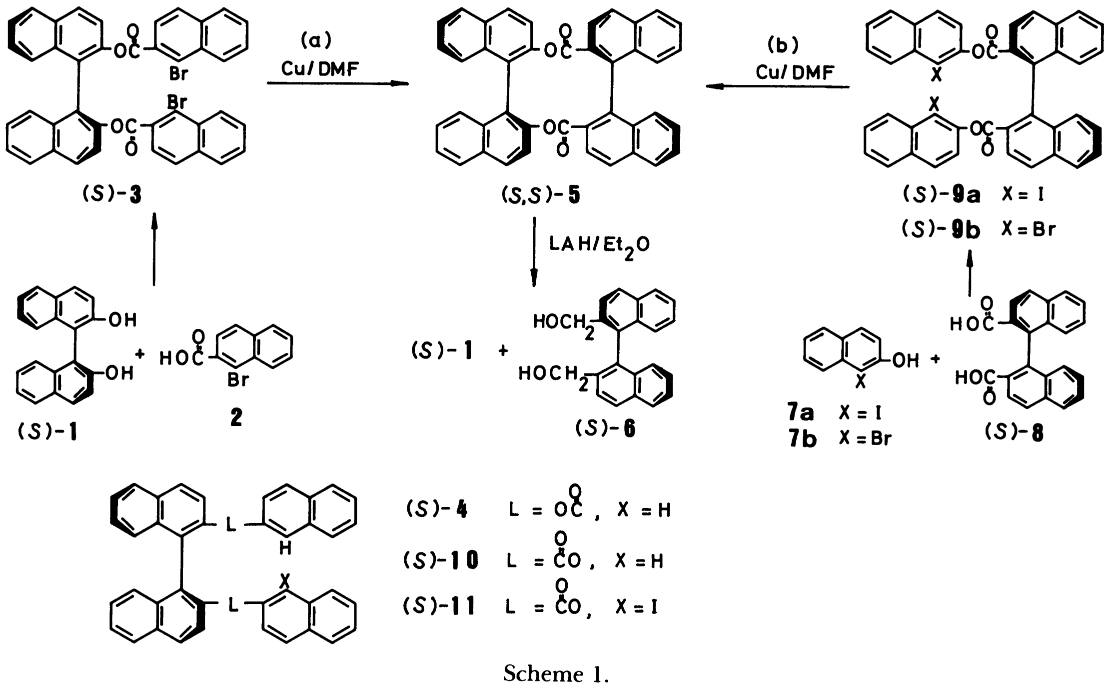
Synopsis. The intramolecular Ullmann coupling of the title diester proceeded in low yield but with virtually complete asymmetric induction in joining the two naphthyl units leading to the 12-membered cyclic diester of (*S*,*S*)-configuration, which is the same diastereomer obtained from the reaction of (*S*)-2,2′-bis(1-bromo-2-naphthoyloxy)-1,1′-binaphthyl.

In our previous paper,[1)] we have reported that the intramolecular Ullmann coupling of chiral diester (*S*)-**3** derived from *chiral diol (S)-***1** and *1-bromo-2-naphthoic acid* **2** proceeds with complete asymmetric induction in joining the two naphthyl units leading to the formation of only (*S*,*S*)-cyclic diester ((*S*,*S*)-**5**) without (*S*,*R*)-diastereomer, although accompanied by the formation of reduction product ((*S*)-**4**) and others derived by intermolecular reactions (Scheme). We reasoned that the remarkable stereoselectivity of the unimolecular coupling should be ascribed to the steric requirement in the product 12-membered cyclic diester which contains two sets of bulky, and rigid 1,1′-binaphthyl moieties; as CPK molecular models of the two possibilities indicate, severe steric compression in (*S*,*R*)-**5** as compared to (*S*,*S*)-**5** would exclude the formation of the former, irrespective of the mechanism of the coupling process.

If this is the case, the other feasible route to the cycle **5** *via* aryl coupling, namely the Ullmann reaction of another chiral bifunctional diester (*S*)-**9**, which is derived from *axially chiral binaphthyldicarboxylic acid (S)-8* and *1-halo-2-naphthol 7*, should also give rise to exclusive formation of (*S*,*S*)-**5** as the unimolecularly coupled product.

To test this hypothesis, optically active (*S*)-**9a** was prepared from axially chiral (*S*)-**8** (91% e.e.) and 1-iodo-2-naphthol **7a**. The Ullmann reaction was carried out by slowly adding a DMF solution of (*S*)-**9a** to a vigorously stirred suspension of an activated copper powder in DMF heated at reflux. Although the ease of copper-promoted halogen displacement from the aromatic ring is generally I>Br, (*S*)-**9a** was much less reactive than (*S*)-**3**, suggesting the importance of the activation of the halogen by the carbonyl function in the *ortho*-position in the latter.[2)] Thus, deiodination of (*S*)-**9a** was incomplete under the comparable conditions where (*S*)-**3** reacted completely.[3,4)] This and concurrent occurrence of intermolecular reaction resulted in somewhat complex products, while HPLC analysis of the mixture revealed only three components, (*S*,*S*)-**5**, (*S*)-**10**, and (*S*)-**11**, as the unimolecular products from (*S*)-**9a**.

Unfortunately, the dominant reaction of (*S*)-**9a** with copper was reductive substitution to (*S*)-**10**.[5)] However, the first eluting component on HPLC, which was recovered in a 11% yield by column chromatography followed by TLC purification, showed the IR and MS spectrum similar to those of the authentic (*S*,*S*)-**5** obtained in the previous work *via* path **a**.[1)] As there seemed little possibility of enantiomeric concentration of the monomeric cycle during the chromatographic purification (see Experimental), the recovered sample of (*S*,*S*)-**5** should represent the component in the reaction mixture. The ester linkage of the sample of (*S*,*S*)-**5** was reductively cleaved by treatment with LAH



Scheme 1.

to give (*S*)-**1** and (*S*)-**6**; the optical purity of these diols was essentially identical (88—90%), as determined by comparison of the optical rotations with those of pure enantiomers.[6] This is likely to suggest that the enantiomeric purity of the recovered (*S*,*S*)-**5** should be close to 90%; this value is in turn in fairly good agreement with that estimated from the optical rotation of the (*S*,*S*)-**5** itself by comparing with that of the enantiomerically pure cycle ($[\alpha]^{23}_{\mathrm{D}}$ −457.6°) obtained in the previous work.[1] Thus, as the enantiomeric purity of the recovered cycle practically coincided with that of the starting (*S*)-**8**, it follows that the unimolecular Ullmann coupling of (*S*)-**9a** (path **b**) also proceeded with virtually complete diastereoselectivity to give the (*S*,*S*)-cycle.

In conclusion, the stereochemistry of the intramolecular coupling of the two aryl units attached, with appropriate spacing groups, at the 2,2′-positions of 1,1′-binaphthyl skeleton is likely to be highly controlled by the axial chirality of the parent binaphthyl moiety as well as the steric requirement of the product cycle.

Experimental

Measurement and materials were similar to those described in the previous paper unless otherwise noted.[1] Melting points are uncorrected. **7a** was prepared by a literature procedure, mp 92—93 °C (lit,[7] 92 °C).

(S)-8. According to the procedure by Hall and Turner,[8] the less soluble quinine salt was recrystallized three times from EtOH to give hexagonal plates, mp 173—175 °C; $[\alpha]^{23}_{\mathrm{D}}$ −85.8° (*c* 1.00, acetone). Decomposition of the salt gave the free acid, which was dried *in vacuo* at 120 °C, mp 152—154 °C; $[\alpha]^{24}_{\mathrm{D}}$ −99.7° (*c* 1.08, 0.1 M NaOH (1 M=1 mol dm^{-3})).[9] Found: C, 77.27; H, 4.06%. Calcd for $\mathrm{C_{22}H_{14}O_4}$: C, 77.18; H, 4.12%. A sample of the (*S*)-**8** was boiled with LAH in ether to give (*S*)-**6**, $[\alpha]^{24}_{546}$ −78.8° (*c* 1.80, acetone).

(S)-9a. After (*S*)-**8** (2.80 g, 8.19 mmol) had been refluxed in $\mathrm{SOCl_2}$ (*ca.* 30 ml) for 3 h, volatiles were removed *in vacuo*. The organic residue was dissolved in benzene (60 ml) and pyridine (10 ml), to which was added **7a** (5.30 g, 19.6 mmol). The mixture was stirred overnight at room temperature and then heated at reflux for 3 h. The reaction was worked up as usual, and the crude diester was purified by an alumina column chromatography with benzene as eluant, 5.95 g (86%); mp 144—147 °C; $[\alpha]^{22}_{\mathrm{D}}$ +72.3° (*c* 1.03, PhH); IR (KBr) 1750, 1200, and 1090 cm^{-1}. Found: C, 60.08; H, 2.93; I, 29.56%. Calcd for $\mathrm{C_{42}H_{24}I_2O_4}$: C, 59.60; H, 2.86; I, 29.98%.

Ullmann Reaction of (S)-9a. According to the procedure described before,[3] (*S*)-**9a** (2.67 g, 3.16 mmol) in 30 ml of DMF was added over a 5 h period to a vigorously stirred copper powder (5.0 g, 79 mmol) in DMF (100 ml) heated at reflux. The mixture was refluxed for another 2 h, and it was worked up as before to give 1.77 g of a pale brown residue, which contained 1.54% of iodine by combustion analysis; $[\alpha]^{22}_{\mathrm{D}}$ −82.0° (*c* 1.1, PhH). HPLC analysis (JASCO SC-01 column, MeCN/$\mathrm{H_2O}$ (10/1)) showed the presence of, in the order of elution, (*S*,*S*)-**5** (1.00), (*S*)-**10** (1.63), and (*S*)-**11** (2.26), and other higher oligomeric products (in parentheses are shown retention volumes relative to (*S*,*S*)-**5**). The mixture (1.70 g) was subjected to a silica-gel column chromatography (Wako Gel C-200) using $\mathrm{CHCl_3}$ (1% EtOH) as eluant to give a 245 mg of the first fraction comprised mostly of (*S*,*S*)-**5** and small amount of (*S*)-**10**; $[\alpha]^{23}_{\mathrm{D}}$ −385° (*c* 1.03, PhH). A part of the sample (*ca.* 85 mg) was treated with LAH, and the products were purified by TLC (silica gel, $\mathrm{CHCl_3}$/AcOEt (4/1)) to give 2-naphthol (trace), (*S*)-**1**, 25 mg, $[\alpha]^{23}_{\mathrm{D}}$ −30.9° (*c* 1.15, THF) and (*S*)-**6**, 32 mg, $[\alpha]^{24}_{546}$ −77.8° (*c* 1.28, acetone). The remainder of the fraction was further purified by TLC (silica gel, PhH) to give (*S*,*S*)-**5** which appeared to be homogeneous by HPLC, 130 mg; $[\alpha]^{24}_{\mathrm{D}}$ −409° (*c* 0.352, PhH); IR (KBr) 1750, 1250, 1220, and *ca.* 1110 cm^{-1}; MS (70 eV) *m/z* (rel intensity) 592 ($\mathrm{M^+}$, 19.0), 280 (9.9), 268 (21.8), and 252 (6.9). LAH treatment of the (*S*,*S*)-**5** (107 mg, 0.181 mmol) gave (*S*)-**1**, 41 mg, $[\alpha]^{23}_{\mathrm{D}}$ −31.4° (*c* 1.18, THF) and (*S*)-**6**, 47 mg, $[\alpha]^{24}_{546}$ −78.0° (*c* 1.31, acetone).

From the second fraction of the column effluent was recovered (*S*)-**10**, 590 mg; $[\alpha]^{23}_{\mathrm{D}}$ +39.0° (*c* 1.03, PhH); 182—185 °C; IR (KBr) 1740, 1230, 1210, and 1120 cm^{-1}. Found: C, 84.57; H, 4.32%. Calcd for $\mathrm{C_{42}H_{26}O_4}$: C, 84.83; H, 4.41%. LAH treatment of the sample (250 mg) gave 2-naphthol (85 mg) and (*S*)-**6**, 110 mg, $[\alpha]^{24}_{546}$ −77.3° (*c* 1.55, acetone). (*S*)-**11** was deduced from MS ($\mathrm{M^+}$ 720) and from positive Beilstein test conducted on the third fraction of the column effluent.

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4) When (*S*)-**9b** was treated with copper under the similar conditions, only 50% of the total bromine was consumed giving (*S*,*S*)-**5** only in poor yield.

5) See for example, F. E. Ziegler and J. A. Schwartz, *J. Org. Chem.*, **43**, 985 (1978).

6) See Ref. 1): (*S*)-**1**: $[\alpha]^{22}_{\mathrm{D}}$ −35.0° (*c* 1.18, THF). (*S*)-**6**: $[\alpha]^{23}_{546}$ −86.0° (*c* 1.43, acetone).

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9) The maximum rotation reported, $[\alpha]_{\mathrm{D}}$ −110°; A. K. Colter and L. M. Clemens, *J. Am. Chem. Soc.*, **87**, 847 (1965).