Synthesis of Enantiomerically Pure Binaphthyl Derivatives. Mechanism of the Enantioselective, Oxidative Coupling of Naphthols and Designing a Catalytic Cycle†

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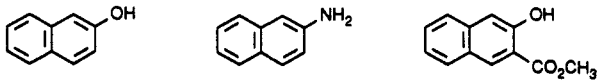
Three different mechanisms have been identified for the $CuCl_2$-mediated oxidative coupling of naphthols to binaphthyls in the presence of chiral amines (sparteine or α-methylbenzylamine); fair to excellent enantioselection has been observed (up to 100% ee). The choice of the dominant mechanism appears to be critically dependent on the structure of the partners to be coupled. Thus, for the self-coupling of 2-naphthol (1) the enantioselection is mainly controlled *via* a second-order asymmetric transformation of the product 4 (up to 100% ee). The same mechanism is responsible for the formation of enantiomerically enriched biphenanthrol 9 (76% ee). By contrast, enantiodifferentiation in the formation of 5 and 7 results from the diastereoselective crystallization of the corresponding Cu(II)–amine–binaphthyl complex (46% and 44% ee, respectively), whereas an enantioselective coupling operates in the preparation of 6 (71% ee). A catalytic cycle has been designed, employing 10 mol % of $CuCl_2$ (with AgCl to regenerate Cu^{II}) and sparteine (20 mol %); when applied to the asymmetric cross-coupling 1 + 3 → 6, the product (−)-6 (32% ee) was obtained in 41% yield.

Introduction

2,2′-Disubstituted derivatives of 1,1′-binaphthyl have been widely used in organic synthesis as chirality inducers.[1] Enantiomerically pure binaphthyl derivatives have been prepared in a number of ways,[2] employing methods ranging from the classical resolution via crystallization of diastereoisomeric salts to enzymatic hydrolysis of esters.[3] Asymmetric oxidative coupling has also been attempted and poor to good stereoselection has been accomplished in a few instances.[4-7] Recently, we have reported on the synthesis of enantiomerically enriched binaphthyl derivatives 4 and 5 from their precursors 1 and 2 by the $CuCl_2$/chiral amine-mediated oxidative coupling and have proposed a mechanistic rationalization for the observed enantioselective processes.[8-11] Herein, we report on the synthesis of the enantiomerically enriched 6, 7, and 9 and on remarkable differences between individual reactions. These differences are interpreted as evidence for the operation of three different mechanisms of enantiodifferentiation producing 4–7 and 9. Two of the mechanisms have been proposed earlier (for 4 and 5, respectively), and we provide further support; the third mechanism is new.



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Results and Discussion

Copper(II)-mediated oxidative coupling of naphthyl derivatives[12] usually results in the formation of a precipitate and a mother liquor, both of which contain the desired product.[6,8] In most cases we have analyzed these two phases separately and compared the results with those obtained from the crude mixtures.

† Dedicated to Dr. Vladimír Hanuš on the occasion of his 70th birthday.

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(1) For reviews, see, e.g.: (a) Morrison, J. D. *Asymmetric Synthesis*; Academic: New York, 1983–1985; Vols. 1–5. (b) Kočovský, P.; Tureček, F.; Hájíček, J. *Synthesis of Natural Products: Problems of Regioselectivity*; CRC: Boca Raton, FL, 1986; Vols. I and II. (c) Jacques, J.; Fouquey, C. *Org. Synth.* **1988**, *67*, 2. (d) Narasaka, K. *Synthesis* **1991**, 1. (e) Trost, B. M. *Pure Appl. Chem.* **1992**, *64*, 315. (f) Kagan, H. B.; Riant, O. *Chem. Rev.* **1992**, *92*, 1007. (g) Mikami, K.; Terada, M.; Narisawa, S.; Nakai, T. *Synlett* **1992**, 255. (h) Mikami, K.; Shimizu, M. *Chem. Rev.* **1992**, *92*, 1021. (i) Hattori, K.; Yamamoto, H. *J. Org. Chem.* **1992**, *57*, 3264 and references cited therein. (j) Parker, D. *Chem. Rev.* **1991**, *91*, 1441. (k) Noyori, R.; Takaya, H. *Acc. Chem. Res.* **1990**, *23*, 345. (l) Takaya, H.; Ohta, T.; Mashima, K.; Noyori, R. *Pure Appl. Chem.* **1990**, *62*, 1135. (m) Hayashi, T.; Kubo, A.; Ozawa, F. *Pure Appl. Chem.* **1992**, *64*, 421. (n) Rossiter, B. E.; Swingle, N. M. *Chem. Rev.* **1992**, *92*, 771. (o) Duthaler, R. O.; Hafner, A. *Chem. Rev.* **1992**, *92*, 807. (p) Blaser, H.-U. *Chem. Rev.* **1992**, *92*, 935. (q) Zassinovich, G.; Mestroni, G.; Gladiali, S. *Chem. Rev.* **1992**, *92*, 1051. (r) Burgess, K.; Ohlmeyer, M. J. *Chem. Rev.* **1991**, *91*, 1179.

(2) (a) For a review, see: Rosini, C.; Franzini, L.; Raffaelli, A.; Salvadori, P. *Synthesis* **1992**, 503. (b) For recent examples, see: (b) Stará, I.; Starý, I.; Závada, J. *Tetrahedron: Asymmetry* **1992**, *3*, 1365. (c) Stará, I.; Starý, I.; Závada, J. *J. Org. Chem.* **1992**, *57*, 6966. (d) Chong, J. M.; MacDonald, G. K.; Park, S. B.; Wilkinson, S. H. *J. Org. Chem.* **1993**, *58*, 1266.

(3) Kazlauskas, R. J. *J. Am. Chem. Soc.* **1989**, *111*, 4953 and references cited therein.

(4) Feringa, B.; Wynberg, H. *Bioorg. Chem.* **1978**, *7*, 397.

(5) Yamamoto, K.; Fukushima, H.; Nakazaki, M. *J. Chem. Soc., Chem. Commun.* **1984**, 1490.

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(7) Yamamoto, K.; Yumioka, H.; Okamoto, Y.; Chikamatsu, H. *J. Chem. Soc., Chem. Commun.* **1987**, 168.

(8) Smrčina, M.; Lorenc, M.; Hanuš, V.; Sedmera, P.; Kočovský, P. *J. Org. Chem.* **1992**, *57*, 1917.

(9) The highly chemoselective formation of 5 from 1 and 2 is the first cross-coupling of this type to produce an optically active binaphthyl derivative (for the racemic version, see ref 11).

(10) From the enantiomerically enriched 4 and 5, enantiomerically pure products were obtained by further crystallization.[8]

(11) Smrčina, M.; Lorenc, M.; Hanuš, V.; Kočovský, P. *Synlett* **1991**, 231.

(12) Other metals have also been explored by other investigators, namely Fe(III)[13] and Mn(III),[14] but to date, Cu(II), first used by Wynberg,[4] has been the most successful oxidant.[4-8,15]

(13) Toda, F.; Tanaka, K.; Iwata, S. *J. Org. Chem.* **1989**, *54*, 3007 and references cited therein.

(14) (a) Yamamoto, H.; Fukushima, H.; Okamoto, Y.; Hatada, K.; Nakazaki, M. *J. Chem. Soc., Chem. Commun.* **1984**, 1111. (b) Diederich F.; Hester, M. R.; Uyeki, M. A. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1705.

(15) (a) Hovorka, M.; Günterová, J.; Závada, J. *Tetrahedron Lett.* **1990**, *31*, 413. (b) Hovorka, M.; Závada, J. *Org. Prep. Proc. Int.* **1991**, *23*, 200. (c) Hovorka, M.; Ščigel, R.; Günterová, J.; Tichý, M.; Závada, J. *Tetrahedron* **1992**, *48*, 9503. (d) Hovorka, M.; Závada, J. *Tetrahedron* **1992**, *48*, 9517.

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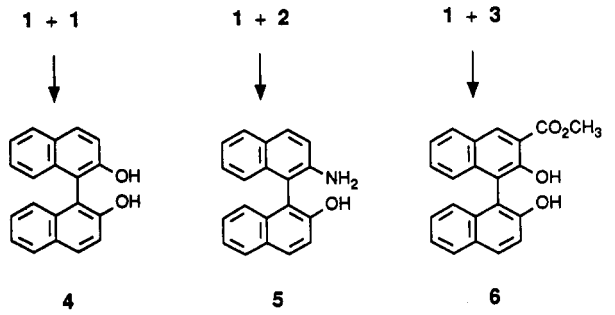
Table I. Preparation of Optically Active Binaphthyls 4–7 and 9

entry	product	method[a]	reagent	isolation[b]	yield,[c] %	ee, %
1	(*S*)-(−)-**4**	A	$CuCl_2$–(−)-sparteine[d]	P	14	100[f]
2	(*S*)-(−)-**4**	A	$CuCl_2$–(−)-sparteine[d]	S	42	20[f]
3	(*S*)-(−)-**4**	B	$CuCl_2$–(−)-sparteine[d]	P	36	100[f]
4	(*S*)-(−)-**4**	B	$CuCl_2$–(−)-sparteine[d]	S	60	59[f]
5	(*S*)-(−)-**5**	A	$CuCl_2$–(+)-$PhCH(NH_2)Me$[e]	P	43	46[f]
6	(*R*)-(+)-**5**	A	$CuCl_2$–(+)-$PhCH(NH_2)Me$[e]	S	42	46[f]
7	(*S*)-(−)-**6**	A	$CuCl_2$–(−)-sparteine[d]	PS	99	41
8	(*S*)-(−)-**6**	A	$CuCl_2$–(−)-sparteine[d]	P	45	71
9	(*S*)-(−)-**6**	A	$CuCl_2$–(−)-sparteine[d]	S	49	27
10	(*S*)-(−)-**7**	A	$CuCl_2$–(−)-$PhCH(NH_2)Me$[d]	P	47	44
11	(*R*)-(+)-**7**	A	$CuCl_2$–(−)-$PhCH(NH_2)Me$[d]	S	40	43
12	(*S*)-(−)-**9**	A	$CuCl_2$–(−)-sparteine[d]	P	80	76
13	(*S*)-(−)-**9**	B	$CuCl_2$–(−)-sparteine[d]	P	95	62

[a] A = coupling experiment; B = deracemization (see the text). [b] P = from precipitate; S = from solution; PS = from a mixture of P and S. [c] For optimized method and overall yields of pure enantiomers, see the text. [d] In MeOH. [e] In *i*-PrOH. [f] See ref 8.

Scheme I



The self-coupling of 2-naphthol (**1**), using an *in situ* generated complex of $CuCl_2$ and (−)-sparteine in methanol,[8] produced mainly (*S*)-(−)-**4**; the same enantiomer was found to predominate in both the precipitate and the mother liquor (Scheme I, Table I, entries 1 and 2).[8] In accord with a pioneering observation by Brussee (made with amphetamine),[6] we have demonstrated that racemic (±)-**4** can be "deracemized" by treatment with the complex of $CuCl_2$ and (−)-sparteine (entries 3 and 4).[8] Since in the case of (−)-sparteine both the precipitate (entry 3) and the mother liquor (entry 4) are enriched in the same enantiomer of **4**, we have suggested[8] that a second-order asymmetric transformation[16] is operating as the main stereodifferentiating process.[17,18] This is fully compatible with the observed gradual racemization of (−)-**4** upon treatment with a complex of $CuCl_2$ and an achiral amine, such as (±)-amphetamine, at rt.

The highly chemoselective cross-coupling of 2-naphthol (**1**) with 2-naphthylamine (**2**)[11] displayed a different behavior, indicating a different mechanism: while the coupling experiment (**1** + **2** → **5**) led again to a fairly good stereodifferentiation (entries 5 and 6),[8] attempted deracemization of (±)-**5** by the Cu(II)/chiral amine system failed and, in turn, no racemization of (−)-**5** has been observed either with $CuCl_2$/TMEDA or with $CuCl_2$/(±)-$PhCH(NH_2)Me$. Furthermore, the precipitate (entry 5) and the mother liquor (entry 6) from the coupling experiment contained the opposite enantiomers. We have rationalized these observations by assuming diastereoselective crystallization of the Cu(II)–amine–product complex as the dominant mechanism of stereodifferentiation.[8]

Yet another situation has now been encountered for the highly chemoselective cross-coupling[19] **1** + **3** → **6**. The $CuCl_2$-mediated coupling in the presence of (−)-sparteine displayed a fairly good enantioselectivity (entries 7–9). In analogy with the synthesis of **4** (but unlike **5**) both the precipitate (entry 8) and the solution (entry 9) turned out to contain the same enantiomer of the product **6**. This finding rules out diastereoselective crystallization as the stereodifferentiating process and might suggest the same mechanism as that operating in the case of **4**. However, the deracemization experiment with (±)-**6** and $CuCl_2$/(−)-sparteine failed as did the attempted racemization of (−)-**6** with $CuCl_2$/TMEDA. Hence, another mechanism must operate in this system, and asymmetric induction in the coupling reaction can be proposed as the most likely one.

Despite the apparent plausibility of the above rationalizations, we felt that further support should be provided. This applies, in particular, to the unsuccessful attempts to perform asymmetric transformations with **5** and **6**. It has been shown in numerous examples[16] that asymmetric transformations (both first and second order) are fastidious processes, requiring a fine tuning of all reaction conditions, namely the right chiral inducer, solvent, temperature, concentration, etc. Thus, it could be argued that in those cases where asymmetric transformation was not observed, these requirements had not been met. Furthermore, the complementary racemization experiments should, strictly, have been done with the complex of $CuCl_2$ and the corresponding racemic amines which, however, were not always available (as in the case of sparteine).

We reasoned that catalytic experiments would address these issues and provide a more detailed insight into the mechanism. Moreover, if successful, they would represent a major improvement of this methodology.

The crucial point for the designing of the catalytic cycle[20]

(16) Jacques, J.; Collet, A.; Wilen, S. H. *Enantiomers, Racemates, and Resolutions*; J. Wiley: New York, 1981.

(17) Brussee[6] has arrived at the same conclusion for (+)-amphetamine.

(18) In the second-order asymmetric transformation, the crystalline product should be of the opposite configuration to that remaining in the solution. This was the case of Brussee who employed (+)-amphetamine[6] but not of our system. The predominance of the same enantiomer of **4** both in the precipitate and the filtrate may be explained assuming a colloidal solution. Thus, a portion of (−)-**4** did not precipitate and in the form of a colloid remained in the filtrate, where it was detected as the main enantiomer (but of much lower enantiomeric purity) after workup.

(19) For the racemic version of this cross-coupling, see ref 15.

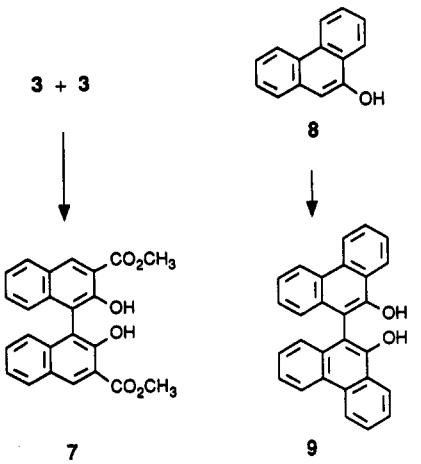
(20) For examples of efficient catalytic oxidation cycles, see, e.g.: (a) Bäckvall, J.-E. *Acc. Chem. Res.* **1983**, *16*, 335. (b) McMurry, J. E.; Kočovský, P. *Tetrahedron Lett.* **1984**, *25*, 4187. (c) Hanson, S.; Heuman, A.; Rein, T.; Akermark, B. *J. Org. Chem.* **1990**, *55*, 975. (d) Byström, S. E.; Larsson, E. M.; Akermark, B. *J. Org. Chem.* **1990**, *55*, 5674. (e) Bäckvall, J.-E.; Awasthi, A. K.; Renko, Z. D. *J. Am. Chem. Soc.* **1987**, *109*, 4750. (f) Bäckvall, J.-E.; Hopkins, R. B.; Grennberg, H.; Mader, M.; Awasthi, A. K. *J. Am. Chem. Soc.* **1990**, *112*, 5160. (g) Bäckvall, J.-E.; Chowdhury, R. L.; Karlsson, U. *J. Chem. Soc., Chem. Commun.* **1991**, 473. (h) Chowdhury, R. L.; Bäckvall, J.-E. *J. Chem. Soc., Chem. Commun.* **1991**, 1063. (i) Wang, G.-Z.; Bäckvall, J.-E. *J. Chem. Soc., Chem. Commun.* **1992**, 337.

is the reoxidation of Cu^{I} to Cu^{II}. This is a difficult task, as the reaction has to be anaerobic and the oxidant must not coordinate to the amine (as this would hamper the stereodifferentiation processes) and must not oxidize the reaction partners and the products. As the most promising candidate we selected silver(I) chloride, for we believed that its insolubility might reduce the inherent tendency of Ag^{+} to coordinate amines and to oxidize phenolic substrates. Another problem was posed by the stoichiometry of the reaction itself, as two molecules of HCl are released per one molecule of the product. Whereas in the stoichiometric reaction HCl is mopped up by the excess of amine, a different method has to be sought for the catalytic version, since the optically active amine would be present only in a substoichiometric amount.[21] Hovorka et al.[15] have shown that the Cu(II)-mediated coupling can be accomplished in the absence of amines if naphthols are first converted to the corresponding sodium salts, and we believed that this might be the solution to this issue.

The catalytic self-coupling of 2-naphthol (in form of its sodium salt) was carried out in MeOH with 10 mol % of $CuCl_2$, 20 mol % of (−)-sparteine[21] and 1.1 equiv of AgCl. The reaction mixture was stirred at rt for 72 h under argon and then worked up to afford (+)-4 (70%; 14 turnovers) of only ~3% ee (as revealed by $[\alpha]_D$ +1°).[22] Although the enantiomeric excess was very low and of no synthetic value, this experiment demonstrated that the reaction conditions allowed for a catalytic process to operate. The failure of the catalytic reaction to exercise better enantioselection (in contrast to the stoichiometric conditions) can be rationalized as follows: in the stoichiometric reaction, the high stereoselection (entries 1 and 2) may be achieved *via* a second-order asymmetric transformation (AT-2) which, by definition, requires a stoichiometric amount of the chiral inducer. By contrast, in the catalytic version, the substoichiometric amount of $CuCl_2$ and (−)-sparteine does not allow for this process to operate efficiently (as the organic substrates mainly stay outside of the complex), so that only a much less efficient first-order asymmetric transformation (AT-1)[16] can occur.[23] Moreover, the catalytic experiment produced (+)-4, whereas the stoichiometric transformation afforded (−)-4. This is an important observation because AT-1 should generally yield the opposite enantiomer to that arising from AT-2.[16,23] Thus, these experiments are strongly supportive of the original hypothesis that AT-2 is the dominant mechanism for the stoichiometric formation of the enantiomerically enriched 4.

The catalytic self-coupling of 2-naphthol (1) demonstrates that the reactions employing asymmetric transformations (or a diastereoselective crystallization) as the main vehicle of stereoselective are not suitable for the development of synthetically useful catalytic methods for preparation of enantiomerically enriched binaphthyl derivatives. Hence, e.g., 4 and 5 of acceptably high enantiomeric purity are unlikely to be obtained via the catalytic reactions of this type. On the other hand, reactions employing asymmetric synthesis as the main tool of stereoselection may be more promising.

Scheme II



In order to verify this hypothesis we have carried out a catalytic cross-coupling of 1 and 3 under the conditions similar to those employed for the self-coupling of 1, i.e., with the equivalent amounts of sodium salts of 1 and 3 with 10 mol % of $CuCl_2$, 20 mol % of (−)-sparteine, and 1.1 equiv of AgCl. The reaction was again run in methanol at rt for 72 h under argon and then worked up to afford (−)-6 (41%; eight turnovers)[24] of 32% ee (as revealed by $[\alpha]_D$ −30° in THF).[25,26] These results rule out the asymmetric transformation (first or second order) in this case and strongly support the mechanism involving asymmetric coupling.

In the absence of 1, ester 3 is known to undergo a self-coupling to produce 7 (Scheme II).[4,15] From a stoichiometric reaction employing $CuCl_2$ and (*S*)-(−)-methylbenzylamine (1:4), isolation of (−)-7 (5.7% ee) was reported.[4] However, in that report the precipitate and the solution were not separated and the yield refers to the workup of the whole mixture. Therefore, we have repeated this experiment and, to our delight, obtained (−)-7 (44% ee) from the precipitate (entry 10), while the mother liquor (entry 11) furnished its enantiomer (+)-7 (43% ee).[27] This finding is not only a noteworthy improvement of the previously reported synthesis, but it also suggests that, as with 5, a diastereoselective crystallization is the major stereodifferentiating mechanism in this case. Furthermore, attempted "deracemization" of (±)-7 employing $CuCl_2$ and (+)-$PhCH(NH_2)Me$ failed, which rules out AT-2 as an alternative mechanism.

Finally, a stoichiometric self-coupling of 9-phenanthrol (8) with $CuCl_2$ and (−)-sparteine has also been achieved,

(21) Stoichiometric experiments[6,8] demonstrated that the amine/$CuCl_2$ ratio should be ≥4:1 and, hence, ≥2:1 for bidentate ligands.

(22) Enantiomerically pure 4 has $[\alpha]_D$ −34° (*c* 1.0, THF): Kyba, E. P.; Gokel, G. W.; de Jong, F.; Koga, K.; Sousa, L. R.; Siegel, M. G.; Kaplan, L.; Sogah, G. D. Y.; Cram, D. J. *J. Org. Chem.* **1977**, *42*, 4173.

(23) In AT-2, the less stable diastereoisomer (i.e., less well stabilized by solvation) which, naturally, is less populated in the solution crystallizes preferentially to reach more stabilization in the crystalline lattice. Continuous equilibrium in the solution may finally produce a diastereoisomerically pure crystalline material in high yield. By contrast, AT-1 affords a mixture which reflects the thermodynamic equilibrium in the solution, which is not perturbed by crystallization. Hence, AT-2 results in the preferential formation of the less stable (in solution) diastereoisomer (van't Hoff–Dimroth rule). For discussion, see, e.g.: Buchanan, C.; Graham, S. H. *J. Chem. Soc.* **1950**, 500.

(24) Starting material 3 (40%) was recovered by flash chromatography; 4 (10%), arising by a self-coupling of 1, was detected as a byproduct.

(25) Enantiomerically pure enantiomers 6 have been obtained by chromatography on triacetyl cellulose[15c] and display $[\alpha]_D$ −92° (*c* 1.0, THF; maximum rotation) or $[\alpha]_D$ −31.0° and +30.5°, respectively (*c* 0.5, $CHCl_3$). The (*S*)-configuration for the laevorotatory enantiomer has been established by Hovorka et al.[15c]

(26) At 50 °C/3 h followed by rt/100 h, only 26% of (−)-6 of the same enantiomeric purity was obtained.

(27) Our (−)-7 had $[\alpha]_D$ −70° (*c* 2.1, THF) while (+)-7 displayed $[\alpha]_D$ +68° (*c* 2.2, THF). Enantiomerically pure (*R*)-(+)-7 shows $[\alpha]_D$ +159° (*c* 1.0; THF).[4] The absolute configuration was determined by Yamada: (a) Akimoto, H.; Shioiri, T.; Iitaka, Y.; Yamada, S. J. *Tetrahedron Lett.* **1968**, 97. (b) Akimoto, H.; Yamada, S. *Tetrahedron* **1971**, *27*, 5999.

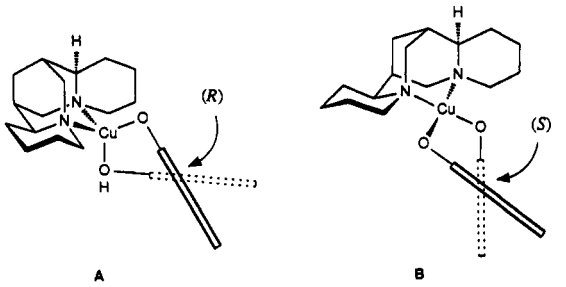


Figure 1. Preferential formation of (*R*)-binaphthol skeleton with tetrahedral Cu (A) and of (*S*)-enantiomer with square-planar Cu (B) complexes of (−)-sparteine.

affording (−)-**9** of 76% ee[28] in 80% isolated yield (entry 12). Similar to **4**, racemic biphenanthrol (±)-**9** was converted to (−)-**9** (62% ee)[29,30] in 95% yield (entry 13). This behavior corresponds to AT-2 in analogy with **4**.

The actual mechanism of the coupling step has been the subject of controversy in the literature. Thus, it has been suggested that the reaction may proceed via an insertion of the radical generated from one naphthol molecule into the C–H bond of the other naphthol molecule, and dimeric species $[L_nCu^{II}(OAr)]_2$ have been proposed to participate in the process. This rationalization seems to best explain the remarkably high chemoselectivity of certain cross-coupling reactions, such as **1** + **3** → **6**.[15] However, the details of the stereodifferentiation remain obscure, namely of that in the asymmetric coupling (**1** + **3** → **6**). Modeling of monomeric species suggests that a complex between (−)-sparteine, tetrahedral copper (presumably Cu^{I}), and binaphthol (or its derivatives) should strongly favor the (*R*)-configuration of the binaphthol unit (A in Figure 1). By contrast, an analogous complex containing square-planar copper (presumably Cu^{II}) should display a strong preference for the (*S*)-configuration (B). The observed formation of (*S*)-(−)-**6** as the major enantiomer is in an excellent agreement with the mechanism involving square-planar Cu^{II} in the crucial step that determines the configuration of the product but more experimental data will be needed to support this rationalization. Nevertheless, this simple hypothesis, as proposed, may be useful in predicting the stereochemical outcome of other coupling reactions.

Conclusions

The *in situ* generated complexes of $CuCl_2$ and chiral amines, sparteine or $PhCH(NH_2)Me$, have been utilized to synthesize enantiomerically enriched biaryl derivatives **4**-**7** and **9** from their respective precursors **1**-**3**, and **8**. The cross-couplings **1** + **2** and **1** + **3** have been found to be highly chemoselective; the self-couplings of **1**, **3**, and **8** are also very efficient.

Dramatic differences have been observed in the stereodifferentiation processes which can be interpreted as stemming from three different mechanisms. Experimental evidence has been accumulated in favor of a second-order asymmetric transformation as the dominant process controlling the production of **4** and **9**. By contrast, the stereodifferentiation observed in the case of **5** and **7** can be ascribed to a diastereoselective crystallization, while formation of the enantiomerically enriched **6** can be best explained by a direct, enantioselective coupling reaction. The choice of mechanism appears to be crucially dependent on the two coupling partners.[31]

A catalytic version of the coupling has been developed and explored for **4** and **6** in more detail. It has been shown to be fairly efficient for both reactions; acceptale stereoselectivity (32% ee) has been achieved in the latter case. This is the first example of a catalytic, oxidative asymmetric coupling that affords a binaphthyl system.[32] The results of the catalytic experiments lend further credence to the mechanistic conclusions and show that the mechanism should be known before a catalytic version is attempted. A simple model has been proposed to account for the stereoselectivity of the asymmetric coupling (B in Figure 1).

Experimental Section

Materials and Equipment. Optical rotations were measured on Pye Unicam 143A polarimeter with an error of <±0.5°. ^1H NMR spectra were recorded on Varian XL-400 (FT mode) and Tesla XBS 100 instruments for acetone-d_6 solutions at 25 °C with TMS as internal reference. The high-resolution mass spectra were measured on a Jeol JMS D-100 double-focusing spectrometer (70 eV, 3 kV) using direct inlet and the lowest temperature enabling evaporation; the accuracy was ≤5 ppm. All the solvents used for the coupling reactions or for crystallization experiments were degassed by purging with argon (20 min; 60 mL Ar/min). Light petroleum refers to the fraction boiling in the range 40–60 °C. Yields are given in mg of isolated product showing one spot on a chromatographic plate and no trace of impurities detectable in the NMR and mass spectra.

Stoichiometric Coupling 1 + 3. To a stirred solution of copper(II) chloride tetrahydrate (400 mg; 2 mmol) in degassed methanol (5 mL) was added (−)-sparteine (1.128 g; 4.8 mmol) under argon. After the solution was purged with argon for 5 min, a solution of 2-naphthol **1** (144 mg; 1 mmol) and methyl 3-hydroxy-2-naphthoate **3** (202 mg; 1 mmol) in degassed methanol (20 mL) was added, and the mixture was stirred at rt for 24 h under argon. The precipitate was filtered off, suspended in methanol (5 mL), decomposed with concd HCl (3 mL), and diluted with water (50 mL). The solid, crude product was chromatographed on silica using a petroleum ether–ether mixture (2:1) as eluent to give (*S*)-(−)-**6** (170 mg; 49%): $[\alpha]_D$ −65° (*c* 1.0, THF; 71% ee);[25] HRMS *m/z* (relative intensity) 344 (100, $M^{\bullet+}$; $C_{22}H_{16}O_4$). The liquid portion (filtrate) from the coupling was worked up separately in the same way to yield (*S*)-(−)-**6** (155 mg; 45%): $[\alpha]_D$ −25° (*c* 1.1, THF; 27% ee).

Stoichiometric Coupling 3 + 3. The self-coupling of **3** (2 mmol) was carried out similarly and on the same scale using (*S*)-(−)-α-methylbenzylamine (8 mmol) as a chiral ligand. The precipitate afforded (*S*)-(−)-**7** (47%): $[\alpha]_D$ −70° (*c* 2.1, THF; 44% ee); HRMS *m/z* (relative intensity) 402 (100, $M^{\bullet+}$; $C_{24}H_{18}O_6$). The liquid phase furnished (*R*)-(+)-**7** (40%): $[\alpha]_D$ +68° (*c* 2.2, THF; 43% ee).[27]

Stoichiometric Coupling 8 + 8. The self-coupling of **8** (2 mmol) was carried out similarly and on the same scale using (−)-sparteine (2.5 mmol) as a chiral ligand. The precipitate

(28) Calculated from $[\alpha]_D$ −54° (*c* 2.3, $CHCl_3$); enantiomerically pure (*S*)-(−)-**9** has $[\alpha]_D$ −71° ($CHCl_3$).[5]

(29) As revealed by $[\alpha]_D$ −44° (*c* 1.9, $CHCl_3$).

(30) Biphenanthrol **9** is much more prone to thermal racemization than **4**. Thus, refluxing in xylene for 2 h results in total racemization. Hence, enantiomerically pure **9** cannot be obtained by crystallization of enriched samples from hot solvents. By contrast, binaphthyl derivatives **4**–**7** arising from the above experiments can readily be purified up to ~100% ee by simple crystallization from benzene.[5,31]

(31) Enantiomeric enrichment (kinetic crystallization), previously reported by us for **4** and **5**,[5] has not been observed with **6**, **7**, and **9**.

(32) Thus far there have been two reports on catalytic, asymmetric coupling to produce a binaphthyl system.[33] However, in both instances the coupling was accomplished between the 1-metalated naphthalenes and 1-substituted naphthalene derivatives rather than by oxidative coupling of two 1-unsubstituted naphthalene units.

(33) (a) Hayashi, T.; Hayashizuka, K.; Kiyoi, T.; Ito, Y. *J. Am. Chem. Soc.* **1988**, *110*, 8153. (b) Shindo, M.; Koga, K.; Tomioka, K. *J. Am. Chem. Soc.* **1992**, *114*, 8732.

afforded (*S*)-(−)-**9** (80%): $[\alpha]_D$ −54° (*c* 2.3, $CHCl_3$; 76% ee);[28] HRMS *m/z* (relative intensity) 386 (100, $M^{\bullet+}$; $C_{28}H_{18}O_2$).

Catalytic Coupling 1 + 3. To a stirred solution of copper(II) chloride tetrahydrate (40 mg; 0.2 mmol) in degassed methanol (5 mL) was added (−)-sparteine (94 mg; 0.4 mmol) under argon. After the solution was purged with argon while being stirred at rt for 5 min, a solution of sodium naphtholate (330 mg; 2 mmol) and sodium 3-(methoxycarbonyl)-2-naphtholate (448 mg; 2 mmol) in degassed methanol (20 mL) was added followed by addition of solid silver(I) chloride (616 mg; 4.4 mmol). The mixture was stirred at rt for 72 h under argon. Concd HCl (3 mL) was then added, the mixture was stirred for 2 min, and then water (50 mL) was added and stirring continued for another 5 min. The suspension was extracted with $CHCl_3$ (3 × 20 mL), and the organic layer was dried with Na_2SO_4 and evaporated. The crude product (426 mg) was chromatographed on a column of silica gel (30 g) using a petroleum ether–ether mixture (2:1) as eluent to yield pure (*S*)-(−)-**6** (281 mg; 41%): $[\alpha]_D$ −30° (*c* 1.0, THF; 32% ee); HRMS *m/z* (relative intensity) 344 (100, $M^{\bullet+}$, $C_{22}H_{16}O_4$).

Catalytic Coupling 1 + 1. The self-coupling of **1** (578 mg; 2.0 mmol), carried out on the same scale in an analogous way as the previous experiment with (−)-sparteine as a chiral ligand, afforded **4** (402 mg; 1.41 mmol; 70%): $[\alpha]_D$ + 1° (*c* 1.0, THF; 3% ee); HRMS *m/z* (relative intensity) 286 (100, $M^{\bullet+}$, $C_{20}H_{14}O_2$).

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