Synthesis of N-Alkylated and N-Arylated Derivatives of 2-Amino-2′-hydroxy-1,1′-binaphthyl (NOBIN) and 2,2′-Diamino-1,1′-binaphthyl and Their Application in the Enantioselective Addition of Diethylzinc to Aromatic Aldehydes†

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High-yield reductive alkylation of (*R*)-(+)-**1** and (*R*)-(+)-**2** has been accomplished with a series of ketones (even as bulky as 2-adamantanone) and $NaBH_4/H_2SO_4$ in THF at room temperature to give the respective N-alkylated binaphthyls **6a**−**c**, **9a**−**c**, and **10a**−**c**. Related *N*-phenyl derivatives **14**, **16**, and **17** were obtained via the Pd(0)-catalyzed coupling of (*R*)-(+)-**1** and (*R*)-(+)-**2**, respectively, with PhBr; no racemization was observed. Subsequent reductive methylation with CH_2O and $NaBH_4/H_2SO_4$ afforded the bidentate ligands **8a**−**c**, **12a**−**c**, **13a**−**c**, **15**, **18**, and **19**, which comprise a new class of binaphthyls. Their utility as chiral ligands has been demonstrated for the addition of Et_2Zn to benzaldehyde and its congeners; the highest level of asymmetric induction was observed for *N*,*N*-dimethyl NOBIN (*R*)-(+)-**3** (3 mol %) in conjunction with *n*-BuLi (5.4 mol %), which gave (*R*)-(+)-**21a** in 88% ee. Derivatives of the amino phenol **1** (NOBIN) proved more efficient than the corresponding diamines derived from **2**. The stereochemical outcome and the enhancement of asymmetric induction by Li^+ are discussed in terms of the chelated transition state **26**.

Introduction

The 1,1′-binaphthyl-based ligands owe their success in asymmetric reactions to the chiral cavity they create around the metal center.[1] Within this class, the prime role is played by C_2-symmetrical 2,2′-disubstituted 1,1′-binaphthyls bearing identical coordinating groups, in particular Noyori's BINOL[2] and BINAP.[3] Their congeners with nonidentical substituents at positions 2 and 2′ (which are no longer C_2-symmetrical) have only recently emerged, and among them, Hayashi's MOP (with 2-OMe and 2′-PPh_2)[4] and our NOBIN[5,6] (**1**) have risen to prominence. In contrast to the wide use of these binaphthyls, the diamine **2**[7] has enjoyed relatively less popularity despite its straightforward, one-step synthesis from 2-naphthol and hydrazine and its ready resolution into enantiomers.[8]

We reasoned that introducing bulky, lipophilic substituent(s) at the amino groups of **1** and **2** should restrict the conformational freedom, thereby creating a more rigid chiral cavity and, in the case of the diamine, enhancing the C_2 twist. A metal catalyst, based on this class of ligands, can therefore be expected to exhibit raised levels of asymmetric induction. Moreover, improved solubility of both the ligands and the complexes in common organic solvents can also be anticipated.

We have recently shown that the NH_2 group of 2-hydroxy-2′-amino-1,1′-binaphthyl (NOBIN, **1**) can be readily dimethylated on reaction with 40% aqueous CH_2O and

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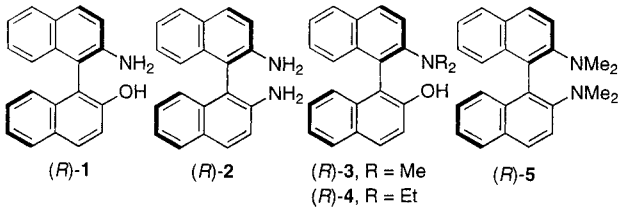
Chart 1



$NaBH_4/H_2SO_4$ in THF[9] to give its *N*,*N*-dimethyl analogue **3** (84%),[9a] whereas the classical Eschweiler−Clarke reaction gave much less satisfactory results.[9a] The permethylated diamine **5** was originally prepared by Snyder from **2** via the Eschweiler−Clarke methylation in modest yield,[10] and we assumed that our $NaBH_4$-mediated reductive methylation,[9] which proved superior in the case of NOBIN, would also be successful here.[9b]

Herein, we report the synthesis of the nitrogen-alkylated or phenylated amines derived from **1** and **2** with alkyl groups of different sizes and their application in the ligand-accelerated addition of diethylzinc to aromatic aldehydes. Also reported are the effects of catalytic amounts of *n*-butyllithium, and the superiority of amino phenols over diamines is demonstrated.

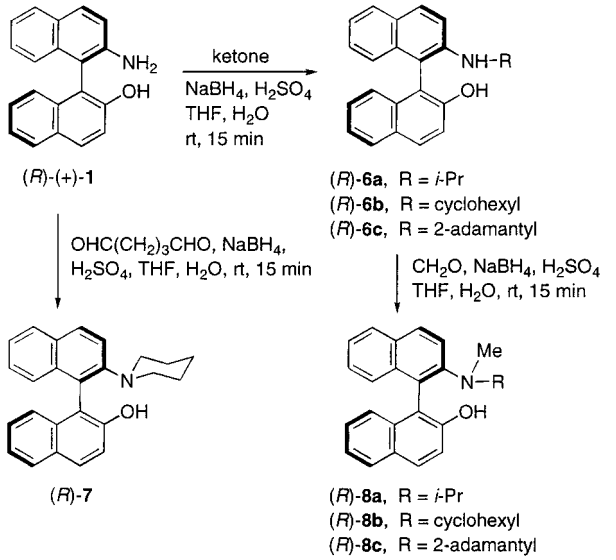
Results and Discussion

Synthesis of the N-Alkylated Binaphthyls. Since the reductive methylation of NOBIN (**1**) with formaldehyde and $NaBH_4$ proved very efficient,[9] it was desirable to explore the scope of this reaction, in particular its feasibility with other carbonyl partners of increased bulk. If successful, this method would open a straightforward entry into an array of binaphthyl-based ligands. In this combinatorial-like approach, amino phenol[5] (*R*)-(+)-**1** and diamine[7,8] (*R*)-(+)-**2** were employed as linchpins (Chart 1), onto whose nitrogen atoms we intended to attach various alkyls; acetaldehyde, acetone, cyclohexanone, 2-adamantanone, and glutaric dialdehyde, in addition to formaldehyde, were selected as representative carbonyl partners.

Reductive alkylation of (*R*)-(+)-**1** (≥99% ee) with acetaldehyde and $NaBH_4/H_2SO_4$ in THF proceeded at ambient temperature in the same way as observed with formaldehyde to afford *N*,*N*-diethyl-NOBIN **4** (91%) as the product of dialkylation (Chart 1). By contrast, only monoalkylation was observed with the sterically more demanding ketones. Thus, acetone and cyclohexanone furnished **6a** (89%) and **6b** (90%), respectively (Scheme 1), as the result of an essentially quantitative conversion of the starting material, whereas 2-adamantanone gave a rather lower yield of **6c** (57%). In the latter instance, the reaction did not proceed to completion; extending the reaction period, varying the temperature, and employing an excess of 2-adamantanone and/or $NaBH_4$ had little effect. On the other hand, glutaric dialdehyde readily afforded the corresponding piperidine derivative **7** (96%).

The monoalkylated amino phenols **6a**−**c** were then methylated with CH_2O (aq) under the same conditions ($NaBH_4$, H_2SO_4, THF, rt) to give **8a** (96%), **8b** (95%), and **8c** (86%), respectively, demonstrating that the second alkylation of the Ar−NHR group can only be attained with a sterically less demanding aldehyde.

Scheme 1[a]



[a] Ketone = acetone, cyclohexanone, or 2-adamantanone.

Reductive alkylation of the diamine (*R*)-(+)-**2** (≥99% ee) with the above ketones and $NaBH_4/H_2SO_4$ in THF has also been found to occur readily at room temperature, affording mixtures of N,N′-bisalkylated and N-monoalkylated products (Scheme 2). Thus, the reaction of (*R*)-(+)-**2** with acetone gave predominantly the *N*,*N*′-bisisopropyldiamine **9a** (82%), accompanied by a small amount of the monoalkylated product **10a** (15%). Enhancing the steric demands of the ketone led to a gradual increase in the proportion of monoderivatization; with cyclohexanone, a ∼2:1 mixture of the bis- and monoalkylated diamines **9b** (64%) and **10b** (28%) was obtained, whereas 2-adamantanone gave mainly the monoalkylated product **10c** (71%), with the bisderivative **9c** being formed in a mere 15% yield. As in the case of **6c**, all attempts to improve the yield of **9c** failed. Glutaric dialdehyde, on the other hand, readily afforded the corresponding bispiperidine derivative **11** (98%).[11] As expected, formaldehyde produced (*R*)-(+)-**5** in high yield (88%).[9b]

The bisalkylated diamines **9a**−**c** were then permethylated with CH_2O (aq) under the same conditions ($NaBH_4$, H_2SO_4, THF, rt) to give **12a** (76%), **12b** (75%), and **12c** (59%), respectively. Similarly, the monoalkylated diamines **10a**−**c** were converted into **13a** (65%), **13b** (68%), and **13c** (64%), respectively.

Synthesis of the N-Arylated Binaphthyls. Appending an alkyl substituent to a nitrogen atom is one of the classical synthetic transformations that can be accomplished, e.g., via a nucleophilic substitution or by reductive alkylation (vide supra). By contrast, N-arylation is much more difficult to attain so that this strategy is normally avoided.[12] It was not only until very recently that a new method emerged, being independently developed by Hartwig[13] and Buchwald.[14] With the aid of a number of simple model substrates, the latter authors have demonstrated that amines can be arylated by aryl

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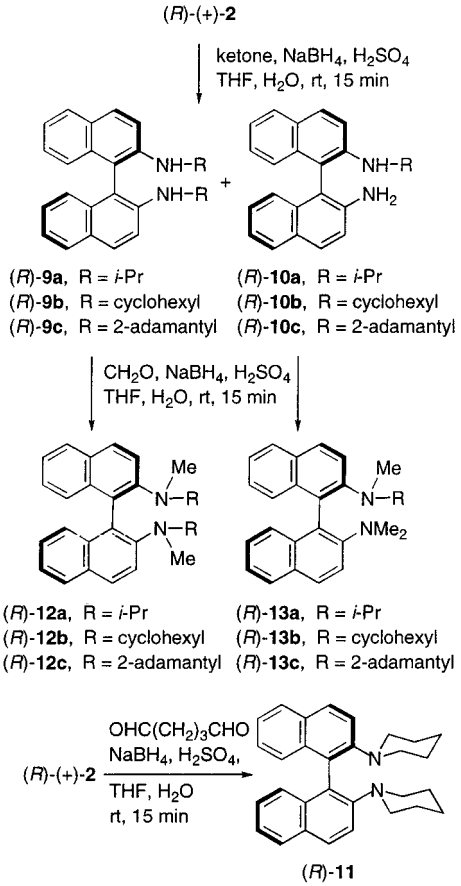
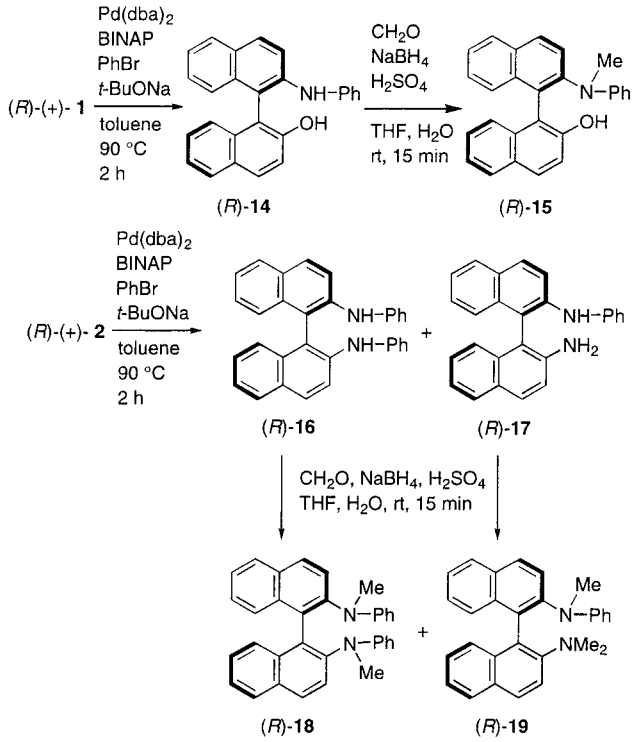
Scheme 2[a]



[a] Ketone = acetone, cyclohexanone, or 2-adamantanone.

halides or triflates in a reaction catalyzed by certain Pd(0) complexes that have a suitable bite angle of the ligand. This new procedure, involving an oxidative addition to the N−H bond, seemed ideally suited to our binaphthyls; not only would it extend the existing array of available ligands by incorporating an important class of N substituents but if successful with these relatively complex and sterically congested, enantiopure substrates, our experiments would further broaden the scope of this promising methodology.[15]

Scheme 3



N-Phenylation, using the Hartwig−Buchwald protocol,[13,14] was first attempted with (*R*)-(+)-**1**. On reaction with bromobenzene, catalyzed by the racemic complex of 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl (BINAP) and Pd(0) at 90 °C for 2 h, the latter substrate readily produced the expected *N*-phenyl derivative **14** in 71% yield (Scheme 3); no traces of the starting amino phenol were detected in the crude reaction mixture.[16] In accordance with a recent report,[14e] no loss of enantiopurity was observed. Standard reductive methylation (CH_2O, $NaBH_4$, H_2SO_4, THF, rt) of the amino phenol **14** thus obtained led to *N*-methyl-*N*-phenyl-NOBIN **15** (81%). The Hartwig−Buchwald method proved equally successful with the diamine (*R*)-(+)-**2**, which under the same conditions, afforded mainly the *N*,*N*′-bisphenyl derivative **16** (70%),[17] contaminated by the monophenylated product **17** (18%). Reductive methylation of each of these diamines furnished the respective permethylated derivatives **18** (85%) and **19** (61%).

The Hartwig−Buchwald method is known to be sensitive to the ligand, with BINAP and the ferrocenyl-derived

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(15) For an early application of the Hartwig−Buchwald protocol by another group, see: Ma, D.; Yao, J. *Tetrahedron: Asymmetry* **1996**, *7*, 3075.

(16) Interestingly, when 2-amino-2′-diphenylphosphino-1,1′-binaphthyl (MAP) was used as the ligand instead of BINAP, the reaction was complete at 60 °C in 5 min, suggesting that aminophosphines may become the ligands of choice for the Hartwig−Buchwald coupling. For the preparation of MAP, see the adjacent paper.

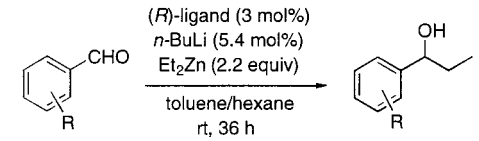
(17) The IR, NMR, and mass spectra of this product were identical to those of an authentic sample of (±)-**16** prepared by the oxidative coupling of *N*-phenyl-2-aminonaphthalene.[5d] No loss of enantiomeric purity was observed for (*R*)-**16** by chiral HPLC.

bisphosphine dppf being identified to give the best results.[13,14] Naturally, if a nonchiral target compound is to be synthesized, economic criteria would dictate that the inherently chiral BINAP be used in its racemic form.[13,14] This raises the question of whether application of the enantiomerically pure BINAP would, in the case of a racemic substrate, lead to any kinetic resolution. To address this issue, racemic NOBIN (±)-**1** was treated under the Hartwig−Buchwald conditions (vide supra) in the presence of (*S*)-BINAP, at a lower temperature than originally, to slow the reaction and increase the chance for resolution. Analysis of the reaction mixture at ∼35% conversion (60 °C, 15 min) by HPLC on a Diacel Chiralpak AD column revealed a preferential formation of (*R*)-**14** in 27% ee, demonstrating the feasibility of this approach. At ∼60% conversion (60 °C, 45 min), the enantioselectivity dropped to 11% ee. Analogous experiments with (±)-**2** gave (*R*)-**16** of 17% ee at ∼45% conversion (60 °C, 1 h).[9b] Although these enantioselectivities could be in principle improved by fine tuning of the ligand and the reaction conditions, this issue was not further pursued in view of the straightforward synthesis of the enantiomerically pure starting materials (*R*)-(+)-**1**[5] and (*R*)-(+)-**2**.[8] On the other hand, successful kinetic resolution of this type may prove useful in the synthesis of other enantiopure compounds, where the classical resolution of the corresponding racemate is more difficult than in the present case.

Enantioselective Addition of Diethylzinc to Selected Aromatic Aldehydes. In contrast to Grignard reagents and alkyllithiums, which react instantaneously with carbonyl compounds, dialkylzinc reagents are inert even to aldehydes at room temperature or below. However, perturbing the rod-type geometry of the stable, sp-hybridized R_2Zn by coordination, followed by replacement of one of the R groups with an electronegative substituent of the bidentate ligand, increases the nucleophilicity of the remaining R group and, at the same time, the Lewis acidity of the Zn atom.[18] As a result, the zinc complexes thus generated in situ become reactive toward aldehydes. This ligand-enhanced reactivity[18,19] has been demonstrated for amino alcohols (particularly those possessing a tertiary amino group) and, to some extent, for diamines. Since R_2Zn itself is inert, only a substoichiometric amount of the ligand is needed to facilitate the reaction, which has an obvious practical advantage in the asymmetric version of the reaction; although it is stoichiometric with respect to the nonexpensive organometallic reagent, it is catalytic in the precious chiral ligand.

Following the pioneering work of Oguni and Omi,[20] numerous chiral amino alcohols have been surveyed as ligands in the R_2Zn addition to aldehydes and some spectacular enantioselectivities have been reported (90−99% ee),[18,19,21−25] especially with DAIB[21,22] and DBNE.[23,24] However, inspection of the impressively long list of these ligands reveals an almost total absence of the representatives of the binaphthyl series.[26] This is hardly surprising, for there was no simple and efficient route to NOBIN-like structures until recently. The scene has now changed owing to our one-step synthesis of NOBIN via the highly selective cross-coupling of 2-naphthol with 2-naphthylamine.[5,27] With the series of the NOBIN-derived amino phenols **3**, **4**, **7**, **8a**−**c**, and **15**, whose syntheses were described above, we could embark on a systematic investigation of the substituent effect on the level of asymmetric induction in the R_2Zn addition to a set of aromatic aldehydes.[28] The corresponding diamines **5**, **11**, **12a**−**c**, **13a**−**c**, **18**, and **19** were also explored to complete the study.

Scheme 4



20a, R = H — **21a**, R = H
20b, R = 4-OMe — **21b**, R = 4-OMe
20c, R = 2-OMe — **21c**, R = 2-OMe
20d, R = 4-Cl — **21d**, R = 4-Cl
20e, R = 2-Cl — **21e**, R = 2-Cl
20f, R = 4-Me — **21f**, R = 4-Me
20g, R = 2-Me — **21g**, R = 2-Me
20h, R = 4-F — **21h**, R = 4-F
20i, 1-naphthaldehyde — **21i**, 1-(1'-naphthyl)-propan-1-ol
20j, 2-naphthaldehyde — **21j**, 1-(2'-naphthyl)-propan-1-ol

The *N*,*N*-dimethylamino phenol (*R*)-(+)-**3** and benzaldehyde (**20a**) were chosen for the initial experiments (Scheme 4). The addition of Et_2Zn to **20a** was carried out at ambient temperature in the presence of 3 mol % of the ligand and was completed in 36 h to give (*R*)-(+)-1-phenyl-2-propanol (**21a**) in 68% ee (Table 1, entry 1). Better enantioselectivities were observed for the catalyst generated in situ from (*R*)-(+)-**3** and *n*-BuLi.[29] An optimum was found for 1.8 equiv of *n*-BuLi (counted with respect to the ligand) and 3 mol % of (*R*)-(+)-**3**, which

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(24) Soai, K.; Yokoyama, S.; Hayasaka, T. *J. Org. Chem.* **1991**, *56*, 4264.

(25) For the use of amino thiols as ligands, see, ref 12j and the following: (a) Hof, R. P.; Poelert, M. A.; Peper, N. C. M. W.; Kellog, R. M. *Tetrahedron: Asymmetry* **1994**, *5*, 31. (b) Kang, J.; Kim, D. S.; Kim, J. I. *Synnlett* **1994**, 842. (c) Kang, J.; Lee, J. W.; Kim, J. I. *J. Chem. Soc., Chem. Commun.* **1994**, 2009. (d) Rijnberg, E.; Jastrzebski, J. T. B. H.; Janssen, M. D.; Boersma, J.; van Koten, G. *Tetrahedron Lett.* **1994**, *35*, 6521. For the most recent examples of amino alcohols, see, e.g.: (e) Jones, G. B.; Guzel, M.; Chapman, B. J. *Tetrahedron: Asymmetry* **1998**, *9*, 901.
(26) The only example of a binaphthyl-type amino alcohol, namely (*S*)-(2,2′-[2-(2-hydroxyethyl)-2-azapropane-1,3-diyl]-1,1′-binaphthalene, exhibited modest enantioselectivity (49% ee): Noyori, R.; Suga, S.; Kawai, K.; Okada, S.; Kitamura, M.; Oguni, N.; Hayashi, M.; Kaneko, T.; Matsuda, Y. *J. Organomet. Chem.* **1990**, *382*, 19.
(27) For a modified version producing (±)-NOBIN, see ref 5f and the following: Ding, K.; Xu, Q.; Wang, Y.; Liu, J.; Yu, Z.; Du, B.; Wu, Y.; Koshima, Y.; Matsuura, T. *Chem. Commun.* **1997**, 693.
(28) Benzaldehyde and its congeners are the standards against which the success of new ligands is measured. Other aldehydes have also been studied but usually found to exhibit lower enantioselectivites. In contrast to the wealth of examples of the reactions of aldehydes, there are only sporadic reports on the corresponding aldimines: (a) Soai, K.; Hatanaka, T.; Miyazawa, T. *J. Chem. Soc., Chem. Commun.* **1992**, 1097. (b) Andersson, P. G.; Guijarro, D.; Tanner, D. *Synlett* **1996**, 727. (c) Andersson, P. G.; Guijarro, D.; Tanner, D. *J. Org. Chem.* **1997**, *62*, 7364. (d) Guijarro, D.; Pinho, P.; Andersson, P. G. *J. Org. Chem.* **1998**, *63*, 2530.
(29) For the use of lithium alkoxides of amino alcohols as ligands in dialkylzinc additions, see refs 18, 19, 23, and the following: (a) de Vries, E. F. J.; Brussee, J.; Kruse, C. C.; van der Gen, A. *Tetrahedron: Asymmetry* **1993**, *4*, 1987. (b) Mehler, T.; Martens, J.; Wallbaum, S. *Synth. Commun.* **1993**, *23*, 2691. (c) De Parrodi, C. A.; Juaristi, E.; Quintero-Cortés, L.; Amador, P. *Tetrahedron: Asymmetry* **1996**, *7*, 1915. (d) Vidal-Ferran, A.; Moyano, A.; Pericàs, M. A.; Riera, A. *J. Org. Chem.* **1997**, *62*, 4970.

Table 1. Enantioselective Addition of Diethylzinc to Benzaldehyde Catalyzed by Complexes of Aminophenols 3, 4, 8a−c, 15, *n*-BuLi, and Diamines 11, 12a−c, 13a−c, 18, 19[a]

entry	catalyst	% yield of **21a**	% ee[b]	configuration of **21a**[c]
1	(*R*)-**3**	89	68	(R)
2	(*R*)-**3**/*n*-BuLi	96	88	(R)
3	(*R*)-**4**/*n*-BuLi	79	45	(R)
4	(*R*)-**5**	94[d,e]	63[e]	(R)[e]
5	(*R*)-**7**/*n*-BuLi	74	58	(R)
6	(*R*)-**8a**/*n*-BuLi	92	75	(R)
7	(*R*)-**8b**/*n*-BuLi	81	71	(R)
8	(*R*)-**8c**/*n*-BuLi	74	15	(S)
9	(*R*)-**11**	34	23	(S)
10	(*R*)-**12a**	64	13	(S)
11	(*R*)-**12b**	48	19	(S)
12	(*R*)-**12c**	40	16	(S)
13	(*R*)-**13a**	69	41	(R)
14	(*R*)-**13b**	47	2	(R)
15	(*R*)-**13c**	43	∼0	
16	(*R*)-**15**/*n*-BuLi	55	19	(R)
17	(*R*)-**18**	41	8	(R)
18	(*R*)-**19**	35	22	(S)

[a] Reactions were carried out in a 2:1 mixture of toluene and hexanes at room temperature for 36 h with 3 mol % of the ligand and 5.4 mol % of BuLi. [b] Determined by GC analysis of diastereoisomeric menthoxycarbonyl esters; see ref 33. [c] See ref 21. [d] NMR yield. [e] See ref 31.

led to 88% ee (Table 1, entry 2); with 1 equiv of *n*-BuLi, the ee dropped to 80%, whereas 2.5 equiv gave 81% ee, and 0.5 equiv led to 74% ee. Employing more than 3 mol % of (*R*)-(+)-**3** did not improve the asymmetric induction, whereas with only 1 mol % it dropped to 67% ee. In accord with the earlier observations,[18,19] running the reaction at lower temperature (0 °C) resulted in lower conversion, practically not affecting the enantioselectivity.

Since the initial experiments with **3** were promising, it was desirable to examine the binaphthyls with bulky groups, in particular **4**, **7**, **8a**−**c**, and **15**, as chiral ligands for the same reaction.[30] The reactions were performed under the optimal conditions identified for the ligand **3** (vide supra), including addition of *n*-BuLi to the ligand as specified above (i.e., 1.8 equiv of *n*-BuLi counted with respect to the ligand). However, both the conversions and enantioselectivities turned out to be generally rather lower than those obtained in the case of (*R*)-(+)-**3** (Table 1, entries 3, 5−8, and 16), with the highest asymmetric induction in the formation of (*R*)-(+)-**21a** being attained with the *N*-isopropyl-*N*-methyl amino phenol (*R*)-(+)-**8a** (75% ee; entry 6) and the lowest with the *N*-phenyl-*N*-methyl derivative (*R*)-(+)-**15** (19% ee; entry 16). Interestingly, the *N*-adamantyl-*N*-methyl amino phenol **8c** gave the addition product with an opposite configuration, i.e., (*S*)-(−)-**21a** (15% ee; entry 8), which apparently reflects a change of mechanism. This finding also shows that caution must be exercised when predicting the configuration of the resulting alcohol[18,19] even within a series of closely related ligands.

Although amino alcohol ligands typically exhibit higher enantioselectivities in dialkylzinc additions than aprotic

Table 2. Enantioselective Addition of Diethylzinc to Aldehydes 20a−j Catalyzed by the Complex of (*R*)-3 and *n*-BuLi[a]

entry	aldehyde **20**	% yield of **21**	% ee	configuration of **21**[b]
1	C_6H_5CHO[c]	96	88[d]	(R)
2	4-MeO−C_6H_5CHO	95	75[e]	(R)
3	2-MeO−C_6H_5CHO	93	62[d]	(R)
4	4-Cl−C_6H_5CHO	93	83[d]	(R)
5	2-Cl−C_6H_5CHO	93	79[e]	(R)
6	4-Me−C_6H_5CHO	96	82[e]	(R)
7	2-Me-C_6H_5CHO	81	81[e]	(R)
8	4-F−C_6H_5CHO	94	79[f]	(R)
9	1-$C_{10}H_7CHO$	87	79[e]	(R)
10	2-$C_{10}H_7CHO$	89	83[e]	(R)

[a] Reactions were carried out in a 2:1 mixture of toluene and hexanes at room temperature for 36 h with 3 mol % of the ligand and 5.4 mol % of BuLi. [b] Determined by comparison of specific rotations with literature data (see the Experimental Section). [c] Copied from Table 1. [d] Determined by GC analysis of diastereoisomeric menthoxycarbonyl esters; see ref 33. [e] Determined by chiral HPLC (see the Experimental Section). [f] Determined by ^{1}H NMR integration of characteristic proton signals in the presence of the chiral shift reagent Eu(hfc)$_3$.

diamines,[18] the binaphthyl derivative **5** has been reported to facilitate the formation of **21a** with the promising 63% ee (entry 4).[31] Therefore, we have explored the potential of our new tetrasubstituted diamines **11**, **12a**−**c**, **13a**−**c**, **18**, and **19**. However, in all instances, the reactions turned out to be much slower than those carried out with the corresponding amino phenols, and the yields and enantioselectivities were inferior (entries 9−15, 17, and 18).

Finally, we employed our champion catalytic system, i.e., (*R*)-(+)-**3** and 1.8 equiv of *n*-BuLi, in reactions with a series of aromatic aldehydes **20** aiming to elucidate the substituent effect on the level of asymmetric induction (Scheme 4). In all the cases examined, the (*R*)-**3** ligand proved to induce formation of the secondary alcohols **21** of (R) configuration (Table 2). In general, introducing a substituent to the aromatic ring resulted in a decrease in enantioselectivity. As expected, the effect of ortho substitution proved slightly more adverse than that of the same para substitution (compare entries 2 vs 3 and 4 vs 5 in Table 2); however, the difference for the *o*- and *p*-methyl-benzaldehydes **20f** and **20g** was negligible (entries 6 and 7). An electron-donating group (MeO) turned out to reduce the level of asymmetric induction rather more than an electron-withdrawing substituent (F, Cl) both in the para (compare entries 2 vs 4 and 8 in Table 2) and ortho series (compare entries 3 vs 5).[32] This result is in accord with earlier reports by Noyori[21] and Soai[23] and in conflict with the behavior of Fréchet's polymer-bound ligands[34b] and with the recent report by Chan,[32d] who observed enhancement of enantioselection

(30) For the effect of the size of the N substituents on the enantioselectivity of Et_2Zn addition, see refs 12j, 23, 28d, and the following: (a) Muchow, Y.; Vannoorenberghe, G. B. *Tetrahedron Lett.* **1987**, *28*, 6163. (b) Chaloner, P. A.; Perera, S. A. R. *Tetrahedron Lett.* **1987**, *28*, 3013. (c) Itsuno, S.; Fréchet, J. M. J. *J. Org. Chem.* **1987**, *52*, 4140. (d) Soai, K.; Yokoyama, S.; Ebihara, K.; Hayasaka, T. *J. Chem. Soc., Chem. Commun.* **1987**, 1690.

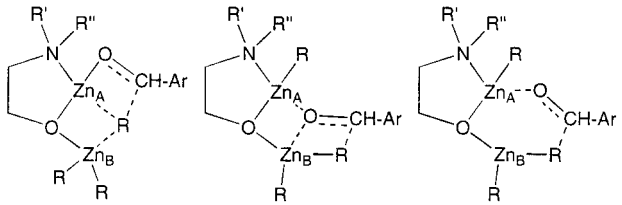
(31) Rosini, C.; Franzini, L.; Iuliano, A.; Pini, D.; Salvadori, P. *Tetrahedron: Asymmetry* **1991**, *2*, 363.

(32) For electronic effects in asymmetric reduction of substituted benzophenones, see: (a) Corey, E. J.; Helal, C. J. *Tetrahedron Lett.* **1995**, *36*, 9153. (b) Corey, E. J.; Helal, C. J. *Tetrahedron Lett.* **1996**, *37*, 5675. For electronic effects in asymmetric cyclopropanation catalyzed by Rh, see: (c) Park, S.-B.; Murata, K.; Matsumoto, H.; Nishiyama, H. *Tetrahedron: Asymmetry* **1995**, *6*, 2487. For electronic effects in addition of Et_2Zn to para substituted benzaldehydes catalyzed by a chiral α-pyridylphenol, see: (d) Zhang, H.; Xue, F.; Mak, T. C. W.; Chan, K. S. *J. Org. Chem.* **1996**, *61*, 8002.

(33) Westley, J. W.; Halpern, B. *J. Org. Chem.* **1968**, *33*, 3979.

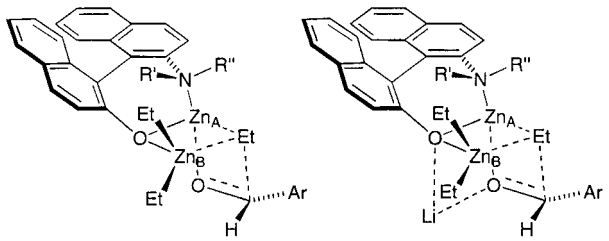
(34) (a) Itsuno, S.; Fréchet, J. M. J. *J. Org. Chem.* **1987**, *52*, 4142. (b) Itsuno, S.; Sakurai, Y.; Ito, K.; Maruyama, T.; Nakahama, S.; Fréchet, J. M. J. *J. Org. Chem.* **1990**, *55*, 304. See also: (c) Watanabe, M.; Araki, S.; Butsugan, Y.; Uemura, M. *J. Org. Chem.* **1991**, *56*, 2218.

Chart 2

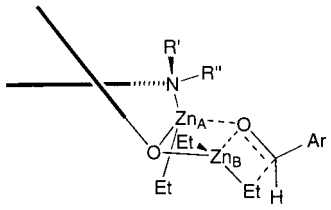


22 **23** **24**

Chart 3



25 **26**



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for benzaldehydes bearing strongly electron-withdrawing groups. On the other hand, little substituent electronic effect (F vs MeO) was recently found by Pericàs for 1-aminopropane-2,3-diol-type ligands.[29d] Hence, it appears that the relationship is rather complex and dependent on the actual ligand, the solvent used, etc.[23] 1-Naphthaldehyde displayed the same enantioselectivity as *o*-chlorobenzaldehyde (79% ee; compare entries 9 and 5 in Table 2), while 2-naphthaldehyde gave the same enantioselectivity as *p*-chlorobenzaldehyde (83% ee, compare entries 10 and 4 in Table 2).

Mechanistic Considerations. The addition of dialkylzinc reagents to aldehydes, facilitated by amino alcohols as bidentate ligands, is generally accepted to occur via dinuclear species. Several transition-state models have been proposed to account for the observed enantioselectivity,[22,23,34,35] which differ in the way the alkyl is transferred to the aldehyde (Chart 2). According to Noyori's mechanism **22**,[22] it is the bridging alkyl originating from the zinc atom coordinated to both nitrogen and oxygen atoms of the amino alcohol (Zn_A) that migrates to the aldehyde, since the $Zn_A-R_{bridging}$ linkage is more polarized than the $Zn_B-R_{terminal}$ bond. By contrast, Fréchet[34] proposed that the alkyl from the other zinc atom (Zn_B) is transferred, i.e., that coordinated to oxygen (**23**). The third model (**24**), postulated by Soai[23] and Corey,[35] differs from **23** in lacking the coordination of the aldehyde oxygen to Zn_B.[36,37]

The effect of added BuLi has previously been demonstrated on several occasions.[18,19,23,29] While in some instances its addition resulted in notable enhancement of asymmetric induction,[18,19,23,29b−d] in other cases it either caused lowering of the ee or reversed the sense of chirality,[29a] thus confirming the mechanistic importance of Li^+.

Our results, obtained with the NOBIN-derived ligands (Table 1), can best be interpreted using the Noyori model **22**. When applied to our system (Chart 3), it shows that the axial twist imposed by the binaphthyl scaffold determines the annulation of the dinuclear chelate (**25**). The downward pointing angular ethyl adjacent to Zn_B must then be directly responsible for determining the stereochemical outcome of the reaction as the aldehyde approaches in a way avoiding repulsive interactions between the Ar and the latter alkyl (i.e., it exposes its *re* face), producing (*R*)-**21**. If Li^+ is taken into account (**26**), we can envisage its chelation between the carbonyl and the naphtholate oxygen, thereby further stabilizing the transition state. The latter effect is likely to improve the enantioselection, which is consonant with the experimental data (compare entries 1 and 2 in Table 1). According to this model, the zinc atom is assumed to coordinate to the soft π-electrons of the carbonyl oxygen, whereas Li^+, a harder Lewis acid, reaches for its hard and more Lewis-basic n orbital.[38] In contrast to this analysis, the two other models (**23** and **24**), although also predicting the correct configuration of the product **21**, do not easily accommodate the Li^+ chelation so that its influence on the level of enantioselection would be difficult to rationalize. Moreover, the corresponding transition state **27** can be assumed to be less rigid than **26** and, consequently, to lead to lower stereoselectivity.

In the instance of the *N*-methyl-*N*-alkyl-NOBIN derivatives **8a**−**c** and **15**, the larger alkyl group (R″ in the transition state **26**) can be predicted to attain the exo

(35) (a) Corey, E. J.; Hannon, F. J. *Tetrahedron Lett.* **1987**, *28*, 5237. (b) Corey, E. J.; Yuen, P.-W.; Hannon, F. J.; Wierda, D. A. *J. Org. Chem.* **1990**, *55*, 784.

(36) An entirely different mechanism operates in the recently reported reaction of Et_2Zn and PhCHO in the presence of (*S*)-(−)-2,2-dimethyl-5,5-diphenyl-4-isopropyl-1,3-oxazolidine, which apparently involves zinc amide as the reactive species lacking chelation: Prasad, K. R. K.; Joshi, N. N. *J. Org. Chem.* **1997**, *62*, 3770.

(37) A titanium(IV) complex of 2,2′-dihydroxy-1,1′-binaphthyl (BINOL) has recently been shown to also catalyze asymmetric addition of Et_2Zn to aldehydes, thus breaking the hegemony of amino alcohol ligands in this area. The mechanism is believed to involve transmetalation so that the ethyl is first transferred from the zinc atom to the titanium chelated by the diol ligand. Presumably, the latter chiral species then reacts with the aldehyde: (a) Mori, M.; Nakai, T. *Tetrahedron Lett.* **1997**, *38*, 6233. Even more recently, functionalized polyBINOLs have been demonstrated to be capable of catalyzing the same reaction without the need of an additive: (b) Hu, Q.-S.; Huang, W.-S.; Vitharana, D.; Zheng, X.-F.; Pu, L. *J. Am. Chem. Soc.* **1997**, *119*, 12454. (c) Huang, W.-S.; Hu, Q.-S.; Pu, L. *J. Org. Chem.* **1998**, *63*, 1364. High enantioselectivities were reported for *N*,*N*′,*N*′-tetraalkyl-2,2′-dihydroxy-1,1′-binaphthyl-3,3′-dicarboxamides employed as ligands in the Et_2Zn addition; additional coordination of the zinc by amide carbonyls has been proposed: (d) Kitajima, H.; Ito, K.; Katsuki, T. *Chem. Lett.* **1996**, 343. For the most recent report on the use of diols as well as amino alcohols as ligands, see: (e) Bringmann, G.; Breuning, M. *Tetrahedron: Asymmetry* **1998**, *9*, 667. 1,2-Bis(trifluoromethanesulfonamido)cyclohexane is another "non-amino alcohol" exhibiting high enantioselectivity in the addition of organozinc reagents to aldehydes: (f) Lutz, C.; Knochel, P. *J. Org. Chem.* **1997**, *62*, 7895. For other bissulfonamide-type ligands, see: (g) Cernerud, M.; Skrinning, A.; Bérgère, I.; Moberg, C. *Tetrahedron: Asymmetry* **1997**, *8*, 3437. For oxazoline-type ligands, see: (h) Allen, J. V.; Frost, C. G.; Williams, J. M. J. *Tetrahedron: Asymmetry* **1993**, *4*, 649−650. (i) Macedo, E.; Moberg, C. *Tetrahedron: Asymmetry* **1995**, *6*, 549. (j) Nakamura, M.; Hirai, A.; Nakamura, E. *J. Am. Chem. Soc.* **1996**, *118*, 8489. For a ferrocene-derived amino aldehyde as the ligand, see: (k) Fukuzawa, S.; Kato, H. *Synlett* **1998**, 727.

(38) For the basicity of π and n orbitals of the C=O group and its manifestation, see: (a) Suga, T.; Imamura, K.; von Rudolf, E. *J. Chem. Soc., Perkin Trans. 1* **1972**, 962. (b) Golfier, M. In *Stereochemistry*; Kagan, H. B., Ed.; Thieme: Stutgart, 1977; Vol. 1, p 39. (c) Tichý, M. *Adv. Org. Chem.* **1965**, *5*, 115. (d) Kočovský, P.; Starý, I. *J. Org. Chem.* **1990**, *55*, 3236. For the ab initio calculations, see: (e) Jaisen, P. G.; Stevens, W. J. *J. Chem. Phys.* **1986**, *84*, 3271.

position in order to avoid clashing with the binaphthyl skeleton (note that, upon chelation, the nitrogen atom becomes stereogeneous). However, the larger the *N*-alkyl (R″), the more serious repulsive interaction with the Ar group of the incoming aldehyde can be identified in the (*re*)-facial approach of ArCHO (**26**).[39] This effect should gradually reduce the degree of enantioselectivity owing to the competing (*si*)-approach. Indeed, the enantioselectivity decreases in the following order **3** > **8a** > **8b** > **7** > **15** (Table 1, entries 2, 5−7, 16), with the extreme of the *N*-(2-adamantyl) derivative **8c**, which preferentially gives the opposite enantiomer. However, for the (*si*)-approach, another serious clash can be identified, this time with the nontransferable ethyl at Zn_B, which is in accord with the low enantioselectivity observed for **8c** (Table 1, entry 8). The increasing steric congestion is reflected in the reaction rate, expressed by the yields attained in the standard period of time (compare, for example, entries 6−8 in Table 1).

The effect of the steric bulk of the *N*-alkyls on the enantioselectivity of Et_2Zn addition to carbonyl compounds has been the subject of several studies.[23,28d,30] While ephedrine-type amino alcohols with NMeR (R = Me, *i*-Pr, $PhCH_2$) or NBu_2 groups turned out to exhibit little difference (within 10% ee),[30a−d] proline derived ligands showed a dramatic increase when the *N*-methyl group was replaced by *N*-neopentyl (from 72 to 100% ee).[23] Similar improvement was attained with amino thiols.[12j] Interestingly, Andersson has recently reported on the reversal of the configuration of the resulting alcohol **21a** as a function of the steric bulk of the N substituent in 2-azanorbornylmethanols as ligands. Thus, while the *N*-Me derivative afforded (*R*)-**21a** of 24% ee, the *N*-Et, *N*-Pr^i, and *N*-CH_2Ph ligands produced (*S*)-**21a** of 48, 53, and 75% ee, respectively.[28d] This behavior was rationalized in the way similar to that in the present study, i.e., by increasing the steric clash of the *N*-R substituent with the Ph group of benzaldehyde.

Bidentate chelation of the diamine ligands can also be assumed. However, the present data do not allow the proposition of a sound hypothesis in view of the rather low enantioselectivities generally observed with diamines. Nevertheless, the trend in this series is similar to that observed for amino phenols—a gradual decrease of enantioselectivity with the increasing steric demands of the N substituents (e.g., **13a** > **13b**; Table 1, entries 13 and 14) leading, eventually, to the reversal of the product configuration with ligands possessing two bulky N,N′-substituents (e.g., **12a**−**c**; Table 1, entries 10−12). As expected, the increased steric bulk of the substituents resulted in lower conversions (compare, for example, the yields in entries 4, 10−12; Table 1).

Conclusions

We have demonstrated that a simple, high-yield reductive alkylation of (*R*)-(+)-**1** and (*R*)-(+)-**2** can be accomplished with ketones even as bulky as 2-adamantanone and $NaBH_4/H_2SO_4$ in THF at room temperature and have established its scope (Schemes 1 and 2); $NaBH_4$ proved to be more efficient than $NaBH_3CN$. Related *N*-phenyl derivatives were obtained via the Pd(0)-catalyzed coupling of (*R*)-(+)-**1** and (*R*)-(+)-**2** with PhBr (Scheme 3). It can be envisaged that the appendices attached to the nitrogen atom(s) via our methodology could bring additional functional group(s), which might further assist the coordination of the metal[6a−c] and enhance the chirality of its environment. We have further demonstrated that our chiral binaphthyls comprise a new, promising class of ligands to be used in asymmetric catalysis. As an example, we have studied the prototype addition of Et_2Zn to benzaldehyde and its congeners in the presence of these ligands; the highest level of asymmetric induction was observed for *N*,*N*-dimethyl NOBIN (*R*)-(+)-**3** (3 mol %) in conjunction with *n*-BuLi (5.4 mol %), which gave (*R*)-(+)-**21a** in 88% ee (Table 1, entry 2). The reactions were carried out at ambient temperature; no increase in the level of enantioselectivity was detected at 0 °C or below, which has obvious practical implications. Generally, derivatives of the amino phenol **1** proved more efficient than the corresponding diamines derived from **2**. The observed enantioselectivities are in the same range as those for established ligands reported by other groups.[18,19,29] The stereochemical outcome and the effect of Li^+ are consistent with the Noyori-type[18,22] transition-state model **26**. Investigation of further applications of the NOBIN-derived complexes in asymmetric catalysis is on the way and will be reported in due course.[40,41]

Experimental Section

General Methods. All reactions were performed under a dry argon atmosphere. Sodium borohydride, diethylzinc (1 M solution in hexanes), *n*-BuLi (1.6 M solution in hexanes[42]), and aldehydes **20** were purchased from Aldrich. Toluene was freshly distilled from a sodium benzophenone still under dry argon. Melting points were determined on a Kofler block and are uncorrected. The optical rotations were measured in THF, $CHCl_3$, benzene, or toluene with an error of $< \pm 0.1$ at 25 °C. The ^{1}H NMR spectra were recorded on 250, 300, or 400 MHz instruments (FT mode) for $CDCl_3$ solutions at 25 °C with TMS as an internal reference. The ^{13}C NMR spectra were recorded on 63 MHz instrument (FT mode) for $CDCl_3$ solutions at 25 °C. The IR spectra were measured in chloroform or dichloromethane. The high-resolution mass spectra (EI) were measured on a double focusing spectrometer (70 eV, 50 μA) using direct inlet and the lowest temperature enabling evaporation; the accuracy was ≤5 ppm. Yields are given in milligrams of isolated product, showing one spot on a chromatographic plate and no impurities detectable in the NMR spectrum. Semipreparative HPLC analyses were carried out on a Magnum 9

(39) Bulky groups attached to the nitrogen normally tend to increase the enantioselectivity of this reaction.[24] The opposite trend, observed in our series, can be understood if *N*,*N*-dimethyl NOBIN (**3**) is assumed to be the upper limit for tolerating the steric bulk; further increasing the steric hindrance apparently has an adverse effect. Alternatively, the bulky N substituent may impair the metal coordination to the sterically hindered nitrogen atom, thereby loosening the transition state. A similarly detrimental effect of the Ph_3C group has been reported for the aziridino alcohols employed as ligands in the Et_2Zn addition to imines.[28b,c]

(40) During the preparation of this manuscript, two papers appeared on the addition of dialkyl zinc reagents to ketones rather than aldehydes. Fu has reported on the successful addition of Ph_2Zn to ketones in the presence of the Noyori's DAIB ligand with 58−83% ee.[41a] Tagliavini has apparently found a more general approach, in which the addition of Et_2Zn and other Knochel-type zinc reagents to ketones is boosted by Me_3SiCl and related silylating agents[41b] (note that a similar effect is known in cuprate chemistry). The latter approach is awaiting its chiral version, thereby opening an exciting new avenue to our NOBIN-derived ligands.

(41) (a) Dosa, P. I.; Fu, G. C. *J. Am. Chem. Soc.* **1998**, *120*, 445. (b) Alvisi, C.; Casolari, S.; Costa, A. L.; Ritiani, M.; Tagliavini, E. *J. Org. Chem.* **1998**, *63*, 1330.

(42) The actual concentration of *n*-BuLi was determined using titration with *o*-phenanthroline as an indicator. For the method, see: Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165.

column (Partisil 10, Whatman) using petroleum ether−ethyl acetate mixtures and refractive index detection. Chiral HPLC analyses were carried out on a Chiralpak AD column (Daicel) using hexanes−ethanol mixtures and UV detection at 254 nm.

(*R*)-(+)-2-(Diethylamino)-2′-hydroxy-1,1′-binaphthyl, (*R*)-(+)-4. A solution of (*R*)-(+)-NOBIN (**1**) (285 mg, 1 mmol, ≥99% ee) in THF (10 mL) and solid $NaBH_4$ (530 mg, 14 mmol) were slowly added (simultaneously) to a solution of acetaldehyde (616 mg, 14 mmol) and 20% aqueous H_2SO_4 (2 mL) in THF (5 mL) over a period of 15 min. The reaction mixture was stirred for an additional 15 min and then poured into 2% aqueous KOH (100 mL). The resulting suspension was extracted with ethyl acetate (3 × 20 mL), and the extract was dried with $MgSO_4$ and evaporated. The crude product was purified by flash chromatography on silica gel (20 g) with toluene to give (*R*)-(+)-**4** (310 mg, 91%): $[\alpha]_D$ +13.1 (*c* 0.5, THF); ^{1}H NMR (250 MHz) δ 0.86 (t, J = 7.1 Hz, 6 H), 2.87−3.05 (m, 4 H), 7.00−7.05 (m, 2 H), 7.09−7.18 (m, 2 H), 7.21−7.38 (m, 3 H), 7.48 (d, J = 9.1 Hz, 1 H), 7.80−7.94 (m, 4 H); ^{13}C NMR δ 12.26 (q), 46.75 (t), 118.47 (s), 119.53 (d), 120.28 (d), 123.06 (d), 124.42 (d), 125.21 (s), 125.61 (d), 126.12 (d), 126.15 (d), 126.28 (d), 127.78 (d), 128.11 (d), 129.18 (d), 129.25 (s), 129.56 (d), 130.32 (s), 134.10 (s), 134.21 (s), 147.35 (s), 151.37 (s); IR (CH_2Cl_2) ν 3525 (OH), 1621 and 1597 (C=C arom) cm^{-1}; MS *m*/*z* (%) 341 (M$^{\bullet+}$, 47), 326 (100).

General Procedure for the Reaction of NOBIN (*R*)-(+)-1 with Ketones and $NaBH_4$. A solution of (*R*)-(+)-NOBIN (**1**) (285 mg, 1 mmol, ≥99% ee) in THF (10 mL) and solid $NaBH_4$ (265 mg, 7 mmol) were slowly added (simultaneously) to a solution of the ketone (7 mmol) and 20% aqueous H_2SO_4 (1 mL) in THF (5 mL) over a period of 15 min at room temperature. The reaction mixture was stirred for an additional 15 min and then poured into 2% aqueous KOH (100 mL). The resulting suspension was extracted with ethyl acetate (3 × 20 mL), and the extract was dried with $MgSO_4$ and evaporated. The crude product was purified by flash chromatography on silica gel (20 g) with toluene to give the monosubstituted amino phenols **6**.

(*R*)-(+)-2-(Isopropylamino)-2′-hydroxy-1,1′-binaphthyl, (*R*)-(+)-6a (291 mg, 89%): mp 50−2 °C (toluene); $[\alpha]_D$ +119 (*c* 0.4, THF); ^{1}H NMR (400 MHz) δ 0.99 (d, J = 6.3 Hz, 3 H), 1.06 (d, J = 6.3 Hz, 3 H), 3.42 (bs, 1 H), 3.71−3.82 (m, 1 H), 5.16 (bs, 1 H), 6.92 (d, J = 7.5 Hz, 1 H), 7.10−7.40 (m, 7 H), 7.77 (d, J = 7.5 Hz, 1 H), 7.80−7.93 (m, 3 H); ^{13}C NMR δ 23.04 (q), 23.13 (q), 44.52 (d), 108.43 (s), 114.09 (s), 114.85 (d), 117.58 (d), 122.12 (d), 123.51 (d), 123.55 (d), 124.58 (d), 126.79 (d), 127.07 (d), 127.41 (s), 128.08 (d), 128.17 (d), 129.46 (s), 130.27 (d), 130.54 (d), 133.37 (s), 134.24 (s), 144.81 (s), 151.92 (s); IR ($CHCl_3$) ν 3515 (OH), 3403 (NH), 1620 and 1598 (C=C arom) cm^{-1}; MS *m*/*z* (%) 327 (M$^{\bullet+}$, 69), 312 (100).

(*R*)-(+)-2-(Cyclohexylamino)-2′-hydroxy-1,1′-binaphthyl, (*R*)-(+)-6b (330 mg, 90%): mp 54−5 °C (toluene); $[\alpha]_D$ +118 (*c* 0.4, THF); ^{1}H NMR (250 MHz) δ 0.70−1.05 (m, 4 H), 1.10−1.36 (m, 2 H), 1.43−1.61 (m, 2 H), 1.74−1.91 (m, 2 H), 3.30−3.43 (m, 1 H), 3.47 (bs, 1 H), 5.19 (bs, 1 H), 6.91 (d, J = 8 Hz, 1 H), 7.05−7.37 (m, 7 H), 7.61−7.88 (m, 4 H); ^{13}C NMR δ 24.72 (2 × t), 25.84 (t), 33.36 (t), 33.42 (t), 51.71 (d), 108.27 (s), 114.09 (s), 114.82 (d), 117.54 (d), 121.97 (d), 123.42 (d), 123.49 (d), 124.57 (d), 126.72 (d), 126.98 (d), 127.32 (s), 128.04 (d), 128.13 (d), 129.39 (s), 130.19 (d), 130.37 (d), 133.36 (s), 134.29 (s), 144.59 (s), 151.89 (s); IR ($CHCl_3$) ν 3514 (OH), 3405 (NH), 1619 and 1598 (C=C arom) cm^{-1}; MS *m*/*z* (%) 367 (M$^{\bullet+}$, 100).

(*R*)-(+)-2-[(2″-Adamantyl)amino]-2′-hydroxy-1,1′-binaphthyl, (*R*)-(+)-6c (240 mg, 57%): mp 153−5 °C (toluene); $[\alpha]_D$ +87 (*c* 0.4, THF); ^{1}H NMR (300 MHz) δ 1.10−1.14 (m, 1 H), 1.20−1.22 (m, 1 H), 1.23−1.27 (m, 1 H), 1.30−1.36 (m, 2 H), 1.48−1.52 (m, 1 H), 1.58−1.62 (m, 1 H), 1.74−1.78 (m, 4 H), 1.79−1.82 (m, 2 H), 1.90−1.94 (m, 1 H), 3.65 (bs, 1 H), 4.02 (bs, 1 H), 5.19 (bs, 1 H), 6.95−7.00 (m, 1 H), 7.14−7.34 (m, 6 H), 7.38 (d, J = 8.8 Hz, 1 H), 7.74−7.78 (m, 1 H), 7.83−7.87 (m, 2 H), 7.91 (d, J = 8.8 Hz, 1 H); ^{13}C NMR δ 26.92 (d), 27.25 (d), 31.12 (t), 31.17 (t), 31.77 (d), 31.92 (d), 37.23 (t), 37.35 (t), 37.48 (t), 56.47 (d), 107.81 (s), 114.21 (s), 114.49 (d), 117.45 (d), 121.87 (d), 123.35 (d), 123.57 (d), 124.72 (d), 126.79 (d), 127.08 (d), 127.17 (s), 128.13 (d), 128.19 (d), 129.46 (s), 130.30 (d), 130.49 (d), 133.41 (s), 134.39 (s), 144.28 (s), 151.95 (s); IR ($CHCl_3$) ν 3511 (OH), 3418 (NH), 1620 and 1599 (C=C arom) cm^{-1}; MS *m*/*z* (%) 419 (M$^{\bullet+}$, 100).

(*R*)-(+)-2-(*N*-Piperidinyl)-2′-hydroxy-1,1′-binaphthyl, (*R*)-(+)-7 (340 mg, 96%): $[\alpha]_D$ +6.3 (*c* 0.8, THF); ^{1}H NMR (250 MHz) δ 1.39 (bs, 6 H), 2.84−2.97 (m, 4 H), 7.05−7.31 (m, 6 H), 7.41−7.46 (m, 2 H), 7.79−7.94 (m, 4 H), 8.12 (bs, 1 H); ^{13}C NMR δ 23.96 (t), 26.20 (t), 53.32 (t), 118.55 (s), 118.65 (d), 120.28 (d), 123.05 (d), 124.35 (d), 125.06 (s), 125.86 (d), 126.02 (d), 126.15 (d), 126.41 (d), 127.82 (d), 128.07 (d), 129.27 (s), 129.53 (d), 129.73 (d), 130.46 (s), 133.71 (s), 134.14 (s), 149.02 (s), 151.66 (s); IR ($CHCl_3$) ν 3527 (OH), 1620 and 1595 (C=C arom) cm^{-1}; MS *m*/*z* (%) 353 (M$^{\bullet+}$, 100).

General Procedure for Methylation of the Amino Phenols (*R*)-6. A solution of the amino phenol (1 mmol) in THF (10 mL) and solid $NaBH_4$ (265 mg, 7 mmol) were slowly added (simultaneously) to a solution of 40% aqueous formaldehyde (1 mL; 12 mmol) and 20% aqueous H_2SO_4 (1 mL) in THF (5 mL) over a period of 15 min at room temperature. The reaction mixture was stirred for an additional 15 min and then poured into 2% aqueous KOH (100 mL). The resulting suspension was extracted with ethyl acetate (3 × 20 mL), and the extract was dried with $MgSO_4$ and evaporated. The crude product was purified by flash chromatography on silica gel (20 g) with toluene to give the amino phenols **8**.

(*R*)-(+)-2-(*N*-Isopropyl-*N*-methylamino)-2′-hydroxy-1,1′-binaphthyl, (*R*)-(+)-8a (327 mg, 96%): mp 106−8 °C (toluene); $[\alpha]_D$ +20.7 (*c* 0.3, THF); ^{1}H NMR (400 MHz) δ 0.70 (d, J = 6.4 Hz, 3 H), 0.77 (d, J = 6.4 Hz, 3 H), 2.66 (s, 3 H), 3.16−3.24 (m, 1 H), 7.01−7.17 (m, 4 H), 7.21−7.28 (m, 2 H), 7.36 (d, J = 8.8 Hz, 1 H), 7.44 (d, J = 8.8 Hz, 1 H), 7.75−7.87 (m, 4 H); ^{13}C NMR δ 16.68 (q), 19.78 (q), 31.21 (q), 54.04 (d), 118.65 (s), 119.66 (d), 120.20 (d), 123.05 (d), 123.95 (s), 124.22 (d), 125.65 (d), 126.12 (d), 126.15 (d), 126.27 (d), 127.79 (d), 128.10 (d), 129.20 (s), 129.40 (d), 129.54 (d), 130.13 (s), 133.93 (s), 134.10 (s), 149.23 (s), 151.50 (s); IR ($CHCl_3$) ν 3526 (OH), 1620 and 1596 (C=C arom) cm^{-1}; MS *m*/*z* (%) 341 (M$^{\bullet+}$, 29), 326 (100).

(*R*)-(+)-2-(*N*-Cyclohexyl-*N*-methylamino)-2′-hydroxy-1,1′-binaphthyl, (*R*)-(+)-8b (364 mg, 95%): mp 103−4 °C (toluene); $[\alpha]_D$ +30.1 (*c* 0.4, THF); ^{1}H NMR (400 MHz) δ 0.04−0.15 (m, 1 H), 0.49−0.59 (m, 1 H), 0.64−0.75 (m, 1 H), 0.91−0.98 (m, 1 H), 1.03−1.19 (m, 3 H), 1.21−1.27 (m, 2 H), 1.37−1.43 (m, 1 H), 2.63 (s, 3 H), 2.65−2.73 (m, 1 H), 6.99−7.14 (m, 4 H), 7.19−7.23 (m, 2 H), 7.26 (d, J = 8.8 Hz, 1 H), 7.38 (d, J = 9.0 Hz, 1H), 7.71−7.83 (m, 4 H); ^{13}C NMR δ 25.62 (t), 25.72 (t), 27.83 (t), 30.55 (t), 32.74 (q), 63.12 (d), 118.71 (s), 119.14 (d), 120.20 (d), 122.47 (s), 123.10 (d), 124.07 (d), 125.44 (d), 125.77 (d), 126.26 (d), 126.42 (d), 127.80 (d), 128.08 (d), 129.24 (s), 129.39 (d), 129.47 (d), 129.94 (s), 134.12 (s), 149.78 (s), 149.82 (s), 151.14 (s); IR ($CHCl_3$) ν 3526 (OH), 1620 and 1596 (C=C arom) cm^{-1}; MS *m*/*z* (%) 381 (M$^{\bullet+}$, 61), 338 (100).

(*R*)-(−)-2-[*N*-(2″-Adamantyl)-*N*-methylamino]-2′-hydroxy-1,1′-binaphthyl, (*R*)-(−)-8c (372 mg, 86%): mp 206−8 °C (toluene); $[\alpha]_D$ −67.5 (*c* 0.4, THF); ^{1}H NMR (400 MHz) δ 0.53−0.62 (m, 1 H), 0.83−0.88 (m, 1 H), 1.13−1.69 (m, 11 H), 2.01−2.07 (m, 1 H), 3.09 (s, 3 H), 3.49 (bs, 1 H), 3.70−3.76 (m, 1 H), 6.79 (d, J = 8.5 Hz, 1 H), 7.05−7.28 (m, 4 H), 7.38−7.42 (m, 1 H), 7.70 (d, J = 8.8 Hz, 1 H), 7.77−7.88 (m, 4 H), 7.99 (d, J = 9.1 Hz, 1 H); ^{13}C NMR δ 26.18 (d), 26.56 (d), 28.66 (d), 28.88 (d), 30.23 (t), 30.52 (t), 36.56 (t), 36.83 (t), 37.01 (t), 43.12 (q), 70.23 (d), 113.20 (s), 119.30 (d), 120.57 (d), 122.92 (d), 124.77 (d), 125.48 (s), 126.23 (d), 126.33 (d), 126.87 (d), 126.93 (d), 127.62 (s), 128.02 (d), 128.26 (d), 128.69 (s), 130.46 (d), 130.97 (d), 132.15 (s), 133.35 (s), 134.17 (s), 153.51 (s); IR ($CHCl_3$) ν 3537 (OH), 1623 and 1597 (C=C arom) cm^{-1}; MS *m*/*z* (%) 433 (M$^{\bullet+}$, 100).

General Procedure for the Reaction of Diamine (*R*)-(+)-2 with Ketones and $NaBH_4$. A solution of diamine (**2**) (284 mg, 1 mmol) in THF (10 mL) and solid $NaBH_4$ (530 mg, 14 mmol) were slowly added (simultaneously) to a solution of the ketone (14 mmol) and 20% aqueous H_2SO_4 (2 mL) in THF (5 mL) over a period of 15 min at room temperature. The reaction mixture was stirred for an additional 15 min and then

poured into 2% aqueous KOH (100 mL). The resulting suspension was extracted with ethyl acetate (3 × 20 mL), and the extract was dried with $MgSO_4$ and evaporated. The crude product was purified by flash chromatography on silica gel (20 g) with toluene to give the disubstituted diamines **9** or **11** and the monosubstituted diamines **10**, respectively.

(*R*)-(+)-2,2′-Bis(isopropylamino)-1,1′-binaphthyl, (*R*)-(+)-9a (301 mg, 82%): mp 83−4 °C (toluene); $[\alpha]_D$ +89 (*c* 0.4, THF); ^{1}H NMR (400 MHz) δ 0.96 (d, J = 6.3 Hz, 6 H), 1.04 (d, J = 6.3 Hz, 6 H), 3.40 (bs, 2 H), 3.73−3.86 (m, 2 H), 6.91 (dd, J = 8.1 Hz, J = 0.9 Hz, 2 H), 7.08−7.22 (m, 4 H), 7.25 (d, J = 9.0 Hz, 2 H), 7.75 (dd, J = 8.1 Hz, J = 0.9 Hz, 2 H), 7.85 (d, J = 9.0 Hz, 2 H); ^{13}C NMR δ 23.20 (q), 44.49 (d), 112.38 (s), 114.95 (d), 121.76 (d), 123.99 (d), 126.46 (d), 127.54 (s), 127.88 (d), 129.42 (d), 134.03 (s), 144.04 (s); IR ($CHCl_3$) ν 3398 (NH), 1619 and 1599 (C=C arom) cm^{-1}; MS *m*/*z* (%) 368 (M$^{\bullet+}$, 100).

(*R*)-(+)-2,2′-Bis(cyclohexylamino)-1,1′-binaphthyl, (*R*)-(+)-9b (288 mg, 64%): mp 66−8 °C (toluene); $[\alpha]_D$ +70.5 (*c* 0.4, THF); ^{1}H NMR (300 MHz) δ 0.72−1.11 (m, 6 H), 1.15−1.34 (m, 4 H), 1.47−1.68 (m, 6 H), 1.80−2.01 (m, 4 H), 3.32−3.41 (m, 2 H), 3.55 (bs, 2 H), 6.92 (d, J = 8.3 Hz, 2 H), 7.09−7.19 (m, 4 H), 7.24 (d, J = 8.8 Hz, 2 H), 7.73 (dd, J = 8.3 Hz, J = 2.2 Hz, 2 H), 7.85 (d, J = 8.8 Hz, 2 H); ^{13}C NMR δ 24.88 (t), 24.96 (t), 25.65 (t) 33.58 (t), 33.68 (t), 51.92 (d), 112.24 (s), 114.91 (d), 121.65 (d), 123.96 (d), 126.40 (d), 127.49 (s), 127.86 (d), 129.30 (d), 134.07 (s), 143.89 (s); IR ($CHCl_3$) ν 3396 (NH), 1618 and 1599 (C=C arom) cm^{-1}; MS *m*/*z* (%) 448 (M$^{\bullet+}$, 100).

(*R*)-(+)-2,2′-Bis[(2″-adamantyl)amino]-1,1′-binaphthyl, (*R*)-(+)-9c (82 mg, 15%): mp 292−4 °C (toluene); $[\alpha]_D$ +16.8 (*c* 0.2, THF); ^{1}H NMR (400 MHz) δ 0.82−0.90 (m, 2 H), 1.08−1.12 (m, 2 H), 1.13−1.16 (m, 2 H), 1.25−1.29 (m, 6 H), 1.41−1.45 (m, 2 H), 1.56−1.59 (m, 4 H), 1.73−1.86 (m, 10 H), 3.61−3.65 (m, 2 H), 4.09 (bs, 2 H), 6.97−7.05 (m, 2 H), 7.09−7.17 (m, 4 H), 7.21 (d, J = 9.1 Hz, 2 H), 7.72−7.80 (m, 2 H), 7.83 (d, J = 9.1 Hz, 2 H); ^{13}C NMR δ 27.00 (d), 27.34 (d), 31.04 (t), 31.28 (t), 31.97 (d), 32.26 (d), 37.37 (t), 37.54 (t), 37.56 (t), 56.65 (d), 112.15 (s), 114.47 (d), 121.50 (d), 123.97 (d), 126.41 (d), 127.27 (s), 127.91 (d), 129.31 (d), 134.14 (s), 143.63 (s); IR ($CHCl_3$) ν 3414 (NH), 1619 and 1598 (C=C arom) cm^{-1}; MS *m*/*z* (%) 552 (M$^{\bullet+}$, 100).

(*R*)-(+)-2-Amino-2′-(isopropylamino)-1,1′-binaphthyl, (*R*)-(+)-10a (50 mg, 15%): mp 158−61 °C (toluene); $[\alpha]_D$ +137 (*c* 0.2, THF); ^{1}H NMR (400 MHz) δ 0.98 (d, J = 6.0 Hz, 3 H), 1.05 (d, J = 6.0 Hz, 3 H), 3.42 (bs, 1 H), 3,64 (bs, 2 H), 3.75−3.83 (m, 1 H), 6.96 (d, J = 7.5 Hz, 1 H), 7.03 (d, J = 8.1 Hz, 1 H), 7.20−7.23 (m, 5 H), 7.27 (d, J = 9.0 Hz, 1 H), 7.75−7.82 (m, 3 H), 7.86 (d, J = 9.0 Hz, 1 H); ^{13}C NMR δ 23.18 (q), 23.33 (q), 44.77 (d), 112.31 (s), 112.85 (s), 115.26 (d), 118.20 (d), 121.90 (d), 122.34 (d), 123.81 (d), 124.10 (d), 126.62 (d), 126.67 (d), 127.65 (s), 128.02 (2 × d), 128.44 (s), 129.45 (2 × d), 133.71 (s), 133.92 (s), 142.88 (s), 144.01 (s); IR ($CHCl_3$) ν 3485 (NH_2, asym), 3393 (NH_2 sym, NH), 1620 and 1598 (C=C arom) cm^{-1}; MS *m*/*z* (%) 326 (M$^{\bullet+}$, 75), 311 (100).

(*R*)-(+)-2-Amino-2′-(cyclohexylamino)-1,1′-binaphthyl, (*R*)-(+)-10b (102 mg, 28%): mp 224−6 °C (toluene); $[\alpha]_D$ +122 (*c* 0.4, THF); ^{1}H NMR (300 MHz) δ 0.79−0.90 (m, 1 H), 0.93−1.09 (m, 2 H), 1.14−1.35 (m, 2 H), 1.47−1.65 (m, 3 H), 1.79−1.88 (m, 1 H), 1.90−1.98 (m, 1 H), 3.32−3.42 (m, 1 H), 3.68 (bs, 3 H), 6.97 (d, J = 7.2 Hz, 1 H), 7.02 (d, J = 7.2 Hz, 1 H), 7.11−7.26 (m, 5 H), 7.32 (d, J = 9.0 Hz, 1 H), 7.75−7.81 (m, 3 H), 7.86 (d, J = 9.0 Hz, 1 H); ^{13}C NMR δ 24.90 (t), 24.98 (t), 25.63 (t), 33.58 (t), 33.76 (t), 52.01 (d), 112.35 (s), 112.62 (s), 115.21 (d), 118.19 (d), 121.78 (d), 122.33 (d), 123.74 (d), 124.13 (d), 126.59 (d), 126.66 (d), 127.58 (s), 127.98 (d), 128.01 (d), 128.41 (s), 129.36 (d), 129.41 (d), 133.77 (s), 133.93 (s), 142.87 (s), 143.77 (s); IR ($CHCl_3$) ν 3485 (NH_2, asym), 3390 (NH_2 sym, NH), 1620 and 1599 (C=C arom) cm^{-1}; MS *m*/*z* (%) 366 (M$^{\bullet+}$, 100).

(*R*)-(+)-2-Amino-2′-[(2″-adamantyl)amino]-1,1′-binaphthyl, (*R*)-(+)-10c (298 mg, 71%): mp 230−3 °C (toluene); $[\alpha]_D$ +107 (*c* 0.2, THF); ^{1}H NMR (400 MHz) δ 1.10−1.14 (m, 1 H), 1.16−1.19 (m, 1 H), 1.25−1.29 (m, 1 H), 1.31−1.35 (m, 2 H), 1.44−1.49 (m, 1 H), 1.57−1.61 (m, 2 H), 1.74−1.82 (m, 5 H), 1.90−1.95 (m, 1 H), 3.62−3.75 (m, 3 H), 4.05 (bs, 1 H), 7.00−7.09 (m, 2 H), 7.12−7.24 (m, 6 H), 7.73−7.85 (m, 4 H); ^{13}C NMR δ 27.00 (d), 27.31 (d), 31.08 (t), 31.25 (t), 31.88 (d), 32.08 (d), 37.35 (t), 37.41 (t), 37.54 (t), 56.65 (d), 112.20 (s), 112.45 (s), 114.70 (d), 118.09 (d), 121.55 (d), 122.31 (d), 123.66 (d), 124.23 (d), 126.58 (d), 126.60 (d), 127.30 (s), 127.97 (d), 128.02 (d), 128.40 (s), 129.32 (d), 129.42 (d), 133.85 (s), 133.96 (s), 142.90 (s), 143.34 (s); IR ($CHCl_3$) ν 3486 (NH_2, asym), 3392 (NH_2 sym, NH), 1620 and 1598 (C=C arom) cm^{-1}; MS *m*/*z* (%) 418 (M$^{\bullet+}$, 100).

(*R*)-(−)-2,2′-Bis(*N*-piperidinyl)-1,1′-binaphthyl, (*R*)-(−)-11 (412 mg, 98%): $[\alpha]_D$ −229 (*c* 0.5, THF); ^{1}H NMR (400 MHz) δ 0.99−1.18 (m, 8 H), 1.21−1.30 (m, 4 H), 2.70 (t, J = 5.2 Hz, 8 H), 7.14−7.18 (m, 4 H), 7.22−7.31 (m, 2 H), 7.48 (d, J = 8.7 Hz, 2 H), 7.81 (d, J = 7.8 Hz, 2 H), 7.87 (d, J = 8.7 Hz, 2 H); ^{13}C NMR δ 24.28 (t), 26.38 (t), 52.89 (t), 120.77 (d), 123.35 (d), 125.64 (d), 126.14 (d), 127.76 (d), 128.21 (d), 129.01 (s), 130.15 (s), 134.23 (s), 150.29 (s); IR ($CHCl_3$) ν 1620 and 1593 (C=C arom) cm^{-1}; MS *m*/*z* (%) 420 (M$^{\bullet+}$, 100).

General Procedure for Methylation of Diamines (*R*)-9 and (*R*)-10. A solution of the diamine (1 mmol) in THF (10 mL) and solid $NaBH_4$ (795 mg, 21 mmol) were slowly added (simultaneously) to a solution of 40% aqueous formaldehyde (2 mL, 24 mmol) and 20% aqueous H_2SO_4 (2 mL) in THF (5 mL) over a period of 15 min at room temperature. The reaction mixture was stirred for an additional 15 min and then poured into a 2% aqueous KOH (100 mL). The resulting suspension was extracted with ethyl acetate (3 × 20 mL), and the extract was dried with $MgSO_4$ and evaporated. The crude product was purified by flash chromatography on silica gel (20 g) with toluene to give the tetrasubstituted diamines **12** or **13**, respectively.

(*R*)-(−)-2,2′-Bis(*N*-isopropyl-*N*-methylamino)-1,1′-binaphthyl, (*R*)-(−)-12a (301 mg, 76%): mp 121−3 °C (toluene); $[\alpha]_D$ −159 (*c* 0.3, THF); ^{1}H NMR (300 MHz) δ 0.33 (d, J = 6.9 Hz, 6 H), 0.69 (d, J = 6.9 Hz, 6 H), 2.53 (s, 6 H), 2.84−2.92 (m, 2 H), 7.13−7.17 (m, 4 H), 7.22−7.30 (m, 2 H), 7.45 (d, J = 8.8 Hz, 2 H), 7.77−7.86 (m, 4 H); ^{13}C NMR δ 17.04 (q), 19.73 (q), 31.50 (q), 52.81 (d), 122.12 (d), 123.11 (d), 125.60 (d), 126.03 (d), 127.66 (2 × d), 128.29 (s), 129.78 (s), 134.48 (s), 150.13 (s); IR ($CHCl_3$) ν 1619 and 1593 (C=C arom) cm^{-1}; MS *m*/*z* (%) 396 (M$^{\bullet+}$, 12), 353 (100).

(*R*)-(−)-2,2′-Bis(*N*-cyclohexyl-*N*-methylamino)-1,1′-binaphthyl, (*R*)-(−)-12b (357 mg, 75%): mp 143−5 °C (toluene); $[\alpha]_D$ −161 (*c* 0.4, THF); ^{1}H NMR (400 MHz) δ −0.26 to −0.09 (m, 2 H), 0.28−0.33 (m, 2 H), 0.49−0.59 (m, 2 H), 0.63−0.75 (m, 2 H), 0.83−0.90 (m, 2 H), 1.14−1.21 (m, 6 H), 1.35−1.44 (m, 4 H), 2.33−2.38 (m, 2 H), 2.62 (s, 6 H), 7.16−7.24 (m, 4 H), 7.26−7.31 (m, 2 H), 7.44 (d, J = 8.8 Hz, 2 H), 7.78−7.84 (m, 4 H); ^{13}C NMR δ 25.66 (t), 25.83 (t), 25.87 (t), 27.86 (t), 30.89 (t), 32.59 (q), 61.94 (d), 122.09 (d), 123.06 (d), 125.70 (d), 125.93 (d), 127.50 (d), 127.72 (d), 128.20 (s), 129.78 (s), 134.84 (s), 150.30 (s); IR ($CHCl_3$) ν 1619 and 1592 (C=C arom) cm^{-1}; MS *m*/*z* (%) 476 (M$^{\bullet+}$, 13), 393 (100).

(*R*)-(−)-2,2′-Bis[*N*-(2″-adamantyl)-*N*-methylamino]-1,1′-binaphthyl, (*R*)-(−)-12c (342 mg, 59%): mp 275−8 °C; $[\alpha]_D$ −116 (*c* 0.1, THF); ^{1}H NMR (400 MHz) δ −0.29 to −0.24 (m, 2 H), 0.40−0.47 (m, 2 H), 1.15−1.25 (m, 12 H), 1.35−1.45 (m, 2 H), 1.51−1.63 (m, 6 H), 1.65−1.73 (m, 2 H), 2.10−2.18 (m, 2 H), 2.78 (s, 6 H), 2.90−2.95 (m, 2 H), 6.92−7.05 (m, 4 H), 7.26−7.33 (m, 2 H), 7.71−7.81 (m, 4 H), 7.92 (d, J = 8.8 Hz, 2 H); ^{13}C NMR δ 27.30 (d), 27.41 (d), 30.07 (d), 30.29 (d), 30.78 (t), 31.68 (t), 26.92 (t), 37.36 (t), 38.10 (t), 42.65 (q), 69.60 (d), 123.40 (d), 124.40 (d), 124.75 (d), 127.30 (d), 128.37 (d), 128.91 (d), 131.43 (s), 133.40 (s), 134.55 (s), 151.53 (s); IR ($CHCl_3$) ν 1619 and 1598 (C=C arom) cm^{-1}; MS *m*/*z* (%) 580 (M$^{\bullet+}$, 1), 445 (100).

(*R*)-(−)-2-(*N*-Isopropyl-*N*-methylamino)-2′-(dimethylamino)-1,1′-binaphthyl, (*R*)-(−)-13a (239 mg, 65%): mp 182−5 °C (toluene); $[\alpha]_D$ −109 (*c* 0.1, THF); ^{1}H NMR (400 MHz) δ 0.44 (d, J = 6.6 Hz, 3 H), 0.71 (d, J = 6.6 Hz, 3 H), 2.34 (s, 6 H), 2.50 (s, 3 H), 2.93−3.09 (m, 1 H), 7.09−7.29 (m, 6 H), 7.42−7.47 (m, 2 H), 7.75−7.85 (m, 4 H); ^{13}C NMR δ 17.50 (q), 19.77 (q), 32.03 (q), 43.38 (2 × q), 52.70 (d), 120.57 (d), 122.02 (d), 123.10 (d), 123.32 (d), 125.74 (d), 125.77 (d), 125.84 (s), 125.89 (d), 126.26 (d), 127.67 (d), 127.70 (d), 127.93 (d), 128.09 (s), 128.23 (d), 129.68 (s), 129.76 (s), 134.52 (s), 134.76 (s),

149.61 (s), 150.22 (s); IR ($CHCl_3$) ν 1619 and 1595 (C=C arom) cm^{-1}; MS *m/z* (%) 368 ($M^{\bullet+}$, 19), 325 (100).

(*R*)-(−)-2-(*N*-Cyclohexyl-*N*-methylamino)-2′-(dimethylamino)-1,1′-binaphthyl, (*R*)-(−)-13b (277 mg, 68%): colorless oil $[\alpha]_D$ −120 (*c* 0.2, THF); ^1H NMR (250 MHz) δ −0.09−0.00 (m, 1 H), 0.42−0.55 (m, 2 H), 0.58−0.72 (m, 1 H), 0.85−1.05 (m, 2 H), 1.08−1.51 (m, 4 H), 2.44 (s, 6 H), 2.43−2.50 (m, 1 H), 2.61 (s, 3 H), 7.12−7.30 (m, 6 H), 7.40−7.48 (m, 2 H), 7.78−7.85 (m, 4 H); ^{13}C NMR δ 25.68 (t), 25.83 (2 × t), 27.92 (t), 30.78 (t), 32.79 (q), 43.47 (2 × q), 61.59 (d), 121.00 (d), 121.74 (d), 123.16 (d), 123.23 (d), 125.79 (d), 125.81 (d), 125.97 (d), 126.11 (d), 126.62 (s), 127.51 (s), 127.66 (d), 127.74 (2 × d), 128.22 (d), 129.56 (s), 129.89 (s), 134.73 (s), 134.83 (s), 149.57 (s), 150.35 (s); IR ($CHCl_3$) ν 1618 and 1593 (C=C arom) cm^{-1}; MS *m/z* (%) 408 ($M^{\bullet+}$, 16), 325 (100).

(*R*)-(−)-2-[*N*-(2″-Adamantyl)-*N*-methylamino]-2′-(dimethylamino)-1,1′-binaphthyl, (*R*)-(−)-13c (294 mg, 64%): mp 173−6 °C (toluene); $[\alpha]_D$ −146 (*c* 0.3, THF); ^1H NMR (250 MHz) δ 0.11−0.17 (m, 1 H), 0.60−0.65 (m, 1 H), 1.12−1.26 (m, 3 H), 1.31−1.48 (m, 5 H), 1.58−1.68 (m, 3 H), 2.00−2.06 (m, 1 H), 2.49 (s, 6 H), 2.57 (s, 3 H), 2.86 (m, 1 H), 6.84 (d, J = 8.5 Hz, 1 H), 6.97−7.03 (m, 1 H), 7.15−7.39 (m, 4 H), 7.46 (d, J = 8.8 Hz, 1 H), 7.67 (d, J = 8.8 Hz, 1 H), 7.75 (d, J = 7.9 Hz, 1 H), 7.82−7.93 (m, 3 H); ^{13}C NMR δ 27.27 (d), 27.37 (d), 29.96 (d), 30.18 (d), 30.65 (t), 31.02 (t), 36.98 (t), 37.37 (t), 37.52 (t), 41.13 (q), 43.47 (2 × q), 66.92 (d), 118.84 (d), 122.86 (d), 124.51 (d), 124.57 (d), 125.23 (d), 125.47 (s), 125.71 (d), 126.36 (d), 127.51 (d), 127.60 (d), 127.66 (d), 128.41 (d), 128.49 (d), 129.62 (s), 131.25 (s), 133.29 (s), 134.64 (s), 134.89 (s), 150.36 (s), 150.43 (s); IR ($CHCl_3$) ν 1619 and 1596 (C=C arom) cm^{-1}; MS *m/z* (%) 460 ($M^{\bullet+}$, 7) 325 (100).

(*R*)-(+)-2-(Phenylamino)-2′-hydroxy-1,1′-binaphthyl, (*R*)-(+)-14. Bis(dibenzylidene acetone)palladium (0.05 mmol, 29 mg, 5 mol %), (±)-2,2′-bis(diphenylphosphino)-1,1′-binaphthyl (BINAP; 0.075 mmol, 49 mg), sodium *tert*-butoxide (6 mmol, 576 mg), NOBIN (**1**) (1 mmol, 285 mg), and bromobenzene (5 mmol, 785 mg, 523 μL) were placed in a Schlenk tube under an argon atmosphere and dissolved in dry toluene (5 mL). The tube was heated at 90 °C with stirring for 2 h. After cooling, the mixture was purified by flash chromatography on silica gel (20 g) with toluene as eluent to give (*R*)-(+)-**14** (255 mg, 71%) as an amorphous solid: $[\alpha]_D$ +146 (*c* 0.3, THF); ^1H NMR (250 MHz) δ 5.13 (bs, 1 H), 5.50 (bs, 1 H), 6.89−7.00 (m, 3 H), 7.05 (d, J = 8.2 Hz, 1 H), 7.13−7.36 (m, 8 H), 7.61 (d, J = 9.1 Hz, 1 H), 7.75−7.91 (m, 4 H); ^{13}C NMR δ 112.42 (s), 113.81 (s), 117.32 (d), 117.73 (d), 120.53 (2 × d), 122.60 (d), 123.51 (d), 123.75 (d), 124.13 (d), 124.29 (d), 127.15 (d), 127.32 (d), 128.21 (d), 128.35 (d), 129.15 (s), 129.24 (2 × d), 129.49 (s), 130.11 (d), 130.58 (d), 133.34 (s), 134.12 (s), 141.46 (s), 141.95 (s), 151.90 (s); IR ($CHCl_3$) ν 3526 (OH), 3407 (NH), 1624 and 1596 (C=C arom) cm^{-1}; MS *m/z* (%) 361 ($M^{\bullet+}$, 100). Chromatography on Daicel Chiralpak AD (elution hexane-2-propanol) 9:1, flow rate 1 mL/min, UV detection at 256 nm) showed 99% ee (t_R = 7.5 min, t_S = 9 min).

(*R*)-(+)-2-(*N*-Methyl-*N*-phenylamino)-2′-hydroxy-1,1′-binaphthyl, (*R*)-(+)-15. A solution of the amino phenol **14** (361 mg, 1 mmol) in THF (10 mL) and solid $NaBH_4$ (265 mg, 7 mmol) were slowly added (simultaneously) to a solution of 40% aqueous formaldehyde (1 mL, 12 mmol) and 20% aqueous H_2SO_4 (1 mL) in THF (5 mL) over a period of 15 min at room temperature. The reaction mixture was stirred for an additional 15 min and then poured into 2% aqueous KOH (100 mL). The resulting suspension was extracted with ethyl acetate (3 × 20 mL), and the extract was dried with $MgSO_4$ and evaporated. The crude product was purified by flash chromatography on silica gel (20 g) with toluene to give (*R*)-(+)-**15** (304 mg, 81%) as an amorphous solid: $[\alpha]_D$ +137 (*c* 0.2, THF); ^1H NMR (400 MHz) δ 2.78 (s, 3 H), 4.95 (s, 1 H), 6.55−6.64 (m, 2 H), 6.93−7.19 (m, 9 H), 7.33−7.45 (m, 1 H), 7.46 (d, J = 8.8 Hz, 1 H), 7.68−7.73 (m, 2 H), 7.80−7.90 (m, 2 H); ^{13}C NMR δ 39.16 (q), 114.83 (2 × d), 116.19 (s), 116.52 (s), 117.80 (d), 118.35 (d), 123.24 (d), 125.07 (d), 125.73 (d), 125.79 (d), 126.33 (d), 126.93 (d), 126.96 (d), 128.07 (d), 128.10 (d), 128.75 (2 × d), 129.10 (s), 129.78 (d), 130.32 (d), 131.90 (s), 133.66 (s), 134.38 (s), 146.94 (s), 148.60 (s), 151.27 (s); IR ($CHCl_3$) ν 3546 (OH), 1621 and 1600 (C=C arom) cm^{-1}; MS *m/z* (%) 375 ($M^{\bullet+}$, 100).

(*R*)-(+)-2,2′-Bis(phenylamino)-1,1′-binaphthyl, (*R*)-(+)-16. Bis(dibenzylidene acetone)palladium (58 mg, 0.1 mmol, 5 mol %), (±)-2,2′-bis(diphenylphosphino)-1,1′-binaphthyl (BINAP; 98 mg, 0.15 mmol), sodium *tert*-butoxide (1.152 g, 12 mmol), diamine **2** (284 mg, 1 mmol, >99% ee), and bromobenzene (1.57 g, 1.046 mL, 10 mmol) were placed in a Schlenk tube under an argon atmosphere and dissolved in dry toluene (5 mL). The tube was heated at 90 °C with stirring for 2 h. After cooling, the mixture was purified by flash chromatography on silica gel (50 g) with toluene as eluent to give (*R*)-(+)-**16** (304 mg, 70%) as an amorphous solid: $[\alpha]_D$ +63.4 (*c* 0.4, THF); ^1H NMR (250 MHz) δ 5.47 (bs, 2 H), 6.79−6.89 (m, 6 H), 7.05−7.24 (m, 10 H), 7.59 (d, J = 9.1 Hz, 2 H), 7.73−7.81 (m, 4 H); ^{13}C NMR δ 116.38 (s), 117.83 (d), 119.94 (2 × d), 122.13 (d), 123.43 (d), 124.42 (d), 127.01 (d), 128.19 (d), 129.20 (2 × d), 129.36 (d), 129.41 (s), 133.96 (s), 140.37 (s), 142.49 (s); IR ($CHCl_3$ ν 3402 (NH), 1620 and 1596 (C=C arom); MS *m/z* (%) 436 ($M^{\bullet+}$, 100).[17] Chromatography on Daicel Chiralpak AD (elution hexanes−ethanol 19:1, flow rate 1 mL/min, UV detection at 256 nm) showed 98% ee (t_S = 4.3 min, t_R = 5.5 min).

(*R*)-(+)-2-Amino-2′-(phenylamino)-1,1′-binaphthyl, (*R*)-(+)-17. (R)-(+)-17 (65 mg, 18%) was isolated from the previous experiment as a slower moving byproduct: mp 240−1 °C (toluene); $[\alpha]_D$ +131 (*c* 0.4, THF); ^1H NMR (400 MHz) δ 3.75 (bs, 2 H), 5.60 (bs, 1 H), 6.91−6.95 (m, 1 H), 6.98−7.02 (m, 2 H), 7.09−7.12 (m, 2 H), 7.14 (d, J = 8.8 Hz, 1 H), 7.18−7.32 (m, 5 H), 7.70 (d, J = 9.1 Hz, 1 H), 7.76−7.88 (m, 5 H); ^{13}C NMR δ 112.03 (s), 116.82 (s), 117.86 (d), 118.27 (d), 119.80 (2 × d), 121.95 (d), 122.53 (d), 123.33 (d), 123.85 (d), 124.52 (d), 126.85 (d), 126.99 (d), 128.13 (d), 128.17 (d), 128.44 (s), 129.09 (d), 129.20 (2 × d), 129.44 (s), 129.75 (d), 133.74 (s), 133.93 (s), 140.19 (s), 142.77 (s), 142.82 (s); IR ($CHCl_3$) ν 3487 (NH_2 asym), 3397 (NH_2 sym, NH), 1621 and 1595 (C=C arom) cm^{-1}; MS *m/z* (%) 360 ($M^{\bullet+}$, 100).

(*R*)-(+)-2,2′-Bis(*N*-methyl-*N*-phenylamino)-1,1′-binaphthyl, (*R*)-(+)-18. A solution of the diamine **16** (436 mg, 10 mmol) in THF (10 mL) and solid $NaBH_4$ (530 mg, 14 mmol) were slowly added (simultaneously) to a solution of 40% aqueous formaldehyde (2 mL, 24 mmol) and 20% aqueous H_2SO_4 (2 mL) in THF (5 mL) over a period of 15 min. The reaction mixture was stirred for an additional 15 min at room temperature and then poured into a 2% aqueous KOH (100 mL). The resulting suspension was extracted with ethyl acetate (3 × 20 mL), and the extract was dried with $MgSO_4$ and evaporated. The crude product was purified by flash chromatography on silica gel (20 g) with toluene to give (*R*)-(+)-**18** (395 mg, 85%): mp 162−4 °C (toluene); $[\alpha]_D$ +401 (*c* 0.2, THF); ^1H NMR (400 MHz) δ 2.64 (s, 6 H), 6.40−6.49 (m, 6 H), 6.74−6.81 (m, 4 H), 7.17 (d, J = 8.8 Hz, 2 H), 7.22−7.28 (m, 2 H), 7.39−7.44 (m, 2 H), 7.46 (d, J = 8.8 Hz, 2 H), 7.82−7.88 (m, 4 H); ^{13}C NMR δ 39.09 (q), 115.09 (2 × d), 117.64 (d), 125.00 (d), 126.26 (d), 126.39 (d), 126.82 (d), 127.82 (2 × d), 128.13 (d), 129.12 (d), 130.85 (s), 131.65 (s), 134.51 (s), 146.17 (s), 148.56 (s); IR (CH_2Cl_2) ν 1605 and 1580 (C=C arom) cm^{-1}; MS *m/z* (%) 464 ($M^{\bullet+}$, 27), 246 (100).

(*R*)-(+)-2-(*N*-Methyl-*N*-phenylamino)-2′-(dimethylamino)-1,1′-binaphthyl, (*R*)-(+)-19. A solution of the diamine **17** (360 mg, 1 mmol) in THF (10 mL) and solid $NaBH_4$ (795 mg, 21 mmol) were slowly added (simultaneously) to a solution of 40% aqueous formaldehyde (3 mL, 36 mmol) and 20% aqueous H_2SO_4 (3 mL) in THF (5 mL) over a period of 15 min. The reaction mixture was stirred for an additional 15 min and then poured into a 2% aqueous KOH (100 mL). The resulting suspension was extracted with ethyl acetate (3 × 20 mL), and the extract was dried with $MgSO_4$ and evaporated. The crude product was purified by flash chromatography on silica gel (20 g) with toluene to give (*R*)-(+)-**19** (246 mg, 61%) as an amorphous solid: $[\alpha]_D$ +335 (*c* 0.6, THF); ^1H NMR (250 MHz) δ 2.19 (s, 6 H), 2.42 (s, 3 H), 6.60−6.64 (m, 3 H), 7.01−7.18 (m, 4 H), 7.20−7.25 (m, 2 H), 7.31−7.46 (m, 3 H), 7.54 (d, J = 8.8 Hz, 1 H), 7.76−7.82 (m, 2 H), 7.87−7.91 (m, 2 H); ^{13}C NMR

δ 38.34 (q), 43.25 (2 × q), 113.49 (2 × d), 116.66 (d), 119.54 (d), 123.25 (d), 124.68 (s), 125.14 (d), 125.44 (d), 126.13 (d), 126.18 (d), 126.70 (d), 128.00 (2 × d), 128.11 (d), 128.15 (2 × d), 128.52 (d), 128.76 (d), 129.67 (s), 131.91 (s), 133.14 (s), 134.14 (s), 135.14 (s), 145.02 (s), 148.84 (s), 150.75 (s); IR ($CHCl_3$) ν 1621 and 1594 (C═C arom) cm^{-1}; MS *m*/*z* (%) 402 ($M^{\bullet+}$, 28), 184 (100).

General Procedure for Addition of Diethylzinc to Aldehydes Using the Amino Phenols 3, 4, 7, 8, and 15 as Chiral Ligands. The (R) ligand (0.03 mmol) was placed in a Schlenk tube and dissolved in degassed toluene (3 mL). The solution was stirred for 5 min, 1.6 M BuLi in hexanes (0.054 mmol, 0.034 mL, 1.8 equiv) was added, and the resulting mixture was stirred for an additional 5 min at room temperature. A 1.0 M solution of diethylzinc in hexanes (2.2 mmol, 2.2 mL) was then added, and after the mixture was stirred for 5 min, a solution of the aldehyde **20** (1 mmol) in degassed toluene (5 mL) was added. The reaction mixture was stirred for 36 h at room temperature and quenched by the addition of 5% aqueous HCl (20 mL), and the product was extracted into ethyl acetate (3 × 10 mL). The combined extracts were washed successively with water, 5% aqueous $KHCO_3$, and water and dried with $MgSO_4$, and the solvent was evaporated in vacuo. The crude product was purified by a semipreparative HPLC (silica gel, Magnum 9 Whatman column, a 4:1 hexanes−ethyl acetate mixture as an eluent) to give the pure alcohol **21** as a colorless oil. The enantiomeric purities were determined by GC analysis of the corresponding menthoxycarbonyl esters[33] or by chiral HPLC (vide infra). The yields are given in Tables 1 and 2.

General Procedure for Addition of Diethylzinc to Aldehydes Using the Diamines 5, 11−13, 16, 18, and 19 as Chiral Ligands. The (R) ligand (0.03 mmol) was placed in a Schlenk tube and dissolved in degassed toluene (3 mL). The solution was stirred for 5 min, a 1.0 M solution of diethylzinc in hexanes (2.2 mmol, 2.2 mL) was then added, and, after the mixture was stirred for 5 min, a solution of the aldehyde **20** (1 mmol) in degassed toluene (5 mL) was added. The reaction mixture was stirred for 36 h at room temperature and quenched by the addition of 5% aqueous HCl (20 mL), and the product was extracted into ethyl acetate (3 × 10 mL). The combined extracts were washed successively with water, 5% aqueous $KHCO_3$, and water and dried with $MgSO_4$, and the solvent was evaporated in vacuo. The crude product was purified by a semipreparative HPLC (silica gel, Magnum 9 Whatman column, a 4:1 mixture hexanes−ethyl acetate as eluent) to give pure alcohol **21** as a colorless oil. The enantiomeric purities were determined by GC analysis of the corresponding menthoxycarbonyl esters[33] or by chiral HPLC (vide infra). The yields are given in Tables 1 and 2.

(*R*)-(+)-1-Phenyl-1-propanol (21a): $[\alpha]_D$ +38.8 (*c* 2, $CHCl_3$) [lit.[21] −47.6 (*c* 6.11, $CHCl_3$) for the (S) enantiomer, 98% ee].

(*R*)-(+)-1-(4′-Methoxyphenyl)-1-propanol (21b): $[\alpha]_D$ +23.9 (*c* 3, benzene) [lit.[21] −32.1 (*c* 1.25, benzene) for the (S) enantiomer, 93% ee].

(*R*)-(+)-1-(2′-Methoxyphenyl)-1-propanol (21c): $[\alpha]_D$ +27.3 (*c* 2, toluene) [lit.[43] −44.9 (*c* 1, toluene) for the (S) enantiomer, 83% ee].

(*R*)-(+)-1-(4′-Chlorophenyl)-1-propanol (21d): $[\alpha]_D$ +17.8 (*c* 3, benzene) [lit.[21] −23.5 (*c* 0.82, benzene) for the (S) enantiomer, 93% ee].

(*R*)-(+)-1-(2′-Chlorophenyl)-1-propanol (21e): $[\alpha]_D$ +37.1 (*c* 4, $CHCl_3$). In this case, the absolute configuration is assumed but not rigorously proven.

(*R*)-(+)-1-(4′-Methylphenyl)-1-propanol (21f): $[\alpha]_D$ +29.8 (*c* 1, benzene) [lit.[44] −23.9 (*c* 5.85, benzene) for the (S) enantiomer, 61% ee].

(*R*)-(+)-1-(2′-Methylphenyl)-1-propanol (21g): $[\alpha]_D$ +44.8 (*c* 1, benzene) [lit.[45] −57.51 (*c* 4, benzene) for the (S) enantiomer].

(*R*)-(+)-1-(4′-Fluorophenyl)-1-propanol (21h): $[\alpha]_D$ +29.7 (*c* 3, $CHCl_3$) [lit.[25] +51.2 (*c* 2.5, $CHCl_3$)].

(*R*)-(+)-1-(1′-Naphthyl)-1-propanol (21i): $[\alpha]_D$ +39.9 (*c* 2, $CHCl_3$) [lit.[46] −55.2 (*c* 8, $CHCl_3$) for the (S) enantiomer, 87% ee].

(*R*)-(+)-1-(2′-Naphthyl)-1-propanol (21j): $[\alpha]_D$ +22 (*c* 3, benzene) [lit.[34c] gives −26.6 (*c* 3.35, benzene) for the (S) enantiomer, 97% ee].

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Supporting Information Available: MS and HRMS data, characterization of **20a**−**j**, and ^1H and ^{13}C NMR spectra of the new compounds prepared (53 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Note Added in Proof: (a) While this paper was in press, Buchwald reported on acceleration of the amination of aryl bromides similar to that we have observed for MAP (see ref 16). In his case, the acceleration was due to a biphenyl analogue of MAP (**9**), namely 2-(dimethylamino)-2′-(dicyclohexylphosphino)-1,1′-biphenyl. See: Old, D. V.; Wolfe, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1998**, *120*, 9722. (b) The first successful resolution of a racemate via the Hartwig−Buchwald coupling has been accomplished in the presence of [2.2]phanephos. See: Rossen, K.; Pye, P. J.; Maliakal, A.; Volante, R. P. *J. Org. Chem.* **1997**, *62*, 6462. (c) Recently, Pericàs reported a new, highly efficient amino alcohol to promote enantioselective addition of Et_2Zn. See Solá, L.; Reddy, K. S.; Vidal-Ferran, A.; Moyano, A.; Pericàs, M. A.; Riera, A.; Alvarez-Larena, A.; Piniella, J.-F. *J. Org. Chem.* **1998**, *63*, 7078.

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