Solvent-Free Asymmetric Aminoalkylation of Electron-Rich Aromatic Compounds: Stereoselective Synthesis of Aminoalkylnaphthols by Crystallization-Induced Asymmetric Transformation

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Electron-rich aromatic compounds such as 2-naphthol give a faster and asymmetric 1-aminoalkylation with high yields when treated with (*R*)-1-phenylethylamine and aromatic aldehydes in solvent-free conditions. An asymmetric transformation of a second kind, probably induced by the preferential crystallization of one diastereomer, affords the straightforward and stereoselective synthesis of aminoalkylnaphthols. Mechanisms predictable for this asymmetric reaction are reported. The absolute configurations and the conformations of the unknown aminonaphthols are widely ascertained.

Introduction

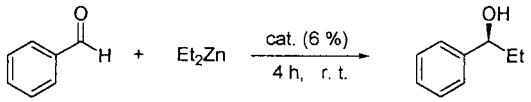
The search for new metal-catalyzed asymmetric reactions has provided some fascinating insights into the effects imposed on the metal catalysts by chiral ligands. A practical consequence is the discovery of ligand-accelerated catalysis (LAC).[1] Thus, an existing catalyzed process is improved by the addition of a specific ligand, which leads to a faster "ligand-accelerated" reaction. The concept is especially valuable in reactions catalyzed by early transition metals.[2]

In previous work, we have found that a catalytic amount of enantiopure aminophenol (*R,R*)-**12a** and aminonaphthol (*R,R*)-**3a** considerably accelerates the addition of dialkylzincs to aldehydes, affording the corresponding alcohols in good enantiomeric purity[3] (see Scheme 1). The precatalyst aminophenol (*R,R*)-**12a** is an accessible compound generally obtained by stereoselective reduction of the corresponding 2-imidoylphenol.[4] The aminoalkylation of electron-rich aromatic compounds (the aromatic Mannich reaction) is an alternative route to aminonaphthol **3**.[5] Here, we report the results of our work in the straightforward and stereoselective synthesis of aminoalkylnaphthols (*R,R*)-**3** (see Scheme 2).

Results and Discussion

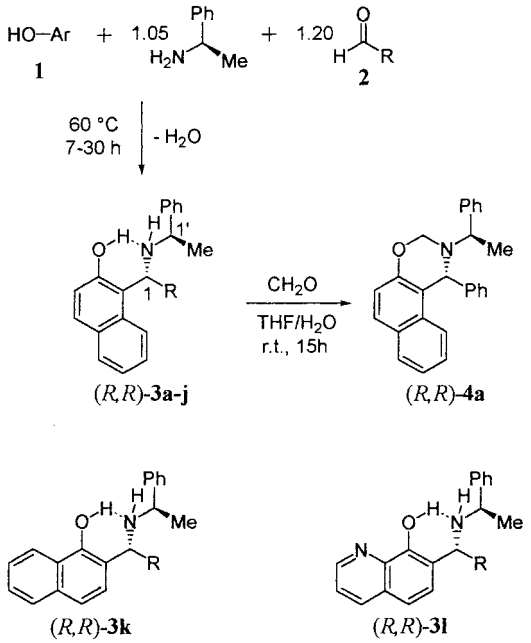
Electron-rich aromatic compounds as 2-naphthol give 1-aminoalkylation with high yields and dr when treated with (*R*)-1-phenylethylamine and aromatic aldehydes (see Scheme 2 and Table 1, entries 1−7). Less reactive 1-naphthol and 8-quinolinol give 2- and 7-aminoalkylation, respectively, with moderate yields (see Scheme 2 and Table 1, entries 11, 12). The use of enantiopure

Scheme 1. Enantioselective Alkylation of Benzaldehyde Catalyzed by the Aminophenol (*R,R*)-12a and the Aminonaphthol (*R,R*)-3a



cat.	yeld	*e.e.*
(*R,R*)-**12a**	93	89
(*R,R*)-**3a**	89	87

Scheme 2. Synthesis of Enantiopure Aminoalkylnaphthols (*R,R*)-3a−l by Solvent-Free Asymmetric Mannich Reaction



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(1) Berrisford, D. J.; Bolm, C.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1059−1070.

(2) Brunner, H. *Synthesis* **1988**, 645−654.

(3) Palmieri, G. *Tetrahedron*: *Asymmetry* **2000**, *11*, 3361−3373.

(4) (a) Palmieri, G. *Eur. J. Org. Chem.* **1999**, 805−811. (b) Cimarelli, C.; Palmieri, G. *Tetrahedron* **1998**, *54*, 15711−15720.

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Table 1. Stereoselective Synthesis of *o*-Hydroxyarylamine (*R,R*)-3 by Mannich Reaction

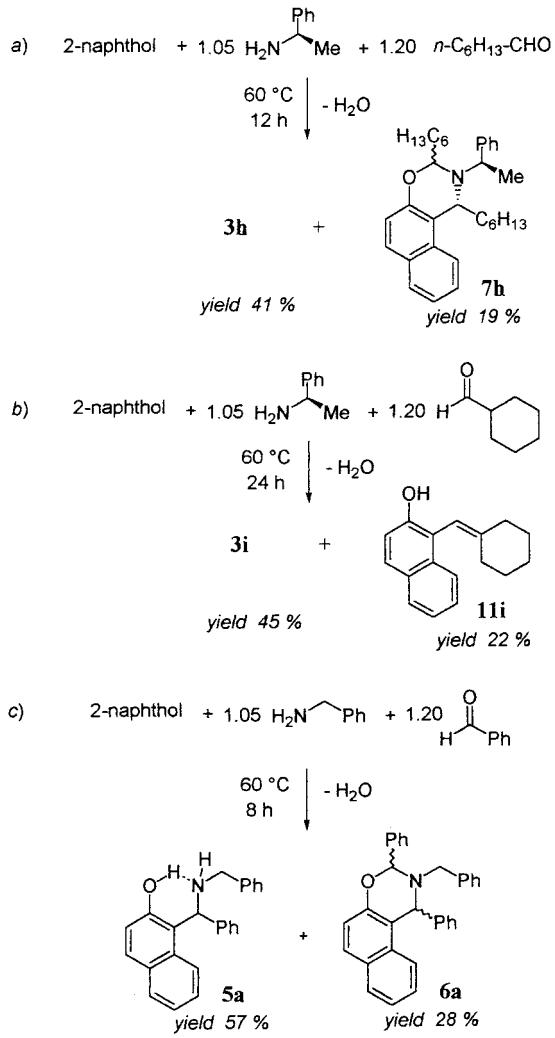
entry	HO-Ar	R	(*R,R*)-**3**	time (h)	yield[a] (%)	dr[b]
1	2-naphthol	C_6H_5	(*R,R*)-**3a**	8	93	99
2	2-naphthol	4-MeC_6H_4	(*R,R*)-**3b**	8	72	24
3	2-naphthol	4-$MeOC_6H_4$	(*R,R*)-**3c**	14	66	4.1
4	2-naphthol	4-ClC_6H_4	(*R,R*)-**3d**	7	72	4.3
5	2-naphthol	3-$NO_2C_6H_4$	(*R,R*)-**3e**	14	86	3.0
6	2-naphthol	1-naphthyl	(*R,R*)-**3f**	20	54	9.5
7	2-naphthol	2-naphthyl	(*R,R*)-**3g**	30	62	4.7
8	2-naphthol	1-hexyl	(*R,R*)-**3h**	12	41	6.1
9	2-naphthol	cyclohexyl	(*R,R*)-**3i**	24	45	66
10	2-naphthol	*i*Pr	(*R,R*)-**3j**	28	48	32
11	1-naphthol	C_6H_5	(*R,R*)-**3k**	8	50	2.4
12	8-quinolinol	C_6H_5	(*R,R*)-**3l**	20	44	1.4

[a] Yields of the pure isolated major diastereomer. [b] The dr value were determined by HPLC or by ^{1}H NMR of the reaction mixture.

1-phenylethylamine, very accessible in both the enantiomeric forms, allows the preparation of both the enantiopure aminonaphthols with moderate to high yields. The reaction was performed in solvent-free conditions: a mixture of naphthol, (*R*)-1-phenylethylamine, and the aldehyde, in a molar ratio of 1.0:1.05:1.2, respectively, was stirred and heated to 60 °C for the time required, under inert atmosphere. It is possible to observe after mixing the separation of some drops of water and, during the course of the reaction, a rise of the reaction mixture viscosity to obtain in some entries a final semisolid and crystalline mass. When high dr were obtained, the pure and crystalline major diastereomer could be isolated in a simpler manner by dispersion of the crude reaction mixture in a few milliliters of ethanol. In all cases, the pure diastereomers were obtained without any workup but by direct chromatographic separation of the crude reaction mixture. All the unknown aminonaphthols **3a**−**l** prepared have been fully characterized by spectroscopic methods.

With aliphatic aldehydes only (Table 1, entries 8−10), a moderate conversion was observed, with the recovery of a considerable amount of the starting 2-naphthol and the formation of byproducts as the naphthoxazine **7h** and the 1-cyclohexylidenemethyl-2-naphthol **11i** deriving from elimination of the auxiliary amine (see Scheme 3a,b). Contrary to that reported for the classical condition adopted in the Betti reaction,[5a−j] in this case the formation of oxazine **7** was generally not observed, probably because of a larger steric hindrance of the 1-phenylethylamine with respect to benzylamine. In fact, when the latter was used, the corresponding oxazine **6a** was isolated as byproduct (28% yield) together with the aminonaphthol **5a**[5f] (57% yield, see Scheme 3c). The

Scheme 3. Synthesis of Aminonaphthols 3h,i, 5a, Naphthoxazines 6a and 7h, and Vinylnaphthol 11i



oxazine **7** was obtained as a byproduct only when heptaldehyde was used (**7h**) and was not obtained with the other aldehydes with major steric hindrance.

The reaction carried out in refluxing ethanol as solvent (the classical conditions adopted for the aminoalkylation[5]) is slow (85% conversion after 15 h, $V_o = 1.7$ mM/min) if compared with our reaction conditions, and the product (*R,R*)-**3a** shows a moderate dr = 1.3. Under our conditions (absence of solvent), the reaction is quicker (V_o = 7.9 and 23.7 mM/min, respectively, at 20 and 60 °C); moreover, an increase of the dr for (*R,R*)-**3** from good to high final value was observed, as reported in the Figure 1 and Table 1. Generally, the progress of the reaction is followed by TLC and HPLC analysis. ^{1}H NMR analysis of the reaction mixture stopped at different times showed the trends reported in Figure 1 for (*R,R*)-**3a**. Although the reaction is faster in solvent-free conditions at 20 °C, the asymmetric transformation in the initial mixture of diastereomers takes place only at 60 °C. This is a typical situation of "asymmetric transformation of second kind" induced by the preferential crystallization of a diastereomer[6] (see Scheme 4a).

The mechanisms theoretically predictable for this asymmetric transformation are reported in Scheme 4. The pathway A, assumed for the synthesis of the aminonaphthol **3**, can be theoretically reversible, allowing the epimerization process, but has been experimentally

(5) (a) Arend, M.; Westermann, B.; Risch, N. *Angew. Chem., Int. Ed.* **1998**, *37*, 1044−1070. (b) Tramontini, M. *Synthesis* **1973**, 703−775. (c) Tramontini, M.; Angiolini, L. *Tetrahedron* **1990**, *46*, 1791−1837. (d) Heaney, H. *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: Oxford, 1991; Vol. 2, p 953−973. (e) Betti, M. *Organic Syntheses*; Wiley: New York, 1941; Collect. Vol. I, pp 381−383. (f) Cardellicchio, C.; Ciccarella, G.; Naso, F.; Schingaro, E.; Scordari, F. *Tetrahedron*: *Asymmetry* **1998**, *9*, 3667−3675. (g) Cardellicchio, C.; Ciccarella, G.; Naso, F.; Perna, F.; Tortorella, P. *Tetrahedron* **1999**, *55*, 14685−14692. (h) Mohrle, H.; Miller, C.; Wendisch, D. *Chem. Ber.* **1974**, *107*, 2675−2682. (i) Burke, W. J.; Nasutavicus, W. A.; Weatherbee, C. *J. Org. Chem.* **1964**, *29*, 407−410. (j) Adamek, M.; Bobulova, P.; Glask, S. Frantisek, G.; Kovacikova, A.; Novak, L.; Strouhal, F. *Czechosl. Patent* 133091, 1969; *Chem. Abstr.* **1970**, *73*, 87933. (k) Burke, W. J.; Kolbezen, M. J.; Stephens, C. W. *J. Am. Chem. Soc.* **1952**, *74*, 3601−3605. (l) Grumbach, H. J.; Arend, M.; Risch, N. *Synthesis* **1996**, 883−887.

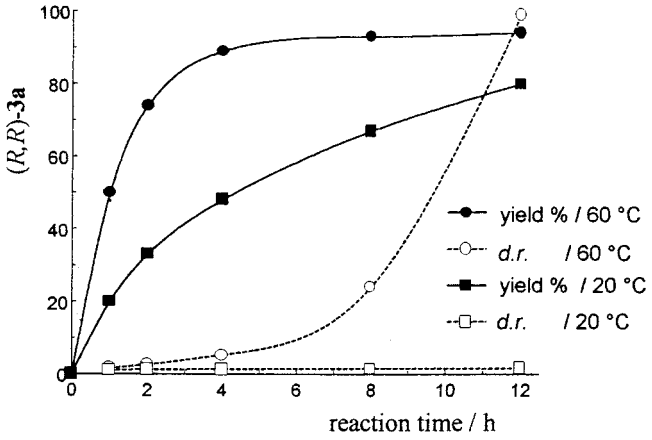
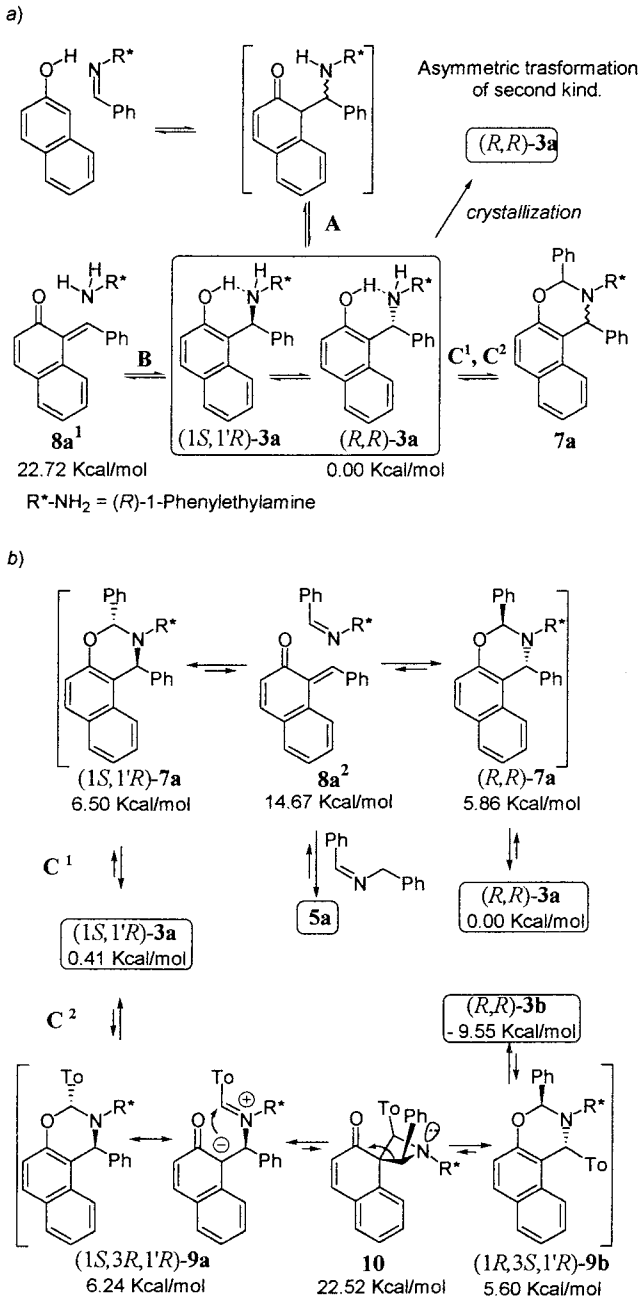


Figure 1. Conversion and dr observed in the solvent-free synthesis of (*R*,*R*)-**3a** at 60 or 20 °C reaction temperature.

verified to be too slow for it: both the pure diastereomers (*R*,*R*)- and (1*S*,1′*R*)-**3a** were stable for many days, also at 60 °C. The pathways B and C are both possible, but the second one has been experimentally found to be faster and so preferentially followed (see Scheme 5). To ascertain which is the way to product (*R*,*R*)-**3a**, some experimental attempts were made on diastereomer (1*S*,1′*R*)-**3a**. Product (1*S*,1′*R*)-**3a** has been refluxed in the presence of a 4-fold excess of benzylamine, and it has scarcely afforded product **5a** (Scheme 5, reaction conditions ii). In the presence of a 4-fold excess of benzaldehyde (reaction conditions i), the same product interconverts almost quantitatively in its diastereoisomer (*R*,*R*)-**3a**, while under the same conditions the transformation from (*R*,*R*)-**3a** to (1*S*,1′*R*)-**3a** does not take place. In the presence of benzaldehyde and benzylamine (reaction conditions iii), product **5a** is easily obtained from (1*S*,1′*R*)-**3a**. All this experimental evidence, allows us to conclude that path C is preferentially followed instead of path B. This pathway C can pass through two alternative intermediates, both theoretically possible: **8a**^{2}, which undergoes the reversible cycloaddition [pathway C^1, followed in the reaction conditions i and iii, Scheme 5, affording (*R*,*R*)-**3a** and **5a**, respectively] or necessarily through the spiroazetidine intermediate **10** [pathway C^2, followed in the reaction conditions iv, Scheme 5, with formation of (*R*,*R*)-**3b**]. It is noteworthy that the difference in the heat of formation of the diastereomer (*R*,*R*)- and (1*S*,1′*R*)-**3a** (0.41 kcal/mol) is too low to justify the high dr obtained even at 60 °C. Therefore, an asymmetric transformation of the second kind induced by the preferential crystallization of a diastereomer may be assumed. None of the aminonaphthols (*R*,*R*)-**3a**−**l** gives a spontaneous asymmetric transformation when dissolved in ethanol or chloroform as we have previously observed in the case of the comparable aminophenol (1*S*,1′*R*)-**12b**, which gives a spontaneous epimerization to (*R*,*R*)-**12b** (dr = 7) when dissolved in chloroform (see Scheme 6). The crystals of starting pure aminophenol (1*S*,1′*R*)-**12b** can again be obtained by slow evaporation of the solvent, and this

Scheme 4. Asymmetric Transformation of the Second Kind Induced by the Preferential Crystallization of the Diastereomer (*R*,*R*)-3a [R*-NH$_2$ = (*R*)-1-Phenylethylamine]



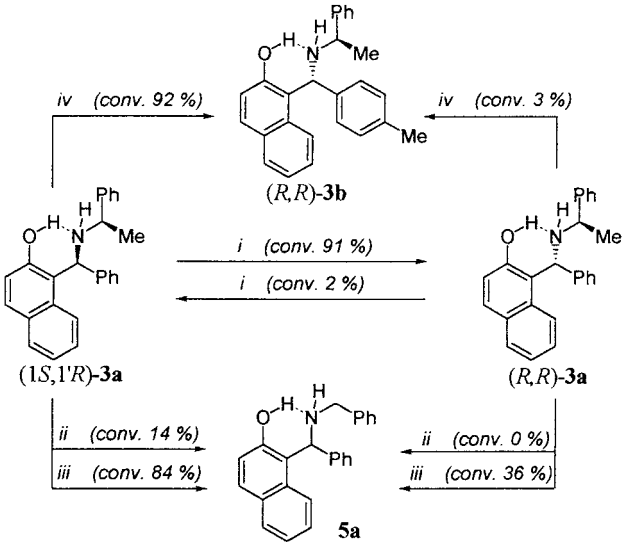
phenomenon can be observed for many of the cycles (unpublished results). The intermediate **13**, sterically less hindered than the comparable **8a**, can be hypothesized as the intermediate of this asymmetric transformation (pathway B, Scheme 4). Because of the lesser steric hindrance, any spontaneous epimerization was observed when aminophenols (*R*,*R*)- and (1*S*,1′*R*)-**12a** were dissolved in chloroform (see Scheme 6).

Stereochemistry

The stereochemistry of the unknown aminonaphthols **3a**−**l** was attributed on the basis of the following considerations. In all the aminonaphthols **3a**−**l**, the H_N of one diastereoisomers is shifted upfield by 0.24−0.57 ppm than the other (see Figure 5 in the Supporting Informa-

(6) (a) Harris, M. M. The Study of Optically Labile Compounds. *Prog. Stereochem.* **1958**, *2*, 157. (b) Jacques, J.; Collet, A.; Wilen, S. H. *Enantiomers, Racemates and Resolutions*; Wiley: New York, 1981, p 374. (c) Buchanan, C.; Graham, S. H. *J. Chem. Soc.* **1950**, 500−507. (d) Eliel, E. *Stereochemistry of Carbon Compounds*; McGraw-Hill: New York, 1962, p 63. (e) Mason, S. F. *Molecular Optical Activity and the Chiral Discriminations*; Cambridge University Press: Cambridge, UK, 1982; p 208.

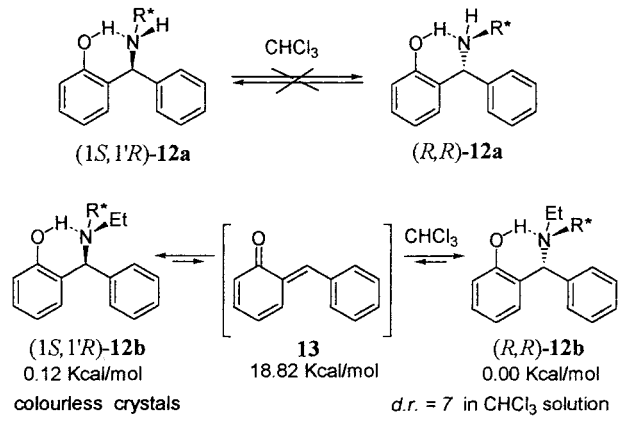
Scheme 5. Asymmetric Transformation of (1*S*,1′*R*)-3a to (*R*,*R*)-3a and to (*R*,*R*)-3b and 5a in the Solvent-Free Reaction[a]



Reagents: i) 4 eq. Ph-CHO, 60 °C, 6 h; *ii*) 4 eq. Bn-NH_2, 60 °C, 6 h; *iii*) 4 eq. Ph-CHO, 4 Bn-NH_2, 60 °C, 6 h; *iv)* 4 eq. *p*To-CHO, 60 °C, 6 h.

[a] Reagents: (i) 4 equiv of Ph-CHO, 60 °C, 6 h; (ii) 4 equiv of Bn-NH_2, 60 °C, 6 h; (iii) 4 equiv of Ph-CHO, 4 equiv of Bn-NH_2, 60 °C, 6 h; (iv) 4 equiv of *p*-Tol-CHO, 60 °C, 6 h.

Scheme 6. Asymmetric Transformation of Second Kind Induced by the Preferential Crystallization of the Diastereomer (1*S*,1′*R*)-12b [R*-NH_2 = (*R*)-1-Phenylethylamine]



R*-NH_2 = (*R*)-(+)-1-phenylethylamine

tion). This trend can be easily rationalized by observing that in the more stable conformations of the possible two diastereoisomers, obtained with PM3 semiempirical minimization,[7] the phenyl group of the auxiliary amine exercises a shielding magnetic anisotropy on the proton H_N at the new stereogenic center in the (*R*,*R*) diastereoisomer (see Figure 2). NOE ^{1}H NMR experiments were carried out on oxazines (*R*,*R*)- and (1*S*,1′*R*)-**4a** and on aminonaphthols (*R*,*R*)- and (1*S*,1′*R*)-**3f** to have experimental confirmation of configurations and conformations of aminonaphthol **3**. The structural assignments of the two diastereoisomers of **4a** (see Figure 3) were achieved by NOE ^{1}H NMR experiments (see Figure 3).[8] Inversion

(7) Semiempirical PM3 calculations were performed with the Spartan 5.0.3, Wavefunction, Inc., 18401 Von Karmen Ave., No. 370, Irvine, CA 92715.

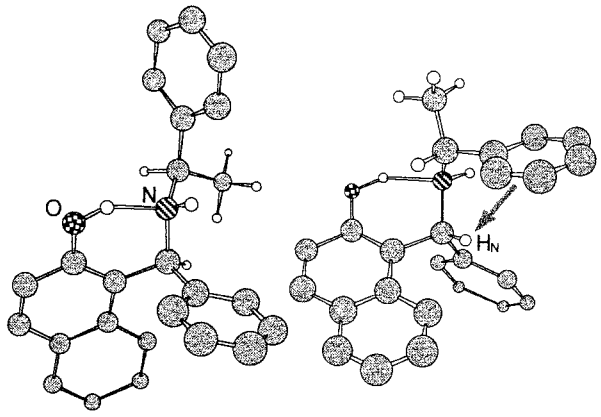


Figure 2. More stable conformations of aminonaphthols (*R*,*R*)- and (1*S*,1′*R*)-**3a** (PM3 semiempirical minimization).

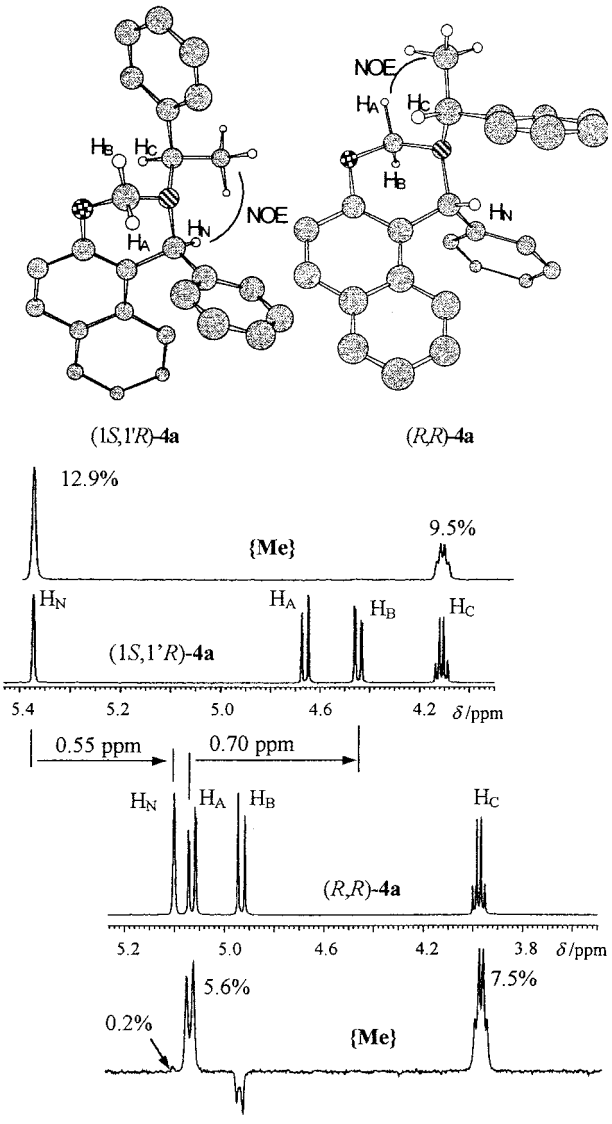


Figure 3. More stable conformations of naphthoxazines (*R*,*R*)- and (1*S*,1′*R*)-**4a** (PM3 semiempirical minimization) and some sections of the ^{1}H NMR spectrum with the respective NOE experiments (Me irradiation).

of the Me lines of (1*S*,1′*R*)-**4a** enhances H_N and the geminal H_C. The same experiment applied to (*R*,*R*)-**4a** enhances H_A and the geminal H_C. A negative effect is

Table 2. Distance Ratio Obtained from Spectral Data (NOE ^{1}H NMR) and Theoretical Calculations (PM3 Minimization Molecular Modeling) for the Diastereomers (*R*,*R*)- and (1*S*,1′*R*)-4a

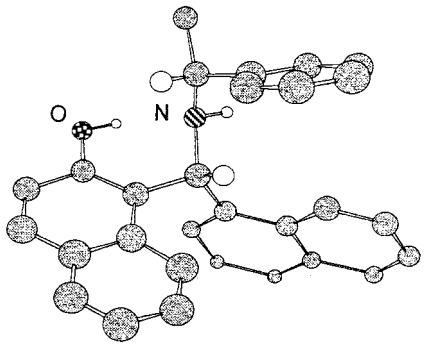
		(*R*,*R*)-**4a**		(1*S*,1′R)-**4a**	
target peak	ratio	NOE ratio	calcd	NOE ratio	calcd
Me	$\sqrt[6]{H_C/H_A}$	1.04	1.04	>2[a]	1.86
Me	$\sqrt[6]{H_A/H_N}$	1.69	1.60	~2[a]	1.77
Me	$\sqrt[6]{H_C/H_N}$	1.76	1.68	0.94	0.96
Me	$\sqrt[6]{H_N/H_B}$			1.88	1.77
Me	$\sqrt[6]{H_N/H_B}$			1.00	1.03
CH(Me)	$\sqrt[6]{H_N/H_A}$	1.43	1.33		
CH(Me)	$\sqrt[6]{H_A/H_B}$	1.16	1.16		
CH(Me)	$\sqrt[6]{H_N/H_B}$	1.66	1.54	1.00	1.03
CH(Me)	$\sqrt[6]{H_{Me}/H_N}$			1.13	1.07
CH(Me)	$\sqrt[6]{H_{Me}/H_B}$			1.13	1.04
CH(N)	$\sqrt[6]{H_C/H_A}$			1.37	1.32
CH(N)	$\sqrt[6]{H_{Me}/H_C}$			1.20	1.11
CH(N)	$\sqrt[6]{H_{Me}/H_A}$			1.60	1.49

[a] The DPFGSE NOE sequence can reveal NOE effects of about 0.1%.[8]

detected over H_B, and a very little effect is detected for H_N. Detailed experimental and theoretical distance ratios are reported in Table 2. The NOE constraints obtained for the two prepared diastereomers (*R*,*R*)- and (1*S*,1′*R*)-**4a** (see Table 2) are consistent with the calculated structure (PM3 minimization), respectively, for (*R*,*R*)- and (1*S*,1′*R*)-**4a**.[7] Assignment of H_A and H_B was possible because of the ^4J coupling with H_N that is observable in six-membered cycles only when the "W" path is available.[9] The ^4J is observable in the (*R*,*R*)-**4a** isomer on H_A (J = 1.9 Hz) and in the (1*S*,1′*R*)-**4a** on H_B (J = 2.1 Hz).

As observed for aminonaphthols **3a**−**l**, the large shift to high field of the H_N signal in the spectrum of the (*R*,*R*)-**4a** isomer with respect to (1*S*,1′*R*)-**4a** ($\Delta\delta$ = 0.55 ppm) and of H_B, which assumes in the (1*S*,1′*R*)-**4a** the equivalent position of H_A in (*R*,*R*)-**4a** ($\Delta\delta$ = 0.70 ppm, see Figure 3), can be understood on the basis of the position of these hydrogens, which are more or less axial with respect to the phenyl group of the auxiliary amine. This feature is known to move significantly upfield the chemical shifts of the hydrogens involved and has already been used as a diagnostic tool to assign the stereochemistry in other compounds of this kind.[10] These findings demonstrate that the strong intermolecular hydrogen bond forces the aminonaphthols **3a**−**l** to assume a conformation very similar to that of the naphthoxazine **4a**.

Structural assignment of the two diastereomers (*R*,*R*)- and (1*S*,1′*R*)-**3f** was analogously achieved through NOE ^{1}H NMR experiments, validating the results obtained by conformational analysis (PM3 minimization)[7] (see Figure 6 in the Supporting Information). Inversion of the Me lines of (1*S*,1′*R*)-**3f** enhances H_N.



syn-(*R*,*R*)-**3f** / X-ray

Figure 4. X-ray crystal structure of *syn*-(*R*,*R*)-**3f**.

Finally, to confirm the structures of aminonaphthols **3a**−**l**, an X-ray study on the (*R*,*R*)-**3f** was carried out (Figure 4). The X-ray structure is very similar to that obtained by molecular modeling (see Figure 6 in the Supporting Information), showing a strong hydrogen bond between OH and N atom, which gives rigidity to the structure and makes it suitable for NOE experiments, without the need to cyclize the aminonaphthol **3** to the corresponding naphthoxazine **4**. In addition, X-ray studies confirm the *syn*-(*R*,*R*)-**3f** structure as more stable than the anti conformations as previously calculated (see Figure 6 in the Supporting Information). This preferred conformation rationalizes the particularly downfield chemical shift [6.80 and 6.31 ppm, respectively, for the (1*S*,1′*R*)- and (*R*,*R*)-**3f**] observed for the benzylic hydrogen atom H_N, which suffers the deshielding effect of the two *syn*-naphthyl groups surrounding it.

Conclusion

In summary, a straightforward and stereoselective synthesis of aminoalkylnaphthols (*R*,*R*)-**3a**−**l**, which are useful chiral ligands for metal-catalyzed asymmetric reactions, is reported. This solvent-free very simple synthetic methodology, through an asymmetric aminoalkylation of electron-rich aromatic compounds, shows a phenomenon of crystallization-induced asymmetric transformation. The absolute configurations and conformations of the products are determined by molecular modeling, NOE ^{1}H NMR experiments, and X-ray crystallography.

Experimental Section

General Procedure for the Synthesis of Aminoalkylnaphthol (*R*,*R*)-3. In the following typical procedure, a mixture of 2-naphthol (0.72 g, 5.0 mmol), benzaldehyde (0.64 g, 6.00 mmol), and (*R*)-(+)-1-phenylethylamine (0.64 g, 5.25 mmol) was stirred at 60 °C for 8 h under nitrogen atmosphere. Following the progress of the reaction by TLC and ^{1}H NMR, it was seen that the formation of the product occurs during the first 4 h but the initial dr of (*R*,*R*)-**3a** (2.6 at 2 h) increases over time (99 at 8 h) with the formation of a solid and crystalline reaction mixture. The reaction mixture was dispersed at room temperature with EtOH (5 mL). The white crystals separated were collected and washed with EtOH (3 × 3 mL). The crystalline white residue, purified by crystallization from EtOAc/hexane, gives the pure (*R*,*R*)-**3a** (1.64 g, 4.65 mmol, yield 93%). The same procedure was used for

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(9) Barfield, M.; Chakrabarti, D. *Chem. Rev.* **1969**, *6*, 757−778.

(10) Harada, N.; Watanabe, M.; Kuwahara, S.; Sugio, A.; Kasai, Y.; Ichikawa, A. *Tetrahedron*: *Asymmetry* **2000**, *11*, 1249−1253.

(11) Since with the DPFGSE sequence it is intrinsically difficult to obtain the NOE percentage enhancements value, the standard NOE-difference sequence was used to find the value of the largest NOE peaks, and the other values were scaled by calculations. See also: Claridge, T. D. W. In *High-resolution NMR techniques in Organic Chemistry*; Pergamon Press: New York, pp 320−322.

1-naphthol and 8-quinolinol. At the end of the reaction time, the pure aminoalkylnaphthol (*R*,*R*)-**3** can be isolated by flash chromatography directly from the reaction mixture without further workup. The characterization of the newly prepared aminonaphthols **3a**−**l** follows. Where only the major diastereomers were obtained pure by chromatography, the ^{1}H NMR signals for the minor diastereomers were deduced from the spectra of the crude reaction mixtures or from enriched chromatographic fractions.

1-[(*R*)-Phenyl[[(1′*R*)-1′-phenylethyl]amino]methyl]-2-naphthol [(*R*,*R*)-3a]: colorless crystals; mp 155−156 °C (AcOEt−hexane); $[\alpha]^{20}_D$ −220.7° (*c* 2.1, $CHCl_3$); IR (Nujol) ν_{max} 3271, 1621, 1238, 1077, 743, 696 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.52 (d, 3 H, J = 6.9 Hz), 2.35 (br s, 1 H), 3.92 (q, 1 H, J = 6.9 Hz), 5.47 (s, 1 H), 7.15−7.83 (m, 16 H), 13.70 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.0, 56.7, 60.3, 113.1, 120.1, 121.1, 122.4, 126.4, 126.7, 127.7, 127.9, 128.0, 128.7, 128.8, 129.0, 129.1, 129.8, 132.6, 141.5, 143.1, 157.3; MS (70 eV) 232 (M^+ − 121, 38), 231 (100), 202 (23), 116 (21). Anal. Calcd for $C_{25}H_{23}NO$ (353.5): C, 84.95; H, 6.56; N, 3.96. Found: C, 85.21; H, 6.37; N, 3.77.

1-[(*S*)-Phenyl[[(1′*R*)-1′-phenylethyl]amino]methyl]-2-naphthol [(1*S*,1′*R*)-3a]: colorless crystals; mp 139−141 °C (AcOEt−hexane); $[\alpha]^{20}_D$ +168.53° (*c* 3.0, $CHCl_3$); IR (Nujol) ν_{max} 3265, 1615, 1240, 1070 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.62 (d, 3 H, J = 6.7 Hz), 2.35 (br s, 1 H), 4.01 (q, 1 H, J = 6.7 Hz), 5.92 (s, 1 H), 7.15−7.80 (m, 16 H), 13.70 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.6, 56.0, 60.7, 114.9, 120.8, 121.5, 122.9, 127.0, 127.1, 128.1, 128.4, 128.5, 129.2, 129.4, 129.5, 129.6, 130.2, 132.8, 141.9, 143.5, 157.2. Anal. Calcd for $C_{25}H_{23}$-NO (353.5): C, 84.95; H, 6.56; N, 3.96. Found: C, 85.18; H, 6.42; N, 3.72.

1-[(*R*)-(4-Methylphenyl)[[(1′*R*)-1′-phenylethyl]amino]-methyl]-2-naphthol [(*R*,*R*)-3b]: crystals; mp 132−134 °C (hexane); $[\alpha]^{20}_D$ −191.9° (*c* 3.1, $CHCl_3$); IR (Nujol) ν_{max} 3309, 1621, 1236, 1077, 744, 700 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.55 (d, 3 H, J = 6.9 Hz), 2.31 (s, 3 H), 2.35 (br s, 1 H), 3.95 (br q, 1 H, J = 6.9 Hz), 5.51 (s, 1 H), 7.07−7.80 (m, 15 H), 13.86 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.6, 23.6, 57.2, 60.6, 113.9, 120.6, 121.7, 122.9, 126.9, 127.3, 128.2, 128.4, 129.2, 129.3, 129.5, 130.2, 130.3, 133.2, 138.3, 139.2, 143.7, 157.8. Anal. Calcd for $C_{26}H_{25}NO$ (367.5): C, 84.98; H, 6.86; N, 3.81. Found: C, 84.87; H, 6.79; N, 3.75. **1-[(*S*)-(4-Methylphenyl)[[(1′*R*)-1′-phenylethyl]amino]methyl]-2-naphthol [(1*S*,1′*R*)-3b]:** ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.61 (d, 3 H, J = 6.7 Hz), 2.32 (s, 3 H), 2.35 (br s, 1 H), 3.98 (q, 1 H, J = 6.7 Hz), 5.88 (s, 1 H), 7.0−7.80 (m, 15 H), 13.80 (br s, 1 H).

1-[(*R*)-(4-Methoxyphenyl[[(1′*R*)-1′-phenylethyl]amino]-methyl]-2-naphthol [(*R*,*R*)-3c]: colorless crystals; mp 109−112 °C (EtOH); $[\alpha]^{20}_D$ −190.4° (*c* 1.9, $CHCl_3$); IR (Nujol) ν_{max} 3307, 1511, 1215, 745 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.51 (d, 3 H, J = 6.8 Hz), 2.20 (br d, 1 H), 3.72 (s, 3 H), 3.90−4.00 (m, 1 H), 5.42 (s, 1 H), 6.75−7.85 (m, 15 H) 13.80 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 23.0, 55.3, 56.6, 59.8, 113.6, 120.1, 121.1, 121.2, 122.6, 126.5, 126.7, 127.8, 128.0, 128.9, 129.0, 129.8, 129.9, 133.6, 143.0, 153.8, 157.0, 159.2. Anal. Calcd for $C_{26}H_{25}NO_2$ (383.5): C, 81.43; H, 6.57; N, 3.65. Found: C, 81.58; H, 6.43; N, 3.72. **1-[(*S*)-(4-Methoxyphenyl-[[(1′*R*)-1′-phenylethyl]amino]methyl]-2-naphthol [(1*S*,1′*R*)-3c]:** ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.60 (d, 3 H, J = 6.7 Hz), 2.20 (br s, 1 H) 3.74 (s, 3 H), 4.01 (q, 1 H, J = 6.7 Hz), 5.84 (s, 1 H), 6.75−7.85 (m, 15 H) 13.80 (br s, 1 H).

1-[(*R*)-(4-Chlorophenyl)[[(1′*R*)-1′-phenylethyl]amino]-methyl]-2-naphthol [(*R*,*R*)-3d]: colorless crystals; mp 132−140 °C (EtOH); $[\alpha]^{20}_D$ −192.0° (*c* 3.5, $CHCl_3$); IR (Nujol) ν_{max} 1619, 1271, 1090, 951, 831, 703 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.51 (d, 3 H, J = 6.8 Hz), 2.25 (br s, 1 H), 3.88 (q, 1 H, J = 6.8 Hz), 5.42 (s, 1 H), 7.05−7.80 (m, 15 H), 13.60 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.5, 57.1, 60.1, 113.2, 120.6, 121.4, 123.1, 127.0, 127.1, 128.5, 129.2, 129.4, 129.5, 129.6, 129.7, 130.5, 132.9, 134.3, 140.4, 143.4, 157.7. Anal. Calcd for $C_{25}H_{22}ClNO$ (387.9): C, 77.41; H, 5.72; N, 3.61. Found: C, 77.64; H, 5.79; N, 3.74. **1-[(*S*)-(4-Chlorophenyl[[(1′*R*)-1′-phenylethyl]amino]methyl]-2-naphthol [(1*S*,1′*R*)-3d]:** ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.58 (d, 3 H, J = 6.7 Hz), 2.25 (br s, 1 H), 3.96 (q, 1 H, J = 6.7 Hz), 5.82 (s, 1 H), 7.05−7.80 (m, 15 H), 13.80 (br s, 1 H).

1-[(*R*)-(3-Nitrophenyl)[[(1′*R*)-1′-phenylethyl]amino]-methyl]-2-naphthol [(*R*,*R*)-3e]: yellow crystals; mp 154−157 °C (EtOH); $[\alpha]^{20}_D$ −215.1° (*c* 1.7, $CHCl_3$); IR (Nujol) ν_{max} 1621, 1529, 1350, 1235, 749 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.55 (d, 3 H, J = 6.9 Hz), 2.30 (br d, 1 H), 3.90−4.05 (m, 1 H), 5.56 (s, 1 H), 7.1−8.3 (m, 15 H), 13.30 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.4, 57.1, 59.9, 112.4, 120.7, 121.0, 123.6, 127.0, 127.1, 128.4, 128.7, 129.3, 129.4, 130.6, 132.7, 134.7, 143.0, 143.6, 149.1, 157.8. Anal. Calcd for $C_{25}H_{22}N_2O_3$ (398.5): C, 75.48; H, 5.39; N, 7.15. Found: C, 77.64; H, 5.79; N, 3.74. **1-[(*S*)-(3-Nitrophenyl)[[(1′*R*)-1′-phenylethyl]amino]-methyl]-2-naphthol [(1*S*,1′*R*)-3e]:** yellow crystals; mp 156−160 °C (EtOH); $[\alpha]^{20}_D$ = +156.9° (*c* 1.9, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.6 (d, 3 H, J = 6.7 Hz), 2.27 (br s, 1 H), 3.96 (q, 1 H, J = 6.7 Hz), 5.95 (s, 1 H), 7.10−8.30 (m, 15 H), 12.75 (br s, 1 H).

1-[(*R*)-(1-Naphthyl)[[(1′*R*)-1′-phenylethyl]amino]methyl]-2-naphthol [(*R*,*R*)-3f]: colorless crystals; mp 195−197 °C (CH_2Cl_2−hexane); $[\alpha]^{20}_D$ −484.73° (*c* 2.1, $CHCl_3$); IR (Nujol) ν_{max} 3307, 1621, 1238, 822, 779, 752, 700 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.54 (d, 3 H, J = 6.9 Hz), 2.22 (br d, 1 H, J = 11.1), 3.97 (br dq, 1 H, J = 11.1, 6.9), 6.31 (s, 1 H), 6.90−7.90 (m, 18 H), 13.70 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.6, 55.5, 56.5, 113.2, 120.0, 121.0, 121.7, 122.5, 125.6, 126.0, 126.6, 126.7, 127.0, 127.6, 128.3, 128.7, 128.77, 128.8, 128.9, 129.3, 129.8, 130.2, 132.8, 134.1, 135.3, 142.1, 158.1. Anal. Calcd for $C_{29}H_{25}NO$ (403.5): C, 86.32; H, 6.24; N, 3.47. Found: C, 86.29; H, 6.23; N, 3.47. **1-[(*S*)-(1-Naphthyl)[[(1′*R*)-1′-phenylethyl]-amino]methyl]-2-naphthol [(1*S*,1′*R*)-3f]:** ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.67 (d, 3 H, J = 6.7), 2.20 (br s, 1 H), 4.20−4.40 (m, 1 H), 6.80 (s, 1 H), 6.88−7.90 (m, 18 H), 13.20 (br s, 1 H).

1-[(*R*)-(2-Naphthyl)[[(1′*R*)-1′-phenylethyl]amino]methyl]-2-naphthol [(*R*,*R*)-3g]: crystals; mp 154−157 °C (CH_2Cl_2−hexane); $[\alpha]^{20}_D$ −261.50° (*c* 2.3, $CHCl_3$); IR (Nujol) ν_{max} 3306, 1623, 1240, 1092, 820, 746, 668 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.54 (d, 3 H, J = 6.9 Hz), 2.38 (br d, 1 H, J = 11.8 Hz), 3.97 (br dq, 1 H, J = 11.8, 6.9 Hz), 5.63 (s, 1 H), 7.18−7.86 (m, 18 H), 13.85 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.5, 57.2, 61.0, 113.5, 120.6, 121.6, 122.9, 126.1, 126.6, 126.7, 127.0, 127.1, 127.3, 128.0, 128.5, 128.6, 128.9, 129.3, 129.5, 129.6, 130.3, 133.1, 133.5, 133.9, 139.4, 143.6, 157.9. Anal. Calcd for $C_{29}H_{25}NO$ (403.5): C, 86.32; H, 6.24; N, 3.47. Found: C, 86.25; H, 6.21; N, 3.45. **1-[(*S*)-(2-Naphthyl)[[(1′*R*)-1′-phenylethyl]amino]methyl]-2-naphthol [(1*S*,1′*R*)-3g]:** ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.64 (d, 3 H, J = 6.7 Hz), 2.35 (br s, 1 H,), 4.15 (q, 1H, J = 6.7 Hz), 6.07 (s, 1 H), 7.18−7.86 (m, 18 H), 13.80 (br s, 1 H).

1-[(1*R*)-1-[[(1′*R*)-1′-Phenylethyl]amino]heptyl]-2-naphthol [(*R*,*R*)-3h]: oil; $[\alpha]^{20}_D$ −3.90° (*c* 1.0, $CHCl_3$); IR (liquid film) ν_{max} 3306, 3060, 1622, 1467, 1378, 1120, 817, 745, 700 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.78−1.92 (m, 17 H), 3.73 (q, 1 H, J = 6.9 Hz), 4.38 (d d, 1 H, J = 8.1, 5.4 Hz), 7.05−7.90 (m, 11 H), 13.10 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 14.6, 23.1, 23.5, 26.5, 29.4, 32.1, 35.4, 55.4, 56.0, 118.5, 120.3, 121.5, 122.8, 126.6, 127.1, 128.2, 129.3, 129.4, 129.5, 130.2, 133.1, 143.8, 156.9. Anal. Calcd for $C_{25}H_{31}NO$ (361.5): C, 83.06; H, 8.64; N, 3.87. Found: C, 83.16; H, 8.63; N, 3.86.

1-[(1*S*)-1-[[(1′*R*)-1′-Phenylethyl]amino]heptyl]-2-naphthol [(1*S*,1′*R*)-3h]: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.78−1.92 (m, 17 H), 3.81 (q, 1 H, J = 6.6 Hz), 4.90 (t, 1 H, J = 6.6 Hz), 7.05−7.90 (m, 11 H), 13.10 (br s, 1 H). **1-[(*R*)-Cyclohexyl-[[(1′*R*)-1′-phenylethyl]amino]methyl]-2-naphthol [(*R*,*R*)-3i]:** crystals; mp 158−161 °C (CH_2Cl_2−hexane); $[\alpha]^{20}_D$ −5.93° (*c* 2.1, $CHCl_3$); IR (Nujol) ν_{max} 3293, 1621, 1456, 1377, 1092, 816, 742, 702 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90−1.28 (m, 6 H), 1.46 (d, 3 H, J = 6.9 Hz), 1.50−1.90 (m, 5 H), 2.27 (br d, 1 H, J = 10.7 Hz), 3.68 (br dq, 1 H, J = 10.7, 6.9 Hz), 4.16 (d, 1 H, J = 6.1 Hz), 7.00−7.80 (m, 11 H), 13.18 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.2, 26.1, 26.2, 26.3, 29.0, 30.5, 42.4, 55.3, 60.1, 114.6, 119.7, 121.7, 122.1, 125.9, 126.7, 127.6, 128.6, 128.7, 128.8, 129.0, 133.4, 143.4, 156.9. Anal. Calcd for $C_{25}H_{29}NO$ (359.5): C, 83.52; H, 8.13; N, 3.90. Found: C, 83.36;

H, 8.14; N, 3.91. **1-[(*S*)-cyclohexyl[[(1′*R*)-1′-phenylethyl]-amino]methyl]-2-naphthol [(1*S*,1′*R*)-3i]:** ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90−1.28 (m, 6 H), 1.46 (d, 3 H, J = 6.9 Hz), 1.50−1.90 (m, 5 H), 2.20−2.38 (m, 1 H), 3.85 (br q, 1 H, J = 6.9 Hz), 4.55 (bd, 1 H, J = 6.2 Hz), 7.00−7.80 (m, 11 H), 13.18 (s, 1 H);

1-[(1*R*)-2-Methyl-1-[[(1′*R*)-1′-phenylethyl]amino]propyl]-2-naphthol [(*R*,*R*)-3j]: crystals; mp 137−139 °C (CH_2Cl_2−hexane), $[\alpha]^{20}_D$ −10.95° (*c* 2.0, $CHCl_3$); IR (Nujol) ν_{max} 3337, 3058, 1620, 1466, 1271, 815, 702 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.74 (d, 3 H, J = 7.0 Hz), 0.97 (d, 3 H, J = 6.8 Hz), 1.47 (d, 3 H, J = 6.8 Hz), 2.05−2.30 (m, 2 H), 3.60−3.80 (m, 1 H), 4.12 (d, 1 H, J = 6.0 Hz), 7.00−7.90 (m, 11 H), 13.10 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.8, 20.7, 23.6, 33.0, 56.18, 61.2, 115.2, 120.2, 122.0, 122.6, 126.4, 127.2, 128.1, 129.1, 129.2, 129.3, 129.6, 133.8, 143.8, 157.3. Anal. Calcd for $C_{22}H_{25}NO$ (319.4): C, 82.72; H, 7.89; N, 4.38. Found: C, 82.75; H, 7.88; N, 4.39. **1-[(1*S*)-2-Methyl-1-[[(1′*R*)-1′-phenylethyl]-amino]propyl]-2-naphthol [(1*S*,1′*R*)-3j]:** ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.75 (d, 3 H, J = 7.1 Hz), 1.07 (d, 3 H, J = 6.9 Hz), 1.50 (d, 3 H, J = 6.8 Hz), 2.05−2.30 (m, 2 H), 3.60−3.80 (m, 1 H), 4.70 (d, 1 H, J = 6.3 Hz), 7.00−7.90 (m, 11 H), 13.00 (br s, 1 H).

2-[(*R*)-Phenyl[[(1′*R*)-1′-phenylethyl]amino]methyl]-1-naphthol [(*R*,*R*)-3k]: oil; $[\alpha]^{20}_D$ −118.87 (dr = 4.6) (*c* 2.0, $CHCl_3$); IR (liquid film) ν_{max} 3312, 1636, 1575, 1085, 803; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.54 (d, 3 H, J = 6.8 Hz), 2.40 (br s, 1 H), 3.94 (br q, 1 H, J = 6.8 Hz), 4.83 (s, 1 H), 6.88 (d, 1 H, J = 8.6 Hz), 7.10−8.00 (m, 15 H), 13.10 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.8, 56.7, 65.7, 116.9, 118.6, 119.2, 123.0, 125.4, 126.7, 127.1, 127.7, 127.8, 128.0, 128.3, 128.4, 129.4, 129.5, 134.4, 142.8, 143.7, 154.4. Anal. Calcd for $C_{25}H_{23}NO$ (353.5): C, 84.95; H, 6.56; N, 3.96. Found: C, 85.17; H, 6.42; N, 3.74. **2-[(*S*)-Phenyl[[(1′*R*)-1′-phenylethyl]amino]methyl]-1-naphthol [(1*S*,1′*R*)-3k]:** ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.53 (d, 3 H, J = 6.6 Hz), 2.40 (br s, 1 H), 3.85 (q, 1 H, J = 6.6 Hz), 5.06 (s, 1 H), 6.72 (d, 1 H, J = 8.6), 7.10−8.0 (m, 15 H), 13.10 (br s, 1 H).

7-[(*R*)-Phenyl[[(1′*R*)-1′-phenylethyl]amino]methyl]quinolin-8-ol [(*R*,*R*)-3l]: oil; $[\alpha]^{20}_D$ −82.0 (*c* 1.6, $CHCl_3$); IR (liquid film) ν_{max} 3368, 1600, 1502, 1374, 760 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.46 (d, 3 H, J = 6.6 Hz), 2.40 (br s, 1H), 3.77 (q, 1 H, J = 6.6 Hz), 4.93 (s, 1 H), 7.00−7.50 (m, 13 H), 8.05 (m, 1H), 8.95 (m, 1 H), 12.00 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.1, 56.2, 63.9, 118.2, 121.9, 127.1, 127.5, 127.9, 128.1, 128.2, 128.3, 129.1, 129.2, 129.3, 136.2, 140.2, 142.9, 144.2, 149.3, 153.4. Anal. Calcd for $C_{24}H_{22}N_2O$ (354.4): C, 81.33; H, 6.26; N, 7.90. Found: C, 81.42; H, 6.41; N, 7.78. **7-[(*S*)-Phenyl[[(1′*R*)-1′-phenylethyl]amino]methyl]quinolin-8-ol [(1*S*,1′*R*)-3l]:** ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.44 (d, 3 H, J = 6.9 Hz), 2.40 (br s, 1H) 3.85 (q, 1H, J = 6.9 Hz), 5.20 (s, 1H), 7.00−7.50 (m, 13 H), 8.00 (m, 1 H), 8.90 (m, 1 H), 12.00 (br s, 1 H).

General Procedure for the Preparation of the 2,3-Dihydro-1*H*-naphtho[1,2-*e*][1,3]oxazine 4. To a solution of aminonaphthol **3** (2 mmol) in THF (3 mL) was added 35% aqueous formaldehyde (2.2 mmol). The solution was stirred for 15 h at room temperature. Solvent was removed and the residue dried under reduced pressure. The crude material was purified by filtration through an SiO_2 pad eluting with CH_2Cl_2.

(1*R*)-1-Phenyl-2-[(1′*R*)-1′-phenylethyl]-2,3-dihydro-1*H*-naphtho[1,2-*e*][1,3]oxazine [(*R*,*R*)-4a]: crystals; mp 125−128 °C (hexane); $[\alpha]^{20}_D$ −132.50° (*c* 3.2, $CHCl_3$); IR (Nujol) ν_{max} 1622, 1233, 950, 744 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.57 (d, 3 H, J = 6.6 Hz), 4.01 (q, 1 H, J = 6.6 Hz), 4.96 (d, 1 H, J_{AB} = 11.0 Hz), 5.17 (dd, 1 H, J_{AB} = 11.0, 2.0 Hz), 5.23 (s, 1H), 7.00−7.80 (m, 16 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.1, 57.6, 59.6, 74.9, 112.6, 118.9, 119.0, 123.1, 123.6, 127.0, 127.6, 128.0, 128.3, 128.6, 129.0, 129.1, 129.4, 129.6, 133.4, 143.6, 145.9, 153.3; MS (70 eV) 232 (M^+ − 133), 231 (100), 202 (23), 105 (83). Anal. Calcd for $C_{26}H_{23}NO$ (365.5): C, 85.45; H, 6.34; N, 3.83. Found: C, 85.43; H, 6.36; N, 3.80.

(1*S*)-1-Phenyl-2-[(1′*R*)-1′-Phenylethyl]-2,3-dihydro-1*H*-naphtho[1,2-*e*][1,3]oxazine [(1*S*,1′*R*)-4a]: crystals; mp 158−160 °C (hexane); $[\alpha]^{20}_D$ +95.5° (*c* 1.2, $CHCl_3$); IR (Nujol) ν_{max} 1630, 1241, 950, 755 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.58 (d, 3 H, J = 6.5 Hz), 4.13 (q, 1 H, J = 6.5 Hz), 4.46 (dd, 1 H, J = 10.6, 2.0), 4.68 (d, 1 H, J_{AB} = 10.6), 5.76 (s, 1 H), 7.10−7.80 (m, 16 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.9, 54.6, 58.1, 76.0, 112.0, 118.8, 122.4, 123.1, 126.6, 127.1, 127.4, 127.8, 128.1, 128.5, 128.6, 128.9, 129.0, 129.3, 132.6, 143.4, 144.0, 152.7; MS (70 eV) 232 (M^+ − 133,), 231 (100), 202 (26), 105 (80). Anal. Calcd for $C_{26}H_{23}NO$ (365.5): C, 85.45; H, 6.34; N, 3.83. Found: C, 85.21; H, 6.46; N, 3.61.

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Supporting Information Available: General methods, the characterization data of (1*S*,1′*R*)-**4k**, (*R*,*R*)-**4k**, **6a**, **7h**, and **11i**, Figures 5 and 6, and the crystallographic data of *syn*-(*R*,*R*)-**3f** are provided. This material is available free of charge via the Internet at http://pubs.acs.org.

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