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Highly regioselective *N*-alkylation of nonracemic Betti base: a novel one-pot synthesis of chiral *N*-methyl-*N*-alkyl Betti bases

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Abstract—A novel one-pot preparation of chiral *N*-methyl-*N*-alkyl Betti bases has been developed involving a highly regioselective *N*-alkylation of (*S*)-(+)-Betti base. The strategy involved formation-cleavage of the oxazine ring and *N*-methylation with $BtCH_2OH$ under neutral conditions.

1. Introduction

Many unnatural homochiral amino-phenol compounds have been reported as excellent ligands in metal ion catalyzed asymmetric reactions in current asymmetric synthesis.[1] The ligands, which have the structure of *N*,*N*-dialkyl Betti base **1** (Chart 1) are gaining increasing importance.[2] Among them, the derivatives of chiral *N*-methyl-*N*-alkyl Betti base **2** have induced satisfactory reactivities and stereoselectivities in their catalyzed asymmetric reactions. The replacement of the *N*-methyl group in *N*-methyl-*N*-alkyl Betti base **2** by a large-sized *N*-alkyl group did not bring any additional satisfactory results, but made the synthetic procedure more difficult.[2g,h]

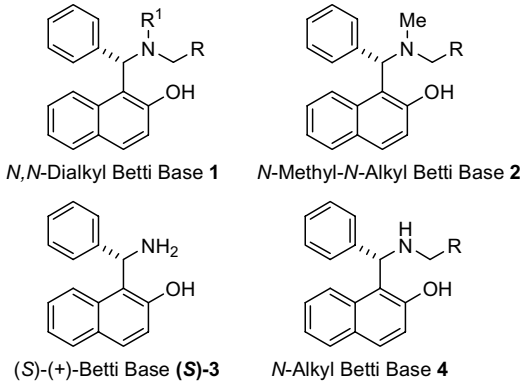

Chart 1.

Because the aliphatic amine moiety of Betti base **3** has a relatively lower nucleophilic reactivity when compared to its phenoxyl group moiety, the *N*-alkylation of Betti base **3** seriously lacks for regioselectivity by using routine methods.[1f,2a,3] Therefore, no derivatives of chiral *N*,*N*-dialkyl Betti base **1** in the literature were prepared from nonracemic Betti base **3**. The chiral *N*-methyl-*N*-alkyl Betti base **2** was prepared mainly by the Mannich condensation of a chiral amine with benzaldehyde and 2-naphthol to yield a *N*-alkyl Betti base **4** followed by a *N*-methylation.[2e,g,h,j] Since few of the *N*-alkyl Betti bases **4**[2h,g,i] prepared by the Mannich condensation had satisfactory diastereopurity, the diversity of the *N*-alkyl group in the *N*-methyl-*N*-alkyl Betti base **2** is quite limited. Herein, we report a highly regioselective *N*-alkylation of (*S*)-(+)-Betti base (*S*)-**3**, by which a series of enantiopure *N*-methyl-*N*-alkyl Betti base **2** was prepared in a convenient one-pot synthesis.

2. Results and discussions

Recently, we achieved the synthesis of enantiopure 1-[α-(1-azacycloalkyl)benzyl]-2-naphthols by direct *N*-alkylation of the (*S*)-Betti bases (*S*)-**3**, in which a strategy that involved the formation-cleavage of an oxazine ring, was employed.[3,4] Following this strategy, *N*-methyl-*N*-alkyl Betti base **2** could be prepared by condensation of (*S*)-(+)-Betti base (*S*)-**3** with aldehyde **5** to yield 2-(*R*)-4-phenyl-naphtho[1,2-*e*][1,3]oxazine **6** as an intermediate

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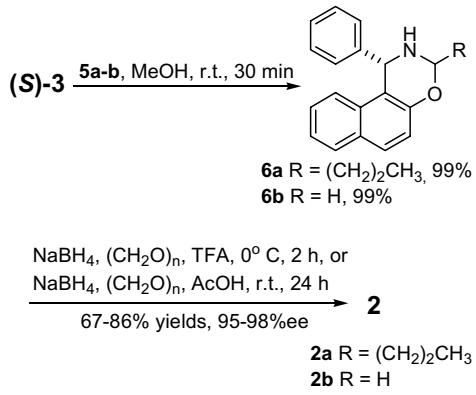
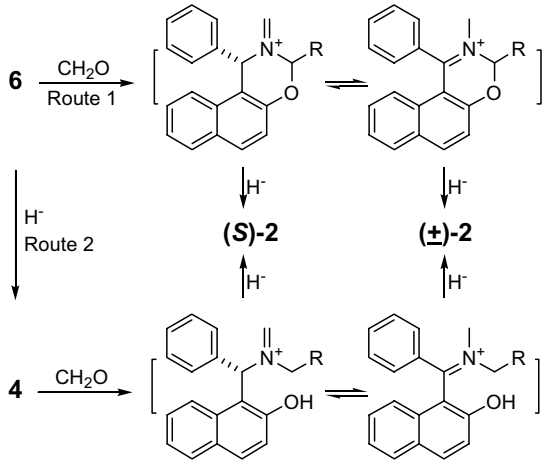


Scheme 1.

followed by simultaneous *N*-methylation and cleavage of the oxazine ring under reductive *N*-methylation conditions (Scheme 1).

The condensation of (*S*)-**3** with *n*-butanal **5a** has been reported to yield 2-propyl-4-phenyl-naphtho[1,2-*e*][1,3]-oxazine **6a** in 68% yield in 95% EtOH at room temperature for 24 h.[2b] When we tried this reaction in MeOH, **6a** was obtained unexpectedly in quantitative yield in just 30 min. Under similar conditions, formaldehyde **5b** (37% aq solution) also gave quantitatively the corresponding 4-phenyl-naphtho[1,2-*e*][1,3]oxazine **6b**. Compound **6a** proved to be a pure single diastereoisomer by its NMR spectra [a single peak (5.45 ppm) for its benzyl proton in ^{1}H NMR and one group peaks in ^{13}C NMR]. However, no special effort was made to identify the absolute conformation of the newly formed stereogenic carbon, since its configuration would disappear in the next step.

The reductive *N*-methylations of **6a** and **b** were then tested by using $NaBH_4$–TFA[2e,g,j] or $NaBH_4$–AcOH,[2h] respectively. As expected, *N*-methylation and cleavage of the oxazine ring occurred smoothly to give the desired compounds **2a** and **b** in 67–86% yields. Unfortunately, the enantiomeric excess of product **2** was found to decrease with a scale-up of the reaction. When the *N*-methylations were made at the scale of 10–50 mmol, 2–5% enantiomeric loss was detected. As shown in Scheme 2, two pathways were hypothesized for the conversion of compound **6** to compound **2**, in which the iminiums are essential intermediates. Thus, the loss of enantiomeric excess must arise from the acid-catalyzed double bond shifts of those iminium intermediates.

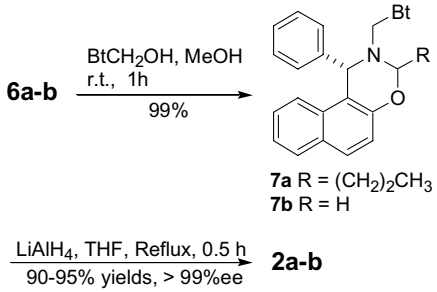


Scheme 2.

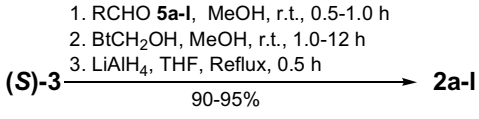
$BtCH_2OH$ (1-hydroxymethylbenzotriazole), a novel *N*-methylation reagent used under neutral conditions developed by Katritzky et al.[5] was then employed for the *N*-methylation of **6**. To our surprise, when the mixture of $BtCH_2OH$ and **6a** was stirred in MeOH at room temperature for 30 min, the desired product *N*-(benzotriazol-1-ylmethyl)-2-propyl-4-phenyl-naphtho-[1,2-*e*][1,3]oxazine **7a** could be isolated with 98% yield. Under similar conditions, **6b** also converted smoothly into **2b** in 98% (Scheme 3). Although $NaBH_4$ was used frequently to cleave the C–Bt bond or C–O bond in oxazoles at room temperature,[6] it failed to reduce oxazines **7a** and **b** possibly due to their heavy steric hindrance. Finally, reduction was achieved by refluxing the mixture of **7a** and **b** and $LiAlH_4$ in THF for 30 min. Since the acidic conditions were obviated, the desired products **2a** and **b** were obtained in 90–95% yields without any loss of enantiomeric excess (Scheme 3).

Realizing that both products **6** and **7** can be readily prepared in quantitative yields in MeOH, the preparation of **2a** and **b** from (*S*)-**3** can be accomplished by a one-pot procedure. Thus, a mixture of (*S*)-**3** and *n*-butanal **5a** or formaldehyde **5b** was stirred in MeOH at room temperature for 30 min (monitored by TLC). $BtCH_2OH$ was then added and stirring continued for another 30 min (monitored by TLC). After removal of MeOH, a solution of $LiAlH_4$ in THF was added and the resultant mixture refluxed for 30 min to give **2a** and **b** in high yields (Scheme 4).

To determine the scope of this one-pot procedure, aldehydes **5c**–**l** were employed in the same reaction. As



Scheme 3.

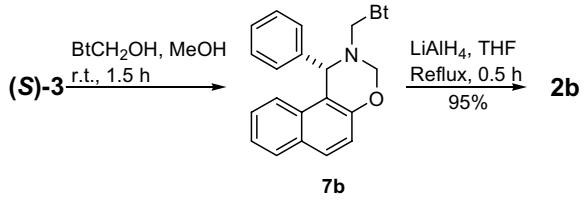


Scheme 4.

Table 1. The *N*-methyl-*N*-alkyl Betti bases **2a**–**l** prepared

5,2	R	*T* (h)[a]	Yield of **2** (%)[b,c]
a	$CH_3(CH_2)_2$–	0.5	90
b	H–	0.5	94
c	CH_3–	0.5	95
d	CH_3CH_2–	0.5	94
e	$CH_3(CH_2)_5$–	1.0	92
f	$CH_3(CH_2)_8$–	1.0	90
g	Me_2CHCH_2–	1.0	91
h	Et_2CH–	1.0	92
i	$C_6H_5CH_2$–	2.0	91
j	Cyclohexyl	2.0	91
k	C_6H_5–	12	92
l	3,4-$(EtO)_2C_6H_3$–	12	90

[a] Time for the *N*-alkylation with $BtCH_2OH$.
[b] The isolated yields.
[c] Enantiopurity was detected by chiral HPLC [Hypersil Pirkle(S) Napht, product of Thermo Electron Cooperation].



Scheme 5.

shown in Table 1, the corresponding enantiopure derivatives of *N*-methyl-*N*-alkyl Betti bases **2c**–**l** were produced in excellent yields. For all of aliphatic aldehydes **5a**–**j**, the step for the *N*-alkylation with $BtCH_2OH$ was accomplished within 0.5–2 h. However a longer reaction time (12 h) was required for aryl aldehydes **5k**–**l** possibly due to the steric hindrance of the benzene rings. It is interesting to note that keeping the addition sequence of aldehyde **5a**–**l** and $BtCH_2OH$ is critical otherwise, a mixture containing **2b** would be obtained because of the competing *N*,*N*-dialkylation that leads to *N*-benzotriazolylmethyl-4-phenyl-naphtho[1,2-*e*][1,3]oxazine **7b** (Scheme 5).

3. Conclusion

In summary, a novel preparation of chiral *N*-methyl-*N*-alkyl Betti base **2** has been developed by highly regioselective *N*-alkylation of (*S*)-(+)-Betti base (*S*)-**3**. 2-(*R*)-4-phenyl-naphtho[1,2-*e*][1,3]oxazine **6**, obtained by condensation of (*S*)-(+)-Betti base (*S*)-**3** and aldehyde **5**, was *N*-methylated with $BtCH_2OH$ under essentially neutral conditions to yield 2-(*R*)-*N*-benzotriazolylmethyl-4-phenyl-naphtho[1,2-*e*][1,3]oxazine **7**. Chiral *N*-methyl-*N*-alkyl Betti base **2** was then obtained by simultaneously cleaving the C–Bt bond and C–O bond in the structure of **7** via $LiAlH_4$. Since every step can be operated in the same solvent and almost in quantitative yields, in practice, they were performed in a one-pot procedure.

4. Experimental

4.1. General considerations

All melting points were determined on a Yanaco melting point apparatus and are uncorrected. IR spectra were recorded on a Nicolet FT-IR 5DX spectrometer as KBr pellets. The ^1H NMR spectra were recorded on a Bruker ACF-300 spectrometer in $CDCl_3$ with TMS as internal reference. The *J* values are given in Hz. MS spectra were obtained on a VG-ZAB-HS mass spectrometer with 70 eV. The elemental analyses were performed on a Perkin–Elmer 240C instrument. Optical rotations were determined on a Perkin–Elmer 343 polarimeter. PE is petroleum ether (60–90 °C).

4.2. General procedure for the preparation of 2-(*R*)-4-phenyl-naphtho[1,2-*e*][1,3]oxazine 6a–b

To a stirred solution of (*S*)-**3** (2.5 g, 10 mmol) in methanol (50 mL) was added aldehyde **5** (11 mmol) in one portion at room temperature. Thirty minutes later, the solvent was removed in vacuum and the residue purified by recrystallization to give desired product **6**.

4.2.1. 2-Propyl-4-phenyl-naphtho[1,2-*e*][1,3]oxazine 6a. Using *n*-butanal **5a**, compound **6a** was obtained as white crystals in 99% yield; mp 96–98 °C (methanol) (Lit.[2b] mp 97–98 °C); $[\alpha]_D^{25} = -19.8$ (*c* 0.50, $CHCl_3$) [Lit.[2b] $= -15.2$ (*c* 1.5, CH_2Cl_2)]; (Found: C, 83.26%; H, 6.99%; N, 4.57%, $C_{21}H_{21}NO$ requires: C, 83.13%; H, 6.98%; N, 4.62%); ν_{max}/cm^{-1} 3323, 2888, 1623, 1466; δ_H 7.08–7.90 (m, 11H), 5.45 (s, 1H), 4.60–4.66 (m, 1H), 2.39 (d, $J = 9.6$ Hz, 1H), 1.68 (m, 2H), 1.49 (m, 2H), 0.88 (t, $J = 7.1$ Hz, 3H); δ_C 152.6, 143.0, 132.0, 129.2 (2C), 129.0, 128.6 (2C), 128.4, 128.1, 127.1, 126.4, 123.0, 122.8, 119.2, 114.0, 82.0, 53.7, 37.3, 17.7, 13.9; *m*/*z*: 303 (M^+, 0.14%), 231 (100).

4.2.2. 4-Phenyl-naphtho[1,2-*e*][1,3]oxazine 6b. Using formaldehyde **5b**, compound **6b** was obtained as white crystals in 99% yield; mp 98–102 °C (methanol); $[\alpha]_D^{25} = -36.3$ (*c* 0.50, $CHCl_3$); (Found: C, 82.78%; H, 5.81%; N, 5.26 %, $C_{18}H_{15}NO$ requires: C, 82.73%; H, 5.79%; N, 5.36%); ν_{max}/cm^{-1} 3344, 2890, 1623, 1468; δ_H 7.08–7.80 (m, 11H), 5.51 (s, 1H), 4.85 (s, 2H), 2.86 (br s, 1H); δ_C 152.1, 142.5, 131.6, 129.4 (2C), 129.1, 128.8 (2C), 128.5, 128.4, 127.4, 126.5, 123.2, 122.8, 119.1, 114.8, 73.6, 53.3; *m*/*z*: 261 (M^+, 1.69%), 231 (100).

4.3. General procedure for the preparation of *N*-benzotriazolylmethyl-2-(*R*)-4-phenyl-naphtho[1,2-*e*][1,3]oxazine 7a–b

A mixture of **6** (10 mmol) and $BtCH_2OH$ (2.2 g, 15 mmol) in methanol (50 mL) was stirred at room temperature for 0.5 h. The solvent was then removed in vacuum and the residue purified by recrystallization to give pure product **7**.

4.3.1. *N*-Benzotriazolylmethyl-4-phenylnaphtho[1,2-*e*]-[1,3]oxazine 7a. Using compound **6a**, product **7a** was obtained as white crystals in 98% yield; mp 162–164 °C (acetone); $[\alpha]_D^{20} = +65.0$ (*c* 0.3, $CHCl_3$); (Found: C, 77.35%; H, 6.33%; N, 12.94%, $C_{28}H_{26}N_4O$ requires: C, 77.39%; H, 6.03%; N, 12.89%); ν_{max}/cm^{-1} 3062, 2946, 1623, 1449; δ_H 6.87–8.07 (m, 15H), 5.50–5.89 (dd, $J = 13.6$ Hz, 2H), 5.62 (s, 1H), 4.86 (t, $J = 6.4$ Hz, 1H), 2.06 (m, 2H), 1.44 (m, 2H), 0.85 (m, 3H); δ_C 152.9, 146.3, 141.5, 133.0, 132.8, 129.5, 129.2 (2C), 128.5, 128.1 (2C), 127.4, 126.8, 126.6, 126.3, 124.0, 123.6, 122.9, 120.2, 118.4, 111.3, 110.0, 84.6, 60.0, 60.1, 34.0, 18.5, 13.5; *m/z*: 434 (M^+, 1.69%), 231 (100).

4.3.2. *N*-Benzotriazolylmethyl-4-phenyl-naphtho[1,2-*e*]-[1,3]oxazine 7b. Using compound **6b**, product **7b** was obtained as white crystals; mp 179–180 °C (acetone); $[\alpha]_D^{20} = +70.2$ (*c* 0.35, $CHCl_3$); (Found: C, 76.57%; H, 5.31%; N, 14.26%. $C_{25}H_{20}N_4O$ requires: C, 76.51%; H, 5.14%; N,14.28%); ν_{max}/cm^{-1} 3062, 2892, 1622, 1451; δ_H 6.88–8.10 (m, 15H), 5.78 (S, 2H), 5.51 (S, 1H), 4.93 (s, 2H); δ_C 151.6, 146.4, 141.3, 133.0, 132.4, 129.6, 129.2 (2C), 129.1, 128.6, 128.3 (2C), 127.6, 126.9, 124.2, 123.7, 122.7, 120.1, 118.4, 111.2, 110.2, 76.2, 65.9, 57.7; *m/z*: 392 (M^+, 3.33%), 231 (100).

4.4. General one-pot procedure for the preparation of (*S*)-1-[-(*N*-methyl-*N*-alkylamino)benzyl]-2-naphthol 2a–l

To a stirred solution of (*S*)-**3** (2.5 g, 10 mmol) in methanol (50 mL) was added aldehyde **5** (11 mmol). After the (*S*)-**3** was exhausted (0.5–1.0 h, monitored by TLC), a solution of $BtCH_2OH$ (2.2 g, 15 mmol) in methanol (20 mL) was added to the system at room temperature. The resultant mixture was stirred until intermediate **6** disappeared completely (0.5–12 h, monitored by TLC). The solvent was then removed in vacuum and a solution of $LiAlH_4$ in THF (1.0 M, 50 mL, 50 mmol) added by syringe. After refluxing for 30 min (monitored by TLC), the reaction was cooled to 0 °C and quenched by the addition of a saturated aqueous solution of NH_4Cl. The mixture was extracted with CH_2Cl_2 and the organic layer washed with water, brine and dried over Na_2SO_4. The solvent was evaporated under reduced pressure to yield the crude product, which was purified by chromatography to give the pure compound **2** (Table 1).

4.4.1. (*S*)-1-[α-(*N*-Methyl-*N*-butylamino)benzyl]-2-naphthol 2a. Using aldehyde **5a**, compound **2a** was obtained as a yellowish gum; $[\alpha]_D^{20} = +198.4$ (*c* 0.31, $CHCl_3$); (Found: C, 82.66%; H, 8.02%; N, 4.32%. $C_{22}H_{25}NO$ requires: 82.72%; H, 7.89%; N, 4.38%); ν_{max}/cm^{-1} 3061, 2959, 1621, 1600, 1473, 1454; δ_H 13.94 (s, 1H), 7.13–7.87 (m, 11H), 5.11 (s, 1H), 2.29–2.40 (br d, 5H), 1.56 (m, 2H), 1.26 (m, 2H), 0.84 (t, $J = 7.2$ Hz, 3H); δ_C 155.57, 140.2, 132.2, 129.4 (2C), 130.0, 128.9 (2C), 128.7, 128.6, 127.9, 126.3, 122.3, 121.0, 120.0, 116.5, 72.0, 55.3, 40.0, 28.9, 20.3, 13.8; *m/z*: 319 (M^+, 1.35%), 231 (100).

4.4.2. (*S*)-1-[α-(*N*,*N*-Dimethylamino)benzyl]-2-naphthol 2b. Using aldehyde **5b**, compound **2b** was obtained as white crystals; mp 136–138 °C (acetone) (Lit.[2a] 158 °C); $[\alpha]_D^{20} = +228.0$ (*c* 0.5, EtOH) [Lit.[2a] +238 (*c* 0.5, EtOH)]; (C, 82.17%; H, 6.87%; N, 5.13%. $C_{19}H_{19}NO$ requires: C, 82.28%; H, 6.90%; N, 5.05%); ν_{max}/cm^{-1} 3062, 2983, 1621, 1600, 1477; δ_H 13.74 (s, 1H), 7.14–7.86 (m, 1H), 4.97 (s, 1H), 2.34 (br s, 6H); δ_C 155.4, 140.3, 132.2, 129.5 (2C), 128.8, 128.7 (2C), 128.0, 126.3 (2C), 122.4, 121.0, 120.0 (2C), 116.2, 73.0, 44.3 (2C); *m/z*: 278 (M^+ +1, 0.33%), 277 (M^+, 1.50), 231 (100).

4.4.3. (*S*)-1-[α-(*N*-Methyl-*N*-ethylamino)benzyl]-2-naphthol 2c. Using aldehyde **5c**, compound **2c** was obtained as yellowish crystals; mp 107–109 °C (PE); $[\alpha]_D^{20} = +187.9$ (*c* 2.0, $CHCl_3$); (Found: C, 82.19%; H, 7.36%; N, 4.88%. $C_{20}H_{21}NO$ requires: C, 82.44%; H, 7.26%; N, 4.81%); ν_{max}/cm^{-1} 3060, 2978, 1622, 1601; δ_H 13.68 (s, 1H), 7.15–7.87 (m, 11H), 5.15 (s, 1H), 2.50–2.78 (br d, 5H), 1.15 (t, $J = 7.0$ Hz, 3H); δ_C 155.7, 140.2, 132.3, 129.4, 129.0 (2C), 128.9 (2C), 128.8, 128.7, 127.9, 126.3, 122.3, 121.0, 120.1, 116.4, 71.4, 49.4, 39.1, 11.9; *m/z*: 291 (M^+, 0.94%), 231 (100).

4.4.4. (*S*)-1-[α-(*N*-Methyl-*N*-propylamino)benzyl]-2-naphthol 2d. Using aldehyde **5d**, compound **2d** was obtained as a yellowish gum; $[\alpha]_D^{20} = +206.5$ (*c* 0.3, $CHCl_3$); (Found: C, 82.46%; H, 7.68%; N, 4.62%. $C_{21}H_{23}NO$ requires: C, 82.58%; H, 7.59%; N, 4.59%); ν_{max}/cm^{-1} 3061, 2966, 2932, 1621, 1601, 1473; δ_H 13.94 (s, 1H), 7.13–7.87 (m, 11H), 5.12 (s, 1H), 2.29 (br d, 5H), 1.60 (m, 2H), 0.84 (t, $J = 7.4$ Hz, 3H); δ_C 155.6, 140.2, 132.2, 129.4 (2C), 128.9 (2C), 128.8, 128.7, 128.6, 127.9, 126.3, 122.3, 121.0, 120.0, 116.5, 72.0, 57.4, 39.9, 19.9, 11.6; *m/z*: 306 (M^++1, 0.28%), 305 (M^+, 1.84), 232 (100), 231 (100), 202 (100), 44 (100).

4.4.5. (*S*)-1-[α-(*N*-Methyl-*N*-hexylamino)benzyl]-2-naphthol 2e. Using aldehyde **5e**, compound **2e** was obtained as a yellowish gum; $[\alpha]_D^{20} = +167.9$ (*c* 0.36, $CHCl_3$); (Found: C, 83.11%; H, 8.51%; N, 3.75%. $C_{25}H_{31}NO$ requires: 83.06%; H, 8.64%; N, 3.87%); ν_{max}/cm^{-1} 3061, 2955, 2928, 2855, 1621, 1600, 1454; δ_H 13.93 (s, 1H), 7.13–7.87 (m, 11H), 5.11 (s, 1H), 2.29–2.38 (br d, 5H), 1.56 (s, 2H), 1.21 (s, 8H), 0.85 (t, $J = 5.6$ Hz, 3H); δ_C 155.6, 140.2, 132.3, 129.4 (2C), 130.0, 128.9 (2C), 128.7, 128.6, 127.9, 126.3, 122.3, 121.0, 120.0, 116.5, 72.0, 55.6, 40.0, 31.6, 29.0, 27.1, 26.7, 22.6, 14.0; *m/z*: 361 (M^+, 0.68%), 232 (100), 231 (100), 44 (100).

4.4.6. (*S*)-1-[α-(*N*-Methyl-*N*-nonylamino)benzyl]-2-naphthol 2f. Using aldehyde **5f**, compound **2f** was obtained as a yellowish gum; $[\alpha]_D^{20} = +142.6$ (*c* 0.3, $CHCl_3$); (Found: C, 83.36%; H, 9.26%; N, 3.31%. $C_{28}H_{37}NO$ requires: C, 83.33%; H, 9.24%; N, 3.47%); ν_{max}/cm^{-1} 3061, 2958, 2925, 1621, 1601, 1455; δ_H 13.94 (s, 1H), 7.13–7.87 (m, 11H), 5.10 (s, 1H), 2.27–2.38 (br d, 5H), 1.56 (s, 2H), 1.21 (s, 14H), 0.87 (t, $J = 6.1$ Hz, 3H); δ_C 155.6, 140.2, 132.3, 129.4 (2C), 129.0, 128.8, 128.7, 128.0, 127.8,

126.3, 122.3, 121.0 (2C), 120.0, 116.5, 72.0, 55.5, 40.0, 31.8, 29.5, 29.4, 29.3, 29.2, 27.1, 26.7, 22.6, 14.1; m/z: 404 (M^++1, 0.38%), 403 (M^+, 1.56), 232 (100), 231 (100), 202 (100), 127 (100), 44 (100).

4.4.7. (*S*)-1-[α-(*N*-Methyl-*N*-(3-methylbutyl)amino)benzyl]-2-naphthol 2g. Using aldehyde **5g**, compound **2g** was obtained as a yellowish solid; mp 76–80 °C (PE); $[\alpha]_D^{20} = +167.9$ (c 0.36, $CHCl_3$); (Found: C, 82.86%; H, 7.97%; N, 4.27%. $C_{23}H_{27}NO$ requires: C, 82.84%; H, 8.16%; N, 4.20%); ν_{max}/cm^{-1} 3061, 2960, 1621, 1600, 1474, 1453; δ_H 13.96 (s, 1H), 7.13–7.87 (m, 11H), 5.11 (s, 1H), 2.27–2.43 (br d, 5H), 1.43–1.54 (m, 3H), 0.76–0.82 (m, 6H); δ_C 155.6, 140.1, 132.2, 129.4 (2C), 129.0, 128.8 (2C), 128.7 (2C), 127.9, 126.3, 122.3, 121.0, 120.0, 116.4, 72.0, 53.6, 40.1, 35.7, 26.1, 22.8, 22.2; m/z: 333 (M^+, 1.15%), 231 (100), 44 (100).

4.4.8. (*S*)-1-[α-(*N*-Methyl-*N*-(2-ethylbutyl)amino)benzyl]-2-naphthol 2h. Using aldehyde **5h**, compound **2h** was obtained as a yellowish solid; mp 76–80 °C (PE); $[\alpha]_D^{20} = +148.6$ (c 0.36, $CHCl_3$); (Found: C, 82.90%; H, 8.56%; N, 4.13%. $C_{24}H_{29}NO$ requires: C, 82.95%; H, 8.41%; N, 4.03%); ν_{max}/cm^{-1} 3062, 2962, 1621, 1600, 1519, 1454; δ_H 13.59 (s, 1H), 6.98-7.88 (m, 11H), 4.56 (s, 1H), 2.13-2.36 (m, 5H), 1.25-1.53 (m, 5H), 0.81 (t, $J = 7.2$ Hz, 3H), 0.72 (t, $J = 7.2$ Hz, 3H); δ_C 155.5, 140.3, 132.4, 129.5, 129.2, 128.9, 128.7, 127.9, 126.3, 122.3 (2C), 121.1 (2C), 120.0, 116.8, 73.2, 59.2, 41.4, 38.4, 24.0, 23.5, 11.0, 9.8; m/z: 347 (M^+, 0.85%), 232 (100), 231 (100), 202 (100), 44 (100).

4.4.9. (*S*)-1-[α-(*N*-Methyl-*N*-benzylamino)benzyl]-2-naphthol 2i. Using aldehyde **5i**, compound **2i** was obtained as a yellowish solid; mp 44–46 °C (PE); $[\alpha]_D^{20} = +143.4$ (c 0.3, $CHCl_3$); (Found: C, 84.29%; H, 6.75%; N, 4.01%. $C_{26}H_{25}NO$ requires: C, 84.98%; H, 6.86%; N, 3.81%); ν_{max}/cm^{-1} 3060, 2968, 1621, 1600, 1469, 1453; δ_H 13.96 (s, 1H), 7.02–7.95 (m, 16H), 5.18 (s, 1H), 2.76–2.86 (br d, 4H), 2.40 (s, 3H); δ_C 155.3, 140.1, 139.1, 132.2, 129.4 (2C), 129.0, 128.8 (2C), 128.7, 128.6, 128.4, 127.9 (2C), 126.3, 126.2, 122.3 (2C), 121.0 (2C), 120.0 (2C), 116.4, 72.0, 53.6, 40.1, 35.7, 26.1, 22.8, 22.2; m/z: 367 (M^+, 0.15%), 232 (100), 231 (100), 44 (100).

4.4.10. (*S*)-1-[α-(*N*-Methyl-*N*-cyclohexylamino)benzyl]-2-naphthol 2j. Using aldehyde **5j**, compound **2j** was obtained as a white solid; mp 134–135 °C (PE); $[\alpha]_D^{20} = +152.0$ (c 0.35, $CHCl_3$); (Found: C, 83.49%; H, 8.22%; N, 3.98%. $C_{25}H_{29}NO$ requires: C, 83.52%; H, 8.13%; N, 3.90%); ν_{max}/cm^{-1} 3025, 2960, 1621, 1600, 1474, 1453; δ_H 13.94 (s, 1H), 7.13–7.87 (m, 11H), 5.07 (s, 1H), 2.23–2.34 (br d, 4H), 1.66 (m, 7H), 1.14 (m, 3H), 0.78 (m, 2H); δ_C 155.2, 140.2, 132.2, 129.4 (2C), 128.8 (2C), 128.7, 128.6, 127.9, 126.3, 122.3 (2C), 121.0 (2C), 120.0, 116.5, 72.8, 62.1, 40.9, 35.3, 31.4, 31.2, 26.4, 26.0, 25.9; m/z: 360 (M^++1, 1.18%), 359 (M^+, 4.69), 232 (100), 231 (100), 202 (100), 44 (100).

4.4.11. (*S*)-1-[α-(*N*-Methyl-*N*-phenylamino)benzyl]-2-naphthol 2k. Using aldehyde **5k**, compound **2k** was obtained as a white solid; mp 54–56 °C (PE); $[\alpha]_D^{20} = +149.8$ (c 0.30, $CHCl_3$); (Found: C, 84.95%; H, 6.63%; N, 3.96%. $C_{25}H_{23}NO$ requires: C, 84.95%; H, 6.56%; N, 3.96%); ν_{max}/cm^{-1} 3061, 2963, 1621, 1600, 1520, 1453; δ_H 13.73 (s, 1H), 7.19–7.92 (m, 16H), 5.24 (s, 1H), 3.60 (br s, 2H), 2.19 (s, 3H); δ_C 155.2, 140.2, 137.0, 132.3, 129.6, 129.4 (2C), 128.9 (2C), 128.8, 128.6, 128.1, 127.6, 126.5, 122.3 (2C), 121.0 (2C), 120.0 (2C), 116.5, 71.8, 60.4, 40.3; m/z: 353 (M^+, 0.20%), 231 (100).

4.4.12. (*S*)-1-[α-(*N*-Methyl-*N*-(3,4-diethoxyphenyl)-amino)-benzyl]-2-naphthol 2l. Using aldehyde **5l**, compound **2l** was obtained as a yellowish solid; mp 51–52 °C (PE); $[\alpha]_D^{20} = +217.2$ (c 0.30, $CHCl_3$); (Found: C, 78.64%; H, 7.13%; N, 3.16%. $C_{29}H_{31}NO_3$ requires: C, 78.88%; H, 7.08%; N, 3.17%); ν_{max}/cm^{-1} 3439, 2977, 1621, 1600, 1514, 1473; δ_H 155.5, 149.3, 148.7, 140.3, 132.4, 129.6 (2C), 129.1, 129.0, 128.9 (2C), 128.0, 126.4, 122.4 (2C), 122.3, 122.2, 121.1, 120.1, 116.4, 115.7, 114.3, 71.5, 65.0, 64.9, 60.2, 40.1, 14.9, 14.8; m/z: 441 (M^+, 0.23%), 232 (100), 231 (100), 202 (100).

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References and notes

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