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Asymmetric reduction of enantiopure imines with zinc borohydride: stereoselective synthesis of chiral amines

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Abstract

The first application of zinc borohydride in the reduction of enantiopure imines for the stereoselective preparation of both the enantiomers of secondary amines is described. A possible explanation of the stereoselectivity and of the reaction mechanism is suggested on the basis of theoretical calculations.

1. Introduction

Chiral enantiopure amines constitute a class of compounds that finds various and important applications in stereoselective organic synthesis; they are used as resolving agents, chiral building blocks and chiral auxiliaries.[1–6] While natural ones are available in a single enantiomeric form, although enantiopure, synthetic procedures often request resolution processes or complex synthetic methodologies. Moreover, our interest is in the application of enantiopure amines **3** as ligands in the preparation of chiral catalysts for enantioselective alkylations of carbonyl compounds with organometallic reagents.[7,8]

Chiral enantiopure amines has been obtained by reductive amination of carbonyl compounds, mainly after reduction,[9–12] or by 1,2-nucleophilic asymmetric addition of organometallic reagents to the C=N double bond.[13–17] In any case these synthetic procedures present some drawbacks, such as careful exclusion of air, large excess of reducing agent, long reaction times, high temperatures and use of toxic and expensive chemicals.

For some years zinc borohydride has been reported to effect very efficient chemo-, regio- and stereoselective reductions in several complex substrates where sodium borohydride failed to produce the desired results.[18–21] In particular it has been reported to reduce imines to secondary

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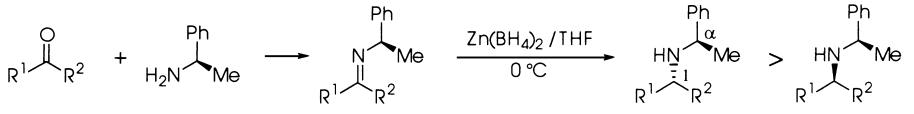
amines.[22–25] This reaction has never been applied before to the reduction of enantiopure imines for the preparation of secondary amines. We describe herein the stereoselective synthesis of chiral amines **3a**–**v** by reduction of enantiopure Schiff bases **2a**–**v** with zinc borohydride.

2. Results and discussion

The starting Schiff bases **2a**–**v** were prepared by conventional condensation of (*R*)-α-methylbenzylamine with ketones **1a**–**v**,[26–30] then reduced using zinc borohydride in anhydrous THF as described in Table 1: The (*R*,*R*)-diastereoisomer is obtained as the main product; yields and diastereoisomeric excesses are generally good, as reported in Table 1. The procedure is very mild and general for a wide variety of amines, does not affect nitro (entry 6) or others groups; the double bond in conjugation does not undergo any isomerization or reduction during the process or during isolation (entries 12, 16).

Table 1
Asymmetric reduction of enantiopure imines (*R*)-**2a**–**v** with zinc borohydride

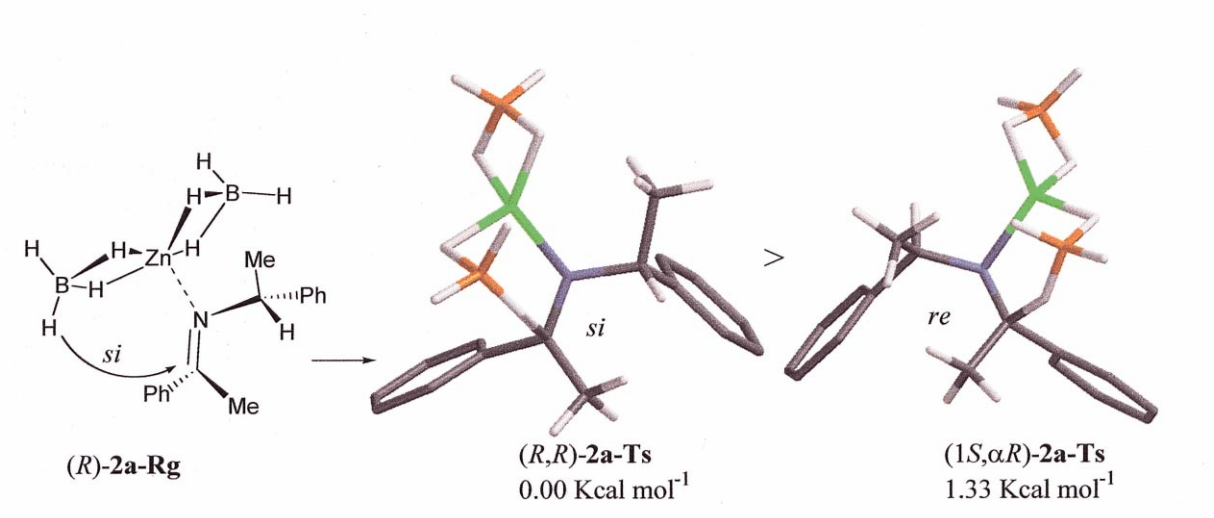


Entry	R^1	R^2	(*R*,*R*)-**3**	Time (min)	Yield (%) [a]	*de* (%) [b]
1	Ph	CH_3	(*R*,*R*)-**3a** [10]	15	82	74
2	2-CH_3O-Ph	CH_3	(*R*,*R*)-**3b** [10]	360	55	24
3	2-pyridyl	CH_3	(*R*,*R*)-**3c** [13]	25	52	57
4	4-pyridyl	CH_3	(*R*,*R*)-**3d** [13]	30	54	68
5	4-Br-Ph	CH_3	(*R*,*R*)-**3e** [9]	60	77	82
6	4-NO_2-Ph	CH_3	(*R*,*R*)-**3f** [9]	60	55	69
7	CH_3CH_2	CH_3	(*R*,*R*)-**3g** [32]	15	51	48
8	$(CH_3)_2CH$	CH_3	(*R*,*R*)-**3h** [33]	60	56	66
9	$(CH_3)_3C$	CH_3	(*R*,*R*)-**3i** [31]	60	78	72
10	$(CH_3CH_2)_2CH$	CH_3	(*R*,*R*)-**3l**	30	66	61
11	$PhCH_2CH_2$	CH_3	(*R*,*R*)-**3m** [4]	60	53	43
12	PhCH=CH	CH_3	(*R*,*R*)-**3n**	60	62	78
13	3-phenanthryl	CH_3	(*R*,*R*)-**3o**	25	77	75
14	2-phenanthryl	CH_3	(*R*,*R*)-**3p**	20	88	95
15	9-phenanthryl	CH_3	(*R*,*R*)-**3q**	15	58	27
16	PhCH=CH	Ph	(1*S*,α*R*)-**3r** [c, 35]	60	45	17
17	2-pyridyl	Ph	(*R*,*R*)-**3s** [34]	60	46	30
18	2-OH-Ph	Ph	(*R*,*R*)-**3t** [7]	60	69	83
19	2-OH-Ph	CH_3	(*R*,*R*)-**3u** [7]	30	54	56
20	2-OH-Ph	CH_3CH_2	(*R*,*R*)-**3v** [7]	30	56	74

Reaction conditions: 1 mmol of **2**, 2 mmol of $Zn(BH_4)_2$, 3 mL of THF, 0 °C.
[a] Chemical yields of purified and isolated (*R*,*R*)-**3**.
[b] Determined by GC analysis or ^1H NMR of the crude reaction mixture.
[c] Product of (*S*,*R*)-configuration because of changed priority numbers.

As became evident from experimental results, *d.e.*s are good when groups R^1 and R^2 constitute a very different steric environment around the C=N double bond (entries 1, 3–6, 8–10 and 12–14) and consequently the imines (*R*)-**2** assumes predominantly the *E*-configuration; in other cases the reaction is less stereoselective (entries 7, 11, 16 and 17). Anyway this feature disappears in the presence of a hydroxy group in *ortho* position with respect to the iminic function, that is when imidoyl phenols **2t**–**v** are used as starting material (entries 18–20). In these substrates a strong intramolecular hydrogen bond constrains the C=N double bond in the *E*-configuration. This evidence suggests two different hypotheses for this mechanism on the basis of the two different groups of substrates.

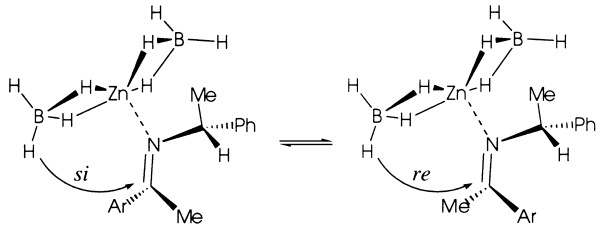
Generally the reduction should take place after the zinc ion coordinates the iminic nitrogen, activating the C=N double bond to nucleophilic attack [Scheme 1, (*R*)-**2a**–**Rg**]. Subsequently an intramolecular hydride transfer from BH_4 to the carbon atom take place both on *si* or *re* face of the C=N double bond. Calculations were performed to find the energies of the transition states (*R*,*R*)-**2a**–**Ts** and (1*S*,α*R*)-**2a**–**Ts**, minimized at the PM3 semiempirical level (Scheme 1), corresponding to the two different situations. Transition state (*R*,*R*)-**2a**–**Ts** was more stable, with a difference of 1.33 Kcal mol^{-1}, and this value is in satisfactory accord with experimental *d.e.* that shows (*R*,*R*)-**3a** as major product. This is in agreement with the fact that for *si* attack hydride enters on the less hindered side, on the same side of the hydrogen atom of the chiral auxiliary (*R*)-α-methyl benzyl group. At the same time the nitrogen lone pair is *gauche* between the phenyl and the methyl group of the same chiral group, in a very favourable position. On the other hand the attack on the *re* face is on the more hindered side (Me) and with the nitrogen lone pair in a less convenient position between phenyl and hydrogen.



Scheme 1. Transition states (*R*,*R*)-**2a**–**Ts** and (1*S*,α*R*)-**2a**–**Ts**, minimized at the PM3 semiempirical level,[36] for the intramolecular hydride transfer on the *si* or *re* face of the imine (*R*)-**2a**–**Rg**

When groups R^1 and R^2 have almost the same steric hindrance around C=N double bond (entries 7, 11, 16 and 17) the imines **2** assume both the two *E*- or *Z*-configuration and consequently a lower diastereoselectivity is found (products **3g**,**m**,**r**,**s**) due to the reduction of both isomeric imines.

The apparently anomalous results obtained with the imines **2b**,**q** (entries 2 and 15) can be explained considering that the hydride complexes (*R*)-**2-Rg** for the *anti* imines **2b**,**q** are less stable than the corresponding complexes of *syn* imines because of the high steric hindrance of the aryl moiety. So the reduction can take place by both pathways (Scheme 2) with a lowering of the stereoselectivity in this case too.

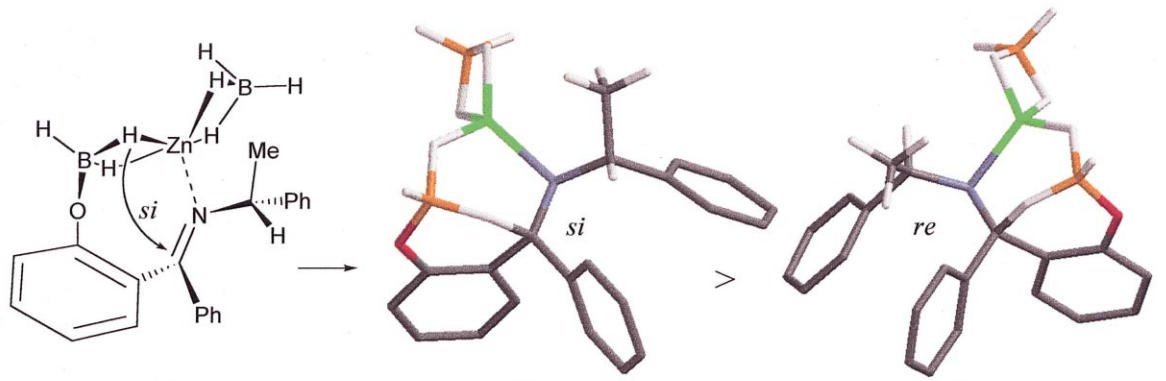


anti-(*R*)-**2b-Rg** *syn*-(*R*)-**2b-Rg**

Scheme 2. The preferred pathways for the intramolecular hydride transfer on the two *anti*- and *syn*-configurations of the imine (*R*)-**2b**–**Rg**

In the reduction of imidoyl phenols **2t**–**v** an acid-base reaction between the phenolic proton and $Zn(BH_4)_2$ takes place, with molecular hydrogen evolution, while the zinc ion coordinates nitrogen (Scheme 3, (*R*)-**2t**–**Rg**). The reducing agent is more tightly bound to the substrate, so hydrogen transfer takes place intramolecularly in a more rigid structure. It is possible to understand why stereoselectivity is so strong although R^1 and R^2 are of almost the same size.

Calculations were made for the product **2t** to build the theorical geometry of transition state minimized at the PM3 semiempirical level (Scheme 3). For this reaction, calculations show that hydride transfer takes place preferably on the less hindered *si* face of C=N double bond, affording to an (*R*,*R*)-**2t**–**Ts** transition state. The corresponding energy differs from that of (1*S*,α*R*)-**2t**–**Ts** transition state of 1.46 Kcal/mol corresponding to product (*R*,*R*)-**3t** as the major diastereomer.



Scheme 3. Transition states (*R*,*R*)-**2t**–**Ts** and (1*S*,α*R*)-**2t**–**Ts**, minimized at the PM3 semiempirical level,[36] for the intramolecular hydride transfer on the *si* or *re* face of the imine (*R*)-**2t**–**Rg**

The configurational assignments of the amines **3** are based upon the following considerations. In all the pairs of diastereoisomeric amines (*R*,*R*)-**3** and (1*S*,α*R*)-**3**, the chemical shifts of benzylic protons H_1 and H_α bonded to the two stereogenic carbon atoms, show a common trend. In the (*R*,*R*)-**3** diastereoisomers these protons are shifted upfield with respect to the corresponding protons of the (1*S*,α*R*)-**3** diastereoisomers; the differences in chemical shift reach up to 0.5 ppm as in the case of **3e**. This feature allowed the absolute configurations to be compared to literature known amines (Fig. 1). On the basis of literature data an (*R*,*R*) configuration has been assigned to amines **3a–i,m,r,t–v** that show this effect, and the same configuration was hypothesized for the other products having a similar spectroscopic behaviour. A further confirmation was found calculating the structure of the more stable conformer for both diastereoisomeric products (*R*,*R*)-**3e** and (1*S*,α*R*)-**3e** (Fig. 2). It was evident that in the (*R*,*R*) structure benzylic protons H_1 and H_α are projected in the shielding cones of the phenyls attached to the opposite carbon atoms. In the product (1*S*,α*R*)-**3e** protons H_1 and H_α lies in the planes of the geminal aromatic rings (deshielding regions).[9,10]

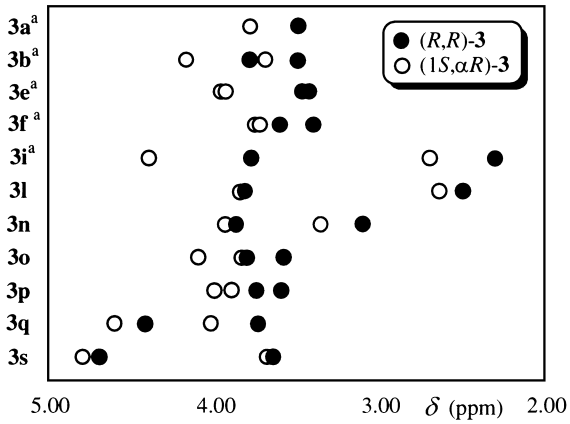


Figure 1. NMR chemical shifts of benzylic proton H_1 and H_α bonded to the two stereogenic carbon atoms of diastereoisomeric amines (*R*,*R*)-**3** and (1*S*,α*R*)-**3** ([a]literature known amines)

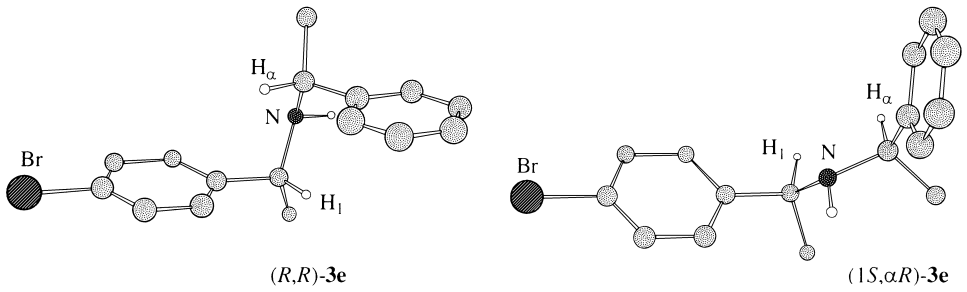


Figure 2. Minimized (PM3) more stable confirmations of amines (*R*,*R*)-**3e** and (1*S*,α*R*)-**3e**[36]

To test the efficacy of this method the same reductions were performed using sodium borohydride, under the classical reaction conditions. Results reported in Table 2 show that sodium borohydride in THF results in comparable diastereoselectivity to zinc borohydride, but in very much longer reaction times although at room temperature (entries 2, 5 and 7); sodium borohydride in methanol is faster but not stereoselective (entries 3 and 8).

Table 2
Stereoselective synthesis of enantiopure amines (*R*,*R*)-**3** with different reductive conditions

Entry	Product	Conditions [a]	T(°C)	Time (h)	Yield (%) [b]	*de* (%) [c]
1	(*R*,*R*)-**3a**	$Zn(BH_4)_2$/THF [a1]	0	0.25	82	74
2	(*R*,*R*)-**3a**	$NaBH_4$/THF [a2]	r.t.	20	77	76
3	(*R*,*R*)-**3a**	$NaBH_4$/MeOH [a3]	0	2	60	49
4	(*R*,*R*)-**3t**	$Zn(BH_4)_2$/THF [a1]	0	1	69	83
5	(*R*,*R*)-**3t**	$NaBH_4$/THF [a2]	r.t.	72	81	80
6	(*R*,*R*)-**3v**	$Zn(BH_4)_2$/THF [a1]	0	0.5	61	74
7	(*R*,*R*)-**3v**	$NaBH_4$/THF [a2]	r.t.	24	70	60
8	(*R*,*R*)-**3v**	$NaBH_4$/MeOH [a3]	0	0.25	54	27

[a] Reaction conditions: [a1] 1 mmol of **2**, 2 mmol of $Zn(BH_4)_2$, 3 mL of THF; [a2] 1 mmol of **2**, 4 mmol of $NaBH_4$, 3 mL of THF; [a3] 1 mmol of **2**, 4 mmol of $NaBH_4$, 3 mL of MeOH.
[b] Chemical yields of purified and isolated (*R*,*R*)-**3**.
[c] Determined by GC analysis or ^{1}H NMR of the crude reaction mixture.

In conclusion, the present procedure using $ZnBH_4$ provides a general, stereoselective and efficient methodology for reductive amination of ketones to obtain chiral secondary amines. Moreover this procedure allows either of the desired enantiomers of the final amine to be obtained, simply by changing the chirality of starting α-methylbenzylamine. The notable advantages of this procedure are good selectivity and yields, operational simplicity, use of cheap or non-toxic chemicals, short reaction times, mild conditions and reduced environmental pollution from waste.

3. Experimental

^{1}H and ^{13}C NMR spectra were recorded with a Varian VXR 300 instrument. Chemical shifts are given in ppm downfield from Me_4Si in $CDCl_3$ solution. Coupling constants are given in hertz. IR spectra were recorded with a Perkin–Elmer 257 spectrometer. GC–MS analyses were performed with an HP 59970 workstation formed by an HP-5890 gas chromatograph equipped with a methyl silicone capillary column and by an HP-5970 mass detector. THF was dried by refluxing over sodium wires until the blue colour of benzophenone ketyl persisted and then distilled into a dry receiver under nitrogen atmosphere. All reagents and solvents were distilled prior to use or were of commercial quality from freshly opened containers. Imines were prepared according to literature methods.[26–30] Zinc borohydride was prepared by known procedures[22,23] and stored in a dry receiver under nitrogen.

3.1. Reduction of imines *2a–v*

Imines **2a–v** (2 mmol) dissolved in THF (2.0 cm^3) were stirred under nitrogen atmosphere and cooled to 0°C, then a freshly prepared solution of zinc borohydride (6.0 cm^3, 4.0 mmol) was added. The reaction was allowed to stand and monitored by TLC and GC. After a variable period the reaction was stopped at constant conversion of starting material. 6 M HCl was then added dropwise to the reaction mixture until hydrogen production ceased, then neutralized with

Na_2CO_3. The aqueous solution was then extracted with CH_2Cl_2 (3×30 cm^3). The organic layer was dried with anhydrous Na_2SO_4 then filtered and the solvent evaporated under reduced pressure. Chromatographic separation on the crude oil obtained, with cyclohexane:ethyl acetate = 70:30 as eluent, afforded to the amines **3** in 45–88% yield. Products (*R*,*R*)-**3a**–**i**,**m**,**r**,**t**–**v** were identified according to literature data. Since only the major diastereomers were obtained pure by chromatography, the ^{1}H NMR signals for the minor diastereoisomers were deduced from the spectra of the crude reaction mixtures or from enriched chromatographic fractions.

3.2. N-*[(1*R*)-2-Ethyl-1-methylbutyl]*-N-*[(1*R*)-1-phenylethyl]amine [(*R,R*)-**3l**]*

Oil, $[\alpha]_D^{20} = +48.7$ (*c* 1.79, $CHCl_3$); NMR ($CDCl_3$): δ_H 0.78 (t, 3H, $J = 7.6$ Hz), 0.83 (d, 3H, $J = 6.5$ Hz), 0.92 (t, 3H, $J = 7.6$ Hz), 1.08–1.37 (m, 4H), 1.29 (d, 3H, $J = 6.4$ Hz), 1.44–1.58 (m, 1H), 2.49 (dq, 1H, $J = 6.4$; 4.3 Hz), 3.75 (br s, 1H), 3.83 (q, 1H, $J = 6.5$ Hz), 7.15–7.35 (m, 5H); δ_C 12.2, 12.6, 16.8, 21.5, 23.2, 24.5, 45.4, 51.6, 55.3, 126.5, 126.6, 128.1, 128.2; m/z 204 (M^+-15, 1), 148 (58), 106 (14), 105 (100). Anal. calcd for $C_{15}H_{25}N$, MW 219.366: C, 82.13; H, 11.49; N, 6.39%. Found: C, 82.27; H, 11.32; N, 6.61%. *N*-[(1*R*)-2-Ethyl-1-methylbutyl]-*N*-[(1*R*)-1-phenylethyl]amine [(1*S*,α*R*)-**3l**]: NMR ($CDCl_3$): δ_H 0.77 (t, 3H, $J = 7.3$ Hz), 0.82 (d, 3H, $J = 6.4$ Hz), 0.94 (t, 3H, $J = 6.1$ Hz), 1.08–1.37 (m, 4H), 1.28 (d, 3H, $J = 6.7$ Hz), 1.44–1.58 (m, 1H), 2.64 (dq, 1H, $J = 6.4$; 3.4 Hz), 3.75 (br s, 1H), 3.85 (q, 1H, $J = 6.7$ Hz), 7.15–7.35 (m, 5H); m/z 204 (M^+-15, 1), 148 (53), 106 (12), 105 (100).

3.3. N-*[(1*R*,2*E*)-1-Methyl-3-phenylprop-2-enyl]*-N-*[(1*R*)-1-phenylethyl]amine [(*E*)-(*R,R*)-**3n**]*

Yellow oil, $[\alpha]_D^{20} = +166.2$ (*c* 1.66, $CHCl_3$): ν_{max} (liquid film) 3306, 1600, 1578, 967, 750, 700 cm^{-1}; NMR ($CDCl_3$): δ_H 1.18 (d, 3H, $J = 6.5$ Hz), 1.34 (d, 3H, $J = 6.7$ Hz), 1.62 (br s, 1H), 3.11 (dq, 1H, $J = 8.1$, 6.5 Hz), 3.88 (q, 1H, $J = 6.7$ Hz), 6.27 (dd, 1H, $J = 16.0$, 6.3 Hz), 6.27 (d, 1H, $J = 16.0$ Hz), 7.15–7.49 (m, 10H); δ_C 23.2, 25.5, 53.7, 55.4, 126.7, 127.1, 127.3, 127.8, 128.9, 129.0, 130.6, 134.7, 137.7, 146.3; m/z 251 (M^+, 9), 236 (20), 160 (50), 132 (59), 131(68), 105 (100). Anal. calcd for $C_{18}H_{21}N$, MW 251.366: C, 86.01; H, 8.42; N, 5.57%. Found: C, 85.95; H, 8.23; N, 5.32%. *N*-[(1*S*,2*E*)-1-Methyl-3-phenylprop-2-enyl]-*N*-[(1*R*)-1-phenylethyl]amine [(1*S,E*),(α*R*)-**3n**]: yellow oil, NMR ($CDCl_3$): δ_H 1.23 (d, 3H, $J = 6.5$ Hz), 1.38 (d, 3H, $J = 7.0$ Hz), 1.69 (br s, 1H), 3.36 (quint, 1H, $J = 4.5$ Hz), 3.93 (q, 1H, $J = 6.6$ Hz), 6.07 (dd, 1H, $J = 7.6$, 15.9 Hz), 6.43 (d, 1H, $J = 15.9$ Hz), 7.17–7.42 (m, 10H); m/z 251 (M^+, 12), 236 (27), 160 (39), 132 (53), 131 (64), 105 (100).

3.4. N-*[(1*R*)-1-(3-Phenanthryl)ethyl]*-N-*[(1*R*)-1-phenylethyl]amine [(*R,R*)-**3o**]*

Yellow oil, $[\alpha]_D^{20} = +124.0$ (*c* 1.61, $CHCl_3$), ν_{max} (liquid film): 3324, 1602, 1123, 841, 748, 701 cm^{-1}; NMR ($CDCl_3$): δ_H 1.34 (d, 3H, $J = 6.7$ Hz), 1.45 (d, 3H, $J = 6.6$ Hz), 1.76 (br s, 1H), 3.58 (q, 1H, $J = 6.7$ Hz), 3.82 (q, 1H, $J = 6.7$ Hz), 7.24–8.00 (m, 12H), 8.47 (s, 1H), 8.72 (m, 1H); δ_C 25.1, 25.1, 55.3, 55.6, 120.9, 122.7, 125.2, 125.4, 126.3, 126.5, 126.5, 126.6, 126.7, 126.9, 127.2, 128.5, 128.6, 128.9, 130.3, 130.3, 131.2, 132.2; m/z 310 (M^+-15, 38), 206 (77), 205 (77), 120 (59), 105 (100). Anal. calcd for $C_{24}H_{23}N$, MW 325.446: C, 88.57; H, 7.12; N, 4.30%. Found: C, 88.30; H, 7.36; N, 4.22%. *N*-[(1*S*)-1-(3-Phenanthryl)ethyl]-*N*-[(1*R*)-1-phenylethyl]amine [(1*S*,α*R*)-**3o**]: NMR ($CDCl_3$): δ_H 1.51 (d, 3H, $J = 6.6$ Hz), 1.66 (d, 3H, $J = 6.4$ Hz), 1.76 (br s, 1H), 3.84 (q, 1H, $J = 6.5$ Hz), 4.09 (q, 1H, $J = 6.5$ Hz), 7.24–8.00 (m, 12H), 8.60–8.80 (m, 2H).

3.5. N-[(1R)-1-(2-Phenanthryl)ethyl]-N-[(1R)-1-phenylethyl]amine [(R,R)-**3p**]

Yellow oil, $[\alpha]_D^{20} = +221.6$ (*c* 2.59, $CHCl_3$), ν_{max} (liquid film): 3324, 1601, 1122, 811, 747, 701 cm^{-1}; NMR ($CDCl_3$): δ_H 1.35 (d, 3H, $J = 6.7$ Hz), 1.43 (d, 3H, $J = 6.7$ Hz), 1.81 (br s, 1H), 3.60 (q, 1H, $J = 6.7$ Hz), 3.77 (q, 1H, $J = 6.7$ Hz), 7.22–8.00 (m, 12H), 8.65–8.76 (m, 2H); δ_C 25.1, 25.1, 55.1, 55.2, 122.6, 123.0, 125.4, 126.4, 126.6, 126.6, 126.7, 126.9, 127.0, 127.0, 128.5, 128.6, 129.4, 130.3, 131.9, 132.2, 144.1, 145.8; m/z 310 (M^+-15, 32), 206 (67), 205 (70), 178 (10), 155 (13), 120 (57), 106 (17), 105 (100). Anal. calcd for $C_{24}H_{23}N$, MW 325.446: C, 88.57; H, 7.12; N, 4.30%. Found: C, 88.36; H, 7.24; N, 4.16%. *N*-[(1*S*)-1-(2-Phenanthryl)ethyl]-*N*-[(1*R*)-1-phenylethyl]-amine [(1*S*,α*R*)-**3p**]: NMR ($CDCl_3$): δ_H 1.42 (d, 3H, $J = 6.6$ Hz), 1.49 (d, 3H, $J = 6.6$ Hz), 2.10 (broad s, 1H), 3.84 (q, 1H, $J = 6.6$ Hz), 4.01 (q, 1H, $J = 6.6$ Hz), 7.20–8.72 (m, 14H).

3.6. N-[(1R)-1-(9-Phenanthryl)ethyl]-N-[(1R)-1-phenylethyl]amine [(R,R)-**3q**]

Yellow oil, $[\alpha]_D^{20} = +87.0$ (*c* 1.92, $CHCl_3$), ν_{max} (liquid film): 3326, 1648, 1130, 749, 726, 701 cm^{-1}; NMR ($CDCl_3$): δ_H 1.43 (d, 3H, $J = 6.8$ Hz), 1.46 (d, 3H, $J = 6.6$ Hz), 1.78 (br s, 1H), 3.75 (q, 1H, $J = 6.8$ Hz), 4.44 (q, 1H, $J = 6.6$ Hz), 7.16–7.40 (m, 4H), 7.48–7.73 (m, 4H), 7.95–8.10 (m, 4H), 8.65–8.82 (m, 2H); δ_C 24.4, 24.7, 51.1, 55.4, 122.5, 123.3, 123.4, 123.7, 126.0, 126.2, 126.3, 126.6, 126.7, 126.9, 128.4, 128.6, 129.8, 130.8, 130.9, 131.9, 139.5, 146.0; m/z 310 (M^+-15, 37), 206 (91), 205 (78), 120 (79), 105 (100). Anal. calcd for $C_{24}H_{23}N$, MW 325.446: C, 88.57; H, 7.12; N, 4.30%. Found: C, 88.41; H, 7.32; N, 4.41%. *N*-[(1*S*)-1-(9-Phenanthryl)ethyl]-*N*-[(1*R*)-1-phenyl-ethyl]amine [(1*S*,α*R*)-**3q**]: yellow oil, NMR ($CDCl_3$): δ_H 1.44 (d, 3H, $J = 6.6$ Hz), 1.59 (d, 3H, $J = 6.5$ Hz), 1.75 (br s, 1H), 4.01 (q, 1H, $J = 6.6$ Hz), 4.59 (q, 1H, $J = 6.6$ Hz), 7.13–7.40 (m, 4H), 7.50–7.75 (m, 4H), 7.95–8.10 (m, 4H), 8.60–8.82 (m, 2H); m/z 310 (M^+-15, 34), 206 (89), 205 (73), 120 (60), 105 (100).

3.7. N-[(1R)-1-Phenylethyl]-N-[(R)-phenyl(pyridin-2-yl)methyl]amine [(R,R)-**3s**]

Yellow oil, $[\alpha]_D^{20} = +101.2$ (*c* 1.23, $CHCl_3$); ν_{max} (liquid film): 3319, 1665, 1588, 748, 699 cm^{-1}; NMR ($CDCl_3$): δ_H 1.42 (d, 3H, $J = 6.6$ Hz), 2.85 (br s, 1H), 3.68 (q, 1H, $J = 6.6$ Hz), 4.72 (s, 1H), 7.00–7.75 (m, 13H), 8.55 (m, 1H). δ_C 25.2, 55.4, 65.4, 122.3, 122.7, 127.4, 127.8, 128.6, 129.1, 129.2, 130.0, 137.0, 143.2, 146.0, 149.6, 162.4; m/z 210 (M^+-78, 11), 169 (100), 168 (49), 120 (38), 105 (30). Anal. calcd for $C_{20}H_{20}N_2$, MW 288.386: C, 83.30; H, 6.99; N, 9.71%. Found: C, 83.48; H, 7.11; N, 9.48%. *N*-[(1*R*)-1-Phenylethyl]-*N*-[(*S*)-phenyl(pyridin-2-yl)methyl]amine [(1*S*,α*R*)-**3s**]: yellow oil, $[\alpha]_D^{20} = +11.5$ ($c = 1$, $CHCl_3$); NMR ($CDCl_3$): δ_H 1.41 (d, 3 H, $J = 6.6$ Hz), 2.65 (br s, 1H), 3.66 (q, 1H, $J = 6.6$ Hz), 4.79 (s, 1H), 7.10–7.75 (m, 13H), 8.6 (m, 1H); δ_C 24.9, 56.3, 65.6, 122.5, 123.2, 127.4, 127.5, 127.6, 128.0, 129.0, 131.5, 136.9, 143.7, 146.0, 150.1, 163.0; m/z 273 (M^+-15, 2), 169 (100), 168 (49), 120 (32), 105 (31).

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