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Stereoselective Grignard reactions to α-amino nitrones. Synthesis of optically active α-aminohydroxylamines and 1,2-diamines

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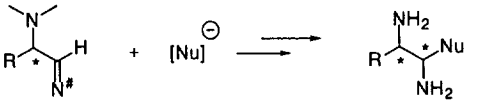
Abstract: α-Aminohydroxylamines are formed stereoselectively from the nucleophilic addition of phenylmagnesium bromide to α-amino nitrones. In contrast, the addition of methylmagnesium bromide occurs in a stereorandom fashion. Nevertheless it is possible to achieve a complete *syn* selectivity by diprotecting the α-amino group in the starting nitrone. Hydrogenation of the obtained α-amino hydroxylamines followed by deprotection of the tert-butoxycarbonyl group affords optically active 1,2-diamines. © 1997 Elsevier Science Ltd

Introduction

The nucleophilic addition of organometallic reagents to a C=N bond is one of the basic reactions in organic synthesis.[1] While several diastereoselective nucleophilic additions to imines,[2] oximes[3] and hydrazones[4] have been reasonably well-documented, the literature contains only a few examples of such reactions with nitrones.[5] In addition, the majority of those correspond to particular cases and, in consequence, exhibit a poor versatility. To the best of our knowledge and excluding the work of Chang and Coates,[5a] and our previous reports,[6] no general studies involving chiral nitrones have been described. In particular, if the nucleophilic addition takes place at a C=N functionality having an α-amino group (Scheme 1),[7] vicinal diamines can be obtained.[8] Although a great variety of synthetic methodologies for the synthesis of 1,2-diamines[9] have been reported none of them makes use of the strategy depicted in Scheme 1. Only Reetz and co-workers[10] have described the addition of several organometallic reagents to α-amino imines to obtain the corresponding α,β-diamines. It is worthy of note that α-amino imines have also been employed by Palomo and co-workers[11] as precursors of β-lactams which have been further converted into 1,2-diamino compounds.



1,2-diamines

$N^{\#}$ = NR, NOR, N-NR^1R^2, $N^+R^1R^2$, $N^+(O^-)R$

Scheme 1.

In our continuing efforts to develop stereoselective nucleophilic additions to chiral nitrones,[6,12] we have found that α-amino nitrones constitute excellent substrates for such reactions.[13] Herein we report the results of our study concerning the reaction of Grignard reagents with several chiral α-amino nitrones. The products so obtained are novel β-amino hydroxylamines[14] which in turn are converted into valuable 1,2-diamines.

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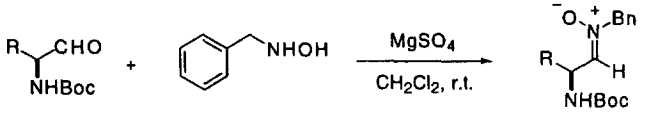
Results and discussion

The starting α-amino nitrones **4–6** were readily prepared by condensation of N-benzyl hydroxylamine[15] with the corresponding α-amino aldehydes[16] **1–3**, following our previously published procedure[17] (Scheme 2). The nitrones **4–6** were crystalline stable compounds in all cases and showed a Z-configuration as demonstrated by n.O.e. experiments which established that the azomethine proton and the benzyl group were on the same side of the nitrone function. In the case of nitrone **4** an X-ray structural analysis[18] further confirmed the previously assigned Z-configuration.

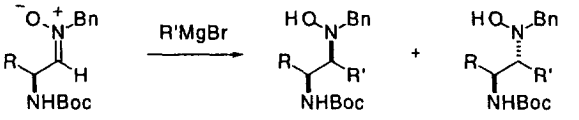


1 R = Me
2 R = ^{i}Pr
3 R = Bn

4 R = Me
5 R = ^{i}Pr
6 R = Bn

Scheme 2.

The reactions of Grignard reagents with N-monoprotected nitrones **4–6** were carried out in THF at −40°C using an excess of 3.0 equivalents of organometallic reagent; with stoichiometric amounts of organometallic reagent the reaction did not go to completion. Aqueous work-up after 4 h provided mixtures of *syn*- and *anti*-α-amino hydroxylamines **7–12** in good yields (Scheme 3). The diastereomeric ratios of the products were determined by analytical ^{1}H NMR spectroscopy of the crude mixtures. The results of the addition reactions are summarized in Table 1.



4-6 **7a-12a** **7b-12b**

Scheme 3.

In all cases methyl magnesium bromide gave modest diastereofacial selectivities whereas phenylmagnesium bromide afforded the *syn* adduct as the only product of the reaction as judged by ^{1}H NMR spectroscopy. No substantial changes in the stereoselectivity were observed by carrying out the reaction at different temperatures. At higher temperatures the yield dropped considerably (50% at 0°C and 32% at 25°C for nitrone **4**) and at lower temperatures the reaction did not go to completion (10% of conversion at −80°C after 48 h). Changes of the solvents (toluene and diethyl ether) did not improve the results either. The obtained diastereomeric hydroxylamines were easily separated by flash chromatography. It is noteworthy that in all cases that the two diastereomers could be observed, the

Table 1. Stereoselective addition of Grignard reagents to nitrones **4–6**[a]

entry	nitrone	R	R'	hydroxylamine	*syn* : *anti*[b]	yield[c] (%)
1	**4**	Me	Me	**7**	66 : 34	83
2	**4**	Me	Ph	**8**	≥95 : 5	89
3	**5**	^{i}Pr	Me	**9**	60 : 40	82
4	**5**	^{i}Pr	Ph	**10**	≥95 : 5	91
5	**6**	Bn	Me	**11**	62 : 38	88
6	**6**	Bn	Ph	**12**	≥95 : 5	92

[a] 3.0 equivalents of Grignard reagent were used. [b] Measured from the intensities of ^{1}H NMR signals. [c] Isolated yield of the crude mixture.

syn adduct showed a higher R_f than that of the *anti* one. A similar behaviour had been observed by us for α-(hydroxyamino) nitriles.[6a]

In order to improve the obtained results with methylmagnesium bromide we next considered the possibility of changing the protective group arrangement in the starting nitrone.[19] Thus, nitrones **13–15** were prepared from the corresponding N,N-diprotected α-amino aldehydes[20] in good yields. The addition of methylmagnesium bromide to those nitrones was carried out using 3.0 equivalents of Grignard reagent at −40°C and in THF as a solvent (Scheme 4).

13 R = Me
14 R = Bn

16 R = Me
17 R = Bn

15

18

Scheme 4.

The results are summarized in Table 2. Although the yields of the resulting hydroxylamines were much lower than those obtained with the N-monoprotected α-amino nitrones, the diastereofacial selectivity was satisfactory. In all cases ^{1}H NMR showed that the obtained hydroxylamines **16–18** consisted of a single isomer. Hence, a total *syn* selectivity for the addition of both methyl and phenylmagnesium bromide to α-amino nitrones had been achieved.

Stereochemical assignments

The relative stereochemistry of the obtained hydroxylamines was based on different techniques. In the case of hydroxylamines **7** and **9** X-ray crystallographic analyses of **7a** (Figure 1) and **9a** (Figure 2), confirmed unequivocally that the relative configuration between the two nitrogen atoms was *syn* in both cases. Consideration of those X-ray structures led us to verify the existence of intramolecular hydrogen bond interactions between the urethane carbonyl and the hydroxylamino group (CO..HO–N bond distance was 2.248 Å for **7a** and 2.544 Å for **9a**; OH..O bond angle was 48.6° for **7a** and 51.0° for **9a**). These intramolecular hydrogen bonds, which has been observed by us in all X-ray structures of chiral hydroxylamines having a tert-butoxycarbonylamino group in α-position,[21] were also shown to exist in solution; bands at c.a. 3600 cm^{-1} remaining unchanged with dilution in non-polar solvents in the infrared spectra of hydroxylamines **7–12**. Also ^{1}H NMR spectra of those hydroxylamines showed in all cases higher values of δs (c.a. 2 ppm) for the hydrogen atom of the hydroxylamino group than other hydroxylamines without a carbamate group in α-position.

Taking advantage of this observation the relative stereochemistry of hydroxylamines **11a,b** in which the two epimers are available, can be determined from their ^{13}C NMR chemical shift nonequivalence. Chemical shifts of the *syn* adducts show a marked upfield shift relative to those of the *anti* compounds (Table 3). Considering that in all cases the coupling constants between H_a and H_b are small (Table 3), thus precluding the possibility of an antiperiplanar disposition of those protons, and the presence of

Table 2. Addition of methyl magnesium bromide to nitrones **13–15**[a]

entry	nitrone	hydroxylamine	*syn* : *anti*[b]	yield[c] (%)
1	**13**	**16**	≥95 : 5	40
2	**14**	**17**	≥95 : 5	41
3	**15**	**18**	≥95 : 5	25

a 3.0 equivalents of Grignard reagent were used. b Measured from the intensities of ^{1}H NMR signals. c Isolated yield of the crude mixture.

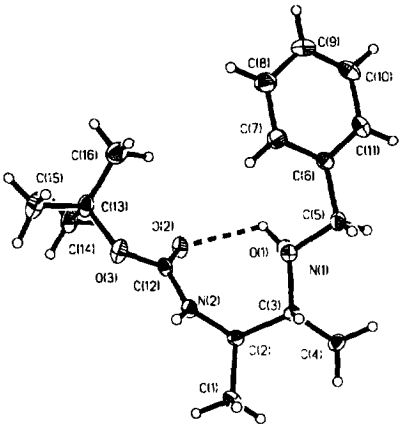


Figure 1. ORTEP view of compound **7a** showing ellipsoids at 30% probability level.

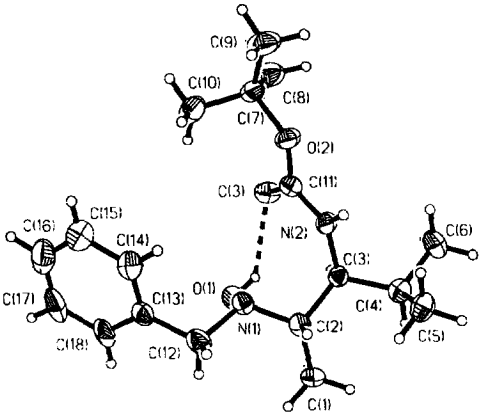


Figure 2. ORTEP view of compound **9a** showing ellipsoids at 30% probability level.

Table 3. Selected NMR data of hydroxylamines

		syn adducts[a]		anti adducts[a]	
	R	$\delta(CH_3)^b$	$J_{a,b}{}^c$	$\delta(CH_3)^b$	$J_{a,b}{}^c$
7	Me	8.58	2.6	10.15	2.8
9	^{i}Pr	8.29	3.6	10.22	3.9
11	Bn	9.03	3.5	10.35	----[d]

[a] syn and anti compounds are referred by **a** and **b** series, respectively. [b] data in ppm. [c] data in Hz. [d] it could not be determined

the above mentioned intramolecular hydrogen bond interaction the most favourable conformations of hydroxylamines **7**, **9** and **11** may be illustrated as shown in Figure 3 ($\alpha \leq 60°$).

According to general rules of ^{13}C NMR spectroscopy,[22] in **7a**, **9a** and **11a** the methyl groups are expected to show upfield shifts due to their pseudoaxial position in the eight-membered ring (Figure 3), in contrast to the pseudoequatorial one found in *anti* hydroxylamines **7b**, **9b** and **11b**. Thus, the major

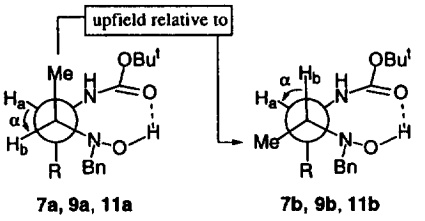


Figure 3. Conformations of hydroxylamines **7**, **9** and **11**.

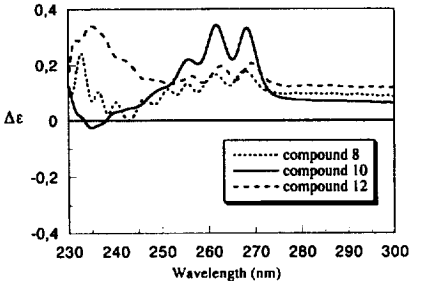


Figure 4. CD spectra of compounds **8**, **10** and **12**.

isomers are proposed to possess a relative *syn* stereochemistry, which is consistent with the above mentioned quite different values of R_f.

For hydroxylamines **8**, **10** and **12** the assignment was based on a CD study of those compounds. Smith and co-workers[23] reported a sector rule for the circular dichroism of the benzene chromophore in a variety of phenylcarbinamines. According to that sector rule, which matches with those previously proposed by us for similar furan[24] and thiazole[25] derivatives, the observed positive Cotton effect in the range 250–270 nm for hydroxylamines **8**, **10** and **12** (Figure 4) is consistent with the (S)-configuration. The stereochemical assignments for hydroxylamines **16–18** were made by comparison, as described below.

Mechanistic considerations

The stereochemical outcome of the additions to N-monoprotected α-amino nitrones **4–6** can be explained as follows. Since the addition to those nitrones does not go to completion using stoichiometric amounts of Grignard reagent it appears reasonable to hypothesize the addition of a second molecule of Grignard reagent to the preformed intermediate chelated magnesium derivative **A** (Figure 5).

On the basis of that six-membered cyclic chelate neither the *Re* face nor the *Si* one are clearly hindered and, in consequence, a small nucleophile such as methylmagnesium bromide leads to a poor

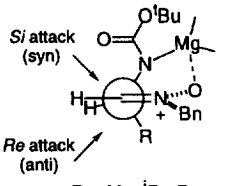


Figure 5. Proposed model for addition to nitrones **4–6**.

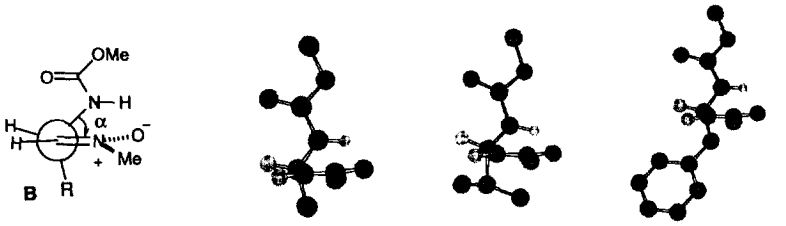


Figure 6. Minima of energy for nitrones **4–6** (other H atoms removed for clarity after minimization).

selectivity. By contrast, a bulkier nucleophile such as phenylmagnesium bromide seems to posses an adequate size for differentiating both faces, only leading to *syn* adducts in all cases. Differences on the behaviour of Grignard reagents such as methyl and phenylmagnesium halides have also been observed in nucleophilic additions to chiral aldehydes. Also in those cases the steric bulk of the reagents has been invoked to rationalize the stereochemical course of the reaction.[26] In order to confirm the proposed model **A** we recourse to semiempirical calculations. The structures of nitrones **4–6** were calculated with the AM1 Hamiltonian[27] in the MOPAC 93 program.[28] The AM1 calculations were started using X-ray data of nitrones[18,29] as guessing parameters. The following clarification of the geometry provided the conformers depicted in Figure 6 with absolute minimal heats of formation.

Since energy barriers between those conformers and others possessing relative minimal heats of formation are greater than 3 Kcal/mol the rate of interconversion is supposed to be low at −40°C and in consequence conformers **B** (Figure 6), which were found to be quite similar to the proposed model **A** (Figure 5), are thought to be predominant.[30] The stability of conformers **B**, in the case of nitrones **4–6** is presumably due to the existence of an intramolecular hydrogen bond interaction between the nitrone oxygen and the hydrogen atom of the carbamate group. That hydrogen bond has also been observed in solution[31] and in solid state.[18]

For the Grignard additions to nitrones **13–15** it seems reasonable that the magnesium atom cannot take the role of the bridging atom between the nitrone oxygen and the carbamate group. Two conformers having minimal heats of formation were obtained from nitrones **13–15**. Conformers **B** (Figure 7) are almost identical to the previously invoked model **A** (Figure 5). On the other hand, conformers **C** (Figure 7) correspond to a model quite similar to that proposed by Houk for additions to double bonds.[32] This model had also been previously proposed by us for nucleophilic additions to α,β-dialkoxy nitrones.[33] Also a quite similar model has been invoked by Reetz and coworkers to explain nucleophilic additions to γ-amino-α,β-unsaturated esters.[14,34] The energy barriers between each couple of conformers **B** and **C** of nitrones **13–15** were found to be less than 1 Kcal/mol (see Figure 7 for relative values of energy). This observation let us propose that the rate of interconversion was rather high even at −40°C, thus allowing equilibration of the conformers. In the case of nitrones **13–15** there is no possibility of intramolecular hydrogen bonds; this could be the reason of the absence of well-defined minima of energy. Reaction of nitrones **13–15** from the *Si* face is presumably less hindered in the case of conformers **C** than from the same face in conformers **B**, and in consequence the reaction proceeds exclusively via the lowest energy conformers **C** (Curtin–Hammett principle) to give *syn*-hydroxylamines **16–18**.

This proposal only indicates a part of the possible reaction courses for the nucleophilic additions to nitrones **4–6** and **13–15**. Further consideration for the stereochemical course of the reaction requires the calculation of not only stable conformers of starting compounds but also transition states formed from the nitrones (perhaps with one or two molecules of Grignard reagent), reaction rates, and so on.

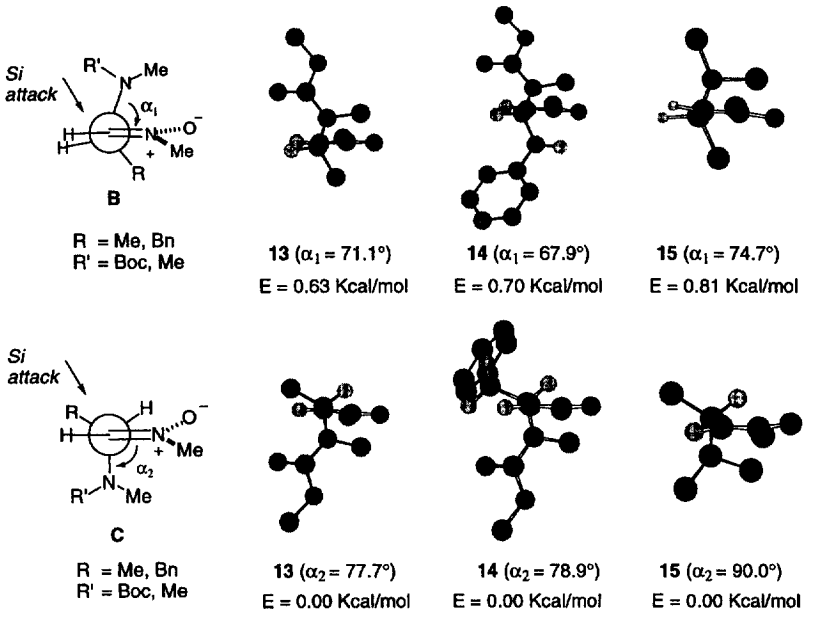
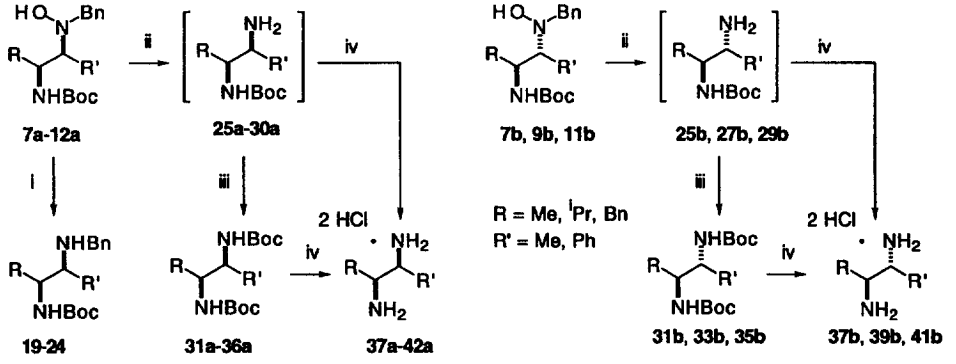


Figure 7. Proposed models and minima of energy for nitrones **13–15** (other H atoms removed for clarity after minimization).

Synthesis of 1,2-diamines

We envisioned that the hydroxylamines **7–12** could serve as intermediates in the preparation of a variety of 1,2-diamines via appropriate functional group transformations. Deoxygenation of the hydroxylamino function of *syn* adducts **7a–12a** (Scheme 5) to the corresponding secondary amines was achieved by zinc–copper(II) acetate, following the procedure reported by Trombini,[5b] the *syn* 1,2-diamines **19–24** being obtained in good yields (Table 4).

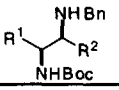


Reagents and conditions: i) Zn dust, $Cu(AcO)_2$, AcOH, 70 °C, 1h. ii) H_2, $Pd(OH)_2$-C, MeOH, r.t., 70 psi, 72 h. iii) Boc_2O, Et_3N, DMAP, r.t., 16 h. iv) 8% HCl - MeOH, 5 °C, 30 min.

Scheme 5.

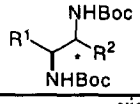
The total reduction of the hydroxylamino functionality was achieved by catalytic hydrogenation (70 psi, 3 days) using palladium hydroxide on charcoal as a catalyst. The resulting crude primary amines **25–30** were treated with ditert-butyldicarbonate to give diprotected 1,2-diamines **31–36**. This protocol was applied to both *syn* hydroxylamines **7a–12a** and *anti* hydroxylamines **7b**, **9b** and **11b** (Scheme 5, Table 5).

Table 4. N-Benzyl-N′-Boc diamines



compound	R^1	R^2	yield(%)
19	Me	Me	83
20	Me	Ph	88
21	^{i}Pr	Me	80
22	^{i}Pr	Ph	73
23	Bn	Me	81
24	Bn	Ph	80

Table 5. N,N′-Bis(tert-butoxycarbonyl)diamines



compound	R^1	R^2	yield(%) *syn*[a]	yield(%) *anti*[a]
31	Me	Me	86	80
32	Me	Ph	83	-----[c]
33	^{i}Pr	Me	47	51
34	^{i}Pr	Ph	0[b]	-----[c]
35	Bn	Me	68	63
36	Bn	Ph	62	-----[c]

[a] *syn* and *anti* compounds are referred by **a** and **b** series, respectively. [b] (see text). [c] not obtained

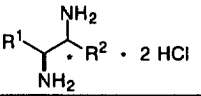
It is worth mentioning that whereas the N,N′-diBoc derivatives **33a** and **33b** were obtained in acceptable yields (47 and 51%, respectively), all attempts to convert efficiently the *syn* diamine **28a** (R=^{i}Pr, R′=Ph) into the di-Boc derivative **34a** failed; several Boc-introduction procedures,[35] including Boc_2O in dioxane, Boc_2O–Et_3N–DMAP and Boc_2O–NaOH, were checked and in all cases the starting primary amine was recovered.[36] The removal of the tert-butoxycarbonyl groups of compounds **31–36** by methanolic hydrochloric acid furnished unprotected 1,2-diamines **37–42** which were characterized as their bishydrochloride salts (Scheme 5). Although the conversion of hydroxylamines **7–12** to vicinal diamines occurred with good overall yields, we envisaged *in situ* deprotection of primary amines **25–30** as an alternative (and more straightforward) route to the targeted 1,2-diamines. Indeed, catalytic hydrogenation of hydroxylamines **7–12** as described above followed by treatment with 8% hydrochloric acid in anhydrous methanol at 5°C for 30 min afforded bishydrochloride salts **37–42** in good isolated chemical yields (Scheme 5, Table 6).

Hydroxylamines **16** and **17** were also subjected to the same sequence of reactions indicated above affording both diamines **37a** and **41a**, and di-(tert-butoxycarbonyl) derivatives **31a** and **35a**, respectively (Scheme 6). This allowed a straightforward assignment of their stereochemistry since the spectral and physical properties (NMR, $[\alpha]_D$) of compounds **37a**, **41a** and **31a**, **35a** (obtained from **16** and **17**, respectively) were in good accord with those of the same compounds obtained from **7a** and **11a**, respectively.

Finally, catalytic hydrogenation (r.t., 70 psi, 3 days) of hydroxylamine **18** using Pearlman's catalyst gave (2S,3S)-2,3-diaminobutane **37a** (Scheme 7) which was characterized as the bishydrobromide salt by treatment with 30% HBr in acetic acid at 5°C.

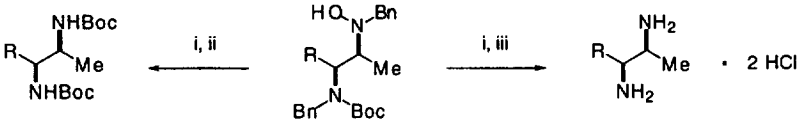
The physical and spectroscopic properties of **37a** (mp 285–290°C (dec.); $[\alpha]_D$ −8.0 (c 1.5, H_2O)) were almost identical, except for the sign of the optical rotation, with those of the previously described (2R,3R)-2,3-diaminobutane (mp 288.4–290.8°C; $[\alpha]_D$ +8.17 (c 1.425, H_2O)).[9a] Hence, the *syn* configuration of **18** appears to be demonstrated.

Table 6. 1,2-Diamines bishydrochloride salts



compound	R^1	R^2	yield(%) *syn*[a]	yield(%) *anti*[a]
37	Me	Me	73	70
38	Me	Ph	74	-----[b]
39	^iPr	Me	76	80
40	^iPr	Ph	81	-----[b]
41	Bn	Me	86	88
42	Bn	Ph	80	-----[b]

[a] *syn* and *anti* compounds are referred by **a** and **b** series, respectively. [b] not obtained



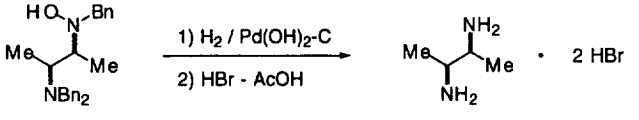
31a R = Me
35a R = Bn

16 R = Me
17 R = Bn

37a R = Me
41a R = Bn

Reagents and conditions: i) H_2, $Pd(OH)_2$-C, MeOH, r.t., 70 psi, 72 h. ii) Bo_2 O, Et_3N, DMAP, r.t., 16 h. iii) 8% HCl - MeOH, 5 °C, 30 min.

Scheme 6.



18 **37a**

Reagents and conditions: i) H_2, $Pd(OH)_2$-C, MeOH, r.t., 70 psi, 72 h. ii) 30% HBr, AcOH, 5 °C, 1 h

Scheme 7.

Conclusions

In summary we have demonstrated that the addition of Grignard reagents to α-amino nitrones shows moderate to extremely high levels of 1,2-asymmetric induction leading to *syn* α-amino hydroxylamines. In addition, this novel methodology should be generally applicable to other α-amino nitrones providing new access to unsymmetrical 1,2-diamines. This provides further evidence of the synthetic potential of nitrones in organic synthesis. A considerable expansion of the scope of this methodology would be to exert a control on the *syn*- and *anti*- addition of the organometallic reagents. Results of our efforts in this direction will be provided in due course.

Experimental section

General methods

All moisture-sensitive reactions were performed under an argon atmosphere using oven-dried glassware. Solvents were dried over standard drying agents[37] and freshly distilled prior to use. Melting points are uncorrected. ^1H and ^{13}C NMR spectra were recorded on a 300 Varian Unity spectrometer at room temperature, unless otherwise specified. Chemical shifts are given in parts per million downfield

from tetramethylsilane. Optical rotations were measured using a Perkin Elmer 214 polarimeter with a thermally jacketed 10 cm cell at 25°C (concentration C given as g/100 mL) and CD spectra on a Jasco J-710 spectrometer. IR spectra were recorded in nujol or chloroform and measured in cm^{-1}, using a Perkin–Elmer 1600 FT-IR infrared spectrophotometer; only representative bands being given. Elemental analyses were performed on a 1106 Microanalyzer Carlo Erba. All reactions were monitored by TLC on silica gel plates (Merck Kiesel gel 60 F254) and visualized by spraying with either 1 M aqueous $KMnO_4$ or a solution of 2,4-dinitrophenylhydrazine in methanolic sulfuric acid and heated. Flash column chromatography was performed on silica gel 60 F254.[38] Methylmagnesium bromide and phenylmagnesium bromide were used in THF from 1.0 M commercial solutions.

Synthesis of α-amino nitrones. General procedure

To a well-stirred solution of the corresponding α-amino aldehyde[16,21] (20 mmol) in dichloromethane (200 ml), anhydrous magnesium sulfate (3.61 g, 30 mmol) and N-benzylhydroxylamine[15] (2.46 g, 20 mmol) were added sequentially and the resulting mixture was stirred at 20°C for 4 h. The reaction mixture was filtered and the filtrate rotatory evaporated to yield the crude product which was purified by column chromatography on silica gel to yield the pure nitrones (eluent is given in brackets for each compound).

(Z)-N-[(2S)-2-(tert-Butoxycarbonylamino)propylidene] benzylamine N-oxide ***4***

(EtOAc; R_f=0.24) (4.62 g, 83%); mp 94–96°C; $[\alpha]_D$ +3.9 (c 1.2, $CHCl_3$); IR ν 1605; ^{1}H NMR ($CDCl_3$, 55°C) δ 1.37 (d, 3H, J=7.3 Hz); 1.39 (s, 9H), 4.50 (m, 1H), 4.84 (s, 2H), 5.75 (bs, 1H), 6.77 (d, 1H, J=5.7 Hz), 7.35 (m, 5H); ^{13}C NMR ($CDCl_3$, 55°C) δ 16.19, 28.30, 44.24, 69.48, 79.60, 128.95, 128.99, 129.18, 132.57, 139.11, 155.22. Anal. Calcd for $C_{15}H_{22}N_2O_3$: C, 64.73; H, 7.97; N, 10.06. Found: C, 64.55; H, 8.22; N, 10.09.

(Z)-N-[(2S)-2-(tert-Butoxycarbonylamino)-3-methylbutylidene] benzylamine N-oxide ***5***

(Et_2O; R_f=0.30) (5.39 g, 88%); mp 128–129°C; $[\alpha]_D$ +6.6 (c 0.65, $CHCl_3$); IR ν 1608; ^{1}H NMR ($CDCl_3$, 55°C) δ 0.87 (d, 3H, J=6.8 Hz), 0.91 (d, 3H, J=6.8 Hz), 1.40 (s, 9H), 2.27 (dq, 1H, J=6.4, 6.8 Hz), 4.19 (dd, 1H, J=6.4, 6.2 Hz), 4.85 (s, 2H), 5.85 (bs, 1H), 6.7 (d, 1H, J=6.2 Hz), 7.36 (m, 5H); ^{13}C NMR ($CDCl_3$, 55°C) δ 18.93, 19.45, 28.26, 30.13, 54.16, 69.85, 79.29, 128.91, 129.13, 132.67, 137.39, 137.52, 155.70. Anal. Calcd for $C_{17}H_{26}N_2O_3$: C, 66.64; H, 8.55; N, 9.14. Found: C, 66.31; H, 8.74; N, 9.25.

(Z)-N-[(2S)-2-(tert-Butoxycarbonylamino)-3-phenylpropylidene] benzylamine N-oxide ***6***

(Et_2O; R_f=0.34) (6.03 g, 85%); mp 150–152°C; $[\alpha]_D$ +10.8 (c 0.54, $CHCl_3$); IR ν 1580; ^{1}H NMR ($CDCl_3$, 55°C) δ 1.37 (s, 9H), 3.02 (dd, 1H, J=13.0, 6.8 Hz), 3.13 (dd, 1H, J=13.0, 7.2 Hz), 4.60 (ddd, 1H, J=7.2, 6.8, 5.5 Hz), 4.80 (s, 2H), 5.80 (s, 1H), 6.66 (d, 1H, J=5.5 Hz), 7.00–7.12 (m, 2H), 7.23–7.40 (m, 8H); ^{13}C NMR ($CDCl_3$, 55°C) δ 28.25, 36.20, 49.80, 69.69, 79.62, 126.63, 128.46, 128.88, 129.06, 129.16, 129.36, 132.35, 137.26, 155.30. Anal. Calcd for $C_{21}H_{26}N_2O_3$: C, 71.16; H, 7.39; N, 7.90. Found: C, 71.42; H, 7.37; N, 8.02.

(Z)-N-[(2S)-2-(N-Benzyl-tert-butoxycarbonylamino)propylidene] benzylamine N-oxide ***13***

(Hexane:diethyl ether, 4:1; R_f=0.40) (5.60 g, 76%); mp 51–53°C; $[\alpha]_D$ +3.3 (c 0.80, $CHCl_3$); IR ν 1590; ^{1}H NMR ($CDCl_3$, 55°C) δ 1.21 (d, 3H, J=7.0 Hz), 1.36 (s, 9H), 4.30 (d, 1H, J=14.5 Hz), 4.50 (dq, 1H, J=7.0, 6.2 Hz), 4.62 (d, 1H, J=14.5 Hz), 4.70 (s, 2H), 6.80 (d, 1H, J=6.2 Hz), 7.25–7.29 (m, 10H); ^{13}C NMR ($CDCl_3$, 55°C) δ 18.03, 28.26, 58.00, 68.88, 71.80, 80.22, 127.14, 127.50, 127.62, 128.35, 128.80, 129.09, 129.21, 136.84, 138.62, 154.50. Anal. Calcd for $C_{22}H_{28}N_2O_3$: C, 71.71; H, 7.66; N, 7.60. Found: C, 71.55; H, 7.81; N, 7.33.

(Z)-N-[(2S)-2-(N-Benzyl-tert-butoxycarbonylamino)-3-phenylpropylidene] benzylamine N-oxide ***14***

(Hexane:diethyl ether, 1:4; R_f=0.32) (6.22 g, 70%); mp 115–116°C; $[\alpha]_D$ −6.0 (c 0.44, $CHCl_3$); IR ν 1605; ^{1}H NMR ($CDCl_3$, 55°C) δ 1.40 (s, 9H), 2.90–3.12 (m, 2H), 4.38 (d, 1H, J=14.1 Hz), 4.51 (m, 1H), 4.64 (d, 1H, J=14.1 Hz), 4.99 (s, 2H), 6.61 (d, 1H, J=6.8 Hz); 7.30–7.50 (m, 15H); ^{13}C NMR ($CDCl_3$, 55°C) δ 21.11, 28.41, 58.05, 69.15, 71.24, 80.41, 126.55, 127.24, 127.76, 128.45, 128.50, 128.63, 128.98, 129.19, 129.24, 130.48, 133.21, 134.28, 138.41, 154.60. Anal. Calcd for $C_{28}H_{32}N_2O_3$: C, 75.65; H, 7.26; N, 6.30. Found: C, 75.88; H, 7.09; N, 6.13.

(Z)-N-[(2S)-2-(Dibenzylamino)propylidene] benzylamine N-oxide ***15***

(Hexane:diethyl ether, 1:4; R_f=0.20) (4.88 g, 68%); oil; $[\alpha]_D$ +52.9 (c 1.5, $CHCl_3$); IR ν 1590; ^{1}H NMR ($CDCl_3$, 55°C) δ 1.10 (d, 3H, J=6.8 Hz), 3.6 (d, 2H, J=13.9 Hz), 3.71 (d, 2H, J=13.9 Hz), 4.26 (dq, 1H, J=6.8, 6.6 Hz), 4.78 (d, 1H, J=13.7 Hz), 4.80 (d, 1H, J=13.7 Hz), 6.70 (d, 1H, J=6.6 Hz), 7.20–7.50 (m, 15H); ^{13}C NMR ($CDCl_3$, 55°C) δ 13.82, 15.07, 52.02, 54.70, 65.59, 69.39, 126.73, 126.78, 127.96, 128.02, 128.16, 128.38, 128.62, 128.66, 128.80, 132.87, 139.29, 140.75. Anal. Calcd for $C_{24}H_{26}N_2O$: C, 80.41; H, 7.31; N, 7.81. Found: C, 80.76; H, 7.08; N, 7.95.

Addition of Grignard reagents to α-amino nitrones. General procedure

To a cold solution (−50°C) of the corresponding nitrone (5 mmol) in THF (30 ml), a solution of Grignard reagent (15 mmol, 15 ml of a 1.0 M solution in THF) was added under Ar atmosphere. The rate of the addition was adjusted so as to keep the temperature of the mixture below −40°C. The reaction mixture was stirred at −40°C for 4 h, then saturated aqueous ammonium chloride (30 ml) was added, and the mixture was allowed to warm to ambient temperature. The layers were separated, and the aqueous layer was extracted with diethyl ether (2×25 ml). The combined organic extracts were dried ($MgSO_4$) and concentrated. Chromatography of the residue on silica gel gave pure hydroxylamines **7–12** (eluent is given in brackets for each compound).

(2S,3S)-N^2-Benzyl-3-(tert-butoxycarbonylamino)-2-(hydroxyamino)butane ***7a***

(Hexane:diethyl ether, 4:1; R_f=0.36) (0.81 g, 55%); mp 122–124°C; $[\alpha]_D$ −11.9 (c 0.95, $CHCl_3$); IR ν 3602, 3420, 1686, 1264; ^{1}H NMR ($CDCl_3$, 55°C) δ 1.11 (d, 3H, J=6.3 Hz), 1.13 (d, 3H, J=6.9 Hz), 1.45 (s, 9H), 2.37 (dq, 1H, J=6.9, 2.6 Hz), 3.67 (m, 1H), 3.68 (d, 1H, J=13.6 Hz), 4.00 (d, 1H, J=13.6 Hz), 4.45 (d, 1H, J=9.5 Hz), 5.90 (bs, 1H), 7.12–7.39 (m, 5H); ^{13}C NMR ($CDCl_3$, 55°C) δ 8.58, 18.30, 28.56, 49.66, 60.20, 65.74, 79.47, 126.89, 128.14, 128.72, 138.60, 157.40. Anal. Calcd for $C_{16}H_{26}N_2O_3$: C, 65.28; H, 8.90; N, 9.52. Found: C, 65.39; H, 8.75; N, 9.59.

X-Ray crystallographic data of compound **7a**: $C_{16}H_{26}N_2O_3$, monoclinic, space group $P2_1$, a=6.358(5), b=10.463(5), c=12.842(5) Å, β=94.57(5)° (from 38 orientation reflections, 10.10°<θ<25.03°), V=851.6(9) Å^3, Z=2, D_{calcd}=1.148 g/cm^3, F(000)=320, μ=0.079 (MoKα radiation, λ=0.71069 A). Intensity data were recorded on a Siemens P4 diffractometer (θ–2θ scans, θ_{max}=25.5°). The intensities of the three standard reflections remeasured every 97 reflections during data collection to monitor crystal stability, indicated a decay of 7.24%. From a total of 1841 measurements those 1458 reflections with I>2σ(I) were retained for the analysis. The crystal structure was solved by direct methods (SIR-92, Giacovazzo). All non-hydrogen atoms were refined anisotropically and the hydrogen atoms at calculated positions. The final cycle of full-matrix least-squares refinement was based on 1749 observed reflections and 195 variable parameters with 1 restraint, and converged with agreement factors of: R=0.050, wR_2=0.129, S=1.055. Crystallographic calculations were performed on a Micro-Vax Alpha using SHELXL-93 software (Sheldrick, 1993). In the least-square iterations, $w=1/[\sigma^2(Fo^2)+(0.0889P)^2]$, $P=(Fo^2-2Fc^2)/3$ was minimized.

(2R,3S)-N^2-Benzyl-3-(tert-butoxycarbonylamino)-2-(hydroxyamino)butane ***7b***

(Hexane:diethyl ether, 4:1; R_f=0.21) (0.41 g, 28%); mp 114–116°C; $[\alpha]_D$ −38.6 (c 0.59, $CHCl_3$); IR ν 3595, 3400, 1660, 1241; ^{1}H NMR ($CDCl_3$, 55°C) δ 1.08 (d, 3H, J=6.5 Hz), 1.15 (d, 3H, J=6.5

Hz), 1.43 (s, 9H), 2.80 (m, 1H), 3.80 (d, 1H, J=14.0 Hz), 4.12 (m, 1H), 4.15 (d, 1H, J=14.0 Hz), 4.66 (bs, 1H), 6.80 (bs, 1H), 7.20–7.51 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 10.15, 17.76, 28.46, 48.11, 60.56, 65.31, 79.33, 126.80, 128.07, 128.81, 138.95, 156.43. Anal. Calcd for $C_{16}H_{26}N_2O_3$: C, 65.28; H, 8.90; N, 9.52. Found: C, 65.53; H, 8.99; N, 9.68.

(1S,2S)-N^1-Benzyl-2-(tert-butoxycarbonylamino)-1-(hydroxyamino)-1-phenylpropane ***8a***

(Hexane:diethyl ether, 4:1; R_f=0.28) (1.51 g, 85%); mp 151–153°C; $[\alpha]_D$ −10.1 (c 0.54, $CHCl_3$); IR ν 3600, 3380, 1680, 1245; ^{1}H NMR ($CDCl_3$) δ 0.95 (d, 3H, J=6.8 Hz), 1.56 (s, 9H), 3.20 (d, 1H, J=9.9 Hz), 3.60 (s, 2H), 4.33 (m, 1H), 4.52 (d, 1H, J=8.5 Hz), 6.81 (bs, 1H), 7.23–7.43 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 18.31, 28.43, 47.56, 60.28, 75.89, 79.78, 127.06, 127.96, 128.02, 128.43, 128.68, 130.06, 136.42, 138.76, 157.64. Anal. Calcd for $C_{21}H_{28}N_2O_3$: C, 70.76; H, 7.92; N, 7.86. Found: C, 70.82; H, 7.83; N, 8.14.

(2S,3S)-N^2-Benzyl-3-(tert-butoxycarbonylamino)-2-(hydroxyamino)-4-methylpentane ***9a***

(Hexane:diethyl ether, 4:1; R_f=0.35) (0.79 g, 49%); mp 123–124°C; $[\alpha]_D$ −51.3 (c 0.24, $CHCl_3$, 55°C); IR ν 3608, 3432, 1677, 1242; ^{1}H NMR ($CDCl_3$) δ 0.74 (d, 3H, J=6.8 Hz), 1.00 (d, 3H, J=6.8 Hz), 1.12 (d, 3H, J=6.3 Hz), 1.47 (s, 9H), 1.99 (dq, 1H, J=6.8, 3.9 Hz), 2.56 (dq, 1H, J=6.3, 3.6 Hz), 3.52 (ddd, 1H, J=10.2, 3.9, 3.6 Hz), 3.71 (d, 1H, J=13.7 Hz), 4.01 (d, 1H, J=13.7 Hz), 4.46 (d, 1H, J=10.2 Hz), 6.01 (bs, 1H), 7.20–7.40 (m, 5H); ^{13}C NMR ($CDCl_3$, 55°C) δ 8.29, 15.25, 20.80, 27.11, 28.43, 58.15, 60.05, 62.26, 79.37, 126.76, 128.04, 128.49, 138.97, 158.45. Anal. Calcd for $C_{18}H_{30}N_2O_3$: C, 67.05; H, 9.38; N, 8.69. Found: C, 66.99; H, 9.56; N, 8.90.

X-Ray crystallographic data of compound **9a**: $C_{18}H_{30}N_2O_3$, monoclinic, space group C2, a=24.234(3), b=10.051(1), c=16.179(2) Å, β=90.47(10)° (from 40 orientation reflections, 10.16°<θ<24.59°), V=3940.7(8) Å^3, Z=8, D_{calcd}=1.087 g/cm^3, F(000)=1408, μ=0.074 (MoKα radiation, λ=0.71069 A). Intensity data were recorded on a Siemens P4 diffractometer (θ–2θ scans, θ_{max}=24.0°). The intensities of the three standard reflections remeasured every 97 reflections during data collection to monitor crystal stability, indicated a decay of 5.09%. From a total of 3624 measurements those 1989 reflections with I>2σ(I) were retained for the analysis. The crystal structure was solved by direct methods (SHELXS-86, Sheldrick). All non-hydrogen atoms were refined anisotropically and the hydrogen atoms at calculated positions. The final cycle of full-matrix least-squares refinement was based on 3164 observed reflections and 422 variable parameters with 1 restraint, and converged with agreement factors of: R=0.061, wR_2=0.131, S=1.077. Crystallographic calculations were performed on a Micro-Vax Alpha using SHELXL-93 software (Sheldrick, 1993). In the least-square iterations, $w=1/[\sigma^2(Fo^2)+(0.0814P)^2]$, $P=(Fo^2-2Fc^2)/3$ was minimized.

(2R,3S)-N^2-Benzyl-3-(tert-butoxycarbonylamino)-2-(hydroxyamino)-4-methylpentane ***9b***

(Hexane:diethyl ether, 4:1; R_f=0.19) (0.53 g, 33%); oil; $[\alpha]_D$ −27.6 (c 1.43, $CHCl_3$); IR ν 3603, 3429, 1680, 1246; ^{1}H NMR ($CDCl_3$, 55°C) δ 0.94 (d, 3H, J=6.8 Hz), 0.97 (d, 3H, J=6.6 Hz), 0.99 (d, 3H, J=6.6 Hz), 1.47 (s, 9H), 1.70 (dq, 1H, J=6.6, 3.9 Hz), 2.87 (dq, 1H, J=6.6, 3.9 Hz), 3.61 (d, 1H, J=13.8 Hz), 3.80 (pseudo dt, 1H, J=10.5, 3.9 Hz), 4.09 (d, 1H, J=13.8 Hz), 4.39 (d, 1H, J=10.5 Hz), 6.51 (bs, 1H), 7.23–7.40 (m, 5H); ^{13}C NMR ($CDCl_3$, 55°C) δ 10.22, 19.70, 19.85, 28.36, 29.64, 57.33, 59.47, 62.16, 79.45, 126.58, 127.94, 128.48, 139.33, 157.45. Anal. Calcd for $C_{18}H_{30}N_2O_3$: C, 67.05; H, 9.38; N, 8.69. Found: C, 67.01; H, 9.09; N, 8.85.

(1S,2S)-N^1-Benzyl-3-(tert-butoxycarbonylamino)-2-(hydroxyamino)-3-methyl-1-phenylbutane ***10a***

(Hexane:diethyl ether, 4:1; R_f=0.25) (1.65 g, 86%); mp 174–176°C; $[\alpha]_D$ −16.5 (c 0.63, $CHCl_3$); IR ν 3596, 3428, 1684, 1268; ^{1}H NMR ($CDCl_3$) δ 0.66 (d, 3H, J=7.1 Hz), 0.90 (d, 3H, J=7.1 Hz), 1.54 (s, 9H), 1.58 (m, 1H), 3.38 (d, 1H, J=10.5 Hz), 3.53 (d, 1H, J=13.9 Hz), 3.61 (d, 1H, J=13.9 Hz), 4.19 (pseudo dt, 1H, J=10.5, 2.5 Hz), 4.60 (d, 1H, J=10.5 Hz), 6.76 (bs, 1H), 7.20–7.40 (m, 10H);

^{13}C NMR ($CDCl_3$) δ 14.60, 20.78, 26.78, 28.47, 56.13, 60.32, 72.80, 79.90, 126.63, 127.60, 127.94, 128.05, 128.34, 130.10, 136.01, 138.86, 158.78. Anal. Calcd for $C_{23}H_{32}N_2O_3$: C, 71.84; H, 8.39; N, 7.29. Found: C, 72.14; H, 8.05; N, 7.50.

(2S,3S)-N^3-Benzyl-2-(tert-butoxycarbonylamino)-3-(hydroxyamino)-1-phenylbutane ***11a***

(Hexane:diethyl ether, 4:1; R_f=0.62) (1.02 g, 55%); mp 120–122°C; $[\alpha]_D$ −59.1 (c 0.20, $CHCl_3$); IR ν 3600, 3408, 1681, 1258; ^{1}H NMR ($CDCl_3$) δ 1.20 (d, 3H, J=6.4 Hz), 1.39 (s, 9H), 2.55 (m, 1H), 2.68 (dd, 1H, J=13.9, 7.2 Hz), 3.04 (dd, 1H, J=13.9, 5.9 Hz), 3.64 (d, 1H, J=13.6 H), 3.20 (m, 1H), 4.00 (d, 1H, J=13.6 Hz), 4.70 (d, 1H, J=8.5 Hz), 5.40 (bs, 1H), 7.11–7.40 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 9.03, 28.50, 37.99, 55.54, 60.92, 62.33, 79.37, 126.38, 127.11, 128.28, 128.45, 128.92, 129.37, 130.30, 138.50, 155.32. Anal. Calcd for $C_{22}H_{30}N_2O_3$: C, 71,32; H, 8.16; N, 7.56. Found: C, 71.24; H, 8.04; N, 7.36.

(2S,3R)-N^3-Benzyl-2-(tert-butoxycarbonylamino)-3-(hydroxyamino)-1-phenylbutane ***11b***

(Hexane:diethyl ether, 4:1; R_f=0.50) (0.61 g, 33%); mp 115–117°C; $[\alpha]_D$ −40.0 (c 0.43, $CHCl_3$); IR ν 3602, 3416, 1680, 1241; ^{1}H NMR ($CDCl_3$) δ 1.08 (d, 3H, J=6.6 Hz), 1.39 (s, 9H), 2.76 (m, 3H), 3.63 (d, 1H, J=13.2 Hz), 4.04 (d, 1H, J=13.2 Hz), 4.41 (m, 1H), 4.50 (d, 1H, J=9.5 Hz), 6.10 (bs, 1H), 7.11–7.40 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 10.35. 28.32, 33.14, 52.90, 59.95, 63.60, 79.61, 126.33, 126.81, 128.11, 128.44, 128.66, 129.08, 138.21, 138.99, 156.74. Anal. Calcd for $C_{22}H_{30}N_2O_3$: C, 71,32; H, 8.16; N, 7.56. Found: C, 71.14; H, 8.31; N, 7.37.

(1S,2S)-N^1-Benzyl-2-(tert-butoxycarbonylamino)-1,3-diphenyl-1-(hydroxyamino)propane ***12a***

(Hexane:diethyl ether, 4:1; R_f=0.31) (1.88 g, 87%); mp 179–181°C; $[\alpha]_D$ +0.8 (c 1.80, $CHCl_3$); IR ν 3599, 3420, 1685, 1246; ^{1}H NMR ($CDCl_3$) δ 1.45 (s, 9H), 2.37 (dd, 1H, J=14.5, 6.1 Hz), 2.54 (dd, 1H, J=14.5, 2.5 Hz), 3.65 (d, 1H, J=8.8 Hz), 3.61 (m, 1H), 3.63 (s, 2H), 4.50 (bs, 1H), 6.51 (bs, 1H), 7.12–7.37 (m, 15H); ^{13}C NMR ($CDCl_3$) δ 28.39, 37.26, 52.34, 60.53, 73.71, 80.04, 126.40, 127.91, 128.02, 128.28, 128.38, 128.54, 129.14, 129.55, 130.34, 135.83, 137.67, 138.59, 157.94. Anal. Calcd for $C_{27}H_{32}N_2O_3$: C, 74.97; H, 7.46; N, 6.48. Found: C, 75.30; H, 7.38; N, 6.16.

(2S,3S)-N^2,N^3-Dibenzyl-3-(tert-butoxycarbonylamino)-2-(hydroxyamino)butane ***16***

(Hexane:diethyl ether, 3:2; R_f=0.11) (0.73 g, 38%); oil; $[\alpha]_D$ −7.9 (c 1.10, $CHCl_3$); IR ν 3604, 1688, 1247; ^{1}H NMR ($CDCl_3$, 55°C) δ 0.85 (d, 3H, J=7.3 Hz), 1.15 (d, 3H, J=7.5 Hz), 1.35 (s, 9H), 2.50 (m, 1H), 3.59 (d, 1H, J=13.7 Hz), 3.99 (d, 1H, J=13.7 Hz), 4.02 (d, 1H, J=14.9 Hz), 4.30 (d, 1H, J=14.9 Hz), 4.35 (m, 1H), 6.24 (bs, 1H), 7.12–7.48 (m, 10H); ^{13}C NMR ($CDCl_3$, 55°C) δ 9.40, 10.10, 20.12, 37.42, 56.37, 63.14, 65.18, 80.12, 127.02, 127.24, 128.32, 128.50. 129.01, 129.03, 138.53, 142.27, 156.38. Anal. Calcd for $C_{23}H_{32}N_2O_3$: C, 71.84; H, 8.39; N, 7.29. Found: C, 72.77; H, 8.69; N, 7.03.

(2S,3S)-N^2,N^3-Dibenzyl-2-(tert-butoxycarbonylamino)-3-(hydroxyamino)-1-phenylbutane ***17***

(Hexane:diethyl ether, 4:1; R_f=0.51) (0.90 g, 39%); oil; $[\alpha]_D$ −8.7 (c 1.70, $CHCl_3$); IR ν 3607, 1676, 1239; ^{1}H NMR ($CDCl_3$, 55°C) δ 1.32 (s, 9H), 1.53 (d, 3H, J=6.8 Hz), 2.80 (m, 1H), 3.03 (m, 1H), 3.53 (d, 1H, J=13.5 Hz), 3.67 (d, 1H, J=13.5 Hz), 3.75 (d, 1H, J=13.5 Hz), 3.86 (m, 1H), 3.90 (d, 1H, J=13.5 Hz), 4.15 (m, 1H), 4.60 (bs, 1H), 7.00–7.08 (m, 2H), 7.10–7.40 (m, 13H); ^{13}C NMR ($CDCl_3$, 55°C) δ 8.90, 19.68, 28.20, 35.08, 59.95, 61.36, 67.18, 79.94, 126.97, 127.18, 127.76, 127.94, 128.11, 128.24, 128.35, 128.58, 128.79, 129.15, 138.56, 143.13, 155.80. Anal. Calcd for $C_{29}H_{36}N_2O_3$: C, 75.62; H, 7.88; N, 6.08. Found: C, 75.92; H, 7.85; N, 5.96.

(2S,3S)-N^2-Benzyl-3-(dibenzylamino)-2-(hydroxyamino)butane ***18***

(Hexane:diethyl ether, 9:1; R_f=0.22) (0.45 g, 24%); oil; $[\alpha]_D$ −5.1 (c 0.20, $CHCl_3$); IR ν 3340; ^1H NMR ($CDCl_3$, 55°C) δ 0.92 (d, 3H, J=6.8 Hz), 1.10 (d, 3H, J=6.8 Hz), 2.97 (dq, 1H, J=8.8, 6.8 Hz), 3.22 (dq, 1H, J=8.8, 6.8 Hz), 3.30 (d, 1H, J=13.1 Hz), 3.51 (d, 2H, J=13.0 Hz), 3.60 (d, 2H, J=13.0 Hz), 3.88 (d, 1H, J=13.1 Hz), 5.80 (bs, 1H), 7.25–7.42 (m, 15H); ^{13}C NMR ($CDCl_3$, 55°C) δ 8.91, 8.94, 36.42, 41.24, 60.52, 66.34, 126.93, 127.19, 128.12, 128.43, 128.80, 129.04, 138.60, 139.37.. Anal. Calcd for $C_{25}H_{30}N_2O$: C, 80.17; H, 8.07; N, 7.48. Found: C, 80.20; H, 8.29; N, 7.73.

Deoxygenation of α-amino hydroxylamines. Synthesis of diamines ***19–24***

To a solution of copper(II) acetate (45 mg, 0.3 mmol) in acetic acid (4 ml), Zn dust (4.0 g, 15.3 mmol) was added and the mixture was stirred at ambient temperature for 15 min under Ar atmosphere. A solution of the hydroxylamine (3 mmol) in acetic acid (4 ml) and water (1.5 ml) was added and the resulting mixture was heated at 70°C for 1 h. After cooling at 20°C the disodium salt of EDTA (3.0 g) was added and the solution was made alkaline (pH=10) by the addition of 3 M aqueous NaOH. The resulting solution was extracted with EtOAc (3×25 ml); the combined organic extracts were washed with saturated aqueous EDTA (40 ml) and brine (30 ml). The organic layer was dried ($MgSO_4$) and the solvent evaporated under reduced pressure. The crude diamines were purified by column chromatography on silica gel (eluent is given in brackets for each compound).

(2S,3S)-2-Benzylamino-3-(tert-butoxycarbonylamino)butane ***19***

(Hexane:diethyl ether, 1:3) (0.693 g, 83%); oil; $[\alpha]_D$ −2.7 (c 0.86, $CHCl_3$); IR ν 3320, 1682, 1245; ^1H NMR ($CDCl_3$) δ 1.03 (d, 3H, 6.6 Hz), 1.10 (d, 3H, 6.8 Hz), 1.41 (s, 9H), 1.70 (bs, 1H, ex. D_2O), 2.70 (m, 1H), 3.60 (m, 1H), 3.64 (d, 1H, J=13.0 Hz), 3.80 (d, 1H, J=13.0 Hz), 4.73 (bs 1H), 7.30–7.36 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 17.06, 17.88, 28.42, 50.36, 51.67, 56.22, 79.03, 127.00, 128.14, 128.40, 140.40, 157.70 Anal. Calcd for $C_{16}H_{26}N_2O_2$: C, 69.03; H, 9.41; N, 10.06. Found: C, 69.33; H, 9.36; N, 10.18.

(1S,2S)-1-Benzylamino-2-(tert-butoxycarbonylamino)-1-phenylpropane ***20***

(Hexane:diethyl ether, 1:4) (0.899 g, 88%); oil; $[\alpha]_D$ −12.6 (c 1.24, $CHCl_3$); IR ν 3382, 1678, 1232; ^1H NMR ($CDCl_3$+D_2O, 55°C) δ 0.90 (d, 3H, J=6.7 Hz), 1.51 (s, 9H), 3.20 (d, 1H, J=9.7 Hz), 3.58 (d, 1H, J=13.4 Hz), 3.61 (d, 1H, J=13.4 Hz), 4.30 (m, 1H), 4.50 (bd, 1H, J=9.2 Hz), 7.31–7.45 (m, 10H); ^{13}C NMR ($CDCl_3$+D_2O, 55°C) δ 18.42, 28.43, 47.63, 60.32, 75.94, 79.90, 126.72, 127.08, 126.76, 128.08, 128.44, 130.11, 136.42, 138.80, 153.70 Anal. Calcd for $C_{21}H_{28}N_2O_2$: C, 74.08; H, 8.29; N, 8.23. Found: C, 74.25; H, 8.42; N, 8.17.

(2S,3S)-2-Benzylamino-3-(tert-butoxycarbonylamino)-4-methylpentane ***21***

(Hexane:diethyl ether, 2:3) (0.735 g, 80%); oil; $[\alpha]_D$ −16.6 (c 0.23, $CHCl_3$); IR ν 3312, 1678, 1244; ^1H NMR ($CDCl_3$) δ 0.87 (d, 3H, J=6.8 Hz), 0.88 (d, 3H, J=6.8 Hz), 1.09 (d, 3H, J=6.4 Hz), 1.40 (s, 9H), 1.60 (bs, 1H, ex. D_2O), 1.76 (m, 1H), 2.86 (dq, 1H, J=3.2, 6.4 Hz), 3.17 (ddd, 1H, J=3.2, 6.8, 10.0 Hz), 3.65 (d, 1H, J=12.9 Hz), 3.86 (d, 1H, J=12.9 Hz), 4.77 (d, 1H, J=10.0 Hz), 7.29–7.40 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 18.19, 18.96, 19.90, 28.41, 30.20, 51.63, 52.30, 60.91, 78.70, 127.02, 128.19, 128.39, 140.51, 156.66 Anal. Calcd for $C_{18}H_{30}N_2O_2$: C, 70.55; H, 9.87; N, 9.14. Found: C, 70.43; H, 10.02; N, 8.99.

(1S,2S)-1-Benzylamino-2-(tert-butoxycarbonylamino)-3-methyl-1-phenybutane ***22***

(Hexane:diethyl ether, 2:3) (0.807 g, 73%); oil; $[\alpha]_D$ −44.1 (c 0.23, $CHCl_3$); IR ν 3405, 1671, 1233; ^1H NMR ($CDCl_3$) δ 0.76 (d, 3H, J=6.8 Hz), 0.95 (d, 3H, J=6.8 Hz), 1.38 (s, 9H), 1.61 (bs, 1H, ex. D_2O), 1.70 (m, 1H), 3.50 (d, 1H, J=13.3 Hz), 3.60 (d, 1H, J=7.0 Hz), 3.74 (m, 1H), 3.66 (d, 1H, J=13.3 Hz), 4.20 (bd, 1H, J=8.3 Hz), 7.26–7.38 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 17.27, 20.66,

28.21, 29.60, 51.01, 59.39, 63.13, 78.73, 127.17, 127.45, 128.08, 128.20, 128.70, 129.78, 140.37 (2C), 156.05. Anal. Calcd for $C_{23}H_{32}N_2O_2$: C, 74.96; H, 8.75; N, 7.60. Found: C, 75.03; H, 8.91; N, 7.66.

(2S,3S)-2-Benzylamino-3-(tert-butoxycarbonylamino)-4-phenylbutane ***23***

(Hexane:diethyl ether, 3:2) (0.861 g, 81%); oil; $[\alpha]_D$ −14.3 (c 0.23, $CHCl_3$); IR ν 3399, 1684, 1260; ^{1}H NMR ($CDCl_3$) δ 1.05 (d, 3H, J=6.8 Hz), 1.39 (s, 9H), 1.91 (bs, 1H, ex. D_2O), 2.70 (dq, 1H, J=3.1, 6.8 Hz), 2.80 (m, 2H), 3.62 (d, 1H, J=13.3 Hz), 3.78 (m, 1H), 3.84 (d, 1H, J=13.3 Hz), 4.88 (bd, 1H, J=9.2 Hz), 7.30–7.40 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 17.83, 28.31, 38.55, 51.82, 53.14, 56.28, 79.00, 126.16, 127.10, 128.34 (2C), 128.45, 129.22, 138.60, 140.34, 155.88. Anal. Calcd for $C_{22}H_{30}N_2O_2$: C, 74.54; H, 8.53; N, 7.90. Found: C, 74.68; H, 8.47; N, 7.71.

(1S,2S)-1-Benzylamino-2-(tert-butoxycarbonylamino)-1,3-diphenylpropane ***24***

(Hexane:diethyl ether, 1:4) (1.00 g, 80%); oil; $[\alpha]_D$ −7.8 (c 0.95, $CHCl_3$); IR ν 3375, 1680, 1258; ^{1}H NMR ($CDCl_3$) δ 1.36 (s, 9H), 1.70 (bs, 1H, ex. D_2O), 2.50 (dd, 1H, J=8.6, 14.0 Hz), 2.81 (dd, 1H, J=5.5, 14.0 Hz), 3.42 (d, 1H, J=13.1 Hz), 3.62 (d, 1H, J=13.1 Hz), 3.70 (d, 1H, J=3.7 Hz), 3.98 (m, 1H), 4.60 (bd, 1H, J=9.1 Hz), 7.29–7.41 (m, 15H); ^{13}C NMR ($CDCl_3$) δ 28.26, 37.80, 51.39, 56.88, 64.18, 79.22, 126.19, 126.96, 127.48, 128.00, 128.22, 128.30, 128.36, 128.47, 129.18, 138.36, 140.35, 140.90, 155.63. Anal. Calcd for $C_{27}H_{32}N_2O_2$: C, 77.85; H, 7.74; N, 6.72. Found: C, 77.73; H, 7.86; N, 6.59.

Synthesis of N,N′-bis(tert-butoxycarbonyl)-1,2-diamines ***31–36***

A mixture of the hydroxylamine (3 mmol) was hydrogenated as described above. The residue was taken up in acetonitrile (30 ml) and the resulting solution was treated with Boc_2O (0.98 g, 4.5 mmol), triethylamine (0.30 g, 3 mmol) and N,N-dimethyl-aminopyridine (6.1 mg, 0.05 mmol). The reaction mixture was stirred at ambient temperature for 16 h at which time the solvent was distilled and the residue was partitioned between dichloromethane (50 ml) and saturated aqueous ammonium chloride (50 ml). The organic layer was separated, dried ($MgSO_4$) and evaporated under reduced pressure to yield the crude products which were purified by column chromatography (eluent is given in brackets for each compound).

(2S,3S)-2,3-Bis-(tert-butoxycarbonylamino)butane ***31a***

(Hexane:diethyl ether, 4:1; R_f=0.28); (0.744 g, 86%); mp 118–120°C; $[\alpha]_D$ −20.9 (c 1.50, $CHCl_3$); IR ν 3380, 1690, 1230; ^{1}H NMR ($CDCl_3$) δ 1.08 (d, 3H, J=6.3 Hz), 1.38 (s, 9H), 3.73 (m, 1H), 4.77 (bs, 1H); ^{13}C NMR ($CDCl_3$) δ 18.83, 28.36, 53.72, 79.11, 149.97, 156.14. Anal. Calcd for $C_{14}H_{28}N_2O_4$: C, 58.31; H, 9.79; N, 9.71. Found: C, 58.47; H, 9.65; N, 9.68.

meso-2,3-Bis-(tert-butoxycarbonylamino)butane ***31b***

(Hexane: diethyl ether, 4:1; R_f=0.10); (0.692 g, 80%); mp 114–116°C; IR ν 3386, 1681, 1242; ^{1}H NMR ($CDCl_3$) δ 1.00 (d, 3H, J=7.5 Hz), 1.42 (s, 9H), 3.65 (m, 1H), 4.81 (bs, 1H); ^{13}C NMR ($CDCl_3$) δ 16.73, 28.37, 50.56, 79.32, 155.34. Anal. Calcd for $C_{14}H_{28}N_2O_4$: C, 58.31; H, 9.79; N, 9.71. Found: C, 58.49; H, 9.90; N, 9.61.

(1S,2S)-1,2-Bis-(tert-butoxycarbonylamino)-1-phenylpropane ***32a***

(Hexane:diethyl ether, 3:2; R_f=0.55); (0.873 g, 83%); mp 117–119°C; $[\alpha]_D$ +7.3 (c 0.65, $CHCl_3$); IR ν 3400, 1686, 1233; ^{1}H NMR ($CDCl_3$) δ 0.94 (d, 3H, J=6.7 Hz), 1.38 (s, 9H), 1.45 (s, 9H), 3.93 (pseudo tq, 1H, J=9.0, 6.7), 4.37 (pseudo t, 1H, J=9.0 Hz), 4.73 (bs, 1H), 5.41 (bs, 1H), 7.11–7.39 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 19.10, 28.34, 29.57, 51.07, 61.60, 79.32, 79.48, 127.19, 127.55, 128.60, 140.70, 155.81, 156.37. Anal. Calcd for $C_{19}H_{30}N_2O_4$: C, 65.12; H, 8.63; N, 7.99. Found: C, 65.30; H, 8.51; N, 8.15.

(2S,3S)-2,3-Bis-(tert-butoxycarbonylamino)-4-methylpentane ***33a***

(Hexane:diethyl ether, 3:2; R_f=0.51); (0.446 g, 47%); oil; $[\alpha]_D$ −31.4 (c 1.20, $CHCl_3$); IR ν 3390, 1685, 1240; ^{1}H NMR ($CDCl_3$) δ 0.91 (d, 3H, J=6.7 Hz), 0.95 (d, 3H, J=6.8 Hz), 1.11 (d, 3H, J=6.9 Hz), 1.41 (s, 9H), 1.42 (s, 9H), 1.79 (m, 1H), 3.22 (m, 1H), 4.10 (m, 1H), 4.54 (bs, 1H), 4.73 (bs, 1H); ^{13}C NMR ($CDCl_3$) δ 16.94, 18.99, 19.39, 22.18, 28.32, 28.41, 48.33, 60.87, 79.05, 79.21, 155.91, 156.84. Anal. Calcd for $C_{16}H_{32}N_2O_4$: C, 60.73; H, 10.19; N, 8.85. Found: C, 60.81; H, 10.30; N, 8.69.

(2R,3S)-2,3-Bis-(tert-butoxycarbonylamino)-4-methylpentane ***33b***

(Hexane:diethyl ether, 3:2; R_f=0.46); (0.484 g, 51%); oil; $[\alpha]_D$ +23.9 (c 1.36, $CHCl_3$); IR ν 3396, 1688, 1238; ^{1}H NMR ($CDCl_3$) δ 0.92 (d, 3H, J=6.8 Hz), 0.97 (d, 3H, J=6.4 Hz), 1.05 (d, 3H, J=6.6 Hz), 1.45 (s, 9H), 1.46 (s, 9H), 1.61 (m, 1H), 3.40 (m, 1H), 3.80 (m, 1H), 4.31 (bs, 1H), 4.72 (bs, 1H); ^{13}C NMR ($CDCl_3$) δ 15.89, 18.29, 19.88, 22.53, 28.29, 28.37, 47.69, 60.21, 79.04, 79.40, 155.18, 156.38. Anal. Calcd for $C_{16}H_{32}N_2O_4$: C, 60.73; H, 10.19; N, 8.85. Found: C, 60.66; H, 10.08; N, 8.72.

(2S,3S)-2,3-Bis-(tert-butoxycarbonylamino)-1-phenylbutane ***35a***

(Hexane:diethyl ether, 3:2; R_f=0.54); (0.744 g, 68%); oil; $[\alpha]_D$ −31.5 (c 1.65, $CHCl_3$); IR ν 3391, 1686, 1245; ^{1}H NMR ($CDCl_3$) δ 1.13 (d, 3H, J=6.4 Hz), 1.42 (s, 9H), 1.46 (s, 9H), 2.83 (dd, 1H, J=14.8, 6.2 Hz), 3.11 (dd, 1H, J=14.8, 10.3 Hz), 4.05 (m, 1H), 4.35 (m, 1H), 5.23 (d, 1H, J=9.3 Hz), 5.65 (d, 1H, J=9.0 Hz), 7.13–7.28 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 19.12, 27.80, 27.93, 35.77, 48.36, 62.39, 82.16, 82.31, 128.10, 129.18, 129.36, 138.44, 153.83, 155.38. Anal. Calcd for $C_{20}H_{32}N_2O_4$: C, 65.91; H, 8.85; N, 7.69. Found: C, 66.09; H, 8.68; N, 7.41.

(2S,3R)-2,3-Bis-(tert-butoxycarbonylamino)-1-phenylbutane ***35b***

(Hexane:diethyl ether, 3:2; R_f=0.23); (0.689 g, 63%); oil; $[\alpha]_D$ −11.7 (c,1.78 $CHCl_3$); IR ν 3379, 1690, 1234; ^{1}H NMR ($CDCl_3$) δ 1.20 (d, 3H, J=6.4 Hz), 1.41 (s, 9H), 1.44 (s, 9H), 2.88 (dd, 1H, J=14.2, 4.0 Hz), 3.10 (dd, 1H, J=14.2, 10.6 Hz), 4.25 (m, 2H), 4.90 (bs, 1H), 5.01 (bs, 1H), 7.7.10–7.30 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 19.71, 27.87, 28.01, 35.30, 53.60, 60.99, 82.03, 82.24, 128.78, 130.86, 132.43, 139.03, 152.32, 153.69. Anal. Calcd for $C_{20}H_{32}N_2O_4$: C, 65.91; H, 8.85; N, 7.69. Found: C, 65.83; H, 8.71; N, 7.57.

(1S,2S)-1,2-Bis-(tert-butoxycarbonylamino)-1,3-diphenylpropane ***36a***

(Hexane:diethyl ether, 3:2; R_f=0.49); (0.793 g, 62%); oil; $[\alpha]_D$ −32.5 (c 0.20, $CHCl_3$); IR ν 3402, 1683, 1234; ^{1}H NMR ($CDCl_3$) δ 1.36 (s, 9H), 1.39 (s, 9H), 2.53 (dd, 1H, J=9.0, 14.4 Hz), 2.79 (dd, 1H, J=4.7, 14.4 Hz), 4.14 (m, 1H), 4.55 (pseudo t, 1H, J=8.1 Hz), 4.65 (bs, 1H), 5.41 (bs, 1H), 7.11–7.42 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 28.41, 29.68, 35.50, 53.71, 62.12, 79.50, 79.12, 127.21, 127.43, 128.70, 128.81, 129.12, 131.40, 139.81, 140.05, 155.78, 156.40. Anal. Calcd for $C_{25}H_{34}N_2O_4$: C, 70.40; H, 8.03; N, 6.57. Found: C, 70.61; H, 8.21; N, 6.48.

Synthesis of 1,2-diamines ***37–42***

A mixture of the hydroxylamine (3 mmol) and 20% palladium hydroxide on activated charcoal (Pearlman's catalyst) (50 mg) in MeOH (30 ml) was degassed under vacuum and saturated with hydrogen three times. The resulting suspension was stirred in a Parr hydrogenation apparatus at ambient temperature for 3 days under 70 psi, then filtered through a plug of Celite, and concentrated. The residue was treated with 8% hydrochloric acid in anhydrous methanol and the resulting solution was stirred at 5°C for 30 min under Ar atmosphere. The reaction mixture was concentrated at high vacuum without exceeding 15°C and the residue was triturated with diethyl ether. The resulting solid was collected by filtration under Ar atmosphere to afford, after drying under high vacuum, the bishydrochloride salts of the 1,2-diamines.

(2S,3S)-2,3-Diaminobutane bishydrochloride salt ***37a***

(0.353 g, 73%); mp 200–202°C; $[\alpha]_D$ −22.9 (c 0.8, MeOH); ^{1}H NMR (D_2O) δ 1.25 (d, 3H, J=6.7 Hz), 3.60 (m, 1H); ^{13}C NMR (D_2O/acetone-d_6) δ 12.09, 48.47. Anal. Calcd for $C_4H_{14}Cl_2N_2$: C, 29.83; H, 8.76; N, 17.39. Found: C, 29.95; H, 8.89; N, 17.50.

meso-2,3-Diaminobutane bishydrochloride salt ***37b***

(0.338 g, 70%); mp 209–210°C; ^{1}H NMR (D_2O) δ 1.29 (d, 3H, J=6.1 Hz), 3.50 (q, 1H, J=6.1 Hz); ^{13}C NMR (D_2O/acetone-d_6) δ 12.89, 48.15. Anal. Calcd for $C_4H_{14}Cl_2N_2$: C, 29.83; H, 8.76; N, 17.39. Found: C, 30.02; H, 8.66; N, 17.20.

(1S,2S)-1,2-Diamino-1-phenylpropane bishydrochloride salt ***38a***

(0.495 g, 74%); mp 203–205°C; $[\alpha]_D$ −19.9 (c 1.00, MeOH); ^{1}H NMR (D_2O) δ 1.14 (d, 3H, J=6.8 Hz), 3.91 (m, 1H), 4.50 (d, 1H, J=4.6 Hz), 7.20–7.40 (m, 5H); ^{13}C NMR (D_2O/acetone-d_6) δ 14.03, 49.30, 57.02, 128.10, 129.03, 129.40, 131.80. Anal. Calcd for $C_9H_{16}Cl_2N_2$: C, 48.44; H, 7.23; N, 12.55. Found: C, 48.33; H, 7.31; N, 12.68.

(2S,3S)-2,3-Diamino-4-methylpentane bishydrochloride salt ***39a***

(0.431 g, 76%); mp 209–211°C; $[\alpha]_D$ −6.3 (c 1.40, MeOH); ^{1}H NMR (D_2O) δ 0.88 (d, 3H, J=6.4 Hz), 0.95 (d, 3H, J=6.4 Hz), 1.21 (d, 3H, J=7.1 Hz), 1.80 (m, 1H), 2.31 (t, 1H, J=4.8 Hz), 3.12 (dq, 1H, J=7.1, 4.8 Hz); ^{13}C NMR (D_2O/acetone-d_6) δ 12.19, 16.04, 17.45, 27.00, 48.40, 58.29. Anal. Calcd for $C_6H_{18}Cl_2N_2$: C, 38.10; H, 9.59; N, 14.81. Found: C, 38.01; H, 9.43; N, 14.99.

(2R,3S)-2,3-Diamino-4-methylpentane bishydrochloride salt ***39b***

(0.454 g, 80%); mp 198–200°C; $[\alpha]_D$ −4.7 (c 1.04, MeOH); ^{1}H NMR (D_2O) δ 0.91 (d, 3H, J=6.8 Hz), 0.96 (d, 3H, J=6.8 Hz), 1.28 (d, 3H, J=6.9 Hz), 1.96 (m, 1H), 3.20 (pseudo t, 1H, J=6.0 Hz), 3.70 (dq, 1H, J=6.0, 6.8 Hz); ^{13}C NMR (D_2O/acetone-d_6) δ 13.55, 16.40, 18.93, 27.86, 46.88, 57.14. Anal. Calcd for $C_6H_{18}Cl_2N_2$: C, 38.10; H, 9.59; N, 14.81. Found: C, 38.34; H, 9.48; N, 14.69.

(1S,2S)-1,2-Diamino-3-methyl-1-phenylbutane bishydrochloride salt ***40a***

(0.610 g, 81%); mp 194–196°C; $[\alpha]_D$ −15.5 (c 0.74, MeOH); ^{1}H NMR (D_2O) δ 0.69 (d, 3H, J=6.6 Hz), 0.85 (d, 3H, J=6.6 Hz), 1.60 (m, 1H), 3.76 (dd, 1H, J=10.5, 2.4 Hz), 4.37 (d, 1H, J=10.5 Hz), 7.29–7.43 (m, 5H); ^{13}C NMR (D_2O/acetone-d_6) δ 12.28, 17.31, 25.81, 61.14, 64.28, 127.08, 128.19, 128.70, 130.12. Anal. Calcd for $C_{11}H_{20}Cl_2N_2$: C, 52.60; H, 8.02; N, 11.15. Found: C, 52.49; H, 8.18; N, 11.23.

(2S,3S)-2,3-Diamino-1-phenylbutane bishydrochloride salt ***41a***

(0.612 g, 86%); mp 199–201°C; $[\alpha]_D$ −43.9 (c 0.89, MeOH); ^{1}H NMR (D_2O) δ 1.40 (d, 3H, J=6.8 Hz), 2.76 (dd, 1H, J=11.2, 14.7 Hz), 3.10 (dd, 1H, J=3.2, 14.7 Hz), 3.71–3.80 (m, 2H), 7.29–7.40 (m, 5H); ^{13}C NMR (D_2O/acetone-d_6) δ 11.03, 30.93, 46.81, 52.73, 126.74, 127.93, 128.09, 132.56. Anal. Calcd for $C_{10}H_{18}Cl_2N_2$: C, 50.64; H, 7.65; N, 11.81. Found: C, 50.72; H, 7.77; N, 11.65.

(2S,3R)-2,3-Diamino-1-phenylbutane bishydrochloride salt ***41b***

(0.626 g, 88%); mp 204–206°C; $[\alpha]_D$ −7.6 (c 1.50, MeOH); ^{1}H NMR (D_2O) δ 1.36 (d, 3H, J=7.0 Hz), 2.85 (dd, 1H, J=9.1, 14.3 Hz), 3.05 (dd, 1H, J=6.1, 14.3 Hz), 3.60 (dq, 1H, J=3.9, 7.0 Hz), 3.78 (ddd, 1H, J=3.9, 6.1, 9.1 Hz), 7.21–7.39 (m, 5H); ^{13}C NMR (D_2O/acetone-d_6) δ 12.97, 35.31, 48.23, 57.56, 128.24, 129.56, 129.71, 135.89. Anal. Calcd for $C_{10}H_{18}Cl_2N_2$: C, 50.64; H, 7.65; N, 11.81. Found: C, 50.52; H, 7.48; N, 11.90.

(1S,2S)-1,2-Diamino-1,3-diphenylpropane bishydrochloride salt ***42a***

(0.718 g, 80%); mp 200–202°C; $[\alpha]_D$ −31.1 (c 0.17, MeOH); ^{1}H NMR (D_2O) δ 2.59 (dd, 1H, J=10.1, 14.4 Hz), 3.05 (dd, 1H, J=6.5, 14.4 Hz), 4.12 (m, 1H), 4.50 (d, 1H, J=10.6 Hz), 7.14–7.42 (m, 10H); ^{13}C NMR (D_2O/acetone-d_6) δ 35.80, 48.86, 52.75, 126.73, 128.00, 128.61, 129.20, 129.85, 130.62, 132.00, 136.12. Anal. Calcd for $C_{15}H_{20}Cl_2N_2$: C, 60.21; H, 6.74; N, 9.36. Found: C, 60.42; H, 6.82; N, 9.48.

(2S,3S)-2,3-Diaminobutane hydrobromide salt ***37a***

Catalytic hydrogenation of hydroxylamine **18** (0.374 mg, 1 mmol) as described above gave the crude diamine **37a** which was treated with a 30% solution of hydrobromic acid in acetic acid at 5°C. After stirring at 5°C for 1 h the solvent was distilled at high vacuum without exceeding 15°C. The residue was triturated with diethyl ether, filtered under Ar atmosphere and dried under high vacuum to afford 98 mg (39%) of the bishydrobromide salt of **37a**. mp 285–290°C (dec); $[\alpha]_D$ −8.0 (1.5, H_2O); [Lit.[9a] (for enantiomer): mp 288.4–290.8°C; $[\alpha]_D$ +8.17 (1.425, H_2O)]; ^{1}H NMR (D_2O) δ 1.39 (d, 3H, J=6.6 Hz), 3.77 (m, 1H); ^{13}C NMR (D_2O) δ 13.8, 50.3. Anal. Calcd for $C_4H_{14}Br_2N_2$: C, 19.22; H, 5.65; N, 11.21. Found: C, 19.45; H, 5.51; N, 11.43.

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