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Synthesis of Chiral C_2-Symmetric 1,2-Diamines by the Addition of Organolithium Reagents to *N*,*N*′-Bis[(*S*)-1-phenylethyl]ethanediimine

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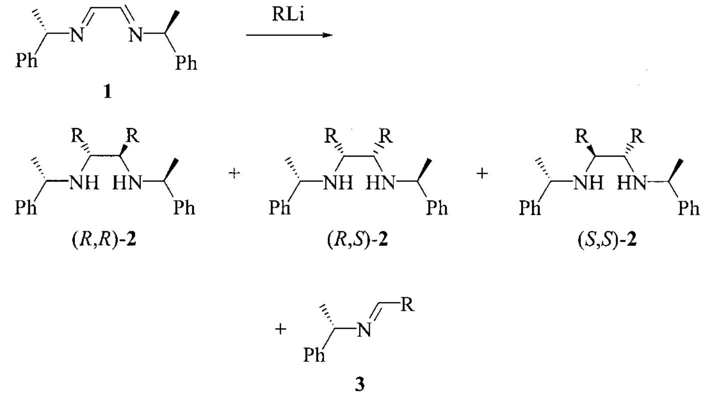
Abstract—The additions of alkyl-, phenyl- and vinyllithium reagents to *N*,*N*′-bis[(*S*)-1-phenylethyl]ethanediimine in THF at −78°C and in DME at −60°C gave high yields of 1,2-diamines with low stereocontrol. Care was taken to quench the reaction mixtures with de-aerated H_2O to avoid formation of *N*-alkylidene-1-phenylethylamines which were formed through homolysis of the dilithium 1,2-diamides to give α-amido radicals which reacted with O_2/H_2O in the quenching step. Pentadienyl-, cinnamyl- and 1-trimethylsilylallyllithium reagents gave only the linear 1,2-diamines with high yields and moderate to good diastereoselectivities. © 2000 Published by Elsevier Science Ltd.

Introduction

Enantiomerically pure 1,2-diamines, especially those having C_2-symmetry, have gained considerable importance in organic synthesis since they are used as reagents, bases or ligands in a large number of asymmetric reactions, most importantly transition metal-catalysed ones,[1,2] and as medicinal agents.[3–6] Among the several methods allowing the asymmetric synthesis of these compounds, the double addition of organometallic reagents to the 1,2-bis-imine **1** derived from glyoxal and 2 equiv. of an optically pure amine (chiral auxiliary) is particularly appealing. Up to now, 1-phenylethylamine has been almost the only chiral auxiliary used,[†] see the 1,2-bis-imine **1** in Scheme 1, because it provides stereocontrol at a high degree, and is inexpensive, available in both enantiomeric forms and easily removed by hydrogenolysis. However, a limited number of 1,2-diamines **2** have been prepared by this route applying Grignard reagents: the reported examples include the additions of allylmagnesium chloride,[8] PhMgCl and MeMgBr in diethyl ether,[9] and *t*-BuMgCl in *n*-hexane at 50°C.[10] In our previous works in this area,[11,12] we described that the additions of allylic zinc reagents in tetrahydrofuran (THF), occurring with allylic inversion, were very efficient and diastereoselective, and determined by X-ray structure analysis the configuration of the newly formed stereocentres,



Scheme 1.

Keywords: amines; diastereoselection; imines; radicals.

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[†] The diastereoselective addition of MeLi–$CeCl_3$ (8 equiv.) to the bis-SAMP-hydrazone of glyoxal, followed by the addition of propionyl chloride (24 equiv.) afforded the protected 1,2-diamine (yield 50%, d.e. 98%).[7]

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so correcting the previous assignment[8] which was based on a stereochemical model proposed for the allylboration of an imine.

Moreover, it was stated that the reactions of Grignard reagents and lithium alkyls in THF gave complex mixtures of diastereomeric products.[9] Despite the fact that these early results did not look promising, we decided to carefully investigate the addition of organolithiums to the 1,2-diimine **1**, because the success of these reactions would enormously widen the scope of this route to enantiopure 1,2-diamines **2** (Scheme 1), considering that diverse, highly reactive organolithium reagents can be prepared by a wider range of methods, as compared to Grignard reagents.

Results and Discussion

The additions of PhLi and *n*-BuLi were preliminarily carried out in THF at −78°C and in all cases GC analyses of the reaction mixtures revealed the formation of the 1,2-diamines **2a** and **2b**,[‡] respectively, with good yields, together with relevant amounts of the imines **3a** and **3b** (Table 1, entries 1 and 4) which were identified by comparison of their GC retention times and mass spectral fragmentations with those of authentic compounds. Column chromatography (SiO_2) of the products allowed the isolation of the main C_2-symmetric diastereomers (*R*,*R*)- and (*S*,*S*)-**2a** and -**2b** with low yields. It was then observed that by carrying out the reactions in 1,2-dimethoxyethane (DME) at −60°C was slightly more efficient, because the yields of the 1,2-diamines **2a**,**b** increased at the expense of the byproducts **3a**,**b**, but the diastereomeric ratios (d.r.) were lower than in THF (entries 2 and 5).

Successively, we examined the reactions of *t*-BuLi in the same solvents as well in diethyl ether and *n*-hexane (entries 7–11). In the less polar solvents, Et_2O and especially *n*-hexane (entries 7 and 8), the temperature had to be increased to achieve complete conversion of the starting 1,2-bis-imine **1**, and the amounts of the imine by-product **3c** reached maximum levels. It is also noteworthy that the d.r. of **2c** prepared in *n*-hexane changed slightly when the reaction mixture was not quenched at the right time: in fact, by stirring the mixture one further hour at 20°C the second-eluted diastereomer (*R*,*S*)-**2c** almost disappeared and the third-eluted one (*S*,*S*)-**2c** became prevalent in the mixture. This observation indicated that an equilibration between the three diastereomeric 1,2-bis-adducts had occurred. On the other hand, the yield and diastereoselectivity of the 1,2-diamine **2c** were higher in DME (entry10), although very similar results were obtained in THF (entry 9); moreover, the d.r. of **2c** did not change significantly with increasing time in DME at −60°C (entry 10).

The imines **3a**–**c** were unexpected by-products, since they were never detected in previous reports dealing with the organometallic additions to the 1,2-diimine **1**.[8–12] We considered that they were produced by a process which involved cleavage and oxidation (dehydrogenation) steps. With this regard, it has been reported that *meso*-1,2-diamines were converted to the more stable D,L-isomers through the following steps: metallation, cleavage of the C1–C2 bond of the dilithium diamides to give α-amido radicals, and recombination of these radicals in an equilibrium process.[14,15] Similarly, in our hands, the pure diamine (*R*,*R*)-**2a** underwent partial loss of diastereomeric purity (6%) after formation of the 1,2-diamide **4a** by treatment with 2 equiv. *n*-BuLi at 0°C and allowing the temperature to rise to 20°C during 1 h (Scheme 2). The formation of the diastereomeric mixture of 1,2-diamines **2a** probably occurred via homolytic cleavage of the C1–C2 bond of (*R*,*R*)-**4a**, followed by recombination of the α-amido radicals **5a** to give an equilibrium mixture of the three diastereomers of **4a**. Moreover, we supposed that imine **3a**, which was detected by GC–MS analysis in the same experiment, was formed from the intermediate radical **5a** through an oxidation step.

In order to shed light on this point, we repeated the preparation of **2a** (**1**-PhLi-THF) taking more care to completely avoid air contamination in the reaction apparatus and using thoroughly de-aerated THF as the solvent, but the outcome of the reaction was the same. Finally, we observed that quenching the reaction mixture at −78°C by the addition of *de-aerated* H_2O in N_2 atmosphere the imine **3a** disappeared (Table 1, entry 3).[§] This result led us to repeat the additions of *t*-BuLi and *n*-BuLi to the 1,2-bis-imine **1** taking care to quench the reaction mixtures with de-aerated H_2O. Using this approach the yields of 1,2-diamines **2b**,**c** were slightly improved at the expense of the imines **3b**,**c** (entries 6 and 11). It should be observed that the diastereomeric ratios (d.r.) of the products **2a**–**c** were not affected by the quenching procedure.

We envisaged a mechanism, described in Scheme 3, which allows a reasonable explanation of the results obtained. The α-amido radicals **5** formed from the dilithium diamides **4** react with H_2O in the quenching step to give α-amino radicals **7**, whose dimerization can afford the 1,2-diamines **2**. In alternative pathways, both the α-amido and α-amino radicals **5** and **7** react with the oxygen dissolved in water to give the α-amido- and α-aminoalkyl peroxy radicals **6** and **8**, respectively, which are the precursors of the imine **3** through elimination or hydrolysis processes. It should be observed that the possibility for the imine **3** to be formed by disproportionation of the α-amino radical **7** can be rejected, since we never detected any of the saturated amines which would have been concomitantly formed. It should also be observed that the relative amounts of imines **3** and 1,2-diamines **2**, as determined by GC–MS analysis of the quenched samples, roughly reflect the corresponding amounts of the radical-anions **5** and 1,2-diamides **4** which are present at the equilibrium in solution; however, the precise determination of the equilibrium constants is presumably hampered by the possibility for the imines **3** to undergo partial hydrolysis during the quenching/extraction procedure.

We also carried out the addition of vinyllithium, prepared

[‡] It is noteworthy that more polar solvents, e.g. THF, favoured the *N*-alkylation in the additions of EtLi and *n*-BuLi to *N*,*N*′-di-*tert*-butyl-bis-1,2-ethanediimine.[13]

[§] Similarly, the formation of oxidized compounds in the reactions of aryllithiums with CO was suppressed by quenching with de-aerated H_2O.[16;17]

Table 1. Addition of organolithium reagents RLi to the 1,2-bis-imine **1** (the reactions were carried out by adding 2.5 equiv. RLi to 5 mmol of the 1,2-bis-imine **1**)

Entry	RLi (R)	Solvent	Temperature (°C), time (h)	Quenching procedure	Diamine **2** (%)[a]	(*R*,*R*/*R*,*S*/*S*,*S*) (%)[a]	Imine **3** (%)[a,b]	Yield % of isolated **2**[c]
1	Ph	THF	−78°C, 1 h	H_2O	**2a**, 82	76:1:23	**3a**, 11	(*R*,*R*)-**2a**, 28 (*S*,*S*)-**2a**, 7
2		DME	−60°C, 1 h	H_2O	**2a**, 94	63:7:30	**3a**, 4	–
3		THF	−78°C, 2 h	De-aerated H_2O	**2a**, 94	69:2:29	–	(*R*,*R*)-**2a**, 42 (*S*,*S*)-**2a**, 10
4	*n*-Bu	THF	−78°C, 1 h	H_2O	**2b**, 68	72:2:26	**3b**, 30	(*R*,*R*)-**2b**, 29 (*S*,*S*)-**2b**, 9
5		DME	−60°C, 0.5 h	H_2O	**2b**, 90	50:23:27	**3b**, 8	–
6		THF	−78°C, 1 h	De-aerated H_2O	**2b**, 85[d]	71:1:28	–	(*R*,*R*)-**2b**, 38 (*S*,*S*)-**2b**, 15
7	*t*-Bu	*n*-Hexane	−78 to 20°C, 2 h; then 20°C, 1 h	H_2O	**2c,** 45;[e] **2c**, 52	50:10:40 43:2:55	**3c**, 41 **3c**, 36	–
8		Et_2O	−78°C, 1 h; to 20°C, 6 h	H_2O	**2c**, 65;[e] **2c**, 75	54:3:43 57:3:40	**3c**, 3 **3a**, 21	–
9		THF	−78°C, 1 h	H_2O	**2c**, 85	67:2:31	**3c**, 11	(*R*,*R*)-**2c**, 45 (*S*,*S*)-**2c**, 25
10		DME	−60°C, 0.1 h; −60°C, 3 h	H_2O	**2c**, 90; **2c**, 88	68:2:30 65:2:33	**3c**, 8 **3c**, 10	–
11		THF	−78°C, 1 h	De-aerated H_2O	**2c**, 95	71:2:27	–	(*R*,*R*)-**2c**, 48 (*S*,*S*)-**2c**, 25
12	Vinyl	THF	−78°C, 1 h	De-aerated H_2O	**2d**, 95	55:2:43[f]	–	(*R*,*R*)/(*S*,*S*)-**2d**, 75 (*R*,*S*)-**2d**, 2

[a] Relative GC peak areas.

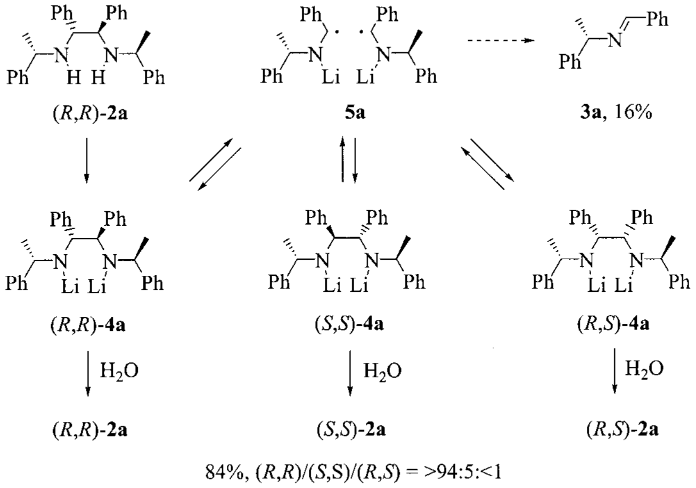
[b] Partial hydrolysis may have occurred.

[c] The diastereomers were separated by column chromatography (SiO_2).

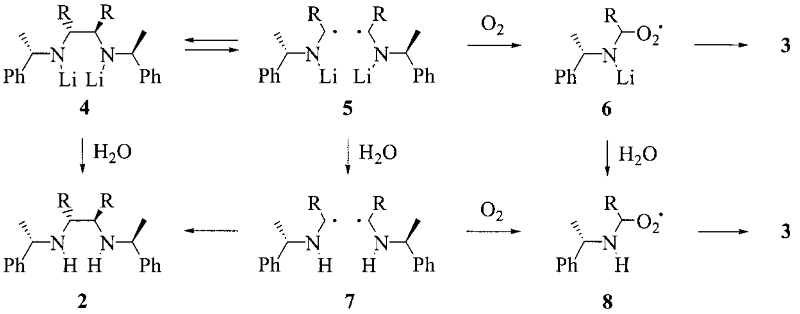
[d] Unreacted **1** (15%) was present.

[e] A by-product, probably the mono-addition product (α-aminoimine), was present in the crude reaction mixture.

[f] The d.r. was determined by ^1H NMR.



Scheme 2.



Scheme 3.

from tetravinyltin and MeLi in THF,[18] and obtained, after quenching with de-aerated H_2O, the expected 1,2-diamine **2d** with very high yield but low diastereoselectivity (Table 1, entry 12); furthermore, the diastereomers could not be separated by column chromatography (SiO_2). It should be underlined that the d.r. could be determined only by ^{1}H NMR spectroscopy of the crude product, because **2d** decomposed during the GC and GC–MS analyses. On the other hand, all the (*R*,*R*)- and (*S*,*S*)-diastereomers of the 1,2-diamines **2a–c** were obtained pure, and with reasonable yields for the main diastereomers, by chromatographic separations on SiO_2 columns (entries 3, 6 and 11).

Aiming to further expand the synthetic scope of the route described herein to C_2-symmetric 1,2-diamines, we then investigated the additions of a few organolithium compounds which can be prepared by metallation of compounds having an acidic C–H bond (Scheme 4). Thus we prepared pentadienyllithium[19–22] by metallation of 1,4-pentadiene **9** using *n*-BuLi as the base in THF–hexane mixtures, as well as phenylallyllithium[23,24] from allylbenzene **10** (*n*-BuLi/TMEDA in THF/*n*-hexane) and trimethylsilylallyllithium[25] from allyltrimethylsilane **11** (*t*-BuLi–TMEDA in THF/*n*-pentane), slightly modifying a procedure described for the lithiation of allyldimethylphenylsilane.[26] After the addition of the 1,2-bis-imine **1** to the organolithiums −78°C, the desired 1,2-diamines **2e–g** were obtained with high yields and moderate to good diastereoselectivities. It is noteworthy that the reactions were not plagued by the formation of imines analogous to **3a–c**, even if care was not taken to use de-aerated H_2O in the quenching step. We cannot give a rationale for this different behaviour. The pure (*R*,*R*)-diastereomers were isolated in pure state by column chromatography. At our knowledge, additions of these substituted allyllithium reagents to imines were never reported, and it is noteworthy that a complete regioselectivity was observed in all the reactions described in Scheme 4, since only the linear products coming from attack of the γ-carbons of the allylic moieties to the C=N bonds were obtained.[‖] This should be compared with previously reported reactions of pentadienyllithium[27] and cinnamyllithium[28] with aldehydes and ketones, where mixtures of branched and linear homoallylic alcohols were generally obtained, contrasting with the reactions of 1-trimethylsilylallyllithium which gave the linear alcohols.[25,29]

It is worth pointing out that higher yields and/or diastereoselectivities in the preparation of the 1,2-diamines **2** were provided by the substituted allyllithium reagents, with respect to alkyl-, phenyl- and vinyllithium reagents. This

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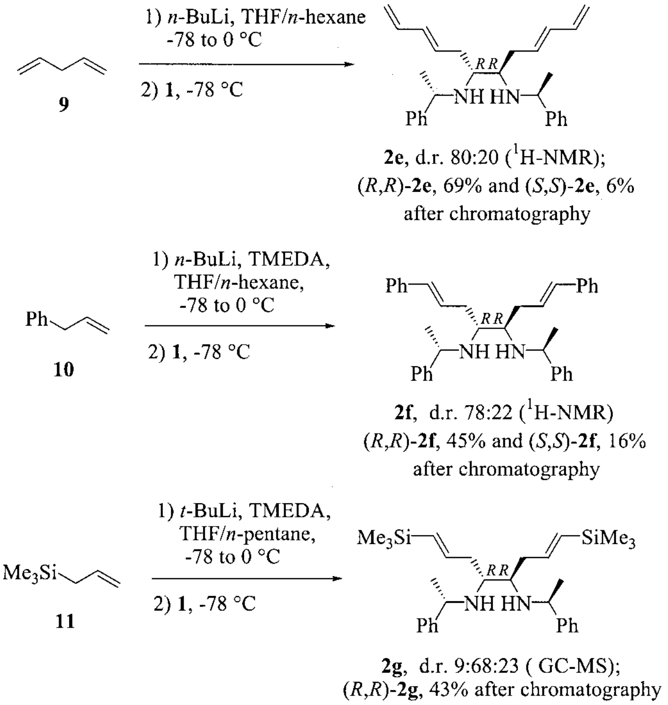
[‖] Our ongoing studies demonstrate that the retro-allyllithiation reactions of branched homoallylic lithium amides occur even at −78°C, so that we cannot exclude that the linear 1,2-diamines **2e–g** are derived from the initially formed branched isomers through a retro-allyllithiation/re-addition sequence.

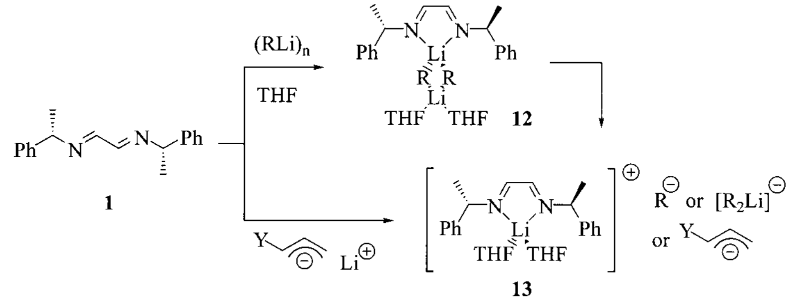


2e, d.r. 80:20 (^{1}H-NMR); (*R,R*)-**2e**, 69% and (*S,S*)-**2e**, 6% after chromatography

2f, d.r. 78:22 (^{1}H-NMR) (*R,R*)-**2f**, 45% and (*S,S*)-**2f**, 16% after chromatography

2g, d.r. 9:68:23 (GC-MS); (*R,R*)-**2g**, 43% after chromatography

Scheme 4.



Scheme 5.

can be explained, in our opinion, by assuming an ionic mechanism for the carbon–carbon bond formation. First, it should be observed that the C–Li bond has a greater ionic character than the C–MgX and C–ZnX bonds. We suppose that the reactions of covalent organolithiums RLi, which are dimeric and tetrameric in THF, take place through the preliminary coordination of lithium by the bidentate 1,2-bis-imine **1** to give the complex **12**, followed by dissociation to ionic species or triple ions (ion triplets) **13** (Scheme 5). We previously took into consideration such a mechanism for organometallic additions to activated imines.[30,31] Moreover, we assume that allylic lithium compounds are ionic, especially those having an electron-withdrawing substituent at the allylic terminus, so their additions to the 1,2-bis-imine **1** should proceed through the corresponding ionic couples **13** (Scheme 5). Since allylic anions are stabilized by resonance, it is likely that the (diastereo)selectivity in their additions to electrophiles is more easily controlled with respect to the reactions of more reactive alkyl, vinyl and phenyl anions. Finally, the occurrence, at least in part, of a mechanism proceeding through the initial single electron transfer (SET) from RLi to the 1,2-bis-imine **1** and the subsequent radical recombination cannot be excluded,[‡13,32] although no experimental result pointing to this mechanism was obtained.

Conclusions

We have demonstrated that the double addition of organolithium reagents to the 1,2-bis-amine **1** is, in certain cases, a practicable method for the synthesis of enantiopure C_2-symmetric 1,2-diamines. A major limitation is the low diastereoselectivity obtained using alkyl, vinyl and phenyl reagents. Moreover, in these reactions care must be taken to quench the mixtures with de-aerated H_2O in order to avoid the formation of imines as by-products coming from the reaction of oxygen with the α-amido-radicals which are formed in equilibrium with the main products, i.e. the dilithium 1,2-diamides. Best results, i.e. high yield and diastereoselectivity and complete regioselectivity, have been obtained with substituted allyllithium compounds. This is important because it opens a stereoselective route to novel 1,2-diamines exploiting a variety of substituted or functionalized organolithium compounds, i.e. allylic, benzylic and α-hetero-substituted reagents, which are easily available by metallation of activated C–H bonds. We are actively pursuing this objective in our laboratory.

Experimental

General conditions

Melting points are uncorrected. Solvents were distilled over the appropriate drying agent in N_2 atmosphere before use: THF (sodium benzophenone ketyl, then $LiAlH_4$), Et_2O and DME (Na, then $LiAlH_4$), *n*-hexane (Na), CH_2Cl_2 (P_2O_5). Optical rotations were measured on a digital polarimeter in a 1-dm cell and $[\alpha]_D$-values are given in 10^{-1} deg cm^3 g^{-1}. ^{1}H NMR spectra were recorded on a Varian Gemini instrument at 300 or 200 MHz for samples in $CDCl_3$ which was stored over Mg: ^{1}H chemical shifts are reported in ppm relative to $CHCl_3$ (δ_H 7.27) and *J*-values are given in Hz. MS spectra were taken at an ionizing voltage of 70 eV on a Hewlett-Packard 5970 or 5890 spectrometer with GLC injection. Chromatographic purifications were performed on columns of SiO_2 (Merck, 230–400 mesh) at medium pressure. The following organolithium reagents and organic compounds were purchased from Aldrich: *n*-BuLi, *t*-BuLi, MeLi, PhLi, glyoxal trimeric dihydrate, (*S*)-1-phenylethylamine, tetravinyltin, TMEDA, 1,4-pentadiene, allylbenzene and allyltrimethylsilane. The 1,2-bis-imine **1** was prepared according to the already described procedure.[11,12] All the organometallic reactions were performed in a flame-dried apparatus under a static atmosphere of dry N_2.

Addition of organolithium compounds to the 1,2-bis-imine 1. Preparation of 1,2-diamines 2a–c

General procedure: To the solution of the 1,2-bis-imine **1** (1.32 g, 5 mmol) in dry THF (20 ml) cooled at −78°C under N_2 was added the organolithium reagent (12.5 mmol) during 30 min. After stirring for 1 h, the mixture was quenched with de-aerated H_2O (10 ml), and the organic phase was extracted with Et_2O (3×20 ml). The collected ethereal phase was dried (Na_2SO_4) and concentrated to leave the crude 1,2-diamine **2** as an oil. The pure diastereomers were obtained by chromatography on an SiO_2 column eluting with cyclohexane–EtOAc mixtures. The hydrochlorides were prepared by treatment with excess 37% HCl, evaporation and thorough drying in vacuo.

1(*R*),2(*R*)-Di-[(*S*)-1-phenylethylamino]-1,2-diphenylethane (*R*,*R*)-2a. Eluted first by column chromatography; white solid, 0.882 g (42%); $[\alpha]_D^{20}=-178.2$ (*c* 0.65, $CHCl_3$); the compound was recrystallized from pentane: colourless crystals, mp 108–110, $[\alpha]_D^{20}=-213.4$ (*c* 0.32, $CHCl_3$); lit:[9] $[\alpha]_D^{20}=-205$ (*c* 0.7, $CHCl_3$); MS *m*/*z* (relative intensity, %) 105 (100), 106 (90), 210 (85, $M^+/2$), 79 (21), 77 (18), 211 (13); the ^{1}H NMR spectrum was identical to that of the compound described in the literature.[9]

(*S*,*S*)-**2a**.Yellowish oil, 0.210 g (10%), containing an unidentified impurity (ca. 10%); $[\alpha]_D^{20}=-56.7$ (*c* 1.6, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.29 (d, *J*=6.6 Hz, 6H, $CHCH_3$), 1.85 (br, 2H, NH), 3.59 (q, *J*=6.3 Hz, 2H, $CHCH_3$), 3.88 (s, 2H, NCHCHN), 7.0–7.42 (m, 20H, Ph).

5(*R*),6(*R*)-Di-[(*S*)-1-phenylethylamino]-decane (*R*,*R*)-2b. Eluted second by column chromatography; yellowish oil, 0.740 g (38%); $[\alpha]_D^{20}=-122.2$ (*c* 1.3, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$–D_2O) δ 0.76 (t, *J*=7.2 Hz, and m, 10H, CH_3 and CH_2), 1.10 (m, 4H, CH_2), 1.37 (m, 4H, CH_2), 1.40 (d, *J*=3.0 Hz, 6H, $CHCH_3$), 2.08 (m, 2H, NCHCHN), 3.81 (m, 2H, $CHCH_3$), 7.10–7.38 (m, 10H, Ph). MS *m*/*e* (relative intensity, %): 105 (100), 190 (85, $M^+/2$), 86 (60). The dihydrochloride (*R*,*R*)-**2b**-2HCl was prepared by routine procedure and purified by several washings with CH_2Cl_2: white solid, mp 218–220°C (dec.); $[\alpha]_D^{20}=-31.9$ (*c* 0.506, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$–D_2O) δ 0.33 and 0.50 (2m, 4H, CH_2), 0.67 (t, *J*=6.9 Hz, 6H, CH_2CH_3), 1.0 (m, 4H, CH_2), 1.64 (m, 2H, CH_2), 1.98 (d, *J*=6.9 Hz, 6H, $CHCH_3$), 2.11 (m, 2H, CH_2), 2.49 (m, 2H, NCHCHN), 4.26 (m, 2H, $CHCH_3$), 7.42 and 7.63 (2m, 10H, Ph), 10.1 and 10.7 (broad, 4H, NH_2). Basic treatment of the salt allowed to recover more pure (*R*,*R*)-**2b**: $[\alpha]_D^{20}=-134.6$ (*c* 0.87, $CHCl_3$). Found: C 82.00, H 10.68, N 7.32%; $C_{26}H_{40}N_2$ requires: C 82.04, H 10.59, N 7.36%.

(*S*,*S*)-**2b**. Eluted first by column chromatography; yellowish oil, 0.292 g (15%); $[\alpha]_D^{20}=-75.8$ (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$–D_2O) δ 0.82 (t, *J*=7.2 Hz, and m, 8H, CH_3 and CH_2), 1.0–1.4 (m, 12H, CH_2 and NH), 1.42 (d, *J*=3.0 Hz, 6H, $CHCH_3$), 2.51 (m, 2H, NCHCHN), 3.6 (m, 2H, $CHCH_3$), 7.10–7.38 (m, 10H, Ph). MS *m*/*e* (relative intensity, %): 105 (100), 190 (85, $M^+/2$), 86 (60). (*S*,*S*)-**2b-2HCl**: white solid, mp 205–207°C (dec.); $[\alpha]_D^{20}=+9$ (*c* 0.36, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.82 (t, *J*=6.7 Hz, 6H, CH_3), 1.12 (m, 8H, CH_2), 1.59 (m, 2H, CH_2), 1.72 (s, 2H, NH), 1.90 (d, *J*=6.6 Hz, 6H, $CHCH_3$), 2.20 (m, 2H, CH_2), 3.24 (m, 2H, NCHCHN), 4.36 (m, 2H, $CHCH_3$), 7.42 (m, 6H, Ph), 7.65 (m, 4H, Ph), 10.4 (broad, 2H, NH).

3(*R*),4(*R*)-Di-[(*S*)-1-phenylethylamino]-2,2,5,5-tetramethylhexane (*R*,*R*)-2c. Eluted first by column chromatography; yellowish oil, 0.936 g (48%); $[\alpha]_D^{20}=+73.4$ (*c* 1.8, $CHCl_3$); we determined the same value for the compound prepared by the reported procedure,[10] where a definitely lower value was given for the crude compound: $[\alpha]_D^{25}=+31.6$ (*c* 0.364, $CHCl_3$); MS *m*/*z* (relative intensity, %) 105 (100), 190 (79, $M^+/2$), 86 (50), 191 (15), 79 (14), 323 (12); the ^{1}H NMR spectrum was identical to that described for the known compound.[10]

(*S*,*S*)-**2c**. Yellowish oil, 0.487 g (25%), contained ca. 5% of (*R*,*R*)-**2c**; $[\alpha]_D^{20}=-75.7$ (*c* 1.2, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.78 (s, 18H, *t*-Bu), 1.37 (d, *J*=6.6 Hz, 6H, $CHCH_3$), 1.91 (s, 2H, NH), 2.34 (s, 2H, NCHCHN), 3.84 (q, *J*=6.6 Hz, 2H, $CHCH_3$), 7.18–7.40 (m, 10H, Ph).

Addition of vinyllithium to the 1,2-bis-imine 1

MeLi (1.6 M in hexane, 7.5 ml, 12 mmol) was slowly added to the solution of tetravinyltin (0.68 g, 3 mmol) in dry THF (20 ml) cooled at −20°C under N_2, and the mixture was stirred during 2.5 h at −20 to 0°C. Then the mixture was cooled to −78°C and the solution of the 1,2-bis-imine **1** (1.056 g, 4 mmol) in dry THF (10 ml) was added during 20 min. After stirring for 1 h, the mixture was quenched with de-aerated H_2O (20 ml), and the organic phase was extracted with Et_2O (3×20 ml). The collected ethereal phase was dried (Na_2SO_4) and concentrated to leave an oil. Chromatography on an SiO_2 column eluting with cyclohexane–EtOAc (5:1) mixture gave 0.970 g (75%) of **2d** as an inseparable mixture of the (*R*,*R*)/(*S*,*S*)-diastereomers (56:44 by ^{1}H NMR), followed by (*R*,*S*)-**2d** (0.030 g, 2%).

3(*R*),4(*R*)-/3(*S*),4(*S*)-Di-[(*S*)-1-phenylethylamino]-1,5-hexadiene (*R*,*R*)/(*S*,*S*)-2d. Eluted first by column chromatography; colourless oil; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.30 and 1.32 (2 d, *J*=6.6 Hz, 6H, CH*Me*), 1.70 (broad, 2H, NH), 2.61 (m, 1H, (*R*,*R*)-NC*H*C*H*N), 3.17 (m, 1H, (*S*,*S*)-NC*H*–C*H*N), 3.79 (2q, *J*=6.2 Hz, 2H, C*H*Me), 4.81–5.21 (m, 4H, CH═C*H*$_2$), 5.32–5.73 (m, 2H, C*H*═CH$_2$), 7.18–7.42 (m, 10H, Ph). Found: C 82.50, H, 8.83, N, 8.71%; $C_{22}H_{28}N_2$ required: C 82.45, H 8.81, N 8.74%.

(*R*,*S*)-**2d**. Colourless oil; $[\alpha]^{25}_{\mathrm{D}}=-91$ (*c* 0.24, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.20 and 1.34 (2d, *J*=6.6 Hz, s H, CH*Me*), 1.66 (broad, 2H, NH), 2.85 and 2.94 (2m, 2H, NCHCHN), 3.47 and 3.76 (2q, 2H, C*H*Me), 4.85–5.20 (m, 4H, CH═C*H*$_2$), 5.46–5.58 (m, 2H, C*H*═CH$_2$), 7.05–7.38 (m, 10H, Ph).

Addition of pentadienyllithium to the 1,2-bis-imine 1

To dry THF (30 ml) cooled at −78°C were added *n*-BuLi (1.6 M in hexane, 15.9 ml, 25.5 mmol) and, after 10 min, 1,4-pentadiene **9** (2.80 ml, 27.2 mmol, taken by a syringe from the holder cooled at 0°C). The mixture was stirred for 1 h, meanwhile the temperature was allowed to reach 0°C. Two phases were observed, the orange upper phase containing pentadienyllithium. The mixture was cooled to −78°C and the 1,2-diimine **1** (2.25 g, 8.5 mmol) dissolved in THF (10 ml) was added dropwise during 1 h while stirring. After a further 1.5 h the reaction was quenched with H_2O (10 ml) and the organic phase was extracted with Et_2O (3×30 ml). The collected ethereal layers were dried (Na_2SO_4), and concentrated to leave crude diamine **2e** as a yellowish thick oil: 3.30 g; d.r. 80:20 by ^{1}H NMR. The pure diastereomers were obtained by chromatography on an SiO_2 column eluting with cyclohexane–AcOEt (15:1).

(*E*,*E*)-6(*R*),7(*R*)-Di-[(*S*)-1-phenylethylamino]-1,3,9,11-dodecatetraene (*R*,*R*)-2e. Eluted second by column chromatography; 2.35 g, 69%: $[\alpha]^{25}_{\mathrm{D}}=-98.7$ (*c* 0.7, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26 (d, *J*=6.6 Hz, CH*Me*), 1.40 (s, 2H, NH), 2.14 (m, 6H, NCHCH$_2$), 3.72 (q, 2H, C*H*Me), 4.85 (d, J_{cis}=10.2 Hz, 1H, CH═C*H*$_2$), 4.92 (d, J_{trans}=16.8 Hz, 1H, CH═C*H*$_2$), 5.20 (m, 1H, C*H*═CH$_2$), 5.53 (dd, *J*=15.3 and 15.3 Hz, 1H, CH═C*H*–CH═CH$_2$), 6.09 (dt, *J*=17.1 and 10.5 Hz, 1H, CH$_2$C*H*═CH), 7.18–7.32 (m, 10H, Ph); the spectrum revealed the absorptions of another compound, perhaps (*R*,*S*)-**2e** (<10%) Found: C 83.93, H 9.04, N 7.00%; $C_{28}H_{36}N_2$ requires: C 83.95, H 9.06, N 6.99%.

(*S*,*S*)-**2e** was eluted first by column chromatography; 0.204 g, 6%: $[\alpha]^{25}_{\mathrm{D}}=+8.6$ (*c* 0.78, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.21 (d, *J*=6.6 Hz, CH*Me*), 1.43 (s, 2H, NH), 1.92 (m, 2H, NCHC*H*$_2$), 2.44 (m, 2H, NCHC*H*$_2$), 2.59 (m, 2H, NCHCHN), 3.63 (q, *J*=6.6 Hz, 2H, C*H*Me), 5.01 (d, J_{cis}=10.5 Hz, 1H, CH═C*H*$_2$), 5.12 (d, J_{trans}=17.1 Hz, 1H, CH═C*H*$_2$), 5.52 (m, 1H, C*H*═CH$_2$), 6.06 (dd, *J*=15.3 and 15.3 Hz, 1H, CH═C*H*–CH═CH$_2$), 6.31 (dt, *J*=16.8 and 10.2 Hz, 1H, CH$_2$C*H*═CH), 7.18–7.40 (m, 10H, Ph).

Addition of cinnamyllithium to the 1,2-bis-imine 1

To dry THF (12 ml) cooled at −78°C were added *n*-BuLi (1.6 M in hexane, 9.4 ml, 15 mmol), then TMEDA (2.39 ml, 16 mmol) and, after 10 min, allylbenzene **10** (2.07 g, 17.5 mmol). The mixture was stirred for 1 h, meanwhile the temperature was allowed to reach 0°C. A deep red colour was observed and attributed to phenylallyllithium. The mixture was cooled to −78°C and the 1,2-bis-imine **1** (1.32 g, 5 mmol) dissolved in THF (7 ml) was added dropwise while stirring. After 1 h the reaction was quenched with H_2O (5 ml) and the organic phase was extracted with Et_2O (3×20 ml). The collected ethereal layers were dried (Na_2SO_4), and concentrated to leave the crude product **2f** as a yellow thick oil: d.r. 78:22 by ^{1}H NMR spectroscopy. The diastereomers were separated by chromatography on an SiO_2 column eluting with cyclohexane–EtOAc (95:5).

(*E*,*E*)-4(*R*),5(*R*)-Di-[(*S*)-1-phenylethylamino]-1,8-diphenyl-1,7-octadiene (*R*,*R*)-2f. Eluted second by column chromatography; yellowish thick oil; 1.12 g, 45%: $[\alpha]^{25}_{\mathrm{D}}=-74$ (*c* 0.7, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.24 (d, *J*=6.6 Hz, 6H, CH*Me*), 1.36 (br, 2H, NH), 2.74 (m, 6H, NCHCH$_2$), 3.82 (q, *J*=6.6 Hz, 2H, C*H*Me), 5.60–5.83 (m, 4H, CH═CH), 7.0–7.35 (m, 20H, Ph). Found: C 86.40, H 8.08, N 5.58%; $C_{36}H_{40}N_2$ requires: C 86.35, H 8.05, N 5.60%.

(*S*,*S*)-**2f**. Eluted first by column chromatography; yellowish thick oil; 0.412 g, 16%: $[\alpha]^{25}_{\mathrm{D}}=-43.7$ (*c* 0.6, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.14 (d, *J*=6.9 Hz, 6H, CH*Me*), 1.46 (br, 2H, NH), 1.98 (m, 2H, NCHC*H*$_2$), 2.50–2.64 (m, 4H, NCHCH$_2$), 3.58 (q, *J*=6.9 Hz, 2H, C*H*Me), 5.96 (m, 2H, CH$_2$C*H*═CH), 6.37 (d, *J*=15.3 Hz, 2H, CH═C*H*–Ph), 7.02–7.30 (m, 20H, Ph).

Addition of 1-trimethylsilylallyllithium to the 1,2-bis-imine 1

To a solution of allyltrimethylsilane **11** (1.71 g, 15 mmol) and TMEDA (0.75 ml, 5 mmol) in dry THF (3 ml), cooled at −78°C, was slowly added *t*-BuLi (1.7 M in pentane, 2.95 ml, 5 mmol). The mixture was allowed to reach slowly −15°C and further stirred at this temperature for 1 h, so assuming an orange colour. The mixture was then cooled to −78°C and the 1,2-bis-imine **1** (0.264 g, 1 mmol) dissolved in THF (3 ml) was added dropwise while stirring. After 1 h the reaction was quenched with de-aerated H_2O (5 ml) and the organic phase was extracted with Et_2O (3×10 ml). The collected ethereal layers were dried (Na_2SO_4), and concentrated to leave the crude product **2g** as a clear yellowish oil: d.r. 9:68:23 by GC–MS analysis. Column chromatography of the crude product coming from the addition of 1-trimethylsilylallyllithium gave the major diastereomer (*R*,*R*)-**2g** in a pure state; fractions containing mixtures of the other two linear diastereomers (*R*,*S*)- and (*S*,*S*)-**2g** were also eluted, but no branched compound was observed.

(*E*,*E*)-1(*R*),2(*R*)-Di-[(*S*)-1-phenylethylamino]-1,8-di-(trimethylsilyl)-1,7-octadiene (*R*,*R*)-2g. Yellowish oil; 0.210 g (43%); $[\alpha]_D^{20}=-97.5$ (c 0.9, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ −0.086 (s, 18H, $SiMe_3$), 1.25 (d, J=6.6 Hz, 6H, CH*Me*), 1.39 (br, 2H, NH), 2.12 (m, 6H, $NCHCH_2$), 3.71 (q, J=6.6 Hz, H, C*H*Me), 5.19 (d, J=18.6 Hz, SiC*H*=CH), 5.54 (dt, J=18.6 and 6.2 Hz, SiCH=C*H*), 7.10–7–38 (m, 10H, Ph); MS m/z 105 (100), 246 (75, $M^+/2$), 73 (22), 142 (21), 247 (17). Found: C 73.05, H 9.84, N 5.69%; $C_{30}H_{48}N_2Si_2$ requires: C 73.10, H 9.82, N 5.68%.

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