Asymmetric Synthesis of Primary Amines by Nucleophilic Addition of Alkyllithium Compounds to Aldehyde SAMP/RAMP Hydrazones[1]

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The aldehydes **1** or **5** are converted to the SAMP hydrazones **2** or the α-alkylated SAMP hydrazones **7** and treated with organolithium compounds at low temperature. Cleavage of the N−N bond of the resulting hydrazines **3** and **8** with Raney-Ni/H_2, or of the *N*-methoxycarbonylhydrazines **9** with Li/NH_3, yield the amines **4** with 61−90% *ee*, the amines **11** with 45−96% *de* and 93 → 99% *ee*. The absolute configuration of the amines **11** was established by X-ray analysis of an appropriate MTPA derivative.

Introduction

Nucleophilic addition to the C=N double bond of imines, oximes and hydrazones is a well established method for the preparation of a variety of amines[2]. Problems were encountered during C−C bond formation reactions by 1,2-addition of C-nucleophiles to aldehyde imines. These difficulties are due to the poor electrophilic nature of the imine moiety compared to corresponding carbonyl compounds and to deprotonation of the α-hydrogen atom by basic nucleophiles. Various approaches were developed to solve these problems. Firstly, activated C=N double bonds were employed by using iminium salts[3], sulfonyl[4], sulfene[5], or acyl imines[6] as carbonyl equivalents in 1,2-additions. Secondly, enolates[7], organocopper[8], organotin compounds[9], and catechol borane[10] were used as weak, non-basic nucleophiles. In some cases an additional activation of the C=N double bond by Lewis acids was necessary to obtain satisfactory results. However, these methods, which were developed in the eighties, were of limited scope because they are restricted to allylic nucleophiles or imines and hydrazones[11] that cannot be deprotonated. Since the mid-eighties, new methods have been developed that include the employment of organolithium[12,13], Grignard[14], in situ generated organoytterbium[15], organocerium[16,17] or allyl barium[18] compounds in 1,2-additions to hydrazones or imines[19]. Recently, we have reported the diastereo- and enantioselective synthesis of C_2-symmetric[20a] and non-symmetric[20b] 1,*n*-diamines, 1,2-amino alcohols[20c] such as (*R,R*)-*statine*[20d], β-amino acids[20e,f,g], and different natural products such as coniine[15] or harmonine[20h], by nucleophilic 1,2-addition to functionalised SAMP/RAMP hydrazones. We would now like to report in detail on our early work on the enantioselective synthesis of primary amines, in which nucleophilic 1,2-addition to a SAMP/RAMP hydrazone is the key reaction step.

Results and Discussion

Amines with One Stereogenic Center

The commercially available aldehydes **1** were converted to the corresponding SAMR/RAMP hydrazones (*S*)-**2a−g** following standard literature procedures[21,12] in 83−96% yield. Nucleophilic 1,2-addition was subsequently carried out at −78°C in diethyl ether or THF, where the highly diastereofacially selective reaction took place upon addition of 1.1−2.0 eq. of the organolithium compound to **2** (Scheme 1). After work up, the extremely air sensitive hydrazines **3** were obtained as pale yellow oils in very good yields (73−98%) and were immediately employed in the N−N bond cleavage reaction, usually without determination of the diastereomeric excess of the 1,2-adducts. However, ^{13}C-NMR spectra of the hydrazines (*S,R*)-**3e** and (*S,R*)-**3h** revealed that the 1,2-addition had taken place with virtually complete diastereoselection (*de* >95%; Table 1).

The N−N bond cleavage of the non-activated hydrazines **3** was accomplished by hydrogenolysis in the presence of a Raney-Ni[22] catalyst. After reductive cleavage of the N−N bond, the desired primary amine **4** and the secondary amine (*S*)-2-(methoxymethyl)pyrrolidine (SMP) were formed. These two compounds could not be separated by column chromatography or by distillation and, therefore, a derivatisation was performed. The amines with low molecular weights were converted to the corresponding azomethines, which were separated by column chromatography from SMP and then hydrolysed under acidic conditions to give amine **4**. Sterically hindered amines were treated with methyl chloroformate to form the corresponding methylcarbamates, which were purified by column chromatography and subsequently cleaved under acidic conditions. Following these procedures, the amines **4** were isolated in 41−73% yield and 61−90% *ee*. Unfortunately, the reductive cleavage

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Scheme 1. Asymmetric synthesis of primary amines starting from aldehydes

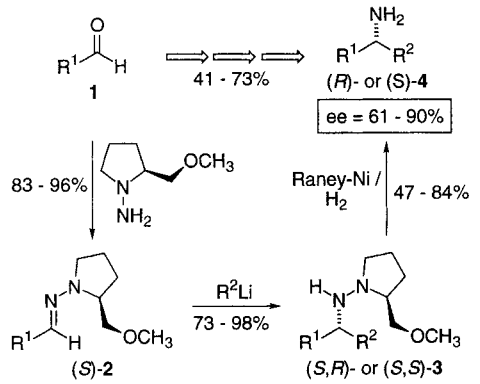


Table 1. Diastereo- and enantioselective synthesis of hydrazines **3** by nucleophilic addition of organolithium compounds to SAMP/RAMP hydrazones (*S*)-**2**

3	R^1	R^2	yield [%]	$[\alpha]_D^{22}$ (c, C_6H_6)	Config.
a	Ph	Me	73	−73.7 (2.26)	(*S*,*R*)
a	Me	Ph	81	+62.7 (2.71)	(*R*,*S*)[a]
b	*p*MeOPh	Me	97	−82.4 (1.94)	(*S*,*R*)
c	*t*Bu	Me	81	−54.4 (1.60)	(*S*,*R*)
c	Me	*t*Bu	98	−77.3 (1.96)	(*S*,*S*)
d	Ph	*t*Bu	87	−32.3 (1.30)	(*S*,*R*)
d	*t*Bu	Ph	95	−101.9 (2.12)	(*S*,*S*)
e	Ph	*n*Bu	91[b]	−88.0 (1.20)	(*S*,*R*)
e	*n*Bu	Ph	88	−58.2 (1.96)	(*S*,*S*)
f	*i*Pr	Ph	98	−58.9 (1.75)	(*S*,*S*)
g	*i*Pr	*n*Bu	92	−90.4 (2.53)	(*S*,*R*)
h	*t*Bu	*n*Bu	91[b]	−104.0 (0.95)	(*S*,*R*)
i	Et	*n*Bu	83	−100.4 (2.35)	(*S*,*S*)

[a] (*R*,*S*)-**3a** was prepared from the corresponding RAMP hydrazone[12]. – [b] *de* >95% (^{13}C NMR).

of the N−N bond proceeds with partial epimerisation at the newly created stereogenic center when Raney-Ni/H_2 is used as the catalyst. Therefore, no correlation between the enantiomeric excess of the isolated amines (*R*)- and (*S*)-**4** and the diastereomeric excess of the hydrazines **3** is possible. Despite this disadvantage, both enantiomers of **4** are available in excess by using either SAMP or RAMP as the chiral auxiliary ((*R*)- and (*S*)-**4a** in Table 2) or by simply exchanging R^1 and R^2 in the reaction sequence (**4c**, **4d**, **4e** in Table 2).

The enantiomeric excesses of known amines were determined by polarimetry. Other amines were converted to the 3,3,3-trifluoro-2-methoxy-2-phenylpropionic acid amides[23] (MTPA amides), and the diastereomeric excesses were measured by NMR spectroscopy (^{13}C,^{19}F). Amine **4h** was converted to the corresponding isopropyl urea derivative and the *ee* determined on a chiral stationary phase[24].

The absolute configurations of the amines were determined by correlation of their optical rotations with literature data. In some cases, CD spectroscopy on the corresponding *N*-salicylidene derivatives was used to determine the configuration of the amines (e.g. **4d**, **4i**) by using the salicylidene amino chirality rule described by Smith et al.[25].

Table 2. Amines **4** prepared by reductive cleavage of the N−N bond with Raney-Ni/H_2

4	R^1	R^2	yield [%]	α_D^{20} (neat)	*ee* [%]	Config.
a	Ph	Me	47	+26.1	81	(*R*)
a[a]	Me	Ph	48	−26.1	81	(*S*)
b	*p*MePh	Me	73	+26.0	72	(*R*)
c	*t*Bu	Me	41	−4.5	81	(*R*)
c	Me	*t*Bu	43	+3.7	69	(*S*)
d[b]	cC_6H_{11}	*t*Bu	64	−25.8	82	(*S*)
d[b]	*t*Bu	cC_6H_{11}	62	+27.4	90	(*R*)
e	Ph	*n*Bu	46	+14.1	85	(*R*)
e	*n*Bu	Ph	58	−13.9	83	(*S*)
f[b]	*i*Pr	cC_6H_{11}	63	+10.5	90	(*S*)
g	*i*Pr	*n*Bu	57	+17.4[c]	86	(*R*)
h	*t*Bu	*n*Bu	78	+14.7	61	(*R*)
i	Et	*n*Bu	57	+5.8	72	(*S*)

[a] (*S*)-**4a** was prepared from the corresponding RAMP hydrazone. [b] The phenyl ring was reduced during N−N bond cleavage. [c] Measured in solution: $[\alpha]_D^{20}$ (c = 3.3, EtOH).

Amines with Two Stereogenic Centers

The highly diastereoselective 1,2-addition reaction of organolithium compounds with the C=N double bond of the hydrazones **2** has shown that the nucleophilic addition proceeds at a faster rate than the enolisation by deprotonation of the α-hydrogen atom. It was evident that the stereochemistry is virtually completely controlled by the chiral auxiliary SAMP or RAMP. Therefore, we directed our efforts to extending this methodology to 2-substituted hydrazones which should be converted to primary amines with two stereogenic centers, as shown in Scheme 2. In addition, the influence of the second stereogenic center on the stereochemical outcome of the reaction was investigated.

Thus, hydrazones **6** were prepared starting from the readily available aldehydes **5** and SAMP/RAMP following literature procedures[21]. The hydrazones were converted under standard conditions[16,21,26] to the α-alkylated hydrazones (*S*,*R*)-**7** in 84−89% yield and 81−93% diastereomeric excess. The organolithium compounds and hydrazones **7** were then allowed to react in THF at −78°C, furnishing the hydrazines **8** as air sensitive oils in moderate to good yields (53−88%) and excellent diastereoselectivities (89 → 98% *ds*). The 1,2-addition at the C=N double bond takes place immediately, and virtually complete diastereoselection is obtained (Table 3).

Usually, the hydrazines **8** were used immediately for the subsequent N−N bond cleavage with Raney-Ni/H_2 or Li/NH_3, respectively. The hydrogenolytic cleavage (Raney-Ni/H_2) resulted in partial epimerisation of the amine. In general, only a slight loss of diastereomeric purity was observed. However, when benzyl-substituted hydrazines (R^3 = C_6H_5) were used in these reactions, up to 50% epimerisation occurred. In addition, the reaction does not terminate after the N−N bond cleavage, leading to subsequent reduction of the benzylic aromatic ring. However, phenyl substituents in non-benzylic positions were tolerated and were not re-

Table 3. Diastereo- and enantioselective synthesis of hydrazines **8** by nucleophilic addition of organolithium compounds to α-alkylated SAMP/RAMP hydrazones **7**

8	R^1	R^2	R^3	yield [%]	$[\alpha]_D^{22}$ (*c*, C_6H_6)	*ds* [%]	Config.
a	Et	Me	*n*Bu	79	−104.8 (1.1)	97	(*S*,*R*,*R*)
b	Et	Me	*t*Bu	67	−98.0 (1.3)	>98	(*S*,*R*,*R*)
c	*n*Pr	Me	Me	74	−92.8 (1.3)	97	(*S*,*R*,*R*)
c[a]	*n*Pr	Me	Me	53	+98.4 (0.5)	89	(*R*,*S*,*R*)
d	*n*Pr	Me	Ph	58	−67.5 (1.2)	96	(*S*,*S*,*R*)
e	*n*Bu	Me	Me	61	−94.2 (1.3)	97	(*S*,*R*,*R*)
e[b]	*n*Bu	Me	Me	48	+95.0 (1.3)	97	(*R*,*S*,*S*)
f	*n*Bu	Me	*t*Bu	66	−91.7 (0.8)	97	(*S*,*S*,*R*)
g	Bzl	Me	*n*Bu	75	−62.3 (0.8)	96	(*S*,*R*,*R*)
g	Me	Bzl	*n*Bu	56	−35.7 (0.7)	94[c]	(*S*,*R*,*S*)
h	Bzl	Me	*t*Bu	53	−74.1 (0.6)	96	(*S*,*S*,*R*)
i	Bzl	Me	Ph	88	−42.9 (0.9)	97	(*S*,*S*,*R*)

[a] The α-alkylated SAMP hydrazone was converted to the corresponding RAMP hydrazone prior to the 1,2-addition[21]; partial racemisation was observed (*de* = 81%). – [b] The RAMP hydrazone was used for α-alkylation and 1,2-addition. – [c] Benzyl group was incorporated during the alkylation step (α-alkylated SAMP hydrazone: *de* = 82%).

duced under these reaction conditions. Other hydrogenation catalysts (Pd/C or PtO_2) did not lead to cleavage of the N–N bond with hydrogen, even under high pressure (160 atm) or any other reaction conditions applied. The amines **11** prepared by this cleavage method were again separated from SMP by derivatisation. Following this protocol, the free amines **11** were isolated in 40–86% yield, 45–90% diastereomeric and 93–99% enantiomeric excess.

Activated *N*-methoxycarbonyl hydrazines **9** were obtained when the lithium hydrazides were treated with methyl chloroformate. However, only hydrazines with small substituents (e.g. $R^3 = CH_3$) were successfully trapped under these conditions. The carbamates **9** were not isolated, but yields and diastereoselectivities (Scheme 2) were determined by GC on the crude reaction mixtures. The N–N bonds in the carbamates **9** were instantly cleaved with lithium in liquid ammonia[16,27], yielding carbamates **10**. Acid-mediated hydrolysis furnished the amines **11** in 18–45% yield, 77–96% *de* and excellent enantiomeric excesses (98 → 99%). Sterically more demanding substituents (R^3, R^2, R^1) resulted in the prevalent cleavage of the N–CO bond instead of the N–N bond in **9** and led to the hydrazines **8**. When phenyllithium was used as the nucleophilic ($R^3 = C_6H_5$), the cleavage of the benzylic C–N bond turned out to be main reaction. Therefore, despite the known disadvantages, some of the hydrazines had to be cleaved using Raney-Ni/H_2 (Table 4).

The diastereo- and enantiomeric excess of **11** were determined by GC on a chiral stationary GC phase "XE-60-(*S*)-valin-(*S*)-α-phenylethylamide"[24,28,29] using the isopropyl urea derivatives or by NMR spectroscopy (^{13}C, ^{19}F) and GC of the corresponding MTPA amides[23].

The absolute configuration of the amines **11** was unambiguously determined by X-ray structure analysis of a corresponding (*R*)-MTPA amide of **11h** (Figure 1)[30]. Suitable crystals were obtained after slowly cooling a petroleum ether solution of the amide to 0°C.

Scheme 2. Asymmetric synthesis of 1,2-disubstituted amines by 1,2-addition to α-alkylated SAMP/RAMP hydrazones

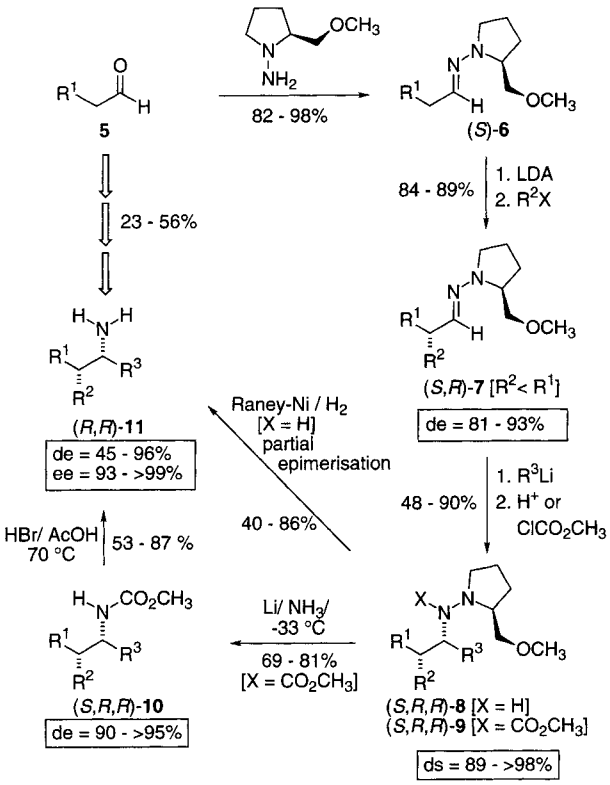


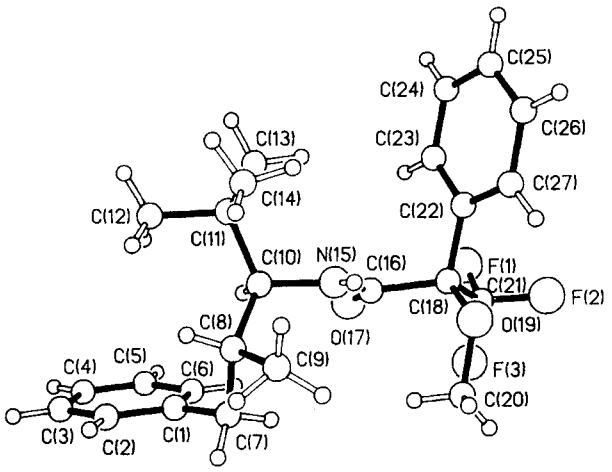
Table 4. Amines **11** prepared by reductive cleavage of the N–N bond by Raney-Ni/H_2 or Li/NH_3 starting from hydrazines **8** and **9**

11	R^1	R^2	R^3	yield [%]	α_D^{20} (neat)	*de*[a] [%]	*ee*[a] [%]	Config.
a	Et	Me	*n*Bu	48	+10.8	87	93	(*R*,*R*)
b	Et	Me	*t*Bu	49	−21.4	90	99	(*S*,*R*)
c	*n*Pr	Me	Me	31[b]	+13.2	90	98	(*R*,*R*)
c[c]	*n*Pr	Me	Me	18[b]	+14.4	77	>99	(*S*,*R*)
d	*n*Pr	Me	cC_6H_{11}	69	+9.1	45	97	(*S*,*R*)
e	*n*Bu	Me	Me	38[b]	+13.0	91	98	(*R*,*R*)
e[d]	*n*Bu	Me	Me	31[b]	−14.4	92	98	(*S*,*S*)
f	*n*Bu	Me	*t*Bu	40	−17.8	86	98	(*S*,*R*)
g	Bzl	Me	*n*Bu	86	−2.6[e]	67	97	(*R*,*R*)
g	Me	Bzl	*n*Bu	79	−3.7	58	93	(*R*,*S*)
h	Bzl	Me	*t*Bu	65	−42.1	85	94	(*S*,*R*)
i	Bzl	Me	cC_6H_{11}	72	−6.9[f]	68	97	(*S*,*R*)
j	cC_6H_{11}	Me	Me	45[b]	+4.5	96	98	(*R*,*R*)

[a] Determined by ^{13}C and ^{19}F NMR of the corresponding MTPA amide. – [b] N–N bond cleavage by Li/NH_3; yields based on 7. – [c] The α-alkylated SAMP hydrazone was converted to the corresponding RAMP hydrazone prior to the 1,2-addition[21]; loss of yield during convertion of the SAMP to the RAMP hydrazone. – [d] The RAMP hydrazone was used for α-alkylation and 1,2-addition. – [e] Measured in solution: $[\alpha]_D^{22}$ (*c* = 1.6, C_6H_6). – [f] Measured in solution: $[\alpha]_D^{22}$ (*c* = 0.87, C_6H_6).

From the structure analysis, the absolute configuration of the stereogenic center generated by the 1,2-addition is established as (*S*) when SAMP was used as auxiliary and if the nucleophile R^3 has a higher priority than R^1R^2CH. The absolute configuration of the α-center of the hydrazine is known from previous investigations[31] but was confirmed by this X-ray structure analysis.

Figure 1. Crystal structure analysis of the (*R*)-MTPA amide of (*S,R*)-**11h**

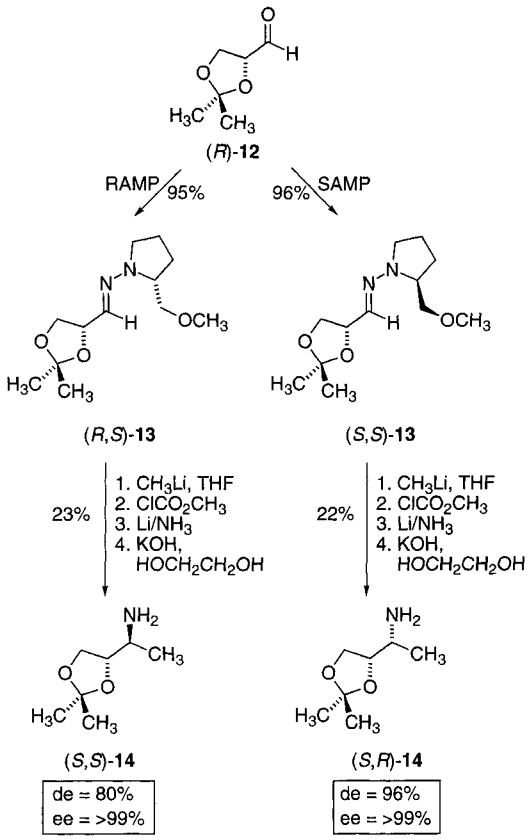


The 1,2-addition is completely controlled by the chiral auxiliary SAMP or RAMP. Table 3 (**8c**, **8g**) shows that the absolute configuration obtained at C-1 changed when RAMP was used as the auxiliary instead of SAMP during the 1,2-addition, starting with the same absolute configuration at the C-2 stereogenic center of the hydrazones. The small differences observed in diastereoselectivity can be traced back to the different diastereomeric excesses of the α-alkylated hydrazones **7**. The same effect was also observed during the nucleophilic addition of alkyllithium compounds to α-alkylated dimethylhydrazones, where poor diastereofacial selectivities of 10–15% were observed[16].

The effect of the configuration at the α-stereogenic center was studied in more detail when isopropylideneglyceroaldehyde[32] (*R*)-**12** was converted to the SAMP and RAMP hydrazone (*S,S*)- and (*R,S*)-**13**, respectively, and treated with organolithium compounds at −78°C (Scheme 3). It is known from previous investigations[12a] that the addition of methyllithium to the dimethylhydrazone of (*R*)-**12** lead to (*S,R*)-**14** with 50% *de* after cleavage of the N–N bond[33]. Thus, the 1,2-addition to (*S,S*)-**13**, using SAMP as the auxiliary, followed by subsequent N–N bond cleavage was performed, giving the amine (*S,R*)-**14** in 22% yield as a virtually diastereo- and enantiomerically pure compound. The corresponding reaction sequence furnished (*S,S*)-**14** in 23% yield with a diastereomeric excess of 80% when the RAMP hydrazone (*R,S*)-**13** was employed in the reaction sequence. Obviously, the SAMP hydrazone pathway represents the *matched* and the RAMP hydrazone the *mismatched* case. The use of RAMP as the auxiliary effectively overrides the stereodirecting effects of the preexisting chirality in the protected glyceraldehyde, leading to the (*S,S*) configuration at the stereogenic center.

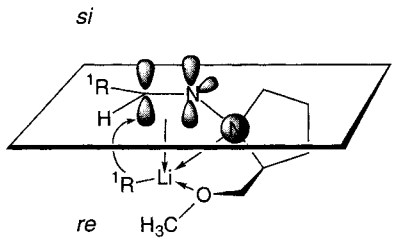
Concerning the mechanism of the highly diastereoselective addition, we do not have to consider the absolute configuration at C-2 of the hydrazone in our mechanistic model. A possible transition state is depicted in Figure 2. As is evident from previous investigations[34], the pyrrolidine ring and the C=N double bond adopt a coplanar conformation in aldehyde SAMP hydrazones. In this transition-

Scheme 3. Diastereoselective nucleophilic addition to protected glyceroaldehyde SAMP or RAMP hydrazone



state model, the chelation of the lithium atom by the pyrrolidine nitrogen atom and the methoxymethyl side-chain changes the preferred aldehyde hydrazone conformation, restricts the rotation around the N–N bond and increases the conformational rigidity. In our model, the free electron pairs of the nitrogen are at an angle of 180° to each other. The nucleophile, i.e. the organolithium compound, is complexed below the plane of the C=N double bond and thus attacks from the *re*-face, giving rise to the absolute configuration observed.

Figure 2. Possible transition state for the diastereoselective nucleophilic 1,2-addition to SAMP hydrazones



Conclusion

We have presented a method for the preparation of α-substituted- and α,β-disubstituted amines, starting from aldehyde hydrazones, in a highly diastereo- and enantioselective fashion. Both enantiomers can be prepared in excess by simple exchange of the readily available chiral auxiliary

SAMP to the optical antipode RAMP or by permutation of R^1 and R^2 in the carbonyl compounds in the diastereoselective α-alkylation of the hydrazones. Alternatively, the chiral auxiliary can be changed to the optical antipode after the α-alkylation step.

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Experimental Section

All reactions were carried out using standard Schlenk techniques under an argon atmosphere. N–N bond cleavages moderated by Raney-Ni were carried out in a Parr hydrogenation apparatus or a stainless steel autoclave. Reagents were purchased from common commercial suppliers and were dried and distilled under argon prior to use. A kugelrohr apparatus was used for distillations. – Column chromatography: Merck silica gel 60, 0.040–0.063 mm (230–400 mesh). – GC: Siemens Sichromat 2 and 3; columns: OV101 (25 m), OV1cb (25 m), SE54 (25 m), OV101 (50 m), XE-60-(*S*)-valin-(*S*)-α-phenylethyl amide (25 m). – IR spectra: Beckman Acculab 4. – NMR: Varian EM 390, Varian VXR 300, Varian CFT 20. – Mass spectra: Varian MAT 212 (EI). – Microanalysis: Heraeus Micro U/D.

General Procedure 1 (GP 1): To a solution of 1.1 to 2.0 equivalents of organolithium compound in diethyl ether or THF (3 ml/mmol) was added dropwise a solution of 1 equivalent of hydrazone **2**, dissolved in THF (1 ml/mmol), at −78°C with stirring. The reaction mixture was allowed to slowly warm to room temperature during 6 to 12 h, water was added for hydrolysis and the reaction mixture was extracted three times with diethyl ether. The combined extracts were dried with $MgSO_4$, and the solvent was removed under vacuum. The air-sensitive hydrazines were purified by column chromatography or kugelrohr distillation.

General Procedure 2 (GP 2): A stainless steel autoclave or a Parr hydrogenation apparatus was charged with hydrazine **3** and methanol (5–10 ml/mmol). Freshly prepared Raney-Ni[22] (0.5–1.0 g/mmol) was added. A hydrogen pressure of 3 to 9 bar was applied, and the reaction mixture was heated with stirring to 50–80°C for 15–140 h. The reaction was followed by TLC, and after termination of the reaction, the mixture was filtered through a Celite plug to remove the catalyst. The solvent was removed under vacuum, the residue dissolved in diethyl ether and dried with $Na_2SO_4/MgSO_4$.

General Procedure 3 (GP 3): The mixture of amines in diethyl ether, obtained by *GP 2*, and 1.5 equivalents of benzaldehyde or *p*-nitrobenzaldehyde, respectively, were combined in the presence of molecular sieves (4 Å). The reaction was monitored by GC until no starting material could be detected (10 to 70 h). The imine (R_f >0.9) and (*S*)-2-(methoxymethyl)pyrrolidine (R_f < 0.2) were separated by column chromatography (silica gel, diethyl ether). The imine was dissolved in 50 ml of diethyl ether, 10 ml of 3 N HCl was added for hydrolysis, and the reaction was followed by TLC. After the hydrolysis was complete, the aqueous phase was separated, saturated with K_2CO_3, extracted with diethyl ether, and dried with $K_2CO_3/MgSO_4$. Finally, the solvent was removed, and the amine was purified by kugelrohr distillation.

General Procedure 4 (GP 4): To a solution of the mixture of amines in diethyl ether, obtained by *GP 2*, 2.1 equivalents of triethyl amine and 2.0 equivalents of methyl chloroformate were added. After stirring for 1 h at ambient temperature, water was added. The organic phase was separated and dried with $MgSO_4$. The solvent was removed under vacuum, and the carbamates were separated by column chromatography (silica gel, petroleum ether/diethyl ether). 10 ml of HBr (33%)/acetic acid and the protected amine were combined and heated to 80°C for 3–5 h. 30 ml of H_2O was added, the aqueous phase was saturated with K_2CO_3 and extracted with diethyl ether (5 × 50 ml). The combined extracts were dried with $K_2CO_3/MgSO_4$, the solvent was removed under vacuum, and the amine was purified by kugelrohr distillation.

General Procedure 5 (GP 5): To a solution of 1 to 1.5 equivalents of the organolithium compound in THF (3 ml/mmol) was added dropwise a solution of 1 equivalent of the aldehyde hydrazone **6** in THF (1 ml/mmol) at −78°C with stirring. The solution was allowed to warm to room temperature during 6 to 12 h. The solution was then cooled to −78°C, and 4 equivalents of methyl chloroformate were added. The cooling bath was removed and the mixture allowed to warm to room temperature. The reaction mixture was poured into a pH-7 buffer and was extracted three times with diethyl ether. The combined extracts were dried with $Na_2SO_4/MgSO_4$, filtered through a pad of silica gel and the solvent removed, yielding the *N*-protected hydrazines in 70–95% purity (GC).

100–150 ml of liquid ammonia was placed in a two-necked flask fitted with a dry-ice condenser. 15 equivalents of lithium wire and the crude reaction mixture, dissolved in 50 ml of diethyl ether, were subsequently added at −78°C. The mixture was refluxed for 3 h and cooled to −50°C. Methanol was added until the violet color completely disappeared. The mixture was allowed to warm to room temperature overnight, and the resulting residue was dissolved in H_2O and extracted three times with 50 ml of diethyl ether. The combined extracts were dried with $Na_2SO_4/MgSO_4$, the solvent was removed under vacuum, and the product was purified by column chromatography (silica gel, petroleum ether/diethyl ether). The carbamate, usually contaminated by the free hydrazine, and 10 ml of HBr (33%)/acetic acid were combined and were heated to 80°C for 3 to 5 h. After cooling to room temperature, 30 ml of H_2O was added, the aqueous phase was saturated with K_2CO_3 and extracted five times with 50 ml of diethyl ether. The combined organic extracts were dried over $K_2CO_3/MgSO_4$, the solvent was removed, and the amine was purified by kugelrohr distillation.

General Procedure 6 (GP 6): $Pb(OAc)_4$ was suspended in toluene (6 ml/mmol) and 1,2:5,6-diisopropylidenemannitol (1 equivalent) was added portionswise with stirring until no oxidising agent remained, as indicated by a KI/starch test. The reaction mixture was filtered through a plug of Celite and stirred with $NaHCO_3$ to neutralise the generated acetic acid. The $NaHCO_3$ was filtered off, and the toluene solution immediately used for the preparation of the hydrazones.

SAMP/RAMP and α-alkylated SAMP/RAMP hydrazones **2**, **6** were prepared and were alkylated according to literature procedures[12,21,16,35].

(−)-(1R,2'S)-1-[2'-(Methoxymethyl)pyrrolidin-1'-yl]amino-1-phenylethane [(*S,R*)-**3a**]: 6.7 ml (10 mmol) of CH_3Li and 1.09 g (5.0 mmol) of (−)-(*S*)-1-benzylideneamino-2-(methoxymethyl) pyrrolidine[12] were allowed to react in Et_2O according to *GP 1*, yielding 0.85 g of (*S,R*)-**3a** (73%) as a bright yellow oil after distillation. – b.p. 65–70°C/0.01 Torr. – $[\alpha]_D^{22} = -73.7$ (c = 2.26, C_6H_6). – IR (film): $\tilde{\nu}$ = 3180 cm^{-1} (w, NH), 3080, 3060, 3020 (m, aromatic CH), 3000–2800 (m, CH), 1600, 1580, 1560, 1450, 1360, 1340, 1320, 1300, 1280, 1200, 1190 (m), 1130, 1100 (s), 1065, 1025, 920, 890, 850, 765, 705 (m). – ^1H NMR (90 MHz, $CDCl_3$, TMS): δ = 1.33 (d, J = 7 Hz, 3H, CH_3), 1.44–2.33 (m, 4H, CH_2CH_2), 2.44 (s, 1H, NH), 2.60 (m, 1H, NC*H*H), 3.00–3.56 (m, 2H, NCH*H*, NCH),

3.38 (s, 3H, OCH_3), 3.69 (d, J = 4 Hz, 2H, OCH_2), 3.98 (q, J = 7 Hz, 1H, $CHCH_3$), 7.31 (m, 5H, aromatic H). – MS (70 eV); *m/z* (%): 234 (6) [M^+], 189 (11) [$M^+ - CH_2OCH_3$], 129 (100). – HRMS ($C_{14}H_{22}N_2O$): calcd. C 234.1732; found 234.1714.

(+)-(1S,2'R)-1-[2'-(Methoxymethyl)pyrrolidin-1'-yl]amino-1-phenylethane [(*R,S*)-**3a**]: 10.0 ml (17.7 mmol) of CH_3Li and 3.27 g (15.0 mmol) of (+)-(*R*)-1-benzylideneamino-2-(methoxymethyl)-pyrrolidine (*R*)-**2a**[12] were allowed to react in Et_2O according to *GP 1*, yielding 2.84 g of (*R,S*)-**3a** (81%) as a bright yellow oil after distillation. – b.p. 150°C/0.1 Torr. – $[\alpha]_D^{20}$ = +62.7 (*c* = 2.7, C_6H_6). – The spectroscopic data were identical with those of (*S,R*)-**3a**.

(–)-(1R,2'S)-1-[2'-(Methoxymethyl)pyrrolidin-1'-yl]amino-1-(4-methoxy)phenylethane [(*S,R*)-**3b**]: 15.0 ml (20.0 mmol) of CH_3Li and 2.48 g (10 mmol) of (–)-(*S*)-1-(4-methoxy)benzylideneamino-2-(methoxymethyl)pyrrolidine[12] were allowed to react in Et_2O according to *GP 1*, yielding 2.54 g of (*R,S*)-**3b** (97%) as an analytically pure, yellow oil. – $[\alpha]_D^{20}$ = –82.4 (*c* = 1.94, C_6H_6): – ^1H NMR (90 MHz, $CDCl_3$, TMS): δ = 1.30 (d, J = 6 Hz, 3H, CH_3), 1.60 (m, 4H, CH_2), 2.09 (m, 1H, NC*H*H), 2.40 (br. s, 1H, NH), 3.24–3.84 (m, 4H, OCH_2, NCH, NCH*H*), 3.38 (s, 3H, OCH_3), 3.76 (s, 3H, C_6H_4-*p*-OCH_3), 3.91 (q, J = 7 Hz, 1H, $CHCH_3$), 7.02 (m, 4H, C_6H_4). – MS (70 eV); *m/z* (%) = 264 (32) [M^+], 219 (8) [$M^+ - CH_2OCH_3$], 135 (100). – $C_{15}H_{24}N_2O_2$ (264.4): calcd. C 68.41, H 8.80, N 10.64; found C 68.12, H 8.79, N 10.27.

(–)-(2R,2'S)-3,3-Dimethyl-2-N-[2'-(methoxymethyl)pyrrolidin-1'-yl]aminobutane [(*S,R*)-**3c**] 34.0 ml (50 mmol) of CH_3Li and 4.96 g (25 mmol) of (–)-(*S*)-1-(2,2-dimethylpropylideneamino)-2-(methoxymethyl)pyrrolidine[12] were allowed to react in Et_2O according to *GP 1*, yielding 4.3 g of (*S,R*)-**3c** (80%) as a red-brown oil after distillation. – b.p. 40°C/0.03 Torr. – $[\alpha]_D^{20}$ = –54.4 (*c* = 1.6, C_6H_6). – IR (film): $\tilde{\nu}$ = 3220 cm^{-1} (w, NH), 1510, 1495, 1480, 1460, 1450, 1400, 1370, 1350, 1290, 1260, 1200 (m), 1130, 1100 (s), 1070, 1020, 1000, 980, 940, 925, 895, 840, 760 (m). – ^1H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.87 (s, 9H, tC_4H_9), 0.97 (d, J = 7 Hz, 3H, $CHCH_3$), 1.41–2.12 (m, 5H, CH_2CH_2, NC*H*H), 2.22 (s, 1H, NH), 2.53 (q, J = 7 Hz, 1H, $CHCH_3$), 3.16–3.64 (m, 4H, OCH_2, NCH*H*, NCH), 3.34 (s, 3H, OCH_3). – MS (70 eV); *m/z* (%) = 214 (16) [M^+], 169 (62) [$M^+ - CH_2OCH_3$], 157 (100) [$M^+ - C_4H_9$]. – $C_{12}H_{26}N_2O$ (214.35): calcd. C 67.24, H 12.24, N 13.07; found C 67.14, H 12.31, N 13.12.

(–)-(2S,2'S)-3,3-Dimethyl-2-N-[2'-(methoxymethyl)pyrrolidin-1'-yl]aminobutane [(*S,S*)-**3c**]: 30 ml (60 mmol) of *t*BuLi and 4.68 g (30 mmol) of (–)-(*S*)-1-ethylideneamino-2-(methoxymethyl)pyrrolidine[36] were allowed to react in Et_2O according to *GP 1*, yielding 6.3 g of crude (*S,S*)-**3c** (98%) as a red oil. $[\alpha]_D^{20}$ = –77.3 (*c* = 1.96, C_6H_6). – The spectroscopic data were identical with those of (*S,R*)-**3c**.

(–)-(1R,2'S)-2,2-Dimethyl-1-[2'-(methoxymethyl)pyrrolidin-1'-yl]amino-1-phenylpropane [(*S,R*)-**3d**]: 10 ml (15 mmol) of *t*BuLi and 2.18 g (10 mmol) of (–)-(*S*)-1-benzylideneamino-2-(methoxymethyl)pyrrolidine[12] were allowed to react in THF according to *GP 1*, yielding 2.4 g of (*S,R*)-**3d** (87%) as bright yellow oil after distillation. – b.p. 86°C/0.02 Torr. – $[\alpha]_D^{20}$ = –32.3 (*c* = 1.3, C_6H_6). – IR (film): $\tilde{\nu}$ = 3200 cm^{-1} (w, NH), 3100, 3070, 3040 (m, aromatic CH), 3000, 2800 (m, CH), 1600, 1480, 1460, 1395, 1370, 1300, 1240, 1200 (m), 1130, 1100 (s), 1070, 1030, 920, 790, 740, 710 (m). – ^1H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.90 (s, 9H, tC_4H_9), 1.04–2.04 (m, 4H, CH_2CH_2), 2.49 (m, 2H, NC*H*H, NH), 3.37 (s, 3H, OCH_3), 3.40–3.76 (m, 5H, OCH_2, NCH*H*, NCH, CHC_6H_5), 7.24 (m, 5H, C_6H_5). – MS (70 eV); *m/z* (%) = 276 (74) [M^+], 231 (14) [$M^+ - CH_2OCH_3$], 219 (86) [$M^+ - C_4H_9$], 129 (100). – $C_{17}H_{28}N_2O$ (276.4): calcd. C 73.87, H 10.21, N 10.13; found C 73.81, H 10.26, N 9.90.

(–)-(1S,2'S)-2,2-Dimethyl-1-[2'-(methoxymethyl)pyrrolidin-1'-yl]amino-1-phenylpropane [(*S,S*)-**3d**]: 18 ml (36 mmol) of PhLi and 3.63 g (18.3 mmol) of (–)-(*S*)-1-(2,2-dimethylpropylideneamino)-2-(methoxymethyl)pyrrolidine[12] were allowed to react in Et_2O according to *GP 1*, yielding 4.8 g of (*S,S*)-**3d** (95%) as bright yellow oil after distillation. – b.p. 140°C/0.05 Torr. – $[\alpha]_D^{20}$ = –101.9 (*c* = 2.12, C_6H_6). – HRMS ($C_{17}H_{28}N_2O$): calcd. 276.2174; found 276.2202. – The spectroscopic data were identical with those of (*S,R*)-**3d**.

(–)-(1R,2'S)-1-[2'-(Methoxymethyl)pyrrolidin-1'-yl]amino-1-phenylpentane [(*S,R*)-**3e**]: 12.5 ml (20 mmol) of *n*BuLi and 2.18 g (10 mmol) of (–)-(*S*)-1-benzylideneamino-2-(methoxymethyl)pyrrolidine[12] were allowed to react in THF according to *GP 1*, yielding 2.5 g of (*S,R*)-**3e** (91%) as a bright yellow oil after distillation. – b.p. 75–85°C/0.01 Torr. – *de* >95% (^{13}C NMR). – $[\alpha]_D^{20}$ = –88.0 (*c* = 1.2, C_6H_6). – IR (film): $\tilde{\nu}$ = 3200 cm^{-1} (w, NH), 3100, 3070, 3040 (m, aromatic CH), 3000–2800 (m, CH), 1610, 1500, 1465, 1350, 1310, 1290, 1200 (m), 1135, 1100 (s), 1035, 925, 765, 735, 710 (m). – ^1H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.82 (t, J = 7 Hz, 3H, CH_3), 0.98–2.22 [m, 10H, $(CH_2)_3CH_3$, CH_2CH_2], 2.56 (m, 2H, NH, NC*H*H), 3.38 (s, 3H, OCH_3), 3.04–3.73 (m, 4H, OCH_2, NCH*H*, CHC_6H_5), 3.89 (t, J = 7 Hz, 1H, CHC_6H_5), 7.27 (m, 5H, C_6H_5). – ^{13}C NMR (20 MHz, $CDCl_3$, TMS): δ = 14.2 (CH_3), 21.3, 23.2, 27.0, 28.5, 35.8 (CH_2), 57.1 (CH_2N), 58.8 (OCH_3), 64.8, 66.0 (CHN), 76.1 (OCH_2), 127.0, 127.6, 128.2 (aromatic CH), 144.3 (aromatic C). – MS (70 eV); *m/z* (%) = 276 (35) [M^+], 231 (77) [$M^+ - CH_2OCH_3$], 219 (10) [$M^+ - C_4H_9$], 129 (100). – $C_{17}H_{28}N_2O$ (276.4): calcd. C 73.87, H 10.21, N 10.13; found C 74.21, H 10.35, N 10.13.

(–)-(1S,2'S)-1-[(2'-(Methoxymethyl)pyrrolidin-1'-yl]amino-1-phenylpentane [(*S,S*)-**3e**]: 20 ml (45 mmol) of PhLi and 4.5 g (22.7 mmol) of (–)-(*S*)-2-(methoxymethyl)-1-pentylideneaminopyrrolidine[21] were allowed to react in Et_2O according to *GP 1*, yielding 5.5 g of (*S,S*)-**3e** (88%) as a yellow oil after distillation. – b.p. 160°C/0.2 Torr. – $[\alpha]_D^{20}$ = –58.2 (*c* = 1.96, C_6H_6). – ^1H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.82 (t, J = 7 Hz, 3H, CH_3), 1.02–2.76 [m, 11H, $(CH_2)_3CH_3$, CH_2CH_2, NC*H*H], 2.48 (br. s, 1H, NH), 2.92–3.36 (m, 4H, OCH_2, NCH*H*, NCH), 3.18 (s, 3H, OCH_3), 3.80 (t, J = 7 Hz, 1H, CHC_6H_5), 7.27 (m, 5H, C_6H_5). – HRMS ($C_{17}H_{28}N_2O$): calcd. 276.2202; found 276.2209. – The IR and MS data were identical with those of (*S,R*)-**3e**.

(–)-(1S,2'S)-2-Methyl-1-[2'-(methoxymethyl)pyrrolidin-1'-yl]-amino-1-phenylpropane [(*S,S*)-**3f**]: 20 ml (40 mmol) of PhLi and 3.45 g (18.75 mmol) of (–)-(*S*)-2-(methoxymethyl)-1-(2-methylpropylideneamino)pyrrolidine[12] were allowed to react in Et_2O according to *GP 1*, yielding 4.83 g of (*S,S*)-**3f** (98%) as bright yellow oil after distillation. – b.p. 130°C/0.02 Torr. – $[\alpha]_D^{20}$ = –58.9 (*c* = 1.75, C_6H_5). – IR (film): $\tilde{\nu}$ = 3200 cm^{-1} (w, NH), 3090, 3070, 3030 (m, aromatic CH), 2960–2860 (m, CH), 1450, 1385, 1370, 1270, 1190 (m), 1130, 1100 (s), 1000, 980, 750, 710 (m). – ^1H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.72, 0.92 [2 d, J = 7 Hz, 6H, $CH(CH_3)_2$], 0.82–2.00 [m, 5H, $CH(CH_3)_2$, CH_2CH_2], 2.18 (m, 1H, NC*H*H), 2.61 (br. s, 1H, NH), 3.18 (s, 3H, OCH_3), 2.89–3.63 (m, 5H, OCH_2, NCH*H*, NCH, CHC_6H_5), 7.24 (m, 5H, C_6H_5). – MS (70 eV); *m/z* (%) = 262 (11) [M^+], 225 (87), 185 (57), 129 (100). – HRMS ($C_{16}H_{26}N_2O$): calcd. 262.2045; found 262.2044.

(–)-(3R,2'S)-2-Methyl-3-N-[2'-(methoxymethyl)pyrrolidin-1'-yl]aminoheptane [(*S,R*)-**3g**]: 19 ml (30 mmol) of *n*BuLi and 2.76 g (15 mmol) of (–)-(*S*)-2-(methoxymethyl)-1-(2-methylpropylideneamino)pyrrolidine[12] were allowed to react in Et_2O according to

GP 1, yielding 3.3 g of (*S,R*)-**3g** (92%) as yellow oil after distillation. – b.p. 120°C/0.01 Torr. – $[\alpha]_D^{20} = -90.4$ (c = 2.53, C_6H_6). – IR (film): $\tilde{\nu}$ = 3200 cm^{-1} (w, NH), 2960–2800 (CH), 1460, 1380, 1350, 1200 (m), 1130, 1100 (s), 1030, 1010, 920 (m). – ^1H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.87 [d, J = 7 Hz, 6H, $CH(CH_3)_2$], 1.11–2.24 [m, 14H, $(CH_2)_3CH_3$, $CH(CH_3)_2$, CH_2CH_2], 2.30 (br. s, 1H, NH), 2.53 (m, 1H, NC*H*H), 3.34 (s, 3H, OCH_3), 3.24–3.64 [m, 5H, OCH_2, NCH*H*, NCH, $CH(CH(CH_3)_2]$. – MS (70 eV); *m/z* (%) = 242 (21) [M^+], 199 (63), 197 (100) [$M^+ - CH_2OCH_3$]. – $C_{14}H_{30}N_2O$ (242.4): calcd. C 69.37, H 12.47, N 11.56; found C 69.67, H 12.07, N 11.29.

(–)-(3R,2'S)-2,2-Dimethyl-3-N-[2'-(methoxymethyl)pyrrolidin-1'-yl]aminoheptane [(*S,R*)-**3h**]: 12.5 ml (20 mmol) of *n*BuLi and 2.97 g (15 mmol) of (–)-(*S*)-1-(2,2-dimethylpropylideneamino)-2-(methoxymethyl)pyrrolidine[12] were allowed to react in THF according to *GP 1*, yielding 3.5 g of (*S,R*)-**3h** (91%) as a yellow oil after distillation. – b.p. 55°C/0.005 Torr. – *de* >95% (^{13}C NMR). – $[\alpha]_D^{20} = -104.0$ (c = 0.95, C_6H_6). – IR (film): $\tilde{\nu}$ = 3220 cm^{-1} (w, NH), 2960–2800 (m, CH), 1470, 1390, 1360, 1200 (m), 1130, 1100 (s), 1020, 970, 920 (m). – ^1H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.89 (s, 9H, tC_4H_9), 1.11–2.34 [m, 13H, CH_2CH_2, $(CH_2)_3CH_3$], 2.25 (br. s, 1H, NH), 2.56 (m, 1H, NC*H*H), 3.17–3.71 [m, 5H, OCH_2, NCH*H*, NCH, $CHC(CH_3)_3$], 3.34 (s, 3H, OCH_3). – ^{13}C NMR (20 MHz, [D_5]pyridine, TMS): δ = 14.2 (CH_3), 21.2, 23.5 (CH_2), 27.0 [$C(CH_3)_3$], 27.2, 31.3, 31.8 (CH_2), 34.0 [$C(CH_3)_3$], 55.9 (CH_2N), 55.9 (CH_2N), 58.6 (OCH_3), 65.3, 66.7 (CHN), 75.8 (CH_2O). – MS (70 eV); *m/z* (%) = 256 (25) [M^+], 211 (18) [$M^+ - CH_2OCH_3$], 199 (92) [$M^+ - C_4H_9$], 70 (100). – $C_{15}H_{32}N_2O$ (256.4): calcd. C 70.26, H 12.56, N 10.92; found C 70.25, H 12.75, N 10.91.

(–)-(3S,2'S)-3-N-[2'-(Methoxymethyl)pyrrolidin-1'-yl]-aminoheptane [(*S,S*)-**3j**]: 25 ml (40 mmol) of *n*BuLi and 3.4 g (20 mmol) of (–)-(*S*)-2-(methoxymethyl)-1-propylideneaminopyrrolidine[21] were allowed to react in Et_2O according to *GP 1*, yielding 3.78 g of (*S,S*)-**3j** (83%) as a yellow oil after distillation. – b.p. 56°C/0.05 Torr. – $[\alpha]_D^{20} = -100.4$ (c = 2.35, C_6H_6). – IR (film): $\tilde{\nu}$ = 3200 cm^{-1} (w, NH), 2960–2800 (m, CH), 1460, 1380, 1200 (m), 1130, 1100 (s), 1030, 920 (m). – ^1H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.89, 0.90 (2 t, 6H, 2 CH_3), 1.14–2.24 [m, 12H, $(CH_2)_3CH_3$, CH_2CH_2, CH_2CH_3], 2.25 (br. s, 1H, NH), 2.33 (m, 1H, NC*H*H), 3.25–3.61 (m, 5H, OCH_2, NCH*H*, NCH, $CHCH_2CH_3$), 3.35 (s, 3H, OCH_3). – MS (70 eV); *m/z* (%) = 228 (13) [M^+], 183 (100) [$M^+ - CH_2OCH_3$]. – HRMS ($C_{13}H_{28}N_2O$): calcd. 228.2201; found 228.2201.

(+)-(R)-1-Amino-1-phenylethane [(*R*)-**4a**]: 2.0 g (8.54 mmol) of (*S,R*)-**3a** was allowed to react according to *GP 2* for 48 h at 20°C, 3.7 bar H_2 pressure and was purified according to *GP 3*, yielding 0.63 g of (*R*)-**4a** (61%) as a colorless oil. – b.p. 80°C/20 Torr. – *ee* = 81% (^1H NMR of the corresponding MTPA amide). – $[\alpha]_D^{20}$ = +26.1 (neat). – The NMR data matched those reported in ref.[37].

(–)-(S)-1-Amino-1-phenylethane [(*S*)-**4a**]: 2.84 g (12.1 mmol) of (*R,S*)-**3a** was allowed to react according to *GP 2* for 48 h at 20°C, 3.8 bar H_2 pressure and was purified according to *GP 3*, yielding 0.92 g of (*S*)-**4a** (63%) as a colorless oil. – b.p. 87°C/25 Torr. – *ee* = 81% (correlation of optical rotation with (*R*)-**4a**). – $[\alpha]_D^{20}$ = –26.1 (neat). – The NMR data matched those reported in ref.[37].

(+)-(R)-1-Amino-1-(4-methoxy)phenylethane [(*R*)-**4b**]: 2.4 g (9.1 mmol) of (*S,R*)-**3b** was allowed to react according to *GP 2* for 24 h at 20°C, 3.8 bar H_2 pressure and was purified according to *GP 3*, yielding 1.1 g of (*R*)-**4b** (80%) as a colorless oil. – b.p. 110–120°C/15 Torr. – *ee* = 72% (correlation of optical rotation). – $[\alpha]_D^{20}$ = +26.0 (neat) {ref.[38] $[\alpha]_D^{20}$ = +21.6 (neat)}. – IR (film): $\tilde{\nu}$ = 3380, 3310 cm^{-1} (w, NH_2), 3070, 3040, 3010 (m, aromatic CH), 1610, 1585, 1510, 1460, 1370, 1300, 1250, 1180 (m), 1100, 1035 (s), 920, 830, 810, 735, 700 (m). – ^1H NMR (90 MHz, $CDCl_3$, TMS): δ = 1.34 (d, J = 7 Hz, 3H, $CHCH_3$), 1.44 (s, 2H, NH_2), 4.07 (q, J = 7 Hz, 1H, $CHCH_3$), 7.07 (m, 4H, C_6H_5).

(–)-(R)-2-Amino-3,3-dimethylbutane [(*R*)-**4c**]: 4.0 g (18.7 mmol) of (*S,R*)-**3c** was allowed to react according to *GP 2* for 24 h at 40°C, 4.0 bar H_2 pressure and was purified according to *GP 3*, yielding 1.1 g of (*R*)-**4c** (58%) as a colorless oil. – b.p. 50–60°C/95 Torr. – *ee* = 81% (correlation of optical rotation). – $[\alpha]_D^{20}$ = –4.5 (neat) {ref.[40] $[\alpha]_D^{23}$ = –5.6 (neat)}. – The spectroscopic data matched those reported in ref.[39].

(+)-(S)-2-Amino-3,3-dimethylbutane [(*S*)-**4c**]: 6.3 g (29.4 mmol) of (*S,S*)-**3c** was allowed to react according to *GP 2* for 24 h at 40°C, 4.0 bar H_2 pressure and was purified according to *GP 3*, yielding 1.38 g of (*S*)-**4c** (47%) as a colorless oil. – b.p. 100–102°C/760 Torr. – *ee* = 69% {correlation of optical rotation[40] and ^1H-NMR shift experiments with Eu(hfc)$_3$}. – $[\alpha]_D^{20}$ = +3.7 (neat) {ref.[40] $[\alpha]_D^{24}$ = +5.3 (neat)}. – The spectroscopic data matched those reported in ref.[39].

(–)-(S)-1-Amino-1-cyclohexyl-2,2-dimethylpropane [(*S*)-**4d**]: 2.0 g (7.2 mmol) of (*S,R*)-**3d** was allowed to react according to *GP 2* for 48 h at 40°C, 3.6 bar H_2 pressure and was purified according to *GP 3*, yielding 0.82 g of (*S*)-**4d** (67%) as a colorless oil. – b.p. 38–40°C/0.4 Torr. – *ee* = 82% (^1H NMR of the corresponding MTPA amide). – $[\alpha]_D^{20} = -25.8$ (neat). – IR (film): $\tilde{\nu}$ = 3400, 3340 cm^{-1} (m, NH_2), 2960–2860 (m, CH), 1615, 1480, 1450, 1400, 1365, 1310, 1260, 1230, 1170 (m), 1130, 1100 (s), 1030, 970, 890, 820, 780, 730 (m). – ^1H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.90 (s, 9H, tC_4H_9), 0.97 (s, 2H, NH_2), 1.06–1.86 (m, 11H, cC_6H_{11}), 1.97 (d, J = 5 Hz, 1H, CHC_4H_9). – MS (70 eV); *m/z* (%) = 170 (5) [M^+ + 1], 154 (6) [$M^+ - CH_3$], 112 (100) [$M^+ - C_4H_9$], 86 (58) [$M^+ - C_6H_{11}$]. – HRMS [$C_{11}H_{24}N$ (M^+ + 1)]: calcd. 170.1909; found 170.1911.

(+)-(R)-1-Amino-1-cyclohexyl-2,2-dimethylpropane [(*R*)-**4d**]: 2.0 g (7.2 mmol) of (*S,S*)-**3d** was allowed to react according to *GP 2* for 48 h at 40°C, 3.7 bar H_2 pressure and was purified according to *GP 3*, yielding 0.9 g of (*R*)-**4d** (74%) as a colorless oil. – b.p. 50–55°C/1.0 Torr. – *ee* = 90% (^1H and ^{19}F NMR of the corresponding MTPA amide). – $[\alpha]_D^{20}$ = +27.4 (neat). – The spectroscopic data were identical with those of (*S*)-**4d**.

(+)-(R)-1-Amino-1-phenylpentane [(*R*)-**4e**]: 1.5 g (5.4 mmol) of (*S,R*)-**3e** was allowed to react according to *GP 2* for 48 h at 20°C, 3.5 bar H_2 pressure and was purified according to *GP 3*, yielding 0.5 g of (*R*)-**4e** (62%) as a colorless oil. – b.p. 59°C/0.5 Torr. – *ee* = 85% (^{19}F NMR of the corresponding MTPA amide). – $[\alpha]_D^{20}$ = +14.1 (neat). – IR (film): $\tilde{\nu}$ = 3380, 3300 cm^{-1} (m, NH_2), 3090, 3060, 3030 (w, aromatic CH), 2960–2860 (m, CH), 1600, 1590, 1450, 1380, 860, 760, 700 (m). – ^1H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.86 (t, J = 6 Hz, 3H, CH_3), 1.47 (s, 2H, NH_2), 1.00–1.84 [m, 6H, $(CH_2)_3$], 3.84 (t, J = 7 Hz, 1H, CHC_6H_5), 7.28 (m, 5H, C_6H_5). – MS (70 eV); *m/z* (%) = 164 (5) [M^+ – 1], 163 (7) [M^+], 162 (47), 106 (100) [$M^+ - C_4H_9$]. – HRMS ($C_{11}H_{17}N$): calcd. C 163.1361; found 163.1339.

(–)-(S)-1-Amino-1-phenylpentane [(*S*)-**4e**]: 5.5 g (19.9 mmol) of (*S,S*)-**3e** was allowed to react according to *GP 2* for 72 h at 20°C, 3.8 bar H_2 pressure and was purified according to *GP 3*, yielding 2.44 g of (*S*)-**4e** (75%) as a colorless oil. – b.p. 65°C/0.6 Torr. – *ee* = 83% (^{19}F NMR of the corresponding MTPA amide). – $[\alpha]_D^{20} = -13.9$ (neat). – HRMS ($C_{11}H_{17}N$): calcd. 163.1361; found 163.1334. – The spectroscopic data were identical with those of (*R*)-**4e**.

(+)-(S)-1-Amino-1-cyclohexyl-2-methylpropane [(*S*)-**4f**]: 3.5 g (13.4 mmol) of (*S,S*)-**3f** was allowed to react according to *GP 2* for 24 h at 40°C, 1.6 bar H_2 pressure and was purified according to *GP 3*, yielding 1.6 g of (*S*)-**4f** (77%) as a colorless oil. – b.p. 38–40°C/0.6 Torr. – *ee* = 90% (^{19}F NMR of the corresponding MTPA amide). – $[\alpha]_D^{20}$ = +10.5 (neat). – IR (film): $\tilde{\nu}$ = 3400, 3330 cm^{-1} (m, NH_2), 2960–2860 (m, CH), 2680, 1615, 1470, 1450, 1390, 1370, 1300, 1270, 1150, 1090, 1010, 970, 900, 835, 770, 660 (m). – ^{1}H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.84, 0.92 [2 d, *J* = 5 Hz, 6H, $CH(CH_3)_2$], 0.95 (s, 2H, NH_2), 1.04–2.00 [m, 12H, cC_6H_{11}, $CH(CH_3)_2$], 2.18 [t, *J* = 5 Hz, 1H, $CHCH(CH_3)_2$]. – MS (70 eV); *m/z* (%) = 156 (5) [M^+ – 1], 112 (78) [$M^+ - C_3H_7$], 72 (100) [$M^+ - C_6H_{11}$]. – HRMS [$C_{10}H_{22}N$ (M^+ – 1)]: calcd. 156.1752; found 156.1736.

(+)-(R)-3-Amino-2-methylheptane [(*R*)-**4g**]: 3.0 g (12.4 mmol) of (*S,R*)-**3g** was allowed to react according to *GP 2* for 48 h at 20°C, 3.8 bar H_2 pressure and was purified according to *GP 3*, yielding 1.35 g of (*R*)-**4g** (84%) as a colorless oil. – b.p. 76°C/40 Torr. – *ee* = 86% (^{19}F NMR of the corresponding MTPA amide). – $[\alpha]_D^{20}$ = +17.4 (*c* = 3.3, EtOH). – IR (film): $\tilde{\nu}$ = 3400, 3320 cm^{-1} (w, NH_2), 2980–2890 (m, CH), 1620, 1475, 1390, 1375, 1130, 1040, 1020, 920, 780, 730 (m). – ^{1}H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.83, 0.91 [2 d, *J* = 7 Hz, 6H, $CH(CH_3)_2$], 1.12 (s, 2H, NH_2), 1.20–1.76 [m, 9H, $(CH_2)_3CH_3$], 2.48 [m, 1H, $CH(CH_3)_2$], 3.47 [q, *J* = 7 Hz, 1H, $CHCH(CH_3)_2$]. – MS (70 eV); *m/z* (%) = 130 (1) [M^+ – 1], 129 (0.24) [M^+], 86 (100) [$M^+ - C_3H_7$], 72 (39) [$M^+ - C_4H_9$]. – HRMS ($C_8H_{19}N$): calcd. 129.1517; found 129.1489.

(+)-(R)-3-Amino-2,2-dimethylheptane [(*R*)-**4h**]: 3.0 g (11.7 mmol) of (*S,R*)-**3h** was allowed to react according to *GP 2* for 48 h at 40°C, 3.5 bar H_2 pressure and was purified according to *GP 3*, yielding 1.3 g of (*R*)-**4h** (78%) as a colorless oil. – b.p. 70–75°C/45 Torr. – *ee* = 61% (^{19}F NMR of the corresponding MTPA amide, GC on CSP). – $[\alpha]_D^{22}$ = +14.7 (neat). – IR (film): $\tilde{\nu}$ = 3400, 3340 cm^{-1} (m, NH_2), 3000–2880 (m, CH), 1620, 1470, 1400, 1380, 1370, 1300, 1230, 1200, 1130, 1100, 1020 (m). – ^{1}H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.87 (s, 9H, tC_4H_9), 1.09 (s, 2H, NH_2), 0.78–2.39 [m, 10H, $(CH_2)_3CH_3$, CHC_4H_9]. – MS (70 eV); *m/z* (%) = 144 (3) [M^+ – 1], 128 (57) [$M^+ - CH_3$], 86 (100) [$M^+ - C_4H_9$]. – HRMS [$C_9H_{22}N$ (M^+ – 1)]: calcd. 144.1752; found 144.1740.

(+)-(S)-3-Aminoheptane [(*S*)-**4j**]: 3.7 g (16.2 mmol) of (*S,S*)-**3j** was allowed to react according to *GP 2* for 24 h at 40°C, 3.8 bar H_2 pressure and was purified according to *GP 3*, yielding 1.35 g of (*S*)-**4j** (72%) as a colorless oil. – b.p. 60–68°C/80 Torr. – *ee* = 72% (^{13}C NMR of the corresponding MTPA amide). $[\alpha]_D^{20}$ = +5.8 (neat)[41]. – IR (film): $\tilde{\nu}$ = 3380, 3300 cm^{-1} (m, NH_2), 2970–2870 (m, CH), 1610, 1460, 1380, 1160, 1140, 820 (m). – ^{1}H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.90 (2 t, 6H, 2 CH_3), 1.09–1.62 [m, 8H, $(CH_2)_3CH_3$, CH_2CH_3], 1.17 (s, 2H, NH_2), 2.59 (m, 1H, $CH(CH_2CH_3)$. – MS (70 eV); *m/z* (%) = 116 (18) [M^+ – 1], 115 (9) [M^+], 86 (97) [$M^+ - C_2H_5$], 58 (100) [$M^+ - C_4H_9$]. – HRMS ($C_9H_{21}N$): calcd. 115.1360; found 115.1353.

(–)-(3R,4R,2'S)-4-N-[2'-(Methoxymethyl)pyrrolidin-1'-yl]-amino-3-methyloctane [(*S,R,R*)-**8a**]: 5.5 ml (8 mmol) of *n*BuLi and 1.39 g (7 mmol) of (–)-(2*S*,2'*R*)-2-(methoxymethyl)-1-[2'-(methyl)-butylideneamino]pyrrolidine[21] were allowed to react in THF according to *GP 1*, yielding 1.42 g of (*S,R,R*)-**8a** (79%) after column chromatography. – *ds* = 97% (^{13}C NMR). – $[\alpha]_D^{20}$ = –104.8 (*c* = 1.1, C_6H_6). – IR (film): $\tilde{\nu}$ = 3200 cm^{-1} (w, NH), 2970–2820 (s, CH), 1460 (s), 1385 (m), 1200 (m), 1140 (s), 1105, 925 (m). – ^{1}H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.7–1.0 (m, 9H, CH_3), 1.0–1.4 (m, 8H, CH_2), 1.4–1.9 (m, 5H, $CHCH_3$, CH_2CH_2), 2.0–2.3 (m, 2H, NH, $NCHH$), 2.4–2.7 (m, 2H, $NCHH$, $CHNH$), 3.3 (s, 3H, OCH_3), 3.15–3.4 (m, 2H, NCH, $OCHH$), 3.52 (dd, *J* = 7 Hz, *J* = 4 Hz, 1H, $OCHH$). – ^{13}C NMR (20 MHz, C_6D_6, TMS): δ = 12.7, 14.5, 14.6 (CH_3), 21.4, 23.7, 25.8, 27.3, 29.3, 30.5 (CH_2), 36.5 (CH), 57.3 (CH_2N), 58.8 (OCH_3), 62.3, 66.2 (CHN), 76.3 (CH_2O). – MS (70 eV); *m/z* (%): 256 (23) [M^+], 211 (89) [$M^+ - CH_2OCH_3$], 199 (100) [$M^+ - C_4H_9$]. – $C_{15}H_{32}N_2O$ (256.4): calcd. C 70.31, H 12.50, N 10.94; found C 70.39, H 12.61, N 10.79.

(–)-(3S,4R,2'S)-3-N-[2'-(Methoxymethyl)pyrrolidin-1'-yl]-amino-2,2,4-trimethylhexane [(*S,S,R*)-**8b**]: 2.4 ml (3.5 mmol) of *t*BuLi and 0.594 g (3 mmol) of (–)-(2*S*,2'*R*)-2-(methoxymethyl)-1-[2'-(methyl)butylideneamino]pyrrolidine[21] were allowed to react in THF according to *GP 1*, yielding 0.515 g of (*S,S,R*)-**8b** (67%) after column chromatography. – *ds* >98% (^{13}C NMR). – $[\alpha]_D^{20}$ = –98.0 (*c* = 1.3, C_6H_6). – IR (film): $\tilde{\nu}$ = 3200 cm^{-1} (w, NH), 2970–2820 (s, CH), 1465 (s), 1395, 1380, 1365, 1200 (m), 1130 (s), 950, 920 (m). – ^{1}H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.9 (s, 9H, tC_4H_9), 0.7–1.0 (m, 6H, CH_3), 1.1–2.1 (m, 8H, CH_2CH_2, $CHCH_3$, NH), 2.2 (m, 1H, $NCHH$), 2.4–2.65 (m, 1H, $NCHH$), 2.42 (d, *J* = 2 Hz, 1 H, $CHNH$), 3.15–3.45 (m, 2H, NCH, $OCHH$), 3.32 (s, 3H, OCH_3), 3.68 (dd, *J* = 9 Hz, *J* = 4 Hz, 1H, $OCHH$). – ^{13}C NMR (20 MHz, C_6D_6, TMS): δ = 13.0, 15.7 (CH_3), 21.2, 27.3 (CH_2), 28.7 [$C(CH_3)_3$], 30.9 (CH_2), 35.3 (CH), 35.8 [$C(CH_3)_3$], 57.0 (CH_2N), 58.8 (OCH_3), 66.4, 68.1 (CHN), 76.0 (CH_2O). – MS (70 eV), *m/z* (%) = 256 (5) [M^+], 211 (4) [$M^+ - CH_2OCH_3$], 199 (100) [$M^+ - C_4H_9$]. – $C_{15}H_{32}N_2O$ (256.4): calcd. C 70.31, H 12.50, N 10.94; found C 70.05, H 12.39, N 10.80.

(–)-(2R,3R,2'S)-2-N-[2'-(Methoxymethyl)pyrrolidin-1'-yl]-amino-3-methylhexane [(*S,R,R*)-**8c**]: 3.7 ml (5.5 mmol) of CH_3Li and 1.06 g (5 mmol) of (–)-(2*S*,2'*R*)-2-(methoxymethyl)-1-[2'-(methyl)pentylideneamino]pyrrolidine[21] were allowed to react in THF according to *GP 1*, yielding 0.84 g of (*S,R,R*)-**8c** (74%) as a colorless oil after distillation. – b.p. 80°C/0.05 Torr. – *ds* = 97% (^{13}C NMR). – $[\alpha]_D^{20}$ = –92.8 (*c* = 1.3, C_6H_6). – IR (film): $\tilde{\nu}$ = 3200 cm^{-1} (w, NH), 2970–2840 (s, CH), 1475, 1465, 1385, 1200 (m), 1140, 1110 (s), 930 (m). – ^{1}H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.7–1.0 (m, 9H, 3 CH_3), 1.0–2.0 (m, 9H, CH_2, CH), 2.0–2.3 (m, 2H, $NCHH$, NH), 2.3–2.9 (m, 2H, $NCHH$, $CHNH$), 3.3 (s, 3H, OCH_3), 3.15–3.4 (m, 2H, NCH, $OCHH$), 3.55 (dd, *J* = 9 Hz, *J* = 4 Hz, 1H, $OCHH$). – ^{13}C NMR (20 MHz, C_6D_6, TMS): δ = 14.7, 16.0, 16.1 (CH_3), 21.3, 21.4, 27.4, 34.4 (CH_2), 37.0 (CH), 57.0 (CH_2N), 58.0 (CHN), 58.8 (OCH_3), 65.9 (CHN), 76.3 (CH_2O). – MS (70 eV); *m/z* (%) = 228 (20) [M^+], 183 (100) [$M^+ - CH_2OCH_3$], 157 (41) [$M^+ - C_5H_{11}$]. – $C_{13}H_{28}N_2O$ (228.4): calcd. C 68.42, H 12.28, N 12.28; found C 68.44, H 12.20, N 12.11.

(+)-(2S,3R,2'R)-2-N-[2'-(Methoxymethyl)pyrrolidin-1'-yl]-amino-3-methylhexane [(*R,S,R*)-**8c**]: 2.7 ml (4 mmol) of CH_3Li and 0.75 g (3.5 mmol) of (+)-(2*R*,2'*R*)-2-(methoxymethyl)-1-[2'-(methyl)pentylideneamino]pyrrolidine[21] were allowed to react in THF according to *GP 1*, yielding 0.42 g of (*R,S,R*)-**8c** (53%) as a pale yellow oil after column chromatography. – *ds* = 89% (^{13}C NMR). – $[\alpha]_D^{24}$ = +98.4 (*c* = 0.5, C_6H_6). – ^{13}C NMR (20 MHz, C_6D_6, TMS): δ = 14.5, 14.2, 14.6 (CH_3), 21.0, 21.4, 27.4 (CH_2), 36.6 (CH), 36.8 (CH_2), 57.1 (CH_2N), 57.6 (CHN), 58.8 (CH_3), 66.0 (CHN), 76.4 (CH_2O). – $C_{13}H_{28}N_2O$ (228.4): calcd. C 68.42, H 12.28, N 12.28; found C 68.46, H 12.23, N 12.16. – The IR- and ^{1}H-NMR data were identical with those of (*S,R,R*)-**8c**.

(–)-(1S,2R,2'S)-1-[2'-(Methoxymethyl)pyrrolidin-1'-yl]amino-2-methyl-1-phenylpentane [(*S,S,R*)-**8d**]: 3 ml (5.5 mmol) of PhLi and 1.06 g (5 mmol) of (–)-(2*S*,2'*R*)-2-(methoxymethyl)-1-[2'-(methyl)-pentylideneamino]pyrrolidine[21] were allowed to react in THF ac-

cording to *GP 1*, yielding 0.84 g of (*S,S,R*)-**8d** (58%) as a bright yellow oil after distillation. – b.p. 130°C/0.2 Torr. – *ds* = 96% (^{13}C NMR). – $[\alpha]_D^{20}$ = −67.5 (*c* = 1.2, C_6H_6). – IR (film): $\tilde{\nu}$ = 3210 cm^{-1} (w, NH), 3100–2820 (s, CH), 1465, 1455, 1385, 1130, 1105, 710 (s). – ^{1}H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.83 (d, 3H, *J* = 7 Hz, CHC*H*$_3$), 0.6–2.0 (m, 12H, CH_3, CH_2, C*H*CH_3), 2.0–2.3 (m, 1H, NC*H*H), 2.3–2.8 (m, 2H, NCH*H*, NH), 3.18 (s, 3H, OCH_3), 2.9–3.6 (m, 3H, OCH_2, CHN), 3.7 (d, *J* = 5 Hz, 1H, C*H*C_6H_5), 7.15 (m, 5H, C_6H_5). – ^{13}C NMR (20 MHz, C_6D_6, TMS): δ = 14.5, 16.4 (CH_3), 20.8, 21.3, 27.3, 35.2 (CH_2), 37.8 (CH), 56.8 (CH_2N), 58.7 (OCH_3), 65.8, 68.7 (CHN), 76.0 (CH_2O), 126.7, 127.7, 128.8 (aromatic CH), 143.6 (aromatic C). – MS (70 eV); *m/z* (%) = 290 (3) [M$^+$], 245 (5) [M$^+$ – CH_2OCH_3], 219 (9) [M$^+$ – C_5H_{11}], 129 (100). – $C_{18}H_{30}N_2O$ (290.4): calcd. C 74.48, H 10.34, N 9.66; found C 74.43, H 10.24, N 9.68.

(−)-(2R,3R,2′S)-2-N-[2′-(Methoxymethyl)pyrrolidin-1′-yl]-amino-3-methylheptane [(*S,R,R*)-**8e**]: 3.7 ml (5.5 mmol) of CH_3Li and 1.13 g (5 mmol) of (−)-(2*S*,2′*R*)-2-(methoxymethyl)-1-[2′-(methyl)hexylideneamino]pyrrolidine[16] were allowed to react in THF according to *GP 1*, yielding 0.74 g of (*S,R,R*)-**8e** (61%) as a pale yellow oil after column chromatography. – *ds* = 97% (^{13}C NMR). – $[\alpha]_D^{20}$ = −94.2 (*c* = 1.2, C_6H_6). – IR (film): $\tilde{\nu}$ = 3200 cm^{-1} (w, NH), 2970–2820 (s, CH), 1460, 1380 (s), 1200 (m), 1135, 1105 (s), 925 (m). – ^{1}H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.93 (t, 3H, *J* = 7 Hz, CH_3), 0.75–1.1 (m, 6H, CH_3), 1.1–2.0 (m, 11H, CH_2, C*H*CH_3), 2.0–2.4 (m, 2H, NH, NC*H*H), 2.4–2.9 (m, 2H, NCH*H*, C*H*NH), 3.4 (s, 3H, OCH_3), 3.2–3.6 (m, 2H, NCH, OC*H*H), 3.58 (dd, *J* = 9 Hz, *J* = 4 Hz, 1H, OCH*H*). – ^{13}C NMR (20 MHz, C_6D_6, TMS): δ = 14.4, 16.1, 16.2 (CH_3), 21.4, 23.58, 27.4, 30.6, 31.8 (CH_2), 37.3 (CH), 57.0 (CH_2N), 58.1 (CHN), 58.8 (OCH_3), 66.0 (CHN), 76.4 (CH_2O). – MS (70 eV); *m/z* (%) = 242 (16) [M$^+$], 197 (100) [M$^+$ – CH_2OCH_3], 157 (50) [M$^+$ – C_6H_{13}]. – $C_{14}H_{30}N_2$ (242.4): calcd. C 69.42, H 12.40, N 11.57; found C 69.35, H 12.35, N 11.68.

(+)-(2S,3S,2′R)-2-N-[2′-(Methoxymethyl)pyrrolidin-1′-yl]-amino-3-methylheptane [(*R,S,S*)-**8e**]: 5.3 ml (8 mmol) of CH_3Li and 1.58 g (7 mmol) of (+)-(2*R*,2′*S*)-2-(methoxymethyl)-1-[2′-(methyl)-hexylideneamino]pyrrolidine[16] were allowed to react in THF according to *GP 1*, yielding 0.82 g of (*R,S,S*)-**8e** (48%) as a colorless oil after distillation. – b.p. 75–80°C/0.05 Torr. – *ds* = 97% (^{13}C NMR). – $[\alpha]_D^{20}$ = +95.0 (*c* = 1.3, C_6H_6). – $C_{14}H_{30}N_2O$ (242.4): calcd. C 69.42, H 12.40, N 11.57; found C 69.59, H 12.42, N 11.40. – The spectroscopic data were identical with those of (*S,R,R*)-**8e**.

(−)-(3S,4R,2′S)-3-N-[2′-(Methoxymethyl)pyrrolidin-1′-yl]-amino-2,2,4-trimethyloctane [(*S,S,R*)-**8f**]: 3.7 ml (5.5 mmol) of *t*BuLi and 1.13 g (5 mmol) of (−)-(2*S*,2′*R*)-2-(methoxymethyl)-1-[2′-(methyl)hexylideneamino]pyrrolidine[16] were allowed to react in THF according to *GP 1*, yielding 0.94 g of (*S,S,R*)-**8f** (66%) as a pale yellow oil after column chromatography. – *ds* = 97% (^{13}C NMR). – $[\alpha]_D^{20}$ = −91.7 (*c* = 0.8, C_6H_6). – IR (film): $\tilde{\nu}$ = 3200 cm^{-1} (w, NH), 2960–2820 (s, CH), 1490, 1450, 1395, 1365, 1205, 1190 (m), 1130, 1100 (s), 920 (m). – ^{1}H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.92 [s, 9H, $C(CH_3)_3$], 0.7–1.0 (m, 6H, CH_3), 1.05–1.4 (m, 6H, CH_2), 1.4–2.1 (m, 6H, C*H*CH_3, NH, NCH_2), 2.2–2.6 (m, 2H, NCH_2), 2.4 (d, *J* = 2 Hz, 1H, C*H*NH), 3.1–3.45 (m, 2H, NCH, OC*H*H), 3.3 (s, 3H, OCH_3), 3.7 (dd, *J* = 9 Hz, *J* = 4 Hz, 1H, OCH*H*). – ^{13}C NMR (20 MHz, C_6D_6, TMS): δ = 14.4, 16.2 (CH_3), 21.2, 23.3, 27.3 (CH_2), 28.7 [$C(CH_3)_3$], 30.0, 33.2 (CH_2), 35.9 [*C*$(CH_3)_3$], 38.1 (CH), 57.0 (CH_2N), 58.8 (OCH_3), 66.4, 68.3 (CHN), 76.0 (OCH_2). – MS (70 eV); *m/z* (%) = 284 (5) [M$^+$], 239 (4) [M$^+$ – CH_2OCH_3], 227 (100) [M$^+$ – C_4H_9], 199 (16) [M$^+$ – C_6H_{13}]. – $C_{17}H_{36}N_2O$ (284.5): calcd. C 71.83, H 12.68, N 9.86; found C 71.72, H 12.73, N 9.85.

(−)-(2R,3R,2′S)-3-N-[2′-(Methoxymethyl)pyrrolidin-1′-yl]-amino-2-methyl-1-phenylheptane [(*S,R,R*)-**8g**]: 3.7 ml (5.5 mmol) of *n*BuLi and 1.3 g (5 mmol) of (−)-(2*S*,2′*R*)-2-(methoxymethyl)-1-[(2′-methyl-3′-phenyl)propylideneamino]pyrrolidine[21] were allowed to react in THF according to *GP 1*, yielding 1.2 g of (*S,R,R*)-**8g** (75%) as a pale yellow oil after column chromatography. – *ds* = 96% (^{13}C NMR). – $[\alpha]_D^{20}$ = −62.3 (*c* = 0.75, C_6H_6). – IR (film): $\tilde{\nu}$ = 3200 cm^{-1} (w, NH), 3100–2810 (s, CH), 1610 (m), 1500, 1470 (s), 1390, 1210 (m), 1140, 1110 (s), 940 (m), 750, 710 (s). – ^{1}H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.87 (t, *J* = 7 Hz, 3H, CH_3), 0.7–1.1 (m, 3H, CH_3), 1.15–1.5 (m, 6H, CH_2), 1.5–1.9 (m, 4H, CH_2CH_2), 2.0–2.5 (m, 4H, NC*H*H, C*H*NH, NH, $CHCH_3$), 2.5–2.9 (m, 3H, NCH*H*, $CH_2C_6H_5$), 3.1–3.4 (m, 2H, NCH, OC*H*H), 3.3 (s, 3H, OCH_3), 3.5 (dd, *J* = 9 Hz, *J* = 4 Hz, 1H, OCH*H*), 7.1–7.35 (m, 5H, C_6H_5). – ^{13}C NMR (20 MHz, C_6D_6, TMS): δ = 14.4, 14.9 (CH_3), 21.5, 23.5, 27.3, 29.4, 30.2 (CH_2), 37.1 (CH), 39.3 ($PhCH_2$), 57.5 (NCH_2), 58.9 (OCH_3), 62.1, 66.4 (CHN), 76.3 (CH_2O), 126.0, 128.5, 129.4 (aromatic CH), 142.2 (aromatic C). – MS (70 eV); *m/z* (%) = 318 (27) [M$^+$], 273 (78) [M$^+$ – CH_2OCH_3], 199 (100) [M$^+$ – C_9H_{11}]. – $C_{20}H_{34}N_2O$ (318.5): calcd. C 75.47, H 10.69, N 8.81; found C 75.37, H 10.54, N 8.77.

(−)-(2S,3R,2′S)-3-N-[2′-(Methoxymethyl)pyrrolidin-1′-yl]-amino-2-methyl-1-phenyl)heptane [(*S,R,S*)-**8g**]: 3.9 ml (5.7 mmol) of *n*BuLi and 1.36 g (5.2 mmol) of (−)-(2*S*,2′*S*)-2-(methoxymethyl)-1-[(2′-methyl-3′-phenyl)propylideneamino]pyrrolidine[21] were allowed to react in THF according to *GP 1*, yielding 0.93 g of (*S,R,S*)-**8g** (56%) as a pale yellow oil after column chromatography. – *ds* = 94% (^{13}C NMR). – $[\alpha]_D^{20}$ = −35.7 (*c* = 0.7, C_6H_6). – ^{13}C NMR (20 MHz, C_6D_6, TMS): δ = 14.5, 14.8 (CH_3), 21.5, 23.6, 27.3, 29.4, 29.5 (CH_2), 37.0 (CH), 40.0 (*C*$H_2C_6H_5$), 57.7 (CH_2N), 58.8 (OCH_3), 62.6, 66.7 (CHN), 76.3 (OCH_2), 125.9, 128.5, 129.4 (aromatic CH), 142.1 (aromatic C). – IR- and ^{1}H-NMR data were identical with those of (*S,R,R*)-**8g**.

(−)-(3S,4R,2′S)-3-N-[2′-(Methoxymethyl)pyrrolidin-1′-yl]-amino-2,2,4-trimethyl-5-phenylpentane [(*S,R,R*)-**8h**]: 3.8 ml (5.5 mmol) of *t*BuLi and 1.3 g (5 mmol) of (−)-(2*S*,2′*R*)-2-(methoxymethyl)-1-[(2′-methyl-3′-phenyl)propylideneamino]-pyrrolidine[21] were allowed to react in THF according to *GP 1*, yielding 0.84 g of (*S,R,R*)-**8h** (53%) as a pale yellow oil after column chromatography. – *ds* = 96% (^{13}C NMR). – $[\alpha]_D^{20}$ = −74.1 (*c* = 0.55, C_6H_6). – IR (film): $\tilde{\nu}$ = 3200 cm^{-1} (w, NH), 3100–2820 (s, CH), 1610 (w), 1500, 1460 (m), 1400, 1370, 1210, 1195 (w), 1135, 1110 (s), 920 (w), 750, 710 (s). – ^{1}H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.85 [s, 9H, $C(CH_3)_3$], 0.7–1.0 (m, 3H, CH_3), 1.5–1.9 (m, 4H, CH_2), 2.0–2.8 (m, 4H, CH_2CH_2, C*H*CH_3, NH), 2.5 (d, *J* = 1 Hz, 1H, C*H*NH), 2.55 (dd, *J* = 8 Hz, *J* = 14 Hz, 1H, C*H*HC_6H_5), 2.78 (dd, *J* = 7 Hz, *J* = 14 Hz, 1H, CH*H*C_6H_5), 3.1–3.45 (m, 2H, NCH, OC*H*H), 3.3 (s, 3H, OCH_3), 3.65 (dd, *J* = 9 Hz, *J* = 4 Hz, 1H, OCH*H*), 7.0–7.3 (m, 5H, C_6H_5). – ^{13}C NMR (20 MHz, C_6D_6, TMS): δ = 15.8, 21.4 (CH_3), 27.3 (CH_2), 28.5 [$C(CH_3)_3$], 35.7 [*C*$(CH_3)_3$], 35.7 (CH), 44.8 (*C*$H_2C_6H_5$), 57.1 (CH_2N), 58.8 (OCH_3), 66.2, 67.9 (CHN), 75.9 (CH_2O), 126.0, 128.4, 129.6 (aromatic CH), 142.2 (aromatic C). – MS (70 eV); *m/z* (%) = 318 (6) [M$^+$], 273 (4) [M$^+$ – CH_2OCH_3], 261 (100) [M$^+$ – C_4H_9], 199 (12) [M$^+$ – C_9H_{11}]. – $C_{20}H_{34}N_2O$ (318.5): calcd. C 75.47, H 10.69, N 8.81; found C 75.39, H 10.88, N 8.69.

(−)-(1S,2R,2′S)-1-[2′-(Methoxymethyl)pyrrolidin-1′-yl]amino-1,3-diphenyl-2-methylpropane [(*S,S,R*)-**8j**]: 5.2 ml (10.3 mmol) of PhLi and 2.44 g (9.4 mmol) of (−)-(2*S*,2′*R*)-2-(methoxymethyl)-1-[(2′-methyl-3′-phenyl)propylideneamino]pyrrolidine[21] were allowed to react in THF according to *GP 1*, yielding 2.8 g of (*S,S,R*)-**8i** (88%) as a pale yellow oil after column chromatography. – *ds* =

97% (^{13}C NMR). – $[\alpha]_D^{20}$ = –42.9 (*c* = 0.9, C_6H_6). – IR (film): $\tilde{\nu}$ = 3200 cm^{-1} (w, NH), 3100–2820 (s, CH), 1605, 1500 (m), 1460 (s), 1380, 1200 (m), 1140–1100 (s), 1040, 765, 745 (m), 710 (s). – ^{1}H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.78 (d, *J* = 7 Hz, 3H, CH_3), 1.4–2.5 (m, 7H, NC*H*H, C*H*CH_3, NH, CH_2CH_2), 2.5–2.9 (m, 3H, $CH_2C_6H_5$, NCH*H*), 2.9–3.65 (m, 3H, NCH, OCH_2), 3.25 (s, 3H, OCH_3), 3.83 (d, *J* = 6 Hz, 1H, C*H*NH), 6.9–7.5 (m, 10H, C_6H_5). – ^{13}C NMR (20 MHz, C_6D_6, TMS): δ = 16.2 (CH_3), 21.4, 27.3 (CH_2), 39.2 (CH), 40.1 ($CH_2C_6H_5$), 57.1 (CH_2N), 58.7 (OCH_3), 66.1, 68.5 (CHN), 76.1 (CH_2O), 126.0 (aromatic CH), 127.0, 127.9, 128.5, 128.9, 129.4, 142.0, 143.0 (aromatic C). – MS (70 eV); *m/z* (%) = 338 (10) [M^+], 293 (9) [$M^+ - CH_2OCH_3$], 219 (11) [$M^+ - C_9H_{11}$], 129 (100). – $C_{22}H_{30}N_2$ (338.5): calcd. C 78.11, H 8.86, N 8.28; found C 77.89, H 8.91, N 8.15.

(+)-(3R,4R)-4-Amino-3-methyloctane [(*R,R*)-**11a**]: 1.27 g (4.96 mmol) of (*S,R,R*)-**8a** was allowed to react according to *GP 2* for 20 h at 50°C, 5.0 bar H_2 pressure and was purified according to *GP 3*, yielding 0.34 g of (*R,R*)-**11a** (48%) as a colorless oil. – b.p. 85°C/20 Torr. – *de* = 87%, *ee* = 93% (^{13}C NMR of the corresponding MTPA amide). – $[\alpha]_D^{20}$ = +10.78 (neat). – IR (film): $\tilde{\nu}$ = 3380, 3320 cm^{-1} (m, NH), 2980–2880 (s, CH), 1620 (m, NH), 1470, 1385 (s), 1130, 1055, 840, 790 (m). – ^{1}H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.7–1.1 (m, 11H, CH_3, NH_2), 1.1–1.6 (m, 9H, CH_2, C*H*CH_3), 2.6 (m, 1H, CHN). – $C_9H_{21}N$ (143.3): calcd. C 75.52, H 14.69, N 9.79; found C 75.33, H 14.50, N 9.59.

(–)-(3S,4R)-3-Amino-2,2,4-trimethylhexane [(*S,R*)-**11b**]: 1.36 g (5.3 mmol) of (*S,S,R*)-**8b** was allowed to react according to *GP 2* for 24 h at 80°C, 50 bar H_2 pressure and was purified according to *GP 4*, yielding 0.37 g of (*S,R*)-**11b** (49%) as a colorless oil and 0.225 g (17%) of hydrazine (*S,S,R*)-**8b**. – b.p. 80°C/20 Torr. – *de* = 90%, *ee* = 99% (GC on a CSP). – $[\alpha]_D^{20}$ = –21.4 (neat). – IR (film): $\tilde{\nu}$ = 3420, 3340 cm^{-1} (w, NH), 2965–2880 (s, CH), 1640 (m, NH), 1480, 1470, 1460, 1400, 1380, 1370, 840 (m). – ^{1}H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.87 [s, 9H, $C(CH_3)_3$], 0.75–1.0 (m, 6H, CH_3), 1.05–1.8 (m, 5H, CH_2, C*H*CH_3, NH_2), 2.32 (d, *J* = 2 Hz, 1H, CHN). – MS (70 eV); *m/z* (%) = 144 (0.1) [$M^+ - 1$], 128 (1.4) [$M^+ - CH_3$], 86 (100) [$M^+ - C_4H_9$].

(+)-(2R,3R)-2-Amino-3-methylhexane [(*R,R*)-**11c**]: 2.12 g (10 mmol) of (–)-(2*S*,2′*R*)-2-(methoxymethyl)-1-[2′-(methyl)pentylideneamino]pyrrolidine[21] and 8.2 ml (11 mmol) of CH_3Li were allowed to react according to *GP 5* in THF, yielding 0.36 g of (*R,R*)-**11c** (31%) as a colorless oil. – b.p. 90°C/75 Torr. – *de* = 89%, *ee* = 97% (GC on CSP). – $[\alpha]_D^{20}$ = +13.2 (neat). – IR (film): $\tilde{\nu}$ = 3370, 3300 cm^{-1} (m, NH), 2970–2880 (s, CH), 1600 (m, NH), 1470, 1465, 1380 (s), 1130 (m), 830 (s). – ^{1}H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.75–1.15 (m, 11H, CH_3, NH_2), 1.15–1.6 (m, 5H, CH_2, C*H*CH_3), 2.65–3.0 (m, 1H, CHN). – $C_7H_{17}N$ (115.2): calcd. C 73.04, H 14.78, N 12.17; found C 72.96, H 14.80, N 12.02.

(+)-(2S,3R)-2-Amino-3-methylhexane [(*S,R*)-**11c**]: 1.37 g (6.46 mmol) of (+)-(2*R*,2*R*)-2-(methoxymethyl)-1-[2′-(methyl)pentylidenamino]pyrrolidine[21] and 6.5 ml (7.75 mmol) of CH_3Li were allowed to react according to *GP 5* in THF, yielding 0.133 g of (*S,R*)-**11c** (18%) as a colorless oil. – b.p. 90°C/75 Torr. – *de* = 77%, *ee* >99% (GC on a CSP). – $[\alpha]_D^{20}$ = +14.4 (neat). – ^{1}H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.75–1.15 (m, 9H, CH_3), 1.15–1.6 (m, 5H, CH_2, C*H*CH_3), 1.2 (s, 2H, NH_2), 2.65–3.0 (m, 1H, CHN). – The IR data were identical with those of (*R,R*)-**11c**.

(+)-(1S,2R)-1-Amino-1-cyclohexyl-2-methylpentane [(*S,R*)-**11d**]: 1.09 g (3.75 mmol) of (*S,S,R*)-**8d** was allowed to react according to *GP 2* for 18 h at 60°C, 5 bar H_2 pressure and was purified according to *GP 4*, yielding 0.47 g of (*S,R*)-**11d** (69%) as a colorless oil. – b.p. 90°C/3 Torr. – *de* = 45%, *ee* >97% (^{13}C of the corresponding MTPA amide). – $[\alpha]_D^{20}$ = +9.05 (neat). – IR (film): $\tilde{\nu}$ = 3400, 3320 (w, NH), 2960–2860 (s, CH), 1620 (m, NH), 1475, 1465 (m), 1455 (s), 1380, 790 (m) cm^{-1}. – ^{1}H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.85 (t, *J* = 7 Hz, 3H, CH_3), 0.75–1.5 (m, 15H, CH_3, CH_2, NH_2, ax. CH), 1.5–2.1 (m, 6H, C*H*CH_3, eq. CH), 2.15–2.4 (m, 1H, CHN). – MS (70 eV); *m/z* (%) = 184 (0.3) [$M^+ + 1$], 183 (0.1) [M^+], 112 (100) [$M^+ - C_5H_{11}$], 100 (77) [$M^+ - C_6H_{13}$].

(+)-(2R,3R)-2-Amino-3-methylheptane [(*R,R*)-**11e**]: 2.26 g (10 mmol) of (–)-(2*S*,2′*R*)-2-(methoxymethyl)-1-[2′-(methyl)hexylideneamino]pyrrolidine[16] and 11 ml (12 mmol) of CH_3Li were allowed to react according to *GP 5* in THF, yielding 0.49 g of (*R,R*)-**11e** (38%) as a colorless oil. – b.p. 100°C/53 Torr. – *de* = 91%, *ee* = 98% (GC on a CSP). – $[\alpha]_D^{22}$ = +13.0 (neat). – IR (film): $\tilde{\nu}$ = 3390, 3310 cm^{-1} (w, NH), 2970–2870 (s, CH), 1620 (m, NH), 1475, 1465, 1455, 1385 (s), 1130, 830 (m). – ^{1}H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.83 (t, *J* = 7 Hz, *J* = 5 Hz, 3H, CH_3), 1.0 (t, *J* = 7 Hz, 3H, CH_3), 1.13 (s, 2H, NH_2), 0.7–1.5 (m, 10H, CH_3, CH_2, C*H*CH), 2.6–2.9 (1H, CHN). – $C_8H_{19}N$ (129.2): calcd. C 74.42, H 14.73, N 10.85; found C 74.14, H 14.61, N 10.86.

(–)-(2S,3S)-2-Amino-3-methylheptane [(*S,S*)-**11e**]: 2.35 g (10.4 mmol) of (+)-(2*R*,2′*S*)-2-(methoxymethyl)-1-[2′-(methyl)hexylideneamino]pyrrolidine[16] and 7.0 ml (11.5 mmol) of CH_3Li were allowed to react according to *GP 5* in THF, yielding 0.41 g of (*S,S*)-**11e** (31%) as a colorless oil. – b.p. 100°C/53 Torr. – *de* = 91%, *ee* = 98% (GC on a CSP). – $[\alpha]_D^{20}$ = –14.35 (neat). – MS (70 eV); *m/z* (%) = 128 (0.06) [$M^+ - 1$], 114 (0.3) [$M^+ - CH_3$], 44 (100) [C_2H_6N]. – IR- and ^{1}H-NMR data were identical with those of (*R,R*)-**11e**.

(–)-(3S,4R)-3-Amino-2,2,4-trimethyloctane [(*S,R*)-**11f**]: 1.59 g (5.59 mmol) of (*S,S,R*)-**8f** was allowed to react according to *GP 2* for 140 h at 70°C, 8.0 bar H_2 pressure and was purified according to *GP 4*, yielding 0.38 g of (*S,R*)-**11f** (40%) as a colorless oil and 0.39 g (24%) of hydrazine (*S,S,R*)-**8f**. – b.p. 90°C/10 Torr. – *de* = 85%, *ee* = 96% (GC on a CSP). – $[\alpha]_D^{23}$ = –17.8 (neat). – IR (film): $\tilde{\nu}$ = 3400, 3320 cm^{-1} (w, NH), 2970–2880 (s, CH), 1620 (w, NH), 1485, 1475, 1470, 1405, 1390, 1370 (m), 820 (w). – ^{1}H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.9 [s, 9H, $C(CH_3)_3$], 0.8–1.1 (m, 8H, CH_3, NH_2), 1.2–1.4 (m, 7H, CH_2, C*H*CH_3), 2.35 (br. s, 1H, CHN). – MS (70 eV); *m/z* (%) = 172 (0.4) [$M^+ + 1$], 156 (3) [$M^+ - CH_3$], 114 (100) [$M^+ - C_4H_9$].

(–)-(2R,3R)-3-Amino-2-methyl-1-phenylheptane [(*R,R*)-**11g**]: 2.49 g (7.8 mmol) of (*S,R,R*)-**8g** was allowed to react according to *GP 2* for 20 h at 60°C, 5.0 bar H_2 pressure and was purified by kugelrohr distillation, yielding 1.37 g of (*R,R*)-**11g** (86%) as a colorless oil. – b.p. 90°C/0.2 Torr. – *de* = 67%, *ee* = 97% (^{19}F NMR of the corresponding MTPA amide). – $[\alpha]_D^{20}$ = –2.6 (*c* = 1.6, C_6H_6). – IR (film): $\tilde{\nu}$ = 3390, 3310 cm^{-1} (w, NH), 3090–3030 (m, aromatic CH), 2960–2860 (s, CH), 1605 (m, NH), 1500 (m), 1460 (s), 1380 (m), 1040 (w), 745, 705 (s). – ^{1}H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.85 (t, *J* = 7 Hz, 3H, CH_3), 1.05 (s, 2H, NH_2), 0.7–1.1 (m, 3H, CH_3), 1.15–1.5 (m, 6H, CH_2), 1.6–2.0 (m, 1H, C*H*CH_3), 2.2–2.9 (m, 3H, $CH_2C_6H_5$, CHN), 7.1–7.4 (m, 5H, C_6H_5). – $C_{14}H_{23}N$ (205.3): calcd. C 81.95, H 11.22, N 6.83; found C 81.84, H 11.28, N 6.90.

(–)-(2S,3R)-3-Amino-2-methyl-1-phenylheptane [(*R,S*)-**11g**]: 2.33 g (7.33 mmol) of (*S,R,S*)-**8g** was allowed to react according to *GP 2* for 18 h at 60°C, 5.0 bar H_2 pressure and was purified by kugelrohr distillation, yielding 1.18 g of (*R,S*)-**11g** (79%) as a colorless oil. – b.p. 80°C/0.05 Torr. – *de* = 58%, *ee* = 93% (^{19}F NMR of the corresponding MTPA amide). – $[\alpha]_D^{20}$ = –3.69 (neat). The spectroscopic data were identical with those of (*R,R*)-**11g**. –

$C_{14}H_{23}N$ (205.3): calcd. C 81.95, H 11.22, N 6.83; found C 82.03, H 11.38, N 6.71.

(−)-(2R,3S)-3-Amino-2,2,4-trimethyl-1-phenylpentane [(*S,R*)-**11h**]: 2.57 g (8.08 mmol) of (*S,S,R*)-**8h** was allowed to react according to *GP 2* for 90 h at 70°C, 9.0 bar H_2 pressure and was purified by kugelrohr distillation, yielding 1.08 g of (*S,R*)-**11h** (65%) as a colorless oil and 0.32 g (13%) of hydrazine (*S,S,R*)-**8h**. − b.p. 70°C/0.05 Torr. − *de* = 85%, *ee* = 94% (GC of the corresponding MTPA amide). − $[\alpha]_D^{20}$ = −42.07 (neat). − IR (film): $\tilde{\nu}$ = 3410, 3340 cm^{-1} (w, NH), 3100−3040 (m, aromatic CH), 2970−2880 (s, CH), 1610 (m, CH), 1500, 1485−1460, 1370 (m), 750, 710 (s). − ^1H NMR (300 MHz, $CDCl_3$, TMS): δ = 0.84 [s, 9H, $C(CH_3)_3$], 0.85 (d, *J* = 7 Hz, 3H, CH_3), 1.17 (br. s, 2H, NH_2), 2.12 (m, 1H, CH), 2.34 (d, *J* = 1 Hz, 1H, CHN), 2.57 (dd, *J* = 7.6 Hz, *J* = 13 Hz, 1H, C*H*HH_6H_5), 2.62 (dd, 1H, *J* = 7.4 Hz, *J* = 13 Hz, CH*H*H_6H_5), 7.16 (m, 3H, C_6H_5), 7.25 (m, 2H, C_6H_5). − ^{13}C NMR (75 MHz, $CDCl_3$, TMS): δ = 14.3 (CH_3), 27.2 [$C(CH_3)_3$], 35.1 (CH), 35.4 [$C(CH_3)_3$], 44.0 ($PhCH_2$), 61.8 (CHN), 125.7, 128.1, 129.2 (aromatic CH), 141.5 (aromatic C). − MS (70 eV); *m/z* (%) = 205 (0.04) [M^+], 190 (3) [$M^+ - CH_3$], 148 (100) [$M^+ - C_4H_9$]. − $C_{14}H_{23}N$ (205.3): calcd. C 81.95, H 11.22, N 6.83; found C 81.89, H 11.38, N 6.85.

(−)-(1S,2R)-1-Amino-1-cyclohexyl-3-phenylpropane [(*S,R*)-**11i**]: 2.78 g (8.22 mmol) of (*S,R,R*)-**8i** was allowed to react according to *GP 2* for 20 h at 80°C, 5.0 bar H_2 pressure and was purified according by kugelrohr distillation, yielding 1.36 g of (*S,R*)-**11i** (72%) as a colorless oil. − b.p. 110°C/0.05 Torr. − *de* = 68%, *ee* = 97% (^{13}C of the corresponding MTPA amide). − $[\alpha]_D^{20}$ = −6.9 (*c* = 0.87, C_6H_6). − IR (film): $\tilde{\nu}$ = 3410, 3340 cm^{-1} (w, NH), 3100−3040 (m, aromatic CH), 2940−2860 (s, CH), 1610 (m, NH), 1500 (m), 1460 (s), 1390, 1040 (m), 750, 710 (s). − ^1H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.8 (d, *J* = 7 Hz, 3H, CH_3), 0.9−1.4 (m, 8H, NH_2, ax. CH), 1.5−2.1 (m, 6H, CH, eq. CH), 2.15−2.8 (m, 3H, $CH_2C_6H_5$, CHN), 7.1−7.4 (m, 5H, C_6H_5). − $C_{16}H_{25}N$ (231.4): calcd. C 83.12, H 10.82, N 6.06; found C 83.31, H 11.01, N 6.00.

(+)-(2R,3R)-2-Amino-3-cyclohexylbutane [(*R,R*)-**11j**]: 1.97 g (7.81 mmol) of (−)-(2*S*,2′*R*)-2-(methoxymethyl)-1-[(2′-cyclohexyl)-propylideneamino]pyrrolidine[35] and 5.5 ml (8.6 mmol) of CH_3Li were allowed to react according to *GP 5* in THF, yielding 0.55 g of (*R,R*)-**11j** (45%) as a colorless oil. − b.p. 100°C/10 Torr. − *de* = 96%, *ee* = 99% (GC on a CSP). − $[\alpha]_D^{20}$ = +4.5 (neat). − IR (film): $\tilde{\nu}$ = 3380, 3260 cm^{-1} (w, NH), 2980−2860 (s, CH), 1620 (w, NH), 1455 (s), 1380, 830 (m). − ^1H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.82 (d, *J* = 7 Hz, 3H, CH_3), 1.05 (d, *J* = 8 Hz, 3H, CH_3), 0.7−1.4 (m, 8H, NH_2, ax. CH), 1.5−1.9 (m, 6H, CH, eq. CH), 2.8−3.1 (m, 1H, CHN). − MS (70 eV); *m/z* (%) = 156 (0.5) [M^+ + 1], 155 (0.2) [M^+], 44 (100).

(−)-(2S,2′S)-2-Methoxymethyl-1-[1′-(2′,3′-isopropylidenedioxy)propylideneamino]pyrrolidine (*S,S*)-**13**: 2.0 g (7.5 mmol) of 1,2:5,6-diisopropylidenemannitol and $Pb(OAc)_4$ were allowed to react according to *GP 6*. The resulting toluene solution and 1.95 g of SAMP (15 mmol) were combined at 0°C and were stirred for 30 min, yielding 3.5 g of (*S,S*)-**13** (96%) as a colorless oil after filtration through silica gel. − $[\alpha]_D^{24}$ = −106.6 (neat). − IR (film): $\tilde{\nu}$ = 2990−2830 cm^{-1} (s, CH), 1600 (m, C=N), 1460 (m), 1380, 1215, 1160, 1130, 1060 (s), 875, 850 (m). − ^1H NMR (90 MHz, $CDCl_3$, TMS): δ = 1.38, 1.45 (2 s, 6H, 2 CH_3), 1.7−2.05 (m, 4H, CH_2CH_2), 2.9 (m, 1H, NC*H*H), 3.2−3.7 (m, 4H, NCH, NCH*H*, CH_2OCH_3), 3.35 (s, 3H, CH_3), 3.75 (t, *J* = 8 Hz, 1H, C*H*HO), 4.10 (d, *J* = 7 Hz, 1H, CH*H*O), 4.65 (br. q, *J* = 8 Hz, 1H, CHO), 6.40 (d, *J* = 7 Hz, CH=N). − MS (70 eV); *m/z* (%) = 242 (9.7) [M^+], 227 (8) [$M^+ - CH_3$], 198 (100) [$M^+ - CH_2OCH_3$], 185 (11), 139 (41), 111 (14), 101 (15), 70 (21), 43 (28). − $C_{12}H_{22}N_2O_3$ (242.3): calcd. C 59.50, H 9.09, N 11.57; found C 59.76, H 9.31, N 11.23.

(−)-(2R,2′S)-2-Methoxymethyl-1-[1′-(2′,3′-isopropylidenedioxy)propylideneamino]pyrrolidine (*R,S*)-**13**: 2.0 g (7.5 mmol) of 1,2:5,6-diisopropylidenemannitol and $Pb(OAc)_4$ were allowed to react according to *GP 6*. The resulting toluene solution and 1.95 g of RAMP (15 mmol) were combined at 0°C and were stirred for 30 min, yielding 3.5 g of (*R,S*)-**13** (95%) as a colorless oil after filtration through silica gel. − $[\alpha]_D^{24}$ = +105.3 (neat). − IR- and ^1H-NMR data were identical with those of (*S,S*)-**13**. − $C_{12}H_{22}N_2O_3$ (242.3): calcd. C 59.50, H 9.09, N 11.57; found C 59.68, H 9.27, N 11.54.

(+)-(4S,1′R)-2,2-Dimethyl-4-(1′-aminoethyl)-1,3-dioxolane (*S,R*)-**14**: 1.87 g (7.75 mmol) of (*S,S*)-**13** and 7.5 ml (11.6 mmol) of CH_3Li were allowed to react according to *GP 5* in THF using KOH/H_2O ethyleneglycol instead of HBr/acetic acid to deprotect the carbamate, yielding 0.25 g of (*S,R*)-**14** (22%) as a colorless oil. − b.p. 90°C/15 Torr. − *de* = 96%, *ee* = 99% (GC of the corresponding MTPA amide). − $[\alpha]_D^{22}$ = 0.75 (*c* = 1, C_6H_6). − IR (film): $\tilde{\nu}$ = 3380, 3310 cm^{-1} (m, NH), 3000−2890 (s, CH), 1600 (m, NH), 1465 (m), 1385, 1375, 1260, 1220, 1165, 1075, 865 (s). − ^1H NMR (90 MHz, $CDCl_3$, TMS): δ = 0.75−1.55 (m, 2H, NH_2), 1.0 (d, *J* = 7 Hz, 3H, $CHCH_3$), 1.35, 1.45 (2 s, 2 3H, 2 CH_3), 2.85 (quin., *J* = 7 Hz, 1H, CHN), 3.5−4.1 (m, 3H, CHO, CH_2O). − MS (70 eV); *m/z* (%) = 146 (0.2) [M^+ + 1], 145 (0.1) [M^+], 130 (3) [$M^+ - CH_3$], 72 (5), 59 (2), 44 (100).

(+)-(4S,1′S)-2,2-Dimethyl-4-(1′-aminoethyl)-1,3-dioxolane (*S,S*)-**14**: 4.5 g (18.6 mmol) of (*R,S*)-**13** and 16.6 ml (27.9 mmol) of CH_3Li were allowed to react according to *GP 5* in THF using KOH/H_2O/ethyleneglycol instead of HBr/acetic acid to deprotect the carbamate, yielding 0.63 g of (*S,S*)-**14** (23%) as a colorless oil. − b.p. 80°C/15 Torr. − *de* = 80%, *ee* = 99% (GC of the corresponding MTPA amide). − $[\alpha]_D^{22}$ = +22.0 (neat). − The spectroscopic data were identical with those of (*S,R*)-**14**.

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