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Synthesis of New, Chiral β-*sec*-Amino Alcohols – Diastereodivergent Addition of Grignard Reagents to α-Amino Aldehydes Based on the (*all-R*)-2-Azabicyclo[3.3.0]octane System ☆

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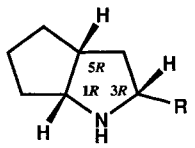
New, chiral β-*sec*-amino alcohols (α*R*,β*R*)-**11a–13a**, (α*S*,β*R*)-**11b–17b**, (α*S*,β*S*)-**11c**, **12c**, **15c**, **17c** and (α*R*,β*S*)-**11d**, **12d**, **15d**, **17d** have been synthesized from the enantiomerically pure amine (*all-R*)-**1a** via diastereomeric, *N-tert*-butoxycarbonyl-protected aldehydes **3**. Grignard additions proceed in fair yields with a high degree of diastereofacial stereoselection (diastereomeric ratios *dr* up to ≥ 95:5) with non-chelation control, generally in favor of the *anti*-(*erythro*) structures. A mechanistic interpretation of the stereochemical course of this reaction is presented. The stereodifferentiating ability of selected stereoisomeric (*erythro*)- and (*threo*)-amino alcohol structures were tested in homogeneous catalysis, e.g. in two model reactions (optical purities up to 95%).

We previously reported the synthesis of (*erythro*)-(α*R*,β*S*)-amino alcohols based on the diastereo- and regioselective α-hydroxyalkylation of the *N*-nitroso derivative of (*all-R*)-2-azabicyclo[3.3.0]octane (*all-R*)-**1c** [1h]. Due to the high diastereoselectivity (up to 90% and 93%, respectively, for the newly generated stereogenic centers in α and β position) for the formation of two contiguous chiral centers on the framework, only the major diastereomers – the (α*R*,β*S*) compounds (α*R*,β*S*)-**11d**, **12d**, **17d** (among others) – have been isolated.

An efficient, alternative synthetic pathway with less stereochemical restriction was needed to have access to the corresponding diastereomeric (α*S*,β*S*)-, (α*R*,β*R*)- and (α*S*,β*R*)-amino alcohol structures. Furthermore, concentration was focussed on the stereochemical correlation of the internal stereogenic centers concerning their sense of induction and the enantioselective-catalytic efficiency of these systems in several asymmetric, homogeneous catalytic reactions. A first short summary of these investigations is given at the end of this report.

In context with our studies on the utilization of industrial waste materials[1] the non-recyclable, enantiomerically pure (*all-R*)-2-azabicyclo[3.3.0]octane-3-carboxylic acid benzyl ester (*all-R*)-**1a** (a waste material which is obtained in the process of synthesizing the ACE-inhibitor ramipril[2] by Hoechst AG), respectively the corresponding (*all-R*)-2-azabicyclo[3.3.0]octane-3-carboxylic acid (*all-R*)-**1b** was used as starting material for the synthesis of β-amino alcohol frameworks based on the diastereoselective conversion of *N*-protected α-amino aldehydes (1*R*,3*R*,5*R*)- and (1*R*,3*S*,5*R*)-**3** with aromatic Grignard reagents.



1	R
a	CO_2CH_2Ph
b	CO_2H
c	H
d	CH_2OH
e	$C(OH)Ph_2$

For the preparation of the diastereomeric (1*R*,3*R*,5*R*) systems, e.g. the (β*R*)-configured (*threo*)-(α*R*,β*R*)-**11a–13a** and (*erythro*)-(α*S*,β*R*)-**11b–17b** amino alcohols (configurations 1 and 2, marked with the letters **a** and **b**, respectively), the *N*-Boc-protected α-amino aldehyde (1*R*,3*R*,5*R*)-**3**, obtained in 94% yield by Swern-oxidation of the corresponding bicyclic *N*-Boc-amino alcohol (*all-R*)-**2**, is the key compound (Scheme 1). In spite of the generally ease of epimerization using the Boc protecting group[3] handling of this

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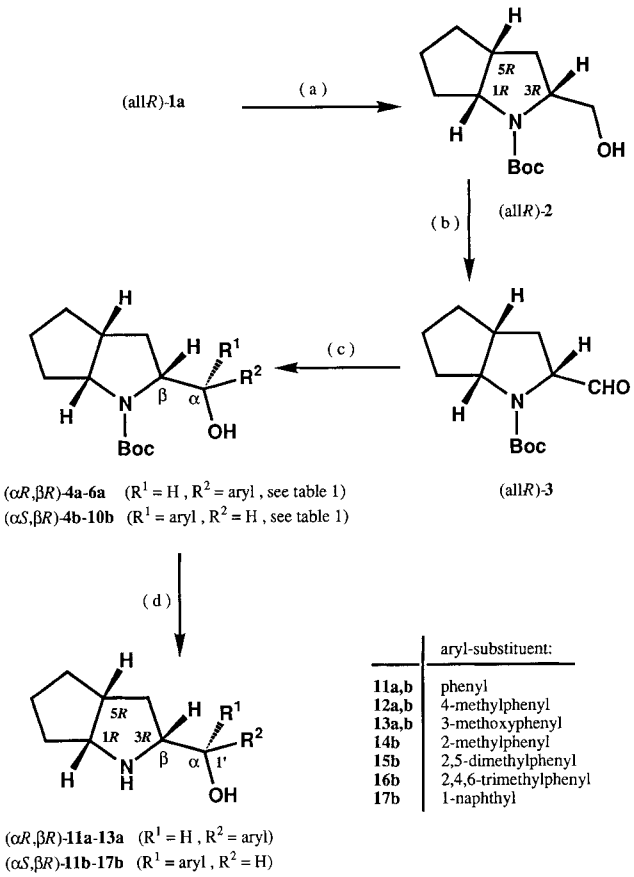
Scheme 1



(a): 1. $LiAlH_4$ in THF[11], 2. $(Boc)_2O$/triethylamine in THF at − 5 to 0 °C. − (b): abs. DMSO, oxalyl chloride in abs. CH_2Cl_2 at −65 to −80 °C. − (c): 1. RMgBr in *anhyd.* THF (for experimental details see Tables 1 and 2), 2. separation of diastereomers by flash chromatography. − (d): (10 equiv.) *p*-toluenesulfonic acid/(1 equiv.) anisole at room temp. or 4 N aqueous HCl at room temp.

chiral aldehyde (1*R*,3*R*,5*R*)-**3** caused no detectable epimerization[3g].

The aldehyde (1*R*,3*R*,5*R*)-**3** is treated with various aromatic Grignard reagents affording the diastereomeric, *N*-Boc-protected amino alcohols **4a−6a** and **4b−10b** (the separation is performed by flash chromatography on silica gel). The stereocontrol observed originates from internal asymmetric induction regulating the introduction of the additional chiral center on the framework. A more detailed description of the results (stereochemical aspects and analytical data) is given in Tables 1 and 2.

Noteworthy is the changing correlation between the diastereofacial stereoselection and the reaction temperature (see Tables 1 and 2: reaction temperature between −5 and −17 °C and between 22−40 °C, respectively) as well as the high level of the α diastereoselectivity. Extent *and* direction of the internal, substrate-induced diastereodivergence are highly dependent on the steric bulkiness of the nucleophilic component. The *re*-side attack is suppressed with increasing steric demand of R^2. The internal asymmetric induction of (1*R*,3*R*,5*R*)-**3** in favor of a significant − although not complete − *syn*, respectively (*threo*) selectivity (93%, Table 2, R^2: phenyl) with the formation of the (α*R*)-configured adducts inverts at a certain crucial bulkiness of the Grignard reagent to an *anti*-(*erythro*) selectivity with (α*S*):(α*R*)-diastereomeric ratios ≥ 95:5 (Tables 1 and 2, R^2: all *ortho*-substituted phenyl systems). The systematic variation of the R^2-substituent, e.g. substitution pattern of the phenyl ring leads to the following results:

Compared to the unsubstituted phenyl system the introduction of an additional substituent, e.g. methyl group in *para* position has − as expected − no significant influence on the stereochemical course of the reaction: the (*threo*) selectivity is almost unchanged with (α*R*)-diastereoselectivities of 70 (Table 1) and 92% (Table 2).

A comparable *meta*-located phenyl substitution (R^2: 3-methoxyphenyl) reveals a decisive effect on the observed *anti*/*syn*-selectivities: with a moderate stereopreference, the *anti*-(*erythro*) adduct is obtained as the major diastereomer. Furthermore, all *ortho*-substituted phenyl systems (R^2: 2-methyl-, 2,5-dimethyl-, 2,4,6-trimethylphenyl and 1-naphthyl) show − independent of the reaction temperature − a highly diastereoselective *anti*-(*erythro*) orientation of the addition products (*dr* values in all cases ≥ 95:5).

The stereochemistry on the ethylenic bridge between the N,O heteroatoms, e.g. the configuration of the new, α-located chiral center was assigned on the basis of the respective ^{1}H-NMR data, e.g. on the relative value of the vicinal coupling observed for the single benzylic proton: the (*threo*)-(α*R*,β*R*) isomers **11a-13a** display a larger vicinal coupling constant appearing at a less downfield region compared to the diastereomeric (*erythro*)-(α*S*,β*R*) structures **11b-13b** in analogy to related literature known compounds[4]. Due to the high diastereoselectivities and the exclusive formation of only one diastereomer this method is not applicable for compounds **14−17**.

Considering the R_f characteristics, we assumed for the *ortho*-substituted phenyl systems **14−17** (and the corresponding *N*-Boc protected structures **7−10**) a *syn*-(*erythro*)-stereochemistry, e.g. a (*S*)-configured chiral center in α position[5]. These attributions have been confirmed by a X-ray analysis for one of these *N*-Boc-protected β-amino alcohols − (α*S*,β*R*)-**9b** (R^2 = 2,4,6-trimethylphenyl) − displaying the expected (*erythro*)-situation between the N,O functionalities (Figure 1).

The synthesis of the complementary (β*S*)-configured (*threo*)- and (*erythro*) systems (diastereomeric configurations 3 and 4, assigned by the letters **c** and **d**) has been accomplished by the following sequence consisting of two distinct diastereoselective reaction steps. First the (*R*) stereochemistry in C-3 position of (1*R*,3*R*,5*R*)-**1b** had to be changed by the salicyl aldehyde-catalyzed epimerization affording a crude mixture of diastereomers [(1*R*,3*S*,5*R*)-**1b** and (1*R*,3*R*,5*R*)-**1b**] with a *dr* value of 66:34 in favor of the (1*R*,3*S*,5*R*)-configured product. This crude reaction mixture is reduced with $LiAlH_4$ to afford *sec*-amino alcohols which are *N*-protected by conversion into the carbamates

Table 1. Experimental and analytical data of compounds **4a, b, 5a, b, 6a, b, 7b–10b**: diastereoselective addition of aromatic Grignard reagents to (*all-R*)-**3** (reaction temperature between −5 and −17 °C; solvent: THF)

Compound[a]	Substituent R^2	Temp. [°C]	Overall yield [%][b]	Yield [%] in[c] (αR)/(αS)	*dr* [%][d] (αR):(αS)
(αR,βR)-**4a**	phenyl	−17	68	38/30	69:31
(αS,βR)-**4b**					
(αR,βR)-**5a**	4-methyl phenyl	−16	55	36/19	70:30
(αS,βR)-**5b**					
(αR,βR)-**6a**	3-methoxy phenyl	− 5	74	35/39	40:60
(αS,βR)-**6b**					
(αS,βR)-**7b**	2-methyl phenyl	− 9	38	−e/38	< 5:> 95
(αS,βR)-**8b**	2,5-dimethyl phenyl	−12	39	−e/39	< 5:> 95
(αS,βR)-**9b**	2,4,6-tri methylphenyl	−14	34	−e/34	< 5:> 95
(αS,βR)-**10b**	1-naphthyl	−11	44	−e/44	< 5:> 95

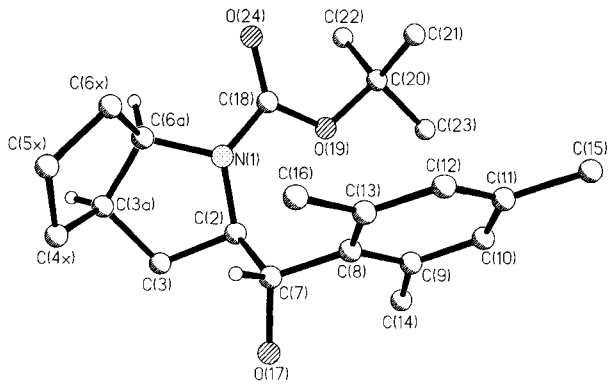
[a] Isolated compounds; for each of these compounds the diastereomeric purity after chromatographic separation is ≥ 95:5. – [b] Overall yields referred to the mixture of diastereomers. – [c] Yields after separation of the diastereomers given as (αR,βR)/(αS,βR) ratio. – [d] Determination by ^{1}H- and ^{13}C-NMR spectroscopy using a sample of the crude product; diastereomeric ratio: (αR,βR)/(αS,βR). – [e] Not isolated and not identified by spectroscopic methods.

Table 2. Experimental and analytical data of compounds **4a**, **5a**, **7b–10b**: diastereoselective addition of Grignard reagents to (*all-R*)-**3** (reaction temperatures between 22 and 40 °C; solvent: THF)

Compound[a]	Substituent R^2	Temp. [°C]	Overall yield [%][b]	Yield in [%][c] (αR)/(αS)	dr [%][d] (αR):(αS)
(αR,βR)-**4a**	phenyl	24	62	62/–	93:7
(αR,βR)-**5a**	4-methylphenyl	26	68	68/–	92:8
(αS,βR)-**7b**	2-methylphenyl	23	42	−e/42	< 5:> 95
(αS,βR)-**8b**	2,5-dimethyl phenyl	35	40	−e/40	< 5:> 95
(αS,βR)-**9b**	2,4,6-trimethyl phenyl	22	37	−e/37	< 5:> 95
(αS,βR)-**10b**	1-naphthyl	40	41	−e/41	< 5:> 95

[a] Isolated compounds; the diastereomeric purity after chromatographic separation is ≥ 95:5. – [b] Overall yields referred to the mixture of diastereomers. – [c] Yields after separation of the diastereomers given as (αR,βR)/(αS,βR) ratio. – [d] Determination by ^{1}H- and ^{13}C-NMR spectroscopy using a sample of the crude product; diastereomeric ratio: (αR,βR)/(αS,βR). – [e] Not isolated and not identified by spectroscopic methods.

Figure 1. Crystal structure of (αS,βR)-**9b** (the numbers of the atoms do not correspond to those used in the nomenclature)



using di-*tert*-butyl dicarbonate/triethylamine in tetrahydrofuran (overall yield after three steps: 63%). Separation of epimers is performed by column chromatography affording the *N*-Boc amino alcohol (1*R*,3*S*,5*R*)-**2** in 54% yield.

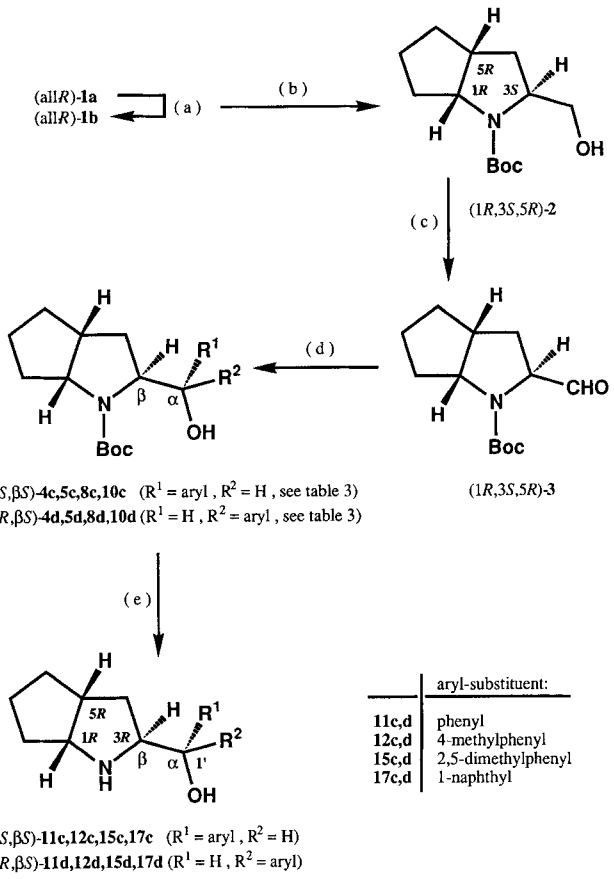
The following steps including the Swern-oxidation of (1*R*,3*S*,5*R*)-**2**, the diastereodivergent Grignard addition to (1*R*,3*S*,5*R*)-**3** and finally the deprotection to give the (β*S*)-*sec*-amino-*sec*-alcohols **11**,**12**,**15**,**17** follow the reaction pathway described in Scheme 2 (a summary of these results is shown in Table 3).

Significant for the second diastereoselective step in this sequence are the uniformly low (αR,β*S*)/(αS,β*S*) proportions with α diastereoselectivities up to 59% in favor of the (*R*)-(*erythro*)-configured adducts. The changing steric demand of the substituent R^2, e.g. the size of the Grignard reagent is not relevant for the stereochemical outcome of this reaction indicated by the almost unchanged (αR,β*S*)/(αS,β*S*) ratios (the diastereomeric ratios for the *N*-Boc-*sec*-amino-*sec*-alcohols are only ranging between 59:41 and 54:46, the yields are between 65 and 83%). The diastereomeric ratios as well as the respective configurations were assigned by ^{1}H-NMR spectroscopy – as described above – using samples of the crude reaction mixtures.

The conformational stability, rigidity of the carbanionic intermediate is essential in order to turn the efficient chiral recognition operating in the transition state to highly diastereoenriched products. The stereochemical aspect of the Grignard addition to (*all-R*)-**3** – considering the changing sense of internal asymmetric induction (dependent on the steric bulkiness of the nucleophilic component) – can be explained on the basis of ground state arguments[6].

For the (3*R*)-configured *N*-Boc-amino aldehyde (1*R*,3*R*,5*R*)-**3** the conformation analysis by MM2-force field calculations[7] provides the conformational arrangement depicted in Figure 2. Noteworthy is the antiperiplanar

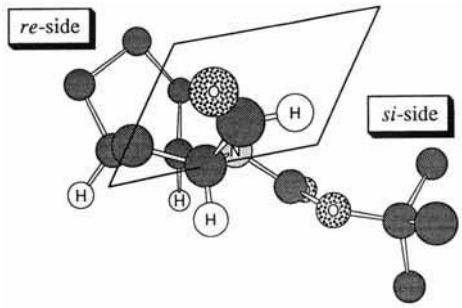
Scheme 2



(a): Pd/C, cyclohexene[11]. – (b): 1. (0.5 equiv.) salicylic aldehyde in conc. acetic acid 4 h under reflux[11]; 2. $LiAlH_4$ in THF; 3. $(Boc)_2O$/triethylamine in THF at −5 to 0 °C. – (c): abs. DMSO, oxalyl chloride in abs. CH_2Cl_2 at −65 to −80 °C.– (d): 1. RMgBr in *anhyd.* THF (for experimental details see Table 3); 2. separation of diastereomers by flash chromatography. – (e): (10 equiv.) *p*-toluenesulfonic acid/(1 equiv.) anisole at room temp. or 4 N aqueous HCl at room temp.

orientation of the carbonyl function and the urethane moiety resulting in a large distance between these electronegative groups. This kind of additional polar or stereoelectronic interaction seems to be the vital element for conformational control. Earlier studies[1d] provide experimental support for this assumption according to the proposal in Figure 2: the reaction of the corresponding (1*R*,3*R*,5*R*)-*N*-benzyl amino aldehyde (e.g. no polar heteroatom moiety as substituent on the nitrogen, but compared to the Boc protecting group with a similar steric bulkiness) with *ortho*-substituted, aromatic Grignard reagents reveals a *reversed* sense of induction with a significant preference for the (α*R*)-configured *syn*-(*threo*) products and diastereomeric ratios between 55:45 and 78:22 [for comparison see Tables 1 and 2: using *N*-Boc amino aldehyde (1*R*,3*R*,5*R*)-**3** as substrate a predominant formation of the (α*S*)-(*erythro*) products with *dr* values ≥ 95:5 is observed].

Figure 2. MM2 force field calculations: Proposed conformation of amino aldehyde (1*R*,3*R*,5*R*)-**3**



Furthermore an almost parallel, "*cis-endo*"-formation between the aldehyde function and the sterically demanding, *cis*-connected cyclopentyl-subunit of the (*all-R*)-azabicyclo[3.3.0]system has to be considered (resulting in a low steric accessibility with only a small opening angle between the planes of these two groups, e.g. the angle for the nucleophilic, *re*-side attack is significantly diminished). According to this formal picture a direct steric hindrance from the *N*-Boc protective group towards the reactive center does not exist. This is in contrast to results published by M. Reetz[6a]: the conversion of *N-bis*-protected, acyclic *N-bis*(benzyl) amino aldehydes reflect an almost completely suppressed, chelate-controlled reaction pathway and the formation of *syn*-(*threo*)-addition products obviously due to the steric bulkiness of the *N*-located substituents. With the assumption that the ground state conformation is the state of the reacting molecule (1*R*,3*R*,5*R*)-**3** ("substrate-like"-transition state), the highly diastereoselective *anti*-(*erythro*) ad-

Table 3. Experimental and analytical data of compounds **4c, d**, **5c, d**, **8c, d** and **10c, d**: diastereoselective addition of Grignard reagents to (1*R*,3*S*,5*R*)-**3** (reaction temperatures between −15 and −18 °C, solvent: THF)

Compound[a]	Substituent R^2	Temp. [°C]	Overall yield [%][b]	Yield in [%][c] (α*R*)/(α*S*)	*dr* [%][d] (α*R*):(α*S*)
(α*R*,β*S*)-**4d** (α*S*,β*S*)-**4c**	phenyl	−15	83	46/37	54:46
(α*R*,β*R*)-**5d** (α*S*,β*S*)-**5c**	4-methyl phenyl	−18	75	39/36	57:43
(α*S*,β*R*)-**8d** (α*S*,β*S*)-**8c**	2,5-dimethyl phenyl	−16	65	35/30	59:41
(α*S*,β*R*)-**10d** (α*S*,β*S*)-**10c**	1-naphthyl	−18	80	45/35	58:42

[a] Isolated compounds; for each of these compounds the diastereomeric purity after chromatographic separation is ≥ 95:5. – [b] Overall yields referred to the mixture of diastereomers. – [c] Yields after separation of the diastereomers given as (α*R*,β*S*)/(α*S*,β*S*) ratios.– [d] Determination by ^{1}H- and ^{13}C-NMR spectroscopy using a sample of the crude product; diastereomeric ratio: (α*R*,β*S*)/(α*S*,β*S*).

dition, especially in cases of larger steric hindrance might be understandable.

At a certain, critical steric demand of the Grignard component (all *ortho*-substituted aromatic systems) the reaction takes exclusively place in only one of the two diastereotopic hemispheres. This proposed mode of addition accounts for the subsequently obtained configuration of the (αS)-addition products **7b**–**10b**: the nucleophilic attack occurs stereospecific on the less hindered side-face of the aldehyde function which is the opposite side of the condensed second ring.

In cases of lower steric interaction the observed favored formation of (αR)-configured products (Tables 1 and 2, R^2 = phenyl, 4-methylphenyl) is more difficult to explain in the context of this model. In general polar substituents, such as the urethane subunit, stabilize transition states in which the incoming nucleophile and the polar group (e.g. the *tert*-butoxycarbonyl group) are remote – in this case – consequently leading to the predominant formation of *syn*-(*threo*) adducts by a *re*-side approach.

Even if this simple, formal picture does not reflect the mechanistic course of the reaction, it allows to predict the major diastereomer formed in a multitude of addition reactions, where the stereochemistry is determined only by steric and presumably by stereoelectronic interactions.

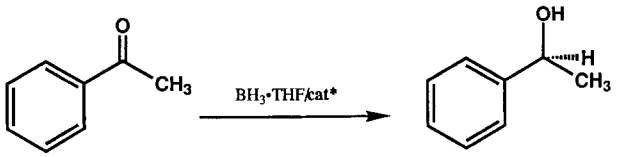
In contrast the corresponding diastereomeric α-amino aldehyde (1*R*,3*S*,5*R*)-**3** with its "*trans-exo*" arrangement of the aldehyde function and the cyclopentane moeity and an obviously much higher steric accessibility of the reactive center furnishes the expected loss of stereocontrol in the diastereodivergent C–C bond formation resulting in low *anti*/*syn* diastereoselectivities (as shown in Table 3) in addition to slightly higher yields.

An extensive study on the variation of the catalyst (e.g. catalyst precursor) structure was conducted to allow a comprehensive investigation on the stereodifferiating ability in homogenous asymmetric catalysis. Therefore a systematic modification of the stereochemical properties, e.g the stereochemical correlation between the internal chiral centers of the bicyclic β-amino alcohols (configurations **a**–**d**) was chosen.

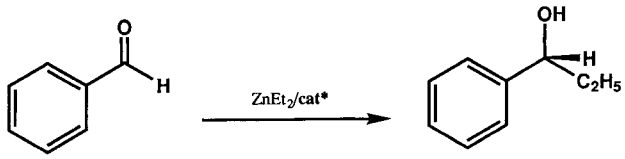
The reactions of choice for this comparison include the enantioselective reduction of prochiral ketones in the presence of catalytic amounts of in situ-formed, chiral oxazaborolidines, the enantioselective catalytic addition of diethylzinc to prochiral aldehydes and the palladium-mediated, enantioselective catalytic formation of optically active 2-alkyl-indan-1-ones (and -tetral-1-ones) from the corresponding racemic β-ketoesters or prochiral enol carbonates[8].

The graphical survey on some of the results obtained so far are given in Scheme 3 (for more detailed information concerning reaction conditions, work-up, determination of the optical yield or enantiomeric excess, etc. see experimental part; studies aimed to improve the enantioselectivity and catalytic efficiency are under investigation at present).

Scheme 3. Survey on results obtained in the enantioselective reduction of prochiral ketones in the presence of catalytic amounts of in situ-formed chiral oxazaborolidines (reaction 1) and the enantioselective catalytic addition of diethylzinc to prochiral ketones (reaction 2)



Reaction 1 : **cat***: 8 mol % ($\alpha S,\beta R$)-**17b**: **91 % *op***
further results: **12a**: 86%, **12b**: 33%, **12c**: 67%, **12d**: 19%
(for **12a-d**: 5 mol % were used)



Reaction 2 : **cat***: 5 mol % ($\alpha R,\beta R$)-*N*-methyl-**12a**: **95 % *op***
further results: **12a**: 9%, **12b**: 6%, **12c**: 14%, **12d**: 45%

By empiric improvement of the correlation between the chiral centers in α and β position (on the "ethylen" bridge between the N- and O-coordination centers of the ligand structure) and subsequently by the variation of the substitution pattern in α position (e.g. the aryl substituent), the development of artificial chiral auxiliaries – suitably designed for each of these asymmetric processes – has been accomplished. For each of these examples an optical purity (*op*) higher than 90% could be reached.

For both catalyzed processes (Scheme 3: reactions 1 and 2) a (1*R*,3*R*,5*R*)-configured, bicyclic backbone, e.g. a "*trans-exo*" substitution at the pyrrolidine ring provides the best results. The results obtained with the four diastereomers **12a**–**d** are given below the respective reaction to underline the importance of the ligand stereochemistry for the catalytic efficiency.

For the stereoselective addition of diethylzinc to benzaldehyde the *N*-methylated ligand *N*-methyl-($\alpha R,\beta R$)-**12a** – synthesized by $LiAlH_4$ reduction of the *N*-Boc-compound ($\alpha R,\beta R$)-**4a** – gives the best result with an optical purity for the product alcohol 1-phenylpropan-1-ol of 95% (result of the corresponding, homochiral *sec*-amino-*sec*-alcohol **12a**: 9% *op*).

For the stereoselective conversion 1 the results using the (*threo*)- or (*erythro*)-*mono*-arylhydroxymethyl systems were found to be significantly better than those obtained with the corresponding ligand based on the azabicyclo[3.3.0]octane system (*all-R*)-**1e** (reaction 1: 63% *op*) featuring a *bis*-arylhydroxymethyl subunit[10].

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Experimental Section

Melting points (uncorrected) were determined in an apparatus according to Linström. – Infrared spectra were recorded with a Beckman IR 4220 spectrometer as films between NaCl plates for liquids and KBr discs for solids. – ^{1}H- and ^{13}C-NMR spectra were recorded with a Bruker AM 300 (300 MHz) and Bruker ARX 500 (500 MHz). $CDCl_3$ was used as solvent and tetramethylsilane (TMS) as internal reference. – Optical rotations were measured with a Perkin-Elmer polarimeter 241 MC. – Mass spectra were measured with a Finnigan-MAT 212 (datasystem SS 300) spectrometer.

General Procedure GP1. – Synthesis of N-Protected N-tert-Butoxycarbonylimino Alcohols: 40 mmol of the amino alcohol component (1*R*,3*R*,5*R*)-**1d**[1l][1m], respectively the corresponding (1*R*,3*RS*,5*R*)-system[1n] were dissolved in 120 ml of anhyd. THF and 8.1 g (80 mmol) of triethylamine were added with stirring. After cooling the resulting clear reaction mixture to −10 °C a solution of di-*tert*-butyl dicarbonate (8.93 g, 39.7 mmol), dissolved in 60 ml of dry THF, was added dropwise within 30 min. To complete the reaction stirring was continued for 18 h at room temp. After the solvents were removed under reduced pressure in a rotary evaporator the oily residue was dissolved in 100 ml of diethyl ether and 80 ml of dist. H_2O. After separation of the layers the aqueous phase was extracted with diethyl ether (2 × 50 ml). The combined organic phases were washed with 2 N HCl solution (40 ml), dist. H_2O (60 ml), saturated $NaHCO_3$ solution (2 × 50 ml), brine (1 × 40 ml) and subsequently dried with anhydrous $MgSO_4$, filtered and concentrated in vacuo. The resulting colourless oil was NMR spectroscopically and microanalytically pure. The oil of compound (1*R*,3*R*,5*R*)-**2** solidified immediately on standing at room temp.

General Procedure GP2. – Synthesis of N-Protected, Bicyclic α-Amino Aldehydes **3** *of the (all-R)-Azabicyclo[3.3.0]octane-3-carboxylic Acid by Swern-Oxidation:* In a 500 ml three-necked flask 3.8 ml (44 mmol) of oxalyl chloride in 100 ml of abs. dichloromethane were placed under argon atmosphere. The clear solution was cooled to −70 °C (ethanol/liquid nitogen bath). A solution of 6.4 ml (88 mmol) abs. DMSO in 10 ml of abs. dichloromethane was added dropwise (during the addition the temp. should be constantly lower than −60 °C). The reaction proceeded with evolution of gas. After the addition was completed the reaction mixture was stirred for further 45 min at −70 °C. Then 40 mmol of the respective *N*-protected amino alcohol (1*R*,3*R*,5*R*)-**2** or (1*R*,3*S*,5*R*)-**2**, dissolved in 40 ml of abs. dichloromethane, were added dropwise over 30 min (again reaction temperatures below −60 °C). After 1.5−2 h of continiously stirring at a constant temperature of −70 °C the reaction mixture was quenched with 28 ml (200 mmol) of triethylamine. Then the cooling bath was removed and the reaction mixture was allowed to warm to room temp. After addition of 200 ml of dist. H_2O layers were separated and the aqueous phase was extracted twice with 120 ml of dichloromethane. The combined organic extracts were dried with $MgSO_4$. The solvent and triethylamine were evaporated in vacuo (temperatures below 30 °C). To remove triethylamine hydrochloride the residue was taken up in 100 ml of diethyl ether. After filtration the filtrate was concentrated under reduced pressure. Without any further work-up the *N*-protected α-amino aldehydes (1*R*,3*R*,5*R*)-**3** and (1*R*,3*S*,5*R*)-**3** were obtained as colourless or slightly yellow oils. A further purification (not necessary for the subsequent conversion according to GP3) of compounds (1*R*,3*R*,5*R*)-**3** and (1*R*,3*S*,5*R*)-**3** by flash chromatography gives NMR spectroscopically and microanalytically pure, colourless oils [(1*R*,3*R*,5*R*)-**3:** eluent: *n*-hexane/EtOAc 8:2, TLC: R_f = 0.44; (1*R*,3*S*,5*R*)-**3:** eluent: *n*-hexane/EtOAc 8:2, TLC: R_f = 0.48]. An epimerization during their chromatographic purification has never been observed (intramolecular control of the diastereomeric purity of the azabicyclo[3.3.0]octane systems by ^{1}H- and ^{13}C-NMR spectroscopy).

General Procedure GP3. – Conversion *of N-Boc-Protected α-Amino Aldehydes (1R,3R,5R)-3 and (1R,3S,5R)-3 with Aromatic Grignard Reagents to Provide the Corresponding N-Boc-Amino sec-Alcohols* **4**−**10**: To a freshly prepared solution of the respective Grignard reagent consisting of 0.96 g (40.0 mmol) of magnesium and 38.5 mmol of aryl halogenide (bromobenzene, 4-bromotoluene, 3-bromoanisole, 2-bromotoluene, 2-bromomesitylene, 2-bromo-*p*-xylene and 1-bromonaphthalene) in 120 ml of dry THF, 4.2 g (17.56 mmol) of the *N*-Boc-amino aldehyde (1*R*,3*R*,5*R*)-**3** or (1*R*,3*S*,5*R*)-**3**, dissolved in 40 ml of dry THF, were added dropwise over 30 min (for the respective reaction temperatures see Tables 1, 2 and 3). After the addition was completed the reaction mixture was stirred for 3 h at constant temp. and then allowed to warm to room temp. (overall reaction time: 16 h). For the hydrolytic work-up, 120 ml sat. NH_4Cl solution were added and after stirring for 1 h at room temp. phases were separated. The aqueous layer was extracted with methyl *t*-butyl ether (2 × 40 ml), the combined organic phases were dried ($MgSO_4$) and the solvents evaporated under reduced pressure. In all cases the diastereomeric ratio was determined by ^{1}H-NMR analysis using samples of the resulting oily crude products. Further details concerning the diastereoselectivity, reaction temp. and isolated yields were given in Tables 1, 2 and 3, the individual chromatographic work-up was described under the name of each compound.

General Procedure GP4. – Cleavage of the tert-Butoxycarbonyl Protecting Group, Synthesis of β-Amino Alcohols with Secondary Amino and Alcohol Function – GP4, Method A: To remove the *tert*-butoxycarbonyl protecting group 1.0 mmol of the respective *N*-Boc-amino alcohol derivative was dissolved in 10 ml of *methanol* [(or in methanol and acetic acid or just acetic acid). Under stirring 15 ml of aqueous 4 N HCl were added at 0 °C. After 3−4 h at room temp. solvents were removed at 40 °C in a rotary evaporator under reduced pressure. After extraction with diethyl ether (3 × 40 ml) the aqueous layer was basified by slow addition of 5% aqueous NaOH under stirring at 0 °C until a pH value of 10 was reached. Dichloromethane was added and after 45 min. at room temp. phases were separated. After extraction of the water phase with dichloromethane (5 × 30 ml) the combined organic extracts were dried ($MgSO_4$), solvents were removed in vacuo and the *sec*-amino alcohol was obtained as colourless or slightly yellow solid (yields generally between 75 and 96%).

GP4, Method B: To remove the *tert*-butoxycarbonyl protecting group 1.0 mmol of the respective *N*-Boc-amino alcohol derivative was dissolved in 15 ml CH_2Cl_2 and under stirring 3 ml of trifluoroacetic acid were added at 0 °C. After 30 min. the reaction mixture was allowed to warm to room temp. and stirring was continued for further 90 min. After basification with 5% aq. NaOH the aqueous phase was saturated with NaCl and then extracted with CH_2Cl_2 or $CH_2Cl_2/CHCl_3$ (5 × 40 ml). The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo. Further purification of the products involves an additional recrystallization with small amounts of *n*-hexane or CH_2Cl_2/*n*-hexane (in some cases a partial

epimerization of the amino alcohols was observed by NMR spectroscopy, after recrystallization the major diastereomer was obtained).

GP4, Method C: The removal of the *tert*-butoxycarbonyl protecting group was accomplished with *p*-toluenesulfonic acid (10.0 mmol for 1 mmol of the *N*-Boc-amino alcohol derivative dissolved in 30 ml of dioxane) and anisole (1.0 mmol). The course and the end of the reaction was monitored by TLC. Then 10 ml of aqueous 2 N HCl were added and after 20 minutes stirring at room temp. the water/dioxane layer was extracted with diethyl ether (3 × 40 ml) to remove the rest of the starting material. The aqueous phase was was basified to pH = 10 by slow addition of 5% aqueous NaOH at 0 °C followed by extraction with CH_2Cl_2 or diethyl ether (4 × 40 ml). After drying with $MgSO_4$ the combined organic layers were evaporated in vacuo to give the *sec*-amino alcohols as colourless or slightly yellow solids. Purification of the crude products – in most cases not necessary – by recrystallization with small amounts of *n*-hexane (or CH_2Cl_2/*n*-hexane) or by shortway distillation ("bulb-to-bulb" distillation under reduced pressure using an Büchi GKR-51 apparatus) affords the analytically pure compounds.

(all-R)-(1-tert-Butyloxycarbonyloctahydrocyclopenta[b]pyrrol-2-yl)methanol [(*all-R*)-**2**]: Reaction: GP1. Yield 9.4 g (97%), colourless solid, m.p. 83 °C. – $[\alpha]^{20}_D$ = −39.0 (*c* = 1.47, CH_2Cl_2). – IR (KBr): $\tilde{\nu}$ = 3680−3230 (OH), 1720−1650 cm^{-1} (−C=O). – ^1H NMR ($CDCl_3$): δ = 1.13−2.00 (m, 7 H, 5-H, 6-H_2, 7-H_2, 8-H_2), 1.43 [s, 9 H, OC(CH_3)$_3$], 2.06−2.26 (m, 1 H, 4-H), 2.44−2.63 (m, 1 H, 4-H), 3.41−3.66 (m, 2 H, CH_2OH), 3.77−4.00 (m, 1 H, 1-H), 4.00−4.17 (m, 1 H, 3-H), 5.29 (s, 1 H, CH_2OH). – ^{13}C NMR ($CDCl_3$): δ = 28.41 [OC(CH_3)$_3$], 24.15, 32.16, 34.46, 34.55 (C-4, C-6, C-7, C-8), 40.97 (C-5), 65.43 (CH_2OH), 62.85, 68.22 (C-1, C-3), 80.17 [O*C*(CH_3)$_3$], 151.15 (R_2NCO_2R). – MS (CI, isobutane); *m/z* (%): 242 (100) [MH^+]. – $C_{13}H_{23}NO_3$ (241.2): calcd. C 64.69, H 9.61, N 5.81; found C 64.62, H 9.54, N 5.76.

(1R,3S,5R)-(1-tert-Butyloxycarbonyloctahydrocyclopenta[b]pyrrol-2-yl)methanol [(1*R*,3*S*,5*R*)-**2**]: Preparation of the starting material (1*R*,3*RS*,5*R*)-**1d:** Conversion of (1*R*,3*R*,5*R*)-**1b** by the salicyl aldehyde-catalyzed epimerization (reaction conditions[11]: 0.5 equiv. of salicyl aldehyde in conc. acetic acid, 4 h under reflux, removal of the solvent under reduced pressure followed by the extractive workup with water/dichloromethane) affording a crude mixture of diastereomers [(1*R*,3*S*,5*R*)-**1b** and (1*R*,3*R*,5*R*)-**1b**] with a *dr* value of 66:34 in favor of the (1*R*,3*S*,5*R*)-configured product. This crude reaction mixture was reduced by treatment with $LiAlH_4$ (3 equiv.) in THF under reflux for 4 h. The epimerized amino alcohol (1*R*,3*RS*,5*R*)-**1d** was isolated by shortway distillation under reduced pressure (yield of this two-step-procedure 68%)[11]. Reaction: GP1. – Starting material: 7.2 g (51.1 mmol) of (1*R*,3*RS*,5*R*)-**1d**. – Diastereomeric ratio (after column chromatography) ≥ 95:5 (eluent: *n*-hexane/EtOAc 6.5:3.5, TLC: R_f = 0.38), minor diastereomer: (*all-R*)-**29** (TLC: R_f = 0.46). Yield 6.6 g (54%, *after* separation of diastereomers, overall yield: 11.4 g, 93%), colourless oil.−$[\alpha]^{20}_D$ = −98.3 (*c* = 0.84, CH_2Cl_2). – IR (NaCl): $\tilde{\nu}$ = 3660−3200 cm^{-1} (OH), 1730−1640 (C=O). – ^1H NMR ($CDCl_3$): δ = 1.29−1.80, 1.86−2.02 (2 m, 7 H, 5-H, 6-H_2, 7-H_2, 8-H_2), 1.44 [s, 9 H, OC(CH_3)$_3$], 2.49−2.68 (m, 1 H, 4-H), 3.48−3.67 (m, 2 H, CH_2OH), 3.86−4.03 (m, 1 H, 4-H), 4.03−4.14 (m, 1 H, 1-H), 4.77−4.86 (m, 1 H, 3-H), 4.77−4.86 (s, 1 H, CH_2OH). – ^{13}C NMR ($CDCl_3$): δ = 28.42 [OC(CH_3)$_3$], 24.69, 31.71, 33.95, 34.49 (C-4, C-6, C-7, C-8), 40.97 (C-5), 61.36, 64.16 (C-1, C-3), 66.66 (CH_2OH), 79.90 [O*C*(CH_3)$_3$], 156.28 (R_2NCO_2R). – MS (CI, isobutane); *m/z* (%): 242 (100) [MH^+]. – $C_{13}H_{23}NO_3$ (241.2): calcd. C 64.69, H 9.61, N 5.81; found C 64.34, H 9.57, N 5.62.

(all-R)-1-(tert-Butyloxycarbonyl)octahydrocyclopenta[b]-pyrrole2-carbaldehyde [(*all-R*)-**3**]: Reaction: GP2. – Starting material: 9.4 g (38.9 mmol) of (*all-R*)-**2**, 3.7 ml (42.8 mmol) of oxalyl chloride, 6.2 ml (85.5 mmol) of abs. DMSO. Yield 8.7 g (94%, crude product), 7.8 g (84%, after flash chromatography). – $[\alpha]^{20}_D$ = + 4.9 (*c* = 2.0, CH_2Cl_2). – IR (NaCl): $\tilde{\nu}$ = 1720−1660 cm^{-1} (−C=O). – ^1H NMR ($CDCl_3$): δ (rotamers) = 1.27−2.00 (m, 16 H, OC(CH_3)$_3$, 5-H, 6-H_2, 7-H_2, 8-H_2), 2.11−2.32 (m, 1 H, 4-H), 2.49−2.74 (m, 1 H, 4-H), 3.83−4.28 (m, 2 H, 1-H, 3-H), 9.48 (d, *J* = 2.6 Hz, 1 H, CHO). – ^{13}C NMR ($CDCl_3$): δ = major rotamer: 28.22 [OC(CH_3)$_3$], 24.20, 31.85, 32.67, 34.29 (C-4, C-6, C-7, C-8), 41.76 (C-5), 64.39, 67.03 (C-1, C-3), 80.12 [O*C*(CH_3)$_3$], 155.16 (R_2NCO_2R), 201.10 (CHO); minor rotamer: 28.34 [OC(CH_3)$_3$], 27.31, 31.48, 33.47, 34.48 (C-4, C-6, C-7, C-8), 42.86 (C-5), 63.97, 65.36 (C-1, C-3), 80.62 [O*C*(CH_3)$_3$], 154.16 (R_2NCO_2R), 200.82 (CHO). – MS (CI, isobutane); *m/z* (%): 240 (100) [MH^+]. – $C_{13}H_{21}NO_3$ (239.2): calcd. C 65.23, H 8.85 , N 5.86; found C 65.10, H 8.67, N 5.78.

(1R,3S,5R)-1-(tert-Butyloxycarbonyl)octahydrocyclopenta[b]-pyrrol-2-carbaldehyde [(1*R*,3*S*,5*R*)-**3**]: Reaction: GP2. – Starting material: 4.8 g (20.0 mmol) of (1*R*,3*S*,5*R*)-**2**. Yield 3.9 g (82%, after flash chromatography, eluent: *n*-hexane/EtOAc 8:2, TLC: R_f = 0.48), colourless oil. – $[\alpha]^{20}_D$ = −158.3 (*c* = 0.24, CH_2Cl_2). – IR (NaCl): $\tilde{\nu}$ = 1730−1680 (C=O, aldehyde). – ^1H NMR ($CDCl_3$): δ (rotamers) = 1.42 [s, 4.5 H, 0.5 × OC(CH_3)$_3$], 1.47 [s, 4.5 H, 0.5 × OC(CH_3)$_3$], 1.34−1.92 (3 m, 7 H, 5-H, 6-H_2, 7-H_2, 8-H_2), 1.92−2.09 (m, 1 H, 4-H), 2.54−2.73 (m, 1 H, 4-H), 4.09−4.31 (2 m, 2 H, 1-H, 3-H), 9.37 (d, *J* = 3.2 Hz, 0.5 H, 0.5 × CHO), 9.46 (d, *J* = 2.8 Hz, 0.5 H, 0.5 × CHO). – ^{13}C NMR ($CDCl_3$): δ (rotamers) = major rotamer: 28.16 [OC(CH_3)$_3$], 24.69, 31.89, 32.30, 34.22 (C-4, C-6, C-7, C-8), 41.31 (C-5), 64.07, 66.28 (C-1, C-3), 80.55 [O*C*(CH_3)$_3$], 154.66 (R_2NCO_2R), 199.34 (CHO); minor rotamer: 28.33 [OC(CH_3)$_3$], 24.56, 31.26, 33.17, 33.46 (C-4, C-6, C-7, C-8), 42.37 (C-5), 63.56, 66.05 (C-1, C-3), 80.11 [O*C*(CH_3)$_3$], 153.54 (R_2NCO_2R), 199.24 (CHO). – MS (CI, isobutane); *m/z* (%): 240 (100) [MH^+]. – $C_{13}H_{21}NO_3$ (239.2): calcd. C 65.23, H 8.85, N 5.86; found C 65.11, H 8.76, N 5.71.

(1'R,1R,3R,5R)-(1-tert-Butyloxycarbonyloctahydrocyclopenta-[b]pyrrol-2-yl)-1'-phenylmethanol [(α*R*,β*R*)-**4a**]: Reaction: GP3. – Starting material: 2.4 g (9.9 mmol) of (*all-R*)-**3**, Grignard reagent prepared from bromobenzene. – Diastereomeric ratio (crude product) 69:31 (reaction temp. −17 °C); diastereomeric ratio (after flash chromatography) ≥ 95:5 (eluent: *n*-hexane/triethylamine 7:3, TLC: R_f = 0.46), second flash chromatography (eluent: *n*-hexane/EtOAc 7:3, TLC: R_f = 0.38). Yield 1.2 g (38%, overall yield, e.g. both diastereomers 68%), colourless oil. – $[\alpha]^{20}_D$ = −31.8 (*c* = 0.50, CH_2Cl_2). – IR (NaCl): $\tilde{\nu}$ = 3630−3210 cm^{-1} (OH). – ^1H NMR ($CDCl_3$): δ = 1.21−1.34, 1.40−1.66, 1.66−2.00 (3 m, 8 H, 5-H, 6-H_2, 7-H_2, 8-H_2, 4-H), 1.54 [s, 9 H, OC(CH_3)$_3$], 2.39−2.57 (m, 1 H, 4-H), 4.09−4.28 (2 m, 2 H, 1-H, 3-H), 4.61 (d, *J* = 8.3 Hz, 1 H, PhC*H*OH), 7.22−7.40 (m, 5 H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 28.41 [OC(CH_3)$_3$], 24.69, 32.55, 34.11, 34.53 (C-4, C-6, C-7, C-8), 41.24 (C-5), 65.79, 66.33 (C-1, C-3), 80.19, 80.72 [Ph*C*HOH, O*C*(CH_3)$_3$], 127.49, 127.55, 128.23 (aromatic C), 142.84 (quat. aromatic C), 154.32 (R_2NCO_2R). – MS (CI, isobutane); *m/z* (%): 318 (100) [MH^+]. – $C_{19}H_{27}NO_3$ (317.2): calcd. C 71.88, H 8.58, N 4.41; found C 71.79, H 8.51, N 4.38.

(1'S,1R,3R,5R)-(1-tert-Butyloxycarbonyloctahydrocyclopenta-[b]pyrrol-2-yl)-1'-phenylmethanol [(α*S*,β*R*)-**4b**]: Reaction: GP3. – Starting material: 2.4 g (9.9 mmol) of (*all-R*)-**3**, Grignard reagent prepared from bromobenzene. – Diastereomeric ratio (crude product) 31:69 (reaction temp. −17 °C); diastereomeric ratio (after flash

chromatography) ≥ 95:5 (eluent: *n*-hexane/triethylamine 7:3, TLC: R_f = 0.57). Yield 0.94 g (30%, overall yield: 68%), colourless oil. – $[\alpha]^{20}_D$ = + 53.1 (*c* = 0.60, CH_2Cl_2). – IR (NaCl): $\tilde{\nu}$ = 3620–3210 cm^{-1} (OH). – ^1H NMR ($CDCl_3$): δ = 1.20–1.83 (2 m, 7 H, 5-H, 6-H_2, 7-H_2, 8-H_2), 1.51 [s, 9 H, OC(CH_3)$_3$], 1.91–2.09 (m, 1 H, 4-H), 2.37–2.58 (m, 1 H, 4-H), 4.04–4.31 (2 m, 2 H, 1-H, 3-H), 4.89–5.03 (s, 1 H, PhC*H*OH), 7.18–7.40 (m, 5 H, aromatic H).– ^{13}C NMR ($CDCl_3$): δ = 28.45 [OC(CH_3)$_3$], 11.53, 23.56, 30.99, 32.65 (C-4, C-6, C-7, C-8), 40.27 (C-5), 46.19, 65.71 (C-1, C-3), 66.44 (Ph*C*OH), 80.09 [O*C*(CH_3)$_3$], 127.10, 127.71, 128.68 (aromatic C), 140.91 (quat. aromatic C), 155.10 (R_2NCO_2R). – MS (CI, isoutane): *m/z* (%): 318 (100) [MH^+]. – $C_{19}H_{27}NO_3$ (317.2): calcd. C 71.88, H 8.58, N 4.41; found C 71.6, H 8.61, N 4.36.

(1'S,1R,3S,5R)-(1-tert-Butyloxycarbonyloctahydrocyclopenta-[b]pyrrol-2-yl)-1'-phenylmethanol [(α*S*,β*S*)-**4c**]: Reaction: GP3. – Starting material: 3.75 g (15.7 mmol) of (1*R*,3*S*,5*R*)-**3**, Grignard reagent bromobenzene. – Diastereomeric ratio (crude product) 46:54 (reaction temp. –15 °C); diastereomeric ratio (after flash chromatography) ≥ 95:5 (eluent: *n*-hexane/triethylamine 8:2, TLC: R_f = 0.55). Yield 1.82 g (37%, over all yield: 83%), colourless solid, m.p. 98 °C. – $[\alpha]^{20}_D$ = – 52.5 (*c* = 0.68, CH_2Cl_2). – IR (KBr): $\tilde{\nu}$ = 3680–3200 cm^{-1} (OH), 1690–1650 (–C=O). – ^1H NMR ($CDCl_3$): δ = 1.51 [s, 9 H, OC(CH_3)$_3$], 1.20–1.61 (3 m, 7 H, 5-H, 6-H_2, 7-H_2, 8-H_2), 1.66–2.02 (m, 1 H, 4-H), 2.39–2.54 (m, 1 H, 4-H), 3.93–4.06 (m, 1 H, 1-H), 4.14–4.29 (m, 1 H, 3-H), 4.77 (d, *J* = 8.8 Hz, 1 H, PhC*H*OH), 5.34 (s, 1 H, PhCHO*H*), 7.20–7.44 (m, 5 H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 28.47 [OC(CH_3)$_3$], 23.95, 30.57, 32.43, 32.87 (C-4, C-6, C-7, C-8), 41.26 (C-5), 63.81, 65.75 (C-1, C-3), 77.80 (Ph*C*HOH), 80.32 [O*C*(CH_3)$_3$], 127.01, 127.59, 128.23 (aromatic C), 142.58 (quat. aromatic C), 157.28 (R_2NCO_2R). – MS (CI, isobutane); *m/z* (%): 318 (100) [MH^+]. – $C_{19}H_{27}NO_3$ (317.2): calcd. C 71.88, H 8.58, N 4.41; found C 71.96, H 8.60, N 4.45.

(1'R,1R,3S,5R)-(1-tert-Butyloxycarbonyloctahydrocyclopenta-[b]pyrrol-2-yl)-1'-phenylmethanol [(α*R*,β*S*)-**4d**]: Reaction: GP3. – Starting material: 3.75 g (15.7 mmol) of (1*R*,3*S*,5*R*)-**3**, Grignard reagent: bromobenzene. – Diastereomeric ratio (crude product) 54:46 (reaction temp. –15 °C); diastereomeric ratio (after flash chromatography) ≥ 95:5 (eluent: *n*-hexane/triethylamine 8:2, TLC: R_f = 0.72). Yield 2.3 g (46%, overall yield: 83%), colourless solid, m.p. 81 °C. – $[\alpha]^{20}_D$ = –129.3 (*c* = 0.57, CH_2Cl_2). – IR (KBr): $\tilde{\nu}$ = 3600–3170 cm^{-1} (OH), 1690–1650 (–C=O). – ^1H NMR ($CDCl_3$) : δ = 1.51 [s, 9 H, OC(CH_3)$_3$], 1.12–2.09 (3 m, 9 H, 5-H, 6-H_2, 7-H_2, 8-H_2, 4-H_2), 3.54–3.69 (m, 1 H, 1-H), 4.45–4.54 (m, 1 H, 3-H), 4.91 (s, 1 H, PhC*H*OH), 5.13 (s, 1 H, PhCHO*H*), 7.20–7.38 (m, 5 H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 28.53 [OC(CH_3)$_3$], 23.88, 31.39, 32.93, 33.73 (C-4, C-6, C-7, C-8), 41.35 (C-5), 64.69, 65.49 (C-1, C-3), 77.54 (Ph*C*HOH), 80.03 [O*C*(CH_3)$_3$], 126.72, 127.20, 127.98 (aromatic C), 141.72 (quat. aromatic C), 153.31 (R_2NCO_2R). – MS (CI, isobutane); *m/z* (%): 318 (100) [MH^+]. – $C_{19}H_{27}NO_3$ (317.2): calcd. C 71.88, H 8.58, N 4.41; found C 71.79, H 8.52, N 4.32.

(1'R,1R,3R,5R)-(1-tert-Butyloxycarbonyloctahydrocyclopenta-[b]pyrrol-2-yl)-1'-(4-methyl-phenyl)methanol [(α*R*,β*R*)-**5a**]: Reaction: GP3. – Starting material: 4.9 g (20.7 mmol) of (*all-R*)-**3**, Grignard reagent prepared from 4-bromotoluene. – Diastereomeric ratio (crude product) 70:30 (reaction temp. –16 °C); diastereomeric ratio (after flash chromatography) ≥ 95:5 (eluent: *n*-hexane/EtOAc 9:1, TLC: R_f = 0.21); subsequent flash chromatography (eluent: *n*-hexane/triethylamine 9:1, TLC: R_f = 0.35). Yield 2.5 g (36%, over all yield, e.g. both diastereomers: 55%), colourless oil. – $[\alpha]^{20}_D$ = –38.6 (*c* = 0.72, CH_2Cl_2). – IR (NaCl): $\tilde{\nu}$ = 3680–3220 cm^{-1} (OH), 1710–1650 (–C=O). – ^1H NMR ($CDCl_3$): δ = 1.21–1.37, 1.40–1.97 (3 m, 8 H, 5-H, 6-H_2, 7-H_2, 8-H_2, 4-H), 1.51 [s, 9 H, OC(CH_3)$_3$], 2.32 (s, 3 H, ArCH_3), 2.41–2.59 (m, 1 H, 4-H), 4.09–4.30 (m, 2 H, 1-H, 3-H), 4.57 (d, *J* = 8.8 Hz, 1 H, ArC*H*OH), 6.31 (s, 1 H, ArCHO*H*), 7.14 (d, *J* = 7.7 Hz, 2 H, aromatic H), 7.24 (d, *J* = 7.7 Hz, 2 H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 28.44 [OC(CH_3)$_3$], 21.10, 24.77, 32.65, 34.14, 34.59 (C-4, C-6, C-7, C-8, CH_3), 41.28 (C-5), 65.77, 66.33 (C-1, C-3), 80.11 (Ar*C*HOH), 80.69 [O*C*(CH_3)$_3$], 127.37, 128.94 (aromatic C), 137.16, 139.96 (quat. aromatic C), 155.10 (R_2NCO_2R). – MS (CI, isobutane); *m/z* (%): 332 (100) [MH^+]. – $C_{20}H_{29}NO_3$ (331.2): calcd. C 72.46, H 8.82, N 4.23; found C 72.27, H 8.79, N 4.28.

(1'S,1R,3R,5R)-(1-tert-Butyloxycarbonyloctahydrocyclopenta-[b]pyrrol-2-yl)-1'-(4-methyl-phenyl)methanol [(α*S*,β*R*)-**5b**]: Reaction: GP3. – Starting material: 4.9 g (20.7 mmol) of (*all-R*)-**3**, Grignard reagent prepared from 4-bromotoluene. – Diastereomeric ratio (crude product) 30:70 (reaction temp. –16 °C); diastereomeric ratio (after flash chromatography) ≥ 95:5 (eluent: *n*-hexane/EtOAc 9:1, TLC: R_f = 0.33). Yield 1.3 g (19%, overall yield, both diastereomers: 55%), colourless oil. – $[\alpha]^{20}_D$ = + 5.28 (*c* = 0.84, CH_2Cl_2). – IR (NaCl): $\tilde{\nu}$ = 3600–3150 cm^{-1} (OH), 1730–1660 (–C=O). – ^1H NMR ($CDCl_3$): δ = 0.83–0.97, 1.20–2.09 (3 m, 8 H, 5-H, 6-H_2, 7-H_2, 8-H_2, 4-H), 1.50 (s, 9 H, OC(CH_3)$_3$], 2.34 (s, 3 H, ArCH_3), 2.38–2.54 (m, 1 H, 4-H), 4.03–4.24 (m, 2 H, 1-H, 3-H), 4.91 (s, 1 H, ArC*H*OH), 6.20 (s, 1 H, ArCHO*H*), 7.11 (d, *J* = 7.7 Hz, 2 H, aromatic H), 7.19 (d, *J* = 7.7 Hz, 2 H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 28.41 (OC(CH_3)$_3$], 21.02, 23.52, 30.97, 32.64, 33.59 (C-4, C-6, C-7, C-8, CH_3), 40.20 (C-5), 65.65, 66.40 (C-1, C-3), 74.37 (Ar*C*HOH), 80.00 (O*C*(CH_3)$_3$], 126.92, 128.36 (aromatic C), 136.53, 137.75 (quat. aromatic C), 154.10 (R_2NCO_2R). – MS (CI, isobutane); *m/z* (%): 332 (100) [MH^+]. – $C_{20}H_{29}NO_3$ (331.2): calcd. C 72.46, H 8.82, N 4.23; found C 72.37, H 8.89, N 4.32.

(1'S,1R,3S,5R)-(1-tert-Butyloxycarbonyloctahydrocyclopenta-[b]pyrrol-2-yl)-1'-(4-methyl-phenyl)methanol [(α*S*,β*S*)-**5c**]: Reaction: GP3. – Starting material: 3.5 g (14.7 mmol) of (1*R*,3*S*,5*R*)-**3**, Grignard reagent: 4-bromotoluene. – Diastereomeric ratio (crude product) 43:57 (reaction temp. –18 °C); diastereomeric ratio (after flash chromatography) ≥ 95:5 (eluent: *n*-hexane/triethylamine 9:1, TLC: R_f = 0.23). Yield 1.74 g (36%, overall yield: 75%), colourless solid, m.p. 122 °C. – $[\alpha]^{20}_D$ = – 54.7 (*c* = 2.74, CH_2Cl_2). – IR (KBr): $\tilde{\nu}$ = 3600–3100 cm^{-1} (OH), 1720–1660 (–C=O). – ^1H NMR ($CDCl_3$): δ = 1.23–1.42, 1.47–1.67, 1.86–1.97 (3 m, 8 H, 5-H, 6-H_2, 7-H_2, 8-H_2, 4-H), 1.51 (s, 9 H, OC(CH_3)$_3$], 2.33 (s, 3 H, ArCH_3), 2.42–2.53 (m, 1 H, 4-H), 3.94–4.05 (s, 1 H, ArCHO*H*), 4.17–4.29 (m, 1 H, 1-H), 4.61–4.68 (m, 1 H, 3-H), 5.24 (d, *J* = 8.4 Hz, 1 H, ArC*H*OH), 7.11 (d, *J* = 7.7 Hz, 2 H, aromatic H), 7.21 (d, *J* = 7.7 Hz, 2 H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 28.48 (OC(CH_3)$_3$], 21.11, 23.96, 30.60, 32.91, 33.54 (C-4, C-6, C-7, C-8, CH_3), 41.27 (C-5), 63.79, 65.76 (C-1, C-3), 77.58 (Ar*C*HOH), 80.26 (O*C*(CH_3)$_3$], 126.89, 128.90 (aromatic C), 137.16, 139.64 (quat. aromatic C), 157.26 (R_2NCO_2R). – MS (CI, isobutane); *m/z* (%): 332 (100) [MH^+]. – $C_{20}H_{29}NO_3$ (331.2): calcd. C 72.46, H 8.82, N 4.23; found C 72.28, H 8.78, N 4.19.

(1'R,1R,3S,5R)-(1-tert-Butyloxycarbonyloctahydrocyclopenta-[b]pyrrol-2-yl)-1'-(4-methyl-phenyl)methanol [(α*R*,β*S*)-**5d**]: Reaction: GP3. – Starting material: 3.5 g (14.7 mmol) of (1*R*,3*S*,5*R*)-**3**, Grignard reagent: 4-bromotoluene. – Diastereomeric ratio (crude product) 57:43 (reaction temp. –18 °C); diastereomeric ratio (after flash chromatography) ≥ 95:5 (eluent: *n*-hexane/triethylamine 9:1,

TLC: R_f = 0.49). Yield 1.90 g (5.73 mmol, 39%, overall yield: 75%), colourless solid, m.p. 129°C. – $[\alpha]^{20}_D$ = – 149.6 (c = 1.28, CH_2Cl_2). – IR (KBr): $\tilde{\nu}$ = 3620–3160 cm^{-1} (OH), 1730–1680 (–C=O). – ^1H NMR ($CDCl_3$): δ = 1.22–1.88 (3 m, 8 H, 5-H, 6-H_2, 7-H_2, 8-H_2, 4-H), 1.51 (s, 9 H, $OC(CH_3)_3$], 1.94–2.11 (m, 1 H, 4-H), 2.32 (s, 3 H, $ArCH_3$), 3.58 (m, 1 H, 1-H), 4.41–4.51 (m, 1 H, 3-H), 4.86 (s, 1 H, ArC*H*OH), 5.09 (s, 1 H, ArCHO*H*), 7.12 (d, J = 7.7 Hz, 2 H, aromatic H), 7.21 (d, J = 7.8 Hz, 2 H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 28.54 [$OC(CH_3)_3$], 21.13, 23.88, 31.39, 32.98, 33.71 (C-4, C-6, C-7, C-8, CH_3), 41.33 (C-5), 64.66, 65.50 (C-1, C-3), 74.69 (Ar*C*HOH), 80.01 [$OC(CH_3)_3$], 126.62, 128.70 (aromatic C), 136.74, 138.61 (quat. aromatic C), 156.77 (R_2NCO_2R). – MS (CI, isobutane); m/z (%): 332 (100) [MH^+]. – $C_{20}H_{29}NO_3$ (331.2): calcd. C 72.46, H 8.82, N 4.23; found C 72.24, H 8.76, N 4.19.

(1'R,1R,3R,5R)-(1-tert-Butyloxycarbonyloctahydrocyclopenta-[b]pyrrol-2-yl)-1'-(3-methoxy-phenyl)methanol(αR,βR)-**6a**]: Reaction: GP3. – Starting material: 4.2 g (17.6 mmol) of (*all-R*)-**3**, Grignard reagent prepared from 3-bromoanisole. – Diastereomeric ratio (crude product) 47:53 (reaction temp. –5 °C); diastereomeric ratio (after flash chromatography) ≥ 95:5 (eluent: *n*-hexane/triethylamine 8:2, DC: R_f = 0.60). Yield 2.40 g (39%, overall yield, both diastereomers: 74%), colourless oil. – $[\alpha]^{20}_D$ = – 21.0 (c = 0.37, CH_2Cl_2). – IR (NaCl): $\tilde{\nu}$ = 3362 cm^{-1} (OH), 1660 (–C=O). – ^1H NMR ($CDCl_3$): δ = 1.22–2.05 (m, 9 H, 5-H, 6-H_2, 7-H_2, 8-H_2, 4-H_2), 1.51 (s, 9 H, $OC(CH_3)_3$], 3.82 (s, 3 H, $ArOCH_3$), 4.08–4.34 (m, 2 H, 1-H, 3-H), 4.56 (d, J = 9.2 Hz, 1 H, ArC*H*OH), 6.26 (s, 1 H, ArCHO*H*), 6.76–7.35 (m, 4 H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 28.44 [$OC(CH_3)_3$], 24.10, 32.65, 34.04, 34.59 (C-4, C-6, C-7, C-8), 41.28 (C-5), 55.12 [OCH_3), 65.42, 65.82 (C-1, C-3), 66.33 (Ar*C*HOH), 80.81 [$OC(CH_3)_3$], 112.73, 113.32, 120.05, 129.23 (aromatic C), 144.42, 159.64 (quat. aromatic C). – MS (CI, isobutane); m/z (%): 348 (18) [MH^+], 155 (100), 110 (98). – $C_{20}H_{29}NO_4$ (347.2).

(1'S,1R,3R,5R)-(1-tert-Butyloxycarbonyloctahydrocyclopenta-[b]pyrrol-2-yl)-1'-(3-methoxy-phenyl)methanol [(αS,βR)-**6b**]: Reaction: GP3. – Starting material: 4.2 g (17.6 mmol) of (*all-R*)-**3**, Grignard reagent prepared from 3-bromoanisole. – Diastereomeric ratio (crude product) 53:47 (reaction temp. –5 °C); diastereomeric ratio (after flash chromatography): ≥ 95:5 (eluent: *n*-hexane/triethylamine 8:2, DC: R_f = 0.27). Yield 2.15 g (35%, overall yield, e.g. both diastereomers: 74%), colourless oil. – $[\alpha]^{20}_D$ = + 22.0 (c = 3.3, CH_2Cl_2). – IR (NaCl): $\tilde{\nu}$ = 3387 cm^{-1} (OH), 1667 (–C=O). – ^1H NMR ($CDCl_3$): δ = 1.21–2.05 (m, 8 H, 5-H, 6-H_2, 7-H_2, 8-H_2, 4-H), 1.53 (s, 9 H, $OC(CH_3)_3$], 2.37–2.58 (m, 1 H, 4-H), 3.79 (s, 3 H, $ArOCH_3$), 4.01–4.29 (m, 2 H, 1-H, 3-H), 4.97 (s, 1 H, ArC*H*OH), 6.12 (s, 1 H, ArCHO*H*), 6.71–7.29 (m, 4 H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 28.51 [$OC(CH_3)_3$], 27.05, 31.15, 32.64, 32.91 (C-4, C-6, C-7, C-8), 40.32 (C-5), 55.24 (OCH_3), 65.82, 66.41 (C-1, C-3), 74.23 (Ar*C*HOH), 80.12 [$OC(CH_3)_3$], 112.71, 113.36, 119.54, 128.74 (aromatic C), 142.75, 159.43 (quat. aromatic C). – MS (CI, isobutane); m/z (%): 348 (94) [MH^+], 347 (74), 110 (100).

(1'S,1R,3R,5R)-(1-tert-Butyloxycarbonyloctahydrocyclopenta-[b]pyrrol-2-yl)-1'-(2-methyl-phenyl)methanol [(αS,βR)-**7b**]: Reaction: GP3. – Starting material: 4.9 g (20.7 mmol) of (*all-R*)-**3**, Grignard reagent prepared from 2-bromotoluene. – Diastereomeric ratio (crude product) ≥ 95:5 (reaction temp. –9 °C); diastereomeric ratio (after flash chromatography) ≥ 95:5 (eluent: *n*-hexane/triethylamine 9:1, TLC: R_f = 0.54); subsequent second flash chromatography (eluents: *n*-hexane/triethylamine 7:3, DC: R_f = 0.77). Yield 2.6 g (38%), colourless oil. – $[\alpha]^{20}_D$ = –19.7 (c = 1.37, CH_2Cl_2). – IR (NaCl): $\tilde{\nu}$ = 3670–3210 cm^{-1} (OH), 1690–1645 (–C=O). – ^1H NMR ($CDCl_3$): δ = 1.09–1.23, 1.40–2.02 (m, 8 H, 5-H, 6-H_2, 7-H_2, 8-H_2, 4-H), 1.51 [s, 9 H, $OC(CH_3)_3$], 2.45 (s, 3 H, $ArCH_3$), 2.40–2.58 (m, 1 H, 4-H), 4.18–4.42 (2 m, 2 H, 1-H, 3-H), 4.87 (d, J = 9.4 Hz, 1 H, Ar-C*H*OH), 6.42 (s, 1 H, ArCHO*H*), 7.08–7.25 (m, 3 H, aromatic H), 7.34–7.43 (m, 1 H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 19.97 ($ArCH_3$), 28.45 [$OC(CH_3)_3$], 24.69, 32.55, 34.21, 34.61 (C-4, C-6, C-7, C-8), 41.10 (C-5), 65.80, 66.12 (C-1, C-3), 75.42 (Ar*C*HOH), 80.77 [$OC(CH_3)_3$], 126.22, 127.28, 127.82 (aromatic C), 130.58, 135.33, 140.90 (quat. aromatic C), 153.87 (R_2NCO_2R). – MS (CI, isobutane); m/z (%): 332 (100) [MH^+]. – $C_{20}H_{29}NO_3$ (331.2): calcd. C 72.46, H 8.82, N 4.23; found C 72.50, H 8.65, N 4.31.

(1'S,1R,3R,5R)-(1-tert-Butyloxycarbonyloctahydrocyclopenta-[b]pyrrol-2-yl)-1'-(2,5-dimethylphenyl)methanol [(αS,βR)-**8b**]: Reaction: GP3. – Starting material: 4.9 g (20.7 mmol) of (*all-R*)-**3**, Grignard reagent prepared from 2-bromo-*p*-xylene. – Diastereomeric ratio (crude product) ≥ 95:5 (reaction temp. –12 °C); diastereomeric ratio (after flash chromatography) ≥ 95:5 (eluent: *n*-hexane/triethylamine 8:2, TLC: R_f = 0.68). Yield 2.8 g (39%), colourless oil. – $[\alpha]^{20}_D$ = –32.1 (c = 0.36, CH_2Cl_2). – IR (NaCl): $\tilde{\nu}$ = 3630–3220 cm^{-1} (OH), 1690–1650 (–C=O). – ^1H NMR ($CDCl_3$): δ = 1.38–2.03 (m, 8 H, 5-H, 6-H_2, 7-H_2, 8-H_2, 4-H), 1.54 [s, 9 H, $OC(CH_3)_3$], 2.31 (s, 3 H, $ArCH_3$), 2.40 (s, 3 H, $ArCH_3$), 2.47–2.56 (m, 1 H, 4-H), 4.21–4.42 (2 m, 2 H, 1-H, 3-H), 4.83 (d, J = 9.2 Hz, 1 H, ArC*H*OH), 6.37 (s, 1 H, ArCHO*H*), 6.94–7.07 (m, 2 H, aromatic H), 7.23 (s, 1 H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 28.46 [$OC(CH_3)_3$], 19.47, 21.00, 24.74, 32.61, 34.14, 34.65 (2 × $ArCH_3$, C-4, C-6, C-7, C-8), 41.16 (C-5), 65.81, 66.26 (C-1, C-3), 76.47 (Ar*C*HOH), 80.74 [$OC(CH_3)_3$], 128.07, 128.27, 130.41 (aromatic C), 132.09, 135.58, 140.73 (quat. aromatic C), 154.32 (R_2NCO_2R).–MS (CI, isobutane); m/z (%): 346 (100) [MH^+]. – $C_{21}H_{31}NO_3$ (345.2): calcd. C 72.9, H 9.05, N 4.06; found C 72.83, H 9.01, N 4.10.

(1'S,1R,3S,5R)-(1-tert-Butyloxycarbonyloctahydrocyclopenta-[b]pyrrol-2-yl)-1'-(2,5-dimethylphenyl)methanol [(αS,βS)-**8c**]: Reaction: GP3. – Starting material: 3.4 g (14.2 mmol) of (1*R*,3*S*,5*R*)-**3**, Grignard reagent: 2-bromo-*p*-xylene. – Diastereomeric ratio (crude product) 41:59 (reaction temp. –16 °C); diastereomeric ratio (after flash chromatography) ≥ 95:5 (eluent: *n*-hexane/triethylamine 9:1, TLC: R_f = 0.48). Yield 1.47 g (30%, overall yield: 65%), colourless oil. – $[\alpha]^{20}_D$ = –14.6 (c = 0.41, CH_2Cl_2). – IR (NaCl): $\tilde{\nu}$ = 3700–3230 cm^{-1} (OH), 1690–1660 (–C=O). – ^1H NMR ($CDCl_3$): δ = 1.34–1.75 (m, 7 H, 5-H, 6-H_2, 7-H_2, 8-H_2), 1.51 [s, 9 H, $OC(CH_3)_3$], 1.91–2.06 (m, 1 H, 4-H), 2.29 (s, 3 H, $ArCH_3$), 2.34 (s, 3 H, $ArCH_3$), 2.54–2.77 (m, 1 H, 4-H), 4.06–4.20 (m, 1 H, 1-H), 4.31–4.42 (m, 1 H, 3-H), 4.89 (d, J = 3.8 Hz, 1 H, Ar-C*H*OH), 5.48 (s, 1 H, ArCHO*H*), 6.91–7.06 (m, 2 H, aromatic H), 7.25 (s, 1 H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 28.47 [$OC(CH_3)_3$], 19.25, 20.99, 23.99, 30.44, 33.04, 33.49 (2 × $ArCH_3$, C-4, C-6, C-7, C-8), 41.93 (C-5), 63.81, 65.95 (C-1, C-3), 74.79 (Ar*C*HOH), 80.47 [$OC(CH_3)_3$], 127.84, 128.06, 130.25 (aromatic C), 132.12, 135.64, 140.73 (quat. aromatic C), 157.74 (R_2NCO_2R). – MS (CI, isobutane); m/z (%): 346 (100) [MH^+]. – $C_{21}H_{31}NO_3$ (345.2): calcd. C 72.99, H 9.05, N 4.06; found C 72.78, H 9.12, N 4.09.

(1'R,1R,3S,5R)-(1-tert-Butyloxycarbonyloctahydrcyclopenta[b]-pyrrol-2-yl)-1'-(2,5-dimethyl-phenyl)methanol [(αR,βS)-**8d**]: Reaction: GP3. – Starting material: 3.4 g (14.2 mmol) of (1*R*,3*S*,5*R*)-**3**, Grignard reagent: 2-bromo-*p*-xylene. – Diastereomeric ratio (crude product) 59:41 (reaction temp. –16 °C); diastereomeric ratio (after flash chromatography) ≥ 95:5 (eluent: *n*-hexane/triethylamine 9:1,

TLC: R_f = 0.69). Yield 1.70 g (35%, overall yield, both diastereomers: 65%), colourless oil. – $[\alpha]^{20}_D$ = – 73.3 (c = 0.24, CH_2Cl_2). – IR (KBr): $\tilde{\nu}$ = 3630–3220 cm^{-1} (OH), 1690–1650 (–C=O). – ^1H NMR ($CDCl_3$): δ = 1.23–1.69 (m, 7 H, 5-H, 6-H_2, 7-H_2, 8-H_2), 1.52 [s, 9 H, OC(CH_3)$_3$], 1.74–1.91 (m, 1 H, 4-H), 1.93–2.11 (m, 1 H, 4-H), 2.32 (s, 3 H, $ArCH_3$), 2.38 (s, 3 H, $ArCH_3$), 3.67 (s, 1 H, ArCHO*H*), 3.82–3.94 (m, 1 H, 1-H), 4.27–4.40 (m, 1 H, 3-H), 5.34 (s, 1 H, ArC*H*OH), 6.94–7.03 (m, 2 H, aromatic H), 7.26 (s, 1 H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 28.60 [OC(CH_3)$_3$], 19.03, 21.15, 23.95, 31.45, 33.93, 41.70 (2 × $ArCH_3$, C-4, C-6, C-7, C-8), 41.95 (C-5), 64.01, 64.68 (C-1, C-3), 71.75 (ArCHOH), 79.56 [O*C*(CH_3)$_3$], 127.15, 127.66, 130.07 (aromatic C), 131.71, 134.94, 139.57 (quat. aromatic C), 155.76 (R_2NCO_2R). – MS (CI, isobutane); *m/z* (%): 346 (100) [MH^+]. – $C_{21}H_{31}NO_3$ (345.2): calcd. C 72.99, H 9.05, N 4.06; found C 73.12, H 9.16, N 4.00.

(1'S,1R,3R,5R)-(1-tert-Butyloxycarbonyloctahydrocyclopenta-[b]pyrrol-2-yl)-1'-(2,4,6-trimethyl-phenyl)methanol [(α*S*,β*R*)-**9b**]: Reaction: GP3. – Starting material: 4.9 g (20.7 mmol) of (*all-R*)-**3**, Grignard reagent prepared from 2-bromomesitylene. – Diastereomeric ratio (crude product) ≥ 95:5 (reaction temp. –14 °C); diastereomeric ratio (after flash chromatography) ≥ 95:5, eluent: *n*-hexane/triethylamine 9:1, TLC: R_f = 0.55). Yield 2.5 g (34%), colourless solid, m.p. 52 °C. – $[\alpha]^{20}_D$ = + 9.4 (c = 0.52, CH_2Cl_2). – IR (KBr): $\tilde{\nu}$ = 3700–3210 cm^{-1} (OH), 1690–1650 (–C=O). – ^1H NMR ($CDCl_3$): δ = 1.42 [s, 9 H, OC(CH_3)$_3$], 1.31–1.80, 1.88–2.07 (2 m, 8 H, 5-H, 6-H_2, 7-H_2, 8-H_2, 4-H), 2.24 (s, 3 H, $ArCH_3$), 2.42–2.58 (m, 1 H, 4-H), 2.45 (s, 6 H, 2 × $ArCH_3$), 4.16–4.37 (m, 2 H, 1-H, 3-H), 5.49 (d, J = 3.0 Hz, 1 H, ArC*H*OH), 6.78 (s, 2 H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 20.59 ($ArCH_3$), 21.51 (2 × $ArCH_3$), 28.27 [OC(CH_3)$_3$], 24.62, 31.52, 31.95, 33.64 (C-4, C-6, C-7, C-8), 41.07 (C-5), 64.08, 65.79 (C-1, C-3), 72.19 (ArC*H*OH), 79.54 [O*C*(CH_3)$_3$], 130.20 (aromatic C), 134.53, 136.06, 136.63 (quat. aromatic C), 156.07 (R_2NCO_2R). – MS (CI, isobutane); *m/z* (%): 360 (100) [MH^+]. – $C_{22}H_{33}NO_3$ (359.2): calcd. C 73.49, H 9.26, N 3.90; found C 73.34, H 9.32, N 3.98.

Further details concerning the crystal structure analysis of (α*S*,β*R*)-**9b** were available on request from the Fachinformationszentrum Karlsruhe, D-76344 Eggenstein-Leopoldshafen, on quoting the depository number CSD-407328, the names of the authors, and the literature citation.

Table 4. Crystallographic data of compound (α*S*,β*R*)-**9b**

Compound	(α*S*,β*R*)-**9b**
Molecular formula	$C_{22}H_{33}NO_3$
Molecular mass	359.49
Crystal system	orthorhombic
Space group	$P2_12_12_1$
Cell parameters:	
a [pm]	1026.50 (10), α = 90°
b [pm]	1281.20 (10), β = 90°
c [pm]	1552.10 (10), γ = 90°
Z	4
Volume [$10^6 \cdot pm^3$]	2041.2 (3)
d [g/cm^3]	1.170
Absorption coefficient [mm^{-1}]	0.077
Reflections collected	2520
Independent reflections	2520 (R_{int} = 0.0000)
Observed reflections [$I > 2.0\ \sigma(I)$]	1762
Final R indices [$I > 2.0\ \sigma(I)$]	R_1 = 0.0621 , wR_2 = 0.1582
Diffractometer used	Siemens STOE AED2
Radiation	Mo-K_α (λ = 0.71073 Å)
Temperature (K)	296(2)
Monochromator	Graphit
System used	Siemens SHELXTL PLUS
Solution	Direct methods
Goodness-of-fit	1.050
2θ range (°)	2.06 to 27.02

(1'S,1R,3R,5R)-(1-tert-Butyloxycarbonyloctahydrocyclopenta-[b]pyrrol-2-yl)-1'-(1-naphthyl)methanol [(α*S*,β*R*)-**10b**]: Reaction: GP3. – Starting material: 4.9 g (20.7 mmol) of (*all-R*)-**3**, Grignard reagent prepared from 1-bromonaphthalene. – Diastereomeric ratio (crude product) ≥ 95:5 (reaction temp. –11 °C); diastereomeric ratio (after flash chromatography) ≥ 95:5, eluent: *n*-hexane/triethylamine 8:2, TLC: R_f = 0.51). Yield 3.3 g (44%), slightly yellow oil. – $[\alpha]^{20}_D$ = –50.1 (c = 0.36, CH_2Cl_2). – IR (NaCl): $\tilde{\nu}$ = 3600–3230 cm^{-1} (OH), 1710–1660 (–C=O). – ^1H NMR ($CDCl_3$): δ = 1.07–2.00 (4 m, 8 H, 5-H, 6-H_2, 7-H_2, 8-H_2, 4-H), 1.57 [s, 9 H, OC(CH_3)$_3$], 2.38–2.53 (m, 1 H, 4-H), 4.02–4.36 (m, 1 H, 1-H), 4.57–4.69 (m, 1 H, 3-H), 5.28 (s, 1 H, ArC*H*OH), 6.67 (s, 1 H, ArCHO*H*), 7.42–7.60 (m, 4 H, aromatic H), 7.84 (m, 2 H, aromatic H), 8.47 (d, J = 8.0 Hz, 1 H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 28.50 [OC(CH_3)$_3$], 24.63, 32.29, 34.41, 34.60 (C-4, C-6, C-7, C-8), 41.13 (C-5), 65.91, 66.31 (C-1, C-3), 79.41 (Ar*C*HOH), 80.87 [O*C*(CH_3)$_3$], 124.54, 125.23, 125.38, 125.83, 126.32, 128.29, 128.76 (aromatic C), 131.94, 134.04, 138.16 (quat. aromatic C), 156.22 (R_2NCO_2R). – MS (CI, isobutane); *m/z* (%): 368 (100) [MH^+]. – $C_{23}H_{29}NO_3$ (367.2): calcd. C 75.16, H 7.96, N 3.81; found C 75.22, H 8.04, N 3.76.

(1'S,1R,3S,5R)-(1-tert-Butyloxycarbonyloctahydrocyclopenta-[b]pyrrol-2-yl)-1'-(1-naphthyl)methanol [(α*S*,β*S*)-**10c**]: Reaction: GP3. – Starting material: 3.4 g (14.2 mmol) of (1*R*,3*S*,5*R*)-**3**, Grignard reagent: 1-bromonaphthalene. – Diastereomeric ratio (crude product) 42:58 (reaction temp. –18 °C); diastereomeric ratio (after flash chromatography) ≥ 95:5 (eluent: *n*-hexane/ triethylamine 9:1, TLC: R_f = 0.34). Yield 1.81 g (35%, overall yield: 80%), colourless, viscous oil. – $[\alpha]^{20}_D$ = – 5.5 (c = 4.01, CH_2Cl_2). – IR (NaCl): $\tilde{\nu}$ = 3680–3200 cm^{-1} (OH), 1690–1650 (–C=O). – ^1H NMR ($CDCl_3$): δ = 1.20–1.71 (m, 7 H, 5-H, 6-H_2, 7-H_2, 8-H_2), 1.51 [s, 9 H, OC(CH_3)$_3$], 1.88–2.05 (m, 1 H, 4-H), 2.46–2.60 (m, 1 H, 4-H), 3.98–4.09 (m, 1 H, 1-H), 4.57–4.69 (m, 1 H, 3-H), 5.44 (d, J = 8.4 Hz, 1 H, ArC*H*OH), 5.66 (s, 1 H, ArCHO*H*), 7.40–7.54, 7.55–7.60 (2 m, 4 H, aromatic H), 7.78 (d, J = 7.8 Hz, 1 H, aromatic H), 7.95 (d, J = 7.8 Hz, 1 H, aromatic H), 8.31 (d, J = 8.0 Hz, 1 H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 28.53 [OC(CH_3)$_3$], 24.01, 30.55, 33.16, 33.60 (C-4, C-6, C-7, C-8), 41.59 (C-5), 63.82, 65.94 (C-1, C-3), 77.48 (Ar*C*HOH), 80.51 [O*C*(CH_3)$_3$], 125.38–138.48 (aromatic C), 177.57 (R_2NCO_2R). – MS (CI, isobutane); *m/z* (%): 368 (100) [MH^+]. – $C_{23}H_{29}NO_3$ (367.2): calcd. C 75.16, H 7.96, N 3.81, found C 75.20, H 7.92, N 3.85.

(1'R,1R,3S,5R)-(1-tert-Butyloxycarbonyloctahydrocyclopenta-[b]pyrrol-2-yl)-1'-(1-naphthyl)methanol [(α*R*,β*S*)-**10d**]: Reaction: GP3. – Starting material: 3.4 g (14.2 mmol) of (1*R*,3*S*,5*R*)-**3**, Grignard reagent: 1-bromonaphthalene. – Diastereomeric ratio (crude product) 58:42 (reaction temp. –18 °C); diastereomeric ratio (after flash chromatography) ≥ 95:5 (eluent: *n*-hexane/triethylamine 9:1, TLC: R_f = 0.63). Yield 2.36 g (45%, overall yield, both diastereomers: 80%), colourless, viscous oil. – $[\alpha]^{20}_D$ = –7.0 (c = 0.53, CH_2Cl_2). – IR (NaCl): $\tilde{\nu}$ = 3610–3100 cm^{-1} (OH), 1690–1660 (–C=O). – ^1H NMR ($CDCl_3$): δ (rotamers) = 1.11–2.09 (4 m, 8 H, 5-H, 6-H_2, 7-H_2, 8-H_2, 4-H), 1.56 [s, 6 H, 0.67 × OC(CH_3)$_3$], 1.66 [s, 3 H, 0.33 × OC(CH_3)$_3$], 2.54–2.72 (m, 1 H, 4-H), 2.96 (s, 0.33 H, 0.33 × ArCHO*H*), 3.20 (s, 0.67 H, 0.67 × ArCHO*H*), 4.00–4.11, 4.39–4.40, 4.40–4.51 (3 m, 2 H, 1-H, 3-H), 5.93 (s, 0.33 H, 0.33 × ArC*H*OH), 6.09 (s, 0.67 H, 0.67 × ArC*H*OH), 7.40–7.61 (m, 3 H, aromatic H), 7.71–7.90 (m, 3 H, aromatic H), 8.23 (d, J = 7.8 Hz, 0.31 H, aromatic H), 8.46 (d,

J = 8.0 Hz, 0.69 H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ (rotamers) = major rotamer: 28.62 [OC(CH_3)$_3$], 23.97, 30.82, 31.75, 34.12 (C-4, C-6, C-7, C-8), 42.32 (C-5), 63.92, 64.75 (C-1, C-3), 70.43 (Ar*C*HOH), 79.36 [O*C*(CH_3)$_3$], 123.43–137.88 (aromatic C), 155.29 (R_2NCO_2R); minor rotamer: 28.85 [OC(CH_3)$_3$], 23.93, 31.54, 31.96, 33.03 (C-4, C-6, C-7, C-8), 41.76 (C-5), 62.99, 65.39 (C-1, C-3), 71.43 (Ar*C*HOH), 80.51 [O*C*(CH_3)$_3$], 123.43–137.88 (aromatic C), 154.34 (R_2NCO_2R). – MS (CI, isobutane); *m/z* (%): 368 (100) [MH^+]. – $C_{23}H_{29}NO_3$ (367.2): calcd. C 75.16, H 7.96, N 3.81; found C 75.09, H 7.87, N 3.77.

(1'R,1R,3R,5R)-(Octahydrocyclopenta[b]pyrrol-2-yl)-1'-phenylmethanol [(α*R*,β*R*)-**11a**]: Reaction: GP4, method A or C. – Starting material: 0.19 g (0.6 mmol) of (α*R*,β*R*)-**4a**. Yield 0.11 g (84%), colourless solid, m.p. 38–43 °C. – $[\alpha]^{20}_D$ = – 26.6 (*c* = 0.49, CH_2Cl_2). – IR (KBr): $\tilde{\nu}$ = 3600–3210 cm^{-1} (OH, NH). – ^{1}H NMR ($CDCl_3$): δ = 0.74–1.00, 1.00–1.94 (3 m, 9 H, 5-H, 6-H_2, 7-H_2, 8-H_2, NH, 4-H), 2.41–2.62 (m, 1 H, 4-H), 3.12–3.31 (m, 1 H, 1-H), 3.40 (s, 1 H, PhCHO*H*), 3.55–3.74 (m, 1 H, 3-H), 4.51 (d, *J* = 4.0 Hz, 1 H, PhC*H*OH), 7.14–7.46 (m, 5 H, aromatic H).- ^{13}C NMR ($CDCl_3$): δ = 23.71, 32.93, 34.78, 36.26 (C-4, C-6, C-7, C-8), 42.11 (C-5), 62.53, 65.96 (C-1, C-3), 74.46 (Ph*C*HOH), 125.72, 127.06, 128.15 (aromatic C), 144.04 (quat. aromatic C). – MS (CI, isobutane); *m/z* (%): 218 (100) [MH^+], 200 (17) [MH^+ – H_2O], 107 (46) [$C_7H_7O^+$]. – $C_{14}H_{19}NO$ (217.2): calcd. C 77.37, H 8.82, N 6.45; found C 77.44, H 8.94, N 6.33.

(1'S,1R,3R,5R)-(Octahydrocyclopenta[b]pyrrol-2-yl)-1'-phenylmethanol [(α*S*,β*R*)-**11b**]: Reaction: GP4, method A or C. – Starting material: 0.2 (0.62 mmol) of (α*S*,β*R*)-**4b**. Yield 0.13 g (96%), colourless solid, m.p. 71–74 °C. – $[\alpha]^{20}_D$ = + 97.7 (*c* = 0.51, CH_2Cl_2). – IR (KBr): $\tilde{\nu}$ = 3550–3140 cm^{-1} (OH, NH), 3090 cm^{-1}, (=C-H). – ^{1}H NMR ($CDCl_3$): δ = 1.20–1.34, 1.34–1.93 (2 m, 9 H, 5-H, 6-H_2, 7-H_2, 8-H_2, NH, 4-H), 2.37–2.56 (m, 1 H, 4-H), 3.06 (s, 1 H, PhCHO*H*), 3.22–3.38 (m, 1 H, 1-H), 3.61–3.73 (m, 1 H, 3-H), 4.74 (d, *J* = 3.7 Hz, 1 H, PhC*H*OH), 7.17–7.40 (m, 5 H, aromatic H).- ^{13}C NMR ($CDCl_3$): δ = 23.63, 31.99, 33.03, 34.89 (C-4, C-6, C-7, C-8), 41.79 (C-5), 62.61, 65.19 (C-1, C-3), 72.41 (Ph*C*HOH), 125.55, 126.91, 128.03 (aromatic C), 142.17 (quat. aromatic C). – MS (CI, isobutane); *m/z* (%): 218 (100) [MH^+], 107 (40) [$C_7H_7O^+$]. – $C_{14}H_{19}NO$ (217.2): calcd. C 77.37, H 8.82, N 6.45; found C 77.43, H 8.86, N 6.38.

(1'S,1R,3S,5R)-(Octahydrocyclopenta[b]pyrrol-2-yl)-1'-phenylmethanol [(α*S*,β*S*)-**11c**]: Reaction: GP4, method B. – Starting material: 0.5 g (1.57 mmol) of (α*S*,β*S*)-**4c**. Yield 0.30 g (88%), colourless solid, m.p. 54 °C. – $[\alpha]^{20}_D$ = + 37.7 (*c* = 0.43, CH_2Cl_2). – IR (KBr): $\tilde{\nu}$ = 3670–3140 cm^{-1} (OH, NH). – ^{1}H NMR ($CDCl_3$): δ = 1.14–1.89 (3 m, 9 H, 5-H, 6-H_2, 7-H_2, 8-H_2, NH, 4-H), 2.46–2.64 (m, 1 H, 4-H), 3.03 (s, 1 H, PhCHO*H*), 3.24–3.36 (m, 1 H, 1-H), 3.61–3.80 (m, 1 H, 3-H), 4.25 (d, *J* = 7.2 Hz, 1 H, PhC*H*OH), 7.14–7.35 (m, 5 H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 25.12, 33.54, 35.58, 36.21 (C-4, C-6, C-7, C-8), 42.88 (C-5), 62.93, 65.38 (C-1, C-3), 74.55 (Ph*C*HOH), 126.43, 127.35, 128.24 (aromatic C), 143.23 (quat. aromatic C). – MS (CI, isobutane); *m/z* (%): 218 (100) [MH^+], 200 (12) [MH^+ – H_2O], 107 (64) [$C_7H_7O^+$]. – $C_{14}H_{19}NO$ (217.2): calcd. C 77.37, H 8.82, N 6.45; found C 77.1, H 8.64, N 6.38.

(1'R,1R,3S,5R)-(Octahydrocyclopenta[b]pyrrol-2-yl)-1'-phenylmethanol [(α*R*,β*S*)-**11d**[1h]]: Reaction: GP4, method B. – Starting material: 0.6 g (1.89 mmol) of (α*R*,β*S*)-**4d**. Yield 0.34 g (83%), almost colourless solid, m.p. 118 °C. – $[\alpha]^{20}_D$ = – 33.7 (*c* = 0.41, CH_2Cl_2). – IR (KBr): $\tilde{\nu}$ = 3670–3210 cm^{-1} (OH, NH). – ^{1}H NMR ($CDCl_3$): δ = 1.03–1.91 (4 m, 9 H, 5-H, 6-H_2, 7-H_2, 8-H_2, NH, 4-H), 2.37–2.58 (m, 1 H, 4-H), 3.29–3.43 (m, 1 H, 1-H), 3.62–3.77 (m, 1 H, 3-H), 3.98 (s, 1 H, PhCHO*H*), 4.69 (d, *J* = 4.4 Hz, 1 H, PhC*H*OH), 7.11–7.33 (m, 5 H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 25.83, 32.61, 33.60, 35.62 (C-4, C-6, C-7, C-8), 42.11 (C-5), 63.20, 63.53 (C-1, C-3), 72.48 (Ph*C*HOH), 125.79, 127.14, 128.15 (aromatic C), 142.32 (quat. aromatic C). – MS (CI, isobutane); *m/z* (%): 218 (100) [MH^+], 200 (12) [MH^+ – H_2O], 107 (40) [$C_7H_7O^+$]. – $C_{14}H_{19}NO$ (217.2): calcd. C 77.37, H 8.82, N 6.45; found C 77.4, H 8.89, N 6.43.

(1'R,1R,3R,5R)-(Octahydrocyclopenta[b]pyrrol-2-yl)-1'-(4-methyl-phenyl)methanol [(α*R*,β*R*)-**12a**]: Reaction: GP4, method C. – Starting material: 1.7 g (5.0 mmol) of (α*R*,β*R*)-**5a**. Yield 0.91 g (79%), colourless solid, m.p. 74 °C. – $[\alpha]^{20}_D$ = – 50.9 (*c* = 0.34, CH_2Cl_2). – IR (KBr): $\tilde{\nu}$ = 3690–3220 cm^{-1} (OH, NH). – ^{1}H NMR ($CDCl_3$): δ = 1.16–1.97 (4 m, 9 H, 5-H, 6-H_2, 7-H_2, 8-H_2, NH, 4-H), 2.34 (s, 3 H, ArCH_3), 2.44–2.62 (m, 1 H, 4-H), 3.03 (s, 1 H, ArCHO*H*), 3.16–3.32 (m, 1 H, 1-H), 3.54–3.60 (m, 1 H, 3-H), 4.50 (d, *J* = 4.1 Hz, 1 H, Ar*C*HOH), 7.01–7.31 (m, 4 H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 21.07 (ArCH_3), 23.72, 33.03, 35.01, 36.27 (C-4, C-6, C-7, C-8), 42.10 (C-5), 62.49, 65.90 (C-1, C-3), 74.23 (Ar*C*HOH), 125.61, 128.89 (aromatic C), 136.66, 141.19 (quat. aromatic C). – MS (CI, isobutane); *m/z* (%): 232 (100) [MH^+], 214 (12) [MH^+ – H_2O], 121 (57) [$C_8H_9O^+$]. – $C_{15}H_{21}NO$ (231.2): calcd. C 77.87, H 9.16, N 6.06; found C 77.65, H 9.12, N 6.10.

(1'R,1R,3R,5R)-(1-Methyloctahydrocyclopenta[b]pyrrol-2-yl)-1'-(4-methyl-phenyl)methanol [(α*R*,β*R*)-*N*-methyl-**12a**]: To a suspension of 1.1 g (29.4 mmol) lithium aluminiumhydride in 70 ml THF – stirred for 1 h under reflux then cooled down to room temp. – 3.0 mmol of the *N-tert*-butoxycarbonyl derivative (α*R*,β*R*)-**5a** (dissolved in 10 ml of THF) were added dropwise within 30 min at room temp. under argon atmosphere. Then the reaction mixture was heated under reflux for 18 h. The heating bath was removed and 5% aqueous KOH was added cautiously at room temp. to destroy the excess reducing reagent. After two additional hours under reflux, the resulting white suspension was filtered, the solids intensively washed with additional solvent and the combined organic phases were concentrated in vacuo after drying with $MgSO_4$ to afford a slightly yellow oil as crude product. Further purification of the crude product was accomplished by flash chromatography. – Starting material: 1.0 g (3.0 mmol) of (α*R*,β*R*)-**5a**. – Work-up: purification by flash chromatography (silica gel 60, eluent: *n*-hexane/EtOAc 2:8, addition of 40 ml triethylamine per liter of the solvent mixture; TLC: R_f = 0.40). Yield 0.57 g (77%), colourless oil. – $[\alpha]^{20}_D$ = – 22.9 (*c* = 0.88, CH_2Cl_2). – IR (NaCl): $\tilde{\nu}$ = 3600–3210 cm^{-1} (OH). – ^{1}H NMR ($CDCl_3$): δ = 1.17–1.68 (m, 7 H, 5-H, 6-H_2, 7-H_2, 8-H_2), 1.94 (s, 3 H, ArCH_3), 2.03–2.14 (m, 1 H, 4-H), 2.27 (s, 3 H, NCH_3), 2.33–2.46 (m, 1 H, 4-H), 2.72–2.90 (m, 2 H, 1-H, 3-H), 3.86 (s, br., 1 H, ArCHO*H*), 4.49 (s, 1 H, Ar*C*HOH), 7.07 (d, *J* = 7.7 Hz, 2 H, aromat.-H), 7.23 (d, *J* = 8.2 Hz, 2 H, aromat.-H). – ^{13}C NMR ($CDCl_3$): δ = 21.02 (ArCH_3), 24.08, 32.98, 33.48, 37.98 (C-4, C-6, C-7, C-8), 39.73 (C-5), 41.59 (NCH_3), 72.17, 72.33 (C-1, C-3), 74.09 (Ar*C*HOH), 125.15, 128.72 (aromat.-C), 135.97, 141.95 (quat. aromat.-C). – MS (CI, isobutane); 246 (100) [MH^+], 121 (23) [$C_8H_9O^+$]. – $C_{16}H_{23}NO$ (245.2): calcd. C 78.31, H 9.45, N 5.71; found: C 78.22, H 9.38, N 5.73.

(1'S,1R,3R,5R)-(Octahydrocyclopenta[b]pyrrol-2-yl)-1'-(4-methyl-phenyl)methanol [(α*S*,β*R*)-**12b**]: Reaction: GP4, method C. – Starting material: 0.75 g (2.26 mmol) of (α*S*,β*R*)-**5b**. Yield 0.49 g (94%), colourless solid, m.p. 106 °C. – $[\alpha]^{20}_D$ = + 96.8 (*c* = 0.50, CH_2Cl_2). – IR (KBr): $\tilde{\nu}$ = 3600–3100 cm^{-1} (OH, NH). – ^{1}H NMR ($CDCl_3$): δ = 1.20–1.81 (m, 9 H, 5-H, 6-H_2, 7-H_2, 8-

H_2, NH, 4-H), 2.34 (s, 3 H, $ArCH_3$), 2.39–2.54 (m, 1 H, 4-H), 3.00 (s, 1 H, ArCHO*H*), 3.20–3.34 (m, 1 H, 1-H), 3.63–3.76 (m, 1 H, 3-H), 4.72 (d, J = 3.8 Hz, 1 H, ArC*H*OH), 7.11 (d, J = 8.2 Hz, 2 H, aromatic H), 7.23 (d, J = 7.9 Hz, 2 H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 21.08 ($ArCH_3$), 23.61, 32.09, 33.04, 34.86 (C-4, C-6, C-7, C-8), 41.79 (C-5), 62.59, 65.24 (C-1, C-3), 72.35 (Ar*C*HOH), 125.50, 128.73 (aromatic C), 136.47, 139.19 (quat. aromatic C). – MS (CI, isobutane); *m/z* (%): 232 (100) [MH^+], 121 (61) [$C_8H_9O^+$]. – $C_{15}H_{21}NO$ (231.2): calcd. C 77.87, H 9.16, N 6.06.; found C 77.90, H 9.18, N 6.00.

(1′S,1R,3S,5R)-(Octahydrocyclopenta[b]pyrrol-2-yl)-1′-(4-methyl-phenyl)methanol [(α*S*,β*S*)-**12c**]: Reaction: GP4, method C. – Starting material: 1.1 g (3.3 mmol), (α*S*,β*S*)-**5c**. Yield 0.67 g (88%), colourless solid, m.p. 86 °C. – $[\alpha]^{20}_D$ = + 33.8 (c = 0.50, CH_2Cl_2). – IR (KBr): $\tilde{\nu}$ = 3600–3100 cm^{-1} (OH, NH). – ^1H NMR ($CDCl_3$): δ = 1.23–1.88 (3 m, 9 H, 5-H, 6-H_2, 7-H_2, 8-H_2, NH, 4-H), 2.34 (s, 3 H, $ArCH_3$), 2.54–2.69 (m, 1 H, 4-H), 3.08 (s, 1 H, ArCHO*H*), 3.31–3.43 (m, 1 H, 1-H), 3.71–3.82 (m, 1 H, 3-H), 4.28 (d, J = 6.9 Hz, 1 H, ArC*H*OH), 7.14 (d, J = 7.7 Hz, 2 H, aromatic H), 7.21 (d, J = 7.8 Hz, 2 H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 21.08 ($ArCH_3$), 25.07, 33.51, 35.41, 36.18 (C-4, C-6, C-7, C-8), 42.88 (C-5), 62.96, 65.44 (C-1, C-3), 74.34 (Ar*C*HOH), 126.36, 128.92 (aromatic C), 136.98, 140.10 (quat. aromatic C). – MS (CI, isobutane); *m/z* (%): 232 (100) [MH^+], 214 (8) [$MH^+ - H_2O$], 121 (54) [$C_8H_9O^+$]. – $C_{15}H_{21}NO$ (231.2): calcd. C 77.87, H 9.16, N 6.06; found C 77.66, H 9.21, N 6.01.

(1′R,1R,3S,5R)-(Octahydrocyclopenta[b]pyrrol-2-yl)-1′-(4-methyl-phenyl)methanol [(α*R*,β*S*)-**12d**[11h]]: Reaction: GP4, method C. – Starting material: 0.8 g (2.4 mmol) of (α*R*,β*S*)-**5d**. Yield 0.43 g (78%), colourless solid, m.p. 128 °C. – $[\alpha]^{20}_D$ = – 44.1 (c = 0.61, CH_2Cl_2). – IR (KBr): $\tilde{\nu}$ = 3610–3100 cm^{-1} (OH). – ^1H NMR ($CDCl_3$): δ = 1.12–1.94 (3 m, 9 H, 5-H, 6-H_2, 7-H_2, 8-H_2, NH, 4-H), 2.33 (s, 3 H, $ArCH_3$), 2.44–2.57 (m, 1 H, 4-H), 3.08 (s, 1 H, ArCHO*H*), 3.30–3.43 (m, 1 H, 1-H), 3.66–3.81 (m, 1 H, 3-H), 4.64 (d, J = 4.9 Hz, 1 H, ArC*H*OH), 7.06 (d, J = 7.9 Hz, 2 H, aromatic H), 7.29 (d, J = 7.7 Hz, 2 H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 21.08 ($ArCH_3$), 25.85, 33.19, 33.71, 36.28 (C-4, C-6, C-7, C-8), 42.16 (C-5), 63.10, 63.54 (C-1, C-3), 73.17 (Ar*C*HOH), 125.82, 128.83 (aromatic C), 136.67, 139.61 (quat. aromatic C). – MS (CI, isobutane); *m/z* (%): 232 (100) [MH^+], 214 (22) [$MH^+ - H_2O$], 121 (58) [$C_8H_9O^+$]. – $C_{15}H_{21}NO$ (231.2): calcd. C 77.87, H 9.16, N 6.06; found C 77.76, H 9.19, N 6.11.

(1′R,1R,3R,5R)-(Octahydrocyclopenta[b]pyrrol-2-yl)-1′-(3-methoxy-phenyl)methanol [(α*R*,β*R*)-**13a**]: Reaction: GP4, method C. – Starting material: 1.02 g (2.94 mmol) of (α*R*,β*R*)-**6a**. Yield 0.62 g (95%), colourless oil. – $[\alpha]^{20}_D$ = –25.9 (c = 0.88, CH_2Cl_2). – IR (KBr): $\tilde{\nu}$ = 3318 cm^{-1} (OH, NH). – ^1H NMR ($CDCl_3$): δ = 1.19–2.05 (m, 9 H, 5-H, 6-H_2, 7-H_2, 8-H_2, NH, 4-H), 2.44–2.62 (m, 1 H, 4-H), 2.97 (s, 1 H, ArCHO*H*), 3.20–3.32 (m, 1 H, 1-H), 3.58–3.60 (m, 1 H, 3-H), 3.80 (s, 3 H, $ArOCH_3$), 4.47 (d, J = 4.0 Hz, 1 H, ArC*H*OH), 6.74–7.28 (m, 4 H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 23.72, 33.03, 35.01, 36.27 (C-4, C-6, C-7, C-8), 42.10 (C-5), 55.12 ($ArOCH_3$), 62.44, 65.70 (C-1, C-3), 73.94 (Ar*C*HOH), 111.21, 112.49, 117.95, 123.43 (aromatic C), 146.19, 159.63 (quat. aromatic C). – MS (CI, isobutane); *m/z* (%): 248 (13) [MH^+], 247 (53), 110 (100). – $C_{15}H_{21}NO_2$ (247.2): calcd. C 72.87, H 8.50, N 5.67; found C 72.35, H 8.85, N 5.57.

(1′S,1R,3R,5R)-(Octahydrocyclopenta[b]pyrrol-2-yl)-1′-(3-methoxy-phenyl)methanol [(α*S*,β*R*)-**13b**]: Reaction: GP4, method C. – Starting material: 0.72 g (2.09 mmol) of (α*S*,β*R*)-**6b**. Yield 0.27 g (52%). – $[\alpha]^{20}_D$ = + 92.5 (c = 0.24, CH_2Cl_2). – IR (KBr): $\tilde{\nu}$ = 3289 cm^{-1} (OH, NH). – ^1H NMR ($CDCl_3$): δ = 1.20–1.80 (m, 9 H, 5-H, 6-H_2, 7-H_2, 8-H_2, NH, 4-H), 2.36–2.54 (m, 1 H, 4-H), 3.01 (s, 1 H, ArCHO*H*), 3.23–3.34 (m, 1 H, 1-H), 3.65–3.74 (m, 1 H, 3-H), 3.80 (s, 3 H, $ArOCH_3$), 4.69 (d, J = 3.8 Hz, 1 H, ArC*H*OH), 6.71–7.27 (m, 4 H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 23.70, 32.08, 33.12, 34.94 (C-4, C-6, C-7, C-8), 41.83 (C-5), 55.16 ($ArOCH_3$), 62.73, 65.23 (C-1, C-3), 72.34 (Ar*C*HOH), 111.15, 112.54, 117.99, 129.03 (aromatic C), 144.04, 159.63 (quat. aromatic C). – MS (CI, isobutane); *m/z* (%): 248 (13) [MH^+], 247 (53), 110 (100). – $C_{15}H_{21}NO_2$ (247.2): calcd. C 72.87, H 8.50, N 5.67; found C 72.38, H 8.71, N 5.56.

(1′S,1R,3R,5R)-(Octahydrocyclopenta[b]pyrrol-2-yl)-1′-(2-methyl-phenyl)methanol [(α*S*,β*R*)-**14b**]: Reaction: GP4, method B. – Starting material: 1.8 g (5.4 mmol) of (α*S*,β*R*)-**7b**. Yield 1.18 g (94%), colourless solid, m.p. 58–69 °C. – $[\alpha]^{20}_D$ = – 51.0 (c = 0.63, CH_2Cl_2). – IR (KBr): $\tilde{\nu}$ = 3600–3210 cm^{-1} (OH, NH). – ^1H NMR ($CDCl_3$): δ = 1.29–2.08 (3 m, 9 H, 5-H, 6-H_2, 7-H_2, 8-H_2, NH, 4-H), 2.33 (s, 3 H, $ArCH_3$), 2.48–2.69 (m, 1 H, 4-H), 3.27–3.45 (m, 1 H, 1-H), 3.60–3.77 (m, 1 H, 3-H), 4.74–5.06 (s, 1 H, ArCHO*H*), 4.89 (d, J = 4.2 Hz, 1 H, ArC*H*OH), 7.07–7.31 (m, 3 H, aromatic H), 7.37–7.51 (m, 1 H, aromatic C).–^{13}C NMR ($CDCl_3$): δ = 19.14 ($ArCH_3$), 23.70, 24.59, 32.78, 34.16 (C-4, C-6, C-7, C-8), 42.10 (C-5), 62.41, 64.53 (C-1, C-3), 76.62 (Ar*C*HOH), 125.23, 126.07, 126.99, 130.36 (aromatic C), 134.44, 141.69 (quat. aromatic C). – MS (CI, isobutane); *m/z* (%): 232 (100) [MH^+], 121 (34) [$C_8H_9O^+$]. – $C_{15}H_{21}NO$ (231.2): calcd. C 77.87, H 9.16, N 6.06; found C 77.63, H 9.10, N 5.98.

(1′S,1R,3R,5R)-(Octahydrocyclopenta[b]pyrrol-2-yl)-1′-(2,5-dimethyl-phenyl)methanol [(α*S*,β*R*)-**15b**]: Reaction: GP4, method A. – Starting material: 1.15 g (3.3 mmol) of (α*S*,β*R*)-**8b**. Yield 0.78 g (96%), colourless solid, m.p. 99 °C. – $[\alpha]^{20}_D$ = –54.1 (c = 0.48, CH_2Cl_2). – IR (KBr): $\tilde{\nu}$ = 3610–3220 cm^{-1} (OH, NH). – ^1H NMR ($CDCl_3$): δ = 1.31–1.86, 1.92–2.11 (4 m, 9 H, 5-H, 6-H_2, 7-H_2, 8-H_2, NH, 4-H), 2.26 (s, 3 H, $ArCH_3$), 2.34 (s, 3 H, $ArCH_3$), 2.49–2.66 (m, 1 H, 4-H), 3.18–3.33 (m, 1 H, 1-H), 3.57–3.71 (m, 1 H, 3-H), 4.73 (d, J = 2.3 Hz, 1 H, ArC*H*OH), 6.91–7.09 (m, 2 H, aromat.-H), 7.20–7.31 (s, 1 H, aromatic H).–^{13}C NMR ($CDCl_3$): δ = 18.57, 21.16 (2 × $ArCH_3$), 23.71, 33.03, 35.21, 36.21 (C-4, C-6, C-7, C-8), 41.99 (C-5), 62.24, 63.84 (C-1, C-3), 69.66 (Ar*C*HOH), 125.57, 127.39, 130.23 (aromatic C), 130.87, 135.33, 142.27 (quat. aromatic C). – MS (CI, isobutane); *m/z* (%): 246 (100) [MH^+]. – $C_{16}H_{23}NO$ (245.2): calcd. C 78.31, H 9.45, N 5.71; found C 78.16, H 9.37, N 5.67.

(1′S,1R,3S,5R)-(Octahydrocyclopenta[b]pyrrol-2-yl)-1′-(2,5-dimethyl-phenyl)methanol [(α*S*,β*S*)-**15c**]: Reaction: GP4, method C. – Starting material: 1.15 g (3.3 mmol) of (α*S*,β*S*)-**8c**. Yield 0.71 g (88%), almost colourless oil. – $[\alpha]^{20}_D$ = + 9.4 (c = 0.33, CH_2Cl_2). – IR (NaCl): $\tilde{\nu}$ = 3690–3220 cm^{-1} (OH, NH). – ^1H NMR ($CDCl_3$): δ = 1.25–1.89 (4 m, 9 H, 5-H, 6-H_2, 7-H_2, 8-H_2, NH, 4-H), 2.31 (s, 3 H, $ArCH_3$), 2.34 (s, 3 H, $ArCH_3$), 2.54–2.71 (m, 1 H, 4-H), 3.26 (s, 1 H, ArCHO*H*), 3.40–3.51 (m, 1 H, 1-H), 3.78–3.87 (m, 1 H, 3-H), 4.62 (d, J = 6.6 Hz, 1 H, ArC*H*OH), 6.94–7.06 (m, 2 H, aromatic H), 7.21 (s, 1 H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 18.91, 21.06 (2 × $ArCH_3$), 25.18, 33.54, 35.61, 36.15 (C-4, C-6, C-7, C-8), 42.94 (C-5), 62.90, 64.34 (C-1, C-3), 69.92 (Ar*C*HOH), 126.51, 127.69, 130.14 (aromatic C), 131.67, 135.39, 141.08 (quat. aromatic C). – MS (CI, isobutane); *m/z* (%): 246 (100) [MH^+], 135 (34) [$C_9H_{11}O^+$]. – $C_{16}H_{23}NO$ (245.2): calcd. C 78.31, H 9.45, N 5.71; found C 78.11, H 9.33, N 5.69.

(1′R,1R,3S,5R)-(Octahydrocyclopenta[b]pyrrol-2-yl)-1′-(2,5-dimethyl-phenyl)methanol [(α*R*,β*S*)-**15d**]: Reaction: GP4, method

C. – Starting material: 0.8 g (2.3 mmol) of (αR,βS)-**8d**. Yield 0.47 g (83%), colourless soild, m.p. 118 °C. – $[\alpha]^{20}_D$ = – 30.2 (*c* = 0.22, CH_2Cl_2). – IR (KBr): $\tilde{\nu}$ = 3700–3210 cm^{-1} (OH, NH). – ^1H NMR ($CDCl_3$): δ = 1.08–1.29, 1.34–2.02 (3 m, 9 H, 5-H, 6-H_2, 7-H_2, 8-H_2, NH, 4-H), 2.28 (s, 3 H, $ArCH_3$), 2.31 (s, 3 H, $ArCH_3$), 2.49–2.62 (m, 1 H, 4-H), 2.91 (s, 1 H, ArCHO*H*), 3.40–3.51 (m, 1 H, 1-H), 3.73–3.82 (m, 1 H, 3-H), 4.94 (d, *J* = 4.9 Hz, 1 H, ArC*H*OH), 6.91–7.06 (m, 2 H, aromatic H), 7.31 (s, 1 H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 18.72, 21.13 (2 × $ArCH_3$), 25.89, 32.69, 33.67, 36.53 (C-4, C-6, C-7, C-8), 42.25 (C-5), 61.16, 63.21 (C-1, C-3), 69.67 (Ar*C*HOH), 126.41, 127.54, 129.99 (aromatic C), 131.19, 135.26, 139.91 (quat. aromatic C). – MS (CI, isobutane); *m/z* (%): 246 (100) [MH^+], 135 (39) [$C_9H_{11}O^+$]. – $C_{16}H_{23}NO$ (245.2): calcd. C 78.31, H 9.45, N 5.71; found C 78.42, H 9.49, N 5.67.

(1'S,1R,3R,5R)-(Octahydrocyclopenta[b]pyrrol-2-yl)-1'-(2,4,6-trimethyl-phenyl)methanol [(αS,β*R*)-**16b**]: Reaction: GP4, method B. – Starting material: 1.7 g (4.7 mmol) of (αS,β*R*)-**9b**. Yield 0.8 g (66%), colourless solid, m.p. 115–119 °C. – $[\alpha]^{20}_D$ = + 5.2 (*c* = 0.27, CH_2Cl_2). – IR (KBr): $\tilde{\nu}$ = 3680–3140 cm^{-1} (OH, NH). – ^1H NMR ($CDCl_3$): δ = 0.94–1.11, 1.34–1.78 (3 m, 9 H, 5-H, 6-H_2, 7-H_2, 8-H_2, NH, 4-H), 2.26 (s, 3 H, $ArCH_3$), 2.45 (s, 6 H, 2 × $ArCH_3$), 2.37–2.54 (m, 1 H, H-4), 3.04 (s, 1 H, ArCHO*H*), 3.44–3.61 (m, 1 H, 1-H), 3.61–3.73 (m, 1 H, 3-H), 4.93 (d, *J* = 7.6 Hz, 1 H, ArC*H*OH), 7.07–7.31 (m, 1 H, aromatic H), 7.37–7.51 (m, 1 H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 20.72 ($ArCH_3$), 21.33 (2 × $ArCH_3$), 23.70, 32.87, 34.87, 36.58 (C-4, C-6, C-7, C-8), 42.35 (C-5), 62.65, 64.04 (C-1, C-3), 74.15 (Ar*C*HOH), 130.10 (aromatic C), 135.64, 136.23, 136.61 (quat. aromatic C). – MS (CI, isobutane); *m/z* (%): 260 (100) [MH^+]. – $C_{17}H_{25}NO$ (259.2): calcd. C 78.71, H 9.72, N 5.40; found C 78.83, H 9.76, N 5.37.

(1'S,1R,3R,5R)-(Octahydrocyclopenta[b]pyrrol-2-yl)-1'-naphthylmethanol [(αS,β*R*)-**17b**]: Reaction: GP4, method A. – Starting material: 1.7 g (4.7 mmol) of (αS,β*R*)-**10b**. Yield 0.9 g (72%), colourless solid, m.p. 84 °C. – $[\alpha]^{20}_D$ = – 109.6 (*c* = 0.50, CH_2Cl_2). – IR (KBr): $\tilde{\nu}$ = 3600–3140 cm^{-1} (OH, NH). – ^1H NMR ($CDCl_3$): δ = 1.34–1.89 (2 m, 8 H, 5-H, 6-H_2, 7-H_2, 8-H_2, NH), 2.05–2.21 (m, 1 H, 4-H), 2.47–2.66 (m, 1 H, 4-H), 3.31 (s, 1 H, ArCHO*H*), 3.47–3.68 (2 m, 2 H, 1-H, 3-H), 5.38 (d, *J* = 2.2 Hz, 1 H, ArC*H*OH), 7.19–8.02 (5 m, 7 H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 23.72, 32.98, 35.06, 36.08 (C-4, C-6, C-7, C-8), 42.05 (C-5), 62.18, 64.03 (C-1, C-3), 69.38 (Ar*C*HOH), 122.35, 122.79, 125.36, 125.40, 125.77, 127.44, 128.86 (aromatic C), 130.13, 133.76, 139.95 (quat. aromatic C). – MS (CI, isobutane); *m/z* (%): 268 (100) [MH^+]. – $C_{18}H_{21}NO$ (267.2): calcd. C 80.85, H 7.92, N 5.24; found C 80.78, H 7.87, N 5.20.

(1'S,1R,3S,5R)-(Octahydrocyclopenta[b]pyrrol-2-yl)-1'-(1-naphthyl)methanol [(αS,βS)-**17c**]: Reaction: GP4, method C. – Starting material: 1.5 g (4.1 mmol) of (αS,βS)-**10c**. Yield 1.05 g (96%), slightly yellow oil. – $[\alpha]^{20}_D$ = + 81.1 (*c* = 0.74, CH_2Cl_2). – IR (NaCl): $\tilde{\nu}$ = 3640–3220 cm^{-1} (OH, NH). – ^1H NMR ($CDCl_3$): δ = 1.20–1.34, 1.37–1.98 (3 m, 9 H, 5-H, 6-H_2, 7-H_2, 8-H_2, NH, 4-H), 2.57–2.71 (m, 1 H, 4-H), 3.66–3.77 (m, 1 H, 1-H), 3.83–3.92 (m, 1 H, 3-H), 3.94 (s, 1 H, ArCHO*H*), 5.25 (d, *J* = 6.1 Hz, 1 H, ArC*H*OH), 7.42–7.54 (2 m, 3 H, aromatic H), 7.61 (d, *J* = 7.7 Hz, 1 H, aromatic H), 7.77 (d, *J* = 8.2 Hz, 1 H, aromatic H), 7.83–7.91 (m, 1 H, aromatic H), 8.12 (d, *J* = 8.8 Hz, 1 H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 25.33, 33.47, 35.41, 36.21 (C-4, C-6, C-7, C-8), 42.81 (C3a), 63.01, 64.03 (C6a, C2), 70.36 (Ar*C*HOH), 123.26, 123.66, 125.35, 125.39, 125.86, 127.80, 128.78 (aromat.-C), 130.77, 133.75, 138.94 (quat. aromat.-C). – MS (CI, isobutane); *m/z* (%): 268 (100) [MH^+]. – $C_{18}H_{21}NO$ (267.2): calcd. C 80.85, H 7.92, N 5.24; found C 80.78, H 7.89, N 5.20.

(1'R,1R,3S,5R)-(Octahydrocyclopenta[b]pyrrol-2-yl)-1'-(1-naphthyl)methanol [(αR,βS)-**17d**[11h]]: Reaction: GP4, method C. – Starting material: 0.87 g (2.4 mmol) of (αR,βS)-**10d**. Yield 0.51 g (79%), colourless solid, m.p. 124–130 °C. – $[\alpha]^{20}_D$ = – 133.3 (*c* = 0.29, CH_2Cl_2). – IR (KBr): $\tilde{\nu}$ = 3690–3210 cm^{-1} (OH, NH). – ^1H NMR ($CDCl_3$): δ = 0.89–0.98, 1.00–1.14, 1.32–2.00 (3 m, 9 H, 5-H, 6-H_2, 7-H_2, 8-H_2, NH, 4-H), 2.46–2.59 (m, 1 H, 4-H), 3.21 (s, 1 H, ArCHO*H*), 3.66–3.75, 3.77–3.86 (2 m, 2 H, 1-H, 3-H), 5.58 (d, *J* = 3.9 Hz, 1 H, ArC*H*OH), 7.34–7.53 (2 m, 3 H, aromatic H), 7.76 (d, *J* = 7.7 Hz, 2 H, aromatic H), 7.76 (d, *J* = 8.2 Hz, 1 H, aromatic H), 7.76 (d, *J* = 8.8 Hz, 1 H, aromatic H). – ^{13}C NMR ($CDCl_3$): δ = 25.94, 32.73, 33.65, 36.54 (C-4, C-6, C-7, C-8), 42.29 (C-5), 61.66, 63.51 (C-1, C-3), 69.31 (Ar*C*HOH), 122.86, 123.16, 125.26, 125.49, 125.81, 127.48, 128.83 (aromatic C), 130.32, 133.56, 137.89 (quat. aromatic C). – MS (CI, isobutane); *m/z* (%): 268 (100) [MH^+]. – $C_{18}H_{21}NO$ (267.2): calcd. C 80.85, H 7.92, N 5.24; found C 80.76, H 7.91, N 5.12.

Reaction 1. – General Procedure for the Reduction of Acetophenone (GP5): The reactions were run under argon atmosphere in oven-dried three-necked, round-bottomed reaction flasks each equipped with a magnetic stirrer, a pressure equalizing dropping funnel and a thermometer. To the reaction flask containing a solution of the respective catalyst (0.5 mmol, 5 mol% or 0.8 mmol, 8 mol%) in 10 ml of anhyd. THF was added at –40 °C a BH_3·THF solution (11 ml, 1.0 M in THF, 11 mmol). The resulting mixture was stirred at constant temp. for 15 minutes, at room temp. for 45 minutes and finally warmed to the reaction temp. (30–35 °C). A solution of acetophenone (1.20 g, 10 mmol) in anhyd. THF (15 ml) was added dropwise via the pressure equalizing addition funnel within 30 min. After the addition was completed, the mixture was stirred for 16 h at constant reaction temp.. The reaction was then quenched at 0 °C with 40 ml 2 N HCl, the layers were separated. After extraction of the aqueous layer with diethyl ether (3 × 50 ml), the combined organic phases were washed with 2 N aqueous NaOH. Then washed with brine, subsequently dried with anhydrous $MgSO_4$, filtered and concentrated in vacuo. The reduction product was isolated and purified by distillation (chemical yields between 65 and 84%, 99.4% pure by GC). The optical purity was determined by optical rotation analysis: $[\alpha]^{20}_D$ = + 43.1 (*c* = 7.19, cyclopentane) for (*R*)-1-phenylethanol[9].

Reaction 2. – General Procedure for the Ethylation of Benzaldehyde (GP6): The amino alcohol catalyst precursor (0.5 mmol, 5 mol%) was dissolved in 20 ml of anhyd. toluene and cooled to –40 °C under argon atmosphere. Diethylzinc (18.2 ml of 1.1 M solution in toluene, 20 mmol) was added dropwise over a period of 10 min. After the addition was completed the mixture was allowed to reach room temp. After 15 min. 1.06 g (10 mmol) of freshly distilled benzaldehyde in 20 ml of anhyd. toluene were added dropwise within 30 min. The reaction mixture was stirred for 40 h at room temp. The reaction was then quenched at 0 °C with 40 ml 2 N HCl, the layers were separated and the aqueous layer was extracted three times with diethyl ether (3 × 40 ml). The combined organic phases were extracted with 3.9% aqueous sodium hydrogen sulfite (3 × 40 ml) and washed with saturated sodium hydrogen carbonate solution and brine, then dried with $MgSO_4$, filtered and concentrated in vacuo. The reduction product was isolated and purified by distillation (chemical yields between 64 and 86%). The optical purity was determined by optical rotation analysis: $[\alpha]^{20}_D$ = + 45.45 (*c* = 5.15, chloroform) for (*R*)-1-phenylpropan-1-ol[10].

☆ Dedicated to Professor *Dieter Seebach* on the occasion of his 60th birthday.

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