Utilization of industrial waste materials. Part 14.† Synthesis of β-amino alcohols and thiols with a 2-azabicyclo[3.3.0]octane backbone and their application in enantioselective catalysis

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New, chiral β-*tert*-amino *tert*-alcohols have been synthesized from the enantiomerically pure *sec*-amine (*all-R*)-**1b** *via* the new glycine, alanine and phenylglycine derivatives **2**–**6**. Grignard additions to these esters provided the new rigid amino alcohols **7**–**11** in fair yields. The absolute configurations of the stereogenic centers, which arose during the alkylation step, were assigned by an independent route leading to some of the optical antipodes of **7**–**10**. Condensation of enantiomerically pure β-amino alcohols **13a**–**g**, **16** and **17** with γ-ketoester *rac*-**12** afforded the *N,O*-acetals **14a**–**g**, **18** and **19**, which were subsequently reduced to the β-*tert*-amino alcohols **10a**,**c** and **15a**–**g**. X-Ray analysis of compound **19** was performed to verify the stereochemistry observed by chemical correlation. The nucleophilic ring opening of enantiomerically pure styrene oxide by amine **1b** resulted in the formation of regioisomeric amino alcohols **9a**, **21a**, and **10a**, **21b**. Amino thiol derivatives **22** and **25a**,**b** were prepared by treatment of **10a** and **15a**,**b**, respectively, with methanesulfonyl chloride followed by regio- and stereoselective cleavage of the *in situ* formed aziridinium ions with potassium thioacetate. Reduction of these compounds to thiols **23** and **26a**,**b** and subsequent oxidation afforded amino disulfides **24** and **27a**,**b**. Finally, the bicyclic β-amino alcohols and thiols were used as chiral ligands in the enantioselective addition of diethylzinc to benzaldehyde and ee values up to 96% were found.

Introduction

During the last decades, the development of new and practical methods of stereoselective synthesis has been among the most challenging subjects in organic chemistry. The invention of new stereoselective reactions *via* the use of both chiral auxiliaries and chiral catalysts has become a major interest of academic and industrial investigations, not least for the reason that enantiomerically pure compounds are of critical importance to pharmaceutical and agricultural chemistry. This is frequently due to the fact that biologically important molecules often show effective activity as one enantiomer whereas the other one is either ineffective or detrimental.[1] Two principal methods were developed for the stereoselective synthesis of enantiomerically pure compounds: the first one is the chiral-auxiliary-based stereoselective synthesis (diastereoselective variant) and the second one is the external chiral-ligand-controlled stereoselective synthesis (enantioselective variant). Although both methods have been intensively studied in a variety of organic reactions, the synthesis of enantiomerically pure compounds by stereoselective formation of C–C bonds is still of major importance.[2] Among the several advances made in this area, the ligand accelerated alkylation of carbonyl compounds (enantioselective asymmetric synthesis) has attracted considerable interest during the past decade. Since the first report of a highly enantioselective amino alcohol catalyzed addition of dialkylzinc reagents to aldehydes,[3] there has been a rapid growth of research aimed at this reaction.[4] Much of these efforts have been directed toward the synthesis of new ligands and so far many good catalysts have been developed.[5]

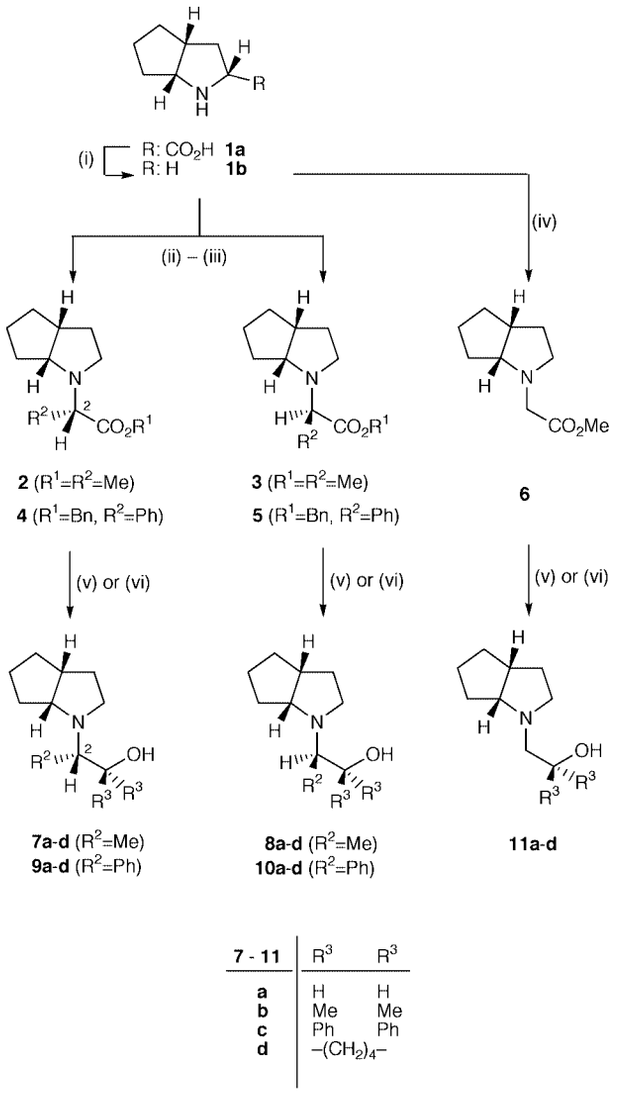
† For part 13 see ref. 7.

However, for a few years our interest in this area has been focused on the design of new ligands with a rigid bi- and tricyclic nitrogen containing backbone.[6] In this paper we report the synthesis of several new ligands with a 2-azabicyclo[3.3.0]-octane framework by the use of derivatives of proteinogenic and non-proteinogenic α-amino acids, as starting materials. Two independent routes for the construction of the same ligands have allowed us to establish the absolute configuration of the newly formed stereogenic centers. Finally, all the ligands were tested for their effectiveness as chiral catalysts in the reaction of benzaldehyde with diethylzinc.

Results and discussion

Synthesis of the ligands

Ligands with (*all-R*)-2-azabicyclo[3.3.0]octane backbone. For the three-step synthesis of the diastereomeric β-amino alcohols **7**–**11** (Scheme 1) we used the enantiomerically pure (*all-R*)-2-azabicyclo[3.3.0]octane-3-carboxylic acid **1a**, a waste material which is generated in the process of synthesizing the ACE-inhibitor Ramipril by Hoechst AG, as the starting material.[7] First of all, chiral **1a** was converted to the chiral heterocyclic amine **1b** by the known cyclohexen-2-one catalyzed thermal decarboxylation process.[8] In the next step the optically pure pyrrolidine derivative **1b** was *N*-alkylated by treatment with methyl 2-bromopropionate or benzyl 2-bromo-2-phenylacetate respectively (Scheme 1, step ii). Separation of the diastereomers (dr = 1 : 1) by column chromatography afforded the new ester derivatives of alanine **2**, **3** and phenylglycine **4**, **5** (step iii). As well as the benzyl ester of phenylglycine derivatives, the methyl and ethyl esters were synthesized, but only in the case of the



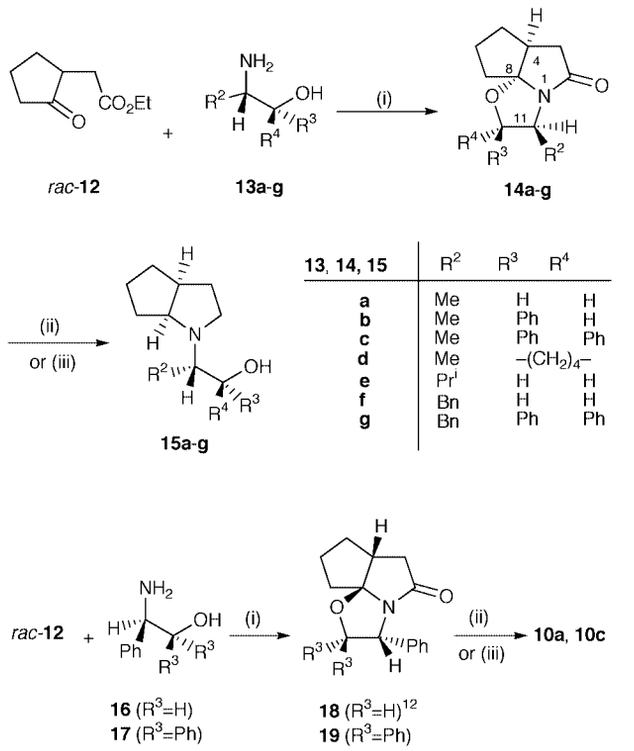
7 - 11	R^3	R^3
a	H	H
b	Me	Me
c	Ph	Ph
d	–$(CH_2)_4$–	

Scheme 1 *Reagents*, *conditions and yields*: i, Pd/C, cyclohexen-2-one;[8] ii, *rac*-$R^2CH(Br)CO_2R^1$ (R^1 = R^2 = Me; R^1 = Bn, R^2 = Ph), NEt_3, reflux, 67–78%; iii, separation of diastereomers by chromatography; iv, $BrCH_2CO_2Me$–NEt_3, reflux, 85%; v, $LiAlH_4$ in THF, 3 h reflux, 82–96%; vi, R^3MgBr in anhydrous THF, 12 h reflux, 43–88%.

benzyl ester was separation of diastereoisomers by column chromatography possible. Subsequently, these esters were converted either to the β-*tert*-amino primary alcohols **7a**–**10a** by lithium aluminium hydride reduction (step v) or to the β-*tert*-amino *tert*-alcohols **7b**–**d**, **8b**–**d**, **9b**–**d** and **10b**–**d** by addition of the corresponding Grignard reagent in refluxing tetrahydrofuran (step vi).

In order to discuss the results and effects of the enantioselective diethylzinc addition to benzaldehyde catalyzed by ligands **7**–**10**, the corresponding alcohol-substituted optically active derivatives of glycinol were also synthesized. Ligands **11a**–**d** were easily provided in two steps by treatment of **1b** with methyl bromoacetate (Scheme 1, step iv), followed by reduction of the resulting chiral ester **6** to β-amino alcohol **11a** or by addition of the respective Grignard reagents to afford **11b**–**d** (steps v–vi).

Ligands with an (*all-S*)-2-azabicyclo[3.3.0]octane backbone. In Scheme 2 an alternative procedure for the synthesis of new β-amino alcohols with an (*all-S*)-2-azabicyclo[3.3.0]octane backbone is presented. Condensation of the racemic ethyl 2-oxocyclopentaneacetate *rac*-**12** with various enantiopure β-amino alcohols **13** (derived from the corresponding α-amino acids) afforded the lactams **14**.[9] The key feature of this highly



13, 14, 15	R^2	R^3	R^4
a	Me	H	H
b	Me	Ph	H
c	Me	Ph	Ph
d	Me	–$(CH_2)_4$–	
e	Pr^i	H	H
f	Bn	H	H
g	Bn	Ph	Ph

Scheme 2 *Reagents*, *conditions and yields*: i, toluene, 16 h reflux, 15–85%; ii, if R^3 = R^4 = H: $LiAlH_4$ in THF, 3 h reflux, 36 h room temp., 81–94%; iii, R^3 = alkyl or aryl: BH_3·THF-complex in THF, 2 h reflux, 3 d room temp., 26–87%; lactams **14b** and **14e**[9] as well as β-amino alcohol **18**[12] have been previously described.

stereoselective step is the simultaneous formation of two contiguous stereogenic centers *via* deracemization of the ketoester. After treatment of *rac*-**12** with the corresponding β-amino alcohols **13a**–**g** in refluxing toluene, the tricyclic lactams **14a**–**g** were isolated in 15–85% yield (Scheme 2, step i). In this context, the lower yields for **14c**,**d** and **g** (R^3 and R^4 = alkyl or aryl, 15–19%), which are probably due to steric hindrance, are noteworthy.

In order to provide new ligands, the *N*,*O*-acetals **14a**–**g** were reductively cleaved either by lithium aluminium hydride (step ii, R^3 = R^4 = H) or by the borane–tetrahydrofuran complex (step iii, R^3 = alkyl, aryl) affording the functionalized 2-azabicyclo-[3.3.0]octanes (a mechanistic explanation for the stereoselective ring opening of *N*,*O*-acetals is given by Meyers and Burgess[10]).

On the basis of their NMR spectra, all these compounds were obtained diastereomerically pure and because the starting β-primary-amino alcohols **13** were enantiopure, it follows that this must hold for the products as well. Their enantiopurity was further confirmed by the same magnitude but opposite sign of optical rotation for the independently synthesized optical antipodes **8a** and **15a** as well as for **8c**, **15c** and **8d**, **15d** (Schemes 1 and 2).

Stereochemical assignment. Based on the assignment of absolute configuration for all compounds synthesized according to Scheme 2[11] and on the complete agreement of the analytical characteristics of the enantiomeric β-amino alcohols obtained as described in Scheme 1 (**8a**,**c**,**d**) and Scheme 2 (**15a**,**c**,**d**), we were able to assign the absolute configurations of all the diastereomeric β-*tert*-amino alcohols **7a**–**d** and **8a**–**d** and consequently those of the alanine methyl ester derivatives **2** and **3** (R^2 = Me). As a result of the fact that (*S*)-alaninol derivatives **13a**,**c**,**d** produced (*all-S*)-configured **15a**,**c**,**d** in Scheme 2, the stereochemistry was determined to be (*all-R*) for **8a**–**d** and **3** and correspondingly (1′*R*,2*S*,5′*R*) for **7a**–**d** as well as for **2**.

Similarly, the absolute configurations of ligands **9a**–**d** and **10a**–**d** and therefore those of the phenylglycine esters **4** and **5**

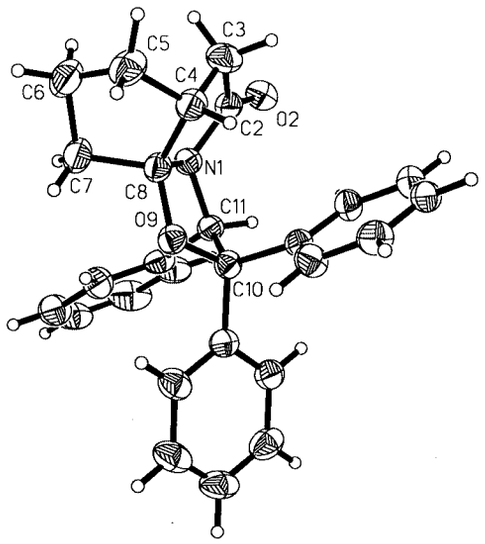


Fig. 1 Selected bond lengths (Å): O2–C2 1.213(3), N1–C2 1.371(3), N1–C8 1.463(3), C8–O9 1.433(3), O9–C10 1.447(3), C10–C11 1.556(3), C11–N1 1.474(3); selected bond angles (°): O9–C8–N1 104.44(17), O9–C8–C4 118.21(19), N1–C11–C10 99.30(17), C2–N1–C11 120.47(19), C3–C4–C8 103.7(2), O9–C10–C11 101.80(18), C2–N1–C8 113.52(19), C8–N1–C11 109.97(18).

(R^2 = Ph) were clarified. A) Reduction of **5** afforded the (*all-R*)-configured amino alcohol **10a** (Scheme 1), which is identical to the product obtained from the condensation of γ-ketoester *rac*-**12** with (*R*)-phenylglycinol (**16**) and subsequent reduction of **18**.[12] B) Likewise, the product **10c** obtained from *rac*-**12** and the α,α-diphenyl-substituted (*R*)-phenylglycinol **17** *via* compound **19** (Scheme 2) is identical with that formed from **5** on treatment with phenylmagnesium bromide (Scheme 1). The magnitude and sign of the optical rotation of the different samples of **10a** as well as of **10c** synthesized on two independent routes were in complete agreement. Thus, the stereochemistry of the newly formed stereogenic carbon of α-amino acid ester **5** was established as being *R* and correspondingly the ester **4** has to be assigned *S*-configured at the 2-position.

Although the absolute configurations of the new bicyclic ligands were proved by chemical correlation, it seemed to be appropriate to verify the observations by a single crystal X-ray study. Thus, analysis of the precursor of **10c**, the crystalline *N,O*-acetal **19**, is given in Figs. 1 and 2. Crystallographic data are given in Table 1.‡ Amazingly, two significantly distinguished structures were found and as can be seen from the figures the different orientation of the phenyl groups causes the overall difference. Moreover, the absolute configuration of compound **19** confirmed the experimental results as described above. A fixed *R* configuration in position C-11 (originating from *R*-configured phenylglycinol derivative) causes the *R* configuration at bridgehead position C-4 (C-4′) and *S* configuration at C-8 (C-8′). It can be observed in the conformation of **19** that the pyrrolidine ring is approximately planar due to the sp^2 hybridized carbonyl group whereas the cyclopentane and the oxazolidine rings exist in envelope forms.

Rigid β-amino alcohols by epoxide ring-opening. The ring-opening reaction of 1,2-epoxides with amines is one of the most widely used methods for the synthesis of β-amino alcohols.[13] This classical procedure involving the direct heating of epoxides with amines has some significant limitations in the reaction with poorly nucleophilic amines. However, due to the previously reported use of pyrrolidine and piperidine as nucleophiles,[14,15] we were prompted to use this method for the synthesis of further rigid β-amino alcohols with a 2-azabicyclo-[3.3.0]octane backbone.

When the chiral amine **1b** was refluxed in ethanol with either enantiomerically pure (*R*)- or (*S*)-styrene oxides **20a** and **20b**, respectively, in both cases a normal as well as an abnormal ring-opening was observed as expected (Scheme 3). As a result of the abnormal nucleophilic attack of **1b** at the benzylic position of the epoxides the formation of the minor regioisomers **9a** and **10a**, respectively, occurred with inversion of configuration. In the case of (*R*)-styrene oxide **20a** as starting compound a regioisomeric ratio of 72:28 in favour of the normal ring-opened product **21a** could be detected (by ^{1}H-NMR spectroscopy) and in approximately the same ratio (rr = 69:31) β-amino alcohols **21b** and **10a** were obtained in the reaction of **20b** with **1b**. However, separation of the respective regioisomers was managed by column chromatography.

‡ CCDC reference number 207/347. See http://www.rsc.org/suppdata/p1/1999/2353 for crystallographic files in .cif format.

Table 1 Crystal data for (4*R*,8*S*,1*R*)-**19**

Compound	(4*R*,8*S*,11*R*)-**19**
Molecular formula	$C_{27}H_{25}NO_2$
Molecular mass	395.50
Crystal system	Triclinic
Space group	*P*1
Cell parameters:	
a/pm	876.6(1) $\alpha = 81.71(10)°$
b/pm	967.3(1) $\beta = 82.07(10)°$
c/pm	1264.7(1) $\gamma = 78.91(10)°$
Z	2
Volume/10^{-6} pm^3	1034.48(3)
d/g cm^{-3}	1.269
Absorption coefficient/mm^{-1}	0.623
Reflections collected	7298
Independent reflections	7298
Observed reflections	7228
Number of parameters refined	7298
Final *R* indices [$I > 2\sigma(I)$]	$R = 0.0542$, $wR_2 = 0.1588$
Diffractometer used	Enraf-Nonius CAD4
Radiation	Cu-Kα ($\lambda = 154.178$ pm)
Temperature/K	213
System used	Siemens SHELXTL Plus
Solution	Direct methods/differences fourier
Goodness-of-fit on F^2	1.092

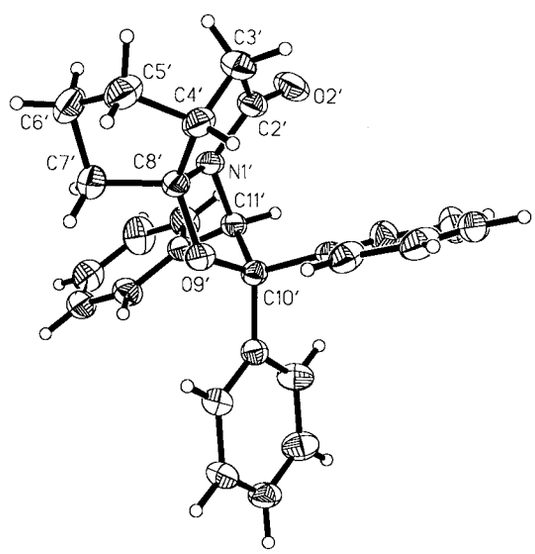
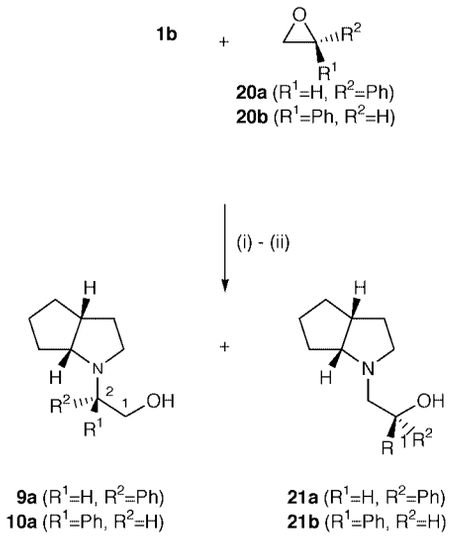


Fig. 2 In this figure the positions of the atoms are marked with '′' (*e.g.* O2′ instead of O2) to stress the difference between this structure and that in Fig. 1; selected bond length (Å): O2′–C2′ 1.217(3), N1′–C2′ 1.376(3), N1′–C8′ 1.455(3), C8′–O9′ 1.437(3), O9′–C10′ 1.439(3), C10′–C11′ 1.563(3), C11′–N1′ 1.468(3); selected bond angles (°): O9′–C8′–N1′ 104.38(17), O9′–C8′–C4′ 117.41(19), N1′–C11′–C10′ 98.51(17), C2′–N1′–C11′ 120.9(2), C3′–C4′–C8′ 104.2(2), O9′–C10′–C11′ 102.76(16), C2′–N1′–C8′ 113.66(19), C8′–N1′–C11′ 109.73(17).



Scheme 3 *Reagents*, *conditions and yields*: i, EtOH, reflux, 51–52%; ii, separation of regioisomers by chromatography; regioisomeric ratio of the crude product: **9a** : **21a** = 28 : 72 and **10a** : **21b** = 31 : 69.

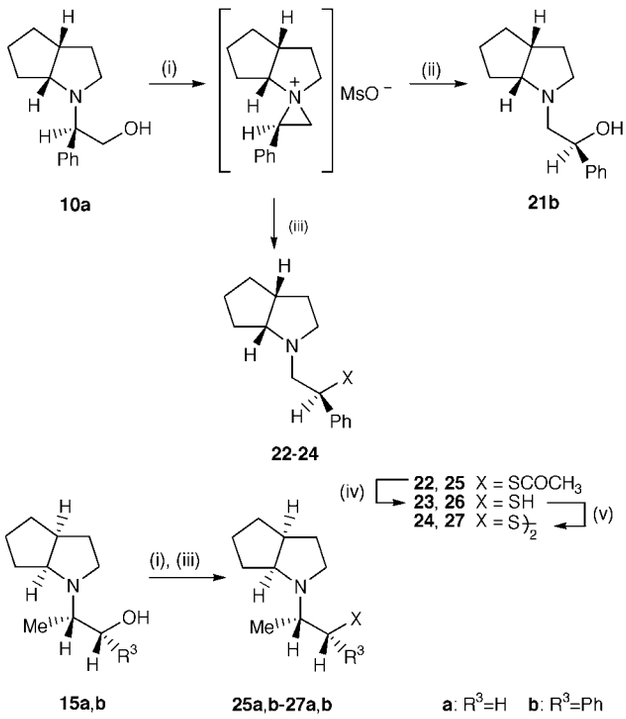
β-Amino alcohols and thiols by aziridinium ion ring opening. Using a procedure developed by Dieter *et al.* for the synthesis of chiral 1,2-diamines by nucleophilic ring-opening of aziridinium ions,[16] we could successfully use a similar method for the conversion of amino alcohol **10a** into its regioisomer **21b** (Scheme 4, steps i, ii). Treatment of **10a** with an excess of methanesulfonyl chloride and triethylamine afforded first of all the corresponding aziridinium salt which was directly converted into the amino alcohol **21b** by basic hydrolysis. The spectral characteristics and optical rotation values of β-amino alcohols **21b** obtained by both routes (ring-opening of epoxide *vs.* ring-opening of aziridinium ion) were in complete agreement. Thus, either the mesylation or hydroxy ion displacement proceeded with inversion of configuration as the hydroxy ion opened the aziridinium ion regio- and stereospecifically at the benzylic position. This is in accord with the well known opening of aziridinium ions by amine nucleophiles.[14–16]

Bearing in mind the known improvement of enantioselectivities in the diethylzinc addition to aldehydes in the presence of β-amino thiols or disulfides in place of amino alcohols,[17] we decided to convert some functionalized 2-azabicyclo[3.3.0]-octanes into the corresponding amino thioacetates, amino thiols and disulfides. Therefore, the aziridinium ion prepared *in situ* from **10a** was treated with potassium thioacetate (Scheme 4, step iii). In the same manner as described above for the basic hydrolysis (step ii), the nucleophilic ring-opening took place at the benzylic position affording thioester **22**,[18] which was reduced by diisobutyl aluminium hydride (DIBAL-H) to β-amino thiol **23**. Subsequently, **23** was converted to disulfide **24** by aerial oxidation while stirring at room temperature for three days. Identical compounds **22**–**24** were also formed from the rearranged amino alcohol **21b** using the same procedure. The retention of configuration during this latter reaction is due to a double inversion at the carbon atom bearing the phenyl group.

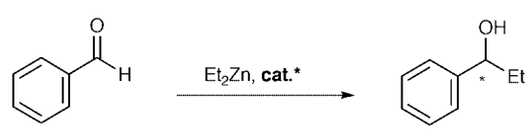
In accordance with amino alcohol **21b** the amino alcohols **15a** and **b** afforded the compounds **25a**,**b** to **27a**,**b**, respectively, without rearrangement, by the same reaction sequence. Thus, in compounds **25b**–**27b** the configuration at the α-C atom should be retained (double inversion).

Enantioselective catalysis

All the presented azabicyclo[3.3.0]octane-based ligands were tested in the enantioselective addition of diethylzinc to benzaldehyde (Scheme 5). The results obtained for this model reaction are summarized in Tables 2 and 3 (for detailed information



Scheme 4 *Reagents*, *conditions and yields*: i, MsCl–NEt_3 in Et_2O, 0 °C, 2 h, without isolation; ii, OH^-/H_2O (pH > 8), 20 h, room temp, 77%; iii, CH_3COSK, 20 h, room temp, 23–73%; iv, DIBAL-H (1 M in *n*-hexane), Et_2O, −10 °C, 2 h, 61–93%; v, O_2 (air), 3 d, room temp, 75–88%.



Scheme 5

about reaction conditions, work-up, determination of the ee value, *etc.* see footnotes of tables and the Experimental section).

The following conclusions concerning the asymmetric induction of the chiral ligands may therefore be drawn. The asymmetric induction caused merely by the stereogenic centers of the bicyclic backbone without a stereogenic center at the amino alcohol moiety is only poor (entries 17–20, compounds **11a**–**d**). As is indicated by comparison of the effect of ligands **21a** and **21b** (entries 25, 26) as well as of ligands **7** and **8** (entries 1–8) or **9** and **10** (entries 9–16) the stereogenic center of the amino alcohol group dictates whether the (*R*)- or the (*S*)-configured 1-phenylpropanol is formed in excess. This asymmetric induction is enforced by the two stereogenic centers of the bicyclic backbone in the (*all-R*)-configured compound **8** and **10** (matched situation), but diminished by the stereogenic centers in **7** and **9** (mismatched situation). In the compounds with primary alcohol groups **7a**–**10a** as well as **15e**,**f** the enantioselectivity does not depend significantly on the bulkiness of the substituent R^2 at the stereogenic center adjacent to the amino group (ee 45–49% and 30–34%, respectively). However, the introduction of two substituents in the α-position to the hydroxy group enhances the enantioselectivity to a different extent. Surprisingly, this effect is much more pronounced with the alkyl groups in **8b**,**d** and **10b**,**d** ($R^3 = R^3$: Me or R^3,R^3: $-(CH_2)_4-$, respectively) compared to the sterically more demanding phenyl groups in **8c** and **10c**. Thus, the highest enantiomeric excess was achieved with **8d** (92%) and **10d** (91%) containing a rigid cyclopentanol framework.

Table 2 Enantioselective addition of diethylzinc to benzaldehyde in the presence of catalytic amounts of chiral β-amino alcohols and thiols; product: 1-phenylpropan-1-ol

Entry[a]	Catalyst	Time/h	Yield (%)	Ee (%)[b]
1	**7a**	42	85	46 (*R*)
2	**7b**	42	78[c]	36 (*R*)
3	**7c**	42	87	35 (*R*)
4	**7d**	42	71[c]	71 (*R*)
5	**8a**	42	87	49 (*S*)
6	**8b**	42	91	80 (*S*)
7	**8c**	42	81	39 (*S*)
8	**8d**	42	93	92 (*S*)
9	**9a**	40	84	45 (*R*)
10	**9b**	40	75[c]	38 (*R*)
11	**9c**	40	79	32 (*R*)
12	**9d**	40	82[c]	52 (*R*)
13	**10a**	40	86	46 (*S*)
14	**10b**	40	88	80 (*S*)
15	**10c**	40	92	66 (*S*)
16	**10d**	40	94	91 (*S*)
17	**11a**	40	86	4 (*S*)
18	**11b**	40	90	6 (*S*)
19	**11c**	40	88	28 (*S*)
20	**11d**	40	94	40 (*S*)
21	**15b**	12	100	86 (*R*)
22	**15e**[d]	12	58[c]	43 (*R*)
23	**15f**[d]	12	93	30 (*R*)
24	**15g**[d]	12	88	74 (*R*)
25	**21a**	42	83	60 (*R*)
26	**21b**	42	88	57 (*S*)
27	**25a**[d]	12	100	82 (*R*)
28	**26a**[d]	12	100	84 (*R*)
29	**22**	12	95	60 (*S*)
30	**23**	12	100	64 (*S*)[e]
31	**24**	12	88	60 (*S*)
32	**25b**	12	100	90 (*R*)
33	**26b**	12	100	90 (*R*)[f]
34	**27b**	12	92	86 (*R*)

[a] Entries 1–34 were carried out according to two different methods: entries 1–20 and 25–26 method A (5 mol% catalyst, room temp), entries 21–24 and 27–34 method B (6 mol% catalyst, 0 °C), see Experimental section. [b] While the ee value of the obtained 1-phenylpropan-1-ol was assigned by chiral GC or NMR (see Experimental section: enantioselective catalysis method A and method B), the absolute configuration of this optically active alcohol was assigned on the basis of the optical rotation. [c] Benzyl alcohol between 4–16% was formed. [d] Ref. 6b. [e] Ligand contained 6% disulfide. [f] Ligand contained 16% disulfide.

A comparison of the result with ligand **15b** (entry 21, 86% ee) with those of ligands **10c** (entry 15, 66% ee) or **8a** (entry 5, 49% ee) reveals the favorable effect of the introduction of an additional stereogenic center at the amino alcohol group.

Whereas the displacement of the hydroxy group by a sulfur-containing substituent brings about a significant improvement of the ee value for compounds **25a** (82% ee) and **26a** (84% ee) compared to **8a** (49% ee), this is not true in the case of the β-amino alcohols **21b** and **15b** compared to the corresponding sulfur compounds **22**–**24** and **25b**–**27b**, respectively. Nevertheless, the amino thioacetate **25b**, the amino thiol **26b** as well as the amino alcohols **8d** and **10d** are the most efficient ligands of the series presented in this paper.

In Table 3 a survey of the results obtained in the addition of diethylzinc to benzaldehyde in the presence of various concentrations of the best ligand **8d** is given. Not surprisingly, the enantiomeric excess as well as the chemical yield is strongly dependent on the catalyst concentration: A decreased amount of the ligand affords lower ee's and chemical yields (entries 35–39) but nevertheless, satisfying results are also obtained for relatively low catalyst concentration of **8d** (1.0 and 0.5 mol%, entries 38 and 39) in this stereoselective C–C bond forming reaction.

Table 3 Enantioselective addition of diethylzinc to benzaldehyde using various concentrations of β-amino alcohol **8d**; product: 1-phenylpropan-1-ol

Entry[a]	Concentration (mol%)	Time/h	Yield (%)	Ee (%)[b]
35	10.0	24	95	96 (*S*)
36	7.5	24	90	93 (*S*)
8	5.0	42	93	92 (*S*)
37	2.5	48	86	86 (*S*)
38	1.0	72	78	72 (*S*)
39	0.5	72	68[c]	50 (*S*)

[a] Carried out according to method B. [b] The ee value of the obtained 1-phenylpropan-1-ol was assigned by chiral GC (see Experimental section: enantioselective catalysis method B) and the absolute configuration of this optically active alcohol was assigned on the basis of optical rotation. [c] 14% benzyl alcohol was formed.

Experimental

Chemicals

(1*S*,2*R*)-(+)-Norephedrin (>98% purity) was purchased from Fluka. (*R*)-(−)- and (*S*)-(+)-styrene oxide, diethylzinc (1.0 M in hexane fraction and 1.1 M in toluene), methyl 2-bromoacetate and methyl 2-bromopropionate were purchased from Aldrich; benzyl 2-bromo-2-phenylacetate was prepared according to a literature described method;[19] *rac*-ethyl (2-oxocyclopentyl)-acetate was prepared in four steps from adipinic acid according to a literature procedure;[20] enantiomerically pure amino alcohols **13a**,**c**–**f** were performed from the respective α-amino acids.[21]

Instrumentation

General. Due to the fact that the compounds described in this paper were prepared in two laboratories, different analytical instruments were used. Melting points (uncorrected) were determined using either a Linström or Kofler apparatus. Infrared spectra were recorded with either a Beckmann IR 4220, Beckmann IR 33 or Bruker IFS 88-FT-IR spectrometer. NMR spectra were recorded on either a Bruker AMX 500, ARX 500, AM 400, AC 300 or AM 300, using the residue of ^{1}H ($\delta = 7.27$) or of ^{13}C ($\delta = 77.0$) of the solvent $CDCl_3$ or tetramethylsilane (TMS) as internal standard. Unless otherwise stated, the ^{1}H NMR spectra were recorded at 300 MHz, the ^{13}C NMR spectra at 75 MHz. *J* values are given in Hz. MS were recorded on either a Varian CH 7 (EI), 711 (FD) or a Finnigan-MAT 212 (datasystem SS 300; CI) spectrometer. Optical rotations were measured using a Perkin-Elmer 241 polarimeter (MC). Optical rotations are given in 10^{-1} deg cm^2 g^{-1}. Elemental analyses were carried out at Division Routine Analytik, Fachbereich Chemie, University of Marburg using a C,H,N-Analyzer Carlo Erba Stumentalione (1104). Gas chromatography (GC) was performed using a Shimadzu (GC-15-A) instrument, 25 m column with the following specifications: SGE Cydex-B (chiral), $\omega_i = 0.25$ mm, film thickness 0.25 μm, 1 μl product in *n*-hexane, FID detection, nitrogen carrier gas. Column chromatography was performed using silica gel 60 (particle size 0.040–0.063 mm) from Merck. Analytical thin layer chromatography (TLC) was performed using Merck silica gel 60 F_{254} aluminium sheets or Polygram Sil G/UV$_{254}$ from Machery-Nagel. TLC spots were detected with UV light and I_2.

Preparation of α-amino acid esters 2–6: general procedure 1 (GP 1)

A solution of amine **1b** (5.55 g, 50 mmol) and triethylamine (5.56 g, 55 mmol) in 100 ml anhydrous THF was cooled down to 0 °C under an argon atmosphere. Within a period of 60 min a solution 50 mmol of the respective α-bromo carboxylic acid ester in 50 ml dry THF was added. The reaction mixture was

heated under reflux for 4 h, then cooled down to room temp and stirred for a further 16 h. After addition of 100 ml of water the layers were separated and the organic solvent was removed *in vacuo*. The residue was dissolved in 50 ml Et_2O, washed with water and brine (30 ml), dried ($MgSO_4$) and evaporated once again. The residue was distilled without fractionating (Kugelröhr distillation) affording the crude product as a 1 : 1 mixture of diastereomers. Separation of the diastereoisomers was performed by column chromatography on silica gel. In all cases, diastereomerically pure amino acid derivatives were obtained.

Preparation of amino alcohols 7a–10a: general procedure 2 (GP 2)

To a suspension of $LiAlH_4$ (0.45 g, 12 mmol) in anhydrous THF (50 ml) the respective α-amino acid esters **2**–**6** (3 mmol in 20 ml THF) were added under vigorous stirring over a period of 15 min. After the addition, the reaction mixture was heated under reflux for 3 h and cooled down to 0 °C. With cautious addition of aqueous KOH solution (10%) the excess reducing reagent was destroyed. The resulting white solid was filtered off and washed with ethyl acetate by heating to reflux for 20 min (2 × 50 ml). The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo* to give the crude amino alcohols which were purified by short-path distillation (bulb-to-bulb) or chromatography (silica gel).

Preparation of β-amino alcohols 7b–d to 11b–d: general procedure 3 (GP 3)

A dried 250 ml, three-necked, round-bottomed flask was equipped with a pressure-equalizing 50 ml dropping funnel, thermometer and reflux condenser. The Grignard reagent was prepared in the usual manner under an argon atmosphere from magnesium (30 mmol) and the alkyl- or arylhalogenide (30 mmol, 15 mmol in the case of 1,4-dibromobutane) in Et_2O (70 ml). The appropriate α-amino acid ester derivative **2**–**6** (5 mmol), dissolved in 20 ml dry Et_2O, was added over 20 min at 0 to 5 °C. After the addition, the cooling bath was removed and the reaction mixture was refluxed for 16 h. For the work-up, the mixture was cooled down to 0 °C and hydrolyzed with saturated NH_4Cl solution. The organic layer was separated and the aqueous layer was extracted with diethyl ether (3 × 40 ml). The combined organic extracts were washed with brine, dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The crude products were purified by either column chromatography (silica gel), distillation or recrystallization (see below).

Preparation of tricyclic lactams 14a–g and 19: general procedure 4 (GP 4)

A mixture of ethyl (2-oxocyclopentyl)acetate (3.41 g, 20 mmol) and 20 mmol of β-amino alcohol **13a**–**g** was refluxed in toluene (100 ml) in a flask fitted with a Dean–Stark trap. After 16 h, the reaction mixture was cooled to room temp. and concentrated *in vacuo*. The resulting crude product was purified by recrystallization or chromatography.

Preparation of 15a,e,f and 10a: general procedure 5 (GP 5)

To a freshly prepared suspension of $LiAlH_4$ (1.39 g, 36.3 mmol) in anhydrous THF (50 ml) a solution of tricyclic lactam **14a**,**e**,**f** or **18** (16.9 mmol) in THF (20 ml) was added dropwise. After refluxing for 3 h the stirring was continued for an additional 36 h at room temp. The reaction mixture was cautiously hydrolyzed by the addition of an aqueous solution of KOH (20%). The white residue was filtered off and washed by three times heating to reflux with Et_2O–THF (1 : 1). The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude products by chromatography or Kugelröhr distillation afforded the analytically pure amino alcohols.

Preparation of 15b–d,g and 10c: general procedure 6 (GP 6)

A solution of lactam **14b**–**d**,**g** or **19** (2.5 mmol) in anhydrous THF (20 ml) was cooled to −78 °C and treated dropwise with a 1 M solution of BH_3·THF (7.5 ml). Stirring was continued at −78 °C for one hour and after warming up to room temp. the reaction mixture was stirred for an additional hour. After heating at reflux for two hours and cooling down again to room temp. the mixture was stirred for a further three days. At a temperature of 0 °C, 5 ml 2 M HCL was cautiously added and the reaction mixture was heated to reflux for 1.5 h. The organic layer was evaporated *in vacuo* and the resulting aqueous layer was adjusted to pH >5 by the addition of 5 M NaOH. After extraction with CH_2Cl_2 (3×) the combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. The resulting crude products were purified by chromatography or recrystallization.

Synthesis of amino alcohols 9a, 10a, 21a–b: general procedure 7 (GP 7)

Enantiomerically pure (*S*)- or (*R*)-styrene oxide (1.0 g, 8.3 mmol) was added dropwise to a stirred solution of amine **1b** (0.93 g, 8.3 mmol) in EtOH (20 ml) and the resulting mixture was heated under reflux for 4 h. After cooling to room temp., the solvent was evaporated under reduced pressure and the residue was diluted in Et_2O (50 ml). Extraction with saturated NH_4Cl solution followed by drying over $MgSO_4$ and concentration *in vacuo* afforded the crude product as a mixture of regioisomers which were separated by column chromatography on silica gel 60.

Preparation of β-amino thioacetate 22 and 25a,b: general procedure 8 (GP 8)

Similar to the synthesis of **21b** by aziridinium ion ring-opening, β-amino alcohol **10a**, **15a** or **15b** (3 mmol) was mesylated with methanesulfonyl chloride (0.52 g, 4.5 mmol) in the presence of triethylamine (0.61 g, 6 mmol) in Et_2O (10 ml) at 0 °C for 2 h. After evaporation of the solvent *in vacuo* the resulting mesylate was directly treated with an aqueous solution of potassium thioacetate (1.03 g, 9 mmol in 10 ml water). The reaction mixture was stirred for 20 h, extracted with Et_2O (3×), dried ($MgSO_4$) and concentrated under reduced pressure. If necessary, the resulting crude product was subsequently purified by column chromatography.

Synthesis of β-amino thiols 23 and 26a,b: general procedure 9 (GP 9)

A solution of the respective thioacetate **22** or **25a**,**b** (1.5 mmol) in anhydrous Et_2O (20 ml) was cooled to −10 °C and treated dropwise with a 1.0 M solution of DIBAL-H in hexane (3.3 ml, 3.3 mmol). After 2 h stirring at 0 °C, 0.1 ml of methanol and 0.1 ml of water were added, resulting in the formation of a jelly-like solid. The solvents were separated by the use of a centrifuge and the residue was washed three times with Et_2O. The dried ($MgSO_4$) combined organic layers were concentrated *in vacuo* affording—after chromatographic work-up (silica gel)—the oxygen sensitive β-amino thiols.

Synthesis of amino disulfides 24 and 27a,b: general procedure 10 (GP 10)

The amino thiol **23** or **26a**,**b** (0.4 g, 1.6 mmol) was dissolved in $CHCl_3$ (50 ml) and stirred for three days at room temp. under air atmosphere. The solvent was removed *in vacuo* and the resulting crude disulfide was purified by column chromatography.

Methyl (2*S*,1′*R*,5′*R*)-(−)-2-(2′-azabicyclo[3.3.0]octan-2′-yl)-propionate 2. Synthesis according to GP 1. Work-up: after

Kugelröhr distillation (120 °C/10 mbar) column chromatography, eluent: *n*-hexane–ethyl acetate 8:2, R_f 0.43; yield 4.08 g (48%) as colorless oil (Found: C 67.01, H 9.68, N 7.12. Calc. for $C_{11}H_{19}NO_2$: C 66.97, H 9.71, N 7.10%); $[\alpha]_D^{20}$ −76.3 (*c* 0.68, CH_2Cl_2); ν_{max} (NaCl)/cm^{-1} 1730; δ_H (500 MHz, $CDCl_3$) 1.27 (3H, d, *J* 7.7, CH_3), 1.30–1.65 (7H, m, 4′-H, 6′-H_2, 7′-H_2, 8′-H_2), 1.89 (1H, m, 4′-H), 2.51 (2H, m, 1′-H, 3′-H), 2.88, 3.12 (2H, m, 3′-H, 5′-H), 3.42 (1H, q, *J* 7.7, 2-H), 3.66 (s, 3H, OCH_3); δ_C (125 MHz, $CDCl_3$) 17.41 (CH_3), 24.37, 31.67, 32.62, 32.90 (C-4′, C-6′, C-7′, C-8′), 42.36 (C-5′), 49.41 (C-3′), 50.95 (OCH_3), 58.61, 66.31 (C-1′, C-2), 174.12 (CO); *m*/*z* 198 (100%) [MH^+].

Methyl (2*R*,1′*R*,5′*R*)-(−)-2-(2′-azabicyclo[3.3.0]octan-2′-yl)-propionate 3. Synthesis according to GP 1. Work-up: after Kugelröhr distillation (120 °C/10 mbar) column chromatography, eluent: *n*-hexane–ethyl acetate 8:2, R_f 0.30; yield 2.96 g (30%) as colorless oil (Found: C 66.84, H 9.69, N 7.03. Calc. for $C_{11}H_{19}NO_2$: C 66.97, H 9.71, N 7.10%); $[\alpha]_D^{20}$ −17.9 (*c* 1.53, CH_2Cl_2); ν_{max} (NaCl)/cm^{-1} 1720; δ_H (500 MHz, $CDCl_3$) 1.28 (3H, d, *J* 7.7, CH_3), 1.32–1.54 (6H, m, 6′-H_2, 7′-H_2, 8′-H_2), 1.62 (1H, m, 4′-H), 1.86 (1H, m, 4′-H), 2.42 (1H, m, 3′-H), 2.53 (1H, m, 3′-H), 2.88 (1H, m, 5′-H), 3.25 (1H, m, 1′-H), 3.31 (1H, q, *J* 7.7, 2-H), 3.64 (3H, s, OCH_3); δ_C (125 MHz, $CDCl_3$) 16.18 (CH_3), 24.78, 31.52, 32.54, 33.05 (C-4′, C-6′, C-7′, C-8′), 42.73 (C-5′), 51.28 (OCH_3), 52.01 (C-3′), 60.51, 66.18 (C-1′, C-2), 174.53 (CO); *m*/*z* 198 (100%) [MH^+].

(2*S*,1′*R*,5′*R*)-(+)-Benzyl 2-phenyl-2-(2′-azabicyclo[3.3.0]-octan-2′-yl)acetate 4. Synthesis according to GP 1. Work-up: after Kugelröhr distillation (100 °C/0.02 mbar) column chromatography, eluent: *n*-hexane–ethyl acetate 9:1, addition of 1% triethylamine, R_f 0.50; yield 4.68 g (28%) as colorless oil, $bp_{(0.02\ mbar)}$ 105 °C (Found: C 78.60, H 7.49, N 4.15. Calc. for $C_{22}H_{25}NO_2$: C 78.78, H 7.51, N 4.18%); $[\alpha]_D^{22}$ +7.24 (*c* 1.16, CH_2Cl_2); ν_{max} (NaCl)/cm^{-1} 1760, 1510, 1480; δ_H (300 MHz, $CDCl_3$) 1.17–1.62 (7H, m, 4′-H, 6′-H_2, 7′-H_2, 8′-H_2), 1.81 (m, 1H, 4′-H), 2.59 (2H, m, 3′-H_2), 2.80 (m, 1H, 5′-H), 3.32 (m, 1H, 1′-H), 4.41 (s, 1H, 2-H), 5.18 (2H, 2d, *J* 12.4 and 12.4, C*H_2*Ph), 7.20–7.51 (m, 10H, arom. H); δ_C (75 MHz, $CDCl_3$) 25.04, 31.69, 33.16 (C-4′, C-6′, C-7′, C-8′), 42.51 (C-5′), 50.85 (O*C*H_2Ph), 66.17, 67.17 (C-1′, C-3′), 69.75 (C-2), 127.89, 128.07, 128.25, 128.41, 128.69, 135.87, 137.60 (arom. C), 171.68 (CO); *m*/*z* 336.3 (100%) [MH^+].

(2*R*,1′*R*,5′*R*)-(−)-Benzyl 2-phenyl-2-(2′-azabicyclo[3.3.0]-octan-2′-yl)acetate 5. Synthesis according to GP 1. Work-up: after Kugelröhr distillation (100 °C/0.02 mbar) column chromatography, eluent: *n*-hexane–ethyl acetate 9:1, addition of 1% triethylamine, R_f 0.40; yield 6.6 g (39%) as colorless oil (Found: C 78.85, H 7.52, N 4.20. Calc. for $C_{22}H_{25}NO_2$: C 78.78, H 7.51, N 4.18%); $[\alpha]_D^{20}$ −37.06 (*c* 1.53, CH_2Cl_2); ν_{max} (NaCl)/cm^{-1} 1740, 1530, 1500; δ_H (300 MHz, $CDCl_3$) 1.19–1.68 (7H, m, 4′-H, 6′-H_2, 7′-H_2, 8′-H_2), 1.92 (1H, m, 4′-H), 2.40 (1H, m, 3′-H), 2.57 (1H, m, 3′-H), 2.82 (1H, m, 5′-H), 3.28 (1H, m, 1′-H), 4.35 (1H, s, 2-H), 5.14 (2H, 2d, *J* 12.4 and 12.5, C*H_2*Ph), 7.17–7.52 (m, 10H, arom. H); δ_C (75 MHz, $CDCl_3$) 25.17, 31.19, 31.56, 33.05 (C-4′, C-6′, C-7′, C-8′), 42.37 (C-5′), 51.92 (O*C*H_2Ph), 66.31, 66.80 (C-1′, C-3′), 70.88 (C-2), 127.92, 127.98, 128.18, 128.38, 128.67, 129.13, 135.81, 136.52 (arom. C), 172.00 (CO); *m*/*z* 336.3 (100%) [MH^+].

Methyl (1′*R*,5′*R*)-(−)-2-(2′-azabicyclo[3.3.0]octan-2′-yl)-acetate 6. Synthesis according to GP 1. Work-up: short-path distillation, $bp_{(0.02\ mbar)}$ 70 °C; yield 7.74 g (85%) as colorless oil (Found: C 65.28, H 9.34, N 7.72. Calc. for $C_{10}H_{17}NO_2$: C 65.54, H 9.35, N 7.64%); $[\alpha]_D^{20}$ −67.7 (*c* 1.55, CH_2Cl_2); ν_{max} (NaCl)/cm^{-1} 1740; δ_H (300 MHz, $CDCl_3$) 1.29–1.68 (7H, m, 4′-H, 6′-H_2, 7′-H_2, 8′-H_2), 1.95 (1H, m, 4′-H), 2.44 (m, 1H, 3′-H), 2.54 (1H, m, 3′-H), 3.01 (2H, m, 1′-H, 5′-H), 3.24 (1H, d, *J* 14.3, 2-H), 3.44 (1H, d, *J* 14.3, 2-H), 3.69 (3H, s, CH_3); δ_C (75 MHz, $CDCl_3$) 24.44, 31.75, 32.21, 33.24 (C-4′, C-6′, C-7′, C-8′), 42.29 (C-5′), 51.35 (OCH_3), 54.45, 55.09 (C-2, C-3′), 68.79 (C-1′), 171.53 (CO); *m*/*z* 184 (100%) [MH^+].

(2*S*,1′*R*,5′*R*)-(+)-2-(2′-Azabicyclo[3.3.0]octan-2′-yl)propan-1-ol 7a. Synthesis according to GP 2. Work-up: short-path distillation, $bp_{(0.02\ mbar)}$ 70 °C; yield 0.49 g (96%) as colorless oil (Found: C 70.82, H 11.20, N 8.27. Calc. for $C_{10}H_{19}NO$: C 70.95, H 11.31, N 8.27%); $[\alpha]_D^{20}$ +39.8 (*c* 1.5, CH_2Cl_2); ν_{max} (NaCl)/cm^{-1} 3400; δ_H (300 MHz, $CDCl_3$) 1.07 (1H, d, *J* 6.7, 3-H), 1.32–1.68 (7H, m, 5′-H, 6′-H, 7′-H, 8′-H), 1.89 (1H, m, 4′-H), 2.51 (2H, m, 3′-H, 4′-H), 2.77 (1H, m, 3′-H), 2.88 (1H, m, 2-H), 3.20 (1H, m, 1′-H), 3.31 (1H, dd, *J* 6.3 and 10.3, 1-H), 3.55 (1H, dd, *J* 4.6 and 10.3, 1-H); δ_C (75 MHz, $CDCl_3$) 13.68 (C-3), 24.77, 31.85, 32.63, 34.45 (C-4′, C-6′, C-7′, C-8′), 43.04 (C-5′), 53.33 (C-3′), 57.96 (C-2), 63.42, 64.55 (C-1, C-1′); *m*/*z* 170 (100%) [MH^+].

(2*S*,1′*R*,5′*R*)-(+)-3-(2′-Azabicyclo[3.3.0]octan-2′-yl)-2-methylbutan-2-ol 7b. Synthesis according to GP 3. Work-up: column chromatography, eluent: *n*-hexane–triethylamine 9:1, R_f 0.60; yield 0.56 g (57%) as colorless oil (Found: C 73.10, H 11.73, N 7.04. Calc. for $C_{12}H_{23}NO$: C 73.04, H 11.75, N 7.10%); $[\alpha]_D^{20}$ +20.8 (*c* 1.67, CH_2Cl_2); ν_{max} (NaCl)/cm^{-1} 3500–3200; δ_H (300 MHz, $CDCl_3$) 1.03 (3H, d, *J* 6.7, 3-H_3), 1.06, 1.15 (6H, 2s, 2CH_3), 1.27–1.85 (8H, m, 4′-H, 5′-H, 6′-H_2, 7′-H_2, 8′-H_2), 2.49 (m, 1H, 4′-H), 2.68 (2H, m, 3′-H_2), 2.86 (1H, m, 2-H), 3.51 (1H, m, 1′-H), 4.52 (1H, br s, OH); δ_C (75 MHz, $CDCl_3$) 10.85 (C-3), 24.12, 28.03 (2CH_3), 25.23, 31.92, 32.50, 33.01 (C-4′, C-5′, C-6′, C-7′), 41.91 (C-5′), 51.45 (C-3′), 64.07, 65.66 (C-1′, C-2′), 71.08 (C-1); *m*/*z* 198 (100%) [MH^+].

(2*S*,1′*R*,5′*R*)-(−)-2-(2′-Azabicyclo[3.3.0]octan-2′-yl)-1,1-diphenylpropan-1-ol 7c. Synthesis according to GP 3. Work-up: column chromatography; eluent: *n*-hexane–diethyl ether 7:3, R_f 0.51; yield 1.12 g (70%) as colorless oil (Found: C 81.98, H 8.50, N 4.32. Calc. for $C_{22}H_{27}NO$: C 82.20, H 8.47, N 4.36%); $[\alpha]_D^{20}$ −64.2 (*c* 0.83, CH_2Cl_2); ν_{max} (NaCl)/cm^{-1} 3400, 1510, 1450; δ_H (500 MHz, $CDCl_3$) 1.04 (3H, d, *J* 6.6, 3-H_3), 0.89, 1.18–1.64 (7H, 2m, 4′-H, 6′-H_2, 7′-H_2, 8′-H_2), 1.72 (1H, m, 4′-H), 2.27 (1H, m, 3′-H), 2.42 (2H, m, 3′-H, 5′-H), 3.28 (1H, m, 1′-H), 3.73 (1H, m, 2-H), 5.56 (1H, br s, OH), 7.14–7.24 (m, 6H, arom. H), 7.51–7.65 (m, 4H, arom. H); δ_C (75 MHz, $CDCl_3$) 15.65 (C-3), 24.94, 32.09, 33.18, 33.51 (C-4′, C-6′, C-7′, C-8′), 41.58 (C-5′), 52.56 (C-3′), 62.32 (C-2), 66.57 (C-1′), 77.82 (C-1), 125.99, 126.16, 126.35, 127.61, 127.86, 146.02, 148.54 (arom. C); *m*/*z* 322 (100%) [MH^+].

(1′*S*,1″*R*,5″*R*)-(+)-1-[1′-(2″-Azabicyclo[3.3.0]octan-2″-yl)-ethyl]cyclopentanol 7d. Synthesis according to GP 3. Work-up: column chromatography; eluent: *n*-hexane–triethylamine 9:1, R_f 0.74; yield 0.49 g (44%) as colorless oil (Found: C 75.28, H 11.09, N 6.31. Calc. for $C_{14}H_{25}NO$: C 75.32, H 11.29, N 6.27%); $[\alpha]_D^{20}$ +4.8 (*c* 0.54, CH_2Cl_2); ν_{max} (NaCl)/cm^{-1} 3350; δ_H (300 MHz, $CDCl_3$) 1.07 (3H, d, *J* 7.0, 2′-H_3), 1.27–1.92 (16H, m, 2-H_2, 3-H_2, 4-H_2, 5-H_2, 4″-H, 5″-H, 6″-H_2, 7″-H_2, 8″-H_2), 2.53, 2.65 (2H, 2m, 3″-H, 4″-H), 2.91 (2H, m, 3″-H, 1′-H), 3.64 (1H, m, 2′-H), 4.58 (1H, br s, OH); δ_C (75 MHz, $CDCl_3$) 10.78 (C-2′), 24.05, 24.90, 31.88, 33.35, 25.00, 32.85, 35.36, 39.54 (C-2, C-3, C-4, C-5, C-4″, C-6″, C-7″, C-8″), 42.54 (C-5″), 52.73 (C-3″), 62.27, 64.38 (C-1′, C-1″), 82.19 (C-1); *m*/*z* 224 (100%) [MH^+].

(2*R*,1′*R*,5′*R*)-(−)-2-(2′-Azabicyclo[3.3.0]octan-2′-yl)propan-1-ol 8a. Synthesis according to GP 2. Work-up: short-path distillation, $bp_{(0.02\ mbar)}$ 75 °C; yield 0.48 g (94%) as colorless oil (Found: C 70.89, H 11.28, N 8.33. Calc. for $C_{10}H_{19}NO$: C 70.95, H 11.31, N 8.27%); $[\alpha]_D^{20}$ −80.5 (*c* 1.5, CH_2Cl_2); $[\alpha]_D^{20}$ −44.1 (*c* 1.1, EtOH); ν_{max} (NaCl)/cm^{-1} 3450, 1450; δ_H (300 MHz, $CDCl_3$) 0.84 (3H, d, *J* 6.6, 3-H), 1.18–1.27, 1.38–1.52 (7H, 2m, 4′-H, 6′-H_2, 7′-H_2, 8′-H_2), 1.90 (1H, m, 4′-H), 2.23 (1H, ddd, *J* 5.5,

8.6 and 11.4, 3′-H), 2.43 (1H, m, 5′-H), 2.58 (1H, dd, *J* 6.7 and 8.6, 3′-H), 2.88 (1H, ddq, *J* 5.0, 6.6 and 10.0, 2-H), 3.08 (1H, dd, *J* 6.3 and 8.2, 1′-H), 3.15 (1H, t, *J* 10.0, 1-H), 3.35 (1H, dd, *J* 5.0 and 10.0, 1-H); δ_C (75 MHz, $CDCl_3$) 9.3 (C-3), 23.7, 32.2, 32.7, 33.2 (C-4′, C-6′, C-7′, C-8′), 41.6 (C-5′), 44.7 (C-3′), 54.4 (C-2), 63.5 (C-1), 65.2 (C-1′); *m*/*z* 170 (100%) [MH^+].

(2*R*,1′*R*,5′*R*)-(−)-3-(2′-Azabicyclo[3.3.0]octan-2′-yl)-2-methylbutan-1-ol 8b. Synthesis according to GP 3. Work-up: column chromatography, eluent: *n*-hexane–triethylamine 95 : 5, R_f 0.5; yield 0.87 g (88%) as colorless oil (Found: C 72.90, H 11.84, N 7.16. Calc. for $C_{12}H_{23}NO$: C 73.04, H 11.75, N 7.10%); $[a]_D^{20}$ −95.5 (*c* 1.5, CH_2Cl_2); ν_{max} (NaCl)/cm^{-1} 3300; δ_H (300 MHz, $CDCl_3$) 0.96 (3H, d, *J* 6.6, 3-H_3), 1.06, 1.14 (6H, 2s, 2CH_3), 1.21–1.71 (7H, m, 5′-H, 6′-H_2, 7′-H_2, 8′-H_2), 1.95 (1H, m, 4′-H), 2.37 (1H, m, 4′-H), 2.63 (1H, q, *J* 6.6, 2-H), 2.74, 3.03 (2H, 2m, 3′-H_2), 4.68 (1H, br s, OH); δ_C (75 MHz, $CDCl_3$) 7.41 (C-3), 23.35, 28.32, 24.97, 32.69, 32.74, 33.30 (2 × CH_3, C-4′, C-5′, C-6′, C-7′), 40.31 (C-5′), 47.36 (C-3′), 62.52, 68.28 (C-1′, C-2′), 70.01 (C-1); *m*/*z* 198 (100%) [MH^+].

(2*R*,1′*R*,5′*R*)-(−)-2-(2′-Azabicyclo[3.3.0]octan-2′-yl)-1,1-diphenylpropan-1-ol 8c. Synthesis according to GP 3. Work-up: column chromatography; eluent: *n*-hexane–triethylamine 8 : 2, R_f 0.82; yield 1.22 g (76%) as slightly yellow oil (Found: C 82.03, H 8.44, N 4.30. Calc. for $C_{22}H_{27}NO$: C 82.20, H 8.47, N 4.36%); $[a]_D^{20}$ −12.8 (*c* 1.06, CH_2Cl_2); $[a]_D^{20}$ −35.9 (*c* 1.0, EtOH); ν_{max} (NaCl)/cm^{-1} 3250, 1490, 1450; δ_H (500 MHz, $CDCl_3$) 1.14 (3H, d, *J* 6.8, 3-H), 1.34, 1.41–1.73, 1.75–1.88 (8H, 3m, 4′-H_2, 6′-H_2, 7′-H_2, 8′-H_2), 1.92–2.06 (2H, m, 3′-H_2), 2.39 (1H, m, 5′-H), 3.17 (1H, m, 1′-H), 3.73 (1H, q, *J* 6.8, 2-H), 6.23 (1H, br s, OH), 7.00–7.28 (6H, m, arom. H), 7.40–7.43 (4H, m, arom. H); δ_C (75 MHz, $CDCl_3$) 9.9 (C-3), 23.6, 32.45, 32.58, 33.25 (C-4′, C-6′, C-7′, C-8′), 40.54 (C-5′), 46.86 (C-3′), 61.19 (C-2), 68.10 (C-1′), 77.2 (C-1), 126.42, 126.93, 127.10, 127.47, 127.91, 128.27, 145.17, 146.25 (arom. C); *m*/*z* 322 (100%) [MH^+].

(1′*R*,1″*R*,5″*R*)-(−)-1-[1′-(2″-Azabicyclo[3.3.0]octan-2″-yl)-ethyl]cyclopentanol 8d. Synthesis according to GP 3. Work-up: column chromatography; eluent: *n*-hexane–ethyl acetate 7 : 3, R_f 0.64; yield 0.77 g (69%) as colorless oil (Found: C 75.46, H 11.18, N 6.26. Calc. for $C_{14}H_{25}NO$: C 75.32, H 11.29, N 6.27%); $[a]_D^{20}$ −74.0 (*c* 0.83, CH_2Cl_2); $[a]_D^{20}$ −45.1 (*c* 0.9, EtOH); ν_{max} (NaCl)/cm^{-1} 3280; δ_H (300 MHz, $CDCl_3$) 0.89 (3H, d, *J* 6.9, 2′-H), 1.16–1.27, 1.29–1.80 (15H, 2m, 2-H_2, 3-H_2, 4-H_2, 5-H_2, 4″-H, 6″-H_2, 7″-H_2, 8″-H_2), 1.90 (1H, ddd, *J* 5.5, 9.1 and 12.0, 4″-H), 2.29 (1H, ddd, *J* 5.5, 8.7 and 11.5, 5″-H), 2.32 (1H, m, 3″-H), 2.57 (1H, dd, *J* 6.7, 8.7, 3″-H), 2.87 (1H, q, *J* 6.9, 1′-H), 3.02 (1H, dd, *J* 6.0 and 8.1, 1″-H), 4.86 (1H, br s, OH); δ_C (75 MHz, $CDCl_3$) 6.43 (C-2′), 23.40, 23.78, 25.19, 32.56, 32.70, 33.31, 35.18, 38.39 (C-2, C-3, C-4, C-5, C-4″, C-6″, C-7″, C-8″), 40.85 (C-5″), 46.63 (C-3″), 58.98 (C-2′), 67.0 (C-1″), 81.00 (s, C-1); *m*/*z* 224 (100%) [MH^+].

(2*S*,1′*R*,5′*R*)-(−)-2-(2′-Azabicyclo[3.3.0]octan-2′-yl)-2-phenylethanol 9a. Synthesis according to GP 2. Work-up: column chromatography; eluent: *n*-hexane–ethyl acetate 1 : 1, R_f 0.22; yield 0.58 g (84%), colorless oil (Found: C 77.9, H 9.16, N 5.97. Calc. for $C_{15}H_{21}NO$: C 77.87, H 9.14, N 6.05%); $[a]_D^{20}$ −5.7 (*c* 1.0, CH_2Cl_2); ν_{max} (NaCl)/cm^{-1} 3350, 1480; δ_H (500 MHz, $CDCl_3$) 1.23–1.43, 1.52–1.64 (7H, 2m, 4′-H, 6′-H_2, 7′-H_2, 8′-H_2), 1.85 (1H, m, 4′-H), 2.43 (1H, m, 3′-H), 2.57 (1H, m, 3′-H), 2.69 (1H, br s, OH), 2.88 (1H, m, 5′-H), 3.16 (1H, m, 1′-H), 3.72 (1H, dd, *J* 6.8 and 13, 2-H), 3.78 (1H, dd, *J* 6.04 and 16.15, 1-H), 3.92 (1H, dd, *J* 7.0 and 10.3, 1-H), 7.27–7.36 (m, 5H, arom. H); δ_C (75 MHz, $CDCl_3$) 25.31, 31.56, 32.59, 32.75 (C-4′, C-5′, C-6′, C-7′); 42.68 (C-5′), 53.39 (C-3′), 63.26 (C-1′), 64.67 (C-2), 67.86 (C-1), 127.59, 128.15, 129.14, 138.54 (arom. C); *m*/*z* 232 (100%) [MH^+].

(2*S*,1′*R*,5′*R*)-(−)-2-(2′-Azabicyclo[3.3.0]octan-2′-yl)-2-phenylethanol 9a. Synthesis according to GP 7. Work-up: column chromatography, eluent: *n*-hexane–ethyl acetate 1 : 1, R_f 0.31; yield 0.18 g (9%); $[a]_D^{20}$ −5.8 (*c* 1.0, CH_2Cl_2); the analytical characteristics were in complete accord with **9a** obtained by GP 2.

(2*S*,1′*R*,5′*R*)-(+)-2-(2′-Azabicyclo[3.3.0]octan-2′-yl)-1,1-dimethyl-2-phenylethanol 9b. Synthesis according to GP 3. Work-up: column chromatography; eluent: *n*-hexane–ethyl acetate 8 : 2, R_f 0.32; yield 0.73 g (56%) as colorless oil (Found: C 78.53, H 9.77, N 5.38. Calc. for $C_{17}H_{25}NO$: C 78.72, H 9.71, N 5.40%); $[a]_D^{20}$ +11.6 (*c* 1.16, CH_2Cl_2); ν_{max} (NaCl)/cm^{-1} 3280, 1510, 1490; δ_H (300 MHz, $CDCl_3$) 1.16, 1.19 (6H, 2s, 2CH_3), 1.21–1.54 (6H, m, 6′-H_2, 7′-H_2, 8′-H_2), 1.69 (1H, m, 4′-H), 1.86 (1H, m, 4′-H), 2.41 (1H, m, 3′-H), 2.70 (1H, m, 3′-H), 2.88 (1H, m, 5′-H), 3.56 (1H, m, 1′-H), 3.68 (1H, s, 2-H), 3.89 (1H, br s, OH), 7.25–7.39 (m, 5H, arom. H); δ_C (75 MHz, $CDCl_3$) 25.47, 26.18, 29.76, 31.65, 32.26, 33.27 (2 × CH_3, C-4′, C-6′, C-7′, C-8′); 41.32 (C-5′); 51.91 (C-3′); 68.74, 74.98 (C-1′, C-2); 72.84 (C-1); 126.97, 127.68, 130.70, 138.56 (arom. C); *m*/*z* 260 (100%) [MH^+].

(2*S*,1′*R*,5′*R*)-(+)-2-(2′-Azabicyclo[3.3.0]octan-2′-yl)-1,1,2-triphenylethanol 9c. Synthesis according to GP 3. Work-up: column chromatography; eluent: *n*-hexane–ethyl acetate 8 : 2, R_f 0.71; yield 1.26 g (66%) as colorless crystals, mp 134 °C (Found: C 84.22, H 7.68, N 3.61. Calc. for $C_{27}H_{29}NO$: C 84.55, H 7.62, N 3.65%); $[a]_D^{20}$ +110.3 (*c* 1.02, CH_2Cl_2); ν_{max} (KBr)/cm^{-1} 3500–3300, 1600, 1490; δ_H (300 MHz, $CDCl_3$) 0.99–1.59 (7H, m, 4′-H, 6′-H_2, 7′-H_2, 8′-H_2), 1.72 (1H, m, 4′-H), 2.27–2.36 (3H, m, 5′-H, 3′-H_2), 2.98 (1H, m, 1′-H), 4.88 (1H, s, 2-H), 6.18 (1H, br s, OH), 6.87–6.96, 7.41–7.82 (15H, 2m, arom. H); δ_C (75 MHz, $CDCl_3$) 25.03, 31.74, 32.84, 33.07 (C-4′, C-6′, C-7′, C-8′), 41.82 (C-5′), 54.87 (C-3′), 66.91 (C-1′), 75.19 (C-2), 78.06 (C-1), 125.19, 126.05, 126.78, 127.21, 127.33, 128.05, 128.73, 131.26, 131.26, 139.29, 146.50, 150.23 (arom. C); *m*/*z* 384 (38%) [MH^+], 200 (100) [M^+ − $C(Ph)_2OH$].

(1′*S*,1″*R*,5″*R*)-(+)-1-[Phenyl(2″-azabicyclo[3.3.0]octan-2″-yl)methyl]cyclopentanol 9d. Synthesis according to GP 3. Work-up: column chromatography; eluent: *n*-hexane–ethyl acetate 1 : 1, R_f 0.58; yield 0.73 g (51%) as colorless oil (Found: C 80.02, H 9.52, N 4.88. Calc. for $C_{19}H_{27}NO$: C 79.95, H 9.53, N 4.91%); $[a]_D^{20}$ +3.6 (*c* 1.03, CH_2Cl_2); ν_{max} (NaCl)/cm^{-1} 3500–3100, 1460; δ_H (300 MHz, $CDCl_3$) 1.12–1.78, 1.83–2.04 (16H, 2m, 2-H_2, 3-H_2, 4-H_2, 5-H_2, 4″-H, 5″-H, 6″-H_2, 7″-H_2, 8″-H_2), 2.48 (2H, m, 4″-H, 3″-H), 2.98 (1H, m, 3 -H), 3.47 (1H, m, 1 -H), 3.56 (1H, s, 1′-H), 5.13 (1H, br s, OH), 7.21–7.47 (2m, 5H, arom. H); δ_C (75 MHz, $CDCl_3$) 23.21, 24.44, 25.34, 32.89 (C-4″, C-6″, C-7″, C-8″), 31.71, 31.95, 42.14, 42.52 (C-2, C-3, C-4, C-5), 39.22 (C-5″), 54.37 (C-3″), 68.14, 75.53 (C-1′, C-1), 82.92 (C-1), 127.25, 127.65, 130.14, 140.34 (arom. C); *m*/*z* 286 (92%) [MH^+], 200 (70) [$C_{14}H_{18}N$], 175 (100) [$C_{12}H_{15}O$].

(2*R*,1′*R*,5′*R*)-(−)-2-(2′-Azabicyclo[3.3.0]octan-2′-yl)-2-phenylethanol 10a. Synthesis according to GP 2. Work-up: column chromatography, eluent: *n*-hexane–ethyl acetate 1 : 1, R_f 0.26; yield 0.57 g (82%) as colorless oil; $[a]_D^{20}$ −49.7 (*c* 1.08, EtOH) [lit.[12] $[a]_D^{25}$ −56.2 (*c* 1.01, EtOH)]; the spectral data are in complete accord with those described in the literature.[12]

(2*R*,1′*R*,5′*R*)-(−)-2-(2′-Azabicyclo[3.3.0]octan-2′-yl)-2-phenylethanol 10a. Synthesis according to GP 7. Work-up: column chromatography, eluent: *n*-hexane–ethyl acetate 1 : 1, R_f 0.58; yield 0.27 g (16%) as colorless oil; $[a]_D^{22}$ −69.3 (*c* 0.98, CH_2Cl_2); $[a]_D^{20}$ −50.2 (*c* 1.0, EtOH); the analytical data are in accord with those described in the literature.[12]

(2*R*,1′*R*,5′*R*)-(−)-2-(2′-Azabicyclo[3.3.0]octan-2′-yl)-1,1-dimethyl-2-phenylethanol 10b. Synthesis according to GP 3. Work-up: column chromatography; eluent: *n*-hexane–ethyl acetate 8:2, R_f 0.63; yield 0.76 g (59%) as colorless oil (Found: C 78.49, H 9.80, N 5.41. Calc. for $C_{17}H_{25}NO$: C 78.72, H 9.71, N 5.40%); $[\alpha]_D^{20}$ −102.3 (*c* 1.04, CH_2Cl_2); ν_{max} (NaCl)/cm^{-1} 3300, 1490; δ_H (300 MHz, $CDCl_3$) 1.14, 1.31 (6H, 2s, $2CH_3$), 1.21–1.70 (7H, m, 4′-H, 6′-H_2, 7′-H_2, 8′-H_2), 1.81–1.95 (2H, m, 3′-H, 4′-H), 2.24 (1H, m, 3′-H), 2.96 (1H, m, 5′-H), 3.16 (1H, m, 1′-H), 3.63 (1H, s, 2-H), 3.92 (1H, br s, OH), 7.33 (5H, m, arom. H); δ_C (75 MHz, $CDCl_3$) 23.76, 26.97, 28.98, 31.89, 32.25, 33.21 (2 × CH_3, C-4′, C-6′, C-7′, C-8′), 39.92 (C-5′), 50.10 (C-3′), 67.49 (C-1′), 71.79 (C-1), 73.61 (C-2), 127.14, 127.51, 131.21, 134.53 (arom. C); *m*/*z* 260 (100%) [MH$^+$].

(2*R*,1′*R*,5′*R*)-(−)-2-(2′-Azabicyclo[3.3.0]octan-2′-yl)-1,1,2-triphenylethanol 10c. Synthesis according to GP 3. Work-up: column chromatography; eluent: *n*-hexane–triethylamine 9:1, R_f 0.21; yield 1.36 g (71%) as colorless crystals, mp 142 °C (Found: C 84.49, H 7.42, N 3.80. Calc. for $C_{27}H_{29}NO$: C 84.56, H 7.62, N 3.65%); $[\alpha]_D^{20}$ −16.7 (*c* 1.01, CH_2Cl_2); $[\alpha]_D^{20}$ −12.5 (*c* 1.1, $CHCl_3$); ν_{max} (KBr)/cm^{-1} 3550, 1450; δ_H (300 MHz, $CDCl_3$) 1.09–1.66 (7H, m, 4′-H, 6′-H_2, 7′-H_2, 8′-H_2), 1.80 (1H, m, 4′-H), 2.08 (1H, m, 3′-H), 2.21 (1H, m, 3′-H), 2.60 (1H, m, 5′-H), 3.20 (1H, m, 1′-H), 4.68 (1H, s, 2-H), 5.88 (1H, br s, OH), 7.00–7.33 (13H, m, arom. H), 7.70–7.73 (2H, m, arom. H); δ_C (75 MHz, $CDCl_3$) 24.6, 30.4, 32.3, 33.3 (C-4′, C-6′, C-7′, C-8′ or C-6′), 40.3 (C-5′), 50.5 (C-3′), 67.9 (C-1′), 72.7 (C-2), 78.6 (C-1), 125.8, 126.1, 126.4, 126.9, 127.0, 127.1, 127.2, 127.8, 131.3, 137.0, 145.9, 148.9 (arom. C); *m*/*z* 384 (38%) [MH$^+$], 200 (100) [$C_{14}H_{18}N^+$].

(2*R*,1′*R*,5′*R*)-(+)-2-(2′-Azabicyclo[3.3.0]octan-2′-yl)-1,1,2-triphenylethanol 10c. Synthesis according to GP 6. Work-up: recrystallization from ethyl acetate–petroleum ether (40–60 °C) 1:1; yield 0.67 g (68%) as colorless needles, mp 159 °C; $[\alpha]_D^{23}$ −11.9 (*c* 1.0, $CHCl_3$); the spectral characteristics are in accord with **10c** synthesized by GP 3.

(1′*R*,1″*R*,5″*R*)-(−)-1-[Phenyl(2″-azabicyclo[3.3.0]octan-2″-yl)methyl]cyclopentanol 10d. Synthesis according to GP 3. Work-up: column chromatography; eluent: toluene–ethyl acetate 3:7, R_f 0.56; yield 0.61 g (43%) as colorless oil (Found: C 79.72, H 9.53, N 4.88. Calc. for $C_{19}H_{27}NO$: C 79.75, H 9.53, N 4.91%); $[\alpha]_D^{20}$ −80.4 (*c* 0.46, CH_2Cl_2); ν_{max} (NaCl)/cm^{-1} 3400–3200, 1480; δ_H (300 MHz, $CDCl_3$) 1.26–1.97 (16H, m, 2-H_2, 3-H_2, 4-H_2, 5-H_2, 4″-H, 5″-H, 6″-H_2, 7″-H_2, 8″-H_2), 2.27 (1H, m, 4″-H), 2.39 (1H, m, 3″-H), 2.99 (2H, m, 3″-H, 1″-H), 3.76 (1H, s, 1′-H), 7.33 (5H, m, arom. H); δ_C (75 MHz, $CDCl_3$) 22.92, 24.02, 24.24, 33.36 (C-4″, C-6″, C-7″, C-8″), 31.62, 32.34, 37.36, 39.50 (C-2, C-3, C-4, C-5), 40.43 (C-5″), 49.84 (C-3″), 66.74, 71.27 (C-1′, C-1″), 82.87 (C-1), 127.13, 127.57, 131.13, 136.09 (arom. C); *m*/*z* 286 (96%) [MH$^+$], 200 (78) [$C_{14}H_{18}N^+$], 175 (100) [$C_{12}H_{15}O$].

(1′*R*,5′*R*)-(−)-2-(2′-Azabicyclo[3.3.0]octan-2′-yl)ethanol 11a. Synthesis according to GP 2. Work-up: short-path distillation, $bp_{(24\ mbar)}$ 120 °C; yield 0.41 g (88%) as colorless oil (Found: C 69.53, H 10.86, N 8.97. Calc. for $C_9H_{17}NO$: C 69.63, H 11.04, N 9.02%); $[\alpha]_D^{20}$ −60.6 (*c* 1.41, $CHCl_3$); ν_{max} (NaCl)/cm^{-1} 3600–3100; δ_H (300 MHz, $CDCl_3$) 1.29–1.67 (7H, m, 4′-H, 6′-H_2, 7′-H_2, 8′-H_2), 1.94–2.18 (2H, m, 4′-H, 5′-H), 2.46–2.59 (2H, m, 2-H_2), 2.77–2.91 (2H, m, 3′-H_2), 2.96–3.02 (1H, m, 1′-H), 3.41 (1H, br s, OH), 3.54–3.67 (2H, m, 1-H_2); δ_C (75 MHz, $CDCl_3$) 24.03, 32.15, 32.30, 33.04 (C-4′, C-6′, C-7′, C-8′), 41.72 (C-5′), 53.89 (C-3′), 56.51 (C-1′), 59.30 (C-1), 69.79 (C-2); *m*/*z* 157 (100%) [MH$^+$].

(1′*R*,5′*R*)-(−)-2-(2′-Azabicyclo[3.3.0]octan-2′-yl)-1,1-dimethylethanol 11b. Synthesis according to GP 3. Work-up: short-path distillation, $bp_{(0.02\ mbar)}$ 60 °C; yield 0.77 g (85%) as colorless oil (Found: C 71.97, H 11.49, N 7.66. Calc. for $C_{11}H_{21}NO$: C 72.08, H 11.55, N 7.64%); $[\alpha]_D^{20}$ −73.7 (*c* 1.67, CH_2Cl_2); ν_{max} (NaCl)/cm^{-1} 3300–3100; δ_H (300 MHz, $CDCl_3$) 1.15, 1.17 (6H, 2s, $2CH_3$), 1.32–1.67 (7H, m, 4′-H, 6′-H_2, 7′-H_2, 8′-H_2), 1.98 (1H, m, 4′-H), 2.32 (1H, m, 5′-H), 2.39 (1H, d, *J* 13.2, 2′-H), 2.48 (1H, m, 1′-H), 2.59 (1H, d, *J* 13.2, 2′-H), 3.08, 3.12 (2H, 2m, 3′-H_2), 3.26 (1H, br s, OH); δ_C (75 MHz, $CDCl_3$) 28.31, 29.05 ($2CH_3$), 23.93, 32.39, 33.10, 33.66 (C-4′, C-6′, C-7′, C-8′), 40.84 (C-5′), 56.67 (C-3′), 65.97 (C-2), 68.59 (C-1), 71.87 (C-1′); *m*/*z* 184 (100%) [MH$^+$].

(1′*R*,5′*R*)-(−)-2-(2′-Azabicyclo[3.3.0]octan-2′-yl)-1,1-diphenylethanol 11c. Synthesis according to GP 3. Work-up: recrystallization from diethyl ether–*n*-hexane; mp 83 °C; yield 1.01 g (66%) as slightly yellow solid (Found: C 82.01, H 8.20, N 4.59. Calc. for $C_{21}H_{25}NO$: C 82.05, H 8.20, N 4.56%); $[\alpha]_D^{20}$ −11.4 (*c* 1.20, CH_2Cl_2); ν_{max} (KBr)/cm^{-1} 3500–3300, 1590, 1470; δ_H (300 MHz, $CDCl_3$) 1.17–1.78 (7H, m, 4′-H, 6′-H_2, 7′-H_2, 8′-H_2), 1.83–2.01 (2H, m, 4′-H, 5′-H), 2.29 (1H, m, 3′-H), 2.47 (1H, m, 1′-H), 3.12 (1H, m, 3′-H), 3.35 (1H, d, *J* 12.6, 2-H), 3.52 (1H, d, *J* 12.7, 2-H), 5.06 (1H, br s, OH), 7.18–7.39, 7.53–7.67 (10H, 2m, arom. H); δ_C (75 MHz, $CDCl_3$) 23.85, 32.14, 32.95, 33.52 (C-4′, C-6′, C-7′, C-8′), 40.67 (C-5′), 54.89 (C-3′), 64.80 (C-2), 71.05 (C-1′), 73.93 (C-1), 125.46, 125.84, 126.32, 126.54, 127.89, 128.05, 147.28 (arom. C), *m*/*z* (100%) [MH$^+$].

(1″*R*,5″*R*)-(−)-1-[Phenyl(2″-azabicyclo[3.3.0]octan-2″-yl)methyl]cyclopentanol 11d. Synthesis according to GP 3. Work-up: short-path distillation, $bp_{(0.02\ mbar)}$ 90 °C; yield 0.85 g (81%) as yellow oil (Found: C 74.49, H 11.11, N 6.65. Calc. for $C_{13}H_{23}NO$: C 74.59, H 11.07, N 6.69%); $[\alpha]_D^{20}$ −69.6 (*c* 2.32, CH_2Cl_2); ν_{max} (NaCl)/cm^{-1} 3500–3100; δ_H (300 MHz, $CDCl_3$) 1.24–1.89 (15H, m, 2-H_2, 3-H_2, 4-H_2, 5-H_2, 4″-H, 6″-H_2, 7″-H_2, 8″-H_2), 2.01 (1H, m, 4″-H), 2.23 (1H, m, 5″-H), 2.36 (1H, d, *J* 12.7, 1′-H), 2.48 (1H, m, 1″-H), 2.84 (1H, d, *J* 12.7, 1′-H), 2.98–3.11 (2H, m, 3″-H); δ_C (75 MHz, $CDCl_3$) 23.48, 23.88, 24.70, 32.35, 33.00, 33.61, 39.03, 40.42 (C-2, C-3, C-4, C-5, C-4″, C-5″, C-6″, C-7″), 41.02 (C-5″), 55.55 (C-3″), 63.75 (C-2′), 71.01 (C-1″), 78.99 (C-1); *m*/*z* 210 (100%) [MH$^+$].

(4*S*,8*R*,11*S*)-(+)-11-Methyl-9-oxa-1-azatricyclo[6.3.0.0^{4,8}]-undecan-2-one 14a.§ Synthesis according to GP 4. Work-up: column chromatography, eluent: ethyl acetate–petroleum ether (40–60 °C) 1:4, R_f 0.20; yield 3.07 g (85%) as colorless oil (Found: C 65.81, H 8.23, N 7.24. Calc. for $C_{10}H_{15}NO_2$: C 66.29, H 8.34, N 7.73%); $[\alpha]_D^{20}$ +91.4 (*c* 1.0, EtOH); ν_{max} (NaCl)/cm^{-1} 3492, 2964, 2870, 1710, 1357, 1330, 1228, 1207, 1030; δ_H (300 MHz, $CDCl_3$) 1.21 (3H, d, *J* 6.6, CH_3), 1.44 (1H, m, 5-H), 1.66–1.76 (3H, m, 6-H_2, 7-H), 1.87–1.94 (2H, m, 5-H, 7-H), 2.29 (1H, dd, *J* 6.9 and 17.5, 3-H), 2.53 (1H, m, 4-H), 2.68 (1H, dd, *J* 10.5 and 17.5, 3-H), 3.53 (1H, dd, *J* 7.0 and 8.1, 10-H), 4.07 (1H, ddq, *J* 6.6, 6.7 and 7.0, 11-H), 4.16 (1H, dd, *J* 6.7 and 8.1, 10-H); δ_C (75 MHz, $CDCl_3$) 19.7 (CH_3), 24.6 (C-6), 32.0 (C-5), 37.6 (C-7), 40.4 (C-3), 41.7 (C-4), 50.3 (C-11), 73.6 (C-10), 110.1 (C-8), 179.5 (C-2); *m*/*z* 152 (100%) [$C_9H_{14}NO^+$], 181 (24) [M$^+$].

(4*S*,8*R*,11*S*)-(−)-11-Methyl-10,10-diphenyl-9-oxa-1-azatricyclo[6.3.0.0^{4,8}]undecan-2-one 14c. Synthesis according to GP 4. Work-up: recrystallization from petroleum ether (40–60 °C); yield 4.83 g (72%) as yellow solid, mp 162 °C (Found: C 79.13, H 6.94, N 4.11. Calc. for $C_{22}H_{23}NO_2$: C 79.26, H 6.95, N 4.20%); $[\alpha]_D^{20}$ −128.3 (*c* 1.0, EtOH); ν_{max} (NaCl)/cm^{-1} 3438, 2969, 2951, 1711, 1449, 1360, 1332, 1227, 1193, 1013, 963, 748, 707; δ_H (300 MHz, $CDCl_3$) 0.95 (3H, d, *J* 7.0, CH_3), 1.48 (1H, m,

§ The IUPAC name for **14a** is (1*R*,4*S*,8*S*)-(+)-4-methyl-2-oxa-5-azatricyclo[6.3.0.0.^{1,5}]undecan-6-one. Compounds **14c**, **14d**, **14f** and **14g** can be named similarly using IUPAC rules.

5-H), 1.60 (1H, m, 6-H), 1.84–1.92 (2H, m, 5-H, 6-H), 2.02 (1H, d, *J* 10.2, 3-H), 2.02 (1H, d, *J* 8.3, 3-H), 2.13 (1H, m, 7-H), 2.17 (1H, m, 7-H), 2.38 (1H, dddd, *J* <2, 7.4, 8.3 and 10.2, 4-H), 5.30 (1H, q, *J* 7.0, 11-H), 7.17–7.36 (8H, m, arom. H), 7.50–7.66 (2H, m, arom. H); δ_C (75 MHz, $CDCl_3$) 16.4 (CH_3), 23.4 (C-6), 31.5 (C-5), 39.0 (C-3), 41.4 (C-7), 43.3 (C-4), 56.7 (C-11), 91.2 (C-10), 109.6 (C-8), 125.9, 126.8, 126.9, 127.5, 128.0, 128.1, 142.0, 143.4 (arom. C), 179.0 (s, C-2); *m*/*z* 151 (100%) [$C_9H_{13}NO^+$]; (field desorption, FD): *m*/*z* [$C_9H_{13}NO^+$], 333 (1) [M^+].

(4*S*,8*R*,11*S*)-(+)-Spiro[cyclopentane-1,10′-11′-methyl-9′-oxa-1′-azatricyclo[6.3.0.0^{4,8}]undecan]-2′-one 14d. Synthesis according to GP 4. Work-up: twofold column chromatography, eluent: diethyl ether–petroleum ether (40–60 °C) 1:1, R_f 0.15; ethyl acetate–petroleum ether (40–60 °C) 1:1, R_f 0.63; yield 0.87 g (19%) pale yellow oil; $[\alpha]_D^{23}$ +33.8 (*c* 1.0, EtOH); ν_{max} (neat)/cm^{-1} 3058, 3032, 2943, 2861, 1493, 1448, 1382, 1327, 1178, 1130, 1099, 1031, 759, 701; δ_H (300 MHz, $CDCl_3$) 1.15 (3H, d, *J* 7.1, CH_3), 1.32–1.88, 1.90–1.99 (14H, 2m, 5-H_2, 6-H_2, 7-H_2, CH_2CH_2CH_2CH_2), 2.17 (1H, dd, *J* 7.7 and 17.1, 3-H), 2.49 (1H, m, 4-H), 2.65 (1H, dd, *J* 10.5 and 17.1, 3-H), 4.05 (1H, q, *J* 7.1, 11-H); δ_C (75 MHz, $CDCl_3$) 15.8 (CH_3), 23.0, 23.2, 23.8, 31.4, 32.6, 38.4 (C-5, C-6, *C*H_2*C*H_2*C*H_2*C*H_2), 39.6 (C-3), 40.8 (C-7), 44.5 (C-4), 58.0 (C-11), 94.6 (C-10), 108.7 (C-8), 179.3 (C-2); *m*/*z* 56 (100%), 138 (59) [$C_9H_{16}N^+$]; (FD): *m*/*z* 138 (100%) [$C_9H_{16}N^+$].

(4*S*,8*R*,11*S*)-(+)-11-Benzyl-9-oxa-1-azatricyclo[6.3.0.0^{4,8}]-undecan-2-one 14f. Synthesis according to GP 4. Work-up: column chromatography, eluent: ethyl acetate–petroleum ether (40–60 °C) 1:3, R_f 0.45; yield 4.13 g (81%) as yellow needles, mp 26–28 °C (Found: C 74.84, H 7.70, N 5.35. Calc. for $C_{16}H_{19}NO_2$: C 74.69, H 7.44, N 5.44%); $[\alpha]_D^{20}$ +66.8 (*c* 1.0, EtOH); ν_{max} (KBr)/cm^{-1} 2979, 2951, 1704, 1453, 1346, 1300, 1213, 1160, 1079, 1052, 733, 724; δ_H (300 MHz, $CDCl_3$) 1.42 (1H, m, 5-H), 1.60–1.74 (4H, m, 6-H_2, 7-H_2), 1.85–1.91 (1H, m, 5-H), 2.27 (1H, dd, *J* 6.8 and 17.1, 3-H), 2.52 (1H, m, 4-H), 2.67 (1H, dd, *J* 10.3 and 17.1, 3-H), 2.70 (1H, dd, *J* 8.8 and 13.7, CH_2Ph), 3.02 (1H, dd, *J* 5.6 and 13.7, CH_2Ph), 3.68 (1H, dd, *J* 6.7 and 8.6, 10-H), 3.95 (1H, dd, *J* 7.3 and 8.6, 10-H), 4.25 (1H, m, 11-H), 7.12–7.24 (5H, m, arom. H); δ_C (75 MHz, $CDCl_3$) 24.5 (C-6), 32.0 (C-5), 37.4 (C-7), 39.6 (*C*H_2Ph), 40.3 (C-3), 41.9 (C-4), 55.7 (C-11), 71.4 (C-10), 110.2 (C-8), 126.5, 128.3, 129.1, 136.9 (arom. C), 179.6 (C-2); *m*/*z* 166 (100%) [$C_9H_{12}NO_2^+$], 257 (36) [M^+].

(4*S*,8*R*,11*S*)-(−)-11-Benzyl-10,10-diphenyl-9-oxa-1-aza-tricyclo[6.3.0.0^{4,8}]undecan-2-one 14g. Synthesis according to GP 4. Work-up: twofold column chromatography, eluent: ethyl acetate–petroleum ether (40–60 °C) 1:5, R_f 0.18, ethyl acetate–petroleum ether (40–60 °C) 1:3, R_f 0.77; yield 1.19 g (15%) as colorless needles, mp 146 °C (Found: C 81.90, H 6.59, N 3.33. Calc. for $C_{28}H_{27}NO_2$: C 82.13, H 6.65, N 3.42%); $[\alpha]_D^{20}$ −96.3 (*c* 1.0, EtOH); ν_{max} (KBr)/cm^{-1} 3483, 3416, 3073, 3031, 2937, 1718, 1639, 1618, 1449, 1351, 762, 701; δ_H (300 MHz, $CDCl_3$) 1.40–1.63, 1.79–1.94 (4H, 2m, 5-H_2, 6-H_2), 1.96 (1H, d, *J* 9.0, 3-H), 1.97 (1H, d, *J* 9.6, 3-H), 2.11–2.30 (2H, m, 7-H_2), 2.36–2.44 (1H, m, 4-H), 2.42 (1H, dd, *J* 4.9 and 15.1, CH_2Ph), 2.60 (1H, dd, *J* 11.3 and 15.1, CH_2Ph), 5.53 (1H, dd, *J* 4.9 and 11.3, 11-H), 7.18–7.30 (13H, m, arom. H), 7.54–7.56 (2H, m, arom. H); δ_C (75 MHz, $CDCl_3$) 23.5 (C-6), 31.5 (C-5), 35.3 (*C*H_2Ph), 39.0 (C-3), 40.7 (C-7), 43.4 (C-4), 61.6 (C-11), 91.1 (C-10), 109.7 (C-8), 126.1, 127.0, 127.6, 128.1, 128.2, 128.3, 128.6, 138.0, 141.7, 143.3 (arom. C), 178.9 (s, C-2); *m*/*z* 227 (100%) [$C_{15}H_{27}NO^+$], 409 (0.3) [M^+]; (FD): *m*/*z* 409 (100%) [M^+].

(2*S*,1′*S*,5′*S*)-(+)-2-(2′-Azabicyclo[3.3.0]octan-2′-yl)propan-1-ol 15a. Synthesis according to GP 5. Work-up: short-path distillation: $bp_{(0.02\ mbar)}$ 75 °C; yield 2.42 g (85%) colorless oil; $[\alpha]_D^{20}$ +44.3 (*c* 1.0, EtOH); the spectral characteristics are in accord with **8a**.

(1*R*,2*S*,1′*S*,5′*S*)-(+)-2-(2′-Azabicyclo[3.3.0]octan-2′-yl)-1-phenylpropanol 15b. Synthesis according to GP 6 starting from the known lactam **14b**.[9] After the reduction of the *N,O*-acetal, **15b** was obtained analytically pure without further purification. Yield 0.25 g (40%) (Found: C 77.13, H 9.44, N 5.75. Calc. for $C_{16}H_{23}NO$: C 78.31, H 9.45, N 5.71%); $[\alpha]_D^{20}$ +41.1 (*c* 1.0, EtOH); ν_{max} (neat)/cm^{-1} 3438, 2948, 2861, 2811, 1450, 1196, 1062, 1026, 751, 701; δ_H (300 MHz, $CDCl_3$) 0.78 (3H, d, *J* 6.7, CH_3), 1.20–1.62 (7H, m, 4′-H, 6′-H_2, 7′-H_2, 8′-H_2), 1.82 (1H, m, 4′-H), 2.32 (1H, m, 3′-H), 2.46 (1H, m, 5′-H), 2.63 (1H, m, 3′-H), 2.72 (1H, dq, *J* 3.9 and 6.7, 2-H), 3.11 (1H, m, 1′-H), 3.69 (1H, br s, OH), 4.76 (1H, d, *J* 3.9, 1-H), 7.12–7.25 (5H, m, arom. H); δ_C (75 MHz, $CDCl_3$) 11.1 (CH_3), 24.5 (C-7′), 32.0 (C-4′), 32.7, 33.0 (C-8′, C-6′), 42.0 (C-5′), 50.7 (C-3′), 63.1 (C-2), 68.5 (C-1′), 73.3 (C-1), 126.1, 126.7, 127.8, 142.1 (arom. C); *m*/*z* 138 (100%) [$C_9H_{16}N^+$].

(2*S*,1′*S*,5′*S*)-(+)-2-(2′-Azabicyclo[3.3.0]octan-2′-yl)-1,1-diphenylpropan-1-ol 15c. Synthesis according to GP 6. Work-up: column chromatography, eluent: ethyl acetate–petroleum ether (40–60 °C) 1:3, R_f 0.44; yield 0.50 g (61%) as yellow oil; $[\alpha]_D^{22}$ +35.7 (*c* 1.0, EtOH); the spectral characteristics are in accord with **8c**.

(1′*S*,1″*S*,5″*S*)-(+)-1-[1′-(2″-Azabicyclo[3.3.0]octan-2″-yl)-ethyl]cyclopentanol 15d. Synthesis according to GP 6. Work-up: column chromatography, eluent: ethyl acetate–petroleum ether (40–60 °C) 1:3, R_f 0.10; yield 0.15 g (26%) as slightly yellow oil; $[\alpha]_D^{25}$ +44.8 (*c* 1.0, EtOH); the spectral characteristics are in accord with **8d**.

(2*S*,1′*S*,5′*S*)-(+)-2-(2′-Azabicyclo[3.3.0]octan-2′-yl)-3-methylbutanol 15e. Synthesis according to GP 5. Work-up: column chromatography, eluent: ethyl acetate–petroleum ether (40–60 °C) 1:1, R_f 0.06; yield 2.70 g (81%) as slightly yellow oil (Found: C 72.94, H 11.62, N 7.38. Calc. for $C_{12}H_{23}NO$: C 73.05, H 11.75, N 7.10%); $[\alpha]_D^{23}$ +35.8 (*c* 1.0, EtOH); ν_{max} (neat)/cm^{-1} 3440, 2951, 2863, 1466, 1450, 1385, 1232, 1166, 1130, 1080, 1013; δ_H (300 MHz, $CDCl_3$) 0.78 (3H, d, *J* 6.7, CH_3), 0.95 (3H, d, *J* 6.7, CH_3), 1.18–1.24, 1.40–1.54 (7H, 2m, 4′-H, 6′-H_2, 7′-H_2, 8′-H_2), 1.81 (1H, m, 3-H), 1.91 (1H, ddd, *J* 3.6, 6.6 and 11.6, 4′-H), 2.44–2.52 (3H, m, 2-H, 3′-H, 5′-H), 2.69 (1H, dd, *J* 7.4 and 8.0, 3′-H), 3.08 (1H, dd, *J* 9.9 and 10.5, 1-H), 3.46 (1H, dd, *J* 5.2 and 9.9, 1-H), 3.40–3.49 (2H, br s, 1′-H, OH); δ_C (75 MHz, $CDCl_3$) 19.6 (CH_3), 22.4 (CH_3′), 23.4 (C-7′), 28.1 (C-3), 32.1, 32.7, 33.0 (C-4′, C-6′, C-8′), 41.5 (C-5′), 44.9 (C-3′), 59.3 (C-1), 63.7 (C-2), 66.7 (C-1′); MS (EI): *m*/*z* 154 (100%) [$C_9H_{14}NO^+$], 197 (2) [M^+].

(2*S*,1′*S*,5′*S*)-(+)-2-(2′-Azabicyclo[3.3.0]octan-2′-yl)-3-phenylpropan-1-ol 15f. Synthesis according to GP 5. Work-up: column chromatography, eluent: ethyl acetate–petroleum ether (40–60 °C) 2:3, R_f 0.21; yield 3.91 g (94%) as orange oil (Found: C 78.12, H 9.41, N 5.87. Calc. for $C_{16}H_{23}NO$: C 78.31, H 9.45, N 5.71%); $[\alpha]_D^{21}$ +32.2 (*c* 1.0, EtOH); ν_{max} (neat)/cm^{-1} 3432, 3026, 2942, 2860, 1494, 1450, 1411, 1326, 1232, 1161, 1128, 1071, 750, 703; δ_H (300 MHz, $CDCl_3$) 1.26–1.44, 1.45–1.61 (7H, 2m, 4′-H, 6′-H_2, 7′-H_2, 8′-H_2), 1.99 (1H, ddd, *J* 5.5, 9.2 and 12.0, 4′-H), 2.36 (1H, dd, *J* 10.1 and 13.1, 3-H), 2.43 (1H, ddd, *J* 5.5, 8.6 and 11.2, 3′-H), 2.50 (1H, m, 5′-H), 2.80 (1H, dd, *J* 6.6 and 8.6, 3′-H), 2.92 (1H, dd, *J* 3.7 and 13.1, 3-H), 2.99 (1H, m, 2-H), 3.24 (1H, dd, *J* 10.0 and 10.1, 1-H), 3.27 (1H, m, 1′-H), 3.37 (1H, d, *J* 4.7 and 10.1, 1-H), 3.54 (1H, br s, OH), 6.94–7.27 (5H, m, arom. H); δ_C (75 MHz, $CDCl_3$) 23.8 (C-7′), 31.9, 32.2, 32.6, 33.2 (C-3, C-4′, C-6′, C-8′), 41.7 (C-5′),

45.4 (C-3′), 60.9 (C-1), 61.3 (C-2), 65.4 (C-1′), 126.0, 128.4, 128.9, 139.4 (arom. C); *m*/*z* 245 (100%) [M^+], 736 (11) [$3M^+$].

(2*S*,1′*S*,5′*S*)-(+)-2-(2′-Azabicyclo[3.3.0]octan-2′-yl)-1,1,3-triphenylpropan-1-ol 15g. Synthesis according to GP 6. Work-up: column chromatography, eluent: ethyl acetate–petroleum ether (40–60 °C) 1 : 3, R_f 0.90; yield 5.73 g (87%) as colorless oil; $[\alpha]_D^{22}$ +81.6 (*c* 1.0, EtOH); ν_{max} (neat)/cm^{-1} 3244, 3086, 3059, 2938, 1494, 1447, 1278, 1162, 1047, 1031, 909, 733, 701; δ_H (300 MHz, $CDCl_3$) 1.06–1.23, 1.33–1.42, 1.43–1.68, 1.88 (7H, 3m, dd, *J* 4.9 and 12.9, 4′-H, 6′-H_2, 7′-H_2, 8′-H_2), 1.76 (1H, ddd, *J* 5.3, 9.1 and 12.0, 4′-H), 2.02–2.18 (2H, m, 3′-H, 5′-H), 2.49 (1H, ddd, *J* 5.3, 8.9 and 11.3, 3′-H), 2.70 (1H, dd, *J* 6.3 and 7.7, 1′-H), 2.90 (1H, dd, *J* 11.3 and 14.4, 3-H), 3.20 (1H, dd, *J* 1.7 and 14.4, 3-H′), 4.18 (1H, dd, *J* 1.7 and 11.3, 2-H), 6.05 (1H, br s, OH), 7.00–7.38 (11H, m, arom. H), 7.57–7.64 (4H, m, arom. H); δ_C (75 MHz, $CDCl_3$) 23.4 (C-7′), 32.0, 32.1, 33.0 (C-4′, C-6′, C-8′), 34.0 (C-3), 40.6 (C-5′), 47.0 (C-3′), 68.3, 68.7 (C-2, C-1′), 77.6 (C-1), 126.2, 126.8, 127.2, 127.4, 128.1, 128.4, 128.5, 129.0, 140.7, 145.0, 145.7 (arom. C); MS (FD): *m*/*z* 182 (100%) [$C_{13}H_{10}O^+$], 398 (64) [M^+].

(4*R*,8*S*,11*R*)-(−)-10,10,11-Triphenyl-9-oxa-1-azatricyclo-[6.3.0.0^{4,8}]undecan-2-one 19. Synthesis according to GP 4. Work-up: recrystallization from ethyl acetate; yield 3.29 g (42%) as colorless crystals, mp 196 °C (Found: C 81.81, H 6.60, N 3.35. Calc. for $C_{27}H_{25}NO_2$: C 82.00, H 6.37, N 3.54%); $[\alpha]_D^{23}$ −11.5 (*c* 1.0, $CHCl_3$); ν_{max} (KBr)/cm^{-1} 3470, 3087, 3054, 2939, 1705, 1344, 1327, 1044, 723, 701; δ_H (300 MHz, $CDCl_3$) 1.48–1.59 (2H, m, 5-H, 6-H), 1.79–1.91 (2H, m, 5-H, 6-H), 2.05 (1H, d, *J* 9.5, 3-H), 2.05 (1H, d, *J* 9.5, 3-H), 2.11–2.24 (2H, m, 7-H_2), 2.55 (1H, dd, *J* 9.4 and 16.9, 4-H), 6.29 (1H, s, 11-H), 6.99–7.31 (13H, m, arom. H), 7.64–7.67 (2H, m, arom. H); δ_C (75 MHz, $CDCl_3$) 23.4 (C-6), 31.0 (C-5), 38.8 (C-3), 40.2 (C-7), 44.2 (C-4), 65.9 (C-11), 92.3 (C-10), 110.7 (C-8), 126.4, 126.5, 127.1, 127.5, 127.6, 128.3, 129.4, 136.6, 142.3, 144.0 (arom. C), 179.0 (C-2); *m*/*z* 213 (100%) [$C_{14}H_{15}NO^+$], 395 (1) [M^+]; (FD): *m*/*z* 395 (100%) [M^+].

(1*R*,1′*R*,5′*R*)-(−)-2-(2′-Azabicyclo[3.3.0]octan-2′-yl)-1-phenylethanol 21a. Synthesis according to GP 7. Work-up: column chromatography, eluent: *n*-hexane–ethyl acetate 1 : 1, R_f 0.61; yield 0.82 g (43%) as colorless oil (Found: C 77.86, H 9.30, N 5.98. Calc. for $C_{15}H_{21}NO$: C 77.87, H 9.14, N 6.05%); $[\alpha]_D^{22}$ −119.4 (*c* 1.61, CH_2Cl_2); ν_{max} (NaCl)/cm^{-1} 3550–3100, 1490, 1450; δ_H (300 MHz, $CDCl_3$) 1.20–1.71 (7H, m, 4′-H, 6′-H_2, 7′-H_2, 8′-H_2), 2.03 (1H, m, 4′-H), 2.14 (1H, m, 5′-H), 2.47 (1H, dd, *J* 3.3 and 12.1, 2-H), 2.52 (1H, m, 2-H), 2.68 (1H, dd, *J* 11.0 and 12.1, 3′-H), 2.93 (1H, dd, *J* 6.3 and 8.1, 3′-H), 3.18 (1H, m, 1′-H), 3.98 (1H, br s, OH), 4.63 (1H, dd, *J* 3.3 and 11.0, 1-H), 7.20–7.39 (5H, m, arom. H); δ_C (75 MHz, $CDCl_3$) 23.91, 32.25, 32.62, 33.52 (C-4′, C-6′, C-7′, C-8′), 41.39 (C-5′), 53.26, 63.08 (C-3′, C-2), 69.58, 69.85 (C-1, C-1′), 125.79, 127.30, 128.18, 142.37 (arom. C); *m*/*z* 232 (100%) [MH^+], 214 (18) [$MH^+ - H_2O$].

(1*S*,1′*R*,5′*R*)-(−)-2-(2′-Azabicyclo[3.3.0]octan-2′-yl)-1-phenylethanol 21b. Synthesis according to GP 7. Work-up: column chromatography, eluent: *n*-hexane–ethyl acetate 1 : 1, R_f 0.49; yield 0.67 g (35%) as colorless oil (Found: C 78.05, H 9.32, N 6.04. Calc. for $C_{15}H_{21}NO$: C 77.87, H 9.14, N 6.05%); $[\alpha]_D^{20}$ +7.3 (*c* 1.38, CH_2Cl_2); ν_{max} (NaCl)/cm^{-1} 3620–3160, 3020, 1490; δ_H (300 MHz, $CDCl_3$) 1.16–1.68 (7H, m, 4′-H, 6′-H_2, 7′-H_2, 8′-H_2), 1.86 (1H, m, 4′-H′), 2.36 (1H, m, 3′-H), 2.53 (1H, m, 5′-H), 2.64 (2H, d, *J* 6.7, 2-H_2), 2.72 (1H, m, 3′-H), 2.99 (1H, m, 1′-H), 3.92 (1H, br s, OH), 4.63 (1H, t, *J* 6.7, 1-H), 7.17–7.32 (5H, m, arom. H); δ_C (75 MHz, $CDCl_3$) 24.8 (C-7′), 32.4, 33.0, 33.0, (C-4′, C-6′, C-8′), 42.8 (C-5′), 55.9 (C-3′), 63.8 (C-2), 70.5 (C-1), 70.5 (C-1′), 125.7, 127.2, 128.2, 142.9 (arom. C); *m*/*z* 232 (100%) [MH^+], 214 (20) [$MH^+ - H_2O$].

Preparation of amino alcohol 21b by aziridinium ion ring-opening. Under argon atmosphere, β-amino alcohol **10a** (0.7 g, 3 mmol) was dissolved in Et_2O (10 ml) and cooled to 0 °C. First of all, triethylamine (0.61 g, 6 mmol), then methanesulfonyl chloride (0.52 g, 4.5 mmol) was added and the reaction mixture was vigorously stirred for 2 h at 0 °C. At this temperature, the solvent was evaporated under reduced pressure and the residue was dissolved in water (pH > 8). After stirring for 20 h at room temp. the mixture was extracted with Et_2O (3×) and the combined organic layers were dried ($MgSO_4$) and finally evaporated *in vacuo* to give the crude amino alcohol **21b** as a slightly yellow oil. Yield 0.53 g (77%); $[\alpha]_D^{26}$ −17.0 (*c* 1.15, EtOH); $[\alpha]_D^{26}$ +14.6 (*c* 1.0, CH_2Cl_2); further purification was not carried out.

(1*S*,1′*R*,5′*R*)-(+)-[2-(2′-Azabicyclo[3.3.0]octan-2′-yl)-1-phenylethyl]thioacetate 22. Synthesis according to GP 8. Work-up: further purification was not necessary; yield 0.84 g (97%) starting from **10a** and 0.64 g (73%) starting from **21a**, yellow oil (Found: C 70.38, H 8.10, N 5.05. Calc. for $C_{17}H_{23}NOS$: C 70.56, H 8.01, N 4.84%); $[\alpha]_D^{26}$ +83.0 (*c* 0.7, EtOH); ν_{max} (neat)/cm^{-1} 3062, 3028, 2949, 2861, 2811, 1692, 1494, 1452, 1354, 1132, 1103, 952, 696, 631; δ_H (300 MHz, $CDCl_3$) 1.20–1.50 (7H, m, 4′-H, 6′-H_2, 7′-H_2, 8′-H_2), 1.89 (1H, dddd, *J* 6.0, 12.1, 9.1 and <2, 4′-H), 2.19 (1H, ddd, *J* 6.0, 8.8 and 10.4, 3′-H), 2.27 (3H, s, CH_3), 2.43 (1H, m, 5′-H), 2.80 (1H, dd, *J* 6.2 and 12.6, 2-H), 2.89 (1H, m, 1′-H), 2.97 (1H, ddd, *J* 8.8, 6.1 and <2, 3′-H), 3.07 (1H, dd, *J* 9.6 and 12.6, 2-H), 4.71 (1H, dd, *J* 6.2 and 9.6, 1-H), 7.20–7.30 (5H, m, arom. H); δ_C (75 MHz, $CDCl_3$) 24.1 (C-7′), 30.4 (CH_3), 32.0, 32.3, 33.3 (C-4′, C-6′, C-8′), 41.8 (C-5′), 47.0 (C-1), 54.1 (C-3′), 59.7 (C-2), 69.8 (C-1′), 127.0, 127.9, 128.5, 140.8 (arom. C), 194.5 (C=O); *m*/*z* 124 (100%) [$C_8H_{14}N^+$].

(1*S*,1′*R*,5′*R*)-2-(2′-Azabicyclo[3.3.0]octan-2′-yl)-1-phenylethanethiol 23. Synthesis according to GP 9. Work-up: without further purification; yield 0.35 g (93%) as slightly yellow oil, highly sensitive to oxidation (contains 6% disulfide); ν_{max} (neat)/cm^{-1} 2949, 2861, 1493, 1452, 1254, 1258, 1225, 1165, 1125, 1092, 1061, 1028, 759, 698; δ_H (300 MHz, $CDCl_3$) 1.19–1.56 (7H, m, 4′-H, 6′-H_2, 7′-H_2, 8′-H_2), 1.83 (1H, m, 4′-H), 2.24 (1H, ddd, *J* 5.9 and 8.7, 10.2, 3′-H), 2.44 (1H, m, 5′-H), 2.75 (1H, dd, *J* 8.5 and 12.5, 2-H), 2.78–2.86 (2H, m, 1′-H, 3′-H), 2.82 (1H, dd, *J* 6.6 and 12.5, 2-H), 4.07 (1H, dd, *J* 6.6 and 8.5 Hz, 1-H), 7.10–7.29 (5H, m, arom. H); δ_C (75 MHz, $CDCl_3$) 24.5 (C-7′), 32.3, 32.6, 33.1 (C-4′, C-6′, C-8′), 42.5 (C-5′), 43.9 (C-3′), 55.2 (C-1), 64.1 (C-2), 70.2 (C-1′); *m*/*z* 42 (23%) (100) [$C_3H_6^+$], 124 (100) [$C_8H_{14}N^+$], 205 (5) [$C_{12}H_{15}NS^+$].

Bis[(1*S*,1′*R*,5′*R*)-(−)-2-(2′-azabicylo[3.3.0]octan-2′-yl)-1-phenylethyl] disulfide 24. Synthesis according to GP 10. Work-up: column chromatography, eluent: *tert*-butyl methyl ether, R_f 0.88; yield 0.33 g (88%) as yellow oil; $[\alpha]_D^{22}$ −1.5 (*c* 0.9, EtOH); ν_{max} (neat)/cm^{-1} 3027, 2948, 2861, 2806, 1493, 1452, 1356, 1258, 1224, 1165, 1125, 1098, 1074, 1029, 696; δ_H (300 MHz, $CDCl_3$) 1.00–1.42 (14H, m, 4′-H, 6′-H_2, 7′-H_2, 8′-H_2), 1.76 (2H, m, 4′-H), 1.96 (2H, ddd, *J* 5.9, 8.7 and 10.5, 3′-H), 2.32 (2H, m, 5′-H), 2.74 (2H, m, 1′-H), 2.80 (2H, dd, *J* 5.6 and 12.6, 2-H), 3.00 (2H, dd, *J* 9.8 and 12.6, 2-H), 3.53 (2H, dd, *J* 5.6 and 9.8, 1-H), 7.08–7.28 (10H, m, arom. H); δ_C (75 MHz, $CDCl_3$) 24.1, 32.0, 32.3, 33.3 (C-4′, C-6′, C-7′, C-8′), 41.8 (C-5′), 54.0 (C-1); 54.1 (C-3′), 58.6 (C-2), 69.8 (C-1′), 127.2, 128.1, 128.5, 140.5 (arom. C); *m*/*z* 124 (100%) [$C_8H_{14}N^+$], 214 (28) [$C_{15}H_{20}N^+$], 246 (16) [$C_{15}H_{20}NS^+$], 279 (11) [$C_{15}H_{21}NS_2^+$].

(2*S*,1′*S*,5′*S*)-(−)-[2-(2′-Azabicyclo[3.3.0]octan-2′-yl)propyl]-thioacetate 25a. Synthesis according to GP 8. Work-up: two-fold column chromatography, eluent: ethyl acetate–petroleum ether (40–60 °C) 1 : 1, R_f 0.25; ethyl acetate, R_f 0.23; yield 0.16 g (23%) as pale yellow oil (Found: C 62.82, H 9.41, N 6.36. Calc.

for $C_{12}H_{21}NOS$: C 63.38, H 9.31, N 6.16%); $[a]_D^{25}$ −29.6 (*c* 1.0, EtOH); ν_{max} (neat)/cm^{-1} 2950, 2862, 2812, 1690, 1375, 1353, 1171, 1135, 954, 631; δ_H (300 MHz, $CDCl_3$) 0.99 (3H, d, *J* 6.4, CH_3), 1.17–1.64 (7H, m, 4′-H, 6′-H_2, 7′-H_2, 8′-H_2), 1.82 (1H, m, 4′-H), 2.23 (3H, s, $COCH_3$), 2.28 (1H, ddd, *J* 5.6, 8.5 and 10.7, 3′-H), 2.41 (1H, m, 5′-H), 2.66–2.73 (2H, m, 2-H, 3′-H), 2.85 (1H, d, *J* 6.3 and 13.2, 1-H), 3.03 (1H, m, 1′-H), 3.04 (1H, dd, *J* 6.9 and 13.2, 1-H); δ_C (75 MHz, $CDCl_3$) 14.6 (CH_3), 24.2 (C-7′), 30.5 (CO*C*H_3), 31.9, 33.0, 33.2 (C-4′, C-6′, C-8′), 35.2 (C-1), 42.1 (C-5′), 48.4 (C-3′), 55.2 (C-2), 66.2 (C-1′), 196.3 (CO); *m*/*z* 138 (100%) [$C_9H_{16}N^+$].

(1*R*,2*S*,1′*S*,5′*S*)-(−)-[2-(2′-Azabicyclo[3.3.0]octan-2′-yl)-1-phenylpropyl]thioacetate 25b. Synthesis according to GP 8. Work-up: column chromatography, eluent: *tert*-butyl methyl ether, R_f 0.71; yield 0.80 g (88%) as yellow oil (Found: C 71.18, H 8.20, N 4.81. Calc. for $C_{18}H_{25}NOS$: C 71.23, H 8.30, N 4.62%); $[a]_D^{23}$ −177.8 (*c* 0.8, EtOH); ν_{max} (neat)/cm^{-1} 3084, 3061, 3027, 2950, 2860, 2830, 1694, 1374, 1352, 1130, 954, 697, 633; δ_H (300 MHz, $CDCl_3$) 0.88–1.36 (7H, m, 4′-H, 6′-H_2, 7′-H_2, 8′-H_2), 1.03 (3H, d, *J* 6.4, CH_3), 1.72 (1H, m, 4′-H), 2.22 (3H, s, $COCH_3$), 2.16–2.32 (2H, m, 3′-H, 5′-H), 2.56 (1H, m, 3′-H), 2.90–3.06 (2H, m, 2-H, 1′-H), 4.56 (1H, d, *J* 8.6, 1-H), 7.08–7.27 (5H, m, arom. H); δ_C (75 MHz, $CDCl_3$) 11.0 (CH_3), 23.5 (C-7′), 30.6 (CO*C*H_3), 32.0, 32.0, 33.1 (C-4′, C-6′, C-8′), 41.5 (C-5′), 46.2 (C-3′), 53.2 (C-1), 58.4 (C-2), 66.2 (C-1′), 126.6, 127.8, 128.1, 142.0 (arom. C), 194.4 (C=O), 194.5 (C=O); *m*/*z* 138 (100%) [$C_9H_{16}N^+$].

(2*S*,1′*S*,5′*S*)-(−)-2-(2′-Azabicyclo[3.3.0]octan-2′-yl)-propanethiol 26a. Synthesis according to GP 7 (starting with 3.8 mmol thioacetate). Work-up: column chromatography, eluent: ethanol, R_f 0.21; yield 0.43 g (61%) as pale yellow oil which undergoes oxidation in air; $[a]_D^{20}$ −28.6 (*c* 1.0, EtOH); ν_{max} (neat)/cm^{-1} 2951, 2861, 2809, 1449, 1435, 1372, 1232, 1169, 1133, 1078; δ_H (300 MHz, $CDCl_3$) 0.96 (3H, d, *J* 6.3, CH_3), 1.10–1.62 (7H, m, 4′-H, 6′-H_2, 7′-H_2, 8′-H_2), 1.76 (1H, m, 4′-H), 2.22 (1H, m, 3′-H), 2.34 (1H, m, 5′-H), 2.53 (1H, dd, *J* 7.3 and 12.1, 1-H), 2.64 (1H, m, 3′-H), 2.81 (1H, m, 2-H), 2.99 (1H, m, 1′-H), 3.04 (1H, dd, *J* 5.9 and 12.1, 1-H); δ_C (75 MHz, $CDCl_3$) 14.2 (C-3), 24.3 (C-7′), 31.9 (C-4′), 33.0, 33.2 (C-6′, C-8′), 42.3 (C-5′), 46.2 (C-1), 48.3 (C-3′), 55.3 (C-2), 66.0 (C-1′); *m*/*z* 138 (100%) [$C_9H_{16}N^+$]; (FD): *m*/*z* 185 (70%) [M^+], 368 (15) [$2M^+ - 2H$ (disulfide)].

(1*R*,2*S*,1′*S*,5′*S*)-(+)-2-(2′-Azabicyclo[3.3.0]octan-2′-yl)-1-phenylpropanethiol 26b. Synthesis according to GP 9. Work-up: column chromatography, eluent: ethyl acetate–petroleum ether 1:3, R_f 0.73; yield 0.29 g (73%) as slightly yellow oil, highly sensitive to oxidation (contains 16% disulfide) (Found: C 73.89, H 8.81, N 5.70. Calc. for $C_{16}H_{23}NS$: C 73.52, H 8.87, N 5.36%); ν_{max} (neat)/cm^{-1} 3026, 2950, 2860, 1599, 1491, 1450, 1374, 1353, 1326, 1227, 1176, 1130, 1074, 896, 741, 697; δ_H (300 MHz, $CDCl_3$) 0.93–1.50 (7H, m, 4′-H, 6′-H_2, 7′-H_2, 8′-H_2), 1.05 (3H, d, *J* 6.4, CH_3), 1.77 (1H, m, 4′-H), 2.18–2.32 (2H, m, 3′-H, 5′-H), 2.59 (1H, m, 3′-H), 2.91 (1H, m, 2-H), 3.01 (1H, m, 1′-H), 4.08 (1H, m, 1-H), 7.10–7.26 (5H, m, arom. H); δ_C (75 MHz, $CDCl_3$) 11.0 (CH_3), 23.8 (C-7′), 32.0, 32.1, 33.0 (C-4′, C-6′, C-8′), 41.7 (C-5′), 47.4 (C-3′), 49.2 (C-1), 61.5 (C-2), 68.9 (C-1′), 126.7, 127.8, 127.9, 143.3 (arom. C); *m*/*z* 138 (100%) [$C_9H_{16}N^+$].

Bis[(1*R*,2*S*,1′*S*,5′*S*)-(−)-2-(2′-azabicylo[3.3.0]octan-2′-yl)-1-phenylpropyl] disulfide 27. Synthesis according to GP 10. Work-up: column chromatography, eluent: *tert*-butyl methyl ether, R_f 0.87; yield 0.32 g (75%) as yellow oil; $[a]_D^{23}$ −186.8 (*c* 0.7, EtOH); ν_{max} (neat)/cm^{-1} 3082, 3059, 3026, 2963, 1599, 1491, 1374, 1228, 897, 738, 694, 615; δ_H (300 MHz, $CDCl_3$) 0.75–1.36 (14H, m, 4′-H, 6′-H_2, 7′-H_2 8′-H_2), 1.04 (6H, d, *J* 6.3, 3-H), 1.62 (2H, m, 4′-H), 2.06–2.21 (6H, m, 3′-H_2, 5′-H), 2.89 (2H, m, 1′-H), 3.07 (2H, m, 2-H), 3.23 (2H, d, *J* 9.2, 1-H), 6.97–7.19 (10H, m, arom. H); δ_C (75 MHz, $CDCl_3$) 10.9 (C-3), 23.1 (C-7′), 32.1, 32.1, 33.2 (C-4′, C-6′, C-8′), 41.3 (C-5′), 45.2 (C-3′), 56.7, 61.5, 65.3 (C-1, C-2, C-1′), 126.4, 127.4, 128.8, 143.7 (arom. C); *m*/*z* 138 (100%) [$C_9H_{16}N^+$], 228 (35) [$C_{16}H_{22}N^+$], 260 (7) [$C_{16}H_{22}NS^+$].

Enantioselective catalysis: method A

Commercially available Et_2Zn (3.75 mmol) in *n*-hexane (1.0 M) or toluene (1.1 M) was added dropwise to a solution of the chiral ligand (0.15 mmol, 6 mol%) in benzaldehyde (2.5 mmol) at 0 °C under argon atmosphere. After stirring for 12 h at 0 °C, the reaction mixture was hydrolyzed by cautiously adding 1.5 M HCl (10 ml). The organic material was extracted with Et_2O (3 × 50 ml), the combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo*.

The absolute configuration of the preferentially obtained 1-phenylpropan-1-ol was assigned from optical rotation of the crude product: $[a]_D^{23}$ +45.45 (*c* 5.15, $CHCl_3$) for (*R*)-1-phenylpropan-1-ol.[22] The enantiomeric excess was determined by chemical derivatisation and NMR spectroscopy. Therefore, the crude product (0.094 g, 0.69 mmol) was cooled to 0 °C under argon. Successively, (*S*)-(+)-*O*-acetylmandelic acid (0.134 g, 0.69 mmol), *N,N*-dimethyl-4-aminopyridine (5 mg, 0.04 mmol) and *N,N*-dicyclohexylcarbodiimide (0.143 g, 0.69 mmol) dissolved in CH_2Cl_2 (1 ml) each, were added. The reaction mixture was stirred for 2 h at 0 °C and for an additional 20 h at room temp. Then the solution was separated from the precipitate and the solvent removed by distillation. Unreacted 1-phenylpropan-1-ol and other volatile residues were removed at 60–70 °C under reduced pressure (1 Torr) to give the diastereomeric esters (*R*,*S*) and (*S*,*S*).

^{1}H NMR: (*R*,*S*), the signals of the diastereomer (*S*,*S*) are given in brackets: δ_H 0.63 [0.88] (3H, t, *J* 7.4, CH_2CH_3), 1.64–1.85 (2H + 2H, m, CH_2CH_3), 2.16 [2.18] (3H, s, CH_3CO_2), 5.66 [5.65] (1H, dd, *J* 6.0 and 7.4, CH_3CH_2CHO), 5.97 [5.98] (1H, s, CH_3CH_3CH), 6.94–7.50 (10H + 10H, m, arom. H); δ_C 9.3 [9.6] (CH_2CH_3), 20.6 (CH_3CO_2), 29.0 [29.2] (CH_2CH_3), 74.5 (CH_3CH_2CHO), 78.6 [78.7] (PhCHCO$_2$), 168.2 [169.0] (C=O), 170.0 [170.2] (C=O), 126–139 (Ar-C).

The enantiomeric excess of 1-phenylpropan-1-ol (corresponding to the diastereomeric excess of the derivative) was determined by the relative intensities of the triplets at 0.63 and 0.88 ppm in the ^{1}H NMR spectra. The absolute configuration of the preferentially obtained 1-phenylpropan-1-ol was again established to be the (*R*)-enantiomer.

Enantioselective catalysis: method B

The amino alcohol (0.25 mmol, 5 mol%) was dissolved in 10 ml anhydrous toluene and cooled to −15 °C under argon atmosphere. Et_2Zn (9.1 ml of 1.1 M solution in toluene, 10 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 0.53 g (5 mmol) of freshly distilled benzaldehyde in 10 ml anhydrous toluene were added within 30 min. The reaction mixture was stirred for a further 40–42 h at ambient temp. The reaction was quenched at 0 °C with 20 ml 2 M HCl, the layers were separated and the aqueous layer was extracted three times with diethyl ether (20 ml). The combined organic phases were extracted with 4% aqueous sodium hydrogen sulfite (3 × 20 ml), washed with saturated sodium hydrogen carbonate solution and brine, then dried ($MgSO_4$) and finally concentrated *in vacuo*. The crude product was purified by distillation (bulb-to-bulb, 125 °C/20 mbar) and the enantiomeric excess was determined by chiral GC (SGE Cydex-B, temperature program 100 °C, 4 °C min^{-1} up to 125 °C, 10 min isotherm; the retention times were (*R*)-1-phenlypropan-1-ol 13.12 min, (*S*)-1-phenylpropan-1-ol 13.46 min).

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