

Formation of Enantiopure β -Amino Alcohols with a 3-Oxa-2,7-diazabicyclo[3.3.0]octane Framework

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Abstract

N-Allylamino alcohols **11a-g** were prepared from enantiopure (*1S*, *2S*)-2-amino-1-phenylpropane-1,3-diol (**8**) by various reaction pathways. Selective Swern oxidation of the primary alcohol group of compounds **11** followed by treatment of the resulting aldehyde with *N*-alkylhydroxylamines afforded the corresponding nitrones that underwent an intramolecular 1,3-dipolar cycloaddition to give the bicyclic compounds **12** and **13**. **12c** and **13c** ($R^3 = \text{allyl}$) were deallylated providing compounds **12i** and **13i**, which could be methylated subsequently yielding **12k** and **13k**, respectively. X-ray analyses of **13a,c** and **12g** were performed indicating different conformations of **13a** and **c** on the one hand and of **12g** on the other hand. Conclusions concerning the conformation of the other compounds **12** and **13** were drawn from their ^1H NMR data. Compounds **12** and **13** act as chiral ligands in the enantioselective addition of diethylzinc to benzaldehyde, however, the enantiomeric excess of the 1-phenylpropane-1-ol is usually low, the best result (79% ee) was achieved with compound **12c**.

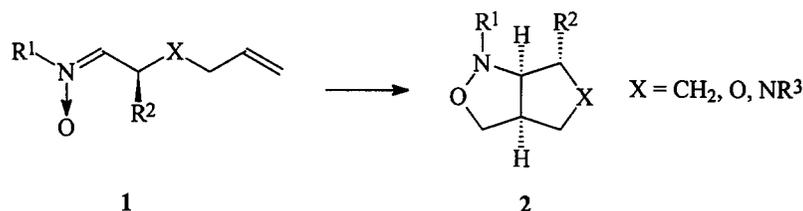
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Key words: Bicyclic heterocyclic compounds; Conformation; Cycloaddition; Enantioselection

1 Introduction

Chiral β -amino alcohols and their heterocyclic derivatives have found widespread use as auxiliaries [1] or enantioselective catalysts [2] in asymmetric synthesis. The high diastereoselectivity in the intramolecular 1,3-dipolar cycloaddition of chiral δ,ϵ -unsaturated nitrones **1** with the stereogenic center adjacent to the nitron carbon atom makes enantiopure bicyclic compounds **2** with an isoxazolidine moiety easily accessible [3]–[7] (Scheme 1). *N*-alkylated nitrones ($R^1 = \text{HO-CR}^2\text{R}^3\text{CR}^4\text{R}^5$ -) prepared with achiral or chiral β -amino alcohols or β -hydroxyamino alcohols provide enantiopure bicyclic compounds **2** ($X = \text{O}$) with an β -amino

alcohol group at its periphery. Such compounds [8] were used as chiral ligands in the enantioselective addition of diethylzinc to aldehydes [9][10]. The intramolecular cycloaddition of modified nitrones **1** ($X = NR^3$) with an α -hydroxyalkyl group as substituent R^2 should make another type of such chiral bicyclic compounds **2** accessible in which an α,β -amino alcohol group is incorporated. Thus, our goal was to synthesize such enantiopure compounds **2** ($X = NR^3$, $R^2 = CH_2OH$, $CH(R)OH$ or CR_2OH) and to test them also as ligands for the enantioselective addition of diethylzinc to benzaldehyde.

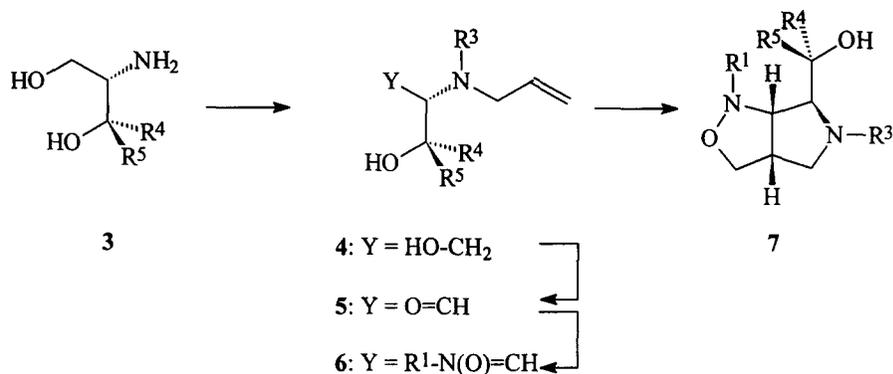


Scheme 1

2 Results and Discussion

Our strategy for the synthesis of target molecules **7** was as follows: Starting from chiral β -amino- α,γ -dialcohols **3** [11] the amino group should be allylated. However, since oxidation of diols with a secondary amino group **4** ($R^3 = H$) failed to give the desired products, compounds **4** with a tertiary amino group ($R^3 \neq H$) must be prepared. Oxidation of the primary alcohol group ($Y = HO-CH_2$) without oxidation of the other alcohol group $-C(R^4R^5)OH$ to give aldehydes **5** would be the crucial step of the reaction sequence. Treatment of compounds **5** with *N*-alkylhydroxylamines should afford nitrones **6**, that were expected to undergo an intramolecular cycloaddition providing the desired chiral 3-oxa-2,7-diazabicyclo[3.3.0]octanes **7** (Scheme 2). Finally, modification of the alkyl substituent R^3 seemed to be possible.

Preliminary experiments with (*S*)-2-amino-1,1-diphenyl-propane-1,3-diol **3** ($R^4 = R^5 = Ph$) [12] failed, because Swern oxidation [13] of the corresponding diallylated compound **4** ($R^3 = CH_2=CH-CH_2$, $R^4 = R^5 = Ph$) caused fragmentation with formation of benzophenone [14]. On the other hand, preparation of 3-oxa-2,7-diazabicyclo[3.3.0]octanes *ent*-**7** ($R^4 = R^5 = H$) is possible in principle, as was exemplified by the synthesis of two compounds ($R^1 = tBu$, $R^3 = CH_2CH=CH_2$; $R^1 = PhCH_2$, $R^3 = CH_2=CH-CH_2$) starting from (*S*)-serine.



Scheme 2

Thus, with allyl bromide threefold allylation took place [6] providing the allylester of *N,N*-diallylserine. Then the hydroxy group was protected by the trityl group before reduction of the ester group yielded the partially protected amino alcohol **4** (Y = TrO-CH₂ instead of HO-CH₂). Swern oxidation of the unprotected group HOCR⁴R⁵ (R⁴ = R⁵ = H) followed by treatment with R¹NHOH and subsequent intramolecular 1,3-dipolar cycloaddition of the resulting nitron yielded the bicyclic compound which was finally deprotected to give the enantiomeric form of **7** (*ent*-**7**) [14].

A shorter reaction sequence arises with the inexpensive, purchaseable (*1S*, *2S*)-2-amino-1-phenylpropane-1,3-diol **3** (R⁴ = Ph, R⁵ = H) as depicted in Scheme 2. If Swern oxidation [13] of the corresponding compound **4** (R⁴ = Ph, R⁵ = H) proceeds selectively at the primary alcohol group no protection of the secondary alcohol group is required. Thus we decided to study the formation of compounds **7** with various substituents R¹ and R³ as well as with additional substituents starting from (*1S*, *2S*)-2-amino-1-phenylpropane-1,3-diol.

2.1 Preparation of the (*1S*, *2S*)-2-amino-1-phenylpropane-1,3-diols **11**

Compounds **11a** and **b** were prepared via *N*-benzylated compounds **9** (R³ = PhCH₂). To this end the enantiopure compound **8** was condensed with benzaldehyde to give the corresponding imine which provided the secondary amine **9** upon reduction with sodium borohydride [15]. Reaction with allyl bromide or methallyl chloride yielded **11a** or **11b**, respectively (Scheme 3). Direct allylation of **8** with allyl bromide [6] afforded only the diallyl compound **11c**, whereas with methallyl chloride a mixture of **11d** and the corresponding mono-allyl compound (R³ = H)

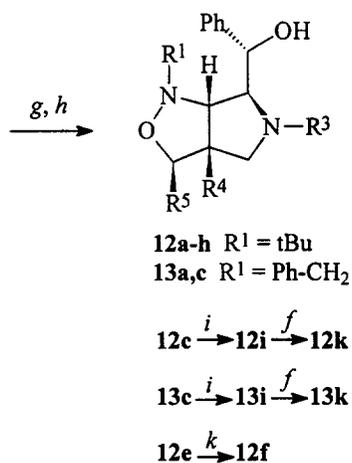
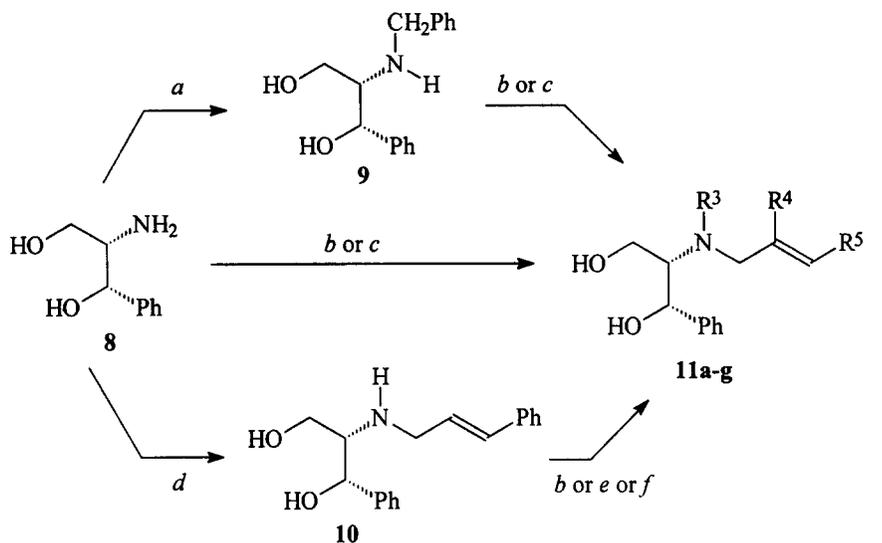
was obtained which could be separated easily by column chromatography. Condensation of amino alcohol **8** with cinnamyl aldehyde followed by reduction of the resulting imine with sodium borohydride provided compound **10** from which the tertiary amino compounds **11e,f** and **g** were accessible by formylation with ethyl formate [16], methylation with methyl iodide or allylation with allyl bromide, respectively.

2.2 Formation of the bicyclic compounds **12** and **13**

Selective oxidation of the primary alcohol group of amino alcohols **11** could be achieved by Swern oxidation [13]. The corresponding aldehydes were treated with *N*-tert-butylhydroxylamine or *N*-benzylhydroxylamine affording nitrones which underwent spontaneously an 1,3-dipolar cycloaddition to give the 3-oxa-2,7-diazabicyclo[3.3.0]octanes **12a-h** and **13a,c**, respectively. Due to the two different dipolarophilic groups in **11g** a mixture of compounds **12g** and **h** arose from cycloaddition of the corresponding nitron. Fivefold chromatographic separation followed by recrystallization provided only 3% of **12g** from which a crystalline structure determination could be performed, whereas **12h** could not be obtained entirely pure. Since the oxidation reaction does not proceed entirely selective, the yields of the cycloadducts **12** and **13** after chromatographic separation from by-products are usually only in the range between 20 and 50%. Nevertheless, this procedure seems to be more economic, because the protection of the secondary alcohol group would require four additional reaction steps (successively protection of the primary group, protection of the secondary group, deprotection of the primary group and finally after formation of the bicyclic compound deprotection of the secondary group).

Deallylation of compounds **12c** and **13c** was performed with *o*-mercaptobenzoic acid in the presence of a mixture of dibenzylideneacetone palladium (0) complex (Pd(dba)₂) and 1,4-bis[(diphenyl-phosphino)butane] (DPPB) [17] as catalyst giving compounds **12i** and **13i**, respectively. Methylation of the latter compounds makes **12k** and **13k** easily accessible. In addition to the general way **12f** was also prepared by reduction of **12e** with lithium aluminium hydride.

All bicyclic compounds **12** and **13** were optically active. They were isolated as enantiopure compounds. This is indicated from their ¹H and ¹³C NMR spectra in which no signals of diastereomers could be recognized. Since the enantiopure starting compound **8** contains two stereogenic centers, formation of diastereomers is expected if one of these two centers would be partially racemized in the reaction sequence.



	R^3	R^4	R^5
a	CH_2Ph	H	H
b	CH_2Ph	Me	H
c	$CH_2-CH=CH_2$	H	H
d	$CH_2-C(Me)=CH_2$	Me	H
e	CHO	H	Ph
f	Me	H	Ph
g	$CH_2-CH=CH_2$	H	Ph
h	$CH_2-CH=CHPh$	H	H
i	H	H	H
k	Me	H	H

a: 1. Ph-CHO, 2. $NaBH_4$, MeOH *b*: $Br-CH_2-CH=CH_2$, K_2CO_3 , H_2O
c: $Cl-CH_2-C(Me)=CH_2$, K_2CO_3 , H_2O , $60^\circ C$ *d*: 1. Ph-CH=CH-CHO, 2. $NaBH_4$, MeOH
e: HCOOEt, *p*-Tol- SO_3H , H_2O , reflux *f*: MeI, $Et(iPr)_2N$, $CHCl_3$, reflux *g*: DMSO, $(COCl)_2$,
 Et_3N , CH_2Cl_2 , $-78^\circ C$ *h*: R^1-NHOH *i*: $o-HS-C_6H_4-COOH$, $Pd(dba)_2$, DPPB, THF, $60^\circ C$
k: $LiAlH_4$, THF, reflux

Scheme 3

2.3 Structure determination

X-ray studies were undertaken with compounds **13a** (Figure 1), **13c** (Figure 2) and **12g** (Figure 3)¹. The five-membered rings of these bicyclic compounds exist in envelope conformation in which the O-atom at position 3 and the N-atom at position 7 protrude in opposite directions from the plane formed by the other four atoms of the respective ring. In **13a** and **c** the O-3 atom is anti-orientated and the N-7 atom syn-orientated with respect to the H-atoms 1-H and 5-H at the bridgehead carbon atoms (Type A). For **12g** the opposite is true (Type B). The latter compound forms an intramolecular hydrogen bond from the OH group to N-7, whereas in **13a** and **c** such an intramolecular hydrogen bond is missing. Obviously, this hydrogen bond is the reason for the quasi-axial position of the allyl group at N-7 of **12g**, while in **13a** and **c** the R³ substituent is in quasi-equatorial position.

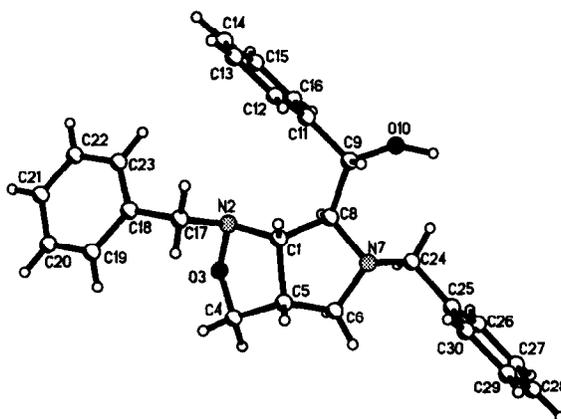


Figure 1: Molecular plot of (*αS*, *1S*, *5S*, *8S*)-(-)-(2,7-dibenzyl-3-oxa-2,7-diazabicyclo[3.3.0]-oct-8-yl)-phenylmethanol **13a**; Selected bond lengths [Å]: C1-N2 1.469 (6), C1-C5 1.551 (6), C1-C8 1.542 (6), N2-O3 1.465 (5), O3-C4 1.433 (6), C4-C5 1.516 (7), C5-C6 1.494 (7), C6-N7 1.462 (6), N7-C8 1.475 (5), C8-C9 1.535 (6); Selected bond angles [°]: N2-C1-C5 107.5 (3), C5-C1-C8 104.8 (3), C1-N2-O3 103.0 (3), N2-O3-C4 106.8 (3), O3-C4-C5 105.1 (4), C4-C5-C1 102.6 (4), C1-C5-C6 103.7 (3), C5-C6-N7 105.0 (4), C6-N7-C8 103.1 (3), N7-C8-C1 102.5 (3)

¹ The atomic coordinates and additional data such as bond lengths and angles for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

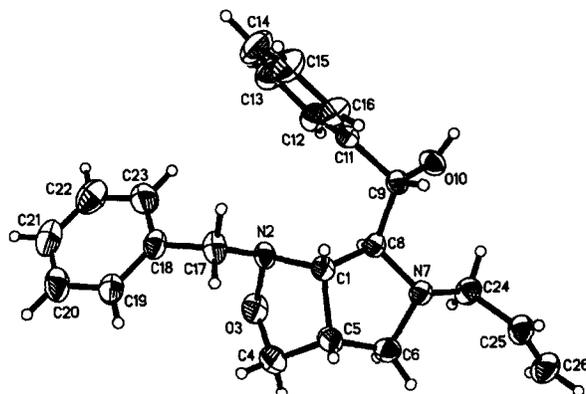


Figure 2: Molecular plot of (αS , $1S$, $5S$, $8S$)-(-)-(7-allyl-2-benzyl-3-oxa-2,7-diazabicyclo[3.3.0]oct-8-yl)-phenylmethanol **13c**; Selected bond lengths [Å]: C1-N2 1.477 (2), C1-C5 1.548 (3), C1-C8 1.531 (3), N2-O3 1.449 (2), O3-C4 1.430 (3), C4-C5 1.524 (3), C5-C6 1.528 (3), C6-N7 1.471 (3), N7-C8 1.483 (2), C8-C9 1.529 (3); Selected bond angles [°]: N2-C1-C5 107.33 (16), C5-C1-C8 106.34 (16), C1-N2-O3 103.25 (14), N2-O3-C4 106.97 (15), O3-C4-C5 105.21 (18), C4-C5-C1 102.25 (17), C1-C5-C6 103.36 (17), C5-C6-N7 104.87 (16), C6-N7-C8 104.32 (15), N7-C8-C1 102.28 (15)

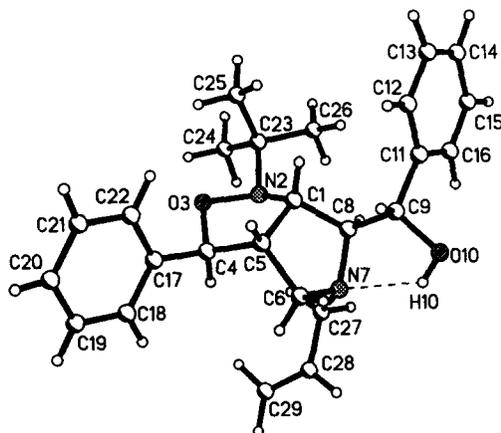


Figure 3: Molecular plot of (αS , $1S$, $4S$, $5S$, $8S$)-(-)-(7-allyl-2-tert-butyl-3-oxa-2,7-diazabicyclo[3.3.0]oct-8-yl)-phenylmethanol **12g**; Selected bond lengths [Å]: C1-N2 1.485 (4), C1-C5 1.543 (4), C1-C8 1.543 (4), N2-O3 1.481 (3), O3-C4 1.421 (3), C4-C5 1.543 (4), C5-C6 1.537 (4), C6-N7 1.483 (4), N7-C8 1.466 (4), C8-C9 1.551 (4); Selected bond angles [°]: N2-C1-C5 104.0 (2), C5-C1-C8 103.6 (2), C1-N2-O3 103.0 (2), N2-O3-C4 102.48 (19), O3-C4-C5 103.9 (2), C4-C5-C1 103.4 (2), C1-C5-C6 105.9 (2), C5-C6-N7 106.6 (2), C6-N7-C8 104.2 (2), N7-C8-C1 107.5 (2)

The ^1H NMR coupling constants for the ring protons of these compound are opposed to coupling constants calculated from the torsional angles evaluated from the X-ray analyses with the aid of the Karplus equation [18] (Table 1). As the accordance between found and calculated coupling constants is good, the coupling constants of the other compounds **12** and **13** can be used for conclusions on their conformations. (NMR data see Tables 2-4)

Table 1

Selected torsional angles φ of compounds **13a,c** and **12g** and comparison of ^1H NMR coupling constants (Hz) with theoretical values calculated from the torsional angles with the aid of the Karplus equation^{a)}

	13a			13c			12g		
	φ ($^\circ$)	$J_{\text{calcd.}}$	J_{found}	φ ($^\circ$)	$J_{\text{calcd.}}$	J_{found}	φ ($^\circ$)	$J_{\text{calcd.}}$	J_{found}
1'-H/5'-H	1.2	8.2	7.9	2.2	8.2	8.3	-2.0	8.2	8.5
1'-H/8'-H	-150.6	6.9	^{b)}	-150.3	6.9	4.7	-93.0	0	2.1
4 α '-H/5'-H	22.1	7.0	6.4	21.3	7.1	6.6	-	-	-
4 β '-H/5'-H	-98.5	0	1.9	-99.5	0	2.1	-152.2	7.2	7.4
5'-H/6 α '-H	26.8	6.5	8.2	23.5	6.9	8.1	-19.0	7.3	7.4
5'-H/6 β '-H	147.6	6.5	8.1	144.4	6.0	8.0	103.3	0.2	3.4

^{a)} See reference [18] ^{b)} not detected

As the ^1H NMR data reveal the conformation of most of the compounds without substituents at position 4 or 5 ($R^4 = R^5 = \text{H}$) resembles those of **13a** and **c** (**12a,c,h,k** and **13k** = type A). This is indicated by the small values for the coupling constants $J_{4\beta/5} < 2.5$ Hz and the large difference between the chemical shifts for 6 α -H and 6 β -H ($\Delta\delta$ 6 α -H/6 β -H: 0.69-1.00 ppm) [19]-[21]. On the other hand, for compounds **12b,d** and **f** substituted at C-4 or C-5 a conformation similar to that of **12g** is supposed (type B). This is indicated either by a large value for $J_{4\beta/5}$ (**12f**: $J_{4\beta/5} = 7.3$ Hz) or by a small difference for $\Delta\delta$ 6 α -H/6 β -H (**12b**: 0.12, **12d**: 0.29 ppm). Presumably, **12e** belongs also to the latter type of compound ($J_{4\beta/5} = 8.8$ Hz), however, the situation is somewhat different, because the N-7 atom substituted by the formyl group is sp^2 -hybridized in contrast to the sp^3 -hybrid N-atom of the other compounds.

A comparison of the NMR data of compounds **12i/13i** ($R^3 = \text{H}$) with those of the corresponding *N*-methyl derivatives ($R^3 = \text{Me}$) reveals considerable differences in $\Delta\delta$ 6 α /6 β (**12i**: 0.27, **13i**: 0.31 vs **12k**: 0.85, **13k**: 1.00 ppm) as well as in the coupling constants $^3J_{4\beta/5}$ (**12i**: 5.9, **13i**: 4.3 vs **12k**: < 2 , **13k**: < 2 Hz) and $^3J_{5/6\beta}$ (**12i**: 2.6, **13i**: 2.8 vs **12k**: 9.0, **13k**: 8.9 Hz). For this reason the former seem to belong to the conformers of type B. (In principle, however, the criterium of $\Delta\delta$ 6 α /6 β is not quite unambiguous in this case. If the H-atom at N-7,

Table 2

Selected ^1H NMR chemical shifts δ (in ppm) of compounds **12** and **13** in CDCl_3 ^{a)}

	1-H	4 α -H	4 β -H	5-H	6 α -H	6 β -H	8-H	CHOH
12a	3.86	3.97	3.70	3.17	3.23	2.54	3.31	4.80
12b	3.39	3.73	3.65	-	2.82	2.70	3.34	4.77
12c	3.70	3.88	3.62	3.06	3.27	2.45	3.04	4.46
12d	3.32	3.70	3.63	-	2.90	2.61	3.18	4.67
12e	4.09	-	4.36	3.04	4.00	3.33	3.84	4.90
12f	3.87	-	4.74	2.94	3.27	2.79	3.14	4.58
12g	3.76	-	4.70	2.93	3.22	2.91	3.24	4.30
12h	3.76	3.91	3.64	3.0-3.2	3.34	2.56	3.0-3.2	4.62
12i	3.53	4.07	3.45	3.06	3.07	2.80	3.16	4.29
12k	3.83	3.88	3.62	3.08	3.24	2.39	2.84	4.70
13a	3.60	4.04	3.65	3.05	3.15	2.29	3.03	4.43
13c	3.51	4.04	3.66	3.10	3.35	2.36	2.92	4.33
13i	3.41	4.18	3.60	3.15	3.19	2.88	3.23	4.28
13k	3.63	4.10	3.72	3.16	3.34	2.34	2.71	4.40

^{a)} Additional chemical shifts see Experimental

Table 3

Selected ^1H NMR coupling constants J (in Hz) in CDCl_3

	3J 1/5	1/8	4 α /5	4 β /5	5/6 α	5/6 β	8/CH	2J 4 α /4 β	6 α /6 β
12a	7.8	3.1	6.1	< 2	8.0	8.6	< 2	8.0	9.0
12b	-	2.8	-	-	-	-	2.5	8.2	9.7
12c	8.0	3.2	6.2	2.4	7.8	7.8	2.9	8.2	9.9
12d	-	2.8	-	-	-	-	2.7	8.2	9.8
12e	9.2	< 1	-	8.8	< 1	7.0	4.0	-	12.2
12f	8.7	3.4	-	7.3	7.3	4.9	3.8	-	10.6
12g	8.5	2.1	-	7.4	7.4	3.4	6.3	-	11.5
12h	8.0	3.4	6.2	2.4	7.8	8.0	2.8	8.1	9.9
12i	8.0	1.6	7.7	5.9	7.0	2.6	8.2	8.1	9.8
12k	8.3	4.3	6.2	< 2	8.2	9.0	< 1	8.1	8.9
13a	7.9	-	6.4	1.9	8.2	8.1	2.5	8.8	9.5
13c	8.3	4.7	6.6	2.1	8.1	8.0	3.3	8.8	9.9
13i	7.7	2.8	7.6	4.3	7.4	2.8	7.6	8.7	11.5
13k	8.5	5.6	6.2	< 2	8.4	8.9	2.2	9.0	8.9

in contrast to all other compounds ($R^3 \neq H$), would adopt a quasi-axial position, the free electron-pair would no longer be anti-periplanar to one of the 6-H protons. Thus $\Delta\delta$ 6 α /6 β would be affected [19]–[21]). Surprisingly after long storage of a sample of **12i** an additional conformer was formed (δ 6 α -H = 3.69, δ 6 β -H = 3.08 ppm; J 4 β /5 = 3.6, J 5/6 β = 5.2 Hz). For **13i** an equilibration of several conformers must be assumed that undergo a fast conversion giving the NMR signals at average values. In fact, we obtained slightly different NMR spectra from different samples dependent on the conditions of preparation and uptake of the spectra.

Table 4

Selected ^{13}C NMR chemical shifts δ (in ppm) of compounds **12** and **13**^{a)}

	C-1	C-4	C-5	C-6	C-8	CHOH	R ¹ ^{b)}	
12a	77.1	72.7	48.8	58.6	69.2	71.3	26.6	59.5
12b	75.6	78.4	55.7 ^{c)}	64.3	79.0	70.9	26.6	61.2 ^{c)}
12c	76.2	72.6	48.7	58.2 ^{d)}	68.8	71.2	26.3	59.2
12d	75.5	78.2	56.6 ^{c)}	64.1	79.0	70.9	26.6	59.2 ^{c)}
12e	74.9	83.7	45.5	56.1	67.1	71.3	25.7/28.0 ^{e)}	58.3/58.5 ^{e)}
12f	76.7	84.5	56.8	59.1	70.1	70.5	25.8	58.0
12g	75.2	84.7	58.1	59.8	69.5	70.8	25.6	58.0
12h	76.2	72.8	48.8	58.4	68.9	71.3	26.5	59.4
12i	70.7 ^{c)}	72.1	50.2	48.3	66.4	72.0 ^{c)}	25.1	58.2
12k	78.0	73.0	48.3	62.5	69.5	70.6	26.7	59.4
13a	75.0	70.3	46.0	60.6	74.6	71.6	59.4 ^{f)}	
13c	74.9	70.4	46.4	60.5	74.0	72.0	59.0	
13i	73.6	71.7	49.3	51.0	70.8	71.8	60.5	
13k	75.1	70.0	46.0	63.2	76.2	71.7	60.4	

^{a)} Additional chemical shifts see Experimental ^{b)} **12**: $R^1 = \text{C}(\text{CH}_3)_3$, **13**: $R^1 = \text{CH}_2\text{Ph}$ ^{c)} An opposite assignment of the two values is possible ^{d)} or 58.3 (see Experimental) ^{e)} The signals of two rotamers were observed ^{f)} or 59.5 (see Experimental)

2.4 Enantioselective catalysis

Most of the bicyclic enantiopure β -amino alcohols **12** and **13** catalyze the addition of diethylzinc to benzaldehyde forming chiral complexes with diethylzinc. However, the enantioselectivity of this reaction achieved with compounds **12** and **13** is low. (Table 5) The best result was achieved with **12c** which afforded 1-phenylpropane-1-ol in 98% yield with an excess of 79% *S*-enantiomer. Replacement of the *N*-tert-butyl group ($R^1 = \text{tBu}$) of **12c** by the

benzyl group ($R^1 = \text{PhCH}_2$) in **13c** reduced the enantiomeric excess dramatically as did also replacement of the allyl group of **12c** ($R^3 = \text{allyl}$) by the benzyl group in **12a**. Substituents $R^3 = \text{H}$ (**12i**) and $R^3 = \text{Me}$ (**12k**) diminish the enantiomeric excess also as compared to **12c**.

Table 5

Enantioselectivity of the addition of Et_2Zn to benzaldehyde in the presence of catalytic amounts of β -amino alcohols **12** and **13**^{a)}

compound	yield (%)	ee (%)	conf. ^{b)}
12a	37	28	<i>S</i>
12c	98	79	<i>S</i>
12i	68 ^{c)}	67	<i>S</i>
12k	82 ^{d)}	56	<i>S</i>
13c	89	22	<i>S</i>

^{a)} 150 mol% Et_2Zn , 6 mol% of **12** or **13**, 0°C ^{b)} configuration of the enantiomer preferently formed ^{c)} in addition 6% of benzylalcohol is formed ^{d)} in addition 3% of benzylalcohol is formed

3 Experimental

Elemental analyses were performed by the division Routine-Analytik, Fachbereich Chemie, University of Marburg. Spectra were recorded with following instruments: NMR: Bruker AMX 500, AM 400 and Bruker AC 300 using the residues of ^1H ($\delta = 7.24$) or of ^{13}C ($\delta = 77.0$ ppm) of the solvent CDCl_3 as internal standard. As far as not stated otherwise ^1H NMR spectra were recorded at 300 MHz, the ^{13}C NMR spectra at 75 MHz, with CDCl_3 as solvent. MS: Varian CH7 (EI) and 711 (FD). Optical rotations: Polarimeter Perkin Elmer 241, at 589 nm. X-ray: 4 circle diffractometer (Enraf-Nonius CAD4).

3.1 Preparation of compounds **9** and **10**

3.1.1 Formation of imines

Benzaldehyde or cinnamylaldehyde (0.05 mol) was added to a solution of **8** (8.36 g, 0.05 mol) in Et_2O (250 ml). The reaction mixture was stirred for 24 h at room temperature. Afterwards the solution was concentrated and stored at -20°C until the imine crystallizes.

(1S, 2S)-(+)-2-(Benzylideneamino)-1-phenylpropane-1,3-diol: Yield: 12.05 g (98%), colourless solid. Exists as a 60:40% mixture with (2,5-diphenyl-oxazolidin-4-yl)methanol. ^1H NMR: δ = 3.19 (dt, 3J = 8.1 and 3.3 Hz, 1H, NCH), 3.58 (dd, 2J = 11.6, 3J = 3.7 Hz, 1H, CH_2OH), 3.79 (dd, 2J = 11.6, 3J = 3.3 Hz, 1H, CH_2OH), 4.81 (d, 3J = 8.1, 1H, Ph-CHOH), 8.15 (s, 1H, N=CH), 7.12–7.36 (m, 10H, Ar-H) and signals of the oxazolidine tautomer at 3.27 (q, 3J = 5.8 Hz, 1H, NCH), 3.98 (dd, 2J = 8.3, 3J = 6.1 Hz, 1H, CH_2OH), 4.43 (dd, 2J = 8.3, 3J = 6.2 Hz, 1H, CH_2OH), 4.73 (d, 3J = 6.1 Hz, 1H, OCH-Ph), 5.54 (s, 1H, N-CHO). ^{13}C NMR: δ = 58.4 (N-CH), 61.6 (CH_2OH), 73.7 (Ph-CHOH), 164.6 (N=CH) and signals of the oxazolidine tautomer at 58.6 (N-CH), 61.4 (CH_2OH), 72.1 (Ph-CHO), 93.1 (N-CHO) + Ar-C between 125.8 and 129.1 and at 140.5 and 140.9.

(1S, 2S)-(+)-2-(3-Phenylprop-2-enylidene)amino-1-phenylpropane-1,3-diol: Yield: 13.01 g (92%), colourless solid, m.p. 184°C, $[\alpha]_{\text{D}}^{21}$ = +147.6 (c = 1.0, EtOH). ^1H NMR (CD_3OD): δ = 3.31 (m, 1H, 2-H), 3.52 (m, 2H, 3-H), 3.91 (s, broad, 2H, OH), 4.74 (d, 3J = 6.3 Hz, 1H, 1-H), 6.80 (dd, 3J = 8.0, 3J = 16.0 Hz, 1H, $\text{CH}=\text{CHPh}$), 6.91 (d, 3J = 16.0 Hz, 1H, $\text{CH}=\text{CHPh}$), 7.20–7.41 (m, 10H, Ar-H), 7.86 (d, 3J = 8.4 Hz, 1H, N=CH). ^{13}C NMR (CD_3OD): δ = 62.9 (C-3), 73.8 (C-2), 77.7 (C-1), 143.6 ($\text{CH}=\text{CHPh}$), 166.2 (N=CH), 126.5–129.4, 135.2, 141.5 (Ar-C + $\text{CH}=\text{CHPh}$). MS (EI): m/z (%): 285 (5) [M^+]. $\text{C}_{18}\text{H}_{19}\text{NO}_2$ (281.4) Calcd C 76.83 H 6.81 N 5.00 Found C 76.63 H 6.71 N 4.92.

3.1.2 Reduction of imines

Sodium borohydride (1.96 g, 0.05 mol) was added in small portions to a solution of the imine (0.04 mol) in methanol (150 ml) at room temperature. The reaction mixture was refluxed for 30 min. and subsequently stirred at room temp. for 1 h. Then 6 M NaOH (0.1 mol) was added dropwise at 0 °C. After evaporation the residue was extracted with Et_2O ten times. After the organic solution had been dried with MgSO_4 the solvent was evaporated.

(1S, 2S)-(+)-2-(Benzylamino)-1-phenylpropane-1,3-diol (9): Yield: 6.66 g (65%), colourless solid. ^1H NMR: δ = 2.30 (s, broad, 2H, OH), 2.77 (m, 3J = 3.7, 3J = 7.1 Hz, 1H, 2-H), 3.35 (dd, 2J = 11.1, 3J = 3.4 Hz, 1H, 3-H), 3.64 (dd, 2J = 11.1, 3J = 3.7 Hz, 1H, 3-H'), 3.66 (d, 2J = 12.9 Hz, 1H, CH_2Ph), 3.78 (d, 2J = 12.9 Hz, 1H, CH_2Ph), 4.63 (d, 3J = 7.1 Hz, 1H, 1-H), 7.20–7.38 (m, 10H, Ar-H). ^{13}C NMR: δ = 51.6 (Ph- CH_2), 60.1 (C-3), 64.1 (C-2), 73.7 (C-1), 126.2–128.5 (Ar-C).

(1S, 2S)-(+)-2-(3-Phenylprop-2-enyl)amino-1-phenylpropane-1,3-diol (10): Yield: 10.54 g (93%), colourless solid, m.p. 105 °C, $[\alpha]_{\text{D}}^{19}$ = +67.2 (c = 1.0, EtOH). ^1H NMR (CD_3OD): δ =

2.71 (dt, $^3J = 6.9$, $^3J = 4.1$ Hz, 1H, 2-H), 3.18 (ddd, $^2J = 13.9$, $^3J = 6.5$, $^4J = 1.3$ Hz, 1H, NCH₂), 3.28 (m, 1H, 3-H), 3.32 (ddd, $^2J = 13.9$, $^3J = 6.2$, $^4J = 1.5$ Hz, 1H, NCH₂), 3.55 (dd, $^2J = 11.3$, $^3J = 4.1$, 1H, 3-H'), 3.80 (s, broad, 3H, OH and NH), 4.57 (d, $^3J = 6.9$ Hz, 1H, 1-H), 6.08 (dt, $^3J = 15.9$, $^3J = 6.3$ Hz, 1H, CH=CHPh), 6.34 (d, $^3J = 15.9$, 1H, CH=CHPh), 7.10-7.29 (m, 10H, Ar-H). ¹³C NMR (CD₃OD): $\delta = 49.8$ (N-CH₂), 59.8 (C-3), 63.8 (C-2), 72.7 (C-1), 131.5 (CH=CHPh), 126.1-128.3, 136.8, 142.0 (Ar-C + CH=CHPh). MS (EI): m/z (%): 284 (5) [M⁺+1]. C₁₈H₂₁NO₂ (283.4) Calcd C 76.29 H 7.47 N 4.94 Found C 76.34 H 7.25 N 4.95.

3.2 Preparation of the *N,N*-disubstituted 2-amino-1-phenylpropane-1,3-diols 11

A solution of the amino alcohol **8** or **9a**, **10** (0.05 mol), allyl bromide (24.22 g, 0.2 mol or 12.11 g, 0.1 mol, resp.) and K₂CO₃ (27.56 g, 0.2 mol) in water (200 ml) was stirred for 24 h at room temp.. Subsequently the reaction mixture was extracted with Et₂O (3x) and the organic solution was dried with MgSO₄. Removal of the solvent yielded compounds **11c** or **11a,g**, respectively.

(1S, 2S)-(+)-2-(*N,N*-Diallylamino)-1-phenylpropane-1,3-diol (11c): Yield: 87%, colourless crystals, m.p. 41-44 °C, $[\alpha]_D^{19} = +23.3$ (c = 1.0, EtOH). ¹H NMR: $\delta = 2.95$ (ddd, $^3J = 9.8$, 7.7, 4.1 Hz, 1H, 2-H), 3.27 (dd, $^2J = 14.0$, $^3J = 7.5$ Hz, 2H, N-CH₂), 3.36 (dd, $^2J = 11.6$, $^3J = 4.1$ Hz, 1H, 3-H), 3.48 (dd, $^2J = 11.6$, $^3J = 7.7$ Hz, 1H, 3-H'), 3.50 (ddt, $^2J = 14.0$, $^3J = 5.4$, $^4J = 2.4$ Hz, 2H, N-CH₂), 4.39 (d, $^3J = 9.8$ Hz, 1H, 1-H), 5.20 (m, 4H, CH=CH₂), 5.86 (m, 2H, CH=CH₂), 7.26-7.33 (m, 10H, Ar-H). ¹³C NMR: $\delta = 53.5$ (N-CH₂), 59.0 (C-3), 66.6 (C-2), 71.5 (C-1), 117.7 (CH=CH₂), 136.5 (CH=CH₂), 127.0, 128.0, 128.5, 142.0 (Ar-C). MS (FD): m/z (%): 247.9 (9) [M⁺], 495.0 (92) [2M⁺], 741.9 (100) [3M⁺].

(1S, 2S)-(+)-2-(*N*-Allyl-*N*-benzylamino)-1-phenylpropane-1,3-diol (11a): Yield: 87%, colourless oil, $[\alpha]_D^{26} = +65.7$ (c = 1.0, EtOH). ¹H NMR: $\delta = 2.94$ (ddd, $^3J = 9.7$, 7.8, 4.0 Hz, 1H, 2-H), 3.27 (dd, $^2J = 14.1$, $^3J = 7.9$ Hz, 1H, CH₂-CH=CH₂), 3.38 (dd, $^2J = 11.7$, $^3J = 4.0$ Hz, 1H, 3-H), 3.47 (ddt, $^2J = 14.1$, $^3J = 6.9$, $^4J = 1.4$ Hz, 1H, CH₂-CH=CH₂), 3.51 (dd, $^2J = 11.7$, $^3J = 7.8$ Hz, 1H, 3-H'), 3.72 (d, $^2J = 13.3$ Hz, 1H, CH₂Ph), 4.04 (d, $^2J = 13.3$ Hz, 1H, CH₂Ph), 4.40 (s, broad, 1H, OH), 4.44 (d, $^3J = 9.7$ Hz, 1H, 1-H), 5.20 (m, 2H, CH=CH₂), 5.84 (m, 1H, CH=CH₂), 7.19-7.32 (m, 10H, Ar-H). ¹³C NMR: $\delta = 53.4$ (CH₂-CH=CH₂), 54.8 (CH₂Ph), 59.0 (C-3), 66.2 (C-2), 71.6 (C-1), 118.0 (CH=CH₂), 136.4 (CH=CH₂), 127.0-129.1, 139.1 (Ar-C). MS (FD): m/z (%): 297.9 (12) [M⁺], 594.9 (100) [2M⁺], 891.9 (34) [3M⁺]. C₁₉H₂₃NO₂ (297.4) Calcd C 76.75 H 7.80 N 4.71 Found C 76.83 H 8.03 N 4.79.

(1*S*, 2*S*)-(+)-2-[*N*-Allyl-(3-phenylprop-2-enyl)amino]-1-phenylpropane-1,3-diol (11g):

Yield: 84%, brown oil, $[\alpha]_D^{19} = +60.1$ ($c = 1.0$, EtOH). $^1\text{H NMR}$ (500 MHz): $\delta = 3.08$ (ddd, $^3J = 9.7, 7.7, 4.1$ Hz, 1H, 2-H), 3.40 (dd, $^2J = 14.0, ^3J = 7.3$ Hz, 1H, $\text{CH}_2\text{-CH}=\text{CH}_2$), 3.46 (dd, $^2J = 11.6, ^3J = 4.1$ Hz, 1H, 3-H), 3.51 (dd, $^2J = 14.0, ^3J = 7.4$ Hz, 1H, $\text{CH}_2\text{-CH}=\text{CHPh}$), 3.57 (dd, $^2J = 11.6, ^3J = 7.7$ Hz, 1H, 3-H'), 3.61 (dd, $^2J = 14.0, ^3J = 5.6$ Hz, 1H, $\text{CH}_2\text{-CH}=\text{CH}_2$), 3.72 (dd, $^2J = 14.0, ^3J = 5.8$ Hz, 1H, $\text{CH}_2\text{-CH}=\text{CHPh}$), 4.51 (d, $^3J = 9.7$ Hz, 1H, 1-H), 5.26 (m, 2H, $\text{CH}=\text{CH}_2$), 5.94 (m, 1H, $\text{CH}=\text{CH}_2$), 6.30 (m, 1H, $\text{CH}=\text{CHPh}$), 6.58 (d, $^3J = 15.9$ Hz, 1H, $\text{CH}=\text{CHPh}$), 7.27-7.43 (m, 10H, Ar-H). $^{13}\text{C NMR}$: $\delta = 53.1$ ($\text{CH}_2\text{-CH}=\text{C}$), 53.8 ($\text{CH}_2\text{-C}=\text{C}$), 59.1 (C-3), 66.9 (C-2), 71.6 (C-1), 118.0 ($\text{CH}=\text{CH}_2$), 133.0 ($\text{CH}=\text{CH}_2$), 136.3 ($\text{CH}=\text{CHPh}$), 126.3-128.5, 137.3, 141.9 (Ar-C + $\text{CH}=\text{CHPh}$). MS (FD): m/z (%): 342 (38) [$\text{M}^+ + 1$], 647 (100) [$2\text{M}^+ + 1$], 970 (14) [$3\text{M}^+ + 1$].

(1*S*, 2*S*)-(+)-2-[*N*-Benzyl-(2-methylprop-2-enyl)amino]-1-phenylpropane-1,3-diol (11b):

was prepared with 3-chloro-2-methylprop-1-ene as described for **11a**, however, the reaction mixture was stirred for 24 h at 60 °C. Yield: 69% after column chromatography (EtOAc, $R_f = 0.66$), light-yellow crystals, m.p. 67 °C, $[\alpha]_D^{22} = +67.6$ ($c = 1.0$, EtOH). $^1\text{H NMR}$: $\delta = 1.79$ (s, 3H, CH_3), 2.94 (m, 1H, 2-H), 3.26 (d, $^2J = 13.2$ Hz, 1H, $\text{CH}_2\text{-C}(\text{CH}_3)=\text{CH}_2$), 3.31 (d, $^2J = 13.2$ Hz, 1H, $\text{CH}_2\text{-C}(\text{CH}_3)=\text{CH}_2$), 3.33 (dd, $^2J = 11.7, ^3J = 4.1$ Hz, 1H, 3-H), 3.55 (dd, $^2J = 11.7, ^3J = 7.4$ Hz, 1H, 3-H'), 3.68 (d, $^2J = 13.1$ Hz, 1H, CH_2Ph), 4.06 (d, $^2J = 13.1$ Hz, 1H, CH_2Ph), 4.52 (d, $^3J = 9.8$ Hz, 1H, 1-H), 4.97 (s, 1H, $\text{C}=\text{CH}_2$), 5.01 (s, 1H, $\text{C}=\text{CH}_2$), 7.20-7.36 (m, 10H, Ar-H). $^{13}\text{C NMR}$: $\delta = 20.6$ (CH_3), 54.6 (CH_2Ph), 56.9 ($\text{CH}_2\text{-C}(\text{CH}_3)=\text{CH}_2$), 58.7 (C-3), 65.0 (C-2), 71.5 (C-1), 114.6 ($\text{C}(\text{CH}_3)=\text{CH}_2$), 139.0 ($\text{C}(\text{CH}_3)=\text{CH}_2$), 127.3-129.3, 142.0, 142.7 (Ar-C). MS (EI): m/z (%): 311 (6) [M^+].

Reaction of amino alcohol **8** (0.05 mol) with 3-chloro-2-methylprop-1-ene (0.2 mol) and K_2CO_3 (0.2 mol) in water (200 ml) at 60 °C afforded after 72 h reaction time a 1:8-mixture of the mono- and diallylated products. Separation by chromatography (t-butylmethyl ether, $R_f = 0.56$) gave a light-yellow oil in 77% yield.

(1*S*, 2*S*)-(+)-2-[*N,N*-{Bis-(2-methylprop-2-enyl)}amino]-1-phenylpropane-1,3-diol (11d):

$[\alpha]_D^{22} = +40.9$ ($c = 1.0$, EtOH). $^1\text{H NMR}$: $\delta = 1.78$ (s, 6H, CH_3), 2.61 (s, broad, 1H, OH), 2.87 (m, 1H, 2-H), 3.08 (d, $^2J = 13.4$ Hz, 2H, N- CH_2), 3.31 (m, 2H, 3-H), 3.32 (d, $^2J = 13.4$ Hz, 2H, N- CH_2), 4.40 (d, $^3J = 9.8$ Hz, 1H, 1-H), 4.71 (s, broad, 1H, OH), 5.11 (s, 4H, $\text{C}(\text{CH}_3)=\text{CH}_2$), 7.22-7.31 (m, 5H, Ar-H). $^{13}\text{C NMR}$: $\delta = 20.5$ (CH_3), 56.6 (N- CH_2), 57.7 (C-3), 64.2 (C-2), 70.8 (C-1), 114.3 ($\text{C}(\text{CH}_3)=\text{CH}_2$), 142.0 ($\text{C}(\text{CH}_3)=\text{CH}_2$), 126.9, 127.6, 128.2, 142.4 (Ar-C). MS (FD): m/z (%): 276 (9) [$\text{M}^+ + 1$], 551 (100) [$2\text{M}^+ + 1$], 826 (53) [$3\text{M}^+ + 1$].

(1*S*, 2*S*)-(+)-(2-Methylprop-2-enyl)amino-1-phenylpropane-1,3-diol was isolated in 9% yield ($R_f = 0.20$) as light-yellow oil, $[\alpha]_D^{21} = +49.3$ ($c = 1.0$, EtOH). $^1\text{H NMR}$: $\delta = 1.69$ (s, 3H, CH_3), 2.66 (dt, $^3J = 7.4$, 3.8 Hz, 1H, 2-H), 2.99 (d, $^2J = 14.2$ Hz, 1H, N- CH_2), 3.13 (d, $^2J = 14.2$ Hz, 1H, N- CH_2), 3.23 (dd, $^2J = 11.3$, $^3J = 3.8$ Hz, 1H, 3-H'), 4.56 (d, $^3J = 7.4$ Hz, 1H, 1-H), 4.81 (s, 2H, $\text{C}(\text{CH}_3)=\text{CH}_2$), 7.22–7.34 (m, 5H, Ar-H). $^{13}\text{C NMR}$: $\delta = 20.3$ (CH_3), 52.9 (N- CH_2), 59.1 (C-3), 63.5 (C-2), 72.8 (C-1), 111.2 ($\text{C}(\text{CH}_3)=\text{CH}_2$), 142.0 ($\text{C}(\text{CH}_3)=\text{CH}_2$), 126.4, 127.4, 128.1, 143.2 (Ar-C). MS (FD): m/z (%): 222 (35) [M^++1], 443 (70) [2M^++1], 664 (100) [3M^++1].

(1*S*, 2*S*)-(+)-*N*-[(1,3-Dihydroxy-1-phenyl)prop-2-yl]-*N*-(3-phenylprop-2-en-1-yl)formamide (11e): A solution of amino alcohol **10** (5.7 g, 0.02 mol) and *p*-toluenesulfonic acid (2.5 mg) in ethyl formate (200 ml) was refluxed for 20h [16]. Removal of the solvent, followed by recrystallization from THF affords **11e**. Yield 6.07 g (98%), colourless solid, m.p. 55 °C. $[\alpha]_D^{22} = +31.1$ ($c = 1.0$, EtOH). As is indicated by the NMR spectra the compound exists in two rotamers. $^1\text{H NMR}$ (CD_3OD): Rotamer I: $\delta = 3.49$ (m, 1H, 2-H), 3.63–3.82 (m, 3H, N- CH_2 and 3-H), 4.11 (dd, $^2J = 15.2$, $^3J = 6.6$ Hz, 1H, 3-H'), 4.88 (d, $^3J = 5.5$ Hz, 1H, 1-H), 5.91 (m, 1H, $\text{CH}=\text{CHPh}$), 6.34 (d, $^3J = 15.9$ Hz, 1H, $\text{CH}=\text{CHPh}$), 7.17–7.29 (m, 10H, Ar-H), 8.11 (s, 1H, $\text{CH}=\text{O}$). - Rotamer II: $\delta = 3.63$ –3.82 (m, 5H, N- CH_2 , 2-H, 2x 3-H), 4.98 (d, $^3J = 5.4$ Hz, 1H, 1-H), 5.42 (m, 1H, $\text{CH}=\text{CHPh}$), 6.39 (d, $J = 15.8$ Hz, 1H, $\text{CH}=\text{CHPh}$), 7.17–7.29 (m, 10H, Ar-H), 7.98 (s, 1H, $\text{CH}=\text{O}$). $^{13}\text{C NMR}$ (CD_3OD): Rotamer I: $\delta = 45.3$ (N- CH_2), 60.5 (C-3), 65.6 (C-2), 72.0 (C-1), 124.4 ($\text{CH}=\text{CHPh}$), 136.6 ($\text{CH}=\text{CHPh}$), 164.6 (C=O). - Rotamer II: $\delta = 49.5$ (N- CH_2), 59.7 (C-3), 65.3 (C-2), 71.6 (C-1), 123.7 ($\text{CH}=\text{CHPh}$), 135.6 ($\text{CH}=\text{CHPh}$), 165.5 (C=O). - 125.6–128.3, 132.7, 134.2, 141.2 (Ar-C). MS (FD): m/z (%): 311 (41) [M^+], 623 (100) [2M^++1], 934 (12) [3M^++1]. $\text{C}_{19}\text{H}_{21}\text{NO}_3$ (311.4) Calcd C 73.28 H 6.80 N 4.50 Found C 73.07 H 6.66 N 4.43.

(1*S*, 2*S*)-(+)-2-[*N*-Methyl-(3-phenylprop-2-en-1-yl)amino]-1-phenylpropane-1,3-diol (11f): A solution of **10** (5.7 g, 0.02 mol), methyl iodide (4.31 g, 0.02 mol) and ethyldiisopropylamine (12.0 g, 0.022 mol) in CHCl_3 (100 ml) was refluxed for 6 h. Then the reaction mixture was washed with water (3x 50 ml). After the organic layer had been dried with MgSO_4 , the solvent was removed. Recrystallization from EtOH afforded colourless crystals, m.p. 100 °C. Yield 4.04 g (68%), $[\alpha]_D^{23} = +92.1$ ($c = 1.0$, EtOH). $^1\text{H NMR}$: $\delta = 2.43$ (s, 3H, CH_3), 2.76 (ddd, $^3J = 9.7$, 8.3, 4.1 Hz, 1H, 2-H), 3.33 (dd, $^2J = 11.4$, $^3J = 4.1$ Hz, 1H, 3-H), 3.46 (ddd, $^2J = 13.9$, $^3J = 6.8$, $^4J < 2$ Hz, 1H, $\text{CH}_2-\text{CH}=\text{CHPh}$), 3.49 (dd, $^2J = 11.4$, $^3J = 8.3$ Hz, 1H, 3-H'), 3.58 (ddd, $^2J = 13.9$, $^3J = 6.4$, $^4J < 2$ Hz, 1H, $\text{CH}_2-\text{CH}=\text{CHPh}$), 4.39 (d, $^3J = 9.7$ Hz, 1H, 1-H), 6.27 (dt, $^3J = 15.8$, 6.6 Hz, 1H, $\text{CH}=\text{CHPh}$), 6.52 (d, $^3J = 15.8$ Hz, 1H, $\text{CH}=\text{CHPh}$), 7.21–7.38 (m, 10H, Ar-H). $^{13}\text{C NMR}$: $\delta = 36.5$ (CH_3), 58.0 (N- CH_2), 58.6 (C-3), 70.2 (C-2), 71.4 (C-1), 132.4

(CH=CHPh), 126.2–128.5, 136.9, 141.8 (Ar-C, CH=CHPh). MS (FD): m/z (%): 144 (100) [C₁₀H₁₀N⁺], 298 (46) [M⁺+1], 595 (75) [2M⁺+1], 892 (46) [3M⁺+1]. C₁₉H₂₃NO₂ (297.4) Calcd C 76.73 H 7.79 N 4.71 Found C 76.66 H 7.90 N 4.64.

3.3 Preparation of the bicyclic compounds 12 and 13

3.3.1 General procedure

A solution of dimethyl sulfoxide (2.1 g, 26.6 mmol) in CH₂Cl₂ (20 ml) was added dropwise to a solution of oxalyl chloride (1.76 g, 14 mmol) in CH₂Cl₂ (50 ml) at -78°C under nitrogen. After 10 min a solution of the amino alcohol 11 (13.3 mmol) in CH₂Cl₂ (20 ml) was added dropwise. Stirring was continued for 2 h at -78°C before triethylamine (3.39 g, 33.25 mmol) was added. Subsequently the temp. was raised to 0°C, then water (0.25 ml, 14 mmol) was added for hydrolysis. Successively MgSO₄ (approxim. 3 g) and *N*-tert-butylhydroxylamine or *N*-benzylhydroxylamine hydrochloride (13.3 mmol) were added. The reaction mixture was stirred for 3 d at room temp.. After filtration the organic layer was washed with water twice and then dried with MgSO₄. After removal of the solvent the crude product was purified either by recrystallization or by column chromatography on silicagel.

(*αS*, *1S*, *5S*, *8S*)-(+)-(7-Benzyl-2-tert-butyl-3-oxa-2,7-diazabicyclo[3.3.0]oct-8-yl)-phenylmethanol (12a): Flash chromatography (EtOAc/petroleum ether 1:1, R_f = 0.71), yellow oil, yield 45%, [α]_D²⁶ = +1.3 (c = 1.0, EtOH). ¹H NMR (500 MHz): see Tables 2/3. Additional signals: δ = 1.14 (s, 9H, tBu), 3.28 (d, ²J = 13.0 Hz, 1H, CH₂Ph), 3.57 (d, ²J = 13.0 Hz, 1H, CH₂Ph), 7.22–7.69 (m, 10H, Ar-H). ¹³C NMR: see Table 4. Additional signals: δ = 60.2 (CH₂-Ph), 125.4–128.6, 139.0, 143.6 (Ar-C). MS (EI): m/z (%): 260 (65) [M⁺-C₇H₇O], 91 (100) [C₇H₇⁺].

(*αS*, *1S*, *5S*, *8S*)-(-)-(7-Benzyl-2-tert-butyl-5-methyl-3-oxa-2,7-diazabicyclo[3.3.0]oct-8-yl)-phenylmethanol (12b): After two chromatographic separations (EtOAc/petroleum ether 1:2, R_f = 0.58; EtOAc/petroleum ether 1:6, R_f = 0.15) and recrystallization from petroleum ether colourless solid, m.p. 114 °C. Yield 0.27 g (5%), [α]_D²² = -9.1 (c = 1.0, EtOH). ¹H NMR: see Tables 2/3. Additional signals: δ = 1.10 (s, 9H, tBu), 1.19 (s, 3H, CH₃), 3.24 (d, ²J = 13.0 Hz, 1H, CH₂Ph), 3.55 (d, ²J = 13.0 Hz, 1H, CH₂Ph), 7.20–7.32 (m, 10H, Ar-H). ¹³C NMR: see Table 4. Additional signals: δ = 21.8 (CH₃), 56.4 (CH₂Ph), 125.4–129.4, 143.7, 149.3 (Ar-C). MS (FD): m/z (%): 380 (42) [M⁺]. C₂₄H₃₂N₂O₂ (380.5) Calcd C 75.76 H 8.48 N 7.36 Found C 75.56 H 8.38 N 7.15.

(αS , $1S$, $5S$, $8S$)-(+)-(7-Allyl-2-tert-butyl-3-oxa-2,7-diazabicyclo[3.3.0]oct-8-yl)-phenylmethanol (12c): Chromatography (Et₂O, R_f = 0.75), brown oil, yield 1.72g (41%), $[\alpha]_D^{19} = +27.9$ (c = 1.0, EtOH). ¹H NMR: see Tables 2/3. Additional signals: $\delta = 0.89$ (s, 9H, tBu), 2.75 (dd, ²J = 13.9, ³J = 7.5 Hz, 1H, CH₂-CH=CH₂), 2.87 (ddt, ²J = 13.9, ³J = 5.2, ⁴J = 1.5 Hz, 1H, CH₂-CH=CH₂), 4.90 (m, 2H, CH₂-CH=CH₂), 5.60 (m, 1H, CH₂-CH=CH₂), 7.12-7.33 (m, 5H, Ar-H). ¹³C NMR: see Table 4. Additional signals: $\delta = 58.3$ or 58.2 (CH₂-CH=CH₂), 116.8 (CH₂-CH=CH₂), 135.2 (CH₂-CH=CH₂), 125.4, 126.8, 128.1, 143.4 (Ar-C). MS (FD): m/z (%): 315.9 (100) [M⁺], 633.0 (95) [2M⁺], 948.9 (95) [3M⁺]. C₁₉H₂₈N₂O₂ (316.4) Calcd C 72.12 H 8.92 N 8.85 Found C 71.90 H 8.30 N 8.35.

(αS , $1S$, $5S$, $8S$)-(-)-[2-tert-Butyl-5-methyl-7-(2-methylprop-2-en-1-yl)-3-oxa-2,7-diazabicyclo[3.3.0]oct-8-yl]-phenylmethanol (12d): Recrystallization from petroleum ether, colourless needles, m.p. 103 °C, yield 0.08 g (20%), $[\alpha]_D^{22} = -23.0$ (c = 1.0, EtOH). ¹H NMR: see Tables 2/3. Additional signals: $\delta = 1.05$ (s, 9H, tBu), 1.35 (s, 3H, CH₃), 1.64 (s, 3H, CH₃), 2.76 (d, ²J = 13.5 Hz, 1H, N-CH₂), 2.78 (d, ²J = 13.5 Hz, 1H, N-CH₂), 4.71 (s, 1H, C=CH₂), 4.74 (s, 1H, C=CH₂), 7.17-7.39 (m, 5H, Ar-H). ¹³C NMR: see Table 4. Additional signals: $\delta = 20.4$ (CH₃), 21.9 (CH₃), 59.2 or 56.6 (C(CH₃)₃), 62.2 (N-CH₂), 112.0 (C=CH₂), 143.6 (C=CH₂), 125.4, 126.9, 128.2, 143.0 (Ar-C). MS (FD): m/z (%): 344 (100) [M⁺]. C₂₁H₃₂N₂O₂ (344.5) Calcd C 73.22 H 9.36 N 8.17 Found C 73.04 H 9.21 N 7.96.

(αS , $1S$, $4S$, $5S$, $8S$)-(+)-(2-tert-Butyl-7-formyl-4-phenyl-3-oxa-2,7-diazabicyclo[3.3.0]oct-8-yl)-phenylmethanol (12e): Chromatography (tert-butylmethyl ether, R_f = 0.36), orange solid, m.p. 115 °C, yield 1.14 g (23%). $[\alpha]_D^{19} = +42.9$ (c = 1.0, EtOH). As is indicated by the ¹³C NMR spectrum the compound exists in two rotamers. ¹H NMR: see Tables 2/3. Additional signals: $\delta = 1.17$ (s, 9H, tBu), 3.50 (s, broad, 1H, OH), 7.29-7.38 (m, 10H, Ar-H), 7.45 (s, 1H, CH=O). ¹³C NMR: see Table 4. Additional signals: Rotamer I: $\delta = 126.4$ -128.8, 138.1, 140.6 (Ar-C), 161.8 (C=O), Rotamer II: $\delta = 126.9$ -129.1, 138.6, 140.8 (Ar-C), 162.0 (C=O). MS (EI): m/z (%): 91 (100) [C₇H₇⁺], 380 (16) [M⁺].

(αS , $1S$, $4S$, $5S$, $8S$)-(+)-(2-tert-Butyl-7-methyl-4-phenyl-3-oxa-2,7-diazabicyclo[3.3.0]oct-8-yl)-phenylmethanol (12f): Chromatography (tert-butylmethyl ether, R_f = 0.36), orange oil, yield 1.13 g (23%). 12f was also obtained by reduction of 12e with LiAlH₄, yield 85%. $[\alpha]_D^{21} = +0.5$ (c = 1.0, EtOH). ¹H NMR: see Tables 2/3. Additional signals: $\delta = 1.07$ (s, 9H, tBu), 2.25 (s, 3H, CH₃), 7.20-7.39 (m, 10H, Ar-H). ¹³C NMR: see Table 4. Additional signals: $\delta = 44.0$ (CH₃), 125.7-128.5, 139.6, 143.2 (Ar-C). MS (FD): m/z (%): 367 (100) [M⁺+1].

(αS , 1*S*, 4*S*, 5*S*, 8*S*)-(-)-(7-Allyl-2-tert-butyl-4-phenyl-3-oxa-2,7-diazabicyclo[3.3.0]oct-8-yl)-phenylmethanol (12g): Chromatography (5x: Me₂CO, R_f = 0.14; Me₂CO/petroleum ether 1:1, R_f = 0.2; EtOAc/petroleum ether 2:1, R_f = 0.79; EtOAc/petroleum ether 1:1, R_f = 0.67; EtOAc/petroleum ether 1:3, R_f = 0.44), recrystallization from petroleum ether, colourless needles, m.p. 117 °C, yield 0.14 g (3%), $[\alpha]_D^{22} = -24.2$ (c = 1.0, EtOH). ¹H NMR: see Tables 2/3. Additional signals: $\delta = 0.87$ (s, 9H, tBu), 3.33 (dd, ²J = 13.7, ³J = 6.7 Hz, 1H, CH₂-CH=CH₂), 3.43 (dd, ²J = 13.7, ³J = 6.1 Hz, 1H, CH₂-CH=CH₂), 5.05 (m, 2H, CH=CH₂), 5.76 (m, 1H, CH=CH₂), 7.29-7.38 (m, 10H, Ar-H). ¹³C NMR: see Table 4. Additional signals: $\delta = 55.0$ (CH₂-CH=CH₂), 117.2 (CH=CH₂), 136.0 (CH=CH₂), 126.3-128.5, 139.7, 142.5 (Ar-C). MS (FD): m/z (%): 392 (100) [M⁺]. C₂₅H₃₂N₂O₂ (392.5) Calcd C 76.50 H 8.22 N 7.14 Found C 75.96 H 8.32 N 6.95.

(αS , 1*S*, 4*S*, 5*S*, 8*S*)-[2-tert-Butyl-7-(3-phenylprop-2-en-1-yl)-3-oxa-2,7-diazabicyclo[3.3.0]oct-8-yl]-phenylmethanol (12h) was formed along with 12g. After separation from 12g it could not be obtained entirely pure. ¹H NMR: see Tables 2/3. Additional signals: $\delta = 1.01$ (s, 9H, tBu), 2.91 (dd, ²J = 14.0, ³J = 7.7 Hz, 1H, CH₂-CH=CHPh), 3.0-3.2 (m, 1H, CH₂-CH=CHPh, superimposed by the signals of 5-H and 8-H), 6.01 (ddd, ³J = 15.9, 7.7, 5.4 Hz, 1H, CH₂-CH=CHPh), 6.16 (d, ²J = 15.9 Hz, 1H, CH=CHPh), 7.18-7.36 (m, 10H, Ar-H). ¹³C NMR: see Table 4. Additional signal: $\delta = 57.6$ (CH₂-CH=CHPh).

(αS , 1*S*, 5*S*, 8*S*)-(-)-(2,7-Dibenzyl-3-oxa-2,7-diazabicyclo[3.3.0]oct-8-yl)-phenylmethanol (13a): Chromatography (EtOAc/petroleum ether 1:3, R_f = 0.69) and recrystallization from Et₂O, colourless crystals, m.p. 109 °C, yield 1.97 g (37%), $[\alpha]_D^{19} = -65.4$ (c = 1.0, EtOH). ¹H NMR (400 MHz): see Tables 2/3. Additional signals: $\delta = 3.02$ (d, ²J = 12.9 Hz, 1H, CH₂Ph), 3.52 (d, ²J = 12.9 Hz, 1H, CH₂Ph), 3.66 (d, ²J = 12.6 Hz, 1H, CH₂Ph), 4.03 (d, ²J = 12.6 Hz, 1H, CH₂Ph), 7.15-7.38 (m, 15H, Ar-H). ¹³C NMR: see Table 4. Additional signals: $\delta = 59.5$ or 59.4 (R³ = CH₂Ph), 125.4-129.3, 136.6, 138.7, 143.1 (Ar-C). MS (FD): m/z (%): 401 (80) [M⁺+1], 801 (67) [2M⁺]. C₂₃H₂₈N₂O₂ (400.5) Calcd C 77.97 H 7.05 N 6.99 Found C 78.81 H 6.93 N 6.99.

(αS , 1*S*, 5*S*, 8*S*)-(-)-(7-Allyl-2-benzyl-3-oxa-2,7-diazabicyclo[3.3.0]oct-8-yl)-phenylmethanol (13c): Chromatography (Et₂O, R_f = 0.62), yellow solid, m.p. 110 °C, yield 1.39 g (30%), $[\alpha]_D^{26} = -39.0$ (c = 1.0, EtOH). ¹H NMR: see Tables 2/3. Additional signals: $\delta = 2.69$ (dd, ²J = 13.9, ³J = 7.8 Hz, 1H, CH₂-CH=CH₂), 3.13 (dd, ²J = 13.9, ³J = 5.9 Hz, 1H, CH₂-CH=CH₂), 3.55 (d, ²J = 12.7 Hz, 1H, CH₂Ph), 3.93 (d, ²J = 12.7 Hz, 1H, CH₂Ph), 4.28 (s broad, 1H, OH), 4.94 (m, 2H, CH=CH₂), 5.65 (m, 1H, CH=CH₂), 7.10-7.33 (m, 10H, Ar-H). ¹³C

NMR: see Table 4. Additional signals: $\delta = 57.8$ ($\text{CH}_2\text{-CH=CH}_2$), 117.4 (CH=CH_2), 134.6 (CH=CH_2), 125.7–129.2, 136.6, 142.9 (Ar-C). MS (FD): m/z (%): 142 (100), 279 (20), 351 (1) [M^+], 702 (12) [2M^+]. $\text{C}_{22}\text{H}_{26}\text{N}_2\text{O}_2$ (350.5) Calcd C 75.40 H 7.48 N 7.99 Found C 74.76 H 7.42 N 7.75.

3.3.2 Preparation of compounds 12i and 13i

A mixture of dibenzylidene acetone palladium (0) ($\text{Pd}(\text{dba})_2$) (96.5 mg, 0.27 mmol) and 1,4-bis-(diphenylphosphino)butane (DPPB) (115.1 mg, 0.27 mmol) in dry THF (10 ml) was stirred for 15 min. under argon. This catalytic mixture and 2-mercapto-benzoic acid were added to a solution of **12c** or **13c** (5.4 mmol) in THF (50 ml). The reaction mixture was stirred for 2 h at 60°C. Subsequently the reaction mixture was treated with HCl (10%, 25 ml) and then extracted with EtOAc. The aqueous layer was made alkaline with 1 N NaOH and again extracted two times with EtOAc. After the combined organic layer had been dried with MgSO_4 , the solvent was removed.

(αS , 1*S*, 5*S*, 8*S*)-(-)-(2-tert-Butyl-3-oxa-2,7-diazabicyclo[3.3.0]oct-8-yl)-phenylmethanol

(12i): Orange solid, m.p. 95 °C, yield 0.91 g (61%). $[\alpha]_D^{21} = -5.3$ ($c = 1.0$, EtOH). ^1H NMR (500 MHz): see Tables 2/3. Additional signals: $\delta = 0.73$ (s, 9H, tBu), 4.21 (s broad, 2H, NH, OH), 7.12–7.40 (m, 5H, Ar-H). ^{13}C NMR: see Table 4. Additional signals: $\delta = 126.7$, 127.3, 127.7, 141.6 (Ar-C). MS (EI): m/z (%): 277 (1) [M^+].

(αS , 1*S*, 5*S*, 8*S*)-(-)-(2-Benzyl-3-oxa-2,7-diazabicyclo[3.3.0]oct-8-yl)-phenylmethanol (13i):

Chromatography (tert-butylmethyl ether/EtOH 1:1, $R_f = 0.25$), colourless crystals, m.p. 125 °C, yield 0.73 g (44%). $[\alpha]_D^{22} = -15.2$ ($c = 1.0$, EtOH). ^1H NMR: see Tables 2/3. Additional signals: $\delta = 3.54$ (d, $^2J = 13.3$ Hz, 1H, CH_2Ph), 3.78 (d, $^2J = 13.3$ Hz, 1H, CH_2Ph), 7.13–7.34 (m, 10H, Ar-H). ^{13}C NMR: see Table 4. Additional signals: $\delta = 126.9$ –129.0, 136.7, 141.7 (Ar-C). MS (FD): m/z (%): 311 (100) [$\text{M}^+ + 1$]. $\text{C}_{19}\text{H}_{22}\text{N}_2\text{O}_2$ (310.4) Calcd C 73.52 H 7.14 N 9.02 Found C 73.15 H 6.86 N 8.69.

3.3.3 Preparation of compounds 12k and 13k

The methylation of compounds **12i** and **13i** with methyl iodide was performed as described for the preparation of **11f**.

(αS , $1S$, $5S$, $8S$)-(-)-(2-tert-Butyl-7-methyl-3-oxa-2,7-diazabicyclo[3.3.0]oct-8-yl)-phenyl-methanol (12k): Chromatography (tert-butylmethyl ether, $R_f = 0.29$), colourless needles, m.p. 118 °C, yield 83%, $[\alpha]_D^{25} = -14.7$ ($c = 1.0$, EtOH). ^1H NMR: see Tables 2/3. Additional signals: $\delta = 1.06$ (s, 9H, tBu), 1.84 (s, 3H, CH_3), 7.12–7.38 (m, 5H, Ar-H). ^{13}C NMR: see Table 4. Additional signals: $\delta = 42.2$ (CH_3), 125.1, 126.6, 128.0, 143.9 (Ar-C). MS (FD): m/z (%): 290 (100) [M^+].

(αS , $1S$, $5S$, $8S$)-(-)-(2-Benzyl-7-methyl-3-oxa-2,7-diazabicyclo[3.3.0]oct-8-yl)-phenyl-methanol (13k): Chromatography (tert-butyl methyl ether/ethanol 1:1, $R_f = 0.27$), beige solid, m.p. 155 °C, yield 52%, $[\alpha]_D^{19} = -15.3$ ($c = 1.0$, EtOH). ^1H NMR: see Tables 2/3. Additional signals: $\delta = 1.96$ (s, 3H, CH_3), 3.66 (d, $^2J = 12.4$ Hz, 1H, CH_2Ph), 4.05 (d, $^2J = 12.4$ Hz, 1H, CH_2Ph), 7.21–7.36 (m, 10H, Ar-H). ^{13}C NMR: see Table 4. Additional signals: $\delta = 41.9$ (CH_3), 125.4–129.2, 136.7, 143.3 (Ar-C). MS (FD): m/z (%): 217 (100) [$\text{C}_{13}\text{H}_{17}\text{N}_2\text{O}^+$], 325 (36) [$\text{M}^+ + 1$], 649 (13) [$2\text{M}^+ + 1$].

3.4 Catalysis of the addition of diethylzinc to benzaldehyde

Freshly distilled benzaldehyde (0.25 ml, 2.5 mmol) was added to the amino alcohol **12** or **13** (0.15 mmol) in a 25 ml flask under argon. The clear solution was cooled to 0 °C, then a 0.1 M solution of diethylzinc in hexane (3.75 ml, 3.75 mmol) was added dropwise within a period of 20 min. The reaction mixture was stirred for 12 h at 0 °C. Subsequently, the reaction was quenched by addition of 1.5 M HCl (10 ml). Then the mixture was extracted with Et_2O (3x). The combined organic layer was dried with MgSO_4 . After filtration and removal of the solvent a non-racemic mixture of (*R*)- and (*S*)-1-phenylpropane-1-ol was obtained.

^1H NMR: $\delta = 0.90$ (t, $^3J = 7.4$ Hz, 3H, 3-H), 1.66–1.89 (m, 2H, 2-H), 2.01 (s broad, 1H, OH), 4.58 (dd, $^3J = 6.5$ and 6.7 Hz, 1H, 1-H), 7.23–7.35 (m, 5H, Ar-H). ^{13}C NMR: $\delta = 10.1$ (C-3), 31.8 (C-2), 76.0 (C-1), 125.9, 127.4, 128.3, 144.6 (Ar-C).

3.5 Treatment of 1-phenylpropane-1-ol with (*S*)-(+)-*O*-acetyl mandelic acid to give the corresponding diastereomeric esters [22]

1-Phenylpropane-1-ol (0.094 g, 0.69 mmol) was cooled to 0 °C under argon. Successively, (*S*)-(+)-*O*-acetyl mandelic acid (0.134 g, 0.69 mmol), *N,N*-dimethyl-4-aminopyridine (5 mg, 0.04 mmol) and *N,N'*-dicyclohexyl carbodiimide (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 additional 20 h at room temp.. Then the solution was separated from the precipitate and the solvent removed by distillation. Non-changed 1-phenylpropane-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*).

^1H NMR: (*R*, *S*), the signals of the diastereomer (*S*, *S*) are given in brackets. $\delta = 0.63$ [0.88] (t, $^3\text{J} = 7.4$ Hz, 3H, CH_2CH_3), 1.64–1.85 (m, 2H + 2H, CH_2CH_3), 2.16 [2.18] (s, 3H, CH_3CO_2), 5.66 [5.65] (dd, $^3\text{J} = 7.4$, $^3\text{J} = 6.0$ Hz, 1H, $\text{CH}_3\text{-CH}_2\text{-CH-O}$), 5.97 [5.98] (s, 1H, $\text{CH}_3\text{CO}_2\text{CH}$), 6.94–7.50 (m, 10H + 10 H, Ar-H). ^{13}C NMR: $\delta = 9.3$ [9.6] ($\text{CH}_2\text{-CH}_3$), 20.6 (CH_3CO_2), 29.0 [29.2] (CH_2CH_3), 74.5 ($\text{CH}_3\text{-CH}_2\text{-CH-O}$), 78.6 [78.7] (Ph-CHCO_2), 168.2 [169.0] (s, C=O), 170.0 [170.2] (s, C=O), 126.0–139.0 (Ar-C).

The diastereomeric excess that corresponds to the enantiomeric excess of 1-phenylpropane-1-ol was determined by the relative intensities of the triplets at 0.63 and 0.88 ppm in the ^1H NMR spectra.

3.6 Crystal Data

3.6.1 Crystal Data for 13a

$\text{C}_{26}\text{H}_{28}\text{N}_2\text{O}_2$, $M_r = 400.50$, $F(000) = 856$, monoclinic, $a = 19.522(2)$, $b = 5.321(1)$, $c = 21.728(1)$ Å, $\beta = 102.530(10)^\circ$, $V = 2203.3(5)$ Å³, space group I2, $Z = 4$, $D_x = 1.207$ g/cm³, $\mu(\text{CuK}\alpha) = 6.01$ cm⁻¹. The experimental data were collected at room temperature on a Nonius CAD4 diffractometer using graphite monochromated $\text{CuK}\alpha$ radiation ($\lambda = 1.5478$ Å). Absorption correction: Semi-empirical from Ψ -scans. The structure was solved by direct and difmap methods [23]. Full matrix refinement on F^2 values lead to the final R values $wR_2 = 0.2183$ (all data) and the conventional R = 0.0726 ($I > 2\sigma(I)$).

3.6.2 Crystal Data for 13c

$\text{C}_{22}\text{H}_{26}\text{N}_2\text{O}_2$, $M_r = 350.45$, $F(000) = 752$, orthorhombic, $a = 7.515(1)$, $b = 13.748(1)$, $c = 18.678(1)$ Å, $V = 1929.8(3)$ Å³, space group P2₁2₁2₁, $Z = 4$, $D_x = 1.206$ g/cm³, $\mu(\text{CuK}\alpha) = 6.11$ cm⁻¹. The experimental data were collected at room temperature on a Nonius CAD4 diffractometer using graphite monochromated $\text{CuK}\alpha$ radiation ($\lambda = 1.54184$ Å). An absorption correction was not applied. The structure was solved by direct methods and difference fourier synthesis [24]. Full matrix refinement on F^2 values lead to the final R values $wR_2 = 0.1192$ (all data) and the conventional R = 0.0450 ($I > 2\sigma(I)$).

3.6.3 Crystal Data for 12g

$\text{C}_{25}\text{H}_{32}\text{N}_2\text{O}_2$, $M_r = 392.53$, $F(000) = 848$, orthorhombic, $a = 6.376(1)$, $b = 18.155(2)$, $c = 19.422(1)$ Å, $V = 2248.2(4)$ Å³, space group P2₁2₁2₁, $Z = 4$, $D_x = 1.160$ g/cm³, $\mu(\text{CuK}\alpha) = 5.73$ cm⁻¹. The experimental data were collected at room temperature on a Nonius CAD4 diffractometer using graphite monochromated $\text{CuK}\alpha$ radiation ($\lambda = 1.54178$ Å). The structure

was solved by direct methods and difference fourier synthesis [25]. Full matrix refinement on F^2 values lead to the final R values $wR_2 = 0.1393$ (all data) and the conventional $R = 0.0530$ ($I > 2\sigma(I)$).

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