Diastereoselective Addition of Chiral (2-Lithiophenyl)acetaldehyde Acetals to Various Imines as Key Step in the Asymmetric Synthesis of 1-Aryltetrahydroisoquinolines, Part 4[+]

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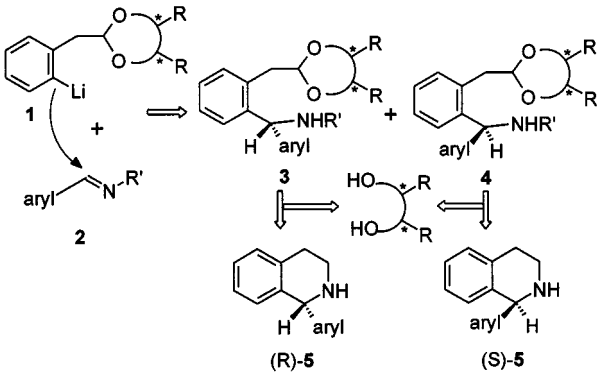
A novel asymmetric synthesis of 1-aryl-1,2,3,4-tetrahydroisoquinolines has been developed. The key step in this synthesis is the diastereoselective addition of homochiral (2-lithiophenyl)acetaldehyde acetals to the sulfonylimine **25** and to the arylimines **28** and **31**. The best diastereoselectivity is obtained by addition of the bis(2-methoxypropan-2-yl)-substituted 1,3-dioxolane **6e** to benzylidene-*p*-anisidine (**31**) with an HPLC-determined diastereomeric ratio **32c**/**33c** = 92.1:7.9. The *N*-tosyl and the *N*-(4-methoxyphenyl) groups of the addition products **26d**, **27d**, **32c**, and **33c** are cleaved with sodium in liquid ammonia and ammonium cerium(IV) nitrate, respectively, to yield the primary amines **35** and **36**. The acid-catalysed cyclization of the sulfonamides **26d** and **27d** and the carbamates **37** and **38**, prepared from **35** and **36**, leads to the enantiomerically pure dihydroisoquinolines **40** and **41**, respectively. During the cyclization of the sulfonamides **26d**, **27d** and the carbamates **37**, **38** the chiral auxiliary – the diol **39** – is cleaved unchanged and can be recovered in good yields.

Introduction

The structure of a great number of pharmacologically active compounds is based on the 1-substituted 1,2,3,4-tetrahydroisoquinoline skeleton.[1] Therefore, several methods for the synthesis of optically active tetrahydroisoquinolines have been developed during the last twenty years.[2] During the course of our work on central nervous system (CNS) receptor ligands we have been engaged in the synthesis of 1-*aryl*-1,2,3,4-tetrahydroisoquinolines **5** possessing antagonistic activity at dopamine D_1[3] and NMDA (*N*-*m*ethyl-*D*-*a*spartate) receptors.[4] For this purpose a novel asymmetric synthesis for 1-aryl-1,2,3,4-tetrahydroisoquinolines **5** has been elaborated, in which the addition of chiral phenylacetaldehyde acetals **1** to activated imine components **2** is the key step. The chiral acetal moiety should thereby control the diastereoselectivity.[5] This strategy differs from the known 1-aryltetrahydroisoquinoline syntheses in two aspects. Firstly, the stereogenic centre in position 1 of **5** is established *before* building up the isoquinoline ring system.[6−10] Secondly, the chiral auxiliary − usually an enantiomerically pure diol − is liberated during the cyclization step without destroying the stereogenic centres and *can be recovered* in good yields.[6−9]

Herein, we report on an extension of our procedure to more stable imine components instead of the highly reactive and thus unstable acylimines **2** (R′ = CO*t*Bu, CO_2Bn). Moreover, additional acetalic heterocycles (see Scheme 2), which should improve the diastereoselectivity during the nucleophilic addition to the imines, are investigated.



Scheme 1

Preparation of Enantiomerically Pure (2-Bromophenyl)acetaldehyde Acetals

The preparation of the 1,3-dioxolanes **6a**, **6b**, **6e**, and **6g** succeeded by transacetalization of the enol ether **10**[11] or the dimethyl acetal **11**[11] with the corresponding 1,2-diols.[5] In analogy, the reaction of **10** and/or **11** with the 1,2-diols **14**,[12] **15**, **20b** or the 1,4-diol **16**[12b,13] provided the 1,3-dioxolanes **6c**, **6d**, **6f**, and the 1,3-dioxepane **8**, respectively.

The 1,2-diol **15** was prepared by alkylation of the tartaric acid derivative **13a**[12b,14] with 1-bromo-2-methoxyethane (→ **13b**) and subsequent hydrolysis. In contrast to a reported method,[15] the diol **20b** could not be obtained by hydrolysis of its acetonide. Therefore, an alternative four-step route for the preparation of **20b** analogous to the described synthesis of tetraaryldialkoxybutane-2,3-diols (TADDOLs)[16] was elaborated. Reaction of the *p*-methoxybenzaldehyde acetal **18** with excess ethylmagnesium iodide led to the diol **19a**, which was alkylated with methyl

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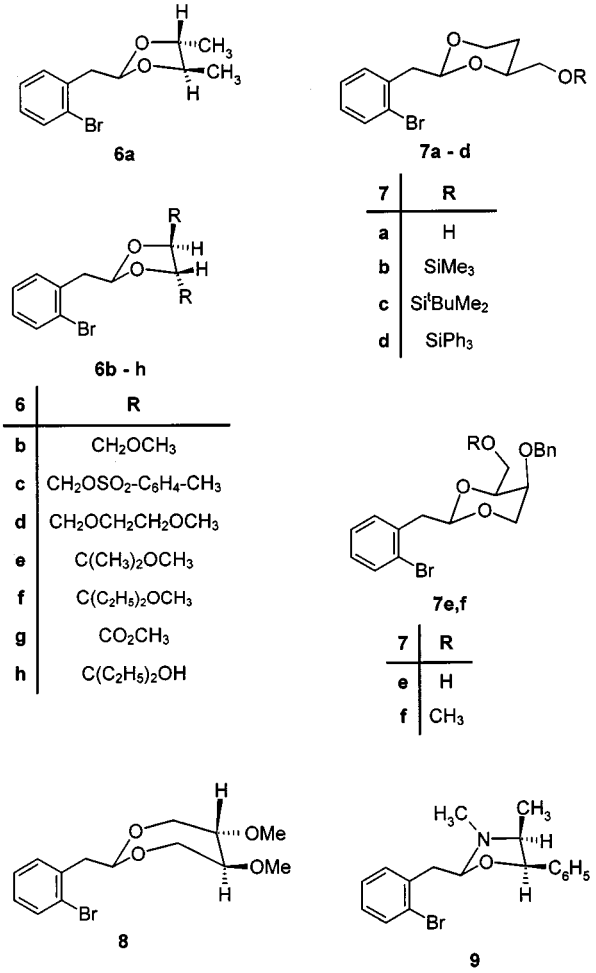
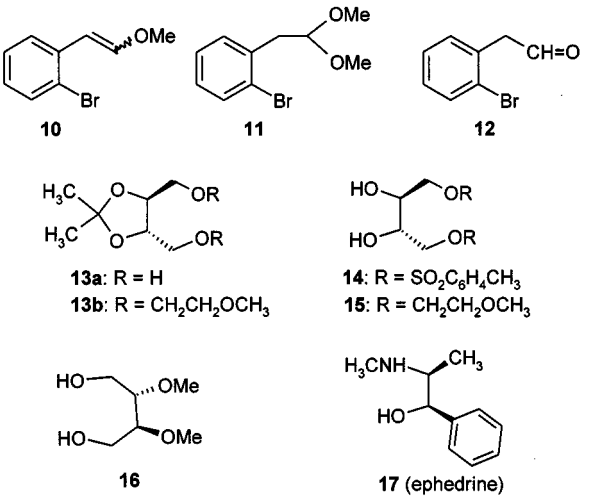


7	R
a	H
b	$SiMe_3$
c	Si^tBuMe_2
d	$SiPh_3$

6	R
b	CH_2OCH_3
c	CH_2OSO_2-C_6H_4-CH_3
d	$CH_2OCH_2CH_2OCH_3$
e	$C(CH_3)_2OCH_3$
f	$C(C_2H_5)_2OCH_3$
g	CO_2CH_3
h	$C(C_2H_5)_2OH$

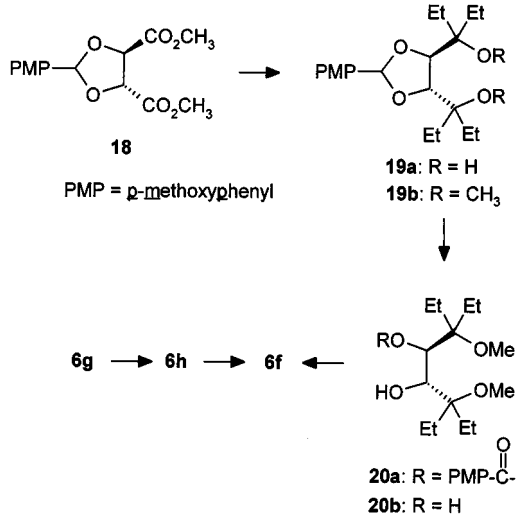
7	R
e	H
f	CH_3

Scheme 2



Scheme 3

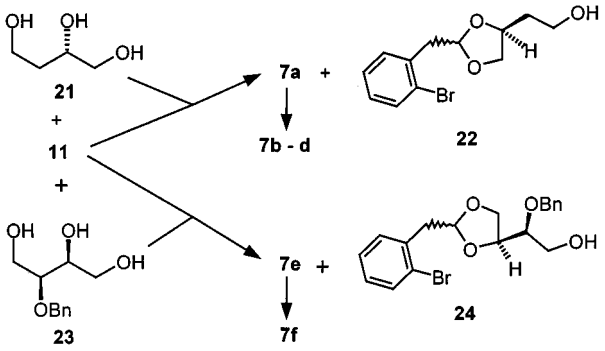
iodide to yield the dimethoxy derivative **19b**. After oxidative cleavage of the acetal moiety with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) the intermediate *p*-methoxybenzoate **20a** was reduced with $LiAlH_4$ to afford the diol **20b**. In the case of the tetraethyl derivative **6f**, Grignard reaction of the diester **6g**[5] with an excess of ethylmagnesium iodide



Scheme 4

and subsequent methylation of the resulting diol **6h** represents an attractive alternative.

Transacetalization of the phenylacetaldehyde dimetyl acetal **11** with the (*S*)-configured butanetriol **21** furnished an 80:20 mixture of the 1,3-dioxane **7a** and the 1,3-dioxolane **22**. Whereas the ^{1}H-NMR spectrum of **7a** displays only signals for the *cis* isomer, two sets of signals appear in the ^{1}H-NMR spectrum of the 1,3-dioxolane **22** (*cis*-**22**/*trans*-**22** = 1:1). A comparable regio- and diastereoselectivity is observed during the acetalization of benzaldehyde derivatives with the butanetriol **21**.[17] Since a halogen/metal exchange reaction was planned as the next step, the hydroxy group of **7a** was protected with sterically different silyl protective groups (**7b**−**7d**). The butanetriol **23** differing from **21** by an additional benzyloxy substituent (and the configuration) was derived from (*R*,*R*)-tartaric acid.[14] Transacetalization of the dimethyl acetal **11** with **23** resulted in a somewhat lower regioselectivity (**7e**/**24** = 60:40). Again, the six-membered acetal **7e**, whose configuration and conformation was deduced from a NOESY spectrum, was formed diastereoselectively, whereas the five-membered 1,3-dioxolane **24** was isolated as 1:1 *cis*/*trans*-isomeric mixture. With methyl iodide the hydroxy group of **7e** was protected to give the methoxymethyl derivative **7f**.



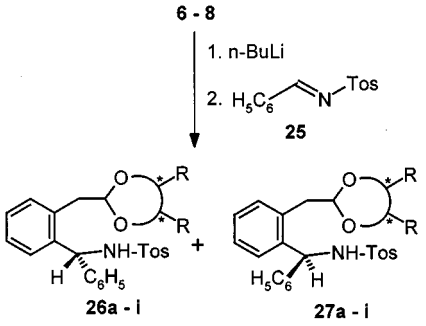
Scheme 5

The 1,3-oxazolidine **9** could not be obtained by transacetalization of the enol ether **10** or the dimethyl acetal **11** with the enantiomerically pure 1,2-amino alcohol (1*R*,2*S*)-ephedrine (**17**). However, reaction of the aldehyde **12**[11] with **17** furnished a diastereomeric mixture of N/O-acetals from which the diastereomer **9** was isolated by fractional crystallization (60% yield).

Addition of Lithiated Phenylacetaldehyde Acetals to Various Imines

At −85°C to −100°C various imine components were added to the aryllithium intermediates, which had been generated by reaction of the aryl bromides **6**−**9** with *n*-butyllithium at −100°C (bromine/lithium exchange).

At first, the diastereoselectivity in the addition of the aryllithium intermediates to the tosylimine **25**, which is easily available by condensation of benzaldehyde or its diethyl acetal with *p*-toluenesulfonamide,[18] was investigated. The activation of the imine moiety by the tosyl group in **25** is comparable to the imine activation by acyl groups in acylimines. In contrast to the acylimines, the crystalline tosylimine **25** is not sensitive to air and moisture and, therefore, can be stored for several months without degradation. Additionally, a different geometry around the imine moiety is caused by the tetrahedral sulfur atom of the tosylimine **25**.



Scheme 6

The results of the addition of various homochiral (2-lithiophenyl)acetaldehyde acetals to the tosylimine **25** are summarized in Table 1. Good chemical yields of the addition products **26**/**27** were obtained with the dioxolanes **6a**, **b**, **d**, **e** (entries 1, 2, 4, 5) and the 1,3-dioxanes **7b**−**d** (entries 9−11). Addition products after reaction of **6c**, **6g**, **7a** (dilithiated derivative generated with two equivalents of *n*-butyllithium), and **8** with the tosylimine **25** even at +25°C could not be detected. In the ^{1}H-NMR spectra of the crude reaction products only signals for the debrominated phenylacetaldehyde acetals (H instead of Br) were identified.

Integration of the separated benzylic methine signals (aryl$_2$C*H*−NH−) in the ^{1}H-NMR spectra of the unpurified addition products provided the diastereomeric ratio of the addition products **26** and **27** (e.g. **26d**: δ = 5.38; **27d**: δ = 5.80). In the case of **26d**/**27d** a HPLC analysis confirmed the ^{1}H-NMR result (**26d**/**27d** = 60.9:39.1).

Table 1. Addition of lithiated **6**−**8** to the tosylimine **25**

entry	acetal	product ratio	yield (%)
1	**6a**	**26a**/**27a** = 45:55	76
2	**6b**	**26b**/**27b** = 55:45	66
3	**6c**	no addition	−
4	**6d**	**26c**/**27c** = 52:48	65
5	**6e**	**26d**/**27d** = 61:39	62
6	**6f**	**26e**/**27e** = 62:38	32
7	**6g**	no addition	−
8	**7a**	no addition	−
9	**7b**	**26f**/**27f** = 44:56	75
10	**7c**	**26g**/**27g** = 33:67	71
11	**7d**	**26h**/**27h** = 32:68	61
12	**7f**	**26i**/**27i** = 56:44	49
13	**8**	no addition	−

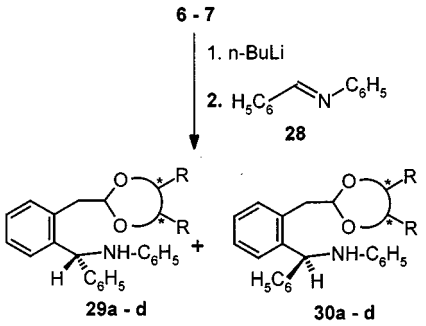
In the dioxolane series electronic or steric variations of the substituents in position 4 and 5 of the dioxolane ring had only little influence on the diastereoselectivity (ratio 55:45 to 62:38, entries 1−7). Protection of the hydroxy group of the 1,3-dioxane **7a** with sterically different silyl protective groups raised the diastereoselectivity from 44:56 (**26f**/**27f**) to 32:68 (**26h**/**27h**, entries 8−12). However, even with the very large triphenylsilyl protective group (**7d**) the diastereomeric ratio did not exceed 32:68. Unexpectedly, enlargement of the 1,3-dioxane ring to the homologous, seven-membered 1,3-dioxepane ring (**8**) reduced the reactivity of the corresponding aryllithium intermediate to such an extent that an addition to the tosylimine **25** did not take place (entry 13).

The configuration of the novel stereogenic centre in the addition products **26** and **27** was determined by transformation of the separated sulfonamides **26d** and **27d** into the known 1-phenyltetrahydroisoquinolines (*R*)-**43** and (*S*)-**43**, respectively [see part Preparation of (*R*)- and (*S*)-1-phenyl-1,2,3,4-tetrahydroisoquinoline]. In the 1,3-dioxane series the diastereomeric mixture **26g**/**27g** (de = 34%) was cyclized to afford the levorotatory 1,2-dihydroisoquinoline (*S*)-**40**. Comparison of the specific optical rotation ($[\alpha]_D^{20}$ = −94.7, *c* = 0.93 in $CHCl_3$, ee = 35%) with the specific optical rotation of the enantiomerically pure 1,2-dihydroisoquinoline (*S*)-**40** prepared from **27d** ($[\alpha]_D^{20}$ = −269.8, *c* = 1.04 in $CHCl_3$) reveals that (*S*) configuration has to be assigned to the novel stereogenic centre in the main diastereomer **27g**. Correlation of the ^{1}H-NMR spectra of all addition products **26** and **27** led to the stereochemical assignment as depicted in Table 1.

The separation of the diastereomers **26** and **27** by flash chromatography or even by HPLC proved to be difficult. After many attempts an eluent was found for the separation of the diastereomeric pair **26d** and **27d**.

Because of the unsatisfactory diastereoselectivity in the addition of the chiral (2-lithiophenyl)acetaldehyde acetals to the tosylimine **25** (Table 1), benzylidenaniline **28** was considered as alternative imine component. The air- and moisture-stable benzylidenaniline **28** is easily prepared by condensation of benzaldehyde with aniline. Compared with acylimines and sulfonylimines the reactivity of the *aryl*imine **28** towards nucleophiles is markedly reduced and, more-

over, the steric environment of the imine moiety of **28**, which exists in a stable *nonplanar* conformation[19], is changed.



Scheme 7

Nevertheless, the addition of the homochiral aryllithium derivatives − generated from the aryl bromides **6a**, **b**, **e**, and **7d** − to benzylidenaniline **28** resulted even in better yields (Table 2) than the corresponding additions to the tosylimine **25** (Table 1). A dramatic enhancement of the diastereoselectivity was observed when the 1,3-dioxolane **6e** with the two large (2-methoxypropan-2-yl) residues was added to benzylidenaniline (**29c**/**30c** = 91:9, entry 3). Aiming at a further enhancement of the diastereoselectivity the homologous doubly (3-methoxy*pentan*-3-yl)-substituted 1,3-dioxolane **6f** was included in the study. Unfortunately, treatment of **6f** with *n*-butyllithium and subsequently with **28** did not provide any addition products even at a reaction temperature of +25°C. In the ^{1}H-NMR spectrum of the unpurified product only debrominated **6f** (H instead of Br) could be detected. Obviously, the very large substituents in the dioxolane ring of **6f** prevent the addition to the arylimine **28** (entry 4) and diminishes the yield in the addition to the tosylimine **25** (entry 6, Table 1).

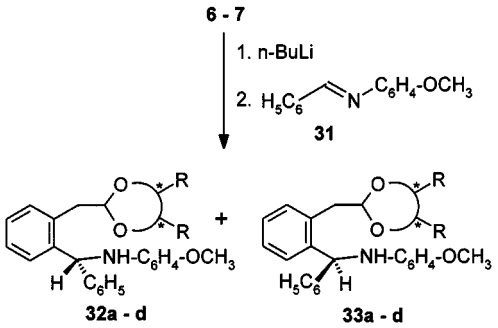
Table 2. Addition of lithiated **6** and **7** to benzylidenaniline **28**

entry	acetal	product ratio	yield (%)
1	**6a**	**29a**/**30a** = 49:51	82
2	**6b**	**29b**/**30b** = 57:43	82
3	**6e**	**29c**/**30c** = 91:9	75
4	**6f**	no addition	−
5	**7d**	**29d**/**30d** = 25:75	69

The addition of the six-membered 1,3-dioxane **7d** to the arylimine **28** also resulted in a better yield and an increased diastereoselectivity (entry 5, Table 2) in comparison with the addition to the tosylimine **25** (entry 11, Table 1).

In summary, the results of the addition to acylimines,[5] benzylimines,[20] to the sulfonylimine **25**, and the arylimine **28** lead to the conclusion that a *N*-aryl-substituted imine component with moderate reactivity (e.g. **28**) seems to be favorable with regard to high diastereoselectivities (and yields). However, the *N*-phenyl group of the benzylideneaniline addition products **29** and **30** cannot be cleaved under mild reaction conditions.

This problem was solved with the imine component benzylidene-*p*-anisidine (**31**), the condensation product of benzaldehyde with 4-methoxyaniline.[21] In **31** the imine reactivity is slightly reduced by the electron-releasing *p*-methoxy substituent. This reduced reactivity of **31** is reflected in the decreased yields of the addition products **32** and **33** (Table 3). However, performing the additions at a reaction temperature of 0°C for two hours instead of −85 to −100°C increased the yields to 62−67% without changing the diastereoselectivity (entries 2/3 and 4/5). Again the 1,3-dioxolane **6f** with the large (3-methoxypentan-3-yl) substituents did not react with benzylidene-*p*-anisidine (**31**) (entry 6). In the 1,3-dioxane series the addition with the *tert*-butyldimethylsilyl-protected derivative **7c** worked well to furnish the addition products **32d**/**33d** (entry 7), whereas the reaction with the triphenylsilyl-protected derivative **7d** failed to give any addition products (entry 8).



Scheme 8

Table 3. Addition of lithiated **6** and **7** to benzylidenanisidine **31**

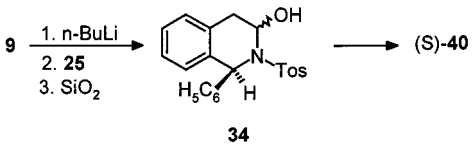
entry	acetal	product ratio	yield (%)
1	**6a**	**32a**/**33a** = 48:52	37
2	**6b**	**32b**/**33b** = 61:39	37
3	**6b**	**32b**/**33b** = 61:39	62
4	**6e**	**32c**/**33c** = 91:9	38
5	**6e**	**32c**/**33c** = 91:9	67
6	**6f**	no addition	−
7	**7c**	**32d**/**33d** = 34:66	58
8	**7d**	no addition	−

[a] Addition: 6 h at −85 to −100°C. − [b] Addition: 2 h at −85 to −100°C, then 2 h at 0°C.

The addition of the aryllithium derivatives to the arylimines **28** and **31** resulted in comparable diastereoselectivities (see Tables 2 and 3). Again, a large diastereoselectivity improvement was observed with the (2-methoxypropan-2-yl)-substituted 1,3-dioxolane **6e** (entries 4, 5). The diastereomeric ratio **32c**/**33c** = 91:9 (entries 4, 5) determined by ^{1}H-NMR spectroscopy was specified by HPLC analysis to be 92.1:7.9.

Reaction of the oxazolidinyl-substituted aryl bromide **9** with *n*-butyllithium and, subsequently, with the tosylimine **25**, or the arylimines **28** or **31** resulted in complex product mixtures. Flash chromatography of the product mixture from the tosylimine addition led to isolation of the hydroxy-substituted isoquinoline **34** in 39% yield (*cis*/*trans* = 1:1). Obviously, the oxazolidine ring containing the chiral auxiliary ephedrine was hydrolysed during workup with NH_4Cl

and/or flash chromatography preventing a diastereomeric separation.



Scheme 9

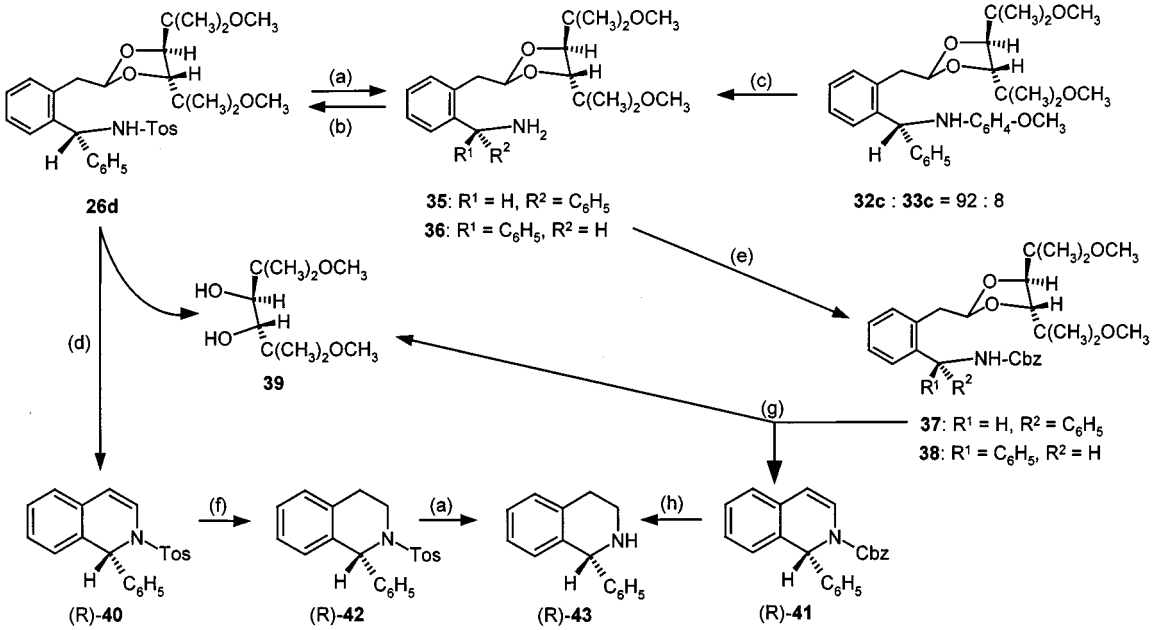
Dehydration of **34** was performed with methanesulfonyl chloride and triethylamine to yield the dihydroisoquinoline (*S*)-**40**. The specific optical rotation of (*S*)-**40** ($[\alpha]_D^{20}$ = −135.6, *c* = 1.90 in $CHCl_3$) indicates an enantiomeric ratio of (*R*)-**40**/(*S*)-**40** = 25:75 [see part Preparation of (*R*)- and (*S*)-1-phenyl-1,2,3,4-tetrahydroisoquinoline]. On the supposition that epimerization and racemization do not occur during workup, FC purification and dehydration, the enantiomeric ratio (25:75) reflects the diastereoselectivity (25:75) of the addition of lithiated **9** to the tosylimine **25**. Starting from this considerable diastereoselectivity further, more stable, chiral oxazolidine and imidazolidine ring systems will be investigated for controlling the diastereoselectivity.

Preparation of (*R*)- and (*S*)-1-Phenyl-1,2,3,4-tetrahydroisoquinoline [(*R*)-43 and (*S*)-43]

For the preparation of (*R*)- and (*S*)-1-phenyltetrahydroisoquinolines (*R*)-**43** and (*S*)-**43** various reaction pathways were investigated. The sulfonyl group of the diastereomerically pure sulfonamide **26d** was cleaved with sodium in liquid ammonia[22] to yield the primary amine **35**. Oxidative cleavage of the *p*-methoxyphenyl group of **32c** (de = 84%) with ammonium cerium(IV) nitrate[23] also furnished the primary amine **35** (de = 84%). A further purification of **35** (de = 84%) succeeded via the chromatographically separable sulfonamides **26d** and **27d**. The enantiomerically pure primary amine **35** was acylated with benzyl chloroformate to yield the carbamate **37**. With *p*-toluenesulfonic acid the carbamate **37** reacted to form the cyclization product (*R*)-**41** liberating the chiral auxiliary, the diol **39**, which could be isolated in 75% yield. Treatment of the dihydroisoquinoline (*R*)-**41** with H_2 and Pd/C furnished the (*R*)-configured 1-phenyltetrahydroisoquinoline (*R*)-**43**.[5]

More directly, heating of the diastereomerically pure sulfonamide **26d** with an excess of HCl and *p*-toluenesulfonic acid led to the tosyl-substituted dihydroisoquinoline (*R*)-**40** and the enantiomerically pure diol **39**, which was recovered in 72% yield. Subsequent reduction of (*R*)-**40** with $LiAlH_4$ provided the tetrahydroisoquinoline (*R*)-**42**. In the last step the *N*-tosyl group of (*R*)-**42** was cleaved with sodium in liquid ammonia[22] to furnish the (*R*)-configured 1-phenyl-1,2,3,4-tetrahydroisoquinoline (*R*)-**43**. The diastereomeric sulfonamide **27d** was transformed analogously into the enantiomeric (*S*)-configured 1-phenyl-1,2,3,4-tetrahydroisoquinoline (*S*)-**43** via the primary amine **36** and the carbamate **38**[5] or via the dihydroisoquinoline (*S*)-**40** and the tetrahydroisoquinoline (*S*)-**42**.

In contrast to previous data,[7a] Wanner and co-workers unequivocally proved, that the configuration of the dextrorotatory isoquinoline enantiomer (+)-**43** is (*S*).[24] This assignment was confirmed by studies of Marazano and co-workers.[9] The stereochemical specifications of the diastereomeric addition products **26**/**27**, **29**/**30**, **32**/**33** and the intermediates **35**−**38**, (*R*)- and (*S*)-**40**, (*R*)- and (*S*)-**41**, and (*R*)- and (*S*)-**42** are based on this assignment.



Scheme 10. Reaction conditions: (a) Na, NH_3 liquid, −78°C, 45 min; (b) TosCl, NEt_3, THF, room temp., 8 h; (c) $(NH_4)_2Ce(NO_3)_6$, CH_3OH, H_2O, room temp., 3 h; (d) *p*-$TolSO_3H$, HCl conc., CH_3OH, H_2O, reflux, 4 d; (e) CbzCl, NEt_3, THF, room temp., 8 h; (f) $LiAlH_4$, THF, reflux, 16 h; (g) *p*-$TolSO_3H$, CH_3OH, reflux, 16 h; (h) H_2, Pd/C, CH_3OH, 1.7 bar, room temp.,4 h[5b]

Table 4. Specific optical rotation $[\alpha]_D^{20}$ of (*R*)-**43** and (*S*)-**43**

	found	references
(*R*)-**43**	$[\alpha] = -10.12$ ($c = 0.98$, $CHCl_3$) [from (*R*)-**41**]	$[\alpha] = -10.2$ ($c = 0.17$, $CHCl_3$)[7a]
	$[\alpha] = -10.20$ ($c = 0.99$, $CHCl_3$) [from (*R*)-**42**]	
(*S*)-**43**	$[\alpha] = +12.20$ ($c = 0.99$, CH_2Cl_2) [from (*S*)-**41**]	$[\alpha] = +12.3$ ($c = 1.0$, CH_2Cl_2)[8a,24]
	$[\alpha] = +12.20$ ($c = 0.85$, CH_2Cl_2) [from (*S*)-**42**]	

According to the specific optical rotation the enantiomeric purity of the prepared tetrahydroisoquinolines (*R*)-**43** and (*S*)-**43** is higher than 99% ee (see Table 4).

Experimental Section

General: Unless otherwise stated, moisture-sensitive reactions were conducted under dry nitrogen. − THF was distilled from sodium benzophenone ketyl prior to use. − Flash chromatography (FC)[25]: Silica gel 60, 0.040−0.063 mm (Merck). − HPLC: Column filled with silica gel (5 µm particles, LiChrosorb Si 60, Merck); pump L-6200 (Merck), pressure 40 bar, rate 1 mL/min; L-4250-UV/VIS detector (Hitachi), λ = 254 nm; eluent petroleum ether/diethyl ether (60:40). − Melting points: Melting point apparatus Dr. Tottoli (Büchi), uncorrected values. − Optical rotation: Polarimeter 241 (Perkin Elmer); 1.0-dm tube; concentration *c* [g/100 mL]; temperature 20°C. − Elemental analyses: CHN elemental analyser Rapid (Heraeus). − MS: Mass spectrometer 5989A (Hewlett Packard); CI = chemical ionization. − IR: IR spectrophotometer 1600 FT-IR and 2000 FT-IR (Perkin−Elmer). − ^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz): GSX FT NMR spectrometer (Jeol), tetramethylsilane as internal standard, δ in ppm.

General Procedure 1. − Preparation of the (2-Bromophenyl)acetaldehyde Acetals 6−8 by Transacetalization of 10 or 11 with Diols: A mixture of **10** or **11**, *p*-toluenesulfonic acid (200 mg per 10 mmol of **10** or **11**), the corresponding diol (ca. 1.1 equiv.) and the appropriate solvent (THF or toluene) was heated to reflux in a Soxhlet apparatus filled with molecular sieves (4 Å) to remove methanol. After 3 d, the solution was diluted with CH_2Cl_2, washed with a saturated solution of $NaHCO_3$ and then with water, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by FC, recrystallization, or distillation.

General Procedure 2. − Bromine/Lithium Exchange at the Aryl Bromides 6−9 and Subsequent Reaction of the Aryllithium Intermediates with the Imines 25, 28, 31: An enantiomerically pure aryl bromide **6−9** was dissolved in THF (20 mL) and cooled to −100°C. A solution of *n*-butyllithium (1.6 mol/L in *n*-hexane, 1.05 equiv.) was added and the reaction mixture was stirred for 15 min at −100°C. Then, a solution of an imine **25**, **28**, or **31** (1.05 equiv.) in THF (10 mL) was added. The reaction mixture was stirred for 6 h at −85 to −100°C and then a saturated solution of NH_4Cl (20 mL) was added. The organic layer was separated, dried ($MgSO_4$), concentrated in vacuo, and the residue was purified by FC. Before carrying out the purification procedure, ^{1}H-NMR spectra were recorded to determine the diastereomeric ratio of the crude products.

(4*S*,5*S*)-(−)-2-(2-Bromobenzyl)-4,5-bis(tosyloxymethyl)-1,3-dioxolane (6c): According to General Procedure 1 a solution of **11** (5.07 g, 20.7 mmol) and **14** (10.0 g, 22.8 mmol) in THF (100 mL) was heated to reflux. The residue was purified by FC: diameter of the column 4 cm, petroleum ether/ethyl acetate (70:30), $R_f = 0.36$. Pale yellow oil, yield 11.1 g (87%), $[\alpha]_{589} = -10.3$ ($c = 1.52$ in $CHCl_3$). − $C_{26}H_{27}BrO_8S_2$ (611.5): calcd. C 51.1, H 4.45: found C 50.8, H 4.74. − MS (CI): m/z = 613/611 ($M + H^+$). − IR (film): $\tilde{\nu}$ = 3066 cm^{-1} (C−H), 2927 (C−H), 1598 (C=C), 1359 (SO_2), 1174 (C−O). − ^{1}H NMR ($CDCl_3$): δ = 2.48 (s, 3 H, aryl-CH_3), 2.50 (s, 3 H, aryl-CH_3), 2.99−3.10 [m, 2 H, CH_2-CH(OR)$_2$], 3.99−4.09 (m, 6 H, 4-H, 5-H and 2 × CH_2OTos), 5.22 (dd, J = 5.1/4.7 Hz, 1 H, 2-H), 7.11−7.25 (m, 3 H, 4-H, 5-H, 6-H arom.), 7.35 (d, J = 8.1 Hz, 2 H, $SO_2C_6H_4CH_3$), 7.40 (d, J = 8.1 Hz, 2 H, SO_2-$C_6H_4CH_3$), 7.55 (d, J = 8.1 Hz, 1 H, 3-H arom.), 7.78 (d, J = 8.1 Hz, 2 H, $SO_2C_6H_4CH_3$), 7.82 (d, J = 8.1 Hz, 2 H, $SO_2C_6H_4CH_3$). − ^{13}C NMR ($CDCl_3$): δ = 21.0 (q, 2 × aryl-CH_3), 40.6 [t, CH_2CH(OR)$_2$], 68.2 (t, CH_2OTos), 68.4 (t, CH_2OTos), 75.2 (d, C-4), 75.4 (d, C-5), 104.2 (d, C-2), 125.0 (s, C-1 arom.), 127.3 (d, C-6 arom.), 128.0 (d, 2 × arom.), 128.6 (d, C-5 arom.), 130.0 (d, 2 × arom.), 132.0 (d, C-4 arom.), 132.3 (s, 2 × arom.), 132.6 (d, C-3 arom.), 134.9 (s, C-2 arom.), 145.3 (s, 2 × arom.).

(4*S*,5*S*)-(+)-2-(2-Bromobenzyl)-4,5-bis[(2-methoxyethoxy)methyl]-1,3-dioxolane (6d): a) According to General Procedure 1, a mixture of **11** (3.10 g, 12.7 mmol), **15** (3.17 g, 13.3 mmol) and THF (50 mL) was heated to reflux. The residue was purified by FC: diameter of the column 3 cm, petroleum ether/ethyl acetate (1:1), $R_f = 0.25$. Colourless oil, yield 4.36 g (82%), $[\alpha]_{589} = +1.20$ ($c = 1.00$ in $CHCl_3$). − $C_{18}H_{27}BrO_6$ (419.3): calcd. C 51.6, H 6.49; found C 51.6, H 6.45. − MS (CI): m/z = 421/419 ($M + H^+$). − IR (film): $\tilde{\nu}$ = 2923 cm^{-1} (C−H), 1473 (C=C), 1136 (C−O). − ^{1}H NMR ($CDCl_3$): δ = 3.11−3.21 [m, 2 H, CH_2CH(OR)$_2$], 3.37 (s, 3 H, CH_2OCH_3), 3.39 (s, 3 H, CH_2OCH_3), 3.53−3.71 (m, 12 H, 2 × CH_2OCH_2CH_2OCH$_3$)$_2$), 3.97−4.03 (m, 2 H, 4-H and 5-H), 5.34 (dd, J = 5.1/4.4 Hz, 1 H, 2-H), 7.09 (td, J = 8.1/2.2 Hz, 1 H, 5-H arom.), 7.25 (td, J = 8.1/2.2 Hz, 1 H, 4-H arom.), 7.36 (dd, J = 8.1/1.5 Hz, 1 H, 6-H arom.), 7.53 (dd, J = 8.1/1.5 Hz, 1 H, 3-H arom.). − b) **10** (3.00 g, 14.1 mmol), **15** (3.42 g, 14.8 mmol) and THF (50 mL) were heated to reflux according to General Procedure 1. FC purification (see under a) provided 4.78 g (81%) of **6d**.

(4*R*,5*R*)-(−)-2-(2-Bromobenzyl)-4,5-bis(3-methoxypentan-3-yl)-1,3-dioxolane (6f): a) According to General Procedure 1 a solution of **11** (4.22 g, 17.2 mmol) and **20b** (5.00 g, 19.1 mmol) in THF (85 mL) was heated to reflux. FC purification [diameter of the column 4 cm, petroleum ether/ethyl acetate (90:10), $R_f = 0.85$] provided a colourless oil, yield 3.86 g (51%), $[\alpha]_{589} = -4.10$ ($c = 1.95$ in $CHCl_3$). − $C_{22}H_{35}BrO_4$ (443.4): calcd. C 59.6, H 7.96; found C 59.9, H 7.69. − MS (CI): m/z = 445/443 ($M + H^+$). − IR (film): $\tilde{\nu}$ = 2968 cm^{-1} (C−H), 1593 (C=C), 1141 (C−O). − ^{1}H NMR ($CDCl_3$): δ = 0.89 (m, 12 H, 4 × CH_2CH_3), 1.45−1.72 (m, 8 H, 4 × CH_2CH$_3$), 3.04 [dd, J = 14.1/5.5 Hz, 1 H, CH_2CH(OR)$_2$], 3.15 [dd, J = 13.9/4.3 Hz, 1 H, CH_2CH(OR)$_2$], 3.20 (s, 3 H, OCH_3), 3.23 (s, 3 H, OCH_3), 4.23 (d, J = 3.9 Hz, 1 H, 4-H), 4.26 (d, J = 3.9 Hz, 1 H, 5-H), 5.38 (dd, J = 5.5/4.3 Hz, 1 H, 2-H), 7.05 (td, J = 7.7/1.7 Hz, 1 H, 5-H arom.), 7.21 (td, J = 7.7/1.3 Hz, 1 H, 4-H arom.), 7.34 (dd, J = 7.7/1.3 Hz, 1 H, 6-H arom.), 7.50 (dd, J = 7.7/1.3 Hz, 1 H, 3-H arom.). − ^{13}C NMR ($CDCl_3$): δ = 7.77 (q, CH_2CH_3), 7.78 (q, CH_2CH_3), 8.04 (q, CH_2CH_3), 8.09 (q, CH_2CH_3), 23.9 (t, CH_2CH_3), 24.8 (t, CH_2CH_3), 25.7 (t, CH_2CH_3), 26.1 (t, CH_2CH_3), 41.1 [t, CH_2CH(OR)$_2$], 50.03 (q, OCH_3), 50.08 (q, OCH_3), 78.6 (d, C-4), 80.0 (d, C-5), 80.5 (s, 2 C, CEt_2OCH_3), 103.7 (d, C-2), 125.0 (s, C-1 arom.), 127.3 (d, C-6 arom.), 128.1 (d,

C-5 arom.), 132.4 (d, C-4 arom.), 132.3 (d, C-3 arom.), 136.4 (s, C-2 arom.). − b) A solution of methyl iodide (9.24 g, 65.1 mmol) and **6h** (9.00 g, 21.7 mmol) in THF (100 mL) was added to a suspension of NaH (1.56 g, 65.1 mmol) in THF (200 mL). The reaction mixture was heated to reflux for 18 h. After addition of H_2O (200 mL), the layers were separated, the aqueous layer was extracted with Et_2O (150 mL), the organic layers were dried ($MgSO_4$) and concentrated in vacuo. FC purification [diameter of the column 5 cm, petroleum ether/ethyl acetate (90:10), R_f = 0.85] of the residue furnished 6.98 g (72%) of **6f**, $[\alpha]_{589}$ = −3.91 (*c* = 1.98 in $CHCl_3$).

(4*R*,5*R*)-2-(2-Bromobenzyl)-4,5-bis(3-hydroxypentan-3-yl)-1,3-dioxolane (6h): A solution of ethyl iodide (34.8 g, 0.22 mol) in Et_2O (50 mL) was added to magnesium (5.35 g, 0.22 mol) in Et_2O (150 mL). The mixture was heated to reflux for 30 min, then it was cooled to 0°C and a solution of **6g** (10.0 g, 27.9 mmol) in THF (60 mL) was added. After stirring at room temperature for 2 h, a saturated solution of NH_4Cl (300 mL) was added, the aqueous layer was separated and extracted with Et_2O (3 × 150 mL). The combined organic layers were dried ($MgSO_4$), econcentrated in vacuo and the residue was methylated (→ **6f**) without further purification. − MS (CI): *m*/*z* = 417/415 ($M + H^+$). − IR (film): $\tilde{\nu}$ = 3354 cm^{-1} (OH), 2984 (C−H), 1465 (C=C), 1108 (C−O). − ^1H NMR ($CDCl_3$): δ = 0.94−1.02 (m, 12 H, 4 × CH_2CH_3), 1.53−1.92 (m, 8 H, 4 × CH_2CH_3), 1.96−2.00 (m, 2 H, 2 × OH, H/D exchange), 3.05 [dd, *J* = 14.1/4.3 Hz, 1 H, $CH_2CH(OR)_2$], 3.12 [dd, *J* = 14.1/4.3 Hz, 1 H, $CH_2CH(OR)_2$], 3.80 (d, *J* = 4.4 Hz, 1 H, 4-H), 3.89 (d, *J* = 4.4 Hz, 1 H, 5-H), 5.38 (t, *J* = 4.3 Hz, 1 H, 2-H), 6.95 (td, *J* = 8.8/1.7 Hz, 1 H, 5-H arom.), 7.21 (td, *J* = 8.8/1.7 Hz, 1 H, 4-H arom.), 7.32 (dd, *J* = 8.1/2.2 Hz, 1 H, 6-H arom.), 7.47 (dd, *J* = 8.1/1.7 Hz, 1 H, 3-H arom.).

(−)-[(2*S*,4*S*)-2-(2-Bromobenzyl)-1,3-dioxan-4-yl]methanol (7a) and 2-[(2*R*,4*S*)- and (2*S*,4*S*)-2-(2-Bromobenzyl)-1,3-dioxolan-4-yl]ethanol (22): According to General Procedure 1, a mixture of **11** (3.11 g, 12.7 mmol), (*S*)-(+)-butane-1,2,4-triol (**21**, 1.32 g, 12.7 mmol), molecular sieves 4 Å and THF (50 mL) was heated to reflux for 4 d. The residue (**7a**/**22** = 80:20 by ^1H-NMR spectroscopy) was purified by FC [diameter of the column 3.5 cm, petroleum ether/ethyl acetate (75:25)].

7a: R_f = 0.33; colourless oil, yield 2.88 g (79%); $[\alpha]_{589}$ = −4.96 (*c* = 1.37 in $CHCl_3$). − $C_{12}H_{15}BrO_3$ (287.3): calcd. C 50.2, H 5.27; found C 50.1, H 5.38. − MS (CI): *m*/*z* = 289/287 ($M + H^+$). − IR (film): $\tilde{\nu}$ = 3442 cm^{-1} (OH), 2925 (C−H), 1473 (C=C), 1141 (C−O), 1028 (C−O). − ^1H NMR ($CDCl_3$): δ = 1.23 (d, *J* = 12.5 Hz, 1 H, 5-H eq.), 1.69 (qd, *J* = 12.5/5.1 Hz, 1 H, 5-H ax.), 1.91 (t, *J* = 5.1 Hz, 1 H, OH H/D exchange), 2.94−3.04 [m, 2 H, $CH_2CH(OR)_2$], 3.40−3.55 (m, 2 H, CH_2OH), 3.58−3.70 (m, 2 H, 4-H ax., 6-H ax.), 3.97−4.04 (m, 1 H, 6-H eq.), 4.73 (t, *J* = 5.1 Hz, 1 H, 2-H ax.), 6.97 (td, *J* = 8.1/1.5 Hz, 1 H, 5-H arom.), 7.13−7.17 (m, 2 H, 4-H, 6-H arom.), 7.42 (d, *J* = 8.1 Hz, 1 H, 3-H arom.). − ^1H NOE ($CDCl_3$, pulse delay 8 s, 37.5 dB): irrad. at δ = 4.73 (2-H ax.), NOE at δ = 2.99 (aryl-CH_2), 3.67 (4-H ax., 6-H ax.). − ^{13}C NMR ($CDCl_3$): δ = 26.8 (t, C-5), 41.7 [t, $CH_2CH(OR)_2$], 65.7 (t, CH_2OH), 66.2 (t, C-6), 77.1 (d, C-4), 100.5 (d, C-2), 124.9 (s, C-1 arom.), 127.2 (d, C-6 arom.), 128.3 (d, C-5 arom.), 132.2 (d, C-4 arom.), 132.7 (d, C-3 arom.), 135.94 (s, C-2 arom.).

22: R_f = 0.25; colourless oil, yield 0.68 g (19%). − $C_{12}H_{15}BrO_3$ (287.3): calcd. C 50.2, H 5.27; found C 50.1, H 5.35. − MS (70 eV): *m*/*z* = 287/285 ($M^+ - H$), 257/255 ($M - CH_2O$). − IR (film): $\tilde{\nu}$ = 3425 cm^{-1} (OH), 2930 (C−H), 1474 (C=C), 1140 (C−O). − ^1H NMR ($CDCl_3$): δ = 1.72−1.82 (m, 2 H, CH_2CH_2OH), 2.52 (m, 1 H, OH, H/D exchange), 3.04−3.16 [m, 2 H, $CH_2CH(OR)_2$], 3.46−3.60 (m, 2 H, CH_2OH), 3.68−3.80 (m, 2 H, 5-H), 4.06−4.22 (m, 1 H, 4-H), 5.17 (t, *J* = 4.4 Hz, 0.5 H, 2-H), 5.29 (t, *J* = 5.1 Hz, 0.5 H, 2-H), 7.08 (td, *J* = 8.1/1.5 Hz, 1 H, 5-H arom.), 7.20−7.33 (m, 2 H, 4-H, 6-H arom.), 7.53 (d, *J* = 8.1 Hz, 1 H, 3-H arom.). − Ratio *cis*-**22**/*trans*-**22** = 1:1.

(2*S*,4*S*)-(−)-2-(2-Bromobenzyl)-4-(trimethylsilyloxymethyl)-1,3-dioxane (7b): Chlorotrimethylsilane (1.08 g, 15.7 mmol) was added to an ice-cold solution of **7a** (3.00 g, 10.5 mmol) and imidazole (1.07 g, 15.7 mmol) in THF (50 mL). After stirring at room temperature for 3 h, the reaction mixture was filtered, washed with H_2O, dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by FC: diameter of the column 3 cm, petroleum ether/ethyl acetate (90:10), R_f = 0.80. Colourless oil, yield 3.25 g (86%), $[\alpha]_{589}$ = −22.8 (*c* = 1.85 in $CHCl_3$). − $C_{15}H_{23}BrO_3Si$ (359.3): calcd. C 50.1, H 6.45; found C 50.3, H 6.34. − MS (70 eV): *m*/*z* = 345/343 ($M - CH_3$). − IR (film): $\tilde{\nu}$ = 2956 cm^{-1} (C−H), 1474 (C=C), 1250 (C−O). − ^1H NMR ($CDCl_3$): δ = 0.04 [s, 9 H, $Si(CH_3)_3$], 1.39 (dq, *J* = 12.5/2.9 Hz, 1 H, 5-H eq.), 1.63 (qd, *J* = 12.5/5.1 Hz, 1 H, 5-H ax.), 2.96−3.06 [m, 2 H, $CH_2CH(OR)_2$], 3.45−3.69 (m, 4 H, 4-H ax., 6-H ax., CH_2OR), 4.05 (dd, *J* = 12.5/2.9 Hz, 1 H, 6-H eq.), 4.75 (t, *J* = 5.1 Hz, 1 H, 2-H ax.), 6.96 (td, *J* = 8.1/1.5 Hz, 1 H, 5-H arom.), 7.11 (td, *J* = 8.1/1.5 Hz, 1 H, 4-H arom.), 7.24 (dd, *J* = 8.1/2.2 Hz, 1 H, 6-H arom.), 7.41 (dd, *J* = 8.1/1.5 Hz, 1 H, 3-H arom.). − ^{13}C NMR ($CDCl_3$): δ = 0.00 [q, $Si(CH_3)_3$], 28.2 (t, C-5), 42.1 [t, $CH_2CH(OR)_2$], 66.1 (t, C-6), 66.8 (t, CH_2OR), 77.1 (d, C-4), 100.8 (d, C-2), 125.3 (s, C-1 arom.), 127.5 (d, C-6 arom.), 128.5 (d, C-5 arom.), 132.7 (d, C-4 arom.), 132.9 (d, C-3 arom.), 136.5 (s, C-2 arom.).

(2*S*,4*S*)-(−)-2-(2-Bromobenzyl)-4-(*tert*-butyldimethylsilyloxymethyl)-1,3-dioxane (7c): As described for **7b**, the alcohol **7a** (3.00 g, 10.5 mmol) was silylated with *tert*-butylchlorodimethylsilane (2.36 g, 15.7 mmol). FC: see **7b**, R_f = 0.90. Colourless oil, yield 3.46 g (82%), $[\alpha]_{589}$ = −29.6 (*c* = 4.76 in $CHCl_3$). − $C_{18}H_{29}BrO_3Si$ (401.4): calcd. C 53.9, H 7.28; found C 53.8, H 7.31. − MS (70 eV): *m*/*z* = 345/343 ($M - t$Bu·). − IR (film): $\tilde{\nu}$ = 2928 cm^{-1} (C−H), 1473 (C=C), 1251 (C−O). − ^1H NMR ($CDCl_3$): δ = 0.00 [s, 6 H, $OSi(CH_3)_2$], 0.82 [s, 9 H, $OSiC(CH_3)_3$], 1.41−1.45 (m, 1 H, 5-H eq.), 1.58−1.68 (m, 1 H, 5-H ax.), 2.97−3.06 [m, 2 H, $CH_2CH(OR)_2$], 3.46−3.69 (m, 4 H, 4-H ax., 6-H ax., CH_2OR), 4.06 (ddd, *J* = 11.5/3.9/1.3 Hz, 1 H, 6-H eq.), 4.75 (t, *J* = 5.1 Hz, 1 H, 2-H ax.), 7.01 (td, *J* = 7.7/1.6 Hz, 1 H, 5-H arom.), 7.15 (td, *J* = 7.5/1.3 Hz, 1 H, 4-H arom.), 7.26 (dd, *J* = 7.7/1.3 Hz, 1 H, 6-H arom.), 7.46 (dd, *J* = 7.7/1.3 Hz, 1 H, 3-H arom.).

(2*S*,4*S*)-(−)-2-(2-Bromobenzyl)-4-(triphenylsilyloxymethyl)-1,3-dioxane (7d): As described for **7b**, the alcohol **7a** (4.00 g, 13.9 mmol) was silylated with chlorotriphenylsilane (4.92 g, 16.7 mmol). FC: diameter of the column 4 cm, petroleum ether/ethyl acetate (85:15), R_f = 0.70. Colourless oil, yield 7.11 g (94%), $[\alpha]_{589}$ = −11.8 (*c* = 0.71 in $CHCl_3$). − $C_{30}H_{29}BrO_3Si$ (545.5): calcd. C 66.0, H 5.36; found C 65.9, H 5.56. − MS (70 eV): *m*/*z* = 469/467 ($M - C_6H_5$). − IR (film): $\tilde{\nu}$ = 3067 cm^{-1} (C−H), 2924 (C−H), 1589 (C=C), 1142 (C−O). − ^1H NMR ($CDCl_3$): δ = 1.36−1.42 (m, 1 H, 5-H eq.), 1.63 (qd, *J* = 12.5/5.1 Hz, 1 H, 5-H ax.), 2.96−3.06 [m, 2 H, $CH_2CH(OR)_2$], 3.66−3.92 (m, 4 H, 4-H ax., 6-H ax., CH_2OR), 4.11 (dd, *J* = 11.8/3.7 Hz, 1 H, 6-H eq.), 4.79 (t, *J* = 5.9 Hz, 1 H, 2-H ax.), 7.04−7.64 (m, 19 H, arom.). − ^{13}C NMR ($CDCl_3$): δ = 27.8 (t, C-5), 41.6 [t, $CH_2CH(OR)_2$], 66.4 (t, C-6), 66.7 (t, CH_2OR), 76.8 (d, C-4), 100.4 (d, C-2), 124.9 (s, C-1 arom.), 127.5 (d, C-6 arom.), 127.8 (d, arom. C), 127.9 (d, C-5 arom.), 130.1 (d, arom. C), 132.3 (d, C-4 arom.), 132.5 (d, C-3 arom.), 134.0 (s, arom. C), 135.3 (d, arom. C), 136.1 (s, C-2 arom.).

(+)-[(2*R*,4*S*,5*S*)-5-Benzyloxy-2-(2-bromobenzyl)-1,3-dioxan-4-yl]-methanol (7e) and (2S)-2-Benzyloxy-2-[(2*R*,4*S*)- and (2*S*,4*S*)-2-(2-bromobenzyl)-1,3-dioxolan-4-yl]ethanol (24): According to General Procedure 1, a mixture of **11** (3.11 g, 12.7 mmol), (2*S*,3*S*)-(+)-3-benzyloxybutane-1,2,4-triol (**23**, 2.69 g, 12.7 mmol), molecular sieves 4 Å and THF (50 mL) was heated to reflux for 4 d. Recrystallization of the residual mixture of **7e** and **24** (60:40 by ^{1}H-NMR spectroscopy) provided **7e**, the dioxolane **24** was isolated by subsequent FC of the mother liquor [diameter of the column 4 cm, petroleum ether/ethyl acetate (75:25), R_f(**7e**) = 0.28, R_f(**24**) = 0.25].

7e: Colourless solid (*i*Pr$_2$O), m.p. 131−133°C; yield 3.00 g (60%), $[\alpha]_{589}$ = +144.4 (*c* = 0.78 in CHCl$_3$). − $C_{19}H_{21}BrO_4$ (393.3): calcd. C 58.0, H 5.38; found C 58.0, H 5.39. − MS (CI): *m*/*z* = 394/392 (M + H$^+$). − IR (film): $\tilde{\nu}$ = 3442 cm^{-1} (OH), 2925 (C−H), 1473 (C=C), 1141 (C−O). − ^{1}H NMR (CDCl$_3$): δ = 1.83 (dd, *J* = 9.5/4.4 Hz, 1 H, OH H/D exchange), 3.15−3.24 [m, 2 H, C*H*$_2$CH(OR)$_2$], 3.29 ("q", *J* = 1.5 Hz, 1 H, 5-H eq.), 3.60 (ddd, *J* = 11.3/4.4/2.2 Hz, 1 H, C*H*$_2$OH), 3.68 (dd, *J* = 12.5/1.5 Hz, 1 H, 6-H ax.), 3.76−3.79 (m, 1 H, 4-H ax.), 3.87−3.92 (m, 1 H, C*H*$_2$OH), 4.29 (dd, *J* = 12.5/1.5 Hz, 1 H, 6-H eq.), 4.46 (d, *J* = 12.1 Hz,1 H, OC*H*$_2$C$_6$H$_5$), 4.82 (d, *J* = 12.4 Hz, 1 H, OC*H*$_2$C$_6$H$_5$), 4.87 (t, *J* = 5.1 Hz, 1 H, 2-H ax.), 7.09 (td, *J* = 8.1/1.5 Hz, 1 H, 5-H arom.), 7.21−7.39 (m, 7 H, 4-H, 6-H arom., OCH$_2$C$_6$*H*$_5$), 7.54 (dd, *J* = 8.1/1.5 Hz, 1 H, 3-H arom.). A H/H COSY spectrum led to this ^{1}H-NMR signal-proton assignment. − ^{1}H NOESY (CDCl$_3$, pulse delay 4.5 s, 37.5 dB): irrad. at δ = 4.87 (2-H ax.), NOE (cross peak) at δ = 3.19 (arylC*H*$_2$), 3.68 (6-H ax.), 3.78 (4-H ax.). − ^{13}C NMR (CDCl$_3$): δ = 41.4 [t, *C*H$_2$CH(OR)$_2$], 62.7 (t, CH$_2$OH), 67.5 (t, C-6), 69.7 (d, C-5), 70.9 (t, OCH$_2$C$_6$H$_5$), 78.8 (d, C-4), 100.8 (d, C-2), 124.8 (s, C-1 arom.), 127.2 (d, C-6 arom.), 128.1 (d, C arom.), 128.2 (d, C arom.), 128.4 (d, C-5 arom.), 128.6 (d, C arom.), 132.5 (d, C-4 arom.), 132.6 (d, C-3 arom.), 135.8 (s, C-2 arom.), 137.6 (s, C arom.).

24: Pale yellow oil, yield 1.85 g (37%). − $C_{19}H_{21}BrO_4$ (393.3): calcd. C 58.0, H 5.38; found C 57.8, H 5.54. − MS (CI): *m*/*z* = 394/392 (M + H$^+$). − IR (film): $\tilde{\nu}$ = 3457 cm^{-1} (OH), 3061 (C−H), 2932 (C−H), 1474 (C=C), 1134 (C−O). − ^{1}H NMR (CDCl$_3$): δ = 2.47 (m, 1 H, OH, H/D exchange), 3.23−3.34 [m, 2 H, C*H*$_2$CH(OR)$_2$], 3.61−3.78 (m, 2 H, C*H*$_2$OH), 3.81−3.88 (m, 1 H, C*H*OBn), 3.95−4.03 (m, 1 H, 4-H), 4.20−4.29 (m, 1 H, 5-H), 4.36−4.44 (m, 1 H, 5-H), 4.83−4.88 (m, 2 H, OC*H*$_2$C$_6$H$_5$), 5.33 (t, *J* = 4.4 Hz, 0.5 H, 2-H; *trans*-**24**), 5.46 (t, *J* = 5.1 Hz, 0.5 H, 2-H; *cis*-**24**), 7.22−7.70 (m, 9 H, arom.). − ^{1}H NOE (CDCl$_3$, pulse delay 8 s, 37.5 dB): irrad. at δ = 5.33 (2-H), NOE at δ = 3.23−3.34 (arylC*H*$_2$), 4.36−4.44 (5-H); irrad. at δ = 5.46 (2-H), NOE at δ = 3.23−3.34 (arylC*H*$_2$), 3.95−4.03 (4-H), 4.20−4.29 (5-H). Ratio *cis*-**24**/*trans*-**24** = 1:1.

(2*R*,4*S*,5*S*)-(+)-5-Benzyloxy-2-(2-bromobenzyl)-4-(methoxymethyl)-1,3-dioxane (7f): A solution of **7e** (2.00 g, 5.09 mmol) and methyl iodide (0.35 mL, 5.60 mmol) in THF (10 mL) was added to a suspension of NaH (0.22 g, 5.60 mmol) in THF (100 mL). The reaction mixture was heated to reflux for 16 h, then it was filtered and concentrated in vacuo. The residue was purified by FC [diameter of the column 3 cm, petroleum ether/ethyl acetate (80:20), R_f = 0.65]. Colourless solid, m.p. 88−90°C, yield 1.96 g (95%), $[\alpha]_{589}$ = +26.6 (*c* = 0.64 in CHCl$_3$). − $C_{20}H_{23}BrO_4$ (407.3): calcd. C 59.0, H 5.69; found C 58.5, H 6.12. − MS (70 eV): *m*/*z* = 408/406 (M$^+$), 317/315 (M − Bn). − IR (KBr): $\tilde{\nu}$ = 3062 cm^{-1} (C−H), 2920 (C−H), 1473 (C=C), 1159 (C−O). − ^{1}H NMR (CDCl$_3$): δ = 3.15−3.25 [m, 2 H, C*H*$_2$CH(OR)$_2$], 3.28−3.33 (m, 1 H, 5-H eq.), 3.34 (s, 3 H, OCH$_3$), 3.58−3.61 (m, 2 H, C*H*$_2$OCH$_3$), 3.68 (dd, *J* = 13.2/1.5 Hz, 1 H, 6-H ax.), 3.89−3.93 (m, 1 H, 4-H ax.), 4.26 (dd, *J* = 12.8/1.5 Hz, 1 H, 6-H eq.), 4.56 (d, *J* = 12.4 Hz, 1 H, OC*H*$_2$C$_6$H$_5$), 4.79 (d, *J* = 12.4 Hz, 1 H, OC*H*$_2$C$_6$H$_5$), 4.90 (t, *J* = 5.1 Hz, 1 H, 2-H ax.), 7.10 (td, *J* = 8.1/1.5 Hz, 1 H, 5-H arom.), 7.22−7.41 (m, 7 H, arom.), 7.55 (dd, *J* = 8.1/1.5 Hz, 1 H, 3-H arom.). − ^{13}C NMR (CDCl$_3$): δ = 41.3 [t, *C*H$_2$CH(OR)$_2$], 59.2 (q, OCH$_3$), 67.9 (t, *C*H$_2$OCH$_3$), 69.5 (t, C-6), 71.3 (d, C-5), 71.7 (t, OCH$_2$C$_6$H$_5$), 77.9 (d, C-4), 100.7 (d, C-2), 124.8 (s, C-1 arom.), 127.1 (d, C-6 arom.), 127.8 (d, C arom.), 128.1 (d, C arom.), 128.2 (d, C-5 arom.), 128.3 (d, C arom.), 132.5 (d, C-4 arom.), 132.5 (d, C-3 arom.), 135.9 (s, C-2 arom.), 137.9 (s, C arom.).

(5*S*,6*S*)-(+)-2-(2-Bromobenzyl)-5,6-dimethoxy-1,3-dioxepane (8): a) According to General Procedure 1, a solution of **11** (5.00 g, 20.4 mmol) and (2*S*,3*S*)-(+)-2,3-dimethoxybutane-1,4-diol (**16**, 3.40 g, 22.5 mmol) in THF (100 mL) was heated to reflux. Recrystallization of the residue provided a colourless solid (*i*Pr$_2$O), m.p. 66−68°C, yield 4.88 g (90%), $[\alpha]_{589}$ = +121.2 (*c* = 1.00 in CHCl$_3$). − $C_{14}H_{19}BrO_4$ (331.2): calcd. C 50.8, H 5.78, Br 24.1; found C 50.6, H 5.66, Br 24.0. − MS (70 eV): *m*/*z* = 332/330 (M$^+$). − IR (KBr): $\tilde{\nu}$ = 3057 cm^{-1} (C−H), 2973 (C−H), 1473 (C=C), 1145 (C−O), 1114 (C−O). − ^{1}H NMR (CDCl$_3$): δ = 3.01−3.99 [m, 2 H, C*H*$_2$CH(OR)$_2$], 3.25−3.35 (m, 2 H, 5-H, 6-H), 3.44 (s, 3 H, OCH$_3$), 3.46 (s, 3 H, OCH$_3$), 3.61−3.75 (m, 2 H, 4-H eq., 7-H eq.), 3.93−4.03 (m, 2 H, 4-H ax., 7-H ax.), 4.97 (dd, *J* = 5.9/5.1 Hz, 1 H, 2-H), 7.06 (td, *J* = 8.1/2.2 Hz, 1 H, 5-H arom.), 7.20−7.27 (m, 2 H, 4-H, 6-H arom.), 7.52 (dd, *J* = 8.1/2.2 Hz, 1 H, 3-H arom.). − ^{13}C NMR (CDCl$_3$): δ = 39.9 [t, CH$_2$CH(OR)$_2$], 57.4 (q, OCH$_3$), 57.5 (q, OCH$_3$), 61.1 (t, C-4), 63.2 (t, C-7), 81.0 (d, C-5), 81.4 (d, C-6), 101.7 (d, C-2), 124.9 (s, C-1 arom.), 127.3 (d, C-6 arom.), 128.2 (d, C-5 arom.), 131.9 (s, C-4 arom.), 132.6 (s, C-3 arom.), 136.3 (s, C-2 arom.). − b) According to General Procedure 1, a solution of **10** (5.00 g, 23.5 mmol) and (2*S*,3*S*)-(+)-2,3-dimethoxybutane-1,4-diol (**16**, 3.85 g, 26.0 mmol) in THF (100 mL) was heated to reflux. Recrystallization furnished a colourless solid (iPr$_2$O), yield 6.85 g (89%), m.p. 66−68°C.

(2*S*,4*S*,5*R*)-(−)-2-(2-Bromobenzyl)-3,4-dimethyl-5-phenyl-1,3-oxazolidine (9): A solution of **12** (5.00 g, 25.2 mmol), (1*R*,2*S*)-(−)-ephedrine (4.98 g, 30.2 mmol), and *p*-toluenesulfonic acid (400 mg) in toluene (100 mL) was heated to reflux. After 36 h, the solvent was evaporated in vacuo and the residue was recrystallized (*i*Pr$_2$O). Colourless solid (*i*Pr$_2$O), m.p. 65−67°C, yield 6.25 g (72%), $[\alpha]_{589}$ = −138.8 (*c* = 1.06 in CHCl$_3$). − $C_{18}H_{20}BrNO$ (346.3): calcd. C 62.4, H 5.82, N 4.05; found C 62.5, H 5.80, N 4.00. − MS (CI): *m*/*z* = 348/346 (M + H$^+$). − IR (KBr): $\tilde{\nu}$ = 3063 cm^{-1} (C−H), 2967 (C−H), 1494 (C=C), 1094 (C−O). − ^{1}H NMR (CDCl$_3$): δ = 0.69 (d, *J* = 6.4 Hz, 3 H, CHC*H*$_3$), 2.40 (s, 3 H, NC*H*$_3$) , 2.82 (dq, *J* = 8.0/6.4 Hz, 1 H, 4-H), 3.02 [dd, *J* = 13.9/8.3 Hz, 1 H, C*H*$_2$CH(OR)$_2$], 3.48 [dd, *J* = 13.9/1.9 Hz, 1 H, C*H*$_2$CH(OR)$_2$], 4.14 (dd, *J* = 8.3/1.9 Hz, 1 H, 2-H), 4.98 (d, *J* = 8.0 Hz, 1 H, 5-H), 7.08 (td, *J* = 7.7/1.7 Hz, 1 H, 5-H arom.), 7.20−7.33 (m, 6 H, arom.), 7.43 (dd, *J* = 7.7/1.7 Hz, 1 H, 6-H arom.), 7.54 (dd, *J* = 8.1/1.7 Hz, 1 H, 3-H arom.). − ^{1}H NOE (CDCl$_3$, pulse delay 8 s, 37.5 dB): irrad. at δ = 2.82 (4-H), NOE at δ = 0.69, 2.40, 4.14 (2-H), 4.98; irrad. at δ = 4.14 (2-H), NOE at δ = 2.40, 2.82 (4-H), 3.02, 3.48, 4.98 (5-H); irrad. at δ = 4.98 (5-H), NOE at δ = 2.82, 4.14 (2-H). − ^{13}C NMR (CDCl$_3$): δ = 14.9 (q, CH*C*H$_3$), 36.7 (q, N*C*H$_3$), 40.4 [t, *C*H$_2$CH(OR)$_2$], 64.1 (d, C-4), 82.1 (d, C-5), 96.5 (d, C-2), 124.7 (s, C-1 arom.), 127.3 (s, C arom.), 127.5 (d, C-6 arom.), 127.7 (d, C arom.), 127.9 (d, C arom.), 128.2 (d, C-5 arom.), 132.4 (s, C-4 arom.), 132.6 (d, C arom.), 137.1 (s, C-3 arom.), 139.9 (s, C-2 arom.).

(4*S*,5*S*)-(+)-4,5-Bis[(2-methoxyethoxy)methyl]-2,2-dimethyl-1,3-dioxolane (13b): At room temperature a solution of 1-bromo-2-me-

thoxyethane (36.4 g, 0.26 mol) and **13a**[12b,14] (20.0 g, 0.12 mol) in THF (150 mL) was added to a suspension of NaH (6.22 g, 0.26 mol) in THF (200 mL). Then, the reaction mixture was heated to reflux for 18 h. After filtration, the mixture was distilled in vacuo. Colourless oil, b.p.$_{0.015}$ 86−88°C, yield 27.9 g (84%), $[\alpha]_{589} = +4.71$ (c = 2.23 in $CHCl_3$). − $C_{13}H_{26}O_6$ (278.3): calcd. C 56.1, H 9.42; found C 56.0, H 9.52. − MS (CI): m/z = 279 ($M + H^+$). − IR (film): $\tilde{\nu}$ = 2984 cm^{-1} (C−H), 1248 (C−O). − ^1H NMR ($CDCl_3$): δ = 1.44 [s, 6 H, $(CH_3)_2C(OR)_2$], 3.40 (s, 6 H, 2 × OCH_3), 3.56−3.80 (m, 12 H, 6 × OCH_2), 4.02−4.06 (m, 2 H, 4-H, 5-H).

(2*S*,3*S*)-(−)-1,4-Bis(2-methoxyethoxy)butane-2,3-diol (15): A mixture of **13b** (5.00 g, 18.0 mmol), H_2O (1.30 g, 72 mmol), *p*-toluenesulfonic acid × 1 H_2O (400 mg), and methanol (75 mL) was heated to reflux for 24 h. Then, the reaction mixture was stirred with K_2CO_3 (400 g) for 1 h, filtered, the solvent was evaporated in vacuo and the residue was filtered through silica gel [*n*-hexane/ethyl acetate (1:1), R_f = 0.75]. Pale yellow oil, yield 3.53 g (82%), $[\alpha]_{589}$ = −2.32 (c = 6.93 in $CHCl_3$). − $C_{10}H_{22}O_6$ (238.3): calcd. C 50.4, H 9.31; found C 49.9, H 9.75. − MS (CI): m/z = 239 ($M + H^+$). − IR (film): $\tilde{\nu}$ = 3388 cm^{-1} (OH), 2923 (C−H), 1245 (C−O), 1098 (C−O). − ^1H NMR ($CDCl_3$): δ = 3.31 (s, 3 H, OCH_3), 3.32 (s, 3 H, OCH_3), 3.39−3.68 (m, 14 H, 6 × OCH_2, 2 × OH, H/D exchange), 4.01−4.06 (m, 2 H, C*H*OH).

(4*R*,5*R*)-(−)-4,5-Bis(3-hydroxypentan-3-yl)-2-(4-methoxyphenyl)-1,3-dioxolane (19a): To an ice-cold solution of EtMgI in Et_2O [prepared from iodoethane (53.0 g, 0.34 mol), magnesium (8.27 g, 0.34 mol) and Et_2O (200 mL)], a solution of **18**[16] (10.0 g, 33.8 mmol) in THF (60 mL) was added and the reaction mixture was stirred at room temperature for 2 h. A saturated solution of NH_4Cl (300 mL) was added, the aqueous layer was separated, and extracted with Et_2O (3 × 150 mL). The combined organid layers were dried ($MgSO_4$), concentrated in vacuo and the residue was purified by FC [diameter of the column 7 cm, petroleum ether/ethyl acetate (85:15), R_f = 0.45]. Colourless oil, yield 9.78 g (82%), $[\alpha]_{589}$ = −4.08 (c = 2.31 in $CHCl_3$). − $C_{20}H_{32}O_5$ (352.5): calcd. C 68.2, H 9.15; found C 67.9, H 9.40. − MS (EI): m/z = 351 ($M^+ - H\cdot$). − IR (film): $\tilde{\nu}$ = 3425 cm^{-1} (OH), 2969 (C−H), 1615 (C=C), 1088 (C−O). − ^1H NMR ($CDCl_3$): δ = 0.92−1.03 (m, 12 H, 4 × CH_2CH_3), 1.53−1.92 (m, 8 H, CH_2CH_3), 1.98 (br. s, 1 H, O*H*, H/D exchange), 2.18 (br. s, 1 H, O*H*, H/D exchange), 3.85 (s, 3 H, aryl-OCH_3), 4.30 (d, J = 5.1 Hz, 1 H, 4-H), 4.39 (d, J = 5.1 Hz, 1 H, 5-H), 6.08 (s, 1 H, 2-H), 6.95 (d, J = 8.8 Hz, 2 H, 3-H, 5-H arom.), 7.47 (d, J = 8.8 Hz, 2 H, 2-H, 6-H arom.).

(4*R*,5*R*)-(−)-4,5-Bis(3-methoxypentan-3-yl)-2-(4-methoxyphenyl)-1,3-dioxolane (19b): A solution of **19a** (9.00 g, 25.6 mmol) and methyl iodide (10.9 g, 76.7 mmol) in THF (100 mL) was added to a suspension of NaH (1.84 g, 76.7 mmol) in THF (200 mL). The reaction mixture was heated to reflux for 18 h, then H_2O (200 mL) was added, the organic layer was separated, dried ($MgSO_4$), concentrated in vacuo, and the residue was purified by FC [diameter of the column 5 cm, petroleum ether/ethyl acetate (85:15), R_f = 0.65]. Pale yellow oil, yield 6.99 g (72%), $[\alpha]_{589}$ = -3.05 (c = 2.13 in $CHCl_3$). − $C_{22}H_{36}O_5$ (380.5): calcd. C 69.4, H 9.54; found C 69.9, H 9.10. − MS (70 eV): m/z = 380 (M^+). − IR (film): $\tilde{\nu}$ = 2969 cm^{-1} (C−H), 1613 (C=C), 1090 (C−O). − ^1H NMR ($CDCl_3$): δ = 0.78−0.89 (m, 12 H, 4 × CH_2CH_3), 1.41−1.74 (m, 8 H, 4 × CH_2CH_3), 3.07 (s, 3 H, OCH_3), 3.09 (s, 3 H, OCH_3), 3.68 (s, 3 H, aryl-OCH_3) , 4.26 (d, J = 4.3 Hz, 1 H, 4-H), 4.32 (d, J = 4.3 Hz, 1 H, 5-H), 5.91 (s, 1 H, 2-H), 6.77 (d, J = 8.6 Hz, 2 H, 3-H, 5-H arom.), 7.32 (d, J = 8.6 Hz, 2 H, 2-H, 6-H arom.).

(−)-[(4*R*,5*R*)-3,6-Diethyl-5-hydroxy-3,6-dimethoxyoctan-4-yl] 4-Methoxybenzoate (20a): At room temperature, DDQ (5.35 g, 23.6 mmol) was added to a solution of **19b** (6.00 g, 15.8 mmol) in CH_2Cl_2 (290 mL) and H_2O (20 mL). After 1.5 h, a saturated solution of $NaHCO_3$ (330 mL) and CH_2Cl_2 (800 mL) were added, the organic layer was separated, dried ($MgSO_4$) and concentrated in vacuo. FC purification [diameter of the column 6 cm, petroleum ether/ethyl acetate (85:15), R_f = 0.42] of the residue provided a pale yellow oil, yield 4.42 g (71%), $[\alpha]_{589}$ = −6.08 (c = 2.20 in $CHCl_3$). − $C_{22}H_{36}O_6$ (396.5): calcd. C 66.6, H 9.15; found C 66.9, H 8.80. − MS (70 eV): m/z = 396 (M^+). − IR (film): $\tilde{\nu}$ = 3528 cm^{-1} (OH), 1713 (C=O), 1604 (C=C), 1169 (C−O). − ^1H NMR ($CDCl_3$): δ = 0.75−0.87 (m, 12 H, 4 × CH_2CH_3), 1.45-1.71 (m, 8 H, 4 × CH_2CH_3), 3.07 (s, 3 H, OCH_3), 3.33 (br. s, 3 H, OCH_3), 3.79 (s, 3 H, aryl-OCH_3) , 4.02−4.08 (m, 2 H, C*H*OH, H/D exchange), 5.47 (s, 1 H, C*H*OCOAr), 6.86 (d, J = 8.8 Hz, 2 H, 3-H, 5-H arom.), 8.00 (d, J = 8.8 Hz, 2 H, 2-H, 6-H arom.).

(4*R*,5*R*)-(+)-3,6-Diethyl-3,6-dimethoxyoctane-4,5-diol (20b): At 0°C, a solution of **20a** (1.94 g, 4.89 mmol) in THF (20 mL) was added to a suspension of $LiAlH_4$ (0.93 g, 24.5 mmol) in Et_2O (150 mL) and the reation mixture was heated to reflux for 14 h. Then, at 0°C H_2O (1.0 mL) was added cautiously, subsequently 2 N NaOH (1.0 mL) and H_2O (3.0 mL) were added. The mixture was filtered, dried ($MgSO_4$), concentrated in vacuo, and the residue was purified by FC [diameter of the column 3 cm, petroleum ether/ethyl acetate (1:1), R_f = 0.82]. Pale yellow oil, yield 0.69 g (54%), $[\alpha]_{589}$ = +0.71 (c = 1.41 in $CHCl_3$). − $C_{14}H_{30}O_4$ (262.4): calcd. C 64.1, H 11.5; found C 64.5, H 11.8. − MS (CI): m/z = 263 ($M + H^+$). − IR (film): $\tilde{\nu}$ = 3420 cm^{-1} (OH), 1108 C−O). − ^1H NMR ($CDCl_3$): δ = 0.93−0.98 (m, 12 H, 4 × CH_2CH_3), 1.55 (q, J = 7.3 Hz, 2 H, CH_2CH_3), 1.71 (q, J = 7.3 Hz, 2 H, CH_2CH_3), 1.80−1.91 (m, 4 H, 2 × CH_2CH_3), 3.44 (s, 6 H, 2 × OCH_3) , 3.85 (d, J = 2.1 Hz, 2 H, 2 × CHO*H*, H/D exchange), 4.16 (d, J = 2.1 Hz, 2 H, C*H*OH).

***N*-[(α*R* and α*S*)-2-{[(4*R*,5*R*)-4,5-Dimethyl-1,3-dioxolan-2-yl]-methyl}benzhydryl]-4-methylbenzenesulfonamide (26a/27a):** According to General Procedure 2, **6a** (120 mg, 0.44 mmol) was treated with **25** (0.13 g, 0.49 mmol). FC purification [diameter of the column 2 cm, petroleum ether/ethyl acetate (85:15), R_f = 0.36] provided a colourless oil, yield 0.15 g (76%). − $C_{26}H_{29}NSO_4$ (451.6): calcd. C 69.2, H 6.47, N 3.10, S 7.10; found C 69.1, H 6.60; N 3.00; S 6.82. − MS (70 eV): m/z = 451 ($M^{\cdot+}$), 296 ($M^{\cdot+}$ − Tos). − IR (film): $\tilde{\nu}$ = 3263 cm^{-1} (NH), 3062 (C−H), 2974 (C−H), 1599 (C=C), 1160 (C−O). − ^1H NMR ($CDCl_3$): δ = 1.21 (d, J = 5.9 Hz, 3 × 0.55 H, $CHCH_3$), 1.26 (d, J = 6.6 Hz, 3 H, $CHCH_3$), 1.32 (d, J = 5.9 Hz, 3 × 0.45 H, $CHCH_3$), 2.37 (s, 3 H, aryl-CH_3), 2.57−2.70 [m, 2 H, $CH_2CH(OR)_2$], 3.50 (dq, J = 6.6/2.2 Hz, 1 × 0.55 H, 4-H), 3.62−3.66 (m, 2 × 0.45 H, 4-H, 5-H), 3.70 (dq, J = 6.6/2.2 Hz, 1 × 0.55 H, 5-H), 5.17−5.20 (m, 1 H, 2-H), 5.52 (d, J = 8.1 Hz, 1 × 0.45 H, C*H*NH-Tos, s after addition of D_2O), 5.66 (d, J = 7.3 Hz, 1 × 0.55 H, C*H*NH-Tos, s after addition of D_2O), 6.65 (d, J = 8.1 Hz, 1 × 0.45 H, CHN*H*-Tos, H/D exchange), 6.73 (d, J = 7.3 Hz, 1 × 0.55 H, CHN*H*-Tos, H/D exchange), 6.89−6.97 (m, 1 H, arom.), 7.10−7.26 (m, 10 H, arom.), 7.56−7.59 (m, 2 H, arom.). Ratio **26a**/**27a** = 45:55.

***N*-[(α*R* and α*S*)-2-{[(4*S*,5*S*)-4,5-Bis(methoxymethyl)-1,3-dioxolan-2-yl]methyl}benzhydryl]-4-methylbenzenesulfonamide (26b/27b):** According to General Procedure 2, **6b** (0.50 g, 1.51 mmol) was treated with **25** (0.41 g, 1.60 mmol). FC [diameter of the column 3 cm, petroleum ether/ethyl acetate (85:15), R_f = 0.24] afforded a colourless oil, yield 0.51 g (66%). − $C_{28}H_{33}NO_6S$ (511.6): calcd. C 65.7, H 6.50, N 2.74, S 6.27; found C 65.3, H 6.74, N 3.01, S 6.35. − MS (70 eV): m/z = 357 (M^+ − Tos). − IR (film): $\tilde{\nu}$ = 3260 cm^{-1} (NH), 3062 (C−H), 2926 (C−H), 1599 (C=C), 1160 (C−O). − ^1H NMR ($CDCl_3$): δ = 2.37 (s, 3 H, aryl-CH_3), 2.69−2.71 [m, 2 H,

$CH_2CH(OR)_2$], 3.34 (s, 3 H, OCH_3), 3.36 (s, 3 H, OCH_3), 3.46−3.48 (m, 4 H, 2 × CH_2OCH_3), 3.98−4.02 (m, 2 H, 4-H, 5-H), 5.19−5.21 (m, 1 H, 2-H), 5.62 (d, J = 8.1 Hz, 1 × 0.55 H, C*H*NH-Tos s after addition of D_2O), 5.68 (d, J = 8.1 Hz, 1 × 0.45 H, C*H*NH-Tos, s after addition of D_2O), 6.52 (d, J = 8.1 Hz, 1 × 0.55 H, CHN*H*-Tos, H/D exchange), 6.75 (d, J = 8.1 Hz, 1 × 0.45 H, CHN*H*-Tos, H/D exchange), 6.78−6.96 (m, 2 H, arom.), 7.09−7.27 (m, 9 H, arom.), 7.57−7.59 (m, 2 H, arom.). − ^{13}C NMR ($CDCl_3$): δ = 21.3 (q, aryl-*C*H_3), 36.8 [t, 1 × 0.45 C, *C*H_2CH(OR)$_2$], 37.2 [t, 1 × 0.55 C, *C*H_2CH(OR)$_2$], 59.0 (q, 1 × 0.45 C, OCH_3), 59.2 (q, 1 × 0.55 C, OCH_3), 59.2 (d, 1 × 0.55 C, *C*HNH-Tos and q, 1 × 0.45 H, OCH_3), 59.5 (d, 1 × 0.45 C, *C*HNH-Tos), 59.7 (q, 1 × 0.55 C, OCH_3), 72.1 (t, 1 × 0.45 C, *C*H_2OCH_3), 72.2 (t, 1 × 0.55 C, *C*H_2OCH_3), 72.4 (t, 1 × 0.45 C, *C*H_2OCH_3), 72.6 (t, 1 × 0.55 C, *C*H_2OCH_3), 77.1 (d, C-4), 77.5 (d, 1 × 0.55 C, C-5), 77.7 (d, 1 × 0.45 C, C-5), 104.9 (d, 1 × 0.55 C, C-2), 105.1 (d, 1 × 0.45 C, C-2), 126.2 (d, arom.), 126.4 (d, arom.), 126.5 (d, arom.), 126.8 (d, arom.), 126.9 (d, arom.), 127.0 (d, arom.), 127.2 (d, arom.), 127.5 (d, arom.), 127.6 (d, arom.), 128.1 (d, arom.), 128.2 (d, arom.), 129.1 (d, arom.), 129.5 (d, arom.), 129.6 (d, arom.), 129.7 (d, arom.), 131.8 (d, arom.), 133.5 (s, arom.), 137.6 (s, arom.), 141.0 (s, arom.), 142.7 (s, arom.). − Ratio **26b**/**27b** = 55:45.

***N*-[(α*R* and α*S*)-2-{[(4*S*,5*S*)-4,5-Bis(2-methoxyethoxymethyl)-1,3-dioxolan-2-yl]methyl}benzhydryl]-4-methylbenzenesulfonamide (26c/27c):** According to General Procedure 2, **6d** (0.63 g, 1.50 mmol) was treated with **25** (0.41 g, 1.60 mmol). FC [diameter of the column 3 cm, petroleum ether/ethyl acetate (50:50), R_f = 0.26] gave a colourless oil, yield 0.59 g (65%). − $C_{32}H_{41}NO_8S$ (599.7): calcd. C 64.1, H 6.89, N 2.34; found C 64.2, H 7.03, N 2.05. − MS (70 eV): *m*/*z* = 599 (M^+), 444 (M − Tos·), 429 (M − NHTos). − IR (film): $\tilde{\nu}$ = 3235 cm^{-1} (NH), 3061 (C−H), 2926 (C−H), 1599 (C=C), 1160 (C−O). − ^{1}H NMR ($CDCl_3$): δ = 2.37 (s, 3 H, aryl-CH_3), 2.69−2.71 [m, 2 H, C*H*$_2$CH(OR)$_2$], 3.33 (s, 3 H, OCH_3), 3.36 (s, 3 H, OCH_3), 3.39−3.69 (m, 12 H, 6 × OCH_2), 3.93−4.16 (m, 2 H, 4-H, 5-H), 5.19−5.21 (m, 1 H, 2-H), 5.58 (d, J = 7.3 Hz, 1 × 0.52 H, C*H*NH-Tos, s after addition of D_2O), 5.63 (d, J = 7.3 Hz, 1 × 0.48 H, C*H*NH-Tos, s after addition of D_2O), 6.50 (d, J = 7.3 Hz, 1 × 0.52 H, CHN*H*-Tos, H/D exchange), 6.71 (d, J = 8.1 Hz, 1 H, arom.), 6.80 (d, J = 7.3 Hz, 1 × 0.48 H, CHN*H*-Tos, H/D exchange), 6.90−6.95 (m, 1 H, arom.), 7.10−7.27 (m, 9 H, arom.), 7.57−7.60 (m, 2 H, arom.). Ratio **26c**/**27c** = 52:48.

(−)-*N*-[(α*R*)-2-{[(4*R*,5*R*)-4,5-Bis(2-methoxypropan-2-yl)-1,3-dioxolan-2-yl]methyl}benzhydryl]-4-methylbenzenesulfonamide (26d) and (+)-*N*-[(α*S*)-2-{[(4*R*,5*R*)-4,5-Bis(2-methoxypropan-2-yl)-1,3-dioxolan-2-yl]methyl}benzhydryl]-4-methylbenzenesulfonamide (27d): a) According to General Procedure 2, **6e** (465 mg, 1.2 mmol) was treated with **25** (0.34 g, 1.30 mmol). The HPLC analysis [eluent petroleum ether/ethyl acetate (85:15)] and the ^{1}H-NMR spectrum of the unpurified product showed a diastereomeric ratio **26d** (retention time 10.4 min)/**27d** (retention time 12.2 min) of 61:39. The diastereomeres were separated by FC: diameter of the column 2 cm, petroleum ether/ethyl acetate (85:15).

26d: R_f = 0.40; colourless oil, yield 0.25 g (37%), $[\alpha]_{589}$ = −4.32 (*c* = 3.92 in $CHCl_3$). − $C_{32}H_{41}NO_6S$ (567.7): calcd. C 67.7, H 7.28, N 2.47; found C 67.8, H 7.40, N 2.25. − MS (CI): *m*/*z* = 568 (M + H^+). − IR (film): $\tilde{\nu}$ = 3204 cm^{-1} (NH), 3062 (C−H), 2977 (C−H), 1600 (C=C), 1160 (C−O). − ^{1}H NMR ($CDCl_3$): δ = 1.08 [s, 3 H, C(CH_3)$_2$], 1.14 [s, 3 H, C(CH_3)$_2$], 1.15 [s, 3 H, C(CH_3)$_2$], 1.19 [s, 3 H, C(CH_3)$_2$], 2.38 (s, 3 H, aryl-CH_3), 2.51 [dd, J = 14.2/8.1 Hz, 1 H, C*H*$_2$CH(OR)$_2$], 2.65 [dd, J = 14.2/2.9 Hz, 1 H, C*H*$_2$CH(OR)$_2$], 3.16 (s, 3 H, OCH_3), 3.23 (s, 3 H, OCH_3), 4.10 (d, J = 3.7 Hz, 1 H, 4-H), 4.11 (d, J = 3.7 Hz, 1 H, 5-H), 5.38 (d, J = 8.1 Hz, 1 H, C*H*NH-Tos, s after addition of D_2O), 5.41 (dd, J = 8.1/2.9 Hz, 1 H, 2-H), 6.52 (d, J = 8.1 Hz, 1 H, CHN*H*-Tos, H/D exchange), 6.88 (dd, J = 8.1/2.2 Hz, 1 H, arom.), 7.10 (d, J = 8.1 Hz, 1 H, arom.), 7.17−7.28 (m, 9 H, arom.), 7.58 (d, J = 8.1 Hz, 2 H, arom.). − ^{13}C NMR ($CDCl_3$): 21.1 [q, C(*C*H_3)$_2$], 21.2 [q, C(*C*H_3)$_2$], 21.4 [q, C(*C*H_3)$_2$ and aryl-*C*H_3], 21.8 [q, C(*C*H_3)$_2$], 38.2 [t, *C*H_2CH(OR)$_2$], 49.2 (q, OCH_3), 49.3 (q, OCH_3), 60.4 (d, *C*HNH-Tos), 75.8 [s, *C*(CH_3)$_2$], 77.1 [s, *C*(CH_3)$_2$], 82.0 (d, C-4), 84.5 (d, C-5), 107.1 (d, C-2), 126.1 (d, arom.), 126.2 (d, arom.), 126.4 (d, arom.), 126.6 (d, arom.), 126.9 (d, arom.), 127.0 (d, arom.), 127.3 (d, arom.), 127.4 (d, arom.), 127.9 (d, arom.), 128.0 (d, arom.), 128.2 (d, arom.), 128.4 (d, arom.), 129.1 (d, arom.), 129.2 (s, arom.), 130.6 (s, arom.), 131.6 (s, arom.), 134.7 (s, arom.), 150.5 (s, arom.).

27d: R_f = 0.38; colourless oil, yield 0.18 g (26%), $[\alpha]_{589}$ = +2.42 (*c* = 2.97 in $CHCl_3$). − $C_{32}H_{41}NO_6S$ (567.7): calcd. C 67.7, H 7.28, N 2.47; found C 67.6, H 7.29, N 2.54. − MS (CI): *m*/*z* = 569 (M + H^+). − IR (film): $\tilde{\nu}$ = 3207 cm^{-1} (NH), 3060 (C−H), 2973 (C−H), 1597 (C=C), 1157 (C−O). − ^{1}H NMR ($CDCl_3$): δ = 1.09 [s, 3 H, C(CH_3)$_2$], 1.12 [s, 3 H, C(CH_3)$_2$], 1.26 [s, 3 H, C(CH_3)$_2$], 1.27 [s, 3 H, C(CH_3)$_2$], 2.37 (s, 3 H, aryl-CH_3), 2.66−2.77 [m, 2 H, C*H*$_2$CH(OR)$_2$], 3.14 (s, 3 H, OCH_3), 3.18 (s, 3 H, OCH_3), 3.79 (d, J = 3.7 Hz, 1 H, 4-H), 4.07 (d, J = 3.7 Hz, 1 H, 5-H), 5.33 (t, J = 3.7 Hz, 1 H, 2-H), 5.80 (d, J = 6.9 Hz, 1 H, C*H*NH-Tos, s after addition of D_2O), 6.22 (d, J = 6.9 Hz, 1 H, CHN*H*-Tos, H/D exchange), 6.89 (d, J = 7.3 Hz, 1 H, arom.), 7.10 (dd, J = 8.1/2.2 Hz, 1 H, arom.), 7.11−7.29 (m, 9 H, arom.), 7.58 (d, J = 8.1 Hz, 2 H, arom.). − ^{13}C NMR ($CDCl_3$): 21.2 [q, C(*C*H_3)$_2$], 21.3 [q, C(*C*H_3)$_2$], 21.4 [q, C(*C*H_3)$_2$ and aryl CH_3], 22.1 [q, C(*C*H_3)$_2$], 36.4 [t, *C*H_2CH(OR)$_2$], 49.1 (q, OCH_3), 49.2 (q, OCH_3), 60.5 (d, *C*HNH-Tos), 75.7 [s, *C*(CH_3)$_2$], 77.2 [s, *C*(CH_3)$_2$], 81.5 (d, C-4), 83.9 (d, C-5), 104.5 (d, C-2), 126.6 (d, arom.), 127.0 (d, 2 C, arom.), 127.1 (d, arom.), 127.2 (d, arom.), 127.3 (d, arom.), 128.0 (d, arom.), 128.1 (d, arom.), 128.3 (d, arom.), 129.1 (d, arom.), 130.1 (d, arom.), 132.9 (s, arom.), 133.8 (s, arom.), 139.3 (s, arom.), 148.7 (s, arom.).

b) *p*-Toluenesulfonyl chloride (87.5 mg, 0.46 mmol) was added to a cooled solution of **35**/**36** (92:8 mixture, 0.18 g, 0.44 mmol) in THF (15 mL) and triethylamine (63 mg, 0.63 mmol). After stirring for 8 h at room temperature, water, 2 N NaOH and Et_2O were added, the organic layer was separated, dried ($MgSO_4$), concentrated in vacuo, and the residue was purified by FC as described under a). Colourless oil (**26d**), yield 0.20 g (81%).

***N*-[(α*R* and α*S*)-2-{[(4*R*,5*R*)-4,5-Bis(3-methoxpentan-3-yl)-1,3-dioxolan-2-yl]methyl}benzhydryl]-4-methylbenzenesulfonamide (26e/27e):** According to General Procedure 2, **6f** (133 mg, 0.30 mmol) was treated with **25** (85.5 mg, 0.33 mmol). FC [diameter of the column 2 cm, petroleum ether/ethyl acetate (90:10), R_f = 0.24] provided a pale yellow oil, yield 59.9 mg (32%). − $C_{36}H_{49}NO_6S$ (623.9): calcd. C 69.3, H 7.92, N 2.25, S 5.14; found C 69.2, H 7.82, N 2.42, S 5.13. − MS (70 eV): *m*/*z* = 454 (M − NHTos). − IR (film): $\tilde{\nu}$ = 3269 cm^{-1} (NH), 3062 (C−H), 2969 (C−H), 1599 (C=C), 1160 (C−O). − ^{1}H NMR ($CDCl_3$): δ = 0.85−1.00 (m, 12 H, 4 × CH_2CH_3), 1.26−1.80 (m, 8 H, 4 × C*H*$_2$CH$_3$), 2.37 (s, 3 × 0.62 H, aryl-CH_3), 2.38 (s, 3 × 0.38 H, aryl-CH_3), 2.57−2.74 [m, 2 H, C*H*$_2$CH(OR)$_2$], 3.10 (s, 3 H, OCH_3), 3.22 (s, 3 H, OCH_3), 4.17 (d, J = 4.3 Hz, 1 × 0.62 H, 4-H), 4.27 (d, J = 4.3 Hz, 1 × 0.62 H, 5-H), 4.32 (d, J = 3.4 Hz, 1 × 0.38 H, 4-H), 4.38 (d, J = 3.4 Hz, 1 × 0.38 H, 5-H), 5.27 (t, J = 3.9 Hz, 1 × 0.62 H, 2-H), 5.32 (dd, J = 4.7/3.0 Hz, 1 × 0.38 H, 2-H), 5.49 (d, J = 8.1 Hz, 1 × 0.62 Hz, C*H*NH-Tos, s after addition of D_2O), 5.84 (d, J = 7.3 Hz, 1

× 0.38 Hz, C*H*NH-Tos, s after addition of D_2O), 5.98−6.02 (m, 1 × 0.62 Hz, CHN*H*-Tos, H/D exchange), 6.63 (d, *J* = 7.3 Hz, 1 × 0.38 Hz, CHN*H*-Tos, H/D exchange), 6.90−7.26 (m, 11 H, arom.), 7.57 (d, *J* = 8.1 Hz, 2 H, arom.). Ratio **26e**/**27e** = 62:38.

***N*-[(α*R* and α*S*)-2-{[(2*S*,4*S*)-4-(Trimethylsiloxymethyl)-1,3-dioxan-2-yl]methyl}benzhydryl]-4-methylbenzenesulfonamide (26f/27f):** According to General Procedure 2, **7b** (108 mg, 0.30 mmol) was treated with **25** (83 mg, 0.32 mmol). FC [diameter of the column 2 cm, petroleum ether/ethyl acetate (90:10), R_f = 0.26] provided a colourless oil, yield 122.1 mg (75%). − $C_{29}H_{37}NO_5SSi$ (539.8): calcd. C 64.5, H 6.91, N 2.59; found C 64.6, H 6.81, N 2.66. − MS (70 eV): *m*/*z* = 524 (M − CH_3). − IR (film): $\tilde{\nu}$ = 3227 cm^{-1} (NH), 3062 (C−H), 2957 (C−H), 1599 (C=C), 1159 (C−O). − ^1H NMR ($CDCl_3$): δ = 0.00 [s, 9 H, OSi(CH_3)$_3$], 1.35−1.49 (m, 1 H, 5-H eq.), 1.51−1.67 (m, 1 H, 5-H ax.), 2.26 (s, 3 × 0.56 H, aryl-CH_3), 2.28 (s, 3 × 0.44 H, aryl-CH_3), 2.49−2.62 [m, 2 H, CH_2CH(OR)$_2$], 3.39−3.62 (m, 4 H, CH_2OSiMe$_3$, 6-H ax., 4-H ax.), 3.99−4.16 (m, 1 H, 6-H eq.), 4.52−4.62 (m, 1 H, 2-H ax.), 5.39 (d, *J* = 7.3 Hz, 1 × 0.56 H, C*H*NH-Tos, s after addition of D_2O), 5.51 (d, *J* = 6.6 Hz, 1 × 0.44 H, C*H*NH-Tos, s after addition of D_2O), 6.24 (d, *J* = 6.6 Hz, 1 × 0.44 H, CHN*H*-Tos, H/D exchange), 6.55 (d, *J* = 7.3 Hz, 1 × 0.56 H, CHN*H*-Tos, H/D exchange), 6.78−6.89 (m, 2 H, arom.), 6.99−7.18 (m, 9 H, arom.), 7.41 (d, *J* = 8.1 Hz, 2 × 0.56 H, arom.), 7.46 (d, *J* = 8.1 Hz, 2 × 0.44 H, arom.). Ratio **26f**/**27f** = 44:56.

***N*-[(α*R* and α*S*)-2-{[(2*S*,4*S*)-4-(*tert*-Butyldimethylsiloxymethyl)-1,3-dioxan-2-yl]methyl}benzhydryl]-4-methylbenzenesulfonamide (26g/27g):** According to General Procedure 2, **7c** (280 mg, 0.70 mmol) was treated with **25** (200 mg, 0.77 mmol). FC [diameter of the column 2 cm, petroleum ether/ethyl acetate (90:10), R_f = 0.30] furnished a colourless oil, yield 290 mg (71%). − $C_{32}H_{43}NO_5SSi$ (581.8): calcd. C 66.1, H 7.45, N 2.41; found C 65.9, H 7.39, N 2.64. − MS (70 eV): *m*/*z* = 524 (M − *tert*-Butyl). − IR (film): $\tilde{\nu}$ = 3266 cm^{-1} (NH), 3063 (C−H), 2928 (C−H), 1599 (C=C), 1160 (C−O). − ^1H NMR ($CDCl_3$): 0.00 [s, 6 H, OSi(CH_3)$_2$], 0.83 [s, 9 H, OSiC(CH_3)$_3$], 1.45−1.52 (m, 1 H, 5-H eq.), 1.61−1.72 (m, 1 H, 5-H ax.), 2.33 (s, 3 × 0.67 H, aryl-CH_3), 2.34 (s, 3 × 0.33 H, aryl-CH_3), 2.50−2.68 [m, 2 H, CH_2CH(OR)$_2$], 3.46−3.70 (m, 4 H, CH_2OSi, 6-H ax., 4-H ax.), 4.12−4.22 (m, 1 H, 6-H eq.), 4.60 (t, *J* = 5.1 Hz, 1 × 0.33 H, 2-H ax.), 4.64 (dd, *J* = 7.2/3.4 Hz, 1 × 0.67 H, 2-H ax.), 5.47 (d, *J* = 8.1 Hz, 1 × 0.67 H, C*H*NH-Tos, s after addition of D_2O), 5.56 (d, *J* = 6.8 Hz, 1 × 0.33 H, C*H*NH-Tos, s after addition of D_2O), 6.64 (d, *J* = 7.7 Hz, 1 × 0.67 H, CHN*H*-Tos, H/D exchange), 6.76 (d, *J* = 6.8 Hz, 1 × 0.33 H, CHN*H*-Tos, H/D exchange), 6.86−7.18 (m, 11 H, arom.), 7.47−7.52 (m, 2 H, arom.). Ratio **26g**/**27g** = 33:67.

***N*-[(α*R* and α*S*)-2-{[(2*S*,4*S*)-4-(Triphenylsiloxymethyl)-1,3-dioxan-2-yl]methyl}benzhydryl]-4-methylbenzenesulfonamide (26h/27h):** According to General Procedure 2, **7d** (163 mg, 0.30 mmol) was treated with **25** (85.5 mg, 0.33 mmol). FC [diameter of the column 2 cm, petroleum ether/ethyl acetate (90:10), R_f = 0.32] gave a pale yellow oil, yield 220 mg (61%). − $C_{44}H_{43}NO_5SSi$ (725.9): calcd. C 72.8, H 5.97, N 1.93, S 4.42; found C 72.6, H 6.21, N 1.90, S 4.27. − MS (CI): *m*/*z* = 649 (M + H^+ − C_6H_5). − IR (film): $\tilde{\nu}$ = 3256 cm^{-1} (NH), 3058 (C−H), 2926 (C−H), 1597 (C=C), 1155 (C−O). − ^1H NMR ($CDCl_3$): δ = 1.37−1.44 (m, 1 H, 5-H eq.), 1.67−1.77 (m, 1 H, 5-H ax.), 2.26 (s, 3 × 0.32 H, aryl-CH_3), 2.32 (s, 3 × 0.68 H, aryl-CH_3), 2.58−2.70 [m, 2 H, CH_2CH(OR)$_2$], 3.60−3.90 (m, 4 H, CH_2OSiPh_3, 6-H ax., 4-H ax.), 4.10−4.21 (m, 1 H, 6-H eq.), 4.60−4.62 (m, 1 H, 2-H ax.), 5.50 (d, *J* = 8.1 Hz, 1 × 0.68 H, C*H*NH-Tos, s after addition of D_2O), 5.56 (d, *J* = 8.1 Hz, 1 × 0.32 H, C*H*NH-Tos, s after addition of D_2O), 6.64−6.76 (m, 1 H, CHN*H*-Tos, H/D exchange), 6.90−7.68 (m, 28 H, arom.). Ratio **26h**/**27h** = 32:68.

***N*-[(α*R* and α*S*)-2-{[(2*R*,4*S*,5*S*)-5-Benzyloxy-4-methoxymethyl-1,3-dioxan-2-yl]methyl}benzhydryl]-4-methylbenzenesulfonamide (26i/27i):** According to General Procedure 2, **7d** (118 mg, 0.30 mmol) was treated with **25** (85.4 mg, 0.33 mmol). FC [diameter of the column 2 cm, petroleum ether/ethyl acetate (75:25), R_f = 0.26] provided a colourless oil, yield 85.9 mg (49%). − MS (CI): *m*/*z* = 589 (M + H^+). − ^1H NMR ($CDCl_3$): δ = 2.23 (s, 3 × 0.44 H, aryl-CH_3), 2.26 (s, 3 × 0.56 H, aryl-CH_3), 2.57−2.70 [m, 2 H, CH_2CH(OR)$_2$], 3.19−3.25 (m, 4 H, 5-H eq., CH_2OCH_3), 3.41−3.45 (m, 1 H, 6-H ax.), 3.50−3.60 (m, 2 H, CH_2OCH$_3$), 3.74−3.82 (m, 1 H, 4-H ax.), 4.25−4.32 (m, 1 H, 6-H eq.), 4.37−4.44 (m, 1 H, OCH_2C$_6$H$_5$), 4.55−4.76 (m, 2 H, 2-H ax., OCH_2C$_6$H$_5$), 5.50 (d, *J* = 8.1 Hz, 1 × 0.56 H, C*H*NH-Tos, s after addition of D_2O), 5.52 (d, *J* = 6.6 Hz, 1 × 0.44 H, C*H*NH-Tos, s after addition of D_2O), 6.27−6.30 (m, 1 H, CHN*H*-Tos, H/D exchange), 6.72−7.32 (m, 16 H, arom.), 7.46 (d, *J* = 7.7 Hz, 2 × 0.56 H, arom.), 7.55 (d, *J* = 8.8 Hz, 2 × 0.44 H, arom.). Ratio **26i**/**27i** = 56:44.

***N*-[(α*R* and α*S*)-2-{[(4*R*,5*R*)-4,5-Dimethyl-1,3-dioxolan-2-yl]methyl}benzhydryl]aniline (29a/30a):** According to General Procedure 2, **6a** (200 mg, 0.74 mmol) was treated with **28** (140 mg, 0.77 mmol). FC [diameter of the column 2 cm, petroleum ether/ethyl acetate (85:15), R_f = 0.41] provided a pale yellow oil, yield 230 mg (82%). − $C_{25}H_{27}NO_2$ (373.5): calcd. C 80.4, H 7.29, N 3.75; found C 80.2, H 7.53, N 3.69. − MS (70 eV): *m*/*z* = 373 (M^+), 282 (M − NHC_6H_5). − IR (film): $\tilde{\nu}$ = 3375 cm^{-1} (NH), 3031 (C−H), 2941 (C−H), 1602 (C=C), 1071 (C−O). − ^1H NMR ($CDCl_3$): 1.09−1.21 (m, 6 H, 2 × CHCH_3), 2.84−2.94 [m, 2 H, CH_2CH(OR)$_2$], 3.42 (q, *J* = 6.6 Hz, 1 H, 4-H), 3.52 (q, *J* = 5.9 Hz, 1 H, 5-H), 4.02−4.08 (m, 1 H, CHN*H*-C_6H_5, H/D exchange), 5.18 (dd, *J* = 5.9/4.4 Hz, 1 H, 2-H), 5.84 (br. s, 1 × 0.49 H, C*H*NHC$_6$H$_5$), 5.86 (br. s, 1 × 0.51 H, C*H*NHC$_6$H$_5$), 6.48−6.61 (m, 3 H, arom.), 7.01−7.27 (m, 11 H, arom.). Ratio **29a**/**30a** = 49:51.

***N*-[(α*R* and α*S*)-2-{[(4*S*,5*S*)-4,5-Bis(methoxymethyl)-1,3-dioxolan-2-yl]methyl}benzhydryl]aniline (29b/30b):** According to General Procedure 2, **6b** (245 mg, 0.74 mmol) was treated with **28** (140 mg, 0.77 mmol). FC [diameter of the column 2 cm, petroleum ether/ethyl acetate (85:15), R_f = 0.35] provided a pale yellow oil, yield 260 mg (82%). − $C_{27}H_{31}NO_4$ (433.5): calcd. C 74.8, H 7.21, N 3.23; found C 74.7, H 7.44, N 3.14. − MS (CI): *m*/*z* = 434 (M + H^+). − IR (film): $\tilde{\nu}$ = 3374 cm^{-1} (NH), 3055 (C−H), 2926 (C−H), 1601 (C=C), 1136 (C−O). − ^1H NMR ($CDCl_3$): δ = 3.00−3.04 [m, 2 H, CH_2CH(OR)$_2$], 3.35 (s, 3 H, OCH_3), 3.38 (s, 3 H, OCH_3), 3.43−3.46 (m, 4 H, 2 × CH_2OCH$_3$), 3.91−3.95 (m, 2 H, 4-H, 5-H), 4.30−4.33 (m, 1 H, CHN*H*C$_6$H$_5$, H/D exchange), 5.27 (dd, *J* = 4.4/3.7 Hz, 1 × 0.57 H, 2-H), 5.34 (t, *J* = 5.1 Hz, 1 × 0.43 H, 2-H), 5.89 (s, 1 × 0.57 H, C*H*NHC$_6$H$_5$), 5.90 (s, 1 × 0.43 H, C*H*NHC$_6$H$_5$;), 6.55 (dd, *J* = 7.3/2.2 Hz, 1 H, arom.), 6.67, (dd, *J* = 7.3/2.2 Hz, 1 H, arom.), 7.07−7.36 (m, 12 H, arom.). Ratio **29b**/**30b** = 57:43.

***N*-[(α*R* and α*S*)-2-{[(4*R*,5*R*)-4,5-Bis(2-methoxypropan-2-yl)-1,3-dioxolan-2-yl]methyl}-benzhydryl]aniline (29c/30c):** According to General Procedure 2, **6e** (232 mg, 0.60 mmol) was treated with **28** (110 mg, 0.62 mmol). FC [diameter of the column 2 cm, petroleum ether/ethyl acetate (90:10), R_f = 0.62] provided a pale yellow oil, yield 220 mg (75%). − $C_{31}H_{39}NO_4$ (489.7): calcd. C 76.0, H 8.03, N 2.86; found C 76.2, H 8.15, N 2.59. − MS (70 eV): *m*/*z* = 489 (M^+), 397 (M − NHC_6H_5). − IR (film): $\tilde{\nu}$ = 3374 cm^{-1} (NH), 3055 (C−H), 2926 (C−H), 1601 (C=C), 1136 (C−O). − ^1H NMR ($CDCl_3$): δ = 0.93 [s, 3 × 0.91 H, C(CH_3)$_2$], 1.00 [s, 3 × 0.91 H,

$C(CH_3)_2$], 1.02 [s, 3 × 0.09 H, $C(CH_3)_2$], 1.03 [s, 3 × 0.09 H, $C(CH_3)_2$], 1.07 [s, 6 × 0.09 H, $C(CH_3)_2$], 1.09 [s, 6 × 0.91 H, $C(CH_3)_2$], 2.84 [dd, J = 14.7/4.4 Hz, 1 × 0.91 H, CH_2CH(OR)$_2$], 2.88−2.90 [m, 2 × 0.09 H, CH_2CH(OR)$_2$], 2.95 84 [dd, J = 14.7/5.1 Hz, 1 × 0.91 H, CH_2CH(OR)$_2$], 3.06 (s, 3 × 0.91 H, OCH_3), 3.08 (s, 3 × 0.09 H, OCH_3), 3.09 (s, 3 × 0.09 H, OCH_3), 3.10 (s, 3 × 0.91 H, OCH_3), 3.75 (d, J = 2.9 Hz, 1 × 0.91 H, 4-H), 3.77 (d, J = 2.9 Hz, 1 × 0.09 H, 4-H), 3.97 (d, J = 2.9 Hz, 1 × 0.09 H, 5-H), 3.99 (d, J = 2.9 Hz, 1 × 0.91 H, 5-H), 4.11 (m, 1 × 0.91 H, CHN*H*-C_6H_5, H/D exchange), 4.16 (m, 1 × 0.09 H, CHN*H*-C_6H_5, H/D exchange), 5.28 (t, J = 4.4 Hz, 1 × 0.09 H, 2-H), 5.37 (dd, J = 5.1/4.4 Hz, 1 × 0.91 H, 2-H), 5.87 (m, 1 H, C*H*NH-C_6H_5, s after addition of D_2O), 6.46 (d, J = 8.1 Hz, 2 H, arom.), 6.56 (t, J = 7.3 Hz, 1 H, arom.), 6.97−7.25 (m, 11 H, arom.). Ratio **29c**/**30c** = 91:9. − ^{13}C NMR ($CDCl_3$): δ = 19.1 [q, 1 × 0.91 C, $C(CH_3)_2$], 21.0 [q, 1 × 0.91 C, $C(CH_3)_2$], 21.2 [q, 1 × 0.09 C, $C(CH_3)_2$], 21.3 [q, 1 × 0.91 C, $C(CH_3)_2$], 22.1 [q, 1 × 0.91 C, $C(CH_3)_2$], 22.1 [q, 1 × 0.09 C, $C(CH_3)_2$], 22.5 [q, 1 × 0.09 C, $C(CH_3)_2$], 25.6 [q, 1 × 0.09 C, $C(CH_3)_2$], 37.5 [t, 1 × 0.09 C, CH_2CH(OR)$_2$], 37.9 [t, 1 × 0.91 C, CH_2CH(OR)$_2$], 49.2 (q, OCH_3), 49.4 (q, OCH_3), 58.6 (d, 1 × 0.91 C, *C*HNHC$_6$H$_5$), 59.0 (d, 1 × 0.09 C, *C*HNHC$_6$H$_5$), 75.8 [s, $C(CH_3)_2$], 76.7 [s, $C(CH_3)_2$], 81.7 (d, 1 × 0.91 C, C-4), 84.0 (d, 2 × 0.09 C, C-4, C-5), 84.1 (d, 1 × 0.91 C, C-5), 105.9 (d, 1 × 0.09 C, C-2), 106.3 (d, 1 × 0.91 C, C-2), 113.2 (d, 2 × 0.09 C, arom.), 113.4 (d, 2 × 0.91 C, arom.), 117.2 (d, C-3 arom.), 126.9 (d, arom.), 127.1 (d, C-4 arom.), 127.2 (d, C-5 arom.), 127.8 (d, C-6 arom.), 128.0 (d, 2 C arom.), 128.5 (d, 2 C arom.), 129.0 (d, 2 C arom.), 131.3 (d, 1 × 0.91 C, arom.), 131.6 (d, 1 × 0.09 C, arom.), 134.9 (s, C-1 arom.), 141.2 (s, C-2 arom.), 142.6 (s, arom.), 147.2 (s, arom.).

***N*-[(α*R* and α*S*)-2-{[(2*S*,4*S*)-4-(Triphenylsiloxymethyl)-1,3-dioxan-2-yl]methyl}benzhydryl]aniline (29d/30d):** According to General Procedure 2, **7d** (164 mg, 0.30 mmol) was treated with **28** (60 mg, 0.33 mmol). FC [diameter of the column 2 cm, petroleum ether/ethyl acetate (90:10), R_f = 0.52] afforded a pale yellow oil, yield 140 mg (70%). − $C_{43}H_{41}NO_3Si$ (647.9): calcd. C 79.7, H 6.38, N 2.16; found C 79.6, H 6.76, N 1.92. − MS (CI): m/z = 648 (M + H$^+$). − IR (film): $\tilde{\nu}$ = 3418 cm^{-1} (NH), 3068 (C−H), 2926 (C−H), 1601 (C=C), 1117 (C−O). − ^{1}H NMR ($CDCl_3$): δ = 1.41−1.52 (m, 1 H, 5-H eq.), 1.56−1.66 (m, 1 H, 5-H ax.), 2.82−3.00 [m, 2 H, CH_2CH(OR)$_2$], 3.50−3.71 (m, 3 H, CH_2OSiPh$_3$, 6-H ax.), 3.84−3.88 (m, 1 H, 4-H ax.), 4.01−4.09 (m, 1 H, 6-H eq.), 4.23−4.29 (m, 1 H, CHN*H*C$_6$H$_5$, H/D exchange), 4.52−4.58 (m, 1 H, 2-H ax.), 5.81 (s, 1 × 0.25 H, C*H*NHC$_6$H$_5$), 5.87 (s, 1 × 0.75 H, C*H*NHC$_6$H$_5$), 6.47−6.65 (m, 3 H, arom.), 7.00−44 (m, 20 H, arom.), 7.58−7.64 (m, 6 H, arom.). Ratio **29d**/**30d** = 25:75.

***N*-[(α*R* and α*S*)-2-{[(4*R*,5*R*)-4,5-Dimethyl-1,3-dioxolan-2-yl]methyl}benzhydryl]-4-methoxyaniline (32a/33a):** According to General Procedure 2, **6a** (0.19 g, 0.70 mmol) was treated with **31** (0.19 g, 0.74 mmol). FC [diameter of the column 2 cm, petroleum ether/ethyl acetate (85:15), R_f = 0.35] provided a pale yellow oil, yield 0.11 g (37%). − $C_{26}H_{29}NO_3$ (403.5): calcd. C 77.4, H 7.24, N 3.47; found C 77.2, H 7.48, N 3.36. − MS (70 eV): m/z = 403 (M$^+$), 281 (M$^+$ − $NHC_6H_4OCH_3$). − IR (film): $\tilde{\nu}$ = 3380 cm^{-1} (NH), 3062 (C−H), 2941 (C−H), 1600 (C=C), 1073 (C−O). − ^{1}H NMR ($CDCl_3$): 1.04−1.17 (m, 6 H, 2 × CHCH_3), 2.81−2.92 [m, 2 H, CH_2CH(OR)$_2$], 3.65 (s, 3 H, aryl-OCH_3), 3.72 (q, J = 6.6 Hz, 1 H, 4-H), 3.82 (q, J = 5.9 Hz, 1 H, 5-H), 4.00−4.06 (m, 1 H, CHN*H*-aryl, H/D exchange), 5.07 (dd, J = 5.9/4.4 Hz, 1 H, 2-H), 5.72 (s, 1 × 0.48 H, C*H*NH-aryl), 5.74 (s, 1 × 0.52 H, C*H*NH-aryl), 6.42−6.59 (m, 3 H, arom.), 7.01−7.20 (m, 10 H, arom.). Ratio **32a**/**33a** = 48:52.

***N*-[(α*R* and α*S*)-2-{[(4*S*,5*S*)-4,5-Bis(methoxymethyl)-1,3-dioxolan-2-yl]methyl}benzhydryl]-4-methoxyaniline (32b/33b):** According to General Procedure 2, **6b** (0.20 g, 0.60 mmol) was treated with **31** (0.13 g, 0.62 mmol). The reaction mixture was stirred for 2 h at −100°C and for 2 h at 0°C. Pruification by FC [diameter of the column 2 cm, petroleum ether/ethyl acetate (75:25), R_f = 0.37] furnished a pale yellow oil, yield 0.17 g (62%). − $C_{28}H_{33}NO_5$ (463.6): calcd. C 72.5, H 7.18, N 3.02; found C 72.7, H 7.56, N 2.47. − MS (70 eV): m/z = 463 (M$^+$), 341 (M − $NHC_6H_4OCH_3$). − IR (film): $\tilde{\nu}$ = 3378 cm^{-1} (NH), 3059 (C−H), 2928 (C−H), 1601 (C=C), 1132 (C−O). − ^{1}H NMR ($CDCl_3$): 2.97−2.99 [m, 2 H, CH_2CH(OR)$_2$], 3.23−3.42 (m, 10 H, 2 × CH_2OCH_3), 3.63 (s, 3 H, aryl-OCH_3), 3.80−3.92 (m, 2 H, 4-H, 5-H), 3.94−4.00 (m, 1 H, CHN*H*-aryl, H/D exchange), 5.18 (dd, J = 4.7/2.1 Hz, 1 × 0.39 H, 2-H), 5.20 (dd, J = 4.3/2.6 Hz, 1 × 0.61 H, 2-H), 5.73 (m, 1 × 0.39 H, C*H*NH-aryl, s after addition of D_2O), 5.74 (m, 1 × 0.61 H, C*H*NH-aryl, s after addition of D_2O), 6.43 (d, J = 8.9 Hz, 2 H, arom.), 6.63 (d, J = 8.9 Hz, 2 H, arom.), 7.08−7.28 (m, 9 H, arom.). Ratio **32b**/**33b** = 61:39.

***N*-[(α*R* and α*S*)-2-{[(4*R*,5*R*)-4,5-Bis(2-methoxypropan-2-yl)-1,3-dioxolan-2-yl]methyl}benzhydryl]-4-methoxyaniline (32c/33c):** According to General Procedure 2, **6e** (0.23 g, 0.60 mmol) was treated with **31** (0.13 g, 0.62 mmol). The reaction mixture was stirred for 2 h at −100°C and for 2 h at 0°C. The HPLC analysis [eluent *n*-heptane/ethyl acetate (90:10)] of the unpurified product showed a diastereomeric ratio **32c** (retention time 17.7 min)/**33c** (retention time 17.2 min) of 92.1:7.9. Purification by FC [diameter of the column 2 cm, petroleum ether/ethyl acetate (90:10), R_f = 0.59] furnished a pale yellow oil, yield 0.21 g (67%). − $C_{32}H_{41}NO_5$ (519.7): calcd. C 74.0, H 7.95, N 2.70; found C 74.0, H 7.97, N 2.60. − MS (70 eV): m/z = 520 (M$^+$), 398 (M − $NHC_6H_4OCH_3$). − IR (film): $\tilde{\nu}$ = 3379 cm^{-1} (NH), 3061 (C−H), 2921 (C−H), 1602 (C=C), 1135 (C−O). − ^{1}H NMR ($CDCl_3$): δ = 0.92 [s, 3 × 0.09 H, $C(CH_3)_2$], 0.93 [s, 3 × 0.91 H, $C(CH_3)_2$], 1.00 [s, 3 × 0.91 H, $C(CH_3)_2$], 1.07 [s, 3 × 0.09 H, $C(CH_3)_2$], 1.08 [s, 6 × 0.09 H, $C(CH_3)_2$], 1.09 [s, 3 × 0.91 H, $C(CH_3)_2$], 1.10 [s, 3 × 0.91 H, $C(CH_3)_2$], 2.84 [dd, J = 14.7/4.4 Hz, 1 × 0.91 H, CH_2CH(OR)$_2$], 2.88−2.90 [m, 2 × 0.09 H, CH_2CH(OR)$_2$], 2.95 [dd, J = 14.7/5.1 Hz, 1 × 0.91 H, CH_2CH(OR)$_2$], 3.07 (s, 3 × 0.91 H, OCH_3), 3.08 (s, 3 × 0.09 H, OCH_3), 3.09 (s, 3 × 0.09 H, OCH_3), 3.11 (s, 3 × 0.91 H, OCH_3), 3.62 (s, 3 × 0.91 H, aryl-OCH_3), 3.62 (s, 3 × 0.09 H, aryl-OCH_3), 3.75 (d, J = 2.9 Hz, 1 × 0.91 H, 4-H), 3.77 (d, J = 2.9 Hz, 1 × 0.09 H, 4-H), 3.88 (br. s, 1 H, CHN*H*-aryl, H/D exchange), 3.97 (d, J = 2.9 Hz, 1 × 0.09 H, 5-H), 3.99 (d, J = 2.9 Hz, 1 × 0.91 H, 5-H), 5.27 (t, J = 4.4 Hz, 1 × 0.09 H, 2-H), 5.36 (dd, J = 5.1/4.4 Hz, 1 × 0.91 H, 2-H), 5.79 (m, 1 H, C*H*NH-aryl, s after addition of D_2O), 6.41 (d, J = 8.8 Hz, 2 H, arom.), 6.60 (d, J = 8.8 Hz, 2 H, arom.), 7.05−7.24 (m, 9 H, arom.). Ratio **32c**/**33c** = 91:9. − ^{13}C NMR ($CDCl_3$): δ = 19.1 [q, 1 × 0.09 C, $C(CH_3)_2$], 21.1 [q, 1 × 0.91 C, $C(CH_3)_2$], 21.4 [q, 1 × 0.91 C, $C(CH_3)_2$], 21.8 [q, 1 C, $C(CH_3)_2$], 22.1 [q, 1 C, $C(CH_3)_2$], 22.2 [q, 1 × 0.09 C, $C(CH_3)_2$], 37.5 [t, 1 × 0.09 C, CH_2CH(OR)$_2$], 37.9 [t, 1 × 0.91 C, CH_2CH(OR)$_2$], 49.3 (q, 2 × 0.09 C, OCH_3], 49.4 (q, 2 × 0.91 C, OCH_3), 55.8 (q, 1 C, OCH_3), 59.3 (d, 1 C, *C*HNH-aryl), 75.8 [s, 1 C, $C(CH_3)_2$], 77.2 [s, 1 C, $C(CH_3)_2$], 81.8 (d, C-4), 84.0 (d, 1 × 0.09 C, C-5), 84.1 (d, 1 × 0.91 C, C-5), 105.9 (d, 1 × 0.09 C, C-2), 106.3 (d, 1 × 0.91 C, C-2), 114.3 (d, 2 × 0.09 C, arom.), 114.4 (d, 2 × 0.91 C, arom.), 114.7 (d, 1 C, arom.), 114.8 (d, 1 C, arom.), 125.1 (d, 1 × 0.09 C, C-4 arom.), 126.8 (d, 1 × 0.91 C, C-4 arom.), 127.1 (d, C-5 arom.), 127.1 (d, C-6 arom.), 127.7 (d, 2 × 0.09 C, arom.), 128.0 (d, 2 × 0.91 C, arom.), 128.5 (d, 1 C, arom.), 131.2 (d, 1 × 0.91 C, arom.), 131.5 (d, 1 × 0.09 C, arom.), 134.9 (s, C-1 arom.),

141.4 (s, C-2 arom.), 141.7 (s, arom.), 142.8 (s, arom.), 151.9 (s, arom.).

***N*-[(α*R* and α*S*)-2-{[(2*S*,4*S*)-4-(*tert*-Butyldimethylsiloxymethy)-1,3-dioxan-2-yl]methyl}benzhydryl]-4-methoxyaniline (32d/33d):** According to General Procedure 2, **7c** (0.24 g, 0.60 mmol) was treated with **31** (0.13 g, 0.62 mmol). The reaction mixture was stirred for 2 h at −100°C and for 2 h at 0°C. FC [diameter of the column 2 cm, petroleum ether/ethyl acetate (90:10), R_f = 0.62] provided a pale yellow oil, yield 0.18 g (58%). − $C_{32}H_{43}NO_4Si$ (533.8): calcd. C 72.0, H 8.12, N 2.62; found C 71.8, H 8.27, N 2.72. − MS (70 eV): *m*/*z* = 533 (M^+), 476 [M − $C(CH_3)_3$], 411 (M − $NHC_6H_4OCH_3$). − IR (film): $\tilde{\nu}$ = 3378 cm^{-1} (NH), 3061 (C−H), 2954 (C−H), 1513 (C=C), 1141 (C−O). − ^1H NMR ($CDCl_3$): δ = 0.00 [s, 6 H, OSi(CH_3)$_2$], 0.85 [s, 9 H, OSiC(CH_3)$_3$], 1.41−1.50 (m, 1 H, 5-H eq.), 1.56−1.67 (m, 1 H, 5-H ax.), 2.84−3.03 [m, 2 H, CH_2CH(OR)$_2$], 3.44−3.68 (m, 7 H, CH_2OSiR$_3$, aryl-OCH_3, 6-H ax., 4-H ax.), 4.02−4.07 (m, 2 H, 6-H eq., CHNHC$_6$H$_4$OCH$_3$, H/D exchange), 4.54−4.58 (m, 1 H, 2-H ax.), 5.73 (br. s, 1 × 0.34 H, CHNH-C$_6$H$_4$OCH$_3$), 5.76 (br. s, 1 × 0.66 H, CHNH-C$_6$H$_4$OCH$_3$), 6.46 (d, *J* = 9.0 Hz, 2 H, arom.), 6.67 (d, *J* = 9.0 Hz, 2 H, arom.), 7.13−7.30 (m, 9 H, arom.). Ratio **32 d**/**33d** = 34:66.

(1*S*,3*R*)- and (1*S*,3*S*)-2-(4-Methylphenylsulfonyl)-1-phenyl-1,2,3,4-tetrahydroisoquinolin-3-ol (34): According to General Procedure 2, **9** (0.21 g, 0.60 mmol) was treated with **25** (0.17 g, 0.66 mmol). After purification by FC [diameter of the column 2 cm, petroleum ether/ethyl acetate (90:10), R_f = 0.30] **34** was obtained as pale yellow oil, yield 88.7 mg (39%). − $C_{22}H_{21}NO_3S$ (379.5): calcd. C 69.6, H 5.58, N 3.70, S 8.45; found C 69.9, H 5.62, N 3.43, S 8.06. − MS (70 eV): *m*/*z* = 362 (M − OH). − IR (film): $\tilde{\nu}$ = 3546 cm^{-1} (OH), 3062 (C−H), 2960 (C−H), 1599 (C=C), 1187 (C−O). − ^1H NMR ($CDCl_3$): δ = 2.21 (s, 3 × 0.84 H, CH_3), 2.26 (s, 3 × 0.16 H, CH_3.), 2.28−2.37 (m, 1 × 0.16 H, 4-H), 2.55 (dd, *J* = 15.0/9.4 Hz, 1 × 0.84 H, 4-H), 2.86 (dd, *J* = 15.0/5.7 Hz, 1 × 0.84 H, 4-H), 2.95 (dd, *J* = 15.4/2.6 Hz, 1 × 0.16 H, 4-H), 3.35−3.40 (m, 1 × 0.16 H, OH, H/D exchange), 3.64−3.68 (m, 1 × 0.84 H, OH, H/D exchange), 5.27−5.30 (m, 1 H, 3-H), 5.92 (s, 1 × 0.84 H, 1-H), 5.96 (s, 1 × 0.16 H, 1-H), 6.93−7.43 (m, 13 H, arom.). − ^{13}C NMR ($CDCl_3$): δ = 21.0 (q, 1 × 0.16 C, CH_3), 21.4 (q, 1 × 0.84 C, CH_3), 34.8 (t, 1 × 0.84 C, C-4), 36.3 (t, 1 × 0.16 C, C-4), 60.2 (d, 1 × 0.16 C, C-1), 61.4 (d, 1 × 0.84 C, C-1), 77.7 (d, 1 × 0.16 C, C-3), 80.0 (d, 1 × 0.84 C, C-3), 126.5 (d, arom.), 126.9 (d, arom.), 127.0 (d, arom.), 127.1 (d, arom.), 127.4 (d, arom.), 127.9 (d, arom.), 128.3 (d, arom.), 128.5 (d, arom.), 129.2 (d, arom.), 129.5 (d, arom.), 129.5 (d, arom.), 132.5 (s, arom.), 135.7 (s, arom.), 136.6 (s, arom.), 139.9 (s, arom.), 143.6 (s, arom.).

(*R*)-(−)-2-{[(4*R*,5*R*)-4,5-Bis(2-methoxypropan-2-yl)-1,3-dioxolan-2-yl]methyl}benzhydrylamine (35): a) At −78°C, a solution of **26d** (150 mg, 0.26 mmol) in THF (4 mL) was added to Na (100 mg) in liquid ammonia. After 45 min at −78°C, H_2O (5 mL) and CH_2Cl_2 (20 mL) were added, the organic layer was separated, dried ($MgSO_4$) and concentrated in vacuo. Colourless oil, yield 73.1 mg (68%), $[\alpha]_{589}$ = −43.5 (*c* = 2.11 in $CHCl_3$). − $C_{25}H_{35}NO_4$ (413.6): calcd. C 72.6, H 8.53, N 3.39; found C 73.0, H 8.60, N 2.95. − MS (70 eV): *m*/*z* = 397 (M − NH_2). − IR (film): $\tilde{\nu}$ = 3382 cm^{-1} (NH_2), 3052 (C−H), 2974 (C−H), 1601 (C=C), 1140 (C−O). − ^1H NMR ($CDCl_3$): δ = 1.14 [s, 3 H, C(CH_3)$_2$], 1.22 [s, 6 H, C(CH_3)$_2$], 1.26 [s, 3 H, C(CH_3)$_2$], 2.09−2.21 (m, 2 H, NH_2, H/D exchange), 3.07−3.14 [m, 2 H, CH_2CH(OR)$_2$], 3.20 (s, 3 H, OCH_3), 3.26 (s, 3 H, OCH_3), 3.89 (d, *J* = 3.4 Hz, 1 H, 4-H), 4.09 (d, *J* = 3.4 Hz, 1 H, 5-H), 5.33 (dd, *J* = 5.6/4.3 Hz, 1 H, 2-H), 5.68 (s, 1 H, C$H$$NH_2$), 7.20−7.42 (m, 9 H, arom.). − b) Ammonium cerium(IV) nitrate (0.35 g, 0.75 mmol) was added to a solution of **32c**/**33c** (92.1:7.9, 0.13 g, 0.25 mmol) in methanol/H_2O (9:1, 20 mL). The reaction mixture was stirred for 3 h at room temperature, then H_2O, 1 N HCl and Et_2O were added and the organic layer was separated. 2 N NaOH and CH_2Cl_2 were added to the aqueous layer, the CH_2Cl_2 layer was separated, dried ($MgSO_4$) and concentrated in vacuo. Colourless oil, yield 55.0 mg (53%). Ratio **35**/**36** = 92:8 (^1H NMR).

(*S*)-(+)-2-{[(4*R*,5*R*)-4,5-Bis(2-methoxypropan-2-yl)-1,3-dioxolan-2-yl]methyl}benzhydrylamine (36): As described for **35**, the tosyl group of **27d** (150 mg, 0.26 mmol) was cleaved with sodium in liquid ammonia. Colourless oil, yield 56.7 mg (52%), $[\alpha]_{589}$ = +15.1 (*c* = 0.70 in $CHCl_3$). − $C_{25}H_{35}NO_4$ (413.6): calcd. C 72.6, H 8.53, N 3.39; found C 72.6, H 8.44, N 3.46. − MS (70 eV): *m*/*z* = 397 (M − NH_2). − IR (film): $\tilde{\nu}$ = 3382 cm^{-1} (NH_2), 3061 (C−H), 2974 (C−H), 1601 (C=C), 1140 (C−O) cm^{-1}. − ^1H NMR ($CDCl_3$): δ = 0.97 [s, 3 H, C(CH_3)$_2$], 1.03 [s, 3 H, C(CH_3)$_2$], 1.09 [s, 3 H, C(CH_3)$_2$], 1.10 [s, 3 H, C(CH_3)$_2$], 2.09−2.21 (m, 2 H, NH_2, H/D exchange), 2.96−3.01 [m, 2 H, CH_2CH(OR)$_2$], 3.17 (s, 3 H, OCH_3), 3.20 (s, 3 H, OCH_3), 3.84 (d, *J* = 3.4 Hz, 1 H, 4-H), 4.04 (d, *J* = 3.4 Hz, 1 H, 5-H), 5.41 (dd, *J* = 5.6/4.3 Hz, 1 H, 2-H), 5.59 (s, 1 H, C$H$$NH_2$), 7.16−7.37 (m, 9 H, arom.).

(−)-Benzyl *N*-[(α*R*)-2-{[(4*R*,5*R*)-4,5-bis(2-methoxypropan-2-yl)-1,3-dioxolan-2-yl]methyl}-benzhydryl]carbamat (37): Benzyl chloroformate (79.0 mg, 0.46 mmol) was added to an ice-cold solution of **35** (0.13 g, 0.31 mmol) and NEt_3 (63 mg, 0.63 mmol) in THF (15 mL). After stirring for 8 h at room temperature, H_2O, 2 N NaOH and Et_2O were added, the organic layer was separated, dried ($MgSO_4$), concentrated in vacuo and the residue was purified by FC [diameter of the column 2 cm, petroleum ether/ethyl acetate (85:15), R_f = 0.22]. − Pale yellow oil, yield 0.14 g (81%), $[\alpha]_{546}$ = −14.1 (*c* = 1.15 in $CHCl_3$). − $C_{33}H_{41}NO_6$ (547.7): calcd. C 72.4, H 7.55, N 2.56; found C 72.4, H 7.77, N 2.30. − MS (70 eV): *m*/*z* = 397 (M − $NHCO_2Bn$). − IR (film): $\tilde{\nu}$ = 3299 cm^{-1} (NH), 3062 (C−H), 2972 (C−H), 1714 (C=O), 1454 (N-H), 1136 (C−O). − ^1H NMR ($CDCl_3$): δ = 0.96 [s, 3 H, C(CH_3)$_2$], 1.02 [s, 3 H, C(CH_3)$_2$], 1.09 [s, 3 H, C(CH_3)$_2$], 1.15 [s, 3 H, C(CH_3)$_2$], 2.90−3.26 [m, 8 H, CH_2CH(OR)$_2$, 2 × OCH_3], 4.01 (d, *J* = 2.9 Hz, 1 H, 4-H), 4.03 (d, *J* = 2.9 Hz, 1 H, 5-H), 5.11−5.13 (m, 2 H, OCH_2C$_6$H$_5$), 5.39 (t, *J* = 4.4 Hz, 1 H, 2-H), 6.07 (d, *J* = 8.1 Hz, 1 H, NH, H/D exchange), 6.29 (d, *J* = 8.1 Hz, 1 H, C$H$$NHCO_2Bn$, s after addition of D_2O), 7.11−7.36 (m, 14 H, arom.).

(+)-Benzyl *N*-[(α*S*)-2-{[(4*R*,5*R*)-4,5-Bis(2-methoxypropan-2-yl)-1,3-dioxolan-2-yl]methyl}benzhydryl]carbamat (38): As described for **37** the diastereomeric amine **36** was acylated with benzyl chloroformate. Colourless oil, yield 0.147 g (85%), $[\alpha]_{546}$ = +20.9 (*c* = 0.80 in $CHCl_3$). − $C_{33}H_{41}NO_6$ (547.7): calcd. C 72.4, H 7.55, N 2.56; found C 72.5, H 7.68, N 2.38. − MS (70 eV): *m*/*z* = 397 (M − $NHCO_2Bn$). − IR (film): $\tilde{\nu}$ = 3299 cm^{-1} (NH), 3062 (C−H), 2972 (C−H), 1714 (C=O), 1454 (N-H), 1136 (C−O). − ^1H NMR ($CDCl_3$): δ = 0.92 [s, 3 H, C(CH_3)$_2$], 1.02 [s, 3 H, C(CH_3)$_2$], 1.13 [s, 3 H, C(CH_3)$_2$], 1.15 [s, 3 H, C(CH_3)$_2$], 2.90−3.26 (m, 8 H, CH_2CH(OR)$_2$, 2 × OCH_3), 3.75−3.81 (m, 2 H, 4-H, 5-H), 5.11−5.13 (m, 2 H, OCH_2C$_6$H$_5$), 5.30 (t, *J* = 4.4 Hz, 1 H, 2-H), 6.09 (d, *J* = 8.1 Hz, 1 H, NH, H/D exchange), 6.14 (d, *J* = 8.1 Hz, 1 H, C$H$$NHCO_2Bn$, s after addition of D_2O), 7.11−7.36 (m,14 H, arom.).

(*R*)-(+)-2-(4-Methylphenylsulfonyl)-1-phenyl-1,2-dihydroisoquinoline [(*R*)-40]: A solution of **26d** (102 mg, 0.18 mmol), *p*-toluenesulfonic acid (0.19 g, 1.08 mmol) and conc. HCl (1 mL) in methanol/H_2O (3:1, 20 mL) was heated to reflux for 4 d. Then, a saturated solution of $NaHCO_3$ (30 mL) and CH_2Cl_2 (25 mL) were added, the organic layer was separated, dried ($MgSO_4$) and concentrated in vacuo. The residue was separated by FC {diameter of the column

2 cm, petroleum ether/ethyl acetate (85:15), R_f = 0.60 [(R)-**40**]}. The chiral diol **39** was isolated by elution of the column with petroleum ether/ethyl acetate (50:50), yield 26.4 mg (71%).

(*R*)-40: Colourless solid (ethyl acetate/*n*-hexane), m.p. 80−82°C, yield 31.0 mg (48%), $[\alpha]_{589}$ = +270.1 (*c* = 1.04 in $CHCl_3$). − $C_{22}H_{19}NO_2S$ (361.5): calcd. C 73.1, H 5.30, N 3.88; found C 72.9, H 5.77, N 3.61. − MS (CI): *m*/*z* = 362 (M + H). − IR (film): $\tilde{\nu}$ = 3061 cm^{-1} (CH), 2927 (C−H), 1663 (C=C), 1597 (C=C), 1135 (C−O). − ^1H NMR ($CDCl_3$): δ = 2.22 (s, 3 H, aryl-CH_3), 5.97 (d, *J* = 7.3 Hz, 1 H, 4-H), 6.21 (s, 1 H, 1-H), 6.63 (d, *J* = 7.3 Hz, 1 H, 3-H), 6.93−7.17 (m, 13 H, arom.). − ^{13}C NMR ($CDCl_3$): δ = 21.4 (q, aryl-CH_3), 59.9 (d, C-1), 113.9 (d, C-4), 125.4 (d, C-3), 125.8 (d, arom.), 127.3 (d, arom.), 127.6 (d, arom.), 127.7 (d, arom.), 128.3 (d, arom.), 128.4 (d, arom.), 128.6 (d, arom.), 128.9 (d, arom.), 130.0 (d, arom.), 127.9 (d, arom.), 140.7 (s, arom.), 143.5 (s, arom.).

(*S*)-(−)-2-(4-Methylphenylsulfonyl)-1-phenyl-1,2-dihydroisoquinoline [(*S*)-40]: a) As described for (*R*)-**40**, the sulfonamide **27d** was cyclized to afford (*S*)-**40**. Pale yellow oil, yield 28.7 mg (44%), $[\alpha]_{589}$ = −269.8 (*c* = 1.04 in $CHCl_3$). − $C_{22}H_{19}NO_2S$ (361.5): calcd. C 73.1, H 5.30 N, 3.88; found C 72.8, H 5.64, N 3.52. In analogy, **39** (26.0 mg, 71%) was isolated by FC with the eluent petroleum ether/ethyl acetate (50:50). − b) Methanesulfonyl chloride (66.3 mg, 0.58 mmol) was added to an ice-cold solution of **34** (0.11 g, 0.29 mmol) and NEt_3 (87.9 mg, 0.87 mmol) in CH_2Cl_2 (20 mL). The reaction mixture was stirred for 4 h at room temperature. Then, the CH_2Cl_2 layer was washed with 1 N HCl (20 mL), 2 N NaOH (20 mL) and H_2O (20 mL), dried ($MgSO_4$) and concentrated in vacuo. Purification by FC provided a colourless oil, yield 0.10 g (97%), $[\alpha]_{589}$ = −135.6 (*c* = 1.90 in $CHCl_3$, ee = 50%).

(*R*)-(+)-Benzyl 1-Phenyl-1,2-dihydroisoquinoline-2-carboxylate [(*R*)-41]: A solution of **37** (100 mg, 0.18 mmol) and *p*-toluenesulfonic acid × H_2O (78.8 mg, 0.41 mmol) in methanol (20 mL) was heated to reflux for 16 h. The reaction mixture was hydrolysed with a saturated solution of $NaHCO_3$ (20 mL), extracted with CH_2Cl_2 (2 × 20 mL), the organic layer was dried ($MgSO_4$) and concentrated in vacuo. FC purification [diameter of the column 2 cm, petroleum ether/ethyl acetate (85:15), R_f = 0.78]. Subsequent elution of the column with petroleum ether/ethyl acetate (50:50) provided the homochiral diol **39** in a yield of 28.2 mg (75%). (*R*)-**41**: Pale yellow oil, yield 51.4 mg (82%), $[\alpha]_{589}$ = +83.0 (*c* = 1.04 in $CHCl_3$).

(*S*)-(−)-Benzyl 1-Phenyl-1,2-dihydroisoquinoline-2-carboxylate [(*S*)-41]: The cyclization of **38** was performed as described for the preparation of (*R*)-**41**. Pale yellow oil, yield 54.5 mg (87%), $[\alpha]_{589}$ = −82.7 (*c* = 1.04 in $CHCl_3$).

(*R*)-(+)-2-(4-Methylphenylsulfonyl)-1-phenyl-1,2,3,4-tetahydroisoquinoline [(*R*)-42]: (*R*)-**40** (60.0 mg, 0.17 mmol), $LiAlH_4$ (1.0 M in THF, 0.34 mL) and THF (20 mL) was heated to reflux for 16 h. Then, H_2O (0.5 mL) was added cautiously, the mixture was filtered, dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by FC [diameter of the column 2 cm, petroleum ether/ethyl acetate (80:20), R_f = 0.23]. Colourless oil, yield 55.4 mg (90%), $[\alpha]_{589}$ = +89.3 (*c* = 1.96 in $CHCl_3$). − $C_{22}H_{21}NO_2S$ (363.5): calcd. C 72.7, H 5.82, N 3.85; found C 72.5, H 5.73, N 3.75. − MS (CI): *m*/*z* = 364 ($M + H^+$). − IR (film): $\tilde{\nu}$ = 3058 cm^{-1} (C−H), 2952 (C−H), 1586 (C=C), 1135 (C−O). − ^1H NMR ($CDCl_3$): δ = 2.11 (s, 3 H, aryl-CH_3), 2.74−2.79 (m, 1 H, 4-H), 2.96−3.01 (m, 1 H, 4-H), 3.03−3.06 (m, 1 H, 3-H), 3.19−3.24 (m, 1 H, 3-H), 5.04 (s, 1 H, 1-H), 6.95−7.27 (m, 13 H, arom.).

(*S*)-(−)-2-(4-Methylphenylsulfonyl)-1-phenyl-1,2,3,4-tetahydroisoquinoline [(*S*)-42]: (*S*)-**40** was reduced with $LiAlH_4$ as described for (*R*)-**42**. Colourless oil, yield 53.4 mg (86%), $[\alpha]_{589}$ = −88.9 (*c* = 1.88 in $CHCl_3$).

(*R*)-(−)-1-Phenyl-1,2,3,4-tetrahydroisoquinoline [(*R*)-43]:[7a,24] A solution of (*R*)-**42** (50 mg, 0.14 mmol) in THF (4 mL) was added to Na (70 mg) in liquid ammonia at −78°C. After stirring for 45 min at −78°C, H_2O (10 mL) and CH_2Cl_2 (20 mL) were added, the CH_2Cl_2 layer was separated, dried ($MgSO_4$) and concentrated in vacuo. FC purification [diameter of the column 2 cm, CH_2Cl_2/methanol (90:10), R_f = 0.25] of the residue afforded a colourless oil, yield 19.7 mg (68%), $[\alpha]_{589}$ = −10.2 (*c* = 0.99 in $CHCl_3$).

(*S*)-(+)-1-Phenyl-1,2,3,4-tetrahydroisoquinoline [(*S*)-43]:[8a,24] As described for (*R*)-**43**, (*S*)-**42** was treated with Na in liquid ammonia. Colourless oil, yield 21.7 mg (75%), $[\alpha]_{589}$ = +12.2 (*c* = 0.85 in CH_2Cl_2).

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