Asymmetric Synthesis of α-Substituted β-Amino Sulfones by Aza-Michael Addition to Alkenyl Sulfones and Subsequent α-Alkylation

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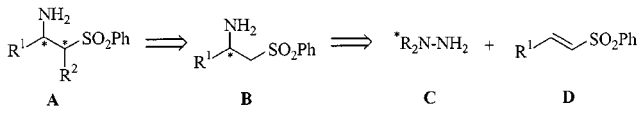
The aza-Michael addition of enantiopure 1-aminopyrrolidines to (*E*)-alkenyl sulfones in the presence of a catalytic amount of ytterbium trifluoromethanesulfonate [$Yb(OTf)_3$] yields β-hydrazino sulfones in moderate to good yields and with diastereoselectivities of up to 98%. The latter undergo reductive N–N bond cleavage with $BH_3 \cdot THF$ and, after *N*-protection with Boc_2O or benzyl bromide, afford *N*-protected β-amino sulfones with moderate to high enantiomeric excesses (*ee* = 42 to ≥96%) without racemization. Subsequent α-alkylation of the *N*,*N*-dibenzyl protected β-amino sulfones with various electrophiles yields α-alkyl-β-amino sulfones in excellent yields (88–97%) with high diastereomeric (*de* ≥96 to ≥98%) and enantiomeric purity (*ee* = 94 to ≥96%). The absolute configuration of the new stereogenic centre was determined by X-ray structural analysis and confirmed by NMR spectroscopy (NOE experiments). Possible reaction mechanisms for the conjugate addition and α-alkylation are presented.

Introduction

The variety of synthetic transformations which may be carried out using sulfones makes them a very valuable and versatile functional group for organic synthesis. Amongst these transformations are the easy α-substitution by electrophiles, and the ability of α,β-unsaturated sulfones to undergo efficient conjugate addition reactions with a wide range of carbon and heteroatom nucleophiles.[1] In particular, the aza-Michael addition is noteworthy as a widely used method for C−N bond formation.[2]

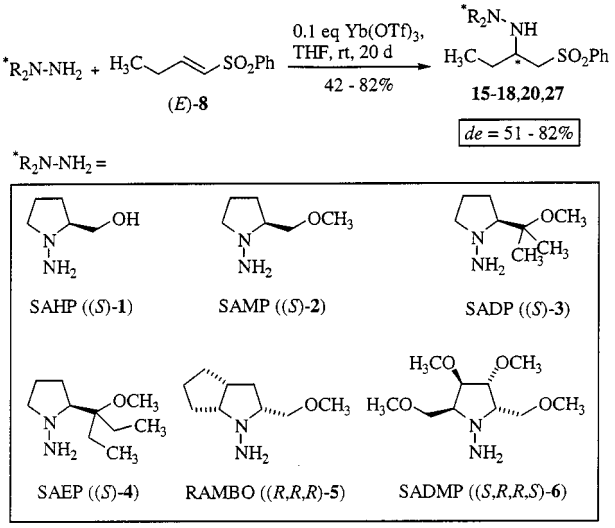
The aim of this project was to develop a stereoselective route to the title compounds **A** by the conjugate addition of an enantiopure ammonia equivalent **C** to the alkenyl sulfones **D** followed by reductive cleavage of the chiral auxiliary and α-alkylation of the resulting β-amino sulfones **B**.



Enantiopure β-amino sulfones play an important role in physiological processes.[3] In addition, they readily undergo electrophilic substitution in the α-position[4] and have, for instance, been used as intermediates in the synthesis of α-amino acids,[5,6] amino alcohols,[7] substituted uridines and adenosines,[8] alkaloids,[9] β-lactams,[10] and nitrogen heterocycles.[11,12] The ease of deprotonation allows sulfone anions to participate, for example, in cyclopropanations,[13] aldol-type reactions,[14] and α-alkylations[15] and demonstrates their importance in organic synthesis. As early as the 1960's Stirling and McDowell investigated the kinetics of the intermolecular addition of achiral amines to alkenyl sulfones.[16] Currently, there exist several procedures for intramolecular[7,9,17] and intermolecular[8,11,12,18] aza-Michael additions to alkenyl sulfones.

Results and Discussion

We now wish to report the intermolecular asymmetric aza-Michael addition of a variety of nitrogen nucleophiles **1–6** to (*E*)-1-butenyl phenyl sulfone **8** in the presence of catalytic amounts of ytterbium trifluoromethanesulfonate [$Yb(OTf)_3$][19] which result in the formation of β-hydrazino sulfones **15–18**, **20**, and **27** (Scheme 1, Table 1).



Scheme 1. Aza-Michael addition of various 1-aminopyrrolidines to alkenyl sulfone **8**

The nitrogen nucleophiles utilised in this study, (*S*)-1-amino-2-(hydroxymethyl)pyrrolidine[20] (SAHP, (*S*)-**1**), (*S*)-1-amino-2-(methoxymethyl)pyrrolidine[21] [SAMP, (*S*)-**2**], (*S*)-1-amino-2-(1′-methoxy-1′-methylethyl)pyrrolidine[22]

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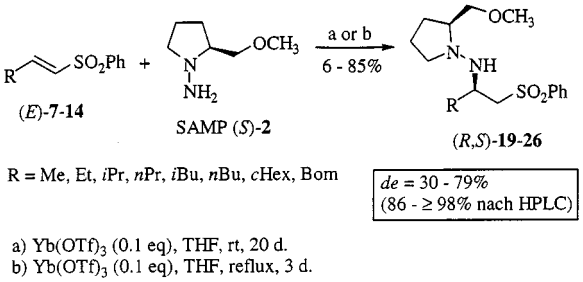
Table 1. Aza-Michael addition of various 1-aminopyrrolidines to alkenyl sulfone **8**

Nucleophile	no.	Product	Config.[a]	Yield [%]	*de* [%]
SAHP	(*S*)-**1**	**15**	(*R*,*S*)	57	51
SAMP	(*S*)-**2**	**20**	(*R*,*S*)	42	64 (≥ 96)[b]
SADP	(*S*)-**3**	**16**	(*R*,*S*)	82	68
SAEP	(*S*)-**4**	**17**	(*R*,*S*)	71	74
RAMBO	(*R*,*R*,*R*)-**5**	**27**	(*S*,*R*,*R*,*R*)	46	82 (≥ 96)[b]
SADMP	(*S*,*R*,*R*,*S*)-**6**	**18**	–[c]	46	71

[a] The absolute configuration of the new stereogenic centre of the major diastereomer was determined by X-ray structural analysis of crystalline (*R*,*S*)-**21** on the assumption that the addition mechanism is the same in all cases. – [b] In the cases of **20** and **27** both epimers were separated by HPLC. – [c] The absolute configuration has not been determined.

[SADP, (*S*)-**3**], (*S*)-1-amino-2-(1′-ethyl-1′-methoxypropyl)-pyrrolidine[22] [SAEP, (*S*)-**4**], (*R*,*R*,*R*)-2-amino-3-methoxymethyl-2-azabicyclo[3.3.0]octane[23] [RAMBO, (*R*,*R*,*R*)-**5**] and (2*S*,3*R*,4*R*,5*S*)-1-amino-3,4-dimethoxy-2,5-bis(methoxymethyl)pyrrolidine[24] [SADMP, (*S*,*R*,*R*,*S*)-**6**] (Scheme 1) are differently substituted 1-aminopyrrolidines, which constitute chiral equivalents of ammonia by reductive cleavage of the hydrazine N−N bond.



Scheme 2. Aza-Michael addition of SAMP [(*S*)-**2**] to alkenyl sulfones

As shown in Scheme 1, β-hydrazino sulfones were prepared in moderate to good yields and with moderate to high diastereoselectivities. In two cases the epimers were separated by preparative HPLC to yield diastereomerically pure Michael adducts (**20** and **27**). In order to demonstrate the general applicability of this method, several (*E*)-alkenyl sulfones (**7–14**) were synthesised by Horner olefination[25] and subsequently used in the conjugate addition with SAMP ((*S*)-**2**) as chiral nucleophile. As shown in Scheme 2, the β-hydrazino sulfones **19–26** were obtained in variable yields and with moderate to high diastereoselectivities[26] (*de* = 43 − ≥98%).

In almost every case, the epimers were separated by preparative HPLC to yield virtually diastereomerically pure Michael adducts (Table 2). It is noteworthy that the chemical yields based on the conversion are usually 90–95% and the isolated starting material can be reused after purification.

The absolute configuration of the newly formed stereogenic centres of the major diastereomers was deduced by an X-ray structural analysis of crystalline (*R*,*S*)-**20** (Figure 1)[27,28,29] on the assumption that the reaction pathway was the same in all cases.

Table 2. Aza-Michael addition of SAMP [(*S*)-**2**] to (*E*)-alkenyl sulfones **7–14**

Sulfone (*E*)	R[a]	Product (*R*,*S*)-	Method	Yield[b] [%]	*de*[c][d] [%]
7	Me	**19**	B	85	41 (≥ 98)
8	Et	**20**	A	42	64 (≥ 96)
8	Et	**20**	B	58	40 (≥ 96)
9	*i*Pr	**21**	A	25	79 (≥ 96)
9	*i*Pr	**21**	B	52	43 (≥ 96)
10	*n*Pr	**22**	A	29	68
10	*n*Pr	**22**	B	52	43
11	*i*Bu	**23**	A	34	54 (93)
11	*i*Bu	**23**	B	58	44 (93)
12	*n*Bu	**24**	A	31	52 (86)
12	*n*Bu	**24**	B	60	40 (86)
13	*c*Hex[e]	**25**	A	6	61 (≥ 96)
13	*c*Hex	**25**	B	35	50 (≥ 96)
14	Bom[f]	**26**	A	32	36 (≥ 96)
14	Bom	**26**	B	65	30 (≥ 96)

[a] 2-Aryl-substituted alkenyl sulfones are not suitable as Michael acceptors for this conjugate addition. – [b] Yield of isolated product. The yield based on the conversion is usually 90−95%. – [c] The *de* values were determined by ^{1}H- and ^{13}C-NMR spectroscopy. – [d] The numbers in parentheses refer to the *de* value after separation of the diastereomers by HPLC (SiO_2, diethyl ether/pentane). – [e] cHex = cyclohexyl. – [f] Bom = benzyloxymethyl.

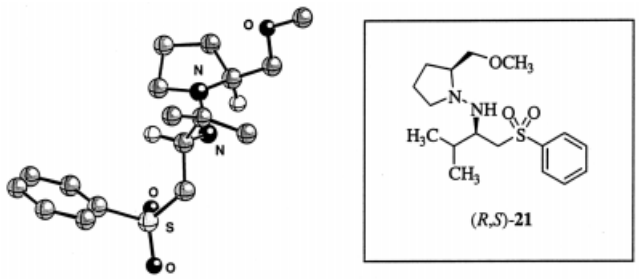


Figure 1. X-ray structure of the β-hydrazino sulfone (*R*,*S*)-**21**

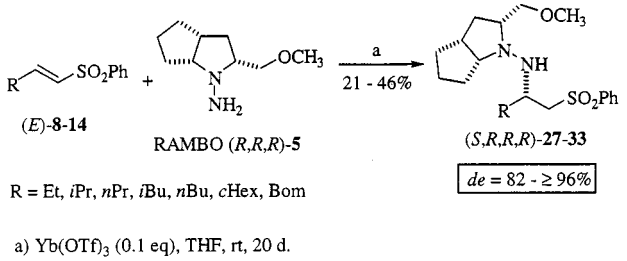
RAMBO [(*R*,*R*,*R*)-**5**], first synthesised as its enantiomer SAMBO by Martens et al.,[23] was also employed as a chiral nitrogen nucleophile in the conjugate addition to several alkenyl sulfones.[26] (*R*,*R*,*R*)-**5** may be obtained by a five-step reaction sequence[30] from the benzyl ester of (*R*,*R*,*R*)-2-azabicyclo[3.3.0]octane-3-carboxylic acid, a precursor to the angiotensin converting enzyme (ACE) inhibitor Ramipril® (from the former Hoechst AG[31]). With RAMBO as a nucleophile considerably higher diastereoselectivities were obtained than with SAMP. The separation of the diastereomers by HPLC was also feasible in these cases (Scheme 3, Table 3).

A possible mechanism for the conjugate addition of SAMP to (*E*)-alkenyl sulfones in the presence of $Yb(OTf)_3$ is shown in Figure 2. If we assume complexation of the oxophilic ytterbium by the oxygen atom of the methoxymethyl group of the incoming nitrogen nucleophile SAMP [(*S*)-**2**] and the oxygen atoms of the sulfone group, then there are two possible faces from which the addition can occur. Attack from the *Si*-face (mechanism A) would result in strong steric interactions between the nucleophile and the substituent R of the alkenyl sulfone, whereas the addition from the

Table 3. Aza-Michael Addition of RAMBO [(*R*,*R*,*R*)-**5**] to (*E*)-alkenyl sulfones **8**–**14**

Sulfone (*E*)-	R[a]	Product (*S*,*R*,*R*,*R*)-	Yield[b] [%]	*de*[c][d] [%]
8	Et	**27**	46	82 (≥ 96)
9	*i*Pr	**28**	21	96
10	*n*Pr	**29**	40	86 (≥ 96)
11	*i*Bu	**30**	32	90 (≥ 96)
12	*n*Bu	**31**	45	86 (≥ 96)
13	*c*Hex	**32**	29	94
14	Bom	**33**	29	90

[a] 2-Aryl-substituted alkenyl sulfones are not suitable as Michael acceptors for this conjugate addition. – [b] Yield of isolated product. The yield based on the conversion is usually 90–95%. – [c] The *de* values were determined by ^{1}H- and ^{13}C-NMR spectroscopy. – [d] The numbers in parentheses refer to the *de* value after separation of the diastereomers by HPLC (SiO_2, diethyl ether/pentane).



Scheme 3. Aza-Michael addition of RAMBO [(*R*,*R*,*R*)-**6**] to alkenyl sulfones

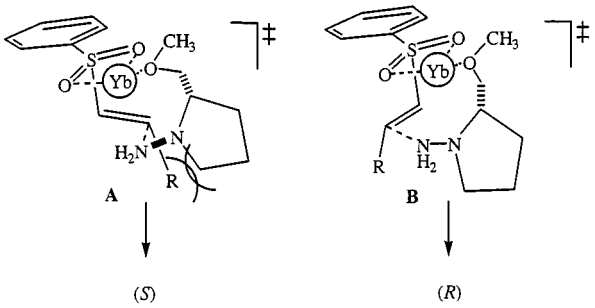
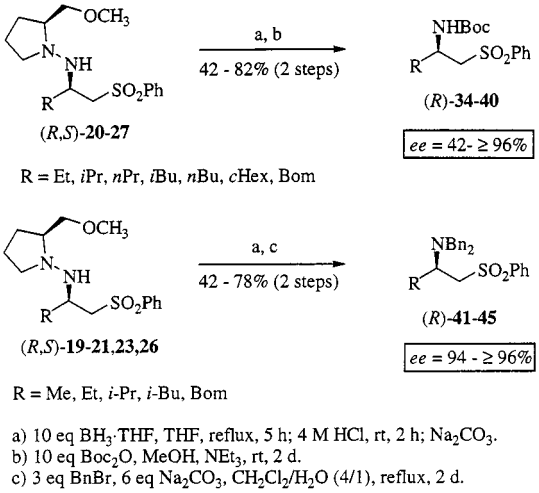


Figure 2. Postulated transition states for the conjugate addition of 1-aminopyrrolidines to alkenyl sulfones in the presence of $Yb(OTf)_3$

Re-face is sterically favoured and leads to the (*R*)-configuration at the newly formed stereogenic centre. The configuration of the stereogenic centre in 2-position of RAMBO [(*R*,*R*,*R*)-**5**] bearing the methoxymethyl group has the opposite configuration to SAMP, which explains the opposite stereochemical outcome of the conjugate addition of this nucleophile to (*E*)-alkenyl sulfones [(*S*) versus (*R*)]. The increase in the diastereoselectivities of the Michael adducts synthesised with RAMBO as nucleophile may be due to a stronger steric interaction of the bicyclic pyrrolidine ring with the R-group of the alkenyl sulfone.

Reductive cleavage of the chiral auxiliary from β-hydrazino sulfones (*R*,*S*)-**19**–**26** with $BH_3 \cdot THF$[32] in refluxing THF afforded β-amino sulfones without racemization as shown by the *de* value of their corresponding Mosher amides[33] (MTPA amides). Treatment with di-*tert*-butyldicarbonate (Boc_2O) or benzyl bromide gave the *N*-Boc (**34**–**40**) or *N*,*N*-dibenzyl (**41**–**45**) protected β-amino sulfones, respectively, in moderate to good yields without any prior purification of the crude amines (Scheme 4, Table 4). After N–N bond cleavage, the chiral auxiliary (*S*)-2-(methoxymethyl)pyrrolidine could be recovered as its *N*-Boc or *N*-benzyl derivative and – after deprotection, nitrosation, and reduction – reused in asymmetric synthesis.



Scheme 4. Asymmetric synthesis of *N*-protected β-amino sulfones

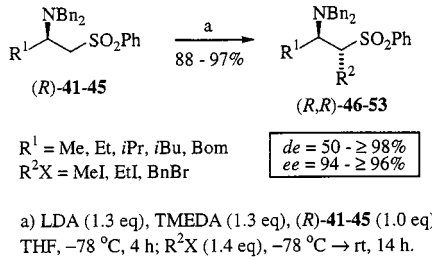
Table 4. Reductive N–N bond cleavage with $BH_3 \cdot THF$ followed by *N*-protection of the resulting β-amino sulfone

Hydrazine (*S*,*R*)-	R	Protecting group(s)	Product (*R*)-	Yield[a] [%]	*ee*[b] [%]
19	Me	Bn_2	**41**	40	≥ 96
20	Et	Boc	**34**	60	≥ 96
20	Et	Bn_2	**42**	78	≥ 96
21	*i*Pr	Boc	**35**	42	≥ 96
21	*i*Pr	Bn_2	**43**	43	≥ 96
22	*n*Pr	Boc	**36**	82	42
23	*i*Bu	Boc	**37**	73	92
23	*i*Bu	Bn_2	**44**	74	94
24	*n*Bu	Boc	**38**	54	84
25	*c*Hex	Boc	**39**	58	≥ 96
26	Bom	Boc	**40**	82	≥ 96
26	Bom	Bn_2	**45**	61	≥ 96

[a] Yield determined over two steps (N–N bond cleavage and *N*-protection). – [b] The *ee* values were determined from the *de* values of the corresponding Mosher amides by ^{1}H NMR spectroscopy.

Similarly, cleavage of the chiral auxiliary from β-hydrazino sulfones (*S*,*R*,*R*,*R*)-**27**–**33** proceeded without racemization.[34] By replacing SAMP with RAMBO both enantiomers are accessible.

An important extension of the outlined protocol is the α-alkylation of β-amino sulfones to generate two neighbouring stereogenic centres. In order to achieve this goal it was necessary to incorporate a protected β-amino sulfone that could selectively deprotonated at the α-carbon atom.



Scheme 5. Asymmetric synthesis of α-alkylated β-amino sulfones

Table 5. Asymmetric synthesis of α-alkylated β-amino sulfones (*R*,*R*)-**46**−**53**

Hydrazine (*R*)-	R^1	R^2X	Product (*R*,*R*)	Yield [%]	*de*[a][b] [%]	*ee*[c] [%]
41	Me	MeI	**46**	91	70 (≥ 98)	≥ 96
42	Et	MeI	**47**	95	>97	≥ 96
42	Et	EtI	**48**	97	68 (> 97)	≥ 96
42	Et	BnBr	**49**	88	64 (> 97)	≥ 96
43	*i*Pr	MeI	**50**	93	50 (≥ 96)	≥ 96
44	*i*Bu	MeI	**51**	93	90 (≥ 96)	94
44	*i*Bu	EtI	**52**	88	50 (≥ 96)	94
45	Bom	MeI	**53**	97	68 (≥ 96)	≥ 96

[a] Determined by GC analysis (**46**) and NMR spectroscopy (**47**−**53**). − [b] The numbers in parentheses refer to the *de* value after isolation of the major diastereomer by recrystallization (**46**,**48**,**49**,**51**,**52**), HPLC (**50**), or column chromatography (**53**). − [c] Based on the *de* values of the corresponding Mosher amides (NMR spectroscopy) of the free amines assuming no overall racemization under subsequent reaction conditions as confirmed by chiral HPLC of compounds **47** and **49** (Chiralpak OD), **51** (Chiralcel OD2), and **52** and **53** ((*S*,*S*)-Whelk 01).

Therefore, *N*,*N*-dibenzyl be protected β-amino sulfones (*R*)-**41**−**45** were metallated with LDA in the presence of TMEDA and alkylated with various electrophiles (Scheme 5, Table 5). Products (*R*,*R*)-**46**−**53** were obtained in excellent yields (88−97%), with medium to high diastereomeric and high enantiomeric excesses (*de* = 50 to >97%, *ee* = 94 to ≥96%).[35]

The major diastereomer of each of the products was obtained practically pure after isolation of the main epimer by recrystallization (**46**,**48**,**49**,**51**,**52**), HPLC (**50**), or column chromatography (**53**). The relative and absolute configuration of the newly formed stereogenic centres of the major diastereomers is based on the X-ray structural analysis of crystalline (*R*,*R*)-**47** (Figure 3). [27,28,29] This result was confirmed by NOE-analysis of compounds (*R*,*R*)-**47** and (*R*,*R*)-**53** (Figure 4).

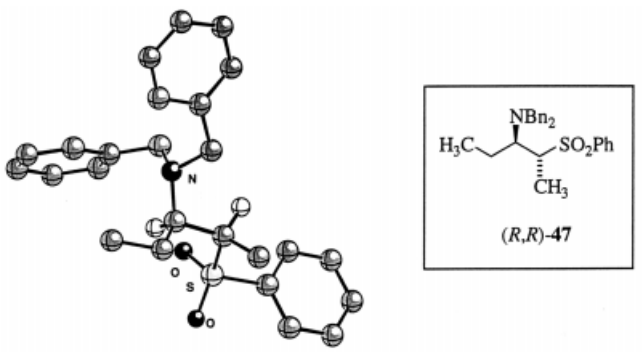


Figure 3. X-ray structure of the α-alkylated β-amino sulfone (*R*,*R*)-**47**

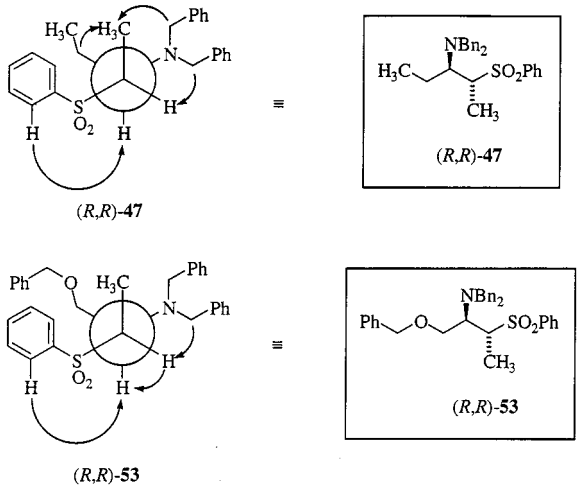


Figure 4. NOE analyses of compounds (*R*,*R*)-**47** and (*R*,*R*)-**53**

A possible transition state in the α-alkylation of *N*,*N*-dibenzyl protected β-amino sulfones is presented in Figure 5. If we assume a planar configuration of the carbanion after deprotonation with LDA and a coordinative bond between the lithium cation and the oxygen atoms of the sulfone group and the nitrogen atom of the dibenzylamino group, there are two possible faces from which the electrophile (E^+) may approach. Owing to steric interactions between the incoming electrophile and the substituent R, the *Si*-face is hindered and the addition from the *Re*-face is favoured and will therefore lead to the (*R*)-configuration at the newly formed stereogenic centre. The stereochemical outcome of the alkylation is consistent with the postulated mechanism.

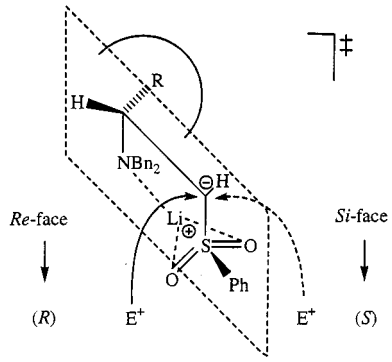


Figure 5. Postulated transition states for the α-alkylation of *N*,*N*-dibenzyl protected β-amino sulfones

Conclusion

In summary, we have synthesised a variety of virtually diastereo- and enantiopure α-alkylated β-amino sulfones. The described asymmetric aza-Michael addition followed by reductive N−N bond cleavage and subsequent α-alkylation opens up an efficient approach to biologically in-

teresting and synthetically valuable *N*-protected α-alkylated β-amino sulfones which can act as intermediates for the creation of acyclic and cyclic carbon frameworks with a nitrogen-bearing stereogenic centre. Application to the asymmetric synthesis of bioactive compounds can be envisaged.

Experimental Section

General: All solvents were dried and purified prior to use. – All reactions were carried out under an atmosphere of dry argon. – Column Chromatography: Merck silica gel 60, 0.040–0.063 mm (230–400 mesh). – Optical rotation values: Perkin–Elmer P 241; solvents Merck Uvasol quality. – IR: Perkin–Elmer FT/IR 1750. – NMR: Varian VXR 300, Gemini 300, Inova 400 and Unity 500, TMS as internal standard. – MS: Finnigan MAT 212 and Finnigan SSQ 7000 (70 eV). – Microanalyses: Elementar vario EL. High-resolution MS: Finnigan MAT, MAT 95. – Melting points (uncorrected): Büchi 510. – THF was dried by distillation from K/benzophenone under Ar. SAHP,[20] SAMP,[21] SADP,[22] SAEP,[22] RAMBO,[23] and SADMP[24] were prepared according to the published procedures.

General Procedure for the Synthesis of the β-Hydrazino Sulfones (15–33, GP 1): In a typical experiment the (*E*)-1-alkenyl sulfone **7–14** (20 mmol) was added dropwise to a solution of ytterbium trifluoromethanesulfonate [$Yb(OTf)_3$] (0.62 g, 2 mmol) in THF (40 mL) under an atmosphere of argon at room temperature and the mixture stirred for 15 min. The corresponding nitrogen nucleophile **1–6** (30 mmol) was added dropwise to the colourless to light yellow solution, and the mixture then stirred for 20 d at room temperature (method A) or heated 3 d under reflux (method B). The solution was then poured into pentane/Et_2O (2:1, 400 mL) and filtered through Celite®. The solvent was evaporated under reduced pressure, and the residue purified by column chromatography or – to provide the major diastereomer – by HPLC (SiO_2, pentane/Et_2O mixtures). The air-sensitive products were isolated as colourless oils. Compound (2*R*/2′*S*)-**21** was recrystallized from CH_2Cl_2/*n*-hexane in order to determine the absolute configuration of the new stereogenic centre.

(2*R*,2′*S*)-2-[(2′-(Hydroxymethyl)pyrrolidin-1′-yl)amino]-butyl Phenyl Sulfone (15): Prepared by method GP 1 from (*E*)-1-butenyl phenyl sulfone **8** and SAHP (*S*)-**1** in the presence of $Yb(OTf)_3$ in THF. The β-hydrazino sulfone **15** was obtained as a colourless oil (3.56 g, 57% yield; method A, *de* = 51%). – $[\alpha]_D^{20}$ = −93.5 (*c* = 0.93, $CHCl_3$). – IR ($CHCl_3$): $\tilde{\nu}$ = 3384 (m), 3065 (w), 2965 (s), 2876 (s), 1586 (w), 1480 (m), 1461 (s), 1448 (s), 1399 (m), 1385 (m), 1305 (s), 1239 (m), 1199 (m), 1182 (m), 1148 (s), 1086 (s), 1039 (s), 1001 (m), 805, (w), 753 (m), 720 (m), 690 (s), 667 (w), 597 (s), 569 (s), 536 (s) cm^{-1}. – ^1H NMR (300 MHz, C_6D_6): δ = 0.62 (t, ^3J = 7.42 Hz, 3 H, CH_3CH$_2$), 1.09–1.92 (m, 7 H, CH$_3$CH_2, CHCH$_2$CH_2CH$_2$, C*H*HN), 2.07–3.10 (m, 4 H, CH*H*N, OCH$_2$C*H*N, CH_2SO$_2$Ph), 3.22–4.60 (m, 5 H, CH$_2$O, C*H*NH, NH, OH), 6.96–7.13 (m, 3 H, *m*-, *p*-Ar-H), 7.75–7.92 (m, 2 H, *o*-Ar-H). – ^{13}C NMR (75 MHz, C_6D_6): δ = 9.05 (*C*H$_3$CH$_2$), 21.03 (*C*H$_2$CH$_2$N), 24.67 (CH$_3$*C*H$_2$), 26.03 (*C*H$_2$CHCH$_2$OH), 54.17 (CHNH), 55.96 (CH$_2$N), 58.04 (CH$_2$S), 66.38 (*C*HCH$_2$OH), 66.48 (CH$_2$OH), 128.16, 129.31, 133.48 (Ar-C), 140.43 (*ipso*-Ar-C). – MS (EI, 70 eV): *m*/*z* (%) = 312 (11) [M^+], 282 (17), 281 (100), 266 (9), 143 (8), 125 (6), 115 (51), 111 (8), 100 (3), 85 (34), 84 (11), 77 (25), 70 (25), 68 (10), 57 (8), 56 (6), 55 (11). – $C_{15}H_{24}O_3N_2S$ (312.332): calcd. C 57.67, H 7.74, N 8.97; found: C 57.80, H 7.76, N 8.94.

(2*R*,2′*S*)-2-[(2′-(1′′-Methoxy-1′′-methylethyl)pyrrolidin-1′-yl)-amino]butyl Phenyl Sulfone (16): Prepared by method GP 1 from (*E*)-1-butenyl phenyl sulfone **8** and SADP (*S*)-**3** in the presence of $Yb(OTf)_3$ in THF. The β-hydrazino sulfone **16** was obtained as a colourless oil (5.81 g, 82% yield; method A, *de* = 68%). – $[\alpha]_D^{20}$ = −13.9 (*c* = 0.80, $CHCl_3$). – IR ($CHCl_3$): $\tilde{\nu}$ = 3373 (w), 3064 (w), 2973 (s), 2937 (s), 2880 (m), 2828 (m), 1715 (w), 1676 (w), 1586 (w), 1462 (s), 1448 (s), 1382 (m), 1365 (m), 1306 (s), 1237 (m), 1148 (s), 1086 (s), 999 (w), 934 (w), 875 (w), 804 (w), 752 (s), 720 (m), 690 (s) cm^{-1}. – ^1H NMR (300 MHz, C_6D_6): δ = 0.71 (t, ^3J = 7.39 Hz, 3 H, CH_3CH$_2$), 1.05, 1.18 (2 s, 6 H, (CH_3)$_2$COCH$_3$), 1.21–2.09 (m, 6 H, CH$_3$CH_2, CHCH_2CH_2CH$_2$), 2.43–2.54 (m, 1 H, C*H*HN), 2.70–2.78 (dd, $^3J_1$ = 9.23 Hz, $^3J_2$ = 6.21 Hz, 1 H, (CH$_3$)$_2$CC*H*N), 2.92 (dd, ^2J = 14.27 Hz, ^3J = 4.20 Hz, 1 H, C*H*HSO$_2$Ph), 3.05 (s, 3 H, OCH$_3$), 3.06–3.17 (m, 2 H, CH*H*SO$_2$Ph, CH*H*N), 3.31–3.47 (m, 2 H, C*H*NH, NH), 6.88–7.01 (m, 3 H, *m*-, *p*-Ar-H), 7.77–7.91 (m, 2 H, *o*-Ar-H). – ^{13}C NMR (75 MHz, C_6D_6): δ = 9.54 (*C*H$_3$CH$_2$), 21.55, 22.14 [(*C*H$_3$)$_2$C], 22.90, 25.47, 26.12 (CH$_3$*C*H$_2$, *C*H$_2$*C*H$_2$CH), 48.89 (OCH$_3$), 55.25 (CHNH), 58.45, 58.79 (CH$_2$S, CH$_2$N), 73.95 (C*C*HN), 77.60 (*C*OCH$_3$), 128.31, 129.16, 133.10 (Ar-C), 141.26 (*ipso*-Ar-C). – MS (EI, 70 eV): *m*/*z* (%) = 354 (0.4) [M^+], 336 (12), 318 (7), 295 (15), 281 (15), 279 (38), 153 (10), 143 (23), 141 (9), 139 (8), 138 (6), 137 (9), 126 (6), 125 (13), 123 (5), 122(14), 121 (8), 111 (13), 110 (8), 109 (6), 99 (18), 97 (6), 94 (5), 85 (6), 84 (7), 83 (17), 82 (5), 81 (6), 79 (5), 78 (7), 77 (37), 74 (5), 73 (100), 71 (6), 70 (14), 69 (16), 68 (7), 67 (6), 59 (5), 57 (8), 56 (10), 55 (36), 54 (5), 53 (5), 51 (11). – $C_{18}H_{30}N_2O_3S$ (354.514): calcd. C 60.98, H 8.53, N 7.90; found: C 61.19, H 8.67, N 7.89.

(2*R*,2′*S*)-2-[(2′-(1′′-Ethyl-1′′-methoxypropyl)pyrrolidin-1′-yl)-amino]butyl Phenyl Sulfone (17): Prepared by method GP 1 from (*E*)-1-butenyl phenyl sulfone **8** and SAEP (*S*)-**4** in the presence of $Yb(OTf)_3$ in THF.

The β-hydrazino sulfone **17** was obtained as a colourless oil (5.43 g, 71% yield; method A, *de* = 74%). – $[\alpha]_D^{20}$ = −8.7 (*c* = 1.02, $CHCl_3$). – IR ($CHCl_3$): $\tilde{\nu}$ = 3389 (w), 3064 (w), 2969 (s), 2938 (s), 2879 (s), 2827 (m), 1711 (w), 1677 (w), 1626 (w), 1586 (w), 1460 (s), 1448 (s), 1381 (m), 1350 (m), 1307 (s), 1237 (m), 1148 (s), 1086 (s), 1026 (m), 999 (w), 922 (m), 881 (w), 835(w), 807 (w), 751 (s), 718 (m), 690 (s), 598 (s) cm^{-1}. – ^1H NMR (300 MHz, C_6D_6): δ = 0.68 (t, ^3J = 7.39 Hz, 3 H, CH_3CH$_2$CH), 0.79–2.02 (m, 17 H, (CH_3CH_2)$_2$C, CHCH_2CH_2C*H*H, CH$_3$CH_2CH), 2.44–3.43 (m, 9 H, CHCH$_2$CH$_2$CH*H*, CH$_3$O, CHNH, OCCHN, CH_2SO$_2$Ph), 6.92–7.03 (m, 3 H, *m*-, *p*-Ar-H), 7.76–7.92 (m, 2 H, *o*-Ar-H). – ^{13}C NMR (75 MHz, C_6D_6): δ = 8.58, 8.88, 9.50 (3 × *C*H$_3$CH$_2$), 23.19, 24.79, 25.22, 25.68, 27.26 (3 × CH$_3$*C*H$_2$, *C*H$_2$*C*H$_2$CHN), 49.84 (CHNH), 55.15 (CO*C*H$_3$), 57.86, 58.74 (CH$_2$S, CH$_2$N), 72.43 (*C*HCCO), 79.93 (*C*OCH$_3$), 127.86, 129.01, 133.18 (Ar-C), 141.04 (*ipso*-Ar-C). – MS (EI, 70 eV): *m*/*z* (%) = 382 (1) [M^+], 283 (6), 282 (18), 281 (100), 279 (15), 266 (10), 143 (8), 125 (5), 111 (5), 99 (18), 97 (6), 94 (5), 85 (8), 84 (8), 83 (5), 77 (11), 70 (12), 69 (8), 68 (5), 59 (7), 57 (6), 56 (5), 55 (13), 45 (5). – $C_{20}H_{34}N_2O_3S$ (382.568): calcd. C 62.79, H 8.96, N 7.32; found: C 63.06, H 8.55, N 6.82.

2-[(3′,4′-Dimethoxy-2′,5′-bis(methoxymethyl)pyrrolidin-1′-yl)-amino]butyl Phenyl Sulfone (18): Prepared by method GP 1 from (*E*)-1-butenyl phenyl sulfone **8** and SADMP (*S*,*R*,*R*,*S*)-**6** in the presence of $Yb(OTf)_3$ in THF. The β-hydrazino sulfone **18** was obtained as a colourless oil (3.96 g, 46% yield; method A, *de* = 71%). – $[\alpha]_D^{20}$ = −8.7 (*c* = 1.02, $CHCl_3$). – IR ($CHCl_3$): $\tilde{\nu}$ = 3284 (w), 3064 (w), 2978 (s), 2928 (s), 2894 (s), 2827 (s), 1586 (w), 1460 (s), 1448 (s), 1384 (m), 1364 (m), 1306 (s), 1236 (m), 1197 (s), 1149 (s), 1107 (s), 1026 (m), 999 (m), 955 (m), 923 (m), 874 (w), 851 (w),

806 (w), 755 (s), 720 (m), 690 (s), 667 (w), 600 (m), 574 (m), 532 (m) cm^{-1}. – ^1H NMR (500 MHz, C_6D_6): δ = 0.75 (t, ^3J = 7.38 Hz, 3 H, CH_3CH$_2$), 1.45–1.63 (m, 1 H, CH$_3$CHH), 1.71–1.88 (m, 1 H, CH$_3$CHH), 2.91 (dd, ^2J = 13.93 Hz, ^3J = 4.70 Hz, 1 H, CHHSO$_2$Ph), 3.08–3.29 (m, 16 H, CHHSO$_2$Ph, 4 × CH$_3$O, CHNH, 2 × CHN), 3.44–3.79 (m, 6 H, CHOCH$_3$, CH_2OCH$_3$), 3.87 (br. s, 1 H, NH), 6.95–7.08 (m, 3 H, *m*-, *p*-Ar-H), 7.79–7.83 (m, 2 H, *o*-Ar-H). – ^{13}C NMR (125 MHz, C_6D_6): δ = 9.67 (*C*H$_3$CH$_2$), 25.19 (CH$_3$*C*H$_2$), 53.58 (CHNH), 58.45, 58.70, (4 × OCH$_3$), 58.84 (CHS), 61.69 (2 × CH*C*HN), 69.22 (2 × *C*H$_2$OCH$_3$), 84.79 (2 × *C*HCHN), 129.22, 133.16 (Ar-C), 141.38 (*ipso*-Ar-C). – MS (EI, 70 eV): *m*/*z* (%) = 431 (5), 430 (20) [M^+], 387 (7), 386 (21), 385 (100), 233 (32), 143 (10), 140 (6), 125 (9), 110 (7), 101 (23), 85 (5), 77 (17), 75 (5), 71 (22), 55 (11), 45 (17). – $C_{20}H_{34}N_2O_6S$ (430.566): calcd. C 55.79, H 7.96, N 6.51; found: C 55.72, H 8.14, N 6.34.

(2*R*,2′*S*)-2-[(2′-(Methoxymethyl)pyrrolidin-1′-yl)amino]propyl Phenyl Sulfone (19): Prepared by method GP 1 from (*E*)-1-propenyl phenyl sulfone **7** and SAMP (*S*)-**2** in the presence of Yb(OTf)$_3$ in THF. The β-hydrazino sulfone **19** was obtained as a colourless oil [5.31 g, 85% yield; method B, *de* = 41% (≥ 98% after HPLC)]. – Major diastereoisomer: $[\alpha]_D^{20}$ = –61.1 (*c* = 2.66, $CHCl_3$) – IR ($CHCl_3$): $\tilde{\nu}$ = 3063 (w), 2969 (m), 2927 (m), 2876 (m), 2826 (m), 1585 (w), 1479 (m), 1447 (m), 1396 (m), 1368 (m), 1305 (s), 1253 (m), 1197 (m), 1147 (s), 1087 (s), 1025 (w), 999 (w), 958 (w), 920 (w), 897 (m), 843 (m), 752 (m), 720 (m), 690 (s), 600 (m), 574 (m), 535 (s) cm^{-1}. – ^1H NMR (300 MHz, C_6D_6): δ = 1.07 (d, ^3J = 6.38 Hz, 3 H, CH_3CH), 1.33–1.59 (m, 4 H, CHCH_2CH_2CH$_2$), 2.17 (q, ^3J = 8.73 Hz, 1 H, CHCH$_2$CH$_2$CHH), 2.61 (m, 1 H, CHCH$_2$CH$_2$CH$_2$), 2.76 (dd, ^2J = 14.10 Hz, ^3J = 4.37 Hz, 1 H, CHHSO$_2$Ph), 3.09–3.54 (m, 8 H, CHCH$_2$CH$_2$CHH, CHHSO$_2$Ph, CH$_2$OCH$_3$, CHNH), 6.90–7.07 (m, 3 H, *m*-, *p*-Ar-H), 7.78–7.81 (m, 2 H, *o*-Ar-H). – ^{13}C NMR (125 MHz, C_6D_6): δ = 20.28 (*C*H$_3$CH), 21.33, 27.02 (*C*H$_2$*C*H$_2$CHN), 49.29 (CHNH), 56.91, 61.11 (CH$_2$S, CH$_2$N), 58.77 (OCH$_3$), 65.97 (CHN), 75.72 (CH$_2$O), 128.10, 129.16, 133.16 (Ar-C), 141.03 (*ipso*-Ar-C). – MS (EI, 70 eV): *m*/*z* (%) = 312 (11) [M^+], 268 (17), 267 (100), 169 (7), 141 (9), 129 (32), 125 (43), 123 (13), 97 (15), 94 (11), 85 (25), 84 (16), 77 (19), 71 (18), 70 (18), 68 (14), 57 (10), 56 (19), 45 (18) cm^{-1}. – $C_{15}H_{24}N_2O_3S$ (312.433): calcd. C 57.67, H 7.82, N 8.97; found: C 57.77, H 7.86, N 9.08.

(2*R*,2′*S*)-2-[(2′-(Methoxymethyl)pyrrolidin-1′-yl)amino]-butyl Phenyl Sulfone (20): Prepared by method GP 1 from (*E*)-1-butenyl phenyl sulfone **8** and SAMP (*S*)-**2** in the presence of Yb(OTf)$_3$ in THF. The β-hydrazino sulfone **20** was obtained as a colourless oil (2.74 g, 42% yield; method A, *de* = 64% (≥ 96% after HPLC) or 3.79 g, 58% yield; method B, *de* = 40% (≥ 96% after HPLC)). – Major diastereoisomer: $[\alpha]_D^{20}$ = –109.5 (*c* = 1.00, $CHCl_3$) – IR ($CHCl_3$): $\tilde{\nu}$ = 3063 (w), 2965 (m), 2930 (m), 2876 (m), 2827 (m), 1585 (w), 1459 (m), 1447 (s), 1384 (w), 1346 (w), 1305 (s), 1239 (w), 1193 (m), 1148 (s), 1086 (s), 1025 (w), 999 (w), 972 (w), 921 (w), 876 (w), 804 (w), 751 (m), 719 (w), 690 (m), 597 (m), 570 (m), 533 (m) cm^{-1}. – ^1H NMR (500 MHz, C_6D_6): δ = 0.67 (t, ^3J = 7.48 Hz, 3 H, CH_3CH$_2$), 1.42–1.60 (m, 4 H, CHCH$_2$CH_2CH$_2$, CH$_3$CHH, CHCHHCH$_2$CH$_2$), 1.65–1.74 (m, 1 H, CH$_3$CHH), 1.76–1.83 (m, 1 H, CHCHHCH$_2$CH$_2$), 2.19–2.24 (m, 1 H, CHHN), 2.62 (m, 1 H, OCH$_2$CHN), 2.92 (dd, ^2J = 14.34 Hz, ^3J = 3.05 Hz, 1 H, CHHSO$_2$Ph), 3.05 (dd, ^2J = 14.34 Hz, ^3J = 8.24 Hz, 1 H, CHHSO$_2$Ph), 3.09 (br. s, 1 H, NH), 3.18 (s, 3 H, CH$_3$O), 3.23–3.29 (m, 2 H, CHHN, CHHO), 3.34 (m, 1 H, CHNH), 3.57 (dd, ^2J = 9.16 Hz, ^3J = 3.97 Hz, 1 H, CHHO), 6.97–701 (m, 2 H, *m*-Ar-H), 7.01–7.05 (m, 1 H, *p*-Ar-H), 7.79–7.81 (m, 2 H, *o*-Ar-H). – ^{13}C NMR (125 MHz, C_6D_6): δ = 9.01 (*C*H$_3$CH$_2$), 21.30 (*C*H$_2$CH$_2$N), 25.97 (CH$_3$*C*H$_2$), 27.00 (*C*H$_2$CHN), 54.72 (CHNH), 56.62 (CH$_2$N), 58.54 (CH$_2$S), 58.78 (OCH$_3$), 65.89 (CHN), 75.61 (CH$_2$O), 128.11, 129.22, 133.26 (Ar-C), 140.82 (*ipso*-Ar-C). – MS (EI, 70 eV): *m*/*z* (%) = 326 (11) [M^+], 283 (8), 282 (16), 281 (100), 266 (5), 143 (18), 141 (2), 139 (7), 129 (38), 111 (8), 97 (10), 85 (15), 84 (23), 83 (10), 77 (13), 71 (14), 70 (39), 69 (8), 68 (21), 56 (10), 55 (15). – $C_{16}H_{26}N_2O_3S$ (326.460): calcd. C 58.87, H 8.03, N 8.58; found: C 58.42, H 7.62, N 8.80.

(2*R*,2′*S*)-2-[(2′-(Methoxymethyl)pyrrolidin-1′-yl)amino]-3-methylbutyl Phenyl Sulfone (21): Prepared by method GP 1 from (*E*)-3-methyl-1-butenyl phenyl sulfone **9** and SAMP (*S*)-**2** in the presence of Yb(OTf)$_3$ in THF. The β-hydrazino sulfone **21** was obtained as a colourless solid [1.70 g, 25% yield; method A, *de* = 79% (≥ 96% after HPLC) or 3.54 g, 52% yield; method B, *de* = 43% (≥ 96% after HPLC)]. **21** was obtained in crystalline form after recrystallization of the major diastereoisomer from CH_2Cl_2/*n*-hexane. – M.p. 63 °C. – $[\alpha]_D^{20}$ = –161.5 (*c* = 0.27, $CHCl_3$) – IR ($CHCl_3$): $\tilde{\nu}$ = 3063 (w), 2960 (s), 2930 (s), 2874 (s), 2825 (s), 1586 (w), 1461 (s), 1447 (s), 1389 (s), 1371 (m), 1305 (s), 1241 (m), 1194 (s), 1145 (s), 1087 (s), 1025 (w), 999 (m), 967 (m), 919 (m), 877 (m), 854 (m), 788 (m), 752 (s), 718 (m), 690 (s), 599 (s), 582 (s), 545 (m) cm^{-1}. – ^1H NMR (300 MHz, C_6D_6): δ = 0.54 [d, ^3J = 7.05 Hz, 3 H, CH_3(CH$_3$)CH], 0.73 [d, ^3J = 6.72 Hz, 3 H, CH$_3$(CH_3)CH], 1.42–1.91 (m, 4 H, CHCH_2CH_2CH$_2$), 2.25 (q, ^3J = 8.73 Hz, 1 H, CHHNH), 2.41 [sepd, $^3J_1$ = 2.86 Hz, $^3J_2$ = 7.05 Hz, 1 H, (CH$_3$)$_2$CH], 2.69–2.74 (m, 1 H, OCH$_2$CHN), 2.78 (dd, ^2J = 14.44 Hz, ^3J = 9.40 Hz, 1 H, CHHSO$_2$Ph), 2.89 (dd, ^2J = 14.44 Hz, ^3J = 2.02 Hz, 1 H, CHHSO$_2$Ph), 3.21 (s, 3 H, CH$_3$O), 3.22–3.44 (m, 1 H, CHNH), 3.65 (dd, ^2J = 9.06 Hz, ^3J = 3.70 Hz, 1 H, CHHO), 6.88–7.01 (m, 3 H, *m*-, *p*-Ar-H), 7.75–7.82 (m, 2 H, *o*-Ar-H). – ^{13}C NMR (75 MHz, C_6D_6): δ = 15.19, 18.53 (2 × CH$_3$), 21.28, 26.97 (*C*H$_2$*C*H$_2$CHN), 27.94 [(CH$_3$)$_2$CH], 56.97, 56.03 (CH$_2$S, CH$_2$N), 58.02, 58.83 (CHNH, OCH$_3$), 65.74 (CHN), 75.56 (CH$_2$O), 128.13, 129.19, 133.25 (Ar-C), 140.48 (*ipso*-Ar-C). – MS (EI, 70 eV): *m*/*z* (%) = 340 (9) [M^+], 297 (6), 296 (17), 295 (100), 294 (2), 155 (10), 143 (5), 130 (2), 129 (26), 125 (2), 111 (8), 97 (6), 85 (5), 84 (6), 71 (5), 70 (9), 69 (5), 68 (4), 55 (3), 45 (4). – $C_{17}H_{28}N_2O_3S$ (340.487): calcd. C 59.97, H 8.29, N 8.23; found: C 60.32, H 8.59, N 8.30.

(2*R*,2′*S*)-2-[(2′-(Methoxymethyl)pyrrolidin-1′-yl)amino]-pentyl Phenyl Sulfone (22): Prepared by method GP 1 from (*E*)-1-pentenyl phenyl sulfone **10** and SAMP (*S*)-**2** in the presence of Yb(OTf)$_3$ in THF. The β-hydrazino sulfone **22** was obtained as a colourless oil (1.97 g, 29% yield; method A, *de* = 68% or 3.54 g, 52% yield; method B, *de* = 43%). – IR ($CHCl_3$): $\tilde{\nu}$ = 3063 (w), 2959 (s), 2930 (s), 2873 (s), 2826 (s), 1723 (w), 1586 (w), 1448 (s), 1383 (m), 1306 (s), 1241 (m), 1186 (m), 1147 (s), 1087 (s), 1000 (w), 967 (m), 921 (m), 860 (m), 791 (m), 753 (s), 721 (m), 690 (s), 601 (m), 574 (s), 535 (s) cm^{-1}. – ^1H NMR (300 MHz, C_6D_6): δ = 0.76–1.84 (m, 11 H, CH$_3$CH$_2$CH$_2$, CHCH_2CH_2CH$_2$), 2.21 (q, *J* = 8.72 Hz, 1 H, CHHN), 2.59–2.7 (m, 1 H, OCH$_2$CHN), 2.90 (dd, ^2J = 11.43 Hz, ^3J = 3.35 Hz, 1 H, CHHSO$_2$Ph), 3.04 (dd, ^2J = 11.43 Hz, ^3J = 6.22 Hz, 1 H, CHHSO$_2$Ph), 3.18 (s, 3 H, CH$_3$O), 3.20–3.41 (m, 3 H, CHHO, CHHN, CHNH), 3.58 (dd, ^2J = 8.73 Hz, ^3J = 4.03 Hz, 1 H, CHHO), 6.89–7.02 (m, 3 H, *m*-, *p*-Ar-H), 7.77–7.84 (m, 2 H, *o*-Ar-H). – ^{13}C NMR (125 MHz, C_6D_6): δ = 14.23 (*C*H$_3$CH$_2$), 18.26 (CH$_3$*C*H$_2$), 21.31, 26.96 (*C*H$_2$*C*H$_2$CHN), 35.57 (CH$_3$CH$_2$*C*H$_2$), 53.48 (CHNH), 56.71, 59.02 (CH$_2$S, CH$_2$N), 56.96 (CHN), 58.77 (OCH$_3$), 75.52 (CH$_2$O), 128.36, 129.17, 133.18 (Ar-C), 140.90 (*ipso*-Ar-C). – MS (EI, 70 eV): *m*/*z* (%) = 340 (8) [M^+], 297 (7), 296 (19), 295 (100), 143

(9), 129 (31), 125 (7), 111 (6), 97 (8), 85 (7), 84 (11), 83 (5), 77 (15), 71 (11), 70 (13), 69 (7), 68 (6), 55 (8), 45 (8). – $C_{17}H_{28}N_2O_3S$ (340.487): calcd. C 59.97, H 8.29, N 8.23; found: C 59.84, H 8.42, N 8.23.

(2*R*,2′*S*)-2-[(2′-(Methoxymethyl)pyrrolidin-1′-yl)amino]-4-methylpentyl Phenyl Sulfone (23): Prepared by method GP 1 from (*E*)-4-methyl-1-pentenyl phenyl sulfone **11** and SAMP (*S*)-**2** in the presence of $Yb(OTf)_3$ in THF. The β-hydrazino sulfone **23** was obtained as a colourless oil [2.41 g, 34% yield; method A, *de* = 54% (93% after HPLC) or 4.11 g, 58% yield; method B, *de* = 44% (93% after HPLC)]. – Major diastereoisomer: $[\alpha]_D^{20}$ = –99.2 (*c* = 1.09, $CHCl_3$) – IR ($CHCl_3$): $\tilde{\nu}$ = 3064 (m), 2956 (s), 2930 (s), 2872 (s), 2827 (s), 1586 (w), 1467 (s), 1448 (s), 1386 (m), 1367 (m), 1306 (s), 1261 (m), 1234 (m), 1183 (s), 1147 (s), 1099 (s), 1087 (s), 1025 (m), 999 (m), 957 (m), 920 (m), 854 (m), 784 (m), 752 (s), 721 (m), 690 (s), 602 (s), 575 (s), 535 (s) cm^{-1}. – ^1H NMR (300 MHz, C_6D_6): δ = 0.71 [d, ^3J = 6.38 Hz, 3 H, CH_3(CH$_3$)CH], 0.86 [d, ^3J = 6.38 Hz, 3 H, CH$_3$(CH_3)CH], 1.20–1.85 (m, 7 H, (CH$_3$)$_2$CHCH$_2$, CHCH_2CH_2CH$_2$), 2.25 (q, *J* = 8.40 Hz, 1 H, C*H*HN), 2.60 (m, 1 H, OCH$_2$C*H*), 2.95 (dd, ^2J = 14.44 Hz, ^3J = 3.36 Hz, 1 H, C*H*HSO$_2$Ph), 3.12 (dd, ^2J = 14.43 Hz, ^3J = 6.71 Hz, 1 H, CH*H*SO$_2$Ph), 3.18 (s, 3 H, CH$_3$O), 3.19–3.46 (m, 3 H, C*H*NH, C*H*HO, CH*H*N), 3.56 (dd, ^2J = 9.06 Hz, ^3J = 4.03 Hz, 1 H, CH*H*O), 6.91–7.03 (m, 3 H, *m*-, *p*-Ar-H), 7.79–7.84 (m, 2 H, *o*-Ar-H). – ^{13}C NMR (125 MHz, C_6D_6): δ = 21.38, 26.98 (*C*H$_2$*C*H$_2$CHN), 22.22, 23.40, 24.86 [(CH$_3$)$_2$CH], 42.90 [(CH$_3$)$_2$CH*C*H$_2$], 52.04 (CHNH), 56.93, 59.41 (CH$_2$S, CH$_2$N), 58.78 (OCH$_3$), 66.05 (CHN), 75.48 (CH$_2$O), 128.19, 129.17, 133,19 (Ar-C), 140.85 (*ipso*-Ar-C). – MS (EI, 70 eV): *m*/*z* (%) = 354 (11) [M$^+$], 311 (6), 310 (17), 309 (100), 129 (44), 111 (8), 97 (12), 85 (8), 84 (10), 83 (8), 77 (16), 71 (9), 70 (17), 68 (7), 55 (8), 45 (10). – $C_{18}H_{30}N_2O_3S$ (354.512): calcd. C 60.98, H 8.53, N 7.90; found: C 60.90, H 8.55, N 7.89.

(2*R*,2′*S*)-2-[(2′-(Methoxymethyl)pyrrolidin-1′-yl)amino]-hexyl Phenyl Sulfone (24): Prepared by method GP 1 from (*E*)-1-hexenyl phenyl sulfone **12** and SAMP (*S*)-**2** in the presence of $Yb(OTf)_3$ in THF. The β-hydrazino sulfone **24** was obtained as a colourless oil (2.20 g, 31% yield; method A, *de* = 52% (86% after HPLC) or 4.25 g, 60% yield; method B, *de* = 40% (86% after HPLC)). – Major diastereoisomer: $[\alpha]_D^{20}$ = –99.7 (*c* = 0.60, $CHCl_3$) – IR ($CHCl_3$): $\tilde{\nu}$ = 3064 (m), 2957 (s), 2929 (s), 2873 (s), 2826 (s), 2280 (w), 1586 (m), 1479 (s), 1462 (s), 1448 (s), 1381 (s), 1305 (s), 1244 (s), 1185 (s), 1142 (s), 1087 (s), 1025 (m), 999 (m), 971 (m), 918 (s), 894 (m), 843 (s), 813 (m), 782 (m), 753 (s), 720 (m), 690 (s), 603 (s), 578 (s), 543 (s), 503 (s) cm^{-1}. – ^1H NMR (300 MHz, C_6D_6): δ = 0.82 (t, ^3J = 7.39 Hz, 3 H, CH_3CH$_2$), 0.85–1.86 (m, 10 H, CH$_3$CH_2CH_2CH_2, NHCHCH_2CH_2CH$_2$), 2.24 (q, *J* = 8.40 Hz, 1 H, C*H*HN), 2.62–2.71 (m, 1 H, OCH$_2$C*H*N), 2.92 (dd, ^2J = 14.44 Hz, ^3J = 3.19 Hz, 1 H, C*H*HSO$_2$Ph), 3.08 (dd, ^2J = 14.44 Hz, ^3J = 8.22 Hz, 1 H, CH*H*SO$_2$Ph), 3.19 (s, 3 H, CH$_3$O), 3.20–3.46 (m, 3 H, C*H*NH, C*H*HO, CH*H*N), 3.58 (dd, ^2J = 9.06 Hz, ^3J = 4.03 Hz, 1 H, CH*H*O), 7.77–7.81 (m, 3 H, *m*-, *p*-Ar-H), 7.88–7.93 (m, 2 H, *o*-Ar-H). – ^{13}C NMR (125 MHz, C_6D_6): δ = 14.23 (*C*H$_3$CH$_2$), 21.32, 23.09, 26.94, 27.14, 33.14 (CH$_3$*C*H$_2$*C*H$_2$*C*H$_2$, *C*H$_2$*C*H$_2$CHN), 53.60 (CHNH), 56.70, 59.03 (CH$_2$S, CH$_2$N), 58.78 (OCH$_3$), 65.94 (CHN), 75.53 (CH$_2$O), 127.72, 128.36, 133.17 (Ar-C), 142.22 (*ipso*-Ar-C). – MS (EI, 70 eV): *m*/*z* (%) = 354 (9) [M$^+$], 311 (6), 309 (100), 143 (5), 129 (10), 125 (3), 111 (5), 97 (7), 85 (5), 84 (7), 77 (7), 70 (8), 55 (6). – $C_{18}H_{30}N_2O_3S$ (354.512): calcd. C 60.98, H 8.53, N 7.90; found: C 60.81, H 8.57, N 7.75.

(2*R*,2′*S*)-2-Cyclohexyl-2-[(2′-(methoxymethyl)pyrrolidin-1′-yl)amino]ethyl Phenyl Sulfone (25): Prepared by method GP 1 from (*E*)-2-cyclohexyl-1-ethenyl phenyl sulfone **13** and SAMP (*S*)-**2** in the presence of $Yb(OTf)_3$ in THF. Theβ-hydrazino sulfone **25** was obtained as a colourless oil [0.46 g, 6% yield; method A, *de* = 61% (≥ 96% after HPLC) or 2.66 g, 35% yield; method B, *de* = 50% (≥ 96% after HPLC)]. – Major diastereoisomer: $[\alpha]_D^{20}$ = –134.1 (*c* = 0.29, $CHCl_3$) – IR ($CHCl_3$): $\tilde{\nu}$ = 3065 (w), 2925 (s), 2852 (s), 2669 (w), 1586 (w), 1498 (m), 1448 (s), 1385 (m), 1344 (m), 1307 (m), 1249 (m), 1230 (m), 1198 (m), 1181 (m), 1150 (s), 1117 (s), 1087 (s), 1025 (w), 999 (w), 957 (m), 937 (m), 923 (m), 890 (m), 840 (w), 806 (m), 788 (m), 754 (s), 723 (m), 690 (s), 666 (m), 633 (m), 567 (m), 543 (m) cm^{-1}. – ^1H NMR (300 MHz, C_6D_6): δ = 0.94–2.15 (m, 15 H, (CH$_2$)$_5$CH, NCHCH_2CH_2CH$_2$), 2.27 (q, *J* = 8.73 Hz, 1 H, C*H*HN), 2.64–2.74 (m, 1 H, OCH$_2$C*H*N), 2.87 (dd, ^2J = 14.44 Hz, ^3J = 9.74 Hz, 1 H, C*H*HSO$_2$Ph), 3.01 (dd, ^2J = 14.44 Hz, ^3J = 1.34 Hz, 1 H, CH*H*SO$_2$Ph), 3.22 (s, 3 H, CH$_3$O), 3.23–3.46 (m, 3 H, C*H*HO, CH*H*N, C*H*N), 3.60 (dd, ^2J = 9.07 Hz, ^3J = 3.69 Hz, 1 H, CH*H*O), 6.99–7.11 (m, 3 H, *m*-, *p*-Ar-H), 7.81–7.85 (m, 2 H, *o*-Ar-H). – ^{13}C NMR (125 MHz, C_6D_6): δ = 21.31, 26.46, 26.66, 26.79, 27.09, 29.64, 32.50 [(*C*H$_2$)$_5$CH, *C*H$_2$*C*H$_2$CHN)], 38.73 [(CH$_2$)$_5$*C*H)], 56.06, 56.08 (CH$_2$S, CH$_2$N), 57.82, 58.86 (CHNH, OCH$_3$), 65.79 (CHN), 75.34 (CH$_2$O), 128.03, 129.26, 133.38 (Ar-C), 140.43 (*ipso*-Ar-C). – MS (EI, 70 eV): *m*/*z* (%) = 380 (11) [M$^+$], 337 (7), 336 (20), 335 (100), 155 (11), 129 (40), 111 (10), 109 (6), 97 (9), 85 (9), 84 (6), 83 (6), 77 (7), 71 (8), 70 (13), 68 (5), 67 (7), 55 (11), 45 (6). – $C_{20}H_{32}N_2O_3S$ (380.450): calcd. C 63.12, H 8.48, N 7.36; found: C 63.22, H 8.47, N 7.67.

(2*R*,2′*S*)-3-Benzyloxy-2-[(2′-(methoxymethyl)pyrrolidin-1′-yl)amino]propyl Phenyl Sulfone (26): Prepared by method GP 1 from (*E*)-3-benzyloxy-1-propenyl phenyl sulfone **14** and SAMP (*S*)-**2** in the presence of $Yb(OTf)_3$ in THF. The β-hydrazino sulfone **26** was obtained as a colourless oil [2.68 g, 32% yield; method A, *de* = 36% (≥ 96% after HPLC) or 5.44 g, 65% yield; method B, *de* = 30% (≥ 96% after HPLC)]. – Major diastereoisomer: $[\alpha]_D^{20}$ = –90.4 (*c* = 0.72, $CHCl_3$) – IR ($CHCl_3$): $\tilde{\nu}$ = 3063 (m), 3029 (m), 2969 (s), 2922 (s), 2873 (s), 1586 (w), 1495 (m), 1449 (s), 1399 (m), 1364 (m), 1305 (s), 1260 (m), 1237 (m), 1188 (s), 1147 (s), 1088 (s), 1027 (m), 1001 (m), 919 (m), 848 (m), 791 (m), 752 (s), 723 (m), 692 (s), 600 (m), 575 (s), 531 (m) cm^{-1}. – ^1H NMR (300 MHz, C_6D_6): δ = 1.36–1.82 (m, 4 H, CHCH_2CH_2CH$_2$), 2.22 (q, *J* = 8.39 Hz, 1 H, C*H*HN), 2.58–2.67 (m, 1 H, CH$_3$OCH$_2$C*H*N), 3.15 (s, 3 H, CH$_3$O), 3.17–3.79 (m, 8 H, OCH_2CHCH$_2$, CH_2OCH$_3$, C*H*CH_2SO$_2$Ph, CH*H*N), 4.22 (s, 2 H, PhCH_2O), 6.83–7.78 (m, 10 H, Ar-H). – ^{13}C NMR (125 MHz, C_6D_6): δ = 21.32, 26.76 (*C*H$_2$*C*H$_2$CHN), 53.94 (CHNH), 56.74, 57.17 (CH$_2$S, CH$_2$N), 58.76 (CHN), 65.89 (OCH$_3$), 71.44, 73.23 (CH$_2$OCH$_2$), 75.14 (*C*H$_2$OCH$_3$), 127.72, 128.04, 128.12, 128.37, 129.13, 133.10 (Ar-C), 138.80, 140.85 (*ipso*-Ar-C). – MS (EI, 70 eV): *m*/*z* (%) = 418 (16) [M$^+$], 375 (7), 374 (20), 373 (100), 155 (12), 129 (15), 111 (8), 97 (5), 91 (31), 85 (15), 84 (7), 77 (5), 71 (5), 70 (7). – $C_{22}H_{30}N_2O_4S$ (418.557): calcd. C 63.13, H 7.22, N 6.69; found: C 63.10, H 7.61, N 7.07.

(2*S*,2′*R*,4′*R*,5′*R*)-2-[(2′-Aza-3′-methoxymethylbicyclo[3.3.0]octan-2′-yl)amino]butyl Phenyl Sulfone (27): Prepared by method GP 1 from (*E*)-1-butenyl phenyl sulfone **8** and RAMBO (*R*,*R*,*R*)-**5** in the presence of $Yb(OTf)_3$ in THF. The β-hydrazino sulfone **27** was obtained as a colourless oil [3.37 g, 46% yield; method A, *de* = 82% (≥ 96% after HPLC)]. – Major diastereoisomer: IR ($CHCl_3$): $\tilde{\nu}$ = 3256 (w), 3064 (w), 2939 (s), 2863 (s), 1586 (w), 1479 (m), 1460 (s), 1447 (s), 1399 (m), 1382 (w), 1348 (w), 1306 (s), 1236 (m), 1196 (m), 1149 (s), 1116 (s), 1087 (s) 1025 (w), 999 (w), 974 (m), 931 (m), 909 (m), 846 (w), 804 (w), 753 (s), 720 (m), 690 (s), 668 (w),

599 (s), 575 (s), 542 (m), 531 (s) cm^{-1}. – ^1H NMR (300 MHz, C_6D_6): δ = 0.68 (t, ^3J = 7.39 Hz, 3 H, CH_3CH$_2$), 0.99–2.06 (m, 10 H, CH$_2$CH$_2$CH$_2$, CH$_3$CH$_2$, CHCH$_2$CHN), 2.21–2.35 (m, 1 H, CHCHN), 2.61–2.76 (m, 1 H, OCH$_2$CHN), 2.90–2.99 (dd, ^2J = 14.60 Hz, ^3J = 3.86 Hz, 1 H, CHHSO$_2$Ph), 3.00–3.53 (m, 9 H, CH$_2$OCH$_3$, NH, CHNH, CHHSO$_2$Ph/CH$_2$CH$_2$CH$_2$CHN), 6.94–7.13 (m, 3 H, *m*-, *p*-Ar-H), 7.82–7.90 (m, 2 H, *o*-Ar-H). – ^{13}C NMR (75 MHz, C_6D_6): δ = 9.08 (CH$_3$CH$_2$), 24.56 (CH$_2$CH$_2$CH), 25.32 (CH$_3$CH$_2$), 33.22, 34.62, 35.66 (CH$_2$CH$_2$CH$_2$CHCH$_2$), 39.34 (CHCHN), 54.33 (CH$_3$CH$_2$), 58.74 (OCH$_3$), 58.93 (CH$_2$S), 68.43, 75.74 (CHCH$_2$O), 75.80 (CHCHN), 128.19, 129.23, 133.29 (Ar-C), 140.84 (*ipso*-Ar-C). – MS (EI, 70 eV): *m*/*z* (%) = 366 (8) [M^+], 322 (21), 321 (100), 179 (8), 169 (36), 125 (47), 111 (29), 109 (23), 97 (38), 95 (30), 85 (24), 83 (32), 81 (34), 77 (23), 71 (40), 69 (41), 67 (36), 57 (64), 55 (62) 45 (9). – $C_{19}H_{30}N_2O_3S$ (366.525): calcd. C 62.26, H 8.25, N 7.64; found: C 62.07, H 7.98, N 8.13.

(2*S*,2′*R*,4′*R*,5′*R*)-2-[(2′-Aza-3′-methoxymethylbicyclo[3.3.0]octan-2′-yl)amino]-3-methylbutyl Phenyl Sulfone (28): Prepared by method GP 1 from (*E*)-3-methyl-1-butenyl phenyl sulfone **9** and RAMBO (*R*,*R*,*R*)-**5** in the presence of Yb(OTf)$_3$ in THF. The β-hydrazino sulfone **28** was obtained as a colourless oil (1.60 g, 21% yield; method A, *de* ≥ 96%). – IR ($CHCl_3$): ṽ = 3388 (w), 3064 (w), 2954 (s), 2863 (s), 1586 (w), 1460 (s), 1448 (s), 1350 (m), 1305 (s), 1237 (m), 1199 (m), 1144 (s), 1115 (s), 1087 (s) 1025 (w), 996 (w), 963 (m), 942 (m), 905 (m), 842 (w), 752 (s), 718 (m), 690 (s), 668 (w), 599 (s), 568 (m), 542 (m), 533 (m) cm^{-1}. – ^1H NMR (500 MHz, C_6D_6): δ = 0.55 [d, ^3J = 7.14 Hz, 3 H, CH_3(CH$_3$)CH], 0.79 [d, ^3J = 6.87 Hz, 3 H, CH$_3$(CH$_3$)CH], 1.12–1.85 [m, 8 H, (CH$_3$)$_2$CH, CH$_2$CH$_2$CH$_2$, CHCHHCH], 2.07 (ddd, ^2J = 12.09 Hz, $^3J_1$ = 9.07 Hz, $^3J_2$ = 5.49 Hz, 1 H, CHCHHCH), 2.29–2.54 (m, 2 H, OCH$_2$CHN, CH$_2$CHCHN), 2.73–2.97 (m, 3 H, CH$_2$SO$_2$Ph, CH$_2$CHCHN), 3.21 (s, 3 H, CH$_3$O), 3.31 (dd, ^2J = 8.79 Hz, ^3J = 6.87 Hz, 1 H, CHHO), 3.52 (dt, $^3J_1$ = 14.83 Hz, $^3J_2$ = 2.47 Hz, 1 H, CHCH$_2$SO$_2$Ph), 3.65 (dd, ^2J = 8.79 Hz, ^3J = 3.58 Hz, 1 H, CHHO), 6.95–7.06 (m, 3 H, *m*-, *p*-Ar-H), 7.79–7.88 (m, 2 H, *o*-Ar-H). – ^{13}C NMR (75 MHz, C_6D_6): δ = 15.24, 18.40 (2 × CH$_3$), 24.87 (CH$_2$CH$_2$CH), 26.76 [(CH$_3$)$_2$CH], 32.82, 35.58, 35.68 (CH$_2$CH$_2$CH$_2$CHCH$_2$), 40.19 (CHCHN), 55.41 (CH$_2$S), 57.29, 58.84 (CHNH, OCH$_3$), 68.27 (CH$_2$CHN), 75.73 (CH$_2$O), 75.99 (CHCHN), 128.04, 129.23, 135.35 (Ar-C), 140.40 (*ipso*-Ar-C). – MS (EI, 70 eV): *m*/*z* (%) = 380 (9) [M^+], 337 (6), 336 (17), 335 (81), 195 (5), 169 (24), 151 (7), 143 (7), 125 (54), 123 (7), 110 (11), 97 (8), 83 (10), 81 (14), 80 (11), 79 (13), 78 (16), 77 (52), 71 (15), 70 (16), 69 (100), 68 (17), 67 (50), 65 (10), 51 (34), 45 (38). – $C_{20}H_{32}N_2O_3S$ (380.552): calcd. C 63.12, H 8.48, N 7.36; found: C 62.67, H 8.42, N 7.23.

(2*S*,2′*R*,4′*R*,5′*R*)-2-[(2′-Aza-3′-methoxymethylbicyclo[3.3.0]octan-2′-yl)amino]pentyl Phenyl Sulfone (29): Prepared method GP 1 from (*E*)-1-pentenyl phenyl sulfone **10** and RAMBO (*R*,*R*,*R*)-**5** in the presence of Yb(OTf)$_3$ in THF. The β-hydrazino sulfone **29** was obtained as a colourless oil [3.04 g, 40% yield; method A, *de* = 86% (≥ 96% after HPLC)]. – Major diastereoisomer: IR ($CHCl_3$): ṽ = 3386 (w), 3064 (w), 2956 (s), 2866 (s), 1727 (w), 1586 (w), 1460 (s), 1447 (s), 1380 (w), 1350 (w), 1307 (s), 1235 (m), 1195 (m), 1145 (s), 1116 (s), 1087 (s) 1024 (w), 999 (w), 950 (m), 932 (m), 902 (m), 875 (w), 861 (w), 790 (m), 753 (s), 721 (m), 690 (s), 625 (m), 600 (s), 575 (s), 532 (s) cm^{-1}. – ^1H NMR (500 MHz, C_6D_6): δ = 0.78 (d, ^3J = 7.32 Hz, 3 H, CH_3CH$_2$), 0.97–1.81 (m, 11 H, CH$_3$CH$_2$CH$_2$, CH$_2$CH$_2$CH$_2$, CHCHHCH), 2.01 (ddd, ^2J = 14.95 Hz, $^3J_1$ = 9.46 Hz, $^3J_2$ = 5.49 Hz, 1 H, CHCHHCH), 2.27 (quind, $^3J_1$ = 9.85 Hz, $^3J_2$ = 2.44 Hz, 1 H, CH$_2$CHCHN), 2.66–2.72 (m, 1 H, OCH$_2$CHN), 2.94 (dd, ^2J = 14.04 Hz, ^3J = 4.07 Hz, 1 H, CHHSO$_2$Ph), 3.02–3.08 (m, 1 H, CH$_2$CHCHN), 3.16 (s, 3 H, CH$_3$O), 3.17 (dd, ^2J = 14.34 Hz, ^3J = 7.33 Hz, 1 H, CHHSO$_2$Ph), 3.19 (dd, ^2J = 8.85 Hz, ^3J = 6.26 Hz, 1 H, CHHO), 3.50 (dd, ^2J = 8.85 Hz, ^3J = 4.58 Hz, 1 H, CHHO), 3.53–3.58 (m, 1 H, CHCH$_2$SO$_2$Ph), 6.94–7.02 (m, 3 H, *m*-, *p*-Ar-H), 7.83–7.90 (m, 2 H, *o*-Ar-H). – ^{13}C NMR (125 MHz, C_6D_6): δ = 14.26 (CH$_3$CH$_2$), 18.29 (CH$_3$CH$_2$), 24.54 (CH$_2$CH$_2$CHN), 33.25, 34.52, 34.92, 35.65 (CH$_3$CH$_2$CH$_2$, CH$_2$CH$_2$CH$_2$CHCH$_2$), 39.27 (CHCHN), 52.91 (CHNH), 58.72 (OCH$_3$), 59.35 (CH$_2$S), 68.47 (CH$_2$CHN), 75.62 (CH$_2$O), 75.78 (CHCHN), 127.78, 127.97, 133.13 (Ar-C), 140.82 (*ipso*-Ar-C). – MS (EI, 70 eV): *m*/*z* (%) = 380 (12) [M^+], 337 (7), 336 (24), 335 (100), 169 (51), 143 (7), 137 (13), 125 (15), 124 (17), 123 (13), 110 (19), 109 (15), 108 (34), 95 (15), 85 (15), 83 (14), 82 (13), 81 (31), 79 (13), 78 (11), 77 (52), 74 (27), 71 (21), 70 (17), 69 (27), 68 (10), 67 (58), 65 (10), 59 (51), 57 (36), 55 (32). – $C_{20}H_{32}N_2O_3S$ (380.552): calcd. C 63.12, H 8.48, N 7.36; found: C 63.56, H 8.62, N 7.83.

(2*S*,2′*R*,4′*R*,5′*R*)-2-[(2′-Aza-3′-methoxymethylbicyclo[3.3.0]octan-2′-yl)amino]-4-methylpentyl Phenyl Sulfone (30): Prepared by method GP 1 from (*E*)-3-methyl-1-pentenyl phenyl sulfone **11** and RAMBO (*R*,*R*,*R*)-**5** in the presence of Yb(OTf)$_3$ in THF. The β-hydrazino sulfone **30** was obtained as a colourless oil [2.53 g, 32% yield; method A, *de* = 90% (≥ 96% after HPLC)]. – Major diastereoisomer: IR ($CHCl_3$): ṽ = 3265 (w), 3062 (w), 2948 (s), 2864 (s), 1585 (w), 1469 (s), 1448 (s), 1403 (w), 1383 (w), 1361 (w), 1303 (s), 1237 (m), 1188 (m), 1141 (s), 1107 (s), 1089 (s) 1027 (w), 997 (w), 948 (m), 896 (m), 850 (m), 810 (m), 753 (s), 689 (s), 577 (s), 541 (s), 499 (s), 479 (s) cm^{-1}. – ^1H NMR (500 MHz, C_6D_6): δ = 0.70 (t, ^3J = 6.71 Hz, 3 H, CH_3(CH$_3$)CH), 0.85 (t, ^3J = 6.41 Hz, 3 H, CH$_3$(CH$_3$)CH), 1.08–1.44 (m, 7 H, NCHCHHCHCHHCH$_2$CHCHH, (CH$_3$)$_2$CHCHH), 1.50–1.72 (m, 1 H, CH$_2$CHHCH$_2$), 1.76–1.85 (m, 2 H, NCHCHHCH$_2$CH$_2$, (CH$_3$)$_2$CHCHH), 2.01–2.07 (m, 1 H, NCHCHCHH), 2.24–2.32 (m, 1 H, CH$_2$CHCHN), 2.66–2.73 (m, 1 H, OCH$_2$CHN), 2.95 (dd, ^2J = 14.65 Hz, ^3J = 3.52 Hz, 1 H, CHHSO$_2$Ph), 3.03–3.11 (m, 1 H, CH$_2$CHCHN), 3.12–3.17 (m, 1 H, CHHSO$_2$Ph), 3.18 (s, 3 H, CH$_3$O), 3.21 (dd, ^2J = 8.85 Hz, ^3J = 6.41 Hz, 1 H, CHHO), 3.53–3.60 (m, 2 H, CHHO, CHCH$_2$SO$_2$Ph), 3.70 (br. s, 1 H, NH), 6.95–7.03 (m, 3 H, *m*-, *p*-Ar-H), 7.82–7.86 (m, 2 H, *o*-Ar-H). – ^{13}C NMR (125 MHz, C_6D_6): δ = 22.20, 23.72 (2 × CH$_3$), 24.53 (CH$_2$CH$_2$CH), 24.79 [(CH$_3$)$_2$CH], 33.30 (CH$_2$CHCH$_2$CHN), 34.46 (CH$_2$CH$_2$CHN), 35.72 (CHCH$_2$CHN), 39.31 (CHCHN), 42.44 [(CH$_3$)$_2$CHCH$_2$], 51.46 (CHNH), 58.77 (OCH$_3$), 59.72 (CH$_2$S), 68.53 (CHCH$_2$O), 75.57 (CH$_2$O), 75.97 (CHCHN), 128.31, 129.25, 133.29 (Ar-C), 140.78 (*ipso*-Ar-C). – MS (EI, 70 eV): *m*/*z* (%) = 394 (11) [M^+], 351 (7), 350 (23), 349 (100), 169 (41), 137 (5), 125 (7), 108 (5), 83 (6), 81 (9), 79 (8), 78 (5), 77 (15), 71 (7), 67 (18), 57 (6), 55 (10). – $C_{21}H_{34}N_2O_3S$ (394.579): calcd. C 63.92, H 8.69, N 7.10; found: C 63.65, H 8.70, N 7.37.

(2*S*,2′*R*,4′*R*,5′*R*)-2-[(2′-Aza-3′-methoxymethylbicyclo[3.3.0]octan-2′-yl)amino]hexyl Phenyl Sulfone (31): Prepared by method GP 1 from (*E*)-1-hexenyl phenyl sulfone **12** and RAMBO (*R*,*R*,*R*)-**5** in the presence of Yb(OTf)$_3$ in THF. The β-hydrazino sulfone **31** was obtained as a colourless oil [3.55 g, 45% yield; method A, *de* = 86% (≥ 96% after HPLC)]. – Major diastereoisomer: IR ($CHCl_3$): ṽ = 3376 (w), 3064 (w), 2954 (s), 2862 (s), 1722 (w), 1586 (w), 1447 (s), 1384 (w), 1350 (m), 1306 (s), 1237 (m), 1197 (m), 1148 (s), 1117 (s), 1087 (s) 1025 (w), 999 (w), 949 (m), 929 (m), 876 (w), 842 (w), 807 (m), 753 (s), 721 (m), 690 (s), 668 (m), 601 (s), 575 (s), 531 (s) cm^{-1}. – ^1H NMR (300 MHz, C_6D_6): δ = 0.82 (d, ^3J = 7.39 Hz, 3 H, CH_3CH$_2$), 0.95–1.86 (m, 13 H, CH$_3$CH$_2$CH$_2$CH$_2$, CH$_2$CH$_2$CH$_2$CHN, CHCHHCH), 2.01 (ddd, ^2J = 14.78 Hz, $^3J_1$ =

9.40 Hz, $^3J_2$ = 5.38 Hz, 1 H, CHCH*H*CH), 2.28 (quind, $^3J_1$ = 8.73 Hz, $^3J_2$ = 2.29 Hz, 1 H, CH_2CHCHN), 2.67–2.73 (m, 1 H, OCH_2CHN), 2.98 (dd, ^2J = 14.44 Hz, ^3J = 4.37 Hz, 1 H, $CHHSO_2Ph$), 3.02–3.09 (m, 1 H, CH_2CHCHN), 3.15–3.39 (m, 5 H, CH_3O, $CHHSO_2Ph$, CHHO), 3.49 (dd, ^2J = 9.06 Hz, ^3J = 4.70 Hz, 1 H, CHHO), 3.50–3.59 (m, 1 H, $CHCH_2SO_2Ph$), 6.97–7.09 (m, 3 H, *m*- *p*-Ar-H), 7.81–7.87 (m, 2 H, *o*-Ar-H). – ^{13}C NMR (75 MHz, C_6D_6): δ = 14.21 (CH_3CH_2), 23.03 (CH_3CH_2), 24.51 ($CH_2CH_2CH_2CHN$), 27.19 ($CH_3CH_2CH_2$), 33.25, 34.51, 35.63, 35.65 ($CH_3CH_2CH_2CH_2$, $CH_2CH_2CH_2CHCH_2$), 39.25 (*C*HCHN), 53.09 (CHNH), 58.72 (OCH_3), 59.37 (CH_2S), 68.46 ($CHCH_2O$), 75.64 (CH_2O), 75.78 (CHCHN), 127.69, 129.21, 133.25 (Ar-C), 140.82 (*ipso*-Ar-C). – MS (EI, 70 eV): *m*/*z* (%) = 394 (12) [M$^+$], 349 (100), 169 (37), 151 (5), 125 (6), 110 (5), 81 (6), 77 (9), 67 (10), 55 (6). – $C_{21}H_{34}N_2O_3S$ (394.579): calcd. C 63.92, H 8.69, N 7.10; found: C 63.92, H 8.74, N 7.25.

(2*S*,2′*R*,4′*R*,5′*R*)-2-[(2′-Aza-3′-methoxymethylbicyclo[3.3.0]octan-2′-yl)amino]-2-cyclohexylethyl Phenyl Sulfone (32): Prepared by method GP 1 from (*E*)-2-cyclohexyl-1-ethenyl phenyl sulfone **13** and RAMBO (*R*,*R*,*R*)-**5** in the presence of $Yb(OTf)_3$ in THF. The β-hydrazino sulfone **32** was obtained as a colourless oil (2.44 g, 29% yield; method A, *de* = 94%). – IR ($CHCl_3$): $\tilde{\nu}$ = 3375 (w), 3064 (w), 2927 (m), 2855 (s), 1728 (w), 1586 (w), 1448 (s), 1385 (w), 1348 (m), 1307 (s), 1248 (m), 1233 (m), 1198 (m), 1148 (s), 1120 (s), 1088 (s) 1025 (w), 999 (w), 955 (w), 931 (w), 909 (m), 888 (w), 840 (w), 804 (w), 754 (s), 723 (m), 690 (s), 667 (w), 631 (m), 567 (m), 543 (s), 533 (s), 457 (w) cm^{-1}. – ^{1}H NMR (300 MHz, C_6D_6): δ = 0.37–2.44 [m, 21 H, $(CH_2)_5CHCH$, $CH_2CH_2CH_2$, $CHCH_2CH$, $CH_2CHCHNNH$], 2.75–2.86 (m, 1 H, OCH_2CHN), 2.91 (dd, ^2J = 14.56 Hz, ^3J = 8.79 Hz, 1 H, $CHHSO_2Ph$), 2.99 (dd, ^2J = 14.56 Hz, ^3J = 2.47 Hz, 1 H, $CHHSO_2Ph$), 3.22 (s, 3 H, CH_3O), 3.36 (dd, ^2J = 8.79 Hz, ^3J = 6.87 Hz, 1 H, CHHO), 3.52 (dt, $^3J_1$ = 8.79 Hz, $^3J_2$ = 2.47 Hz, 1 H, $CHCH_2SO_2Ph$), 3.64 (dd, ^2J = 8.79 Hz, ^3J = 3.85 Hz, 1 H, CHHO), 6.92–7.07 (m, 3 H, *m*-, *p*-Ar-H), 7.79–7.87 (m, 2 H, *o*-aryl-H). – ^{13}C NMR (75 MHz, C_6D_6): δ = 24.94, 26.61, 26.67, 26.88, 27.08 [$(CH_2)_5CH$], 29.42 (CH_2CH_2CHN), 32.89, 35.53, 35.68 ($CH_2CH_2CH_2CHCH_2CH$), 37.70, 40.14 [$(CH_2)_5CH$, *C*HCHN], 56.57 (CH_2S), 57.19, 58.90 (CHNH, OCH_3), 68.57 (*C*HCH$_2$O), 75.64 (CH_2O), 76.05 (CHCHN), 128.05, 128.24, 133.29 (Ar-C), 140.59 (*ipso*-Ar-C). – MS (EI, 70 eV): *m*/*z* (%) = 420 (3) [M$^+$], 376 (5), 170 (6), 169 (16), 126 (9), 125 (98), 110 (14), 109 (84), 108 (21), 93 (15), 91 (33), 81 (17), 80 (12), 79 (29), 78 (12), 77 (35), 68 (11), 67 (100), 65 (13), 59 (18), 57 (20), 55 (31), 53 (14), 51 (19), 45 (9). – $C_{23}H_{36}N_2O_3S$ (420.617): calcd. C 65.68, H 8.63, N 6.66; found: C 65.78, H 8.50, N 6.84.

(2*S*,2′*R*,4′*R*,5′*R*)-2-[(2′-Aza-3′-methoxymethylbicyclo[3.3.0]octan-2′-yl)amino]-3-benzyloxypropyl Phenyl Sulfone (33): Prepared by method GP 1 from (*E*)-3-benzyloxy-1-propenyl phenyl sulfone **14** and RAMBO (*R*,*R*,*R*)-**5** in the presence of $Yb(OTf)_3$ in THF. The β-hydrazino sulfone **33** was obtained as a colourless oil (2.66 g, 29% yield; method A, *de* = 90%). – IR ($CHCl_3$): $\tilde{\nu}$ = 3529 (w), 3261 (w), 3087 (w), 3063 (w), 3030 (w), 2938 (m), 2863 (s), 1586 (w), 1496 (m), 1478 (m), 1448 (s), 1397 (w), 1364 (w), 1343 (m), 1306 (s), 1235 (m), 1198 (m), 1148 (s), 1118 (s), 1086 (s) 1028 (w), 1000 (w), 975 (w), 950 (w), 929 (w), 902 (m), 880 (w), 819 (w), 792 (w), 752 (s), 723 (m), 698 (s), 690 (s), 668 (w), 647 (w), 601(s), 574 (s), 546 (m), 532 (s) cm^{-1}. – ^{1}H NMR (500 MHz, C_6D_6): δ = 1.04–1.82 (m, 7 H, $CH_2CH_2CH_2$, CHC*H*HCH), 2.00 (ddd, ^2J = 12.09 Hz, $^3J_1$ = 9.40 Hz, $^3J_2$ = 5.37 Hz, 1 H, CHCH*H*CH), 2.24 (quind, $^3J_1$ = 8.39 Hz, $^3J_2$ = 2.35 Hz, 1 H, CH_2CHCHN), 2.61–2.68 (m, 1 H, OCH_2CHN), 3.06 (m, 1 H, CH_2CHCHN), 3.14 (s, 3 H, CH_3O), 3.15 (dd, ^2J = 9.07 Hz, ^3J = 6.38 Hz, 1 H, C*H*HOCH$_3$), 3.25 (dd, ^2J = 14.44 Hz, ^3J = 7.72 Hz, 1 H, C*H*HSO$_2$Ph), 3.41 (dd, ^2J = 14.44 Hz, ^3J = 4.03 Hz, 1 H, CH*H*SO$_2$Ph), 3.45–3.52 (m, 2 H, CH*H*OCH$_3$, CHC*H*HOCH$_2$), 3.72 (dd, ^2J = 9.73 Hz, ^3J = 5.03 Hz, 1 H, CHCH*H*OCH$_2$), 3.85–3.94 (m, 1 H, C*H*CH$_2$SO$_2$Ph), 4.22 (d, ^2J = 11.75 Hz, 1 H, C*H*HPh), 4.29 (d, ^2J = 12.08 Hz, 1 H, CH*H*Ph), 6.92–7.26 (m, 8 H, CH$_2$-Ar-*H*, SO$_2$-*m*-, *p*-Ar-H), 7.81–7.88 (m, 2 H, SO$_2$-*o*-Ar-H). – ^{13}C NMR (125 MHz, C_6D_6): δ = 24.54 (*C*H$_2$CH$_2$CH), 33.98, 34.54, 35.48 (*C*H$_2$CH$_2$*C*H$_2$CH*C*H$_2$), 39.25 (*C*HCHN), 53.88 (CHNH), 57.49 (CH_2S), 58.74 (OCH_3), 68.34 (N*C*HCH$_2$O), 71.04 (NHCH*C*H$_2$O), 73.06 (Ph*C*H$_2$O), 75.18 (OCH_2), 75.81 (CH*C*HN), 127.69, 127.80, 128.50, 128.57, 129.20, 133.26 (Ar-C), 138.76, 140.58 (*ipso*-Ar-C). – MS (EI, 70 eV): *m*/*z* (%) = 458 (39) [M$^+$], 415 (27), 414 (65), 413 (100), 195 (21), 170 (6), 169 (48), 125 (17), 110 (8), 92 (8), 91 (67), 79 (12), 77 (12), 71 (9), 67 (20), 45 (7). – $C_{25}H_{34}N_2O_4S$ (458.622): calcd. C 65.47, H 7.47, N 6.11; found: C 65.31, H 7.48, N 6.61.

General Procedure for the Synthesis of *N*-Protected β-Amino Sulfones (34–45) by Reductive N–N Bond Cleavage with BH_3·THF and Subsequent *N*-Protection of the Free Amine (GP 2): In a typical experiment the β-hydrazino sulfone **19–26** (10 mmol) was dissolved in THF (50 mL) under an atmosphere of argon. $BH_3 \cdot THF$[32] (100 mL, 1.0 M in THF) was added, and the reaction mixture heated under reflux for 5 h. The solution was cooled to room temperature, hydrochloric acid (30 mL, 4.0 M) slowly (!) added and the solution stirred for 2 h at room temperature. The solvent was evaporated under reduced pressure, and the residue treated with saturated aqueous Na_2CO_3 solution. The aqueous phase was extracted with CH_2Cl_2/Et_2O (3:1), and the combined organic layer washed with brine. The organic phase was dried with Na_2SO_4 and the solvent evaporated in vacuo to yield a colourless oil. Without further purification, the crude β-amino sulfone was treated with Boc_2O or benzyl bromide.

Conversion to the *N*-Boc-Protected β-Amino Sulfone: The crude β-amino sulfone was dissolved in methanol (300 mL) and Boc_2O (100 mmol) and triethyl amine (3 mL) added at 0 °C. The reaction mixture was stirred for 2 d at room temperature. The solvent was evaporated under reduced pressure, and the residue diluted with Et_2O. The mixture was washed with saturated aqueous NH_4Cl solution and then brine, dried with $MgSO_4$ and concentrated under reduced pressure. After purification by column chromatography (SiO_2, pentane/Et_2O-mixtures), the products **34–40** were obtained as colourless oils.

Conversion to the *N*,*N*-Dibenzyl-Protected β-Amino Sulfone: The crude β-amino sulfone was dissolved in a mixture of CH_2Cl_2/H_2O (4:1, 100 mL) and solid Na_2CO_3 (60 mmol) and benzyl bromide (30 mmol) added at room temperature. The reaction mixture was heated under reflux for 1−3 d (monitored by TLC). The organic layer was separated, the aqueous phase extracted twice with CH_2Cl_2, and the combined organic phases washed with a saturated aqueous Na_2CO_3 solution and then brine. The organic solution was dried with $MgSO_4$, the solvent evaporated, and the products purified by chromatography (SiO_2, pentane/Et_2O mixtures) to yield compounds **41**−**45** as colourless solids.

(*R*)-2-(*tert*-Butoxycarbonylamino)butyl Phenyl Sulfone (34): Prepared by method GP 2 by cleavage of hydrazine **20** with $BH_3 \cdot THF$ and subsequent protection of the resulting crude amine with Boc_2O. Compound **34** was obtained as a colourless solid (1.88 g, 60%, 2 steps). – M.p. 107 °C. – $[\alpha]_D^{20}$ = –2.1 (*c* = 0.78, $CHCl_3$) – IR (KBr) $\tilde{\nu}$ = 3386 (s), 3062 (w), 3011 (m), 2965 (m), 2932 (m), 2875 (m), 1689 (s), 1654 (w), 1586 (w), 1520 (s), 1482 (w), 1453

(m), 1391 (m), 1367 (m), 1318 (m), 1297 (s), 1251 (s), 1285 (s), 1242 (s), 1170 (s), 1151 (s), 1112 (m), 1082 (s), 1052 (m), 1029 (w), 1015 (w), 987 (m), 933 (w), 747 (m), 694 (m), 621 (m), 573 (s), 548 (m), 530 (s) cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 0.91 (t, ^3J = 7.39 Hz, 3 H, CH_3CH_2), 1.41 [s, 9 H, $C(CH_3)_3$], 1.64–181 (m, 2 H, CH_3CH_2), 3.25 (dd, ^2J = 14.44 Hz, ^3J = 4.37 Hz, 1 H, $CHHSO_2Ph$), 3.45 (dd, ^2J = 14.44 Hz, ^3J = 7.05 Hz, 1 H, $CHHSO_2Ph$), 3.80–3.92 (m, 1 H, CHNH), 4.92 (br. s, 1 H, NH), 7.54–7.67 (m, 3 H, *m*-, *p*-Ar-H), 7.01–7.94 (m, 2 H, *o*-Ar-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.26 (CH_3CH_2), 27.52 (CH_3CH_2), 28.33 [$(CH_3)_3C$], 48.72 (CHNH), 59.16 (CH_2S), 79.57 [$(CH_3)_3C$], 127.89, 129.35, 133.76 (Ar-C), 140.01 (*ipso*-Ar-C), 155.03 (NHCO). – MS (CI, isobutane): *m*/*z* (%) = 314 (17) [M^++1], 260 (5), 259 (12), 258 (100), 214 (15). – $C_{15}H_{23}NO_4S$ (313.418): calcd. C 57.48, H 7.40, N 4.47; found: C 57.45, H 7.31, N 4.28.

(*R*)-2-(*tert*-Butoxycarbonylamino)-3-methylbutyl Phenyl Sulfone (35): Prepared by method GP 2 by cleavage of hydrazine **21** with $BH_3 \cdot$ T HF and subsequent protection of the resulting crude amine with Boc_2O. Compound **35** was obtained as a colourless solid (1.38 g, 42%, 2 steps). – M.p. 94 °C. – $[\alpha]_D^{20}$ = –12.9 (*c* = 0.31, $CHCl_3$) – IR (KBr): ṽ = 3389 (s), 3070 (w), 2971 (s), 2931 (s), 2875 (m), 1585 (m), 1516 (s), 1452 (s), 1390 (s), 1369 (s), 1310 (s), 1297 (s), 1247 (s), 1169 (s), 1147 (s), 1105 (m), 1083 (s), 1041 (m), 1018 (s), 998 (m), 957 (w), 938 (w), 876 (m), 844 (w), 783 (m), 754 (s), 695 (s), 621 (m), 574 (s), 527 (s) cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 0.88 [2 d, ^3J = 6.72 Hz, 6 H, $C(CH_3)_2CH$], 1.42 [s, 9 H, $C(CH_3)_3$], 1.92–2.10 [m, 1 H, $(CH_3)_2CH$], 3.22–3.40 (m, 2 H, CH_2SO_2Ph), 3.65–3.88 (m, 1 H, CHNH), 4.75 (br. s, 1 H, NH), 7.54–7.70 (m, 3 H, *m*-, *p*-Ar-H), 7.89–7.94 (m, 2 H, *o*-Ar-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 17.95, 18.86 [$(CH_3)_2CH$], 28.34 [$(CH_3)_3C$], 31.92 [$(CH_3)_2CH$], 52.13 (CHNH), 57.58 (CH_2S), 79.40 [$(CH_3)_3C$], 128.06, 129.33, 133.77 (Ar-C), 138.20 (*ipso*-Ar-C), 155.16 (NHCO). – MS (CI, isobutane): *m*/*z* (%) = 328 (14) [M^++1], 272 (100), 254 (12), 228 (48), 143 (6), 132 (13), 131 (6). – $C_{16}H_{25}NO_4S$ (327.445): calcd. C 58.69, H 7.70, N 4.28; found: C 58.87, H 7.53, N 4.03.

(*R*)-2-(*tert*-Butoxycarbonylamino)pentyl Phenyl Sulfone (36): Prepared by method GP 2 by cleavage of hydrazine **22** with $BH_3 \cdot$ THF and subsequent protection of the resulting crude amine with Boc_2O. Compound **34** was obtained as a colourless solid (2.69 g, 82%, 2 steps). – M.p. 98 °C. – IR (KBr): ṽ = 3384 (s), 2976 (m), 2932 (m), 2871 (w), 1689 (s), 1519 (s), 1450 (m), 1391 (m), 1365 (m), 1304 (s), 1289 (s), 1264 (m), 1230 (m), 1169 (s), 1150 (s), 1085 (m), 1053 (w), 1013 (m), 879 (w), 854 (w), 785 (m), 756 (m), 743 (m), 690 (m), 611 (w), 587 (m), 548 (m), 530 (m) cm^{-1}. – ^1H NMR (400 MHz, $CDCl_3$): δ = 0.89 (t, ^3J = 7.29 Hz, 3 H, CH_3CH_2), 1.21–1.50 (m, 2 H, CH_3CH_2), 1.40 [s, 9 H, $C(CH_3)_3$], 1.62–1.76 (m, 2 H, $CH_3CH_2CH_2$), 3.26 (dd, ^2J = 14.29 Hz, ^3J = 3.85 Hz, 1 H, $CHHSO_2Ph$), 3.38–3.48 (m, 1 H, $CHHSO_2Ph$), 3.89–3.99 (m, 1 H, CHNH), 4.88 (br. s 1 H, NH), 7.54–7.68 (m, 3 H, *m*-, *p*-Ar-H), 7.90–7.97 (m, 2 H, *o*-Ar-H). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.62 (CH_3CH_2), 19.13 (CH_3CH_2), 28.34 [$(CH_3)_3C$], 36.43 ($CH_3CH_2CH_2$), 47.21 (CHNH), 59.43 (CH_2S), 79.64 [$(CH_3)_3C$], 127.88, 129.35, 133.75 (Ar-C), 140.14 (*ipso*-Ar-C), 154.97 (NHCO). – MS (EI, 70 eV): *m*/*z* (%) = 327 (1) [M^+], 284 (14), 271 (10), 228 (13), 186 (6), 185 (15), 184 (100), 143 (18), 141 (6), 130 (5), 129 (6), 125 (5), 77 (12), 72 (10), 69 (6), 58 (7), 57 (60). – $C_{16}H_{25}NO_4S$ (327.445): calcd. C 58.69, H 7.70, N 4.28; found: C 58.61, H 7.63, N 4.16.

(*R*)-2-(*tert*-Butoxycarbonylamino)-4-methylpentyl Phenyl Sulfone (37): Prepared by method GP 2 by cleavage of hydrazine **23** with $BH_3 \cdot$ THF and subsequent protection of the resulting crude amine with Boc_2O. Compound **37** was obtained as a colourless solid (2.49 g, 73%, 2 steps). – M.p. 89 °C. – $[\alpha]_D^{20}$ = +7.1 (*c* = 1.25, $CHCl_3$) – IR (KBr): ṽ = 3387 (s), 3067 (w), 2974 (s), 2962 (s), 2928 (s), 2898 (s), 2872 (s), 1689 (s), 1586 (m), 1516 (s), 1451 (s), 1402 (s), 1391 (s), 1366 (s), 1326 (s), 1304 (s), 1291 (s), 1246 (s), 1230 (s), 1169 (s), 1144 (s), 1110 (m), 1085 (s), 1046 (m), 1024 (s), 999 (m), 938 (w), 922 (w), 878 (m), 862 (m), 846 (w), 781 (s), 754 (s), 693 (s), 622 (m), 592 (s), 552 (s), 530 (s) cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 0.88 [d, ^3J = 6.05 Hz, 6 H, $(CH_3)_2CH$], 1.40 [s, 9 H, $C(CH_3)_3$], 1.45–1.75 [m, 3 H, $(CH_3)_2CHCH_2$], 3.26 (dd, ^2J = 14.10 Hz, ^3J = 3.36 Hz, 1 H, $CHHSO_2Ph$), 3.38–3.52 (m, 1 H, $CHHSO_2Ph$), 3.94–4.08 (m, 1 H, CHNH), 4.88 (br. s, 1 H, NH), 7.54–7.69 (m, 3 H, *m*-, *p*-Ar-H), 7.91–7.97 (m, 2 H, *o*-Ar-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.87, 22.73 [$(CH_3)_2CH$], 24.78 [$(CH_3)_2CH$], 28.32 [$(CH_3)_3C$], 43.23 [$(CH_3)_2CHCH_2$], 45.68 (CHNH), 59.69 (CH_2S), 79.56 [$(CH_3)_3C$], 127.86, 129.33, 133.73 (Ar-C), 140.15 (*ipso*-Ar-C), 154.90 (NHCO). – MS (CI, isobutane): *m*/*z* (%) = 342 (19) [M^++1], 288 (6), 287 (15), 286 (100), 242 (23), 146 (4), 143 (6). – $C_{17}H_{27}NO_4S$ (341.472): calcd. C 59.80, H 7.97, N 4.10; found: C 59.60, H 8.21, N 3.95.

(*R*)-2-(*tert*-Butoxycarbonylamino)hexyl Phenyl Sulfone (38): Prepared by method GP 2 by cleavage of hydrazine **24** with $BH_3 \cdot$ THF and subsequent protection of the resulting crude amine with Boc_2O. Compound **38** was obtained as a colourless solid (1.84 g, 54%, 2 steps). – M.p. 101 °C. – $[\alpha]_D^{20}$ = +10.3 (*c* = 0.88, $CHCl_3$) – IR (KBr): ṽ = 3387 (s), 3065 (m), 2980 (s), 2957 (s), 2934 (s), 2870 (m), 1692 (s), 1519 (s), 1482 (m), 1449 (s), 1390 (s), 1366 (s), 1293 (s), 1251 (s), 1172 (s), 1149 (s), 1103 (m), 1086 (s), 1037 (m), 1022 (s), 933 (w), 874 (m), 785 (s), 747 (s), 690 (s), 622 (m), 575 (s), 530 (s) cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 0.86 (t, ^3J = 6.72 Hz, 3 H, CH_3CH_2), 1.23–1.35 (m, 4 H, $CH_3CH_2CH_2$), 1.41 [s, 9 H, $C(CH_3)_3$], 1.60–1.78 (m, 2 H, $CH_3CH_2CH_2CH_2$), 3.24 (dd, ^2J = 14.44 Hz, ^3J = 4.54 Hz, 1 H, $CHHSO_2Ph$), 3.44 (dd, ^2J = 14.44 Hz, ^3J = 5.54 Hz, 1 H, $CHHSO_2Ph$), 3.85–3.99 (m, 1 H, CHNH), 4.90 (br. s, 1 H, NH), 7.53–7.68 (m, 3 H, *m*-, *p*-Ar-H), 7.91–7.95 (m, 2 H, *o*-Ar-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.92 (CH_3CH_2), 22.24 (CH_3CH_2), 27.98 ($CH_3CH_2CH_2$), 28.33 [$(CH_3)_3C$], 34.08 ($CH_3CH_2CH_2CH_2$), 47.39 (CHNH), 59.46 (CH_2S), 81.41 [$(CH_3)_3C$], 127.88, 129.34, 133.74 (Ar-C), 140.11 (*ipso*-Ar-C), 154.97 (NHCO). – MS (EI, 70 eV): *m*/*z* (%) = 341 (0.2) [M^+], 285 (17), 242 (5), 228 (5), 186 (5), 185 (10), 184 (100), 157 (5), 144 (9), 143 (20), 141 (7), 130 (5), 125 (6), 100 (5), 99 (12), 93 (5), 86 (15), 83 (6), 77 (16), 58 (9), 57 (83), 55 (8). – $C_{17}H_{27}NO_4S$ (341.472): calcd. C 59.80, H 7.97, N 4.10; found: C 59.67, H 8.33, N 4.00.

(*R*)-2-(*tert*-Butoxycarbonylamino)-2-cyclohexylethyl Phenyl Sulfone (39): Prepared by method GP 2 by cleavage of hydrazine **25** with $BH_3 \cdot$ THF and subsequent protection of the resulting crude amine with Boc_2O. Compound **39** was obtained as a colourless solid (2.13 g, 58%, 2 steps). – M.p. 135 °C. – $[\alpha]_D^{20}$ = –8.1 (*c* = 0.16, $CHCl_3$) – IR (KBr): ṽ = 3363 (s), 3063 (m), 2979 (s), 2931 (s), 2851 (s), 1689 (s), 1587 (m), 1525 (s), 1478 (m), 1449 (s), 1386 (s), 1368 (s), 1347 (s), 1308 (s), 1247 (s), 1171 (s), 1149 (s), 1122 (s), 1085 (s), 1055 (m), 1039 (m), 1018 (s), 962 (m), 936 (w), 893 (w), 873 (m), 845 (w), 807 (w), 779 (m), 743 (s), 720 (m), 691 (s), 641 (w) cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 0.86–1.78 [kB, 20 H, $(CH_2)_5CH$, $C(CH_3)_3$], 3.20–3.42 (m, 2 H, CH_2SO_2Ph), 3.70–3.88 (m, 1 H, CHNH), 7.51–7.69 (m, 3 H, *m*-, *p*-Ar-H), 7.85–7.94 (m, 2 H, *o*-Ar-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 25.85, 26.12, 29.56 [$(CH_2)_5CH$], 28.37 [$(CH_3)_3C$], 41.39 [$(CH_2)_5CH$], 51.80 (CHNH), 57.52 (CH_2S), 80.05 [$(CH_3)_3C$], 128.04, 129.34, 133.75 (Ar-C), 140.00 (*ipso*-Ar-C), 155.10 (NHCO). – MS (CI, isobutane): *m*/*z*

(%) = 368 (50) [M$^+$+1], 314 (6), 313 (15), 312 (100), 228 (27), 172 (53), 143 (11), 113 (8), 112 (7), 99 (5). – $C_{19}H_{29}NO_4S$ (367.510): calcd. C 62.10, H 7.95, N 3.81; found: C 61.81, H 8.60, N 3.60.

(*R*)-3-Benzyloxy-2-(*tert*-Butoxycarbonylamino)propyl Phenyl Sulfone (40): Prepared by method GP 2 by cleavage of hydrazine **26** with $BH_3 \cdot THF$ and subsequent protection of the resulting crude amine with Boc_2O. Compound **40** was obtained as a colourless solid (3.33 g, 82%, 2 steps). – M.p. 97 °C. – $[\alpha]_D^{20} = -9.7$ (c = 0.57, $CHCl_3$) – IR (KBr): $\tilde{\nu}$ = 3384 (s), 3062 (m), 2979 (s), 2918 (s), 2868 (m), 2761 (w), 1685 (m), 1585 (m), 1522 (s), 1473 (m), 1449 (s), 1392 (s), 1366 (s), 1327 (s), 1294 (s), 1285 (s), 1248 (s), 1206 (m), 1172 (s), 1151 (s), 1120 (m), 1084 (s), 1053 (s), 1027 (s), 999 (m), 965 (m), 938 (w), 868 (m), 850 (m), 789 (s), 752 (s), 732 (s), 694 (s), 640 (s), 608 (m), 583 (m), 558 (s), 530 (s) cm^{-1}. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.40 [s, 9 H, $C(CH_3)_3$], 3.45 (br. d, ^3J = 6.05 Hz, 2 H, CH_2SO_2Ph), 3.56 (dd, ^2J = 9.34 Hz, ^3J = 4.95 Hz, 1 H, OC*H*HCH), 3.69 (dd, ^2J = 9.34 Hz, ^3J = 3.71 Hz, 1 H, OCH*H*CH), 4.11–4.23 (m, 1 H, C*H*NH), 4.46 (s, 2 H, $PhCH_2O$), 5.05–5.25 (br. s, 1 H, CHN*H*), 7.22–7.96 (m, 10 H, Ar-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.89 [(CH_3)$_3$C], 46.52 (CHNH), 57.13 (CH_2S), 71.60, 73.90 (CH_2OCH_2), 80.30 [(CH_3)$_3$*C*], 128.36, 128.50, 128.56, 129.07, 129.28, 129.94, 134.41, 138.19 (Ar-C), 155.30 (NHCO). – MS (CI, isobutane): *m*/*z* (%) = 406 (31) [M$^+$+1], 352 (6), 351 (18), 350 (100), 307 (6), 306 (33), 266 (5), 210 (9), 143 (15). – $C_{21}H_{27}NO_5S$ (405.515): calcd. C 62.20, H 6.71, N 3.45; found: C 62.07, H 6.83, N 3.23.

(*R*)-2-Dibenzylaminopropyl Phenyl Sulfone (41): Prepared by method GP 2 by cleavage of hydrazine **19** with $BH_3 \cdot THF$ and subsequent protection of the resulting crude amine with benzyl bromide. Compound **41** was obtained as a colourless oil (1.52 g, 40%, 2 steps). – $[\alpha]_D^{20} = -10.5$ (c = 2.16, $CHCl_3$) – IR ($CHCl_3$): $\tilde{\nu}$ = 3400 (m), 3085 (m), 3062 (m), 3029 (m), 3004 (m), 2971 (m), 2923 (m), 2876 (m), 2806 (m), 1954 (w), 1877 (w), 1812 (w), 1603 (w), 1586 (w), 1495 (s), 1453 (s), 1400 (m), 1375 (m), 1305 (s), 1260 (m), 1207 (m), 1149 (s), 1084 (s), 1024 (s), 911 (w), 841 (w), 797 (w), 746 (s), 699 (s), 625 (m), 595 (m), 587 (m), 570 (s), 545 (m), cm^{-1}. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.30 (d, ^3J = 6.59 Hz, 3 H, CH_3), 3.07 (dd, ^2J = 13.73 Hz, ^3J = 9.06 Hz, 1 H, C*H*HSO$_2$Ph), 3.23–3.34 (m, 1 H, CHN), 3.39 (d, ^2J = 14.01 Hz, 2 H, C*H*HPh), 3.47 (dd, ^2J = 13.73 Hz, ^3J = 2.74 Hz, 1 H, CH*H*SO$_2$Ph), 3.56 (d, ^2J = 14.01 Hz, 2 H, CH*H*Ph), 7.16–7.80 (kB, 15 H, Ar-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.49 (*C*H$_3$CH), 48.88 (CH$_3$*C*H), 53.50 (NCH_2), 59.34 (CH_2S), 126.99, 127.03, 128.28, 128.53, 129.23, 133.49 (Ar-C), 139.00, 139.52 (*ipso*-Ar-C). – MS (EI, 70 eV): *m*/*z* (%) = 379 (2) [M$^+$], 364 (9), 288 (18), 225 (17), 224 (100), 181 (15), 146 (10), 105 (6), 91 (85). – $C_{23}H_{25}NO_2S$: calcd. 379.1606; found 379.1606 (HRMS).

(*R*)-2-Dibenzylaminobutyl Phenyl Sulfone (42): Prepared by method GP 2 by cleavage of hydrazine **20** with $BH_3 \cdot THF$ and subsequent protection of the resulting crude amine with benzyl bromide. Compound **42** was obtained as a colourless solid (3.07 g, 78%, 2 steps). – M.p. 124 °C. – $[\alpha]_D^{20} = +40.3$ (c = 2.16, $CHCl_3$) – IR (KBr): $\tilde{\nu}$ = 2972 (s), 2949 (w), 2923 (s), 2866 (w), 2832 (w), 1958 (w), 1809 (w), 1602 (s), 1494 (s), 1448 (w), 1401 (w), 1380 (s), 1359 (s), 1316 (w), 1301 (s), 1249 (w), 1199 (s), 1146 (s), 1083 (s), 1028 (s), 985 (w), 965 (w), 953 (w), 928 (w), 907 (w), 856 (w), 836 (s), 791 (s), 745 (s), 727 (w), 698 (s), 687 (w), 622 (s), 589 (s), 566 (s), 548 (m), 526 (w), 495 (w), 468 (m) cm^{-1}. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.88 (t, ^3J = 7.00 Hz, 3 H, C*H*$_3$CH$_2$), 1.52–1.78 (m, 2 H, CH$_3$C*H*$_2$), 2.96 (dd, ^2J = 13.54 Hz, ^3J = 8.24 Hz, 1 H, C*H*HSO$_2$Ph), 3.02–3.11 (m, 1 H, C*H*CH$_2$SO$_2$Ph), 3.22 (d, ^2J = 13.74 Hz, 2 H, C*H*HPh), 3.49 (dd, ^2J = 13.54 Hz, ^3J = 2.20 Hz, 1 H, CH*H*SO$_2$Ph), 3.67 (d, ^2J = 13.74 Hz, 2 H, CH*H*Ph), 7.18–7.85 (m, 15 H, Ar-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.30 (*C*H$_3$CH$_2$), 25.60 (CH$_3$*C*H$_2$), 53.32 (NCH_2), 54.90 (CHN), 56.05 (CH_2S), 127.02, 128.02, 128.19, 128.92, 129.32, 129.34 (Ar-C), 138.95, 139.84 (*ipso*-Ar-C). – MS (CI, isobutane): *m*/*z* (%) = 394 (100) [M$^+$+1], 304 (4), 254 (2), 162 (2). – $C_{24}H_{27}NO_2S$ (393.550): calcd. C 73.25, H 6.92, N 3.56; found: C 72.83, H 6.98, N 3.41.

(*R*)-2-Dibenzylamino-3-methylbutyl Phenyl Sulfone (43): Prepared by method GP 2 by cleavage of hydrazine **21** with $BH_3 \cdot THF$ and subsequent protection of the resulting crude amine with benzyl bromide. Compound **43** was obtained as a colourless solid (1.75 g, 43%, 2 steps). – M.p. 112 °C. – $[\alpha]_D^{20} = +31.0$ (c = 1.05, $CHCl_3$) – IR ($CHCl_3$): $\tilde{\nu}$ = 3085 (w), 3062 (m), 3028 (m), 2961 (m), 2931 (m), 2873 (m), 2839 (w), 2803 (w), 1585 (w), 1494 (m), 1466 (m), 1447 (s), 1402 (w), 1386 (m), 1364 (m), 1307 (s), 1255 (m), 1205 (m), 1150 (s), 1087 (s), 1070 (m), 1028 (m), 999 (m), 974 (m), 924 (w), 690 (s), 668 (w), 647 (w), 632 (w), 614 (w), 588 (s), 572 (m), 558 (m), 523 (w), 486 (w), 465 (w) cm^{-1}. – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.78 (d, ^3J = 6.87 Hz, 3 H, C*H*$_3$(CH$_3$)CH), 0.95 [d, ^3J = 6.60 Hz, 3 H, CH$_3$(C*H*$_3$)CH], 1.81–1.93 [m, 1 H, (CH$_3$)$_2$C*H*], 3.08–3.15 (m, 2 H, C*H*$_2$SO$_2$Ph), 3.43–3.50 (m, 1 H, CHN), 3.47 (d, ^2J = 13.47 Hz, 2 H, C*H*HPh), 3.69 (d, ^2J = 13.47 Hz, 2 H, CH*H*Ph), 7.20–7.88 (m, 15 H, Ar-H). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.91, 20.09 [(*C*H$_3$)$_2$CH], 31.59 [(CH$_3$)$_2$*C*H], 54.65 (NCH_2), 54.79 (CH_2S), 58.34 (CHN), 127.00, 127.88, 128.16, 129.19, 129.32, 133.52 (Ar-C), 139.21, 140.38 (*ipso*-Ar-C). – MS (EI, 70 eV): *m*/*z* (%) = 407 (1) [M$^+$], 367 (2), 366 (8), 365 (17), 364 (100), 252 (2), 238 (2), 223 (2), 222 (3), 181 (9), 132 (8), 129 (2), 105 (3), 104 (2), 92 (6), 91 (70), 78 (2), 77 (5), 65 (5), 51 (2). – $C_{25}H_{29}NO_2S$ (407.575): calcd. C 73.67, H 7.12, N 3.44; found: C 73.43, H 7.34, N 3.34.

(*R*)-2-Dibenzylamino-4-methylpentyl Phenyl Sulfone (44): Prepared by method GP 2 by cleavage of hydrazine **23** with $BH_3 \cdot THF$ and subsequent protection of the resulting crude amine with benzyl bromide. Compound **42** was obtained as a colourless oil (3.12 g, 74%, 2 steps). – $[\alpha]_D^{20} = +22.9$ (c = 4.97, $CHCl_3$) – IR (KBr): $\tilde{\nu}$ = 3085 (w), 3063 (m), 3029 (m), 2952 (s), 2922 (s), 2867 (m), 2838 (m), 2812 (m), 1603 (w), 1586 (w), 1495 (m), 1468 (m), 1447 (s), 1407 (m), 1384 (m), 1384 (m), 1364 (m), 1323 (s), 1303 (s), 1276 (m), 1247 (m), 1208 (w), 1189 (m), 1147 (s), 1117 (m), 1085 (s), 1075 (m), 1047 (w), 1028 (m), 986 (m), 959 (m), 921 (w), 907 (w), 854 (m), 828 (w), 802 (w), 783 (m), 747 (s), 732 (s), 719 (s), 699 (s), 687 (s) cm^{-1}. – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.36 [d, ^3J = 6.60 Hz, 3 H, C*H*$_3$(CH$_3$)CH], 0.79 [d, ^3J = 6.60 Hz, 3 H, CH$_3$(C*H*$_3$)CH], 1.24–1.32 [m, 1 H, (CH$_3$)$_2$CHC*H*H], 1.57–1.65 [m, 1 H, (CH$_3$)$_2$CHCH*H*], 1.77–1.88 [m, 1 H, (CH$_3$)$_2$C*H*], 2.93 (dd, ^2J = 14.02 Hz, ^3J = 8.52 Hz, 1 H, C*H*HSO$_2$Ph), 3.11–3.17 (m, 1 H, CHN), 3.17 (d, ^2J = 13.47 Hz, 2 H, C*H*HPh), 3.51 (dd, ^2J = 14.02 Hz, ^3J = 2.20 Hz, 1 H, CH*H*SO$_2$Ph), 3.65 (d, ^2J = 13.47 Hz, 2 H, CH*H*Ph), 7.16–7.84 (m, 15 H, Ar-H). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.79, 23.62 [(*C*H$_3$)$_2$CH], 24.00 [(CH$_3$)$_2$*C*H], 41.69 [(CH$_3$)$_2$CH*C*H$_2$] 50.93 (CHN), 53.31 (NCH_2), 55.84 (CH_2S), 127.04, 127.97, 128.06, 129.12, 129.36 (Ar-H), 139.00, 139.62 (*ipso*-Ar-H). – MS (EI, 70 eV): *m*/*z* (%) = 421 (3) [M$^+$], 366 (7), 365 (21), 364 (82), 330 (16), 267 (11), 266 (53), 196 (6), 121 (12), 132 (9), 106 (6), 92 (9), 91 (100), 77 (5), 65 (5), 57 (3). – $C_{26}H_{31}NO_2S$ (421.604): calcd. C 74.07, H 7.41, N 3.32; found: C 73.86, H 7.361, N 3.33.

(*R*)-2-Dibenzylamino-3-benzyloxypropyl Phenyl Sulfone (45): Prepared by method GP 2 by cleavage of hydrazine **26** with $BH_3 \cdot THF$ and subsequent protection of the resulting crude amine with benzyl bromide. Compound **45** was obtained as a colourless solid (2.96 g,

61%, 2 steps). – $[\alpha]_D^{20} = -30.2$ ($c = 1.39$, $CHCl_3$) – IR (film): $\tilde{\nu}$ = 3753 (w), 3524 (w), 3394 (w), 3167 (w), 3086 (m), 3062 (s), 3029 (s), 3005 (m), 2925 (s), 2860 (s), 2806 (m), 2721 (w), 1603 (m), 1586 (m), 1545 (w), 1495 (s), 1448 (s), 1364 (s), 1306 (s), 1254 (m), 1205 (m), 1150 (s), 1105 (s), 1087 (s), 1074 (s), 1028 (s), 1001 (m), 974 (m), 910 (m), 860 (m), 798 (m), 748 (s), 720 (s), 699 (s), 672 (w), 622 (m), 588 (m) cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 3.33–3.78 (m, 5 H, CH_2CHC$H_2$$SO_2$Ph), 3.52 (d, ^2J = 14.29 Hz, 2 H, CHHPh), 3.74 (d, ^2J = 13.74 Hz, 2 H, CHHPh), 4.39 (s, 2 H, CH_2O), 7.15–7.79 (20 H, Ar-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.88 (CHN), 54.04 (CH_2S), 54.73 (NCH_2), 70.57, 73.09 (CH_2OCH_2), 127.00, 127.56, 127.59, 127.83, 128.34, 128.53, 128.74, 129.22, 133.48 (Ar-C), 138.07, 139.23, 139.67 (*ipso*-Ar-C). – MS (CI, isobutane): *m*/*z* (%) = 487 (31) [M^++1], 486 (100) [M^+], 419 (3), 396 (3), 364 (6), 346 (36), 332 (6), 291 (4), 254 (11), 198 (10), 143 (16), 107 (11). – $C_{22}H_{22}NO_2S$ ($M^+ - C_8H_9O$): calcd. 364.1371; found 364.1370 (HRMS).

General Procedure for the Synthesis of *N*,*N*-Dibenzyl-Protected α-Alkylated β-Amino Sulfones (46–53, GP 3): In a typical experiment the *N*,*N*-dibenzyl-protected β-amino sulfone **41**−**45** (5 mmol) was dissolved in THF (25 mL) and added dropwise to a solution of LDA (6.5 mmol) in THF (10 mL) at –78 °C under an atmosphere of argon. Tetramethylethylendiamine (TMEDA) (6.5 mmol) was added, and the reaction mixture stirred at –78 °C for 4 h. The corresponding electrophile (7.0 mmol, MeI: **46**,**47**,**50**,**51**,**53**, EtI: **48**,**52**, BnBr: **49**) was slowly added (neat) and the solution stirred for 1 h at –78 °C and then overnight at room temperature. After quenching with pH-7-buffer, the aqueous phase was extracted three times with Et_2O. The combined organic phases were washed with brine, dried with $MgSO_4$, and the solvent removed under reduced pressure. Purification by column chromatography (SiO_2, pentane/Et_2O mixtures) afforded products **46**−**53** as colourless oils.

(*R*,*R*)-2-Dibenzylamino-1-methylpropyl Phenyl Sulfone (46): The *N*,*N*-dibenzyl-protected β-amino sulfone **41** was metallated with LDA and allowed to react with iodomethane by the method described in GP 3 to yield product **46** as a colourless oil (1.42 g, 91%, *de* = 70% (≥ 98% after recryst. from CH_2Cl_2/*n*-hexane)). – Major diastereoisomer: M.p. 112 °C. – $[\alpha]_D^{20} = -1.4$ ($c = 1.43$, $CHCl_3$) – IR ($CHCl_3$): $\tilde{\nu}$ = 3528 (w), 3388 (m), 3085 (m), 3062 (m), 3027 (m), 2927 (m), 2940 (m), 2880 (m), 2831 (m), 2831 (m), 2803 (m), 1603 (w), 1585 (w), 1494 (m), 1447 (s), 1383 (m), 1362 (m), 1304 (s), 1235 (m), 1219 (m), 1147 (s), 1084 (s), 1075 (s), 1050 (m), 1027 (m), 1000 (m), 970 (w), 944 (w), 909 (w), 875 (w), 841 (w), 819 (w), 751 (s), 732 (s), 699 (s), 668 (w), 626 (m), 597 (m), 588 (m), 574 (m), 551 (m), 530 (m), 506 (w), 465 (w) cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 1.19 (d, ^3J = 7.14 Hz, 3 H, CH_3), 1.36 (d, ^3J = 7.14 Hz, 3 H, CH_3), 3.43 (dq, $^3J_1$ = 7.14 Hz, $^3J_2$ = 2.21 Hz, 1 H, CH_3CHN), 3.48 (d, ^2J = 13.73 Hz, 2 H, CHHPh), 3.62 (dq, $^3J_1$ = 7.14 Hz, $^3J_2$ = 1.92 Hz, 1 H, C$H$$SO_2$Ph), 3.65 (d, ^2J = 14.01 Hz, 2 H, CHHPh), 7.41–7.74 (m, 15 H, Ar-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.13, 12.73 (2 × CH_3), 51.19 (CHN), 54.15 (NCH_2), 60.78 (CHS), 126.96, 128.57, 128.23, 128.50, 129.07, 133.44 (Ar-C), 137.97, 139.44 (*ipso*-Ar-C). – MS (EI, 70 eV): *m*/*z* (%) = 393 (1, M^+), 236 (6), 225 (18), 224 (100), 181 (8), 91 (65), 65 (5). – $C_{24}H_{27}NO_2S$ (393.550): calcd. C 73.25, H 6.92, N 3.56; found: C 73.18, H 6.65, N 3.54.

(*R*,*R*)-2-Dibenzylamino-1-methylbutyl Phenyl Sulfone (47): The *N*,*N*-dibenzyl-protected β-amino sulfone **42** was metallated with LDA and allowed to react with iodomethane by the method described in GP 3 to yield product **47** as a colourless solid (1.94 g, 95%, *de* = 70%). – M.p. 105 °C. – $[\alpha]_D^{20} = +54.7$ ($c = 1.30$, $CHCl_3$) – IR ($CHCl_3$): $\tilde{\nu}$ = 3085 (w), 3062 (m), 3028 (s), 2962 (w), 2933 (w), 2873 (w), 2801 (w), 2732 (w), 2605 (w), 2336 (w), 1952 (w), 1899 (w), 1814 (w), 1729 (w), 1601 (s), 1494 (s), 1448 (s), 1361 (w), 1304 (s), 1240 (m), 1218 (w), 1146 (s), 1102 (w), 1085 (s), 1027 (s), 1001 (s), 962 (s), 912 (s), 867 (s), 848 (m), 825 (w), 750 (s), 699 (s), 668 (s), 625 (s), 594 (w), 572 (s), 551 (s), 522 (s), 487 (w), 464 (w) cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$): δ = 0.89 (t, ^3J = 7.17 Hz, 3 H, C$H_3$$CH_2$), 1.24–1.38 (m, 1 H, CH_3CHH), 1.35 (d, ^3J = 7.33 Hz, 3 H, CH_3CH), 1.54–1.66 (m, 1 H, CH_3CHH), 3.29 (d, ^2J = 13.42 Hz, 2 H, CHHPh), 3.38 (dd, $^3J_1$ = 11.60 Hz, $^3J_2$ = 2.75 Hz, 1 H, CHCHSO_2Ph), 3.52 (q, ^3J = 7.32 Hz, 1 H, C$H$$SO_2$Ph), 3.79 (d, ^2J = 13.42 Hz, 1 H, CHHPh), 7.17–7.24 (m, 2 H, CH_2-*p*-Ar-H), 7.24–7.31 (m, 8 H, CH_2-*m*-Ar-H, CH_2-*o*-Ar-H), 7.46–7.52 (m, 2 H, SO_2-*m*-Ar-H), 7.57–7.62 (m, 1 H, SO_2-*p*-Ar-H), 7.76–7.80 (m, 2 H, SO_2-*o*-Ar-H). – ^{13}C NMR (125 MHz, $CDCl_3$): δ = 11.52 ($C$$H_3$$CH_2$), 11.58 ($CH_3CH$), 20.76 ($CH_3$$CH_2$), 53.38 ($NCH_2$), 56.43 (CHN), 58.10 (CHS), 126.87, 128.00, 128.63, 128.88, 128.98, 133.48 (Ar-C), 137.73, 139.25 (*ipso*-Ar-C). – MS (CI, isobutane): *m*/*z* (%) = 408 (100) [M^++1], 268 (6), 266 (6), 238 (4). – $C_{25}H_{29}NO_2S$ (407.577): calcd. C 73.67, H 7.17, N 3.44; found: C 73.47, H 7.09, N 3.40.

(*R*,*R*)-2-Dibenzylamino-1-ethylbutyl Phenyl Sulfone (48): The *N*,*N*-dibenzyl-protected β-amino sulfone **42** was metallated with LDA and allowed to react with iodoethane by the method described in GP 3 to yield product **48** as a colourless oil [2.04 g, 97%, *de* = 68% (>97% after recryst. from CH_2Cl_2/*n*-hexane)]. – Major diastereoisomer: M.p. 108 °C. – $[\alpha]_D^{20} = +19.9$ ($c = 1.23$, $CHCl_3$) – IR (film): $\tilde{\nu}$ = 3085 (m), 3062 (m), 3029 (m), 2965 (s), 2934 (s), 2876 (m), 2801 (m), 2254 (w), 1602 (w), 1585 (w), 1494 (m), 1449 (s), 1377 (m), 1363 (m), 1303 (s), 1255 (m), 2111 (m), 1145 (s), 1085 (s), 1045 (m), 1028 (m), 963 (s), 911 (w), 865 (w), 824 (w), 730 (s), 699 (s), 624 (s), 609 (m), 587 (m), 574 (s), 551 (m), 526 (m), 466 (w) cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 0.83 (t, ^3J = 7.19 Hz, 3 H, CH_3), 0.98 (t, ^3J = 7.41 Hz, 3 H, CH_3), 1.16–1.96 (m, 4 H, 2 × CH_3CH_2), 3.19–3.26 (m, 2 H, CHC$H$$SO_2$Ph), 2.28 (d, ^2J = 13.74 Hz, 2 H, CHHPh), 3.78 (d, ^2J = 13.46 Hz, 2 H, CHHPh), 7.18–7.80 (m, 15 H, Ar-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.92, 13.41 (2 × $C$$H_3$$CH_2$), 18.80, 20.91 (2 × CH_3CH_2), 53.48 (NCH_2), 58.44 (CHN), 65.77 (CHS), 126.89, 128.89, 128.07, 129.01, 129.13, 133.54 (Ar-C), 138.72, 139.33 (*ipso*-Ar-C). – MS (CI, isobutane): *m*/*z* (%) = 422 (100) [M^++1], 296 (7), 283 (10), 280 (18), 268 (5), 192 (2), 190 (8). – $C_{24}H_{27}NO_2S$ (421.037): calcd. C 73.25, H 6.92, N 3.56; found: C 73.18, H 6.65, N 3.54.

(*R*,*R*)-2-Dibenzylamino-1-benzylbutyl Phenyl Sulfone (49): The *N*,*N*-dibenzyl-protected β-amino sulfone **42** was metallated with LDA and allowed to react with benzyl bromide by the method described in GP 3 to yield product **49** as a colourless oil [2.13 g, 88%, *de* = 64% (> 97% after recryst. from CH_2Cl_2/*n*-hexane)]. – Major diastereoisomer: M.p. 133 °C. – $[\alpha]_D^{20} = +45.8$ ($c = 3.00$, $CHCl_3$) – IR (film): $\tilde{\nu}$ = 3534 (m), 3165 (w), 3085 (s), 3062 (s), 3029 (s), 3005 (s), 2966 (s), 2932 (s), 2874 (s), 2833 (s), 2801 (s), 2729 (m), 2606 (w), 2253 (w), 1953 (w), 1889 (w), 1811 (w), 1603 (s), 1586 (m), 1495 (s), 1451 (s), 13.65 (s), 1303 (s), 1253 (s), 1207 (s), 1144 (s), 1084 (s), 1046 (s), 1028 (s), 1000 (m), 972 (s), 911 (s), 872 (m), 826 (w), 734 (s), 698 (s), 647 (w), 624 (s), 612 (s), 584 (s), 553 (s), 532 (m) cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 0.98 (t, ^3J = 7.14 Hz, 3 H, CH_3), 1.53–1.68 (m, 1 H, CH_3CHH), 1.72–87 (m, 1 H, CH_3CHH), 3.15 (dd, ^2J = 15.66 Hz, ^3J = 4.67 Hz, 1 H, PhCHHCH), 3.26 (dd, ^2J = 15.93 Hz, ^3J = 7.30 Hz, 1 H, PhCHHCH), 3.34 (d, ^2J = 13.73 Hz, 2 H, NCHHPh), 3.56–3.85 (m, 2 H, CHC$H$$SO_2$Ph), 3.72 (d, ^2J = 13.74 Hz, 2 H, NCHHPh), 6.68–7.60 (m, 20 H, Ar-H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 12.16 (CH_3), 21.70 (CH_3CH_2), 31.25 (CHCH_2), 54.18 (NCH_2),

58.58 (CHN), 65.42 (CHS), 126.47, 126.98, 128.17, 128.41, 128.46, 128.64, 128.88, 128.94, 133.94 (Ar-C), 138.26, 139.20, 133.39 (*ipso*-Ar-C). – MS (CI, isobutane): *m*/*z* (%) = 484 (100) [M^++1], 394 (20), 342 (5), 287 (7), 247 (7), 238 (16). – $C_{31}H_{33}NO_2S$, (483.675): calcd. C 76.98, H 6.88, N 2.90; found: C 76.76, H 6.93, N 2.82.

(*R*,*R*)-2-Dibenzylamino-1,3-dimethylbutyl Phenyl Sulfone (50): The *N*,*N*-dibenzyl-protected β-amino sulfone **43** was metallated with LDA and allowed to react with iodomethane by the method described in GP 3 to yield product **50** as a colourless oil [1.96 g, 93%, *de* = 50% (≥ 96% after HPLC)]. – Major diastereoisomer: M.p. 134 °C. – $[\alpha]_D^{20}$ = +117.7 (*c* = 0.30, $CHCl_3$) – IR (KBr): $\tilde{\nu}$ = 3404 (w), 3063 (m), 3028 (m), 2993 (m), 2959 (m), 2926 (m), 2788 (m), 2704 (w), 1602 (w), 1585 (w), 1495 (m), 1448 (s), 1384 (m), 1384 (m), 1362 (m), 1304 (s), 1237 (m), 1207 (w), 1144 (s), 1087 (s), 1071 (m), 1044 (w), 1027 (m), 1009 (m), 970 (m), 910 (w), 861 (m), 844 (w), 805 (w), 766 (m), 754 (s), 736 (s), 701 (s), 692 (s), 497 (w), 466 (w) cm^{-1}. – ^1H NMR (500 MHz, $CDCl_3$): δ = 0.92 [d, ^3J = 6.60 Hz, 3 H, CH_3(CH$_3$)CH], 1.10 [d, ^3J = 6.60 Hz, 3 H, CH$_3$(CH_3)CH], 1.39 (d, ^3J = 7.14 Hz, 3 H, CH_3CHSO$_2$Ph), 1.82–2.01 [m, 1 H, (CH$_3$)$_2$C*H*], 3.29 (d, ^2J = 13.16 Hz, 2 H, C*H*HPh), 3.37 (d, ^3J = 9.61 Hz, 1 H, C*H*CHSO$_2$Ph), 3.51 (q, ^3J = 7.23 Hz, 1 H, CHC*H*SO$_2$Ph), 3.91 (d, ^2J = 13.46 Hz, 2 H, CH*H*Ph), 7.20–7.98 (m, 15 H, Ar-H). – ^{13}C NMR (125 MHz, $CDCl_3$): δ = 12.01 (*C*H$_3$CH), 21.29, 21.31 [(*C*H$_3$)$_2$CH], 27.11 [(CH$_3$)$_2$*C*H], 53.88 (NCH$_2$), 59.10, 60.28 (CHCHS), 127.03, 128.08, 128.10, 129.03, 129.20, 133.41 (Ar-C), 139.15, 139.59 (*ipso*-Ar-C) – MS (CI, isobutane): *m*/*z* (%) = 422 (100) [M^++1], 296 (9), 282 (15), 281 (8), 280 (30), 190 (21). – $C_{26}H_{31}NO_2S$ (421.604): calcd. C 74.07, H 7.41, N 3.32; found: C 73.70, H 7.53, N 3.29.

(*R*,*R*)-2-Dibenzylamino-1,4-dimethylpentyl Phenyl Sulfone (51): The *N*,*N*-dibenzyl-protected β-amino sulfone **44** was metallated with LDA and allowed to react with iodomethane by the method described in GP 3 to yield product **51** as a colourless oil [1.96 g, 93%, *de* = 90% (≥ 96% after recryst. from CH_2Cl_2/*n*-hexane)]. – Major diastereoisomer: M.p. 128 °C. – $[\alpha]_D^{20}$ = +40.6 (*c* = 1.40, $CHCl_3$) – IR (KBr): $\tilde{\nu}$ = 3083 (w), 3059 (m), 3027 (m), 3001 (w), 2959 (s), 2942 (s), 2926 (s), 2905 (s), 2866 (m), 2833 (m), 2817 (m), 2796 (m), 2712 (w), 1602 (w), 1585 (w), 1495 (m), 1471 (m), 1447 (s), 1401 (w), 1383 (m), 1366 (m), 1341 (m), 1305 (s), 1295 (s), 1270 (m), 1234 (m), 1207 (m), 1163 (s), 1150 (s), 1080 (s), 1020 (s), 970 (m), 860 (m), 825 (m), 765 (m), 750 (s), 740 (s), 700 (s), 630 (s), 600 (s), 570 (s), 560 (s), 530 (m) cm^{-1}. – ^1H NMR (400 MHz, $CDCl_3$): δ = 0.35 [d, ^3J = 6.60 Hz, 3 H, CH_3(CH$_3$)CH], 0.87 [d, ^3J = 6.87 Hz, 3 H, CH$_3$(CH_3)CH], 0.90–1.99 [m, 3 H, (CH$_3$)$_2$C*H*CH_2], 1.38 (d, ^3J = 7.42 Hz, 3 H, CH_3CHSO$_2$Ph), 3.27 (d, ^2J = 13.19 Hz, 2 H, C*H*HPh), 3.52–3.59 (m, 2 H, C*H*C*H*SO$_2$Ph), 3.78 (d, ^2J = 13.20 Hz, 2 H, CH*H*Ph), 7.17–7.85 (m, 15 H, Ar-H). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.11 (*C*H$_3$CH), 20.50, 23.94 [(*C*H$_3$)$_2$CH], 24.26 [(CH$_3$)$_2$*C*H], 37.00 [(CH$_3$)$_2$CH*C*H$_2$], 52.21 (CHS), 53.45 (NCH$_2$), 58.00 (CHN), 127.00, 128.11, 128.62, 129,01, 129.21, 130.99 (Ar-C), 137.97, 139.39 (*ipso*-Ar-C). – MS (CI, isobutane): *m*/*z* (%) = 436 (100) [M^++1], 346 (6), 296 (18), 295 (5), 294 (5), 266 (12), 204 (4), 190 (9), 143 (7). – $C_{27}H_{33}NO_2S$ (435.628): calcd. C 74.44, H 7.64, N 3.22; found: C 74.20, H 7.36, N 3.11.

(*R*,*R*)-2-Dibenzylamino-1-ethyl-4-methylpentyl Phenyl Sulfone (52): The *N*,*N*-dibenzyl-protected β-amino sulfone **44** was metallated with LDA and allowed to react with iodomethane by the method described in GP 3 to yield product **52** as a colourless oil [1.98 g, 88%, *de* = 50% (≥ 96% after recryst. from CH_2Cl_2/*n*-hexane)]. – Major diastereoisomer: M.p. 131 °C. – $[\alpha]_D^{20}$ = +24.8 (*c* = 0.77, $CHCl_3$) – IR (KBr): $\tilde{\nu}$ = 3425 (m), 3058 (m), 3028 (m), 2956 (s), 2899 (s), 2873 (s), 2815 (m), 2801 (m), 2226 (w), 1960 (w), 1898 (w), 1813 (w), 1703 (w), 1639 (w), 1601 (m), 1585 (m), 1546 (w), 1495 (m), 1448 (s), 1381 (m), 1368 (s), 1347 (m), 1305 (s), 1282 (s), 1209 (m), 1146 (s), 1085 (s), 1026 (m), 1000 (m), 967 (s), 917 (m), 856 (m), 830 (w), 748 (s), 727 (s), 696 (s), 626 (s), 610 (m), 573 (s), 536 (s), 494 (m), 469 (w) cm^{-1}. – ^1H NMR (400 MHz, $CDCl_3$): δ = 0.38 [d, ^3J = 6.32 Hz, 3 H, CH_3(CH$_3$)CH], 0.86 [d, ^3J = 6.59 Hz, CH$_3$(CH_3)CH], 0.93–1.08 [m, 1 H, (CH$_3$)$_2$C*H*], 0.96 (t, ^3J = 7.29 Hz, 3 H, CH_3CH$_2$), 1.56–1.95 [m, 4 H, CH$_3$CH_2, (CH$_3$)$_2$CHCH_2], 3.21–3.27 (m, 3 H, C*H*HPh, C*H*SO$_2$Ph), 3.40 (d, ^3J = 10.17 Hz, 1 H, CHN), 3.77 (d, ^2J = 13.20 Hz, 2 H, CH*H*Ph), 7.16–7.86 (m, 15 H, Ar-H). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.42 (*C*H$_3$CH$_2$), 18.59 (CH$_3$*C*H$_2$), 20.72, 24.19 [(*C*H$_3$)$_2$CH], 24.31 [(CH$_3$)$_2$*C*H], 37.05 [(CH$_3$)$_2$CH*C*H$_2$], 53.49 (NCH$_2$), 54.04 (CHN), 65.39 (CHS), 127.01, 128.12, 128.95, 129.18, 129.26, 133.57 (Ar-C), 139.20, 139.43 (*ipso*-Ar-C). – MS (CI, isobutane): *m*/*z* (%) = 450 (100) [M^++1], 360 (9), 311 (5), 310 (22), 309 (7), 308 (23), 266 (10), 218 (8), 143 (32). – $C_{28}H_{35}NO_2S$ (449.655): calcd. C 74.79, H 7.85, N 3.12; found: C 74.49, H 7.85, N 3.06.

(*R*,*R*)-2-Dibenzylamino-3-benzyloxy-1-methylpropyl Phenyl Sulfone (53): The *N*,*N*-dibenzyl-protected β-amino sulfone **45** was metallated with LDA and allowed to react with iodomethane by the method described in GP 3 to yield product **53** as a colourless oil [2.42 g, 97%, *de* = 68% (≥ 96% after column chromatography)]. – Major diastereoisomer: – $[\alpha]_D^{20}$= –12.1 (*c* = 1.16, $CHCl_3$) – IR ($CHCl_3$): $\tilde{\nu}$ = 3535 (w), 3085 (m), 3063 (m), 3028 (s), 2928 (m), 2862 (m), 2805 (m), 1603 (w), 1586 (w), 1495 (m), 1450 (s), 1364 (m), 1305 (s), 1253 (m), 1218 (m), 1147 (s), 1107 (s), 1085 (s), 1028 (m), 1000 (m), 910 (w), 872 (w), 800 (w), 752 (s), 699 (s), 668 (m), 624 (m), 593 (m), 571 (w), 538 (w) cm^{-1}. – ^1H NMR (400 MHz, $CDCl_3$): δ = 1.31 (d, ^3J = 7.43 Hz, 3 H, CH_3CH), 3.45 (qd, $^3J_1$ = 7.42 Hz, $^3J_2$ = 2.75 Hz, 1 H, CH$_3$C*H*), 3.66–3.89 (m, 7 H, OCH_2C*H*, NCH_2Ph), 4.42 (d, ^2J = 12.10 Hz, 1 H, OC*H*HPh), 4.48 (d, ^2J = 11.82 Hz, 1 H, OCH*H*Ph), 7.17–7.87 (m, 20 H, Ar-H). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.80 (CH$_3$), 55.11 (NCH$_2$), 55.71, 60.57 (*C*H*C*HS), 68.21, 72.96 (CH$_2$OCH$_2$), 126.92, 127.53, 127.58, 128.62, 128.13, 128.58, 128.83, 129.02, 133.42 (Ar-C), 138.07, 138.29, 139.56 (*ipso*-Ar-C). – MS (CI, isobutane): *m*/*z* (%) = 500 (100) [M^++1], 408 (5), 394 (32), 360 (20), 358 (11), 289 (7), 198 (7), 143 (17). – $C_{23}H_{24}NO_2S$ (M^+ – C_8H_9O): calcd. 378.1528; found 378.1528 (HRMS).

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[1] [1a] N. S. Simpkins, in: *Sulfones in Organic Synthesis, Tetrahedron Organic Chemistry Series, Vol. 10* (Eds.: J. E. Baldwin, P. D. Magnus), Pergamon, Oxford, **1993**. – [1b] *The Chemistry of Functional Groups: The Chemistry of Sulfones and Sulfoxides* (Eds.: S. Patai, Z. Rappoport, C. J. Stirling), Wiley, Chichester, **1988**. – [1c] K. Schank, *Methoden Org. Chem. (Houben-Weyl) 4th ed.* **1985**, Vol. E11/2, p. 1132–1136. – [1d] T. Durst, in: *Comprehensive Organic Chemistry, Vol. 3* (Eds.: D. H. R. Barton, W. D. Ollis), Pergamon, Oxford, **1979**, p. 171–213. – [1e] N. S. Simpkins, *Tetrahedron* **1990**, *46*, 6951–6984. – [1f] L. Field, *Synthesis* **1978**, 713–740.

[2] [2a] M. Schäfer, K. Drauz, M. Schwarm, *Methoden Org. Chem. (Houben- Weyl) 4th ed.* **1995**, vol. E21/5, pp. 5588–5642. – [2b] P. Perlmutter, in: *Conjugate Addition Reactions in Organic Synthesis, Tetrahedron Organic Chemistry Series, Vol. 9* (Eds.: J. E. Baldwin P. D. Magnus), Pergamon, Oxford, **1992**. – [2c] D. Enders, H. Wahl, W. Bettray, *Angew. Chem.* **1995**, *107*, 527–529;

Angew. Chem. Int. Ed. Engl. **1995**, *34*, 527–529, and references cited therein.
[3] [3a] D. Braghiroli, R. Avallone, M. D. Di Bella, *Tetrahedron: Asymmetry* **1997**, *8*, 2209–2213. – [3b] H. Nakamura, H. Wu, J. Kobayashi, M. Kobayashi, Y. Ohizumi, Y. Hirata, *J. Org. Chem.* **1985**, *50*, 2494–2497. – [3c] Y. Ichikawa, *Tetrahedron Lett.* **1988**, *29*, 4957–4958. – [3d] B. Beagley, P. H. Crackett, R. G. Pritchard, R. J. Stoodley, *J. Chem. Soc., Perkin Trans. 1* **1990**, 773–781. – [3e] Y. Girard, M. Larue, T. R. Jones, J. Rokach, *Tetrahedron Lett.* **1982**, *23*, 1023–1026.
[4] N. A. Sasaki, M. Dockner, A. Chiaroni, C. Riche, P. Potier, *J. Org. Chem.* **1997**, *62*, 765–770, and references cited therein.
[5] R. Pauly, A. Sasaki, P. Portier, *Tetrahedron Lett.* **1994**, *35*, 237–240.
[6] M. Hirama, H. Hioki, S. Ito, *Tetrahedron Lett.* **1988**, *29*, 3125–3128.
[7] J. de Blas, J. C. Carretero, E. Domínguez, *Tetrahedron Lett.* **1994**, *35*, 4603–4606.
[8] J. C. Wu, T. Pathak, W. Tong, J. M. Vial, G. Remaud, J. Chattopadhyaya, *Tetrahedron* **1988**, *44*, 6705–6722.
[9] [9a] J. C. Carretero, R. G. Arrayás, *Synlett* **1999**, 49–52. – [9b] J. de Vincente, R. G. Arrayás, J. C. Carretero, *Tetrahedron Lett.* **1999**, 40, 6083–6086. – [9c] J. C. Carretero, R. G. Arrayás, J. S. de Garcia, *Tetrahedron Lett.* **1997**, *38*, 8537–8540.
[10] D. DiPetro, R. M. Borzilleri, S. M. Weinreb, *J. Org. Chem.* **1994**, *59*, 5856–5857.
[11] D. A. Alonso, A. Costa, B. Mancheño, C. Najerá, *Tetrahedron* **1997**, *53*, 4791–4814.
[12] R. Giovannini, M. Petrini, *Synlett* **1997**, 90–92.
[13] [13a] R. Tanikaga, N. Shibata, T. Yoneda, *J. Chem. Soc., Perkin Trans. 1* **1997**, 2253–2257. – [13b] R. V. M. Campbell, L. Crombie, D. Findley, R. W. King, G. Pattenden, D. A. Whiting, *J. Chem. Soc., Perkin Trans. 1* **1975**, 897–913.
[14] Recent examples: [14a] D. W. Knight, A. W. Sibley, *J. Chem. Soc., Perkin Trans. 1* **1997**, 2179–2187. – [14b] D. J. Hart, J. Li, W.-L. Wu, A. P. Kozikowski, *J. Org. Chem.* **1997**, *62*, 5023–5033. – [14c] N. Magnus, P. Magnus, *Tetrahedron Lett.* **1997**, *38*, 3491–3494. – [14d] A. Solladié-Cavallo, D. Roche, J. Fischer, A. De Cian, *J. Org. Chem.* **1996**, *61*, 2690–2694. – [14e] I. E. Markó, F. Murphy, S. Dolan, *Tetrahedron Lett.* **1996**, *37*, 2089–2092.
[15] Recent examples: [15a] H. Tanimoto, T. Oritani, *Tetrahedron* **1997**, *53*, 3527–3536. – [15b] D. A. Alonso, L. R. Falvello, B. Mancheño, C. Nájera, M. Tomás, *J. Org. Chem.* **1996**, *61*, 5004–5012. – [15c] P. Bonete, C. Nájera, *Tetrahedron* **1996**, *52*, 4111–4122. – [15d] T. A. Houston, M. Koreeda, *Synth. Commun.* **1994**, *24*, 393–398. – [15e] S. H. Pine, G. Shen, J. Bautista, C. Sutton, Jr., W. Yamada, L. Apodaca, *J. Org. Chem.* **1990**, *55*, 2234–2237. – [15f] M. Isobe, J. Obeyama, Y. Funabashi, T. Goto, *Tetrahedron Lett.* **1988**, *29*, 4773–4776.
[16] [16a] C. J. M. Stirling, S. T. McDowell, *J. Chem. Soc. B* **1967**, 343–348. – [16b] C. J. M. Stirling, S. T. McDowell, *J. Chem. Soc. B* **1967**, 348–351.
[17] H. Hirama, H. Hioki, S. Ito, C. Kubuto, *Tetrahedron Lett.* **1988**, *29*, 3121–3124.
[18] A. Padwa, B. H. Norman, *J. Org. Chem.* **1990**, *55*, 4801–4807.
[19] S. Matsubara, M. Yoshioka, K. Utimoto, *Chem. Lett.* **1994**, 827–830.
[20] H. Eichenauer, Ph. D. Dissertation, Justus-Liebig-Universität Gießen, **1980**.
[21] [21a] D. Enders, H. Eichenauer, *Chem. Ber.* **1979**, *112*, 2933–2960. – [21b] D. Enders in *Asymmetric Synthesis*, Vol. 3B (Hrsg.: J. D. Morrison), Academic Press, Orlando, **1984**, p. 275–339. – [21c] D. Enders, P. Fey, H. Kipphardt, *Org. Synth.* **1987**, *65*, 173–182; 183–202.
[22] [22a] D. Enders, H. Kipphardt, P. Gerdes, L. J. Breña-Valle, V. Bhushan, Bu*ll. Soc. Chim. Belg.* **1988**, *97*, 691–704. – [22b] D. Enders, *Acros Organics Acta* **1995**, *1*, 35–36.
[23] [23a] J. Martens, S. Lübben, *Liebigs Ann. Chem.* **1990**, 949–952. – [23b] J. Wilken, C. Theorey, H. Gröger, D. Haase, W. Saak, S. Pohl, J. Muzart, J. Martens, *Liebigs Ann. Chem.* **1997**, 2133–2146, and references cited therein.
[24] H. Kempen, Ph. D. Dissertation, RWTH Aachen, **1994**.
[25] M. W. Rathke, M. Nowak, *J. Org. Chem.* **1985**, *50*, 2624–2626.
[26] D. Enders, S. F. Müller, G. Raabe, *Angew. Chem.* **1999**, *111*, 212–214; *Angew. Chem. Int. Ed.* **1999**, *38*, 195–197.
[27] S. R. Hall, H. D. Flack, J. M. Stewart, *XTAL3.2 Reference Manual*, Universities of West Australia, Geneva, Maryland, Lamb, Perth, **1992**.
[28] Software for preparing the ball-and-stick plot representation: Ball Stick Version 2.2, A. Falk, N. Müller, G. Schoppel, L. Webb, Linz (Austria), Stafford (UK).
[29] Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-102345 and CCDC-115145. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (Fax: (internat.) +44–1223/336-033, E-mail: deposit@ccdc.cam.ac.uk).
[30] Preparation analogous to that of SAMP (*S*)-**2**. See ref. [21]
[31] V. Teetz, R. Geiger, R. Henning, H. Urbach, *Arzneim. Forsch.* **1984**, *34*, 1399–1401.
[32] D. Enders, R. Lochtman, M. Meiers, S. F. Müller, R. Lazny, *Synlett* **1998**, 1182–1184.
[33] [33a] J. A. Dale, D. L. Dull, H. S. Mosher, *J. Org. Chem.* **1969**, *34*, 2543–2549. – [33b] J. A. Dale, H. S. Mosher, *J. Am. Chem. Soc.* **1973**, *95*, 512–519.
[34] The starting material for the synthesis of RAMBO (**5**) – (*R*,*R*,*R*)-azabicyclo[3.3.0]octane-3-carboxylic acid benzyl ester hydrochloride, which was supplied by the former Hoechst AG – showed an *ee* value of 80% (determined by NMR spectroscopy from the *de* value of the corresponding Mosher amide).
[35] D. Enders, S. F. Müller, G. Raabe, *Synlett* **1999**, 741–743.

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