Asymmetric β-Aminoethylation of Ketones and Nitriles with Tosylaziridines Employing the SAMP-Hydrazone Method

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The nucleophilic ring-opening of tosylaziridines with chiral aza-enolates is reported. The SAMP-/ RAMP-hydrazones **1a**–**h** derived from aldehydes or ketones were reacted with tosylaziridine **2a** to give the β-aminoethylated hydrazones **3a**–**h** with good diastereoselectivity. Removal of the chiral auxiliary resulted in the formation of the γ-amino nitriles **4a**–**e** or γ-amino ketones **6f**–**h** in good yields and excellent enantiomeric excesses (*ee* ≥ 98%). Ring-opening of the enantiopure, benzyl-substituted tosylaziridine **2b** with aza-enolates was achieved selectively at the less-substituted ring-carbon atom, again with excellent diastereoselectivity. Subsequent cleavage of the chiral auxiliary yielded the γ-benzyl-substituted γ-amino nitrile **4j** or γ-amino ketone **6i** with *de*,*ee* ≥ 98%, respectively. The relative and absolute configuration of the new stereogenic centre of the aminoethylated hydrazones **3a**–**j** was determined by NOE measurements and confirmed by X-ray structure analysis on the Mosher amide of **6h**.

Introduction

Aziridines are versatile intermediates of great importance to organic synthesis.[1] In particular, the ability of *N*-activated aziridines to undergo highly regio- and stereoselective ring-opening reactions[2] has received much attention in asymmetric synthesis. Activation of the aziridine,[3] which is essential for effective ring-opening, can be achieved by the presence of an electron-withdrawing protecting group on the ring nitrogen atom. The correct choice of the protecting group is crucial to determining the reactivity of the aziridine. For example, reaction of benzoyl-substituted aziridines with dianions derived from β-keto esters results in acylation, while the use of sulfonyl aziridines leads to the desired γ-amino ketones.[4] Aziridines are known to undergo ring-opening reactions with enolates,[5] and therefore we decided to investigate their reaction with chiral aza-enolates in order to develop an efficient asymmetric β-aminoethylation protocol for ketones and nitriles.[6] α-Alkylation of SAMP/RAMP-hydrazones is a well-established method in asymmetric synthesis,[7] but β-amino alkylations with halogenated electrophiles have so far proved unreliable owing to competing elimination reactions.

Results and Discussion

In our study four different *N*-protected aziridines were reacted with enantiopure aza-enolates generated by metallation of the chiral SAMP-/RAMP-hydrazones **1a**−**h**. With a urethane derivative (Boc) no reaction was observed. Activation of the aziridine with either a *p*-nitro-benzosulfonyl-[8] or a diphenylphosphinyl group[9] resulted in complex mixtures, while the use of tosylaziridine[10] **2a** led smoothly to the desired β-aminoethylated products **3a**−**h**. Hydrazones **1f**−**h** derived from ketones gave the β-aminoalkylated hydrazone products **3f**−**h** in good yields (79−88%) and virtually complete asymmetric inductions (*de* ≥ 98%), which were determined by ^{13}C NMR spectroscopy. The electrophilic α-substitutions of the simple aldehyde hydrazones **1a**−**c** were less successful and unchanged starting materials were isolated. Thus, the yields were low (24−43%) and the diastereomeric excesses not as high as expected. However, simple flash chromatography of the product hydrazones **3a,b** yielded the diastereomerically pure compounds. The sterically more-hindered aldehyde SAMP-hydrazones **3d,e** gave β-aminoalkylated products with excellent diastereomeric excesses (*de* ≥ 98%) and substantially better yields of 63% and 88%, respectively.

Next we turned our attention to the reaction of the enantiopure, benzyl-substituted tosylaziridine **2b**, which was synthesized in three steps from L-phenylalanine.[11] The ring-opening reaction with the aza-enolates of the hydrazones (*R*)-**1e** and (*S*)-**1f** led exclusively to the formation of the hydrazones **3i,j**. As expected, the nucleophilic attack of the aza-enolate was directed to the less-substituted ring-carbon atom and, again, a virtually complete asymmetric induction (*de* ≥ 98%) could be determined by ^{13}C NMR spectroscopy for the ring-opening α-alkylation of the hydrazones (Scheme 1 and Table 1).

The removal of the chiral auxiliary was accomplished by subsequent oxidative cleavage of the aminoethylated aldehyde hydrazones **3a**−**e,j** with magnesium monoperoxyphthalate (MMPP).[12] Under these conditions the pyrrolidine nitrogen is oxidized to the corresponding *N*-oxide, which undergoes a aza-analogous Cope type elimination. In this way, the γ-amino nitriles **4a**−**e** were obtained in good yields (71−87%) and excellent enantiomeric excesses (*ee* ≥ 98%). Compound **4j** was isolated in quantitative yield and as a

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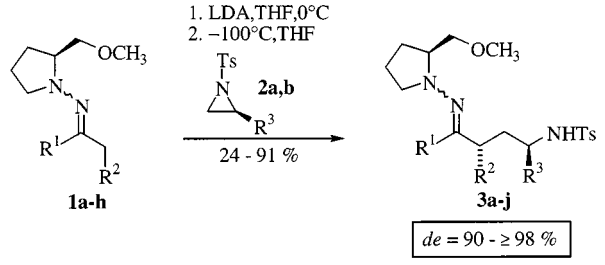
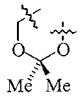
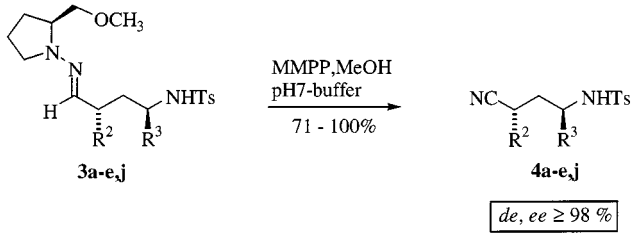


Scheme 1. β-Aminoethylation with tosylaziridines

Table 1. Synthesis of β-aminoethylated hydrazones **3a−j**

Product	R^1	R^2	R^3	Yield (%)	*de*[a,b] (%)	$[\alpha]_D^{26}$ (*c*, $CHCl_3$)[c]
(*S*,*S*)–**3a**	H	Me	H	32	90 (≥ 98)	− 29.2 (1.00)
(*S*,*S*)–**3b**	H	Et	H	43	93 (≥ 98)	− 14.3 (1.00)
(*R*,*S*)–**3c**	H	*i*Pr	H	24	≥ 98	− 1.7 (1.00)
(*R*,*S*)–**3d**	H	Bn	H	63	≥ 98	− 39.5 (0.75)
(*R*,*S*)–**3e**	H	3,4-OCH_2O-Ph	H	88	≥ 98	− 42.9 (1.00)
(*S*,*R*)–**3e**[d]	H	3,4-OCH_2O-Ph	H	91	≥ 98	+ 44.0 (1.00)
(*S*,*S*)–**3f**	Et	Me	H	79	≥ 98	+ 174.9 (2.27)
(*S*,*S*)–**3g**	Ph	Me	H	88	≥ 98	+ 354.7 (1.00)
(*S*,*S*)–**3h**			H	87	≥ 98	+ 98.6 (0.72)
(*S*,*S*,*R*)–**3i**	Et	Me	Bn	81	≥ 98	+ 89.1 (1.00)
(*S*,*R*,*R*)–**3j**[d]	H	3,4-OCH_2O-Ph	Bn	64	≥ 98	+ 81.8 (0.99)

[a] Determined by ^{13}C NMR spectroscopy. − [b] Numbers in parentheses indicate the value after column chromatography. − [c] All optical rotations were measured in Uvasol grade $CHCl_3$ at temperatures T = 26 ± 1 °C. − [d] RAMP was used as chiral auxiliary.



Scheme 2. Oxidative hydrazone cleavage to γ-amino nitriles

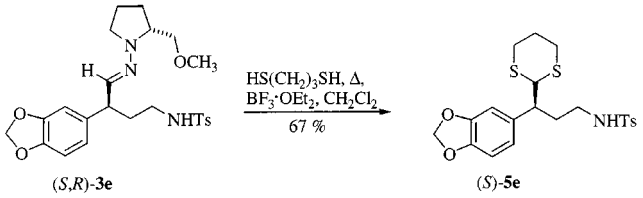
single stereoisomer (*de*, *ee* ≥ 98%) (Scheme 2 and Table 2). These compounds should be ideal precursors for the synthesis of γ-amino acids or γ-lactams.

Alternatively, recovery of the aldehyde functionality is feasible under different reaction conditions.[13] The direct transformation of the RAMP-hydrazone (*S*,*R*)-**3e**, promoted by a Lewis acid, to the corresponding dithioacetal (*S*)-**5e**[14] was accomplished using 1,3-propanedithiol and BF_3−diethyl ether in refluxing dichloromethane in 67% yield (Scheme 3). Therefore, the hydrazones **3a−e** are precursors of versatile bifunctional, diastereo- and enantiomerically pure building blocks in synthesis.

Table 2. Synthesis of γ-amino nitriles **4a−e,j** by cleavage of the hydrazones **3a−e,j** with MMPP

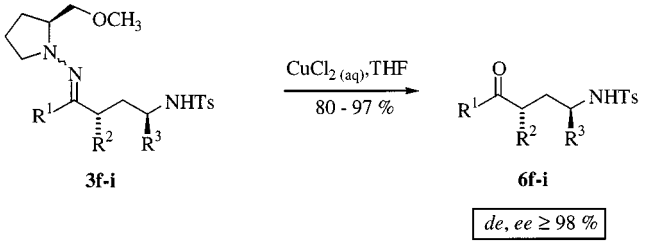
Product	R^2	R^3	Yield (%)	*de*[a] (%)	*ee*[b] (%)	$[\alpha]_D^{26}$ (*c*, $CHCl_3$)[c]
(*S*)-**4a**	Me	H	78	−	≥ 98	+32.2 (1.00)
(*S*)-**4b**	Et	H	80	−	≥ 98	+25.0 (1.00)
(*R*)-**4c**	*i*Pr	H	87	−	≥ 98	+31.7 (1.23)
(*R*)-**4d**	Bn	H	84	−	≥ 98	+16.0 (1.12)
(*R*)-**4e**	3,4-OCH_2O-Ph	H	71	−	≥ 98	+34.5 (1.08)
(*S*)-**4e**	3,4-OCH_2O-Ph	H	83	−	≥ 98	−38.5 (1.32)
(*S*,*R*)-**4j**	3,4-OCH_2O-Ph	Bn	100	≥98	≥ 98	−61.2 (1.00)

[a] Determined by ^{13}C NMR spectroscopy. − [b] Based on the *de* value of the corresponding Mosher-amide [HPLC, Chiralpak AD (4.6×250 mm)]. − [c] All optical rotations were measured in Uvasol grade $CHCl_3$ at temperatures T = 26 ± 1°C.



Scheme 3. Direct RAMP-hydrazone/1,3-dithiane conversion

The ketone hydrazones **3f−i** were cleaved with a 1 M aqueous solution of copper(II) chloride[15] to remove the chiral auxiliary and to regenerate the parent ketone functionality. The *N*-tosyl-protected γ-amino ketones **6f−i** were obtained in good to excellent yields (80−97%) and excellent enantiomeric excesses (*ee* ≥ 98%) (**6i**: *de*, *ee* ≥ 98%) (Scheme 4 and Table 3).



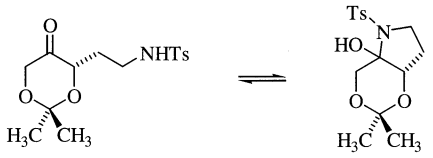
Scheme 4. Hydrazone cleavage to γ-amino ketones

Table 3. Synthesis of γ-amino ketones **6f−i** by cleavage of the hydrazones **3f−i** with aqueous copper (II) chloride solution

Product	R^1	R^2	R^3	Yield (%)	*de*[a] (%)	*ee*[b] (%)	$[\alpha]_D^{26}$ (*c*, $CHCl_3$)[c]
(*S*)–**6f**	Et	Me	H	97	–	≥ 98	− 9.1 (1.05)
(*S*)–**6g**	Ph	Me	H	83	–	≥ 98	− 6.0 (1.00)
(*S*)–**6h**			H	80	–	≥ 98	+ 4.4 (1.00)
(*S*,*R*)–**6i**	Et	Me	Bn	96	≥ 98	≥ 98	− 8.7 (1.00)

[a] Determined by ^{13}C NMR spectroscopy. − [b] Based on the *de* value of the corresponding Mosher-amide [HPLC, Chiralpak AD (4.6 × 250 mm)]. − [c] All optical rotations were measured in Uvasol grade $CHCl_3$ at temperatures T = 26 ± 1 °C.

Ketone **6h** was obtained as an equilibrium mixture of the amino ketone **6h** and its hemi-*N*,*O*-acetal **6h′** (Scheme 5). Compound **6h′** was formed as a single stereoisomer as determined by ^{1}H and ^{13}C NMR spectroscopy. The configuration of the newly generated stereocentre remains unclear. Presumably, the intramolecular nucleophilic attack of the protected amino group occurs from the *si* face of the ketone moiety giving rise to the (*R*,*S*)-configuration.



Scheme 5. Amino ketone/hemi-*N*,*O*-acetal equilibrium

The relative configuration of the new stereogenic centre of the aminoethylated hydrazones was determined by NOE experiments on (*S*,*S*)-**3h**.[6] These findings were confirmed by an X-ray structure analysis on the Mosher amide of **6h** showing the *S*-configuration alpha to the ketone carbonyl group (Figure 1).[16]

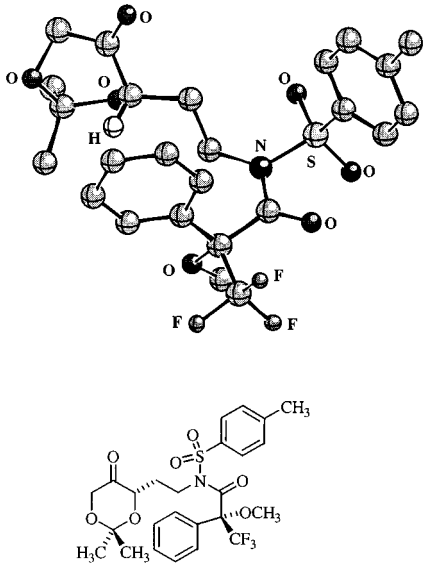


Figure 1. Crystal structure of the Mosher amide of **6h**

The stereochemical outcome as indicated in Table 1 is in accordance with the proposed general mechanism for electrophilic substitutions by SAMP-/RAMP-hydrazones.[7a] The enantiomeric excesses of γ-amino nitriles **4a−e** and γ-amino ketones **6f−i** were determined by HPLC of the corresponding Mosher amides.[17]

Conclusion

In summary, a practical method for the diastereo- and enantioselective synthesis of *N*-protected γ-amino nitriles and γ-amino ketones has been developed. After the trapping of lithiated SAMP-/RAMP-hydrazones with unsubstituted or enantiopure, 2-substituted tosylaziridines as electrophiles, and removal of the chiral auxiliary, the bifunctional title compounds were obtained in good yields and excellent diastereomeric and enantiomeric excesses. This new protocol will prove attractive for asymmetric synthesis due to the ready accessibility of enantiopure, 2-substituted aziridines[11,18] and the virtually complete asymmetric inductions achieved in the β-aminoethylation process.

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. − Melting points (uncorrected): Büchi 510. − THF was dried by distillation from K/benzophenone under Ar. The SAMP hydrazones of propanal **(1a)**,[19] butanal **(1b)**,[19] 3-methyl-butanal **(1c)**,[19] 3-phenyl-propanal **(1d)**,[20] 3-pentanone **(1f)**,[21] propiophenone **(1g)**,[22] and 2,2-dimethyl-1,3-dioxan-5-one **(1h)**[23] were prepared according to the published procedures.

General Procedure 1 for the Formation of SAMP-/RAMP Hydrazones [(*S*)-1e, (*R*)-1e, GP1]: One equivalent of SAMP (RAMP)[24] was slowly added to 1 equiv. homopiperonal[25] (neat) at 0 °C and stirred at room temp. for 2−3 h (TLC control). The resulting yellow solution was diluted with ether and dried over $MgSO_4$. After removal of the solvent, the residue was purified by flash chromatography (SiO_2, ether/pentane 1:2 containing 2% NEt_3) to afford the chiral hydrazone (*S*)-**1e** or (*R*)-**1e**.

(*S*)-*E*-(2-Benzo[1,3]dioxol-5-yl-ethylidene)-(2-methoxymethyl-pyrrolidine-1-yl)-amine, (*S*)-1e: According to GP1, (*S*)-**1e** was obtained as a yellow oil after purification by column chromatography (SiO_2, ether/pentane 1:2, containing 2% NEt_3). Yield 13.26 g (97%) − TLC: R_f = 0.41 (ether/pentane = 1:2) − $[\alpha]_D^{26}$ = −91.0 (*c* = 1.37, $CHCl_3$) − IR ($CHCl_3$): $\tilde{\nu}$ = 2972 (m), 2887 (s), 2827 (m), 1606 (w), 1503 (s), 1489 (s), 1460 (m), 1442 (s), 1342 (m), 1287 (w), 1246 (s), 1195 (s), 1120 (s), 1098 (s), 1040 (s), 973 (w), 929 (s), 862 (w), 810 (m) cm^{-1}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.76−1.99 (m, 4 H, $NCH_2CH_2CH_2$), 2.75 (m, 1 H, $NCHCH_2CH_2$), 3.29−3.60 (m, 4 H, CH_3OCH_2, $NCH_2CH_2CH_2$), 3.38 (s, 3 H, OCH_3), 3.46 (d, 2 H, *J* = 5.7 Hz, CH_2CHN), 5.90 (s, 2 H, OCH_2O), 6.63 (t, *J* = 5.7 Hz, 1 H, CH_2CHN), 6.68−6.76 (m, 3 H, Ar*H*). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.27, 26.72, 39.39, 50.28, 59.30, 63.44, 74.94, 100.90, 108.29, 109.35, 121.63, 132.80, 136.51, 146.10, 147.79. − MS (CI): *m*/*z* (%) = 277 (100, $[MH]^+$), 276 (50, M^+), 231 (17), 135 (100), 115 (24), 105 (14), 77 (30). − $C_{15}H_{20}N_2O_3$ (276.34): calcd. C 65.20, H 7.30, N 10.14; found C 65.20, H 7.32, N 10.45.

(*R*)-*E*-(2-Benzo[1,3]dioxol-5-yl-ethylidene)-(2-methoxymethyl-pyrrolidine-1-yl)-amine, (*R*)-1e: According to GP1, (*R*)-**1e** was obtained as a yellow oil after purification by column chromatography (SiO_2, ether/pentane 1:2, containing 2% NEt_3). Yield 2.13 g (84%) − TLC: R_f = 0.41 (ether/pentane = 1:2) − $[\alpha]_D^{26}$ = + 91.9 (*c* = 1.35, $CHCl_3$).

General Procedure 2 for the Aminoethylation of SAMP-/RAMP-Hydrazones (1a−h, GP2): The hydrazones **1a−g** were slowly added to a solution of 1.05 equiv. of LDA in THF (5 mL/mmol) at 0 °C

and stirred for 4 h. (Hydrazone **1h** was metallated at −78 °C with 1 equiv. of *t*BuLi for 2 h). The resulting yellow solutions were cooled to −100 °C and a solution of 1 equiv. tosylaziridine **2a** or **2b** in the minimum amount of THF was added dropwise with a syringe pump over 30 min. The mixtures were stirred at −100 °C for 2 h and allowed to reach room temperature overnight. The reactions were quenched by the addition of a saturated aqueous NH_4Cl solution (10 mL). The aqueous phases were extracted with CH_2Cl_2 (3 × 25 mL). The combined organic phases were washed with H_2O (20 mL) and brine (20 mL) and dried over $MgSO_4$. After removal of the solvent, the residues were purified by flash chromatography (SiO_2, ether/pentane 1:1, containing 2% NEt_3) to afford the aminoethylated products (*E*)-**3a−e,g,h** or (*E*/*Z*)-**3f,i**.

(3*S*,4*E*,2′*S*)-*N*-{4-[2′-(Methoxymethyl)pyrrolidin-1′-ylimino]-3-methylbutyl}-4-methylbenzenesulfonamide, (*S*,*S*)-3a: According to GP2, (*S*,*S*)-**3a** was obtained as a colourless oil after purification by column chromatography (SiO_2, ether/pentane 1:1, containing 2% NEt_3). Yield 0.24 g (32%) − TLC: R_f = 0.32 (ether/pentane 2:1) − $[\alpha]_D^{26}$ = −29.2 (*c* = 1.00, $CHCl_3$) − *de* = 90% (^{13}C NMR) (≥ 98% after column chromatography) − IR ($CHCl_3$): $\tilde{\nu}$ = 3279 (m), 3064 (m), 2962 (s), 2928 (s), 2874 (s), 2829 (m), 1599 (m), 1495 (m), 1456 (m), 1382 (m), 1330 (s), 1306 (m), 1290 (m), 1251 (m), 1197 (m), 1185 (m), 1161 (s), 1095 (s), 1020 (m), 974 (m), 904 (m), 844 (m), 816 (m), 760 (w), 708 (m), 663 (s), 573 (m), 552 (s) cm^{-1}. − ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.99 (d, *J* = 7.2 Hz, 3 H, CHC*H*$_3$), 1.57−1.97 (m, 6 H, C*H*$_2$CH$_2$NH, NCH$_2$C*H*$_2$C*H*$_2$), 2.33 (m, 1 H, C*H*CH$_3$), 2.41 (s, 3 H, CC*H*$_3$), 2.63 (m, 1 H, NC*H*CH$_2$CH$_2$), 2.96 (m, 2 H, C*H*$_2$NH), 3.20−3.36 (m, 2 H, NC*H*$_2$CH$_2$CH$_2$), 3.37 (s, 3 H, OC*H*$_3$), 3.42 (dd, *J* = 6.6/9.3 Hz, 1 H, *H*CHOCH$_3$), 3.51 (dd, *J* = 4.1/9.3 Hz, 1 H, HC*H*OCH$_3$), 5.55 (s, 1 H, N*H*), 6.38 (d, *J* = 5.8 Hz, 1 H, C*H*NN), 7.29 (d, *J* = 8.0 Hz, 2 H, C*H*CCH$_3$), 7.73 (d, *J* = 8.2 Hz, 2 H, C*H*CSO$_2$). − ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.21, 21.47, 22.08, 26.48, 34.40, 34.84, 41.44, 50.22, 59.15, 63.38, 74.72, 127.05, 129.57, 137.26, 141.71, 143.03. − MS (CI): *m*/*z* (%) = 369 (17), 368 (100) $[MH]^+$, 238 (19), 114 (12), 84 (11). − $C_{18}H_{29}N_3O_3S$ (367.51): calcd. C 58.83, H 7.95, N 11.43; found C 58.90, H 8.09, N 11.70.

(3*S*,4*E*,2′*S*)-*N*-{3-Ethyl-4-[2′-(methoxymethyl)pyrrolidin-1′-ylimino]-butyl}-4-methylbenzenesulfonamide, (*S*,*S*)-3b: According to GP2, (*S*,*S*)-**3b** was obtained as a colourless oil after purification by column chromatography (SiO_2, ether/pentane 1:1, containing 2% NEt_3). Yield 0.44 g (43%) − TLC: R_f = 0.31 (ether/pentane 2:1) − $[\alpha]_D^{26}$ = −14.3 (*c* = 1.00, $CHCl_3$) − *de* = 93% (^{1}H NMR) (≥ 98% after column chromatography) − IR ($CHCl_3$): $\tilde{\nu}$ = 3279 (m), 3063 (w), 2961 (s), 2928 (s), 2875 (m), 1599 (m), 1495 (m), 1460 (m), 1383 (m), 1330 (s), 1306 (m), 1290 (m), 1197 (m), 1185 (m), 1161 (s), 1095 (s), 1020 (m), 972 (w), 907 (m), 816 (m), 757 (w), 708 (m), 663 (m), 576 (m), 552 (m) cm^{-1}. − ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.83 (t, *J* = 7.4 Hz, 3 H, CH$_2$C*H*$_3$), 1.48−1.97 (m, 8 H, C*H*$_2$CH$_2$NH, NCH$_2$C*H*$_2$C*H*$_2$, C*H*$_2$CH$_3$), 2.10 (m, 1 H, C*H*CHNN), 2.41 (s, 3 H, CC*H*$_3$), 2.63 (m, 1 H, NC*H*CH$_2$CH$_2$), 2.86−3.08 (m, 2 H, C*H*$_2$NH), 3.20−3.34 (m, 2 H, NC*H*$_2$CH$_2$CH$_2$), 3.36 (s, 3 H, OC*H*$_3$), 3.42 (dd, *J* = 6.6/9.3 Hz, 1 H, *H*CHOCH$_3$), 3.52 (dd, *J* = 4.1/9.3 Hz, 1 H, HC*H*OCH$_3$), 5.57 (s, 1 H, N*H*), 6.36 (d, *J* = 6.3 Hz, 1 H, C*H*NN), 7.28 (d, *J* = 8.0 Hz, 2 H, C*H*CCH$_3$), 7.73 (d, *J* = 8.2 Hz, 2 H, C*H*CSO$_2$). − ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.38, 21.41, 22.02, 26.42, 26.77, 32.20, 41.47, 41.54, 50.22, 59.03, 63.25, 74.60, 126.86, 129.36, 137.06, 140.75, 142.80. − MS (CI): *m*/*z* (%) = 383 (21), 382 (100) $[MH]^+$, 336 (7), 267 (19), 252 (36), 131 (7), 116 (6), 114 (22), 98 (14). − $C_{19}H_{31}N_3O_3S$ (381.50): calcd. C 59.81, H 8.19, N 11.01; found C 59.38, H 8.33, N 11.15.

(3*R*,3*E*,2′*S*)-*N*-{3-Isopropyl-4-[2′-(Methoxymethyl)pyrrolidin-1′-ylimino]-butyl}-4-methylbenzenesulfonamide, (*R*,*S*)-3c: According to GP2, (*R*,*S*)-**3c** was obtained as a yellow oil after purification by column chromatography (SiO_2, ether/pentane 1:1, containing 2% NEt_3). Yield 0.22 g (24%) − TLC: R_f = 0.38 (ether/pentane 2:1) − $[\alpha]_D^{26}$ = −1.7 (*c* = 1.00, $CHCl_3$) − *de* ≥ 98% (^{13}C NMR) − IR ($CHCl_3$): $\tilde{\nu}$ = 3279 (m), 3064 (m), 3029 (m), 2958 (s), 2929 (s), 2874 (s), 2829 (s), 1599 (m), 1495 (m), 1462 (s), 1386 (m), 1369 (m), 1330 (s), 1306 (s), 1290 (m), 1249 (m), 1197 (m), 1185 (m), 1161 (s), 1095 (s), 1020 (m), 972 (m), 925 (m), 900 (m), 816 (s), 760 (m), 708 (m), 663 (s), 578 (m), 552 (s), 504 (m) cm^{-1}. − ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.82 (d, *J* = 6.9 Hz, 3 H, CHC*H*$_3$), 0.84 (d, *J* = 6.9 Hz, 3 H, CHC*H*$_3$), 1.49−2.02 (m, 8 H, C*H*$_2$CH$_2$NH, C*H*C*H*CHN, NCH$_2$C*H*$_2$C*H*$_2$), 2.41 (s, 3 H, CC*H*$_3$), 2.65 (m, 1 H, NC*H*CH$_2$CH$_2$), 2.90 (m, 1 H, HC*H*NH), 3.01 (m, 1 H, *H*CHNH), 3.25−3.35 (m, 2 H, NC*H*$_2$CH$_2$CH$_2$), 3.36 (s, 3 H, OC*H*$_3$), 3.42 (dd, *J* = 6.6/9.3 Hz, 1 H, *H*CHOCH$_3$), 3.53 (dd, *J* = 4.1/9.3 Hz, 1 H, HC*H*OCH$_3$), 5.44 (s, 1 H, N*H*), 6.41 (d, *J* = 6.3 Hz, 1 H, C*H*NN), 7.29 (d, *J* = 8.0 Hz, 2 H, C*H*CCH$_3$), 7.72 (d, *J* = 8.2 Hz, 2 H, C*H*CSO$_2$). − ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.68, 20.12, 21.64, 22.24, 26.64, 29.80, 31.62, 42.20, 46.40, 50.61, 59.35, 63.58, 74.95, 127.25, 129.74, 137.54, 140.10, 143.21. − MS (CI): *m*/*z* (%) = 397 (22), 396 (100) $[MH]^+$, 266 (10), 253 (5). − $C_{20}H_{33}N_3O_3S$ (395.56): calcd. C 60.73, H 8.41, N 10.62; found C 60.92, H 8.78, N 10.84.

(3*R*,4*E*,2′*S*)-*N*-{3-Benzyl-4-[2′-(methoxymethyl)pyrrolidin-1′-ylimino]-butyl}-4-methylbenzenesulfonamide, (*R*,*S*)-3d: According to GP2, (*R*,*S*)-**3d** was obtained as a colourless oil after purification by column chromatography (SiO_2, ether/pentane 1:1, containing 2% NEt_3). Yield 1.17 g (63%) − TLC: R_f = 0.41 (ether/pentane 2:1) − $[\alpha]_D^{26}$ = −39.5 (*c* = 0.75, $CHCl_3$) − *de* ≥ 98% (^{13}C NMR) − IR ($CHCl_3$): $\tilde{\nu}$ = 3279 (m), 3084 (m), 3061 (m), 3026 (m), 2970 (s), 2926 (s), 2876 (s), 2829 (m), 1599 (m), 1495 (m), 1454 (m), 1382 (m), 1331 (s), 1305 (m), 1290 (m), 1197 (m), 1185 (m), 1161 (s), 1119 (m), 1095 (s), 1031 (m), 1020 (m), 1003 (w), 971 (m), 901 (w), 816 (m), 749 (m), 702 (m), 662 (m), 551 (m) cm^{-1}. − ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.49−1.93 (m, 6 H, C*H*$_2$CH$_2$NH, NCH$_2$C*H*$_2$C*H*$_2$), 2.40 (s, 3 H, CC*H*$_3$), 2.52−2.75 (m, 4 H, NC*H*CH$_2$CH$_2$, C*H*$_2$C*H*CHN), 2.87−3.04 (m, 2 H, C*H*$_2$NH), 3.23−3.38 (m, 2 H, NC*H*$_2$CH$_2$CH$_2$), 3.34 (s, 3 H, OC*H*$_3$), 3.42−3.49 (m, 2 H, C*H*$_2$OCH$_3$), 5.28 (s, 1 H, N*H*), 6.36 (d, *J* = 5.5 Hz, 1 H, C*H*NN), 7.05−7.28 (m, 7 H, C$_6$*H*$_5$, C*H*CCH$_3$), 7.68 (d, *J* = 8.2 Hz, 2 H, C*H*CSO$_2$). − ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.71, 22.29, 26.73, 31.98, 40.65, 41.75, 41.89, 50.36, 59.41, 63.45, 74.86, 126.30, 127.27, 128.50, 129.38, 129.79, 137.49, 139.62, 139.66, 143.25. − MS (CI): *m*/*z* (%) = 445 (23), 444 (100) $[MH]^+$, 412 (5), 398 (18), 329 (5), 314 (26), 114 (6). − $C_{24}H_{33}N_3O_3S$ (443.60): calcd. C 64.98, H 7.50, N 9.47; found C 64.88, H 7.72, N 9.81.

(3*R*,4*E*,2′*S*)-*N*-{3(*R*)-(Benzo[1,3]dioxol-5-yl)-4-[2′-(methoxymethyl)pyrrolidin-1′-ylimino]-butyl}-4-methylbenzenesulfonamide, (*R*,*S*)-3e: According to GP2, (*R*,*S*)-**3e** was obtained as a yellow oil after purification by column chromatography (SiO_2, ether/pentane 1:1, containing 2% NEt_3). Yield 0.90 g (88%) − TLC: R_f = 0.53 (ether/pentane 2:1) − $[\alpha]_D^{26}$ = − 42.9 (*c* = 1.00, $CHCl_3$) − *de* ≥ 98% (^{13}C NMR) − IR ($CHCl_3$): $\tilde{\nu}$ = 3282 (m), 3018 (m), 2972 (m), 2927 (m), 2879 (m), 1598 (m), 1504 (m), 1487 (s), 1441 (m), 1382 (w), 1328 (s), 1305 (m), 1289 (m), 1247 (s), 1197 (m), 1185 (m), 1160 (s), 1119 (m), 1095 (s), 1040 (s), 971 (w), 934 (m), 865 (m), 815 (m), 757 (s), 708 (m), 666 (m), 551 (m) cm^{-1}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.75−2.10 (m, 6 H, C*H*$_2$CH$_2$NHSO$_2$, NCH$_2$C*H*$_2$C*H*$_2$), 2.42 (s, 3 H, CC*H*$_3$), 2.70 (m, 1

H, NC*H*CH$_2$CH$_2$), 2.95 (m, 2 H, C*H*$_2$NHSO$_2$), 3.25−3.60 (m, 5 H, C*H*CH=N, CH$_3$OC*H*$_2$, NC*H*$_2$CH$_2$CH$_2$), 3.37 (s, 3 H, OC*H*$_3$), 5.30 (s, 1 H, N*H*), 5.92 (s, 2 H, OC*H*$_2$O), 6.50−6.60 (m, 3 H, Ar*H*), 6.69 (d, J = 8.0 Hz, 1 H, *H*C=N), 7.29 (d, J = 8.0 Hz, 2 H, SO$_2$CC*H*), 7.69 (d, J = 8.0 Hz, 2 H, H$_3$CCC*H*). − ^{13}C NMR (75 MHz, CDCl$_3$): δ = 21.95, 22.58, 27.07, 34.29, 41.87, 46.57, 50.41, 59.63, 63.76, 75.26, 101.41, 108.59, 108.75, 121.32, 127.59, 130.09, 136.71, 137.86, 138.94, 143.53, 146.71, 148.31. − MS (CI): *m*/*z* (%) = 474 (100) [MH]$^+$, 344 (22), 334 (8), 190 (22), 172 (16), 131 (10), 116 (37), 114 (43), 74 (6). − C$_{24}$H$_{31}$N$_3$O$_5$S (473.60): calcd. C 60.87, H 6.60, N 8.87; found C 60.64, H 6.55, N 9.02.

(3*S*,4*E*,2′*R*)-*N*-{3(*S*)-(Benzo[1,3]dioxol-5-yl)-4-[2′-(methoxymethyl)-pyrrolidin-1′-ylimino]-butyl}-4-methylbenzenesulfonamide, (*S*,*R*)-3e: According to GP2, (*S*,*R*)-**3e** was obtained as a yellow oil after purification by column chromatography (SiO$_2$, ether/pentane 1:1, containing 2% NEt$_3$). Yield 1.93 g (91%) − TLC: R_f = 0.53 (ether/pentane 2:1) − $[\alpha]_D^{26}$ = +44.0 (c = 1.00, CHCl$_3$) − *de* ≥ 98% (^{13}C NMR).

(3*S*,4*E*/*Z*,2′*S*)-*N*-{4-[2′-(methoxymethyl)pyrrolidin-1′-ylimino]-3-methylhexyl}-4-methylbenzenesulfonamide, (*S*,*S*)-3f: According to GP2, (*S*,*S*)-**3f** was obtained as a yellow oil after purification by column chromatography (SiO$_2$, ether/pentane 1:1). Yield 1.28 g (79%) − TLC: R_f = 0.60 (ether/pentane 2:1) − $[\alpha]_D^{26}$ = +174.9 (c = 2.27, CHCl$_3$) − *de* ≥ 98% (^{13}C NMR) − IR (CHCl$_3$): $\tilde{\nu}$ = 3279 (m), 2967 (m), 2933 (m), 2874 (m), 1599 (w), 1495 (m), 1460 (m), 1379 (m), 1331 (s), 1305 (m), 1290 (m), 1184 (m), 1160 (s), 1095 (s), 1021 (w), 974 (m), 913 (m), 816 (m), 708 (m), 662 (m), 552 (m) cm^{-1}. − ^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.88−1.06 (m, 6 H, CHC*H*$_3$, CH$_2$C*H*$_3$), 1.31−2.62 (m, 11 H, NC*H*$_2$C*H*$_2$C*H*$_2$, C*H*$_2$CH$_2$NHSO$_2$, C*H*CH$_3$, C*H*$_2$CH$_3$), 2.41 (s, 3 H, CC*H*$_3$), 2.98−3.02 (m, 2 H, C*H*$_2$NHSO$_2$), 3.13−3.43 (m, 6 H, N*H*CHCH$_2$CH$_2$, C*H*$_2$OC*H*$_3$), 5.81 (s, 1 H, N*H*), 7.29 (m, 2 H, CHCCH$_3$), 7.75 (m, 2 H, C*H*CSO$_2$). − ^{13}C NMR (100 MHz, CDCl$_3$): *E*-isomer δ = 10.92, 17.30, 21.48, 22.12, 23.59, 25.99, 34.47, 37.17, 40.91, 55.01, 58.99, 65.89, 74.41, 127.08, 129.55, 139.34, 142.97, 172.20. *Z*-isomer δ = 11.91, 18.94, 21.45, 21.99, 23.53, 26.46, 31.86, 32.84, 41.00, 55.63, 58.79, 66.73, 75.59, 126.76, 129.41, 137.36, 142.67, 174.31. − MS (CI): *m*/*z* (%) = 397 (21), 396 (100) [MH]$^+$, 131 (6), 116 (16), 114 (31), 112 (16). − C$_{20}$H$_{33}$N$_3$O$_3$S (395.60): calcd. C 60.73, H 8.41, N 10.62; found C 60.55, H 8.30, N 10.83.

(3*S*,4*E*,2′*S*)-*N*-{4-[2′-(methoxymethyl)pyrrolidin-1′-ylimino]-3-methyl-4-phenyl-butyl}-4-methylbenzenesulfonamide, (*S*,*S*)-3g: According to GP2, (*S*,*S*)-**3g** was obtained as a yellow solid after purification by column chromatography (SiO$_2$, ether/pentane 1:1, containing 2% NEt$_3$). Yield 0.80 g (88%) − TLC: R_f = 0.50 (ether/pentane 2:1) − $[\alpha]_D^{26}$ = +354.7 (c = 1.00, CHCl$_3$) − *de* ≥ 98% (^{13}C NMR) − m.p. 80 °C − IR (KBr): $\tilde{\nu}$ = 3215 (m), 3058 (m), 2965 (m), 2944 (m), 2879 (m), 2852 (m), 1596 (w), 1557 (m), 1493 (m), 1442 (m), 1399 (m), 1383 (m), 1324 (s), 1304 (m), 1291 (m), 1151 (s), 1114 (s), 1089 (s), 1033 (m), 1003 (m), 975 (m), 913 (m), 817 (m), 776 (m), 701 (m), 654 (m), 579 (m), 556 (m), 525 (m) cm^{-1}. − ^{1}H NMR (400 MHz, CDCl$_3$): δ = 1.06 (d, J = 7.4 Hz, 3 H, CHC*H*$_3$), 1.27−1.62 (m, 3 H, NCH$_2$C*H*$_2$CH*H*), 1.73−2.06 (m, 4 H, C*H*$_2$CH$_2$NH, NCH$_2$CH$_2$C*H*H, C*H*CH$_3$), 2.42 (s, 3 H, CC*H*$_3$), 2.60 (m, 1 H, NHC*H*CH$_2$), 2.70 (m, 1 H, N*H*CHCH$_2$), 3.19 (m, 1 H, NC*H*CH$_2$CH$_2$), 3.30 (s, 3 H, OC*H*$_3$), 3.31−3.59 (m, 4 H, HC*H*OCH$_3$, C*H*$_2$NH), 7.27−7.36 (m, 7 H, C$_6$*H*$_5$, CHCCH$_3$), 7.76 (d, J = 8.5 Hz, 2 H, C*H*CSO$_2$). − ^{13}C NMR (100 MHz, CDCl$_3$): δ = 18.19, 21.44, 22.61, 25.89, 31.78, 34.39, 40.72, 56.21, 58.75, 66.61, 74.26, 126.60, 127.50, 127.93, 128.27, 129.23, 137.17, 138.87, 142.53, 169.54. − MS (CI): *m*/*z* (%) = 444 (100) [MH]$^+$, 263 (26), 245 (13), 198 (12), 102 (100), 100 (15). − C$_{24}$H$_{33}$N$_3$O$_3$S (443.22): calcd. C 64.98, H 7.50, N 9.47; found C 64.96, H 7.77, N 9.77.

(4*S*,5*E*,2′*S*)-*N*-{2-[5-(2′-(Methoxymethyl)pyrrolidin-1′-ylimino)-2,2-dimethyl-[1,3]dioxan-4-yl]ethyl}-4-methylbenzenesulfonamide, (*S*,*S*)-3h: According to GP2, (*S*,*S*)-**3h** was obtained as a yellow oil after purification by column chromatography (SiO$_2$, ether/pentane 1:1, containing 2% NEt$_3$). Yield 0.87 g (87%) − TLC: R_f = 0.22 (ether/pentane 2:1) − $[\alpha]_D^{26}$ = +98.6 (c = 0.72, CHCl$_3$) − *de* ≥ 98% (^{13}C NMR) − IR (CHCl$_3$): $\tilde{\nu}$ = 3287 (m), 2983 (m), 2937 (m), 2875 (m), 1599 (w), 1495 (m), 1448 (m), 1382 (m), 1331 (s), 1305 (m), 1290 (m), 1226 (s), 1185 (m), 1161 (s), 1095 (s), 1072 (s), 1019 (m), 974 (m), 873 (m), 842 (w), 816 (m), 756 (s), 708 (m), 665 (m), 552 (m) cm^{-1}. − ^{1}H NMR (400 MHz, CDCl$_3$): δ = 1.33 (s, 3 H, OCC*H*$_3$), 1.35 (s, 3 H, OCC*H*$_3$), 1.65 (m, 1 H, NCH$_2$HC*H*CH$_2$), 1.83 (m, 3 H, HC*H*CH$_2$NH, NCH$_2$*H*CHHC*H*), 2.00 (m, 2 H, *H*CHCH$_2$NH, NCH$_2$CH$_2$*H*CH), 2.29 (m, 1 H, N*H*CHCH$_2$), 2.42 (s, 3 H, CC*H*$_3$), 3.00 (m, 1 H, NHC*H*CH$_2$), 3.10 (m, 2 H, C*H*$_2$NH), 3.24 (dd, J = 6.6/9.1 Hz, 1 H, *H*CHOCH$_3$), 3.32 (m, 1 H, NC*H*CH$_2$CH$_2$), 3.34 (s, 3 H, OC*H*$_3$), 3.40 (dd, J = 4.1/9.1 Hz, 1 H, HC*H*OCH$_3$), 4.08 (dd, J = 1.9/15.7 Hz, 1 H, OHC*H*C=N), 4.34 (m, 1 H, OC*H*C=N), 4.44 (d, J = 15.9 Hz, 1 H, O*H*CHC=N), 5.81 (t, J = 5.2 Hz, 1 H, N*H*), 7.31 (d, J = 8.5 Hz, 2 H, C*H*CCH$_3$), 7.73 (d, J = 8.5 Hz, 2 H, C*H*CSO$_2$). − ^{13}C NMR (100 MHz, CDCl$_3$): δ = 21.42, 22.84, 23.87, 23.97, 26.67, 31.00, 40.18, 55.80, 59.08, 59.75, 66.74, 69.76, 75.39, 100.40, 127.06, 129.55, 137.18, 143.01, 161.35. − MS (CI): *m*/*z* (%) = 441 (24), 440 (100) [MH]$^+$, 382 (20), 172 (5), 114 (5). − C$_{21}$H$_{33}$N$_3$O$_5$S (439.57): calcd. C 57.38, H 7.57, N 9.56; found C 57.21, H 7.73, N 9.85.

(1*R*,3*S*,4*E*/*Z*,2′*S*)-*N*-{1-Benzyl-4-[2′-(methoxymethyl)pyrrolidin-1′-ylimino]-3-methyl-hexyl}-4-methylbenzenesulfonamide, (*R*,*S*,*S*)-3i: According to GP2, (*R*,*S*,*S*)-**3i** was obtained as a colourless solid after purification by column chromatography (SiO$_2$, ether/pentane 1:1, containing 2% NEt$_3$). Yield 0.75 g (81%) − TLC: R_f = 0.38 (ether/pentane 2:1) − $[\alpha]_D^{26}$ = + 89.1 (c = 1.00, CHCl$_3$) − *de* ≥ 98% (^{13}C NMR) − m.p. 133 °C − IR (KBr): $\tilde{\nu}$ = 3237 (s), 3027 (m), 2976 (s), 2962 (s), 2922 (s), 2895 (m), 2875 (m), 2835 (m), 2812 (s), 1619 (m), 1598 (w), 1495 (m), 1456 (s), 1428 (m), 1401 (m), 1379 (m), 1321 (s), 1308 (m), 1289 (m), 1246 (m), 1163 (s), 1126 (s), 1093 (s), 1071 (m), 1039 (s), 1071 (w), 1039 (m), 1027 (m), 984 (m), 965 (m), 942 (m), 914 (m), 818 (m), 753 (m), 705 (m), 672 (m), 577 (s), 550 (m) cm^{-1}. − ^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.83 (d, J = 6.9 Hz, 3 H, CHC*H*$_3$), 1.00 (t, J = 7.6 Hz, 3 H, CH$_2$C*H*$_3$), 1.38−2.13 (m, 8 H, NCH$_2$C*H*$_2$C*H*$_2$, HC*H*CHNHSO$_2$, C*H*CH$_3$, C*H*$_2$CH$_3$), 2.33−2.61 (m, 6 H, NC*H*$_2$CH$_2$CH$_2$, *H*CHCHNHSO$_2$, CC*H*$_3$), 2.82−3.62 (m, 9 H, C*H*NHSO$_2$, NC*H*CH$_2$CH$_2$, C*H*$_2$OC*H*$_3$, C*H*$_2$C$_6$H$_5$), 6.42 (d, J = 6.0 Hz, 1 H, N*H*), 7.00−7.27 (m, 7 H, C$_6$*H*$_5$, CHCCH$_3$), 7.75 (m, 2 H, C*H*CSO$_2$). − ^{13}C NMR (100 MHz, CDCl$_3$), *E*-isomer: δ = 10.69, 18.69, 21.48, 22.08, 24.06, 26.56, 35.14, 37.09, 41.72, 52.60, 54.84, 59.15, 65.93, 75.46, 126.32, 127.02, 128.32, 129.52, 129.63, 137.71, 138.59, 142.83, 174.78. *Z*-isomer: δ = 11.73, 17.92, 21.48, 22.19, 23.20, 25.51, 30.99, 37.60, 39.95, 55.63, 55.76, 58.22, 65.09, 74.77, 126.19, 126.77, 128.36, 129.03, 129.24, 139.01, 139.94, 142.36, 173.57. − MS (CI): *m*/*z* (%) = 487 (32), 486 (100) [MH]$^+$, 288 (7). − C$_{27}$H$_{39}$N$_3$O$_3$S (485.68): calcd. C 66.77, H 8.09, N 8.65; found C 66.80, H 8.23, N 8.60.

(1*R*,3*S*,4*E*,2′*R*)-*N*-{3-(Benzo[1,3]dioxol-5-yl)-1-benzyl-4-[2′-(methoxymethyl)pyrrolidin-1′-ylimino]-butyl}-4-methylbenzenesulfonamide, (*R*,*S*,*R*)-3j: According to GP2, (*R*,*S*,*R*)-**3j** was obtained as a yellow oil after purification by column chromatography (SiO$_2$, ether/pentane 1:1, containing 2% NEt$_3$). Yield 0.22 g (64%) − TLC:

R_f = 0.27 (ether/pentane 2:1) − $[\alpha]_D^{26}$ = + 81.8 (c = 0.99, $CHCl_3$) − *de* ≥ 98% (^{13}C NMR) − IR ($CHCl_3$): $\tilde{\nu}$ = 3280 (m), 3085 (m), 3063 (m), 3027 (m), 2925 (s), 2880 (s), 2831 (m), 1598 (m), 1503 (s), 1487 (s), 1441 (s), 1330 (s), 1304 (s), 1291 (m), 1246 (s), 1197 (s), 1185 (s), 1158 (s), 1119 (s), 1094 (s), 1040 (s), 971 (m), 937 (s), 862 (m), 814 (s), 754 (s), 703 (s), 666 (s), 585 (m), 568 (m), 551 (s) cm^{-1}. − ^1H NMR (400 MHz, $CDCl_3$): δ = 1.61−2.08 (m, 6 H, $CH_2CHNHSO_2$, $NCH_2CH_2CH_2$), 2.40 (s, 3 H, CCH_3), 2.65 (m, 1 H, $NCHCH_2CH_2$), 2.76 (dd, J = 7.1/13.1 Hz, 1 H, $HCHC_6H_5$), 2.82 (dd, J = 5.0/13.1 Hz, 1 H, $HCHC_6H_5$), 3.06 (m, 1 H, $CHNHSO_2$), 3.22 (m, 1 H, $CHCH{=}N$), 3.36−3.45 (m, 3 H, $HCHOCH_3$, $NCH_2CH_2CH_2$), 3.39 (s, 3 H, OCH_3), 3.59 (m, 1 H, $HCHOCH_3$), 5.68 (s, 1 H, NH), 5.87 (d, J = 3.0 Hz, 1 H, OHCHO), 5.88 (d, J = 2.7 Hz, 1 H, OHCHO), 6.29 (dd, J = 1.6/8.0 Hz, 1 H, ArH), 6.32 (d, J = 1.6 Hz, 1 H, ArH), 6.34 (d, J = 4.7 Hz, 1 H, CHNN), 6.59 (d, J = 8.0 Hz, 1 H, ArH), 7.02−7.23 (m, 7 H, C_6H_5, $CHCCH_3$), 7.65 (d, J = 8.3 Hz, 2 H, $CHCSO_2$). − ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.44, 22.06, 26.62, 37.82, 42.26, 45.63, 49.84, 54.24, 59.06, 63.17, 74.82, 100.68, 107.91, 107.96, 120.43, 126.14, 126.90, 128.08, 129.23, 129.39, 136.40, 137.30, 137.74, 139.05, 142.73, 145.84, 147.44. − MS (CI): *m*/*z* (%) = 565 (37), 564 (100, $[MH]^+$), 518 (6), 280 (41), 131 (16), 129 (7), 114 (5). − $C_{31}H_{37}N_3O_5S$ (563.71): calcd. C 66.05, H 6.62, N 7.45; found C 65.64, H 6.75, N 7.32.

General Procedure 3 for the Cleavage of SAMP-/RAMP Aldehyde Hydrazones with Magnesium Monoperoxyphthalate (3a−e,j, GP3): Magnesium monoperoxyphthalate (2 equiv.) was dissolved in MeOH (20 mL/mmol) and pH 7−buffer solution (10 mL/mmol). The resulting suspension was cooled to 0 °C and treated with a solution of hydrazones **3a−e,j** (1 equiv.) dissolved in MeOH (2 mL/mmol). The reaction mixtures were allowed to warm to room temperature, stirred for 4 h and finally 50 mL H_2O was added. The aqueous phases were extracted with ether (3 × 50 mL). The combined organic phase was washed with H_2O (20 mL) and brine (2 × 50 mL) and dried over $MgSO_4$. After removal of the solvent, the residues were purified by flash chromatography (SiO_2, ether/pentane 1:1) to afford γ-amino nitriles **4a−e,j**.

***N*-[(3*S*)-Cyanobutyl]-4-methylbenzenesulfonamide, (*S*)-4a:** According to GP3, (*S*)-**4a** was obtained as a colourless oil after purification by column chromatography (SiO_2, ether/pentane 1:1). Yield 0.124 g (78%) − TLC: R_f = 0.23 (ether/pentane 2:1) − $[\alpha]_D^{26}$ = +32.2 (c = 1.00, $CHCl_3$) − ee ≥ 98% − IR ($CHCl_3$): $\tilde{\nu}$ = 3275 (s), 3065 (m), 2981 (m), 2940 (m), 2879 (m), 2242 (m), 1599 (m), 1495 (m), 1455 (s), 1429 (m), 1385 (m), 1328 (s), 1307 (s), 1291 (m), 1211 (w), 1185 (m), 1158 (s), 1093 (s), 1019 (m), 982 (w), 904 (m), 882 (m), 817 (s), 707 (m), 665 (s), 586 (m), 568 (m), 552 (s) cm^{-1}. − ^1H NMR (400 MHz, $CDCl_3$): δ = 1.28 (d, J = 6.9 Hz, 3 H, $CHCH_3$), 1.77 (m, 2 H, CH_2CH_2NH), 2.43 (s, 3 H, CCH_3), 2.77 (m, 1 H, CHCN), 3.04 (m, 2 H, CH_2CH_2NH), 5.44 (s, 1 H, NH), 7.33 (d, J = 8.0 Hz, $CHCCH_3$, 2 H), 7.74 (d, J = 8.2 Hz, 2 H, $CHCSO_2$). − ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.83, 21.74, 22.86, 34.13, 40.69, 122.65, 127.28, 130.10, 136.65, 143.96. − MS (CI): *m*/*z* (%) = 254 (13), 253 (100) $[MH]^+$, 99 (6). − $C_{12}H_{16}N_2O_2S$ (252.33): calcd. C 57.12, H 6.39, N 11.10; found C 56.74, H 6.59, N 11.45.

***N*-[(3*S*)-Cyanopentyl]-4-methylbenzenesulfonamide, (*S*)-4b:** According to GP3, (*S*)-**4b** was obtained as a colourless oil after purification by column chromatography (SiO_2, ether/pentane 1:1). Yield 0.22 g (80%) − TLC: R_f = 0.34 (ether/pentane 2:1) − $[\alpha]_D^{26}$ = +25.0 (c = 1.00, $CHCl_3$) − ee ≥ 98% − IR ($CHCl_3$): $\tilde{\nu}$ = 3277 (s), 3065 (m), 2970 (m), 2936 (m), 2879 (m), 2239 (m), 1599 (m), 1495 (m), 1460 (m), 1430 (m), 1386 (m), 1329 (s), 1292 (m), 1242 (w), 1185 (m), 1161 (s), 1094 (s), 1033 (m), 935 (m), 817 (s), 777 (w), 707 (m), 665 (m), 569 (m), 552 (s) cm^{-1}. − ^1H NMR (400 MHz, $CDCl_3$): δ = 1.03 (t, J = 7.4 Hz, 3 H, CH_2CH_3), 1.52 (m, 2 H, CH_2CH_2NH), 1.77 (q, J = 7.4 Hz, 2 H, CH_2CH_3), 2.42 (s, 3 H, CCH_3), 2.63 (m, 1 H, CHCN), 3.03 (m, 2 H, CH_2CH_2NH), 5.46 (t, J = 6.4 Hz, 1 H, NH), 7.33 (d, J = 8.2 Hz, 2 H, $CHCCH_3$), 7.74 (d, J = 8.4 Hz, 2 H, $CHCSO_2$). − ^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.39, 21.52, 25.19, 30.28, 31.97, 40.66, 121.54, 127.08, 129.88, 136.48, 143.74. − MS (CI): *m*/*z* (%) = 268 (15), 267 (100) $[MH]^+$, 113 (6). − $C_{13}H_{18}N_2O_2S$ (266.36): calcd. C 58.62, H 6.81, N 10.52; found C 58.23, H 6.71, N 10.72.

***N*-[(3*R*)-Cyano-4-methylpentyl]-4-methylbenzenesulfonamide, (*R*)-4c:** According to GP3, (*R*)-**4c** was obtained as a colourless oil after purification by column chromatography (SiO_2, ether/pentane 1:1). Yield 0.43 g (87%) − TLC: R_f = 0.56 (ether/pentane 2:1) − $[\alpha]_D^{26}$ = +31.7 (c = 1.23, $CHCl_3$) − ee ≥ 98% − IR ($CHCl_3$): $\tilde{\nu}$ = 3274 (m), 3021 (m), 2966 (m), 2933 (m), 2876 (m), 2238 (m), 1599 (m), 1495 (m), 1465 (m), 1452 (m), 1430 (m), 1394 (m), 1374 (m), 1328 (s), 1307 (m), 1291 (m), 1235 (w), 1216 (w), 1185 (m), 1160 (s), 1094 (s), 1020 (w), 939 (w), 851 (m), 816 (m), 707 (m), 666 (m), 552 (s) cm^{-1}. − ^1H NMR (400 MHz, $CDCl_3$): δ = 0.98 (d, J = 6.9 Hz, 3 H, $CHCH_3$), 1.00 (d, J = 6.9 Hz, 3 H, $CHCH_3$), 1.71−1.83 (m, 3 H, CH_2CH_2NH, $CH(CH_3)_2$), 2.42 (s, 3 H, CCH_3), 2.58 (dt, J = 5.2/8.0 Hz, 1 H, CHCN), 3.07 (m, 2 H, CH_2CH_2NH), 5.46 (t, J = 6.3 Hz, 1 H, NH), 7.33 (d, J = 8.5 Hz, 2 H, $CHCCH_3$), 7.75 (d, J = 8.5 Hz, 2 H, $CHCSO_2$). − ^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.63, 21.06, 21.73, 30.02, 30.47, 36.17, 41.11, 120.75, 127.30, 130.08, 136.73, 143.93. − MS (CI): *m*/*z* (%) = 282 (15), 281 (100, $[MH]^+$). − $C_{14}H_{20}N_2O_2S$ (280.39): calcd. C 59.97, H 7.19, N 9.99; found C 59.93, H 6.97, N 9.88.

***N*-[(3*R*)-Cyano-4-phenylbutyl]-4-methylbenzenesulfonamide, (*R*)-4d:** According to GP3, (*R*)-**4d** was obtained as a colourless solid after purification by column chromatography (SiO_2, ether/pentane 1:1). Yield 0.33 g (84%) − TLC: R_f = 0.50 (ether/pentane 2:1) − $[\alpha]_D^{26}$ = +16.0 (c = 1.12, $CHCl_3$) − ee: ≥ 98% − m.p. 115 °C − IR (KBr): $\tilde{\nu}$ = 3239 (s), 3062 (w), 2986 (w), 2930 (m), 2892 (m), 2857 (m), 2242 (m), 1595 (m), 1495 (m), 1476 (m), 1456 (m), 1429 (m), 1396 (m), 1370 (m), 1339 (m), 1317 (s), 1303 (m), 1292 (m), 1243 (m), 1166 (s), 1156 (s), 1120 (m), 1093 (m), 1083 (m), 1066 (m), 1016 (m), 945 (m), 918 (m), 901 (m), 824 (m), 736 (m), 702 (s), 613 (m), 591 (m), 563 (m), 551 (s) cm^{-1}. − ^1H NMR (400 MHz, $CDCl_3$): δ = 1.70−1.86 (m, 2 H, CH_2CH_2NH), 2.41 (s, 3 H, CCH_3), 2.76−3.15 (m, 5 H, $CH_2CHCH_2CH_2NH$), 5.24 (s, 1 H, NH), 7.15−7.33 (m, 7 H, C_6H_5, $CHCCH_3$), 7.73 (d, J = 8.2 Hz, 2 H, $CHCSO_2$). − ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.49, 30.71, 31.88, 37.80, 40.49, 120.90, 126.86, 127.13, 128.54, 128.84, 129.69, 136.18, 136.20, 143.54. − MS (CI): *m*/*z* (%) = 330 (19), 329 (100) $[MH]^+$, 173 (6). − $C_{18}H_{20}N_2O_2S$ (328.43): calcd. C 65.83, H 6.14, N 8.53; found C 65.57, H 6.27, N 8.49.

***N*-[(3*R*)-Benzo[1,3]dioxol-5-yl-3-cyanopropyl]-4-methylbenzenesulfonamide, (*R*)-4e:** According to GP3, (*R*)-**4e** was obtained as a colourless oil after purification by column chromatography (SiO_2, ether/pentane 1:1). Yield 0.54 g (71%) − TLC: R_f = 0.35 (ether/pentane 2:1) − $[\alpha]_D^{26}$ = +34.5 (c = 1.08, $CHCl_3$) − ee ≥ 98% − IR ($CHCl_3$): $\tilde{\nu}$ = 3280 (m), 3022 (m), 2925 (m), 2895 (m), 2242 (w), 1598 (m), 1505 (s), 1490 (s), 1446 (s), 1368 (m), 1329 (s), 1306 (s), 1291 (m), 1276 (m), 1250 (s), 1186 (m), 1160 (s), 1094 (s), 1040 (s), 932 (m), 858 (m), 814 (s), 757 (s), 707 (m), 667 (m), 552 (m) cm^{-1}. − ^1H NMR (400 MHz, $CDCl_3$): δ = 2.04 (m, 2 H, CH_2CH_2NH), 2.44 (s, 3 H, CH_3), 3.04 (m, 2 H, CH_2NH), 3.87 (t, J = 7.4 Hz, 1 H, CHCN), 4.95 (t, J = 6.3 Hz, 1 H, NH), 5.97 (s, 2 H, OCH_2O), 6.70−6.77 (m, 3 H, ArH), 7.32 (d, J = 8.0 Hz, 2 H, H_3CCCH),

7.73 (d, J = 8.0 Hz, 2 H, SO_2CCH). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.52, 33.82, 35.71, 40.26, 101.47, 107.67, 108.70, 120.41, 120.90, 127.14, 128.32, 129.93, 136.38, 143.88, 147.65, 148.34. − MS (CI): m/z (%) = 360 (36), 359 (100) $[MH]^+$, 358 (40), 75 (5). − $C_{18}H_{18}N_2O_4S$ (358.42): calcd. C 60.32, H 5.06, N 7.82; found C 60.32, H 5.41, N 7.91.

***N*-[(3*S*)-Benzo[1,3]dioxol-5-yl-3-cyanopropyl]-4-methylbenzenesulfonamide, (*S*)-4e:** According to GP3, (*S*)-**4e** was obtained as a colourless oil after purification by column chromatography (SiO_2, ether/pentane 1:1). Yield 0.25 g (83%) − $[\alpha]_D^{26}$ = −38.5 (c = 1.32, $CHCl_3$) − *ee*: ≥ 98%.

(1*R*,3*S*)-*N*-[3-Benzo[1,3]dioxol-5-yl-1-benzyl-3-cyanopropyl]-4-methylbenzenesulfonamide, (*R*,*S*)-4j: According to GP3, (*R*,*S*)-**4j** was obtained as a colourless solid after purification by column chromatography (SiO_2, ether/pentane 1:1). Yield 77 mg (100%) − TLC: R_f = 0.33 (ether/pentane 2:1) − $[\alpha]_D^{26}$ = −61.2 (c = 1.00, $CHCl_3$) − de ≥ 98% (^{13}C NMR) − m.p. 59 °C − IR (KBr): $\tilde{\nu}$ = 3275 (m), 3062 (m), 3028 (m), 2923 (m), 2240 (m), 1599 (m), 1505 (s), 1490 (s), 1445 (s), 1332 (s), 1304 (m), 1246 (s), 1185 (m), 1158 (s), 1121 (m), 1088 (s), 1039 (s), 934 (m), 901 (m), 856 (m), 814 (s), 748 (m), 703 (m), 666 (s), 586 (m), 550 (m) cm^{-1}. − ^1H NMR (400 MHz, $CDCl_3$): δ = 2.01 (m, 2 H, CH_2CHNH), 2.42 (s, 3 H, CH_3), 2.59 (m, 2 H, J = 6.6 Hz, $CH_2C_6H_5$), 3.35 (m, 1 H, $CHNH$), 3.79 (dd, J = 6.3/8.5 Hz, 1 H, $CHCN$), 4.79 (m, 1 H, J = 8.5 Hz, NH), 5.96 (d, J = 4.4 Hz, 1 H, $OHCHO$), 5.97 (d, J = 4.4 Hz, 1 H, $OHCHO$), 6.55 (d, J = 1.9 Hz, 1 H, ArH), 6.58 (dd, J = 1.7/8.0 Hz, 1 H, ArH), 6.70 (d, J = 8.0 Hz, 1 H, ArH), 6.85 (m, 2 H, C_6H_5), 7.18 (m, 3 H, C_6H_5), 7.26 (d, J = 8.0 Hz, 2 H, H_3CCCH), 7.64 (d, J = 8.2 Hz, 2 H, SO_2CCH). − ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.51, 32.62, 40.11, 40.85, 52.09, 101.22, 107.82, 108.39, 120.97, 121.20, 126.80, 126.91, 128.12, 128.53, 128.99, 129.70, 135.60, 136.94, 143.54, 147.36, 147.98. − MS (CI): m/z (%) = 450 (30), 449 (100) $[MH]^+$, 295 (19), 293 (14), 240 (5), 203 (16). − $C_{25}H_{24}N_2O_4S$ (448.54): calcd. C 66.94, H 5.39, N 6.25; found C 66.62, H 5.68, N 6.20.

***N*-[(3*S*)-Benzo[1,3]dioxol-5-yl-3-[1,3]dithian-2-ylpropyl]-4-methylbenzenesulfonamide, (*S*)-5e:** Hydrazone (*S*,*R*)-**3e** (0.22 g, 0.46 mmol) was dissolved in dry dichloromethane (5 mL) and then treated with 1,3-propanedithiol (0.06 mL, 0.56 mmol) and finally boron trifluoride−diethyl ether (0.20 g, 1.38 mmol). The reaction mixture was refluxed for 72 h, diluted with dichloromethane (15 mL) and cooled to 0 °C. The solution was neutralized with aqueous, saturated $NaHCO_3$ and extracted with dichloromethane (3×25 mL). The combined organic phase was washed with H_2O (20 mL) and brine (25 mL) and dried over Na_2SO_4. After removal of the solvent, the residue was purified by flash chromatography (SiO_2, ether/pentane 1:1) to afford dithioacetal (*S*)-**5e** as a colourless solid. Yield 0.14 g (67%) − TLC: R_f = 0.30 (ether/pentane 2:1) − $[\alpha]_D^{26}$ = +25.8 (c = 1.08, $CHCl_3$) − m.p. 67 °C − IR (KBr): $\tilde{\nu}$ = 3278 (m), 2894 (m), 1598 (w), 1503 (s), 1488 (s), 1441 (s), 1375 (m), 1326 (s), 1277 (m), 1244 (s), 1185 (m), 1158 (s), 1094 (s), 1038 (s), 933 (m), 864 (m), 814 (m), 774 (w), 730 (w), 707 (w), 663 (m), 550 (m) cm^{-1}. − ^1H NMR (400 MHz, $CDCl_3$): δ = 1.80 (m, 2 H, $SCH_2CH_2CH_2S$), 2.03 (m, 1 H, $CHHCH_2N$), 2.21 (m, 1 H, $CHHCH_2N$), 2.42 (s, 3 H, CH_3), 2.70−2.90 (m, 7 H, $SCH_2CH_2CH_2S$, CH_2N, $CHCHS$), 4.13 (d, J = 7.4 Hz, 1 H, $CHCHS$), 4.76 (t, J = 6.0 Hz, 1 H, NH), 5.93 (s, 2 H, OCH_2O), 6.57 (dd, J = 1.6/8.0 Hz, 1 H, ArH), 6.62 (d, J = 1.6 Hz, 1 H, ArH), 6.69 (d, J = 7.7 Hz, 1 H, ArH), 7.29 (d, J = 8.0 Hz, 2 H, H_3CCCH), 7.66 (d, J = 8.5 Hz, 2 H, SO_2CCH). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.52, 25.77, 30.46, 30.73, 32.64, 41.31, 47.54, 53.54, 101.06, 108.06, 108.07, 121.85, 127.10, 129.69, 133.24, 136.69, 143.36, 146.84, 147.71. − MS (EI) m/z (%) = 451 (10, $[M]^+$), 184 (10), 155 (16), 121 (10), 119 (100), 91 (17). − $C_{21}H_{25}NO_4S_3$ (451.63): calcd. C 55.85, H 5.58, N 3.10; found C 55.38, H 5.81, N 2.96.

General Procedure 4 for the Cleavage of SAMP-/RAMP Ketone Hydrazones with a 1 M Aqueous Solution of Copper(II) Chloride (3f−i, GP4): To an ice-cooled solution of the hydrazones **3f−i** in THF (10 mL/mmol) was slowly added a 1 M aqueous solution of copper(II) chloride (1.2 equiv.) and the resulting mixtures were stirred for 12 h. Then NH_3 aq (10 mL) was added and the reaction mixtures extracted with ether (3 × 25 mL). The combined organic phases were washed with brine (2×25 mL) and dried over $MgSO_4$. After removal of the solvent, the residues were purified by flash chromatography (SiO_2, ether/pentane 1:2) to afford the γ-amino ketones **6f−i**.

4-Methyl-*N*-[(3*R*)-methyl-4-oxohexyl]benzenesulfonamide, (*S*)-6f: According to GP4, (*S*)-**6f** was obtained as a colourless oil after purification by column chromatography (SiO_2, ether/pentane 1:1). Yield 0.50 g (97%) − TLC: R_f = 0.40 (ether/pentane 2:1) − $[\alpha]_D^{26}$ = −9.1 (c = 1.05, $CHCl_3$) − ee ≥ 98% − IR ($CHCl_3$): $\tilde{\nu}$ = 3279 (m), 3030 (w), 2973 (m), 2937 (m), 2878 (m), 1708 (s), 1598 (w), 1495 (w), 1460 (m), 1425 (m), 1378 (m), 1328 (s), 1307 (m), 1290 (m), 1184 (m), 1161 (s), 1094 (s), 1020 (m), 977 (m), 816 (m), 708 (m), 664 (m), 575 (m), 552 (m) cm^{-1}. − ^1H NMR (500 MHz, C_6D_6): δ = 0.77 (d, J = 7.3 Hz, 3 H, $CHCH_3$), 0.97 (t, J = 7.3 Hz, 3 H, CH_2CH_3), 1.19 (m, 1 H, $CHCH_2$), 1.79 (m, 1 H, $CHCH_2$), 1.92 (s, 3 H, CCH_3), 2.12 (m, 2 H, CH_2CH_3), 2.35 (m, 1 H, CH), 2.75 (m, 2 H, CH_2NH), 5.09 (t, J = 6.4 Hz, 1 H, NH), 6.84 (d, J = 8.4 Hz, 2 H, $CHCCH_3$), 7.82 (d, J = 8.3 Hz, 2 H, $CHCSO_2$). − ^{13}C NMR (100 MHz, $CDCl_3$): δ = 7.93, 16.81, 21.09, 32.58, 34.47, 41.52, 43.02, 127.45, 129.75, 138.17, 142.90, 213.53. − MS (CI): m/z (%) = 285 (14), 284 (100) $[MH]^+$, 130 (6), 112 (5). − $C_{14}H_{21}NO_3S$ (283.39): calcd. C 59.34, H 7.47, N 4.94; found C 59.43, H 7.51, N 5.23.

4-Methyl-*N*-[(3*S*)-methyl-4-oxo-4-phenyl-butyl]benzenesulfonamide, (*S*)-6g: According to GP4, (*S*)-**6g** was obtained as a colourless oil after purification by column chromatography (SiO_2, ether/pentane 1:1). Yield 0.136 g (83%) − TLC: R_f = 0.38 (ether/pentane 2:1) − $[\alpha]_D^{26}$ = −6.0 (c = 1.00, $CHCl_3$) − ee ≥ 98% − IR ($CHCl_3$): $\tilde{\nu}$ = 3280 (m), 3063 (w), 2972 (m), 2933 (m), 2875 (m), 1680 (s), 1597 (m), 1495 (w), 1448 (m), 1427 (m), 1379 (m), 1327 (s), 1306 (m), 1291 (m), 1235 (m), 1202 (m), 1184 (m), 1160 (s), 1094 (s), 1002 (m), 975 (m), 816 (m), 796 (m), 707 (m), 686 (m), 664 (m), 574 (m), 552 (m) cm^{-1}. − ^1H NMR (400 MHz, $CDCl_3$): δ = 1.12 (d, J = 6.9 Hz, 3 H, $CHCH_3$), 1.59 (m, 1 H, $HCHCH_2NH$), 2.03 (m, 1 H, $HCHCH_2NH$), 2.36 (s, 3 H, CCH_3), 2.97 (m, 2 H, CH_2NH), 3.59 (m, 1 H, $CHCH_3$), 5.35 (t, J = 6.2 Hz, 1 H, NH), 7.22 (d, J = 8.0 Hz, 2 H, $CHCCH_3$), 7.42 (m, 3 H, C_6H_5), 7.53 (m, 2 H, C_6H_5), 7.71 (d, J = 8.3 Hz, 2 H, $CHCSO_2$). − ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.59, 21.43, 32.39, 37.70, 41.04, 126.81, 128.18, 128.46, 129.47, 132.89, 135.76, 136.49, 143.09, 203.44. − MS (CI): m/z (%) = 333 (20), 332 (100) $[MH]^+$, 176 (8), 161 (21), 135 (17), 71 (6). − $C_{18}H_{21}NO_3S$ (331.43): calcd. C 65.23, H 6.39, N 4.23; found C 64.92, H 6.66, N 4.44.

(*S*)-*N*-[2-(2,2-Dimethyl-5-oxo-[1,3]dioxan-4-yl)-ethyl]-4-methylbenzenesulfonamide, (*S*)-6h /(2,2-Dimethyl-5-(toluene-4-sulfonyl)-tetrahydro-[1,3]dioxino[5,4-b]pyrrol-4a-ol, (*S*)-(6h′): According to GP4, (*S*)-**6h, 6h′** were obtained as colourless oils after purification by column chromatography (SiO_2, ether/pentane 1:1). Yield 0.14 g (80%) − TLC: R_f = 0.44 (ether/pentane 2:1) − $[\alpha]_D^{26}$ = +4.4 (c = 1.00, $CHCl_3$) − ee ≥ 98% − IR (KBr): $\tilde{\nu}$ = 3465 (m), 3298 (m),

3062 (m), 2991 (m), 2941 (m), 2894 (m), 1747 (m), 1599 (m), 1496 (m), 1441 (m), 1377 (m), 1329 (m), 1307 (m), 1290 (m), 1269 (m), 1254 (m), 1224 (m), 1160 (s), 1102 (s), 1078 (m), 1066 (m), 1037 (m), 1017 (m), 1002 (m), 952 (w), 927 (w), 868 (m), 816 (m), 737 (m), 706 (m), 670 (m), 598 (m) cm^{-1}. – ^1H NMR (400 MHz, $CDCl_3$): δ (**6h**) = 1.41 (s, 3 H, OCCH_3), 1.43 (s, 3 H, OCCH_3), 1.73 (m, 1 H, CH_2CH$_2$NH), 2.05 (m, 1 H, CH_2CH$_2$NH), 2.42 (s, 3 H, CCH_3), 3.06 (m, 2 H, CH$_2$CH_2NH), 3.97 (d, J = 17.0 Hz, 1 H, CH_2O), 4.21 (dd, J = 1.7/17.0 Hz, 1 H, CH_2O), 4.35 (ddd, J = 1.4/4.1/5.5 Hz, 1 H, CHO), 5.07 (t, J = 6.0 Hz, 1 H, NH), 7.31 (m, J = 8.0 Hz, 2 H, CHCCH$_3$), 7.74 (d, J = 8.2 Hz, 2 H, CHCSO$_2$). – δ (**6h′**) = 1.22 (s, 3 H, OCCH_3), 1.42 (s, 3 H, OCCH_3), 1.80 (m, 1 H, CH_2CH$_2$N), 2.28 (dddd, J = 5.0/9.0/10.4/15.4 Hz, 1 H, CH_2CH$_2$N), 2.42 (s, 3 H, CCH_3), 3.50 (ddd, J = 6.6/9.5/10.4 Hz, 1 H, CH$_2$CH_2N), 3.67 (dt, J = 1.6/8.8 Hz, 1 H, CH$_2$CH_2N), 3.75 (s, 1 H, OH), 3.98 (d, J = 12.6 Hz, 1 H, CH_2O), 4.16 (m, 1 H, CHO), 4.31 (d, J = 12.8 Hz, 1 H, CH_2O), 7.31 (m, J = 8.0 Hz, 2 H, CHCCH$_3$), 7.82 (d, J = 8.2 Hz, 2 H, CHCSO$_2$). – ^{13}C NMR (75 MHz, $CDCl_3$): δ (**6h**) = 20.71, 23.62, 23.76, 28.02, 39.62, 66.40, 72.71, 100.93, 126.88, 129.53, 136.58, 143.21, 208.70. δ (**6h′**) = 20.71, 21.48, 26.42, 28.19, 47.60, 65.28, 77.36, 89.82, 98.89, 126.96, 129.28, 137.07, 143.24. – MS (CI): m/z (%) = 329 (10), 328 (52) $[MH]^+$, 311 (20), 310 (100), 270 (46), 156 (5), 75 (5). – $C_{15}H_{21}NO_5S$ (327.40): calcd. C 55.03, H 6.47, N 4.28; found C 54.93, H 6.51, N 4.26.

(1*R*,3*S*)-*N*-(1-Benzyl-3-methyl-4-oxohexyl)-4-methylbenzenesulfonamide (*R*,*S*)-6i. According to GP4, (*R*,*S*)-**6i** was obtained as a colourless oil after purification by column chromatography (SiO_2, ether/pentane 1:1). Yield 0.19 g (96%) – TLC: R_f = 0.59 (ether/pentane 2:1) – $[\alpha]_D^{26}$ = −8.7 (c = 1.00, $CHCl_3$) – de ≥ 98% (^{13}C NMR) – IR ($CHCl_3$): $\tilde{\nu}$ = 3281 (m), 3025 (m), 2973 (m), 2937 (m), 1708 (m), 1496 (m), 1455 (m), 1421 (m), 1379 (m), 1331 (m), 1305 (m), 1290 (m), 1217 (m), 1158 (s), 1094 (s), 1054 (m), 1033 (m), 974 (m), 950 (m), 816 (m), 756 (s), 702 (m), 667 (m), 583 (m), 551 (m) cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 1.02 (d, J = 7.4 Hz, 3 H, CHCH_3), 1.03 (t, J = 7.2 Hz, 3 H, CH$_2$CH_3), 1.13 (ddd, J = 3.3/10.4/13.8 Hz, 1 H, CHHCHCH), 1.95 (ddd, J = 3.3/10.0/13.7 Hz, 1 H, CHHCHCH), 2.30–2.60 (m, 4 H, CH_2CH$_3$, CH_2C$_6$H$_5$), 2.40 (s, 3 H, CCH_3), 2.57 (m, 1 H, CH$_3$CH), 3.44 (m, 1 H, CHNH), 4.51 (d, J = 9.0 Hz, 1 H, NH), 6.92 (m, 2 H, CHCCH$_3$), 7.14–7.28 (m, 5 H, C$_6$H$_5$), 7.61 (d, J = 8.4 Hz, 2 H, CHCSO$_2$). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 7.67, 18.16, 21.49, 34.21, 37.82, 41.65, 42.19, 52.81, 126.63, 126.93, 128.50, 129.55, 129.72, 136.44, 137.92, 143.23, 214.99. – MS (CI): m/z (%) = 375 (21), 374 (100, $[MH]^+$), 282 (14), 203 (27). – $C_{21}H_{27}NO_3S$ (373.51): calcd. C 67.53, H 7.29, N 3.75; found C 67.26, H 7.51, N 4.05.

(3*S*,2′*R*)-4-Methyl-*N*-[2-(2,2-dimethyl-5-oxo-[1,3]dioxan-4-yl)-ethyl]*N*-(3,3,3-trifluoro-2′-methoxy-2′-phenylpropionyl)benzenesulfonamide, (*S*,*R*)-7h: Hydrazone **3h** (0.20 g, 0.46 mmol) was dissolved in dry CH_2Cl_2 (5 mL) and treated successively with NEt_3 (0.068 g, 0.68 mmol), a catalytic amount of DMAP and (*S*)-methoxytrifluoromethylphenyl acetic acid chloride (Mosher-chloride) (0.18 g, 0.68 mmol) at 0 °C. The reaction mixture was allowed to warm to room temp. over a period of 12 hours and concentrated. The residue was diluted with ether and washed successively with aqueous $KHSO_4$, $NaHCO_3$ and brine. The product was dried over $MgSO_4$. Treatment of the crude Mosher amide according to GP4 furnished (*S*,*R*)-**7i** as a colourless solid after purification by column chromatography (SiO_2, ether/pentane 1:1). Yield 0.18 g (72%) – de ≥ 98% (HPLC) – TLC: R_f = 0.31 (ether/pentane 1:2) – $[\alpha]_D^{26}$ = +51.6 (c = 1.00, $CHCl_3$) – m.p. 147 °C – IR (KBr): $\tilde{\nu}$ = 2991 (m), 1755 (m), 1693 (s), 1597 (m), 1496 (m), 1456 (m), 1424 (m), 1365 (s), 1311 (m), 1280 (m), 1258 (m), 1237 (m), 1222 (m), 1185 (s), 1170 (s), 1105 (m), 1087 (m), 1049 (m), 1000 (m), 975 (m), 956 (m), 911 (m), 873 (m), 768 (m), 740 (m), 723 (s), 708 (m), 686 (m), 657 (m), 644 (m), 562 (m), 543 (m) cm^{-1}. – ^1H NMR (400 MHz, $CDCl_3$): δ = 1.31 (s, 3 H, CH$_3$CCH_3), 1.38 (s, 3 H, CH$_3$CCH_3), 1.47 (m, 1 H, HCHCH$_2$N), 1.85 (m, 1 H, HCHCH$_2$N), 2.47 (s, 3 H, CCH_3), 3.56 (m, 1 H, HCO), 3.64 (s, 3 H, OCH_3), 3.70 (m, 1 H, HCHN), 3.81 (m, 1 H, HCHN), 3.90 (d, J = 17.0 Hz, 1 H, HCHO), 4.13 (dd, J = 1.4/17.0 Hz, 1 H, HCHO), 7.30–7.42 (m, 7 H, CHCCH$_3$, C$_6$H$_5$), 7.90 (m, 2 H, CHCSO$_2$). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.70, 23.47, 23.65, 28.33, 43.60, 56.49, 66.21, 72.53, 85.00, 100.54, 124.12, 126.14, 128.55, 128.95, 129.22, 129.90, 131.95, 135.46, 145.09, 165.74, 207.35. – MS (CI): m/z (%) = 545 (14), 544 (52) $[MH]^+$, 486 (14), 390 (46), 372 (38), 332 (100), 234 (5), 189 (5), 157 (10), 89 (7), 75 (9). – $C_{25}H_{28}F_3NO_7S$ (543.55): calcd. C 55.24, H 5.19, N 2.58; found C 55.38, H 5.38, N 2.49.

X-ray Diffraction Study: Crystal data for $C_{25}H_{28}NO_7F_3S$ (**7i**):[16] The compound crystallizes in the orthorhombic space group $P2_12_12_1$ (19). a = 8.0188(9), b = 13.426(3), c = 24.007(3)Å. M_r = 543.56, Z = 4, D_c = 1.397gcm^{-3}, μ = 16.68 cm^{-1}, no absorption correction. 6269 reflections were collected at 150 K on an ENRAF NONIUS CAD4 diffractometer using Cu-K_α radiation (λ = 1.54179 Å). The structure was solved by direct methods (GENSIN/GENTAN) as implemented in the XTAL3.4 program package of crystallographic routines.[26] 4492 observed reflections [I >2σ(I)] in the final least-squares full-matrix refinement of 334 parameters on F terminating at $R(R_w)$ = 0.069(0.085, w = 1/(σ^2(F) + 0.0005F^2), a goodness of fit of 1.988 and a residual electron density of −0.63/+1.28eÅ^{-3}. The absolute configuration of the molecule as shown in Figure 1 was determined by Flack's method[27] resulting in an absolute structure parameter of X_{abs} = 0.05(5).

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