Asymmetric Synthesis of β-Amino Cyclohexyl Sulfonates, β-Sultams and γ-Sultones

Dieter Enders,* Stefan Wallert, Jan Runsink

Institut für Organische Chemie, Rheinisch-Westfälische Technische Hochschule, Professor-Pirlet-Straße 1, 52074 Aachen, Germany
Fax +49(241)8092127; E-mail: enders@rwth-aachen.de

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Dedicated to Professor Wolfgang Steglich on the occasion of his 70th birthday.

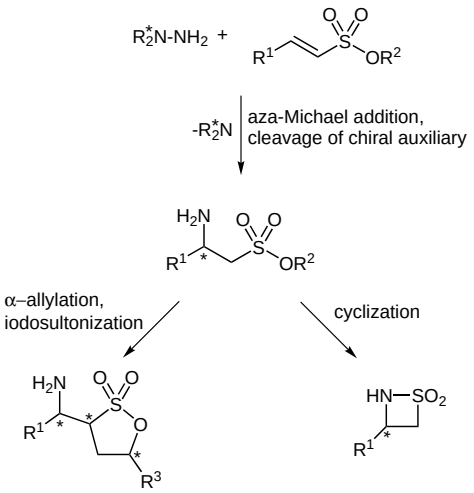
Abstract: An efficient asymmetric synthesis of β-aminocyclohexyl sulfonates, β-sultams and γ-sultones has been developed. The key step of the synthesis is the Lewis acid catalyzed aza-Michael addition of the enantiopure hydrazines SAMP [(*S*)-**1**] or RAMBO [(*R*,*R*,*R*)-**2**] to alkenylcyclohexyl sulfonates **3**. This leads to β-hydrazino sulfonates **4a**–**k** in moderate to good yields (41–85%) and diastereomeric excesses (de = 44–90%). The epimers were separated by preparative HPLC. Subsequent reductive N–N bond cleavage with BH_3·THF and protection of the resulting amines with CbzCl gave *N*-Cbz-protected β-aminocyclohexyl sulfonates **6a**–**k** in moderate to good yields (38–68% over 2 steps) and high enantiomeric excesses (ee ≥ 96%). α-Alkylation of **6** with various electrophiles afforded α-alkyl-β-aminocyclohexyl sulfonates **10a**–**g** in good to excellent yields (67–92%) and moderate to high diastereomeric excesses (de = 71–93%). After alkylation with allyl iodide, the first asymmetric iodosultonization was achieved with high selectivities. Compounds **6g**–**k** were also cyclized in a four-step synthesis to highly enantio-enriched 3-substituted-1,2-thiazetidine 1,1-dioxides (β-sultams) **9a**–**e**.

Key words: asymmetric synthesis, Michael addition, sulfonates, β-sultams, γ-sultones, hydrazines

There is constant need for the synthesis of unnatural amino acids, since these compounds can provide new biological activities and their peptides are attractive targets for drug discovery. The best-known β-aminosulfonic acid is taurine, which is important for the evolution of the central nervous system of many mammals. Moreover, derivatives like 2-amino-2-phenylethanesulfonic acid,[1] a potential $GABA_B$ receptor antagonist or flavocristamides A and B,[2] which have inhibitory activity against DNA polymerase α, demonstrate the demanding interest for the asymmetric synthesis of taurine derivatives.

Furthermore, the exchange of α- or β-amino acids in peptides for β-aminosulfonic acids or the synthesis of β-sulfonopeptides have drawn great attention.[3] White et al. designed β-sulfonopeptides as inhibitors of D-alanyl-D-alanine transpeptidase containing taurine instead of a penultimate amino acid.[4] Liskamp et al. synthesized oligopetido sulfonamides on solid-phase starting from α-amino acids in order to analyze their secondary and tertiary structure as well as their biological activity.[5]

As we have described in a previous communication, the aza-Michael addition provides an efficient access to taurine derivatives.[6] As shown in Scheme 1, the reaction starts with 1,4-addition of enantiopure nitrogen nucleophiles to alkenyl sulfonates, followed by cleavage of the chiral auxilaries. This leads to chiral β-amino sulfonates, which can be used in the synthesis of 3-substituted 1,2-thiazetidine 1,1-dioxides (β-sultams) and γ-sultones.



Scheme 1 Asymmetric synthesis of β-aminocyclohexyl sulfonates, γ-sultones and β-sultams by aza-Michael addition

β-Sultams are the sulfonyl analogues of β-lactams. Therefore, they are interesting building blocks for the synthesis of new antibiotics, corresponding to β-lactam antibiotics.[7] But so far none of the synthesized compounds have shown remarkable antibacterial activities.

Due to their higher reactivity compared to β-lactams (approx. 10^3-fold more reactive),[8] β-sultams are important compounds from a chemical and pharmacological point of view. For example, *N*-benzoyl β-sultam is an irreversible inhibitor of porcine pancreatic elastase (PPE).[9] PPE is related to the human neutrophil elastase (HNE), which causes diseases such as emphysema, cystic fibrosis and rheumatoid arthritis. Furthermore, it has been found that the C–S and C–N bonds can be broken under different experimental conditions, thus making β-sultams interesting building blocks for the synthesis of other heterocyclic systems.[10]

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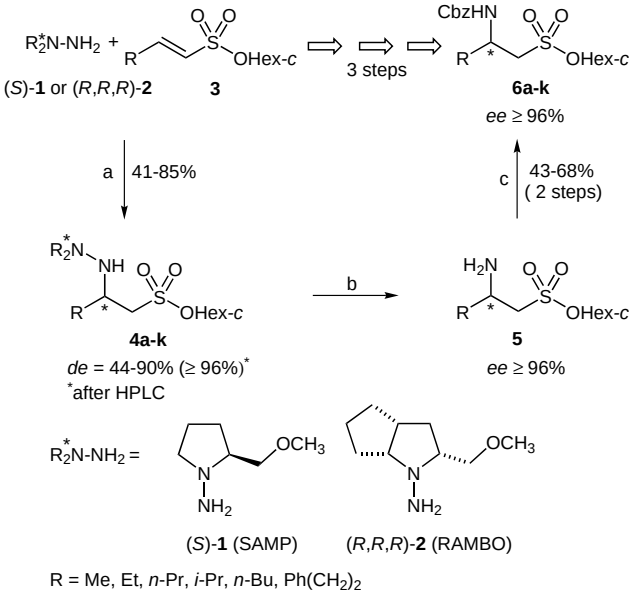
The term sultone was first introduced by Erdmann in 1888.[11] Since then sultones have emerged as valuable heterocyclic intermediates. They are very reactive towards nucleophiles and are therefore used as sulfoalkylating agents.[12] Propane sultone found application in industry as modifier of proteins, fungicides, fire-resistant polymers, oil additives, emulsifying agents and cation exchange resins.[13]

We now wish to report our results on the asymmetric synthesis of β-sultams and γ-sultones, starting from enantioenriched β-aminosulfonates.

The first aza-Michael addition of primary and secondary amines to ethenesulfonates was published in 1970.[14] Progress has been made in the last years towards the aza-Michael addition,[15] but to our knowledge we have described the first enantioselective 1,4-addition with enantiopure nitrogen-nucleophiles to alkenyl sulfonates.[6]

As shown in Scheme 2, (*S*)-1-amino-2-methoxymethylpyrrolidine [SAMP, (*S*)-**1**][16] or (*R*,*R*,*R*)-2-amino-3-methoxymethyl-2-azabicyclo[3.3.0]octane [RAMBO, (*R*,*R*,*R*)-**2**][17] could be added to (*E*)-alkenylcyclohexyl sulfonates **3** in the presence of catalytic amounts of zinc bromide in moderate to good yields and moderate to good diastereomeric excesses (Tables 1 and 2). The excess of (*S*)-**1** or (*R*,*R*,*R*)-**2** can be recovered after column chromatography. α,β-Unsaturated sulfonates **3** were obtained by modification of the Horner–Wadsworth–Emmons olefination reported by Masamune et al.[18] and Rathke et al.[19]



Scheme 2 Enantioselective synthesis of *N*-Cbz-protected β-aminocyclohexyl sulfonates. *Reagents and conditions*: a) $ZnBr_2$, MeOH, r.t.; b) BH_3·THF, THF, reflux; c) CbzCl, Na_2CO_3, CH_2Cl_2–H_2O (4:1), reflux

Addition of a Lewis acid to the reaction mixture is essential. Therefore we tested different Lewis acids [$Yb(OTf)_3$, $Zn(OTf)_2$, $Sn(OTf)_2$, $Pr(OTf)_3$, $CeCl_3$, $Sc(OTf)_3$, $SnCl_4$, $ZrCl_4$, $TiCl_4$, $FeCl_3$, $MgCl_2$, $MgBr_2$, ZnF_2, $ZnBr_2$, $Sm(OTf)_3$, LiBr, $Cu(OTf)_2$, $Eu(OTf)_3$, AgOTf], starting with ytterbium triflate [$Yb(OTf)_3$], which has shown good results in the addition of (*S*)-**1** and (*R*,*R*,*R*)-**2** to alkenylsulfones.[20] For our system zinc bromide proved to be the best Lewis acid.

Table 1 Aza-Michael Addition of SAMP [(*S*)-**1**] to 1-(*E*)-Alkenylcyclohexyl Sulfonates **3**

4	R	Yield (%)	de[a] (%)
(*R*,*S*)–**4a**	Me	78	44 (≥96)[b]
(*R*,*S*)–**4b**	Et	74	55 (≥96)[b]
(*R*,*S*)–**4c**	*n*-Pr	73	58 (≥96)[b]
(*R*,*S*)–**4d**	*i*-Pr	41	80 (≥96)[b]
(*R*,*S*)–**4e**	$Ph(CH_2)_2$	66	60 (≥96)[b]

[a] Determined by ^{13}C NMR spectroscopy.
[b] After HPLC on chiral stationary phase (Daicel AD 2).

Table 2 Aza-Michael Addition of RAMBO [(*R*,*R*,*R*)-**2**] to 1-(*E*)-Alkenylsulfonic Esters **3**

4	R	Yield (%)	de[a] (%)
(*S*,*R*,*R*,*R*)–**4f**	Me	77	64 (≥96)[b]
(*S*,*R*,*R*,*R*)–**4g**	Et	85	77 (≥96)[b]
(*S*,*R*,*R*,*R*)–**4h**	*n*-Pr	62	82 (≥96)[b]
(*S*,*R*,*R*,*R*)–**4i**	*n*-Bu	65	80 (≥96)[b]
(*S*,*R*,*R*,*R*)–**4j**	*i*-Pr	44	90 (≥96)[b]
(*S*,*R*,*R*,*R*)–**4k**	$Ph(CH_2)_2$	63	78 (≥96)[b]

[a] Determined by ^{13}C NMR spectroscopy.
[b] After HPLC on chiral stationary phase (Daicel AD 2).

After the aza-Michael addition, the epimers could be separated by preparative HPLC to yield virtually diastereomerically pure β-hydrazinocyclohexyl sulfonates **4a**–**k**. In the following step the chiral auxiliary was removed by racemization-free reductive N–N bond cleavage utilizing BH_3·THF.[21] After workup and column chromatographic purification the auxiliaries [in the case of SAMP: (*S*)-(methoxymethyl)pyrrolidine] could be recovered as its *N*-Cbz derivative and - after deprotection, nitrosation and reduction - reused in further asymmetric reactions. The resulting crude amines **5** were not purified, but directly protected with CbzCl to yield *N*-Cbz-protected β-aminocyclohexyl sulfonates **6a**–**k** in moderate to good yields and high enantiomeric excesses (Table 3). Other protecting groups, e.g. FmocCl, BnBr or BOC-anhydride have been tested without satisfying results.

The relative configuration of the new stereogenic center was determined by NOE experiments on the major diastereoisomer of (*R*,*S*)-**4d** (Figure 1) and (*S*,*R*,*R*,*R*)-**4j**. The (*R*,*S*)- or (*S*,*R*,*R*,*R*)-configuration follows from the known

Table 3 Synthesis of *N*-Cbz-Protected Amines **6a**–**k**

6	R	Yield[a] (%)	ee[b] (%)
(*R*)–**6a**	Me	68	≥96
(*R*)–**6b**	Et	53	≥96
(*R*)–**6c**	*n*-Pr	43	≥96
(*R*)–**6d**	*i*-Pr	61	≥96
(*R*)–**6e**	$Ph(CH_2)_2$	53	≥96
(*S*)–**6f**	Me	56	≥96
(*S*)–**6g**	Et	53	≥96
(*S*)–**6h**	*n*-Pr	38	≥96
(*S*)–**6i**	*n*-Bu	63	≥96
(*S*)–**6j**	*i*-Pr	57	≥96
(*S*)–**6k**	$Ph(CH_2)_2$	56	≥96

[a] Over 2 steps.
[b] Determined by HPLC (Daicel AD 2).

absolute configuration of SAMP [(*S*)-**1**] or RAMBO [(*R*,*R*,*R*)-**2**].

As shown in Scheme 2, *N*-Cbz-protected β-aminocyclohexyl sulfonates **6a**–**f** can now be cyclized to 3-substituted β-sultams.

The cyclization of β-aminosulfonyl chlorides has been carried out quite often.[22] For example Otto et al. synthesized different β-sultams to analyze their biological activities compared to β-lactam antibiotics.[7]

Another approach to β-sultams is the [2+2] cycloaddition of a sulfene intermediate with chiral imines.[23] Due to the increasing interest in chemical libraries of small and reactive biological compounds Gordeev et al. investigated the [2+2] cycloaddition on a solid phase support.[24]

To the best of our knowledge, only one enantioselective synthesis of β-sultams exists. Baldoli et al. used chiral tricarbonyl(η^6-arene)chromium(0) complexes in the synthesis of 3-(2-phenyl-substituted) *N*-*tert*-butyl-1,2-thiazetidine 1,1-dioxide derivatives. The products are enantiomerically pure, but restricted in the C-3 position (*o*-substituted phenyls).[25]

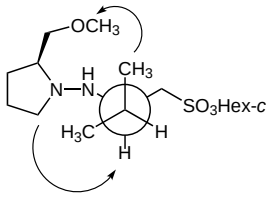
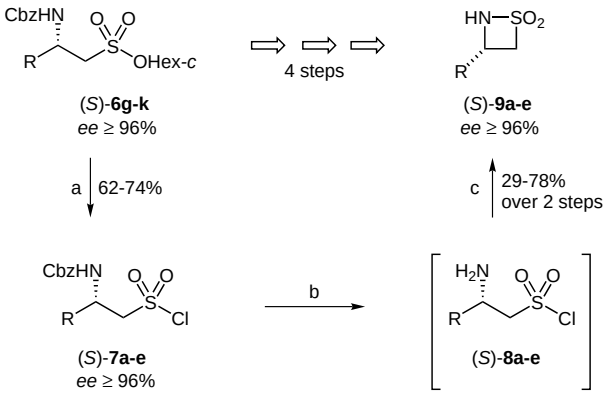


Figure 1 NOE connectivitiy in (*R*,*S*)-**4d**

In an earlier communication we have described a four step asymmetric synthesis of 3-substituted β-sultams.[26] Cleavage of the sulfonates (*S*)-**6g**–**k** in order to achieve free acids succeeded by refluxing in a mixture of EtOH–H_2O (Scheme 3). Without further purification the crude acids were transferred to their sodium salts. The Cbz-protected β-aminosulfonyl chlorides (*S*)-**7a**–**e** were synthesized by adding a solution of phosgene in toluene in good yields (62–74% over 2 steps) and high enantiomeric excesses (ee ≥96%, Table 4). The enantiomeric excesses were determined for the β-sultams (*S*)-**9a**–**e** synthesized in the last step.



R = Et, *n*-Pr, *i*-Pr, *n*-Bu, $Ph(CH_2)_2$

Scheme 3 Enantioselective synthesis of β-sultams. *Reagents and conditions*: a)1. EtOH, H_2O, reflux → r.t., 2. NaOAc, DMF, 3. CH_2Cl_2, 20% $COCl_2$ in toluene; b) 33% HBr in HOAc, r.t. c) NEt_3, 0 °C → r.t.

Table 4 Synthesis of Cbz-Protected β-Aminosulfonyl Chlorides (*S*)-**7a**–**e**

(*S*)-7	R	Yield[a] (%)	ee[b] (%)
(*S*)-**7a**	Et	64	≥96
(*S*)-**7b**	*n*-Pr	74	≥96
(*S*)-**7c**	*i*-Pr	67	≥96
(*S*)-**7d**	*n*-Bu	64	≥96
(*S*)-**7e**	$Ph(CH_2)_2$	62	≥96

[a] Over 2 steps.
[b] Based on the ee values of **9**.

The Cbz-protected β-aminosulfonyl chlorides were deprotected utilizing HBr·AcOH, resulting in β-aminosulfonyl chlorides, which were cyclized in situ using an excess of triethylamine (Scheme 3).

C-3 Substituted β-sultams (*S*)-**9a**–**e** were obtained in moderate to good yields (29–78% over 2 steps) and high enantiomeric excesses (ee ≥96%, Table 5). The enantiomeric excesses were determined by GC on a chiral stationary phase (Daicel AD) by comparison with racemic samples. As shown in Table 5, the β-sultams containing

longer alkyl chains were obtained in higher yields, due to their increasing stability towards hydrolysis.

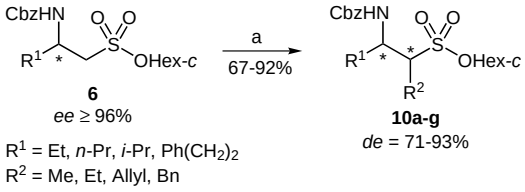
Table 5 Synthesis of 3-Substituted β-Sultams (*S*)-**9a–e**

(*S*)-**9**	R	Yield[a] (%)	ee[b] (%)
(*S*)-**9a**	Et	29	≥96
(*S*)-**9b**	*n*-Pr	68	≥96
(*S*)-**9c**	*i*-Pr	47	≥96
(*S*)-**9d**	*n*-Bu	78	≥96
(*S*)-**9e**	$Ph(CH_2)_2$	55	≥96

[a] Over 2 steps.
[b] Determined by GC on chiral stationary phase (Daicel AD) by comparison with racemic samples.

Besides the synthesis of β-aminosulfonates and β-sultams, we investigated the α-alkylation of **6** with various electrophiles. As shown in Scheme 4 (Table 6), 2.2 equivalents of LDA were necessary, due to the formation of a dianion species. The four equivalents of the corresponding electrophile had no side effects, for example, no alkylation at the nitrogen atom occurred. Only in the case of the most reactive electrophile, methyl iodide, we obtained a small amount of double α-alkylated product. The yields of the α-alkylation reactions were good to excellent (67–92% over 2 steps) and only twice we decided to separate the diastereoisomers by preparative HPLC [(*R*,*R*)-**10a**, (*R*,*R*)-**10e**], due to a lower selectivity (de = 73–85%).

The addition of electrophiles is controlled by the already existing stereocenter and always resulted in *anti*-products, which was confirmed by a NOE experiment on (*R*,*R*)-**10a**. Addition of HMPA, DMPU or LiCl to the reaction mixture had no significant effect on yields or selectivities.



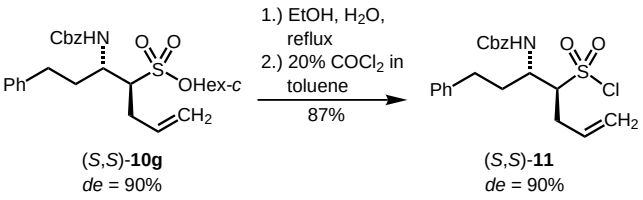
Scheme 4 α-Alkylation of *N*-Cbz-protected β-aminocyclohexyl sulfonates. *Reagents and conditions*: a) LDA, R^2X, –78 °C

The α-alkyl-β-aminocyclohexyl sulfonates **10a–g** can be used in the synthesis of new β-sultams. As shown in Scheme 5 no epimerization in the α-position occurred, during the conversion of the sulfonate to the sulfonyl chloride.

Table 6 α-Alkylation of *N*-Cbz-Protected β-Aminocyclohexyl Sulfonates **10a–g**

10	R^1	R^2X	Yield (%)	de[a] (%)
(*R*,*R*)-**10a**	Et	MeI	67	71 (≥96)[b]
(*R*,*R*)-**10b**	Et	BnBr	79	93
(*R*,*R*)-**10c**	Et	2-Methylallyl bromide	87	90
(*R*,*R*)-**10d**	*n*-Pr	allyl iodide	92	91
(*R*,*R*)-**10e**	*n*-Pr	EtI	83	85 (≥96)[b]
(*R*,*R*)-**10f**	*i*-Pr	allyl iodide	89	90
(*S*,*S*)-**10g**	$Ph(CH_2)_2$	allyl iodide	86	90

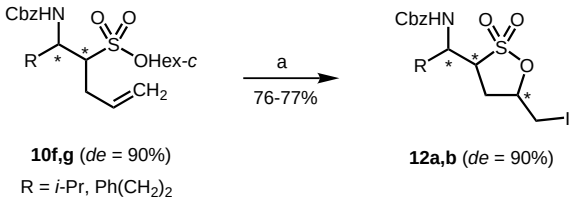
[a] Determined by ^{13}C NMR spectroscopy.
[b] After HPLC (Chiracel-OD).



Scheme 5 Conversion of the β-aminocyclohexyl sulfonate (*S*,*S*)-**10g** to the sulfonyl chloride (*S*,*S*)-**11**

Only a few diastereoselective syntheses of γ-sultones are described in literature. For example Yamamoto et al. published a synthesis of γ-sultones using an intramolecular Michael addition of γ-alkylsulfonyloxy-α,β-unsaturated esters involving higher order cyano copper or silver amides as a base.[27] Another example is the intramolecular stereocontrolled Diels–Alder reaction of vinyl sulfonates by Metz et al.[28] Furthermore, the first auxiliary controlled enantioselective synthesis of γ-sultones was developed in our group.[29]

The 'halolactonization' reaction is a valuable tool in asymmetric synthesis of lactones,[30] but to the best of our knowledge no substrate-controlled stereoselective iodosultonization has been described in the literature. As shown in Scheme 6, after cleavage of the sulfonate the cyclization was obtained by addition of three equivalents iodine to the sodium salts at –78 °C. The yields of the γ-sultones were good (76–77% over 2 steps) and complete induction of the new stereocenter was achieved. Cyclization of (*R*,*R*)-**10c** failed, probably due to steric reasons.



10f,g (*de* = 90%)
R = *i*-Pr, $Ph(CH_2)_2$

12a,b (*de* = 90%)

Scheme 6 Enantioselective synthesis of γ-sultones by iodosultonization. *Reagents and conditions*: a) EtOH, H_2O, reflux → r.t., THF, –78 °C, I_2

The relative configuration of the new stereogenic center was determined by NOE analysis on the major diastereoisomer of (*R*,*R*)-**12a** (Figure 2).

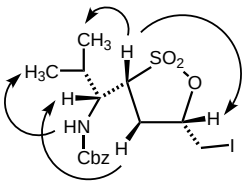


Figure 2 NOE connectivity in (*S*,*R*,*R*)-**12a**

In summary, we have developed a novel asymmetric synthesis of β-aminocyclohexyl sulfonates, β-sultams and γ-sultones. Starting with the aza-Michael addition of the enantiopure hydrazines SAMP or RAMBO to alkenyl sulfonates, N–N-cleavage of the hydrazine 1,4-adducts and protection of the resulting amines leads to the *N*-Cbz-protected β-aminocyclohexyl sulfonates of high enantiomeric purity. After α-alkylation of the sulfonates and iodosultonization a novel class of γ-sultones is obtained (de = 71–93%). In addition, the sulfonates can directly be cyclized to highly enantio-enriched 3-substituted β-sultams.

Melting points were measured with a Büchi 510 apparatus and are not corrected. IR: Perkin Elmer FT 1750 spectrometer. ^{1}H NMR spectra (300, 400, 500 MHz) and ^{13}C NMR spectra (75, 100 MHz): Varian VXR 300, Varian Gemini 300, Varian Inova 400 and Varian VXR 500 spectrometer, internal standard TMS. MS: Varian MAT 212 and Finnegan MAT SSQ 7000 spectrometer (EI 70 eV). Elemental analyses: Heraeus CHN-O-RAPID and Elementar Vario EL. GC: Siemens Sichromat 2 and 3, FID, using SE-54, OV1-CB, OV-5 or OV-17 capilliary columns. Optical rotations: Perkin-Elmer P 241 polarimeter. THF, CH_2Cl_2, MeOH and diisopropylamine were dried and distilled prior to use by standard procedures. *n*-BuLi (1.6 molar solution in hexane), BH_3·THF (1 M solution in THF) and $ZnBr_2$ were purchased from Merck and Aldrich. The pH 7 buffer was prepared from NaOH (11.6 g) and KH_2PO_4 (68 g) in H_2O (1 L). All experiments were performed under argon.

β-Hydrazinocyclohexyl Sulfonates 4a–k; General Procedure

$ZnBr_2$ (0.2 equiv) and the corresponding sulfonate **3** were dissolved in anhyd MeOH (1 mL/mmol **3**). (*S*)-**1** or (*R*,*R*)-**2** was added after 10 min and the reaction mixture was stirred for 7–14 d at r.t. The solution was poured into a mixture of *n*-pentane and Et_2O (2:1, 30 mL/mmol **3**) to precipitate the Lewis acid. After filtration through Celite, the product was purified by column chromatography (silica gel, *n*-pentane–Et_2O) to afford **4a–k** as colorless oils.

(2*R*,2′*S*)-2-{[2′-(Methoxymethyl)pyrrolidine-1′yl]amino}propane-1-cyclohexyl Sulfonate [(*R*,*S*)-4a]

Reaction of **3** (0.409 g, 2 mmol) and SAMP (*S*)-**1** (0.781 g, 6 mmol) gave 0.521 g (78%) of pure (*R*,*S*)-**4a**; $[\alpha]_D^{24}$ –60.6 (*c* = 1.1, $CHCl_3$).

IR ($CHCl_3$): 2937, 2863, 2826, 1452, 1345, 1263, 1195, 1168, 1119, 1032, 1004, 937, 894, 871, 829, 799, 770, 643, 598, 566, 532, 489 cm^{-1}.

^{1}H NMR (400 MHz, C_6D_6): δ = 0.90–1.80 (m, 14 H, $CH_2CH_2CH_2CHN$, CH_2, *c*-Hex), 1.16 (d, 3 H, *J* = 6.32 Hz, CH_3CH), 2.20 (q, 1 H, *J* = 8.79 Hz, $CHHCH_2CH_2CHN$), 2.61 (m, 1 H, $CH_2CH_2CH_2CHN$), 2.85 (dd, 1 H, *J* = 14.29, 5.50 Hz, $CHHSO_2$), 3.10–3.60 (m, 6 H, $CHHCH_2CH_2CHN$, CH_2O, CHNH, $CHHSO_2$, NH), 3.18 (s, 3 H, OCH_3), 4.63 (m, 1 H, CH, *c*-Hex).

^{13}C NMR (100 MHz, C_6D_6): δ = 19.84 (CH_3CH), 21.28, 23.43, 24.99, 26.97 ($OCHCH_2CH_2CH_2$, $NCH_2CH_2CH_2$), 32.83, 32.89 ($OCHCH_2$), 50.33 (CHNH), 56.60 (CH_2SO_2), 57.06 (NCH_2), 58.70 (OCH_3), 66.06 ($NCHCH_2O$), 75.66 (CH_2O), 80.10 (OCH).

MS (EI, 70 eV): *m*/*z* (%) = 334 (1, [M^+]), 332 (5), 287 (17), 221 (7), 207 (27), 206 (9), 205 (100), 169 (6), 141 (7), 125 (45), 123 (6), 115 (26), 84 (8), 83 (52), 73 (11), 71 (76), 69 (6), 57 (7), 56 (14), 55 (57), 45 (42).

Anal. Calcd for $C_{15}H_{30}N_2O_4S$ (334.48): C, 53.86; H, 9.04; N, 8.38. Found: C, 53.77; H, 8.94; N, 8.64.

(2*R*,2′*S*)-2-{[2′-(Methoxymethyl)pyrrolidine-1′yl]amino}butane-1-cyclohexyl Sulfonate [(*R*,*S*)-4b]

Reaction of **3** (0.437 g, 2 mmol) and SAMP (*S*)-**1** (0.781 g, 6 mmol) gave 0.516 g (74%) of pure (*R*,*S*)-**4b**; $[\alpha]_D^{24}$ –88.1 (*c* = 1.1, $CHCl_3$).

IR ($CHCl_3$): 3401, 2937, 2864, 1671, 1454, 1343, 1265, 1248, 1194, 1167, 1119, 1032, 1004, 936, 870, 831, 643, 596, 531 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.92 (t, 3 H, *J* = 7.42 Hz, CH_3CH_2), 1.20–2.05 (m, 16 H, $CH_2CH_2CH_2CHN$, CH_3CH_2, CH_2, *c*-Hex), 2.31 (q, 1 H, *J* = 8.59 Hz, $CHHCH_2CH_2CHN$), 2.61 (m, 1 H, $CH_2CH_2CH_2CHN$), 3.03 (br s, 1 H, NH), 3.12 (m, 1 H, $CHHSO_2$), 3.10–3.60 (m, 5 H, $CHHCH_2CH_2CHN$, CH_2O, CHNH, $CHHSO_2$), 3.36 (s, 3 H, OCH_3), 4.72 (sept, 1 H, *J* = 4.13 Hz, CH, *c*-Hex).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 9.27 (CH_3CH_2), 20.88, 23.47, 24.86, 25.78, 25.88 ($OCHCH_2CH_2CH_2$, CH_3CH_2, $NCH_2CH_2CH_2$), 32.77, 32.80 ($OCHCH_2$), 53.71, 56.88 (CH_2SO_2, NCH_2), 55.56 (CHNH), 59.05 (OCH_3), 65.93 ($NCHCH_2O$), 74.41 (CH_2O), 81.15 (OCH).

MS (EI, 70 eV): *m*/*z* (%) = 348 (6, [M^+]), 266 (14), 221 (100), 219 (10), 129 (10), 71 (5), 55 (10), 45 (8).

Anal. Calcd for $C_{16}H_{32}N_2O_4S$ (348.51): C, 55.14; H, 9.25; N, 8.04. Found: C, 55.12; H, 9.66; N, 8.15.

(2*R*,2′*S*)-2-{[(2′-(Methoxymethyl)pyrrolidine-1′yl]amino}pentane-1-cyclohexyl Sulfonate [(*R*,*S*)-4c]

Reaction of **3** (0.232 g, 1 mmol) and SAMP (*S*)-**1** (0.39 g, 3 mmol) gave 0.265 g (73%) of pure (*R*,*S*)-**4c**; $[\alpha]_D^{24}$ –64.1 (*c* = 1.0, $CHCl_3$).

IR ($CHCl_3$): 2937, 2870, 2827, 1455, 1345, 1264, 1168, 1119, 1096, 1032, 1002, 937, 871, 829, 643, 598, 566, 532 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.94 (t, 3 H, *J* = 7.42 Hz, CH_3CH_2), 1.20–2.05 (m, 18 H, $CH_2CH_2CH_2CHN$, $CH_3CH_2CH_2$, CH_2, *c*-Hex), 2.32 (q, 1 H, *J* = 8.90 Hz, $CHHCH_2CH_2CHN$), 2.62 (m, 1 H, $CH_2CH_2CH_2CHN$), 2.90 (br s, 1 H, NH), 3.10–3.60 (m, 5 H, $CHHCH_2CH_2CHN$, CHHO, CHNH, CH_2SO_2), 3.35 (s, 3 H, OCH_3), 3.48 (dd, 1 H, *J* = 9.40, 3.95 Hz, CHHO), 4.71 (sept, 1 H, *J* = 3.95 Hz, CH, *c*-Hex).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.12 (CH_3CH_2), 18.26 (CH_3CH_2), 20.92, 23.43, 24.84, 25.95 ($OCHCH_2CH_2CH_2$, $NCH_2CH_2CH_2$), 32.71, 32.76 ($OCHCH_2$), 35.24 ($CH_3CH_2CH_2$),

54.10, 56.95 (CH_2SO_2, NCH_2), 54.33 (CHNH), 58.91 (OCH_3), 65.92 (N*C*HCH$_2$O), 74.42 (CH_2O), 80.89 (OCH).

MS (EI, 70 eV): *m*/*z* (%) = 362 (8, [M$^+$]), 280 (16), 236 (12), 235 (100), 129 (10).

Anal. Calcd for $C_{17}H_{34}N_2O_4S$ (362.53): C, 56.32; H, 9.45; N, 7.73. Found: C, 56.29; H, 9.19; N, 7.66.

(2*R*,2′*S*)-2-{[2′-(Methoxymethyl)pyrrolidine-1′yl]amino}-3-methylpropane-1-cyclohexyl Sulfonate [(*R*,*S*)-4d]

Reaction of **3** (3.252 g, 14 mmol) and SAMP (*S*)-**1** (5.468 g, 42 mmol) gave 2.08 g (41%) of pure (*R*,*S*)-**4d**; $[\alpha]_D^{24}$ –87.7 (*c* = 1.0, $CHCl_3$).

IR ($CHCl_3$): 2940, 2869, 2826, 1499, 1455, 1344, 1247, 1196, 1167, 1117, 1033, 995, 935, 870, 830, 774, 733, 643, 600, 564, 530 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.80 (d, 3 H, *J* = 6.87 Hz, C*H*$_3$CH), 0.91 (d, 3 H, *J* = 7.14 Hz, C*H*$_3$CH), 1.20–2.05 (m, 14 H, CH$_2$C*H*$_2$C*H*$_2$CHN, CH_2, *c*-Hex), 2.26 (m, 2 H, C*H*HN, CH_3CH), 2.58 (m, 1 H, NC*H*OCH$_2$), 2.84 (dd, 1 H, *J* = 14.56, 8.89 Hz, C*H*HSO$_2$), 2.96 (br s, 1 H, NH), 3.06 (d, 1 H, *J* = 14.56 Hz, CH*H*SO$_2$), 3.34 (s, 3 H, OCH_3), 3.39 (dd, 1 H, *J* = 9.06, 5.77 Hz, C*H*HO), 3.48 (m, 2 H, CH*H*O, CH*H*N), 3.86 (m, 1 H, C*H*NH), 4.73 (sept, 1 H, *J* = 3.85 Hz, CH, *c*-Hex).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.11, 18.94 [(*C*H$_3$)$_2$CH], 20.70, 23.40, 24.83, 25.57 (OCHCH$_2$*C*H$_2$*C*H$_2$, NCH$_2$*C*H$_2$*C*H$_2$), 28.01 [(CH$_3$)$_2$*C*H], 32.72, 32.75 (OC*H*CH$_2$), 50.16 (CH_2SO_2), 55.96 (NCH_2), 58.42 (CHNH), 58.95 (OCH_3), 65.62 (N*C*HCH$_2$O), 73.88 (CH_2O), 81.01 (OCH).

MS (EI, 70 eV): *m*/*z* (%) = 362 (7, [M$^+$]), 280 (18), 236 (11), 235 (100), 129 (10).

Anal. Calcd for $C_{17}H_{34}N_2O_4S$ (362.53): C, 56.32;, H, 9.45; N, 7.73. Found: C, 56.29; H, 9.53; N, 7.83.

(2*R*,2′*S*)-2-{[2′-(Methoxymethyl)pyrrolidine-1′yl]amino}-4-phenylbutane-1-cyclohexyl Sulfonate [(*R*,*S*)-4e]

Reaction of **3** (2.944 g, 10 mmol) and SAMP (*S*)-**1** (3.905 g, 30 mmol) gave 2.802 g (66%) of pure (*R*,*S*)-**4e**; $[\alpha]_D^{24}$ –55.7 (*c* = 1.0, $CHCl_3$).

IR ($CHCl_3$): 3085, 3061, 3026, 2938, 2862, 1603, 1496, 1454, 1344, 1265, 1169, 1118, 1031, 1003, 935, 870, 829, 747, 700, 644, 595, 533, 489, 457 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.20–2.08 (m, 16 H, NCH$_2$C*H*$_2$C*H*$_2$, PhCH$_2$C*H*$_2$, CH_2, *c*-Hex), 2.33 (q, 1 H, *J* = 8.79 Hz, C*H*HN), 2.80 (br s, 1 H, NH), 2.61–2.78 (m, 3 H, PhC*H*$_2$CH$_2$, CHN), 3.18 (dd, 1 H, *J* = 14.29, 4.12 Hz, C*H*HSO$_2$), 3.25 (dd, 1 H, *J* = 14.29, 7.42 Hz, CH*H*SO$_2$), 3.30 (m, 1 H, CH*H*N), 3.31 (s, 3 H, OCH_3), 3.34 (dd, 1 H, *J* = 9.07, 6.04 Hz, CH*H*O), 3.40 (m, 1 H, C*H*NH), 3.50 (dd, 1 H, *J* = 9.07, 4.12 Hz, C*H*HO), 4.70 (m, 1 H, CH, *c*-Hex), 7.15–7.30 (m, 5 H, C_6H_5).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.24 (NCH$_2$*C*H$_2$CH$_2$), 23.69, 25.07 (OCHCH$_2$*C*H$_2$*C*H$_2$), 26.39 (NCH$_2$CH$_2$*C*H$_2$), 31.45 (Ph*C*H$_2$), 32.95, 33.02 (OCH*C*H$_2$), 34.52 (PhCH$_2$*C*H$_2$), 54.36 (*C*HNH), 54.42 (*C*H$_2$SO$_2$), 57.16 (CH_2N), 59.26 (OCH_3), 66.15 (N*C*HCH$_2$O), 75.04 (CH_2O), 81.40 (OCH), 126.14, 128.59, 128.62 (CH, Ph), 141.89 (C, Ph).

MS (EI, 70 eV): *m*/*z* (%) = 424 (7, [M$^+$]), 342 (16), 299 (6), 298 (18), 297 (100), 129 (17), 91 (5), 70 (6).

Anal. Calcd for $C_{22}H_{36}N_2O_4S$ (424.60): C, 62.23; H, 8.54; N, 6.60. Found: C, 62.33; H, 8.80; N, 6.69.

(2*S*,2′*R*,4′*R*,5′*R*)-2-[(2′-Aza-3′-methoxymethylbicyclo[3.3.0]octane-2′yl)amino]propane-1-cyclohexyl Sulfonate [(*S*,*R*,*R*,*R*)-4f]

Reaction of **3** (0.613 g, 3 mmol) and RAMBO (*R*,*R*,*R*)-**2** (1.532 g, 9 mmol) gave 0.865 g (77%) of pure (*S*,*R*,*R*,*R*)-**4f**; $[\alpha]_D^{28}$ +5.3 (*c* = 1.0, $CHCl_3$).

IR ($CHCl_3$): 2939, 2862, 1451, 1346, 1264, 1249, 1196, 1169, 1119, 1096, 1033, 1004, 938, 911, 893, 870, 831, 790, 757, 704, 643, 624, 602, 564, 533, 490, 460 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.92–2.10 (m, 18 H, C*H*$_2$CH$_2$C*H*$_2$, CHC*H*$_2$CHN, CH_2, *c*-Hex), 1.17 (d, 3 H, *J* = 6.32 Hz, C*H*$_3$CH), 2.45 (m, 1 H, C*H*CHN), 2.70 (m, 1 H, CHCH$_2$C*H*N), 2.92 (dd, 1 H, *J* = 13.46, 6.86 Hz, C*H*HSO$_2$), 3.04 (m, 1 H, CHC*H*N), 3.32 (s, 3 H, OCH_3), 3.34 (dd, 1 H, *J* = 9.89, 4.94 Hz, C*H*HO), 3.40–3.58 (m, 3 H, C*H*HO, C*H*HSO$_2$, C*H*NH), 4.70 (sept, 1 H, *J* = 4.12 Hz, CH, *c*-Hex).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.17 (*C*H$_3$), 23.74, 24.12, 25.11 (OCHCH$_2$*C*H$_2$*C*H$_2$, CH$_2$*C*H$_2$CH$_2$), 33.06, 33.27, 33.51, 35.46 (OCH*C*H$_2$, *C*H$_2$CH$_2$*C*H$_2$, CH*C*H$_2$CHN), 38.37 (*C*HCHN), 50.28 (CHNH), 56.83 (CH_2SO_2), 59.18 (OCH_3), 68.84 (N*C*HCH$_2$O), 75.20 (CH*C*HN), 75.99 (CH_2O), 81.32 (OCH).

MS (EI, 70 eV): *m*/*z* (%) = 374 (4, [M$^+$]), 327 (9), 292 (8), 249 (5), 248 (11), 247 (100), 246 (5), 245 (41), 169 (14), 165 (16), 67 (10), 55 (8), 45 (11).

Anal. Calcd for $C_{18}H_{34}N_2O_4S$ (374.54): C, 57.72; H, 9.15; N, 7.49. Found: C, 58.07; H, 8.96; N, 7.58.

(2*S*,2′*R*,4′*R*,5′*R*)-2-[(2′-Aza-3′-methoxymethylbicyclo[3.3.0]octane –2′yl)amino]butane-1-cyclohexyl Sulfonate [(*S*,*R*,*R*,*R*)-4g]

Reaction of 3 (0.655 g, 3 mmol) and RAMBO (*R*,*R*,*R*)-**2** (1.532 g, 9 mmol) gave 0.99 g (85%) of pure (*S*,*R*,*R*,*R*)-**4g**; $[\alpha]_D^{24}$ +23.4 (*c* = 1.0, $CHCl_3$).

IR ($CHCl_3$): 2939, 2862, 1452, 1346, 1272, 1245, 1196, 1168, 1118, 1032, 1004, 936, 868, 830, 788, 642, 601, 530 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.91 (t, 3 H, *J* = 7.41 Hz, C*H*$_3$CH$_2$), 1.01–2.10 (m, 20 H, CH$_3$C*H*$_2$, C*H*$_2$C*H*$_2$C*H*$_2$, CHC*H*$_2$CHN, CH_2, *c*-Hex), 2.50 (m, 1 H, C*H*CHN), 2.70 (m, 1 H, CHCH$_2$C*H*N), 3.07 (dd, 1 H, *J* = 14.28, 5.22 Hz, C*H*HSO$_2$), 3.08 (m, 1 H, CHC*H*N), 3.26 (dd, 1 H, *J* = 9.62, 6.60 Hz, C*H*HO), 3.32 (s, 3 H, OCH_3), 3.30–3.43 (m, 2 H, C*H*HSO$_2$, C*H*NH), 3.53 (dd, 1 H, *J* = 9.07, 4.94 Hz, C*H*HO), 4.70 (sept, 1 H, *J* = 4.12 Hz, CH, *c*-Hex).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 9.42 (*C*H$_3$CH$_2$), 23.71, 24.42, 25.11, 25.35 (OCHCH$_2$*C*H$_2$*C*H$_2$, CH$_3$*C*H$_2$, CH$_2$*C*H$_2$CH$_2$), 33.04, 33.28, 33.94, 35.56 (OCH*C*H$_2$, *C*H$_2$CH$_2$*C*H$_2$, CH*C*H$_2$CHN), 38.94 (*C*HCHN), 54.47 (CH_2SO_2), 55.15 (CHNH), 59.16 (OCH_3), 68.67 (N*C*HCH$_2$O), 75.57 (CH*C*HN), 75.86 (CH_2O), 81.25 (OCH).

MS (EI, 70 eV): *m*/*z* (%) = 388 (5, [M$^+$]), 306 (12), 263 (5), 262 (13), 261 (100), 169 (15), 67 (7), 55 (8), 45 (5).

Anal. Calcd for $C_{19}H_{36}N_2O_4S$ (388.57): C, 58.73; H, 9.34; N, 7.21. Found: C, 59.06; H, 9.84; N, 7.44.

(2*S*,2′*R*,4′*R*,5′*R*)-2-[(2′-Aza-3′-methoxymethylbicyclo[3.3.0]octane-2′yl)amino]pentane-1-cyclohexyl Sulfonate [(*S*,*R*,*R*,*R*)-4h]

Reaction of **3** (1.859 g, 8 mmol) and RAMBO (*R*,*R*,*R*)-**2** (4.086 g, 24 mmol) gave 1.997 g (62%) of pure (*S*,*R*,*R*,*R*)-**4h**; $[\alpha]_D^{24}$ +17.7 (*c* = 1.0, $CHCl_3$).

IR ($CHCl_3$): 2937, 2863, 1451, 1347, 1265, 1240, 1195, 1168, 1119, 1033, 1004, 937, 869, 833, 791, 643, 603, 531 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.94 (t, 3 H, *J* = 7.42 Hz, C*H*$_3$CH$_2$), 1.00–2.14 (m, 22 H, CH$_3$C*H*$_2$CH$_2$, CH$_3$CH$_2$C*H*$_2$, C*H*$_2$C*H*$_2$C*H*$_2$, CHC*H*$_2$CHN, CH_2, *c*-Hex), 2.50 (m, 1 H, C*H*CHN), 2.69 (m, 1 H, CHCH$_2$C*H*N), 3.06 (m, 2 H, CHC*H*N, C*H*HSO$_2$),

3.32 (s, 3 H, OCH_3), 3.30–3.60 (m, 4 H, C*H*HSO_2, C*H*NH, CH_2O), 4.71 (sept, 1 H, *J* = 3.84 Hz, CH, *c*-Hex).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.60 (*C*H_3CH_2), 18.61 (CH_3*C*H_2), 23.84, 24.50, 25.23 (OCHCH$_2$*C*H$_2$*C*H$_2$, CH$_2$*C*H$_2$CH$_2$), 33.16, 33.42, 33.88, 35.10, 35.72 (OCH*C*H$_2$, CH$_3$CH$_2$*C*H$_2$, *C*H$_2$CH$_2$*C*H$_2$, CH*C*H$_2$CHN), 38.93 (*C*HCHN), 54.01 (CHNH), 55.00 (CH_2SO_2), 59.23 (OCH_3), 68.81 (N*C*HCH$_2$O), 75.58 (CH*C*HN), 75.91 (CH_2O), 81.24 (OCH).

MS (EI, 70 eV): *m*/*z* (%) = 402 (8, [M$^+$]), 320 (15), 277 (6), 276 (14), 275 (100), 169 (15), 67 (5).

Anal. Calcd for $C_{20}H_{38}N_2O_4S$ (402.60): C, 59.67; H, 9.51; N, 6.96. Found: C, 59.50; H, 9.64; N, 7.16.

(2*S*,2′*R*,4′*R*,5′*R*)-2-[(2′-Aza-3′-methoxymethylbicyclo[3.3.0]octane-2′yl)amino]hexane-1-cyclohexyl Sulfonate [(*S*,*R*,*R*,*R*)-4i]

Reaction of **3** (0.246 g, 1 mmol) and RAMBO (*R*,*R*,*R*)-**2** (0.51 g, 3 mmol) gave 0.271 g (65%) of pure (*S*,*R*,*R*,*R*)-**4i**; $[\alpha]_D^{24}$ +18.6 (*c* = 0.8, $CHCl_3$).

IR (film): 2938, 2862, 1452, 1346, 1264, 1247, 1196, 1168, 1119, 1096, 1032, 1004, 937, 870, 829, 790, 733, 643, 601, 530 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.92 (t, 3 H, *J* = 6.87 Hz, C*H*$_3$CH$_2$), 1.00–2.14 (m, 24 H, CH$_3$C*H*$_2$C*H*$_2$C*H*$_2$, C*H*$_2$C*H*$_2$C*H*$_2$, CHC*H*$_2$CHN, CH$_2$, *c*-Hex), 2.50 (m, 1 H, C*H*CHN), 2.70 (m, 1 H, CHCH$_2$C*H*N), 3.06 (m, 2 H, CHC*H*N, C*H*HSO_2), 3.32 (s, 3 H, OCH_3), 3.30–3.60 (m, 4 H, C*H*HSO_2, C*H*NH, CH_2O), 4.71 (sept, 1 H, *J* = 3.84 Hz, CH, *c*-Hex).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.27 (*C*H_3CH_2), 23.08, 23.68, 24.31, 25.10, 27.33 (OCHCH$_2$*C*H$_2$*C*H$_2$, CH$_3$CH$_2$*C*H$_2$, CH$_2$*C*H$_2$CH$_2$), 32.45, 33.02, 33.31, 33.74, 35.58 (OCH*C*H$_2$, CH$_3$CH$_2$CH$_2$*C*H$_2$, *C*H$_2$CH$_2$*C*H$_2$, CH*C*H$_2$CHN), 38.75 (*C*HCHN), 54.04 (CHNH), 54.83 (CH_2SO_2), 59.10 (OCH_3), 68.68 (N*C*HCH$_2$O), 75.46 (CH*C*HN), 75.82 (CH_2O), 81.13 (OCH).

MS (EI, 70 eV): *m*/*z* (%) = 416 (8, [M$^+$]), 334 (16), 289 (100), 169 (19), 67 (6), 55 (7), 45 (5).

Anal. Calcd for $C_{21}H_{40}N_2O_4S$ (416.62): C, 60.54; H, 9.68; N, 6.72. Found: C, 60.72; H, 10.14; N, 6.54.

(2*S*,2′*R*,4′*R*,5′*R*)-2-[(2′-Aza-3′-methoxymethylbicyclo[3.3.0]octane-2′yl)amino]-3-methylbutane-1-cyclohexyl Sulfonate [(*S*,*R*,*R*,*R*)-4j]

Reaction of **3** (0.697 g, 3 mmol) and RAMBO (*R*,*R*,*R*)-**2** (1.532 g, 9 mmol) gave 0.531 g (44%) of pure (*S*,*R*,*R*,*R*)-**4j**; $[\alpha]_D^{24}$ +17.2 (*c* = 0.9, $CHCl_3$).

IR ($CHCl_3$): 2940, 2863, 1498, 1452, 1351, 1264, 1238, 1196, 1168, 1118, 1095, 1004, 937, 870, 830, 734, 641, 601, 567, 503 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.83 (d, 3 H, *J* = 6.86 Hz, C*H*$_3$CH), 0.89 (d, 3 H, *J* = 7.14 Hz, C*H*$_3$CH), 1.00–2.14 (m, 18 H, C*H*$_2$C*H*$_2$C*H*$_2$, CHC*H*$_2$CHN, CH$_2$, *c*-Hex), 2.39 (m, 1 H, CH$_3$C*H*), 2.57 (m, 1 H, C*H*CHN), 2.70 (m, 1 H, CHCH$_2$C*H*N), 2.88 (dd, 1 H, *J* = 14.56, 9.06 Hz, C*H*HSO_2), 3.05 (dd, 1 H, *J* = 14.56, 2.48 Hz, C*H*HSO_2), 3.10 (m, 1 H, CHC*H*N), 3.27 (dd, 1 H, 9.06, 6.87 Hz, C*H*HO), 3.32 (s, 3 H, OCH_3), 3.46 (m, 1 H, C*H*NH), 3.57 (dd, 1 H, *J* = 9.06, 3.85 Hz, CH*H*O), 4.73 (sept, 1 H, *J* = 3.85, CH, *c*-Hex).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.53, 18.79 [(*C*H$_3$)$_2$CH], 23.67, 24.97, 25.10 (OCHCH$_2$*C*H$_2$*C*H$_2$, CH$_2$*C*H$_2$CH$_2$), 27.12 [(CH$_3$)$_2$*C*H], 32.81, 33.00, 33.04, 35.20, 35.43 (OCH*C*H$_2$, *C*H$_2$CH$_2$*C*H$_2$, CH*C*H$_2$CHN), 40.01 (*C*HCHN), 51.01 (CH_2SO_2), 58.00 (CHNH), 59.28 (OCH_3), 68.31 (N*C*HCH$_2$O), 75.56 (CH_2O), 75.97 (CH*C*HN), 81.33 (OCH).

MS (EI, 70 eV): *m*/*z* (%) = 402 (6, [M$^+$]), 320 (14), 277 (7), 276 (15), 275 (100), 169 (18), 67 (6), 55 (2).

Anal. calcd for $C_{20}H_{38}N_2O_4S$ (402.60): C, 59.67; H, 9.51; N, 6.96. Found: C, 59.47; H, 9.42; N, 7.17.

(2*S*,2′*R*,4′*R*,5′*R*)-2-[(2′-Aza-3′-methoxymethylbicyclo[3.3.0]octane-2′yl)amino]-4-phenylbutane-1-cyclohexyl Sulfonate [(*S*,*R*,*R*,*R*)-4k]

Reaction of **3** (1.324 g, 4.5 mmol) and RAMBO (*R*,*R*,*R*)-**2** (2.298 g, 13.5 mmol) gave 1.317 g (63%) of pure (*S*,*R*,*R*,*R*)-**4k**; $[\alpha]_D^{24}$ +20.7 (*c* = 1.0, $CHCl_3$).

IR ($CHCl_3$): 3061, 3026, 2939, 2862, 1496, 1452, 1345, 1238, 1216, 1196, 1169, 1118, 1031, 1002, 934, 869, 830, 756, 700, 643, 599, 531 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.00–2.12 (m, 20 H, C*H*$_2$C*H*$_2$C*H*$_2$, CHC*H*$_2$CHN, PhCH$_2$C*H*$_2$, CH$_2$, *c*-Hex), 2.45–2.74 (m, 4 H, PhC*H*$_2$CH$_2$, OCH$_2$C*H*N, C*H*CHN), 3.10 (m, 1 H, C*H*HO), 3.12 (dd, 1 H, *J* = 14.29, 5.22 Hz, C*H*HSO_2), 3.28 (s, 3 H, OCH_3), 3.20–3.60 (m, 4 H, CHC*H*N, C*H*NH, CH*H*SO_2, CH*H*O), 4.70 (sept, 1 H, *J* = 3.85 Hz, CH, *c*-Hex), 7.18–7.32 (m, 5 H, C_6H_5).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 23.74, 24.43, 25.13 (OCHCH$_2$*C*H$_2$*C*H$_2$, CH$_2$*C*H$_2$CH$_2$), 31.42, 33.04, 33.09, 33.26, 33.88, 34.11, 35.64 (OCH*C*H$_2$, PhCH$_2$*C*H$_2$, *C*H$_2$CH$_2$*C*H$_2$, CH*C*H$_2$CHN, PhCH$_2$*C*H$_2$), 39.00 (*C*HCHN), 53.64 (*C*HNH), 54.77 (CH_2SO_2), 59.21 (OCH_3), 68.62 (N*C*HCH$_2$O), 75.61 (CH*C*HN), 75.92 (CH_2O), 81.35 (OCH), 126.19, 128.68 (CH, Ph), 141.90 (C, Ph).

MS (EI, 70 eV): *m*/*z* (%) = 464 (4, [M$^+$]), 382 (9), 339 (7), 338 (20), 337 (100), 170 (2), 169 (18), 91 (7), 67 (8), 55 (5), 45 (6).

Anal. Calcd for $C_{25}H_{40}N_2O_4S$ (464.67): C, 64.62; H, 8.67; N, 6.03. Found: C, 64.63; H, 8.67; N, 6.07.

***N*-Cbz-Protected β-Aminocyclohexyl Sulfonates 6a–k; General Procedure**

The β-hydrazino sulfonates **4a**–**k** were dissolved in anhyd THF (10 mL/mmol **4a**–**k**). BH_3·THF (10 equiv, 1.0 M in THF) was added and the reaction mixture was refluxed for 5 h. After cooling to r.t., the solution was slowly quenched with MeOH (3 mL/mmol **4a**–**k**). The solvents were carefully evaporated under reduced pressure and the mixture was treated again with MeOH (30 mL/mmol **4a**–**k**). The solution was refluxed for 30 min after which the solvent was removed. The crude amines were dissolved in a mixture of CH_2Cl_2 and H_2O (4:1, 10mL/mmol **4a**–**k**). After the addition of Na_2CO_3 (6 equiv) and CbzCl (3 equiv), the reaction mixture was refluxed for 1–3 d. Then the organic layer was separated and the aqueous phase was extracted three times with CH_2Cl_2 (30 mL/mmol **4a**–**k**). The combined organic layers were washed with sat. aq Na_2CO_3 and NaCl solutions. After drying ($MgSO_4$), the solvent was evaporated and the products were purified by column chromatography (silica gel,; *n*-pentane–Et_2O) to afford **6a**–**k** as colorless solids.

2-Benzyloxycarbonylaminopropane-1-cyclohexyl Sulfonate [6a/f]

Reaction of (*R*,*S*)-**4a** (0.334 g, 1 mmol) or (*S*,*R*,*R*,*R*)-**4f** (0.187 g, 0.5 mmol) with BH_3·THF and CbzCl gave 0.242 g (68%) of pure (*R*)-**6a** or 0.100 g (56%) of pure (*S*)-**6f**; mp 85 °C; $[\alpha]_D^{24}$ +8.5 [*c* = 0.9, $CHCl_3$; for (*R*)-**6a**].

IR (KBr): 3356, 2934, 2865, 1694, 1541, 1455, 1382, 1343, 1327, 1271, 1256, 1208, 1197, 1172, 1108, 1053, 935, 893, 875, 835, 729, 695, 648, 595, 568, 528, 476 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.43 (d, 3 H, *J* = 6.87 Hz, C*H*$_3$CH), 1.20–2.00 (m, 10 H, CH$_2$, *c*-Hex), 3.23 (dd, 1 H, *J* = 14.01, 4.74 Hz, SO_2CH*H*), 3.23 (dd, 1 H, *J* = 14.15, 4.74 Hz, SO_2C*H*H), 4.22 (sept, 1 H, *J* = 6.68 Hz, C*H*NH), 4.72 (sept, 1 H, *J* = 3.84 Hz, CH, *c*-Hex), 5.10 (s, 2 H, OCH_2), 5.15 (d, 1 H, *J* = 9.34 Hz, NH), 7.28–7.38 (m, 5 H, C_6H_5).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.10 (CH_3CH), 23.68, 25.04 ($OCHCH_2CH_2CH_2$), 32.91, 32.99 ($OCHCH_2$), 43.96 (CHNH), 56.28 (CH_2SO_2), 67.05 (OCH_2), 81.93 (OCH), 128.31, 128.42, 128.77 (CH, Ph), 136.47 (C, Ph), 155.57 (OCNH).

MS (CI, isobutane): *m*/*z* (%) = 356 (74, [M$^+$ + 1]), 274 (100).

HRMS: *m*/*z* calcd for $C_{17}H_{25}NO_5S - C_6H_5$ (273.07, M$^+$): 273.0671; found: 273.0670.

2-Benzyloxycarbonylaminobutane-1-cyclohexyl Sulfonate [6b/g]

Reaction of (*R*,*S*)-**4b** (1.394 g, 4 mmol) or (*S*,*R*,*R*,*R*)-**4g** (1.749 g, 4.5 mmol) with BH_3·THF and CbzCl gave 0.783 g (53%) of pure (*R*)-**6b** or 0.881g (53%) of pure (*S*)-**6g**; mp 99 °C; $[\alpha]_D^{24}$ +8.6 [*c* = 0.9, $CHCl_3$; for (*R*)-**6b**].

IR ($CHCl_3$): 3354, 3035, 2969, 2936, 2868, 2852, 1692, 1660, 1588, 1537, 1499, 1453, 1441, 1421, 1411, 1385, 1343, 1333, 1320, 1282, 1265, 1240, 1195, 1168, 1115, 1092, 1056, 1020, 993, 967, 934, 892, 877, 859, 832, 774, 745, 727, 694, 649, 591, 567, 533, 481, 457 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.96 (t, 3 H, *J* = 7.15 Hz, CH_3), 1.20–2.00 (m, 12 H, CH_2, *c*-Hex, CH_3CH_2), 3.25 (dd, 1 H, *J* = 14.01, 4.26 Hz, $CHHSO_2$), 3.40 (dd, 1 H, *J* = 14.01, 4.26 Hz, $CHHSO_2$), 4.00 (m, 1 H, CHNH), 4.70 (m, 1 H, CH, *c*-Hex), 5.10 (s, 2 H, OCH_2), 5.38 (d, 1 H, *J* = 8.24 Hz, NH), 7.28–7.38 (m, 5 H, C_6H_5).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.74 (CH_3CH_2), 23.71, 25.08 ($OCHCH_2CH_2CH_2$), 26.98 (CH_3CH_2), 33.01, 32.93 ($OCHCH_2$), 49.60 (CHNH), 54.80 (CH_2SO_2), 67.02 (OCH_2), 81.87 (OCH), 128.26, 128.39, 128.78 (CH, Ph), 136.63 (C, Ph), 156.00 (OCNH).

MS (EI, 70 eV): *m*/*z* (%) = 370 (1, [M$^+$]), 288 (5), 287 (38), 214 (6), 108 (72), 107 (83), 92 (7), 91 (100), 83 (6), 79 (5), 65 (7), 55 (18).

Anal. Calcd for $C_{18}H_{27}NO_5S$ (369.48): C, 58.51; H, 7.37; N, 3.79. Found: C, 58.70; H, 7.33; N, 3.59.

2-Benzyloxycarbonylaminopentane-1-cyclohexyl Sulfonate [6c/h]

Reaction of (*R*,*S*)-**4c** (0.363 g, 1 mmol) or (*S*,*R*,*R*,*R*)-**4h** (0.201 g, 0.5 mmol) with BH_3·THF and CbzCl gave 0.165 g (43%) of pure (*R*)-**6c** or 0.072 g (38%) of pure (*S*)-**6h**; mp 98 °C; $[\alpha]_D^{24}$ +9.8 [*c* = 1.0, $CHCl_3$; for (*R*)-**6c**].

IR (KBr): 3365, 3035, 2993, 2929, 2869, 2850, 1698, 1535, 1460, 1359, 1331, 1290, 1260, 1225, 1195, 1170, 1109, 1059, 1039, 1027, 1006, 935, 878, 830, 731, 694, 635, 605, 526, 457 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.94 (t, 3 H, *J* = 7.28 Hz, CH_3), 1.20–2.00 (m, 14 H, CH_2, *c*-Hex, $CH_3CH_2CH_2$, $CH_3CH_2CH_2$), 3.29 (dd, 1 H, *J* = 14.43, 4.26 Hz, $CHHSO_2$), 3.42 (dd, 1 H, *J* = 14.42, 5.63 Hz, $CHHSO_2$), 4.09 (m, 1 H, CHNH), 4.72 (sept, 1 H, *J* = 4.12 Hz, CH, *c*-Hex), 5.10 (s, 2 H, OCH_2), 5.22 (d, 1 H, *J* = 8.24 Hz, NH), 7.28–7.37 (m, 5 H, C_6H_5).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.62 (CH_3CH_2), 19.28 (CH_3CH_2), 23.47, 24.83 ($OCHCH_2CH_2CH_2$), 32.71, 32.78 ($OCHCH_2$), 35.58 ($CH_3CH_2CH_2$), 47.74 (CHNH), 54.91 (CH_2SO_2), 66.83 (OCH_2), 81.62 (OCH), 128.05, 128.18, 128.54 (CH, Ph), 136.30 (C, Ph), 155.65 (OCNH).

MS (CI, isobutane): *m*/*z* (%) = 384 (100, [M$^+$ + 1]), 303 (12), 302 (75), 250 (7), 168 (5), 91 (5).

HRMS: *m*/*z* calcd for $C_{19}H_{29}NO_5S$ (383.18, M$^+$): 383.1766; found: 383.1766.

2-Benzyloxycarbonylamino-3-methylbutane-1-cyclohexyl Sulfonate [6d/j]

Reaction of (*R*,*S*)-**4d** (1.088 g, 3 mmol) or (*S*,*R*,*R*,*R*)-**4j** (0.684 g, 1.7 mmol) with BH_3·THF and CbzCl gave 0.701 g (61%) of pure (*R*)-**6d** or 0.371 g (57%) of pure (*S*)-**6j**; mp 102 °C; $[\alpha]_D^{24}$ +8.8 [*c* = 1.0, $CHCl_3$; for (*R*)-**6d**].

IR (KBr): 3374, 2938, 2906, 2868, 1698, 1531, 1469, 1453, 1411, 1387, 1331, 1304, 1273, 1241, 1195, 1171, 1128, 1104, 1035, 1025, 1004, 934, 890, 877, 829, 751, 726, 695, 641, 591, 569, 534, 526, 482 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93 (d, 3 H, *J* = 6.86 Hz, CH_3), 0.98 (d, 3 H, *J* = 6.86 Hz, CH_3), 1.19–2.15 (m, 11 H, CH_2, *c*-Hex, CH_3CH), 3.26 (dd, 1 H, *J* = 14.63, 4.12 Hz, $CHHSO_2$), 3.36 (dd, 1 H, *J* = 14.56, 7.14 Hz, $CHHSO_2$), 3.92 (m, 1 H, CHNH), 4.72 (sept, 1 H, *J* = 4.28 Hz, CH, *c*-Hex), 5.11 (s, 2 H, OCH_2), 5.19 (d, 1 H, *J* = 9.34 Hz, NH), 7.28–7.37 (m, 5 H, C_6H_5).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.53, 19.63 [$(CH_3)_2CH$], 23.82, 25.19 ($OCHCH_2CH_2CH_2$), 31.48 [$(CH_3)_2CH$], 33.04, 33.12 ($OCHCH_2$), 53.28 (CH_2SO_2), 53.39 (CHNH), 67.15 (OCH_2), 81.83 (OCH), 128.22, 128.32, 128.72 (CH, Ph), 136.57 (C, Ph), 156.00 (OCNH).

MS (CI, isobutane): *m*/*z* (%) = 383 (6, [M$^+$]), 303 (13), 302 (80), 168 (7).

HRMS: *m*/*z* calcd for $C_{19}H_{29}NO_5S$ (383.18, M$^+$): 383.1766; found: 383.1766.

2-Benzyloxycarbonylaminohexane-1-cyclohexyl Sulfonate [6i]

Reaction of (*S*,*R*,*R*,*R*)-**4i** (0.708 g, 1.7 mmol) with BH_3·THF and CbzCl gave 0.426 g (63%) of pure (*S*)-**6i**; mp 114 °C; $[\alpha]_D^{24}$ –12.1 (*c* = 1.0, $CHCl_3$).

IR (KBr): 3360, 3034, 2930, 2863, 2185, 1696, 1535, 1454, 1411, 1329, 1254, 1217, 1193, 1169, 1109, 1038, 1006, 935, 875, 832, 774, 731, 694, 644, 602, 569, 541, 526, 486, 456 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.89 (t, 3 H, *J* = 7.28 Hz, CH_3), 1.20–2.00 (m, 16 H, CH_2, *c*-Hex, $CH_3CH_2CH_2CH_2$, $CH_3CH_2CH_2CH_2$, $CH_3CH_2CH_2CH_2CH_2$), 3.28 (dd, 1 H, *J* = 14.29, 4.12 Hz, $CHHSO_2$), 3.40 (dd, 1 H, *J* = 14.56, 5.77 Hz, $CHHSO_2$), 4.07 (m, 1 H, CHNH), 4.71 (m, 1 H, CH, *c*-Hex), 5.10 (s, 2 H, OCH_2), 5.31 (d, 1 H, *J* = 8.79 Hz, NH), 7.28–7.38 (m, 5 H, C_6H_5).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.19 (CH_3), 22.52 ($CH_3CH_2CH_2CH_2$), 23.71, 25.07 ($OCHCH_2CH_2CH_2$), 28.37 ($CH_3CH_2CH_2CH_2$), 32.95, 33.02 ($OCHCH_2$), 33.53 ($CH_3CH_2CH_2CH_2$), 48.20 (CHNH), 55.15 (CH_2SO_2), 67.06 (OCH_2), 81.88 (OCH), 128.29, 128.42, 128.79 (CH, Ph), 136.58 (C, Ph), 155.93 (OCNH).

MS (EI, 70 eV): *m*/*z* (%) = 397 (1, [M$^+$]), 315 (22), 214 (7), 108 (100), 107 (17), 92 (8), 91 (91), 83 (10), 82 (7), 67 (13), 57 (11), 55 (18).

Anal. Calcd for $C_{20}H_{31}NO_5S$ (397.54): C, 60.43; H, 7.86; N, 3.52. Found: C, 60.01; H, 8.05; N, 3.65.

2-Benzyloxycarbonylamino-4-phenylbutane-1-cyclohexyl Sulfonate [6e/k]

Reaction of (*R*,*S*)-**4e** (0.425 g, 1 mmol) or (*S*,*R*,*R*,*R*)-**4k** (1.394 g, 3 mmol) with BH_3·THF and CbzCl gave 0.236 g (53%) of pure (*R*)-**6e** or 0.842 g (63%) of pure (*S*)-**6k**; mp 121 °C; $[\alpha]_D^{24}$ +14.4 [*c* = 1.0, $CHCl_3$; for (*R*)-**6e**].

IR (KBr): 2936, 2863, 1533, 1498, 1454, 1328, 1294, 1247, 1214, 1127, 1049, 1010, 930, 875, 742, 700, 614 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.20–2.20 (m, 12 H, CH_2, *c*-Hex, $PhCH_2CH_2$), 3.26 (dd, 1 H, *J* = 14.56, 4.12 Hz, $CHHSO_2$), 2.68 (m, 2 H, $PhCH_2CH_2$), 3.40 (dd, 1 H, *J* = 14.56, 5.76 Hz, $CHHSO_2$), 4.07 (m, 1 H, CHNH), 4.68 (m, 1 H, CH, *c*-Hex), 5.10 (s, 2 H, OCH_2), 5.37 (d, 1 H, *J* = 8.51 Hz, NH), 7.24–7.36 (m, 5 H, C_6H_5).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.82, 25.18 ($OCHCH_2CH_2CH_2$), 32.60 ($PhCH_2CH_2$), 33.03, 33.08 ($OCHCH_2$), 35.44 ($PhCH_2CH_2$),

47.86 (*C*HNH), 55.19 (CH_2SO_2), 67.17 (OCH_2), 82.04 (OCH), 126.41, 128.28, 128.41, 128.63, 128.75, 128.77 (CH, Ph), 136.53, 140.85 (C, Ph), 155.84 (OCNH).

MS (EI, 70 eV): *m*/*z* (%) = 445 (1, [M^+]), 363 (11), 272 (32), 211 (42), 168 (25), 130 (7), 129 (38), 124 (18), 108 (6), 107 (6), 105 (6), 104 (11), 92 (13), 91 (100), 83 (8), 82 (9), 79 (6), 67 (17), 65 (6), 55 (13), 54 (16).

Anal. Calcd for $C_{24}H_{31}NO_5S$ (445.58): C, 64.69; H, 7.01; N, 3.14. Found: C, 64.63; H, 7.44; N, 3.06.

N-Cbz-Protected β-Aminocyclohexylsulfonyl Chlorides 7a–e and (*S*,*S*)-11; General Procedure

N-Cbz-Protected β-aminocyclohexyl sulfonates (*S*)-**6g–k**, (*S*,*S*)-**10g** were dissolved in a mixture of EtOH [30 mL/mmol **6g–k**, (*S*,*S*)-**10g**] and H_2O [1 mL/mmol **6g–k**, (*S*,*S*)-**10g**] and refluxed for 4 h. After cooling to r.t., NaOAc (1.1 equiv) was added and the solution was stirred for 1 h. The solvents were removed under reduced pressure and the crude sodium salts were dissolved in anhyd CH_2Cl_2 (10 mL/mmol **6g–k**, (*S*,*S*)-**10g**) and anhyd DMF (0.12 mL/mmol **6g–k**, (*S*,*S*)-**10g**). Then a solution, containing 20% $COCl_2$ in toluene [1 mL/mmol **6g–k**, (*S*,*S*)-**10g**] was added dropwise and the mixture was stirred for 2 h at r.t. Products were purified by column chromatography (silica gel, *n*-pentane–Et_2O) to afford **7a–e**, (*S*,*S*)-**11** as colorless solids.

(*S*)-2-Benzyloxycarbonylaminobutane-1-sulfonyl Chloride [(*S*)-7a]

Reaction of (*S*)-**6g** (0.222 g, 0.6 mmol) and 20% $COCl_2$ in toluene (0.6 mL, 0.6 mmol) gave 0.117 g (64%) of pure (*S*)-**7a**; mp 104 °C; $[\alpha]_D^{24}$ –13.2 (*c* = 0.8, $CHCl_3$).

IR (KBr): 3324, 2971, 2934, 1693, 1544, 1499, 1458, 1350, 1313, 1286, 1247, 1165, 1116, 1092, 1055, 994, 967, 835, 777, 743, 730, 697, 534 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.98 (t, *J* = 7.14 Hz, 3 H, CH_3), 1.76 (m, 1 H, CH_3CH_2), 3.86 (d, 1 H, *J* = 10.12 Hz, C*H*HSO_2), 4.06 (d, 1 H, *J* = 6.59 Hz, CH*H*SO_2), 4.11 (m, 1 H, C*H*CH_2SO_2), 5.10 (s, 2 H, OCH_2), 5.33 (m, 1 H, NH), 7.28–7.38 (m, 5 H, C_6H_5).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.36 (CH_3CH_2), 26.61 (CH_3CH_2), 49.96 (CHNH), 66.96 (OCH_2), 68.30 (CH_2SO_2), 127.86, 128.09, 128.38 (CH, Ph), 135.86 (C, Ph), 155.38 (OCNH).

MS (EI, 70 eV): *m*/*z* (%) = 306 (2, [M^+]), 126 (6), 108 (51), 107 (20), 105 (11), 99 (6), 92 (9), 91 (100), 79 (7), 77 (7), 65 (7), 58 (7).

Anal. Calcd for $C_{12}H_{16}ClNO_4S$ (305.78): C, 47.14; H, 5.27; N, 4.58. Found: C, 47.29; H, 5.39; N, 4.52.

(*S*)-2-Benzyloxycarbonylaminopentane-1-sulfonyl Chloride [(*S*)-7b]

Reaction of (*S*)-**6h** (0.307 g, 0.8 mmol) and 20% $COCl_2$ in toluene (0.8 mL, 0.8 mmol) gave 0.189 g (74%) of pure (*S*)-**7b**; mp 106 °C; $[\alpha]_D^{24}$ –4.7 (*c* = 1.0, $CHCl_3$).

IR (KBr): 3309, 3071, 2965, 2925, 2871, 1690, 1551, 1462, 1368, 1291, 1265, 1229, 1166, 1119, 1098, 1056, 1016, 907, 835, 750, 729, 694, 674, 599, 581, 532 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$):δ = 0.93 (t, 3 H, *J* = 7.41 Hz, CH_3), 1.40 (m, 2 H, CH_3CH_2), 1.70 (m, 2 H, $CH_3CH_2CH_2$), 3.86 (dd, 1 H, *J* = 14.29, 4.12 Hz, CH*H*SO_2), 4.06 (dd, 1 H, *J* = 14.28, 6.54 Hz, C*H*HSO_2), 4.20 (m, 1 H, C*H*NH), 5.10 (m, 2 H, OCH_2), 5.32 (d, 1 H, *J* = 7.97 Hz, NH), 7.28 (m, 5 H, C_6H_5).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.88 (CH_3CH_2), 19.50 (CH_3CH_2), 35.81 ($CH_3CH_2CH_2$), 48.74 (*C*HNH), 67.38 (OCH_2), 69.06 (CH_2SO_2), 128.28, 128.52, 128.81 (CH, Ph), 136.29 (C, Ph), 155.78 (OCNH).

MS (EI, 70 eV): *m*/*z* (%) = 320 (0.2, [M^+]), 109 (8), 108 (100), 107 (12), 92 (7), 91 (29), 79 (7), 65 (8).

Anal. Calcd for $C_{13}H_{18}ClNO_4S$ (319.81): C, 48.82; H, 5.67; N, 4.38. Found: C, 48.40; H, 5.74; N, 4.28.

(*S*)-2-Benzyloxycarbonylamino-3-methylbutane-1-sulfonyl Chloride [(*S*)-7c]

Reaction of (S)-**6j** (0.307 g, 0.8 mol) and 20% $COCl_2$ in toluene (0.8 mL, 0.8 mol) gave 0.171 g (67%) of pure (*S*)-**7c**; mp 111 °C; $[\alpha]_D^{24}$ +17.2 (*c* = 1.0, $CHCl_3$).

IR (KBr): 3328, 3033, 2978, 2893, 1692, 1544, 1467, 1356, 1338, 1301, 1251, 1165, 1130, 1112, 1039, 1009, 970, 851, 776, 752, 728, 696, 676, 567, 533 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.93 (d, 3 H, *J* = 6.81 Hz, CH_3), 0.98 (d, 3 H, *J* = 6.82 Hz, CH_3), 2.04 (m, 1 H, CH_3CH), 3.84 (dd, 1 H, *J* = 14.06, 3.07 Hz, CH*H*SO_2), 4.00 (dd, 1 H, *J* = 14.28, 8.13 Hz, C*H*HSO_2), 4.15 (m, 1 H, C*H*NH), 5.10 (s, 2 H, OCH_2), 5.35 (d, 1 H, *J* = 8.79 Hz, NH), 7.26–7.40 (m, 5 H, C_6H_5).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.33, 19.61 [(CH_3)$_2$CH], 32.04 [(CH_3)$_2$*C*H], 53.82 (CHNH), 67.44 (OCH_2), 67.51 (CH_2SO_2), 128.25, 128.46, 128.78 (CH, Ph), 136.37 (C, Ph), 156.00 (OCNH).

MS (EI, 70 eV): *m*/*z* (%) = 319 (6, [M^+]), 108 (67), 91 (100), 65 (7).

Anal. Calcd for $C_{13}H_{18}ClNO_4S$ (319.81): C, 48.82; H, 5.67; N, 4.38. Found: C, 48.89; H, 5.63; N, 4.09.

(*S*)-2-Benzyloxycarbonylaminohexane-1-sulfonyl Chloride [(*S*)-7d]

Reaction of (*S*)-**6i** (0.358 g, 0.9 mmol) and 20% $COCl_2$ in toluene (0.9 mL, 0.9 mmol) gave 0.229 g (64%) of pure (*S*)-**7d**; mp 98 °C; $[\alpha]_D^{26}$ –8.3 (*c* = 1.1, $CHCl_3$).

IR (KBr): 3328, 3067, 3032, 2956, 2927, 2861, 1693, 1545, 1456, 1363, 1295, 1259, 1218, 1161, 1125, 1107, 1051, 1029, 834, 776, 732, 696, 670, 608, 528, 455 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89 (t, 3 H, *J* = 7.28 Hz, CH_3), 1.33 (m, 4 H, $CH_3CH_2CH_2CH_2$, $CH_3CH_2CH_2CH_2$), 1.71 (m, 2 H, $CH_3CH_2CH_2CH_2$), 3.86 (dd, 1 H, *J* = 14.01, 4.12 Hz, CH*H*SO_2), 4.08 (dd, 1 H, *J* = 14.29, 6.60 Hz, C*H*HSO_2), 4.18 (m, 1 H, C*H*NH), 5.10 (s, 2 H, OCH_2), 5.29 (d, 1 H, *J* = 7.69 Hz, NH), 7.28–7.38 (m, 5 H, C_6H_5).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.83 (CH_3CH_2), 22.09 (CH_3CH_2), 27.91 ($CH_3CH_2CH_2$), 33.06 ($CH_3CH_2CH_2CH_2$), 48.59 (CHNH), 66.96 (OCH_2), 68.61 (CH_2SO_2), 127.87, 128.10, 128.38 (CH, Ph), 135.86 (C, Ph), 155.31 (OCNH).

MS (EI, 70 eV): *m*/*z* (%) = 334 (1, [M^+]), 216 (8), 197 (6), 181 (17), 179 (7), 167 (8), 165 (7), 128 (12), 127 (5), 126 (45), 125 (8), 112 (6), 108 (5), 92 (8), 91 (88), 83 (8), 69 (6), 65 (31).

Anal. Calcd for $C_{14}H_{20}ClNO_4S$ (333.84): C, 50.37; H, 6.04; N, 4.20. Found: C, 50.19; H, 5.73; N, 4.19.

(*S*)-2-Benzyloxycarbonylamino-4-phenylbutane-1-sulfonyl Chloride [(*S*)-7e]

Reaction of (*S*)-**6k** (0.356 g; 0.8 mmol) and 20% $COCl_2$ in toluene (0.8 mL, 0.8 mmol) gave 0.189 g (62%) of pure (*S*)-**7e**; mp 116 °C; $[\alpha]_D^{24}$ –11.4 (*c* = 1.0, $CHCl_3$).

IR (KBr): 3676, 3653, 3590, 3331, 3062, 3030, 2927, 2861, 1695, 1541, 1498, 1454, 1383, 1356, 1285, 1255, 1212, 1166, 1083, 1049, 907, 847, 774, 743, 697, 608, 528 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.10 (m, 2 H, PhCH_2CH_2), 2.68 (m, 2 H, $PhCH_2CH_2$), 3.83 (dd, 1 H, *J* = 14.00, 3.99 Hz, C*H*HSO_2), 4.04 (dd, 1 H, *J* = 14.15, 6.73 Hz, CH*H*SO_2), 4.15 (m, 1 H, C*H*CH_2SO_2), 5.09 (s, 2 H, OCH_2), 5.41 (d, *J* = 8.24 Hz, 1 H, NH) 7.10–7.36 (m, 10 H, C_6H_5).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 32.46, 35.26 (Ph*C*H_2*C*H_2), 48.64 (CHNH), 67.49 (OCH_2), 68.94 (CH_2SO_2), 126.69, 128.35, 128.62, 128.88, 128.93 (CH, Ph), 136.30, 140.32 (C, Ph), 155.80 (OCNH).

MS (EI, 70 eV): *m*/*z* (%) = 381(1, [M$^+$]), 290 (34), 186 (30), 142 (10), 129 (23), 108 (6), 104 (7), 91 (100), 65 (10).

Anal. Calcd for $C_{18}H_{20}ClNO_4S$ (381.88): C, 56.61; H, 5.28; N, 3.67. Found: C, 56.69; H, 5.50; N, 3.36.

(*S*,*S*)-5-Benzyloxycarbonylamino-7-phenylhept-1-en-4-sulfonyl Chloride [(*S*,*S*)-11]

Reaction of (*S*,*S*)-**10g** (0.243 g, 0.5 mmol) and 20% $COCl_2$ in toluene (0.5 mL, 0.5 mmol) gave 0.184 g (87%) of pure (*S*,*S*)-**11**.

IR (KBr): 3406, 3333, 3063, 3030, 2929, 2861, 1692, 1643, 1532, 1453, 1372, 1299, 1247, 1163, 1039, 997, 930, 753, 699, 633, 589, 540, 491, 473 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.12 (m, 2 H, PhCH_2CH$_2$), 2.40–2.95 (m, 4 H, PhCH$_2$CH_2, CH_2CHSO$_2$), 3.86 (m, 1 H, CHSO$_2$), 4.38 (m, 1 H, C*H*NH), 5.13 (d, 2 H, *J* = 2.72 Hz, OCH_2), 4.95–5.32 (m, 3 H, CH_2CHCH_2, NH), 5.75 (m, 1 H, CH_2C*H*CH$_2$), 7.10–7.38 (m, 10 H, C_6H_5).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 32.33, 32.67, 34.93 (Ph*C*H_2*C*H_2, *C*H_2CHSO$_2$), 50.89 (CHNH), 67.38 (OCH_2), 79.56 (CHSO$_2$), 120.56 (CH_2CH*C*H_2), 126.42, 128.45, 128.67 (CH, Ph), 131.78 (CH_2*C*HCH$_2$), 136.09, 140.22 (C, Ph), 156.03 (OCNH).

MS (EI, 70 eV): *m*/*z* (%) = 421 (2, [M$^+$]), 332 (7), 330 (17), 266 (8), 226 (6), 224 (6), 169 (14), 162 (5), 126 (9), 92 (9), 91 (100), 82 (7), 65 (8).

Anal. Calcd for $C_{21}H_{24}ClNO_4S$ (421.94): C, 59.78; H, 5.73; N, 3.32. Found: C, 59.45; H, 5.69; N, 3.54.

β-Sultams 9a–e; General Procedure

To a mixture of *N*-Cbz-protected β-aminocyclohexyl sulfonyl chloride (*S*)-**7a**–**e** in CH_2Cl_2 (20 mL/mmol (*S*)-**7a**–**e**) was added a 33% solution of HBr in HOAc (1.5 equiv). After stirring for 3 h at r.t., the reaction mixture was cooled to 0 °C and Et_3N was added (12 mL/mmol (*S*)-**7a**–**e**). The solution was stirred for 2 h while it warmed up to r.t. After separation of the organic layer, the aqueous phase was extracted with CH_2Cl_2 [3 × 30 mL/mmol (*S*)-**7a**–**e**]. The combined organic layers were dried ($MgSO_4$) and the solvent was removed under reduced pressure. Products were purified by column chromatography (silica gel, *n*-pentane–Et_2O) to afford **9a**,**b**,**d** as colorless oils and **9c**,**e** as colorless solids.

(*S*)-3-Ethyl-1,2-thiazetidine 1,1 Dioxide [(*S*)-9a]

Reaction of (*S*)-**7a** (0.306 g, 1 mmol) with a solution of HBr in HOAc and Et_3N gave 0.039 g (29%) of pure (*S*)-**9a**; $[\alpha]_D^{24}$ +8.6 (*c* = 0.7, $CHCl_3$).

IR ($CHCl_3$): 3552, 3290, 3031, 2967, 2935, 2879, 2854, 1744, 1462, 1414, 1383, 1316, 1234, 1192, 1159, 1052, 981, 956, 927, 901, 793, 759, 665, 628, 505 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.97 (t, 3 H, *J* = 7.47 Hz, CH_3), 1.80 (m, 2 H, CH_3CH_2), 3.57 (m, 1 H, NHC*H*), 3.87 (dd, 1 H, *J* = 12.53, 5.50 Hz, C*H*HSO$_2$), 4.30 (ddd, 1 H, *J* = 12.75, 7.69, 3.07 Hz, CH*H*SO$_2$), 5.40 (s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 10.07 (CH_3), 29.03 (CH_3*C*H_2), 42.10 (CHNH), 64.34 (CH_2SO_2).

MS (EI, 70 eV): *m*/*z* (%) = 135 (4) [M$^+$], 106 (100), 56 (15).

HRMS: *m*/*z* calcd for $C_4H_9NO_2S$ (135.04, M$^+$): 135.0354; found: 135.0354.

(*S*)-3-Propyl-1,2-thiazetidine 1,1-Dioxide [(*S*)-9b]

Reaction of (*S*)-**7b** (0.320 g, 1 mmol) with a solution of HBr in HOAc and Et_3N gave 0.051 g (68%) of pure (*S*)-**9b**; $[\alpha]_D^{24}$ +5.8 (*c* = 1.0, $CHCl_3$).

IR (film): 3291, 2961, 2934, 2874, 1466, 1414, 1382, 1308, 1224, 1189, 1159, 1114, 1070, 810, 783, 659, 499, 466 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.96 (t, 3 H, *J* = 7.25 Hz, CH_3), 1.36 (m, 2 H, CH_3CH_2CH$_2$), 1.74 (m, 2 H, CH_3CH_2CH_2), 3.63 (m, 1 H, C*H*NH), 3.87 (dd, 1 H, *J* = 12.52, 5.50 Hz, C*H*HSO$_2$), 4.31 (ddd, 1 H, *J* = 12.52, 7.69, 3.08 Hz, CH*H*SO$_2$), 5.56 (s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.97 (*C*$H_3CH_2CH_2$), 19.68 (CH_3*C*H_2CH_2), 38.38 (CH_3CH_2*C*H_2), 41.08 (CHNH), 65.16 (CH_2SO_2).

MS (EI, 70 eV): *m*/*z* (%) = 149 (2, [M$^+$]), 106 (100), 69 (21), 56 (18).

Anal. Calcd for $C_5H_{11}NO_2S$ (149.21): C, 40.25; H, 7.43; N, 9.39. Found: C, 40.16; H, 7.51; N, 9.68.

(*S*)-3-(1-Methylethyl)-1,2-thiazetidine 1,1-Dioxide [(*S*)-9c]

Reaction of (*S*)-**7c** (0.320 g, 1 mmol) with a solution of HBr in HOAc and Et_3N gave 0.070 g (47%) of pure (*S*)-**9c**; mp 87 °C; $[\alpha]_D^{24}$ +10.2 (*c* = 1.0, $CHCl_3$).

IR (KBr): 3675, 3653, 3334, 3048, 2965, 2932, 2881, 1738, 1703, 1654, 1624, 1472, 1413, 1383, 1343, 1298, 1231, 1199, 1148, 1121, 1036, 1013, 987, 929, 882, 801, 762, 682, 602, 507 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.94 (d, 3 H, *J* = 6.59 Hz, CH_3), 0.98 (d, 3 H, *J* = 6.59 Hz, CH_3), 1.90 (m, 1 H, CH_3C*H*), 3.33 (m, 1 H, C*H*NH), 3.93 (dd, 1 H, *J* = 12.64, 6.04 Hz, C*H*HSO$_2$), 4.22 (ddd, 1 H, *J* = 12.64, 7.97, 3.85 Hz, CH*H*SO$_2$), 5.51 (s, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.27, 18.76 [(*C*H_3)$_2$CH], 33.95 [(CH$_3$)$_2$*C*H], 46.91 (CHNH), 63.35 (CH_2SO_2).

MS (EI, 70 eV): *m*/*z* (%) = 149 (1, [M$^+$]), 108 (5), 106 (100), 69 (10), 55 (6), 45 (6).

Anal. Calcd for $C_5H_{11}NO_2S$ (149.21): C, 40.25; H, 7.43; N, 9.39. Found: C, 40.26; H, 7.81; N, 9.09.

(*S*)-3-Butyl-1,2-thiazetidine 1,1-Dioxide [(*S*)-9d]

Reaction of (*S*)-**7d** (0.167 g, 0.5 mmol) with a solution of HBr in HOAc and Et_3N gave 0.064 g (78%) of pure (*S*)-**9d**; $[\alpha]_D^{24}$ +6.8 (*c* = 1.1, $CHCl_3$).

IR ($CHCl_3$): 3171, 3019, 2976, 2932, 2875, 1716, 1380, 1217, 1045, 758, 668, 615 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92 (t, 3 H, *J* = 6.87 Hz, CH_3), 1.22–1.42 (m, 4 H, CH_3CH_2CH_2), 1.76 (m, 2 H, $CH_3CH_2CH_2$CH_2), 3.60 (m, 1 H, C*H*NH), 3.87 (dd, 1 H, *J* = 12.63, 5.50 Hz, C*H*HSO$_2$), 4.30 (ddd, 1 H, *J* = 12.37, 7.80, 3.02 Hz, CH*H*SO$_2$), 5.45 (s, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.90 (*C*$H_3CH_2CH_2$), 22.20 (CH_3*C*H_2CH_2), 28.09 (CH_3CH_2*C*H_2), 35.75 ($CH_3CH_2CH_2$*C*H_2), 40.92 (CHNH), 64.78 (CH_2SO_2).

MS (EI, 70 eV): *m*/*z* (%) = 164 (2, [M$^+$ + 1]), 122 (6), 106 (100), 70 (9), 67 (8), 57 (10), 56 (23), 55 (13).

Anal. Calcd for $C_6H_{13}NO_2S$ (163.24): C, 44.15; H, 8.03; N, 8.58. Found: C, 43.93; H, 8.00; N, 8.73.

(*S*)-3-(2-Phenylethyl)-1,2-thiazetidine 1,1-Dioxide [(*S*)-9e]

Reaction of (*S*)-**7e** 0.191 g (0.5 mmol) with a solution of HBr in HOAc and Et_3N gave 0.058 g (55%) of pure (*S*)-**9e**; mp 95 °C; $[\alpha]_D^{24}$ +3.6 (*c* = 1.0, $CHCl_3$).

IR (KBr): 3676, 3654, 3632, 3273, 3032, 2925, 2856, 1656, 1604, 1497, 1456, 1384, 1331, 1302, 1265, 1231, 1203, 1156, 1098, 1083, 1060, 1031, 972, 934, 805, 753, 701, 629, 572, 519, 479 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.08 (m, 2 H, PhCH_2CH$_2$), 2.68 (m, 2 H, PhCH$_2$CH_2), 3.59 (m, 1 H, C*H*NH), 3.81 (dd, 1 H, *J* = 12.64, 5.49 Hz, C*H*HSO$_2$), 4.22 (ddd, 1 H, *J* = 12.63, 7.69, 3.30 Hz, CH*H*SO$_2$), 5.50 (s, 1 H, NH), 7.13–7.32 (m, 5 H, C_6H_5).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 32.69 (Ph*C*H$_2$CH$_2$), 37.76 (PhCH$_2$*C*H$_2$), 40.80 (CHNH), 65.14 (CH$_2$SO$_2$), 126.77, 128.56, 128.98 (CH, Ph), 139.97 (C, Ph).

MS (EI, 70 eV): *m*/*z* (%) = 211 (1, [M$^+$]), 130 (100), 106 (32), 91 (44), 77 (12), 65 (12), 51 (7).

Anal. Calcd for $C_{10}H_{13}NO_2S$ (211.28): C, 56.85; H, 6.20; N, 6.63. Found: C, 56.58; H, 6.56; N, 6.22.

α-Alkylation of *N*-Cbz-Protected β-Aminocyclohexyl Sulfonates 10a–g; General Procedure

β-Aminocyclohexyl sulfonates **6** were dissolved in anhyd THF (3 mL/mmol **6**) and added to a solution of LDA (2.2 equiv) in anhyd THF (10 mL/mmol **6**) at –78 °C. The mixture was warmed up to –45 °C and after 15 min cooled down to –78 °C. After 45 min at this temperature, the corresponding electrophile (4.0 equiv) was added slowly to the reaction mixture. The reaction was quenched after ca. 16 h at –78 °C with pH 7 buffer and the aqueous phase was extracted with CH_2Cl_2 (3 × 30 mL/mmol **6**). The combined organic layers were washed with sat. aq $NaHCO_3$ and NaCl solutions, dried ($MgSO_4$) and the solvent was removed under reduced pressure. Products were purified by column chromatography (silica gel, *n*-pentane–Et_2O) to afford **10a**–**g** as colorless oils.

(*R*,*R*)-3-Benzyloxycarbonylaminopentane-2-cyclohexyl Sulfonate [(*R*,*R*)-10a]

Reaction of (*R*)-**6b** (0.111 g, 0.3 mmol) and MeI (0.170 g, 1.2 mmol) gave 0.077 g (67%) of pure (*R*,*R*)-**10a**; $[\alpha]_D^{25}$ +24.3 (*c* = 0.7, $CHCl_3$).

IR ($CHCl_3$): 3367, 3032, 2939, 2862, 1720, 1522, 1454, 1339, 1283, 1235, 1169, 1091, 1029, 972, 928, 865, 825, 792, 753, 698, 634, 600 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.98 (t, 3 H, *J* = 7.41 Hz, CH_3CH$_2$), 1.20–2.00 (m, 12 H, CH$_2$, *c*-Hex, CH$_3$CH_2), 1.42 (d, 3 H, *J* = 7.14 Hz, CH_3CH), 3.44 (m, 1 H, CHSO$_2$), 4.00 (m, 1 H, C*H*NH), 4.76 (sept, 1 H, *J* = 4.12 Hz, CH, *c*-Hex), 5.12 (d, 2 H, *J* = 1.65 Hz, CH_2Ph), 5.22 (d, 1 H, *J* = 9.34 Hz, NH), 7.28–7.40 (m, 5 H, C_6H_5).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.04 (*C*H$_3$CH$_2$), 12.49 (*C*H$_3$CH), 23.44, 24.86, 25.63 (OCHCH$_2$*C*H$_2$*C*H$_2$, CH$_3$*C*H$_2$), 32.65, 32.78 (OCH*C*H$_2$), 54.26 (CHNH), 59.48 (CHSO$_2$), 66.85 (OCH$_2$), 81.34 (OCH), 127.96, 128.15, 128.53 (CH, Ph), 136.39 (C, Ph), 156.36 (OCNH).

MS (EI, 70 eV): *m*/*z* (%) = 383 (1, [M$^+$]), 302 (7), 301 (42), 228 (19), 192 (5), 148 (15), 109 (7), 108 (91), 107 (14), 91 (100), 55 (7).

Anal. Calcd for $C_{19}H_{29}NO_5S$ (383.51): C, 59.51; H, 7.62; N, 3.65. Found: C, 59.09; H, 7.56; N, 3.99.

(*R*,*R*)-3-Benzyloxycarbonylamino-1-phenylpentane-2-cyclohexyl Sulfonate [(*R*,*R*)-10b]

Reaction of (*R*)-**6b** (0.111 g, 0.3 mmol) and benzyl bromide (0.205 g, 1.2 mmol) gave 0.109 g (79%) of pure (*R*,*R*)-**10b**.

IR ($CHCl_3$): 3372, 3063, 3030, 2938, 2861, 1720, 1604, 1515, 1454, 1333, 1281, 1230, 1166, 1122, 1076, 1029, 1000, 971, 925, 865, 823, 790, 754, 699, 664, 634, 515 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.96 (t, 3 H, *J* = 7.42 Hz, CH_3CH$_2$), 1.20–2.00 (m, 12 H, CH$_2$, *c*-Hex, CH$_3$CH_2), 2.97 (dd, 1 H, *J* = 14.01, 9.61 Hz, C*H*HCHSO$_2$), 3.34 (dd, 1 H, *J* = 14.28, 3.85 Hz, CH*H*CHSO$_2$), 3.50 (m, 1 H, CHSO$_2$), 3.97 (m, 1 H, C*H*NH), 4.79 (sept, 1 H, *J* = 4.12 Hz, CH, *c*-Hex), 5.12 (s, 2 H, CH_2Ph), 5.27 (d, 1 H, *J* = 9.06 Hz, NH), 7.18–7.38 (m, 10 H, C_6H_5).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.01 (*C*H$_3$CH$_2$), 23.39, 24.84, 26.73 (OCHCH$_2$*C*H$_2$*C*H$_2$, CH$_3$*C*H$_2$), 32.68, 32.77 (OCH*C*H$_2$), 33.19 (*C*H$_2$CHSO$_2$), 51.86 (CHNH), 66.43 (CHSO$_2$), 66.82 (OCH$_2$), 81.53 (OCH), 127.07, 128.01, 128.13, 128.51, 128.80, 129.25 (CH, Ph), 136.50, 137.13 (C, Ph), 156.27 (OCNH).

MS (EI, 70 eV): *m*/*z* (%) = 459 (1, [M$^+$]), 304 (11), 297 (11), 296 (52), 295 (15), 266 (7), 222 (4), 205 (7), 192 (32), 148 (24), 145 (18), 143 (8), 108 (6), 107 (6), 92 (8), 91 (100), 55 (7).

Anal. Calcd for $C_{25}H_{33}NO_5S$ (459.61): C, 65.32; H, 7.24; N, 3.05. Found: C, 64.82; H, 7.31; N, 3.27.

(*R*,*R*)-5-Benzyloxycarbonylamino-6-methylhept-1-en-4-cyclohexyl Sulfonate [(*R*,*R*)-10c]

Reaction of (*R*)-**6d** (0.230 g, 0.6 mmol) and allyl iodide (0.403 g, 2.4 mmol) gave 0.231 g (89%) of pure (*R*,*R*)-**10c**.

IR ($CHCl_3$): 3425, 3068, 3027, 2941, 2864, 1724, 1641, 1588, 1514, 1453, 1418, 1332, 1227, 1164, 1116, 1027, 1001, 924, 893, 866, 824, 756, 698, 666, 572, 547 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.97 (d, 3 H, *J* = 6.60 Hz, CH$_3$), 0.99 (d, 3 H, *J* = 6.59 Hz, CH$_3$), 1.20–2.00 (m, 10 H, CH$_2$, *c*-Hex), 2.16 (m, 1 H, CH$_3$C*H*), 2.47 (m, 1 H, CHC*H*HCH), 2.75 (m, 1 H, CHCH*H*CH), 3.42, (dt, 1 H, *J* = 9.61, 3.30 Hz, CHSO$_2$), 3.76 (dt, 1 H, *J* = 10.43, 2.47 Hz, C*H*NH), 4.81 (sep, 1 H, *J* = 4.12 Hz, CH, *c*-Hex), 5.12 (d, 2 H, *J* = 5.49 Hz, CH_2Ph), 5.14 (m, 2 H, CH$_2$CHCH_2), 5.47 (d, 1 H, *J* = 10.32 Hz, NH), 5.82 (m, 1 H, CH$_2$C*H*CH$_2$), 7.25–7.38 (m, 5 H, C_6H_5).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.88, 20.29 [(*C*H$_3$)$_2$CH], 23.34, 24.79 (OCHCH$_2$*C*H$_2$*C*H$_2$), 31.36 [(CH$_3$)$_2$*C*H], 32.29, 32.63, 32.80 (OCH*C*H$_2$, *C*H$_2$CHSO$_2$), 56.48 (CHNH), 62.52 (CHSO$_2$), 66.68 (OCH$_2$), 81.02 (OCH), 119.41 (CH$_2$CH*C*H$_2$), 127.71, 127.84, 128.26 (CH, Ph), 132.82 (CH$_2$*C*HCH$_2$), 136.40 (C, Ph), 156.36 (OCNH).

MS (EI, 70 eV): *m*/*z* (%) = 423 (2, [M$^+$]), 380 (19), 341 (13), 298 (18), 254 (64), 108 (7), 91 (100), 55 (9).

HRMS: *m*/*z* calcd for $C_{22}H_{33}NO_5S$ (423.21, M$^+$): 423.2079; found: 423.2079.

(*R*,*R*)-5-Benzyloxycarbonylaminooct-1-en-4-cyclohexyl Sulfonate [(*R*,*R*)-10d]

Reaction of (*R*)-**6c** (0.115 g, 0.3 mmol) and allyl iodide (0.202 g, 1.2 mmol) gave 0.117 g (92%) of pure (*R*,*R*)-**10d**.

IR ($CHCl_3$): 3422, 3375, 3066, 3032, 2937, 2863, 1722, 1641, 1515, 1453, 1335, 1252, 1224, 1167, 1108, 1054, 1025, 1002, 926, 865, 825, 754, 698, 603, 576 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.92 (t, 3 H, *J* = 7.18 Hz, CH_3CH$_2$), 1.20–2.05 (m, 14 H, CH$_2$,*c*-Hex, CH$_3$CH_2CH$_2$, CH$_3$CH$_2$CH_2), 2.52 (m, 1 H, C*H*HCHSO$_2$), 2.74 (m, 1 H, CH*H*CHSO$_2$), 3.27 (m, 1 H, CHSO$_2$), 4.18 (m, 1 H, C*H*NH), 4.79 (sept, 1 H, *J* = 4.20 Hz, CH, *c*-Hex), 5.10 (s, 2 H, CH_2Ph), 5.16 (m, 2 H, CH$_2$CHCH_2), 5.31 (d, 1 H, *J* = 9.15 Hz, NH), 5.79 (m, 1 H, CH$_2$C*H*CH$_2$), 7.28–7.40 (m, 5 H, C_6H_5).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.90 (*C*H$_3$CH$_2$), 19.96 (CH$_3$*C*H$_2$), 23.64, 25.10 (OCHCH$_2$*C*H$_2$*C*H$_2$), 31.84 (*C*H$_2$CHSO$_2$), 32.99, 33.03 (OCH*C*H$_2$), 35.89 (CH$_3$CH$_2$*C*H$_2$), 50.46 (CHNH), 64.91 (CHSO$_2$), 67.07 (OCH$_2$), 81.66 (OCH), 119.45 (CH$_2$CH*C*H$_2$), 128.24, 128.38, 128.76 (CH, Ph), 133.65 (CH$_2$*C*HCH$_2$), 136.70 (C, Ph), 156.41 (OCNH).

MS (EI, 70 eV): *m*/*z* (%) = 423 (4, [M$^+$]), 341 (24), 298 (6), 260 (11), 254 (29), 234 (5), 206 (17), 162 (22), 109 (7), 108 (40), 92 (9), 91 (100), 83 (5), 82 (6), 67 (10), 55 (10).

Anal. Calcd for $C_{22}H_{33}NO_5S$ (423.57): C, 62.38; H, 7.85; N, 3.31. Found: C, 62.82; H, 8.17; N, 3.55.

(*R*,*R*)-4-Benzyloxycarbonylaminoheptane-3-cyclohexyl Sulfonate [(*R*,*R*)-10e]

Reaction of (*R*)-**6c** (0.115 g, 0.3 mmol) and EtI (0.187 g, 1.2 mmol) gave 0.103 g (83%) of pure (*R*,*R*)-**10e**; $[\alpha]_D^{25}$ +8.4 (*c* = 1.0, $CHCl_3$).

IR (film): 3423, 3372, 3064, 3033, 2938, 2864, 1722, 1516, 1454, 1331, 1257, 1230, 1167, 1096, 1061, 1025, 1025, 1004, 927, 867, 823, 790, 777, 736, 699, 647, 604, 577, 457 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.93 (t, 3 H, *J* = 7.42 Hz, C*H*$_3$H$_2$CH$_2$), 1.10 (t, 3 H, *J* = 7.42 Hz, CH$_3$C*H*$_3$CHCH$_2$), 1.20–2.10 (m, 10 H, CH_2, *c*-Hex), 3.12 (m, 1 H, $CHSO_2$), 4.19 (m, 1 H, C*H*NH), 4.79 (sept, 1 H, *J* = 4.12 Hz, CH, *c*-Hex), 5.11 (s, 2 H, C*H*$_2$Ph), 5.35 (d, 1 H, *J* = 9.89 Hz, NH), 7.25–7.38 (m, 5 H, C_6H_5).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.07, 13.67 (*C*H$_3$CH$_2$CH$_2$, *C*H$_3$CH$_2$CH), 19.79 (CH$_3$*C*H$_2$CH$_2$), 20.67 (CH$_3$CH$_2$*C*H$_2$), 23.38, 24.84 (OCHCH$_2$*C*H$_2$CH$_2$), 32.74, 32.77 (OCH*C*H$_2$), 35.88 (CH$_3$CH$_2$CH), 50.03 (CHNH), 66.56 ($CHSO_2$), 66.72 (OCH_2), 80.92 (OCH), 127.74, 127.90, 128.31 (CH, Ph), 136.23 (C, Ph), 156.11 (OCNH).

MS (EI, 70 eV): *m*/*z* (%) = 411 (1, [M^+]), 330 (5), 329 (30), 286 (5), 242 (29), 206 (15), 162 (29), 136 (11), 119 (6), 108 (49), 107 (9), 91 (100), 55 (9).

Anal. Calcd for $C_{21}H_{33}NO_5S$ (411.56): C, 61.29; H, 8.08; N, 3.43. Found: C, 60.94; H, 8.38; N, 3.55.

(*R*,*R*)-5-Benzyloxycarbonylamino-2-methylhept-1-en-4-cyclohexyl Sulfonate [(*R*,*R*)-10f]

Reaction of (*R*)-**6b** (0.296 g, 0.8 mmol) and 2-methylprop-2-ene bromide (0.432 g, 3.2 mmol) gave 0.295 g (87%) of pure (*R*,*R*)-**10f**.

IR (film): 3420, 3373, 3071, 3034, 2939, 2863, 1721, 1651, 1516, 1453, 1333, 1276, 1230, 1166, 1123, 1087, 1051, 1031, 976, 925, 866, 824, 776, 740, 699, 522 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.96 (t, 3 H, *J* = 7.42 Hz, C*H*$_3$CH$_2$), 1.20–2.00 (m, 12 H, CH$_3$C*H*$_2$, CH_2, *c*-Hex), 1.72 (s, 3 H, CCH_3), 2.51 (dd, 1 H, *J* = 14.34, 9.89 Hz, C*H*HCHSO$_2$), 2.63 (dd, *J* = 14.59, 3.71 Hz, 1 H, CH*H*CHSO$_2$), 3.43 (m, 1 H, $CHSO_2$), 4.05 (m, 1 H, C*H*NH), 4.79 (sept, *J* = 4.21 Hz, 1 H, CH, *c*-Hex), 4.89 (d, 2 H, *J* = 16.82 Hz, CCH_2), 5.10 (s, 2 H, C*H*$_2$Ph), 5.35 (d, 1 H, *J* = 9.64 Hz, NH), 7.29–7.37 (m, 5 H, C_6H_5).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 11.10 (*C*H$_3$CH$_2$), 21.69 (*C*H$_3$C), 23.38, 24.87 (OCHCH$_2$*C*H$_2$*C*H$_2$), 26.33 (CH$_3$*C*H$_2$), 32.78, 32.72 (OCH*C*H$_2$), 35.08 (*C*H$_2$CHSO$_2$), 52.15 (CHNH), 62.12 ($CHSO_2$), 66.75 (OCH_2), 81.33 (OCH), 115.04 (C*C*H$_2$), 128.01, 128.09, 128.48 (CH, Ph), 136.55 (C, Ph), 140.10 (CH$_3$*C*), 156.21 (OCNH).

MS (EI, 70 eV): *m*/*z* (%) = 423 (1, [M^+]), 260 (24), 216 (6), 206 (10), 192 (5), 148 (9), 108 (12), 107 (12), 91 (100), 55 (10).

Anal. Calcd for $C_{22}H_{33}NO_5S$ (423.57): C, 62.38; H, 7.85; N, 3.31. Found: C, 62.18; H, 7.62; N, 3.66.

(*S*,*S*)-5-Benzyloxycarbonylamino-7-phenylhept-1-en-4-cyclohexyl Sulfonate [(*S*,*S*)-10g]

Reaction of (*S*)-**6k** (0.267 g, 0.6 mmol) and allyl iodide (0.404 g, 2.4 mmol) gave 0.251 g (86%) of pure (*S*,*S*)-**10g**.

IR ($CHCl_3$): 3421, 3063, 3632, 3027, 2939, 2861, 1720, 1513, 1452, 1334, 1234, 1165, 1031, 1001, 924, 893, 866, 826, 756, 699, 667 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.20–2.13 (m, 12 H CH_2, *c*-Hex, PhCH$_2$C*H*$_2$), 2.45–2.77 (m, 4 H, PhC*H*$_2$CH$_2$, C*H*$_2$CHSO$_2$), 3.27 (m, 1 H, $CHSO_2$), 4.23 (m, 1 H, C*H*NH), 4.76 (sept, 1 H, *J* = 4.70 Hz, CH, *c*-Hex), 5.12 (s, 2 H, C*H*$_2$Ph), 5.14 (m, 2 H, CH$_2$CHC*H*$_2$), 5.40 (d, 1 H, *J* = 9.89 Hz, NH), 5.77 (m, 1 H, CH$_2$C*H*CH$_2$), 7.15–7.37 (m, 10 H, C_6H_5).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.33, 24.78 (OCHCH$_2$*C*H$_2$*C*H$_2$), 31.55 (PhCH$_2$CH$_2$), 32.67, 32.62 (OCH*C*H$_2$, *C*H$_2$CHSO$_2$), 35.23 (PhCH$_2$*C*H$_2$), 50.08 (CHNH), 64.60 ($CHSO_2$), 66.80 (OCH_2), 81.47 (OCH), 119.07 (CH$_2$CH*C*H$_2$), 125.86, 127.83, 127.98, 128.21, 128.24, 128.33, (CH, Ph), 132.99 (CH$_2$*C*HCH$_2$), 136.18, 140.68 (C, Ph), 155.87 (OCNH).

MS (EI, 70 eV): *m*/*z* (%) = 485 (1, [M^+]), 403 (5), 394 (8), 313 (5), 312 (30), 251 (12), 224 (6), 208 (15), 169 (58), 126 (6), 91 (100), 82 (11), 67 (12), 65 (5), 55 (15).

Anal. Calcd for $C_{27}H_{35}NO_5S$ (485.64): C, 66.78; H, 7.26; N, 2.88. Found: C, 66.30; H, 7.08; N, 3.21.

Sultones 12a,b; General Procedure

N-Cbz-Protected β-aminocyclohexyl sulfonate (*R*,*R*)-**10f** or (*S*,*S*)-**10g** was dissolved in a mixture of EtOH (30 mL/mmol **10**) and H_2O (1 mL/mmol **10**) and refluxed for 4 h. After cooling to r.t., NaOAc (1.1 equiv) was added and the solution was stirred for 1 h. The solvents were removed under reduced pressure and the crude sodium salts were dissolved in anhyd THF (6 mL/mmol **10**) and cooled to –78 °C. Iodine (3.0 equiv) was added and the reaction mixture was stirred overnight while it warmed up to r.t. Then the solution was diluted with CH_2Cl_2, washed with sat. aq $NaHCO_3$ and 10% $Na_2S_2O_3$ solution and dried ($MgSO_4$). Products were purified by column chromatography (silica gel, *n*-pentane–Et_2O) to afford **12a**,**b** as colorless solids.

(*S*,*R*,*R*)-[1-(5-Iodomethyl-2,2-dioxo-2λ^6-[1,2]oxathiolan-3-yl)-2-methylpropyl]carbamic Acid Benzyl Ester [(*S*,*R*,*R*)-12a]

Reaction of (*R*,*R*)-**10f** (0.191 g, 0.45 mmol) and I_2 (0.342 g, 1.35 mmol) gave 0.162 g (77%) of pure (*S*,*R*,*R*)-**12a**; $[\alpha]_D^{25}$ –27.7 (*c* = 1.0, $CHCl_3$).

IR (film): 3340, 3287, 3030, 2965, 2933, 1695, 1530, 1453, 1371, 1336, 1289, 1263, 1169, 1108, 1089, 1061, 1010, 976, 871, 838, 779, 754, 700, 600 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.01 (d, 3 H, *J* = 6.59 Hz, CH_3), 1.11 (d, 3 H, *J* = 6.59 Hz, CH_3), 2.14 (m, 2 H, CH$_3$C*H* C*H*HCHSO$_2$), 2.78 (m, 1 H, CH*H*CHSO$_2$), 3.19 (dd, 1 H, *J* = 10.16, 8.24 Hz, C*H*HI), 3.19 (dd, 1 H, *J* = 10.16, 4.95 Hz, CH*H*I), 3.83 (m, 2 H, C*H*NH, $CHSO_2$), 4.60 (m, 1 H, C*H*CH$_2$I), 5.14 (d, 2 H, *J* = 7.69 Hz, C*H*$_2$Ph), 5.44 (d, 1 H, *J* = 10.44 Hz, NH), 7.32–7.39 (m, 5 H, C_6H_5).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 3.47 (CH*C*H$_2$I), 19.51, 20.17 [(*C*H$_3$)$_2$CH], 31.36 [(CH$_3$)$_2$*C*H], 34.30 (*C*H$_2$CHSO$_2$), 55.88, (CHNH), 59.92 ($CHSO_2$), 67.09 (CH_2O), 78.14 (SO*C*HCH$_2$I), 127.86, 128.10, 128.40 (CH, Ph), 136.02 (C, Ph), 156.50 (OCNH).

MS (EI, 70 eV): *m*/*z* (%) = 467 (19, [M^+]), 424 (6), 380 (22), 108 (49), 91 (100), 65 (6).

Anal. Calcd for $C_{16}H_{22}INO_5S$ (467.32): C, 41.12; H, 4.74; N, 3.00. Found: C, 41.34; H, 5.22; N, 2.84.

(*R*,*S*,*S*)-[1-(5-Iodomethyl-2,2-dioxo-2λ^6-[1,2]oxathiolan-3-yl)-3-phenylpropyl]carbamic Acid Benzyl Ester [(*R*,*S*,*S*)-12b]

Reaction of (*S*,*S*)-**10g** (0.146 g, 0.3 mmol) and I_2 (0.229 g, 0.9 mmol) gave 0.121 g (76%) of pure (*R*,*S*,*S*)-**12b**; $[\alpha]_D^{22}$ +12.2 (*c* = 1.0, $CHCl_3$).

IR (film): 3337, 3061, 3029, 2931, 2861, 1695, 1533, 1498, 1451, 1343, 1281, 1263, 1244, 1214, 1161, 1066, 973, 853, 780, 739, 698, 603, 474 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.10 (m, 3 H, PhCH$_2$C*H*$_2$, C*H*HCHSO$_2$), 2.70 (m, 3 H, PhC*H*$_2$CH$_2$, CH*H*CHSO$_2$), 3.15 (dd, 1 H, *J* = 10.39, 8.16 Hz, C*H*HI), 3.38 (dd, 1 H, *J* = 10.39, 5.19 Hz,

CH*H*I), 3.68 (m, 1 H, $CHSO_2$), 4.06 (sept, 1 H, J = 5.19 Hz, C*H*NH), 4.54 (m, 1 H, C*H*CH_2I), 5.14 (d, 2 H, J = 4.94 Hz, CH_2Ph), 5.51 (d, 1 H, J = 10.14 Hz, NH), 7.08–7.40 (m, 10 H, C_6H_5).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 3.55 (CH*C*H_2I), 32.31, 33.94, 34.81 (*C*H_2CHSO$_2$, PhCH_2*C*H_2), 49.50 (CHNH), 62.27 ($CHSO_2$), 67.18 (CH_2O), 78.20 (SO*C*HCH$_2$I), 126.34, 128.09, 128.34, 128.41, 128.45, 128.60 (CH, Ph), 136.17, 140.25 (C, Ph), 156.36 (OCNH).

MS (EI, 70 eV): *m*/*z* (%) = 529 (3, [M^+]), 439 (14), 438 (78), 421 (8), 377 (7), 333 (36), 295 (32), 290 (21), 289 (11), 168 (21), 167 (15), 108 (18), 107 (11), 105 (5), 91 (100), 79 (15), 77 (8), 65 (8).

Anal. Calcd for $C_{21}H_{24}INO_5S$ (529.39): C ,47.65; H, 4.57; N, 2.65. Found: C, 48.15; H, 4.93; N, 2.50.

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