α-Amino Acids and *N*-Protected α-Amino Aldehydes by Stereoselective Additions of a Chiral Vinyllithium Reagent to Sulfonylimines

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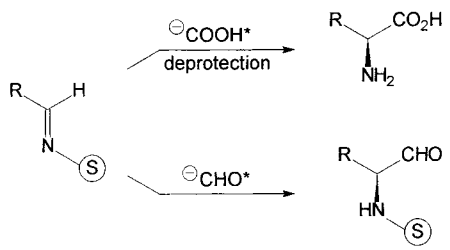
The chiral vinyllithium reagent (*S*)-**1b**, readily generated from dibromoalkene (*S*)-**1a** by bromine/lithium exchange, adds stereoselectively to mesitylsulfonylimines **2a–f** so that the diastereomers **3** are obtained in ≥98% *d.e.* after column chromatography. The bromoalkenes **3a–d** are submitted to ozonolysis in methanol to give α-mesitylsulfonylamino esters (*S*)-**8a–d** which can be hydrolyzed to deliver *N*-protected α-amino acids in >95% *e.e.* On the other hand, α-mesitylsulfonylamino aldehydes **12a–d** are available when bromoalkenes **3a**, **d–f** are first debrominated (→ **11a–d**) and subsequently ozonized. In order to avoid reacemization, the aldehydes **12a–d** are not purified but submitted to a Mukaiyama-type aldol addition whereby hydroxyesters **15a–d** are formed as single diastereomers in a chelate-controlled reaction. The relative configuration of the esters **15a–d** is proven by conversion into the oxazolidinones **16a–d** whose optical purity is determined to exceed 92% *e.e.* by ^{1}H-NMR measurements in the presence of chiral shift reagents. The sulfonylimine **21a** and a series of *para*-substituted derivatives **21b–h** are also allowed to react with the vinyllithium reagent **1b** to give mixtures of diastereomers **22/23**. The logarithms of the diastereomeric ratios **22**:**23** correlate with Hammett's σ-values.

There is a continuous interest in syntheses of naturally occurring as well as non-natural α-amino acids in view of their importance in biology, biochemistry, and chemistry. As a consequence, an enormous number of methods affording routes to enantiomerically pure α-amino acids has been developed in recent years. Remarkably, that large diversity of methods is based on only a few fundamental concepts. They include, besides enzymatic methods, asymmetric hydrogenation of dehydroamino acids, alkylation of chiral glycine enolates, electrophilic and nucleophilic amination, addition of carbon nucleophiles to α-imino esters, and nucleophilic addition of CO_2H equivalents to chiral imines[1]. In this paper, we report for the first time[2] on a different approach: the stereoselective addition of chiral $^-CO_2H$* and ^-CHO* synthons to prochiral sulfonylimines[3] provides not only non-racemic α-amino acids but, even more importantly, leads to *N*-protected α-amino aldehydes as well (Scheme 1). These latter compounds turn out to be valuable synthetic building blocks[4] as illustrated by a highly diastereoselective Mukaiyama-type aldol addition[5] which is also described here.

Scheme 1



Diastereoselective Addition of Vinyllithium Reagent (*S*)-1b to Sulfonylimines 2

An equivalent of $^-CO_2H$* and ^-CHO* synthons is available from the vinyllithium reagents (*R*)- and (*S*)-**1b**, readily accessible by stereoselective (*E*/*Z* > 99:1) bromine/lithium exchange in the dibromoalkene **1a**. Both enantiomers of the latter reagent are available on 100 g scale from (*R*)-isobutyl or (*S*)-ethyl lactate, respectively[6]. As far as the prochiral imine is concerned, a suitable group S (Scheme 1) should fulfil three requirements: i) efficient protection of the amino group avoiding racemization, ii) cleavage under mild conditions, and iii) activation of the imine moiety towards attack of the nucleophilic carbenoid **1b**. A fairly tedious search revealed that a series of imines (S = $SiMe_3$, SPh, Ph, CO_2Me, SO_2CF_3) were either completely unreactive or provided insufficient chemical yields and/or diastereoselectivities when treated with **1b**. The *N*-mesitylsulfonyl imines **2**, however, turned out to be not only sufficiently reactive but also highly stereoselective. Thus, addition of the sulfonylimines **2** to solutions of the vinyllithium reagent (*S*)-**1b** at −110 °C in tetrahydrofuran resulted predominantly in the sulfonamides **3**. After chromatography of the diastereomeric mixtures of **3** and **4**, the major isomers **3** were ob-

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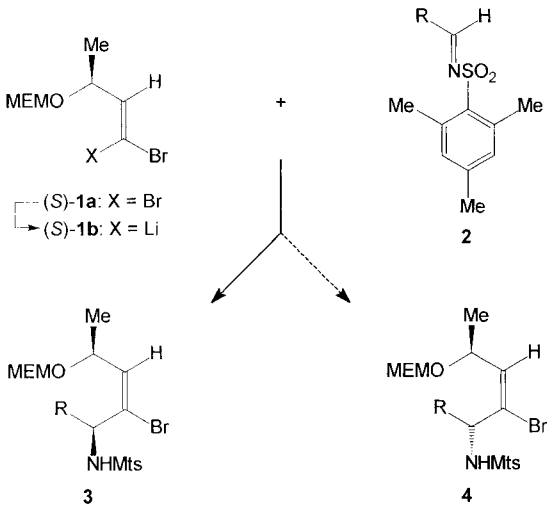
tained with ≥98% *d.e.* each. The yields of the main products **3** purified in that way, as well as the diastereomeric ratios of the crude mixtures of **3** and **4** are given in Table 1.



MEM = $CH_2OCH_2CH_2OCH_3$

Mts = 2,4,6-trimethylbenzenesulfonyl (mesitylsulfonyl)

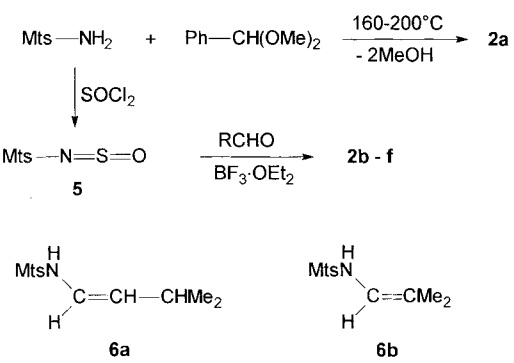
2, 3, 4	R
a	Ph
b	4-$MeOC_6H_4$
c	4-$(ThexMe_2SiO)C_6H_4$
d	Me_2CHCH_2
e	Me_2CH
f	Me_3C

Table 1. Ratio of diastereomers **3/4** formed by the addition of the vinyllithium reagent (*S*)-**1b** to mesitylsulfonylimines **2**

Sulfonylimine	Products	Diastereomeric ratio	Yield[a]
2a	**3a**:**4a**	96:4	62 %
2b	**3b**:**4b**	96:4	63 %
2c	**3c**:**4c**	96:4	54 %
2d	**3d**:**4d**	97:3	21 %
2e	**3e**:**4e**	97:3	34 %
2f	**3f**:**4f**	98:2	52 %

[a] Purified **3** (*d.e.* ≥98%).

The imine **2a** was prepared by heating a mixture of mesitylsulfonamide and the dimethylacetal of benzaldehyde as described by Kresze et al.[7a] A protocol originating from the same group[8] was used to prepare the imines **2b**–**f**: Mesityl sulfonamide was first converted to the *N*-sulfinyl sulfonamide **5** which was subsequently allowed to react with the corresponding aldehyde in the presence of boron trifluoride etherate, to give the sulfonylimines **2b**–**f**, thereby liberating sulfur dioxide. Whereas pure products **2b**, **c**, and **f** were obtained from 4-methoxybenzaldehyde, 4-(dimethylthexylsilyloxy)benzaldehyde and 2,2-dimethylpropanal, respectively, the sulfonylimines **2d**, **e** derived from isobutyraldehyde and 3-methylbutanal, respectively, could not be obtained free from the corresponding tautomeric enamines **6a** and **6b**. As a consequence, only moderate chemical yields were achieved in the case of the sulfonamides **3d** and **3e** (Table 1).

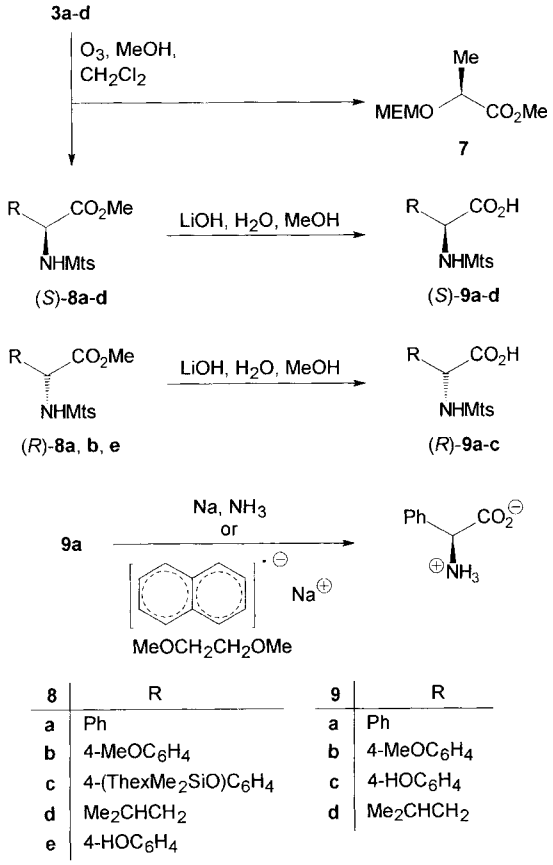


Synthesis of α-Amino Acids and *N*-Sulfonyl α-Amino Aldehydes

The bromoalkenes **3a**–**d** obtained in ≥98% *d.e.* after column chromatography (see above) were submitted to an ozonolysis in methanol/dichloromethane[9]. Thereby, *N*-protected amino acid methyl esters (*S*)-**8a**–**d** were obtained directly together with *O*-MEM-protected methyl lactate **7**. When the reaction was run on a larger scale, the lactate **7** was isolated by distillation and could be reused for the preparation of the dibromoalkene **1a**. In order to prove the absolute configuration and the optical purity of the products **8**, authentic samples of **8d** as well as enantiomeric (*R*)-**8a** and (*R*)-**8b** were prepared from commercially available methyl esters of (*S*)-leucine, (*R*)-phenylglycine, and (*R*)-4-hydroxyphenylglycine.

Comparison of the optical rotations allowed the assignment of the (*S*) configuration to the amino acid esters **8a**–**d** and of the (*S*,*S*) configuration to their precursors **3a**–**d**. The diastereomeric excess of the latter compounds corresponded to the optical purity of the esters (*S*)-**8a**–**d**, whose alkaline hydrolysis provided the *N*-mesitylsulfonyl-protected amino acids (*S*)-**9a**–**d**. Under those conditions, the silyloxy protecting group[10] was cleaved so that *N*-mesitylsulfonyl-4-hydroxyphenylglycine (**9c**) was obtained from the ester **8c**. Here again, samples of (*S*)-**9d** as well as (*R*)-**9a**–**c** were prepared from the authentic amino acids via the *N*-sulfonyl methyl esters (*S*)-**8d** and (*R*)-**8a**, **b**, **e** which were also saponified. The chemical yields and the optical purities of *N*-protected amino acids **9a**–**d** generated from alkenes **3a**–**d** are given in Table 2. The synthesis of (*S*)-phenylglycine from (*S*)-**9a** serves to illustrate the cleavage of the *N*-mesitylsulfonyl protecting group. In our hands, either treatment with sodium in liquid ammonia[11] or reaction with sodium naphthalenide[12] were found to be suitable methods for deprotection. Thus, (*R*)-phenylglycine was formed in 59% and 78% chemical yield, respectively, without racemization. The cleavage of the bromoalkenes **3e**, **f** was not fea-

sible by ozonolysis, presumably due to steric hindrance at the carbon–carbon double bond.



8	R
a	Ph
b	4-$MeOC_6H_4$
c	4-(ThexMe$_2$SiO)C_6H_4
d	Me_2CHCH_2
e	4-HOC_6H_4

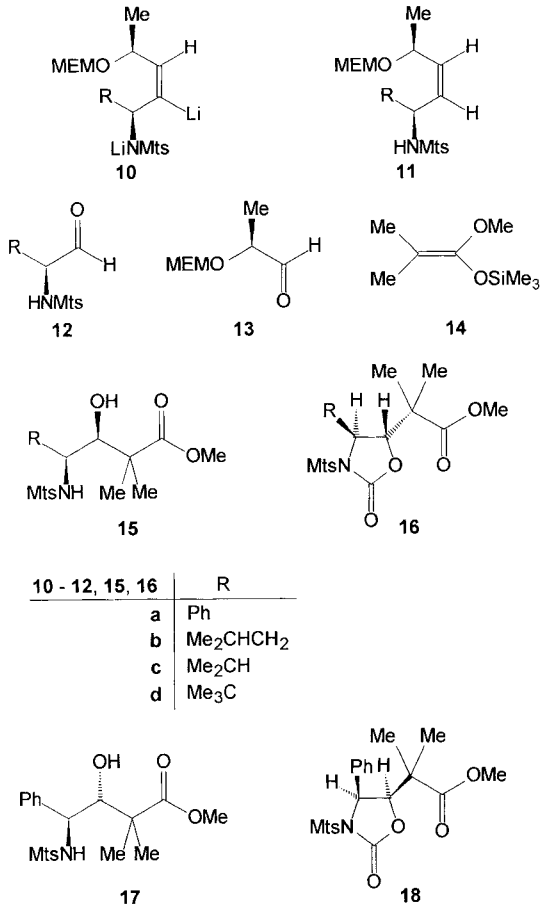
9	R
a	Ph
b	4-$MeOC_6H_4$
c	4-HOC_6H_4
d	Me_2CHCH_2

Table 2. *N*-Mesitylsulfonyl protected α-amino esters **8** and acids **9** formed from bromoalkenes **3**

Bromoalkene	Ester (*S*)-**8** (Yield)	Acid (*S*)-**9** (Yield) [e.e.]
3a	**a** (78%)	**a** (91%) [98%]
3b	**b** (75%)	**b** (89%) [98%]
3c	**c** (68%)	**c** (88%) [99%]
3d	**d** (45%)	**d** (99%) [95%]

N-Mesitylsulfonyl α-Amino Aldehydes: Preparation and Diastereoselective Mukaiyama Aldol Addition

With respect to their oxidation number, debrominated alkenes **11** are more suitable precursors of *N*-protected aldehydes **12** than the bromoolefins **3**. Therefore, compounds **3a**, **d**, **e**, **f** (*d.e.* ≥98%) were submitted to another bromine/lithium exchange reaction by means of *tert*-butyllithium (→ **10a–d**), followed by protonation. Thus, alkenes **11a–d** were not only obtained in high enantiomeric and diastereomeric excesses (*e.e.* >99%, *d.e.* >98%) and good chemical yields (92–95%), but also as pure *Z*-isomers. Ozonolysis followed by work-up with dimethyl sulfide provided *N*-mesitylsulfonyl-protected α-amino aldehydes **12** in almost quantitative yields. The lactaldehyde **13** formed simultaneously was condensed under high vacuum at 25°C in a trap cooled with liquid nitrogen and could be reused for the preparation of the dibromoalkene **1a**. When the temperature of the remaining α-amino aldehydes **12** was strictly kept below 25°C, racemization was largely suppressed. In view of the lability of α-amino-substituted aldehydes, the intermediates **12a–d** were not purified but submitted immediately to subsequent conversions.



When *N*-protected α-amino aldehydes are attacked by nucleophiles, the stereochemical outcome of the reaction depends mainly on the protecting group so that either chelate-controlled or non-chelate-controlled products result[13]. Since *N*-mesitylsulfonyl-substituted α-amino aldehydes have never been used as intermediates in diastereoselective reactions, we decided to bring about a Mukaiyama-type aldol reaction of the crude aldehydes **12a–d**. For this purpose, methyl isobutyrate was first converted into the silyl ketene acetal **14**, which was subsequently treated with the aldehydes **12a–d** in the presence of titanium tetrachloride. Thereby, remarkably high diastereoselectivity was achieved: the crude products **15a–d** were formed as single diastereomers according to their ^{1}H-NMR spectra (Table 3). In order to assign the relative configurations to the carbinols **15**, they were treated with phosgene to give the oxazolidinones **16**. It is known from various series of 4,5-disubstituted oxazolidin-2-ones that the smaller 4-H,5-H coupling constant (ca. 5 Hz) has to be assigned to the *trans*-diastereomer, whereas the *cis*-isomers display substantially larger coupling constants which range from 7.5 to 9.5 Hz[14]. Since the ^{1}H-NMR spectra of the heterocycles **16** derived from aldol adducts **15** clearly show a *trans* relation of the substituents in position 4 and 5, the *syn* configuration has to be assigned to the *N*-protected amino alcohols **15**. Obviously, the alde-

hydes **12** are attacked exclusively at the *Si* face during the Mukaiyama aldol reaction. This stereochemical outcome is plausibly explained by assuming chelate control, as indicated in the transition state model **19**.

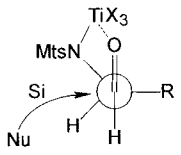


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Table 3. Hydroxy esters **15** obtained from alkenes **11** by ozonolysis and Mukaiyama aldol addition; oxazolidinones **16** derived from **15**

Alkene	Ester **15**[a] (Yield)	Oxazolidinone **16**[a] (Yield)
11a	**a** (72%)	**a** (90%)
11b	**b** (78%)	**b** (88%)
11c	**c** (75%)	**c** (94%)
11d	**d** (73%)	**d** (96%)

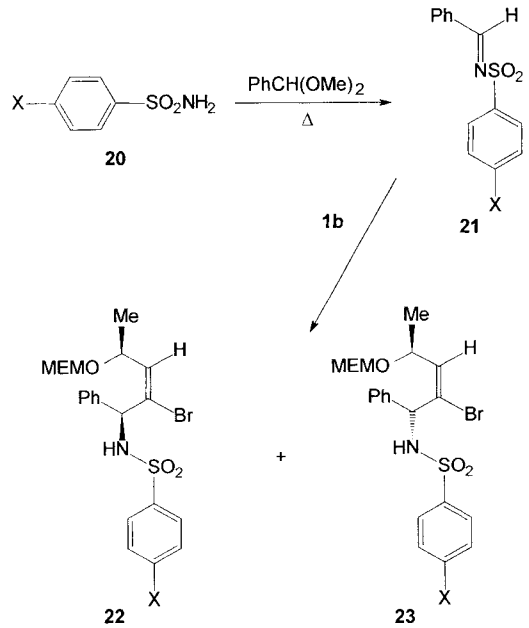
[a] Single diastereomer.

In contrast to the excellent stereoselectivity obtained in Mukaiyama-type aldol reactions of the aldehydes **12**, diastereomeric mixtures of **15a** and **17** were formed when the aldehyde **12a** was treated with the lithium enolate of methyl isobutyrate. Even poorer diastereoselectivity resulted from the transmetallation of that lithium enolate with chloro triisopropyloxy titanate. As expected, oxazolidinone **18** formed from **17** clearly differs from the corresponding diastereomer **16a** in the NMR spectra.

In order to find out whether substantial racemization had occurred during the formation and isolation of the aldehydes **12**, as well as during the aldol addition, the final products **16** were investigated by ^{1}H-NMR spectroscopy in the presence of the chiral europium shift reagent Eu(hfc)$_3$[15]. Under these conditions, a racemic mixture of **16a** and *ent*-**16a** had been found to differ in the chemical shift values of the 4-H and 5-H signals. For this purpose, an "artifical" racemate had been prepared by combining equal amounts of **16a** and *ent*-**16a**. The latter stereoisomer is available by the enantiomeric series, which starts from (*R*)-dibromoalkene **1a**, available from (*R*)-lactate. It turned out that the enatiomeric purities of the final products **16a**, **c**, **d** were slightly lower than expected according to the *d.e.* values of the corresponding bromoolefins **3a**, **e**, **f** (≥98%). This indicates that marginal degrees of racemization occur during the sequence which is undoubtedly due to the lability of the aldehydes **12a**, **c**, **d**. Complete retention of the configuration, however, was found in the aldehyde **12b** as indicated by the optical purity of the oxazolidinone **16**. The Mukaiyama aldol additions underline the versatility of *N*-mesitylsulfonyl protected α-amino aldehydes **12**, both enantiomers of which are available according to the protocol outlined above.

Addition of 1-Bromo-1-lithio-1-alkene (*S*)-1b to *para*-Substituted Arylsulfonylimines; a Linear Free-Energy Relationship

In the key step of our route to α-amino acids and *N*-protected α-amino aldehydes, the (*S*)-vinyllithium reagent **1b** attacks mesityl sulfonylimines predominantly at their *Re*-face. When the mesityl-protected derivative **2a** is replaced by phenylsulfonylimine **21a**, the diastereoselectivity decreases dramatically (Table 4). Undoubtedly, this effect is mainly caused by steric interference of the two *ortho*-methyl groups in **2a**. Since we were wondering whether the diastereoselectivity of that key step is also influenced by electronic effects, a series of *para*-substituted arylsulfonylimines **21b–h** was treated under *identical conditions* (temperature, reaction time) with the chiral carbenoid (*S*)-**1b** to give mixtures of **22** and **23**. The imines **21a–h** were readily available[7] by heating the dimethylacetal of benzaldehyde with the corresponding sulfonamides **20a–h**. The ratio of diastereomers **22**:**23** shown in Table 4 was easily determined by ^{1}H-NMR spectroscopy. It turned out that increased diastereoselectivity was observed when electron-donating substituents were introduced in the sulfonylimine (i.e. **21b–d**) whereas lower diastereomeric ratios resulted in the case of electron-withdrawing substituents (i.e. **21e–h**).



20 - 23	R
a	H
b	NMe_2
c	OMe
d	Me
e	F
f	Cl
g	CF_3
h	NO_2

The Hammett equation offers a simple as well as versatile solution when the influence of *meta*- and *para*-substituents in aromatic substrates has to be correlated with their reactivity[16]. There are very few reports on linear free-energy

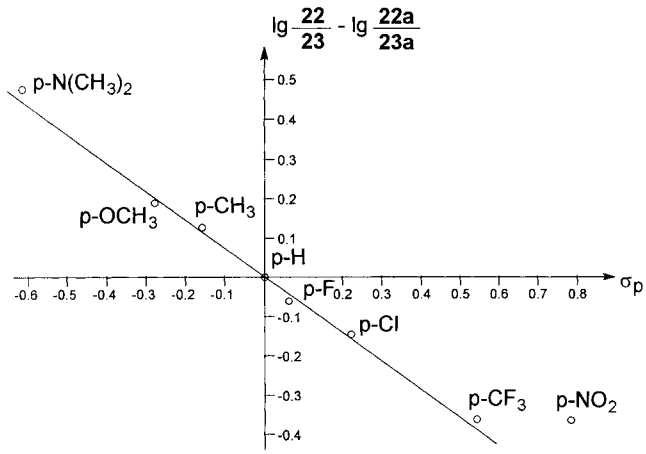
relationships for asymmetric syntheses. Only recently, the stereoselectivity of manganese-catalyzed epoxidations has been related to Hammett's σ-parameters ("electron tuning")[17,18]. When, under kinetic control, a chiral reagent (e.g. **1b**) adds to the *Re*- or *Si*-face of the sulfonylimines **21** (or any other prochiral molecule), the rate constants k_{Re} and k_{Si} of the competing reactions can be correlated as shown in equations (1a) and (1b). The corresponding rate constants of the unsubstituted sulfonylimine **21a** (X = H) are termed k^0_{Re} and k^0_{Si}. Being aware that – in competing reactions starting from identical compounds – the ratio of the rate constants equals the ratio of products, the terms $k^0_{Re}:k^0_{Si}$ and $k_{Re}:k_{Si}$ can be replaced by the ratio **22a**:**23a** and **22**:**23**, respectively. Thus, equation (2) results which may be termed a linear free-energy relationship for an asymmetric synthesis.

$$\lg \frac{k_{Re}}{k^\circ_{Re}} = \rho_{Re} \cdot \sigma \qquad (1a)$$

$$\lg \frac{k_{Si}}{k^\circ_{Si}} = \rho_{Si} \cdot \sigma \qquad (1b)$$

$$\lg \frac{\mathbf{22}}{\mathbf{23}} - \lg \frac{\mathbf{22a}}{\mathbf{23a}} = \Delta\rho \cdot \sigma \qquad (2)$$

Figure 1

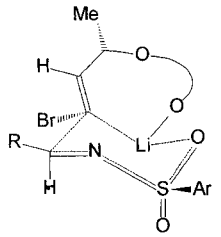


The difference of the logarithms of the diastereomeric ratios of substituted and unsubstituted products **22/23** is plotted against Hammett's σ-values (Table 4). As shown in Figure 1, all derivatives except the nitro-substituted one are clearly arranged in a linear plot. The exception is probably caused by insufficient solubility of sulfonylimine **21h** so that, in this particular case, the reaction cannot be run in an homogeneous phase. Furthermore, the nitro substituent may cause single-electron transfer processes so that the mechanism of the addition of **1b** to **21h** is completely different from that of the other sulfonylimines **21a–g**. Obviously, the diastereoselectivity increases with the strength of the electron donating effect of the substituent X. It seems that the enhancement of electron density at the sulfonylimine moiety leads to a more tightened transition state, wherein the lithium atom of **1b** is coordinated to the oxygen. The tightness maximizes the steric and/or stereoelectronic effects which arise from the chiral information of the vinyllithium reagent **1b**. A six-membered transition state model **24** is proposed to account for the predominant (*S*)/*Re* topicity in the addition of (*S*)-**1b** to sulfonylimines **2** and **21**. It is assumed that the bulky substituents R, bromine, and the aryl group of the sulfonyl moiety occupy equatorial positions. In the unfavored (*S*)/*Si* topicity the methyl group at the stereogenic center of the vinyllithium reagent would be directed towards the sulfonylimine.

Table 4. Diastereomeric Sulfonamides **22/23** formed by the addition of (*S*)-**1b** to sulfonylimines **21**

Sulfonylimine **21**	Products **22/23** (Diastereomeric ratio)	σ_p [a]	$\lg\frac{22}{23} - \lg\frac{22a}{23a}$
a: X = H	**a** (74.0:26.0)	0	0
b: X = NMe_2	**b** (89.5:10.5)	–0.63	+0.477
c: X = OMe	**c** (81.5:18.5)	–0.28	+0.190
d: X = Me	**d** (79.5:20.5)	–0.16	+0.135
e: X = F	**e** (71.5:28.5)	+0.06	–0.055
f: X = Cl	**f** (67.0:33.0)	+0.22	–0.147
g: X = CF_3	**g** (55.0:45.0)	+0.54	–0.367
h: X = NO_2	**h** (55.0:45.0)	+0.78	–0.367

[a] Hammett σ values (cf. ref.[16b]).



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It is reasonable to look for linear free-energy relations in asymmetric syntheses performed with a series of reagents or substrates which differ in their electronic properties? At least *nonlinearity* gives a valuable piece of information: namely that in the selectivity-determining step there are *several* reactive species (e.g. different aggregates of organometallic compounds like monomers, dimers, tetramers, various kinds of mixed aggregates).

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Experimental Section

Melting points: Büchi 510. – IR: Perkin-Elmer 710B and 1420. – NMR: Varian EM 360, EM 390, and VXR 300; all spectra were recorded in $CDCl_3$ with tetramethylsilane as internal standard. – MS: Varian MAT CH5 (70 eV). – Specific rotations: Perkin Elmer 141. – TLC: DC-Alufolien 60 F_{254} and Sil-G 60/UV_{254} (Merck). – Column chromatography: MN-Kieselgel 60, mesh size 0.04–0.063 mm (Macherey-Nagel). – Elemental analysis: Mikroanalytisches Laboratorium Beller (Göttingen) and Institut für Pharmazeutische Chemie, Universität Düsseldorf.

Solvents and Reagents: Tetrahydrofuran (THF) was predried with KOH and distilled under N_2 from sodium/benzophenone or from $LiAlH_4$. It was taken from the receiving flask, which was

closed by a septum, using syringes or cannulas. Dichloromethane, chloroform, *n*-pentane, *n*-hexane, and acetone were refluxed for several hours with di-phosphorus pentoxide, distilled, and kept over molecular sieves (4 Å). The aldehydes and imines as well as chlorotrimethylsilane and thionyl chloride were distilled before use. Neat diisobutylaluminiumhydride (DIBAH) was diluted with *n*-hexane to give a 1 M soluton. The organolithium compunds *n*- and *tert*-butyllithium were purchased as solutions in *n*-hexane and *n*-pentane, respectively.

General Remarks Concerning the Handling of Organolithium Coupounds: See ref.[19].

(3S)- and (3R)-1,1-Dibromo-[(2-methoxyethoxy)methyoxy]-1-butene (**1a**) were prepared according to ref.[6].

N-(Phenylmethylene)benzenesulfonamide (**21a**), *4-Methyl-N-(phenylmethylene)benzenesulfonamide* (**21d**), *4-Chloro-N-(phenylmethylene)benzenesulfonamide* (**21f**), and *4-Nitro-N-(phenylmethylene)benzenesulfonamide* (**21h**) were prepared according to ref.[7a].

4-(Dimethylamino)-N-(phenylmethylene)benzenesulfonamide (**21b**): A mixture of 4-dimethylaminobenzenesulfonamide[20] (6.0 g, 30 mmol) and α,α-dimethoxytoluene (4.5 ml, 30 mmol) was heated to 160 °C in a one-necked flask equipped with a short Vigreux column with a Zincke distillation apparatus. Heating was continued for 30 min. The temp. was then raised for a short time to 200 °C in order to distill the 1.7 ml of methanol formed during the condensation. After cooling to room temp. the residue was recrystallized three times from petroleum ether (b.p. 100 °C–140 °C) or 1,4-dioxane to give 4.1 g (47%) of colorless **21b**; m.p. 173 °C. – ^{1}H NMR (60 MHz): δ = 3.05 [s, 6H, $N(CH_3)_2$], 6.56–6.86 (m, 4H, aromatic H), 7.23–8.05 (m, 5H, aromatic H), 8.92 (s, 1H, $C{=}CHC_6H_5$). – MS (70 eV); *m/z* (%): 288 (100) [M^+], 184 (68) [$M^+ - N{=}CHC_6H_5$]. – $C_{15}H_{16}N_2O_2S$ (288.4): calcd. C 62.48, H 5.59, N 9.71; found C 62.43, H 5.57, N 9.66.

4-Methoxy-N-(phenylmethylene)benzenesulfonamide (**20c**): Prepared analogously from 4-methoxybenzenesulfonamide[21] (3.74 g, 20 mmol) and α,α-dimethoxytoluene (2.94 ml, 20 mmol), which were heated to 160 °C for 10 min and thereafter for a short time to 200 °C. The crude residue was recrystallized twice from petroleum ether (b.p. 100 °C–140 °C) to give 2.86 g (52%) of colorless **20c**. – ^{1}H NMR (60 MHz): δ = 3.82 (s, 3H, OCH_3), 6.81–7.10 (m, 5H, aromatic H), 7.30–7.90 (m, 4H, aromatic H), 8.93 (s, 1H, $N{=}CHC_6H_5$).

4-Fluoro-N-(phenylmethylene)benzenesulfonamide (**20e**): 4-Fluorobenzenesulfonamide was prepared by refluxing a mixture of 4-fluorobenzenesulfonyl chloride (9.73 g, 50 mmol), ammonium carbonate (25 g, 260 mmol), and 50 ml of a conc. aqueous solution of ammonia for 1 h. After cooling to room temp., water (100 ml) was added, and the mixture was filtered. The residue was washed with water and recrystallized from water/ethanol (1:3) to give 7.72 g (88%) of crystalline product; m.p. 122 °C.

4-Fluorobenzenesulfonamide (3.52 g, 20 mmol) thus obtained was heated with α,α-dimethoxytoluene (4.4 ml, 30 mmol) as described above. The residue was recrystallized from petroleum ether (b.p. 60 °C–80 °C) to give 3.66 g (67%) of **20e**; m.p. 76 °C. – ^{1}H NMR (300 MHz): δ = 7.20–7.52 (m, 4H, aromatic H), 7.61–7.66 (m, 1H, aromatic H), 7.92–8.06 (m, 4H, aromatic H), 9.06 (s, 1H, $N{=}CHC_6H_5$). – MS (70 eV); *m/z* (%): 263 (3) [M^+], 159 (68) [C_6H_4FS], 95 (100) [C_6H_4F]. – $C_{13}H_{10}FNO_2S$ (263.3): calcd. C 59.31, H 3.83, N 5.32; found C 59.44, H 4.05, N 5.32.

N-(Phenylmethylene)-4-(trifluoromethyl)benzenesulfonamide (**21g**): A 250-ml three-necked flask equipped with a thermometer and an inlet tube was charged with CuCl (4.95 g, 50 mmol) and 150 ml of anhydrous acetic acid. After cooling to 5 °C, a stream of SO_2 was passed through the solution for 2 h. During the course of this, the temp. was kept below 10 °C. In a 100-ml two-necked flask equipped with a thermometer and a dropping funnel, a mixture of 4-(trifluoromethyl)aniline (8.05 g, 50 mmol) and 17 ml of conc. hydrochloric acid was cooled to 0 °C. A solution of $NaNO_2$ (4.0 g, 52 mmol) in 8 ml of water was added through the dropping funnel at such a rate that the temp. did not exceed 5 °C. The solution of the 4-(trifluoromethyl)benzenediazonium salt thus formed was added slowly under stirring through the dropping funnel to the saturated solution of SO_2 in acetic acid. Stirring was continued for 2 h at room temp. The mixture was then transferred to a separatory funnel and extracted three times with toluene. The combined organic layers were washed with a 1 M aqueous solution of $NaHCO_3$ (100 ml) and with 100 ml of water and dried with $CaCl_2$. After removal of the solvent in a rotary evaporator, the crude 4-(trifluoromethyl)benzenesulfonyl chloride was treated with 150 ml of a saturated aqueous solution of ammonia and refluxed for 1 h. After cooling to room temp., 4-(trifluoromethyl)benzenesulfonamide crystallized and was filtered, washed with water, and recrystallized from toluene to give 7.89 g (70%) of a colorless solid; m.p. 174 °C.

4-(Trifluoromethyl)benzenesulfonamide (3.38 g, 15 mmol) thus obtained was heated with α,α-dimethoxytoluene for 10 min as described above. Recrystallization of the crude product from petroleum ether afforded 3.42 g (73%) of **21g**; m.p. 99 °C. – ^{1}H NMR (300 MHz): δ = 7.27–7.83 (m, 5H, aromatic H), 7.94–8.18 (m, 4H, aromatic H), 9.12 (s, 1H, $N{=}CHC_6H_5$). – MS (70 eV); *m/z* (%): 313 (12) [M^+], 209 (20) [$C_7H_4F_3O_2S$], 145 (100) [$C_7H_4F_3$]. – $C_{14}H_{10}F_3NO_2S$ (313.3): calcd. C 53.67, H 3.22, N 4.47; found C 53.83, H 3.29, N 4.51.

2,4,6-Trimethyl-N-(phenylmethylene)benzenesulfonamide (**2a**): A mixture of 2,4,6-trimethylbenzenesulfonamide[22] (9.96 g, 50 mmol) and α,α-dimethoxytoluene (8 ml, 53 mmol) was heated for 10 min as described above. The remaining crude product was recrystallized three times from *n*-hexane to give 12.2 g (85%) of **2a**; m.p. 91 °C. – ^{1}H NMR (60 MHz): δ = 2.29 (s, 3H, CH_3), 2.68 (s, 6H, CH_3), 6.89 (s, 2H, aromatic H), 7.19–8.0 (m, 5H, aromatic H), 8.98 (s, 1H, $N{=}CHC_6H_5$). – MS (70 eV); *m/z* (%): 287 (1) [M^+], 119 (100) [C_9H_{11}]. – $C_{16}H_{17}NO_2S$ (287.4): calcd. C 66.87, H 5.96, N 4.87; found C 66.84, H 5.93, N 5.08.

4-[Dimethyl(1,1,2-trimethylpropyl)silyloxy]benzaldehyde: 4-Hydroxybenzaldehyde (15 g, 123 mmol) was added to a mixture of dimethylhexylsilyl chloride (24.2 ml, 123 mmol), diisopropylethylamine (25.8 ml, 148 mmol), and 60 ml of dichloromethane. After stirring for 15 h at 70 °C, *n*-hexane (300 ml) was added, the mixture was transferred to a separatory funnel, washed with three 150 ml portions of water and dried with $MgSO_4$. The solvent was removed under reduced pressure, and the residue was distilled in vacuo. Yield: 24.8 g (76%); b.p. 78–81 °C/0.02 Torr. – ^{1}H NMR (60 MHz): δ = 0.28 [s, 6H, $Si(CH_3)_2$], 0.80–1.05 (m, 12H, CH_3), 1.65 [m, 1H, $HC(CH_3)_2$], 6.70–7.70 (m, 4H, aromatic H), 9.74 (s, 1H, CHO).

N-Sulfinyl-(2,4,6-trimethylbenzene)sulfonamide: A mixture of 2,4,6-trimethylbenzenesulfonamide (4.68 g, 23.3 mmol) and thionyl chloride (7.25 ml, 100 mmol) was refluxed under N_2 for 8 h. Excess thionyl chloride was removed by distillation and the residue was distilled in vacuo. Yield: 3.26 g (57%); b.p. 130–135 °C/0.03 Torr.

General Procedure (G. P. 1) for the Preparation of N-Benzylidene- and N-Alkylidene-(2,4,6-trimethylbenzene)sulfonamides **2b–f**: A 50-ml two-necked flask was equipped with a magnetic stirrer, a

septum, and a reflux condenser which was connected to a combined nitrogen/vacuum line, and charged with 30 mmol of *N*-sulfinyl-(2,4,6-trimethylbenzene)sulfonamide. The air in the flask was replaced by nitrogen, and dry dichloromethane (15 ml) was added by syringe through the septum. Thereafter, the corresponding aldehyde (neat or dissolved in 5 ml of dichloromethane) was injected under stirring. The connection to the nitrogen/vacuum line was replaced by a bubbler, and 5–7 drops of boron trifluoride etherate were added. The production of gaseous sulfur dioxide started immediately. When the mixture had been refluxed for 1–2 h, the condenser was replaced by a Zincke distillation apparatus, and the solvent as well as most of the excess aldehyde and the catalyst were distilled off. The crude products thus obtained were either recrystallized or purified by distillation under reduced pressure (oil-diffusion pump).

Using this procedure, the following were obtained:

N-[(4-Methoxyphenyl)methylene](2,4,6-trimethylbenzene)-sulfonamide (**2b**): Prepared from 8.09 g of *N*-sulfinyl(2,4,6-trimethylbenzene)sulfonamide (33 mmol) and 4-methoxybenzaldehyde (4.45 ml, 36.3 mmol). The crude product was recrystallized from petroleum ether/chloroform (10:1). Yield: 7.8 g (75%); m.p. 117°C. – ^{1}H NMR (60 MHz): δ = 2.20 (s, 3H, CH_3), 2.61 (s, 6H, CH_3), 3.75 (s, 3H, OCH_3), 6.70–6.86 (m, 4H, aromatic H), 7.50–7.75 (m, 2H, aromatic H), 8.72 (s, 1H, N=C*H*-Ar). – MS (70 eV); *m/z* (%): 317 (28) [M^+], 146 (100), 119 (78) [C_9H_{11}]. – $C_{17}H_{19}NO_3S$ (317.4): calcd. C 64.33, H 6.03, N 4.41; found C 64.24, H 5.89, N 4.43.

N-({4-[Dimethyl(1,1,2-trimethylpropyl)silyloxy]-phenyl}methylene)2,4,6-trimethylbenzenesulfonylamide (**2c**): Prepared from 6.4 g of *N*-sulfinyl(2,4,6-trimethylbenzene)sulfonylamide (25.7 mmol) and 4-[dimethyl(1,1,2-trimethylpropyl)silyloxy]-benzaldehyde (6.88 g, 26 mmol). The oily crude product was used without further purification. Yield: 10.05 g (87%). – ^{1}H NMR (300 MHz): δ = 0.26 [s, 6H, $Si(CH_3)_2$], 0.92–0.96 [m, 12H, $C(CH_3)_2CH(CH_3)_2$], 1.60–1.80 [m, 1H, $CH(CH_3)_2$], 2.29 (s, 3H, $ArCH_3$), 2.70 (s, 6H, $ArCH_3$), 6.88–7.84 (m, 6H, aromatic H), 8.94 (s, 1H, N=CHAr).

N-(3-Methylbutylidene)(2,4,6-trimethylbenzene)sulfonamide (**2d**) *and N-(3-Methylbutenyl)(2,4,6-trimethylbenzene)sulfonamide* (**6a**): Prepared from 9.81 g of 2,4,6-trimethyl-*N*-sulfinylbenzenesulfonamide (40 mmol) and 3-methylbutanal (4.3 ml, 40 mmol). According to the ^{1}H NMR spectrum, the product which was purified by distillation, consisted of a mixture (approximately 1:1) of the tautomers **2d** and **6a**. Yield: 6.52 g (61%); b.p. 150°C/0.0001 Torr.

2d: ^{1}H NMR (300 MHz): δ = 0.89–1.22 [m, 6H, $CH(CH_3)_2$], 1.70–1.85 [m, 1H, $CH(CH_3)_2$], 2.30 (s, 3H, $ArCH_3$), 2.60 (s, 6H, $ArCH_3$), 2.90–3.10 (m, 2H, CH_2CH), 6.91–7.03 (m, 2H, aromatic H), 8.58 (t, *J* = 5 Hz, 1H, N=C*H*CH_2).

6a: ^{1}H NMR (300 MHz) differs from that of **2d** in: δ = 2.35–2.45 [m, 1H, $CH(CH_3)_2$], 4.81 (broad s, 1H, NH), 6.38–6.50 (m, 2H, C*H*=C*H*).

N-(2-Methylpropylidene)-2,4,6-trimethylbenzenesulfonamide (**2e**) *and N-(2-Methylpropenyl)-2,4-6-trimethylbenzenesulfonamide* (**6b**): Prepared from 10.2 g of 2,4,6-trimethyl-*N*-sulfinylbenzenesulfonamide (42 mmol) and 2-methylpropanal (5.5 ml, 60 mmol). According to the ^{1}H-NMR spectrum, the product distilled in vacuo consisted of the tautomers **2e** and **6b** in a ratio of 2:1. Yield: 7.8 g (73%); b.p. 124°C/0.0001 Torr; m.p. 55°C.

2e: ^{1}H NMR (60 MHz): δ = 1.13 [d, *J* = 7 Hz, 6H, $CH(CH_3)_2$], 1.60–1.80 [m, 1H, $CH(CH_3)_2$], 2.25 (s, 3H, $ArCH_3$), 2.60 (s, 6H, $ArCH_3$), 6.90–7.00 (m, 2H, aromatic H), 8.40 [d, *J* = 4 Hz, 1H, N=C*H*-$CH(CH_3)_2$].

6b: ^{1}H NMR (60 MHz) differs from that of **2e** in: δ = 1.50 and 1.60 [2 s, 3H each, C*H*=$C(CH_3)_2$], 5.03 (broad s, 1H, NH), 5.58 [d, *J* = 9 Hz, 1H, C*H*=$C(CH_3)_2$].

N-(2,2-Dimethylpropylidene)-2,4,6-trimethylbenzenesulfonamide (**2f**): Prepared from 9.0 g of 2,4,6-trimethyl-*N*-sulfinylbenzenesulfonamide (36.7 mmol) and 2,2-dimethylpropanal (6 ml, 55 mmol). The crude product was purified by distillation. Yield: 8.67 g (88%); b.p. 110°C/0.01 Torr; m.p. 60°C. – ^{1}H NMR (60 MHz): δ = 1.08 [s, 9H, $C(CH_3)_3$], 2.27 (s, 3H, $ArCH_3$), 2.58 (s, 6H, $ArCH_3$), 6.90 (s, 2H, ArH), 8.37 (s, 1H, N=CH).

General Procedure (G. P. 2) for the Addition of Dibromoalkene **1a** *to Sulfonylimines* **2a–f** *and* **21a–h**: A solution of **1a** (3.18 g, 10.0 mmol) in 50 ml of absolute diethyl ether was stirred at −108°C under nitrogen in a 100-ml two-necked flask equipped with a magnetic stirrer, a septum, and a connection to a combined nitrogen/vacuum line. A thermocouple was introduced through the septum, and *n*-butyllithium (6.0 ml of a 1.6 M solution in *n*-hexane, 9.6 mmol) was added slowly to the vigorously stirred mixture by means of a cannula. During the course of the addition, the temp. monitored by an electronic thermometer was not allowed to exceed −105°C. Care was taken to avoid an excess of butyllithium. A fine white precipitate formed gradually during the addition of *n*-butyllithium. After stirring for 15 min at −105°C another 0.25 ml portion (0.4 mmol) of the solution of butyllithium was added. Stirring was continued for 20 min at −105 to −100°C in order to complete the formation of **1b**.

The mixture was then diluted with 2 ml of THF at −110°C, stirring was continued for 1 min, and a precooled (−100°C) solution of the sulfonylimine **2** or **21** (10.0 mmol) in THF (30 to 40 ml) was added through a cannula at such a rate that the temp. did not exceed −110°C. Thereafter, the mixture was allowed to reach −78°C within 8 h. A satd. aqueous solution of NH_4Cl (10 ml) was added, and the cooling bath was removed so that the mixture could reach room temp. The organic layer was separated, the aqueous phase was diluted with water (20 ml) and extracted four times with a total amount of 100 ml of diethyl ether. The combined organic layers were washed with brine (30 ml) and then dried with $MgSO_4$. The solvent was removed in a rotary evaporator and the residue was transferred into a 25-ml one-necked flask which was connected via a short bent glass tube to a two-necked flask. The latter flask was plunged into a bath of liquid nitrogen and connected to an oil pump (0.001 Torr), while the crude product was warmed to 50–70°C. This procedure was maintained for 2 to 3 h in order to remove smaller amounts of dibromoalkene **1a** as well as (*E*)-1-bromo-3-[(2-methoxyethoxy)methoxy]-1-butene which arose from protonation of the lithiated alkene **1b**. The crude products thus obtained were first submitted to ^{1}H-NMR investigation so that the diastereomeric ratio could be determined. Thereafter, they were purified by column chromatography.

Using this procedure, the following were obtained:

(1S,2E,4S)- and (1R,2E,4S)-N-{2-Bromo-4-[(2-methoxyethoxy)methoxy]-1-phenyl-2-pentenyl}-2,4,6-trimethylbenzenesulfonamide (**3a** and **4a**): Prepared by reaction of (*S*)-**1a** (15.9 g, 50.0 mmol) with **2a** (14.4 g, 50.0 mmol) dissolved in 200 ml of THF. The diastereomeric ratio of the crude mixture **3a/4a** was determined as 96:4. Column chromatography (hexane/ethyl acetate/chloroform, 1:1:2) afforded 16.16 g (62%) of crystalline **3a** (>98% *d.e.*); R_f = 0.7; m.p. 55°C. – $[\alpha]_D^{20}$ = −92.5 (*c* = 3.5 in 95% aqueous ethanol). – ^{1}H NMR (300 MHz): δ = 1.03 [d, *J* = 6.3 Hz, 3H, $CH(O-)CH_3$], 2.29 (s, 3H, $ArCH_3$), 2.65 (s, 6H, $ArCH_3$), 3.32 (s, 3H, OCH_3), 3.42–3.68 (m, 4H, OCH_2CH_2O), 4.35–4.45 [dq, J_d = 9.0 Hz, J_q = 6.3 Hz, 1H, $CH(O-)CH_3$], 4.65 (s, 2H, OCH_2O), 5.5 (d, *J* = 9.2 Hz, 1H, NH), 5.62 [d, *J* = 9.2 Hz, 1H,

CH(N−)], 5.93 (d, J = 9.0 Hz, 1 H, BrC=CH), 6.94−7.42 (m, 7 H, aromatic H). − MS (70 eV); *m/z* (%): 421, 419 (100) [M^+ − $C_4H_9O_3$], 343, 341 (45) [M^+ − $C_9H_{11}O_2S$]. − $C_{24}H_{32}BrNO_5S$ (526.5): calcd. C 54.75, H 6.13, N 2.66; found C 54.80, H 6.22, N 2.69.

^{1}H NMR (300 MHz) of the minor diastereomer **4a** differs from that of **3a** in: δ = 1.18 (d, J = 6.3 Hz), 3.39 (s, 3 H, OCH_3), 6.04 (d, J = 9.0 Hz).

(1S,2E,4S)- and (1R,2E,4S)-N-{2-Bromo-4-[(2-methoxyethoxy)methoxy]-1-(4-methoxyphenyl)-2-pentenyl}-2,4,6-trimethylbenzenesulfonamide (**3b** and **4b**): Synthesized by reaction of (*S*)-**1a** (9.54 g, 30 mmol) with sulfonylimine **2b** (7.93 g, 25.0 mmol) dissolved in 120 ml of THF. The ^{1}H-NMR spectrum showed the diastereomeric ratio of **3b** and **4b** to be 96:4. Column chromatography (hexane/ethyl acetate/chloroform, 3:2:3) afforded 8.71 g (63%) of oily, viscous **3b** (98% *d.e.*); R_f = 0.65. − $[\alpha]_D^{20}$ = −95.7 (c = 1.95 in 95% aqueous ethanol). − ^{1}H NMR (300 MHz): δ = 1.03 (d, J = 6.2 Hz, 3 H, CH(O−)CH_3], 2.28 (s, 3 H, $ArCH_3$), 2.64 (s, 6 H, $ArCH_3$), 3.32 (s, 3 H, CH_2OCH_3), 3.43−3.75 (m, 4 H, OCH_2CH_2O), 3.77 (s, 3 H, $ArOCH_3$), 4.38 [dq, J_d = 9.2 Hz, J_q = 6.2 Hz, 1 H, C*H*(O−)CH_3], 4.63 (s, 2 H, OCH_2O), 5.46 (d, J = 9.0 Hz, 1 H, NH), 5.54 [d, J = 9.0 Hz, 1 H, CH(N−)], 5.90 (d, J = 9.2 Hz, 1 H, BrC=CH), 6.79−7.88 (m, 6 H, aromatic H). − MS (70 eV); *m/z* (%): 450, 448 (64, 60) [M^+ − C_7H_7O], 119 (50) [C_9H_{11}], 59 (100) [$C_2H_3O_2$]. − $C_{25}H_{34}BrNO_6S$ (556.5): calcd. C 53.96, H 6.16, N 2.52; found C 53.79, H 6.13, N 2.45.

^{1}H NMR (300 MHz) of the minor diastereomer **4b** differs from that of **3b** in: δ = 1.10 (d, J = 6.2 Hz), 6.01 (d, J = 9.2 Hz).

(1S,2E,4S)- and (1R,2E,4S)-N-{2-Bromo-1-(4-[dimethyl(1,1,2-trimethylpropyl)silyloxy]phenyl}-4-[(2-methoxyethoxy)-metoxy]-2-pentenyl}-2,4,6-trimethylbenzenesulfonamide (**3c** and **4c**): Prepared by reaction of (*S*)-**1b** (6.36 g, 20.0 mmol) and sulfonylimine **2c** (8.91 g, 20.0 mmol) dissolved in 80 ml of THF. The diastereomeric ratio **3c**/**4c** was determined as 96:4, according to the ^{1}H-NMR spectrum of the crude product. Purification by column chromatography (hexane/ethyl acetate/chloroform, 3:1:3) afforded 7.31 g (53.9%) of oily, viscous **3c** (98% *d.e.*); R_f = 0.6. − $[\alpha]_D^{20}$ = −84.6 (c = 1.7 in 95% aqueous ethanol). − ^{1}H NMR (300 MHz): δ = 0.20 [s, 6 H, $Si(CH_3)_2$], 0.94 [m, 12 H, $C(CH_3)_2CH(CH_3)_2$], 1.05 [d, J = 6.3 Hz, 3 H, CH(O−)CH_3], 1.71 [sept, J = 6.8 Hz, 1 H, $C(CH_3)_2CH(CH_3)_2$], 2.28 (s, 3 H, $ArCH_3$), 2.63 (s, 6 H, $ArCH_3$), 3.32 (s, 3 H, OCH_3), 3.43−3.75 (m, 4 H, OCH_2CH_2O), 4.42 [dq, J_d = 9.2 Hz, J_q = 6.2 Hz, 1 H, C*H*(O−)CH_3], 4.63 (s, 2 H, OCH_2O), 5.45 (d, J = 8.9 Hz, 1 H, NH), 5.55 [d, J = 8.9 Hz, 1 H, CH(N−)], 5.90 (d, J = 9.2 Hz, 1 H, BrC=CH), 6.70−7.83 (m, 6 H, aromatic H). − MS (70 eV); *m/z* (%): 685, 683 (1) [M^+], 578, 576 (100, 93) [M^+ − $C_4H_9O_3$], 501, 499 (30, 28) [M^+ − $C_9H_{11}O_2S$]. − $C_{32}H_{50}BrNO_6SSi$ (684.8): calcd. C 56.12, H 7.36, N 2.05; found C 56.26, H 7.42, N 2.00.

^{1}H NMR (300 MHz) of the minor isomer **4c** differs from that of **3c** in δ = 6.02 (d, J = 9.2 Hz).

(1S,2E,4S)- and (1R,2E,4S)-N-{2-Bromo-4-[(2-methoxyethoxy)methoxy]-1-(2-methylpropyl)-2-pentenyl}-2,4,6-trimethylbenzenesulfonamide (**3d** and **4d**): Prepared by reaction of (*S*)-**1a** (7.95 g, 25.0 mmol) and a distilled mixture of the tautomeric compounds **2d** and **6a** (6.39 g, 23.9 mmol) dissolved in 80 ml of THF. The ratio of the diastereomeric products **3d** and **4d** in the crude mixture was determined as 97:3 from the ^{1}H-NMR spectra. Column chromatography (hexane/ethyl acetate/chloroform, 3:2:3) gave 2.48 g (21%) of oily, viscous **3d** (>98% *d.e.*; the minor isomer **4d** could not be detected by ^{1}H-NMR spectroscopy in the purified product); R_f = 0.76. − $[\alpha]_D^{20}$ = −86.4 (c = 1.6 in 95% aqueous ethanol). − ^{1}H NMR (300 MHz): δ = 0.83, 0.87 [2 d, J = 6.5 Hz, 3 H each, $CH(CH_3)_2$], 1.06 [d, J = 6.3 Hz, 3 H, CH(O−)CH_3], 1.61 [m, 2 H, $CH_2CH(CH_3)_2$], 2.29 (s, 3 H, $ArCH_3$), 2.66 (s, 6 H, $ArCH_3$), 3.37 (s, 3 H, OCH_3), 3.51−3.78 (m, 4 H, OCH_2CH_2O), 4.28−4.35 [m, 1 H, CH(N−)], 4.36−4.42 [m, 1 H, C*H*(O−)CH_3], 4.63 (AB system, J_{AB} = 7.1 Hz, 2 H, OCH_2O), 4.84 (d, J = 9.7 Hz, 1 H, NH), 5.69 (d, J = 9.4 Hz, 1 H, BrC=CH), 6.91−6.94 (m, 2 H, aromatic H). − MS (70 eV); *m/z* (%): 505, 507 (5) [M^+], 468, 466 (20) [M^+ − C_3H_7], 400, 398 (30, 32) [M^+ − $C_4H_9O_3$], 268 (58) [$C_{14}H_{22}NO_2S$], 211 (100) [$C_{10}H_{13}NO_2S$]. − $C_{22}H_{36}BrNO_5S$ (506.5): calcd. C 53.07, H 7.36, N 2.69; found C 53.37, H 7.37, N 2.79.

^{1}H NMR (300 MHz) spectrum of the minor isomer **4d** (detected in the crude product only) differs from that of **3d** in: δ = 1.10 (d, J = 6.3 Hz), 3.38 (s), 5.80 (d, J = 9.4 Hz).

(1S,2E,4S)- and (1R,2E,4S)-N-{2-Bromo-4-[(2-methoxyethoxy)methoxy]-1-(1-methylethyl)-2-pentenyl}-2,4,6-trimethylbenzenesulfonamide (**3e** and **4e**): Synthesized by reaction of (*S*)-**1a** (9.54 g, 30.0 mmol) with a distilled mixture of the tautomeric compounds **2e** and **6b** (7.37 g, 29.0 mmol) dissolved in 100 ml of THF. According to the ^{1}H-NMR spectra, the ratio of diastereomers **3e** and **4e** in the crude mixture amounted to 97:3. The crude product was submitted to column chromatography (hexane/ethyl acetate/chloroform, 3:1:2) to give 4.8 g (34%) of oily **3e** (98% *d.e.*); R_f = 0.78. − $[\alpha]_D^{20}$ = −70.2 (c = 1.5 in 95% aqueous ethanol). − ^{1}H NMR (300 MHz): δ = 0.91 and 0.94 [2 d, J = 6.9 Hz, 3 H each, $CH(CH_3)_2$], 1.02 [d, J = 6.2 Hz, 3 H, CH(O−)CH_3], 1.79 [m, 1 H, C*H*$(CH_3)_2$], 2.28 (s, 3 H, $ArCH_3$), 2.66 (s, 6 H, $ArCH_3$), 3.39 (s, 3 H, OCH_3), 3.54−3.78 (m, 4 H, OCH_2CH_2O), 3.85 [dd, J= 9.7 Hz, J = 9.6 Hz, 1 H, CH(N−)], 4.42 [dq, J_d = 9.5 Hz, J_q = 6.2 Hz, 1 H, CH(O−)CH_3], 4.67 (AB system, J_{AB} = 7.1 Hz, 2 H, OCH_2O), 4.87 (d, J = 9.7 Hz, 1 H, NH), 5.80 (d, J = 9.5 Hz, 1 H, BrC=CH), 6.94 (s, 2 H, aromatic H). − MS (70 eV); *m/z* (%): 450, 448 (25) [M^+ − C_3H_7], 387, 385 (70) [M^+ − $C_4H_{10}O_3$], 211 (100) [$C_{10}H_{13}NO_2S$]. − $C_{21}H_{34}BrNO_5S$ (492.5): calcd. C 51.22, H 6.69, N 2.84; found C 51.07, H 6.84, N 2.99.

The ^{1}H-NMR (300 MHz) spectrum of the minor isomer **4e** (detected in the crude product only) differs from that of **3e** in: δ = 1.09 (d, J = 6.2 Hz), 5.85 (d, J = 9.5 Hz).

(1S,2E,4S)- and (1R,2E,4S)-N-{2-Bromo-1-(1,1-dimethylethyl)-4-[(2-methoxyethoxy)-methoxy]-2-pentenyl}-2,4,6-trimethylbenzenesulfonamide (**3f** and **4f**): Prepared by reaction of (*S*)-**1a** (3.18 g, 10 mmol) and **2f** (2.67 g, 10 mmol) dissolved in 30 ml of THF. The ratio of diastereomers **3f** and **4f** amounted to 98:2 in the crude product, according to the ^{1}H-NMR spectrum. Purification by column chromatography (hexane/ethyl acetate/chloroform, 3:2:3) afforded crystalline **3f** (2.55 g, 52%); R_f = 0.85; m.p. 61 °C; $[\alpha]_D^{20}$ = −67.6 (c = 1.1 in 95% aqueous ethanol). − ^{1}H NMR (300 MHz): δ = 0.94 [s, 9 H, $C(CH_3)_3$], 1.18 [d, J = 6.2 Hz, 3 H, CH(O−)CH_3], 2.29 (s, 3 H, $ArCH_3$), 2.62 (s, 6 H, $ArCH_3$), 3.38 (s, 3 H, OCH_3), 3.52−3.78 (m, 4 H, OCH_2CH_2O), 4.05 [d, J = 10.2 Hz, 1 H, C*H*(N−)], 4.53 [m, 1 H, C*H*(O−)CH_3], 4.71 (s, 2 H, OCH_2O), 5.03 (d, J = 10.2 Hz, 1 H, NH), 5.93 (d, J = 9.1 Hz, 1 H, BrC=CH), 6.95 (m, 2 H, aromatic H). − MS (70 eV); *m/z* (%). 448, 446 (4) [M^+ − C_4H_7], 344, 342 (35) [M^+ − $C_8H_{18}O_3$], 211 (100) [$C_{10}H_{13}NO_2S$]. − $C_{22}H_{36}BrNO_5S$ (506.5): calcd. C 52.17, H 7.16, N 2.77; found C 52.07, H 7.23, N 2.76.

The ^{1}H-NMR (300 MHz) spectrum of the minor isomer **4f** (detected in the crude product only) differs from that of **3f** in: δ = 1.26 (d, J = 6.2 Hz), 6.00 (d, J = 9.1 Hz).

(1S,2E,4S)- and (1R,2E,4S)-N-{2-Bromo-4-[(2-methoxyethoxy)methoxy]-1-phenyl-2-pentenyl}benzenesulfamide (**22a** and **23a**): Prepared by reaction of (*S*)-**1a** (3.18 g, 10.0 mmol) and **21a**

(2.45 g, 10.0 mmol) dissolved in 15 ml of THF; diastereomeric ratio: 74:26; yield: 3.71 g (77%). A sample of **22a/23a** (0.34 g) was submitted to column chromatography (hexane/ethyl acetate/chloroform, 1:1:2) to give an analytically pure, oily mixture of **22a** and **23a** (0.16 g); R_f = 0.6. – MS (70 eV); *m/z* (%): 378, 376 (12) [$M^+ - C_4H_9O_3$], 157 (52) [$C_8H_{13}O_3$], 141 (35) [$C_6H_5O_2S$], 77 (100) [C_6H_5]. – **22a** (major distereomer): ^{1}H NMR (300 MHz): δ = 1.10 [d, *J* = 6.5 Hz, 3H, CH(O−)C*H*$_3$], 3.33 (s, 3H, OCH_3), 3.45−3.69 (m, 4H, OCH_2CH_2O), 4.46 dq, J_d = 6.5 Hz, J_q = 9 Hz, 1H, C*H*(O−)CH_3], 4.65 (s, 2H, OCH_2O), 5.70 [broad s, 1H, CH(N−)], 5.89 (d, *J* = 9 Hz, 1H, BrC=CH), 7.25−8.03 (m, 10H, aromatic H). – **23a** (minor diastereomer): ^{1}H NMR (300 MHz): Differs in δ = 1.18 (d, *J* = 6.5 Hz), 3.39 (s), 4.72 (AB system, J_{AB} = 7 Hz, OCH_2O), 6.02 (d, *J* = 9 Hz). – $C_{21}H_{26}BrNO_5S$ (484.4): calcd. C 52.07, H 5.41, N 2.89; found C 51.91, H 5.50, N 2.83.

(1S,2E,4S)- and (1R,2E,4S)-N-{2-Bromo-4-[(2-methoxyethoxy)methoxy]-1-phenyl-2-pentenyl}-4-(dimethylamino)-benzenesulfonamide (**22b** and **23b**): Prepared by reaction of (*S*)-**1a** (3.18 g, 10.0 mmol) and **21b** (2.88 g, 10.0 mmol) dissolved in 40 ml of THF; diastereomeric ratio: 89.5:10.5; yield: 2.95 g (56%). A sample of **22b/23b** (0.40 g) was submitted to column chromatography (hexane/ethyl acetate/chloroform, 1:1:1) to give an oily mixture of **22b** and **23b** (0.35 g); R_f = 0.6. – MS (70 eV); *m/z* (%): 527, 525 (17) [M^+], 184 (90) [$C_8H_{10}NO_2S$], 59 (100) [$C_2H_3O_2$]. – **22b** (major diastereomer): ^{1}H NMR (300 MHz): δ = 1.15 [d, *J* = 6.3 Hz, 3H, CH(O−)C*H*$_3$], 3.00 [s, 6H, $N(CH_3)_2$], 3.33 (s, 3H, OCH_3), 3.45−3.68 (m, 4H, OCH_2CH_2O), 4.48 [dq, J_d = 6.3 Hz, J_q = 9 Hz, 1H, C*H*(O−)CH_3], 4.65 (s, 2H, OCH_2O), 5.62 [s, 1H, CH(N−)], 5.92 (d, *J* = 9 Hz, 1H, BrC=CH), 6.59−7.71 (m, 9H, aromatic H). – **23b** (minor diastereomer): ^{1}H NMR (300 MHz): Differs in δ = 1.19 (d, *J* = 6.3 Hz), 3.37 (s), 4.73 (AB system, J_{AB} = 7 Hz, OCH_2O), 6.06 (d, *J* = 9 Hz). – $C_{23}H_{31}BrN_2O_5S$ (527.5): calcd. C 52.37, H 5.92, N 5.31; found C 52.41, H 6.04, N 5.31.

(1S,2E,4S)- and (1R,2E,4S)-N-{2-Bromo-4-[(2-methoxyethoxy)methoxy]-1-phenyl-2-pentenyl}-4-methoxybenzenesulfonamide (**22c** and **23c**): Prepared by reaction of (*S*)-**1b** (2.23 g, 7.1 mmol) and **21c** (1.95 g, 7.1 mmol) dissolved in 20 ml of THF; diastereomeric ratio: 81.5:18.5; yield: 2.83 g (78%). A sample of **22c/23c** (0.54 g) was submitted to column chromatography (hexane/ethyl acetate/chloroform, 1:1:2) to give an oily, viscous mixture of **22c** and **23c** (0.46 g); R_f = 0.7. – MS (70 eV); *m/z* (%): 408, 406 (100) [$M^+ - C_7H_7O$], 343, 341 (70) [$M^+ - C_7H_8O_3S$], 186 (80) [$C_7H_8NO_3S$], 171 (100) [$C_7H_7O_3S$]. – **22c** (major diastereomer): ^{1}H NMR (300 MHz): δ = 1.14 [d, *J* = 6.3 Hz, 3H, CH(O−)C*H*$_3$], 3.32 (s, 3H, CH_2OCH_3), 3.51−3.78 (m, 4H, OCH_2CH_2O), 3.84 (s, 3H, $ArOCH_3$), 4.50 [dq, J_d = 6.3 Hz, J_q = 9 Hz, 1H, C*H*(O−)CH_3], 4.65 (s, 2H, OCH_2O), 5.67 [broad s, 1H, CH(N−)], 5.91 (d, *J* = 9 Hz, 1H, BrC=CH), 6.90−7.94 (m, 9H, aromatic H). – **23c** (minor diastereomer): ^{1}H NMR (300 MHz): Differs in δ = 1.18 (d, *J* = 6.3 Hz), 3.39 (s), 3.85 (s), 4.72 (AB system, J_{AB} = 8.5 Hz, OCH_2O), 6.04 (d, *J* = 9 Hz). – $C_{22}H_{28}BrNO_6S$ (514.4): calcd. C 51.37, H 5.49, N 2.72; found C 51.59, H 5.53, N 2.75.

(1S,2E,4S)- and (1R,2E,4S)-N-{2-Bromo-4-[(2-methoxyethoxy)methoxy]-1-phenyl-2-pentenyl}-4-methylbenzenesulfonamide (**22d** and **23d**): Prepared by reaction of (*S*)-**1a** (3.10 g, 9.8 mmol) and **21d** (2.59 g, 10.0 mmol) dissolved in 20 ml of THF; diastereomeric ratio: 79.5:20.5; yield: 3.22 g (66%). A sample of **22d/23d** (0.30 g) was purified by column chromatography (diethyl ether/hexane, 3:1) to give a yellowish, oily mixture of **22d/23d** (0.22 g); R_f = 0.5. – MS (70 eV); *m/z* (%): 394, 392 (12) [$M^+ - C_4H_{10}O_3$], 171 (32) [$C_7H_9NO_2S$], 91 (100) [C_7H_7]. – **22d** (major diastereomer): ^{1}H NMR (300 MHz): δ = 1.11 [d, *J* = 6.3 Hz, 3H, CH(O−)C*H*$_3$], 2.40 (s, 3H, $ArCH_3$), 3.32 (s, 3H, OCH_3), 3.44−3.70 (m, 4H, OCH_2CH_2O), 4.54 [dq, J_d = 6.3 Hz, J_q = 9.0 Hz, 1H, C*H*(O−)CH_3], 4.64 (s, 2H, OCH_2O), 5.68 [broad s, 1H, CH(N−)], 5.90 (d, *J* = 9.0 Hz, 1H, BrC=CH), 7.23−7.93 (m, 9H, aromatic H). – **23d** (minor diastereomer): ^{1}H NMR (300 MHz): Differs in δ = 1.18 (d, *J* = 6.3 Hz), 2.43 (s), 3.38 (s), 4.66 (AB system, J_{AB} = 8.5 Hz, OCH_2O), 6.03 (d, *J* = 9 Hz). – $C_{22}H_{28}BrNO_5S$ (498.4): calcd. C 53.01, H 5.66, Br 16.03; found C 52.92, H 5.71, Br 15.86.

(1S,2E,4S)- and (1R,2E,4S)-N-{2-Bromo-4-[(2-methoxyethoxy)methoxy]-1-phenyl-2-pentenyl}-4-fluorobenzenesulfonamide (**22e** and **23e**): Prepared by reaction of (*S*)-**1a** (1.91 g; 6.0 mmol) and **21e** (1.58 g, 6.0 mmol) dissolved in 30 ml of THF; diastereomeric ratio: 70.5:29.5. The crude product was purified by column chromatography (hexane/ethyl acetate/chloroform, 3:1:1) to give a mixture of **22e** and **23e** (1.78 g, 59%); R_f = 0.8. – MS (70 eV); *m/z* (%): 398, 396 (18) [$M^+ - C_4H_9O_3$], 157 (64) [$C_6H_4FO_2S$], 95 (29) [C_6H_4F], 89 (51) [$C_3H_7O_3$], 59 (100) [C_3H_7O]. – **22e** (major diastereomer): ^{1}H NMR (300 MHz): δ = 1.14 [d, *J* = 6.3 Hz, 1H, CH(O−)C*H*$_3$], 3.34 (s, 3H, OCH_3), 3.47−3.73 (m, 4H, OCH_2CH_2O), 4.50 [dq, J_d = 9 Hz, J_q = 6.3 Hz, 1H, C*H*(O−)CH_3], 4.65 (s, 2H, OCH_2O), 5.71 (d, *J* = 9.4 Hz, 1H, NH), 5.85 [d, *J* = 9.4 Hz, 1H, C*H*(N−)], 5.91 (d, *J* = 9 Hz, 1H, BrC=CH), 7.10−7.39 (m, 7H, aromatic H), 7.87−7.91 (m, 2H, aromatic H). – **23e** (minor diastereomer): ^{1}H NMR (300 MHz): Differs in δ = 1.18 (d, *J* = 6.3 Hz), 3.40 (s), 4.71 (AB system, J_{AB} = 7.8 Hz, OCH_2O), 5.60 (d, *J* = 8.7 Hz). – $C_{21}H_{25}BrFNO_5S$ (502.4): calcd. C 50.21, H 5.02, N 2.79; found C 50.27, H 4.96, N 2.63.

(1S,2E,4S)- and (1R,2E,4S)-N-{2-Bromo-4-[(2-methoxyethoxy)methoxy]-1-phenyl-2-pentenyl}-4-chlorobenzenesulfonamide (**22f** and **23f**): Prepared by reaction of (*S*)-**1a** (3.15 g, 9.9 mmol) and **21f** (3.07 g, 11.0 mmol) dissolved in 15 ml of THF; diastereomeric ratio: 67:33; yield: 4.20 g (82%). A sample (0.40 g) of the crude product was purified by column chromatography (hexane/ethyl acetate/chloroform, 2:1:2) to give an oily, viscous mixture of **22f** and **23f** (0.21 g); R_f = 0.6. – MS (70 eV); *m/z* (%): 413 (16), 411 (22) [$M^+ - C_4H_9O_3$], 177 (6), 175 (18) [$C_6H_4ClNO_2S$], 59 (100) [C_3H_7O]. – **22f** (major diastereomer): ^{1}H NMR (300 MHz): δ = 1.13 [d, *J* = 6.5 Hz, 3H, CH(O−)C*H*$_3$], 3.32 (s, 3H, OCH_3), 3.45−3.72 (m, 4H, OCH_2CH_2O), 4.48 [dq, J_d = 9.0 Hz, J_q = 6.3 Hz, 1H, C*H*(O−)CH_3], 4.64 (s, 2H, OCH_2O), 5.73 [broad s, 1H, CH(N−)], 5.91 (d, *J* = 9.0 Hz, 1H, BrC=CH), 7.27−7.86 (m, 9H, aromatic H). – **23f** (minor diastereomer): ^{1}H NMR (300 MHz): Differs in δ = 1.17 (d, *J* = 6.5 Hz), 3.38 (s), 4.69 (AB system, J_{AB} = 7.0 Hz, OCH_2O), 6.03 (d, *J* = 9.0 Hz). – $C_{21}H_{25}BrClNO_5S$ (518.9): calcd. C 48.61, H 4.86, N 2.70; found C 48.85, H 4.95, N 2.60.

(1S,2E,4S)- and (1R,2E,4S)-N-{2-Bromo-4-[(2-methoxyethoxy)methoxy]-1-phenyl-2-pentenyl}-4-(trifluoromethyl)-benzenesulfonamide (**22g** and **23g**): Prepared by reaction of (*S*)-**1a** (1.91 g, 6.0 mmol) and **21g** (1.88 g, 6.0 mmol) dissolved in 30 ml of THF; diastereomeric ratio: 55:45. The crude product was purified by column chromatography (hexane/ethyl acetate/chloroform, 2:1:1) to give an oily mixture of **22g/23g** (2.03 g, 61%), R_f = 0.65. – MS (70 eV); *m/z* (%): 448, 446 (21) [$M^+ - C_4H_9O_3$], 157 (73) [$C_8H_{13}O_3$], 145 (31) [$C_7H_4F_3$], 59 (100) [C_3H_7O]. – **22g** (major diastereomer): ^{1}H NMR (300 MHz): δ = 1.10 [d, *J* = 6.3 Hz, 3H, CH(O−)C*H*$_3$], 3.35 (s, 3H, OCH_3), 3.48−3.72 (m, 4H, OCH_2-CH_2O), 4.49 [dq, J_d = 9.2 Hz, J_q = 6.3 Hz, 1H, C*H*(O−)CH_3], 4.64 (s, 2H, OCH_2O), 5.75 (d, *J* = 9.6 Hz, 1H, NH), 5.80 [d, *J* = 9.6 Hz, 1H, C*H*(N−)], 5.90 (d, *J* = 9.2 Hz, 1H, BrC=CH), 7.26−7.37 (m, 5H, aromatic H), 7.70−8.05 (m, 4H, aromatic H).

– **23g** (minor diastereomer): ^{1}H NMR (300 MHz): Differs in δ = 1.18 (d, J = 6.3 Hz), 3.40 (s), 4.67 (AB system, J_{AB} = 7.8 Hz, OCH_2O), 6.03 (d, J = 9.2 Hz). – $C_{22}H_{25}BrFNO_5S$ (552.4): calcd. C 47.84, H 4.56, N 2.54; found C 47.81, H 4.58, N 2.42.

(1S,2E,4S)- and (1R,2E,4S)-N-{2-Bromo-4-[(2-methoxyethoxy)methoxy]-1-phenyl-2-pentenyl}-4-nitrobenzenesulfonamide (**22h** and **23h**): Prepared by reaction of (*S*)-**1a** (3.07 g, 9.66 mmol) and **21h** (2.81 g, 9.7 mmol). The sulfonamide was added as a suspension in 40 ml of THF; diastereomeric ratio: 55:45; yield 1.26 g (25%). A sample (0.50 g) of the crude product was purified by column chromatography (hexane/ethyl acetate/chloroform, 1:1:2) to give a yellowish, oily mixture of **21h** and **22h** (0.21 g); R_f = 0.7. – MS (70 eV); *m/z* (%): 424, 422 (44) [M^+ – $C_4H_9O_3$], 157 (68) [$C_8H_{13}O_3$], 90 (94) [$C_4H_{10}O_2$], 59 (100) [C_3H_7O]. – **22h** (major diastereomer): ^{1}H NMR (300 MHz): δ = 1.12 [d, J = 6.5 Hz, 3H, CH(O–)CH_3], 3.39 (s, 3H, OCH_3), 3.52–3.77 (m, 4H, OCH_2CH_2O), 4.39–4.52 [m, 1H, CH(O–)CH_3], 4.64 (s, 2H, OCH_2O), 5.76 [broad s, 1H, CH(N–)], 5.90 (d, J = 9.0 Hz, 1H, BrC=CH), 7.28–7.36 (m, 9H, aromatic H). – **23h** (minor diastereomer): ^{1}H NMR (300 MHz): Differs in δ = 1.18 (d, J = 6.3 Hz), 3.41 (s), 4.73 (AB system, J_{AB} = 7.0 Hz, OCH_2O), 6.05 (d, J = 9.0 Hz). – $C_{21}H_{25}BrN_2O_7S$ (529.4): calcd. C 47.64, H 4.76, N 5.29; found C 47.75, H 4.94, N 5.17.

General Procedure (G. P. 3) for the Conversion of the Vinyl Bromides **3a** *and* **3d–f** *into Alkenes* **11a–d**: An approximately 0.2 M solution of the vinyl bromides **3a** and **3d–f** in THF was stirred under nitrogen at –105 °C in a 250-ml two-necked flask equipped with a stirring bar, a connection to the combined nitrogen/vacuum line, and a thermocouple which was introduced through a septum. A 1.5 M solution of *tert*-butyllithium in pentane (26.7 ml, 40 mmol) was added to the vigorously stirred solution in such a way that the temp. did not exceed –95 °C. The mixture, which turned into a dark orange color, was allowed to reach –30 °C within 1 h. Thereafter, the solution was cooled to –78 °C and methanol (3 ml) and a satd. aqueous solution of NH_4Cl (20 ml) were added. The mixture was poured into diethyl ether (100 ml) and the organic layer was separated. The aqueous phase was extracted with three 20 ml portions of diethyl ether. The combined organic layers were washed with brine (30 ml) and dried with $MgSO_4$. The solvent was removed in a rotary evaporator, and the residue was purified by column chromatography.,

Using this procedure, the following were obtained:

(1R,2Z,4S)-N-{4-[(2-Methoxyethoxy)methoxy]-1-phenyl-2-pentenyl}-2,4,6-trimethylbenzenesulfonamide (**11a**): Prepared from **3a** (5.36 g, 10.0 mmol; >98% *d.e.*). The crude product (4.4 g) was purified by column chromatography (hexane/ethyl acetate/chloroform, 3:2:2) to give colorless, oily **11a** in 92% yield (4.09 g); R_f = 0.46; $[\alpha]_D^{20}$ = –96.8 (c = 1 in 95% aqueous ethanol). – ^{1}H NMR (300 MHz): δ = 1.11 [d, J = 6.3 Hz, 3H, CH(O–)CH_3], 2.25 (s, 3H, $ArCH_3$), 2.55 (s, 6H, $ArCH_3$), 3.35 (s, 3H, OCH_3), 3.45–3.68 (m, 4H, OCH_2CH_2O), 4.45 [dq, J_d = 9.8 Hz, J_q = 6.3 Hz, 1H, CH(O–)CH_3], 4.50 (AB system, J_{AB} = 6.9 Hz, 2H, OCH_2O), 5.18–5.25 (m, 2H, HC=CH), 5.28–5.35 [m, 1H, CH(N–)], 5.62 (d, J = 8.5 Hz, 1H, NH), 6.85–7.21 (m, 7H, aromatic H). – MS (70 eV); *m/z* (%): 341 (7) [M^+ – $C_4H_{10}O_3$], 198 (45) [$C_9H_{12}NO_2S$], 119 (100) [C_9H_{11}]. – $C_{24}H_{33}NO_5S$ (447.6): calcd. C 64.40, H 7.43, N 3.13; found C 64.30, H 7.41, N 3.26.

(1S,2Z,4S)-N-{4-[(2-Methoxyethoxy)methoxy]-1-(2-methylpropyl)-2-pentenyl}-2,4,6-trimethylbenzenesulfonamide (**11b**): Prepared from **3d** (1.36 g, 2.7 mmol; >98% *d.e.*). The crude product was purified by column chromatography (hexane/ethyl acetate/chloroform, 1:1:1) to give colorless, crystalline **11b** (1.09 g, 95%); R_f = 0.82; m.p. 58 °C; $[\alpha]_D^{20}$ = –51.9 (c = 1.1 in 95% aqueous ethanol). – ^{1}H NMR (300 MHz): δ = 0.79 and 0.84 [2 d, J = 6.6 Hz, 3H each, CH(CH_3)$_2$], 1.03 [d, J = 6.3 Hz, 3H, CH(O–)CH_3], 1.18–1.43 [m, 2H, CH_2CH$(CH_3)_2$], 1.53–1.64 [m, 1H, CH_2C$H$$(CH_3)_2$], 2.29 (s, 3H, $ArCH_3$), 2.64 (s, 6H, $ArCH_3$), 3.37 (s, 3H, OCH_3), 3.51–3.76 (m, 4H, OCH_2CH_2O), 4.01–4.12 [m, 1H, CH(N–)], 4.33 (dq, J_d = 8.9 Hz, J_q = 6.3 Hz, 1H, CH(O–)CH_3], 4.60 (AB system, J_{AB} = 7.0 Hz, 2H, OCH_2O), 4.65 (d, J = 8.1 Hz, 1H, NH), 5.12–5.31 (m, 2H, CH=HC), 6.94 (s, 2H, aromatic H). – MS (70 eV); *m/z* (%): 322 (16) [M^+ – $C_4H_9O_3$], 321 (18) [M^+ – $C_4H_{10}O_3$], 183 (23) [$C_9H_{11}O_2S$], 119 (82) [C_9H_{11}], 89 (83) [$C_4H_9O_2$], 59 (100) [C_3H_7O]. – $C_{22}H_{37}NO_5S$ (427.6): calcd. C 61.80, H 8.72, N 3.28; found C 61.94, H 8.77, N 3.19.

(1S,2Z,4S)-N-{4-[(2-Methoxyethoxy)methoxy]-1-(1-methylethyl)-2-pentenyl}-2,4,6-trimethylbenzenesulfonamide (**11c**): Prepared from **3e** (3.94 g, 8.0 mmol; 98% *d.e.*). The crude product was purified by column chromatography (hexane/ethyl acetate/chloroform, 3:2:3) to give colorless, oily **11c** (3.10 g, 94%); R_f = 0.65; $[\alpha]_D^{20}$ = –31.6 (c = 1.1 in 95% aqueous ethanol). – ^{1}H NMR (300 MHz): δ = 0.83 and 0.87 [2 d, J = 6.8 Hz, 3H each, CH(CH_3)$_2$], 0.97 [d, J = 6.3 Hz, 3H, CH(O–)CH_3], 1.72–1.81 [m, 1H, C$H$$(CH_3)_2$], 2.28 (s, 3H, $ArCH_3$), 2.64 (s, 6H, $ArCH_3$), 3.37 (s, 3H, OCH_3), 3.51–3.71 (m, 4H, OCH_2CH_2O), 3.83–3.92 [m, 1H, CH(N–)], 4.31 [dq, J_d = 8.3 Hz, J_q = 6.3 Hz, 1H, CH(O–)CH_3], 4.61 (AB system, J_{AB} = 7.0 Hz, 2H, OCH_2O), 4.84 (broad s, 1H, NH), 5.22–5.37 (m, 2H, HC=CH), 6.93 (s, 2H, aromatic H). – MS (70 eV); *m/z* (%): 198 (17) [$C_9H_{12}NO_2S$], 183 (19) [$C_9H_{11}O_2S$], 119 (63) [C_9H_{11}], 89 (69) [$C_4H_9O_2$], 59 (100) [$C_3H_7O_2$]. – $C_{21}H_{35}NO_5S$ (413.6): calcd. C 59.01, H 7.26, N 2.29; found C 59.21, H 7.23, N 2.21.

(1R,2Z,4S)-N-{1-(1,1-Dimethylethyl)-4-[(2-methoxyethoxy)methoxy]-2-pentenyl}-2,4,6-trimethylbenzenesulfonamide (**11d**): Prepared from **3f** (5.06 g, 10.0 mmol; >98% *d.e.*). The crude product was purified by column chromatography (hexane/ethyl acetate/chloroform, 3:2:3) to give colorless solid **11d** (4.05 g, 95%); R_f = 0.74; m.p. 56 °C; $[\alpha]_D^{20}$ = –47.5 (c = 1.2 in 95% aqueous ethanol). – ^{1}H NMR (300 MHz): δ = 0.82 [s, 9H, C$(CH_3)_3$], 1.04 [d, J = 6.3 Hz, 3H, CH(O–)CH_3], 2.28 (s, 3H, $ArCH_3$), 2.64 (s, 6H, $ArCH_3$), 3.39 (s, 3H, OCH_3), 3.53–3.78 (m, 4H, OCH_2CH_2O), 3.78–3.84 [m, 1H, CH(N–)], 4.41–4.47 [m, 1H, CH(O–)CH_3], 4.66 (AB system, J_{AB} = 5.5 Hz, 2H, OCH_2O), 4.67 (broad s, 1H, NH), 5.32–5.35 (m, 2H, CH=CH), 6.92 (s, 2H, aromatic H). – MS (70 eV); *m/z* (%): 370 (4) [M^+ – C_4H_9], 322 (10) [M^+ – $C_4H_9O_3$], 212 (100) [$C_{10}H_{14}NO_2S$], 89 (25) [$C_4H_9O_2$], 83 (49) [$C_6H_{11}^+$]. – $C_{22}H_{37}NO_5S$ (427.6): calcd. C 61.80, H 8.72, N 3.28; found C 61.72, H 8.74, N 3.20.

General Procedure (G. P. 4) for the Ozonolysis of Bromoalkenes **3a–d**: A stream of ozone in O_2 was passed, via a frit, through a solution of the bromoalkene **3a–d** (10 mmol) in 75 ml of a mixture of dry dichloromethane and absolute methanol (8:1) at –78 °C until the blue color persisted. The mixture was allowed to reach –40 °C gradually, while the stream of ozone was maintained. Thereafter, the solution was cooled again to –78 °C, treated successively with streams of O_2 and N_2, and transferred to a separatory funnel. A 0.5 M aqueous solution of Na_2CO_3 (100 ml) was then added. The phases were separated, and the organic layer was extracted three times with dichloromethane. The combined organic layers were washed with brine and dried with $MgSO_4$. After the removal of the solvent in a rotary evaporator, lactate **7** was distilled off under reduced pressure (see below). The residue which contained *N*-sulfonyl protected amino acid esters **8a–d** was purified by column chromatography.

Using this procedure, the following were obtained:

Methyl (S)-α-{(2,4,6-Trimethylphenyl)sulfonyl]amino}benzeneacetate (**8a**): Prepared by ozonolysis of **3a** (2.0 g, 3.8 mmol). Slightly impure lactate **7** (0.475 g, 65%) was obtained from distillation of the crude product; b.p. 70°C/0.1 Torr; $[\alpha]_D^{20} = -68.1$ (c = 2.3 in 95% aqueous ethanol) {ref.[6] $[\alpha]_D^{20} = -74.9$ (c = 0.64 in 95% aqueous ethanol)}. The residue was submitted to column chromatography (hexane/ethyl acetate, 2:1) and recrystallized from carbon tetrachloride to give 1.03 g (78%) of colorless **8a**; R_f = 0.76; m.p. 107°C; $[\alpha]_D^{20} = +67.0$ (c = 1.8 in 95% aqueous ethanol). – ^{1}H NMR ([D$_6$]DMSO; 60 MHz): δ = 2.20 (s, 3H, $ArCH_3$), 2.54 (s, 6H, $ArCH_3$), 3.40 (s, 3H, OCH_3), 4.83 [d, J = 10 Hz, 1H, CH(–N)], 6.88–7.22 (m, 7H, aromatic H), 8.67 (d, J = 10 Hz, 1H, NH). – MS (70 eV); *m/z* (%): 347 (15) [M$^+$], 287 (100) [M$^+$ – $C_2H_4O_2$]. – $C_{18}H_{21}NO_4S$ (347.4): calcd. C 62.23, H 6.09, N 4.03; found C 62.21, H 6.19, N 4.01.

Methyl (S)-4-Methoxy-α-{[(2,4,6-trimethylphenyl)sulfonyl]-amino}benzeneacetate (**8b**): Prepared by ozonolysis of **3b** (4.29 g, 7.70 mmol). Purification of the residue by column chromatography (hexane/ethyl acetate, 2:1) afforded crystalline **8b** (2.18 g, 75%); R_f = 0.7; m.p. 79°C; $[\alpha]_D^{20} = +65.7$ (c = 1.85 in 95% aqueous ethanol). The spectroscopic data were identical with those of (*R*)-**8b**, obtained according to G. P. 5 (see below).

Methyl (S)-4-{[Dimethyl(1,1,2-trimethylpropyl)silyl]oxy}-α-⟨[(2,4,6-trimethylphenyl)sulfonyl]amino⟩benzeneacetate (**8c**): Prepared by ozonolysis of **3c** (2.3 g, 3.3 mmol). Purification of the residue by column chromatography (hexane/ethyl acetate/chloroform, 2:1:1) afforded solid **8c** (1.13 g, 68%); R_f = 0.85; m.p. 87°C. – ^{1}H NMR (60 MHz): δ = 0.20 [s, 6H, $Si(CH_3)_2$], 0.90 [m, 12H, $C(CH_3)_2CH(CH_3)_2$], 1.72 [m, 1H, $CH(CH_3)_2$], 2.16 (s, 3H, $ArCH_3$), 2.50 (s, 6H, $ArCH_3$), 3.47 (s, 3H, OCH_3), 4.82 [d, J = 7 Hz, 1H, CH(N)], 5.56 (d, J = 7 Hz, 1H, NH), 6.35–7.10 (m, 6H, aromatic H). – MS (70 eV); *m/z* (%): 505 (10) [M$^+$], 445 (100) [M$^+$ – $C_2H_4O_2$]. – $C_{26}H_{39}NO_3SSi$ (505.7): calcd. C 61.75, H 7.77, N 2.77; found C 61.81, H 7.78, N 2.82.

Methyl (S)-4-Methyl-2-{[(2,4,6-trimethylphenyl)sulfonyl]-amino}pentanoate (**8d**): Synthesized by ozonolysis of **3d** (0.98 g, 1.9 mmol). The residue was purified by column chromatography (hexane/ethyl acetate/chloroform, 1:1:1) and subsequently recrystallized from carbon tetrachloride to give colorless, **8d**; yield 0.282 g (45%); R_f = 0.9; m.p. 80°C; $[\alpha]_D^{20} = +33.9$ (c = 1 in 95% aqueous ethanol). The spectroscopic data corresponded to those of a sample of (*S*)-**8d** which was prepared from leucine methyl ester (see G. P. 5).

General Procedure (G. P. 5) for the Conversion of α-Amino Acid Esters into α-Sulfonylamino Acid Esters **8**: The hydrochloride of the corresponding α-amino acid methyl ester **8** (30.0 mmol) was dissolved in 10 ml of pyridine and stirred at 0°C under N_2. A solution of 2,4,6-trimethylbenzenesulfonyl chloride (6.56 g, 30.0 mmol) in pyridine (10 ml) was added dropwise by a syringe. Stirring was continued for 48 h at room temp. The mixture was poured into water (100 ml) and extracted several times with diethyl ether (250 ml). The combined organic layers were washed several times with 1 N hydrochloric acid and with a satd. aqueous solution of $NaHCO_3$, dried with $MgSO_4$ and concentrated under reduced pressure. The residue was recrystallized from carbon tetrachloride.

Using this procedure, the following were obtained:

(*R*)-**8a**: Synthesized from the hydrochloride of (*R*)-phenylglycine methyl ester[23] (6.05 g, 30 mmol). Yield: 7.8 g (74.9%); $[\alpha]_D^{20}$ = –69.2 (c = 0.2 in 95% aqueous ethanol). The spectroscopic data were in accordance with those of *S*-**8a** described above.

(*R*)-**8b**: Synthesized from the hydrochloride of (*R*)-4-methoxyphenylglycine methyl ester[24] (6.95 g, 30 mmol). Yield: 7.69 g (68%); $[\alpha]_D^{20} = -63.0$ (c = 1.4 in 95% aqueous ethanol). – ^{1}H NMR (60 MHz): δ = 2.20 (s, 3H, $ArCH_3$), 2.55 (s, 6H, $ArCH_3$), 3.46 (s, 3H, CO_2CH_3), 3.64 (s, 3H, $ArOCH_3$), 3.82 [d, J = 7 Hz, 1H, CH(N–)], 4.64 (d, J = 7 Hz, 1H, NH), 6.40–7.15 (m, 6H, aromatic H). – MS (70 eV); *m/z* (%): 377 (4) [M$^+$], 317 (80) [M$^+$ – $C_2H_4O_2$], 119 (100) [C_9H_{11}]. – $C_{19}H_{23}NO_5S$ (377.5): calcd. C 60.46, H 6.14, N 3.71; found C 60.44, H 6.11, N 3.69.

(*S*)-**8d**: Synthesized by reaction of the hydrochloride of (*S*)-leucine methyl ester (9.08 g, 50 mmol) with 2,4,6-trimethylbenzenesulfonyl chloride (10.93 g, 50 mmol). Yield: 15.35 g (94%); m.p. 80°C; $[\alpha]_D^{20} = -36.2$ (c = 2.0 in 95% aqueous ethanol). – ^{1}H NMR (300 MHz): δ = 0.80, 0.88 [2 d, J = 6.6 Hz, 3H each, $CH(CH_3)_2$], 1.39–1.56 (m, 2H, CH_2), 1.67–1.77 [m, 1H, $CH(CH_3)_2$], 2.29 (s, 3H, $ArCH_3$), 2.64 (s, 6H, $ArCH_3$), 3.43 (s, 3H, OCH_3), 3.80–3.88 [m, 1H, CH(N–)], 5.20 (d, J = 10.2 Hz, 1H, NH), 6.91 (s, 2H, aromatic H). – MS (70 eV); *m/z* (%): 327 (4) [M$^+$], 267 (24) [M$^+$ – $C_2H_4O_2$], 119 (100) [C_9H_{11}]. – $C_{16}H_{25}NO_4S$ (327.4): calcd. C 58.69, H 7.70, N 4.28; found C 58.69, H 7.67, N 4.25.

General Procedure (G. P. 6) for the Conversion of Methyl Esters **8** *into α-Sulfonylamino Acids* **9**: The methyl esters **8** (1.0 mmol) were stirred in 7.0 ml of a 0.5 M aqueous solution of LiOH. A few drops of methanol were added in order to dissolve the ester **8**. Stirring was continued for 5 h at room temp. Thereafter, the mixture was acidified by addition of 1 M hydrochloric acid and extracted several times with ethyl acetate and with diethyl ether. The combined organic layers were washed with brine, dried with $MgSO_4$ and concentrated under reduced pressure. The residue was purified by recrystallization.

Using this procedure, the following were obtained:

(S)- and (R)-α-{[(2,4,6-Trimethylphenyl)sulfonyl]amino}-benzeneacetic Acid (**9a**): (*S*)-**9a**: Prepared by hydrolysis of (*S*)-**8a** (0.30 g, 0.86 mmol). The crude product was recrystallized from chloroform/methanol (4:1) to give colorless (*S*)-**9a** (0.261 g, 91%); m.p. 157°C; $[\alpha]_D^{25} = +104.5$ (c = 2.3 in 95% aqueous ethanol). – (*R*)-**9a**: Prepared by hydrolysis of (*R*)-**8a** (1.0 g, 2.9 mmol). Yield: 0.90 g (97%); m.p. 157°C, $[\alpha]_D^{25} = -107$ (c = 2.1 in 95% aqueous ethanol). – ^{1}H NMR ([D$_6$]DMSO; 60 MHz): δ = 2.42 (s, 3H, $ArCH_3$), 2.75 (s, 6H, $ArCH_3$), 6.95–7.30 (m, 7H, aromatic H), 8.46 (d, J = 10 Hz, 1H, NH). – $C_{17}H_{19}NO_4S$ (333.4): calcd. C 61.24, H 5.74, N 4.20; found C 61.25, H 5.77, N 4.18.

(S)- and (R)-4-Methoxy-α-{[(2,4,6-trimethylphenyl)sulfonyl]-amino}benzeneacetic Acid (**9b**): (*S*)-**9b**: Prepared by hydrolysis of (*S*)-**8b** (0.30 g, 0.79 mmol). Recrystallization from chloroform and a few drops of methanol afforded (*S*)-**9b** (0.256 g, 89%); m.p. 131°C; $[\alpha]_D^{25} = +105.0$ (c = 1.8 in 95% aqueous ethanol). – (*R*)-**9b**: Prepared by hydrolysis of (*R*)-**8b** (0.30 g, 0.79 mmol). Yield. 0.235 g (82%); m.p. 131°C, $[\alpha]_D^{20} = -107.2$ (c = 2.0 in 95% aqueous ethanol). – ^{1}H NMR ([D$_6$]DMSO; 60 MHz): δ = 2.15 (s, 3H, $ArCH_3$), 2.45 (s, 6H, $ArCH_3$), 3.64 (s, 3H, $ArOCH_3$), 4.61 [d, J = 10 Hz, 1H, CH(N–)], 6.64–7.20 (m, 6H, aromatic H), 8.28 (d, J = 10 Hz, 1H, NH). – $C_{18}H_{21}NO_3S$ (363.4): calcd. C 59.49, H 5.82, N 3.85; found C 59.52, H 5.87, N 3.83.

(S)- and (R)-4-Hydroxy-α-{[(2,4,6-trimethylphenyl)sulfonyl]-amino}benzeneacetic Acid (**9c**): (*S*)-**9c**: Prepared by hydrolysis of silyl-protected methyl ester (*S*)-**8c** (0.21 g, 0.42 mmol). Recrystallization of the crude product from chloroform and a few drops of methanol afforded (*S*)-**9c** (0.129 g, 87.7%); m.p. 186°C (decomp.); $[\alpha]_D^{25} = +106.1$ (c = 1 in 95% aqueous ethanol). – (*R*)-**9c**: Prepared from 4-hydroxyphenylglycine by following the general procedures G. P. 5 [to give (*R*)-**8e** which is not purified] and G. P. 6.

Yield: 72%; $[\alpha]_D^{25} = -106.9$ ($c = 1$ in 95% aqueous ethanol). – ^{1}H NMR ([D$_6$]DMSO; 60 MHz): δ = 2.35 (s, 3H, $ArCH_3$), 2.70 (s, 6H, $ArCH_3$), 6.69–7.29 (m, 6H, aromatic H), 8.41 (d, $J = 10$ Hz, 1H, NH), 9.6 (broad s, 1H, OH). – $C_{17}H_{19}NO_5S$ (349.4): calcd. C 58.44, H 5.48, N 4.01; found C 58.41, H 5.45, N 4.00.

(S)-4-Methyl-2-{[(2,4,6-trimethylphenyl)sulfonyl]amino}-pentanoic Acid (**9d**): Prepared by hydrolysis of (*S*)-**8d** (0.24 g, 0.73 mmol). Yield: 0.23 g (99%) of waxy (*S*)-**9d**: $[\alpha]_D^{20} = -13.7$ ($c = 1.8$ in 95% aqueous ethanol, sample prepared by the sulfonylimine route); $[\alpha]_D^{20} = -14.4$ [$c = 1.9$ in 95% aqueous ethanol, sample prepared from (*S*)-leucine methyl ester]. – ^{1}H NMR (300 MHz): δ = 0.72, 0.87 [2 d, $J = 6.5$ Hz, 3H each, $CH(CH_3)_2$], 1.47–1.53 (m, 2H, CH_2), 1.67–1.72 [m, 1H, $CH(CH_3)_2$], 2.28 (s, 3H, $ArCH_3$), 2.63 (s, 6H, $ArCH_3$), 3.78–3.84 [m, 1H, CH(N–)], 5.37 (d, $J = 10$ Hz, 1H, NH), 6.94 (s, 2H, aromatic H), 9.50 (broad s, 1H, CO_2H). – $C_{15}H_{23}NO_4S$ (313.4): calcd. C 57.49, H 7.40, N 4.47; found C 57.42, H 7.33, N 4.44.

(R)-α-Aminobenzeneacetic Acid (Phenylglycine) by Deprotection of **9a** *with Sodium/Ammonia:* Approximately 80 ml of ammonia were condensed in a 250-ml two-necked flask at –50°C. For the purpose of drying, small pieces of sodium were added until a blue color persisted. Thereafter, the ammonia was allowed to evaporate and recondensed in a pressure-equalized dropping funnel with a mantle which was filled with dry ice/acetone. The dropping funnel was fitted with a 100-ml two-necked flask equipped with a connection to the combined vacuum/nitrogen line, and charged with (*R*)-**9a** (1.0 g, 3.0 mmol). The solid **9a** was dissolved by addition of about 20 ml of ammonia through the dropping funnel. The resulting solution was stirred with a *glass-coated* stirring bar at –50°C. Small, freshly cut pieces of sodium (0.23 g, 10 mmol) were added to the dropping funnel so that a deep blue colored solution formed. This solution was added dropwise to the stirred mixture of **9a** until the blue color no longer disappeared. Thereafter, a small amount (about 10–20 mg) of NH_4Cl was added, and the ammonia was allowed to evaporate. The white solid residue (1.21 g) was dissolved in 50 ml of deionized water. Amberlite IRC 50 (NH_4^+ form, 2 g) was added, and the mixture was stirred for 30 min. The resin was filtered and washed with water. The combined filtrates were passed through a column containing 15 g of amberlite 120 (H^+ form). Thereafter, the amino acid was eluted by 200 ml of a 3% aqueous solution of ammonia. The eluate was concentrated in a rotary evaporator and the dry residue was recrystallized from water to give 0.269 g (59%) of (*R*)-phenylglycine; $[\alpha]_D^{20} = -153.1$ ($c = 1$ in 1 M hydrochloric acid) {authentic sample[25] $[\alpha]_D^{20} = -155$ ($c = 1$ in 1 M hydrochloric acid)}.

(R)-α-Aminobenzeneacetic Acid (Phenylglycine) by Deprotonation of **9a** *with Sodium Naphthalenide:* A solution of naphthalene (1.56 g, 12.0 mmol) in 1,2-dimethoxyethane (70 ml) was stirred under N_2 in a 250-ml two-necked flask, equipped with a septum, a concentration to the combined nitrogen/vacuum line and a *glass-coated* stirring bar. Small pieces of sodium (0.28 g, 12 mmol) were added to the mixture which was stirred vigorously at room temp. Stirring was continued for 1 h and the dark green mixture was cooled to –40°C. A solution of (*R*)-**9a** (1.0 g, 3.0 mmol) in 1,2-dimethoxyethane (5 ml) was injected dropwise by a syringe through the septum. A clear, light green solution formed. Stirring was continued for 30 min at –40°C. Then, 24 ml of 0.5 M hydrochloric acid and 50 ml of diethyl ether were added. The layers were separated and the aqueous phase was concentrated in vacuo. The residue was redissolved in 25 ml of 0.5 M hydrochloric acid and washed with diethyl ether. The aqueous layer was neutralized by addition of a 1 M solution of NaOH and, thereafter, submitted to purification by ion exchange resins as described above. Thus, 0.359 g (78%) of (*R*)-phenylglycine was obtained; $[\alpha]_D^{20} = -153.8$ ($c = 1$ in 1 M hydrochloric acid).

General Procedure (G. P. 7) for Ozonolysis of Alkenes **11** *and the Subsequent Conversion of Aldehydes* **12** *into Amino Hydroxy Esters* **15** *by Mukaiyama Aldol Addition:* A stream of ozone was passed, via a frit, through a solution of **11** (2.0 mmol) in 40 ml of dichloromethane at –30°C. A fivefold excess of ozone was used compared to the amount which was calculated based on the parameters of the ozone generator. Thereafter, streams of O_2 and N_2 were passed successively through the solution at –60°C and dimethyl sulfide (0.3 ml, 4 mmol) was added. The mixture was allowed to reach room temp. within 2 h, transferred to a separatory funnel, washed twice with water, and dried with $MgSO_4$. The solvent was removed in a rotary evaporator at room temp., and the residue was exposed to oil pump vacuum at room temp. Lactaldehyde **13** evaporated when the residue was heated gently (30°C) at 0.0001 Torr, and was isolated via a short-path distillation apparatus, the receiving flask of which was cooled by liquid nitrogen.

The oily residue consisting of the aldehydes **12** was transferred, without further purification, to a two-necked flask equipped with a stirring bar, a septum, and a connection to the combined nitrogen/vacuum line. The aldehyde **12** was dissolved in 20 ml of dichloromethane, cooled to –78°C and treated dropwise with $TiCl_4$ (0.22 ml, 2.0 mmol). The mixture was allowed to reach –40°C within 30 min and cooled again to –78°C. A solution of ketene acetal **14**[26] (0.372 g, 2.0 mmol) in dichloromethane (10 ml) was precooled to –78°C and added slowly. Stirring was continued for 1 h, the mixture was allowed to warm to –40°C and then recooled to –78°C. A satd. aqueous solution of NH_4Cl (40 ml) was added and the mixture was transferred to a separatory funnel. The organic layer was separated, and the aqueous phase was extracted four times with a total volume of 150 ml of dichloromethane. The combined organic layers were washed with brine, dried with $MgSO_4$ and concentrated in a rotary evaporator. The residue was purified by column chromatography.

Using this procedure, the following were obtained:

Methyl (3S,4S)-3-Hydroxy-2,2-dimethyl-4-phenyl-4-{[(2,4,6-trimethylphenyl)sulfonyl]amino}butanoate (**15a**): Prepared by ozonolysis of **11a** (1.31 g, 2.93 mmol). The crude aldehyde **12a** thus formed was characterized by ^{1}H NMR (60 MHz): δ = 2.20 (s, 3H, $ArCH_3$), 2.50 (s, 6H, $ArCH_3$), 4.87 [d, $J = 5$ Hz, 1H, CH(N–)], 5.90 (d, $J = 6$ Hz, 1H, NH), 6.67 (s, 2H, aromatic H), 7.05 (s, 5H, aromatic H), 9.22 (s, 1H, CHO).

Reaction of crude aldehyde **12a** with **14** afforded **15a** as a single diastereomer according to its ^{1}H-NMR spectra. Purification by column chromatography (hexane/ethyl acetate/chloroform, 1:1:1) gave waxy **15a** (0.88 g, 72%); $R_f = 0.65$; $[\alpha]_D^{20} = +17.9$ ($c = 1$ in 95% aqueous ethanol). – ^{1}H NMR (300 MHz): δ = 1.25, 1.33 [2 s, 3H each, $C(CH_3)_2$], 2.15 (s, 3H, $ArCH_3$), 2.42 (s, 6H, $ArCH_3$), 3.63 (s, 3H, OCH_3), 3.78 [dd, $J = 6.1$ Hz, $J = 3.5$ Hz, 1H, $CH(OH)$], 3.85 (d, $J = 6.1$ Hz, 1H, OH), 4.44 [dd, $J = 8.4$ Hz, $J = 3.5$ Hz, 1H, $CH(NH)$], 5.57 (d, $J = 8.4$ Hz, 1H, NH), 6.64 (s, 2H, aromatic H), 6.90–7.05 (m, 5H, aromatic H). – MS (70 eV); *m/z* (%): 419 (1) [M^+], 287 (90) [$M^+ - C_{16}H_{17}NO_2S$], 131 (100) [$C_6H_{11}O_3$]. – $C_{22}H_{29}NO_5S$ (419.5): calcd.C 62.98, H 6.97, N 3.34; found C 62.99, H 7.05, N 3.49.

(3*R*,4*R*)-**15a** was obtained in the same way from (*R*)-**11a**; $[\alpha]_D^{20} = -17.8$ ($c = 1$ in 95% aqueous ethanol).

Methyl (3S,4S)-3-Hydroxy-2,2,6-trimethyl-4-{[(2,4,6-trimethylphenyl)sulfonyl]amino}heptanoate (**15b**): Prepared by ozonolysis of **11b** (0.9 g, 2.1 mmol). Crude aldehyde **12b** formed thereby was

characterized by ^{1}H NMR (300 MHz): δ = 0.78, 0.87 [2 d, *J* = 7.9 Hz, 3H each, $CH(CH_3)_2$], 1.35–1.60 (m, 2H, CH_2), 1.66–1.79 [m, 1H, $CH(CH_3)_2$], 2.29 (s, 3H, $ArCH_3$), 2.65 (s, 6H, $ArCH_3$), 3.73–3.81 [m, 1H, CH(NH)], 5.46 (d, *J* = 7.5 Hz, 1H, NH), 6.93 (s, 2H, aromatic H), 9.45 (d, *J* = 0.7 Hz, 1H, CHO). Reaction of crude **12b** with **14** gave **15b** as a single diastereomer according to the ^{1}H-NMR spectrum of the crude product. Column chromatography (hexane/ethyl acetate/chloroform, 1:1:1) afforded crystalline **15b** (0.65 g, 78%); R_f = 0.8, m.p. 101 °C; $[\alpha]_D^{20}$ = −14.0 (*c* = 1.1 in 95% aqueous ethanol). – ^{1}H NMR (300 MHz): δ = 0.52 (m, 1H, CH*H*), 0.61, 0.65 [2 d, *J* = 6.5 Hz, 3H each, $CH(CH_3)_2$], 1.32, 1.35 [2 s, 3H each, $C(CH_3)_2$], 1.48–1.55 [m, 2H, C*H*H and $CH(CH_3)_2$], 2.30 (s, 3H, $ArCH_3$), 2.61 (s, 6H, $ArCH_3$), 3.45 [dd, *J* = 7.4 Hz, *J* = 3.1 Hz, 1H, C*H*(OH)], 3.52–3.61 [m, 1H, C*H*(NH)], 3.80 (s, 3H, OCH_3), 4.31 (d, *J* = 7.4 Hz, 1H, OH), 4.64 (d, *J* = 10.4 Hz, 1H, NH), 6.95 (s, 2H, aromatic H). – MS (70 eV); *m/z* (%): 399 (1) [M^+], 342 (17) [$M^+ - C_4H_9$], 267 (56) [$M^+ - C_4H_9NO_2S$] 119 (100) [C_9H_{11}]. – $C_{20}H_{33}NO_5S$ (399.5): calcd. C 60.12, H 8.32, N 3.51; found C 60.22, H 8.29, N 3.45.

Methyl (3S,4S)-3-Hydroxy-2,2,5-trimethyl-4-{[(2,4,6-trimethylphenyl)sulfonyl]amino}hexanoate (**15c**): Prepared by ozonolysis of **11c** (1.08 g, 2.6 mmol). The crude aldehyde **12c** formed thereby was characterized by ^{1}H NMR (60 MHz): δ = 0.9 [d, *J* = 7 Hz, 6H, $CH(CH_3)_2$], 1.32–1.62 [m, 1H, $CH(CH_3)_2$], 2.30 (s, 3H, $ArCH_3$), 2.64 (s, 6H, $ArCH_3$), 4.58–4.79 [m, 1H, C*H*(NH)], 5.42 (d, *J* = 7.5 Hz, 1H, NH), 6.84 (s, 2H, aromatic H), 9.34 (s, 1H, CHO). Reaction of crude **12c** with **14** afforded **15c** as a single diastereomer according to the ^{1}H-NMR spectrum of the crude product. Column chromatography (hexane/ethyl acetate/chloroform, 1:1:1) resulted incrystalline **15c** (0.75 g, 75%); R_f = 0.74; m.p. 106 °C; $[\alpha]_D^{20}$ = −18.8 (*c* = 1.1 in 95% aqueous ethanol). – ^{1}H NMR (300 MHz): δ = 0.69, 0.72 [2 d, *J* = 7.0 Hz, 3H each, $CH(CH_3)_2$], 1.24, 1.25 [2 s, 3H each, $C(CH_3)_2$], 1.53–1.59 [m, 1H, $CH(CH_3)_2$], 2.28 (s, 3H, $ArCH_3$), 2.63 (s, 6H, $ArCH_3$), 3.47–3.52 [m, 1H, C*H*(NH)], 3.70–3.72 [m, 1H, C*H*(OH)], 3.74 (s, 3H, OCH_3), 3.82 (d, *J* = 5.2 Hz, 1H, OH), 5.23 (d, *J* = 8.6 Hz, 1H, NH), 6.92 (s, 2H, aromatic H). – MS (70 eV); *m/z* (%): 385 (1) [M^+], 354 (25) [$M^+ - CH_3O$], 342 (50) [$M^+ - C_3H_7$], 253 (70) [$C_{13}H_{19}NO_2S$], 131 (50) [$C_6H_{11}O_3$], 102 (100) [$C_5H_{12}NO$]. – $C_{19}H_{31}NO_5S$ (385.5): calcd. C 59.20, H 8.10, N 3.63; found C 59.12, H 8.09, N 3.77.

Methyl (3S,4S)-3-Hydroxy-2,2,5,5-tetramethyl-4-{[(2,4,6-trimethylphenyl)sulfonyl]amino}hexanoate (**15d**): Prepared by ozonolysis of **11d** (1.50 g, 3.5 mmol). The crude aldehyde **12d** formed thereby was characterized by: ^{1}H NMR (60 MHz): δ = 1.00 [s, 9H, $C(CH_3)_3$], 2.25 (s, 3H, $ArCH_3$), 2.65 (s, 6H, $ArCH_3$), 3.55 [m, 1H, C*H*(NH)], 5.46 (d, *J* = 8 Hz, 1H, NH), 6.90 (s, 2H, aromatic H), 9.66 (s, 1H, CHO). Reaction of crude **12d** with **14** gave **15d** as a single diastereomer according to the ^{1}H-NMR spectrum of the crude material. Column chromatography (hexane/ethyl acetate/chloroform, 1:1:1) afforded crystalline **15d** (1.02 g, 73%); R_f = 0.71; m.p. 112 °C; $[\alpha]_D^{20}$ = −36.2 (*c* = 1.2 in 95% aqueous ethanol). – ^{1}H NMR (300 MHz): δ = 0.70 [s, 9H, $C(CH_3)_3$], 0.93, 0.94 [2 s, 3H each, $C(CH_3)_2$], 2.27 (s, 3H, $ArCH_3$), 2.64 (s, 6H, $ArCH_3$), 3.50 [d, *J* = 7.8 Hz, 1H, C*H*(NH)], 3.76 (s, 3H, OCH_3), 3.92 [d, *J* = 5.5 Hz, 1H, C*H*(OH)], 4.13 (d, *J* = 5.5 Hz, 1H, OH), 5.38 (d, *J* = 7.8 Hz, 1H, NH), 6.90 (s, 2H, aromatic H). – MS (70 eV); *m/z* (%): 368 (4) [$M^+ - CH_3O$], 342 (38) [$M^+ - C_4H_9$], 268 (39) [$C_{14}H_{22}NO_2S$], 183 (27) [$C_9H_{11}O_2S$], 119 (100) [C_9H_{11}]. – $C_{20}H_{33}NO_5S$ (399.5): calcd. C 60.12, H 8.32, N 3.51; found C 60.08, H 8.24, N 3.49.

General Procedure (G. P. 8) for the Conversion of Methyl Esters **15** *into Oxazolidinones* **16**: A 100-ml two-necked flask was charged with 1.0 mmol of methyl ester **15** and equipped with a stirring bar, a septum, and a connection to the combined vacuum/nitrogen line. Dry toluene (50 ml) was added, and the solution was cooled to −20 °C. Pyridine (0.16 ml, 2.0 mmol) or triethylamine (0.28 ml, 2.0 mmol) was added. The mixture was stirred for 10 min and a 1.9 M solution of phosgene in toluene (0.6 ml, 1.14 mmol) was injected through the septum. A white precipitate formed after a few min. The mixture was stirred at 0 °C for 12 h, transferred to a separatory funnel and washed twice with water. The combined aqueous phases were re-extracted with diethyl ether and the combined organic layers were dried with $MgSO_4$. The solvent was removed in a rotary evaporator and the residue was purified by chromatography on a short column.

Using this procedure, the following were obtained:

Methyl (4S,5S)-α,α-Dimethyl-2-oxo-4-phenyl-3-[(2,4,6-trimethylphenyl)sulfonyl]-5-oxazolidineacetate (**16a**): Prepared from **15a** (0.31 g, 0.75 mmol) and purified by column chromatography (hexane/ethyl acetate/chloroform, 1:1:1). Yield: 0.30 g (90%) of colorless, waxy **16a**: R_f = 0.76; $[\alpha]_D^{20}$ = +13.7 (*c* = 0.9 in 95% aqueous ethanol). – ^{1}H NMR (300 MHz): δ = 1.29, 1.31 [2 s, 3H each, $C(CH_3)_2$], 2.24 (s, 3H, $ArCH_3$), 2.45 (s, 6H, $ArCH_3$), 3.62 (s, 3H, OCH_3), 4.59 [d, *J* = 4.5 Hz, 1H, CH(O–)], 5.19 [d, *J* = 4.5 Hz, 1H, CH(N–)], 6.84 (s, 2H, aromatic H), 7.18–7.32 (m, 5H, aromatic H). – MS (70 eV); *m/z* (%): 445 (5) [M^+], 380 (25) [$M^+ - C_5H_5$], 119 (80) [C_9H_{11}], 91 (100) [C_7H_7]. – $C_{23}H_{27}NO_6S$ (445.5): calcd. C 62.01, H 6.11, N 3.14; found C 61.74, H 6.04, N 2.91.

16a *and* **18**: Prepared from a diastereomeric mixture of **15a**/**17a**. ^{1}H NMR of the minor diastereomer **18** differs from that of **16a** in: δ = 2.34 (s, 6H), 3.69 (s, 3H), 4.91 (d, *J* = 6.8 Hz, 1H), 5.69 (d, *J* = 6.8 Hz, 1H).

Methyl (4S,5S)-α,α-Dimethyl-4-(2-methylpropyl)-2-oxo-3-[(2,4,6-trimethylphenyl)-sulfonyl]-5-oxazolidineacetate (**16b**): Prepared by reaction of **15b** (0.28 g, 0.70 mmol) with phosgene in the presence of triethylamine. Column chromatography (hexane/ethyl acetate/chloroform, 1.25:1:1) afforded colorless waxy **16b** (0.26 g, 88%); R_f = 0.95; $[\alpha]_D^{20}$ = +91.0 (*c* = 1.0 in 95% aqueous ethanol). – ^{1}H NMR (300 MHz): δ = 0.96, 0.98 [2 d, *J* = 6.4 Hz, 3H each, $CH(CH_3)_2$], 1.58–1.69 [m, 1H, $CH(CH_3)_2$], 1.68–2.01 (m, 2H, CH_2), 2.31 (s, 3H, $ArCH_3$), 2.68 (s, 6H, $ArCH_3$), 3.68 (s, 3H, OCH_3), 4.22 [m, 1H, C*H*(N–)], 4.39 [d, *J* = 2.2 Hz, 1H, C*H*(O–)], 6.98 (s, 2H, aromatic H). – MS (70 eV); *m/z* (%): 394 (1) [$M^+ - OCH_3$], 119 (100) [C_9H_{11}]. – $C_{21}H_{31}NO_6S$ (425.5): calcd. C 59.27, H 7.34, N 3.29; found C 59.20, H 7.29, N 3.31.

Methyl (4S,5S)-α,α-Dimethyl-4-(1-methylethyl)-2-oxo-3-[(2,4,6-trimethylphenyl)sulfonyl]-6-oxazolidineacetate (**16c**): Prepared by reaction of **15c** (0.29 g, 0.75 mmol) with phosgene in the presence of triethylamine. Column chromatography (hexane/ethyl acetate/chloroform, 1:1:1.5) afforded colorless, waxy **16c** (0.29 g, 94%); R_f = 0.92; $[\alpha]_D^{20}$ = +75.0 (*c* = 1.0 in 95% aqueous ethanol). – ^{1}H NMR (300 MHz): δ = 0.92, 1.03 [2 d, *J* = 7.0 Hz, 3H each, $CH(CH_3)_2$], 1.18, 1.24 [2 s, 3H each, $C(CH_3)_2$], 1.55 [m, 1H, $CH(CH_3)_2$], 2.31 (s, 3H, $ArCH_3$), 2.69 (s, 6H, $ArCH_3$), 3.66 (s, 3H, OCH_3), 4.21 [dd, *J* = 3.0 Hz, *J* = 2.5 Hz, 1H, CH(N–)], 4.43 [d, *J* = 2.5 Hz, 1H, CH(O–)], 6.98 (s, 2H, aromatic H). – MS (70 eV); *m/z* (%): 411 (1) [M^+], 380 (3) [$M^+ - CH_3O$], 352 (25) [$M^+ - C_2H_3O_2$], 292 (67) [$M^+ - C_9H_{11}$], 183 (22) [$C_9H_{11}NO_2S$], 119 (100) [C_9H_{11}]. – $C_{20}H_{29}NO_6S$ (411.5): calcd. C 58.38, H 7.10, N 3.40; found C 58.29, H 7.08, N 3.33.

Methyl (4S,5S)-α,α-Dimethyl-4-(1,1-dimethylethyl)-2-oxo-3-[(2,4,6-trimethylphenyl)sulfonyl]-5-oxazolidineacetate (**16d**): Prepared by reaction of **15d** (0.40 g, 1.0 mmol) with phosgene in the presence of triethylamine. Column chromatography (hexane/ethyl

acetate/chloroform, 1:1:3) afforded colorless, waxy **16d** (0.41 g, 96%); R_f = 0.9; $[\alpha]_D^{20}$ = +77.8 (c = 1.4 in 95% aqueous ethanol). – ^{1}H NMR (300 MHz): δ = 0.99 [s, 9H, $C(CH_3)_3$], 1.18, 1.24 [2 s, 3H each, $C(CH_3)_2$], 2.30 (s, 3H, $ArCH_3$), 2.72 (s, 6H, $ArCH_3$), 3.70 (s, 3H, OCH_3), 4.10 [d, J = 2.0 Hz, 1H, CH(N–)], 4.55 [d, J = 2.0 Hz, 1H, CH(O–)], 6.97 (s, 2H, aromatic H). – MS (70 eV); m/z (%): 425 (1) [M^+], 367 (30) [$M^+ - C_4H_{10}$], 306 (75) [$M^+ - C_9H_{11}$], 183 (80) [$C_9H_{11}NO_2S$], 119 (100) [C_9H_{11}]. – $C_{21}H_{31}NO_6S$ (425.5): calcd. C 59.27, H 7.34, N 3.29; found C 59.21, H 7.30, N 3.22.

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