154. Asymmetric Synthesis of 3-Hydroxyprolines by Photocyclization of C(1')-Substituted *N*-(2-Benzoylethyl)glycine Esters

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The chiral *N*-(2-benzoylethyl)-*N*-tosylglycine esters **5a–h** and the α-amino-γ-keto ester **6** were prepared from γ-(tosylamino) alcohols **7a–h**. Irradiation of compounds **5a–c,e** gave *cis*-3-hydroxyproline esters **20–23** (*Scheme 6*), partly with complete asymmetric induction by the C(1')-substituent, whereas **6** gave enantiomerically pure 4-hydroxy-4-phenyl-L-proline esters **24** in good yield but low de (*Scheme 6*). The de of the photocyclization depended on the nature and/or size of the C(1')-substituents. Irradiation of ketones **5d** and **5f**, bearing H-atoms at C(γ) with respect to the keto function, gave cyclobutanols (*Scheme 9*) in low yields besides the preferred *Norrish*-type-II cleavage product. Cyclopentanol **25** was a by-product of the photocyclization of **5c** as a result of H–C(δ) abstraction from the *t*-Bu group. The structure of products **20**, **22**, and **24a,b** was established by NMR or X-ray analyses.

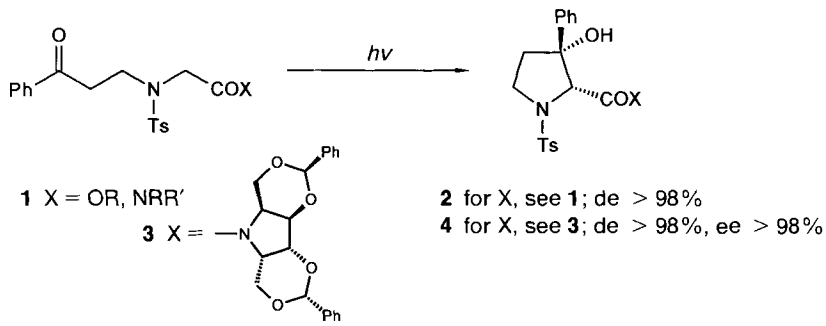
Introduction. – Proline-type α-amino acids are widely distributed in nature (for an early review on proline derivatives, see [1]). *E.g.*, both diastereoisomers of 3-hydroxy-L-proline have been isolated from the peptide antibiotic telomycin [2]. *trans*-3-Hydroxy-L-proline is a component of Mediterranean sponge [2] and of cattle achilles-tendon collagen [3]. In addition to the well-known occurrence of *cis*-4-hydroxy-L-proline in gelatins and collagens, *trans*-4-hydroxy-L-proline is a constituent of the toxic cyclopeptides from *Amanita phalloides* such as phalloidin [4].

The stereoselective synthesis of enantiomerically pure analogues of the naturally occurring prolines is an interesting field of modern organic synthesis. These compounds, bearing additional functional groups, unusual substitution patterns or arrangement of substituents, possess some interest as constituents of modified peptides. For this reason, enantiomerically pure prolines are valuable target compounds. Recently, *Henning* and coworkers [5] [6] demonstrated, that *N*-(2-benzoylethyl)-*N*-tosylglycine derivatives **1** undergo a highly diastereoselective photocyclization to 3-hydroxy-3-phenylprolines **2** (see *Scheme 1*). The reaction proceeds *via* an 1-hydroxy-1,5-biradical, which is presumably stabilized by a strong intramolecular H-bond, providing the *cis*-3-hydroxyproline derivative after recombination [7].

Recently, we developed an enantioselective version of this reaction by means of C_2-symmetric chiral auxiliaries [7]. Asymmetric induction by the chiral pyrrolidine moiety led from **3** to the (2*R*,3*R*)-3-hydroxyproline derivative **4**, exclusively.

In this paper, we report on the substrate-controlled asymmetric induction of stereogenic centers at C(2) and C(3) of the formed proline ring during the photocyclization of

Scheme 1

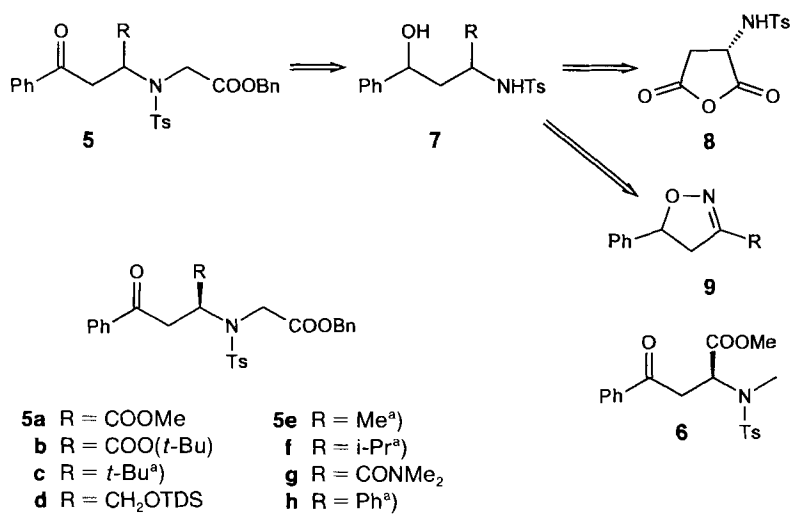


n–π*-excited chiral glycine derivatives **5a–h**. In addition, the α-amino-γ-keto ester **6** was investigated (*Scheme 2*).

Results and Discussion. – *Synthesis of* **5a–h** *and* **6.** β-(Tosylamino)propiophenone undergoes facile β-cleavage on treatment with base, yielding tosylamide and phenyl vinyl ketone. Therefore, our approach to ketones **5** and **6** needed to include an oxidation step at the end of the synthesis. We decided that γ-(tosylamino) alcohols **7** should be useful intermediates in the synthesis of the target compounds. *Scheme 2* shows our retrosynthetic approach to ketones **5**. The known (*S*)-*N*-tosylaspartic anhydride (**8**) [8] and 5-phenylisoxazolines **9** were regarded as useful precursors.

Anhydride **8** served as the starting compound for the preparation of the enantiomerically pure amino alcohols **7a, b, d, g**, which were used as mixtures of diastereoisomers. No

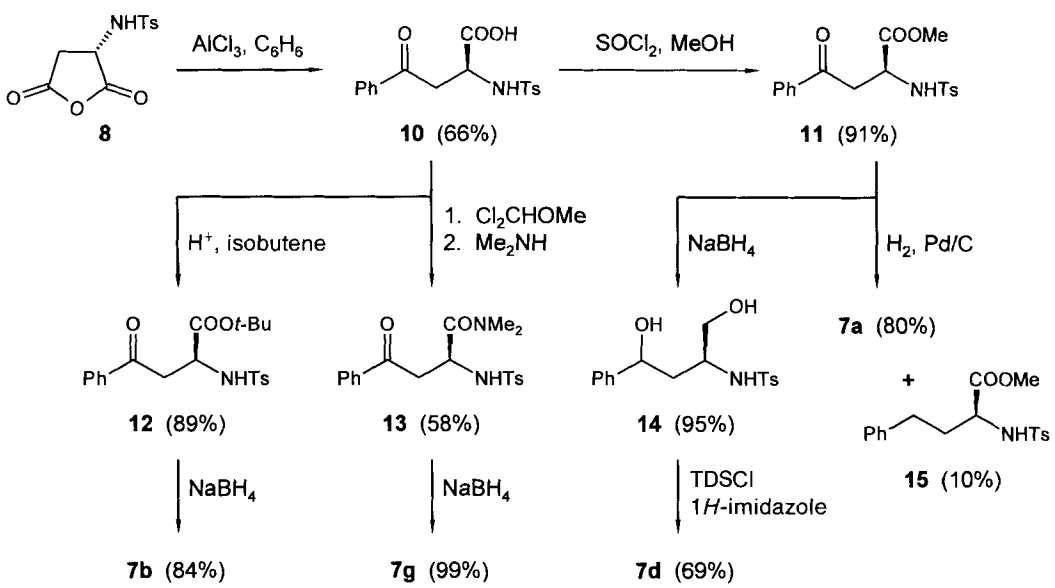
Scheme 2



[a]) Racemic, only one enantiomer is displayed.

extended efforts were made either to separate the diastereoisomers or to assign major diastereoisomers to the *syn*- or *anti*-configuration, because the final oxidation step destroyed the second chirality center. First, (*S*)-3-benzoyl-2-(tosylamino)propanoic acid (**10**) was prepared from **8** similarly as described by *Nordlander* and coworkers [9] for the *N*-(trifluoroacetyl)-protected compounds (*Scheme 3*). Esterification using either $SOCl_2$/MeOH or H_2SO_4/isobutene gave esters **11** and **12**, respectively, whereas treatment of **10** with dichloromethyl methyl ether and subsequent reaction of the non-isolated acid chloride with Me_2NH yielded the *N*,*N*-dimethylamide **13** (this was found to be the only method for preparing this compound in an acceptable yield). Reduction of the keto group of **12** and **13** with $NaBH_4$ gave the γ-hydroxy acid derivatives **7b** and **7g**, each as diastereoisomer mixture with poor diastereoselectivity, whereas reduction of methyl ester **11** did not stop at this stage. Instead, diol **14** (diastereoisomer mixture) was isolated in excellent yield, which could be selectively monosilylated at the primary alcohol function by thexyldimethylsilyl chloride ([$Me_2CHC(Me)_2$]Me_2SiCl; TDSCl) to give **7d**. The methyl ester **11** could be reduced to the hydroxy ester **7a** using H_2 and Pd/C. Under the reaction conditions described in the *Exper. Part*, the by-product **15** was formed in low yield, only.

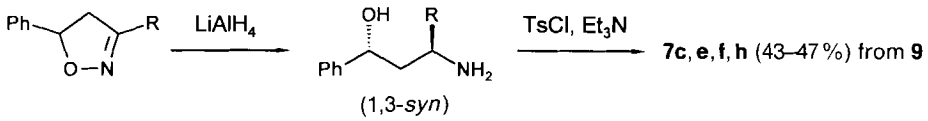
Scheme 3



TDS = (thexyl)dimethylsilyl

The second approach to racemic amino alcohols **7** included diastereoselective reduction of easily accessible 5-phenylisoxazolines **9** to racemic 1,3-*syn*-γ-amino alcohols **16** as described for **16a**, **b** by *Jäger* and *Buß* [10] (see *Scheme 4*). Subsequent *N*-acylation with tosyl chloride gave the racemic γ-(tosylamino) alcohols **7c**, **e**, **f**, **h**.

Scheme 4

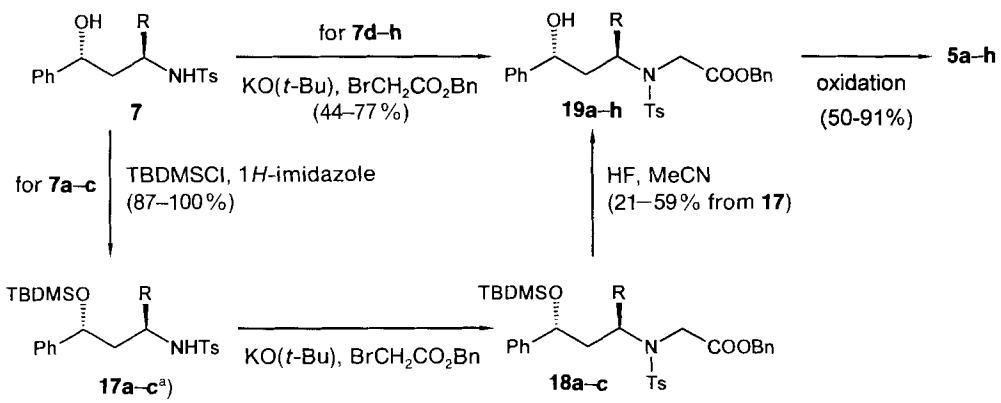


9a R = Me
b R = Ph
c R = *t*-Bu
d R = i-Pr

rac-**16a** R = Me
b R = Ph
c R = *t*-Bu
d R = i-Pr

The final steps towards the ketones **5** are shown in *Scheme 5*. A two-step alkylation-oxidation procedure led from **7d–h** *via* **19d–h** to **5d–h** in moderate to good yields. Unfortunately, the alkylation step often proceeded with low yields. Alcohols **7a–c** were converted to the silyl ethers **17a–c** before alkylation to **18a–c**, because direct alkylation gave non-separable mixtures of reactants and products. Desilylation of **18a–c** with excess 40% aqueous HF solution in MeCN led to the corresponding alcohols **19a–c**. Compound **6** was prepared from silyl ether **17a** similarly to **5a** using MeI in the alkylation step (52% overall yield). Oxidation of alcohols **19a–h** using standard methods (*e.g.* [11]) led to ketones **5** (for details, see *Exper. Part*).

Scheme 5



a R = COOMe[a])
b R = COO(*t*-Bu)[a])
c R = *t*-Bu (rac.)
d R = CH_2OTDS[a])
e R = Me (rac.)
f R = i-Pr (rac.)
g R = $CONMe_2$[a])
h R = Ph (rac.)

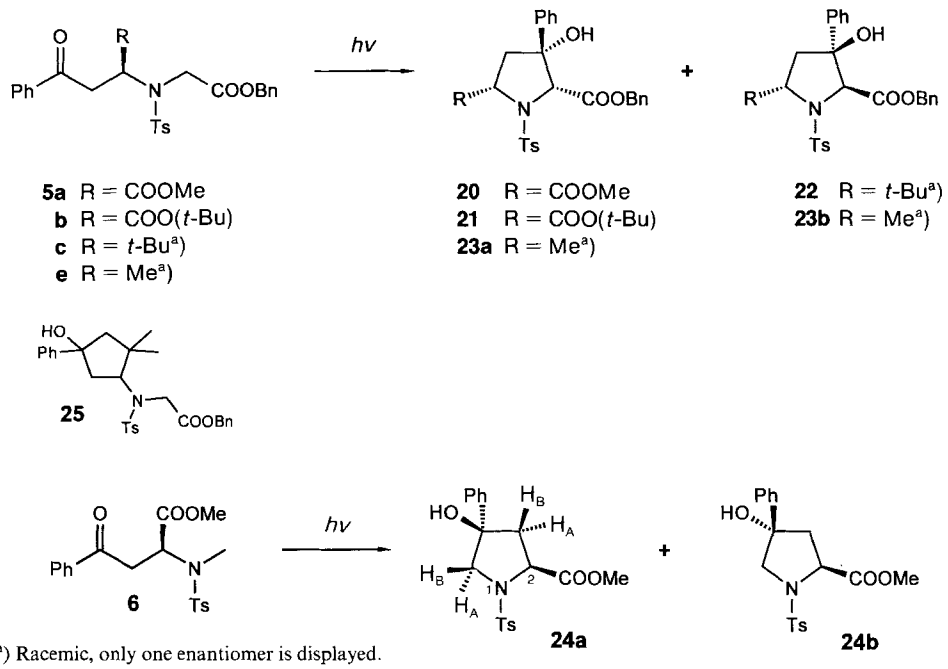
TBDMS = (*t*-Bu)Me_2Si, TDS = (thexyl)dimethylsilyl

[a]) Only one (of two) diastereoisomer is displayed in the case of **7**, **18** and **19**.

In order to establish that no racemization had taken place during the synthesis of enantiomerically pure ketones **5a, b, d, g**, the ee of **5a** (> 98%) was determined by HPLC (*Chiralcel-OD* column; for details, see *Exper. Part*). Racemic **5a**, which was needed to discriminate between the (*R*)- and (*S*)-enantiomer, was synthesized independently from racemic 2-amino-3-benzoylpropanoic acid [12].

Photochemical Behaviour of Compounds **5a–c, e** *and* **6**. Generally, three aspects determine the outcome of photolysis of **5** and **6**: *1*) the regioselectivity of H-abstraction to form an 1-hydroxy-1,*n*-biradical (relevant for ketones **5c–g**), *2*) the diastereoselectivity with respect to the generated bond, which was expected to be high for ketones **5** (see *e.g.* [5]), and *3*) the asymmetric induction by the C(1′)-substituent as the most important point. The irradiation results of ketones **5a–c, e** and **6** are summerized in *Scheme 6* and *Table 1*.

Scheme 6



[a]) Racemic, only one enantiomer is displayed.

As expected, proline derivatives **20–24** were formed in moderate-to-good yields by H-abstraction at C(γ) with respect to the keto function. Low regioselectivity was observed in the case of ketones **5c** and **5e**. The irradiation of **5a** gave the diester **20** exclusively, in good yield. Other diastereoisomers could not be detected. The configuration of **20** was established by X-ray crystallography (*Fig. 1*). Compound **20** can be regarded both as a (*R*)-3-hydroxy- or (*S*)-4-hydroxyproline derivative. The ester functions at C(2) and C(5) may be cleaved separately, providing a (*R*)- or (*S*)-proline derivative, respectively. Since cleavage of methyl esters requires harsh reaction conditions, we additionally investigated compound **5b**, which contains a *t*-Bu ester function as C(1′)-substituent.

Table 1. *Photoproducts from Ketones* **5a–c, e** *and* **6**

Starting ketone (solvent[a]))	R (config.)[b])	Photoproducts (yield [%]; config.)[c])	By-product (yield [%])	de [%]	ee [%][d])
5a (*A*)	COOMe (*S*)	**20** (65, (2*R*,3*R*,5*S*))	–	> 98	> 98
5b (*A*)	COO(*t*-Bu) (*S*)	**21** (57, (2*R*,3*R*,5*S*))	–	> 98	> 98
5c (*A*)	*t*-Bu (*RS*)	**22** (24, (2*r*,3*c*,5*t*))	**25** (36)	> 98	0
5e (*A*)	Me (*RS*)	**23a** (20, (2*r*,3*c*,5*c*))/ **23b** (20, (2*r*,3*c*,5*t*))	$TsHNCH_2CO_2Bn$ (24)	0	0
6 (*B*)	–	**24a** (27, (2*S*,4*R*))/ **24b** (48, (2*S*,4*S*))	–	28% (**24b**)	> 98[e])

[a]) *A* = cyclohexane/benzene; *B* = CH_2Cl_2. [b]) Absolute configuration at the chirality center. [c]) Yield of non-isolated products (HPLC); rel. (abs.) configuration of prolines **20–24**. [d]) Refers to the ee of the starting compounds (determined for **5a** as a representative example; see *Exper. Part*). No racemization should occur at the initial chirality center during photolysis, thus the ee of products is of the same magnitude as the ee of the starting compounds. [e]) For each pure isolated diastereoisomer.

Again, only one diastereoisomer **21** was formed, though after extensively long irradiation and in poor yield. We assume, that the bulky *t*-Bu ester group shields the radical centers, causing cleavage reactions and reformation of the starting compound. We assign to **21** the same configuration as to **20**.

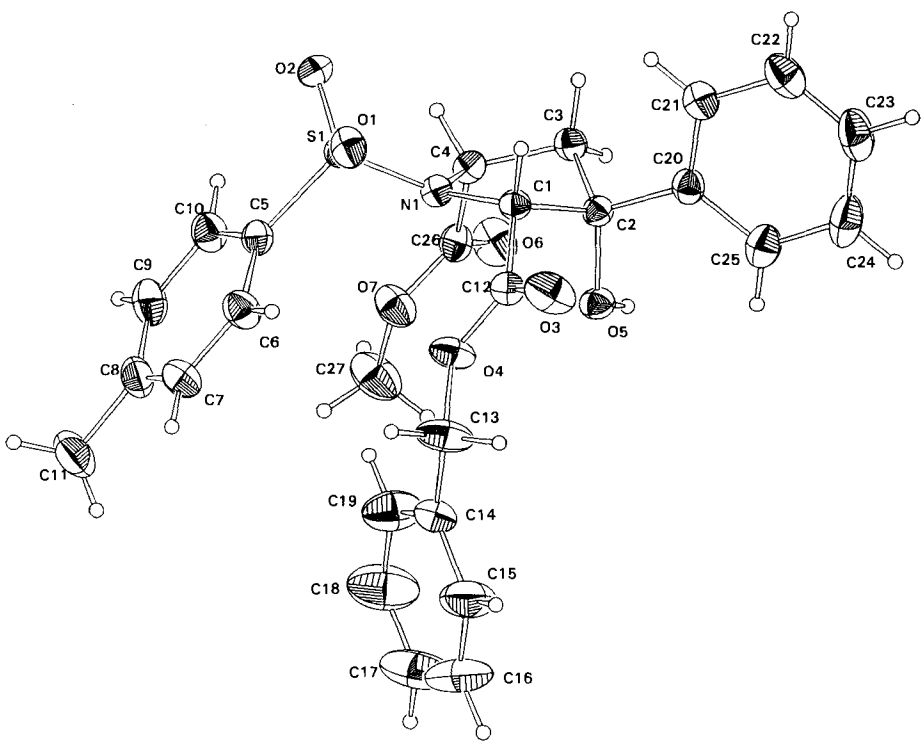
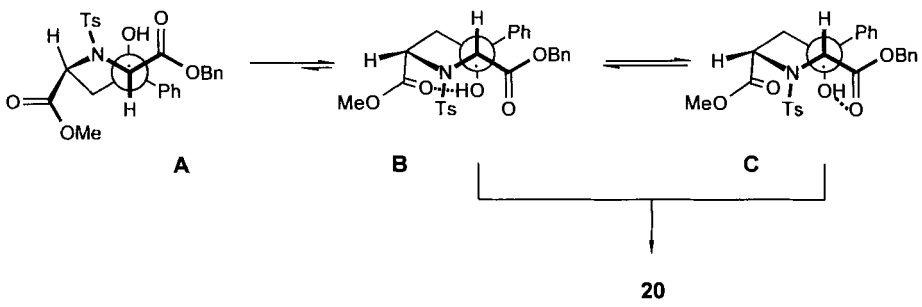


Fig. 1. *Crystal structure of* **20**. Arbitrary numbering.

Explanation of the stereoselectivity observed during photolysis of **5a** and **5b** is difficult. The substituents at C(2) and C(5) in **20** prefer a *cis*-arrangement although it was found by calculations[1]) to have a higher heat of formation (*ca.* 2 kcal/mol) than the *trans*-arrangement. Therefore, selectivity may be explained by preferred conformations of the intermediate 1-hydroxy-1,5-biradical (see *Scheme 7*). After H-abstraction, the relatively stable hydroxy-biradical forms conformer **B**, which can be stabilized by an intramolecular H-bond in contrast to conformer **A**. If the radical centers get closer, **C** can be generated by cleaving this H-bond to form another one with the glycine ester carbonyl group. This dynamic process takes place until the biradical recombines. Thus, alternating H-bonds could force the two ester functions into the observed *cis*-arrangement.

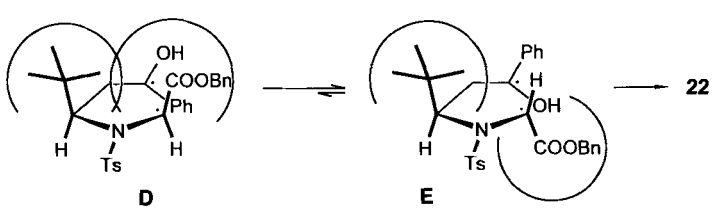
Scheme 7



The bulky *t*-Bu group of **5c** caused complete asymmetric induction, too, though the regioselectivity was poor. Two diastereoisomerically pure compounds could be isolated: proline ester **22** and cyclopentanol **25**, which was formed by abstraction of H–C(δ) from the *t*-Bu group. The arrangement of substituents in **22** was proved by NOE experiments (see *Fig. 2*), whereas the configuration of cyclopentanol **25** was not established.

The high stereoselectivity of the reaction from **5c** to **22** can be explained by the steric hindrance in the intermediate 4-hydroxy-1,5-biradical, caused by the bulky *t*-Bu group. Though the *cis*-conformation of the OH and ester group is not affected, the large *t*-Bu group forces the ester group from **D** into the *trans*-conformation **E**, leading to the observed product **22** after recombination (see *Scheme 8*).

Scheme 8



[1]) The calculations were performed using the UHF/PM3 method with the program MOPAC 7 [13].

Irradiation of H_B–C(4) (1.94 ppm) of **22** produces NOE's at H–C(2) and *t*-Bu–C(5), indicating *trans*-arrangement of *t*-Bu–C(5) and COOBn–C(2). In addition, NOE difference signals appear in the region above 7 ppm, caused by Ph–C(3), proving the *cis*-arrangement of OH–C(3) and COOBn–C(2). In a second experiment *t*-Bu–C(5) (0.85 ppm) was irradiated. The observed NOE's at H_B–C(4) and H–C(2) verify the relative (2*r*,3*c*,5*t*)-configuration for **22**.

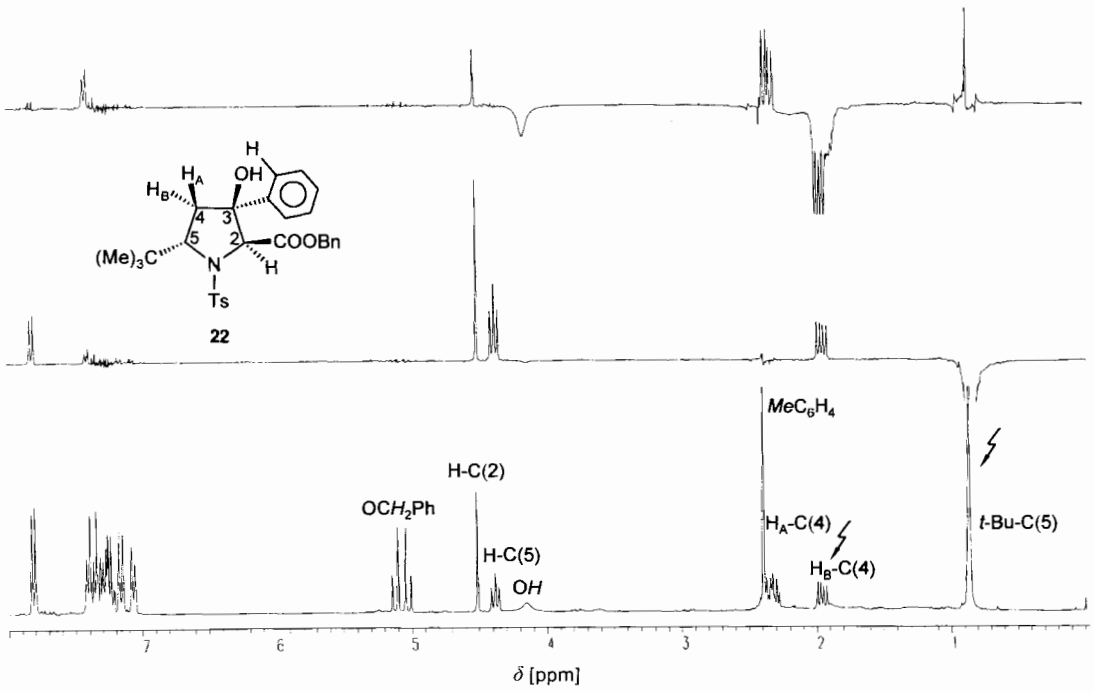


Fig. 2. *^{1}H-NMR Spectrum, NOE difference spectra and configuration of* **22**

The C(1′)-methyl substituted compound **5e** gave only 40% of cyclization products **23a,b** in a ratio of 1:1, compared with 48% of *Norrish*-type-II cleavage product as a result of abstraction of H–C(γ) (see *Scheme 6*, *Table 1*). The regioselectivity during the photolysis of **5e** was found to be solvent dependent. In CH_2Cl_2, cleavage of **5e** was observed exclusively. Obviously, the more polar solvent is able to stabilize the 1-hydroxy-1,4-biradical better than the 1,5-biradical, leading to almost complete *Norrish*-type-II cleavage. The primary cleavage product, benzyl *N*-vinyl-*N*-tosylglycinate could not be detected. Instead, we isolated benzyl *N*-tosylglycinate, only. Because no asymmetric induction during the reaction of **5e** to **23a,b** took place (*cf.* irradiation result of **5c**), no assignments of product configuration were made (temptative assignments in *Scheme 6* and in the *Exper. Part*).

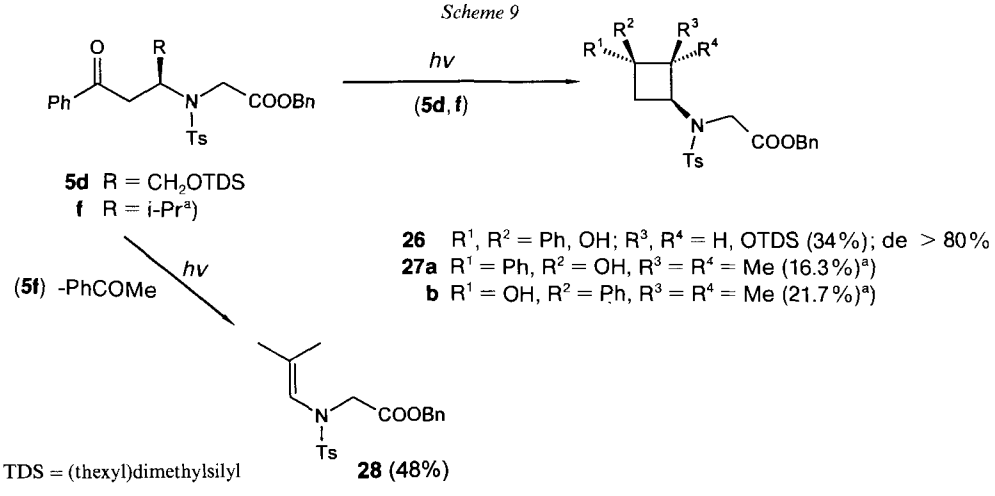
As pointed out before, both ester groups in **5a** are responsible for the observed efficient asymmetric induction. Evidence for this fact is the irradiation result of **6**. This compound contains only the methyl ester function, whereas the (benzyloxycarbonyl)methyl moiety is replaced by a Me group. Irradiation led to methyl (2*S*,4*R*)- and (2*S*,4*S*)-4-hydroxy-4-phenyl-1-tosylprolinate (**24a** and **24b**, resp.; see *Scheme 6*). The observed de (28%) is low compared with the photolysis of the diesters **5a** and **5b**

(de > 98%), indicating that asymmetric induction is poor if the glycine ester function is absent. In addition, not the expected *cis*-4-hydroxyproline **24a** was the major diastereoisomer, but the *trans*-isomer **24b**. The *cis*-arrangement for **24a** was proved by NOE experiments. In spite of the low de, the photolysis of **6** provided 4-hydroxyprolines **24a, b** in the highest cyclization yield (75%) as compared to those from ketones **5**. The enantiomerically pure compound **24a** is a fully protected 4-phenylated analogue of the naturally occurring *cis*-4-hydroxy-L-proline and should, therefore, possess some importance for peptide syntheses.

Irradition of H–C(2) (4.53 ppm) of **24a** produces a NOE at H_A–C(3) (2.53 ppm), indicating the *cis*-arrangement. Irradiation of H_A–C(3) gave NOE's at H–C(2) and H_A–C(5) (3.49 ppm). In addition, NOE difference signals appear in the region above 7 ppm, caused by Ph–C(4), proving the *cis*-arrangement of H–C(2) and Ph–C(4). The observed long-range coupling between H_B–C(3) and H_B–C(5) (J = 1.5 Hz) verifies the existence of a strong intramolecular H-bond between COOMe–C(2) and OH–C(5). A molecular model shows that due to this H-bond, the proline ring is folded to achieve a planar W-shape connection between H_B–C(3) and H_B–C(5). Another evidence for a short H-bond is the fact, that the OH signal of the *cis*-isomer **24a** is low-field-shifted by *ca.* 2.2 ppm, as compared to the *trans*-isomer **24b**. Obviously, this shift is caused by the anisotropic effect of the ester carbonyl group.

Photochemical Behaviour of Compounds **5d, f, g–h**. Whereas the ketones **5a–c, e** and **6** gave the desired hydroxyproline derivatives, ketones **5d, f, g–h** showed a somewhat different photochemical behaviour, which should be mentioned. Alkoxy groups are able to stabilize an adjacent radical center [14]. That seems to be true for silyloxy groups, too, as shown by the irradiation result of **5d** (see *Scheme 9*). No abstraction of H–C(δ) was found. Instead, we isolated the H–C(γ) abstraction product **26**, exclusively. Besides the cyclization, *Norrish*-type-II cleavage took place. Cyclobutanol **26** was obtained as a 90% pure compound (relative configuration not determined). Therefore, the de can be estimated to be > 80%. The impurity (presumably another diastereoisomer) could not be identified, even after various separation efforts. The observed high regio- and diastereoselectivity of the reaction of **5d** to **26** seems to be characteristic for such compounds, because we found comparable results in the case of similar compounds [15].

Scheme 9



a) Racemic, only one enantiomer is displayed.

Compound **5f** gave 86% H–C(γ) abstraction (see *Scheme 9*). This regioselectivity can be explained by the high stability of the formed tertiary radical. The 1-hydroxy-1,4-biradical recombined to cyclobutanols **27a,b** in only 38% cyclization yield with poor diastereoselectivity, besides 48% *Norrish*-type-II cleavage. In contrast to **5e**, the primary cleavage product **28** was isolated and characterized. The diastereoisomeric cyclobutanols **27a,b** could not be separated and their relative configuration was not established (temptative assignments in *Scheme 9* and *Exper. Part*).

N,N-Dimethylamide **5g** (see *Scheme 2*) bears H-atoms at C(δ) as well as C(ε) with respect to the keto function. The formation of δ-lactams from β-benzoylpropan amides has been intensively investigated [16] [17]. Unfortunately, the existence of two different sets of abstractable H-atoms, combined with a low diastereoselectivity, led to a variety of products upon irradiation of **5g**. Variation of solvent did not change the observed low regio- and diastereoselectivity. Due to the absence of H–C(γ)'s and the size of the C(1')-substituent, compound **5h** was expected to react as selectively as **5c**, but without formation of by-products. Surprisingly, no photoreaction was observed at all. Extremely long irradiation times resulted in slow thermal decomposition, only. We assume that charge-transfer interactions between the phenyl substituent and the keto carbonyl group could dissipate the excitation energy.

Conclusion. – Photocyclization of enantiomerically pure C(1')-substituted *N*-(2-benzoylethyl)glycine esters **5a** and **5b** provided (2*r*,3*c*,5*c*)-configurated proline derivatives **20** and **21** with high de (> 98%). In contrast to **5a,b**, irradiation of **5c** gave the (2*r*,3*c*,5*t*)-configurated proline **22**, indicating a different selection mechanism. Whereas steric effects are responsible for the formation of **22**, products **20** and **21** can be explained by electronic stabilization of the intermediate hydroxy-biradicals (H-bonds). Thus, one should be able to control the relative 2,5-configuration of the formed 3-hydroxyproline by proper choice of the C(1')-substituent in compounds **5**. *cis*-Diastereoselectivity with respect to the formed bond in the new proline rings was always high, as expected by previous investigations [5–7]. Regioselectivity of H-abstraction was almost always low, if additional abstractable H-atoms were available in ketones **5**, as exemplified by the formation of cyclopentanol **25** from **5c**. Ketones **5d** and **5f** formed stable 1-hydroxy-1,4-biradicals, resulting in the formation of cyclobutanols **26**–**27** and *Norrish*-type-II cleavage. C(1')-Phenyl-substituted compound **5h** seemed to be a poor reactant for selective photocyclization as well as *N,N*-dimethylamide **5g**. α-Amino-γ-keto ester **6** provided both diastereoisomers of the 4-phenylated analogue of naturally occurring 4-hydroxy-L-proline in excellent yield, but low de.

The diastereo- and enantioselective formation of 3-hydroxyprolines described in this paper is an interesting alternative to other asymmetric syntheses of 3-hydroxyprolines.

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Experimental Part

General. All solvents were distilled and dried. The reagents were of reagent grade and used without further purification, if not specified otherwise. Org. extracts were dried ($MgSO_4$) and evaporated below 40°. High vacuum (h.v.) means < 0.05 Torr. Photochemistry: see [7]; isolated photoproducts were used to determine the non-isolated yields by anal. HPLC (correlation function between peak areas and concentration). TLC: alumina

sheets coated with silica gel *60 F_{254} (Merck)*; detection by UV light or with a soln. of $Ce(SO_4)_2 \cdot 4\ H_2O$ (1 g) and $(NH_4)_6Mo_7O_{24} \cdot 4\ H_2O$ (2.5 g) in 1.8M H_2SO_4 (100 ml) followed by heating. Flash chromatography (FC): silica gel (40–63 μm, *Merck*). High-pressure liquid chromatography (HPLC): anal., *SIX [NH_2]* column (150 × 3.3 mm, 5 μm, *Laboratorni Pristroje Prag*), flow 1 ml/min; semiprep., *LiChrosorb Si-60* (250 × 20 mm, 7 μm, *Knauer*), flow 10 ml/min; prep. *Eurospher 100* (250 × 32 mm, 5 μm, *Knauer*), flow 30 ml/min; UV detection; mobile phase (semiprep. and prep.), CH_2Cl_2/MeOH (λ_{max} values in parentheses refer to the UV/VIS absorption of a soln. of 2,6-diphenyl-4-(2,4,6-triphenyl-pyridinium-1-yl)phenolate hydrate (*Reichardt*'s dye) in the specified mobile phase (ε up to 1.0); this was used to recover the mobile phase). M.p.: *Boetius* micro melting point apparatus (*Küster Nachf. KG*); uncorrected. IR: *Perkin-Elmer-881*; in cm^{-1}. UV: *Uvikon 930* (*Kontron*); λ_{max} in nm. Polarimetry: *DIP 370* (*JASCO*); d = 100 mm. NMR: *Bruker AM 300* (^1H, 300 MHz; ^{13}C, 75.5 MHz); chemical shifts in ppm rel. to internal reference $SiMe_4$ (= 0 ppm), J in Hz; ^1H-NMR spectra of diastereoisomer mixtures with major diastereoisomers were analyzed for *each* diastereoisomer, **A** being the major and **B** the minor diastereoisomer, without assignment of configuration (except for **7bA** and **7bB** which were assigned by comparison with similar compounds [18]), whereas ^{13}C-NMR assignments refer to equal atoms in *both* diastereoisomers. EI-MS: *HP 5995 A*; 70 eV at 293–593 K.

(S)-3-Benzoyl-2-(tosylamino)propanoic Acid (**10**). (*S*)-*N*-Tosylaspartic anhydride (**8**) [8] (8.08 g, 30 mmol) was suspended in dry benzene (150 ml), and $AlCl_3$ (9.33 g, 70 mmol) was added in one portion. After stirring for 20 h at r.t., the resulting brown soln. was poured into a mixture of ice (150 g) and conc. HCl soln. (80 ml). After stirring for 30 min, the mixture was filtrated and the remaining solid (crude **10**) washed with 6N HCl (2 × 50 ml) and benzene (2 × 50 ml) and dried. Recrystallization of the crude product (9.9 g) from 75% aq. MeOH yielded 6.88 g (66%) of **10**. Colourless needles. M.p. 174–176°. $[\alpha]_D^{16} = +51.5$ (c = 2, MeOH). IR (KBr): 3307, 1752, 1679, 1321, 1153. ^1H-NMR ((D_6)DMSO): 2.51 (*s*, *Me*C_6H_4); 3.26 (*m*, 1 H–C(3)); 3.35 (*m*, 1 H–C(3)); 3.50 (br. *s*, COOH); 4.26 (*m*, H–C(2)); 7.28–7.83 (*m*, 9 arom. H); 8.1 (*d*, J = 8.8, NH). ^{13}C-NMR ((D_6)DMSO): 21 (*Me*C_6H_4); 41 (C(3)); 51.8 (C(2)); 126.6, 127.9, 128.8, 129.4, 133.5, 136, 138.4, 142.5 (arom. C); 171.9 (C(1)); 196.3 (Ph*C*O). EI-MS: 302 (2, $[M - COOH]^+$), 192 (5, $[M - Ts]^+$), 176 (6, $[M - TsNH_2]^+$), 155 (18, Ts^+), 131 (10, PhCOCH=CH^+), 105 (100, $PhCO^+$), 91 (91, $C_7H_7^+$).

Methyl (S)-3-Benzoyl-2-(tosylamino)propanoate (**11**). To dry MeOH (120 ml) was added dropwise at −10° freshly distilled $SOCl_2$ (11 ml, 150 mmol). The soln. was stirred for 10 min, and solid **10** (13.9 g, 40 mmol) was added. The suspension was allowed to come to r.t. and stirred overnight. The mixture was evaporated, the residue dissolved in CH_2Cl_2 (150 ml), and the soln. extracted with H_2O (80 ml), 5% $NaHCO_3$ soln. (80 ml), and H_2O (80 ml). The dried org. phase was evaporated and the residue recrystallized (75% aq. MeOH): 13.17 g (91%) of **11**. Colourless needles. M.p. 114–115°. $[\alpha]_D^{16} = +74.1$ (c = 1, $CHCl_3$). IR (KBr): 3302, 1739, 1680, 1342, 1167. ^1H-NMR ($CDCl_3$): 2.38 (*s*, *Me*C_6H_4); 3.58 (*s*, MeO); 3.62 (*m*, 2 H–C(3)); 4.28 (*m*, H–C(2)); 5.79 (*d*, J = 8, NH); 7.25–7.88 (*m*, 9 arom. H). ^{13}C-NMR ($CDCl_3$): 21.5 (*Me*C_6H_4); 42.0 (C(3)); 51.7 (C(2)); 127.2, 128.1, 128.7, 129.6, 133.8, 135.7, 136.9, 143.6 (arom. C); 170.9 (C(1)); 196.9 (Ph*C*O). EI-MS: 302 (3, $[M - COOMe]^+$), 206 (11, $[M - Ts]^+$), 131 (1, PhCOCH=CH^+), 155 (3, Ts^+), 105 (100, $PhCO^+$), 91 (23, $C_7H_7^+$).

tert-*Butyl (S)-3-Benzoyl-2-(tosylamino)propanoate* (**12**). Solid **10** (12.26 g, 35.3 mmol) was added to a stirred mixture of conc. H_2SO_4 (0.35 ml) and dry CH_2Cl_2 (150 ml). After cooling to −15°, gaseous isobutene (7.1 g, 125 mmol) was bubbled into the suspension. The mixture was allowed to come to r.t., stirred for 2 d, and then evaporated. The residue was dissolved in AcOEt (150 ml) and the soln. extracted with sat. $NaHCO_3$ soln. (3 × 60 ml), H_2O (60 ml), and brine (60 ml). The dried org. phase was evaporated and the residue recrystallized (CH_2Cl_2/hexane): 12.62 g (89%) of **12**. M.p. 118–120°. $[\alpha]_D^{16} = +22.6$ (c = 1, MeOH). IR (KBr): 3282, 2981, 2930, 1732, 1679, 1344, 1159. ^1H-NMR ($CDCl_3$): 1.25 (*s*, *Me*$_3$CO); 2.34 (*s*, *Me*C_6H_4); 3.54 (*m*, 2 H–C(3)); 4.15 (*m*, H–C(2)); 5.69 (*d*, J = 7.3, NH); 7.21–7.84 (*m*, 9 arom. H). ^{13}C-NMR ($CDCl_3$): 21.5 (*Me*C_6H_4); 27.5 (*Me*$_3$C); 42.2 (C(3)); 52.4 (C(2)); 82.8 (Me$_3$*C*); 127.3, 128.1, 128.6, 129.6, 133.6, 136.1, 137.0, 143.4 (arom. C); 169.1 (C(1)); 196 (Ph*C*O). EI-MS: 302 (4, $[M - COO(t\text{-}Bu)]^+$), 192 (3), 105 (100, $PhCO^+$), 91 (14, $C_7H_7^+$).

(S)-3-Benzoyl-N,N-dimethyl-2-(tosylamino)propanamide (**13**). To a suspension of **10** (13.9 g, 40 mmol) and Na_2CO_3 (12.72 g, 120 mmol) in dry CH_2Cl_2 (200 ml), dichloromethyl methyl ether (10.86 ml, 120 mmol) was added. After stirring for 5 h at r.t., the mixture was cooled to 0° and gaseous Me_2NH bubbled in. The red mixture was allowed to come to r.t., stirred for 20 h, and then evaporated. The residue was partitioned between H_2O (200 ml) and AcOEt (150 ml), the aq. phase extracted with AcOEt (2 × 60 ml), the combined org. phase extracted with 2N HCl (60 ml) and brine (60 ml), dried, and evaporated, and the residue purified by FC (CH_2Cl_2/MeOH 100:4) and recrystallized from toluene: 8.74 g (58%) of **13**. White solid. M.p. 131–133°. $[\alpha]_D^{20} = -10.5$ (c = 1, Me_2CO). IR (KBr): 3255, 1666, 1649, 1339, 1167. ^1H-NMR ($CDCl_3$): 2.38 (*s*, *Me*C_6H_4); 2.75, 3.05 (2*s*, Me_2N); 3.19 (*m*, 1 H–C(3)); 3.47 (*m*, 1 H–C(3)); 4.89 (*m*, H–C(2)); 6.22 (*d*, J = 9.7, NH); 7.21–7.79 (*m*, 9 arom. H). ^{13}C-NMR

($CDCl_3$): 21.5 (*Me*C_6H_4); 35.9, 37.3 (Me_2N); 42.4 (C(3)); 48.7 (C(2)); 127.1, 128.1, 128.6, 129.6, 133.6, 136.0, 137.4, 143.5 (arom. C); 170.4 (C(1)); 197 (Ph*C*O). EI-MS: 302 (10, $[M - CONMe_2]^+$), 155 (2, $[M - Ts]^+$), 105 (100, $PhCO^+$), 91 (16, $C_7H_7^+$).

(1RS,3S)-1-Phenyl-3-(tosylamino)butane-1,4-diol (**14**). A suspension of **11** (9.04 g, 25 mmol) in 96% EtOH soln. (200 ml) was treated with $NaBH_4$ (5.67 g, 150 mmol). After stirring for 4 h at r.t., the solvent was removed. The residue was taken up in H_2O (100 ml), cooled (0°), and 2N HCl (90 ml) was added dropwise. The mixture was extracted with CH_2Cl_2 (3 × 70 ml), the combined org. phase extracted with 3% $NaHCO_3$ soln. (50 ml), dried, and evaporated. Removal of remaining solvent traces (h.v.) gave 7.97 g (95%) of **14**. Colourless resin (^{1}H-NMR: 1:1 diastereoisomer mixture). IR (film): 3530, 3288, 1321, 1152.

Methyl (2S,4RS)-4-Hydroxy-4-phenyl-2-(tosylamino)butanoate (**7a**) *and Methyl (S)-4-phenyl-2-(tosylamino)butanoate* (**15**). A mixture of **7a** (8.31 g, 23 mmol), 3% Pd/C (2 g), AcOEt (80 ml), and MeOH (300 ml) was cooled to −10°, and a slow stream of H_2 was bubbled through (atmospheric pressure was preferred to prevent an exhaustive formation of the by-product **15**). The reaction was monitored by TLC and stopped when only traces of starting material remained (3–4 h). The mixture was rinsed with Ar to remove dissolved H_2, filtrated through *Celite*, and evaporated. FC (CH_2Cl_2/MeOH 100:3) of the remaining oil gave **15** (0.8 g, 10%) followed by **7aA**/**7aB** 1.7:1 (by ^{1}H-NMR: 6.69 g, 80%; colourless resin).

Data of **7aA**/**7aB**: IR (film): 3517, 3273, 1784, 1739, 1341, 1161. ^{1}H-NMR ($CDCl_3$): **7aA**: 1.79, 2.11 (2*m*, 2 H–C(3) (**7aA**/**7aB**)); 2.39 (*s*, *Me*C_6H_4 (**7aA**/**7aB**)); 2.92 (*d*, *J* = 3.7, OH); 3.53 (*s*, MeO); 3.98 (*m*, H–C(2)); 4.85 (*m*, H–C(4)); 5.77 (*d*, *J* = 7.3, NH); 7.17–7.74 (*m*, 9 arom. H (**7aA**/**7aB**)); **7aB**: 2.38 (*s*, OH); 3.46 (*s*, MeO); 4.24 (*m*, H–C(2)); 4.95 (*m*, H–C(4)); 5.64 (*d*, *J* = 9.5, NH). ^{13}C-NMR ($CDCl_3$): 21.5 (*Me*C_6H_4); 41.5, 42.4 (C(3)); 52.7, 53.2 (MeO); 53.7 (C(2)); 69.6, 70.6 (C(4)); 125.6, 125.8, 127.3, 127.6, 128.5, 129.7, 136.2, 136.5, 143.4, 143.8, 143.9 (arom. C); 172.2 (C(1)).

Data of **15**: M.p. 88–92° (MeOH/H_2O). $[\alpha]_D^{18} = +55.6$ (*c* = 1, $CHCl_3$). IR (KBr): 3270, 1739, 1343, 1162. ^{1}H-NMR ($CDCl_3$): 1.98 (*m*, 2 H–C(3)); 2.41 (*m*, (*Me*C_6H_4); 2.67 (*m*, 2 H–C(4)); 3.46 (*s*, MeO); 3.94 (*m*, H–C(2)); 5.32 (*d*, *J* = 9.5, NH); 7.09–7.73 (*m*, 9 arom. H). ^{13}C-NMR ($CDCl_3$): 21.5 (*Me*C_6H_4); 31.1, 34.9 (C(3), C(4)); 52.5 (C(2)); 55.3 (MeO); 126.2, 127.3, 128.5, 129.6, 136.6, 140.3, 143.7 (arom. C); 172 (C(1)). EI-MS: 347 (2, M^+), 288 (9, $[M - COOMe]^+$), 192 (4, $[M - Ts]^+$), 155 (18, Ts^+), 132 (11), 117 (34, $PhCH_2CH{=}CH^+$), 91 (100, $C_7H_7^+$).

tert-*Butyl (2S,4S)- and (2S,4R)-4-Hydroxy-4-phenyl-2-(tosylamino)butanoate* (**7bA** and **7bB**, resp.). A soln. of **12** (8.97 g, 22.2 mmol) in i-PrOH (150 ml) was treated with $NaBH_4$ (440 mg, 11.6 mmol). After stirring for 3 h at r.t., the solvent was removed and the residue taken up in H_2O (200 ml). Dil. HCl soln. was added until foaming ceased, and the mixture was extracted with CH_2Cl_2 (3 × 70 ml). The dried org. phase was evaporated and the residue recrystallized from 80% aq. MeOH: 7.58 (84%) of **7bA**/**7bB** 1.1:1 (by ^{1}H-NMR). M.p. 110–155°. IR (KBr): 3530, 3426, 3285, 1734, 1724, 1346, 1162. An anal. sample of each diastereoisomer was obtained by FC (CH_2Cl_2/MeOH 100:4): **7bA** followed by **7bB**.

Data of **7bA**: ^{1}H-NMR ($CDCl_3$): 1.18 (*s*, Me_3CO); 1.72 (*m*, 1 H–C(3)); 2.01 (*m*, 1 H–C(3)); 2.39 (*s*, *Me*C_6H_4); 3.08 (*d*, *J* = 4.4, OH); 4.07 (*m*, H–C(2)); 5.05 (*m*, H–C(4)); 5.48 (*d*, *J* = 9.6, NH); 7.24–7.76 (*m*, 9 arom. H). ^{13}C-NMR ($CDCl_3$): 21.5 (*Me*C_6H_4); 27.6 (Me_3C); 42.7 (C(3)); 53.6 (C(2)); 69.3 (C(4)); 82.7 (Me_3C); 125.6, 127.5, 128.5, 129.7, 135.9, 143.5, 143.9 (arom. C); 170.8 (C(1)). EI-MS: 348 (1, $[M - (t\text{-Bu})]^+$), 304 (1, $[M - COO(t\text{-Bu})]^+$), 198 (36), 194 (7), 155 (29, Ts^+), 132 (100), 116 (30), 107 (9, $PhCHOH^+$), 105 (85, $PhCO^+$), 91 (76, $C_7H_7^+$).

Data of **7bB**: ^{1}H-NMR ($CDCl_3$): 1.27 (*s*, Me_3CO); 2.02–2.18 (*m*, 2 H–C(3)); 2.36 (br. *s*, OH); 2.38 (*s*, *Me*C_6H_4); 3.84 (*m*, H–C(2)); 4.88 (*m*, H–C(4)); 5.59 (*d*, *J* = 7.3, NH); 7.25–7.73 (*m*, 9 arom. H). ^{13}C-NMR ($CDCl_3$): 21.5 (*Me*C_6H_4); 27.7 (Me_3C); 41.9 (C(3)); 54.4 (C(2)); 71.0 (C(4)); 82.7 (Me_3C); 125.8, 127.4, 127.8, 128.5, 129.7, 136.5, 143.6 (arom. C); 170.5 (C(1)). EI-MS: 348 (2, $[M - (t\text{-Bu})]^+$), 304 (3, $[M - COO(t\text{-Bu})]^+$), 198 (91), 194 (18), 155 (64, Ts^+), 132 (10), 121 (13), 107 (40, $PhCHOH^+$), 105 (31, $PhCO^+$), 91 (100, $C_7H_7^+$).

rac-*1,3*-syn-*3-Amino-4,4-dimethyl-1-phenylpentan-1-ol* (**16c**) was prepared similarly to **16d** (see below) from *3-(*tert*-butyl)-5-phenylisoxazoline* (**9c**) [19] (20.33 g, 100 mmol), $LiAlH_4$ (6.8 g, 179 mmol), and Et_2O (520 ml) at −15° (4 h warming up, then 19 h). Workup with 1.4M H_2SO_4 (590 mmol), filtration, extraction with Et_2O (2 × 80 ml), addition of KNa(tartrate)·4 H_2O (200 mmol) and 30% NaOH soln. (110 ml) followed by extraction with CH_2Cl_2 (4 × 80 ml) and evaporation of the dried org. phase gave 13.47 g (65%) of **16c**. Yellow oil. IR (film): 3387, 3296, 2960, 700. ^{1}H-NMR ($CDCl_3$): 0.84 (*s*, Me_3CH); 1.28 (*m*, 1 H–C(2)); 1.83 (*m*, 1 H–C(2)); 2.66 (*m*, H–C(3)); 3.38 (br. *s*, OH, NH_2); 4.85 (*m*, H–C(1)); 7.19–7.40 (arom. H). ^{13}C-NMR ($CDCl_3$): 25.8 (Me_3C); 34.8 (C(4)); 39.7 (C(2)); 62.4 (C(3)); 75.8 (C(1)); 125.7, 126.9, 128.2, 145.7 (arom. C). EI-MS: 150 (14, $[M - (t\text{-Bu})]^+$), 107 (18, $PhCHOH^+$), 105 (11).

General Procedure 1: N-*Acylation of Amino Alcohols* **16** *with Tosyl Chloride*. A mixture of **16** (30 mmol), TsCl (5.81 g, 30.5 mmol), Et_3N (4.25 ml, 30.5 mmol), and dry CH_2Cl_2 (80 ml) was stirred at r.t. till completion

(2–3 h). The soln. was extracted with H_2O (2 × 50 ml, containing 2 ml of Et_3N), 2N HCl (2 × 50 ml), and H_2O (50 ml), dried, and evaporated. Recrystallization or FC afforded pure *N*-(tosylamino) alcohols **7c, e, f, h**.

rac-*1,3*-syn-*4,4-Dimethyl-1-phenyl-3-(tosylamino)pentan-1-ol* (**7c**). From **16c** according to the *General Procedure 1*. Recrystallization from toluene: 7.16 g (66%) of **7c**. M.p. 164–166°. IR (KBr): 3479, 3182, 2969, 1320, 1148. ^{1}H-NMR ($CDCl_3$): 0.68 (*s*, Me_3C); 1.81 (*m*, 1 H–C(2)); 1.99 (*m*, 1 H–C(2)); 2.40 (*s*, MeC_6H_4); 2.78 (*d*, J = 2.9, OH); 3.18 (*m*, H–C(3)); 4.64 (*m*, H–C(1)); 5.11 (*d*, J = 8.8, NH); 7.20–7.41 (arom. H). ^{13}C-NMR ($CDCl_3$): 21.5 (MeC_6H_4); 26.3 (Me_3C); 35.3 (C(4)); 41.3 (C(2)); 61.1 (C(3)); 72.9 (C(1)); 126.1, 127.2, 127.6, 128.5, 129.5, 138.5, 143.2, 144.4 (arom. C). EI-MS: 304 (8, $[M - (t\text{-Bu})]^+$), 198 (100), 155 (56, Ts^+), 107 (23, $PhCHOH^+$), 91 (66, $C_7H_7^+$).

(1RS,3S)-1-Phenyl-4-[(thexyl)dimethylsilyloxy]-3-(tosylamino)butan-1-ol (**7d**). A mixture of **14** (7.08 g, 21.1 mmol; diastereoisomer mixture), thexyldimethylsilyl chloride (4.99 ml, 25.4 mmol), 1*H*-imidazole (3.61 g, 53 mmol), and dry DMF (35 ml) was stirred for 20 h at r.t. H_2O (150 ml) was added and the mixture extracted with Et_2O (3 × 50 ml). The dried org. phase was evaporated, residual solvent removed (h.v.), and the residue purified by FC (CH_2Cl_2/MeOH 100:2): 6.96 g (69%) of **7dA**/**7dB** 1:1 (by ^{1}H-NMR). Colourless resin. IR (film): 3503, 3285, 2958, 2869, 1331, 1161. An anal. sample of each diastereoisomer was obtained by FC (CH_2Cl_2/MeOH 100:3) of the diastereoisomer mixture.

Data of **7dA**: ^{1}H-NMR ($CDCl_3$): −0.12, −0.11 (2*s*, MeSi); 0.69 (*s*, $C(Me_2)Si$); 0.75 (*d*, J = 7.3, Me_2CH); 1.47 (*m*, Me_2CH); 1.56 (*m*, 1 H–C(2)); 1.82 (*m*, 1 H–C(2)); 2.36 (*s*, MeC_6H_4); 2.92 (*d*, J = 3.7, OH); 3.14, 3.27 (2*m*, 2 H–C(4)); 3.53 (*m*, H–C(3)); 4.90 (*m*, H–C(1)); 5.11 (*d*, J = 8.8, NH); 7.15–7.72 (*m*, 9 arom. H). ^{13}C-NMR ($CDCl_3$): −3.8, −3.7 (MeSi); 18.5, 20.2, 20.3 ($Me_2CHC(Me)_2Si$); 21.6 (MeC_6H_4); 25.1 ($C(Me)_2Si$); 34.1 (Me_2CH); 41.9 (C(2)); 51.9 (C(3)); 64.1 (C(4)); 70.1 (C(1)); 125.6, 127.0, 127.3, 128.4, 129.8, 137.8, 143.6, 144.2 (arom. C).

Data of **7dB**: ^{1}H-NMR ($CDCl_3$): −0.09, −0.06 (2*s*, MeSi); 0.71 (*s*, $C(Me)_2Si$); 0.76 (*d*, J = 6.6, Me_2CH); 1.48 (*m*, Me_2CH); 1.83 (*m*, 2 H–C(2)); 2.35 (*s*, MeC_6H_4); 2.53 (*d*, J = 3.7, OH); 3.29 (*m*, 1 H–C(4), H–C(3)); 3.47 (*m*, 1 H–C(4)); 4.56 (*m*, H–C(1)); 5.12 (*d*, J = 7.3, NH); 7.14–7.68 (*m*, 9 arom. H). ^{13}C-NMR ($CDCl_3$): −3.6 (MeSi); 18.5, 20.2 ($Me_2CHC(Me)_2Si$); 21.5 (MeC_6H_4); 25.1 ($C(Me)_2Si$); 34.1 (Me_2CH); 41.3 (C(2)); 53.3 (C(3)); 64.3 (C(4)); 71.9 (C(1)); 125.8, 127.2, 127.6, 128.5, 129.7, 137.8, 143.4, 144.2 (arom. C).

rac-*1,3*-syn-*1-Phenyl-2-(tosylamino)butan-1-ol* (**7e**). From *rac-1,3*-syn-*3-amino-1-phenylbutanol* (**16a**) [10] according to the *General Procedure 1*. Recrystallization from toluene: 7.47 g (78%) of **7e**. M.p. 137–144°. IR (KBr): 3536, 3280, 1313, 1160. ^{1}H-NMR ((D_6)DMSO): 0.92 (*d*, J = 6.6, 3 H–C(4)); 1.42 (*m*, 1 H–C(2)); 1.67 (*m*, 1 H–C(2)); 2.38 (*s*, MeC_6H_4); 3.24 (*m*, H–C(1)); 3.35 (*d*, J = 7.3, OH); 4.45 (*m*, H–C(3)); 5.19 (*d*, J = 4.4, NH); 7.15–7.67 (*m*, 9 arom. H). ^{13}C-NMR ((D_6)DMSO): 20.5 (C(4)); 21.0 (MeC_6H_4); 46.8 (C(2)); 69.2, 69.4 (C(1), C(3)); 125.8, 126.5, 128, 129.6, 139.2, 142.4, 146 (arom. C). EI-MS: 318 (2, $[M - H]^+$), 198 (32), 164 (6, $[M - Ts]^+$), 155 (40, Ts^+), 105 (23, $PhCO^+$), 91 (100, $C_7H_7^+$).

3-Isopropyl-5-phenylisoxazoline (**9d**). To a stirred soln. of N-*hydroxy-2-methylpropanimidoyl chloride* [20] (18.84 g, 155 mmol) and freshly distilled styrene (36 ml, 310 mmol) in dry Et_2O (120 ml) was added a soln. of Et_3N (22.7 ml, 163 mmol) in dry Et_2O (30 ml) within 30 min. After standing for 21 h, the mixture was filtrated, the filter cake washed with Et_2O (2 × 50 ml), and the soln. extracted with H_2O (2 × 100 ml), dried, and evaporated. After removal of the excess styrene (h.v.), the yellow liquid was purified by FC (CH_2Cl_2): 9.2 g (31%) of **9d**. Colourless liquid. B.p. 120–124°/3.6 Torr. n_D^{18} = 1.527. IR (film): 2969, 2933, 2875, 1467, 1456, 758, 700. ^{1}H-NMR ($CDCl_3$): 1.17, 1.18 (2*d*, J = 6.6, Me_2CH); 2.74 (*m*, Me_2CH); 2.89, 3.36 (2*m*, 2 H–C(4)); 5.51 (*m*, H–C(5)); 7.16–7.36 (*m*, 5 arom. H). ^{13}C-NMR ($CDCl_3$): 20.1 (Me_2CH); 27.9 (Me_2CH); 43.2 (C(4)); 81.2 (C(5)); 125.6, 127.9, 128.6, 141.4 (arom. C); 163.0 (C(3)). EI-MS: 189 (37, $[M - H]^+$), 188 (25, $[M - 2H]^+$), 174 (7, $[M - H - Me]^+$), 128 (13), 117 (12), 112 (17), 105 (54), 104 (100), 91 (15).

rac-*1,3*-syn-*3-Amino-4-methyl-1-phenylpentan-1-ol* (**16d**). A soln. of **9d** (8.7 g, 46 mmol) in dry Et_2O (40 ml) was added within 30 min to a stirred suspension of $LiAlH_4$ (2.47 g, 65 mmol) in dry Et_2O (180 ml) at −15°. The mixture was allowed to come to r.t. in 1.5 h and stirred for 16 h. After cooling (−5°), 1.4M H_2SO_4 (152 ml, 213 mmol) was added dropwise with shaking and the mixture filtrated through *Celite*. The *Celite* was washed with H_2O (2 × 100 ml) and the aq. phase extracted with Et_2O (2 × 60 ml). Solid KNa(tartrate) · 4 H_2O (62 g, 220 mmol) was added to the aq. phase, and the suspension was made strongly alkaline (pH 12) with 10% NaOH soln. (*ca.* 130 ml). The resulting clear soln. was extracted with CH_2Cl_2 (4 × 60 ml) and the combined org. phase washed with 10% NaOH soln. (70 ml), dried, and evaporated: 7.02 g (79%) of **16d**. Yellow oil. IR (film): 3374, 3332, 2958, 700. ^{1}H-NMR ($CDCl_3$): 0.83, 0.87 (2*d*, J = 6.6, Me_2CH); 1.40 (*m*, 1 H–C(2)); 1.56 (*m*, H–C(4)); 1.71 (*m*, 1 H–C(2)); 2.83 (*m*, H–C(3)); 3.20 (br. *s*, OH, NH_2); 4.87 (*m*, H–C(1)); 7.19–7.39 (*m*, 5 arom. H). ^{13}C-NMR ($CDCl_3$): 16.9, 18.6 (Me_2CH); 35.3 (C(4)); 42.2 (C(2)); 58.4 (C(3)); 75.7 (C(1)); 125.6, 126.9, 128.2, 145.5 (arom. C). EI-MS: 150 (17, $[M - (i\text{-Pr})]^+$), 107 (18, $PhCHOH^+$).

rac-*1,3*-syn-*4-Methyl-1-phenyl-3-(tosylamino)pentan-1-ol* (**7f**). From **16d** according to the *General Procedure 1*. Purification by FC (CH_2Cl_2/MeOH 100:2): 6.25 g (60%) of **7f**. Pale yellow oil. IR (film): 3494, 3286, 2962, 1320, 1158. ^{1}H-NMR ($CDCl_3$): 0.69, 0.74 (2*d*, J = 6.6, Me_2CH); 1.71 (*m*, 2 H–C(2)); 1.86 (*m*, H–C(4)); 2.41 (MeC_6H_4); 2.56 (*d*, J = 3.7, OH); 3.23 (*m*, H–C(3)); 4.50 (*m*, H–C(1)); 5.44 (*d*, J = 7.3, NH); 7.15–7.78 (*m*, 9 arom. H). ^{13}C-NMR ($CDCl_3$): 16.9, 17.9 (Me_2CH); 21.5 (MeC_6H_4); 31.2 (C(4)); 39.0 (C(2)); 57.9 (C(3)); 73.0 (C(1)); 125.8, 127.3, 127.8, 128.5, 129.6, 137.9, 143.2, 144.2 (arom. C).

*(2S,4RS)-4-Hydroxy-*N,N*-dimethyl-4-phenyl-2-(tosylamino)butanamide* (**7g**). A suspension of **13** (5.29 g, 14.1 mmol) in 96% EtOH (100 ml) was treated with $NaBH_4$ (2.1 g, 55 mmol). After stirring for 2 h at r.t., the solvent was evaporated the residue taken up in H_2O (80 ml), and 2N HCl added to the cooled (0°) soln. until foaming ceased. The mixture was extracted with CH_2Cl_2 (4 × 30 ml) and the combined org. phase extracted with 3% $NaHCO_3$ soln., dried and evaporated. Removal of remaining solvent traces (h.v.) yielded 5.25 g (99%) of **7gA**/**7gB** 1.3:1 (by ^{1}H-NMR). White solid. M.p. 44–50°. $[\alpha]_D^{20}$ = +57 (c = 1, $CHCl_3$). IR (KBr): 3415, 3350, 1641, 1336, 1159. ^{1}H-NMR ($CDCl_3$): **7gA**: 1.69, 1.81, 1.97 (3*m*, 2 H–C(3) (**7gA**/**7gB**)); 2.40 (*s*, MeC_6H_4); 2.59, 2.79 (2*s*, Me_2N); 3.47 (*d*, J = 4.4, OH); 4.39 (*m*, H–C(2)); 5.03 (*m*, H–C(4)); 6.11 (*d*, J = 8.8, NH); 7.14–7.69 (*m*, 9 arom. H (**7gA**/**7gB**)); **7gB**: 2.38 (*s*, MeC_6H_4); 2.53, 2.58 (2*s*, Me_2N); 3.27 (*s*, OH); 4.08 (*m*, H–C(2)); 4.73 (*m*, H–C(4)); 6.08 (*d*, J = 8.8, NH). ^{13}C-NMR ($CDCl_3$): 21.5 (MeC_6H_4); 35.5, 35.7, 36.4, 36.5 (Me_2N); 42.7 (C(3)); 50.4 (C(2)); 69.2, 70.5 (C(4)); 125.5, 126.1, 127.3, 127.8, 128.4, 128.5, 129.4, 129.5, 136.1, 136.7, 143.5, 143.8 (arom. C); 170.6, 170.7 (C(1)).

General Procedure 2: Preparation of Silyl Ethers **17a–c**. A mixture of alcohol **7a–c** (30 mmol), (*t*-Bu)Me_3SiCl (5.43 g, 36 mmol), 1*H*-imidazole (5.11 g, 75 mmol), and dry DMF (30–50 ml) was stirred at r.t. overnight. H_2O (200 ml) was added and the mixture extracted with Et_2O (3–4 × 80 ml). The combined org. phase was dried, evaporated, and residual solvent removed (h.v.). For further purification, see below.

*Methyl (2S,4RS)-4-[(*tert*-Butyl)dimethylsilyloxy]-4-phenyl-2-(tosylamino)butanoate* (**17a**). From **7a** (diastereoisomer mixture). Purification by FC (CH_2Cl_2): 12.46 g (87%) of **17aA**/**17aB** 1.7:1 (by ^{1}H-NMR). Colourless resin. IR (film): 3273, 2955, 2929, 2888, 2857, 1744, 1344, 1163. ^{1}H-NMR ($CDCl_3$): **17aA**: –0.27, 0.09 (2*s*, MeSi); 0.82 (*s*, Me_3CSi); 1.81–2.16 (*m*, 2 H–C(3) of (**17aA**/**17aB**)); 2.41 (*s*, MeC_6H_4 (**17aA**/**17aB**)); 3.49 (*s*, MeO); 3.9 (*m*, H–C(2)); 4.77 (*m*, H–C(4)); 5.30 (*d*, J = 8.1, NH); 7.15–7.69 (*m*, 9 arom. H (**17aA**/**17aB**)); **17aB**: –0.28, 0.0 (2*s*, MeSi); 0.88 (*s*, Me_3CSi); 3.41 (*s*, MeO); 4.09 (*m*, H–C(2)); 4.85 (*m*, H–C(4)); 5.65 (*d*, J = 8.8, NH). ^{13}C-NMR ($CDCl_3$): –5.2, –4.9, –4.6, –4.5 (MeSi); 18.0 (Me_3CSi); 25.8 (Me_3CSi); 21.5 (MeC_6H_4); 43.1,43.5 (C(3)); 52.2, 52.4, 53.1, 53.6 (C(2), Me); 71.6, 72.1 (C(4)); 126.1, 126.3, 127.3, 127.4, 127.6, 128.2, 128.3, 129.5, 129.6, 136.5, 136.8, 143.4, 143.5, 143.7 (arom. C); 171.9 (C(1)).

tert-Butyl *(2S,4RS)-4-[(*tert*-Butyl)dimethylsilyloxy]-4-phenyl-2-(tosylamino)butanoate* (**17b**). From **7b** (diastereoisomer mixture). The crude **17bA**/**17bB** (15.59 g (100); 1.1:1 mixture by ^{1}H-NMR; colourless resin) was used in the next step without further purification. IR (film): 3276, 2956, 2930, 2890, 2858, 1730, 1345, 1157. ^{1}H-NMR ($CDCl_3$): **17bA**: –0.32, 0.11 (2*s*, MeSi); 0.88 (*s*, Me_3C); 1.23 (*s*, Me_3CO); 1.71 (*m*, 1 H–C(3)); 1.89–2.05 (*m*, 1 H–C(3) and 2 H–C(3) of **17bB**); 2.38 (*s*, MeC_6H_4 (**17bA**/**17bB**)); 3.97 (*m*, H–C(2)); 4.83 (*m*, H–C(4)); 5.47 (*d*, J = 9.6, NH); 7.20–7.69 (*m*, 9 arom. H (**17bA**/**17bB**)); **17bB**: –0.23, 0.0 (2*s*, MeSi); 0.82 (*s*, Me_3Si); 1.21 (*s*, Me_3CO); 3.72 (*m*, H–C(2)); 4.76 (*m*, H–C(4)); 5.12 (*d*, J = 8.8, NH). ^{13}C-NMR ($CDCl_3$): –4.9, –4.3 (MeSi); 18.1 (Me_3CSi); 21.5 (MeC_6H_4); 25.9 (Me_3CSi); 27.6, 27.7 (Me_3CO); 44.4, 44.6 (C(3)); 53.7, 54.2 (C(2)); 72.1 (C(4)); 82.0, 82.4 (Me_3CO); 126.1, 126.5, 127.5, 127.6, 128.3, 129.6, 136.8, 136.9, 143.4, 143.5, 143.8, 143.9 (arom. C); 170.7 (C(1)).

rac-*1,3*-syn-*1-[(*tert*-Butyl)dimethylsilyloxy]-4,4-dimethyl-1-phenyl-3-(tosylamino)pentane* (**17c**). From **7c**. The crude product (13.75 g, 96%) was used in the next step without further purification. M.p. 116–118°. IR (KBr): 3307, 2955, 2928, 2885, 2855, 1339, 1158. ^{1}H-NMR ($CDCl_3$): –0.24, –0.06 (2*s*, MeSi); 0.60 (*s*, *t*-Bu); 0.82 (*s*, Me_3CSi); 1.65, 2.03 (2*m*, 2 H–C(2)); 2.42 (*s*, MeC_6H_4); 2.89 (*m*, H–C(3)); 4.43 (*d*, J = 9.5, NH); 4.70 (*m*, H–C(1)); 7.21–7.81 (*m*, 9 arom. H). ^{13}C-NMR ($CDCl_3$): –4.9, –4.6 (MeSi); 18.1 (Me_3CSi); 21.5 (MeC_6H_4); 25.8, 26.2 (Me_3CO, Me_3CSi); 34.9 (C(4)); 44.4 (C(2)); 59.3 (C(3)); 72.5 (C(1)); 127.0, 127.1, 127.3, 128.0, 129.5, 139.3, 143.0, 144.1 (arom. C). EI-MS: 418 (27, $[M - (t\text{-Bu})]^+$), 314 (26), 228 (24), 221 (54, $PhCHOSiMe_2(t\text{-Bu})^+$), 155 (19, Ts^+), 149 (20), 131 (29, $OSiMe_2(t\text{-Bu})^+$), 100 (62), 91 (93, $C_7H_7^+$).

General Procedure 3: Alkylation of Tosylamides **7d–h** *and* **17a–c** *with Benzyl Bromoacetate*. To a stirred soln. of **7d–h** or **17a–c** in dry DMF was added KO(*t*-Bu) (1.0 equiv.) in portions at r.t. or below. Stirring was continued for 30–60 min or until all of the KO(*t*-Bu) was dissolved. Freshly distilled benzyl bromoacetate (1.0–1.2 equiv.) was added and the mixture stirred overnight. Crushed ice was added and the mixture repeatedly extracted with Et_2O. The combined org. phase was dried, evaporated, residual solvent removed (h.v.), and the residue purified as outlined below.

Methyl (2S,4RS)-2-{N-[(Benzyloxycarbonyl)methyl]-N-tosylamino}-4-hydroxy-4-phenylbutanoate (**19a**). *Methyl (2S,4RS)-2-{N-[(Benzyloxycarbonyl)methyl]-N-tosylamino}-4-[(*tert*-butyl)dimethylsilyloxy]-4-phenylbutanoate* (**18a**) was prepared from **17a** (diastereoisomer mixture, 15.15 mmol), DMF (50 ml), and benzyl bromoacetate (17 mmol) at r.t. Workup afforded a complex mixture of non-reacted **17a** with **18a** (both as a diastereoisomer mixture) which could not be separated by FC and was used directly in the next step. The mixture **17a**/**18a** was dissolved in MeCN (80 ml) and treated with 40% aq. HF soln. (15 ml). After stirring for 20 h at r.t., H_2O (150 ml) and CH_2Cl_2 (150 ml) were added. The aq. phase was extracted with CH_2Cl_2 (80 ml) and the combined org. phase dried and evaporated. Purification by FC (CH_2Cl_2/MeOH 100:2): 4.57 g (59% rel. to **17a**) of **19a** (1.7:1 diastereoisomer mixture). Pale yellow resin. IR (film): 3526, 1785, 1738, 1344, 1158.

tert-*Butyl (2S,4RS)-2-{N-[(Benzyloxycarbonyl)methyl]-N-tosylamino}-4-[(*tert*-butyl)dimethylsilyloxy]-4-phenylbutanoate* (**18b**). From **17b** (diastereoisomer mixture, 16.6 mmol), DMF (35 ml), and benzyl bromoacetate (16.6 mmol) at r.t. Workup and purification by FC (CH_2Cl_2) yielded 6.72 g (60%) of **18bA**/**18bB** 1.1:1 (by ^{1}H-NMR). Colourless resin. IR (film): 2956, 2930, 2890, 2856, 1756, 1734, 1348, 1160, 1150. ^{1}H-NMR ($CDCl_3$): **18bA**: −0.34, 0.14 (2*s*, MeSi); 0.88 (*s*, Me_3CSi); 1.21 (*s*, Me_3CO); 1.69, 2.05 (2*m*, 2 H–C(3)); 2.37 (*s*, MeC_6H_4); 4.00, 4.03 (2*d*, *J* = 16.5, CH_2N); 4.56 (*m*, H–C(2)); 4.99 (*m*, H–C(4)); 5.06–5.12 (*m*, $PhCH_2O$ (**18bA**/**18bB**)); 7.16–7.81 (*m*, 14 arom. H **18bA**/**18bB**); **18bB**: −0.32, −0.03 (2*s*, MeSi); 0.83 (*s*, Me_3CSi); 1.31 (*s*, Me_3CO); 1.98 (*m*, 2 H–C(3)); 2.39 (*s*, MeC_6H_4); 4.21, 4.25 (2*d*, *J* = 12.5, CH_2N); 4.42 (*m*, H–C(2)); 4.62 (*m*, H–C(4)). ^{13}C-NMR ($CDCl_3$): −5.4, −5.1, 4.2 (MeSi); 18.0, 18.1 (Me_3CSi); 21.5 (MeC_6H_4); 25.8, 25.9 (Me_3CSi); 27.7, 27.8 (Me_3CO); 42.0, 42.6, 45.8, 46.6 (CH_2N, C(3)); 57.0 (C(2)); 67.0, 67.1 ($PhCH_2O$); 71.0, 71.9 (C(4)); 81.9, 82.3 (Me_3CO); 126.2, 126.4, 127.4, 127.5, 127.6, 128.1, 128.2, 128.4, 128.5, 128.6, 129.5, 129.6, 135.3, 135.5, 136.1, 143.5, 144.1, 144.4 (arom. C); 169.5, 169.8, 169.9, 170.3 (C(1), $COOCH_2Ph$).

tert-*Butyl (2S,4RS)-2-{N-[(Benzyloxycarbonyl)methyl]-N-tosylamino}-4-hydroxy-4-phenylbutanoate* (**19b**). A soln. of **18b** (6.10 g, 9.12 mmol; diastereoisomer mixture) in MeCN (70 ml) was treated with 40% aq. HF soln. (9 ml). After stirring for 3 h at r.t., H_2O (100 ml) and CH_2Cl_2 (100 ml) were added. The aq. phase was extracted with CH_2Cl_2 (100 ml) and the combined org. phase dried and evaporated: 4.85 g (96%) of **19b** (1.1:1 diastereoisomer mixture). Colourless resin. IR (film): 3534, 1753, 1733, 1344, 1155.

rac-*1,3*-syn-*3-{N-[(Benzyloxycarbonyl)methyl]-N-tosylamino}-4,4-dimethyl-1-phenylpentan-1-ol* (**19c**). rac-*1,3*-syn-*3-{N-[(Benzyloxycarbonyl)methyl]-N-tosylamino}-1-[(*tert*-butyl)dimethylsilyloxy]-4,4-dimethyl-1-phenylpentane* (**18c**) was prepared according to the *General Procedure 3* from **17c** (25 mmol), DMF (70 ml), and benzyl bromoacetate (25 mmol) at 0°. Then, 5 h after the addition of benzyl bromoacetate, the temp. was raised to r.t. and stirring was continued for 24 h. Workup afforded a mixture of non-reacted **17c** with **18c** which could not be separated by FC and was used directly in the next step. A soln. of **17c**/**18c** in MeCN (90 ml) was treated with 40% aq. HF soln. (15 ml). After stirring for 3 h at r.t., H_2O (250 ml) and CH_2Cl_2 (80 ml) were added. The aq. phase was extracted with CH_2Cl_2 (2 × 60 ml), the combined org. phase dried and evaporated, and the residue recrystallized from toluene: 5.32 g of pure **7c**. The mother liquor was evaporated and purified by FC (CH_2Cl_2/MeOH 200:3): 0.76 g of **7c** and 2.67 g (21% rel. to **17c**) of **19c** as an oil. **19c**: IR (film): 3503, 1755, 1332, 1153. ^{1}H-NMR ($CDCl_3$): 0.70 (*s*, *t*-Bu); 1.82, 1.97 (2*m*, 2 H–C(2)); 2.39 (*s*, MeC_6H_4); 3.15 (*d*, *J* = 5.1, OH); 3.71 (*m*, H–C(3)); 3.89, 4.25 (2*d*, *J* = 18.4, CH_2N); 4.84 (*m*, H–C(1)); 5.12 (*s*, $PhCH_2O$); 7.19–7.84 (*m*, 14 arom. H). ^{13}C-NMR ($CDCl_3$): 21.6 (MeC_6H_4); 27.5 (*t*-Bu); 36.5 (C(4)); 39.4 (CH_2N); 46.5 (C(2)); 63.9 (C(3)); 67.3 ($PhCH_2O$); 73.2 (C(1)); 125.8, 127.5, 128.4, 128.6, 128.8, 129.3, 135.2, 136.2, 143.9, 144.6, 144.9 (arom. C); 170.0 (COO).

(1RS,3S)-3-{N-[(Benzyloxycarbonyl)methyl]-N-tosylamino}-1-phenyl-4-[(thexyl)dimethylsilyloxy]-butan-1-ol (= *Benzyl N-[1-(Thexyl)dimethylsilyloxymethyl-3-hydroxy-3-phenylpropyl]-N-tosylglycinate*; **19d**). According to the *General Procedure 3* from **7d** (4.69 mmol; diastereoisomer mixture), DMF (30 ml), and benzyl bromoacetate (4.86 mmol) at r.t. Workup and purification by FC (CH_2Cl_2/MeOH 100:2) gave 2.26 g (77%) of **19d** (1:1 diastereoisomer mixture). Colourless resin. IR (film): 3466, 2958, 2866, 1756, 1338, 1156.

rac-*1,3*-syn-*3-{N-[(Benzyloxycarbonyl)methyl]-N-tosylamino}-1-phenylbutan-1-ol* (= *Benzyl N-[3-Hydroxy-1-methyl-3-phenylpropyl]-N-tosylglycinate*; **19e**). According to the *General Procedure 3* from **7e** (15 mmol), DMF (30 ml), and benzyl bromoacetate at 0°. Workup and purification by FC (CH_2Cl_2/MeOH 200:3) followed by treatment with Et_2O/hexane 4:1 gave 4.42 g (63%) of **19e**. White solid. M.p. 93–97°. IR (KBr): 3539, 1732, 1325, 1151. ^{1}H-NMR ($CDCl_3$): 0.97 (*d*, *J* = 6.6, 3 H–C(4)); 1.64, 1.90 (2*m*, 2 H–C(2)); 2.42 (*s*, MeC_6H_4); 2.52 (*d*, *J* = 3.7, OH); 3.89–4.07 (*m*, H–C(3), CH_2N); 4.65 (*m*, H–C(1)); 5.19 (*s*, $PhCH_2O$); 7.22–7.82 (*m*, 14 arom. H). ^{13}C-NMR ($CDCl_3$): 18.2 (C(4)); 21.6 (MeC_6H_4); 43.8, 44.6 (C(2), CH_2N); 51.6 (C(3)); 67.4 ($PhCH_2O$); 71.8 (C(1)); 125.9, 127.6, 127.8, 128.5, 128.6, 129.6, 135.2, 136.9, 143.6, 144.4 (arom. C); 170.3 (COO).

rac-*1,3*-syn-*3-{N-[(Benzyloxycarbonyl)methyl]-N-tosylamino}-4-methyl-1-phenylpentan-1-ol* (= *Benzyl N-[3-Hydroxy-1-isopropyl-3-phenylpropyl]-N-tosylglycinate*; **19f**). According to the *General Procedure 3* from **7f**

(17.9 mmol), DMF (90 ml), and benzyl bromoacetate (18 mmol) at r.t. Workup and purification by FC (CH_2Cl_2/MeOH 200:3): 3.9 g (44%) of **19f**. Colourless resin. IR (film): 3517, 1963, 1755, 1341, 1154. ^{1}H-NMR ($CDCl_3$): 0.54, 0.81 (2*d*, J = 6.6, Me_2CH); 1.60 (*m*, H–C(4)); 1.86 (*m*, 2 H–C(2)); 2.40 (*s*, MeC_6H_4); 2.90 (*d*, J = 4.4, OH); 3.53 (*m*, H–C(3)); 3.95, 4.02 (2*d*, J = 17.6, CH_2N); 4.76 (*m*, H–C(1)); 5.17 (*s*, PhCH_2O); 7.21–7.81 (*m*, 14 arom. H). ^{13}C-NMR ($CDCl_3$): 19.7, 20.0 (Me_2CH); 21.6 (MeC_6H_4); 32.1 (C(4)); 41.3, 45.4 (C(2), CH_2N); 61.8 (C(3)); 67.4 (PhCH_2O); 72.5 (C(1)); 125.8, 127.5, 128.3, 128.4, 128.5, 128.6, 129.4, 135.2, 136.6, 143.7, 144.7 (arom. C); 170.2 (CO).

*(S)-2-{N-[(Benzyloxycarbonyl)methyl]-*N*-tosylamino}-*N*,*N*-dimethyl-4-oxo-4-phenylbutanamide* (= *Benzyl* N-{*1-[(Dimethylamino)carbonyl]-3-oxo-3-phenylpropyl*}-N-*tosylglycinate*; **5g**). *(2S,4RS)-2-{N-[(Benzyloxycarbonyl)methyl]-*N*-tosylamino}-4-hydroxy-*N*,*N*-dimethyl-4-phenylbutanamide* (= *Benzyl* N-{*1-[(Dimethylamino)carbonyl]-3-hydroxy-3-phenylpropyl*}-N-*tosylglycinate*; **19g**) was prepared according to the *General Procedure 3* from **7g** (7.5 mmol, diastereoisomer mixture), DMF (20 ml), and benzyl bromoacetate (7.5 mmol) at r.t. Workup afforded a mixture of non-reacted **19g** and **7g** (both as a diastereoisomer mixture) which was used in the next step without further purification. Crude **19g** was dissolved in dry CH_2Cl_2 (50 ml), and *Dess-Martin* periodinane [11] (3.82 g, 9 mmol) was added. After stirring for 1 h at r.t., Et_2O (90 ml) and sat. $NaHCO_3$ soln. (70 ml, containing 25 g $Na_2S_2O_3 \cdot 5\ H_2O$/100 ml) were added, and stirring was continued for 20 min. The org. phase was extracted with 5% $NaHCO_3$ soln. (70 ml) and H_2O (70 ml), dried, and evaporated. Purification by FC (CH_2Cl_2/MeOH 100:2): 1.96 g (50% rel. to **7g**) of **5g**. Colourless resin. IR (film): 1756, 1680, 1648, 1346, 1161. $[\alpha]_D^{20} = -43.6$ (c = 1, $CHCl_3$). ^{1}H-NMR ($CDCl_3$): 2.35 (*s*, MeC_6H_4); 2.69 (*m*, 1 H–C(3)); 2.75, 3.09 (2*s*, Me_2N); 3.79 (*m*, 1 H–C(3)); 4.14, 4.32 (2*d*, J = 18.1, CH_2N); 5.09, 5.14 (2*d*, J = 12.3, PhCH_2O); 5.31 (*m*, H–C(2)); 7.22–7.76 (*m*, 14 arom. H). ^{13}C-NMR ($CDCl_3$): 21.5 (MeC_6H_4); 36.1, 37.2 (Me_2N); 38.7 (CH_2N); 45.5 (C(3)); 51.3 (C(2)); 67.1 (PhCH_2O); 127.7, 127.9, 128.3, 128.4, 128.6, 129.8, 133.4, 135.4, 136.0, 136.5, 144.2 (arom. C); 168.2, 169.3 (C(1), CH_2COO). EI-MS: 450 (2, $[M - CONMe_2]^+$), 184 (8, $TsNHCH_2^+$), 155 (19, Ts^+), 105 (99, $PhCO^+$), 91 (100, $C_7H_7^+$).

rac-*1,3-syn-3-{N-[(Benzyloxycarbonyl)methyl]-*N*-tosylamino}-1,3-diphenylpropan-1-ol* (= *Benzyl* N-*[3-Hydroxy-1,3-diphenylpropyl]-*N*-tosylglycinate*; **19h**). According to the *General Procedure 3* from rac-*1,3-syn-3-(tosylamino)-1,3-diphenylpropanol* (**7h**) [21] (6.5 mmol), DMF (25 ml), and benzyl bromoacetate (7 mmol) at r.t. (17 h) and 80° (4 h). Workup and purification by FC (CH_2Cl_2/MeOH 100:2): 2.06 g (60%) of **19h**. Colourless resin. IR (film): 3507, 1755, 1333, 1154.

*Methyl (S)-2-{N-[(Benzyloxycarbonyl)methyl]-*N*-tosylamino}-4-oxo-4-phenylbutanoate* (**5a**). A soln. of DMSO (1.21 ml, 17 mmol) in dry CH_2Cl_2 (3 ml) was added dropwise to a cooled ($< -60°$) soln. of oxalyl chloride (0.69 ml, 8 mmol) in CH_2Cl_2 (15 ml) under Ar. After stirring for 30 min, a soln. of **19a** (3.35 g, 6.55 mmol; diastereoisomer mixture) in CH_2Cl_2 (15 ml) was added below $-60°$. Stirring was continued for 45 min, and Et_3N (4.74 ml, 34 mmol) was added. After the addition, the mixture was allowed to come to r.t., and H_2O (40 ml) was added. The aq. phase was extracted with CH_2Cl_2 (2 × 15 ml) and the combined org. phase washed with 2N HCl and 3% $NaHCO_3$ soln., dried, and evaporated. Purification by FC (CH_2Cl_2/MeOH 100:1) followed by treatment with Et_2O/hexane 2:1 gave 2.21 g (66%) of **5a**, optically pure (ee > 98%; HPLC). White solid. M.p. 91–97°. HPLC (*Daicel-Chiralcel-OD* column, hexane/i-PrOH 80:20, detection at 220 nm): t_R of *rac*-**5a**: 23.3 (*S*) and 28.5 min (*R*). $[\alpha]_D^{18} = -27.5$ (c = 0.5, $CHCl_3$). IR (KBr): 1748, 1724, 1670, 1342, 1160. ^{1}H-NMR ($CDCl_3$): 2.39 (*s*, MeC_6H_4); 3.52 (*s*, MeO); 3.49 (*m*, 1 H–C(3)); 3.79 (*m*, 1 H–C(3)); 4.25, 4.29 (2*d*, J = 18.5, CH_2N); 4.97 (*m*, H–C(2)); 4.99, 5.04 (2*d*, J = 12.2, PhCH_2O); 7.22–7.79 (*m*, 14 arom. H). ^{13}C-NMR ($CDCl_3$): 21.5 (MeC_6H_4); 40.8 (C(3)); 47.5 (CH_2N); 52.4, 55.4 (C(2), MeO); 67.1 (PhCH_2O); 127.7, 128, 128.2, 128.4, 128.5, 129.5, 133.5, 135.2, 135.8, 136.4, 143.8 (arom. C); 170.1, 175.9 (C(1), C$OOCH_2$Ph); 196.7 (PhCO). EI-MS: 450 (1, $[M - COOMe]^+$), 354 (6, $[M - Ts]^+$), 190 (7, $[M - TsNHCH_2CO_2CH_2Ph]^+$), 184 (24, $TsNHCH_2^+$), 155 (54, Ts^+), 131 (9, $PhCOCH{=}CH^+$), 105 (67, $PhCO^+$), 91 (100, $C_7H_7^+$).

tert-*Butyl (S)-2-{N-[(Benzyloxycarbonyl)methyl]-*N*-tosylamino}-4-oxo-4-phenylbutanoate* (**5b**). A mixture of **19b** (4.81 g, 8.69 mmol; diastereoisomer mixture), CH_2Cl_2 (140 ml), pyridinium dichromate (PDC; 4.75 g, 12.62 mmol) was stirred at r.t. for 63 h. The soln. was filtrated through a plug of silica gel (60–200 μm, *Merck*; 20 g) and the latter washed with CH_2Cl_2/MeOH 100:2 (2 × 30 ml). The combined org. phase was extracted with 2N HCl (2 × 40 ml) and H_2O (40 ml), dried, and evaporated. Purification by FC (CH_2Cl_2, then CH_2Cl_2/MeOH 100:2) followed by treatment with Et_2O/hexane 2:1 gave 2.39 g (50%) of **5b**. White solid. M.p. 76–78°. $[\alpha]_D^{17} = -30.8$ (c = 1, $CHCl_3$). IR (KBr): 1748, 1723, 1679, 1343, 1154. ^{1}H-NMR ($CDCl_3$): 1.25 (*s*, Me_3CO); 2.39 (MeC_6H_4); 3.49, 3.73 (2*m*, 2 H–C(3)); 4.25, 4.26 (2*d*, J = 19.1, CH_2N); 4.85 (*m*, H–C(2)); 5.01, 5.04 (2*d*, J = 11.8, PhCH_2O); 7.25–7.79 (*m*, 14 arom. H). ^{13}C-NMR ($CDCl_3$): 21.5 (MeC_6H_4); 27.6 (Me_3CO); 41.0, 47.4 (C(3), CH_2N); 56.3 (C(2)); 67.1 (PhCH_2O); 82.4 (Me_3CO); 127.7, 128.0, 128.2, 129.5, 133.3, 135.2, 136.0, 136.6, 143.7 (arom. C); 168.5, 169.8 (C(1), CH_2COO); 196.8 (PhCO). EI-MS: 450 (1, $[M - COO(t\text{-}Bu)]^+$), 210 (3), 184 (4, $TsNHCH_2^+$), 155 (10, Ts^+), 105 (100, $PhCO^+$), 91 (76, $C_7H_7^+$).

rac-*3*-{N-*[(Benzyloxycarbonyl)methyl]*-N-*tosylamino*}-*4,4-dimethyl-1-phenylpentan-1-one* (= *Benzyl* N-*[1-(*tert-*Butyl)-3-oxo-3-phenylpropyl)*-N-*tosylglycinate*; **5c**) was prepared similarly to **5a** from **19c** (5 mmol). Purification by FC (CH_2Cl_2) and treatment with Et_2O/hexane 2:1 gave 1.95 g (77%) of **5c**. White solid. M.p. 87–92°. IR (KBr): 2957, 1755, 1685, 1342, 1158. ^{1}H-NMR ($CDCl_3$): 0.88 (*s*, Me_3C); 2.24 (*s*, MeC_6H_4); 2.41 (*m*, 1 H–C(2)); 3.19 (*m*, 1 H–C(2)); 3.76, 4.06 (2*d*, *J* = 18.4, CH_2N); 4.55 (*m*, H–C(3)); 5.20 (*s*, PhCH_2O); 7.11–7.78 (*m*, 14 arom. H). ^{13}C-NMR ($CDCl_3$): 21.4 (MeC_6H_4); 27.0 (Me_3C); 36.4 (Me_3C); 37.6 (CH_2N); 47.8 (C(2)); 60.7 (C(3)); 67.3 (PhCH_3O); 127.8, 128.3, 128.4, 128.5, 129.4, 133.2, 135.2, 135.3, 136.5, 143.7 (arom. C); 169.4 (COO); 195.9 (C(1)). EI-MS: 450 (22, $[M - (t\text{-Bu})]^+$), 155 (8, Ts^+), 105 (100, $PhCO^+$), 91 (60, $C_7H_7^+$).

(S)-3-{N-*[(Benzyloxycarbonyl)methyl]*-N-*tosylamino*}-*1-phenyl-4-[(thexyl)dimethylsilyloxy]butan-1-one* (= *Benzyl* N-{*3-Oxo-3-phenyl-1-[(thexyl)dimethylsilyl]propyl*}-N-*tosylglycinate*; **5d**) was prepared similarly to **5a** from **19d** (3.55 mmol). Purification by FC (CH_2Cl_2): 2.01 g (91%) of **5d**. Pale yellow resin. $[\alpha]_D^{25} = -2.1$ (*c* = 1, $CHCl_3$). IR (film): 2958, 2869, 1755, 1684, 1340, 1157. ^{1}H-NMR ($CDCl_3$): −0.24, −0.18 (2*s*, MeSi); 0.55, 0.56 (2*s*, C(Me)$_2$Si); 0.59 (*d*, *J* = 7.3, Me_2CH); 1.33 (*m*, Me_2CH); 2.22 (*s*, MeC_6H_4); 3.00, 3.35 (2*m*, 2 H–C(2)); 3.64 (*m*, 2 H–C(4)); 4.19 (*m*, H–C(3)); 4.23, 4.29 (2*d*, *J* = 18.4, CH_2N); 5.02, 5.07 (2*d*, *J* = 12.1, PhCH_2O); 7.05–7.65 (*m*, 14 arom. H). ^{13}C-NMR ($CDCl_3$): −4.0, −3.7 (MeSi); 18.3, 18.4, 20.0, 20.1 (Me_2CHC(Me)$_2$Si); 21.5 (MeC_6H_4); 24.9 (*C*(Me)$_2$Si); 33.9 (Me_2CH); 38.2 (C(2)); 46.8 (CH_2N); 55.0 (C(3)); 64.1 (C(4)); 67.0 (PhCH_2O); 124.4, 127.6, 127.9, 128.3, 128.4, 128.5, 128.6, 129.5, 133.2, 135.4, 136.4, 137.1, 143.4 (arom. C); 170.2 (CH_2COO); 197.2 (PhCO).

rac-*3*-{N-*[(Benzyloxycarbonyl)methyl]*-N-*tosylamino*}-*1-phenylbutan-1-one* (= *Benzyl* N-*(1-Methyl-3-oxo-3-phenylpropyl)*-N-*tosylglycinate*; **5e**) was prepared similarly to **5b** from **19e** (7.9 mmol), CH_2Cl_2 (60 ml), and PDC (14.7 mmol). After stirring at r.t for 40 h, the solvent was removed and the residue extracted with Et_2O (3 × 60 ml). Filtration through silica gel, washing with 2N HCl and H_2O followed by FC (CH_2Cl_2/MeOH 300:1) and treatment with Et_2O/hexane 2:1 gave 3.16 g (86%) of **5e**. White solid. M.p. 74–77°. IR (KBr): 1734, 1681, 1334, 1150. ^{1}H-NMR ($CDCl_3$): 1.12 (*d*, *J* = 6.7, 3 H–C(4)); 2.38 (*s*, MeC_6H_4); 2.98 (*m*, 1 H–C(2)); 3.40 (*m*, 1 H–C(2)); 4.15, 4.19 (2*d*, *J* = 18.3, CH_2N); 4.35 (*m*, H–C(3)); 5.18 (*s*, PhCH_2O); 7.21–7.81 (*m*, 14 arom. H). ^{13}C-NMR ($CDCl_3$): 18.4 (C(4)); 21.5 (MeC_6H_4); 44.6, 45.0 (C(2), CH_2N); 50.6 (C(3)); 67.3 (PhCH_2O); 127.7, 128.1, 128.4, 128.5, 128.6, 128.7, 129.6, 133.3, 135.2, 136.3, 137.1, 143.5 (arom. C); 170.0 (CH_2COO); 197.2 (C(1)). EI-MS: 310 (11, $[M - Ts]^+$), 184 (5, $TsNHCH_2^+$), 155 (13, Ts^+), 105 (80, $PhCO^+$), 91 (100, $C_7H_7^+$).

rac-*3*-{N-*[(Benzyloxycarbonyl)methyl]*-N-*tosylamino*}-*4-methyl-1-phenylpentan-1-one* (= *Benzyl* N-*(1-Isopropyl-3-oxo-3-phenylpropyl)*-N-*tosylglycinate*; **5f**) was prepared from **19f** (7.73 mmol), CH_2Cl_2 (65 ml), and PDC (14.8 mmol) as described for **5e** (reaction time: 4 d). Purification by FC (CH_2Cl_2/MeOH 200:1) gave 2.89 g (76%) of **5f**. Colourless resin. ^{1}H-NMR ($CDCl_3$): 0.70 (*d*, *J* = 6.6, 3 H, Me_2CH); 0.74 (*d*, *J* = 7.3, 3 H, Me_2CH); 1.87 (*m*, H–C(4)); 2.29 (*s*, MeC_6H_4); 3.05–3.25 (*m*, 2 H–C(2)); 4.07 (*m*, H–C(3)); 4.11 (*s*, CH_2N); 5.10 (*s*, PhCH_2O); 7.15–7.76 (*m*, 14 arom. H). ^{13}C-NMR ($CDCl_3$): 19.5, 20.0 (Me_2CH); 21.5 (MeC_6H_4); 31.6 (C(4)); 41.7, 46.3 (C(2), CH_2N); 59.7 (C(3)); 67.1 (PhCH_2O); 127.9, 128.4, 128.5, 129.4, 133.1, 135.3, 136.6, 136.8, 143.4 (arom. C); 169.9 (COO); 197.0 (C(1)). EI-MS: 450 (3, $[M - (i\text{-Pr})]^+$), 338 (1, $[M - Ts]^+$), 155 (13, Ts^+), 105 (100, $PhCO^+$), 91 (91, $C_7H_7^+$).

rac-*3*-{N-*[(Benzyloxycarbonyl)methyl]*-N-*tosylamino*}-*1,3-diphenylpropan-1-one* (= *Benzyl* N-*(3-Oxo-1,3-di-phenylpropyl)*-N-*tosylglycinate*; **5h**) was prepared from **19h** (4.9 mmol), CH_2Cl_2 (40 ml), and PDC (7.4 mmol) as described for **5e** (reaction time: 24 h). Purification by FC (CH_2Cl_2/MeOH 200:1) followed by treatment of the non-reacted **19h** in the same way gave 1.91 g (74%) of **5h**. Pale yellow resin. IR (film): 1752, 1685, 1339, 1153. ^{1}H-NMR ($CDCl_3$): 2.40 (MeC_6H_4); 3.59 (*m*, 1 H–C(2)); 3.69 (*d*, *J* = 18.3, CH_2N); 3.90 (*m*, 1 H–C(2)); 4.13 (*d*, *J* = 18.3, CH_2N); 5.04, 5.08 (each *d*, *J* = 12.2, PhCH_2O); 5.60 (*m*, H–C(3)); 6.89–7.96 (*m*, 19 arom. H). ^{13}C-NMR ($CDCl_3$): 21.6 (MeC_6H_4); 41.2, 45.9 (C(2), CH_2N); 56.8 (C(3)); 67.1 (PhCH_2O); 127.8, 128.0, 128.2, 128.4, 128.5, 128.6, 129.7, 133.3, 135.2, 136.3, 136.5, 137.0, 143.8 (arom. C); 169.9 (COO); 196.6 (PhCO).

*Methyl (S)-2-(*N-*Methyl*-N-*tosylamino)-4-oxo-4-phenylbutanoate* (**6**). NaH (0.45 g, 80% in mineral oil, 15 mmol) was added within 30 min to a soln. of **17a** (3.69 g, 7.72 mmol; diastereoisomer mixture) and MeI (1.87 ml, 30 mmol) in dry DMF (30 ml) at 0°. The mixture was allowed to come to r.t. and stirred for 2.5 h. To the cooled (0°) mixture 2N HCl (15 ml) and H_2O (50 ml) were added. The mixture was extracted with Et_2O (4 × 15 ml) and the combined org. phase extracted with 5% $NaHCO_3$ soln. (20 ml) and 5% $Na_2S_3O_3$ soln. (20 ml), dried, and evaporated. Removal of solvent traces (h.v.) yielded 3.5 g (92%) of crude *methyl (2S,4RS)-4-[(*tert-*butyl)-dimethylsilyloxy]-2-(*N-*methyl*-N-*tosylamino)-4-phenylbutanoate* (diastereoisomer mixture) as a yellow resin, which was used in the next step without further purification. A mixture of the latter (3.43 g), MeCN (25 ml), and 40% aq. HF soln. (2.8 ml) was stirred for 5 h at r.t. H_2O (30 ml) and CH_2Cl_2 (30 ml) were added and the aq. phase extracted with CH_2Cl_2 (10 ml). The combined org. phase was extracted with 3% $NaHCO_3$ soln. (30 ml), dried and

evaporated. FC (CH_2Cl_2/MeOH 100:3) gave 1.66 g (63%) of *methyl (2S,4RS)-4-hydroxy-2-(*N*-methyl-*N*-tosylamino)phenylbutanoate* (diastereoisomer mixture). Oxidation of this alcohol (1.66 g, 4.4 mmol) with *Dess-Martin* periodinane (2.85 g, 6.73 mmol) in dry CH_2Cl_2 (20 ml) and workup as described for **5g** followed by treatment with Et_2O/hexane 2:1 gave 1.48 g (52% rel. to **17a**) of **6**. White solid. M.p. 71–73°. $[\alpha]_D^{16} = -50.9$ ($c = 1$, $CHCl_3$). IR (KBr): 1737, 1677, 1333, 1160. ^{1}H-NMR ($CDCl_3$): 2.39 (*s*, *Me*C_6H_4); 2.85 (*s*, MeN); 3.15 (*m*, 1 H–C(3)); 3.56 (*s*, MeO); 3.76 (*m*, 1 H–C(3)); 5.25 (*m*, H–C(2)); 7.26–7.92 (*m*, 9 arom. H). ^{13}C-NMR ($CDCl_3$): 21.5 (*Me*C_6H_4); 31.8 (MeN); 38.8 (C(3)); 52.3 (C(2)); 56.0 (MeO); 127.4, 127.9, 128.3, 128.6, 133.5, 143.4, 135.9 (arom. C); 170.0 (C(1)); 196.1 (Ph*C*O). EI-MS: 316 (5, $[M - COOMe]^+$), 220 (14, $[M - Ts]^+$), 155 (3, Ts^+), 105 (100, $PhCO^+$), 91 (21, $C_7H_7^+$).

Preparation of **20**–**29**. A soln. of ketone **5a**–**h** or **6** in the appropriate solvent (*ca.* $3.5 \cdot 10^{-3}$ mol/l) was rinsed with dry, O_2-free Ar for 30 min, if not specified otherwise. The stirred soln. was irradiated until practically no starting material was left (monitored by anal. HPLC). After evaporation, the crude photoproducts were separated by FC and purified by FC or HPLC.

*Benzyl (2*R*,3*R*,5*S*)-3-Hydroxy-5-(methoxycarbonyl)-3-phenyl-1-tosylprolinate* (= *1-Benzyl 5-Methyl 3-Hydroxy-3-phenyl-1-tosylpyrrolidine-1,5-dicarboxylate*; **20**). From **5a** (0.8 g) in cyclohexane/benzene 6:4 for 6 h. Non-isolated yield (anal. HPLC): 65%. FC (CH_2Cl_2/MeOH 100:2): 400 mg (50%) of crude **20**. Yellow resin. Treatment with Et_2O/hexane gave 160 mg (20%) of **20**. M.p. 99–103°. $[a]_D^{17} = -19.4$ ($c = 0.1$, $CHCl_3$). IR (KBr): 3477, 1759, 1727, 1354, 1158. ^{1}H-NMR ($CDCl_3$): 2.42 (*s*, *Me*C_6H_4); 2.43 (*m*, 1 H–C(4)); 2.58 (*m*, 1 H–C(4)); 3.56 (*s*, MeO); 4.69 (*m*, H–C(5)); 4.79 (*s*, H–C(2)); 4.83 (*s*, OH); 5.02, 5.12 (2*d*, $J = 12.5$, PhCH_2O); 7.03–7.86 (*m*, 14 arom. H). ^{13}C-NMR ($CDCl_3$): 21.6 (*Me*C_6H_4); 45.3 (C(4)); 52.9 (C(5)); 60.2 (MeO); 67.0 (Ph*C*H_2O); 72.3 (C(2)); 82.5 (C(3)); 125.1, 127.9, 128, 128.3, 128.4, 129.5, 135.1, 140.2, 144.4 (arom. C); 168.1, 173.1 (*C*O–C(2) and *C*O–C(5)). EI-MS: 354 (2, $[M - Ts]^+$), 155 (11, Ts^+), 123 (10), 105 (20, $PhCO^+$), 91 (100, $C_7H_7^+$).

*Benzyl (2*R*,3*R*,5*S*)-5-[(*tert*-Butoxy)carbonyl]-3-hydroxy-3-phenyl-1-tosylprolinate* (= *1-Benzyl 5-(*tert*-Butyl) 3-Hydroxy-3-phenyl-1-tosylpyrrolidine-1,5-dicarboxylate*; **21**). From **5b** (0.9 g) in cyclohexane/benzene 4:6 for 100 h. Non-isolated yield (anal. HPLC): 57%. FC (CH_2Cl_2/MeOH 200:1): 153 mg (17%) of **21**. Yellow resin. Treatment with Et_2O/hexane gave 17 mg (2%) of solid **21**. M.p. 96–99°. $[\alpha]_D^{20} = -42.8$ ($c = 0.25$, $CHCl_3$). IR (KBr): 3351, 1763, 1711, 1334, 1160. ^{1}H-NMR ($CDCl_3$): 1.32 (*s*, Me_3CO); 2.32 (*m*, 1 H–C(4)); 2.43 (*s*, *Me*C_6H_4); 2.65 (*m*, 1 H–C(4)); 4.58 (*m*, H–C(5)); 4.87 (*s*, H–C(2)); 5.04 , 5.18 (2*d*, $J = 12.5$, PhCH_2O); 5.25 (*s*, O*H*); 7.05–7.92 (*m*, 14 arom. H). ^{13}C-NMR ($CDCl_3$): 21.6 (*Me*C_6H_4); 27.6 (*Me*$_3$C); 45.7 (C(4)); 61.1 (C(5)); 66.8 (Ph*C*H_2O); 72.8 (C(2)); 82.5, 83.5 (C(3), Me_3C); 125.2, 127.7, 127.9, 128.2, 128.3, 128.5, 129.6, 135.3, 135.4, 140.2, 144.3 (arom. C); 167.9, 172.2 (*C*O–C(2), *C*O–C(5)). EI-MS: 315 (1, $[M - COO(t\text{-Bu}) - COOMe]^+$), 155 (3, Ts^+), 143 (11), 105 (16, $PhCO^+$), 91 (49, $C_7H_7^+$), 18 (100).

rac-r-*2-Benzyl* c-*3-Hydroxy*-c-*5-methyl-3-phenyl-1-tosylprolinate* (**23a**), rac-r-*2-Benzyl* c-*3-Hydroxy*-t-*5-methyl-3-phenyl-1-tosylprolinate* (23b), *and Benzyl* N-*Tosylglycinate*. From **5e** (1.2 g) in cyclohexane/benzene 4:6 (the soln. was rinsed with dry air instead of Ar; with Ar, the photolysis was 24 times slower) for 3 h. Non-isolated yields (anal. HPLC): **23a** (20%), **23b** (20%), $TsNHCH_2CO_2Bn$ (24%). FC (CH_2Cl_2/MeOH 100:1) followed by treatment with Et_2O/hexane and recrystallization from 75% aq. MeOH gave 50 mg (4%) of **23a**, 81 mg (7%) of **23b**, and 132 mg (16%) of $TsNHCH_2CO_2Bn$, which was identical in all issues with a prepared authentic sample.

Data of **23a**: M.p. 96–103°. IR (KBr): 3495, 1748, 1334, 1159. ^{1}H-NMR ($CDCl_3$): 1.16 (*d*, $J = 6.6$, Me–C(5)); 2.02 (*m*, 1 H–C(4)); 2.41 (*s*, *Me*C_6H_4); 2.64 (*m*, 1 H–C(4)); 3.11 (*s*, OH); 4.20 (*m*, H–C(5)); 4.85 (*s*, H–C(2)); 5.10 (*s*, PhCH_2O); 7.19–7.77 (14 arom. H). ^{13}C-NMR ($CDCl_3$): 20.8 (*Me*–C(5)); 21.6 (*Me*C_6H_4); 48.6 (C(4)); 55.5 (C(5)); 67.3 (Ph*C*H_2O); 69.9 (C(2)); 79.4 (C(3)); 125.2, 127.5, 128.1, 128.3, 128.5, 128.6, 135.2, 137.4, 143.1, 143.5 (arom. C); 170.3 (*C*O–C(2)). EI-MS: 330 (2, $[M - COOCH_2Ph]^+$), 310 (8, $[M - Ts]^+$), 155 (7, Ts^+), 105 (27, $PhCO^+$), 91 (100, $C_7H_7]^+$).

Data of **23b**: M.p. 104–108°. IR (KBr): 3472, 1746, 1332, 1155. ^{1}H-NMR ($CDCl_3$): 1.48 (*d*, $J = 6.6$, Me–C(5)); 2.13 (*m*, 1 H–C(4)); 2.34 (*m*, 1 H–C(4)); 2.39 (*s*, *Me*C_6H_4); 3.09 (*s*, OH); 3.93 (*m*, H–C(5)); 4.59 (*s*, H–C(2)); 5.11, 5.17 (2*d*, $J = 12.5$, PhCH_2O); 7.16–7.68 (*m*, 14 arom. H). ^{13}C-NMR ($CDCl_3$): 21.6 (*Me*C_6H_4); 22.4 (*Me*–C(5)); 47.1 (C(4)); 56.3 (C(5)); 67.3 (Ph*C*H_2O); 70.8 (C(2)); 81.0 (C(3)); 124.9, 127.5, 127.9, 128.1, 128.3, 128.6, 129.6, 135.2, 142.3, 143.7 (arom. C); 170.1 (*C*O–C(2)). EI-MS: 330 (3, $[M - COOCH_2Ph]^+$), 310 (9, $[M - Ts]^+$), 155 (10, Ts^+), 105 (22, $PhCO^+$), 91 (100, $C_7H_7^+$).

rac-r-*2-Benzyl* t-*5-(*tert*-Butyl)*-c-*3-hydroxy-3-phenyl-1-tosylprolinate* (**22**) *and* rac-*4-*{N-*[(Benzyloxycarbonyl)methyl]*-N-*tosylamino*}*-3,3-dimethyl-1-phenylcyclopentan-1-ol* (= *Benzyl* N-*(4-Hydroxy-2,2-dimethyl-4-phenylcyclopentyl)*-N-*tosylglycinate*; **25**). From **5c** (0.8 g) in cyclohexane/benzene 6:4 for 40 h (20% **5c** left). Non-isolated yields (anal. HPLC): **22** (24%), **25** (36%). FC (CH_2Cl_2/MeOH 100:1): 150 mg of impure **25** followed by 188 mg of impure **22**. Purification by semiprep. HPLC (for **22**, CH_2Cl_2/MeOH (686 nm; t_R 12.8 min); for **25**, CH_2Cl_2/MeOH (690 nm; t_R 9.5 min)) gave 60.5 mg (7%) of **22** and 70.5 mg (9%) of **25**.

Data of **22**: Viscous oil. IR (film): 3491, 2935, 1730, 1345, 1156. ^{1}H-NMR ($CDCl_3$): 0.85 (*s*, *t*-Bu); 1.94 (*m*, 1 H–C(4)); 2.32 (*m*, 1 H–C(4)); 2.38 (*s*, *Me*C_6H_4); 4.14 (br. *s*, OH); 4.37 (*m*, H–C(5)); 4.49 (*s*, H–C(2)); 5.02, 5.10 (2*d*, *J* = 11.8, PhCH_2O); 7.04–7.81 (*m*, 14 arom. H). ^{13}C-NMR ($CDCl_3$): 21.5 (*Me*C_6H_4); 26.5 (*Me*$_3$C); 36.0 (Me_3C); 43.9 (C(4)); 68.2 (Ph*C*H_2O); 69.4, 71.1 (C(2), C(5)); 81.2 (C(3)); 124.8, 127.3, 127.5, 127.7, 128.4, 128.6, 128.7, 129.0, 129.4, 134.4, 139.4, 141.9, 142.7 (arom. C); 167.9 (*C*O–C(2)). EI-MS: 450 (1, [*M* – (*t*-Bu)]$^+$), 352 (5, [*M* – Ts]$^+$), 155 (6, Ts$^+$), 105 (45, PhCO$^+$), 91 (100, $C_7H_7^+$).

Data of **25**: Viscous oil. ^{1}H-NMR ($CDCl_3$): 0.99, 1.15 (2*s*, 2 Me–C(3)); 1.90–1.97, 2.15–2.27 (2*m*, 2 H–C(5)); 1.95 (*s*, 2 H–C(2)); 2.39 (*s*, *Me*C_6H_4); 3.97, 4.24 (2*d*, *J* = 18.4, CH_2N); 5.08, 5.13 (2*d*, *J* = 11.8, PhCH_2O); 7.19–7.84 (*m*, 14 arom. H). ^{13}C-NMR ($CDCl_3$): 21.6 (*Me*C_6H_4); 25.4, 30.4 (2 *Me*–C(3)); 41.0 (C(3)); 43.6, 47.1, 55.2 (CH_2N, C(2), C(5)); 65.2 (C(4)); 67.0 (Ph*C*H_2O); 79.3 (C(1)); 124.7, 127.1, 127.9, 128.2, 128.6, 129.4, 135.3, 136.7, 143.5, 146.2 (arom. C); 169.7 (COO). EI-MS: 334 (2, [*M* – H_2O-Ts]$^+$), 184 (2, TsNHCH_2]), 155 (8, Ts$^+$), 105 (41, PhCO$^+$), 91 (100, $C_7H_7^+$).

*Methyl (2*S*,4*R*)-4-Hydroxy-4-phenyl-1-tosylprolinate* (**24a**) *and Methyl (2*S*,4*S*)-4-Hydroxy-4-phenyl-1-tosylprolinate* (**24b**). From **6** (0.5 g) in CH_2Cl_2 for 10 h. Non-isolated yields (anal. HPLC): **24a** (27%), **24b** (48%); de (**24b**) 28%. FC (CH_2Cl_2/MeOH 200:5): 352 mg of impure **24a,b** (diastereoisomer mixture). Separation by prep. HPLC (666 nm; t_R 40 (**24b**) and 46 min (**24a**)) gave 89 mg (18%) of **24a** and 137 mg (27%) of **24b** as resins which were pure (HPLC, NMR). Treatment with Et_2O/hexane yielded the crystalline compounds: 67 mg (13%) of **24a** and 101 mg (20%) of **24b**.

Data of **24a**: M.p. 104–106°. Pale yellow solid. $[\alpha]_D^{17} = -26.1$ (*c* = 0.5, $CHCl_3$). IR (KBr): 3479, 1768, 1341, 1164. ^{1}H-NMR ($CDCl_3$): 2.35 (*m*, 1 H–C(3)); 2.45 (*s*, *Me*C_6H_4); 2.53 (*m*, 1 H–C(3)); 3.49 (*d*, *J* = 9.5, 1 H–C(5)); 3.71 (*dd*, *J* = 9.5, 1.5, 1 H–C(5)); 3.83 (*s*, MeO); 4.24 (*s*, OH); 4.53 (*m*, H–C(2)); 7.26–7.80 (*m*, 9 arom. H). ^{13}C-NMR ($CDCl_3$): 21.6 (*Me*C_6H_4); 43.9 (C(3)); 53.2 (C(2)); 59.3 (MeO); 61.4 (C(5)); 80.1 (C(4)); 125.2, 127.7, 128.0, 128.5, 129.9, 134.2, 140.1, 144.2 (arom. C); 174.2 (*C*O–C(2)). EI-MS: 316 (22, [*M* – COOMe]$^+$), 299 (11), 220 (61, [*M* – Ts]$^+$), 160 (22), 155 (22, Ts$^+$), 144 (60), 105 (100, PhCO$^+$), 91 (90, $C_7H_7^+$).

Data of **24b**: M.p. 114–116°. $[\alpha]_D^{17} = -21.4$ (*c* = 2, $CHCl_3$). IR (KBr): 3516, 1761, 1330, 1155. ^{1}H-NMR ($CDCl_3$): 2.06 (br. *s*, OH); 2.38 (*m*, 1 H–C(3)); 2.42 (*s*, *Me*C_6H_4); 2.53 (*m*, 1 H–C(3)); 3.70 (*dd*, *J* = 11.8, 2.2, 1 H–C(5)); 3.78 (*s*, MeO, and *d*, *J* = 11.8, 1 H–C(5)); 4.60 (*m*, H–C(2)); 7.26–7.82 (*m*, 9 arom. H). ^{13}C-NMR ($CDCl_3$): 21.6 (*Me*C_6H_4); 44.7 (C(3)); 52.6 (C(2)); 60.3 (MeO); 61.0 (C(5)); 80.1 (C(4)); 125.0, 127.8, 128.2, 128.6, 129.5, 134.9, 140.3, 143.8 (arom. C); 172.5 (*C*O–C(2)). EI-MS: 357 (2, [*M* – H_2O]$^+$), 316 (8, [*M* – COOMe]$^+$), 298 (26, [*M* – Ph]$^+$), 220 (37, [*M* – Ts]$^+$), 155 (37, Ts$^+$), 115 (31), 105 (81, PhCO$^+$), 91 (100, $C_7H_7^+$).

3-{N-[(Benzyloxycarbonyl)methyl]-N-tosylamino}-1-phenyl-2-[(thexyl)dimethylsilyloxy]cyclobutanol (= *Benzyl* N-{*3-Hydroxy-3-phenyl-2-[(thexyl)dimethylsilyloxy]cyclobutyl*}-N-*tosylglycinate*; **26**). From **5d** (1.0 g) in Et_2O for 4.5 h. Non-isolated yield (anal. HPLC): 34%. FC (CH_2Cl_2/MeOH 200:3): 147 mg of impure **26**. Purification by semiprep. HPLC (688 nm; t_R 12 min): 89 mg (9%) of **26** (*ca.* 90% pure, impurity not identified). Pale yellow oil. IR (film): 3520, 2958, 2868, 1753, 1345, 1158. ^{1}H-NMR ($CDCl_3$): –0.06, –0.04 (2*s*, MeSi); 0.53 (*s*, C(Me)$_2$Si); 0.59 (*d*, *J* = 6.6, *Me*$_2$CH); 1.33 (*m*, Me$_2$C*H*); 2.01 (*m*, 1 H–C(4)); 2.33 (*s*, OH); 2.38 (*s*, *Me*C_6H_4); 2.62 (*m*, 1 H–C(4)); 3,77 (*m*, H–C(3)); 4.09, 4.18 (2*d*, *J* = 18.4, NCH_2); 4.29 (*d*, *J* = 7.4, H–C(2)); 5.11 (*s*, PhCH_2O); 7.19–7.73 (*m*, 14 arom. H). ^{13}C-NMR ($CDCl_3$): –3.2, –2.2 (MeSi); 18.3, 18.9, 20.0 (Me_2CHC(Me)$_2$Si); 21.6 (*Me*C_6H_4); 24.5 (*C*(Me)$_2$Si); 33.8 (Me$_2$*C*H); 36.6 (C(4)); 46.7 (CH_2N); 54.6 (C(2), C(3)); 67.3 (Ph*C*H_2O); 80.6 (C(1)); 125.8, 126.7, 127.5, 127.9, 128.2, 128.6, 129.2, 129.6, 135.1, 136.8, 140.4, 143.6 (arom. C); 169.3 (COO).

rac-cis- *and* rac-trans-*3-{N-[(Benzyloxycarbonyl)methyl]-N-tosylamino}-2,2-dimethyl-1-phenylcyclobutanol* (= *Benzyl* N-*(3-Hydroxy-2,2-dimethyl-3-phenylcyclobutyl)*-N-*tosylglycinate*; **27a** and **27b**, resp.) *and Benzyl* N-*(2-Methylprop-1-enyl)*-N-*tosylglycinate* (**28**). From **5f** (1 g) in Et_2O for 11 h (15% **5f** left). Non-isolated yields: **27a**/**27b** (38%, diastereoisomer mixture; de (**27b**) 14% (HPLC, NMR)) and **28** (48%). FC (CH_2Cl_2/MeOH 200:3): 311 mg (31%) of **27a**/**27b** (diastereoisomeric mixture) followed by 340 mg (45%) of impure **28**. Purification of **28** by treatment with Et_2O/hexane afforded 303 mg (40%) of **28**. The separation of **27a**/**27b** by semiprep. HPLC was not successful. ^{1}H-NMR ($CDCl_3$): **27a**: 0.60, 1.21 (2*s*, 2 Me–C(2)); 2.29 (*m*, 1 H–C(4)); 2.41 (*s*, *Me*C_6H_4); 2.65 (*s*, OH); 2.89 (*m*, 1 H–C(4)); 3.69 (*m*, H–C(3)); 4.28, 4.45 (2*d*, *J* = 18.8, CH_2N); 4.96, 5.12 (2*d*, *J* = 12.1, PhCH_2O); 7.14–7.68 (*m*, 14 arom. H); **27b**: 0.72, 1.31 (2*s*, 2 Me–C(2)); 1.82 (*s*, OH); 2.12 (*m*, 1 H–C(4)); 2.41 (*s*, *Me*C_6H_4); 2.72 (*m*, 1 H–C(4)); 4.06 (*d*, *J* = 18.4, CH_2N); 4.20 (*m*, H–C(3)); 4.37 (*d*, *J* = 18.4, CH_2N); 5.04, 5.08 (2*d*, *J* = 12.5, PhCH_2O); 7.14–7.75 (*m*, 14 arom. H). ^{13}C-NMR ($CDCl_3$): 17.7, 20.1, 21.3, 24.9 (*Me*–C(2)); 21.6 (*Me*C_6H_4); 35.4, 38.7 (C(4)); 47.7, 48.1 (CH_2N); 50.6, 50.9 (C(2)); 55.3, 57.4 (C(3)); 67.0 (Ph*C*H_2O); 75.1, 76.9 (C(1)); 125.7, 126.9, 127.3, 127.5, 127.9, 128.3, 128.5, 128.6, 129.4, 129.7, 135.1, 135.2, 136.3, 136.7, 142.3, 142.9, 143.4, 143.5 (arom. C); 169.4, 169.6 (COO).

Data of **28**: M.p. 58–60°. IR (KBr): 1756, 1351, 1164, 1095. ^{1}H-NMR ($CDCl_3$): 1.67 (*s*, Me_2C); 2.41 (*s*, *Me*C_6H_4); 4.04 (*s*, CH_2N); 5.08 (*s*, PhCH_2O); 5.39 (*t*, *J* = 1.5, olef. H); 7.24–7.66 (*m*, 9 arom. H). ^{13}C-NMR

($CDCl_3$): 18.1, 22.1 (Me_2C); 21.6 (MeC_6H_4); 52.1 (CH_2N); 67.0 ($PhCH_2O$); 120.3 (olef. CH); 127.6, 128.3, 128.4, 128.6, 129.4, 135.2, 135.6, 142.1, 143.5 (arom. and olef. C); 168.4 (COO). EI-MS: 373 (3, M^+), 218 (11, $[M - Ts]^+$), 155 (6, Ts^+), 91 (100, $C_7H_7^+$), 82 (14).

X-Ray Structure Analysis of **20**. The X-ray structure of **20** is shown in *Fig. 1*. Crystal data and parameters of data collection are summarized in *Table 2*. Unit-cell parameters were determined by accurate centering of 25 strong independent reflections by the least-squares method. Reflection intensities were collected at r.t. on a four-circle *Enraf-Nonius-CAD4* diffractometer equipped a graphite monochromator and using MoK_α radiation. Three standard reflections monitored every 2 h during data collection showed an intensity decay of −1.7%. The usual corrections were applied. Direct-method strategies used the program SHELXS-86 [22]. Anisotropic least-squares refinement was carried out on all non-H-atoms using the program SHELXL-93 [23]. Scattering factors were taken from 'International Tables of Crystallography', Vol. C. Fractional coordinates are deposited in the *Cambridge Crystallographic Data Base*.

Table 2. *Crystal Data and Parameters of Data Collection for* **20**

Molecular formula	$C_{27}H_{27}NO_7S$	Temperature [K]	296 (2)
Crystal system	triclinic	Θ_{max} [°]	23.0
Space group	$P\bar{1}$	Radiation	MoK_α, $\lambda = 0.71073$ Å
a [Å]	10.251 (7)	Scan type	$\omega/2\Theta$
b [Å]	11.208 (6)	No. of measured refl.	3631
c [Å]	11.711 (5)	No. of independent refl.	3430
α [°]	81.55 (4)	No. of refl. ($I > 2\sigma I$)	3076
β [°]	79.92 (5)	No. of parameters	328
γ [°]	69.45 (5)	Final R (F^2)	3.97
V [Å^3]	1253.1 (12)	Final R_w (F^2)	11.07
Z	2	Weighting scheme	$w^{-1} = [\sigma^2 F_o^2 + (0.2065P)^2 + 6.6719P]$, where $P = (F_o^2 + 2F_c^2)/3$
Crystal dimensions [mm]	0.27 × 0.33 × 0.53		

REFERENCES

[1] A. B. Mauger, B. Witkop, *Chem. Rev.* **1965,** *65,* 47.
[2] F. Irreverre, K. Morita, A. V. Robertson, B. Witkop, *J. Am. Chem. Soc.* **1963,** *85,* 2824.
[3] J. D. Ogle, R. B. Aringhaus, M. A. Logan, *J. Biol. Chem.* **1962,** *237,* 3667.
[4] T. Wieland, H. W. Schnabel, *Liebigs Ann. Chem.* **1962,** *657,* 225.
[5] H. Haber, H. Buchholz, R. Sukale, H.-G. Henning, *J. Prakt. Chem.* **1985,** *327,* 51.
[6] K. Walther, U. Kranz, H.-G. Henning, *J. Prakt. Chem.* **1987,** *329,* 859.
[7] P. Wessig, P. Wettstein, B. Giese, M. Neuburger, M. Zehnder, *Helv. Chim. Acta* **1994,** *77,* 829.
[8] S. C. Bergmeier, W. K. Lee, H. Rapoport, *J. Org. Chem.* **1993,** *58,* 5019.
[9] J. E. Nordlander, M. J. Payne, F. G. Njoroge, V. M. Vishwanath, G. R. Han, G. D. Laikos, M. A. Balk, *J. Org. Chem.* **1985,** *50,* 3619.
[10] V. Jäger, V. Buß, *Liebigs Ann. Chem.* **1980,** 101.
[11] D. B. Dess, J. C. Martin, *J. Am. Chem. Soc.* **1991,** *113,* 7277.
[12] O. Wiss, F. Fuchs, *Helv. Chim. Acta* **1952,** *35,* 407.
[13] F. J. Seiler, Res. Lab., U.S. Air Force Academy, Colorado Springs, CO 80840.
[14] P. Yates, J. Pal, *J. Chem. Soc., Chem. Commun.* **1970,** 553.
[15] P. Wessig, unpublished results.
[16] A. Azzouzi, M. Dufour, J.-C. Gramain, R. Remuson, *Heterocycles* **1988,** *27,* 133.
[17] U. Lindemann, P. Wessig, unpublished results.
[18] R. F. W. Jackson, A. B. Rettie, A. Wood, M. J. Wythes, *J. Chem. Soc., Perkin Trans.1* **1994,** 1719, 1722.
[19] D. P. Curran, S. A. Scanga, C. J. Fenk, *J. Org. Chem.* **1984,** *49,* 3474.
[20] M. H. Benn, *Can. J. Chem.* **1964,** *42,* 2393.
[21] B. F. Powell, J. Reichenthal, C. G. Overberger, J.-P. Anselme, *J. Heterocycl. Chem.* **1980,** *17,* 219.
[22] G. M. Sheldrick, 'SHELXS-86', Universität Göttingen, 1990.
[23] G. M. Sheldrick, 'SHELXL-93', Universität Göttingen, 1993.