

N-Monoalkylation of α -Amino Acid Esters under Solid-Liquid PTC Conditions

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N-(2-Nitrophenylsulfonyl)- (*o*-NBS-AA-OMe, **4**) and *N*-(4-Nitrophenylsulfonyl)- α -amino acid methyl esters (*p*-NBS-AA-OMe, **5**) were *N*-alkylated with a variety of alkyl halides **6** under solid-liquid phase-transfer catalysis (SL-PTC) condi-

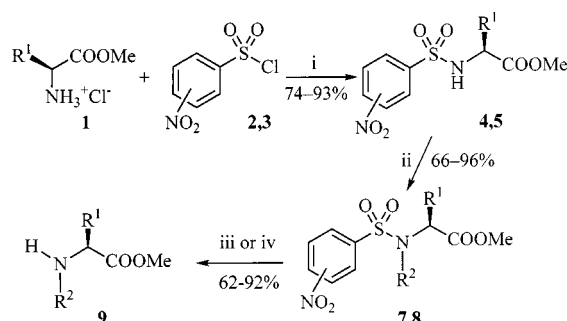
tions, affording the alkylated products *o*-NBS-*N*-R²-AA-OMe **7** and *p*-NBS-*N*-R²-AA-OMe **8** in excellent yields without any detectable racemization.

Introduction

N-Monoalkylated α -amino acids and esters are very important intermediates in the synthesis of many biologically active compounds.^[1] Therefore, the interest in developing new protocols for the selective *N*-monoalkylation of optically pure α -amino acid derivatives is increasing in recent years. However, the numerous methods reported so far^[1a,1c–1e,2] are not generally applicable and most of them deal only with *N*-methylation reactions.^[1b–1e,2b,2c]

Recently Bowman and Coghlan^[3] described a general procedure for the *N*-monoalkylation of α -amino acid esters

1, AA-OMe·HCl	2, <i>o</i> -NBS-Cl (2-NO ₂)	3, <i>p</i> -NBS-Cl (4-NO ₂)
4, <i>o</i> -NBS-AA-OMe	5, <i>p</i> -NBS-AA-OMe	
7, <i>o</i> -NBS- <i>N</i> -R ² -AA-OMe	8, <i>p</i> -NBS- <i>N</i> -R ² -AA-OMe	9, AA- <i>N</i> -R ² -OMe



i) TEA, CH₂Cl₂, 25 °C; ii) R²X (**6**), K₂CO₃, TEBA_{cat}, solvent, 25–80 °C; iii) PhSH, K₂CO₃, MeCN, 50 °C; iv) PhS[−]K⁺, DMF, 25 °C

R ² X	R ² X
6a CH ₂ =CHCH ₂ Br	6d CH ₂ =CH(CH ₂) ₃ Br
6b C ₄ H ₉ Br	6e MeI
6c PhCH ₂ Br	6f HC≡C-CH ₂ Br

Scheme 1. Preparation of *N*-alkylated α -amino acids **9** by alkylation under SL-PTC of *N*-(nitrophenylsulfonyl)- α -amino acid methyl esters **4,5**

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by reaction of *N*-(nitrophenylsulfonyl)- α -amino acid methyl esters (e.g. *L*-isomers **4a** and **5a**) with an alkyl bromide **6**, using a stoichiometric amount of cesium carbonate as base in anhydrous DMF (Scheme 1). Under these conditions the isolated yields of the *N*-alkyl derivatives **7** and **8** reached 72–87%, whereas they were lower with acetonitrile as solvent and/or potassium carbonate as base.

Here we report that *N*-(2-nitrophenylsulfonyl)- and *N*-(4-nitrophenylsulfonyl)- α -amino acid esters **4** and **5** are advantageously *N*-alkylated under solid-liquid phase-transfer catalysis (SL-PTC) conditions^[4] in the presence of anhydrous potassium carbonate, which is widely used as a non-nucleophilic base, especially in *N*-alkylations.^[4,5] Since the nitrophenylsulfonyl groups of sulfonamides **7** and **8** can be easily removed,^[6] this protocol represents a useful procedure for the synthesis of selective *N*-monoalkylated α -amino acid esters **9** (Scheme 1).

Results and Discussion

The nitrophenylsulfonamides *o*-NBS-AA-OMe (**4**) and *p*-NBS-AA-OMe (**5**) were obtained in 74–90% yields as enantiopure compounds (Table 1)^[6] by reacting the corresponding sulfonyl chloride *o*-NBS-Cl (**2**) or *p*-NBS-Cl (**3**) with the optically pure α -amino ester hydrochlorides AA-OMe·HCl (**1**) in the presence of TEA, according to a previously described procedure (Scheme 1).^[6]

Table 1. Preparation of *N*-(nitrophenylsulfonyl)- α -amino acid methyl esters **4,5** from the corresponding hydrochlorides of α -amino acid methyl esters (AA-OMe·HCl) **1**

1,4,5R ¹	AA	t [h]	Product	Yield [%]
a <i>i</i> -Pr	<i>L</i> -Val	18	<i>o</i> -NBS- <i>L</i> -Val-OMe	4a 86 (93) ^[a]
b CH ₂ OH	<i>L</i> -Ser	1.5	<i>o</i> -NBS- <i>L</i> -Ser-OMe	4b 77
c CH ₂ CH ₂ SMe	<i>L</i> -Met	3	<i>o</i> -NBS- <i>L</i> -Met-OMe	4c 74
d <i>R</i> -CH(OH)Me	<i>L</i> -Thr	2	<i>o</i> -NBS- <i>L</i> -Thr-OMe	4d 86
e H	Gly	1	<i>o</i> -NBS-Gly-OMe	4e 90
f PhCH ₂	<i>L</i> -Phe	24	<i>o</i> -NBS- <i>L</i> -Phe-OMe	4f 83
g Ph	<i>L</i> -PhGly	24	<i>o</i> -NBS- <i>L</i> -PhGly-OMe	4g 88
a <i>i</i> -Pr	<i>L</i> -Val	12	<i>p</i> -NBS- <i>L</i> -Val-OMe	5a 80

^[a] In parentheses isolated yield of **4a** (purity $\geq$ 98%) without chromatographic purification.

The *N*-alkylation reactions of the sulfonamides **4,5** were performed by stirring a heterogeneous mixture of anhydrous potassium carbonate and an acetonitrile or dioxane solution of **4** or **5**, alkylating agent **6** and triethylbenzylammonium chloride (TEBA) as phase-transfer catalyst at 25 or 80 °C. The reaction between the L-valine derivative *o*-NBS-Val-OMe (**4a**) and allyl bromide (**6a**) was chosen for the process optimisation (Table 2).

Table 2. *N*-Alkylation of *o*-NBS-L-Val-OMe (**4a**) with allyl bromide (**6a**) under SL-PTC conditions

Entry ^[a]	6a [mol equiv]	T [°C]	t [h]	7a , Yield [%] ^[b]
1	2	25	7	88
2	2	25	46	91 ^[c]
3	2	80	1	90
4	1.05	80	2	93
5	1.05	80	8	94 ^[d]
6	1.05	80	3	95 ^[e]
7	1.05	80	3.5	97 ^[f]
8	1.05	80	1.5	93 ^[g]
9	1.05	80	1	97 ^[f,g]

^[a] Substrate **4a** (10 mmol), **6a** (10.5–20 mmol), K₂CO₃ (15 mmol), TEBA (1 mmol), anhydrous CH₃CN (100 mL). – ^[b] **7a**: *o*-NBS-*N*-allyl-L-Val-OMe. – ^[c] Without TEBA. – ^[d] In the presence of 0.1 mmol of TEBA. – ^[e] Commercial non-anhydrous acetonitrile. – ^[f] In dioxane (100 mL). – ^[g] In the presence of 1 mmol of tetrabutylammonium bromide (TBAB) as catalyst.

The alkylation reactions were complete in 1–8 h and, as expected for a PTC process,^[4] the reaction time increased by decreasing the amount of the catalyst (Table 2, entries 4 and 5). In the absence of TEBA (Table 2, entry 2) the reaction was much slower than the catalysed alkylation (Table 2, entry 1), the yields remaining high. The catalytic efficiency of tetrabutylammonium bromide (TBAB) was found to be superior to that of TEBA (Table 2, entries 4, 8 and 7, 9). This behaviour can be likely explained assuming that the ion pair formed by the anion derived from the sulfonamide and the tetrabutylammonium cation has higher solubility and reactivity than the ion pair containing the triethylben-

zylammonium cation.^[4a,4d,7,8] Only a small excess of alkylating agent **6** (1.05 mol equiv.) was required for the complete conversion of the substrates **4,5**. However, as shown for **4a** (Table 2, entries 3 and 4), a 100% excess of **6** increased the reaction rate without causing bisalkylation and represents the best compromise between reaction time and amount of alkylating agent in the case of the non-activated electrophiles **6b,d** (Table 3, entries 2, 4, 14 and 19).

The alkylation was shown to be very sensitive to steric hindrance, e.g. *o*-NBS-L-Val-OMe (**4a**), *p*-NBS-L-Val-OMe (**5a**) and *o*-NBS-Gly-OMe (**4e**) were recovered unchanged after 24 h from the crude of the reaction with 3-bromopentane or 1-bromo-3,3-dimethylpropane. Both non-anhydrous analar grade acetonitrile or dioxane can be used as purchased, even if the reaction times were shorter under anhydrous conditions (Table 2, entries 4, 6 and 7).

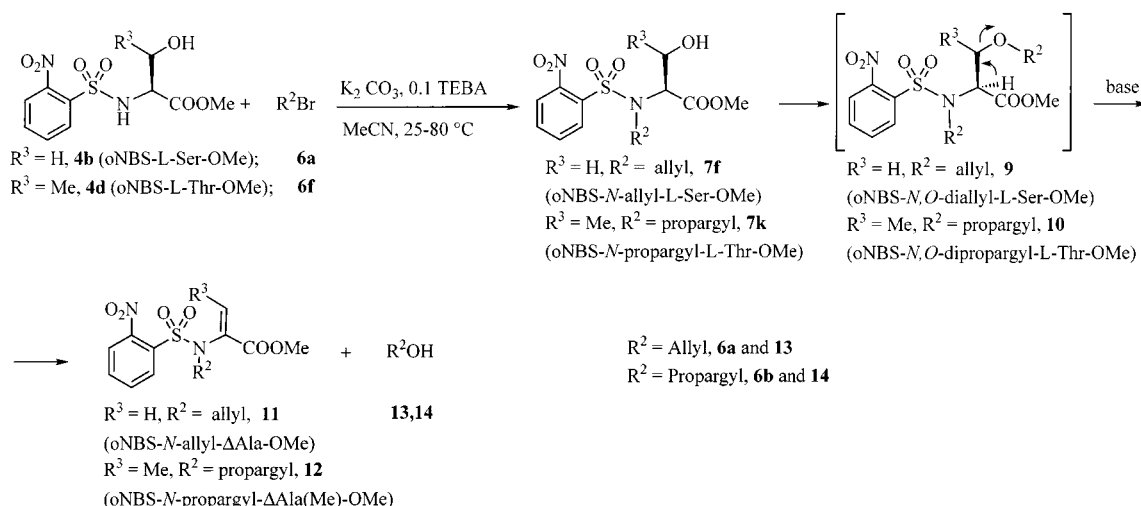
Under the best reaction conditions (Table 3) the sulfonamides **4,5,21** reacted with various electrophiles **6** affording the corresponding *N*-alkylated products **7,8,22** in excellent yields (86–96%).

In contrary to that found by Bowman and Coghlan,^[3] under SL-PTC conditions we did not observe decomposition or rearrangement of the products **7a–e,g,h,j–m** and **8a,d**, even in the presence of a molar excess of potassium carbonate (1.5 mol equiv.). However, the alkylation of *o*-NBS-L-Ser-OMe (**4b**) with allyl bromide (**6a**) in acetonitrile at 80 °C (Table 3, entry 6) afforded only 12% of the expected *o*-NBS-*N*-allyl-L-Ser-OMe (**7f**) and major amounts (35%) of *o*-NBS-*N*-allyl-ΔAla-OMe (**11**). When the reaction was performed at 25 °C the yields of **7f** and **11** became 46% and 19%, respectively, although the reaction rate was much lower (120 h) (Table 3, entry 7). A further yield increase of **7f** (76%) in an acceptable reaction time (7 h) was obtained by using anhydrous DMF instead of MeCN, at room temperature (Table 3, entry 8). The ester **11** probably derives from the intermediate *o*-NBS-*N,O*-diallyl-L-Ser-OMe (**9**) through a base-catalysed β-elimination of a molecule of

Table 3. Alkylation of *o*-NBS-AA-OMe **4,21** and *p*-NBS-AA-OMe **5** with alkyl halides **6** under SL-PTC conditions

Entry ^[a]	R ² X	mol equiv.	t [h]	Product	Yield [%]
1	4a	6a	1.05	<i>o</i> -NBS- <i>N</i> -allyl-L-Val-OMe (7a)	91
2	4a	6b	2	<i>o</i> -NBS- <i>N</i> -C ₄ H ₉ -L-Val-OMe (7b)	89
3	4a	6c	1.05	<i>o</i> -NBS- <i>N</i> -Bn-L-Val-OMe (7c)	96
4	4a	6d	2	<i>o</i> -NBS- <i>N</i> -(4-pentenyl)-L-Val-OMe (7d)	96
5	4a	6e	1.05	<i>o</i> -NBS- <i>N</i> -Me-L-Val-OMe (7e)	87
6	4b	6a	1.05	<i>o</i> -NBS- <i>N</i> -allyl-L-Ser-OMe (7f)	12 ^[b]
7	4b	6a	1.05	<i>o</i> -NBS- <i>N</i> -allyl-L-Ser-OMe (7f)	46 ^[c] ^[d]
8	4b	6a	1.05	<i>o</i> -NBS- <i>N</i> -allyl-L-Ser-OMe (7f)	76 ^[e]
9	4c	6a	1.05	<i>o</i> -NBS- <i>N</i> -allyl-L-Met-OMe (7g)	94
10	4c	6c	1.05	<i>o</i> -NBS- <i>N</i> -Bn-L-Met-OMe (7h)	91
11	4d	6f	1.05	<i>o</i> -NBS- <i>N</i> -propargyl-L-Thr-OMe (7i)	66
12	4d	6f	1.05	<i>o</i> -NBS- <i>N</i> -propargyl-L-Thr-OMe (7i)	84 ^[e]
13	21	6f	1.05	<i>o</i> -NBS- <i>N</i> -propargyl-D- <i>allo</i> -Thr-OMe (22)	86 ^[e]
14	4e	6b	2	<i>o</i> -NBS- <i>N</i> -C ₄ H ₉ -Gly-OMe (7j)	80
15	4f	6a	1.05	<i>o</i> -NBS- <i>N</i> -allyl-L-Phe-OMe (7k)	88
16	4f	6e	1.05	<i>o</i> -NBS- <i>N</i> -Me-L-Phe-OMe (7l)	86
17	4g	6e	2	<i>o</i> -NBS- <i>N</i> -Me-L-PhGly-OMe (7m)	91 ^[c]
18	5a	6a	1.05	<i>p</i> -NBS- <i>N</i> -allyl-L-Val-OMe (8a)	91
19	5a	6d	2	<i>p</i> -NBS- <i>N</i> -(4-pentenyl)-L-Val-OMe (8d)	91

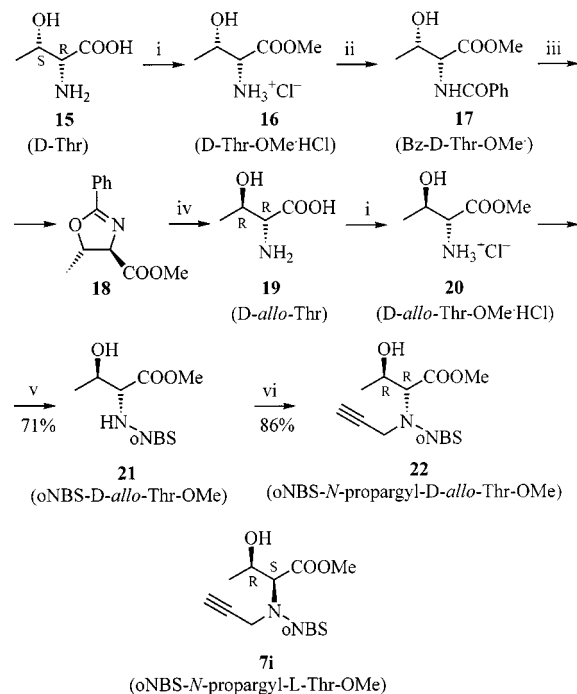
^[a] Reaction conditions: K₂CO₃ (1.5 mol equiv.), TEBA (0.1 mol equiv.), MeCN (0.1 M), 80 °C. – ^[b] Together with 35% of *o*-NBS-*N*-allyl-ΔAla-OMe (**11**). – ^[c] At 25 °C in anhydrous MeCN. – ^[d] Together with 15% of **11**. – ^[e] At 25 °C in anhydrous DMF.



Scheme 2. Synthesis of *o*-NBS-*N*-allyl-L-Ser-OMe (**7f**) and *o*-NBS-*N*-propargyl-L-Thr-OMe (**7i**) and mechanism of the elimination to the corresponding acrylic derivatives **11** and **12**

allyl alcohol (**13**) (Scheme 2).^[2c,9] A similar behaviour was found in the alkylation of *o*-NBS-L-Thr-OMe (**4d**) with propargyl alcohol (**6f**) (Scheme 2 and Table 3, entries 11 and 12), even if, in this case, the yields of the expected product **7i** in both MeCN and DMF were higher (66 and 84%, respectively). These results indicate that both temperature and solvent are crucial factors for the outcome of the *N*-alkylation reaction. Clearly, at higher temperature (80 °C) the bisalkylation process favourably competes with *N*-monoalkylation, affording the unstable *N,O*-dialkylated products **11** or **12**. In contrast, at 25 °C *N*-monoalkylation is the favoured process, especially in anhydrous DMF. This behaviour is probably due to the higher solubility of the sulfonamide onium salt in DMF than in MeCN or dioxane. The lower acidity and higher steric requirements of the hydroxy group of **4d** with respect to that of **4b** account for the good yield of *N*-monoalkylated product **7i** obtained. The *D*-*allo*-threonine derivative **21** (Scheme 3), possessing a less-hindered nitrogen, is more reactive than the diastereoisomeric L-threonine derivative **7i** and its alkylation with propargyl bromide (**6f**) is complete in 2.5 h, producing *o*-NBS-*N*-propargyl-*D*-*allo*-Thr-OMe (**22**) in 86% yield (Table 3, entry 13).

The products **7a,e,k** and **8a** were chosen to check the deprotection procedure to the corresponding amino esters **9**. The substrates **7,8** were reacted at 50 °C with excess PhSH and solid potassium carbonate in MeCN,^[6,3] or at 25 °C with a 0.5 M solution of PhS[−]K⁺^[1c,1d] and the deprotected enantiopure esters **9** were isolated in 62–92%. The sulfonamides *o*-NBS-*N*-R²-AA-OMe (**7,21**) and *p*-NBS-*N*-R²-AA-OMe (**8**) were isolated as optically pure compounds, indicating that no racemization took place during the PTC alkylation of the enantiopure substrates *o*-NBS-AA-OMe (**4**) and *p*-NBS-AA-OMe (**5**). Only in the case of *o*-NBS-L-PhGly-OMe (**4g**), whose benzylic α -proton has a high acidity, did the alkylation with MeI proceed to *o*-NBS-*N*-Me-PhGly-OMe (**7m**) with partial racemization. The *ee* of **7m** was determined by deprotecting this sulfonamide to the known amino ester **9m**, obtained in 21% *ee*, and repro-



Scheme 3. Preparation of *o*-NBS-*N*-propargyl-*D*-*allo*-Thr-OMe (**22**) from D-Thr (**15**)

tecting this latter with *o*-NBS-Cl. The determination of the $[\alpha]_D$ of the resulting racemized **7m** allowed the calculation of the value of the pure enantiomer and the amount of racemization in the alkylation (50%) and deprotection (29%) steps (see Experimental Section).

Whereas **7a,b,d,f** are known compounds and their physical properties match those of products reported in literature, the optical purities of the new compounds **7c,e,g,h,k** were determined by ¹H NMR spectroscopy in comparison with the corresponding racemized material **7-rac**, by using

an appropriate shift reagent (see Experimental Section). The sulfonamides **7a** and **8a** were deprotected to the known **9a**; similarly **7c** and **7l** were transformed into the corresponding known α -amino esters **9c** and **9l**, respectively. Finally, ^1H NMR analysis of the L-threonine derivative **7i** shows minor amounts ($\leq 3\%$) of the α -racemized product derived from D-*allo*-threonine **22** (and vice versa), which in turn is synthesised starting from D-threonine (**15**)^[10] by selective inversion of the C-3 stereogenic centre via the oxazoline **18** and subsequent alkylation of the sulfonamide **21** (Scheme 3).

Conclusion

In conclusion, the results indicate that SL-PTC is an effective procedure for the *N*-alkylation of (nitrophenyl)sulfonamides of α -amino acid esters. The procedure is particularly suitable for the scale-up of the process since it involves the use of cheap and environmentally friendly reagents. The enantiopure compounds **7,8** can be isolated with excellent yields and purities after an aqueous workup.

Experimental Section

General Remarks: Melting points were determined on a Büchi 535 apparatus and are corrected. $[\alpha]_D^{20}$'s were measured at 589 nm on a Perkin–Elmer 241 polarimeter using a 10 cm $\times$ 5 mL cell and *c* is in g/100 mL. ^1H NMR spectra were recorded on a Bruker AC 300 spectrometer operating at 300.133 MHz; TMS was used as external reference; δ are in ppm and *J* are in Hz. IR spectra were recorded on a Perkin–Elmer FT-IR 1725 spectrometer and frequency values are in cm^{-1} . Reagent-grade commercially available reagents and solvents were used and dried, when required, before use. Petroleum ether (PE) having boiling range 40–60 °C was used in the chromatographic purifications. Amino esters AA-OMe-HCl (**1**) are commercially available products, whereas **20** was prepared by a known procedure.^[10]

General Method for the Preparation of Sulfonamides 4, 5, 21:^[6] In a well-dried round bottomed flask was dissolved AA-OMe-HCl (**1**) (10 mmol) in anhydrous dichloromethane (80 mL). This solution was cooled to 0 °C and anhydrous TEA (2.3 g, 22.7 mmol) was added under stirring in 5 min. The corresponding (nitrophenyl)sulfonyl chloride **2** or **3** (10 mmol) was added in portions in 10 min and the stirring was continued at 25 °C until no starting material was detectable (TLC). The reaction mixture was washed with water (3 $\times$ 20 mL) and the organic phase was dried over sodium sulfate, evaporated to dryness under vacuum and purified by flash column chromatography on silica gel (230–400 mesh). Starting amino ester hydrochloride and (nitrophenyl)sulfonyl chloride, reaction time, chromatographic eluent, yield and physical, spectroscopic and analytical data of **4a–g, 5a, 21** are as follows:

***o*-NBS-L-Val-OMe (4a):** L-Val-OMe-HCl (**1a**), *o*-NBS-Cl (**2**), 18 h, AcOEt–PE 1:3; **4a**, 2.71 g (86%). Ester **4a** with a sufficient purity ($\geq 98\%$) for the alkylation step can be obtained in 93% yield without chromatographic purification; oil, $[\alpha]_D^{20} = -213.9$ (*c* = 3.8 in CHCl_3) {ref.^[3] $[\alpha]_D^{28.5} = -214.5$ (*c* = 3.8 in CHCl_3)}

***o*-NBS-L-Ser-OMe (4b):** L-Ser-OMe-HCl (**1b**), *o*-NBS-Cl (**2**), 1.5 h, AcOEt–PE 2:3; **4b**, 2.34 g (77%), m.p. 109–110 °C (ref.^[3] 110.5–112

°C). – $[\alpha]_D^{20} = -103.0$ (*c* = 3.0 in MeOH) {ref.^[3] $[\alpha]_D^{28.5} = -103.5$ (*c* = 3.0 in MeOH)}

***o*-NBS-L-Met-OMe (4c):** L-Met-OMe-HCl (**1c**), *o*-NBS-Cl (**2**), 3 h, AcOEt–PE 1:2; **4c**, 2.52 g (74%); oil, $[\alpha]_D^{20} = -176.7$ (*c* = 0.67 in CHCl_3). – ^1H NMR (CDCl_3): δ = 1.92–2.17 (m, 2 H, $\text{CH}_2\text{CH}_2\text{S}$), 2.05 (s, 3 H, SCH_3), 2.50–2.66 (m, 2 H, CH_2S), 3.47 (s, 3 H, OCH_3), 4.29–4.36 (m, 1 H, CHCOOR), 6.22 (d, 3J = 8.9 Hz, 1 H, NH), 7.70–7.73 (m, 2 H, Ar), 7.89–7.91 (m, 1 H, Ar), 8.04–8.07 (m, 1 H, Ar). – $\text{C}_{12}\text{H}_{16}\text{N}_2\text{O}_6\text{S}_2$ (348.40): calcd. C 41.37, H 4.63, N 8.04; found C 41.48, H 4.57, N 8.00.

***o*-NBS-L-Thr-OMe (4d):** L-Thr-OMe-HCl (**1d**), *o*-NBS-Cl (**2**), 2 h, AcOEt–PE 1:1; **4d**, 2.74 g (86%); m.p. 80–81 °C. – $[\alpha]_D^{20} = -97.1$ (*c* = 0.82 in MeOH). – ^1H NMR (CDCl_3): δ = 1.32 (d, 3J = 6.4 Hz, 3 H, CH_3CH), 2.11 (bd, 3J = 4.9 Hz, 1 H, OH), 3.50 (s, 3 H, OCH_3), 4.13 (dd, 3J = 9.4, 2.7 Hz, 1 H, CHCOOR), 4.27–4.38 (m, 1 H, CHOH), 6.34 (d, 3J = 9.4 Hz, 1 H, NH), 7.70–7.74 (m, 2 H, Ar), 7.91–7.94 (m, 1 H, Ar), 8.00–8.07 (m, 1 H, Ar). – $\text{C}_{11}\text{H}_{14}\text{N}_2\text{O}_7\text{S}$ (318.30): calcd. C 41.51, H 4.43, N 8.80; found C 41.40, H 4.36, N 8.77.

***o*-NBS-*allo*-D-Thr-OMe (21):** D-*allo*-Thr-OMe-HCl (**20**),^[10] $[\alpha]_D^{20} = -22.8$ (*c* = 5.0 in MeOH; ref.^[10] $[\alpha]_D^{23} = -23.1$ (*c* = 5.0 in MeOH)), *o*-NBS-Cl (**2**), 3.5 h, AcOEt–PE 5:4; **21**, 2.26 g (71%); oil, $[\alpha]_D^{20} = +202.7$ (*c* = 2.96 in CHCl_3). – ^1H NMR (CDCl_3): δ = 1.24 (d, 3J = 6.3 Hz, 3 H, CH_3CH), 2.18 (bd, 3J = 4.8 Hz, 1 H, OH), 3.52 (s, 3 H, OCH_3), 4.12–4.17 (m, 1 H, CHOH), 4.19 (dd, 3J = 9.2, 4.2 Hz, 1 H, CHCOOR), 6.39 (d, 3J = 9.2 Hz, 1 H, NH), 7.73–7.76 (m, 2 H, Ar), 7.92–7.95 (m, 1 H, Ar), 8.07–8.10 (m, 1 H, Ar). – $\text{C}_{11}\text{H}_{14}\text{N}_2\text{O}_7\text{S}$ (318.30): calcd. C 41.51, H 4.43, N 8.80; found C 41.38, H 4.40, N 8.72.

***o*-NBS-Gly-OMe (4e):** Gly-OMe-HCl (**1e**), *o*-NBS-Cl (**2**), 1 h, AcOEt–PE 3:4; **4e**, 2.43 g (90%), m.p. 112–113 °C. – ^1H NMR (CDCl_3): δ = 3.60 (s, 3 H, OCH_3), 4.01 (d, 3J = 5.7 Hz, 2 H, CH_2COOR), 6.05 (t, 3J = 5.7 Hz, 1 H, NH), 7.72–7.75 (m, 2 H, Ar), 7.91–7.94 (m, 1 H, Ar), 8.07–8.10 (m, 1 H, Ar). – $\text{C}_9\text{H}_{10}\text{N}_2\text{O}_6\text{S}$ (274.25): calcd. C 39.42, H 3.68, N 10.21; found C 39.53, H 3.60, N 10.15.

***o*-NBS-L-Phe-OMe (4f):** L-Phe-OMe-HCl (**1f**), *o*-NBS-Cl (**2**), 24 h, AcOEt–PE 2:3; **4f**, 3.03 g (83%), m.p. 81–82 °C. – $[\alpha]_D^{20} = -93.7$ (*c* = 1.0 in CHCl_3). – ^1H NMR (CDCl_3): δ = 3.06 (dd, 2J = 13.9 Hz, 3J = 5.7 Hz, 1 H, HCHPh), 3.15 (dd, 2J = 13.9 Hz, 3J = 7.0 Hz, 1 H, HCHPh), 3.51 (s, 3 H, OCH_3), 4.42–4.48 (m, 1 H, CHCOOR), 6.01 (d, 3J = 7.9 Hz, 1 H, NH), 7.09–7.11 (m, 2 H, Ar), 7.16–7.22 (m, 3 H, Ar), 7.64–7.69 (m, 2 H, Ar), 7.81–7.84 (m, 1 H, Ar), 7.93–7.96 (m, 1 H, Ar). – $\text{C}_{16}\text{H}_{16}\text{N}_2\text{O}_6\text{S}$ (364.37): calcd. C 52.74, H 4.43, N 7.69; found C 52.81, H 4.32, N 7.60.

***o*-NBS-L-PhGly-OMe (4g):** L-PhGly-OMe-HCl (**1g**), *o*-NBS-Cl (**2**), 24 h, AcOEt–PE 1:1; **4g**, 3.02 g (88%), m.p. 97–98 °C. – $[\alpha]_D^{20} = +87.4$ (*c* = 1.0 in CHCl_3). – ^1H NMR (CDCl_3): δ = 3.61 (s, 3 H, OCH_3), 5.26 (d, 3J = 8.0 Hz, 1 H, CHCOOR), 6.64 (d, 3J = 8.0 Hz, 1 H, NH), 7.15–7.19 (m, 3 H, Ar), 7.22–7.25 (m, 2 H, Ar), 7.45 (dd, 3J = 7.9, 7.9 Hz, 1 H, Ar), 7.59 (dd, 3J = 7.9, 7.9 Hz, 1 H, Ar), 7.68 (d, 3J = 7.9 Hz, 1 H, Ar), 7.79 (d, 3J = 7.9 Hz, 1 H, Ar). – $\text{C}_{15}\text{H}_{14}\text{N}_2\text{O}_6\text{S}$ (350.35): calcd. C 51.42, H 4.03, N 8.00; found C 51.37, H 4.12, N 7.89.

***p*-NBS-L-Val-OMe (5a):** L-Val-OMe-HCl (**1a**), *p*-NBS-Cl (**3**), 20 h, AcOEt–PE 1:2; **5a**, 2.52 g (80%), m.p. 102 °C. – $[\alpha]_D^{20} = +33.2$ (*c* = 0.9 in CHCl_3) {ref.^[3] $[\alpha]_D^{26} = +36.4$ (*c* = 3.1 in CHCl_3)}

General Method for the Alkylation of Sulfonamides 4,5,21: In a dried flask connected to a CaCl_2 tube, anhydrous potassium car-

bonate (2.07 g, 15 mmol) was added to an acetonitrile (or DMF) solution (50 mL) of sulfonamide **4,5** (10 mmol), alkyl halide **6** (10.5–20 mmol) and TEBA (0.23 g, 1 mmol). The heterogeneous mixture was magnetically stirred at 25–80 °C until no starting **4,5** was detectable (TLC analysis, AcOEt–PE 1:1) and then cooled to room temperature, diluted with water (50 mL) and extracted with Et₂O or CH₂Cl₂ (3 × 20 mL). The organic layer was washed with water (2 × 20 mL), dried over Na₂SO₄ and evaporated under vacuum to give pure *N*-alkyl sulfonamides **7,8,22**. Starting sulfonamide and alkyl halide, reaction time, yield and physical, spectroscopic and analytical data of **7a–m,8a,8d,22** are as follows:

***o*-NBS-*N*-allyl-L-Val-OMe (7a):** *o*-NBS-L-Val-OMe (**4a**), allyl bromide (**6a**), 2 h; **7a**, 3.24 g (91%); oil, $[\alpha]_D^{20} = -61.8$ ($c = 3.5$ in CHCl₃) {ref.^[3] $[\alpha]_D^{20} = -62.4$ ($c = 3.6$ in CHCl₃)}.

***o*-NBS-*N*-C₄H₉-L-Val-OMe (7b):** *o*-NBS-L-Val-OMe (**4a**), butyl bromide (**6b**), 12 h; **7b**, 3.30 g (89%); oil, $[\alpha]_D^{20} = -70.1$ ($c = 5.0$ in CHCl₃) {ref.^[3] $[\alpha]_D^{20} = -70.0$ ($c = 4.7$ in CHCl₃)}.

***o*-NBS-*N*-Bn-L-Val-OMe (7c):** *o*-NBS-L-Val-OMe (**4a**), benzyl bromide (**6c**), 1 h; **7c**, 3.93 g (96%), 76–77 °C. – $[\alpha]_D^{20} = -17.4$ ($c = 0.66$ in CHCl₃). – ¹H NMR (CDCl₃): $\delta = 0.88$ (d, ³*J* = 6.7 Hz, 3 H, CHCH₃), 0.91 (d, ³*J* = 6.6 Hz, 3 H, CHCH₃), 2.07–2.19 (m, 1 H, CHCH₃), 3.55 (s, 3 H, OCH₃), 4.31 (d, ³*J* = 10.2 Hz, 1 H, CHCOOR), 4.54 (d, ²*J* = 15.2 Hz, 1 H, HCHPh), 4.91 (d, ²*J* = 15.2 Hz, 1 H, HCHPh), 7.15–7.25 (m, 3 H, Ar), 7.34–7.43 (m, 3 H, Ar), 7.55–7.65 (m, 3 H, Ar). – C₁₉H₂₂N₂O₆S (406.45): calcd. C 56.14, H 5.46, N 6.89; found C 56.00, H 5.35, N 6.81.

***o*-NBS-*N*-(4-pentenyl)-L-Val-OMe (7d):** *o*-NBS-L-Val-OMe (**4a**), 4-pentenyl bromide (**6d**), 8 h; **7d**, 3.68 g (96%); oil, $[\alpha]_D^{20} = -65.7$ ($c = 3.0$ in CHCl₃) {ref.^[3] $[\alpha]_D^{20} = -63.8$ ($c = 3.0$ in CHCl₃)}.

***o*-NBS-*N*-Me-L-Val-OMe (7e):** *o*-NBS-L-Val-OMe (**4a**), methyl iodide (**6e**), 1.5 h; **7e**, 2.88 g (87%), m.p. 66–67 °C. – $[\alpha]_D^{20} = -13.5$ ($c = 0.78$ in CHCl₃). – ¹H NMR (CDCl₃): $\delta = 0.93$ (d, ³*J* = 6.7 Hz, 3 H, CHCH₃), 0.96 (d, ³*J* = 6.6 Hz, 3 H, CH₃CH), 2.11–2.23 (m, 1 H, CHCH₃), 3.03 (s, 3 H, NCH₃), 3.54 (s, 3 H, OCH₃), 4.11 (d, ³*J* = 10.2 Hz, 1 H, CHCOOR), 7.61–7.69 (m, 3 H, Ar), 7.98–8.01 (m, 1 H, Ar). – C₁₃H₁₈N₂O₆S (330.36): calcd. C 47.26, H 5.49, N 8.48; found C 47.11, H 5.37, N 8.44.

***o*-NBS-*N*-allyl-L-Ser-OMe (7f):** (using anhydrous DMF instead of MeCN, Table 3, entry 8) *o*-NBS-L-Ser-OMe (**4b**), allyl bromide (**6a**); 7 h; purified by flash column chromatography: **7f**, 2.62 g (76%); oil, $[\alpha]_D^{20} = -11.4$ ($c = 0.59$ in CHCl₃) {ref.^[3] $[\alpha]_D^{20} = -12.2$ ($c = 2.4$ in CHCl₃)}. Compound **11** was also obtained as an oil (0.49 g, 15%). – ¹H NMR (CDCl₃): $\delta = 3.63$ (s, 3 H, OCH₃), 4.20 (d, ³*J* = 6.7 Hz, 2 H, CH₂N), 5.12–5.19 (m, 2 H, CH₂=), 5.71–5.84 (m, 2 H, CH₂=), 5.95 (s, 1 H, CH=), 6.55 (s, 1 H, NH), 7.58–7.69 (m, 3 H, Ar), 7.97–8.00 (m, 1 H, Ar). – C₁₃H₁₄N₂O₆S (326.33): calcd. C 47.85, H 4.32, N 8.58; found C 47.92, H 4.22, N 8.49.

***o*-NBS-*N*-allyl-L-Met-OMe (7g):** *o*-NBS-L-Met-OMe (**4c**), allyl bromide (**6a**), 1 h; **7g**, 3.66 g (94%); oil, $[\alpha]_D^{20} = +9.4$ ($c = 0.63$ in CHCl₃). – ¹H NMR (CDCl₃): $\delta = 1.95$ –2.11 (m, 1 H, HCHCH₂S), 2.11 (s, 3 H, SCH₃), 2.24–2.38 (m, 1 H, HCHCH₂S), 2.53–2.67 (m, 2 H, CH₂S), 3.59 (s, 3 H, OCH₃), 3.88 (dd, ²*J* = 16.5 Hz, ³*J* = 7.3 Hz, 1 H, HCHN), 4.14 (dd, ²*J* = 16.5 Hz, ³*J* = 5.6 Hz, 1 H, HCHN), 4.79 (dd, ³*J* = 9.1, 5.5 Hz, 1 H, CHCOOR), 5.14 (d, ³*J*_{cis} = 10.1 Hz, 1 H, HCH=), 5.24 (d, ³*J*_{trans} = 17.2 Hz, 1 H, HCH=), 5.86–5.97 (m, 1 H, CH=), 7.61–7.64 (m, 1 H, Ar), 7.69–7.74 (m, 2 H, Ar), 8.07–8.11 (m, 1 H, Ar). – C₁₅H₂₀N₂O₆S₂ (388.46): calcd. C 46.38, H 5.19, N 7.21; found C 46.46, H 5.25, N 7.26.

***o*-NBS-*N*-Bn-L-Met-OMe (7h):** *o*-NBS-L-Met-OMe (**4c**), benzyl bromide (**6c**), 0.25 h; **7h**, 3.98 g (91%); oil, $[\alpha]_D^{20} = -12.9$ ($c = 0.68$ in CHCl₃). – ¹H NMR (CDCl₃): $\delta = 1.76$ –1.93 (m, 1 H, HCHCH₂S), 1.90 (s, 3 H, SCH₃), 2.05–2.17 (m, 1 H, HCHCH₂S), 2.31–2.51 (m, 2 H, CH₂S), 3.51 (s, 3 H, OCH₃), 4.34 (d, ²*J* = 15.7 Hz, 1 H, HCHPh), 4.81 (m, 1 H, CHCOOR), 4.82 (d, ²*J* = 15.7 Hz, 1 H, HCHPh), 7.22–7.24 (m, 3 H, Ar), 7.37–7.39 (m, 2 H, Ar), 7.53–7.64 (m, 3 H, Ar), 7.82 (d, 1 H, *J* = 7.9 Hz, Ar). – C₁₉H₂₂N₂O₆S₂ (438.52): calcd. C 52.04, H 5.06, N 6.39; found C 52.00, H 5.17, N 6.37.

***o*-NBS-*N*-propargyl-L-Thr-OMe (7i):** (using anhydrous DMF instead of MeCN, Table 3, entry 12) *o*-NBS-L-Thr-OMe (**4d**), propargyl bromide (**6f**), 6 h; purified by flash column chromatography using AcOEt–EP 5:6; **7i**, 2.98 g (84%); oil, $[\alpha]_D^{20} = +12.8$ ($c = 1.6$ in CHCl₃). – ¹H NMR (CDCl₃): $\delta = 1.38$ (d, ³*J* = 6.2 Hz, 3 H, CH₃CH), 2.33 (t, ⁴*J* = 2.4 Hz, 1 H, CH≡), 2.43 (d, ³*J* = 5.4 Hz, 1 H, OH), 3.62 (s, 3 H, OCH₃), 4.45 (dd, ⁴*J* = 2.4, 1.5 Hz, 2 H, CH₂N), 4.46–4.56 (m, 1 H, CHOH), 4.57 (dd, ³*J* = 5.0 Hz, ⁴*J* = 1.5 Hz, 1 H, CHCOOR), 7.59–7.62 (m, 1 H, Ar), 7.66–7.71 (m, 2 H, Ar), 8.14–8.17 (m, 1 H, Ar). – C₁₄H₁₆N₂O₇S (356.35): calcd. C 47.19, H 4.53, N 7.86; found C 47.06, H 4.44, N 7.96.

***o*-NBS-*N*-propargyl-D-*allo*-Thr-OMe (22):** (using anhydrous DMF instead of MeCN, Table 3, entry 13) *o*-NBS-D-*allo*-Thr-OMe (**21**), propargyl bromide (**6f**), 2.5 h; purified by flash column chromatography using AcOEt–EP 4:5; **7i**, 3.05 g (86%); oil, $[\alpha]_D^{20} = +96.6$ ($c = 1.64$ in CHCl₃). – ¹H NMR (CDCl₃): $\delta = 1.43$ (d, ³*J* = 6.2 Hz, 3 H, CH₃CH), 2.20 (t, ⁴*J* = 2.5 Hz, 1 H, CH≡), 2.48 (br. s, 1 H, OH), 3.61 (s, 3 H, OCH₃), 4.39 (dd, ⁴*J* = 2.5, 0.8 Hz, 2 H, CH₂N), 4.46 (q, ³*J* = 6.2 Hz, 1 H, CHOH), 4.50 (d, ³*J* = 5.5 Hz, 1 H, CHCOOR), 7.63–7.69 (m, 1 H, Ar), 7.70–7.75 (m, 2 H, Ar), 8.14–8.17 (m, 1 H, Ar). – C₁₄H₁₆N₂O₇S (356.35): calcd. C 47.19, H 4.53, N 7.86; found C 47.06, H 4.44, N 7.96.

***o*-NBS-*N*-C₄H₉-Gly-OMe (7j):** *o*-NBS-Gly-OMe (**4e**), butyl bromide (**6b**), 1.5 h; **7j**, 2.65 g (80%); oil. – ¹H NMR (CDCl₃): $\delta = 0.86$ (t, ³*J* = 7.3 Hz, 3 H, CH₃ aliph), 1.19–1.32 (m, 2 H, CH₂ aliph), 1.45–1.55 (m, 2 H, CH₂ aliph), 3.37 (t, ³*J* = 7.6 Hz, 2 H, CH₂N), 3.64 (s, 3 H, OCH₃), 4.16 (s, 2 H, CH₂COOR), 7.58–7.61 (m, 1 H, Ar), 7.65–7.69 (m, 2 H, Ar), 8.05–8.08 (m, 1 H, Ar). – C₁₃H₁₈N₂O₆S (330.36): calcd. C 47.26, H 5.49, N 8.48, O 29.06, S 9.71; found C 47.11, H 5.47, N 8.55.

***o*-NBS-*N*-allyl-L-Phe-OMe (7k):** *o*-NBS-L-Phe-OMe (**4f**), allyl bromide (**6a**), 0.5 h; **7k**, 3.54 g (88%); oil, $[\alpha]_D^{20} = -24.6$ ($c = 0.56$ in CHCl₃). – ¹H NMR (CDCl₃): $\delta = 3.04$ (dd, ²*J* = 14.1 Hz, ³*J* = 7.5 Hz, 1 H, HCHPh), 3.35 (dd, ²*J* = 14.1 Hz, ³*J* = 7.7 Hz, 1 H, HCHPh), 3.56 (s, 3 H, OCH₃), 3.80 (dd, ²*J* = 16.5 Hz, ³*J* = 6.5 Hz, 1 H, HCHN), 4.11 (dd, ²*J* = 16.5 Hz, ³*J* = 6.3 Hz, 1 H, HCHN), 4.91 (t, ³*J* = 7.6 Hz, 1 H, CHCOOR), 5.11 (dd, ³*J*_{cis} = 10.8 Hz, ²*J* = 0.8 Hz, 1 H, HCH=), 5.22 (dd, ³*J*_{trans} = 17.2 Hz, ²*J* = 0.8 Hz, 1 H, HCH=), 5.72–5.86 (dm, ³*J* = 6.7 Hz, 1 H, CH=), 7.20–7.29 (m, 5 H, Ar), 7.53–7.68 (m, 3 H, Ar), 7.82–7.85 (m, 1 H, Ar). – C₁₉H₂₀N₂O₆S (404.44): calcd. C 56.42, H 4.98, N 6.93; found C 56.31, H 4.80, N 6.99.

***o*-NBS-*N*-Me-L-Phe-OMe (7l):** *o*-NBS-L-Phe-OMe (**4f**), methyl iodide (**6e**), 0.15 h; **7l**, 3.25 g (86%); oil, $[\alpha]_D^{20} = +55.2$ ($c = 1.45$ in CHCl₃). – ¹H NMR (CDCl₃): $\delta = 2.98$ (dd, ²*J* = 14.3 Hz, ³*J* = 9.5 Hz, 1 H, HCHPh), 3.04 (s, 3 H, NCH₃), 3.36 (dd, ²*J* = 14.3 Hz, ³*J* = 6.2 Hz, 1 H, HCHPh), 3.65 (s, 3 H, OCH₃), 4.94 (dd, ³*J* = 6.2, 9.5 Hz, 1 H, CHCOOR), 7.20–7.28 (m, 5 H, Ar), 7.54–7.74 (m, 3 H, Ar), 7.74–7.77 (m, 1 H, Ar). – C₁₇H₁₈N₂O₆S (378.40): calcd. C 53.96, H 4.79, N 7.40; found C 53.78, H 4.71, N 7.33.

***o*-NBS-*N*-Me-*L*-PhGly-OMe (7m):** *o*-NBS-*L*-PhGly-OMe (4g), methyl iodide (6e), 15 h; **7m**, 3.32 g (91%); oil, $[\alpha]_D^{20} = +56.0$ ($c = 1.1$ in CHCl_3). – ^1H NMR (CDCl_3): $\delta = 2.84$ (s, 3 H, NCH_3), 3.70 (s, 3 H, OCH_3), 5.98 (s, 1 H, CHCOOR), 7.24–7.28 (m, 2 H, Ar), 7.35–7.38 (m, 3 H, Ar), 7.64–7.72 (m, 3 H, Ar), 8.05–8.08 (m, 1 H, Ar). – $\text{C}_{16}\text{H}_{16}\text{N}_2\text{O}_6\text{S}$ (364.37): calcd. C 52.74, H 4.43, N 7.69; found C 52.61, H 4.36, N 7.61.

***p*-NBS-*N*-allyl-*L*-Val-OMe (8a):** *p*-NBS-*L*-Val-OMe (5a), allyl bromide (6a), 2 h; **8a**, 3.24 g (91%); oil, $[\alpha]_D^{20} = -124.2$ ($c = 0.65$ in CHCl_3). – ^1H NMR (CDCl_3): $\delta = 0.93$ (d, $^3J = 6.6$ Hz, 3 H, CH_3CH), 1.02 (d, $^3J = 6.6$ Hz, 3 H, CH_3CH), 2.14–2.21 (m, 1 H, CHCH_3), 3.46 (s, 3 H, OCH_3), 3.88 (ddt, $^2J = 16.4$ Hz, $^3J = 5.3$ Hz, $^4J = 1.4$ Hz, 1 H, HCHN), 4.06 (dd, $^2J = 16.4$ Hz, $^3J = 7.8$ Hz, 1 H, HCHN), 4.16 (d, $^3J = 10.5$ Hz, 1 H, CHCOOR), 5.09 (dd, $^3J_{\text{cis}} = 10.1$ Hz, $^2J = 0.9$ Hz, 1 H, HCH=), 5.19 (dd, $^3J_{\text{trans}} = 17.2$ Hz, $^2J = 0.9$ Hz, 1 H, HCH=), 5.65–5.79 (m, 1 H, CH=), 8.00 (dd, 2 H, $^3J = 6.9$ Hz, $^4J = 2.1$ Hz, Ar), 8.31 (dd, 2 H, $^3J = 6.9$ Hz, $^4J = 2.1$ Hz, Ar). – $\text{C}_{15}\text{H}_{20}\text{N}_2\text{O}_6\text{S}$ (356.40): calcd. C 50.55, H 5.66, N 7.86; found C 50.45, H 5.52, N 7.93.

***p*-NBS-*N*-(4-pentenyl)-*L*-Val-OMe (8d):** *p*-NBS-*L*-Val-OMe (5a), 4-pentenyl bromide (6d), 6 h; **8d**, 3.49 g (91%); oil, $[\alpha]_D^{20} = -77.7$ ($c = 0.6$ in CHCl_3) {ref.^[3] $[\alpha]_D^{25} = -82.3$ ($c = 2.5$ in CHCl_3)}

Determination of Optical Purities: ^1H NMR analyses to determine the optical purities of new compounds were made by recording the spectrum of a solution of **7** (2.6 mg) in CDCl_3 (0.5 mL) after the addition of an appropriate amount of a CDCl_3 solution of $\text{Eu}(\text{hfc})_3$ (100 mg/mL CDCl_3) or $\text{Eu}(\text{tfc})_3$ (75 mg/mL CDCl_3) as shift reagents. The same procedure was applied to the corresponding racemized sulfonamide **7-rac**, obtained by reacting the enantiopure **7** (0.2 mmol) with sodium methylate (1 mmol) in anhydrous methanol (1 mL) at 25–65 °C. The starting enantiopure **7**, temperature and time for the racemization, *ee* of the racemized **7-rac**, type and amount of the solution of the shift reagent and signals involved in the shift are as follows.

7c: 25 °C, 8 h, **7c-rac** *ee* = 55%; $\text{Eu}(\text{hfc})_3$, 60 μL ; $\delta = 4.31, 4.54, 4.91$.

7e: 65 °C, 4 h, **7e-rac** *ee* = 0%; $\text{Eu}(\text{hfc})_3$, 80 μL ; $\delta = 4.11$.

7g: 25 °C, 30 h, **7g-rac** *ee* = 0%; $\text{Eu}(\text{hfc})_3$, 60 μL ; $\delta = 3.88$.

7h: 25 °C, 25 h, **7h-rac** *ee* = 0%; $\text{Eu}(\text{hfc})_3$, 60 μL ; $\delta = 4.34$.

7k: 25 °C, 3 h, **7k-rac** *ee* = 45%; $\text{Eu}(\text{tfc})_3$, 200 μL ; $\delta = 4.91$.

Deprotection of Sulfonamides 7,8:

Method A:^[3,6] Sulfonamide **7** or **8** (0.4 mmol), PhSH (1.2 mmol), acetonitrile (10 mL) and anhydrous potassium carbonate (1.6 mmol), were stirred at 50 °C for 1 h. Under these reaction conditions the following esters **9** were obtained:

***N*-Allyl-*L*-Val-OMe (9a):** 43 mg (62%) from **7a**, 40 mg (58%) from **8a**; oil, $[\alpha]_D^{20} = -21.8$ ($c = 1.6$ in CHCl_3) {ref.^[3] $[\alpha]_D^{25} = -21.8$ ($c = 1.6$ in CHCl_3)}

***N*-Bn-*L*-Val-OMe (9c):** 74 mg (83%); oil, $[\alpha]_D^{20} = -51.1$ ($c = 2.1$ in CHCl_3) {ref.^[3] $[\alpha]_D^{24} = -51.5$ ($c = 2.1$ in CHCl_3)}

***N*-Allyl-*L*-Phe-OMe (9k):** 62 mg (72%); oil, $[\alpha]_D^{20} = +16.8$ ($c = 1.2$ in CHCl_3). – ^1H NMR (CDCl_3): $\delta = 1.65$ (br. s, 1 H, NH), 2.95 (d, $^3J = 6.8$ Hz, 2 H, CH_2Ph), 3.10 (ddt, $^2J = 13.0$ Hz, $^3J = 6.1$ Hz, $^4J = 1.3$ Hz, 1 H, HCHN), 3.25 (ddt, $^2J = 13.0$ Hz, $^3J = 5.9$ Hz, $^4J = 1.3$ Hz, 1 H, HCHN), 3.55 (t, $^3J = 6.8$ Hz, 1 H, CHCOOR), 3.63 (s, 3 H, OCH_3), 5.03–5.14 (m, 2 H, $\text{CH}_2=$), 5.73–5.86 (m, 1

H, CH=), 7.15–7.31 (m, 5 H, Ar). – $\text{C}_{13}\text{H}_{17}\text{NO}_2$ (219.28): calcd. C 71.21, H 7.81, N 6.39; found C 71.10, H 7.69, N 6.33.

***N*-Me-*L*-PhGly-OMe (9m):** 63 mg (88%); oil, $[\alpha]_D^{20} = +27.5$ ($c = 1.0$ in CHCl_3) {ref.^[11] $[\alpha]_D^{28} = +131.3$, *c* not reported, in CHCl_3 solution}, 21% *ee*. Compound **9m** was reprotected as previously described in this section. **7m**, $[\alpha]_D^{20} = +23.3$ ($c = 1.0$ in CHCl_3) corresponding to 21% *ee*. Theoretical value of the pure enantiomer **7m**: $[\alpha]_D^{20} = +111.0$. The measured $[\alpha]_D^{20} = +55.5$ of the starting **7m** corresponds to 50% *ee*.

Method B:^{[1c][1d]} sulfonamide **7** (0.4 mmol) in 0.8 mL of a 0.5 M solution of PhS^-K^+ in DMF was left to stand at 25 °C until no starting **7** was detectable by TLC. After usual workup, the following esters **9** were isolated:

***N*-Me-*L*-Phe-OMe (9l):** 71 mg (92%); oil, $[\alpha]_D^{20} = +28.0$ ($c = 0.95$ in CHCl_3) {ref.^[10] $[\alpha]_D^{28} = +28.6$, *c* not reported, in CHCl_3 solution}

***N*-Me-*L*-PhGly-OMe (9m):** 49 mg (68%); oil, $[\alpha]_D^{20} = +15.0$ ($c = 1.1$ in CHCl_3), 11% *ee*.

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