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Synthesis and Reactivity of β-Bromo-β-Substituted Dehydroalanines

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The methyl ester of *N*-*tert*-butoxycarbonyl-(*Z*)-β-bromo-β-(1,2,4-triazol-1-yl)dehydroalanine was prepared by treatment of the methyl ester of *N*-*tert*-butoxycarbonyl-(*E*)-β-(1,2,4-triazol-1-yl)dehydroalanine with *N*-bromosuccinimide (NBS), followed by Et_3N. The reactivities of this compound and of our previously synthesized methyl ester of *N*-*tert*-butoxycarbonyl-β,β-dibromodehydroalanine towards several nucleophiles were studied, and it was found that these compounds react with oxygen nucleophiles to give the corresponding α-alkoxy-β,β-disubstituted alanines. Addition to the α-carbon atom also occurred when the β,β-dibromodehydroalanine derivative was treated with primary amines, giving α-amino-β,β-dibromoalanines. Treatment of the β-bromo-β-(1,2,4-triazol-1-yl)dehydroalanine derivative with amines gave α-(alkylamino)-β-(alkylimino)alanines in high yields. These iminoalanines afforded α-aminoglycines when treated with silica in dichloromethane.

Introduction

Nonproteinogenic amino acids constitute an important class of organic compounds due to their intrinsic biological activity and their application in peptide and combinatorial chemistry. These compounds can be used as conformationally constrained components or as molecular scaffolds in structure–activity relationship studies and in the development of peptidomimetics,[1] so research towards efficient methods that will allow the synthesis of this type of compounds is an important area of peptide chemistry.

We have recently become interested in the synthesis of new α- or β-substituted amino acid and dehydroamino acid derivatives. One of our approaches towards the synthesis of these compounds has been the reaction of β-substituted dehydroamino acid derivatives, namely β-(1,2,4-triazol-1-yl)-dehydroalanine, β-(1,2,4-triazol-1-yl)dehydroaminobutyric acid, β-(1,2,4-triazol-1-yl)dehydrophenylalanine and β-(4-tolylsulfinyl)dehydroserine, with nucleophiles.[2,3]

Here we describe the synthesis of the methyl ester of (*Z*)-*N*-*tert*-butoxycarbonyl-β-bromo-β-(1,2,4-triazol-1-yl)dehydroalanine from the corresponding β-triazolyldehydroalanine derivative by treatment with NBS, followed by Et_3N. The reactivity of this compound towards amines and oxygen nucleophiles was studied, together with that of a previously synthesized β,β-dibromodehydroalanine derivative.[4] Several α-alkoxy-β-substituted alanines were prepared by treating these dehydroalanine derivatives with oxygen nucleophiles. The same reactivity was observed when the β,β-dibromodehydroalanine derivative was treated with primary amines, giving the corresponding α-amino-β,β-dibromoalanines. When the β-triazolyldehydroalanine derivative was treated with amines in methanol, α-alkylamino-β-alkyliminoalanines were obtained in high yields. These were then converted into the corresponding α-aminoglycines by treatment with silica.

α-Aminoglycines have recently been used for introducing chemical diversity into bioactive peptides and in the synthesis of retro-inverso-peptides potentially more stable towards proteolytic degradation.[5–10] The methods used for the synthesis of this type of compounds are low-yielding and multistep, and include the treatment of α-hydroxyglycines with thiols followed by displacement of the alkylthio group by an alkylamine through the use of mercuric salts,[11] the displacement of sulfur from α-isopropylthioglycines with amines in the presence of *N*-bromosuccinimide,[12] reduction of α-azidoglycines,[13] conversion of α-hydroxyglycines into the corresponding acetates followed by treatment with amines[14] and the treatment of α-haloglycines with nitrogen nucleophiles.[15]

Results and Discussion

We recently described the synthesis of β-aminodehydroamino acids from β-triazolyldehydroamino acids by displacement of the triazole moiety with primary amines.[3] With these results in mind we decided to study the reactivity towards nucleophiles of a β-bromo-β-triazolyldehydroalanine derivative. The methyl ester of *N*-*tert*-butoxycarbonyl-(*Z*)-β-bromo-β-(1,2,4-triazol-1-yl)-dehydroalanine was thus synthesised in good yield by treating the methyl ester of (*E*)-*N*-*tert*-butoxycarbonyl-β-(1,2,4-triazol-1-yl)dehydroalanine[16] with NBS followed by Et_3N (Scheme 1).

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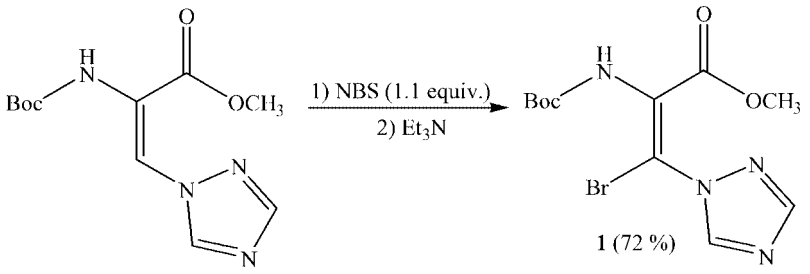


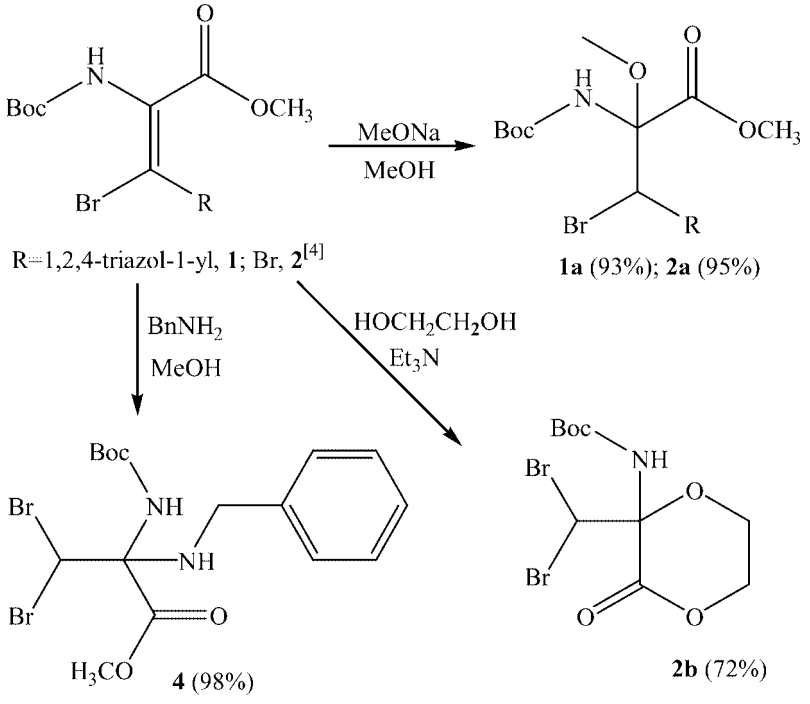
Scheme 1.

The stereochemistry of compound **1** was determined by NOE difference experiments by irradiation of the α-NH and OMe protons. No NOE effect was detected when the α-NH was irradiated, but a NOE enhancement on 3-H and 5-H of the triazole ring was observed when the OMe protons were irradiated, thus indicating that compound **1** is the (*Z*) isomer.

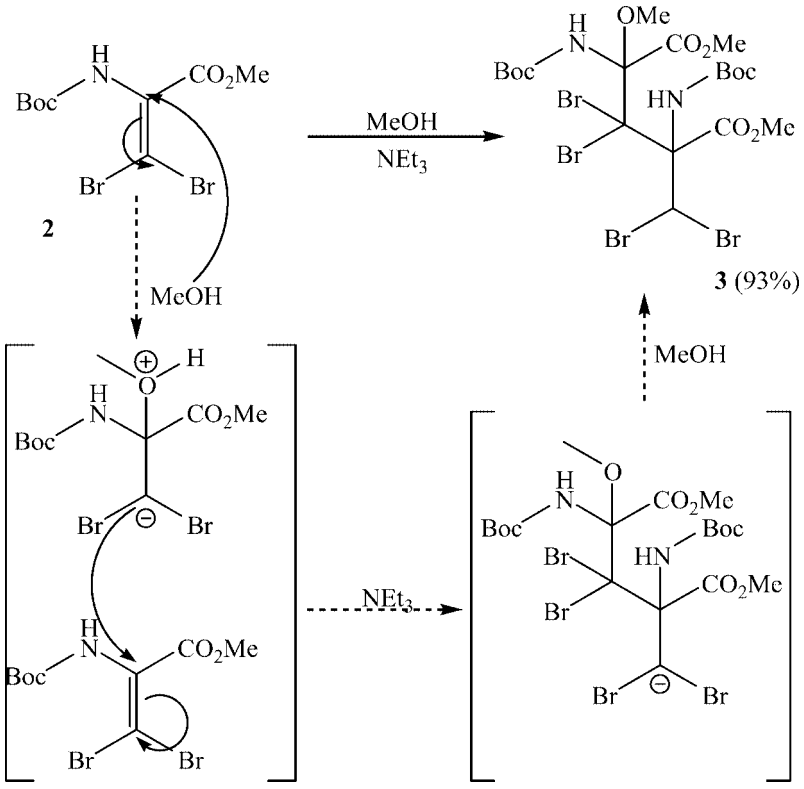
Compound **1** was treated with sodium methoxide to give the α-methoxy-β-bromo-β-triazolylalanine derivative (compound **1a**, Scheme 2). Two stereocenters are generated in this reaction, but the ^{1}H NMR spectrum only showed the formation of one diastereomer. Previously it had been found that the methyl ester of *N*-*tert*-butoxycarbonyl-β-(1,2,4-triazol-1-yl)dehydroalanine reacted with sodium methoxide to give, after substitution of the triazole group and β-addition, the β,β-dimethoxyalanine derivative.[3] The different reactivity now observed for compound **1** can be attributed to the electron-withdrawing effect of the bromine, which induces α-addition. When the methyl ester of *N*-*tert*-butoxycarbonyl-β,β-dibromodehydroalanine[4] was treated with sodium methoxide (compound **2**, Scheme 2) the α-addition product was also obtained (compound **2a**, Scheme 2). Compound **2** and ethylene-1,2-diol in the presence of an excess of triethylamine gave the lactone resulting from α-addition and transesterification (compound **2b**). The α-methoxy-β-bromo-β-triazolylalanine derivative (compound **1a**) was also obtained when compound **1** was treated with an excess of Et_3N (10 equiv.) in methanol, although compound **2** gave an α-methoxy dimer (compound **3**) under the same conditions (Scheme 3). We believe that this compound is the result of α-addition of a methoxide, with subsequent nucleophilic attack of the β-carbon atom on another β,β-dibromoalanine derivative.

A study of the reactivity of compounds **1** and **2** with primary amines was also carried out. Compound **2** reacted with benzylamine to give the α-benzylamino-β,β-dibromoalanine derivative (compound **4**, Scheme 2), thus exhibiting similar reactivity to that shown towards oxygen nucleophiles.

The results presented above are all consistent with the addition to the α-carbon atom previously reported by us when a β-(4-tolylsulfinyl)dehydroserine derivative was



Scheme 2.



Scheme 3.

treated with nucleophiles.[3] This was attributed to the electron-withdrawing effect of the 4-tolylsulfinyl group. In compounds **1** and **2** the β-bromine atoms produce the same effect, activating the α-carbon atom towards addition.

The reaction between compound **1** and benzylamine in methanol gave – after α-addition, β-substitution and β-elimination – the α-benzylamino-β-(benzylimino)alanine derivative in good yield (compound **5a**, Scheme 4). Similar compounds were obtained with several other primary amines (compounds **5b**–**5e**, Scheme 4).

NMR assignments for compounds **5a**–**e** were done using HMQC and HMBC spectra. A correlation between the CH_2 (two doublets at δ = 4.57 and 4.61 ppm) and the β carbon atom (δ =159.84 ppm) in the HMBC spectrum of compound **5a**, for example, allowed the identification of the $=NCH_2$ function. The stereochemistry of the β-C–N double bond in compound **5a** was studied by NOE difference experiments, by irradiation of the β-CH and observation of an NOE enhancement on the $=NCH_2$ protons. This result indicates an (*E*) configuration (Figure 1).

Compounds **5a**–**e** were treated with silica (SiO_2) in dichloromethane at room temperature, giving racemic α-(alkylamino)glycines **6a**–**e** in good to high yields (Scheme 5).

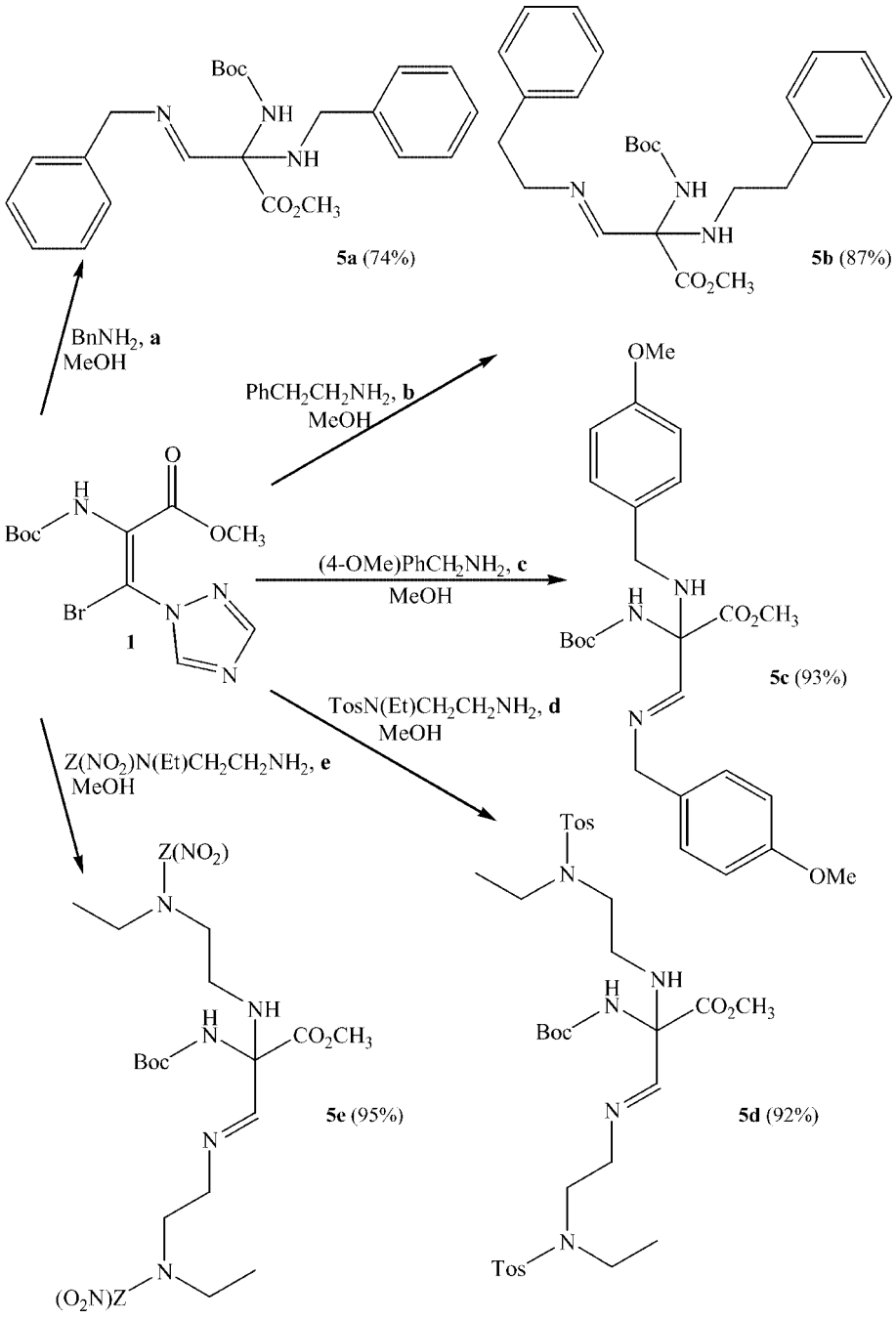
This reaction may involve addition of water to the imine carbon atom and elimination of an amide (Scheme 6). An acidic medium is necessary in order to activate the imine carbon atom towards nucleophilic attack. Support for the proposed mechanism was obtained observing by HPLC the formation of benzylformamide in the reaction of **5a** to give **6a**.

The use of 10 equiv. of amine in a two-step, one-pot procedure gave the corresponding amides of the α-(alkylamino)glycines (compounds **7a** and **7b**, Scheme 7).

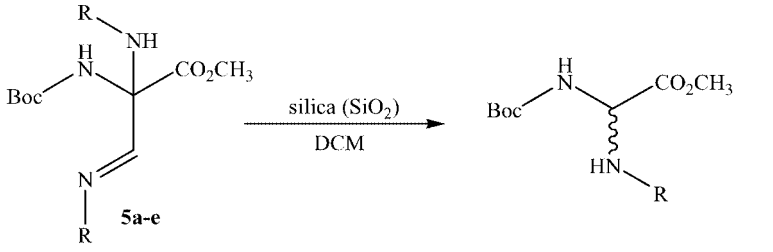
The possibility of using this reaction to cross-link amino acids was also investigated. Thus, compound **1** was treated with the methyl ester of glycine in a two-step, one-pot procedure, giving compound **6f** in high yield (Scheme 7). The synthesis of this compound shows that this strategy can be used to create cross-links between the α-carbon atom of glycine and an amino function of another amino acid derivative.

Conclusions

Several nonproteinogenic amino acids – namely α-substituted β-bromo-β-substituted alanines and α-amino-β-iminoalanines – were synthesized by treatment of β-bromo-β-substituted dehydroalanines with oxygen and nitrogen nucleophiles. Treatment of the β-bromo-β-substituted dehydroalanine derivatives with alkoxides afforded the corresponding α-alkoxy-β-bromo-β-substituted alanines in high yields. When the β,β-dibromodehydroalanine derivative was treated with primary amines the corresponding α-amino-β,β-dibromoalanines were obtained. It thus seems that the electron-withdrawing effect of the β-bromine atoms activates the α-carbon atoms of these compounds towards ad-



Scheme 4.



R = **a**: Bn, **b**: $PhCH_2CH_2$, **c**: (4-OMe)$PhCH_2$, **d**: $TosN(Et)CH_2CH_2$, **e**: $Z(NO_2)N(Et)CH_2CH_2$,

6a (83%), **6b** (76%), **6c** (63%), **6d** (91%), **6e** (87%)

Scheme 5.

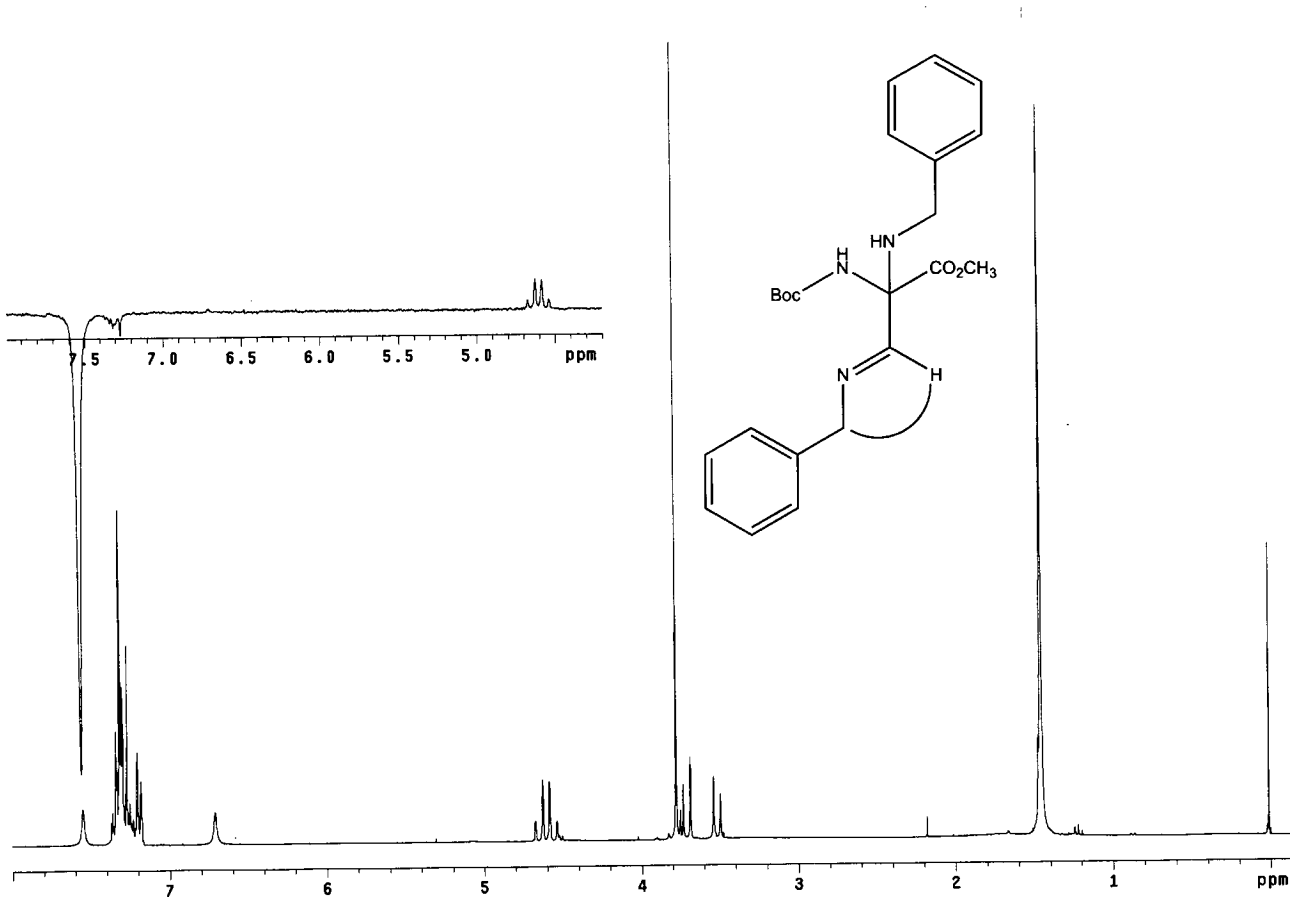
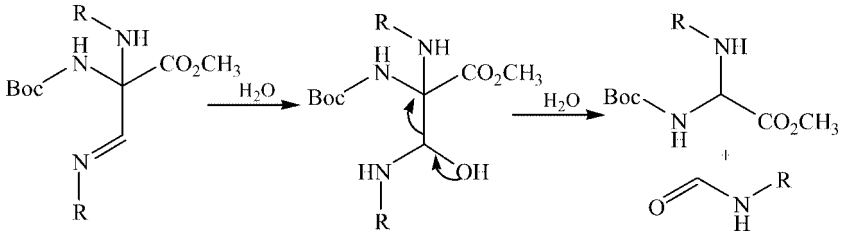
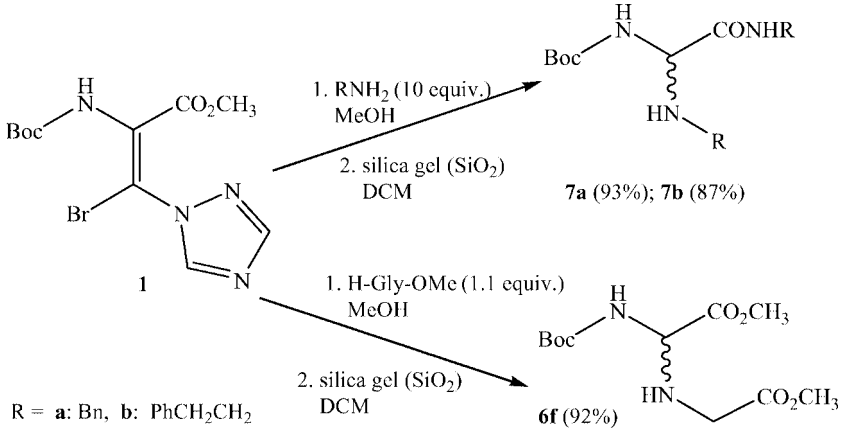


Figure 1. NOE difference experiment on compound **5a** on irradiation of the β-CH proton.



Scheme 6.



Scheme 7.

dition. The reactions between primary amines and a β-bromo-β-(1,2,4-triazol-1-yl)dehydroalanine gave iminoalanines that were easily converted into aminoglycines by treatment with silica. The compounds synthesized could have biological activity, since anticonvulsant activity has been reported for several α-aminoglycines.[11] Furthermore, these amino acids can be introduced into bioactive peptides to enhance chemical diversity and to increase stability towards proteolytic enzymes and/or can be used in structure–activity relationship studies.

Experimental Section

1. General Remarks: Melting points (°C) were determined in a Gallenkamp apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Unity Plus instrument at 300 and 75.4 MHz, respectively. Chemical shifts are given in ppm and coupling constants in Hz. MS and HRMS data were recorded by the mass spectrometry service of the University of Vigo, Spain. Elemental analysis was performed on a LECO CHNS 932 elemental analyser.

The reactions were monitored by thin-layer chromatography (TLC). Column chromatography was performed on Macherey–Nagel silica gel (230–400 mesh). Petroleum ether refers to the boiling range 40–60 °C.

2. Boc-ΔAla[3-(1,2,4-triazol-1-yl)]-OMe: The synthesis of this compound was described elsewhere.[16]

3. Methyl (*Z*)-3-Bromo-2-(*tert*-butoxycarbonylamino)-3-(1*H*-1,2,4-triazol-1-yl)acrylate, Boc-(*Z*)-ΔAla[3-Br,3-(1,2,4-triazol-1-yl)]-OMe (1): NBS (1.10 equiv.) was added with rapid stirring to a solution of (*E*)-Boc-ΔAla[3-(1,2,4-triazol-1-yl)]-OMe (268 mg, 1.00 mmol) in dichloromethane (0.100 mol·dm^{-3}). After the mixture had been kept for 18 h at room temperature, Et_3N (2.00 equiv.) was added and the solution was left stirring for another hour. Dichloromethane (90 cm^3) was then added and the solution was washed with water and brine (3 × 30 cm^3 each). The organic layer was dried with $MgSO_4$ and the solvent was evaporated at reduced pressure to give a yellow oil. Column chromatography (diethyl ether in petroleum ether, 30%) afforded compound **1** (250 mg, 72%) as a white solid, m.p. 119.0–120.0 °C. ^{1}H NMR ($CDCl_3$): δ = 1.49 [s, 9 H, OC(CH_3)$_3$], 3.64 (s, 3 H, CO_2CH_3), 6.61 (s, 1 H, αNH), 8.03 (s, 1 H, 3-H or 5-H triaz.), 8.32 (s, 1 H, 3-H or 5-H triaz.) ppm. ^{13}C NMR ($CDCl_3$): δ = 27.95 [C(*C*H$_3$)$_3$], 53.25 (OCH_3), 83.40 [O*C*(CH_3)$_3$], 103.02 (C), 132.61 (C), 145.94 (CH), 151.07 (C=O Boc), 152.73 (CH), 160.90 (*C*O$_2$CH$_3$) ppm. $C_{11}H_{15}BrN_4O_4$ (347.17): calcd. C 38.06, H 4.35, N 16.14; found C 38.27, H 4.50, N 15.91.

4. Methyl 3,3-Dibromo-2-(*tert*-butoxycarbonylamino)acrylate, Boc-ΔAla(3-Br,3-Br)-OMe (2): The synthesis of this compound was described elsewhere.[4]

5.1. Methyl 3-Bromo-2-(*tert*-butoxycarbonylamino)-2-methoxy-3-(1*H*-1,2,4-triazol-1-yl)propanoate, Boc-Ala[3-Br,2-methoxy,3-(1,2,4-triazol-1-yl)]-OMe (1a): Sodium methoxide (1.10 equiv.) was added with rapid stirring to a solution of (*Z*)-Boc-ΔAla[3-Br, 3-(1,2,4-triazol-1-yl)]-OMe (174 mg, 0.500 mmol) in methanol (0.100 mol·dm^{-3}). After the mixture had been kept for 3 h at room temperature, ethyl acetate (100 cm^3) was added and the solution was washed with water and brine (3 × 30 cm^3 each). The organic layer was dried with $MgSO_4$ and the solvent was evaporated at reduced pressure to give an oil. Crystallization from diethyl ether/petroleum ether afforded compound **1a** (176 mg, 93%) as a white solid, m.p. 103.5–105.0 °C. ^{1}H NMR ($CDCl_3$): δ = 1.46 [s, 9 H, OC(CH_3)$_3$], 3.56 (s, 3 H, OCH_3), 3.75 (s, 3 H, CH_3, CO_2CH_3), 5.69 (s, 1 H, 2-NH), 6.88 (s, 1 H, 3-CH), 7.91 (s, 1 H, 3-H triaz.), 8.32 (s, 1 H, 5-H triaz.) ppm. ^{13}C NMR ($CDCl_3$): δ = 28.00 [C(*C*H$_3$)$_3$], 52.81 (OCH_3), 53.43 (CO_2CH_3), 63.26 (βCH), 81.96 [O*C*(CH_3)$_3$], 86.17 (2-C), 145.39 (5-*C*H triaz.), 151.58 (3-*C*H triaz.), 153.44 (C=O Boc), 165.16 (*C*O$_2$CH$_3$) ppm. $C_{12}H_{19}BrN_4O_5$ (379.21): calcd. C 38.01, H 5.05, N 14.77; found C 38.25, H 5.20, N 14.50.

5.2. Methyl 3,3-Dibromo-2-(*tert*-butoxycarbonylamino)-2-methoxypropanoate: Boc-Ala(3-Br,3-Br,2-methoxy)-OMe (2a): Sodium methoxide (1.10 equiv.) was added with rapid stirring to a solution of Boc-ΔAla(3-Br, 3-Br)-OMe (180 mg, 0.500 mmol) in methanol (0.100 mol·dm^{-3}). After the mixture had been kept for 3 h at room temperature, ethyl acetate (100 cm^3) was added and the solution was washed with water and brine (3 × 30 cm^3 each). The organic layer was dried with $MgSO_4$ and the solvent was evaporated at reduced pressure to give **2a** (186 mg, 95%) as an oil. ^{1}H NMR ($CDCl_3$): δ = 1.44 [s, 9 H, OC(*C*H$_3$)$_3$], 3.49 (s, 3 H, OCH_3), 3.86 (s, 3 H, CO_2CH_3), 5.62 (s, 1 H, 2-NH), 6.11 (s, 1 H, 3-CH) ppm. ^{13}C NMR ($CDCl_3$): δ = 27.99 [C(*C*H$_3$)$_3$], 52.93 (OCH_3), 53.37 (CO_2CH_3), 45.87 (3-*C*H), 81.60 [O*C*(CH_3)$_3$], 87.07 (2-C), 153.02 (C=O Boc), 165.99 (*C*O$_2$CH$_3$) ppm. HRMS (FAB) [M + H]$^+$ found 389.9562; calcd. for $C_{10}H_{18}Br_2NO_5$ 389.9552.

5.3. *tert*-Butyl 2-(Dibromomethyl)-(3-oxo-1,4-dioxan-2-yl)carbamate (2b): Et_3N (10.0 equiv.) was added with rapid stirring to a solution of Boc-ΔAla(3-Br,3-Br)-OMe (90.0 mg, 0.250 mmol) in ethane-1,2-diol (0.100 mol·dm^{-3}). After the mixture had been kept for 18 h at room temperature, diethyl ether (100 cm^3) was added and the solution was washed with water and brine (3 × 30 cm^3 each). The organic layer was dried with $MgSO_4$ and the solvent was evaporated at reduced pressure to give **2b** (71.0 mg, 72%) as an oil. ^{1}H NMR ($CDCl_3$): δ = 1.46 [s, 9 H, OC(CH_3)$_3$], 4.12–4.18 (m, 1 H, CH_2), 4.51–4.67 (m, 2 H, CH_2), 4.75–4.83 (m, 1 H, CH_2), 5.65 (s, 1 H, 2-NH), 5.98 (s, 1 H, CH) ppm. ^{13}C NMR ($CDCl_3$): δ = 28.08 [C(*C*H$_3$)$_3$], 47.67 (CH), 60.89 (5-CH_2), 68.60 (6-CH_2), 82.41 [*C*(CH_3)$_3$], 84.76 (3-C), 153.93 (C=O Boc), 162.71 (2-C=O) ppm. $C_{10}H_{15}Br_2NO_5$ (389.04): calcd. C 30.87, H 3.89, N 3.60; found C 31.26, H 3.92, N 3.65.

5.4. Compound 3: Et_3N (10.0 equiv.) was added with rapid stirring to a solution of Boc-ΔAla(3-Br,3-Br)-OMe (90.0 mg, 0.250 mmol) in methanol (0.100 mol·dm^{-3}). After the mixture had been kept for 4 h at room temperature, diethyl ether (100 cm^3) was added and the solution was washed with water and brine (3 × 30 cm^3 each). The organic layer was dried with $MgSO_4$ and the solvent was evaporated at reduced pressure to give **3** (87.0 mg, 93%) as an oil. ^{1}H NMR ($CDCl_3$): δ = 1.46 [s, 9 H, OC(CH_3)$_3$], 1.47 [s, 9 H, OC(CH_3)$_3$], 3.51 (s, 3 H, OCH_3), 3.87 (s, 3 H, OCH_3), 3.88 (s, 3 H, OCH_3), 5.63 (s, 1 H, NH), 6.18 (s, 1 H, CH), 6.37 (s, 1 H, NH) ppm. ^{13}C NMR ($CDCl_3$): δ = 27.99 [C(*C*H$_3$)$_3$], 28.05 [C(*C*H$_3$)$_3$CO], 45.91 (*C*H), 52.99 (CO_2CH_3), 53.43 (CO_2CH_3), 81.67 [*C*(CH_3)$_3$], 82.69 (C), 87.14 (OCH_3), 150.88 (C=O Boc), 153.07 (C=O Boc), 162.53 (*C*O$_2$CH$_3$), 166.07 (CO_2CH_3) ppm. $C_{19}H_{30}Br_4N_2O_9$ (750.07): calcd. C 30.43, H 4.03, N 3.73; found C 31.08, H 4.15, N 3.77.

6.1. Methyl 2-(Benzylamino)-3,3-dibromo-2-(*tert*-butoxycarbonylamino)propanoate, Boc-Ala(2-benzylamino,3-Br,3-Br)-OMe (4): Benzylamine (2.50 equiv.) was added with rapid stirring to a solution of Boc-ΔAla(3-Br, 3-Br)-OMe (179 mg, 0.500 mmol) in methanol (0.100 mol·dm^{-3}). After the mixture had been kept for 18 h at room temperature, diethyl ether (100 cm^3) was added and the solution was washed with water and brine (3 × 30 cm^3 each). The organic layer was dried with $MgSO_4$ and the solvent was evaporated

at reduced pressure to give compound **4** (229 mg, 98%) as an oil. Recrystallization from *n*-hexane gave white crystals, m.p. 86.0–86.5 °C. ^{1}H NMR ($CDCl_3$): δ = 1.48 [s, 9 H, $OC(CH_3)_3$], 3.22 (s, 1 H, NH), 3.65 (d, J = 12.6 Hz, 1 H, CH_2), 3.82 (s, 3 H, CO_2CH_3), 3.86 (d, J = 12.6 Hz, 1 H, CH_2), 5.87 (s, 1 H, 2-NH), 6.24 (s, 1 H, 3-CH), 7.25–7.40 (m, 5 H, ArH) ppm. ^{13}C NMR ($CDCl_3$): δ = 28.18 [$C(CH_3)_3$], 46.16 (CH_2), 48.64 (βCH), 53.63 (OCH_3), 78.16 (2-C), 80.84 [$C(CH_3)_3$], 127.20 (CH), 128.32 (CH), 128.36 (CH), 139.07 (C), 153.53 (C=O Boc), 168.29 (CO_2CH_3) ppm. $C_{16}H_{22}Br_2N_2O_4$ (466.16): calcd. C 41.22, H 4.76, N 6.01; found C 41.21, H 4.77, N 6.00.

7.1. 2-[Ethyl(4-tolylsulfonyl)amino]ethylammonium Trifluoroacetate (d): This compound was obtained by treatment of *N*-(*tert*-butoxycarbonyl)-2-[ethyl(4-tolylsulfonyl)amino]ethylamine[17] (685 mg, 2.00 mmol) with TFA (10 cm^3) to give a white solid (683 mg, 96%). Recrystallization from methanol/diethyl ether gave white crystals, m.p. 115.5–116.5 °C. ^{1}H NMR ($CDCl_3$): δ = 1.04 (t, J = 7.2 Hz, 3 H, CH_3), 2.41 (s, 3 H, Tos CH_3), 3.19–3.26 (m, 4 H, 2×CH_2), 3.34–3.38 (m, 2 H, CH_2), 7.29 (d, J = 8.1 Hz, 2 H, ArH), 7.68 (d, J = 8.1 Hz, 2 H, ArH), 8.21 (br. s, 3 H, NH_3) ppm. ^{13}C NMR ($CDCl_3$): δ = 13.20 (CH_3CH_2), 21.46 (CH_3 Tos), 39.30 (CH_2), 44.50 (CH_2), 44.92 (CH_2), 127.25 (2×CH), 129.94 (2×CH), 135.17 (C), 143.95 (C) ppm. $C_{13}H_{19}F_3N_2O_4S$ (356.36): calcd. C 43.83, H 5.40, N 7.85, S 9.25; found C 43.82, H 5.37, N 7.86, S 9.00.

7.2. 2-[Ethyl(4-nitrobenzyloxycarbonyl)amino]ethylammonium Trifluoroacetate (e): *N*-(*tert*-Butoxycarbonyl)-2-[ethyl(4-nitrobenzyloxycarbonyl)amino]ethylamine was obtained from *N*-(*tert*-butoxycarbonyl)-2-(ethylamino)ethylamine[18] (940 mg, 5.00 mmol) by addition of 4-nitrobenzyloxycarbonyl chloroformate (1.00 equiv.) in dioxane/NaOH (2.00 mol·dm^{-3}) (5:1) in an ice bath. After the mixture had been stirred overnight the dioxane was removed and the residue was partitioned between ethyl acetate (150 cm^3) and $KHSO_4$ (1 mol·dm^{-3}, 50 cm^3). The organic layer was washed with $KHSO_4$ (1 mol·dm^{-3}), $NaHCO_3$ (1 mol·dm^{-3}) and brine (3 × 30 cm^3 each). The organic layer was dried with $MgSO_4$ and the solvent was evaporated at reduced pressure to give *N*-(*tert*-butoxycarbonyl)-2-[ethyl(4-nitrobenzyloxycarbonyl)amino]ethylamine (1.70 g, 92%) as an oil. Crystallization from ethyl acetate/*n*-hexane gave a white solid, m.p. 83.5–84.0 °C. ^{1}H NMR ($CDCl_3$): δ = 1.16 (t, J = 7.2 Hz, 3 H, CH_3), [s, 9 H, $OC(CH_3)_3$], 3.29–3.42 (comp. signal, 6 H, 3×CH_2), 4.67, 4.90 (2×br s, 1 H, NH), 5.24 [s, 2 H, Z(NO_2) CH_2], 7.52 (br. d, J = 7.8 Hz, 2 H, ArH), 8.23 (d, J = 8.4 Hz, 2 H, ArH) ppm. ^{13}C NMR ($CDCl_3$): δ = 13.94 (CH_3CH_2), 28.35 [$C(CH_3)_3$], 39.35 (CH_2), 42.66 (CH_2), 46.89 (CH_2), 65.67 [CH_2 Z(NO_2)], 79.59 [$C(CH_3)_3$], 123.79 (2×CH), 127.96 (2×CH), 144.13 (C), 147.55 (C), 155.39 (C=O Boc), 156.14 [C=O Z(NO_2)] ppm. $C_{17}H_{25}N_3O_6$ (367.40): calcd. C 55.54, H 6.98, N 11.37; found C 55.58, H 6.86, N 11.44.

Treatment of *N*-(*tert*-butoxycarbonyl)-2-[ethyl(4-nitrobenzyloxycarbonyl)amino]ethylamine (1.42 g, 3.90 mmol) with TFA (12.0 cm^3) gave compound **e** (1.30 g, 87%). Crystallization from methanol/diethyl ether gave a white solid, m.p. 130.0–131.0 °C. ^{1}H NMR (DMSO): δ = 1.07 (t, J = 6.6 Hz, 3 H, CH_3), 2.96 (t, J = 6.6 Hz, 2 H, CH_2CH_3), 3.29–3.46 (complex signal, 4 H, 2×CH_2), 5.22 [s, 2 H, Z(NO_2) CH_2], 7.63 (d, J = 8.7 Hz, 2 H, ArH), 7.95 (br. s, 3 H, NH_3), 8.23 (d, J = 8.1 Hz, 2 H, ArH) ppm. ^{13}C NMR ($CDCl_3$): δ = 13.54 (CH_3CH_2), 37.34 (CH_2), 41.78 (CH_2), 44.16 (CH_2), 65.25 [CH_2 Z(NO_2)], 123.58 (2×CH), 128.13 (2×CH), 144.76 (C), 146.98 (C), 155.44 [C=O Z(NO_2)] ppm. $C_{14}H_{18}F_3N_3O_6$ (381.31): calcd. C 44.05, H 4.73, N 10.99; found C 44.10, H 4.76, N 11.02.

8. General Procedure for the Synthesis of α-(Alkylamino)-β-(alkylimino)alanines 5a–e: The amine (2.20 equiv.) and Et_3N (10.0 equiv.) were added with rapid stirring to a solution of Boc-(*Z*)-ΔAla[3-Br, 3-(1,2,4-triazol-1-yl)]-OMe (174 mg, 0.500 mmol) in methanol (0.100 mol·dm^{-3}). After the mixture had been kept for 18 h at room temperature, ethyl acetate (45 cm^3) was added and the solution was washed with water and brine (3 × 15 cm^3 each). The organic layer was dried with $MgSO_4$ and the solvent was evaporated at reduced pressure to give compounds **5a–e**.

8.1. Methyl (*E*)-2-(Benzylamino)-3-(benzylimino)-2-(*tert*-butoxycarbonylamino)propanoate, Boc-Ala[2-benzylamino,3-(*E*)-benzylimino]-OMe (5a): The general procedure described above was used with benzylamine. Crystallization from diethyl ether/*n*-hexane afforded compound **5a** (151 mg, 74%) as a white solid, m.p. 88.5–89.5 °C. ^{1}H NMR ($CDCl_3$): δ = 1.49 [s, 9 H, $OC(CH_3)_3$], 3.51 (d, J = 12.9 Hz, 1 H, CH_2), 3.72 (d, J = 12.9 Hz, 1 H, CH_2), 3.77 (s, 3 H, CO_2CH_3), 4.57 (d, J = 14.1 Hz, 1 H, =NCH_2), 4.61 (d, J = 14.1 Hz, 1 H, =NCH_2), 6.72 (s, 1 H, NH), 7.19–7.37 (m, 11 H, ArH + NH), 7.56 (s, 1 H, 3-CH) ppm. ^{13}C NMR ($CDCl_3$): δ = 28.20 [$C(CH_3)_3$], 45.99 (CH_2), 53.25 (OCH_3), 62.88 (=NCH_2), 75.01 (2-C), 80.10 [$C(CH_3)_3$], 127.00 (CH), 127.28 (CH), 127.91 (CH), 128.15 (CH), 128.35 (CH), 128.54 (CH), 137.73 (C), 139.62 (C), 154.28 (C=O Boc), 159.84 (3-CH), 169.08 (CO_2CH_3) ppm. $C_{23}H_{29}N_3O_4$ (411.50): calcd. C 67.13, H 7.10, N 10.21; found C 67.20, H 6.95, N 9.96.

8.2. Methyl (*E*)-2-(*tert*-Butoxycarbonylamino)-2-(phenethylamino)-3-(phenethylimino)propanoate, Boc-Ala[2-(2-phenyl)ethylamino,3-(*E*)-(2-phenyl)ethylimino]-OMe (5b): The general procedure described above was used with 2-(phenyl)ethylamine, giving compound **5b** (192 mg, 87%) as an oil. ^{1}H NMR ($CDCl_3$): δ = 1.44 [s, 9 H, $OC(CH_3)_3$], 2.63–2.87 (m, 4 H, 2CH_2), 2.96–3.05 (m, 2 H, CH_2), 3.59–3.84 (m, 5 H, =NCH_2 + CO_2CH_3), 6.51 (s, 1 H, NH), 7.05–7.36 (m, 12 H, ArH + 3-CH + NH) ppm. ^{13}C NMR ($CDCl_3$): δ = 28.20 [$C(CH_3)_3$], 36.02 (CH_2), 36.44 (CH_2), 45.87 (CH_2), 52.68 (OCH_3), 60.65 (2-C), 65.77 (=NCH_2), 80.10 [$C(CH_3)_3$], 126.22 (CH), 128.34 (CH), 128.43 (CH), 128.62 (CH), 128.80 (CH), 138.96 (C), 139.40 (3-CH), 139.59 (C), 155.07 (C=O Boc), 170.63 (CO_2CH_3) ppm. HRMS (FAB) found 440.2565 [M + H]$^+$, calcd. for $C_{25}H_{34}N_3O_4$ 440.2471.

8.3. Methyl (*E*)-2-(*tert*-Butoxycarbonylamino)-2-(4-methoxybenzylamino)-3-(4-methoxybenzylimino)propanoate, Boc-Ala{2-(4-methoxybenzylamino),3-[(*E*)-4-methoxybenzylimino]}-OMe (5c): The general procedure described above was used with 4-methoxybenzylamine, giving compound **5c** (151 mg, 93%) as an oil. Crystallization from diethyl ether/*n*-hexane gave compound **5c** as white solid, m.p. 99.0–99.5 °C. ^{1}H NMR ($CDCl_3$): δ = 1.45 [s, 9 H, $OC(CH_3)_3$], 3.44 (d, J = 12.6 Hz, 1 H, CH_2), 3.63 (d, J = 12.6 Hz, 1 H, CH_2), 3.77 (s, 3 H, OCH_3), 3.80 (s, 3 H, OCH_3), 3.81 (s, 3 H, OCH_3), 4.51 (d, J = 13.8 Hz, 1 H, =NCH_2), 4.60 (d, J = 13.8 Hz, 1 H, =NCH_2), 6.69 (s, 1 H, NH), 6.18–6.88 (m, 5 H, ArH), 7.11 (d, J = 8.7 Hz, 2 H, ArH), 7.22 (d, J = 8.4 Hz, 2 H, ArH), 7.51 (s, 1 H, 3-CH) ppm. ^{13}C NMR ($CDCl_3$): δ = 28.23 [$C(CH_3)_3$], 45.41 (CH_2), 53.25 (OCH_3), 55.26 (2×OCH_3), 62.35 (=NCH_2), 74.99 (2-C), 80.08 [$C(CH_3)_3$], 113.73 (CH), 113.96 (CH), 129.21 (CH), 129.58 (CH), 129.83 (C), 131.75 (C), 154.33 (C=O Boc), 158.66 (C), 158.86 (C), 159.48 (3-CH), 169.16 (CO_2CH_3) ppm. $C_{25}H_{33}N_3O_6$ (324.37): calcd. C 63.68, H 7.05, N 8.91; found C 63.66, H 7.06, N 8.96.

8.4. Boc-Ala{2-[2-ethyl,2-(4-tolylsulfonylamino)ethylamino],3-(*E*)-[2-ethyl,2-(4-tolylsulfonylamino)ethylimino]}-OMe (5d): The general procedure described above was used with 2-[ethyl(4-tolylsulfonyl)-amino]ethylamine trifluoroacetate, giving compound **5d** (313 mg, 92%) as an oil. ^{1}H NMR ($CDCl_3$): δ = 1.04–1.11 (m, 6 H, 2×CH_3), 1.42 [s, 9 H, $OC(CH_3)_3$], 2.40 (s, 6 H, 2×Tos CH_3), 2.48–2.76 (m,

2 H, CH_2), 3.12–3.25 (m, 7 H, 3×CH_2 + NH), 3.34–3.39 (m, 2 H, CH_2), 3.68–3.72 (m, 2 H, =NCH_2), 3.76 (s, 3 H, CO_2CH_3), 6.51 (s, 1 H, BocNH), 7.25–7.29 (m, 4 H, ArH), 7.44 (m, 1 H, 3-H), 7.65–7.70 (m, 4 H, ArH) ppm. ^{13}C NMR ($CDCl_3$): δ = 13.83 (CH_3CH_2), 13.90 (CH_3CH_2), 21.38 (2×CH_3, Ar–CH_3), 28.10 [C(CH_3)$_3$], 43.81 (CH_2), 43.91 (CH_2), 47.54 (CH_2 N=CH_2CH_2), 48.05 (CH_2), 53.27 (OMe), 58.79 (N=CH_2), 74.57 (2-C), 80.09 [$C(CH_3)_3$], 127.00 (2×CH), 127.06 (2×CH), 129.55 (2×CH), 129.62 (2×CH), 136.53 (C), 136.68 (C), 143.05 (C), 143.18 (C), 154.21 (C=O Boc), 160.08 (3-CH), 168.78 (CO_2CH_3) ppm. HRMS (FAB) [M + H]$^+$ found 682.2935; calcd. for $C_{31}H_{49}N_5O_8S_2$ 682.2944.

8.5. Boc-Ala{2-[2-ethyl,2-(4-nitrobenzyloxycarbonylamino)ethylamino],3-(*E*)-[2-ethyl,2-(4-nitrobenzyloxycarbonylamino)ethylimino]}-OMe (5e): The general procedure described above was used with 2-[ethyl(4-nitrobenzyloxycarbonyl)amino]ethylamine trifluoroacetate, giving compound **5e** (347 mg, 95%) as an oil. ^{1}H NMR ($CDCl_3$): δ = 1.11–1.20 (m, 6 H, CH_3 Et), 1.43 [s, 9 H, OC(CH_3)$_3$], 2.76–2.84 (m, 1 H, CH_2), 3.30–3.47 (m, 11 H, 6×CH_2), 3.76 (s, 3 H, CO_2CH_3), 5.02 (s, 1 H, NH), 5.21 [s, 2 H, Z(NO_2)-CH_2], 5.23 [s, 2 H, Z(NO_2) CH_2], 6.40 (s, 1 H, NH), 7.48–7.52 (m, 4 H, ArH), 8.13–8.24 (m, 5 H, ArH + 3-CH) ppm. ^{13}C NMR ($CDCl_3$): δ = 13.11 (CH_2CH_3), 13.84 (CH_2CH_3), 28.19 [C(CH_3)$_3$], 37.68 (=NCH_2), 42.56 (CH_2), 43.07 (CH_2), 43.14 (CH_2), 46.10 (CH_2), 47.18 (CH_2), 65.52 [CH_2 Z(NO_2)], 65.82 [CH_2 Z(NO_2)], 79.59 (2-C), 80.33 [$C(CH_3)_3$], 123.72 (CH), 123.77 (CH), 127.88 (2×CH), 143.85 (C), 144.26 (C), 147.44 (C), 147.55 (C), 155.12 (C=O Boc), 161.56 (CO_2CH_3), 170.46 (3-CH) ppm. HRMS (FAB) found 732.3207 [M + H]$^+$, calcd.for $C_{33}H_{46}N_7O_{12}$ 732.3204.

9. Synthesis of α-Alkylaminoglycines

9.1. Methyl 2-(Benzylamino)-2-(*tert*-butoxycarbonylamino)acetate, Boc-Gly(2-benzylamino)-OMe (6a): Treatment of Boc-Ala[2-benzylamino,3-(*E*)-benzylimino]-OMe (**5a**) (104 mg, 0.300 mmol) with silica (1.00 g) in dichloromethane (5.00 cm^3) for 1 h afforded compound **6a** (80.0 mg, 83%) as a white solid, m.p. 69.0–70.0 °C. ^{1}H NMR ($CDCl_3$): δ = 1.47 [s, 9 H, OC(CH_3)$_3$], 3.75 (s, 3 H, CO_2CH_3), 3.83 (s, 2 H, CH_2), 5.07 (d, J = 6.3 Hz, 1 H, 2-CH), 5.37 (s, 1 H, NH), 7.26–7.35 (m, 6 H, ArH + NH) ppm. ^{13}C NMR ($CDCl_3$): δ = 28.27 [C(CH_3)$_3$], 48.83 (CH_2), 52.69 (OCH_3), 65.77 (CH), 80.26 [$C(CH_3)_3$], 127.20 (CH), 128.24 (CH), 128.44 (CH), 139.20 (C), 155.24 (C=O Boc), 170.63 (CO_2CH_3) ppm. MS (FAB) *m*/*z* (%): 295.16 (100) [M + H]$^+$, 235.15 (27.5) [M – CO_2Me]$^+$. $C_{15}H_{22}N_2O_4$ (294.35): calcd. C 61.22, H 7.48, N, 9.52; found C 61.08, H 7.39, N 9.52.

9.2. Methyl 2-(*tert*-Butoxycarbonylamino)-2-(phenethylamino)acetate,Boc-Gly[2-(2-phenyl)ethylamino]-OMe (6b): The same procedure as described above was used, with substitution of compound **5a** by compound **5b**, giving compound **6b** (71.0 mg, 76%) as an oil. ^{1}H NMR ($CDCl_3$): δ = 1.45 [s, 9 H, OC(CH_3)$_3$], 2.76–2.97 (m, 4 H, CH_2), 3.80 (s, 3 H, CO_2CH_3), 5.06 (d, J = 7.2 Hz, 1 H, CH), 5.30 (s, 1 H, NH), 7.04–7.29 (m, 6 H, ArH + NH) ppm. ^{13}C NMR ($CDCl_3$): δ = 28.20 [C(CH_3)$_3$], 36.02 (CH_2), 45.87 (CH_2), 52.67 (OCH_3), 65.77 (CH), 80.10 [$C(CH_3)_3$], 126.22 (CH), 128.43 (CH), 128.62 (CH), 139.40 (C), 155.07 (C=O Boc), 170.63 (CO_2CH_3) ppm. HRMS (EI) found 308.1741, calcd. for $C_{16}H_{24}N_2O_4$ [M]$^+$ 308.1736.

9.3. Methyl 2-(*tert*-Butoxycarbonylamino)-2-(4-methoxybenzylamino)acetate, Boc-Gly[2-(4-methoxybenzylamino)]-OMe (6c): The same procedure as described above was used, with substitution of compound **5a** by compound **5c**, giving compound **6c** (61.0 mg, 63%) as a white solid, m.p. 47.0–48.0 °C. ^{1}H NMR ($CDCl_3$): δ = 1.47 [s, 9 H, OC(CH_3)$_3$], 3.74 (s, 3 H, OCH_3), 3.75 (s, 2 H, CH_2), 3.79 (s, 3 H, OCH_3), 5.03 (br. s, 1 H, CH), 5.40 (s, 1 H, NH), 6.85 (d, J = 8.7 Hz, 2 H, ArH), 7.24 (d, J = 8.7 Hz, 2 H, ArH) ppm. ^{13}C NMR ($CDCl_3$): δ = 28.25 [C(CH_3)$_3$], 48.20 (CH_2), 52.64 (OCH_3), 52.22 (OCH_3), 65.61 (CH), 80.15 [$C(CH_3)_3$], 113.79 (CH), 129.46 (CH), 131.25 (C), 155.04 (C=O Boc), 158.76 (C), 170.68 (CO_2CH_3) ppm. MS (FAB) *m*/*z* (%): 325.12 (100) [M + H]$^+$, 265.11 (19) [M – CO_2Me]$^+$. $C_{16}H_{24}N_2O_5$ (324.37): calcd. C 59.24, H 7.46, N 8.64; found C 59.05, H 7.31, N 8.64.

9.4. Boc-Gly{2-[2-[ethyl(4-tolylsulfonyl)amino]ethylamino]}-OMe (6d): The same procedure as described above was used, with substitution of compound **5a** by compound **5d**, giving compound **6d** (117 mg, 91%) as an oil. ^{1}H NMR ($CDCl_3$): δ = 1.12 (t, J = 7.2 Hz, 3 H, CH_3), 1.46 [s, 9 H, OC(CH_3)$_3$], 2.43 (s, 3 H, Tos CH_3), 2.84–2.90 (m, 2 H, CH_2), 3.20–3.24 (m, 4 H, 2×CH_2), 3.80 (s, 3 H, CO_2CH_3), 5.02 (d, J = 8.4 Hz, 1 H, BocNH or CH_2NH), 5.34 (comp. signal, 1 H, BocNH or CH_2NH), 7.30 (d, J = 8.1 Hz, 2 H, ArH), 7.70 (d, J = 8.1 Hz, 2 H, ArH) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.08 (CH_3CH_2), 21.42 (CH_3 Tos), 28.21 [C(CH_3)$_3$], 43.78 (CH_2), 43.91 (CH_2), 47.62 (CH_2), 52.72 (OCH_3), 65.65 (αCH), 80.22 [$C(CH_3)_3$], 127.11 (2×CH), 129.61 (2×CH), 136.53 (C), 143.17 (C), 155.15 (C=O Boc), 170.29 (CO_2CH_3) ppm. HRMS (FAB) [M + H]$^+$ found 430.2021, calcd. for $C_{19}H_{32}N_3O_6S$ 430.2012.

9.5. Boc-Gly{2-[2-[ethyl(4-nitrobenzyloxycarbonyl)amino]-ethylamino]}-OMe (6e): The same procedure as described above was used, with substitution of compound **5a** by compound **5e**, giving compound **6e** (119 mg, 87%) as an oil. ^{1}H NMR ($CDCl_3$): δ = 1.14 (t, J = 7.5 Hz, 3 H, CH_3), 1.45 [s, 9 H, OC(CH_3)$_3$], 2.83 (br. d, J = 5.4 Hz, 2 H, CH_2), 3.31–3.41 (m, 4 H, 2×CH_2), 3.73 (s, 3 H, CO_2CH_3), 5.01 (comp. signal, 1 H, αCH), 5.22 [s, 2 H, Z(NO_2), CH_2], 5.35 (br. s, 1 H, CONH), 7.51 (d, J = 8.1 Hz, 2 H, ArH), 8.22 (d, J = 9.0 Hz, 2 H, ArH) ppm. ^{13}C NMR ($CDCl_3$): δ = 13.90 (CH_3CH_2), 28.23 [C(CH_3)$_3$], 42.45 (CH_2), 43.11 (CH_2), 46.43 (CH_2), 47.22 (CH_2), 52.76 (OCH_3), 65.54 (αCH), 80.40 [$C(CH_3)_3$], 123.76 (2×CH), 127.97 (2×CH), 144.29 (C), 147.50 (C), 155.15 (C=O Boc), 164.68 [CO Z(NO_2)], 170.47 (CO_2CH_3) ppm. HRMS (FAB) [M + H]$^+$ found 455.2132, calcd. for $C_{20}H_{31}N_4O_8$ 455.2142.

10.1. Methyl 2-(*tert*-Butoxycarbonylamino)-2-(2-methoxy-2-oxoethylamino)acetate,Boc-Gly[2-(methoxycarbonylmethylamino)]-OMe (6f): H-Gly-OMe (2.20 equiv.) was added with rapid stirring to a solution of (*Z*)-Boc-ΔAla[3-Br, 3-(1,2,4-triazol-1-yl)-OMe (174 mg, 0.500 mmol) in methanol (0.100 mol·dm^{-3}). After the mixture had been kept for 18 h at room temperature, diethyl ether (45 cm^3) was added and the solution was washed with water and brine (3×15 cm^3 each). The organic layer was dried with $MgSO_4$, and the solvent was evaporated at reduced pressure to give an oil, which was subjected to column chromatography with diethyl ether/petroleum ether (2:1) to give compound **6f** (79.0 mg, 92%) as an oil. ^{1}H NMR ($CDCl_3$): δ = 1.44 [s, 9 H, OC(CH_3)$_3$], 3.48 (d, J = 3.3 Hz, 2 H, CH_2), 3.73 (s, 3 H, OCH_3), 3.79 (s, 3 H, OCH_3), 5.05 (d, J = 8.4 Hz, 1 H, 2-CH), 5.36 (br. d, J = 8.4 Hz, 1 H, NH) ppm. ^{13}C NMR ($CDCl_3$): δ = 28.20 [C(CH_3)$_3$], 46.27 (CH_2), 52.00 (OCH_3), 52.83 (OCH_3), 65.53 (2-CH), 80.35 [$C(CH_3)_3$], 155.12 (C=O Boc), 170.04 (CO_2CH_3), 172.42 (CO_2CH_3) ppm. HRMS (FAB) found 277.1410 [M + H]$^+$, calcd. for $C_{11}H_{21}N_2O_6$ 277.1400.

10.2. *tert*-Butyl 1,2-Bis(benzylamino)-2-oxoethylcarbamate, Boc-Gly(2-benzylamino)-NHBn (7a): The same procedure as described above was used, with substitution of H-Gly-OMe (2.20 equiv.) by benzylamine (10.0 equiv.) to give compound **7a** (103 mg, 93%). Crystallization from diethyl ether/*n*-hexane afforded a white solid, m.p. 134.0–135.5 °C. ^{1}H NMR ($CDCl_3$): δ = 1.48 [s, 9 H, OC(CH_3)$_3$], 3.54 (d, J = 13.2 Hz, 1 H, CH_2), 3.80 (d, J = 13.2 Hz, 1 H, CH_2), 4.44 (d, J = 5.7 Hz, 2 H, CH_2), 4.95 (d, J = 4.8 Hz, 1 H, CH), 5.89 (s, 1 H, NH), 7.25–7.42 (m, 12 H, ArH + 2NH) ppm.

^{13}C NMR ($CDCl_3$): δ = 28.29 [C(CH_3)$_3$], 43.65 (CH_2), 47.32 (CH_2), 66.49 (CH), 80.01 [C(CH_3)$_3$], 127.14 (CH), 127.58 (CH), 127.65 (CH), 127.82 (CH), 128.09 (CH), 128.47 (CH), 128.71 (CH), 137.77 (C), 139.31 (C), 155.94 (C=O Boc), 169.28 (CO_2CH_3) ppm. $C_{21}H_{27}N_3O_3$ (369.46): calcd. C 68.27, H 7.37, N 11.37; found C 68.07, H 7.25, N 10.98.

10.3. *tert*-Butyl 2-Oxo-1,2-bis(phenethylamino)ethylcarbamate, Boc-Gly[2-(2-phenyl)ethylamino]-NHCH$_2$CH$_2$Ph (7b): The same procedure as described above was used, with substitution of H-Gly-OMe (2.20 equiv.) by phenylethylamine (10.0 equiv.), giving compound **7b** (104 mg, 87%) as an oil. Crystallization from diethyl ether/*n*-hexane afforded a white solid, m.p. 121.0–123.0 °C. ^1H NMR ($CDCl_3$): δ = 1.44 [s, 9 H, OC(CH_3)$_3$], 2.37–2.46 (m, 1 H, CH_2), 2.60–2.71 (m, 4 H, CH_2), 2.88–3.00 (m, 1 H, CH_2), 3.28–3.49 (m, 2 H, CH_2), 4.78 (d, J = 3.9 Hz, 3 H, 2-CH), 5.72 (s, 1 H, NH), 6.83 (s, 1 H, NH), 7.10–7.33 (m, 11 H, ArH + NH) ppm. ^{13}C NMR ($CDCl_3$): δ = 28.24 [C(CH_3)$_3$], 35.40 (CH_2), 36.31 (CH_2), 40.56 (CH_2), 43.99 (CH_2), 66.39 (CH), 79.72 [C(CH_3)$_3$], 126.18 (CH), 126.48 (CH), 128.35 (CH), 128.55 (CH), 128.59 (CH), 128.77 (CH), 138.54 (C), 139.91 (C), 155.89 (C=O Boc), 169.15 (CO_2CH_3) ppm. $C_{23}H_{31}N_3O_3$ (397.51): calcd. C 69.49, H 7.86, N 10.57; found C 69.40, H 7.89, N 10.66.

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