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Synthesis of bis-α-amino acids through proline catalyzed asymmetric α-amination of higher homologs of Garner's aldehyde

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ABSTRACT

A very convenient synthesis of bis-α-amino acids from the higher homologs of Garner's aldehyde is reported. The key step is proline catalyzed asymmetric amination of the aldehydes using dibenzylazodicarboxylate. The aldehydes used are either commercially available or can easily be prepared from aspartic or glutamic acid. One of the two chiral centers in the bis-amino acids comes from the aldehyde and the other one is generated through the proline catalyzed reaction, which were high yielding and proceeded with very high diastereoselectivity (93–99%). The reported route offers a general method for the synthesis of the title compounds with desired stereochemical outcome.

1. Introduction

Bis-α-amino acids, **1** are involved in a number of very vital functions in various microorganisms (Fig. 1) and two of the most commonly discussed examples are diaminopimelic acid (**1a**) and diaminosuberic acid (**1b**). Compound **1a** plays an important role in bacterial biosynthesis of L-lysine and provides structural stability to the peptidoglycan units of bacterial cell walls by functioning as cross-linking units between polysaccharides.[1] The absence of a **1a** based biosynthetic pathway in mammals has spurred an interest in the synthesis and study of **1a** and related analogs. Compound **1b** on the other hand, has received attention for its structural similarity to cystine and has been used as a structural replacement for cystine in biologically active peptides.[2]

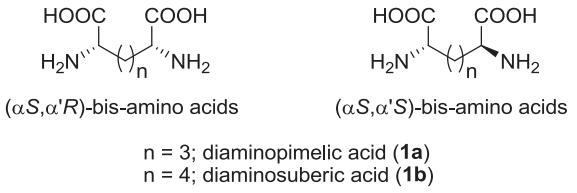

Fig. 1. Bis-α-amino acids.

The importance of these molecules has resulted in a number of reports dealing with their synthesis. Synthetic strategies based on olefin metathesis and metal mediated cross coupling reactions of chiral precursors predominate the available syntheses of these molecules.[3] Procedures based on stereoselective and stereospecific transformations are also available.[4] Most of these procedures are limited to the synthesis of **1a** and/or **1b** or their specific lower analogs and general methods available for the synthesis of **1** of any length are limited. Very recently, Soloshonok et al. have reported a general procedure for the synthesis of bis-α-amino acids through bis-alkylation of 2 equiv of a glycine equivalent using suitable dihalogenated reagents.[5] We report here an easy and efficient procedure for the synthesis of **1** with various chain lengths from the higher homologs, **2** of Garner's aldehyde through proline catalyzed asymmetric α-amination (Scheme 1).[6] The strategy reported here is based on using a starting material with one of the stereo centers fixed and generating the second one using an asymmetric functionalization. The current method provides the opportunity to generate two different diastereomers of the target compounds from the same aldehyde using L or D-proline as the catalyst (Scheme 1).

2. Results and discussion

The methodology is based on the assumption that aldehydes **2** are ideal starting materials for the synthesis of **1** through proline catalyzed asymmetric α-hydrazination[6,7] followed by reduction to

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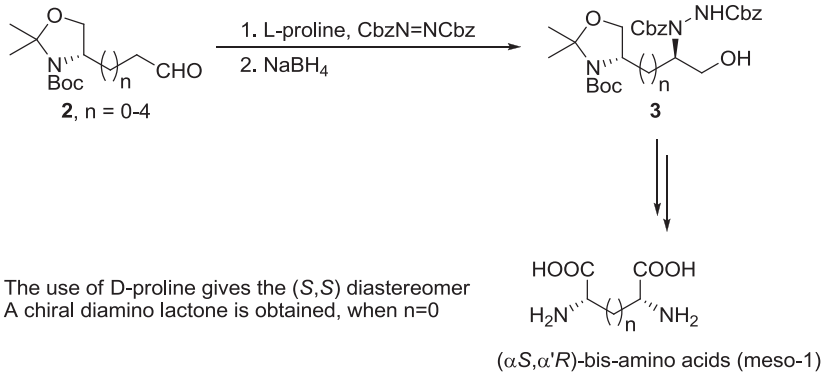
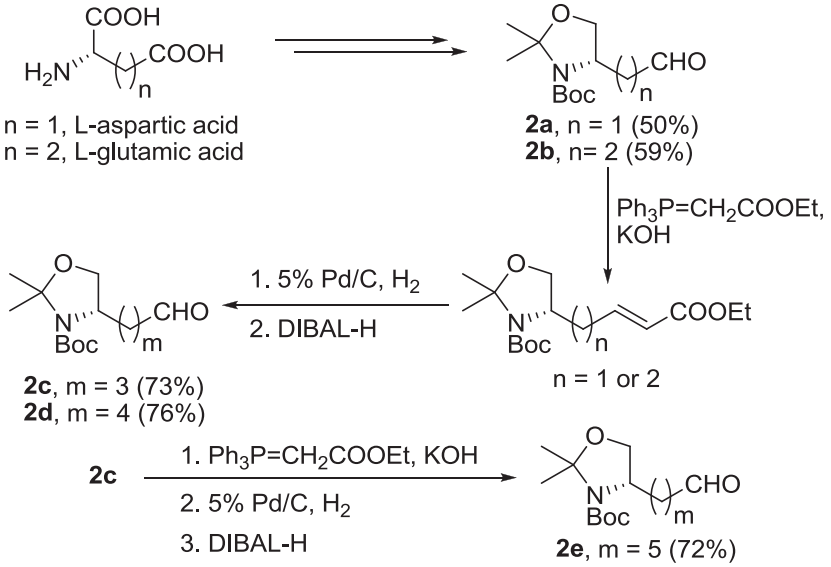


Scheme 1. Synthesis of bis-α-amino acids through asymmetric amination of aldehydes, **2**.

get asymmetric α-amino alcohols, which in turn can be converted to the title compounds. The required starting materials, **2** are commercially available or can easily be synthesized from aspartic or glutamic acid (Scheme 2).[8] The derivatives **2a** and **2b** are prepared directly from L-aspartic and L-glutamic acids. A chain extension of **2a** and **2b** through Wittig reaction followed by reduction gives the aldehydes **2c** and **2d**, respectively. Homologating **2c** further as above yielded the aldehyde **2e**.

yielded the other diastereomer, **3′** with equally high selectivity (Table 1), which was expected from similar reports available in the literature.[10] However, the reaction of **2a**, with dibenzylazodicarboxylate in the presence of D-proline was very slow and proceeded without any diastereoselectivity. We assume that the presence of an adjacent chiral center to the α-CH_2 and steric factors resulting from it could have resulted in the differential reaction of **2a**. A similar difference in reactivity of an oxygenated analog of **2a**

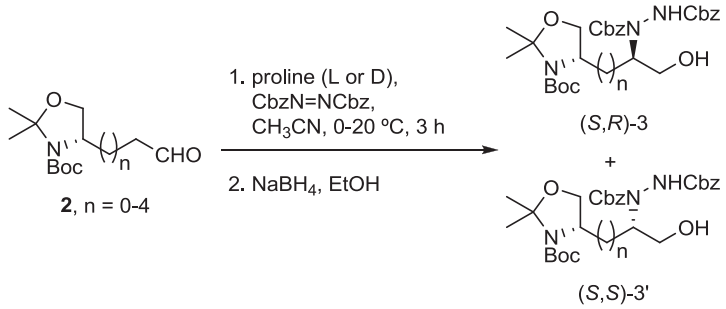


Scheme 2. Synthesis of the aldehydes **2**.

Asymmetric electrophilic α-amination of aldehydes is a widely explored strategy for the synthesis of α-amino acids in general and the proline catalyzed α-functionalization of aldehydes using dialkyl azodicarboxylates is a particularly effective method,[6,7,9] which we presumed could yield us the targeted compounds. Accordingly, **2** was treated with dibenzylazodicarboxylate (1 equiv) in the presence of L-proline (10 mol %, 0–30 °C, CH_3CN, 3 h) followed immediately with reduction of the aldehyde function to the primary alcohol ($NaBH_4$, C_2H_5OH) to get the hydrazine derivatives **3** in very high yields and diastereoselectivity (Table 1). The diastereomeric ratio of these compounds was estimated using chiral HPLC and was established by comparing the chromatograms with that of a 1:1 mixture of the diastereomers obtained through reactions catalyzed by DL-proline. Using D-proline instead of the L-isomer as a catalyst in L- and D-proline catalyzed amination reactions were earlier reported by Greck et al.[10b] The reactions proceeded smoothly and the isolated products were the major isomers in each case and were obtained in very high yields. The presence of a number of diastereotopic groups, a flexible oxazolidine ring and the possibility of having rotamers resulting from the geometry of the Boc group in **3** and **3′** yielded very complex ^1H and ^{13}C NMR spectra for them at room temperature. The ^1H NMR spectra of these compounds recorded at 90 °C in DMSO-d_6 were simpler and easy to interpret.

The hydrazine derivatives **3** and **3′** were reduced with Raney-Ni/H_2 (CH_3OH/CH_3CO_2H, 30 °C, 16 h) to get the 2-amino alcohol derivatives, which were treated with $(Boc)_2O$ and were isolated as the *N*-Boc derivatives **4** and **4′** in excellent yields (Table 2). Oxidation of the primary alcohol group to the carboxylic acid, followed by

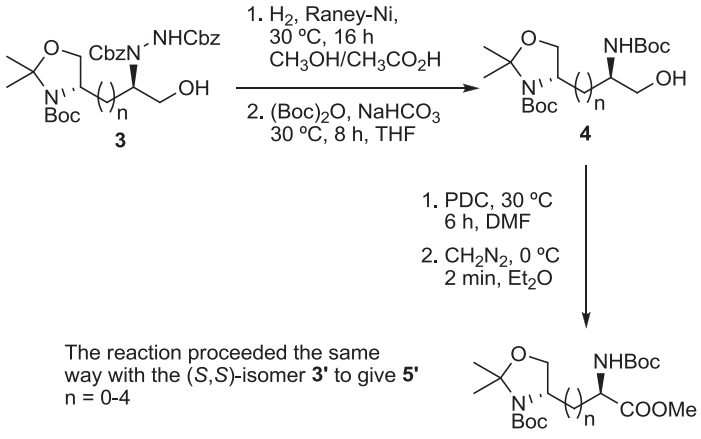
Table 1
Asymmetric α-hydrazination of **2**



Entry	Aldehyde **2**	Catalyst	Yield[a] (%)	**3**(*S*,*R*)/**3′**(*S*,*S*)[b]
1	*n*=0, **2a**	L-Proline	91	96:4
2	*n*=1, **2b**	L-Proline	93	97:3
3	*n*=1, **2b**	D-Proline	94	3:97
4	*n*=2, **2c**	L-Proline	95	99:1
5	*n*=2, **2c**	D-Proline	95	4:96
6	*n*=3, **2d**	L-Proline	97	98:2
7	*n*=3, **2d**	D-Proline	95	6:94
8	*n*=4, **2e**	L-Proline	96	93:7
9	*n*=4, **2e**	D-Proline	97	3:97

[a] Isolated yield.
[b] Estimated from chiral HPLC.

Table 2
Synthesis of the amino esters **5** and **5′**



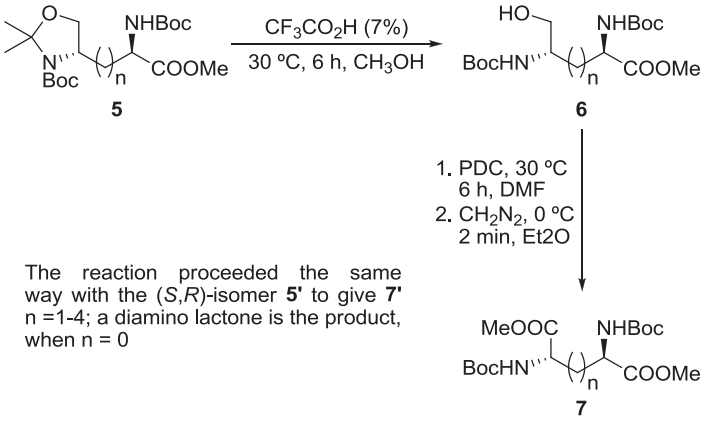
No	Hydrazine derivative	*N*-Boc amino alcohol (% yield)[a]	Amino ester (% yield)[a]
1	**3a**	**4a** (85)	**5a** (82)
2	**3b**	**4b** (86)	**5b** (85)
3	**3b′**	**4b′** (86)	**5b′** (85)
4	**3c**	**4c** (87)	**5c** (83)
5	**3c′**	**4c′** (88)	**5c′** (84)
6	**3d**	**4d** (88)	**5d** (84)
7	**3d′**	**4d′** (87)	**5d′** (85)
8	**3e**	**4e** (88)	**5e** (80)
9	**3e′**	**4e′** (85)	**5e′** (81)

[a] Isolated yield.

esterification using diazomethane yielded the α-amino esters **5** and **5′** in very good yields (Table 2). Our initial attempts were to hydrolyze the oxazolidine group in **4**, and to oxidize both the primary hydroxy groups together using Jones' reagent. Although the starting materials were consumed, the reactions yielded very polar mixtures and the diaminodicarboxylic acids could not be isolated.

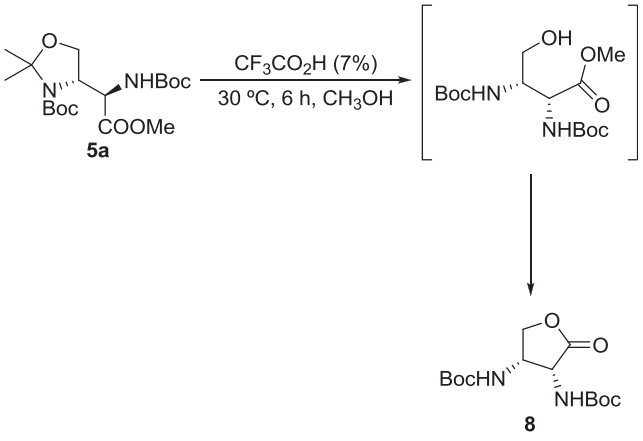
The amino esters **5** and **5′** bearing an oxazolidine group were converted to the target molecules in two steps. Acidolysis of the oxazolidine group with TFA (7% in CH_3OH) provided the diaminohydroxy esters **6** and **6′** in high yields (Table 3). Oxidation of the primary hydroxyl group in **6** and **6′**, followed by the esterification of the carboxylic acid group with diazomethane yielded the targeted bis-α-amino acids **1** as their *N*-Boc protected methyl ester derivatives **7** and **7′** (Table 3). However, the reaction did not proceed as expected for **5a**, acidolysis of this derivative gave the diamino lactone **8** (Scheme 3).

Table 3
Synthesis of the bis-α-amino esters **7** and **7′**



No	Amino ester	Diaminohydroxy ester (% yield)[a]	Bis-α-amino esters (% yield)[a]
1	**5b**	**6b** (90)	**7b** (86)
2	**5b′**	**6b′** (89)	**7b′** (86)
3	**5c**	**6c** (90)	**7c** (85)
4	**5c′**	**6c′** (88)	**7c′** (84)
5	**5d**	**6d** (91)	**7d** (86)
6	**5d′**	**6d′** (92)	**7d′** (85)
7	**5e**	**6e** (93)	**7e** (86)
8	**5e′**	**6e′** (94)	**7e′** (87)

[a] Isolated yield.



Scheme 3. Cyclization of **5a** to the diamino lactone **8**.

The stereochemical outcomes of the reactions were confirmed from the X-ray crystal structure of **7c** (Fig. 2).[11] All the *meso* derivatives, **7** synthesized using L-proline were optically inactive as expected. The asymmetric α-hydrazination of **2** should be following a very ordered transition state similar to the one proposed by List and Jorgensen.[6] The orientation of the carboxylic acid function of proline decides the outcome of the reaction and thus the stereochemistry of the products. While L-proline prefers the attack on the *re*-face, the reaction using D-proline proceeds on the *si*-face.[6]

3. Conclusions

In conclusion, we have achieved a very efficient synthesis of α,α′-diaminodiacids in their protected forms starting from aspartic or glutamic acids using organocatalytic asymmetric α-amination as the key step. The method is very general and can be applied for the synthesis of both diastereomers of the diaminodiacids, by choosing the suitable isomer of proline as the catalyst. The strategy can be

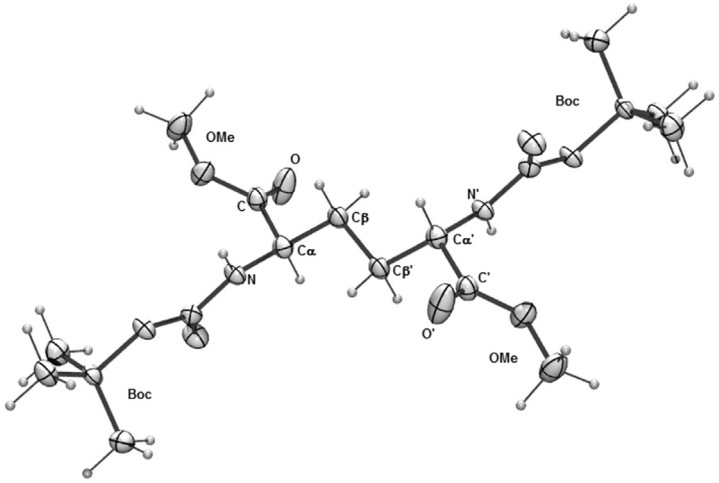


Fig. 2. X-ray crystal structure of **7c**.[11]

used for making diaminodiacids of any length, which is a definite advantage.

4. Experimental section

4.1. General experimental methods

All the commercially available reagents were used directly without any further purification. All the reactions were carried out under inert atmosphere unless otherwise mentioned. Acetonitrile was distilled out initially from phosphorus pentoxide and subsequently from calcium hydride; dichloromethane was distilled out from calcium hydride. Yields reported are for compounds purified using column chromatography. All the reactions were monitored by analytical thin layer chromatography carried out on 0.25 mm Merck silica gel plates (60F-254) using UV light as a visualizing agent and ninhydrin as a staining agent. Merck silica gel (particle size 60–120 and 100–200 mesh) was used for column chromatography. All proton NMR spectra were recorded at either 400 or 500 MHz using a Jeol spectrometer and ^{13}C NMR spectra were run at 100 or 125 MHz. ^1H NMR splitting pattern was designated as singlet (s), doublet (d), doublet of doublet (dd), triplet (t) and multiplet (m), broad singlet (br s). IR spectra were recorded as neat for liquids and as KBr pellets for solids. High-resolution mass spectra were obtained using a Waters Q/Tof Premier micromass HAB 213 spectrometer with an ESI source. Optical rotation was measured using 6.0 mL cell with a 10 dm path length and are reported as $[\alpha]_D^{25}$ (*c* in g per 100 mL solvent). The diastereoselectivity was determined by chiral HPLC analysis using Daicel chiralpack IA-3 column with 254 nm UV detector and by using a mixture of isopropanol and *n*-hexane as eluant at 25 °C.

4.2. General procedure for the asymmetric α-hydrazination of aldehydes

The aldehyde, **2** (2 mmol, 1 equiv) in dry acetonitrile (15 mL) was treated with dibenzylazodicarboxylate (0.59 g, 2 mmol, 1 equiv) and proline (either D or L, 0.02 g, 10 mol %) at 0 °C. The mixture was stirred for 2 h and the temperature was raised to 20 °C over a period of 1 h. The mixture was stirred until the color changed from yellow to colorless (1–2 h) and was cooled to 0 °C and then treated with sodium borohydride (0.05 g) in ethanol (15 mL). Then stirring was continued for 5 min and the reaction was quenched with saturated ammonium chloride solution (20 mL). Organic layer was extracted with ethyl acetate (3×30 mL) and the combined organic phases were dried over anhydrous Na_2SO_4, filtered, concentrated, and purified by column chromatography using ethyl acetate and petroleum ether of suitable composition.

4.2.1. Dibenzyl 1-((R)-1-((S)-3-(tert-butoxycarbonyl)-2,2-dimethyloxazolidin-4-yl)-2-hydroxyethyl)hydrazine-1,2-dicarboxylate ***3a***. R_f=0.3 (petroleum ether/EtOAc, 7:3); oily liquid (0.97 g, 91%); $[\alpha]_D^{25}$ −12.7 (*c* 2.83, $CHCl_3$); IR ν_{max} (thin film): 3469, 3258, 1718, 1693 cm^{-1}; ^1H NMR (DMSO-d_6, 90 °C, 500 MHz): δ=1.36–1.45 (m, 15H), 3.54–4.21 (m, 6H), 5.06–5.10 (m, 4H), 7.30–7.36 (m, 10H), 8.95 (br s, 1H) ppm; ^{13}C NMR (DMSO-d_6, 125 MHz): δ=28.2, 28.4, 56.2, 59.8, 60.2, 64.8, 66.4, 67.1, 67.4, 67.7, 79.7, 81.0, 93.8, 127.6, 127.9, 128.3, 128.7, 128.8, 128.9, 129.0, 136.5, 136.5, 137.0, 153.7, 155.9, 157.0, 157.1 ppm; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd for $C_{28}H_{38}N_3O_8$: 544.2659; found 544.2655.

4.2.2. Dibenzyl 1-((R)-1-((S)-3-(tert-butoxycarbonyl)-2,2-dimethyloxazolidin-4-yl)-3-hydroxypropan-2-yl)hydrazine-1,2-dicarboxylate ***3b***. R_f=0.3 (petroleum ether/EtOAc, 7:3); oily liquid (1.05 g, 93%); $[\alpha]_D^{25}$ −13.1 (*c* 0.16, $CHCl_3$); IR ν_{max} (thin film): 3469, 3258, 1718, 1693 cm^{-1}; ^1H NMR (DMSO-d_6, 90 °C, 500 MHz): δ=1.37 (br s, 3H), 1.39 (s, 9H), 1.44 (s, 3H), 1.58 (br s, 1H), 1.92 (br s, 1H), 3.37 (br s, 1H), 3.42 (br s, 1H), 3.67–3.68 (m, 1H), 3.79–3.89 (m, 1H), 4.08 (m, 1H), 4.23 (br s, 1H), 5.08 (s, 4H), 7.30 (s, 10H), 8.91 (br s, 1H) ppm; ^{13}C NMR (DMSO-d_6, 125 MHz): δ=27.2, 27.8, 28.4, 54.5, 54.7, 61.8, 66.7, 67.1, 67.3, 67.7, 79.4, 93.2, 93.4, 127.6, 128.0, 128.2, 128.5, 128.8, 128.9, 136.8, 151.7, 156.0 ppm; HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ calcd for $C_{29}H_{39}N_3NaO_8$ 580.2635; found: 580.2634.

4.2.3. Dibenzyl 1-((S)-1-((S)-3-(tert-butoxycarbonyl)-2,2-dimethyloxazolidin-4-yl)-3-hydroxypropan-2-yl)hydrazine-1,2-dicarboxylate ***3b′***. R_f=0.3 (petroleum ether/EtOAc, 7:3); oily liquid (1.05 g, 94%); $[\alpha]_D^{25}$ +25.0 (*c* 0.2, $CHCl_3$); IR ν_{max} (thin film): 3469, 3258, 1718, 1693 cm^{-1}; ^1H NMR (DMSO-d_6, 90 °C, 500 MHz): δ=1.36 (br s, 3H), 1.38 (s, 9H), 1.42 (s, 3H), 1.66 (br s, 1H), 1.76 (br s, 1H), 3.38–3.48 (m, 2H), 3.73 (br s, 1H), 3.81–3.83 (m, 1H), 4.01 (br s, 1H), 4.25 (br s, 1H), 5.08 (s, 4H), 7.27–7.30 (m, 10H), 9.09 (br s, 1H) ppm; ^{13}C NMR (DMSO-d_{63}, 125 MHz): δ=27.1, 28.0, 28.5, 55.6, 58.5, 60.9, 66.7, 66.9, 67.1, 67.3, 67.7, 79.4, 93.1, 127.7, 127.9, 128.2, 128.3, 128.5, 128.8, 128.9, 136.8, 151.3, 155.7, 157.0, ppm; HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ calcd for $C_{29}H_{39}N_3NaO_8$ 580.2635; found 580.2634.

4.2.4. Dibenzyl 1-((R)-4-((S)-3-(tert-butoxycarbonyl)-2,2-dimethyloxazolidin-4-yl)-1-hydroxybutan-2-yl)hydrazine-1,2-dicarboxylate ***3c***. R_f=0.3 (petroleum ether/EtOAc, 7:3); oily liquid (1.09 g, 95%); $[\alpha]_D^{25}$ −8.0 (*c* 0.2, $CHCl_3$); IR ν_{max} (thin film): 3471, 3261, 1719, 1698 cm^{-1}; ^1H NMR (DMSO-d_6, 90 °C, 500 MHz): δ=1.34–1.44 (m, 15H), 1.46–1.63 (m, 4H), 3.28–3.33 (m, 1H), 3.40–3.44 (m, 1H), 3.66 (br s, 1H), 3.79–3.82 (m, 1H), 4.03–4.05 (m, 1H), 4.20 (br s, 1H), 5.08 (s, 4H), 7.28 (s, 10H), 9.10 (br s, 1H) ppm; ^{13}C NMR (DMSO-d_6, 125 MHz): δ=23.6, 25.0, 25.4, 27.1, 27.9, 28.5, 57.4, 57.6, 60.0, 60.9, 61.7, 61.9, 66.3, 66.6, 66.9, 67.1, 67.3, 67.6, 79.1, 79.5, 92.9, 93.1, 127.5, 127.6, 127.8, 128.2, 128.4, 128.5, 128.8, 128.9, 136.6, 136.9, 151.6, 151.8, 156.1, 156.3, 157.2, 158.5 ppm; HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ calcd for $C_{31}H_{43}N_3O_8$ 594.2791; found 594.2795.

4.2.5. Dibenzyl 1-((S)-4-((S)-3-(tert-butoxycarbonyl)-2,2-dimethyloxazolidin-4-yl)-1-hydroxybutan-2-yl)hydrazine-1,2-dicarboxylate ***3c′***. R_f=0.3 (petroleum ether/EtOAc, 7:3); oily liquid (1.09 g, 95%); $[\alpha]_D^{25}$ +18.6 (*c* 0.22, $CHCl_3$); IR ν_{max} (thin film): 3471, 3261, 1719, 1698 cm^{-1}; ^1H NMR (DMSO-d_6, 90 °C, 500 MHz): δ=1.38–1.46 (m, 15H), 1.50–1.73 (m, 4H), 3.32–3.37 (m, 1H), 3.40–3.45 (m, 1H), 3.62 (br s, 1H), 3.76–3.81 (m, 1H), 4.03–4.08 (m, 1H), 4.18 (br s, 1H), 5.09 (s, 4H), 7.29 (s, 10H), 9.01 (br s, 1H) ppm; ^{13}C NMR (DMSO-d_6, 125 MHz): δ=22.5, 23.4, 24.0, 24.5, 24.7, 26.8, 27.1, 27.7, 27.9, 28.5, 29.3, 29.5, 30.0, 30.8, 56.6, 56.8, 60.1, 60.5, 60.9, 61.1, 61.3, 61.6, 61.7, 66.6, 66.9, 67.2, 67.4, 67.6, 79.2, 79.5, 93.1, 93.3, 127.6, 127.8, 128.2, 128.5, 128.8, 128.9, 136.6, 136.8, 151.8, 152.0, 156.1, 156.3, 157.1, 158.6 ppm; HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ calcd for $C_{31}H_{43}N_3O_8$ 594.2791; found 594.2795.

4.2.6. Dibenzyl 1-((R)-5-((S)-3-(tert-butoxycarbonyl)-2,2-dimethyloxazolidin-4-yl)-1-hydroxypentan-2-yl)hydrazine-1,2-dicarboxylate ***3d***. R_f=0.3 (petroleum ether/EtOAc, 7:3); oily liquid (1.13 g, 97%); $[\alpha]_D^{25}$ −16.8 (*c* 0.28, $CHCl_3$); IR ν_{max} (thin film): 3463, 3265, 1718, 1694 cm^{-1}; ^1H NMR (DMSO-d_6, 90 °C, 500 MHz): δ=1.12–1.22 (m, 2H), 1.34–1.51 (m, 15H), 1.43–1.51 (m, 4H), 3.28 (br s, 1H), 3.35–3.39 (m, 2H), 3.64–3.82 (m, 2H), 4.05–4.18 (m, 2H), 5.07 (s, 4H), 7.29 (s, 10H), 9.02 (br s, 1H) ppm; ^{13}C NMR (DMSO-d_6, 90 °C, 125 MHz): δ=22.9, 28.3, 28.5, 28.7, 57.2, 57.5, 60.9, 66.9, 67.4, 79.3, 79.5, 93.1, 127.5, 127.9, 128.0, 128.2, 128.3, 128.4, 128.5, 128.6, 128.9, 129.0, 136.8, 137.0, 151.8, 156.3 ppm; HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ calcd for $C_{31}H_{43}N_3O_8$ 608.2498; found 608.2495.

4.2.7. Dibenzyl-1-((S)-5-((S)-3-(tert-butoxycarbonyl)-2,2-dimethyloxazolidin-4-yl)-1-hydroxypentan-2-yl)hydrazine-1,2-dicarboxylate ***3d′***. R_f=0.3 (petroleum ether/EtOAc, 7:3); oily liquid

(1.16 g, 95%); $[\alpha]_D^{25}$ +11.9 (*c* 0.42, $CHCl_3$); IR ν_{max} (thin film): 3463, 3265, 1718, 1694 cm^{-1}; ^1H NMR (DMSO-d_6, 90 °C, 500 MHz): δ=1.12–1.22 (m, 2H), 1.34–1.51 (m, 15H), 1.43–1.51 (m, 4H), 3.28 (br s, 1H), 3.35–3.39 (m, 2H), 3.64–3.82 (m, 2H), 4.05–4.18 (m, 2H), 5.07 (s, 4H), 7.29 (s, 10H), 9.12 (br s, 1H) ppm; ^{13}C NMR (DMSO-d_6, 90 °C, 125 MHz): δ=22.9, 28.3, 28.5, 28.7, 57.2, 57.5, 60.9, 66.9, 67.4, 79.3, 79.5, 93.1, 127.5, 127.9, 128.0, 128.2, 128.3, 128.4, 128.5, 128.6, 128.9, 129.0, 136.8, 137.0, 151.8, 156.3 ppm; HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ calcd for $C_{31}H_{43}N_3O_8$ 608.2498; found 608.2495.

4.2.8. Dibenzyl 1-((R)-6-((S)-3-(tert-butoxycarbonyl)-2,2-dimethyloxazolidin-4-yl)-1-hydroxyhexan-2-yl)hydrazine-1,2-dicarboxylate ***3e***. R_f=0.3 (petroleum ether/EtOAc, 7:3); oily liquid (1.06 g, 96%); $[\alpha]_D^{25}$ −4.2 (*c* 0.23, $CHCl_3$); IR ν_{max} (thin film): 3472, 3275, 1719, 1695 cm^{-1}; ^1H NMR (DMSO-d_6, 90 °C, 500 MHz): δ=1.14–1.25 (m, 4H), 1.33–1.38 (m, 15H), 1.44–1.56 (m, 4H), 3.28 (br s, 1H), 3.37 (br s, 2H), 3.59–3.68 (m, 2H), 3.81–3.82 (m, 1H),4.02–4.05 (m, 1H), 5.07 (s, 4H), 7.30 (s, 10H), 9.03 (br s, 1H) ppm; ^{13}C NMR (DMSO-d_6, 125 MHz): δ=23.5, 24.9, 26.0, 27.1, 28.0, 28.5, 32.6, 33.5, 57.1, 57.4, 59.4, 60.9, 61.6, 61.9, 66.4, 66.5, 66.8, 67.1, 67.3, 79.0, 79.5, 92.9, 93.1, 127.5, 127.7, 127.8, 128.1, 128.3, 128.4, 128.6, 128.8, 128.8, 128.9, 136.6, 136.9, 137.0, 151.5, 151.7, 156.2, 156.3, 157.0, 158.5 ppm; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd for $C_{32}H_{46}N_3O_8$ 600.3285; found 600.3281.

4.2.9. Dibenzyl 1-((S)-6-((S)-3-(tert-butoxycarbonyl)-2,2-dimethyloxazolidin-4-yl)-1-hydroxyhexan-2-yl)hydrazine-1,2-dicarboxylate ***3e′***. R_f=0.3 (petroleum ether/EtOAc, 7:3); oily liquid (1.16 g, 97%); $[\alpha]_D^{25}$ +15.5 (*c* 0.45, $CHCl_3$); IR ν_{max} (thin film): 3463, 3273, 1716, 1694 cm^{-1}; ^1H NMR (DMSO-d_6, 90 °C, 500 MHz): δ=1.14–1.25 (m, 4H), 1.38–1.39 (m, 15H), 1.42–1.57 (m, 4H), 3.29 (br s, 1H), 3.37–3.40 (br s, 1H), 3.59–3.70 (m, 2H), 3.82–3.85 (m, 1H),4.01–4.07 (m, 1H), 5.08 (s, 4H), 7.30 (s, 10H), 8.99 (br s, 1H) ppm; ^{13}C NMR (DMSO-d_6, 125 MHz): δ=23.5, 24.9, 26.0, 27.1, 28.0, 28.5, 32.9, 33.6, 57.0, 57.1, 57.4, 59.5, 60.9, 61.6, 61.9, 66.4, 66.6, 67.0, 67.1, 67.3, 67.3, 79.0, 79.5, 79.7, 92.9, 93.1, 127.5, 127.8, 128.1, 128.3, 128.3, 128.4, 128.6, 128.8, 128.8, 128.9, 136.6, 136.9, 136.9, 137.0, 151.6, 151.6, 156.2, 156.3, 157.0, 157.1, 158.6 ppm; HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ calcd for $C_{32}H_{46}N_3O_8$ 622.3104; found 622.3109.

4.3. General procedure for the preparation of *N*-Boc protected amino alcohols 4 from the corresponding hydrazino alcohols 3

Freshly prepared Raney-nickel (around 0.80 g, pre-washed with absolute ethanol) was added to the stirred solution of **3** (2 mmol) in dry methanol (15 mL) followed with 40 drops of acetic acid. The reaction mixture was hydrogenated at atmospheric pressure for 16 h at 30 °C. After complete disappearance of starting material on TLC, the reaction mixture was passed over Celite and concentrated. The crude amines were protected as Boc derivatives using the following procedure, before purification.

Boc anhydride (2 mmol) was added drop wise to the stirred solution of the crude amine (0.48 g, 2.2 mmol) and $NaHCO_3$ (0.55 g, 6 mmol) in THF at 0 °C. Stirring was continued for 12 h, filtered, concentrated, and purified by column chromatography (3:7, ethyl acetate/pet ether mixture).

4.3.1. (S)-tert-Butyl 4-((R)-1-(tert-butoxycarbonylamino)-2-hydroxyethyl)-2,2-dimethyloxazolidine-3-carboxylate ***4a***. R_f=0.3 (petroleum ether/EtOAc, 3:2); oily liquid (0.61 g, 85%); $[\alpha]_D^{25}$ −24.7 (*c* 0.21, $CHCl_3$); IR ν_{max} (thin film): 3356, 1698 cm^{-1}; ^1H NMR (DMSO-d_6, 90 °C, 500 MHz): δ=1.34 (s, 9H), 1.39 (s, 3H), 1.42 (s, 9H), 1.45 (s, 3H), 3.41 (br s, 2H), 3.66 (br s, 1H), 3.80–3.83 (m, 1H), 3.88–3.90 (m, 1H), 3.97 (br s, 1H), 4.40 (br s, 1H), 5.67 (br s, 1H) ppm; ^{13}C NMR (DMSO-d_6, 125 MHz): δ=23.0, 24.5, 26.2, 27.1, 28.5, 28.6, 54.3, 55.0, 57.5, 60.9, 61.8, 65.2, 65.3, 78.0, 78.2, 79.6, 79.6, 80.0, 93.4, 93.8, 151.9, 153.3, 155.5, 155.7 ppm; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd for $C_{17}H_{33}N_2O_6$ 361.2339; found 361.2335.

4.3.2. (S)-tert-Butyl 4-((R)-2-(tert-butoxycarbonylamino)-3-hydroxypropyl)-2,2-dimethyloxazolidine-3-carboxylate ***4b***. R_f=0.3 (petroleum ether/EtOAc, 3:2); oily liquid (0.64 g, 86%); $[\alpha]_D^{25}$ −11.79 (*c* 0.195, $CHCl_3$); IR ν_{max} (thin film): 3355, 1695 cm^{-1}; ^1H NMR (DMSO-d_6, 90 °C, 500 MHz):δ=1.35 (s, 9H), 1.37 (s, 3H), 1.39 (s, 9H), 1.44 (s, 3H), 1.47–1.61 (m, 2H), 3.23–3.33 (m, 3H), 3.62–3.64 (m, 1H), 3.72–3.74 (m, 1H), 3.84–3.87 (m, 1H), 4.18 (br s, 1H), 5.94 (br s, 1H) ppm; ^{13}C NMR (DMSO-d_6, 125 MHz): δ=23.5, 24.9, 27.1, 27.3, 28.1, 28.5, 28.7, 28.7, 29.6, 30.5, 34.9, 36.8, 50.5, 55.1, 55.2, 57.2, 60.9, 61.1, 64.1, 64.2, 66.4, 66.9, 77.9, 78.0, 79.0, 79.1, 79.5, 92.9, 93.0, 93.1, 151.3, 151.4, 151.6, 151.7, 155.9, 157.0 ppm; HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ calcd for $C_{18}H_{34}N_2NaO_6$ 397.2315; found 397.2313.

4.3.3. (S)-tert-Butyl 4-((S)-2-(tert-butoxycarbonylamino)-3-hydroxypropyl)-2,2-dimethyloxazolidine-3-carboxylate ***4b′***. R_f=0.3 (petroleum ether/EtOAc, 3:2); oily liquid (0.64 g, 86%); $[\alpha]_D^{25}$ +17.18 (*c* 0.19, $CHCl_3$); IR ν_{max} (thin film): 3355, 1695 cm^{-1}; ^1H NMR (DMSO-d_6, 90 °C, 500 MHz): δ=1.37 (s, 9H), 1.39 (s, 3H), 1.41 (s, 9H), 1.46 (s, 3H), 1.51–1.65 (m, 2H), 3.24–3.34 (m, 3H), 3.63–3.65 (m, 1H), 3.73–3.75 (m, 1H), 3.86–3.89 (m, 1H), 4.19 (br s, 1H), 5.95 (br s, 1H) ppm; ^{13}C NMR (DMSO-d_6, 125 MHz): δ=23.5, 24.9, 27.1, 27.3, 28.1, 28.5, 28.7, 28.7, 29.6, 30.5, 34.9, 36.8, 50.5, 55.1, 55.2, 57.2, 60.9, 61.1, 64.1, 64.2, 66.4, 66.9, 77.9, 78.0, 79.0, 79.1, 79.5, 92.9, 93.0, 93.1, 151.3, 151.4, 151.6, 151.7, 155.9, 157.0 ppm; HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ calcd for $C_{18}H_{34}N_2NaO_6$ 397.2315; found 397.2313.

4.3.4. (S)-tert-Butyl 4-((R)-3-(tert-butoxycarbonylamino)-4-hydroxybutyl)-2,2-dimethyloxazolidine-3-carboxylate ***4c***. R_f=0.3 (petroleum ether/EtOAc, 3:2); oily liquid (0.85 g, 87%); $[\alpha]_D^{25}$ −13.9 (*c* 0.23, $CHCl_3$); IR ν_{max} (thin film): 3355, 1695 cm^{-1}; ^1H NMR (DMSO-d_6, 90 °C, 500 MHz): δ=1.36 (s, 9H), 1.37 (s, 3H), 1.40 (s, 9H), 1.44 (s, 3H), 1.43–1.65 (m, 4H), 3.25–3.34 (m, 3H), 3.64–3.66 (m, 1H), 3.70 (br s, 1H), 3.83–3.86 (m, 1H), 4.21 (br s, 1H), 6.00 (br s, 1H) ppm; ^{13}C NMR (DMSO-d_6, 125 MHz): δ=23.4, 24.8, 27.1, 28.0, 28.7, 28.7, 29.6, 30.2, 52.7, 52.9, 57.4, 57.6, 64.0, 64.2, 66.2, 66.8, 77.8, 79.0, 79.5, 92.8, 93.1, 151.6, 155.9 ppm; HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ calcd for $C_{19}H_{36}N_2NaO_6$ 411.2471; found 411.2473.

4.3.5. (S)-tert-Butyl 4-((S)-3-(tert-butoxycarbonylamino)-4-hydroxybutyl)-2,2-dimethyloxazolidine-3-carboxylate ***4c′***. R_f=0.3 (petroleum ether/EtOAc, 3:2); oily liquid (0.85 g, 87%); $[\alpha]_D^{25}$ +12.12 (*c* 0.33, $CHCl_3$); IR ν_{max} (thin film): 3355, 1695 cm^{-1}; ^1H NMR (DMSO-d_6, 90 °C, 500 MHz): δ=1.35 (s, 9H), 1.37 (s, 3H), 1.40 (s, 9H), 1.45 (s, 3H), 1.43–1.70 (m, 4H), 3.27–3.33 (m, 3H), 3.62–3.64 (m, 1H), 3.71 (br s, 1H), 3.84–3.87 (m, 1H), 4.20–4.21 (m, 1H), 5.98 (br s, 1H) ppm; ^{13}C NMR (DMSO-d_6, 125 MHz): δ=23.5, 24.8, 27.0, 28.1, 28.5, 28.7, 29.4, 30.3, 52.7, 57.4, 63.9, 66.5, 66.9, 77.8, 79.1, 79.1, 79.4, 92.9, 93.1, 151.6, 155.9 ppm; HRMS (ESI-TOF) *m*/*z*: calcd for $C_{19}H_{36}N_2NaO_6$ $[M+Na]^+$: 411.2471; found: 411.2473.

4.3.6. (S)-tert-Butyl 4-((R)-4-(tert-butoxycarbonylamino)-5-hydroxypentyl)-2,2-dimethyloxazolidine-3-carboxylate ***4d***. R_f=0.3 (petroleum ether/EtOAc, 3:2); oily liquid (0.69 g, 87%); $[\alpha]_D^{25}$ 15.7 (*c* 0.14, $CHCl_3$); IR ν_{max} (thin film): 3355, 1695 cm^{-1}; ^1H NMR (DMSO-d_6, 90 °C, 500 MHz): δ=1.23–1.26 (m, 2H), 1.35 (s, 9H), 1.37 (s, 3H), 1.39 (s, 9H), 1.43 (s, 3H), 1.43–1.58 (m, 4H), 3.24–3.34 (m, 3H), 3.60–3.67 (m, 1H), 3.71 (br s, 1H), 3.84–3.89 (m, 1H), 4.20 (br s, 1H), 5.99 (br s, 1H) ppm; ^{13}C NMR (DMSO-d_6, 125 MHz): δ=22.7, 23.4, 24.9, 27.1, 27.9, 28.5, 28.7, 31.3, 32.9, 33.9, 52.5, 57.2, 57.4, 64.1, 66.5, 67.0, 77.7, 79.1, 79.5, 92.9, 93.1, 151.6, 151.7, 155.9 ppm; HRMS (ESI-

TOF) *m*/*z*: $[M+Na]^+$ calcd for $C_{20}H_{38}N_2NaO_6$ 425.2628; found 425.2622.

4.3.7. (S)-tert-Butyl 4-((S)-4-(tert-butoxycarbonylamino)-5-hydroxypentyl)-2,2-dimethyloxazolidine-3-carboxylate ***4d′***. R_f=0.3 (petroleum ether/EtOAc, 3:2); oily liquid (0.69 g, 87%); $[\alpha]_D^{25}$ +11.53 (*c* 0.26, $CHCl_3$); IR ν_{max} (thin film): 3355, 1695 cm^{-1}; ^1H NMR (DMSO-d_6, 90 °C, 500 MHz): δ=1.17–1.30 (m, 2H), 1.35 (s, 9H), 1.37 (s, 3H), 1.39 (s, 9H), 1.44 (s, 3H), 1.47–1.53 (m, 2H), 1.57–1.63 (m, 2H), 3.27–3.36 (m, 3H), 3.63 (dd, *J*=8.5 Hz, *J*=1.8 Hz, 1H), 3.73 (m, 1H), 3.84–3.87 (m, 1H), 4.18 (br s, 1H), 5.93 (br s, 1H) ppm; ^{13}C NMR (DMSO-d_6, 125 MHz): δ=22.4, 23.4, 24.8, 27.1, 27.8, 28.5, 28.7, 31.4, 33.0, 34.0, 52.6, 52.7, 57.1, 57.3, 64.1, 66.5, 67.1, 77.7, 79.0, 79.4, 92.9, 93.1, 151.6, 151.7, 155.9 ppm; HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ calcd for $C_{20}H_{38}N_2NaO_6$ 425.2628; found 425.2622.

4.3.8. (S)-tert-Butyl 4-((R)-5-(tert-butoxycarbonylamino)-6-hydroxyhexyl)-2,2-dimethyloxazolidine-3-carboxylate ***4e***. R_f=0.3 (petroleum ether/EtOAc, 3:2); oily liquid (0.73 g, 88%); $[\alpha]_D^{25}$ +19.0 (*c* 0.21, $CHCl_3$); IR ν_{max} (thin film): 3356, 1694 cm^{-1}; ^1H NMR (DMSO-d_6, 90 °C, 500 MHz): δ=1.20–1.28 (m, 4H), 1.36 (s, 9H), 1.37 (s, 3H), 1.39 (s, 9H), 1.44 (s, 3H), 1.43–1.60 (m, 4H), 3.23–3.35 (m, 3H), 3.62–3.64 (m, 1H), 3.71–3.72 (m, 1H), 3.84–3.87 (m, 1H), 4.17 (br s, 1H), 5.93 (br s, 1H) ppm; ^{13}C NMR (DMSO-d_6, 125 MHz): δ=23.5, 24.8, 24.9, 25.8, 26.0, 27.1, 28.5, 28.7, 31.4, 33.7, 33.7, 52.4, 52.5, 57.0, 57.1, 64.1, 66.9, 66.9, 67.0, 77.7, 79.0, 79.4, 92.9, 93.1, 151.5, 151.7, 155.9; HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ calcd for $C_{21}H_{40}N_2NaO_6$ 439.2784; found 439.2781.

4.3.9. (S)-tert-Butyl 4-((S)-5-(tert-butoxycarbonylamino)-6-hydroxyhexyl)-2,2-dimethyloxazolidine-3-carboxylate ***4e′***. R_f=0.3 (petroleum ether/EtOAc, 3:2); oily liquid (0.73 g, 85%); $[\alpha]_D^{25}$ +13.3 (*c* 0.15, $CHCl_3$); IR ν_{max} (thin film): 3356, 1694 cm^{-1}; ^1H NMR (DMSO-d_6, 90 °C, 500 MHz): δ=1.23–1.29 (m, 4H), 1.36 (s, 9H), 1.37 (s, 3H), 1.39 (s, 9H), 1.44 (s, 3H), 1.42–1.61 (m, 4H), 3.23–3.36 (m, 3H), 3.62–3.64 (m, 1H), 3.70–3.72 (m, 1H), 3.84–3.87 (m, 1H), 4.17 (br s, 1H), 5.94 (br s, 1H) ppm; ^{13}C NMR (DMSO-d_6, 125 MHz): δ=23.5, 24.9, 26.0, 27.1, 28.5, 28.7, 31.4, 33.8, 52.5, 57.1, 57.5, 64.1, 66.4, 66.9, 77.7, 79.0, 79.4, 92.9, 93.1, 151.5, 151.7, 155.9 ppm; HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ calcd for $C_{21}H_{40}N_2NaO_6$ 439.2784; found 439.2781.

4.4. Procedure for the oxidation of *N*-Boc protected amino alcohols 4 to the corresponding amino carboxylic acid methyl esters 5

Pyridinium dichromate (7.51 g, 21.4 mmol) was added to the stirred solution of *N*-Boc protected amino alcohol (2 mmol) in dry DMF (8 mL) under nitrogen at 30 °C and stirring was continued for 6 h. After complete disappearance of the starting material on TLC, the reaction was quenched by adding water (50 mL) and the mixture was extracted diethyl ether (2×50 mL). The ether solution was extracted with 10% $NaHCO_3$ solution (2×30 mL), the aqueous extracts containing the carboxylate salts were combined and acidified with saturated $KHSO_4$ solution and was extracted with diethyl ether (2×30 mL). The ether layers were combined, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude carboxylic acids were converted to the methyl ester derivatives using diazomethane before purification.

N-Nitroso methyl urea (1 g) was added to a stirred of mixture of 60% KOH solution (25 mL) and diethyl ether (15 mL) at 0 °C and was stirred for 5 min. Color of the ether layer changes to yellow indicating the presence of diazomethane. The ether layer was separated and passed through KOH pellets. This solution of diazomethane in ether was added to the crude solution of carboxylic acids in ether. Esterification was finished within 5 min. The reaction mixture was concentrated and purified by column chromatography.

4.4.1. (S)-tert-Butyl 4-((R)-1-(tert-butoxycarbonylamino)-2-methoxy-2-oxoethyl)-2,2-dimethyloxazolidine-3-carboxylate ***5a***. R_f=0.5 (petroleum ether/EtOAc, 4:1); oily liquid (0.64 g, 82%); $[\alpha]_D^{25}$ −14.9 (*c* 0.26, $CHCl_3$); IR ν_{max} (thin film): 3355, 1745, 1698 cm^{-1}; ^1H NMR (DMSO-d_6DMSO-d_6, 90 °C, 500 MHz): δ=1.22–1.42 (m, 24H), 3.60 (s, 3H), 3.87–4.02 (m, 3H), 4.35 (br s, 1H), 6.57 (br s, 1H) ppm; ^{13}C NMR (DMSO-d_6, 125 MHz): δ=22.8, 24.2, 26.0, 26.8, 28.4, 28.5, 52.3, 54.7, 58.4, 58.7, 64.3, 79.1, 80.0, 80.4, 93.7, 93.9, 151.6, 152.5, 155.4, 155.6, 171.5 ppm; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd for $C_{18}H_{33}N_2O_7$ 389.2288; found 389.2284.

4.4.2. (S)-tert-Butyl 4-((R)-2-(tert-butoxycarbonylamino)-3-methoxy-3-oxopropyl)-2,2-dimethyloxazolidine-3-carboxylate ***5b***. R_f=0.5 (petroleum ether/EtOAc, 4:1); oily liquid (0.68 g, 85%); $[\alpha]_D^{25}$ −10.2 (*c* 0.19, $CHCl_3$); IR ν_{max} (thin film): 3355, 1745, 1698 cm^{-1}; ^1H NMR (DMSO-d_6, 90 °C, 500 MHz): δ=1.35 (s, 9H), 1.38 (s, 3H), 1.40 (s, 9H), 1.45 (s, 3H), 1.90 (br s, 2H), 3.61 (s, 3H), 3.70–3.75 (m, 1H), 3.84–3.87 (m, 2H), 4.01 (br s, 1H), 6.67 (br s, 1H) ppm; ^{13}C NMR (DMSO-d_6, 125 MHz): δ=23.3, 24.7, 27.2, 27.9, 28.4, 28.6, 38.1, 51.3, 52.4, 55.0, 66.4, 66.7, 78.7, 79.5, 79.8, 93.3, 151.3, 151.7 ppm; HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ calcd for $C_{19}H_{34}N_2NaO_7$ 425.2264; found 425.2261.

4.4.3. (S)-tert-Butyl 4-((S)-2-(tert-butoxycarbonylamino)-3-methoxy-3-oxopropyl)-2,2-dimethyloxazolidine-3-carboxylate ***5b′***. R_f=0.5 (petroleum ether/EtOAc, 4:1); oily liquid (0.68 g, 85%); $[\alpha]_D^{25}$ +17.18 (*c* 0.25, $CHCl_3$); IR ν_{max} (thin film): 3355, 1745, 1698 cm^{-1}; ^1H NMR (DMSO-d_6, 90 °C, 500 MHz):δ=1.35 (s, 9H), 1.38 (s, 3H), 1.39 (s, 9H), 1.44 (s, 3H), 2.05 (br s, 2H), 3.61 (s, 3H), 3.72–3.74 (m, 1H), 3.81–3.86 (m, 2H), 3.98 (br s, 1H), 6.92 (br s, 1H) ppm; ^{13}C NMR (DMSO-d_6, 125 MHz): δ=23.4, 24.8, 27.3, 28.4, 28.6, 31.8, 35.8, 52.3, 52.5, 55.5, 67.2, 78.8, 79.5, 93.1, 151.4, 155.2, 173.2 ppm; HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ calcd for $C_{19}H_{34}N_2NaO_7$ 425.2264; found 425.2261.

4.4.4. (S)-tert-Butyl 4-((R)-3-(tert-butoxycarbonylamino)-4-methoxy-4-oxobutyl)-2,2-dimethyloxazolidine-3-carboxylate ***5c***. R_f=0.5 (petroleum ether/EtOAc, 4:1); oily liquid (0.55 g, 83%); $[\alpha]_D^{25}$ −15.38 (*c* 0.26, $CHCl_3$); IR ν_{max} (thin film): 3353, 1746, 1697 cm^{-1}; ^1H NMR (DMSO-d_6, 90 °C, 500 MHz):δ=1.35 (s, 9H), 1.36 (s, 3H), 1.38 (s, 9H), 1.44 (s, 3H), 1.49–1.69 (m, 4H), 3.59 (s, 3H), 3.61–3.66 (m, 1H), 3.73 (br s, 1H), 3.82–3.87 (m, 1H), 3.93 (br s, 1H), 6.85 (br s, 1H) ppm; ^{13}C NMR (DMSO-d_6, 125 MHz): δ=27.1, 27.9, 28.3, 28.4, 28.5, 28.5, 28.7, 28.7, 28.9, 28.9, 30.1, 51.9, 52.1, 54.4, 56.8, 56.9, 57.1, 57.2, 66.9, 67.1, 67.3, 78.8, 79.4, 93.3, 93.3, 151.8, 151.8, 155.8, 173.1, 173.2 ppm; HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ calcd for $C_{20}H_{36}N_2NaO_7$ 439.2420; found 439.2423.

4.4.5. (S)-tert-Butyl 4-((S)-3-(tert-butoxycarbonylamino)-4-methoxy-4-oxobutyl)-2,2-dimethyloxazolidine-3-carboxylate ***5c′***. R_f=0.5 (petroleum ether/EtOAc, 4:1); oily liquid (0.71 g, 84%); $[\alpha]_D^{25}$ +35.2 (*c* 0.17, $CHCl_3$); IR ν_{max} (thin film): 3353, 1746, 1697 cm^{-1}; ^1H NMR (DMSO-d_6, 90 °C, 500 MHz):δ=1.35 (s, 9H), 1.36 (s, 3H), 1.38 (s, 9H), 1.44 (s, 3H), 1.49–1.69 (m, 4H), 3.59 (s, 3H), 3.61–3.66 (m, 1H), 3.73 (br s, 1H), 3.82–3.87 (m, 1H), 3.93 (br s, 1H), 6.85 (br s, 1H) ppm; ^{13}C NMR (DMSO-d_6, 125 MHz): δ=27.1, 27.9, 28.3, 28.4, 28.5, 28.5, 28.7, 28.7, 28.9, 28.9, 30.1, 51.9, 52.1, 54.4, 56.8, 56.9, 57.1, 57.2, 66.9, 67.1, 67.3, 78.8, 79.4, 93.3, 93.3, 151.8, 151.8, 155.8, 173.1, 173.2 ppm; HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ calcd for $C_{20}H_{36}N_2NaO_7$ 439.2420; found 439.2423.

4.4.6. (S)-tert-Butyl 4-((R)-4-(tert-butoxycarbonylamino)-5-methoxy-5-oxopentyl)-2,2-dimethyloxazolidine-3-carboxylate

5d. R_f=0.5 (petroleum ether/EtOAc, 4:1); oily liquid (0.75 g, 84%); $[\alpha]_D^{25}$ +3.75 (*c* 0.16, $CHCl_3$); IR ν_{max} (thin film): 3353, 1746, 1697 cm^{-1}; ^1H NMR (DMSO-d_6, 90 °C, 500 MHz):δ=1.23–1.33 (m, 2H), 1.35 (s, 9H), 1.37 (s, 3H), 1.39 (s, 9H), 1.44 (s, 3H), 1.46–1.68 (m, 4H), 3.60 (s, 3H), 3.63 (dd, *J*=8.85, 1.85 Hz, 1H), 3.73 (br s, 1H), 3.84–3.87 (m, 1H), 3.90–3.94 (m, 1H), 6.72 (br s, 1H) ppm; ^{13}C NMR (DMSO-d_6, 125 MHz): δ=22.5, 23.4, 24.8, 27.1, 27.9, 28.5, 28.6, 31.0, 33.3, 52.1, 52.1, 53.9, 57.0, 66.6, 67.0, 78.6, 79.1, 79.5, 93.0, 93.2, 151.5, 151.8, 156.0, 173.6 ppm; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd for $C_{21}H_{39}N_2O_7$ 431.2757; found 431.2753.

4.4.7. (S)-tert-Butyl 4-((S)-4-(tert-butoxycarbonylamino)-5-methoxy-5-oxopentyl)-2,2-dimethyloxazolidine-3-carboxylate ***5d′***. R_f=0.5 (petroleum ether/EtOAc, 4:1); oily liquid (0.75 g, 85%); $[\alpha]_D^{25}$ +24.1 (*c* 0.29, $CHCl_3$); IR ν_{max} (thin film): 3353, 1746, 1697 cm^{-1}; ^1H NMR (DMSO-d_6, 90 °C, 500 MHz): δ=1.27–1.34 (m, 2H), 1.36 (s, 9H), 1.39 (s, 3H), 1.40 (s, 9H), 1.46 (s, 3H), 1.53–1.71 (m, 4H), 3.61 (s, 3H), 3.64 (dd, *J*=8.85, 1.85 Hz, 1H), 3.74 (br s, 1H), 3.86–3.88 (m, 1H), 3.91–3.95 (m, 1H), 6.72 (br s, 1H) ppm; ^{13}C NMR (DMSO-d_6, 125 MHz): δ=22.6, 23.4, 24.9, 27.1, 28.1, 28.7, 28.8, 31.1, 33.4, 52.3, 52.5, 54.2, 57.2, 66.8, 67.2, 78.8, 79.1, 79.5, 93.0, 93.2, 151.7, 151.9, 156.1, 173.7 ppm; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd for $C_{21}H_{39}N_2O_7$ 431.2757; found 431.2753.

4.4.8. (S)-tert-Butyl 4-((R)-5-(tert-butoxycarbonylamino)-6-methoxy-6-oxohexyl)-2,2-dimethyloxazolidine-3-carboxylate ***5e***. R_f=0.5 (petroleum ether/EtOAc, 4:1); oily liquid (0.75 g, 80%); $[\alpha]_D^{25}$ +18.75 (*c* 0.16, $CHCl_3$); IR ν_{max}(thin film): 3353, 1746, 1697 cm^{-1}; ^1H NMR (DMSO-d_6, 90 °C, 500 MHz):δ=1.19–1.30 (m, 4H), 1.35 (s, 9H), 1.37 (s, 3H), 1.39 (s, 9H), 1.44 (s, 3H), 1.46–1.65 (m, 4H), 3.60 (s, 3H), 3.63 (dd, *J*=8.8, 1.85 Hz, 1H), 3.71 (br s, 1H), 3.84–3.87 (m, 1H), 3.90–3.95 (m, 1H), 6.72 (br s, 1H) ppm; ^{13}C NMR (DMSO-d_6, 125 MHz): δ=23.4, 24.8, 25.4, 25.6, 25.8, 27.1, 27.9, 28.6, 29.5, 31.10, 32.2, 33.4, 52.1, 52.2, 53.7, 53.9, 56.9, 57.0, 57.2, 57.3, 66.3, 66.5, 66.8, 66.9, 78.6, 79.1, 79.5, 92.9, 92.9, 93.1, 93.1, 151.5, 151.7, 156.0, 173.7 ppm; HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ calcd for $C_{22}H_{40}N_2NaO_7$ 467.2733; found 467.2733.

4.4.9. (S)-tert-Butyl 4-((S)-5-(tert-butoxycarbonylamino)-6-methoxy-6-oxohexyl)-2,2-dimethyloxazolidine-3-carboxylate ***5e′***. R_f=0.5 (petroleum ether/EtOAc, 4:1); oily liquid (0.75 g, 81%); $[\alpha]_D^{25}$ +13.33 (*c* 0.15, $CHCl_3$); IR ν_{max}(thin film): 3353, 1746, 1697 cm^{-1}; ^1H NMR (DMSO-d_6, 90 °C, 500 MHz):δ=1.19–1.33 (m, 4H), 1.35 (s, 9H), 1.37 (s, 3H), 1.39 (s, 9H), 1.44 (s, 3H), 1.47–1.67 (m, 4H), 3.60 (s, 3H), 3.63 (dd, *J*=8.85, 1.50 Hz, 1H), 3.71 (br s, 1H), 3.84–3.87 (m, 1H), 3.90–3.94 (m, 1H), 6.72 (br s, 1H) ppm; ^{13}C NMR (DMSO-d_6, 125 MHz): δ=23.4, 25.4, 25.7, 25.9, 27.1, 27.1, 28.6, 28.6, 31.0, 33.4, 52.1, 52.2, 53.8, 53.8, 57.1, 57.3, 66.5, 66.9, 78.6, 79.1, 79.5, 92.9, 93.1, 150.2, 151.6, 156.0, 173.7 ppm; HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ calcd for $C_{22}H_{40}N_2NaO_7$ 467.2733; found 467.2733.

4.5. General procedure for the conversion of 5 to 6 (oxazolidine ring opening)

The oxazolidine derivatives **5** (2 mmol) were treated with 25 mL of 7% trifluoroacetic acid in MeOH at 0 °C under nitrogen. After stirring the reaction mixture for 16 h at 30 °C, the mixture was concentrated under reduced pressure and purified by column chromatography (1:1 ethyl acetate and petroleum ether).

4.5.1. (2R,4S)-Methyl 2,4-bis(tert-butoxycarbonylamino)-5-hydroxypentanoate ***6b***. R_f=0.4 (petroleum ether/EtOAc, 1:1); oily liquid (0.65 g, 90%); $[\alpha]_D^{25}$ −3.5 (*c* 0.28, $CHCl_3$); IR ν_{max} (thin film): 3354, 1741, 1692 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ=1.41 (s, 18H), 1.98–2.02 (m, 2H), 3.03 (br s, 1H), 3.60–3.65 (m, 3H), 3.70 (s, 3H), 4.37–4.39 (m, 1H), 5.02 (d, *J*=7.9 Hz, 1H), 5.64 (d, *J*=7.9 Hz, 1H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ=28.3, 28.4, 33.7, 48.9, 51.0, 52.5, 64.6, 79.9, 80.1, 155.7, 156.0, 173.0 ppm; HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ calcd for $C_{16}H_{30}N_2NaO_7$ 385.1959; found 385.1954.

4.5.2. (2S,4S)-Methyl 2,4-bis(tert-butoxycarbonylamino)-5-hydroxypentanoate ***6b′***. R_f=0.4 (petroleum ether/EtOAc, 1:1); oily liquid (0.65 g, 90%); $[\alpha]_D^{25}$ +13.0 (*c* 0.23, $CHCl_3$); IR ν_{max} (thin film): 3354, 1741, 1692 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ=1.41 (s, 18H), 1.81–2.05 (m, 2H), 3.60–3.67 (m, 3H), 3.72 (s, 3H), 4.25 (m, 1H), 5.17 (br s, 1H), 5.43 (br s, 1H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ=28.3, 28.4, 29.7, 34.3, 49.9, 51.0, 52.6, 64.9, 79.9, 80.3, 155.7, 156.2, 173.1 ppm; HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ calcd for $C_{16}H_{30}N_2NaO_7$ 385.1959; found 385.1954.

4.5.3. (2R,5S)-Methyl 2,5-bis(tert-butoxycarbonylamino)-6-hydroxyhexanoate ***6c***. R_f=0.4 (petroleum ether/EtOAc, 1:1); pale yellow solid; mp 57–60 °C (0.61 g, 90%); $[\alpha]_D^{25}$ −9.6 (*c* 0.23, $CHCl_3$); IR ν_{max} (KBr): 3359, 1744, 1698 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ=1.41 (s, 18H), 1.46–1.69 (m, 2H), 1.87–2.02 (m, 2H), 2.72 (br s, 1H) 3.54–3.59 (m, 3H), 3.71 (s, 3H), 4.25–4.26 (m, 1H), 4.87 (d, *J*=7.90 Hz, 1H), 5.21 (d, *J*=6.7 Hz, 1H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ=27.5, 28.3, 28.4, 29.5, 52.4, 53.5, 65.4, 79.7, 80.1, 155.6, 156.4, 173.1 ppm; HRMS (ESI-TOF) *m*/*z*: calcd for $C_{17}H_{33}N_2O_7$ 377.2288; found 377.2285.

4.5.4. (2S,5S)-Methyl 2,5-bis(tert-butoxycarbonylamino)-6-hydroxyhexanoate ***6c′***. R_f=0.4 (petroleum ether/EtOAc, 1:1); oily liquid (0.61 g, 90%); $[\alpha]_D^{25}$ +8.6 (*c* 0.23, $CHCl_3$); IR ν_{max} (thin film): 3354, 1741, 1692 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ=1.41 (s, 18H), 1.57–2.14 (m, 4H), 2.76 (br s, 1H), 3.54–3.61 (m, 3H), 3.71 (s, 3H), 4.79–4.88 (m, 1H), 5.16 (br s, 1H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ=27.4, 28.3, 28.4, 29.5, 52.1, 52.4, 53.2, 65.3, 79.7, 80.1, 155.6, 156.3, 173.2 ppm; HRMS (ESI-TOF) *m*/*z*: $[M+H]^+$ calcd for $C_{17}H_{33}N_2O_7$ 377.2288; found 377.2286.

4.5.5. (2R,6S)-Methyl 2,6-bis(tert-butoxycarbonylamino)-7-hydroxyheptanoate ***6d***. R_f=0.4 (petroleum ether/EtOAc, 1:1); oily liquid (0.71 g, 91%); $[\alpha]_D^{25}$ −10.0 (*c* 0.10, $CHCl_3$); IR ν_{max} (thin film): 3357, 1740, 1689 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ=1.28–1.35 (m, 2H), 1.41 (s, 18H), 1.54–1.82 (m, 4H), 3.56 (m, 3H), 3.71 (s, 3H), 4.30 (m, 1H), 4.92 (m, *J*=3.95 Hz, 1H), 5.18 (m, *J*=9 Hz, 1H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ=21.5, 28.3, 28.4, 30.3, 33.1, 52.2, 52.4, 52.5, 64.4, 79.5, 80.2, 155.9, 156.3, 173.3 ppm; HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ calcd for $C_{18}H_{34}N_2NaO_7$ 413.2264; found 413.2263.

4.5.6. (2S,6S)-Methyl 2,6-bis(tert-butoxycarbonylamino)-7-hydroxyheptanoate ***6d′***. R_f=0.4 (petroleum ether/EtOAc, 1:1); white solid; mp 81–85 °C (0.71 g, 92%); $[\alpha]_D^{25}$ 4.34 (*c* 0.23, $CHCl_3$); IR ν_{max} (KBr): 3357, 1741, 1691 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ=1.28–1.35 (m, 2H), 1.40 (s, 18H), 1.46–1.75 (m, 4H), 2.61 (br s, 1H), 3.53–3.59 (m, 3H), 3.70 (s, 3H), 4.23 (br s, 1H), 4.85 (m, *J*=4.6 Hz, 1H), 5.19 (m, *J*=6.1 Hz, 1H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ=21.8, 28.4, 28.4, 30.7, 32.6, 52.2, 52.4, 53.0, 65.9, 79.6, 80.0, 155.7, 156.7, 173.4 ppm; HRMS (ESI-TOF) *m*/*z*: $[M+Na]^+$ calcd for $C_{18}H_{34}N_2NaO_7$ 413.2264; found 413.2269.

4.5.7. (2R,7S)-Methyl 2,7-bis(tert-butoxycarbonylamino)-8-hydroxyoctanoate ***6e***. R_f=0.4 (petroleum ether/EtOAc, 1:1); pale yellow solid; mp 90–95 °C (0.75 g, 93%); $[\alpha]_D^{25}$ −12.5 (*c* 0.24, $CHCl_3$); IR ν_{max} (KBr): 3360, 1744, 1691 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ=1.18–1.35 (m, 4H), 1.41 (s, 18H), 1.49–1.87 (m, 4H), 2.62 (br s, 1H), 3.50–3.62 (m, 3H), 3.71 (s, 3H), 4.25–4.26 (m, 1H), 4.70 (br s, 1H), 5.05 (br s, 1H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ=25.1, 25.5, 28.3,

28.4, 29.7, 31.3, 32.6, 52.3, 52.6, 53.3, 65.8, 79.6, 79.9, 155.5, 156.5, 173.4 ppm; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{19}H_{37}N_2O_7$ 405.2601; found 405.2605.

4.5.8. (2S,7S)-Methyl 2,7-bis(tert-butoxycarbonylamino)-8-hydroxyoctanoate ***6e′***. R_f=0.4 (petroleum ether/EtOAc, 1:1); oily liquid (0.75 g, 93%); $[\alpha]_D^{25}$ +2.8 (*c* 0.34, $CHCl_3$); IR ν_{max}(thin film): 3356, 1741, 1691 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ=1.17–1.33 (m, 4H), 1.40 (s, 18H), 1.44–1.74 (m, 4H), 2.83 (br s, 1H), 3.54–3.59 (m, 3H), 3.70 (s, 3H), 4.25–4.26 (m, 1H), 4.75 (br s, 1H), 5.09 (d, *J*=6.7 Hz, 1H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ=25.1, 25.4, 28.3, 28.4, 29.7, 31.3, 32.6, 52.3, 52.6, 53.2, 65.5, 79.6, 80.0, 155.5, 156.4, 173.4 ppm; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{19}H_{37}N_2O_7$ 405.2601; found 405.2604.

4.6. Oxidation of *N*-Boc protected amino alcohols 6 to the bis-amino acid derivatives 7

Oxidation of *N*-Boc protected amino alcohols **6** to the bis-amino acid derivatives **7** was carried out using the same procedure that was used for the oxidation of **4** to **5**.

4.6.1. (2R,4S)-Dimethyl-2,4-bis(tert-butoxycarbonylamino)pentanedioate ***7b***. R_f=0.3 (petroleum ether/EtOAc, 4:1); oily liquid (0.67 g, 86%); $[\alpha]_D^{25}$ 0.00 (*c* 0.24, $CHCl_3$); IR ν_{max} (thin film): 3354, 1741, 1692 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ=1.42 (s, 18H), 2.23 (t, *J*=5.75 Hz, 2H), 3.73 (s, 3H), 4.31 (br s, 2H), 5.25 (br s, 2H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ=28.2, 28.3, 29.7, 34.7, 50.8, 52.6, 80.3, 155.4, 172.5 ppm; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{17}H_{30}N_2NaO_8$ 413.1900; found 413.1902.

4.6.2. (2S,4S)-Dimethyl-2,4-bis(tert-butoxycarbonylamino)pentanedioate ***7b′***. R_f=0.3 (petroleum ether/EtOAc, 4:1); oily liquid (0.67 g, 86%); $[\alpha]_D^{25}$ +20.68 (*c* 0.29, $CHCl_3$); IR ν_{max} (thin film): 3354, 1741, 1692 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ=1.42 (s, 18H), 2.23 (t, *J*=5.75 Hz, 2H), 3.73 (s, 3H), 4.31 (br s, 2H), 5.25 (br s, 2H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ=28.2, 28.3, 29.7, 34.7, 50.8, 52.6, 80.3, 155.4, 172.5 ppm; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{17}H_{30}N_2NaO_8$ 413.1900; found 413.1902.

4.6.3. (2R,5S)-Dimethyl-2,5-bis(tert-butoxycarbonylamino)hexanedioate ***7c***. R_f=0.3 (petroleum ether/EtOAc, 4:1); crystalline solid (0.69 g, 85%); mp 120–125 °C; $[\alpha]_D^{25}$ 0.0 (*c* 0.31, $CHCl_3$); IR ν_{max} (KBr): 3361, 1741, 1714 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ=1.39 (s, 18H), 1.54–1.92 (m, 4H), 3.72 (s, 6H), 4.30 (m, 2H), 5.04 (d, *J*=6.1 Hz, 2H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ=28.3, 28.9, 52.4, 52.9, 80.1, 155.4, 172.9 ppm; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{18}H_{32}N_2NaO_8$ 427.2056; found 427.2053.

4.6.4. (2S,5S)-Dimethyl-2,5-bis(tert-butoxycarbonylamino)hexanedioate ***7c′***. R_f=0.3 (petroleum ether/EtOAc, 4:1); white solid; mp 81–85 °C (0.69 g, 85%); $[\alpha]_D^{25}$ +17.3 (*c* 0.23, $CHCl_3$); IR ν_{max} (KBr): 3361, 1741, 1714 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ=1.37 (s, 18H), 1.58–1.89 (m, 4H), 3.73 (s, 6H), 4.28 (m, 2H), 5.07 (br s, 2H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ=28.3, 28.9, 52.5, 53.2, 80.1, 155.4, 172.8 ppm; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{18}H_{32}N_2NaO_8$ 427.2056; found 427.2053.

4.6.5. (2R,6S)-Dimethyl-2,6-bis(tert-butoxycarbonylamino)heptanedioate ***7d***. R_f=0.3 (petroleum ether/EtOAc, 4:1); oily liquid (0.71 g, 86%); $[\alpha]_D^{25}$ 0.0 (*c* 0.28, $CHCl_3$); IR ν_{max} (thin film): 3361, 1741, 1714 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ=1.22–1.38 (m, 2H), 1.41 (s, 18H), 1.57–1.79 (m, 4H), 3.71 (s, 6H), 4.25–4.26 (m, 2H), 5.05 (d, *J*=6.4 Hz, 2H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ=21.1, 28.3, 32.2, 52.3, 53.1, 80.0, 155.5, 173.1 ppm; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{19}H_{34}N_2NaO_8$ 441.2213; found 441.2212.

4.6.6. (2S,6S)-Dimethyl-2,6-bis(tert-butoxycarbonylamino)heptanedioate ***7d′***. R_f=0.3 (petroleum ether/EtOAc, 4:1); oily liquid (0.71 g, 86%); $[\alpha]_D^{25}$ +9.4 (*c* 0.42, $CHCl_3$); IR ν_{max} (thin film): 3364, 1744, 1714 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ=1.20–1.27 (m, 2H), 1.33 (s, 18H), 1.55–1.70 (m, 4H), 3.62 (s, 6H), 4.14 (m, 2H), 5.17 (d, *J*=7.3 Hz, 2H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ=21.4, 28.3, 32.0, 52.2, 53.0, 79.7, 155.6, 173.2 ppm; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{19}H_{35}N_2O_8$ 419.2393; found 419.2390.

4.6.7. (2R,7S)-Dimethyl-2,7-bis(tert-butoxycarbonylamino)octanedioate ***7e***. R_f=0.3 (petroleum ether/EtOAc, 4:1); oily liquid (0.75 g, 87%); $[\alpha]_D^{25}$ 0.0 (*c* 0.31, $CHCl_3$); IR ν_{max} (thin film): 3362, 1744, 1714 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ=1.27–1.34 (m, 4H), 1.21–1.34 (m, 4H), 1.40 (s, 18H), 1.52–1.59 (m, 2H), 1.73–1.74 (m, 2H), 3.69 (s, 6H), 4.23–4.24 (m, 2H), 5.04 (d, *J*=7.0 Hz, 2H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ=24.9, 28.3, 32.5, 52.3, 53.2, 79.9, 155.4, 173.3 ppm; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{20}H_{37}N_2O_8$ 432.2550; found 433.2556.

4.6.8. (2S,7S)-Dimethyl-2,7-bis(tert-butoxycarbonylamino)octanedioate ***7e′***. R_f=0.3 (petroleum ether/EtOAc, 4:1); oily liquid (0.75 g, 87%); $[\alpha]_D^{25}$ +14.6 (*c* 0.47, $CHCl_3$); IR ν_{max} (thin film): 3363, 1744, 1715 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ=1.25–1.33 (m, 4H), 1.38 (s, 18H), 1.51–1.72 (m, 4H), 3.68 (s, 6H), 4.22–4.23 (m, 2H), 5.04 (d, *J*=7.6 Hz, 2H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz): δ=24.9, 28.3, 32.5, 52.2, 53.3, 79.9, 155.4, 173.3 ppm; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{20}H_{37}N_2O_8$ 433.2550; found 433.2556.

4.6.9. (3R,4S)-3,4-Di(tert-butoxycarbonylamino)dihydrofuran-2(3H)-one ***8***. R_f=0.3 (petroleum ether/EtOAc, 4:1); oily liquid (0.52 g, 85%); $[\alpha]_D^{25}$ −40.7 (*c* 2.7, $CHCl_3$); IR ν_{max} (thin film): 3355, 1787, 1693 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ=1.42 (s, 18H), 3.96–4.13 (m, 2H), 4.37 (br s, 1H), 4.78 (br s, 1H), 5.28 (d, *J*=5.7 Hz, 1H), 6.00 (br s, 1H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ=28.3, 28.3, 54.8, 55.3, 70.1, 80.4, 81.4, 155.9, 156.6, 172.4 ppm; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{14}H_{24}N_2NaO_6$ 339.1532; found 339.1533.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2014.10.048.

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11. CCDC-1001499 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.