

Preparation of Optically Pure δ -Lactones Using Diastereomeric Resolution with Amino Acid as Resolving Agent

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Abstract: Synthesis of optically pure δ -lactones by diastereomeric resolution was investigated. Amino acid derivatives, which can be obtained at a relatively low cost, were used as resolving agents. Six optically pure δ -lactones were efficiently synthesized using Cbz-L-alanine without other expensive resolving agents. Both enantiomers of δ -lactone obtained had over 98% enantiomeric excesses. This diastereomeric resolution is very efficient for the preparation of optically pure δ -lactones.

Key words: δ -lactone, diastereomeric resolution, resolving agent, amino acid

1 INTRODUCTION

δ -Lactones are well-known natural flavor compounds¹⁻⁵, pheromone components⁶ and useful building blocks⁷⁻⁹ for pharmaceutical purposes. These lactones are approved for use in a wide variety of foods and beverages including ice cream, soft drinks, candy, and sweet cakes. However, the odor characteristics of δ -lactones depend to a large extent on their chiral configuration and enantiomeric composition¹⁰. In coconut, mango, passion fruit, and strawberry, δ -octalactone is found naturally in an enantiomeric excess with the *R*-enantiomer dominant. On the other hand, δ -decalactone is found in raspberries and is *S*-enantiomer dominant¹¹. Therefore, use of a similar enantiomeric excess of optically active δ -lactones is prerequisite to artificially simulate a natural flavor. These interesting and useful properties have encouraged much research to explore effective and low cost methods for obtaining optically active δ -lactones. Among the various methods that have been developed to prepare optically active δ -lactones are transition metal-catalyzed hydrogenation^{12,13}, microbiological reduction^{14,15}, and enzymatic resolution¹⁶⁻¹⁸. Among the various new and attractive techniques now available for preparation of enantiopure compounds, resolution *via* diastereomeric resolution is still a useful technique on an industrial scale because it is generally simple and clean and laboratory-level data can be easily reproduced on a larger scale¹⁹⁻²¹. In fact, it has been estimated

that more than half of the chiral drugs on the pharmaceutical market are produced by a diastereomeric resolution procedure using enantiopure resolving agents²². Many researchers have reported the preparation of optically active lactones *via* diastereomeric resolution^{23,24}. However, problems such as low yields and the need for expensive resolving reagents remain. Amino acid derivatives are used as resolving agents because these are commercially available and relatively inexpensive, and many examples have been reported²⁴⁻²⁶. In this paper, we attempted to prepare both enantiomers of δ -lactones selectively *via* diastereomeric resolution using amino acid derivatives as a resolving agent.

2 EXPERIMENTAL

2.1 General

¹H and ¹³C NMR spectra were recorded on a JNM-ECA-400 spectrometer (JEOL, Tokyo, Japan) at 399.78 and 100.53 MHz, respectively, with CDCl₃ as a solvent and TMS as the internal standard. Chemical shifts are reported in delta (δ) units. Coupling constants are reported in Hertz (Hz). Diastereomeric excesses are determined by ¹H NMR. Infrared (IR) spectra were recorded on a Fourier transform (FT)IR-4100 spectrometer from JASCO Corp. (Tokyo, Japan) and are reported as wave numbers (cm⁻¹). Melting

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points (mp) were recorded on a MP-500D micro-melting-point apparatus from Yanaco Technical Science Co., Ltd. (Kyoto, Japan) and are uncorrected. Capillary GC was performed using a CycloSil-B (30m × 0.25 mm I.D. 0.25 μm film thickness, Agilent Technologies, Santa Clara, CA, USA) column (Inj. 250°C, Det. 250°C). Optical rotations were obtained on a P-1010 polarimeter from JASCO Corp. (Tokyo, Japan). High-resolution mass spectra (HRMS) were analyzed on an AccuTof GCv 4G (JEOL, Tokyo, Japan). Analytical thin-layer chromatography (TLC) was carried out on precoated plates (silica gel 60 F254). Flash column chromatography was carried out with silica gel FL60D.

2.2 General procedure for preparation of *N*-alkyl-5-hydroxyalkylamides (*rac*-1a-d and *rac*-5a-d)

Racemic *N*-alkyl-5-hydroxyalkylamides (*rac*-1a-c and *rac*-5a-d) were prepared by stirring a solution of the corresponding δ-lactone (10.0 mmol) and amine (20.0 mmol) at room temperature. On the other hand, racemic *N*-methyl-5-hydroxydodecanamide (*rac*-4d) was prepared by adding δ-dodecalactone (2.0 g, 10.0 mmol) to a stirred 40% methylamine aqueous solution (30 mL) for two days at room temperature, and neutralized by hydrochloric acid. The aqueous phase was extracted with CHCl₃. The combined organic phase was dried over NaSO₄ and concentrated under reduced pressure. The residue was purified by flash chromatography on silica (eluent: AcOEt) to afford the corresponding *N*-alkyl-5-hydroxyalkylamides (*rac*-1a-c and *rac*-5a-d).

2.2.1 *N*-Benzyl-5-hydroxydodecanamide (*rac*-1a)

Yield: 0.28 g, 93%; Colorless solid; mp = 70–71°C; *R*_f = 0.10 (eluent: *n*-hexane-AcOEt, 1:1, *v/v*). IR (KBr): cm⁻¹ 3289 (O-H, N-H), 3033 (Ar, C-H), 2922 (CH₃), 2850 (CH₂), 1634 (NHC(=O)), 1553, 1454 (Ar, C=C), 729, 696 (Ar, C-H). ¹H NMR (399.78 MHz, TMS/CDCl₃): δ 0.88 (t, *J* = 6.9 Hz, 3H, -CH₃), 1.17–1.34 (m, 10H, -CH₂- × 5), 1.35–1.55 (m, 4H, -CH₂CH(OH)CH₂-), 1.76 (m, 2H, -NHC(=O)CH₂CH₂-), 2.13 (br s, 1H, OH), 2.25 (t, *J* = 7.3 Hz, 2H, -NHC(=O)CH₂-), 3.56 (m, 1H, -CH(OH)-), 4.42 (d, *J* = 5.7 Hz, 2H, PhCH₂NHC(=O)-), 6.05 (br s, 1H, NH), 7.22–7.38 (m, 5H, Ph). ¹³C NMR (100.53 MHz, TMS/CDCl₃): δ 14.1 (-CH₃), 21.6 (-NHC(=O)CH₂CH₂-), 22.6 (-CH₂CH₃), 25.7, 29.3, 29.6 (-CH₂-), 31.8 (-CH₂CH₂CH₃), 36.2 (-NHC(=O)CH₂-), 36.6 (-CH₂CH(OH)CH₂-), 37.5 (-CH₂CH(OH)CH₂-), 43.5 (PhCH₂NHC(=O)-), 71.2 (-CH(OH)-), 127.4, 127.8, 128.6, 138.3 (Ph), 173.0 (-NHC(=O)-). HRMS (FI) calcd. for C₁₉H₃₁NO₂ (M)⁺, 305.23548; found: (M)⁺, 305.23712.

2.2.2 *N*-Cyclohexyl-5-hydroxydodecanamide (*rac*-1b)

Yield: 0.29 g, 98%; Colorless solid; mp = 81–82°C; *R*_f = 0.11 (eluent: *n*-hexane-AcOEt, 1:1, *v/v*). IR (KBr): cm⁻¹ 3303 (O-H, N-H), 2918 (CH₃), 2853 (CH₂), 1631 (NHC(=O)). ¹H NMR (399.78 MHz, TMS/CDCl₃): δ 0.88 (t, *J* = 6.9 Hz, 3H, -CH₃), 1.03–1.21 (m, 3H, -CH₂- × 2), 1.21–1.34 (m, 10H, -CH₂- × 5), 1.33–1.39 (m, 2H, -CH₂-), 1.39–1.55 (m, 4H,

-CH₂CH(OH)CH₂-), 1.59–1.66 (m, 1H, -CH₂-), 1.66–1.79 (m, 4H, -CH₂- × 2), 1.86–1.95 (t, *J* = 7.3 Hz, 2H, -CH₂-), 2.13–2.25 (m, 3H, -NHC(=O)CH₂-), 3.58 (m, 1H, -CH(OH)-), 3.77 (m, 1H, -CHNHC(=O)-), 5.53 (br s, 1H, NH). ¹³C NMR (100.53 MHz, TMS/CDCl₃): δ 14.1 (-CH₃), 21.6 (-NHC(=O)CH₂CH₂-), 22.6 (-CH₂CH₃), 24.8, 25.7, 29.3, 29.6 (-CH₂-), 31.8 (-CH₂CH₂CH₃), 33.2 (-CH₂-), 36.5 (-NHC(=O)CH₂-), 36.6 (-CH₂CH(OH)CH₂-), 37.5 (-CH₂CH(OH)CH₂-), 48.1 (-CHNHC(=O)-), 71.2 (-CH(OH)-), 172.2 (-NHC(=O)-). HRMS (FI) calcd. for C₁₈H₃₅NO₂ (M)⁺, 297.26678; found: (M)⁺, 297.26803.

2.2.3 *N*-iso-Propyl-5-hydroxydodecanamide (*rac*-1c)

Yield: 0.23 g, 91%; Colorless solid; mp = 59–60°C; *R*_f = 0.08 (eluent: *n*-hexane-AcOEt, 1:1, *v/v*). IR (KBr): cm⁻¹ 3034 (O-H, N-H), 2920 (CH₃), 2851 (CH₂), 1641 (NHC(=O)). ¹H NMR (399.78 MHz, TMS/CDCl₃): δ 0.88 (t, *J* = 6.9 Hz, 3H, -CH₃), 1.14 (t, *J* = 6.6 Hz, 6H, (CH₃)₂CH-), 1.21–1.35 (10H, m, -CH₂- × 5), 1.37–1.54 (m, 4H, -CH₂CH(OH)CH₂-), 1.74 (m, 2H, -NHC(=O)CH₂CH₂-), 2.18 (t, *J* = 7.3 Hz, 2H, -NHC(=O)CH₂-), 2.28 (br s, 1H, OH), 3.58 (m, 1H, -CH(OH)-), 4.08 (m, 1H, (CH₃)₂CH-), 5.54 (br s, 1H, NH). ¹³C NMR (100.53 MHz, TMS/CDCl₃): δ 14.1 (-CH₃), 21.5 (-NHC(=O)CH₂CH₂-), 22.6 (-CH₂CH₃), 22.7 ((CH₃)₂CH-), 25.7, 29.3, 29.6 (-CH₂-), 31.8 (-CH₂CH₂CH₃), 36.4 (-NHC(=O)CH₂-), 36.6 (-CH₂CH(OH)CH₂-), 37.5 (-CH₂CH(OH)CH₂-), 41.2 ((CH₃)₂CH-), 71.2 (-CH(OH)-), 172.3 (-NHC(=O)-). HRMS (FI) calcd. for C₁₅H₃₁NO₂ (M)⁺, 257.23548; found: (M)⁺, 257.23249.

2.2.4 *N*-Methyl-5-hydroxydodecanamide (*rac*-1d)

Yield: 0.21 g, 90%; Colorless solid; mp = 70–71°C; *R*_f = 0.02 (eluent: *n*-hexane-AcOEt, 1:1, *v/v*). IR (KBr): cm⁻¹ 3289 (O-H, N-H), 2956 (CH₃), 2849 (CH₂), 1639 (NHC(=O)). ¹H NMR (399.78 MHz, TMS/CDCl₃): δ 0.88 (t, *J* = 6.9 Hz, 3H, -CH₃), 1.20–1.35 (m, 10H, -CH₂- × 5), 1.38–1.55 (m, 4H, -CH₂CH(OH)CH₂-), 1.74 (m, 2H, -NHC(=O)CH₂CH₂-), 2.23 (t, *J* = 7.3 Hz, 2H, -NHC(=O)CH₂-), 2.48 (br s, 1H, OH), 2.80 (d, *J* = 4.8 Hz, 3H, CH₃NHC(=O)-), 3.58 (m, 1H, -CH(OH)-), 5.96 (br s, 1H, NH). ¹³C NMR (100.53 MHz, TMS/CDCl₃): δ 14.0 (-CH₃), 21.6 (-NHC(=O)CH₂CH₂-), 22.6 (-CH₂CH₃), 25.7 (-CH₂-), 26.2 (CH₃NHC(=O)-), 29.2, 29.6 (-CH₂-), 31.8 (-CH₂CH₂CH₃), 36.1 (-NHC(=O)CH₂-), 36.6 (-CH₂CH(OH)CH₂-), 37.5 (-CH₂CH(OH)CH₂-), 71.2 (-CH(OH)-), 173.9 (-NHC(=O)-). HRMS (FI) calcd. for C₁₃H₂₇NO₂ (M)⁺, 229.20418; found: (M)⁺, 229.20216.

2.2.5 *N*-Benzyl-5-hydroxydecanamide (*rac*-5a)

Yield: 0.28 g, 93%; Colorless solid; mp = 69–70°C; *R*_f = 0.08 (eluent: *n*-hexane-AcOEt, 1:1, *v/v*). IR (KBr): cm⁻¹ 3289 (O-H, N-H), 3028 (Ar, C-H), 2922 (CH₃), 2853 (CH₂), 1631 (NHC(=O)), 1550, 1454 (Ar, C=C), 729, 696 (Ar, C-H). ¹H NMR (399.78 MHz, TMS/CDCl₃): δ 0.89 (t, *J* = 6.9 Hz, 3H, -CH₃), 1.18–1.34 (m, 6H, -CH₂- × 3), 1.36–1.55 (m, 4H, -CH₂CH(OH)CH₂-), 1.76 (m, 2H, -NHC(=O)CH₂CH₂-), 2.15 (br s, 1H, OH), 2.25 (t, *J* = 7.3 Hz, 2H, -NHC(=O)CH₂-), 3.56 (m, 1H, -CH₂CH(OH)CH₂-), 4.42 (d, *J* = 5.7 Hz,

2H, PhCH₂NHC(=O)-), 6.07 (br s, 1H, NH), 7.17-7.42 (m, 5H, Ph). ¹³C NMR (100.53 MHz, TMS/CDCl₃) δ 14.0 (-CH₃), 21.6 (-NHC(=O)CH₂CH₂-), 22.6 (-CH₂CH₃), 25.3 (-CH₂-), 31.8 (-CH₂CH₂CH₃), 36.2 (-NHC(=O)CH₂-), 36.6 (-CH₂CH(OH)CH₂-), 37.5 (-CH₂CH(OH)CH₂-), 43.5 (PhCH₂NHC(=O)-), 71.2 (-CH₂CH(OH)CH₂-), 127.4, 127.8, 128.6, 138.3 (Ph), 173.02 (-NHC(=O)-). HRMS (FI) calcd. for C₁₇H₂₇NO₂ (M)⁺, 277.20418; found: (M)⁺, 277.20209.

2.2.6 *N*-Benzyl-5-hydroxyundecanamide (*rac*-5b)

Yield: 0.24 g, 83%; Colorless solid; mp = 77-78°C; R_f = 0.09 (eluent: *n*-hexane-AcOEt, 1:1, *v/v*). IR (KBr): cm⁻¹ 3292 (O-H, N-H), 3032 (Ar, C-H), 2924 (CH₃), 2853 (CH₂), 1641 (NHC(=O)), 1549, 1450 (Ar, C=C), 729, 698 (Ar, C-H). ¹H NMR (399.78 MHz, TMS/CDCl₃) δ 0.89 (t, *J* = 6.9 Hz, 3H, -CH₃), 1.17-1.35 (m, 8H, -CH₂- × 4), 1.36-1.55 (m, 4H, -CH₂CH(OH)CH₂-), 1.76 (m, 2H, -NHC(=O)CH₂CH₂-), 2.15 (br s, 1H, OH), 2.25 (t, *J* = 7.3 Hz, 2H, -NHC(=O)CH₂-), 3.56 (m, 1H, -CH₂CH(OH)CH₂-), 4.42 (d, *J* = 5.7 Hz, 2H, PhCH₂NHC(=O)-), 6.06 (br s, 1H, NH), 7.18-7.43 (m, 5H, Ph). ¹³C NMR (100.53 MHz, TMS/CDCl₃) δ 14.1 (-CH₃), 21.6 (-NHC(=O)CH₂CH₂-), 22.6 (-CH₂CH₃), 25.6, 29.3 (-CH₂-), 31.8 (-CH₂CH₂CH₃), 36.2 (-NHC(=O)CH₂-), 36.6 (-CH₂CH(OH)CH₂-), 37.5 (-CH₂CH(OH)CH₂-), 43.5 (PhCH₂NHC(=O)-), 71.2 (-CH₂CH(OH)CH₂-), 127.4, 127.8, 128.6, 138.3 (Ph), 173.0 (-NHC(=O)-). HRMS (FI) calcd. for C₁₈H₂₉NO₂ (M)⁺, 291.21983; found: (M)⁺, 291.21992.

2.2.7 *N*-Benzyl-5-hydroxytridecanamide (*rac*-5c)

Yield: 0.29 g, 91%; Colorless solid; mp = 84-85°C; R_f = 0.12 (eluent: *n*-hexane-AcOEt, 1:1, *v/v*). IR (KBr): cm⁻¹ 3300 (O-H, N-H), 3032 (Ar, C-H), 2918 (CH₃), 2850 (CH₂), 1639 (NHC(=O)), 1551, 1454 (Ar, C=C), 728, 697 (Ar, C-H). ¹H NMR (399.78 MHz, TMS/CDCl₃) δ 0.88 (t, *J* = 6.9 Hz, 3H, -CH₃), 1.18-1.34 (m, 12H, -CH₂- × 6), 1.35-1.54 (m, 4H, -CH₂CH(OH)CH₂-), 1.76 (m, 2H, -NHC(=O)CH₂CH₂-), 2.18-2.30 (br s, 1H, OH), 2.24 (t, *J* = 7.3 Hz, 2H, -NHC(=O)CH₂-), 3.56 (m, 1H, -CH₂CH(OH)CH₂-), 4.41 (d, *J* = 5.7 Hz, 2H, PhCH₂NHC(=O)-), 6.14 (br s, 1H, NH), 7.19-7.40 (m, 5H, Ph). ¹³C NMR (100.53 MHz, TMS/CDCl₃) δ 14.1 (-CH₃), 21.6 (-NHC(=O)CH₂CH₂-), 22.6 (-CH₂CH₃), 25.7, 29.2, 29.6, 29.7 (-CH₂-), 31.8 (-CH₂CH₂CH₃), 36.2 (-NHC(=O)CH₂-), 36.6 (-CH₂CH(OH)CH₂-), 37.5 (-CH₂CH(OH)CH₂-), 43.5 (PhCH₂NHC(=O)-), 71.2 (-CH₂CH(OH)CH₂-), 127.4, 127.7, 128.6, 138.3 (Ph), 173.1 (-NHC(=O)-). HRMS (FI) calcd. for C₂₀H₃₃NO₂ (M)⁺, 319.25113; found: (M + H)⁺, 319.25216.

2.2.8 *N*-Benzyl-5-hydroxytetradecanamide (*rac*-5d)

Yield: 0.26 g, 77%; Colorless solid; mp = 76-77°C; R_f = 0.13 (eluent: *n*-hexane-AcOEt, 1:1, *v/v*). IR (KBr): cm⁻¹ 3300 (O-H, N-H), 3032 (Ar, C-H), 2918 (CH₃), 2849 (CH₂), 1637 (NHC(=O)), 1551, 1453 (Ar, C=C), 729, 696 (Ar, C-H). ¹H NMR (399.78 MHz, TMS/CDCl₃) δ 0.89 (t, *J* = 6.9 Hz, 3H, -CH₃), 1.18-1.34 (m, 14H, -CH₂- × 7), 1.35-1.50 (m, 4H, -CH₂CH(OH)CH₂-), 1.77 (m, 2H, -NHC(=O)CH₂CH₂-),

2.06-2.21 (br s, 1H, OH), 2.14 (t, *J* = 7.2 Hz, 2H, -NHC(=O)CH₂-), 3.56 (m, 1H, -CH₂CH(OH)CH₂-), 4.42 (d, *J* = 5.7 Hz, 2H, PhCH₂NHC(=O)-), 6.07 (br s, 1H, NH), 7.23-7.40 (m, 5H, Ph). ¹³C NMR (100.53 MHz, TMS/CDCl₃) δ 14.1 (-CH₃), 21.6 (-NHC(=O)CH₂CH₂-), 22.6 (-CH₂CH₃), 25.7, 29.3, 29.5, 29.6, 29.7 (-CH₂-), 31.9 (-CH₂CH₂CH₃), 36.2 (-NHC(=O)CH₂-), 36.6 (-CH₂CH(OH)CH₂-), 37.5 (-CH₂CH(OH)CH₂-), 43.5 (PhCH₂NHC(=O)-), 71.2 (-CH₂CH(OH)CH₂-), 127.4, 127.8, 128.6, 138.3 (Ph), 173.0 (-NHC(=O)-). HRMS (FI) calcd. for C₂₁H₃₅NO₂ (M)⁺, 333.26678; found: (M)⁺, 333.26884.

2.2.9 *N*-Benzyl-5-hydroxyhexadecanamide (*rac*-5e)

Yield: 0.30 g, 83%; Colorless solid; mp = 82-83°C; R_f = 0.15 (eluent: *n*-hexane-AcOEt, 1:1, *v/v*). IR (KBr): cm⁻¹ 3296 (O-H, N-H), 3031 (Ar, C-H), 2918 (CH₃), 2849 (CH₂), 1639 (NHC(=O)), 1557, 1456 (Ar, C=C), 730, 695 (Ar, C-H). ¹H NMR (399.78 MHz, TMS/CDCl₃) δ 0.89 (t, *J* = 6.9 Hz, 3H, -CH₃), 1.19-1.33 (m, 18H, -CH₂- × 9), 1.36-1.54 (m, 4H, -CH₂CH(OH)CH₂-), 1.77 (m, 2H, -NHC(=O)CH₂CH₂-), 2.09 (br s, 1H, OH), 2.25 (t, *J* = 7.3 Hz, 2H, -NHC(=O)CH₂-), 3.56 (m, 1H, -CH₂CH(OH)CH₂-), 4.42 (d, *J* = 5.7 Hz, 2H, PhCH₂NHC(=O)-), 6.02 (br s, 1H, NH), 7.22-7.36 (m, 5H, Ph). ¹³C NMR (100.53 MHz, TMS/CDCl₃) δ 14.1 (-CH₃), 21.6 (-NHC(=O)CH₂CH₂-), 22.7 (-CH₂CH₃), 25.7, 29.3, 29.6, 29.4, 29.6 (-CH₂-), 31.9 (-CH₂CH₂CH₃), 36.3 (-NHC(=O)CH₂-), 36.6 (-CH₂CH(OH)CH₂-), 37.6 (-CH₂CH(OH)CH₂-), 43.5 (PhCH₂NHC(=O)-), 71.2 (-CH₂CH(OH)CH₂-), 127.5, 127.8, 128.7, 138.3 (Ph), 173.0 (-NHC(=O)-). HRMS (FI) calcd. for C₂₃H₃₉NO₂ (M)⁺, 361.29810; found: (M)⁺, 361.29748.

2.3 Esterification of *rac*-1a-d and *rac*-5a-e

EDCI (0.35 mL, 2.0 mmol) was added dropwise to a solution of the corresponding *N*-alkyl-5-hydroxyalkylamides (*rac*-1a-d and *rac*-5a-e) (1.0 mmol), *N*-(*tert*-butoxycarbonyl)-L-alanine (0.38 g, 2.0 mmol) or *N*-(benzyloxycarbonyl)-L-alanine (0.45 g, 2.0 mmol), DMAP (0.12 g, 1.0 mmol) in THF (5 mL) with stirring at 0°C. The reaction mixture was stirred at the same temperature for a further two hours and then stirred at room temperature for two hours. After evaporation, H₂O was added to the reaction mixture, and it was neutralized with hydrochloric acid. The organic phases were extracted with AcOEt, and the combined organic layers were washed with aqueous NaHCO₃ water and brine, and dried over Na₂SO₄. The AcOEt was removed under reduced pressure, and the residue was purified by column chromatography on silica gel (eluent: toluene-AcOEt, 4:1, *v/v*) to give the corresponding *N*-Alkyl-5-[*N*-(benzyloxy)carbonyl]-2-aminopropanoyloxydodecanamides (2a_{1st}-d_{1st} and 2a_{2nd}-d_{2nd}), *N*-Alkyl-5-[*N*-(*tert*-butyloxy)carbonyl]-2-aminopropanoyloxydodecanamides (3a_{1st}-d_{1st} and 3a_{2nd}-d_{2nd}), and *N*-Benzyl-5-[*N*-(benzyloxy)carbonyl]-2-aminopropanoyloxyalkylamides (6a_{1st}-e_{1st} and 6a_{2nd}-e_{2nd}).

2.3.1 *N*-Benzyl-5-[*N*-(benzyloxy) carbonyl]-2-aminopropanoyloxidodecanamide (**2a**)Data for (5*S*)-**2a**_{1st}

Yield: 0.24 g, 47%; Colorless solid; mp = 82-84°C; $[\alpha]_{\text{D}}^{20} = -19.1$ ($c = 1.0$, MeOH, 99% d.e.). IR (KBr): cm^{-1} 3297 (N-H), 3064 (Ar, C-H), 2927 (CH_2), 2857 (CH_3), 1734 ($\text{OC}(\text{=O})$), 1646 ($\text{NHC}(\text{=O})$), 1456 (CH_2), 1214 (C-O), 731 (Ar, C=C), 695 (Ar, C=C). ^1H NMR (399.78 MHz, TMS/ CDCl_3) δ 0.87 (t, $J = 6.9$ Hz, 3H, $-\text{CH}_3$), 1.14-1.36 (m, 10H, $-\text{CH}_2 \times 5$), 1.39 (d, $J = 7.6$ Hz, 3H, $-\text{CH}(\text{CH}_3)\text{NHC}(\text{=O})-$), 1.44-1.61 (m, 4H, $-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 1.65 (quint, $J = 7.6$ Hz, 2H, $-\text{NHC}(\text{=O})\text{CH}_2\text{CH}_2-$), 2.19 (t, $J = 7.3$ Hz, 2H, $-\text{NHC}(\text{=O})\text{CH}_2-$), 4.26 (quint, $J = 7.3$ Hz, 1H, $-\text{CH}(\text{CH}_3)\text{NHC}(\text{=O})-$), 4.41 (dd, $J = 1.8, 3.7$ Hz, 2H, $\text{PhCH}_2\text{NHC}(\text{=O})-$), 4.91 (quint, $J = 6.2$ Hz, 1H, $-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 5.03 (dd, $J = 4.6, 12.4$ Hz, 2H, $-\text{NHC}(\text{=O})\text{OCH}_2\text{Ph}$), 5.34 (d, $J = 7.8$ Hz, 1H, $-\text{CHNHC}(\text{=O})\text{O}-$), 6.05 (br s, 1H, $\text{BnNHC}(\text{=O})-$), 7.18-7.41 (m, 10H, Ph). ^{13}C NMR (100.53 MHz, TMS/ CDCl_3) δ 14.1 ($-\text{CH}_3$), 18.5 ($-\text{CH}(\text{CH}_3)\text{NHC}(\text{=O})-$), 22.5 ($-\text{CH}_2\text{CH}_3$), 24.7 ($-\text{CH}_2-$), 25.2 ($-\text{NHC}(\text{=O})\text{CH}_2\text{CH}_2-$), 25.4, 29.0 ($-\text{CH}_2-$), 31.7 ($-\text{CH}_2\text{CH}_2\text{CH}_3$), 33.5 ($-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 34.0 ($-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 36.5 ($-\text{NHC}(\text{=O})\text{CH}_2-$), 43.5 ($\text{PhCH}_2\text{NHC}(\text{=O})-$), 49.8 ($-\text{CH}(\text{CH}_3)\text{NHC}(\text{=O})-$), 66.8 ($-\text{NHC}(\text{=O})\text{OCH}_2\text{Ph}$), 75.5 ($-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 127.4, 127.8, 128.0, 128.1, 128.5, 128.6, 136.2, 138.5 (Ph), 155.7 ($-\text{NHC}(\text{=O})\text{O}-$), 172.8 ($-\text{OC}(\text{=O})\text{CH}(\text{CH}_3)-$), 172.8 ($\text{BnNHC}(\text{=O})-$). HRMS (FD) calcd. for $\text{C}_{31}\text{H}_{44}\text{N}_2\text{O}_5$ (M^+), 510.30937; found: (M^+), 510.30687.

Data for (5*R*)-**2a**_{2nd}

Yield: 0.25 g, 48%; Colorless solid; mp = 41-43°C; $[\alpha]_{\text{D}}^{20} = -17.7$ ($c = 1.0$, MeOH, 99% d.e.). IR (KBr): cm^{-1} 3308 (N-H), 3040 (Ar, C-H), 2928 (CH_2), 2861 (CH_3), 1734 ($\text{OC}(\text{=O})$), 1653 ($\text{NHC}(\text{=O})$), 1507 (Ar, C=C), 1457 (CH_2), 1216 (C-O), 746 (Ar, C=C), 697 (Ar, C=C). ^1H NMR (399.78 MHz, TMS/ CDCl_3) δ 0.88 (t, $J = 6.6$ Hz, 3H, $-\text{CH}_3$), 1.15-1.35 (m, 10H, $-\text{CH}_2 \times 5$), 1.39 (d, $J = 6.9$ Hz, 3H, $-\text{CH}(\text{CH}_3)\text{NHC}(\text{=O})-$), 1.43-1.59 (m, 4H, $-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 1.65 (quint, $J = 7.6$ Hz, 2H, $-\text{NHC}(\text{=O})\text{CH}_2\text{CH}_2-$), 2.18 (t, $J = 7.3$ Hz, 2H, $-\text{NHC}(\text{=O})\text{CH}_2-$), 4.33 (quint, $J = 7.1$ Hz, 1H, $-\text{CH}(\text{CH}_3)\text{NHC}(\text{=O})-$), 4.42 (d, $J = 6.2$ Hz, 2H, $\text{PhCH}_2\text{NHC}(\text{=O})-$), 4.89 (quint, $J = 5.6$ Hz, 1H, $-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 5.09 (s, 2H, $-\text{NHC}(\text{=O})\text{OCH}_2\text{Ph}$), 5.35 (d, $J = 7.6$ Hz, 1H, $-\text{CHNHC}(\text{=O})\text{O}-$), 5.81 (br s, 1H, $\text{BnNHC}(\text{=O})-$), 7.20-7.40 (m, 10H, Ph). ^{13}C NMR (100.53 MHz, TMS/ CDCl_3) δ 14.1 ($-\text{CH}_3$), 18.8 ($-\text{CH}(\text{CH}_3)\text{NHC}(\text{=O})-$), 22.5 ($-\text{CH}_2\text{CH}_3$), 24.9 ($-\text{CH}_2-$), 25.1 ($-\text{NHC}(\text{=O})\text{CH}_2\text{CH}_2-$), 25.4, 29.1 ($-\text{CH}_2-$), 31.6 ($-\text{CH}_2\text{CH}_2\text{CH}_3$), 33.6 ($-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 34.0 ($-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 36.4 ($-\text{NHC}(\text{=O})\text{CH}_2-$), 43.6 ($\text{PhCH}_2\text{NHC}(\text{=O})-$), 49.8 ($-\text{CH}(\text{CH}_3)\text{NHC}(\text{=O})-$), 66.8 ($-\text{NHC}(\text{=O})\text{OCH}_2\text{Ph}$), 75.5 ($-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 127.5, 127.8, 128.0, 128.1, 128.5, 128.7, 136.3, 138.4 (Ph), 155.5 ($-\text{NHC}(\text{=O})\text{O}-$), 171.9 ($-\text{OC}(\text{=O})\text{CH}(\text{CH}_3)-$), 172.5 ($\text{BnNHC}(\text{=O})-$). HRMS (FD) calcd. for $\text{C}_{31}\text{H}_{44}\text{N}_2\text{O}_5$ (M^+), 510.30937; found: (M^+), 510.31173.

2.3.2 *N*-Cyclohexyl-5-[*N*-(benzyloxy) carbonyl]-2-aminopropanoyloxidodecanamide (**2b**)Data for (5*S*)-**2b**_{1st}

Yield: 0.24 g, 48%; Colorless solid; mp = 80-82°C; $[\alpha]_{\text{D}}^{20} = -17.1$ ($c = 1.0$, MeOH, 99% d.e.). IR (KBr): cm^{-1} 3304 (N-H), 2925 (CH_2), 2853 (CH_3), 1735 ($\text{OC}(\text{=O})$), 1637 ($\text{NHC}(\text{=O})$), 1507 (Ar, C=C), 1457 (CH_2), 1260 (C-O), 745 (Ar, C=C), 696 (Ar, C=C). ^1H NMR (399.78 MHz, TMS/ CDCl_3) δ 0.87 (t, $J = 7.1$ Hz, 3H, $-\text{CH}_3$), 1.02-1.18 (m, 3H, $-\text{CH}_2 \times 2$), 1.18-1.31 (m, 10H, $-\text{CH}_2 \times 5$), 1.31-1.38 (m, 2H, $-\text{CH}_2-$), 1.42 (d, $J = 7.1$ Hz, 3H, $-\text{CH}(\text{CH}_3)\text{NHC}(\text{=O})-$), 1.46-1.74 (m, 9H, $-\text{CH}_2\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$, $-\text{CH}_2 \times 2$), 1.89 (m, 2H, $-\text{CH}_2-$), 2.13 (m, 2H, $-\text{NHC}(\text{=O})\text{CH}_2-$), 3.74 (m, 1H, $-\text{CH}_2\text{CH}(\text{CH}_2)\text{NHC}(\text{=O})-$), 4.32 (quint, $J = 7.3$ Hz, 1H, $-\text{CH}(\text{CH}_3)\text{NHC}(\text{=O})-$), 4.93 (quint, $J = 5.7$ Hz, 1H, $-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 5.11 (dd, $J = 8.5, 12.1$ Hz, 2H, $-\text{NHC}(\text{=O})\text{OCH}_2\text{Ph}$), 5.36 (d, $J = 7.3$ Hz, 1H, $-\text{CHNHC}(\text{=O})\text{O}-$), 5.69 (d, $J = 7.8$ Hz, 1H, $\text{cHxNHC}(\text{=O})-$), 7.28-7.40 (m, 5H, Ph). ^{13}C NMR (100.53 MHz, TMS/ CDCl_3) δ 14.0 ($-\text{CH}_3$), 18.4 ($-\text{CH}(\text{CH}_3)\text{NHC}(\text{=O})-$), 21.7 ($-\text{NHC}(\text{=O})\text{CH}_2\text{CH}_2-$), 22.6 ($-\text{CH}_2\text{CH}_3$), 24.9, 25.2, 25.5, 29.1, 29.3 ($-\text{CH}_2-$), 31.7 ($-\text{CH}_2\text{CH}_2\text{CH}_3$), 33.2, 33.2 ($-\text{CH}_2-$), 33.2 ($-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 34.1 ($-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 36.3 ($-\text{NHC}(\text{=O})\text{CH}_2-$), 48.0 ($-\text{CH}_2\text{CH}(\text{CH}_2)\text{NHC}(\text{=O})-$), 49.9 ($-\text{CH}(\text{CH}_3)\text{NHC}(\text{=O})-$), 66.9 ($-\text{NHC}(\text{=O})\text{OCH}_2\text{Ph}$), 75.2 ($-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 127.9, 128.1, 128.5, 136.2 (Ph), 155.7 ($-\text{NHC}(\text{=O})\text{O}-$), 171.7 ($\text{cHxNHC}(\text{=O})-$), 173.0 ($-\text{OC}(\text{=O})\text{CH}(\text{CH}_3)-$). HRMS (FD) calcd. for $\text{C}_{30}\text{H}_{48}\text{N}_2\text{O}_5$ (M^+), 502.34067; found: (M^+), 502.33840.

Data for (5*R*)-**2b**_{2nd}

Yield: 0.24 g, 48%; Colorless solid; mp = 102-105°C; $[\alpha]_{\text{D}}^{20} = -18.1$ ($c = 1.0$, MeOH, 99% d.e.). IR (KBr): cm^{-1} 3308 (N-H), 3034 (Ar, C-H), 2931 (CH_2), 2854 (CH_3), 1734 ($\text{OC}(\text{=O})$), 1635 ($\text{NHC}(\text{=O})$), 1507 (Ar, C=C), 1457 (CH_2), 1215 (C-O), 746 (Ar, C=C), 695 (Ar, C=C). ^1H -NMR (399.78 MHz, TMS/ CDCl_3) δ 0.87 (t, $J = 7.1$ Hz, 3H, $-\text{CH}_3$), 1.03-1.18 (m, 3H, $-\text{CH}_2 \times 2$), 1.18-1.31 (m, 10H, $-\text{CH}_2 \times 5$), 1.31-1.38 (m, 2H, $-\text{CH}_2-$), 1.42 (d, $J = 7.1$ Hz, 3H, $-\text{CH}(\text{CH}_3)\text{NHC}(\text{=O})-$), 1.47-1.74 (m, 9H, $-\text{CH}_2\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$, $-\text{CH}_2 \times 2$), 1.89 (m, 2H, $-\text{CH}_2-$), 2.11 (m, 2H, $-\text{NHC}(\text{=O})\text{CH}_2-$), 3.74 (m, 1H, $-\text{CH}_2\text{CH}(\text{CH}_2)\text{NHC}(\text{=O})-$), 4.35 (quint, $J = 7.1$ Hz, 1H, $-\text{CH}(\text{CH}_3)\text{NHC}(\text{=O})-$), 4.91 (quint, $J = 5.7$ Hz, 1H, $-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 5.11 (s, 2H, $-\text{NHC}(\text{=O})\text{OCH}_2\text{Ph}$), 5.36 (d, $J = 7.6$ Hz, 1H, $-\text{CHNHC}(\text{=O})\text{O}-$), 5.44 (d, $J = 7.6$ Hz, 1H, $\text{cHxNHC}(\text{=O})-$), 7.28-7.42 (m, 5H, Ph). ^{13}C NMR (100.53 MHz, TMS/ CDCl_3) δ 14.0 ($-\text{CH}_3$), 18.8 ($-\text{CH}(\text{CH}_3)\text{NHC}(\text{=O})-$), 21.3 ($-\text{NHC}(\text{=O})\text{CH}_2\text{CH}_2-$), 22.6 ($-\text{CH}_2\text{CH}_3$), 24.8, 25.2, 25.5, 29.1, 29.3, 30.9 ($-\text{CH}_2-$), 31.7 ($-\text{CH}_2\text{CH}_2\text{CH}_3$), 33.2 ($-\text{CH}_2-$), 33.3 ($-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 34.0 ($-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 36.2 ($-\text{NHC}(\text{=O})\text{CH}_2-$), 48.1 ($-\text{CH}_2\text{CH}(\text{CH}_2)\text{NHC}(\text{=O})-$), 49.9 ($-\text{CH}(\text{CH}_3)\text{NHC}(\text{=O})-$), 66.8 ($-\text{NHC}(\text{=O})\text{OCH}_2\text{Ph}$), 75.2 ($-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 128.0, 128.1, 128.5, 136.3 (Ph), 155.6 ($-\text{NHC}(\text{=O})\text{O}-$), 171.4 ($\text{cHxNHC}(\text{=O})-$), 172.8 ($-\text{OC}(\text{=O})\text{CH}(\text{CH}_3)-$). HRMS (FD) calcd. for $\text{C}_{30}\text{H}_{48}\text{N}_2\text{O}_5$

(M)⁺, 502.34067; found: (M)⁺, 502.33782.

2.3.3 *N*-iso-Propyl-5-[*N*-(benzyloxy) carbonyl]-2-amino-propanoxydodecanamide (**2c**)

Data for (5*S*)-**2c**_{1st}

Yield: 0.22 g, 47%; Colorless solid; mp = 59-63°C; [α]_D²⁰ = -19.3 (*c* = 1.0, MeOH, 99% d.e.). IR (KBr): cm⁻¹ 3308 (N-H), 3040 (Ar, C-H), 2922 (CH₂), 2853 (CH₃), 1734 (OC(=O)), 1653 (NHC(=O)), 1507 (Ar, C=C), 1457 (CH₂), 1220 (C-O), 748 (Ar, C=C), 698 (Ar, C=C). ¹H NMR (399.78 MHz, TMS/CDCl₃) δ 0.87 (t, *J* = 7.1 Hz, 3H, -CH₃), 1.12 (d, *J* = 6.6 Hz, 6H, (CH₃)₂CH-), 1.18-1.33 (m, 10H, -CH₂- \times 5), 1.41 (d, *J* = 7.3 Hz, 3H, -CH(CH₃)NHC(=O)-), 1.54 (m, 2H, -CH₂CH(O-)CH₂-), 1.57-1.71 (m, 4H, -CH₂CH₂CH(O-)CH₂-), 2.12 (m, 2H, -NHC(=O)CH₂-), 4.06 (m, 1H, (CH₃)CH-), 4.32 (quint, *J* = 7.3 Hz, 1H, -CH(CH₃)NHC(=O)-), 4.93 (quint, *J* = 5.7 Hz, 1H, -CH₂CH(O-)CH₂-), 5.11 (dd, *J* = 5.0, 12.3 Hz, 2H, -NHC(=O)OCH₂Ph), 5.35 (d, *J* = 7.3 Hz, 1H, -CHNHC(=O)O-), 5.61 (d, *J* = 7.1 Hz, 1H, *i*-PrNHC(=O)-), 7.29-7.37 (m, 5H, Ph). ¹³C NMR (100.53 MHz, TMS/CDCl₃) δ 14.0 (-CH₃), 18.4 (-CH(CH₃)NHC(=O)-), 21.6 (-NHC(=O)CH₂CH₂-), 22.6 (-CH₂CH₃), 22.7 ((CH₃)₂CH-), 22.8 ((CH₃)₂CH-), 25.0 (-CH₂-), 29.1, 29.3 (-CH₂-), 31.7 (-CH₂CH₂CH₃), 33.3 (-CH₂CH(O-)CH₂-), 34.1 (-CH₂CH(O-)CH₂-), 36.2 (-NH(C=O)CH₂-), 41.1 ((CH₃)₂CH-), 49.9 (-CH(CH₃)NHC(=O)-), 66.9 (-NHC(=O)OCH₂Ph), 75.2 (-CH₂CH(O-)CH₂-), 128.0, 128.2, 128.5, 136.2 (Ph), 155.7 (-NHC(=O)O-), 171.8 (*i*-PrNHC(=O)-), 173.0 (-OC(=O)CH(CH₃)-). HRMS (FD) calcd. for C₂₇H₄₄N₂O₅(M)⁺, 462.30937; found: (M)⁺, 462.31160.

Data for (5*R*)-**2c**_{2nd}

Yield: 0.22 g, 48%; Colorless solid; mp = 87-90°C; [α]_D²⁰ = -19.7 (*c* = 1.0, MeOH, 99% d.e.). IR (KBr): cm⁻¹ 3304 (N-H), 3035 (Ar, C-H), 2927 (CH₂), 2855 (CH₃), 1725 (OC(=O)), 1636 (NHC(=O)), 1507 (Ar, C=C), 1457 (CH₂), 1224 (C-O), 745 (Ar, C=C), 694 (Ar, C=C). ¹H NMR (399.78 MHz, TMS/CDCl₃) δ 0.87 (t, *J* = 7.1 Hz, 3H, -CH₃), 1.12 (d, *J* = 1.83 Hz, 3H, (CH₃)₂CH-), 1.14 (d, *J* = 1.83 Hz, 3H, (CH₃)₂CH-), 1.18-1.35 (m, 10H, -CH₂- \times 5), 1.43 (d, *J* = 7.1 Hz, 3H, -CH(CH₃)NHC(=O)-), 1.46-1.71 (m, 6H, -CH₂CH₂CH(O-)CH₂-), 2.09 (m, 2H, -NHC(=O)CH₂-), 4.06 (m, 1H, (CH₃)₂CH-), 4.35 (quint, *J* = 7.1 Hz, 1H, -CH(CH₃)NHC(=O)-), 4.91 (quint, *J* = 5.7 Hz, 1H, -CH₂CH(O-)CH₂-), 5.11 (s, 2H, -NHC(=O)OCH₂Ph), 5.25-5.48 (m, 2H, *i*-PrNHC(=O)-, -CHNHC(=O)O-), 7.28-7.39 (m, 5H, Ph). ¹³C NMR (100.53 MHz, TMS/CDCl₃) δ 14.1 (-CH₃), 18.8 (-CH(CH₃)NHC(=O)-), 21.3 (-NHC(=O)CH₂CH₂-), 22.6 (-CH₂CH₃), 22.8 ((CH₃)₂CH-), 25.2, 29.1, 29.4 (-CH₂-), 31.7 (-CH₂CH₂CH₃), 33.3 (-CH₂CH(O-)CH₂-), 33.9 (-CH₂CH(O-)CH₂-), 36.2 (-NHC(=O)CH₂-), 41.2 ((CH₃)₂CH-), 49.9 (-CH(CH₃)NHC(=O)-), 66.8 (-NHC(=O)OCH₂Ph), 75.2 (-CH₂CH(O-)CH₂-), 128.0, 128.1, 128.5, 136.3 (Ph), 155.4 (-NHC(=O)O-), 171.5 (*i*-PrNHC(=O)-), 172.8 (-OC(=O)CH(CH₃)-). HRMS (FD) calcd. for C₂₇H₄₄N₂O₅(M)⁺, 462.30937; found: (M)⁺, 462.30697.

2.3.4 *N*-Methyl-5-[*N*-(benzyloxy) carbonyl]-2-aminopropanoxydodecanamide (**2d**)

Data for (5*S*)-**2d**_{1st}

Yield: 0.20 g, 45%; Colorless solid; mp = 91-91°C; [α]_D²⁰ = -20.0 (*c* = 1.0, MeOH, 99% d.e.). IR (KBr): cm⁻¹ 3314 (N-H), 3063 (Ar, C-H), 2941 (CH₂), 2851 (CH₃), 1734 (OC(=O)), 1646 (NHC(=O)), 1454 (CH₂), 1215 (C-O), 752 (Ar, C=C), 697 (Ar, C=C). ¹H NMR (399.78 MHz, TMS/CDCl₃) δ 0.87 (t, *J* = 7.2 Hz, 3H, -CH₃), 1.16-1.33 (m, 10H, -CH₂- \times 5), 1.41 (d, *J* = 7.2 Hz, 3H, -CH(CH₃)NHC(=O)-), 1.53 (m, 2H, -CH₂CH(O-)CH₂-), 1.61 (m, 2H, -CH₂CH(O-)CH₂-), 1.66 (m, 2H, -NHC(=O)CH₂CH₂-), 2.16 (m, 2H, -NHC(=O)CH₂-), 2.76 (d, *J* = 4.9 Hz, 3H, CH₃NHC(=O)-), 4.29 (quint, *J* = 7.2 Hz, 1H, -CH(CH₃)NHC(=O)-), 4.95 (quint, *J* = 6.0 Hz, 1H, -CH₂CH(O-)CH₂-), 5.10 (2H, dd, *J* = 11.17, 12.32 Hz, 1H, -NHC(=O)OCH₂Ph), 5.36 (d, *J* = 7.2 Hz, 1H, -CHNHC(=O)O-), 6.01 (br s, 1H, CH₃NHC(=O)-), 7.29-7.43 (m, 5H, Ph). ¹³C NMR (100.53 MHz, TMS/CDCl₃) δ 14.0 (-CH₃), 18.2 (-CH(CH₃)NHC(=O)-), 21.7 (-NHC(=O)CH₂CH₃-), 22.6 (-CH₂CH₃), 25.2 (-CH₂-), 26.2 (CH₃NHC(=O)-), 29.1, 29.3 (-CH₂-), 31.7 (-CH₂CH₂CH₃), 33.4 (-CH₂CH(O-)CH₂-), 34.3 (-CH₂CH(O-)CH₂-), 36.0 (-NHC(=O)CH₂-), 49.9 (-CH(CH₃)NHC(=O)-), 66.9 (-NHC(=O)OCH₂Ph), 75.0 (-CH₂CH(O-)CH₂-), 127.9, 128.2, 128.5, 136.2 (Ph), 155.9 (-NHC(=O)O-), 173.1 (-OC(=O)CH(CH₃)-), 173.4 (CH₃NHC(=O)-). HRMS (FD) calcd. for C₂₅H₄₀N₂O₅(M)⁺, 434.27807; found: (M)⁺, 434.27661.

Data for (5*R*)-**2d**_{2nd}

Yield: 0.21 g, 48%; Colorless solid; mp = 58-59°C; [α]_D²⁰ = -21.3 (*c* = 1.0, MeOH, 99% d.e.). IR (KBr): cm⁻¹ 3336 (N-H), 3040 (Ar, C-H), 2924 (CH₂), 2851 (CH₃), 1737 (OC(=O)), 1653 (NHC(=O)), 1457 (CH₂), 1206 (C-O), 750 (Ar, C=C), 697 (Ar, C=C). ¹H NMR (399.78 MHz, TMS/CDCl₃) δ 0.87 (t, *J* = 7.2 Hz, 3H, -CH₃), 1.15-1.34 (m, 10H, -CH₂- \times 5), 1.43 (d, *J* = 7.2 Hz, 3H, -CH(CH₃)NHC(=O)-), 1.47-1.72 (m, 6H, -CH₂CH₂CH(O-)CH₂-), 2.14 (m, 2H, -NHC(=O)CH₂-), 2.78 (d, *J* = 4.9 Hz, 3H, CH₃NHC(=O)-), 4.34 (quint, *J* = 7.2 Hz, 1H, -CH(CH₃)NHC(=O)-), 4.91 (quint, *J* = 6.0 Hz, 1H, -CH₂CH(O-)CH₂-), 5.11 (s, 2H, -NHC(=O)OCH₂Ph), 5.36 (d, *J* = 7.2 Hz, 1H, -CHNHC(=O)O-), 5.64 (br s, 1H, CH₃NHC(=O)-), 7.28-7.42 (m, 5H, Ph). ¹³C NMR (100.53 MHz, TMS/CDCl₃) δ 14.1 (-CH₃), 18.7 (-CH(CH₃)NHC(=O)-), 21.2 (-NHC(=O)CH₂CH₂-), 22.6 (-CH₂CH₃), 25.2 (-CH₂-), 26.2 (CH₃NHC(=O)-), 29.1, 29.3 (-CH₂-), 31.7 (-CH₂CH₂CH₃), 33.3 (-CH₂CH(O-)CH₂-), 34.0 (-CH₂CH(O-)CH₂-), 35.9 (-NHC(=O)CH₂-), 49.9 (-CH(CH₃)NHC(=O)-), 66.8 (-NHC(=O)OCH₂Ph), 75.1 (-CH₂CH(O-)CH₂-), 128.0, 128.2, 128.5, 136.2 (Ph), 155.7 (-CHNHC(=O)O-), 172.7 (-OC(=O)CH(CH₃)-), 173.0 (CH₃NHC(=O)-). HRMS (FD) calcd. for C₂₅H₄₀N₂O₅(M)⁺, 434.27807; found: (M)⁺, 434.27749.

2.3.5 *N*-Benzyl-5-[*N*-(*tert*-butyloxy) carbonyl]-2-amino-propanoyloxylododecanamide (**3a**)Data for (5*S*)-**3a**_{1st}

Yield: 0.22 g, 46%; Colorless solid; mp = 62-64°C; $[\alpha]_D^{20} = 23.7$ ($c = 1.0$, MeOH, 99% d.e.). IR (KBr): cm^{-1} 3344 (N-H), 2933 (CH₂), 2855 (CH₃), 1733 (OC(=O)), 1636 (NHC(=O)), 1507 (Ar, C=C), 1457 (CH₂), 1253 (C-O), 789 (Ar, C=C), 669 (Ar, C=C). ¹H NMR (399.78 MHz, TMS/CDCl₃) δ 0.88 (t, $J = 6.4$ Hz, 3H, -CH₃), 1.15-1.30 (m, 10H, -CH₂- \times 5), 1.34 (d, $J = 7.3$ Hz, 3H, -CH(CH₃)NHC(=O)-), 1.38 (s, 9H, -OC(CH₃)₃), 1.51 (m, 2H, -CH₂CH(O)-CH₂-), 1.60 (m, 2H, -CH₂CH(O)-CH₂-), 1.69 (m, 2H, -NHC(=O)CH₂CH₂-), 2.21 (m, 2H, -NHC(=O)CH₂-), 4.13 (quint, $J = 7.3$ Hz, 1H, -CH(CH₃)NHC(=O)-), 4.41 (t, $J = 6.6$ Hz, 2H, PhCH₂NHC(=O)-), 4.91 (quint, $J = 6.0$ Hz, 1H, -CH₂CH(O)-CH₂-), 5.16 (d, $J = 7.6$ Hz, 1H, -CHNHC(=O)O-), 6.85 (br s, 1H, BnNHC(=O)-), 7.19-7.36 (m, 5H, Ph). ¹³C NMR (100.53 MHz, TMS/CDCl₃) δ 13.9 (-CH₃), 17.9 (-CH(CH₃)NHC(=O)-), 21.7 (-NHC(=O)CH₂CH₂-), 22.4 (-CH₂CH₃), 25.0 (-CH₂-), 28.1 (-OC(CH₃)₃), 29.0, 29.2 (-CH₂-), 31.6 (-CH₂CH₂CH₃), 33.1 (-CH₂CH(O)-CH₂-), 34.2 (-CH₂CH(O)-CH₂-), 35.7 (-NHC(=O)CH₂-), 43.1 (PhCH₂NHC(=O)-), 49.3 (-CH(CH₃)NHC(=O)-), 74.7 (-CH₂CH(O)-CH₂-), 79.6 (-OC(CH₃)₃), 127.0, 127.5, 128.3, 138.5 (Ph), 155.2 (-CHNHC(=O)O-), 172.9 (-OC(=O)CH(CH₃)-), 173.3 (BnNHC(=O)-). HRMS (FD) calcd. for C₂₈H₄₆N₂O₅ (M)⁺, 476.32502; found: (M)⁺, 476.32630.

Data for (5*R*)-**3a**_{2nd}

Yield: 0.23 g, 49%; Colorless solid; mp = 74-76°C; $[\alpha]_D^{20} = -23.5$ ($c = 1.0$, MeOH, 99% d.e.). IR (KBr): cm^{-1} 3344 (N-H), 2933 (CH₂), 2855 (CH₃), 1733 (OC(=O)), 1636 (NHC(=O)), 1507 (Ar, C=C), 1457 (CH₂), 1220 (C-O), 789 (Ar, C=C), 669 (Ar, C=C). ¹H NMR (399.78 MHz, TMS/CDCl₃) δ 0.88 (t, $J = 6.9$ Hz, 3H, -CH₃), 1.15-1.31 (m, 10H, -CH₂- \times 5), 1.34 (d, $J = 7.1$ Hz, 3H, -CH(CH₃)NHC(=O)-), 1.43 (s, 9H, -OC(CH₃)₃), 1.49-1.76 (m, 6H, -CH₂CH₂CH(O)-CH₂-), 2.19 (m, 2H, -NHC(=O)CH₂-), 4.22 (quint, $J = 7.1$ Hz, 1H, -CH(CH₃)NHC(=O)-), 4.41 (d, $J = 5.7$ Hz, 2H, PhCH₂NHC(=O)-), 4.90 (quint, $J = 6.0$ Hz, 1H, -CH₂CH(O)-CH₂-), 5.08 (d, $J = 6.9$ Hz, 1H, -CHNHC(=O)O-), 6.28 (br s, 1H, BnNHC(=O)-), 7.19-7.40 (m, 5H, Ph). ¹³C NMR (100.53 MHz, TMS/CDCl₃) δ 14.0 (-CH₃), 18.5 (-CH(CH₃)NHC(=O)-), 21.2 (-NHC(=O)CH₂CH₂-), 22.5 (-CH₂CH₃), 25.1 (-CH₂-), 28.2 (-OC(CH₃)₃), 29.0, 29.3 (-CH₂-), 31.6 (-CH₂CH₂CH₃), 33.2 (-CH₂CH(O)-CH₂-), 33.9 (-CH₂CH(O)-CH₂-), 35.8 (-NHC(=O)CH₂-), 43.3 (PhCH₂NHC(=O)-), 49.3 (-CH(CH₃)NHC(=O)-), 74.7 (-CH₂CH(O)-CH₂-), 79.6 (-OC(CH₃)₃), 127.3, 127.6, 128.5, 138.4 (Ph), 155.0 (-CHNHC(=O)O-), 172.4 (-OC(=O)CH(CH₃)-), 173.1 (BnNHC(=O)-). HRMS (FD) calcd. for C₂₈H₄₆N₂O₅ (M)⁺, 476.32502; found: (M)⁺, 476.32648.

2.3.6 *N*-Cyclohexyl-5-[*N*-(*tert*-butyloxy) carbonyl]-2-aminopropanoyloxylododecanamide (**3b**)Data for (5*S*)-**3b**_{1st}

Yield: 0.22 g, 46%; Colorless solid; mp = 70-72°C; $[\alpha]_D^{20} = -19.8$ ($c = 1.0$, MeOH, 99% d.e.). IR (KBr): cm^{-1} 3324 (N-H), 2929 (CH₂), 2857 (CH₃), 1748 (OC(=O)), 1661 (NHC(=O)), 1457 (CH₂), 1258 (C-O). ¹H NMR (399.78 MHz, TMS/CDCl₃) δ 0.87 (t, $J = 7.2$ Hz, 3H, -CH₃), 1.05-1.19 (m, 3H, -CH₂- \times 2), 1.19-1.31 (m, 10H, -CH₂- \times 5), 1.31-1.36 (m, 2H, -CH₂-), 1.38 (d, $J = 6.6$ Hz, 3H, -CH(CH₃)NHC(=O)-), 1.45 (s, 9H, -OC(CH₃)₃), 1.49-1.74 (m, 9H, -CH₂CH₂CH(O)-CH₂-), -CH₂- \times 2), 1.90 (m, 2H, -CH₂-), 2.14 (m, 2H, -NHC(=O)CH₂-), 3.75 (m, 1H, -CH₂CH(CH₂)NHC(=O)-), 4.24 (quint, $J = 7.2$ Hz, 1H, -CH(CH₃)NHC(=O)-), 4.92 (quint, $J = 6.0$ Hz, 1H, -CH₂CH(O)-CH₂-), 5.07 (d, $J = 7.7$ Hz, 1H, -CHNHC(=O)O-), 5.74 (d, $J = 5.7$ Hz, 1H, cHxNHC(=O)-). ¹³C NMR (100.53 MHz, TMS/CDCl₃) δ 14.0 (-CH₃), 18.4 (-CH(CH₃)NHC(=O)-), 21.7 (-NHC(=O)CH₂CH₂-), 22.6 (-CH₂CH₃), 24.9, 25.2, 25.5 (-CH₂-), 28.3 (-OC(CH₃)₃), 29.1, 29.3 (-CH₂-), 31.7 (-CH₂CH₂CH₃), 33.2 (-CH₂-), 33.2 (-CH₂CH(O)-CH₂-), 33.2 (-CH₂CH(O)-CH₂-), 36.2 (-NHC(=O)CH₂-), 48.1 (-CH(CH₃)NHC(=O)-), 49.4 (-CH₂CH(CH₂)NHC(=O)-), 75.0 (-CH₂CH(O)-CH₂-), 155.0 (-CHNHC(=O)O-), 171.8 (cHxNHC(=O)-), 173.5 (-OC(=O)CH(CH₃)-). HRMS (FD) calcd. for C₂₇H₅₀N₂O₅ (M)⁺, 468.35632; found: (M)⁺, 468.35629.

Data for (5*R*)-**3b**_{2nd}

Yield: 0.22 g, 47%; Colorless solid; mp = 43-45°C; $[\alpha]_D^{20} = -23.3$ ($c = 1.0$, MeOH, 99% d.e.). IR (KBr): cm^{-1} 3337 (N-H), 2927 (CH₂), 2856 (CH₃), 1749 (OC(=O)), 1639 (NHC(=O)), 1457 (CH₂), 1246 (C-O). ¹H NMR (399.78 MHz, TMS/CDCl₃) δ 0.88 (t, $J = 6.6$ Hz, 3H, -CH₃), 1.05-1.20 (m, 3H, -CH₂- \times 2), 1.20-1.32 (m, 10H, -CH₂- \times 5), 1.32-1.38 (m, 2H, -CH₂-), 1.39 (d, $J = 6.6$ Hz, 3H, -CH(CH₃)NHC(=O)-), 1.45 (s, 9H, -OC(CH₃)₃), 1.49-1.65 (m, 6H, -CH₂CH(O)-CH₂-), -CH₂-), 1.65-1.74 (m, 3H, -NHC(=O)CH₂CH₂-), -CH₂-), 1.90 (m, 2H, -CH(CH₃)NHC(=O)-), 2.13 (m, 2H, -NHC(=O)CH₂-), 3.75 (m, 1H, -CH₂CH(CH₂)NHC(=O)-), 4.27 (quint, $J = 6.9$ Hz, 1H, -CH(CH₃)NHC(=O)-), 4.91 (quint, $J = 5.7$ Hz, 1H, -CH₂CH(O)-CH₂-), 5.05 (d, $J = 6.59$ Hz, 1H, -CHNHC(=O)O-), 5.44 (1H, d, $J = 7.7$ Hz, cHxNHC(=O)-). ¹³C NMR (100.53 MHz, TMS/CDCl₃) δ 14.0 (-CH₃), 18.8 (-CH(CH₃)NHC(=O)-), 21.4 (-NHC(=O)CH₂CH₂-), 22.6 (-CH₂CH₃), 24.8, 25.2, 25.5 (-CH₂-), 28.3 (-OC(CH₃)₃), 29.1, 29.4 (-CH₂-), 31.7 (-CH₂CH₂CH₃), 33.2 (-CH₂-), 33.3 (-CH₂CH(O)-CH₂-), 34.0 (-CH₂CH(O)-CH₂-), 36.3 (-NHC(=O)CH₂-), 48.1 (-CH(CH₃)NHC(=O)-), 49.5 (-CH₂CH(CH₂)NHC(=O)-), 74.9 (-CH₂CH(O)-CH₂-), 155.2 (-CHNHC(=O)O-), 171.4 (cHxNHC(=O)-), 173.1 (-OC(=O)CH(CH₃)-). HRMS (FD) calcd. for C₂₇H₅₀N₂O₅ (M)⁺, 468.35632; found: (M)⁺, 468.35629.

2.3.7 *N*-iso-Propyl-5-[*N*-(*tert*-butyloxy) carbonyl]-2-aminopropanoxydodecanamide (**3c**)Data for (5*S*)-**3c**_{1st}

Yield: 0.20 g, 47%; Colorless oil; $[\alpha]_D^{20} = -23.8$ ($c = 1.0$, MeOH, 99% d.e.). IR (KBr): cm^{-1} 3306 (N-H), 2930 (CH_2), 2856 (CH_3), 1721 ($\text{OC}(=\text{O})$), 1659 ($\text{NHC}(=\text{O})$), 1455 (CH_2), 1252 (C-O). ^1H NMR (399.78 MHz, TMS/ CDCl_3) δ 0.87 (t, $J = 7.2$ Hz, 3H, $-\text{CH}_3$), 1.14 (t, $J = 6.0$ Hz, 6H, $(\text{CH}_3)_2\text{CH}-$), 1.19-1.33 (m, 10H, $-\text{CH}_2-\times 5$), 1.38 (d, $J = 7.2$ Hz, 3H, $-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 1.45 (s, 9H, $-\text{OC}(\text{CH}_3)_3$), 1.54 (m, 2H, $-\text{CH}_2\text{CH}(\text{O}-)\text{CH}_2-$), 1.61 (m, 2H, $-\text{CH}_2\text{CH}(\text{O}-)\text{CH}_2-$), 1.66 (m, 2H, $-\text{NHC}(=\text{O})\text{CH}_2\text{CH}_2-$), 2.13 (m, 2H, $-\text{NHC}(=\text{O})\text{CH}_2-$), 4.07 (d, $J = 4.8$ Hz, 1H, $(\text{CH}_3)_2\text{CH}-$), 4.24 (quint, $J = 7.2$ Hz, 1H, $-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 4.92 (quint, $J = 5.7$ Hz, 1H, $-\text{CH}_2\text{CH}(\text{O}-)\text{CH}_2-$), 5.10 (d, $J = 7.7$ Hz, 1H, $-\text{CHNHC}(=\text{O})\text{O}-$), 5.82 (br s, 1H, *i*-PrNHC(=O)-). ^{13}C NMR (100.53 MHz, TMS/ CDCl_3) δ 14.0 ($-\text{CH}_3$), 18.3 ($-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 21.6 ($-\text{NHC}(=\text{O})\text{CH}_2\text{CH}_2-$), 22.5 ($-\text{CH}_2\text{CH}_3$), 22.7 ($(\text{CH}_3)_2\text{CH}-$), 22.8 ($(\text{CH}_3)_2\text{CH}-$), 25.2 ($-\text{CH}_2-$), 28.3 ($-\text{OC}(\text{CH}_3)_3$), 29.1, 29.3 ($-\text{CH}_2-$), 31.7 ($-\text{CH}_2\text{CH}_2\text{CH}_3$), 33.2 ($-\text{CH}_2\text{CH}(\text{O}-)\text{CH}_2-$), 34.2 ($-\text{CH}_2\text{CH}(\text{O}-)\text{CH}_2-$), 36.1 ($-\text{NHC}(=\text{O})\text{CH}_2-$), 41.1 ($(\text{CH}_3)_2\text{CH}-$), 49.4 ($-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 75.0 ($-\text{CH}_2\text{CH}(\text{O}-)\text{CH}_2-$), 79.7 ($-\text{OC}(\text{CH}_3)_3$), 155.3 ($-\text{CHNHC}(=\text{O})\text{O}-$), 171.8 ($-\text{OC}(=\text{O})\text{CH}(\text{CH}_3)-$), 173.4 (*i*-PrNHC(=O)-). HRMS (FD) calcd. for $\text{C}_{24}\text{H}_{46}\text{N}_2\text{O}_5$ (M^+), 428.32502; found: (M^+), 428.32508.

Data for (5*R*)-**3c**_{2nd}

Yield: 0.20 g, 47%; Colorless oil; $[\alpha]_D^{20} = -25.0$ ($c = 1.0$, MeOH, 99% d.e.). IR (KBr): cm^{-1} 3305 (N-H), 2930 (CH_2), 2858 (CH_3), 1721 ($\text{OC}(=\text{O})$), 1656 ($\text{NHC}(=\text{O})$), 1454 (CH_2), 1212 (C-O). ^1H NMR (399.78 MHz, TMS/ CDCl_3) δ 0.88 (t, $J = 6.9$ Hz, 3H, $-\text{CH}_3$), 1.13 (d, $J = 1.718$ Hz, 3H, $(\text{CH}_3)_2\text{CH}-$), 1.15 (d, $J = 1.718$ Hz, 3H, $(\text{CH}_3)_2\text{CH}-$), 1.20-1.34 (m, 10H, $-\text{CH}_2-\times 5$), 1.39 (d, $J = 7.2$ Hz, 3H, $-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 1.45 (s, 9H, $-\text{OC}(\text{CH}_3)_3$), 1.48-1.72 (m, 6H, $-\text{CH}_2\text{CH}_2\text{CH}(\text{O}-)\text{CH}_2-$), 2.12 (m, 2H, $-\text{NHC}(=\text{O})\text{CH}_2-$), 4.06 (m, 1H, $(\text{CH}_3)_2\text{CH}-$), 4.27 (quint, $J = 7.2$ Hz, 1H, $-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 4.91 (quint, $J = 5.7$ Hz, 1H, $-\text{CH}_2\text{CH}(\text{O}-)\text{CH}_2-$), 5.07 (d, $J = 6.59$ Hz, 1H, $-\text{CHNHC}(=\text{O})\text{O}-$), 5.50 (d, $J = 6.87$ Hz, 1H, *i*-PrNHC(=O)-). ^{13}C NMR (100.53 MHz, TMS/ CDCl_3) δ 14.0 ($-\text{CH}_3$), 18.7 ($-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 21.2 ($-\text{NHC}(=\text{O})\text{CH}_2\text{CH}_2-$), 22.6 ($-\text{CH}_2\text{CH}_3$), 22.7 ($(\text{CH}_3)_2\text{CH}-$), 25.2 ($-\text{CH}_2-$), 28.3 ($-\text{OC}(\text{CH}_3)_3$), 29.1, 29.3 ($-\text{CH}_2-$), 31.7 ($-\text{CH}_2\text{CH}_2\text{CH}_3$), 33.3 ($-\text{CH}_2\text{CH}(\text{O}-)\text{CH}_2-$), 34.0 ($-\text{CH}_2\text{CH}(\text{O}-)\text{CH}_2-$), 36.2 ($-\text{NHC}(=\text{O})\text{CH}_2-$), 41.2 ($(\text{CH}_3)_2\text{CH}-$), 50.0 ($-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 74.9 ($-\text{CH}_2\text{CH}(\text{O}-)\text{CH}_2-$), 79.7 ($-\text{OC}(\text{CH}_3)_3$), 154.9 ($-\text{CHNHC}(=\text{O})\text{O}-$), 171.6 ($-\text{OC}(=\text{O})\text{CH}(\text{CH}_3)-$), 173.2 (*i*-PrNHC(=O)-). HRMS (FD) calcd. for $\text{C}_{24}\text{H}_{46}\text{N}_2\text{O}_5$ (M^+), 428.32502; found: (M^+), 428.32404.

2.3.8 *N*-Methyl-5-[*tert*-butyloxy) carbonyl]aminopropanoxydodecanamide (**3d**)Data for (5*S*)-**3d**_{1st}

Yield: 0.19 g, 47%; Colorless oil; $[\alpha]_D^{20} = -29.1$ ($c = 1.0$, MeOH, 99% d.e.). IR (KBr): cm^{-1} 3372 (N-H), 2829 (CH_2),

2856 (CH_3), 1735 ($\text{OC}(=\text{O})$), 1660 ($\text{NHC}(=\text{O})$), 1247 (C-O). ^1H NMR (399.78 MHz, TMS/ CDCl_3) δ 0.88 (t, $J = 6.9$ Hz, 3H, $-\text{CH}_3$), 1.18-1.33 (m, 10H, $-\text{CH}_2-\times 5$), 1.39 (d, $J = 7.6$ Hz, 3H, $-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 1.45 (s, 9H, $-\text{OC}(\text{CH}_3)_3$), 1.54 (m, 2H, $-\text{CH}_2\text{CH}(\text{O}-)\text{CH}_2-$), 1.61 (m, 2H, $-\text{CH}_2\text{CH}(\text{O}-)\text{CH}_2-$), 1.68 (m, 2H, $-\text{NHC}(=\text{O})\text{CH}_2\text{CH}_2-$), 2.18 (m, 2H, $-\text{NHC}(=\text{O})\text{CH}_2-$), 2.78 (d, $J = 4.8$ Hz, 3H, $\text{CH}_3\text{NHC}(=\text{O})-$), 4.20 (quint, $J = 7.3$ Hz, 1H, $-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 4.95 (quint, $J = 6.0$ Hz, 1H, $-\text{CH}_2\text{CH}(\text{O}-)\text{CH}_2-$), 5.27 (d, $J = 7.6$ Hz, 1H, $-\text{CHNHC}(=\text{O})\text{O}-$), 6.58 (br s, 1H, $\text{CH}_3\text{NHC}(=\text{O})-$).

^{13}C NMR (100.53 MHz, TMS/ CDCl_3) δ 13.9 ($-\text{CH}_3$), 17.8 ($-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 21.7 ($-\text{NHC}(=\text{O})\text{CH}_2\text{CH}_2-$), 22.4 ($-\text{CH}_2\text{CH}_3$), 25.0 ($-\text{CH}_2-$), 26.0 ($\text{CH}_3\text{NHC}(=\text{O})-$), 28.1 ($-\text{OC}(\text{CH}_3)_3$), 28.9, 29.2 ($-\text{CH}_2-$), 31.5 ($-\text{CH}_2\text{CH}_2\text{CH}_3$), 33.2 ($-\text{CH}_2\text{CH}(\text{O}-)\text{CH}_2-$), 34.2 ($-\text{CH}_2\text{CH}(\text{O}-)\text{CH}_2-$), 35.8 ($-\text{NHC}(=\text{O})\text{CH}_2-$), 49.4 ($-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 74.5 ($-\text{CH}_2\text{CH}(\text{O}-)\text{CH}_2-$), 79.6 ($-\text{OC}(\text{CH}_3)_3$), 155.4 ($-\text{CHNHC}(=\text{O})\text{O}-$), 173.2 ($-\text{OC}(=\text{O})\text{CH}(\text{CH}_3)-$), 173.6 ($\text{CH}_3\text{NHC}(=\text{O})-$). HRMS (FD) calcd. for $\text{C}_{22}\text{H}_{42}\text{N}_2\text{O}_5$ (M^+), 400.29372; found: (M^+), 400.29621.

Data for (5*R*)-**3d**_{2nd}

Yield: 0.18 g, 46%; Colorless oil; $[\alpha]_D^{20} = -29.1$ ($c = 1.0$, MeOH, 99% d.e.). IR (KBr): cm^{-1} 3305 (N-H), 2930 (CH_2), 2859 (CH_3), 1721 ($\text{OC}(=\text{O})$), 1658 ($\text{NHC}(=\text{O})$), 1453 (CH_2), 1251 (C-O). ^1H NMR (399.78 MHz, TMS/ CDCl_3) δ 0.88 (t, $J = 6.6$ Hz, 3H, $-\text{CH}_3$), 1.16-1.35 (m, 10H, $-\text{CH}_2-\times 5$), 1.39 (d, $J = 6.9$ Hz, 3H, $-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 1.44 (s, 9H, $-\text{OC}(\text{CH}_3)_3$), 1.47-1.75 (m, 6H, $-\text{CH}_2\text{CH}_2\text{CH}(\text{O}-)\text{CH}_2-$), 2.03 (m, 2H, $-\text{NHC}(=\text{O})\text{CH}_2-$), 2.79 (d, $J = 4.8$ Hz, 3H, $\text{CH}_3\text{NHC}(=\text{O})-$), 4.25 (quint, $J = 7.3$ Hz, 1H, $-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 4.92 (quint, $J = 6.0$ Hz, 1H, $-\text{CH}_2\text{CH}(\text{O}-)\text{CH}_2-$), 5.17 (d, $J = 7.8$ Hz, 1H, $-\text{CHNHC}(=\text{O})\text{O}-$), 6.05 (br s, 1H, $\text{CH}_3\text{NHC}(=\text{O})-$). ^{13}C NMR (100.53 MHz, TMS/ CDCl_3) δ 13.9 ($-\text{CH}_3$), 18.5 ($-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 21.2 ($-\text{NHC}(=\text{O})\text{CH}_2\text{CH}_2-$), 22.5 ($-\text{CH}_2\text{CH}_3$), 25.1 ($-\text{CH}_2-$), 26.1 ($\text{CH}_3\text{NHC}(=\text{O})-$), 28.2 ($-\text{OC}(\text{CH}_3)_3$), 29.0, 29.2 ($-\text{CH}_2-$), 31.6 ($-\text{CH}_2\text{CH}_2\text{CH}_3$), 33.3 ($-\text{CH}_2\text{CH}(\text{O}-)\text{CH}_2-$), 33.9 ($-\text{CH}_2\text{CH}(\text{O}-)\text{CH}_2-$), 35.8 ($-\text{NHC}(=\text{O})\text{CH}_2-$), 49.4 ($-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 74.7 ($-\text{CH}_2\text{CH}(\text{O}-)\text{CH}_2-$), 79.6 ($-\text{OC}(\text{CH}_3)_3$), 155.1 ($-\text{CHNHC}(=\text{O})\text{O}-$), 173.1 ($-\text{OC}(=\text{O})\text{CH}(\text{CH}_3)-$), 173.2 ($\text{CH}_3\text{NHC}(=\text{O})-$). HRMS (FD) calcd. for $\text{C}_{22}\text{H}_{42}\text{N}_2\text{O}_5$ (M^+), 400.29372; found: (M^+), 400.29299.

2.3.9 *N*-Benzyl-5-[*N*-(benzyloxy) carbonyl]-2-aminopropanoxydodecanamide (**6a**)Data for (5*S*)-**6a**_{1st}

Yield: 0.23 g, 48%; Colorless solid; mp = 87-88°C; $[\alpha]_D^{20} = -18.5$ ($c = 1.0$, MeOH, 99% d.e.). IR (KBr): cm^{-1} 3316 (N-H), 3030 (Ar, C-H), 2959 (CH_2), 2841 (CH_3), 1732 ($\text{OC}(=\text{O})$), 1636 ($\text{NHC}(=\text{O})$), 1470 (Ar, C=C), 1455 (CH_2), 1211 (C-O), 753 (Ar, C=C), 699 (Ar, C=C). ^1H NMR (399.78 MHz, TMS/ CDCl_3) δ 0.87 (t, $J = 6.9$ Hz, 3H, $-\text{CH}_3$), 1.15-1.34 (m, 6H, $-\text{CH}_2-\times 3$), 1.38 (d, $J = 7.6$ Hz, 3H, $-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 1.53 (m, 2H, $-\text{CH}_2\text{CH}(\text{O}-)\text{CH}_2-$), 1.63 (m, 2H, $-\text{CH}_2\text{CH}(\text{O}-)\text{CH}_2-$), 1.71 (m, 2H, $-\text{NHC}(=\text{O})$)

CH₂CH₂-), 2.22 (m, 2H, -NHC(=O)CH₂-), 4.23 (quint, *J* = 7.3 Hz, 1H, -CH(CH₃)NHC(=O)-), 4.42 (d, *J* = 5.7 Hz, 2H, PhCH₂NHC(=O)-), 4.83-5.00 (m, 3H, -CH₂CH(O-)CH₂-), -NHC(=O)OCH₂Ph), 5.29 (d, *J* = 6.9 Hz, 1H, -CHNHC(=O)O-), 6.43 (br s, 1H, BnNHC(=O)-), 7.13-7.43 (m, 10H, Ph). ¹³C NMR (100.53 MHz, TMS/CDCl₃) δ 14.0 (-CH₃), 18.6 (-CH(CH₃)NHC(=O)-), 21.3 (-NHC(=O)CH₂CH₂-), 22.5, 24.8 (-CH₂-), 31.5 (-CH₂CH₂CH₃), 33.3 (-CH₂CH(O-)CH₂-), 33.9 (-CH₂CH(O-)CH₂-), 35.9 (-NHC(=O)CH₂-), 43.5 (PhCH₂NHC(=O)-), 49.8 (-CH(CH₃)NHC(=O)-), 66.8 (-NHC(=O)OCH₂Ph), 75.0 (-CH₂CH(O-)CH₂-), 127.5, 127.8, 128.0, 128.1, 128.5, 128.7, 136.2, 138.4 (Ph), 158.7 (-CHNHC(=O)O-), 172.3 (-OC(=O)CH(CH₃)-), 172.8 (BnNHC(=O)-). HRMS (FD) calcd. for C₂₉H₄₀N₂O₅ (M)⁺, 482.27807; found: (M)⁺, 482.28028.

Data for (5*R*)-**6a**_{2nd}

Yield: 0.23 g, 47%; Colorless solid; mp = 91-93°C; [α]_D²⁰ = -18.2 (*c* = 1.0, MeOH, 99% d.e.). IR (KBr): cm⁻¹ 3313 (N-H), 3034 (Ar, C-H), 2930 (CH₂), 2859 (CH₃), 1734 (OC(=O)), 1635 (NHC(=O)), 1507 (Ar, C=C), 1457 (CH₂), 1215 (C-O), 751 (Ar, C=C), 697 (Ar, C=C). ¹H NMR (399.78 MHz, TMS/CDCl₃) δ 0.87 (t, *J* = 6.6 Hz, 3H, -CH₃), 1.13-1.33 (m, 6H, -CH₂- × 3), 1.39 (d, *J* = 7.6 Hz, 3H, -CH(CH₃)NHC(=O)-), 1.44-1.74 (m, 6H, -CH₂CH₂CH(O-)CH₂-), 2.17 (m, 2H, -NHC(=O)CH₂-), 4.31 (quint, *J* = 7.3 Hz, 1H, -CH(CH₃)NHC(=O)-), 4.42 (d, *J* = 6.0 Hz, 2H, PhCH₂NHC(=O)-), 4.91 (quint, *J* = 6.0 Hz, 1H, -CH₂CH(O-)CH₂-), 5.06 (s, 2H, -NHC(=O)OCH₂Ph), 5.29 (d, *J* = 7.3 Hz, 1H, -CHNHC(=O)O-), 5.97 (br s, 1H, BnNHC(=O)-), 7.19-7.41 (m, 10H, Ph). ¹³C NMR (100.53 MHz, TMS/CDCl₃) δ 13.9 (-CH₃), 18.1 (-CH(CH₃)NHC(=O)-), 21.8 (-NHC(=O)CH₂CH₂-), 22.4 (-CH₂CH₃), 24.8 (-CH₂-), 31.5 (-CH₂CH₂CH₃), 33.3 (-CH₂CH(O-)CH₂-), 34.3 (-CH₂CH(O-)CH₂-), 36.0 (-NHC(=O)CH₂-), 43.4 (PhCH₂NHC(=O)-), 49.9 (-CH(CH₃)NHC(=O)-), 66.8 (-NHC(=O)OCH₂Ph), 75.0 (-CH₂CH(O-)CH₂-), 127.3, 127.7, 128.0, 128.1, 128.5, 128.6, 136.0, 142.2 (Ph), 155.8 (-CHNHC(=O)O-), 172.7 (-OC(=O)CH(CH₃)-), 173.1 (BnNHC(=O)-). HRMS (FD) calcd. for C₂₉H₄₀N₂O₅ (M)⁺, 482.27807; found: (M)⁺, 482.27971.

2.3.10 *N*-Benzyl-5-[*N*-(*tert*-butyloxy)carbonyl]-2-amino-propanoylexyundecanamide (**6b**)

Data for (5*S*)-**6b**_{1st}

Yield: 0.22 g, 45%; Colorless solid; mp = 40-43°C; [α]_D²⁰ = -19.2 (*c* = 1.0, MeOH, 99% d.e.). IR (KBr): cm⁻¹ 3314 (N-H), 3033 (Ar, C-H), 2930 (CH₂), 2857 (CH₃), 1734 (OC(=O)), 1653 (NHC(=O)), 1507 (Ar, C=C), 1457 (CH₂), 1212 (C-O), 751 (Ar, C=C), 696 (Ar, C=C). ¹H NMR (399.78 MHz, TMS/CDCl₃) δ 0.87 (t, *J* = 7.2 Hz, 3H, -CH₃), 1.16-1.33 (m, 8H, -CH₂- × 4), 1.38 (d, *J* = 7.2 Hz, 3H, -CH(CH₃)NHC(=O)-), 1.53 (m, 2H, -CH₂CH(O-)CH₂-), 1.63 (m, 2H, -CH₂CH(O-)CH₂-), 1.71 (m, 2H, -NHC(=O)CH₂CH₂-), 2.22 (m, 2H, -NHC(=O)CH₂-), 4.23 (quint, *J* = 7.2 Hz, 1H, -CH(CH₃)NHC(=O)-), 4.41 (d, *J* = 5.7 Hz, 2H,

PhCH₂NHC(=O)-), 4.84-4.99 (m, 3H, -CH₂CH(O-)CH₂-), -NHC(=O)OCH₂Ph), 5.30 (d, *J* = 7.2 Hz, 1H, -CHNHC(=O)O-), 6.43 (br s, 1H, BnNHC(=O)-), 7.18-7.39 (m, 10H, Ph). ¹³C NMR (100.53 MHz, TMS/CDCl₃) δ 14.0 (-CH₃), 18.1 (-CH(CH₃)NHC(=O)-), 21.7 (-CH₂CH₃), 22.5 (-NHC(=O)CH₂CH₂-), 25.1, 29.0 (-CH₂-), 31.6 (-CH₂CH₂CH₃), 33.3 (-CH₂CH(O-)CH₂-), 34.3 (-CH₂CH(O-)CH₂-), 36.0 (-NHC(=O)CH₂-), 43.4 (PhCH₂NHC(=O)-), 49.9 (-CH(CH₃)NHC(=O)-), 66.8 (-NHC(=O)OCH₂Ph), 75.3 (-CH₂CH(O-)CH₂-), 127.3, 127.7, 127.9, 128.1, 128.4, 128.5, 136.1, 138.4 (Ph), 155.7 (-CHNHC(=O)O-), 172.7 (-OC(=O)CH(CH₃)-), 173.1 (BnNHC(=O)-). HRMS (FD) calcd. for C₃₀H₄₂N₂O₅ (M)⁺, 496.29372; found: (M)⁺, 496.29570.

Data for (5*R*)-**6b**_{2nd}

Yield: 0.23 g, 46%; Colorless solid; mp = 101-102°C; [α]_D²⁰ = -17.6 (*c* = 1.0, MeOH, 99% d.e.). IR (KBr): cm⁻¹ 3336 (N-H), 3065 (Ar, C-H), 2940 (CH₂), 2859 (CH₃), 1730 (OC(=O)), 1635 (NHC(=O)), 1496 (Ar, C=C), 1447 (CH₂), 1219 (C-O), 750 (Ar, C=C), 698 (Ar, C=C). ¹H NMR (399.78 MHz, TMS/CDCl₃) δ 0.87 (t, *J* = 7.2 Hz, 3H, -CH₃), 1.14-1.33 (m, 8H, -CH₂- × 4), 1.39 (d, *J* = 7.2 Hz, 3H, -CH(CH₃)NHC(=O)-), 1.45-1.74 (m, 6H, -CH₂CH₂CH(O-)CH₂-), 2.18 (m, 2H, -NHC(=O)CH₂-), 4.31 (quint, *J* = 7.2 Hz, 1H, -CH(CH₃)NHC(=O)-), 4.41 (dd, *J* = 2.8, 5.7 Hz, 2H, PhCH₂NHC(=O)-), 5.29 (quint, *J* = 7.2 Hz, 1H, -CH₂CH(O-)CH₂-), 5.06 (s, 2H, -NHC(=O)OCH₂Ph), 5.29 (d, *J* = 7.4 Hz, 1H, -CHNHC(=O)O-), 5.97 (br s, 1H, BnNHC(=O)-), 7.19-7.41 (m, 10H, Ph). ¹³C NMR (100.53 MHz, TMS/CDCl₃) δ 14.0 (-CH₃), 18.7 (-CH(CH₃)NHC(=O)-), 21.3 (-CH₂CH₃), 22.5, 25.1, 29.0 (-CH₂-), 31.6 (-CH₂CH₂CH₃), 33.3 (-CH₂CH(O-)CH₂-), 34.0 (-CH₂CH(O-)CH₂-), 35.9 (-NHC(=O)CH₂-), 43.5 (PhCH₂NHC(=O)-), 49.9 (-CH(CH₃)NHC(=O)-), 66.8 (-NHC(=O)OCH₂Ph), 75.1 (-CH₂CH(O-)CH₂-), 127.5, 127.8, 128.0, 128.1, 128.5, 128.7, 136.2, 138.4 (Ph), 155.6 (-CHNHC(=O)O-), 172.3 (-OC(=O)CH(CH₃)-), 172.8 (BnNHC(=O)-). HRMS (FD) calcd. for C₃₀H₄₂N₂O₅ (M)⁺, 496.29372; found: (M)⁺, 496.29670.

2.3.11 *N*-Benzyl-5-[*N*-(*tert*-butyloxy)carbonyl]-2-amino-propanoylexytridecanamide (**6c**)

Data for (5*S*)-**6c**_{1st}

Yield: 0.25 g, 47%; Colorless solid; mp = 47-49°C; [α]_D²⁰ = -18.7 (*c* = 1.0, MeOH, 99% d.e.). IR (KBr): cm⁻¹ 3313 (N-H), 3032 (Ar, C-H), 2924 (CH₂), 2852 (CH₃), 1734 (OC(=O)), 1653 (NHC(=O)), 1507 (Ar, C=C), 1457 (CH₂), 1212 (C-O), 751 (Ar, C=C), 696 (Ar, C=C). ¹H NMR (399.78 MHz, TMS/CDCl₃) δ 0.88 (t, *J* = 7.2 Hz, 3H, -CH₃), 1.16-1.33 (m, 12H, -CH₂- × 6), 1.38 (d, *J* = 7.2 Hz, 3H, -CH(CH₃)NHC(=O)-), 1.53 (m, 2H, -CH₂CH(O-)CH₂-), 1.63 (m, 2H, -CH₂CH(O-)CH₂-), 1.71 (m, 2H, -NHC(=O)CH₂CH₂-), 2.22 (m, 2H, -NHC(=O)CH₂-), 4.23 (quint, *J* = 7.2 Hz, 1H, -CH(CH₃)NHC(=O)-), 4.42 (d, *J* = 5.7 Hz, 2H, PhCH₂NHC(=O)-), 4.82-5.00 (m, 3H, -CH₂CH(O-)CH₂-), -NHC(=O)OCH₂Ph), 5.28 (d, *J* = 7.2 Hz, 1H, -CHNHC(=

O)O-), 6.40 (br s, 1H, BnNHC(=O)-), 7.17-7.38 (m, 10H, Ph). ^{13}C NMR (100.53 MHz, TMS/ CDCl_3) δ 14.0 ($-\text{CH}_3$), 18.1 ($-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 21.7 ($-\text{NHC}(=\text{O})\text{CH}_2\text{CH}_2-$), 22.6 ($-\text{CH}_2\text{CH}_3$), 25.2, 29.2, 29.4 ($-\text{CH}_2-$), 31.8 ($-\text{CH}_2\text{CH}_2\text{CH}_3$), 33.3 ($-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 34.3 ($-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 36.0 ($-\text{NHC}(=\text{O})\text{CH}_2-$), 43.4 (Ph $\text{CH}_2\text{NHC}(=\text{O})-$), 49.9 ($-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 66.8 ($-\text{NHC}(=\text{O})\text{OCH}_2\text{Ph}$), 75.1 ($-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 127.3, 127.7, 128.0, 128.1, 128.5, 128.6, 136.1, 138.6 (Ph), 155.7 ($-\text{CHNHC}(=\text{O})\text{O}-$), 172.7 ($-\text{OC}(=\text{O})\text{CH}(\text{CH}_3)-$), 173.1 (BnNHC(=O)-). HRMS(FD) calcd. for $\text{C}_{32}\text{H}_{46}\text{N}_2\text{O}_5(\text{M})^+$, 524.32502; found: (M) $^+$, 524.32552.

Data for (5*R*)-6c_{2nd}

Yield: 0.24 g, 45%; Colorless solid; mp = 92-93°C; $[\alpha]_{\text{D}}^{20}$ = -16.4 (c = 1.0, MeOH, 99% d.e.). IR (KBr): cm^{-1} 3313 (N-H), 3034 (Ar, C-H), 2920 (CH_2), 2852 (CH_3), 1733 ($\text{OC}(=\text{O})$), 1636 ($\text{NHC}(=\text{O})$), 1507 (Ar, C=C), 1456 (CH_2), 1224 (C-O), 744 (Ar, C=C), 696 (Ar, C=C). ^1H NMR (399.78 MHz, TMS/ CDCl_3) δ 0.88 (t, J = 7.2 Hz, 3H, $-\text{CH}_3$), 1.15-1.33 (m, 12H, $-\text{CH}_2-\times 6$), 1.39 (d, J = 7.2 Hz, 3H, $-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 1.45-1.74 (m, 6H, $-\text{CH}_2\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 2.18 (m, 2H, $-\text{NHC}(=\text{O})\text{CH}_2-$), 4.31 (quint, J = 7.2 Hz, 1H, $-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 4.41 (dd, J = 3.2, 5.7 Hz, 2H, Ph $\text{CH}_2\text{NHC}(=\text{O})-$), 4.91 (quint, J = 5.7 Hz, 1H, $-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 5.06 (s, 2H, $-\text{NHC}(=\text{O})\text{OCH}_2\text{Ph}$), 5.29 (d, J = 7.4 Hz, 1H, $-\text{CHNHC}(=\text{O})\text{O}-$), 5.96 (br s, 1H, BnNHC(=O)-), 7.21-7.40 (m, 10H, Ph). ^{13}C NMR (100.53 MHz, TMS/ CDCl_3) δ 14.1 ($-\text{CH}_3$), 18.7 ($-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 21.3 ($-\text{NHC}(=\text{O})\text{CH}_2\text{CH}_2-$), 22.6 ($-\text{CH}_2\text{CH}_3$), 25.2, 29.2, 29.4 ($-\text{CH}_2-$), 31.8 ($-\text{CH}_2\text{CH}_2\text{CH}_3$), 33.3 ($-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 34.0 ($-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 36.0 ($-\text{NHC}(=\text{O})\text{CH}_2-$), 43.5 ($-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 66.8 ($-\text{NHC}(=\text{O})\text{OCH}_2\text{Ph}$), 75.1 ($-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 127.5, 127.8, 128.0, 128.1, 128.5, 128.7, 136.3, 138.4 (Ph), 155.6 ($-\text{CHNHC}(=\text{O})\text{O}-$), 172.3 ($-\text{OC}(=\text{O})\text{CH}(\text{CH}_3)-$), 172.8 (BnNHC(=O)-). HRMS(FD) calcd. for $\text{C}_{32}\text{H}_{46}\text{N}_2\text{O}_5(\text{M})^+$, 524.32502; found: (M) $^+$, 524.32411.

2.3.12 *N*-Benzyl-5-[*N*-(*tert*-butyloxy) carbonyl]-2-amino-propanoyloxyltetradecanamide (6d)

Data for (5*S*)-6d_{1st}

Yield: 0.25 g, 46%; Colorless solid; mp = 64-66°C; $[\alpha]_{\text{D}}^{20}$ = -17.6 (c = 1.0, MeOH, 99% d.e.). IR (KBr): cm^{-1} 3321 (N-H), 3031 (Ar, C-H), 2919 (CH_2), 2849 (CH_3), 1729 ($\text{OC}(=\text{O})$), 1646 ($\text{NHC}(=\text{O})$), 1507 (Ar, C=C), 1456 (CH_2), 1222 (C-O), 748 (Ar, C=C), 696 (Ar, C=C). ^1H NMR (399.78 MHz, TMS/ CDCl_3) δ 0.88 (t, J = 7.1 Hz, 3H, $-\text{CH}_3$), 1.16-1.33 (m, 14H, $-\text{CH}_2-\times 7$), 1.38 (d, J = 7.1 Hz, 3H, $-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 1.53 (m, 2H, $-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 1.62 (m, 2H, $-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 1.71 (m, 2H, $-\text{NHC}(=\text{O})\text{CH}_2\text{CH}_2-$), 2.21 (m, 2H, $-\text{NHC}(=\text{O})\text{CH}_2-$), 4.22 (quint, J = 7.2 Hz, 1H, $-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 4.41 (d, J = 5.7 Hz, 2H, Ph $\text{CH}_2\text{NHC}(=\text{O})-$), 4.79-5.01 (m, 3H, $-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$, $-\text{NHC}(=\text{O})\text{OCH}_2\text{Ph}$), 5.32 (d, J = 7.6 Hz, 1H, $-\text{CHNHC}(=\text{O})\text{O}-$), 6.48 (br s, 1H, BnNHC(=O)-), 7.15-7.41 (m, 10H,

Ph). ^{13}C NMR (100.53 MHz, TMS/ CDCl_3) δ 14.4 ($-\text{CH}_3$), 18.0 ($-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 21.7 ($-\text{NHC}(=\text{O})\text{CH}_2\text{CH}_2-$), 22.6 ($-\text{CH}_2\text{CH}_3$), 25.2, 29.2, 29.3, 29.4 ($-\text{CH}_2-$), 31.8 ($-\text{CH}_2\text{CH}_2\text{CH}_3$), 33.2 ($-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 34.3 ($-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 36.0 ($-\text{NHC}(=\text{O})\text{CH}_2-$), 43.4 (Ph $\text{CH}_2\text{NHC}(=\text{O})-$), 49.9 ($-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 66.8 ($-\text{NHC}(=\text{O})\text{OCH}_2\text{Ph}$), 75.0 ($-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 127.2, 127.7, 127.9, 128.1, 128.4, 128.5, 136.1, 138.6 (Ph), 155.8 ($-\text{CHNHC}(=\text{O})\text{O}-$), 172.7 ($-\text{OC}(=\text{O})\text{CH}(\text{CH}_3)-$), 173.1 (BnNHC(=O)-). HRMS(FD) calcd. for $\text{C}_{33}\text{H}_{48}\text{N}_2\text{O}_5(\text{M})^+$, 538.34067; found: (M) $^+$, 538.34215.

Data for (5*R*)-6d_{2nd}

Yield: 0.25 g, 47%; Colorless solid; mp = 88-92°C; $[\alpha]_{\text{D}}^{20}$ = -15.3 (c = 1.0, MeOH, 99% d.e.). IR (KBr): cm^{-1} 3313 (N-H), 3031 (Ar, C-H), 2916 (CH_2), 2850 (CH_3), 1733 ($\text{OC}(=\text{O})$), 1636 ($\text{NHC}(=\text{O})$), 1507 (Ar, C=C), 1457 (CH_2), 1224 (C-O), 747 (Ar, C=C), 698 (Ar, C=C). ^1H NMR (399.78 MHz, TMS/ CDCl_3) δ 0.88 (t, J = 6.9 Hz, 3H, $-\text{CH}_3$), 1.14-1.33 (m, 14H, $-\text{CH}_2-\times 7$), 1.39 (d, J = 7.3 Hz, 3H, $-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 1.43-1.75 (m, 6H, $-\text{CH}_2\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 2.18 (m, 2H, $-\text{NHC}(=\text{O})\text{CH}_2-$), 4.31 (quint, J = 7.6 Hz, 1H, $-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 4.41 (d, J = 5.7 Hz, 2H, Ph $\text{CH}_2\text{NHC}(=\text{O})-$), 4.91 (quint, J = 5.7 Hz, 1H, $-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 5.06 (s, 2H, $-\text{NHC}(=\text{O})\text{OCH}_2\text{Ph}$), 5.30 (d, J = 7.6 Hz, 1H, $-\text{CHNHC}(=\text{O})\text{O}-$), 6.00 (br s, 1H, BnNHC(=O)-), 7.18-7.41 (m, 10H, Ph). ^{13}C NMR (100.53 MHz, TMS/ CDCl_3) δ 14.4 ($-\text{CH}_3$), 18.7 ($-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 21.3 ($-\text{NHC}(=\text{O})\text{CH}_2\text{CH}_2-$), 22.6 ($-\text{CH}_2\text{CH}_3$), 25.2, 29.3, 29.3, 29.4, 29.5 ($-\text{CH}_2-$), 31.8 ($-\text{CH}_2\text{CH}_2\text{CH}_3$), 33.3 ($-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 34.0 ($-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 35.9 ($-\text{NHC}(=\text{O})\text{CH}_2-$), 43.5 (Ph $\text{CH}_2\text{NHC}(=\text{O})-$), 49.9 ($-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 66.8 ($-\text{NHC}(=\text{O})\text{OCH}_2\text{Ph}$), 75.1 ($-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 127.5, 127.8, 128.0, 128.1, 128.5, 128.7, 136.1, 138.4 (Ph), 155.6 ($-\text{CHNHC}(=\text{O})\text{O}-$), 172.3 ($-\text{OC}(=\text{O})\text{CH}(\text{CH}_3)-$), 172.8 (BnNHC(=O)-). HRMS(FD) calcd. for $\text{C}_{33}\text{H}_{48}\text{N}_2\text{O}_5(\text{M})^+$, 538.34067; found: (M) $^+$, 538.34287.

2.3.13 *N*-Benzyl-5-[*N*-(*tert*-butyloxy) carbonyl]-2-amino-propanoyloxylhexadecanamide (6e)

Data for (5*S*)-6e_{1st}

Yield: 0.27 g, 47%; Colorless solid; mp = 61-63°C; $[\alpha]_{\text{D}}^{20}$ = -16.9 (c = 1.0, MeOH, 99% d.e.). IR (KBr): cm^{-1} 3288 (N-H), 3034 (Ar, C-H), 2917 (CH_2), 2848 (CH_3), 1742 ($\text{OC}(=\text{O})$), 1654 ($\text{NHC}(=\text{O})$), 1507 (Ar, C=C), 1457 (CH_2), 1211 (C-O), 741 (Ar, C=C), 695 (Ar, C=C). ^1H NMR (399.78 MHz, TMS/ CDCl_3) δ 0.88 (t, J = 7.1 Hz, 3H, $-\text{CH}_3$), 1.14-1.34 (m, 18H, $-\text{CH}_2-\times 8$), 1.38 (d, J = 7.1 Hz, 3H, $-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 1.53 (m, 2H, $-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 1.63 (m, 2H, $-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$), 1.71 (m, 2H, $-\text{NHC}(=\text{O})\text{CH}_2\text{CH}_2-$), 2.22 (m, 2H, $-\text{NHC}(=\text{O})\text{CH}_2-$), 4.23 (quint, J = 7.3 Hz, 1H, $-\text{CH}(\text{CH}_3)\text{NHC}(=\text{O})-$), 4.42 (d, J = 5.7 Hz, 2H, Ph $\text{CH}_2\text{NHC}(=\text{O})-$), 4.80-5.01 (m, 3H, $-\text{CH}_2\text{CH}(\text{O})\text{CH}_2-$, $-\text{NHC}(=\text{O})\text{OCH}_2\text{Ph}$), 5.27 (d, J = 7.6 Hz, 1H, $-\text{CHNHC}(=\text{O})\text{O}-$), 6.40 (br s, 1H, BnNHC(=O)-), 7.11-7.41 (m, 10H, Ph). ^{13}C NMR (100.53 MHz, TMS/ CDCl_3) δ 14.1 ($-\text{CH}_3$), 18.1

(-CH(CH₃)NHC(=O)-), 21.7(-NHC(=O)CH₂CH₂-), 22.7(-CH₂CH₃), 25.2, 29.3, 29.4, 29.5, 29.5, 29.6(-CH₂-), 31.9(-CH₂CH₂CH₃), 33.3(-CH₂CH(O-)CH₂-), 34.3(-CH₂CH(O)CH₂-), 36.0(-NHC(=O)CH₂-), 43.4(PhCH₂NHC(=O)-), 49.9(-CH(CH₃)NHC(=O)-), 66.9(-NHC(=O)OCH₂Ph), 75.1(-CH₂CH(O-)CH₂-), 127.3, 127.7, 128.0, 128.1, 128.5, 128.6, 135.1, 138.6(Ph), 155.8(-CHNHC(=O)O-), 172.7(-OC(=O)CH(CH₃)-), 173.1(BnNHC(=O)-). HRMS(FD) calcd. for C₃₅H₅₂N₂O₅(M)⁺, 566.37197; found: (M)⁺, 566.37451.

Data for (5*R*)-6e_{2nd}

Yield: 0.27 g, 47%; Colorless solid; mp = 51–53°C; [α]_D²⁰ = -15.0 (*c* = 1.0, MeOH, 99% d.e.). IR(KBr): cm⁻¹ 3308(N-H), 3034(Ar, C-H), 2921(CH₂), 2852(CH₃), 1734(OC(=O)), 1647(NHC(=O)), 1507(Ar, C=C), 1457(CH₂), 1211(C-O), 749(Ar, C=C), 696(Ar, C=C). ¹H NMR(399.78 MHz, TMS/CDCl₃) δ 0.88(t, *J* = 7.1 Hz, 3H, -CH₃), 1.15–1.33(m, 18H, -CH₂- × 8), 1.38(d, *J* = 7.3 Hz, 3H, -CH(CH₃)NHC(=O)-), 1.44–1.75(m, 6H, -CH₂CH₂CH(O)CH₂-), 2.18(m, 2H, -NHC(=O)CH₂-), 4.31(quint, *J* = 7.3 Hz, 1H, -CH(CH₃)NHC(=O)-), 4.41(t, *J* = 5.7 Hz, 2H, PhCH₂NHC(=O)-), 4.91(quint, *J* = 5.7 Hz, 1H, -CH₂CH(O-)CH₂-), 5.06(s, 2H, -NHC(=O)OCH₂Ph), 5.31(d, *J* = 7.8 Hz, 1H, -CHNHC(=O)O-), 6.01(br s, 1H, BnNHC(=O)-), 7.17–7.44(m, 10H, Ph). ¹³C NMR(100.53 MHz, TMS/CDCl₃) δ 14.1(-CH₃), 18.6(-CH(CH₃)NHC(=O)-), 21.3(-NHC(=O)CH₂CH₂-), 22.6(-CH₂CH₃), 25.2, 29.3, 29.3, 29.4, 29.5, 29.6, 29.6(-CH₂-), 31.9(-CH₂CH₂CH₃), 33.3(-CH₂CH(O-)CH₂-), 34.0(-CH₂CH(O-)CH₂-), 35.9(-NHC(=O)CH₂-), 43.5(PhCH₂NHC(=O)-), 49.8(-CH(CH₃)NHC(=O)-), 66.8(-NHC(=O)OCH₂Ph), 75.1(-CH₂CH(O-)CH₂-), 127.4, 127.8, 128.0, 128.1, 128.5, 128.6, 136.2, 138.4(Ph), 155.6(-CHNHC(=O)O-), 172.3(-OC(=O)CH(CH₃)-), 172.8(BnNHC(=O)-). HRMS(FD) calcd. for C₃₅H₅₂N₂O₅(M)⁺, 566.37197; found: (M)⁺, 566.37353.

2.4 General procedure for lactonization of 2, 3, and 6

Lactonization of 2, 3, and 6 was performed by hydrolysis under alkaline conditions and subsequent methyl esterification in 10% H₂SO₄/MeOH, and intraesterification under acidic conditions²⁷.

2.4.1 δ-Dodecalactone (4)

Yield: 0.07 g, 71% [(*S*)-4], 0.07 g, 73% [(*R*)-4]; Colorless oil; R_f = 0.85 (eluent: *n*-hexane-AcOEt, 1:1, *v/v*). Enantiomeric excess determined by GC on a CycloSil-B (30m × 0.25 mm i.d. × 0.25 μm film thickness) column, temperature: 130°C (isothermal), flow rate: 2.0 mL/min, *t_R* = 73.193 min, *t_S* = 74.375 min; [α]_D²⁰ = -45.2 [*c* = 0.2, MeOH, (*S*)-4 with 99% e.e., lit [α]_D²⁵ = -42.4 (*c* = 1.06, MeOH, 92% e.e.)]²⁸, [α]_D²⁰ = +43.2 [*c* = 0.2, MeOH, (*R*)-4 with 99% e.e., lit [α]_D²⁵ = +42.6 (*c* = 1.10, MeOH, 93% e.e.)]²⁸]. IR (NaCl): cm⁻¹ 2953(CH₃), 2927(CH₂), 2872(CH₃), 2857(CH₂), 1738(OC(=O)), 1240(C-O). ¹H NMR(399.78 MHz, TMS/CDCl₃) δ 0.88(t, *J* = 6.8 Hz, 3H, -CH₃), 1.22–1.40(m, 8H, -CH₂- × 4),

1.42–1.62(m, 4H, -CH₂- × 2), 1.68(m, 1H, -CH₂CH(CH₂-)OC(=O)-), 1.78–1.96(3H, m, -CH₂CH₂H(CH₂-)OC(=O)-), 2.38–2.62(m, 2H, -OC(=O)CH₂-), 4.28(m, 1H, -CH₂CH(CH₂-)OC(=O)-). ¹³C NMR(100.53 MHz, TMS/CDCl₃) δ 14.1(-CH₃), 18.5(-CH₂CH₂CH(CH₂-)OC(=O)-), 22.6, 24.9(-CH₂-), 27.8(-CH₂CH₂CH₃), 29.2(-CH₂CH₃), 29.4(-CH₂-), 29.5(-CH₂CH(CH₂-)OC(=O)-), 31.8(-CH₂CH(CH₂-)OC(=O)-), 35.9(-CH₂C(=O)O-), 80.6(-CH₂CH(CH₂-)OC(=O)-), 172.0(-C(=O)O-). HRMS(FI) calcd. for C₁₂H₂₁O₂(M)⁺, 198.16198; found: (M)⁺, 198.16121.

2.4.2 δ-Decalactone (7a)

Yield: 0.06 g, 75% [(*S*)-7a], 0.06 g, 73% [(*R*)-7a]; Colorless oil; R_f = 0.80 (eluent: *n*-hexane-AcOEt, 1:1, *v/v*). Enantiomeric excess determined by GC on a CycloSil-B (30m × 0.25 mm i.d. × 0.25 μm film thickness) column, temperature: 110°C (isothermal), flow rate: 2.0 mL/min, *t_R* = 69.773 min, *t_S* = 70.953 min; [α]_D²⁰ = -60.0 [*c* = 0.2, MeOH, (*S*)-7a with 99% e.e., lit [α]_D²⁰ = -60.2 (*c* = 1.58, >98% e.e.)]²⁹, [α]_D²⁰ = +60.1 [*c* = 0.2, MeOH, (*R*)-7a with 99% e.e., lit [α]_D²⁰ = +60.2 (*c* = 1.74, THF, >98% e.e.)]³⁰]. IR (NaCl): cm⁻¹ 2954(CH₃), 2933(CH₂), 2872(CH₃), 2861(CH₂), 1736(OC(=O)), 1244(C-O). ¹H NMR(399.78 MHz, TMS/CDCl₃) δ 0.89(t, *J* = 6.7 Hz, 3H, -CH₃), 1.24–1.43(m, 4H, -CH₂CH₂CH₃), 1.44–1.62(m, 4H, -CH₂- × 2), 1.70(m, 1H, -CH₂CH(CH₂-)OC(=O)-), 1.80–1.95(m, 2H, -CH₂CH₂CH(CH₂-)OC(=O)-), 2.40–2.62(m, 2H, -CH₂C(=O)O-), 4.27(1H, m, -CH₂CH(CH₂-)OC(=O)-). ¹³C NMR(100.53 MHz, TMS/CDCl₃) δ 14.0(-CH₃), 18.5(-CH₂CH₂CH(CH₂-)OC(=O)-), 22.5(-CH₂CH₂CH₃), 24.6(-CH₂CH₃), 27.8(-CH₂-), 29.5(-CH₂CH(CH₂-)OC(=O)-), 31.7(-CH₂CH(CH₂-)OC(=O)-), 35.8(-CH₂C(=O)O-), 80.6(-CH₂CH(CH₂-)OC(=O)-), 172.0(-C(=O)O-). HRMS(FI) calcd. for C₁₀H₁₇O₂(M)⁺, 170.13068; found: (M)⁺, 170.12893.

2.4.3 δ-Undecalactone (7b)

Yield: 0.06 g, 70% [(*S*)-7b], 0.07 g, 71% [(*R*)-7b]; Colorless oil; R_f = 0.82 (eluent: *n*-hexane-AcOEt, 1:1, *v/v*). Enantiomeric excess determined by GC on a CycloSil-B (30m × 0.25 mm i.d. × 0.25 μm film thickness) column, temperature: 120°C (isothermal), flow rate: 2.0 mL/min, *t_R* = 73.098 min, *t_S* = 74.44 min; [α]_D²⁰ = -44.1 [*c* = 0.2, MeOH, (*S*)-7a with 99% e.e., lit [α]_D²⁵ = -44.8 (*c* = 1.05, MeOH, 89% e.e.)]²⁸, [α]_D²⁰ = +45.5 [*c* = 0.2, MeOH, (*R*)-7a with 99% e.e., lit [α]_D²⁵ = +44.9 (*c* = 1.02, MeOH, 89% e.e.)]²⁸]. IR (NaCl): cm⁻¹ 2953(CH₃), 2930(CH₂), 2871(CH₃), 2859(CH₂), 1735(OC(=O)), 1241(C-O). ¹H NMR(399.78 MHz, TMS/CDCl₃) δ 0.88(t, *J* = 7.2 Hz, 3H, -CH₃), 1.26–1.40(m, 6H, -CH₂- × 3), 1.46–1.62(m, 4H, -CH₂- × 2), 1.71(m, 1H, -CH₂CH(CH₂-)OC(=O)-), 1.80–1.98(m, 3H, -CH₂CH₂CH(CH₂-)OC(=O)-), 2.40–2.62(m, 2H, -CH₂C(=O)O-), 2.48(1H, m, -CH₂CH(CH₂-)OC(=O)-). ¹³C NMR(100.53 MHz, TMS/CDCl₃) δ 14.0(-CH₃), 22.6(-CH₂CH₂CH(CH₂-)OC(=O)-), 25.2(-CH₂-), 28.0(-CH₂CH₂CH₃), 28.8(-CH₂CH₃), 29.3(-CH₂-), 31.7(-CH₂CH(CH₂-)OC(=O)-), 35.6(-CH₂C(=O)O-), 81.0(-CH₂CH(CH₂-)OC(=O)-), 177.2(-C(=O)

O-). HRMS (FI) calcd. for $C_{11}H_{19}O_2(M)^+$, 184.14633; found: $(M)^+$, 184.14614.

2.4.4 δ -tridecalactone (**7c**)

Yield: 0.08 g, 76% [(*S*)-**7c**], 0.08 g, 72% [(*R*)-**7c**]; Colorless oil; $R_f = 0.87$ (eluent: *n*-hexane-AcOEt, 1:1, *v/v*). Enantiomeric excess determined by GC on a CycloSil-B (30 m \times 0.25 mm i.d. \times 0.25 μ m film thickness) column, temperature: 130°C (isothermal), flow rate: 2.0 mL/min, $t_R = 124.715$ min, $t_S = 126.942$ min; $[\alpha]_D^{20} = -35.4$ [$c = 0.2$, MeOH, (*S*)-**7c** with 99% e.e., lit $[\alpha]_D = -35.0$ ($c = 1.38$, $CHCl_3$, >98% e.e.)]³¹, $[\alpha]_D^{20} = +38.0$ [$c = 0.2$, MeOH, (*R*)-**7c** with 99% e.e., lit $[\alpha]_D = +45.2$ ($c = 1.58$, THF, >98% e.e.)]³⁰. IR (NaCl): cm^{-1} 2953 (CH_3), 2926 (CH_2), 2872 (CH_3), 2855 (CH_2), 1734 ($OC(=O)$), 1241 (C-O). 1H NMR (399.78 MHz, TMS/ $CDCl_3$) δ 0.88 (t, $J = 7.0$ Hz, 3H, $-CH_3$), 1.22-1.34 (m, 10H, $-CH_2 \times 5$), 1.42-1.62 (m, 4H, $-CH_2 \times 2$), 1.68 (m, 1H, $-CH_2CH(CH_2)OC(=O)-$), 1.79-1.94 (m, 3H, $-CH_2CH_2CH(CH_2)OC(=O)-$), 2.40-2.62 (m, 2H, $-CH_2C(=O)O-$), 2.48 (m, 1H, $-CH_2CH(CH_2)OC(=O)-$). ^{13}C NMR (100.53 MHz, TMS/ $CDCl_3$) δ 14.1 ($-CH_3$), 18.5 ($-CH_2CH_2CH(CH_2)OC(=O)-$), 22.6, 24.9, 27.8 ($-CH_2-$), 29.2 ($-CH_2CH_2CH_3$), 29.3 ($-CH_2CH_3$), 29.4 ($-CH_2-$), 29.5 ($-CH_2CH(CH_2)OC(=O)-$), 31.8 ($-CH_2CH(CH_2)OC(=O)-$), 35.8 ($-CH_2C(=O)O-$), 80.6 ($-CH_2CH(CH_2)OC(=O)-$), 172.0 ($-C(=O)O-$). HRMS (FI) calcd. for $C_{13}H_{23}O_2(M)^+$, 212.17763; found: $(M)^+$, 212.17757.

2.4.5 δ -tetradecalactone (**7d**)

Yield: 0.08 g, 72% [(*S*)-**7d**], 0.09 g, 76% [(*R*)-**7d**]; Colorless oil; $R_f = 0.88$ (eluent: *n*-hexane-AcOEt, 1:1, *v/v*). Enantiomeric excess determined by GC on a CycloSil-B (30 m \times 0.25 mm i.d. \times 0.25 μ m film thickness) column, temperature: 140°C (isothermal), flow rate: 2.0 mL/min, $t_R = 118.837$ min, $t_S = 120.807$ min; $[\alpha]_D^{20} = -40.8$ [$c = 1.0$, MeOH, (*S*)-**7d** with 99% e.e.], $[\alpha]_D^{20} = +40.2$ [$c = 1.0$, MeOH, (*R*)-**7d** with 99% e.e.]. IR (NaCl): cm^{-1} 2954 (CH_3), 2925 (CH_2), 2870 (CH_3), 2855 (CH_2), 1734 ($OC(=O)$), 1248 (C-O). 1H NMR (399.78 MHz, TMS/ $CDCl_3$) δ 0.88 (t, $J = 6.8$ Hz, 3H, $-CH_3$), 1.22-1.34 (m, 12H, $-CH_2 \times 6$), 1.45-1.62 (m, 4H, $-CH_2 \times 2$), 1.70 (m, 1H, $-CH_2CH(CH_2)OC(=O)-$), 1.77-1.96 (m, 3H, $-CH_2CH_2CH(CH_2)OC(=O)-$), 2.38-2.62 (m, 2H, $-CH_2C(=O)O-$), 4.28 (1H, m, $-CH_2CH(CH_2)OC(=O)-$).

^{13}C NMR (100.53 MHz, TMS/ $CDCl_3$) δ 14.1 ($-CH_3$), 18.5 ($-CH_2CH_2CH(CH_2)OC(=O)-$), 22.7, 24.9, 27.8, 29.3 ($-CH_2-$), 29.4 ($-CH_2CH_2CH_3$), 29.5 ($-CH_2CH_3$), 29.5 ($-CH_2-$), 31.9 ($-CH_2CH(CH_2)OC(=O)-$), 35.9 ($-CH_2CH(CH_2)OC(=O)-$), 80.6 ($-CH_2CH(CH_2)OC(=O)-$), 172.0 ($-C(=O)O-$). HRMS (FI) calcd. for $C_{14}H_{25}O_2(M)^+$, 226.19328; found: $(M)^+$, 226.19376.

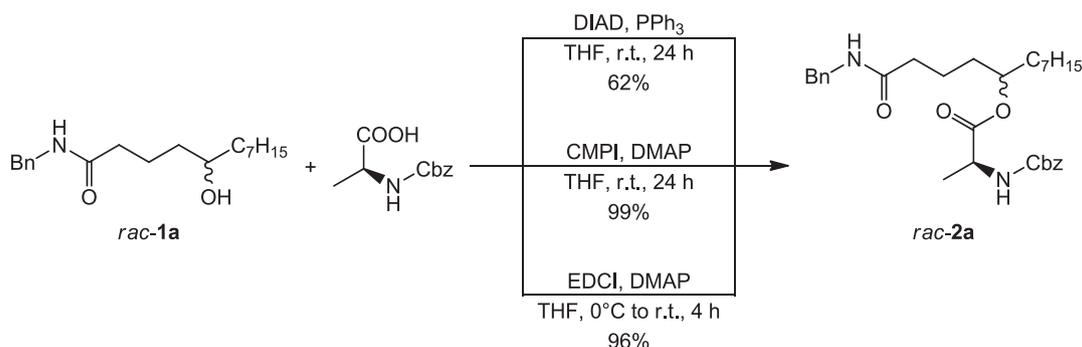
2.4.6 δ -Hexadecalactone (**7e**)

Yield: 0.10 g, 77% [(*S*)-**7e**], 0.10 g, 75% [(*R*)-**7e**]; Colorless solid; mp = 33-34°C; $R_f = 0.90$ (eluent: *n*-hexane-AcOEt, 1:1, *v/v*). Enantiomeric excess determined by GC on a CycloSil-B (30 m \times 0.25 mm i.d. \times 0.25 μ m film thickness) column, temperature: 160°C (isothermal), flow rate: 2.0 mL/min, $t_R = 101.303$ min, $t_S = 102.223$ min; $[\alpha]_D^{20} = +42.1$ [$c = 1.0$, THF, (*S*)-**7e** with 99% e.e., lit $[\alpha]_D^{25} = -40.2$ ($c = 1.66$, THF, >99% e.e.)]³², $[\alpha]_D^{20} = +42.0$ [$c = 1.0$, THF, (*R*)-**7e** with 99% e.e., lit $[\alpha]_D^{21.5} = +40.2$ ($c = 1.76$, THF, >99% e.e.)]³². IR (KBr): cm^{-1} 2927 (CH_3), 2848 (CH_3), 1727 ($OC(=O)$), 1242 (C-O). 1H NMR (500 MHz, $CDCl_3$): δ 0.88 (t, $J = 6.9$ Hz, 3H, $-CH_2CH_3$), 1.26-1.40 (m, 18H, $-CH_2 \times 9$), 1.44-1.62 (m, 2H, $-CH_2CHCH_2CH_2-$), 1.64-1.75, 1.78-1.97 (m, 4H, $-C(=O)CH_2CH_2CH_2CH-$), 2.39-2.49, 2.54-2.63 (m, 2H, $C(=O)CH_2CH_2-$), 4.24-4.31 (m, 1H, $-CH_2CHCH_2-$). ^{13}C NMR (126 MHz, $CDCl_3$): δ 14.1 ($-CH_2CH_3$), 18.5, 22.6, 24.9, 27.8, 29.3, 29.4, 29.5, 29.6, 31.9 ($-CH_2-$), 35.8 ($-CH_2CH(CH_2)OC(=O)-$), 80.6 ($-CH_2CH(CH_2)OC(=O)-$), 171.9 ($-OC(=O)-$). HRMS (FD) calcd. for $C_{16}H_{32}O_2(M)$, 254.22458; found (M), 254.22240.

3 Results and discussion

3.1 Esterification of *rac*-**1a** by various methods

L-Alanine was selected as a resolving agent because optically active carboxylic acids are readily available at relatively low cost. We also selected Cbz-L-alanine, which is protected by a benzyloxyl carbonyl group at an amino group, in consideration of the crystallinity of the diastereomeric esters (*N*-benzyl-5-[(*N*-(benzyloxy)carbonyl]-2-aminopropanoyloxy)dodecanamide (*rac*-**2a**) produced. Esterification of Cbz-L-alanine for *rac*-**1a** was examined with



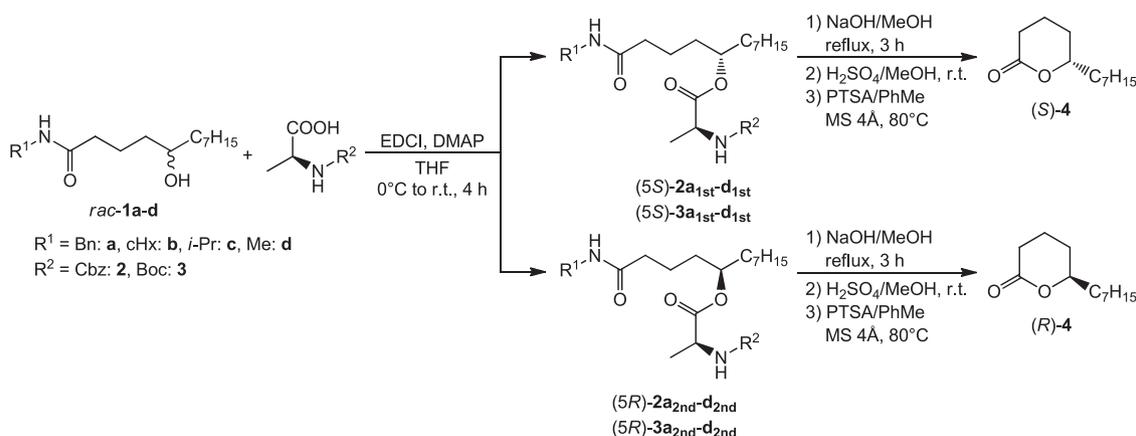
Scheme 1 Various esterification methods.

various methods (Scheme 1). First, Fischer esterification was performed. A toluene solution of racemic *N*-benzyl-5-hydroxydodecanamide (*rac*-1a) was stirred with *p*-TsOH as an acid catalyst and MS 4Å at 80°C for two hours. *Rac*-2a was not observed, and all *rac*-1a was converted into δ -dodecalactone (4). Therefore, the reaction was performed at room temperature to reduce the reactivity, but *rac*-4 was produced instead of *rac*-2a. The production of 4 was confirmed, even when the solution of *rac*-1a was stirred with two equal amounts of Cbz-L-alanine at room temperature. It was assumed that hydrolysis of the amide bond proceeded only by stirring under acidic conditions to give hydroxyl carboxylic acid, and 4 was produced by intramolecular esterification. These results indicated that other esterification methods under neutral or basic conditions were required. The Mitsunobu reaction was attempted to esterify *rac*-1a under weakly basic to neutral conditions^{33–35}. This method gave *rac*-2a with a 62% yield. However, the production of 4 was also observed. It was assumed that addition of two equal amounts of Cbz-L-alanine to *rac*-1a acidified the reaction conditions, and this caused the hydrolysis of *rac*-1a, which progressed to *rac*-2a, and the intramolecular esterification proceeded to give 4. Therefore, in order to carry out esterification under basic conditions, two condensation agents such as 2-chloro-1-methylpyridinium iodide (CMPI)^{36–38} and 1-ethyl-3-(3-dimethylamino-propyl) carbodiimide (EDCI)^{39–41} was used. When CMPI was used as a condensation agent, *rac*-2a was obtained with 99% yield in a reaction time of 24 hours. In contrast, esterification using EDCI as a condensation agent gave *rac*-2a with 96% yield in four hours. Generally, the reactivity in esterification with carbodiimides as a condensation agent is improved by adding a catalytic amount of DMAP. In this case, DMAP in stoichiometric amounts was added in order to perform the esterification under basic conditions. There was no great difference in the yield of *rac*-2a between the two condensation agents. However, esterification with EDCI was faster than that of CMPI. Therefore,

esterification with EDCI was found to be the optimum condition for the preparation of diastereomeric esters.

3.2 Comparison of R¹ group and resolving agents

For separation of each diastereomer of *rac*-2a, TLC was performed with various eluents. When an eluent with the ratio of toluene/AcOEt = 2/1 was used for TLC analysis of *rac*-2a, two spots was observed (*R_f* values = 0.49 and 0.40). These two compounds could be easily separated by silica gel column chromatography. These two compounds were confirmed to be related to diastereomers by COSY and HMQC, HMBC NMR spectra. Therefore, these compounds are referred to as **2a_{1st}** with lower polarity and **2a_{2nd}** with higher polarity. Both diastereomeric excesses showed 99% d.e. Absolute configurations of **2a** were determined by comparison with the corresponding **4** in the literature data. It was clarified that **2a_{1st}** and **2a_{2nd}** had 5*S* and 5*R* configurations, respectively. In addition, the enantiomeric excesses of **2a_{1st}** and **2a_{2nd}** were 98% and 99% determined by the corresponding **4**. These values were lower than diastereomeric excesses. It was seemed that racemization was not occurred in lactonization process. Sensitivity of GC was higher than that of NMR. Therefore, almost all enantiomeric excesses showed somewhat low values compared with diastereomeric excesses. In the optical resolution by a diastereomeric method, separation by recrystallization utilizing the different solubilities in the solvent of each diastereomer is common. **2a_{2nd}** and **2a_{1st}** were a colorless solid together. No great difference in between the solubility of diastereomers in various solvents was confirmed. In order to confirm the effect of the R¹ group, diastereomeric esters from *rac*-1 possessing *c*Hx, *i*-Pr, and Me groups were prepared (Scheme 2). The *R_f* values and eluent that produced the biggest difference in *R_f* values between each diastereomer in TLC analysis of **2** are shown in Table 1. Regardless of the differences in the R¹ groups, there was no great difference in diastereomeric excesses of all diastereomers with more than 98% d.e. However, **2a** showed the



Scheme 2 Esterification of *rac*-1a-d using Cbz-alanine and Boc-alanine as resolving agent.

Table 1 Effect R¹ group on R_f value using Cbz-alanine as resolving agent.

Entry	R ¹	Product	R _f value ¹	Yield [%]	Diastereomeric excess [% d.e.] ²	Config. ³	Appearance	Enantiomeric excess [% e.e.] ⁴ of 4
1	Bn	2a _{1st}	0.49	47	99	5 <i>S</i>	Solid	99
		2a _{2nd}	0.40	48	99	5 <i>R</i>		98
2	cHx	2b _{1st}	0.52	48	99	5 <i>S</i>		97
		2b _{2nd}	0.45	48	99	5 <i>R</i>		99
3	<i>i</i> -Pr	2c _{1st}	0.35	47	99	5 <i>S</i>		99
		2c _{2nd}	0.28	48	99	5 <i>R</i>		97
4	Me	2d _{1st}	0.43	45	99	5 <i>S</i>		99
		2d _{2nd}	0.35	48	99	5 <i>R</i>		99

1) PhMe/AcOEt = 2/1 for **2a**, 1/1 for **2b** and **2c**, 1/2 for **2d**

2) Determined by ¹H NMR.

3) Configuration was determined from **4**.

4) Determined by GC using a CycloSil-B column.

Table 2 Effect R¹ group on R_f value using Boc-alanine as resolving agent.

Entry	R ¹	Product	R _f value ¹	Yield [%]	Diastereomeric excess [% d.e.] ²	Config. ³	Appearance	Enantiomeric excess [% e.e.] ⁴ of 4
1	Bn	3a _{1st}	0.33	46	99	5 <i>S</i>	Solid	99
		3a _{2nd}	0.26	49	99	5 <i>R</i>		99
2	cHx	3b _{1st}	0.55	46	99	5 <i>S</i>	Oil	99
		3b _{2nd}	0.48	47	99	5 <i>R</i>		99
3	<i>i</i> -Pr	3c _{1st}	0.40	47	99	5 <i>S</i>		99
		3c _{2nd}	0.33	47	99	5 <i>R</i>		98
4	Me	3d _{1st}	0.25	47	99	5 <i>S</i>		98
		3d _{2nd}	0.19	46	99	5 <i>R</i>		97

1) PhMe/AcOEt = 2/1 for **2a**, 1/1 for **2b** and **2c**, 1/2 for **2d**

2) Determined by ¹H NMR.

3) Configuration was determined from **4**.

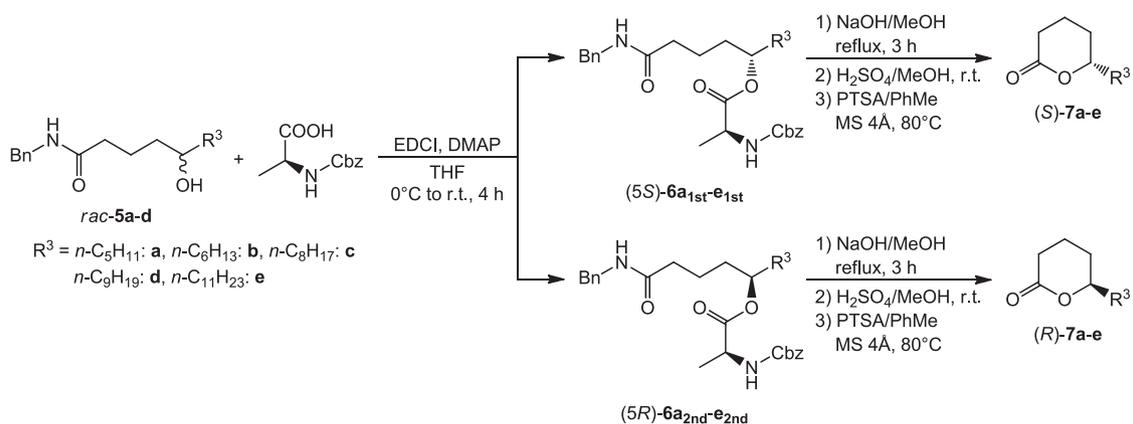
4) Determined by GC using a CycloSil-B column.

biggest difference in R_f values between diastereomers, and the separation of **2a**_{1st} and **2a**_{2nd} was easy. The synthesis of diastereomers using Boc-*L*-alanine was carried out in order to confirm the effect of amino acids (Table 2). It was possible to separate the diastereomers respectively using mixed toluene/AcOEt eluents in all cases. As with Cbz-*L*-alanine, **3a**_{1st}-**d**_{1st} and **3a**_{2nd}-**d**_{2nd} had 5*S* and 5*R* configurations, respectively. Furthermore, there was no difference in diastereomeric excesses of all diastereomers with 99% d.e. Both diastereomers possessing Bn and cHx groups as the R₁ group were colorless solids. In contrast, both diastereomers were colorless oils for *i*-Pr and Me groups in the R¹ group. It was considered that the crystallinity was decreased for Boc-*L*-alanine, which does not have a benzene ring, unlike Cbz-*L*-alanine. Boc-*L*-alanine tended to produce a small difference in R_f values between diastereomers compared with Cbz-*L*-alanine. Based on these results, Cbz-*L*-alanine was an

appropriate resolving agent for the separation of both diastereomers. Furthermore, Bn groups as the R¹ group showed the biggest difference in R_f values with 0.09 between each diastereomer. Both enantiomers of δ -dodecalactone (**4**) could be synthesized with over 98% enantiomeric excesses by a combination of Cbz-*L*-alanine as a resolving agent and Bn groups as the R¹ group.

3.3 Preparation of various δ -lactones using Cbz-alanine as resolving agent

The objective was to synthesize both enantiomers of various δ -lactones with high optical purities. Esterification of *N*-benzyl-5-hydroxyalkylamides (**5a-d**) possessing different R₃ groups with Cbz-*L*-alanine was performed (Scheme 3, Table 3). As in the case of **2a**, it was possible to separate all *N*-benzyl-5-[*N*-(benzyloxy)carbonyl]-2-aminopropanoyloxyalkylamides (**6a-e**) into each diastereomer. The



Scheme 3 Synthesis of various optically active δ -lactones using Cbz-alanine as resolving agent.

Table 3 Preparation of various δ -lactones using Cbz-alanine.

Entry	R ³	Product	R _f value ¹	Yield [%]	Diastereomeric excess [% d.e.] ²	Config. ³	Appearance	Enantiomeric excess [% e.e.] ⁴ of 7
1	<i>n</i> -C ₅ H ₁₁	6a _{1st}	0.48	48	99	5 <i>S</i>	Solid	99
		6a _{2nd}	0.39	47	99	5 <i>R</i>		99
2	<i>n</i> -C ₆ H ₁₃	6b _{1st}	0.50	45	99	5 <i>S</i>	Solid	99
		6b _{2nd}	0.42	46	99	5 <i>R</i>		99
3	<i>n</i> -C ₈ H ₁₇	6c _{1st}	0.54	47	99	5 <i>S</i>	Solid	99
		6c _{2nd}	0.44	45	99	5 <i>R</i>		99
4	<i>n</i> -C ₉ H ₁₁	6d _{1st}	0.54	46	99	5 <i>S</i>	Solid	99
		6d _{2nd}	0.45	47	99	5 <i>R</i>		99
5	<i>n</i> -C ₁₁ H ₂₃	6e _{1st}	0.55	47	99	5 <i>S</i>	Solid	99
		6e _{2nd}	0.47	47	99	5 <i>R</i>		99

1) PhMe/AcOEt = 4/3

2) Determined by ¹H NMR.

3) Configuration was determined from **7**.

4) Determined by GC using a CycloSil-B column.

difference in R_f values between diastereomers was 0.08–0.10, and they could be easily separated. Regardless of the difference of the R₃ group, **6a**_{1st}–**d**_{1st} and **6a**_{2nd}–**d**_{2nd} showed the 5*S* and 5*R* configuration, respectively. Diastereomeric excesses of diastereomers separated were 99% in all cases. From these results, both enantiomers of various δ -lactones could be efficiently synthesized both enantiomers of various δ -lactones by using Cbz-*L*-alanine as a resolving agent. Six optically pure δ -lactones could be efficiently synthesized by diastereomeric resolution using only Cbz-*L*-alanine as a resolving agent. These results indicate that this synthetic procedure is very useful for the preparation of optically pure δ -lactones.

4 CONCLUSIONS

Diastereomer esters were prepared by esterification of

N-benzyl-5-hydroxyalkylamides with an *L*-alanine derivative, which is a commercially available and relatively low cost optically active carboxylic acid, as a resolving agent. It was possible to synthesize diastereomer esters almost quantitatively by using EDCI or CMPI as condensing agents. EDCI had a short reaction time compared with CMPI. When a combination of a Bn group as the R¹ group and Cbz-*L*-alanine as a resolving agent was used, the difference in R_f values between the diastereomers was largest. Two diastereomers were separated relatively easily by silica gel column chromatography using an eluent of toluene/AcOEt regardless of the difference in the R³ group. Additionally, both enantiomers of δ -lactones were selectively synthesized with over 98% enantiomeric excesses regardless of R³ groups. Six optically pure δ -lactones were selectively synthesized using only Cbz-*L*-alanine without other expensive resolving agents. It was suggested that this diastereomeric resolution is a very efficient procedure for

the preparation of optically pure δ -lactones.

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