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Successive diastereoselective C(sp^3)–H arylation and Suzuki coupling toward enantioenriched polyaryl unnatural amino acid motifs†

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This paper reports the preliminary efforts in constructing (teraryl-, quateraryl- and hexaryl-based) polyaryl unnatural amino acid motifs. At first, chemo- and diastereoselective Pd(II)-catalyzed bidentate directing group-aided arylation of prochiral β-C(sp^3)–H bonds of carboxamides of amino acids with 4-bromo-4′-iodo-1,1′-biphenyl was performed. This process generated amino acid motifs possessing the 4-bromobiphenyl unit. Subsequently, the Suzuki–Miyaura coupling reaction with the 4-bromobiphenyl unit present in amino acid motifs has led to the assembling of a library of teraryl-, quateraryl-, and hexaaryl-based polyaryl unnatural amino acid motifs. Emission spectra of representative teraryl-, quateraryl-, and hexaaryl-based unnatural amino acid motifs are recorded, and some are found to be fluorescent. In the literature, various teraryl- and quateraryl-based molecules have been reported as medicinally relevant compounds. Consequently, there is scope for synthesizing novel and functionalized teraryl-, quateraryl-, and hexaaryl-based molecules to aid future investigations into the biological activities of such scaffolds. Thus, this work on the construction of teraryl-, quateraryl-, and hexaaryl-based unnatural amino acid motifs *via* successive sp^3 C–H arylation and Suzuki coupling would be a valuable effort toward strengthening the library of polyaryl-based unnatural amino acid scaffolds.

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Introduction

Oligoaryls or π-extended biaryls (*e.g.*, teraryls, quateraryls, hexaaryls, *etc*) have gained significant attention in materials, organic synthesis, and drug discovery/medicinal chemistry.[1,2] Of particular interest, various naturally occurring and synthetically derived teraryls are known to exhibit potential bioactivities and medicinal properties (Fig. 1).[2–4] Several teraryls, quateraryls, and hexaaryls are vital motifs in developing various functional organic materials and additionally, various terphenyls are known to exhibit fluorescence properties.[5]

On the other hand, the secondary structures of protein were imagined as templates in the design of drug-like small molecules that may act as proteomimetics.[6,7] It is reported that various types of biaryl, terphenyl-inspired templates, polycyclic ether, benzodiazepinedione, and indane motifs were envisioned to act as drug-like non-peptidyl α-helix mimetics, which may disrupt protein–protein interactions (Fig. 1).[6] Along these lines, various non-peptidyl teraryl-based α-helix mimetics (*e.g.*, **1i**, and **1f**, Fig. 1),

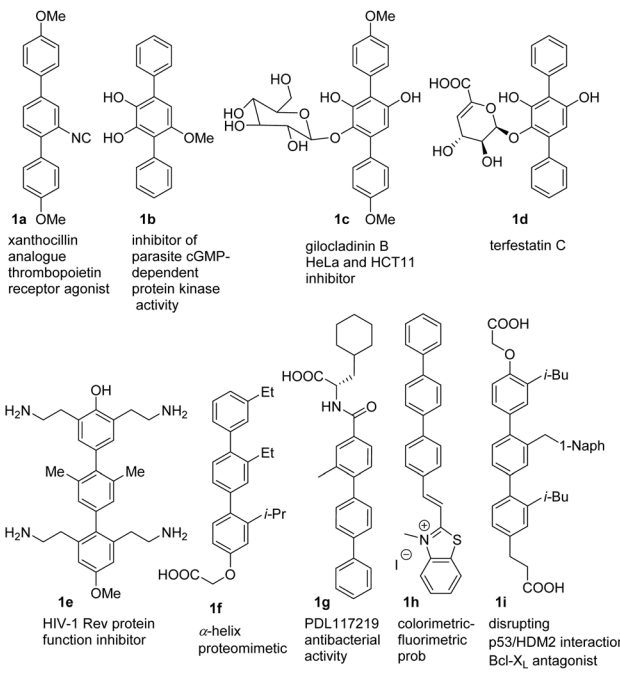

Fig. 1 Examples of bio-active polyaryls.

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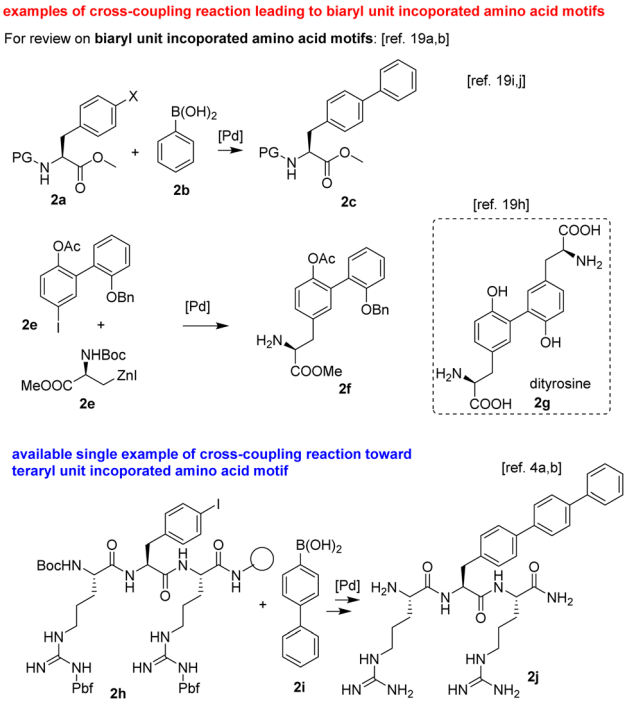
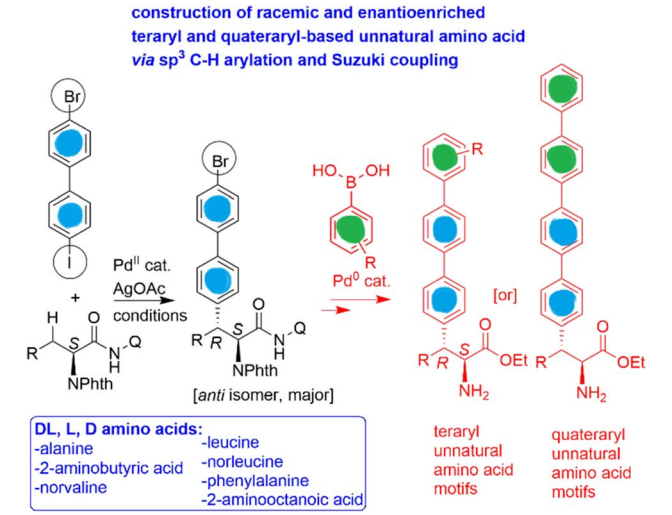


Scheme 1 Representative cross-coupling approaches toward the synthesis of bio-active polyaryl-based unnatural amino acid motifs.



Scheme 2 Successive diastereoselective C(sp^3)–H arylation and Suzuki coupling toward (teraryl, quateraryl, hexaaryl-based) polyaryl unnatural amino acid motifs.

were tested as potent Bcl-X_L antagonists[7b,c] and acted to disrupt the p53/HDM2 interaction.[7d]

In general, the transition metal-catalyzed cross-coupling method has been used as a viable route for obtaining biaryl and oligoaryl-based compounds.[8–11] Along these lines, the synthesis of bio-active and non-peptidyl teraryl-based α-helix mimetics (*e.g.*, **1i**,[7c] **1f**,[7a,g] **1e**,[3a] **2j**,[4a,b]) and pyridine-based teraryl/quateraryl α-helix mimetics[7e,f,h] have been accomplished using the sequential cross-coupling reactions (Scheme 1).

Unnatural amino acid derivatives (*viz.*, noncanonical or non-proteinogenic amino acids) have proven to be vital and privileged molecules in various research fields, including organic synthesis, chemical biology, and drug discovery.[12] Diverse unnatural amino acid molecules have been used as starting materials for synthesizing natural products, drug molecules, and peptides, *etc.* Furthermore, a wide range of L- and D-unnatural amino acids are used as organocatalysts, ligands, tools, or probes to study and understand the functions of macromolecules and biomolecules.[12]

In recent years, the C–H functionalization of sp^3 C–H bonds has facilitated the regio- or site-selective installation of a wide range of functional groups in aliphatic chains.[13] Especially, the Pd(II)-catalyzed, bidentate directing group-aided C–H functionalization[14,15] of the prochiral or diastereotopic sp^3 C–H bonds has enabled the installation of a wide range of functional groups in the backbone of carboxamides of α-amino acids.[16–18]

Given the importance of teraryls and quateraryls as inhibitors of medicinally relevant protein–protein and protein–nucleic acid interactions.[6,7] There is scope for synthesizing new teraryls and quateraryls. In this work, we explored the construction of teraryl-, quateraryl-, and hexaaryl-based unnatural amino acid motifs *via* the successive sp^3 C–H arylation and Suzuki coupling. We envisaged that this approach would be a valuable effort and a contribution towards strengthening the library of polyaryl-based unnatural amino acid motifs.

With regard to polyaryl-based unnatural amino acid motifs, while the synthesis of biaryl-based unnatural amino acid molecules *via* the traditional cross-coupling reaction has been well documented (Scheme 1).[18a,19] However, apart from the Suzuki coupling-based synthesis of arginine-based tripeptide **2j** encompassing a terphenyl unit (Scheme 1),[4a,b] to the best of our knowledge, the synthesis of teraryl-, quateraryl, and hexaaryl-based unnatural amino acid analogues is rarely explored *via* the C–H functionalization route. Recently, we reported the synthesis of biaryl-based unnatural amino acid molecules *via* the sp^3 C–H arylation method.[18a] As a part of the extension of our previous report, this work aimed to generate teraryl-, quateraryl, and hexaaryl-based unnatural amino acid motifs (Scheme 2), which may be useful in developing amino acid-based proteomimetics.

Results and discussion

To commence with the conceived teraryl and quaternary unnatural amino acid targets, initially, we planned to assemble various amino acid derivatives possessing a 4-bromobiphenyl moiety, which then can be subjected to the Suzuki coupling reaction. Based on previous experience,[18a,20] we prepared carboxamide of 2-aminobutyric acid **3b-(DL)** linked with the bidentate directing group 8-aminoquinoline for performing the Pd(II)-catalyzed arylation of the prochiral β-C(sp^3)–H bond of 2-aminobutyric acid **3b-(DL)** with 4-bromo-4′-iodobiphenyl (**4**). Carboxamide **3b-(DL)** was treated with 4-bromo-4′-iodobiphenyl (**4**) under the standard C–H arylation conditions[16–18] involving $Pd(OAc)_2$ catalyst, AgOAc (iodide ion scavenging additive) in

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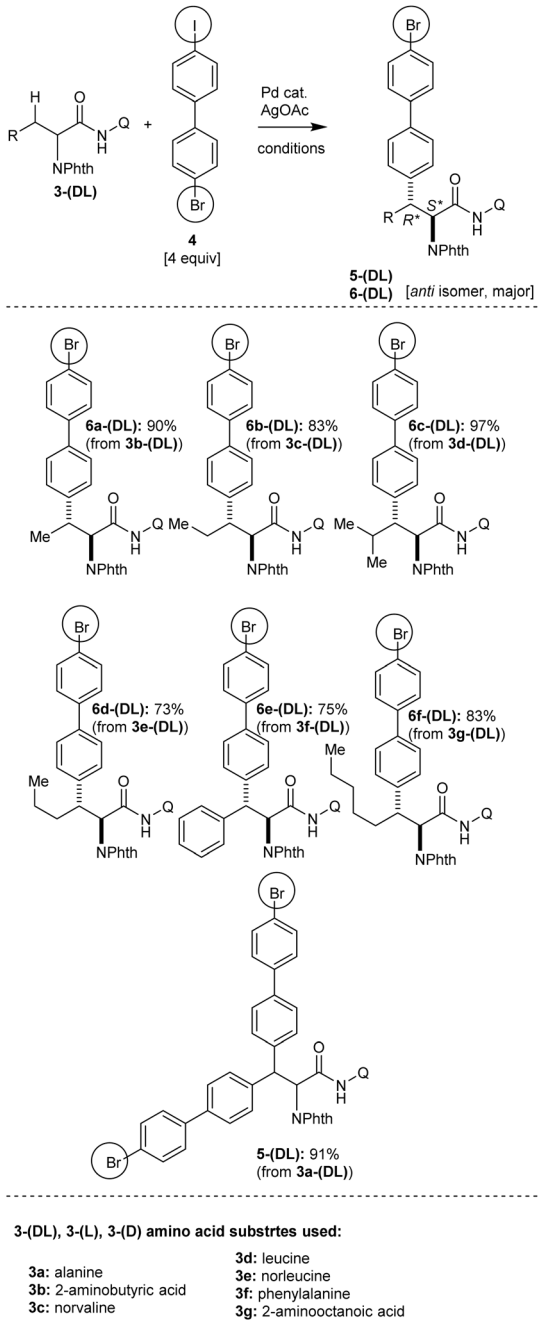

Scheme 3 Construction of amino acid derivatives possessing a 4-bromobiphenyl moiety *via* the Pd(II)-catalyzed sp^3 C–H arylation. Conditions: **3-(DL)** (0.25–4.6 mmol), $Pd(OAc)_2$ (10 mol%), AgOAc (2.5 equiv), toluene (3 mL), 110 °C, 48 h, sealed tube (purged with N_2). Products **6-(DL)** were obtained from their corresponding carboxamides of 2-aminobutyric acid **3b-(DL)**, norvaline **3c-(DL)**, leucine **3d-(DL)**, norleucine **3e-(DL)**, phenylalanine **3f-(DL)** and 2-aminooctanoic acid **3g-(DL)** linked with 8-aminoquinoline directing group. Products **5-(DL)** were obtained from their corresponding carboxamides of alanine **3a-(DL)** linked with 8-aminoquinoline directing group.

toluene at 110 °C for 48 h (Scheme 3). This reaction afforded the expected 2-aminobutyric acid derivative **6a-(DL)**, possessing a 4-bromobiphenyl moiety in 90% yield as the major diastereomer (having the *anti*-stereochemistry).

Similarly, carboxamides of norvaline **3c-(DL)**, leucine **3d-(DL)**, norleucine **3e-(DL)**, phenylalanine **3f-(DL)** and 2-aminooctanoic acid **3g-(DL)** possessing 8-aminoquinoline directing group were assembled.[18,20] Then, the carboxamides **3c-g-(DL)** were subjected to the β-C(sp^3)–H arylation with 4-bromo-4′-iodobiphenyl (**4**) in the presence of $Pd(OAc)_2$ and AgOAc in toluene at 110 °C for 48 h (Scheme 3). These reactions afforded the corresponding norvaline **6b-(DL)**, leucine **6c-(DL)**, norleucine **6d-(DL)**, phenylalanine **6e-(DL)**, and 2-aminooctanoic acid **6f-(DL)** possessing a 4-bromobiphenyl moiety in 73–97% yields (major diastereomers having the *anti*-stereochemistry).

Next, we assembled enantioenriched carboxamides of L-amino acids, such as L-2-aminobutyric acid **3b-(L)**, L-norvaline **3c-(L)**, L-leucine **3d-(L)**, L-norleucine **3e-(L)**, and L-phenylalanine **3f-(L)**, possessing an 8-aminoquinoline directing group. Subsequently, enantioenriched carboxamides of L-amino acids **3b-f-(L)** were subjected to the $Pd(OAc)_2$-catalyzed β-C(sp^3)–H arylation with 4-bromo-4′-iodobiphenyl (**4**) in toluene at 110 °C for 48 h (Scheme 4). These reactions afforded the corresponding enantioenriched 2-aminobutyric acid **6a-(L)**, norvaline **6b-(L)**, leucine **6c-(L)**, norleucine **6d-(L)** and phenylalanine **6e-(L)** possessing 4-bromobiphenyl moiety in 74–95% yields (major diastereomers, *anti*-stereochemistry) with good enantiopurity.

Along this line, we then assembled enantioenriched carboxamides of D-amino acids such as D-norvaline **3c-(D)**, D-leucine **3d-(D)**, D-norleucine **3e-(D)**, and D-phenylalanine **3f-(D)** possessing an 8-aminoquinoline directing group. Subsequently, enantiopure carboxamides of D-amino acids **3c-f-(D)** were subjected to the $Pd(OAc)_2$-catalyzed β-C(sp^3)–H arylation with 4-bromo-4′-iodobiphenyl (**4**) (Scheme 4). These reactions afforded the corresponding enantioenriched norvaline **6b-(D)**, leucine **6c-(D)**, norleucine **6d-(D)**, and phenylalanine **6e-(D)** possessing a 4-bromobiphenyl moiety in 76–96% yields (major diastereomers, *anti*-stereochemistry) with good enantiopurity.

Additionally, we assembled racemic and enantiopure carboxamides of alanine, such as DL-alanine **3a-(DL)**, D-alanine **3a-(D)**, and L-alanine **3a-(L)** possessing an 8-aminoquinoline directing group.[18a] Carboxamide **3a-(DL)** was treated with 4-bromo-4′-iodobiphenyl (**4**) under the standard β-C(sp^3)–H conditions involving $Pd(OAc)_2$ and AgOAc in toluene at 110 °C for 48 h (Scheme 3). This reaction afforded the alanine derivative **5-(DL)**, possessing two 4-bromobiphenyl moieties *via* double β-C(sp^3)–H arylation of **3a-(DL)**. Along this line, enantiopure L- or D-alanine carboxamides **3a-(L)** or **3a-(D)** were subjected to the β-C(sp^3)–H arylation with 4-bromo-4′-iodobiphenyl (**4**) in the presence of $Pd(OAc)_2$ and AgOAc in toluene at 110 °C for 48 h (Scheme 4). These reactions afforded the corresponding enantioenriched alanine derivatives **5-(L)** and **5-(D)** possessing two 4-bromobiphenyl moieties *via* double β-C(sp^3)–H arylation of respective carboxamides **3a-(L)** and **3a-(D)**.

Initially, we tried to perform the Suzuki cross-coupling reaction with the 4-bromobiphenyl moiety present in the amino acid derivative having 8-aminoquinoline and phthalimide protecting groups (see ESI†). Unfortunately, we could not achieve the expected Suzuki cross-coupling and the synthesis of the π-extended biaryl, such as teraryl- or quateraryl-based unnatural amino acid motifs having 8-aminoquinoline and

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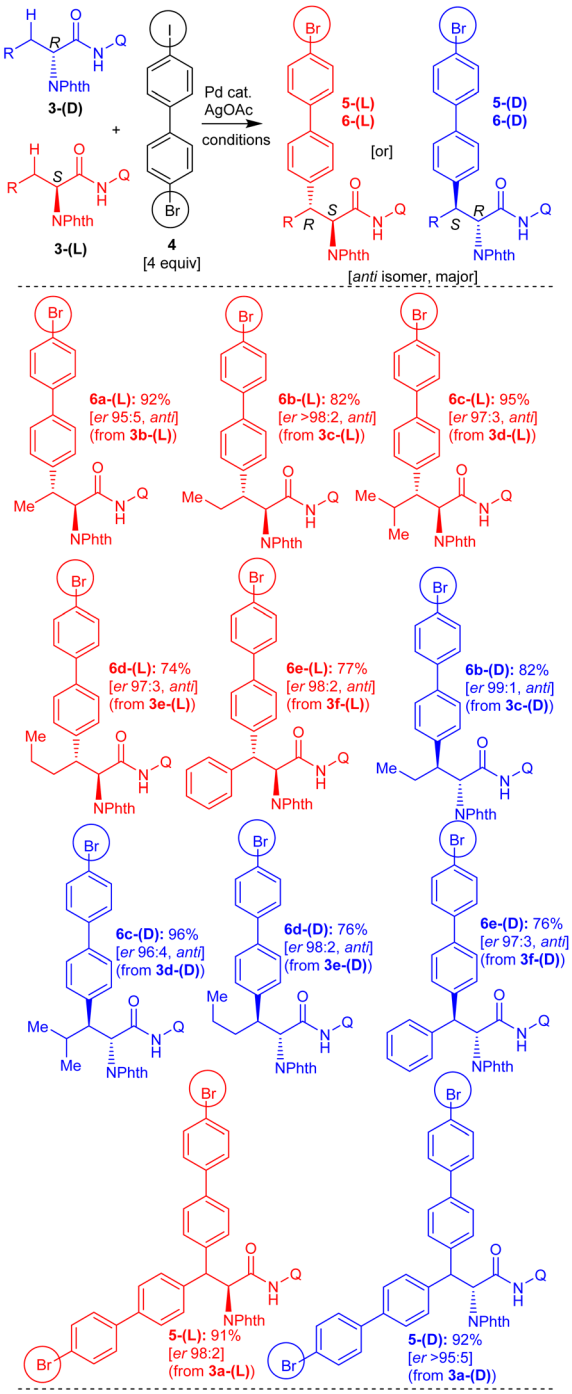

Scheme 4 Construction of enantioenriched amino acid derivatives possessing a 4-bromobiphenyl moiety *via* the Pd(II)-catalyzed sp^3 C–H arylation. Conditions: **3-(D)** or **3-(L)** (0.25–4.6 mmol), $Pd(OAc)_2$ (10 mol%), AgOAc (2.5 equiv.), toluene (3 mL), 110 °C, 48 h, sealed tube (purged with N_2). Products **6-(L)** (or) **6-(D)** were obtained from their corresponding carboxamides of 2-aminobutyric acid **3b-(L)**, norvaline **3c-(L/D)**, leucine **3d-(L/D)**, norleucine **3e-(L/D)**, phenylalanine **3f-(L/D)** and 2-aminooctanoic acid **3g-(DL)** linked with 8-aminoquinoline directing group. Products **5-(L)** (or) **5-(D)** were obtained from their corresponding carboxamides of alanine **3a-(L/D)** linked with 8-aminoquinoline directing group.

phthalimide protecting groups. The presence of 8-aminoquinoline and phthalimide protecting groups presumably interfered with the Suzuki cross-coupling reaction conditions, and thereby, the expected Suzuki cross-coupling with the 4-bromobiphenyl moiety present in the amino acid derivative did not occur.

Therefore, we attempted the removal of the directing group (8-aminoquinoline) and phthalimide protecting groups from the amino acid derivatives **5-(DL)**, **6-(DL)**, **5-(D)**, **6-(D)**, **5-(L)** and **6-(L)** which were obtained *via* the Pd(II)-catalyzed β-C(sp^3)–H arylation reactions. Based our previous experience,[18] we performed the $BF_3 \cdot Et_2O$-mediated direct amide to ester conversion reactions in the substrates **5-(DL)**, **6-(DL)**, **5-(D)**, **6-(D)**, **5-(L)** and **6-(L)**. Accordingly, carboxamide of norvaline **6b-(DL)**, having 8-aminoquinoline and phthalimide protecting group, was treated with ethanol in the presence of $BF_3 \cdot Et_2O$ at 130 °C for 36 h. This reaction enabled the removal of the 8-aminoquinoline directing group and afforded the corresponding norvaline ethyl ester derivative **8a-(DL)** in 61% yield (Scheme 5). Similarly, the substrates leucine **6c-(DL)**, norleucine **6d-(DL)**, and phenylalanine **6e-(DL)**, having the 8-aminoquinoline directing group, were treated with ethanol/methanol in the presence of $BF_3 \cdot Et_2O$ at 130 °C for 36 h. These reactions afforded the corresponding products including leucine **8b-(DL)**, norleucine **8c-(DL)**, phenylalanine **8d-(DL)** and phenylalanine **8e-(DL)** ester derivatives (Scheme 5).

Subsequently, enantioenriched L-carboxamide substrates including norvaline **6b-(L)**, leucine **6c-(L)**, norleucine **6d-(L)**, phenylalanine **6e-(L)** and D-carboxamide substrates including norvaline **6b-(D)**, leucine **6c-(D)**, norleucine **6d-(D)**, phenylalanine **6e-(D)** were treated with EtOH in the presence of $BF_3 \cdot Et_2O$ to remove the 8-aminoquinoline group. These reaction afforded the corresponding enantioenriched products including norvaline **8a-(L)**, leucine **8b-(L)**, norleucine **8c-(L)**, phenylalanine **8d-(L)** and norvaline **8a-(D)**, leucine **8b-(D)**, norleucine **8c-(D)**, phenylalanine **8d-(D)** ester derivatives (Scheme 6). Additionally, the carboxamides of alanine **5-(DL)**, enantioenriched alanine **5-(D)**, and alanine **5-(L)** were treated with EtOH in the presence of $BF_3 \cdot Et_2O$ to remove the 8-aminoquinoline group. These reactions afforded the corresponding products, including alanine **7-(DL)**, enantioenriched alanine **7-(D)** and alanine **7-(L)** ester derivatives (Schemes 5 and 6).

Before performing the Suzuki coupling reaction using the amino acid derivatives **7-(DL)**, **8-(DL)**, **7-(D)**, **8-(D)**, **7-(L)** and **8-(L)** possessing the phthalimide group, we decided to deprotect the phthalimide group also. Accordingly, we attempted the deprotection of phthalimide group from the amino acid ester derivatives **7-(DL)**, **8-(DL)**, **7-(D)**, **8-(D)**, **7-(L)** and **8-(L)** to obtain the amino acid ester derivatives **9-(DL)**, **10-(DL)**, **9-(D)**, **10-(D)**, **9-(L)** and **10-(L)** possessing the free amino group and 4-bromobiphenyl moiety (Schemes 7 and 8).

Based on our previous works, we treated norvaline ethyl ester derivative **8a-(DL)** with 1,2-ethylenediamine in *t*-BuOH at rt, which enabled the phthalimide deprotection. The norvaline ethyl ester derivative **10a-(DL)**, having the free amino group, was obtained in 81% yield (Scheme 7). Similarly, ester derivatives of leucine **8b-(DL)**, norleucine **8c-(DL)**, phenylalanine **8d-(DL)**, and

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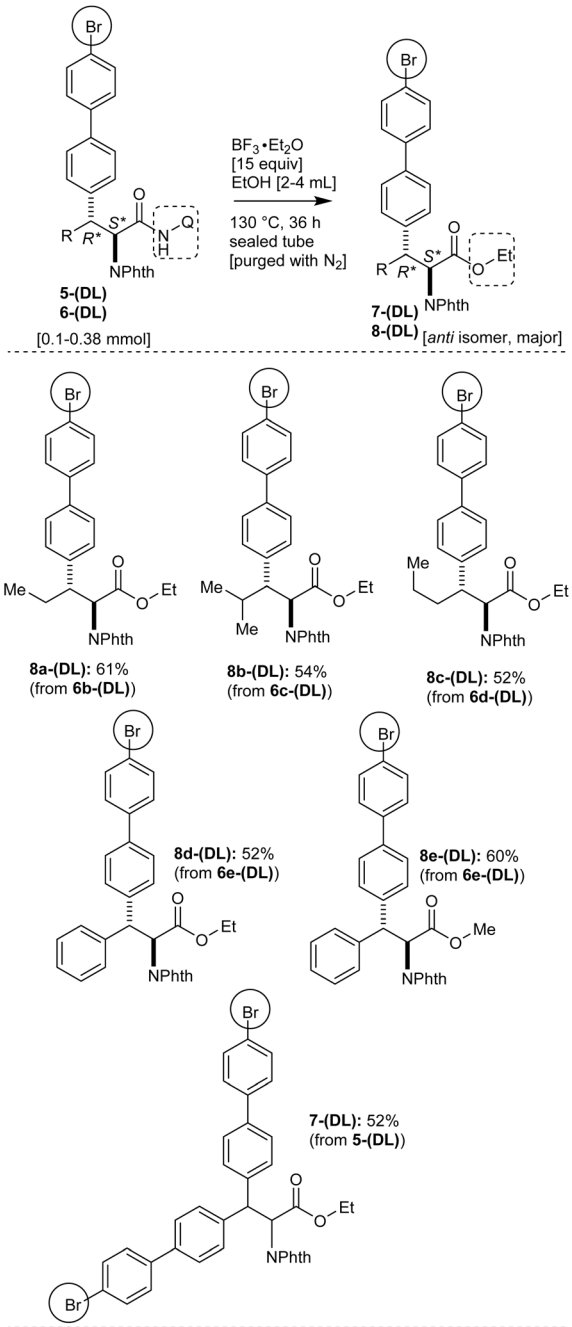
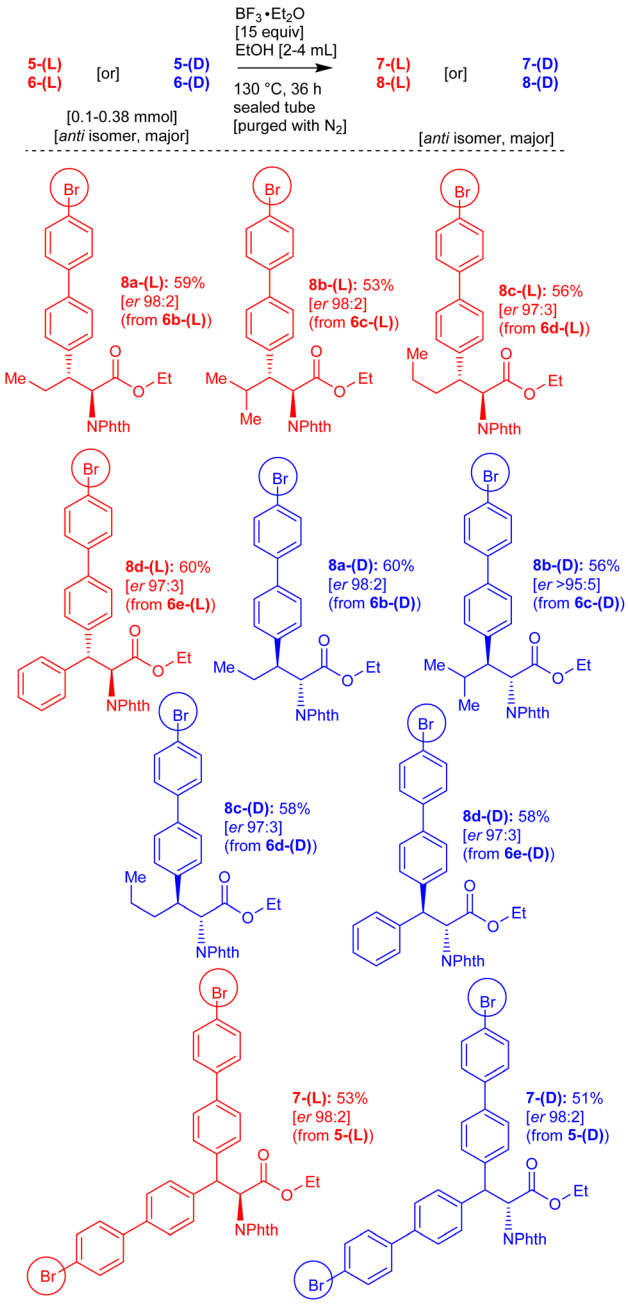


Scheme 5 Removal of the 8-aminoquinoline group and $BF_3 \cdot Et_2O$-mediated direct amide to ester conversion in substrates 5-(DL), and 6-(DL), affording the corresponding ester derivatives 7-(DL), and 8-(DL).



Scheme 6 Removal of the 8-aminoquinoline group and $BF_3 \cdot Et_2O$-mediated direct amide to ester conversion in substrates 5-(D), 6-(D), 5-(L) and 6-(L) affording the corresponding ester derivatives 7-(D), 8-(D), 7-(L) and 8-(L).

phenylalanine **8e-(DL)** were treated with 1,2-ethylenediamine in *t*-BuOH at rt. These reactions afforded the corresponding ethyl ester derivatives of leucine **10b-(DL)**, norleucine **10c-(DL)**, phenylalanine **10d-(DL)**, and phenylalanine **10e-(DL)** possessing the free amino group.

Subsequently, enantioenriched ester derivatives of norvaline **8a-(L)**, leucine **8b-(L)**, norleucine **8c-(L)**, phenylalanine **8d-(L)**, and norvaline **8a-(D)**, leucine **8b-(D)**, norleucine **8c-(D)** and phenylalanine **8d-(D)** were treated with 1,2-ethylenediamine in *t*-BuOH at rt. These reactions afforded the corresponding enantioenriched ester derivatives of norvaline **10a-(L)**, leucine **10b-(L)**, norleucine **10c-(L)**, phenylalanine **10d-(L)** and norvaline **10a-(D)**, leucine **10b-(D)**, norleucine **10c-(D)** and phenylalanine **10d-(D)** having the free amino group (Scheme 8). Additionally, alanine ester derivatives **7-(DL)**, enantioenriched alanine **7-(D)**, and alanine **7-(L)** were treated with 1,2-ethylenediamine in *t*-BuOH at rt. These reactions afforded the corresponding alanine ester derivatives **9-(DL)**, enantioenriched alanine **9-(D)**, and

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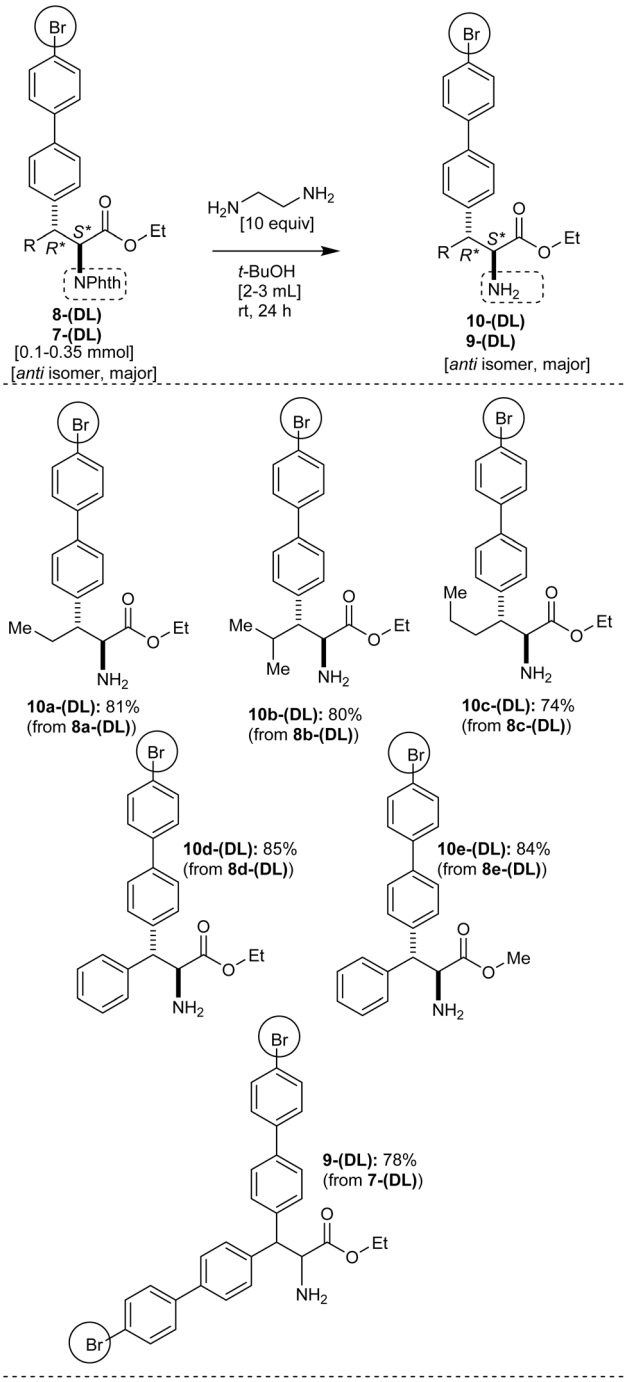
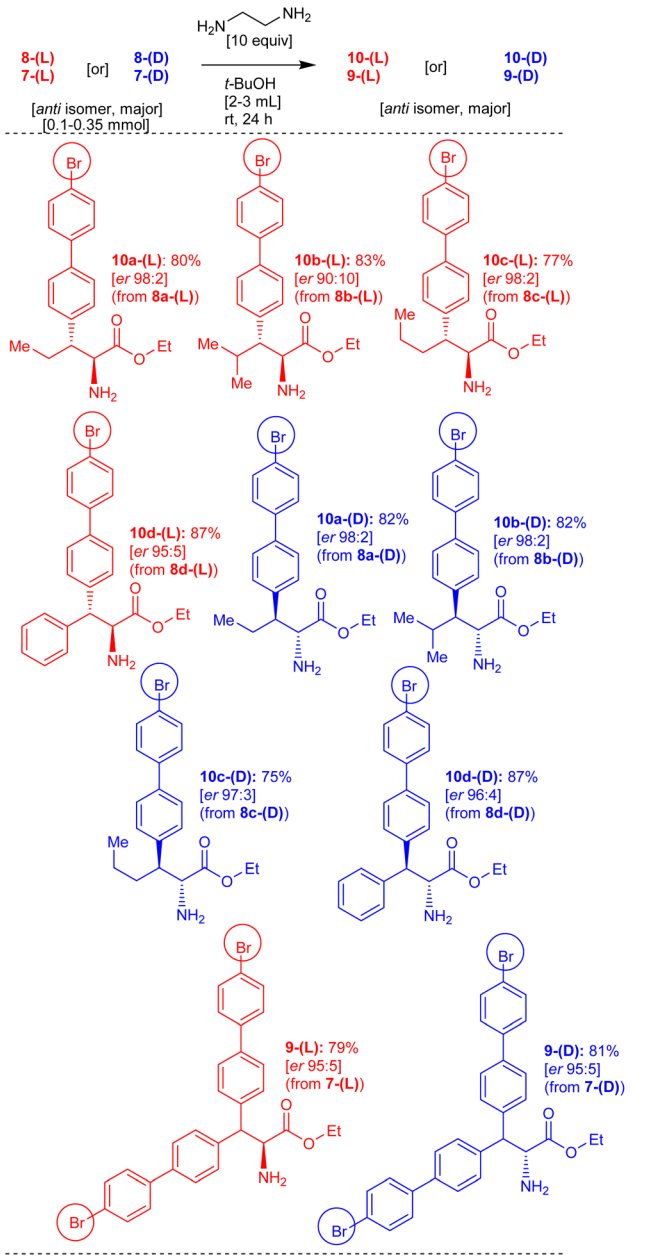


Scheme 7 Deprotection of the phthalimide group in substrates 7-(DL), and 8-(DL), affording ester derivatives of 9-(DL), and 10-(DL), having free amino group.



Scheme 8 Deprotection of the phthalimide group in substrates 7-(D), 8-(D), 7-(L) and 8-(L) affording ester derivatives of 9-(D), 10-(D), 9-(L) and 10-(L) having free amino group.

alanine **9-(L)** possessing the free amino group (Schemes 7 and 8).

Having obtained amino acid ester derivatives **9-(DL)**, **10-(DL)**, **9-(D)**, **10-(D)**, **9-(L)** and **10-(L)** possessing free amino group and 4-bromobiphenyl moiety, we then commenced the synthesis of teraryl- and quateraryl amino acid motifs *via* the Suzuki coupling. Firstly, we attempted the Suzuki coupling reaction on norvaline **10a-(DL)** containing a 4-bromobiphenyl moiety with (4-methoxyphenyl)boronic acid in the presence of $Pd(PPh_3)_4$ (5 mol%) and K_2CO_3 in toluene : EtOH : H_2O (2 : 1 : 1 mL) at 110 °C for 24 h. This reaction afforded the targeted teraryl-based norvaline **12a-(DL)** in 84% yield (Scheme 9). Then, the Pd-catalyzed Suzuki coupling reaction was performed using enantioenriched norvalines **10a-(D)** and **10a-(L)** containing a 4-bromobiphenyl moiety with (4-methoxyphenyl)boronic acid. These reactions afforded the targeted enantioenriched teraryl-based norvalines **12a-(D)** and **12a-(L)** in 78–83% yields (*anti* isomers) with good enantiopurity (Scheme 10). Next, we performed the Pd-catalyzed Suzuki coupling reaction on leucine **10b-(DL)**, norleucine **10c-(DL)**, and phenylalanine **10d-(DL)** containing

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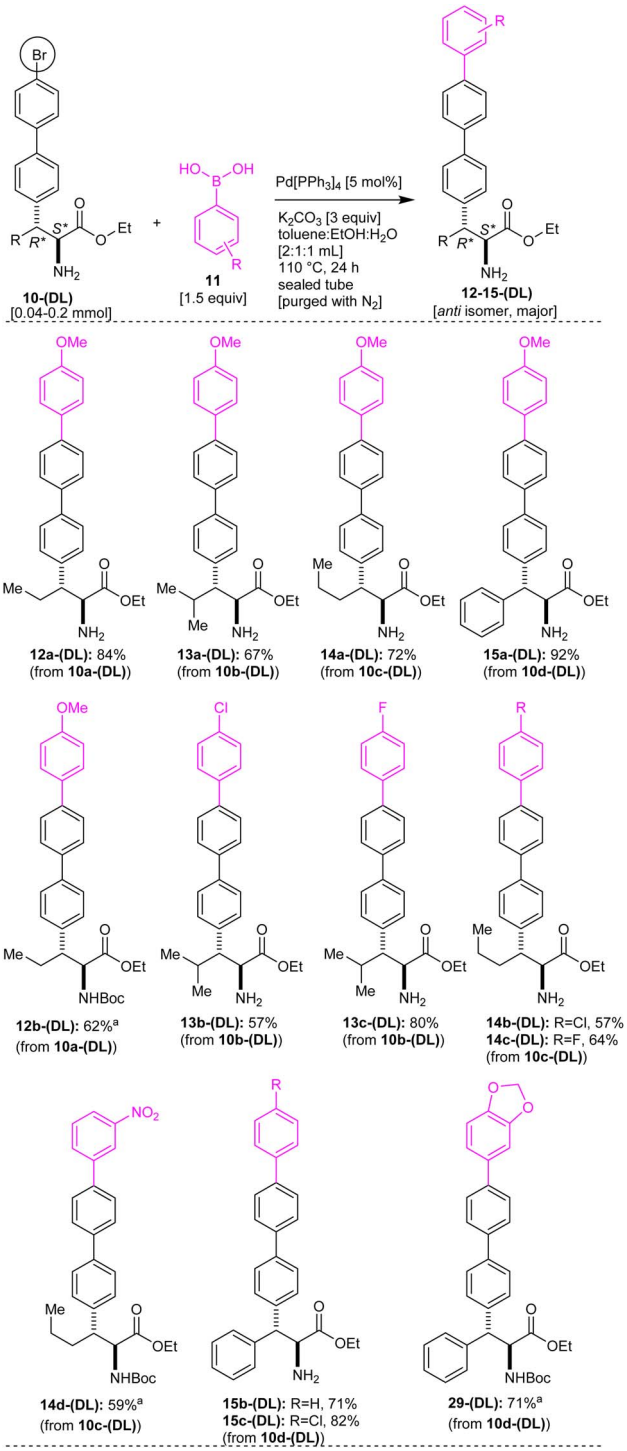
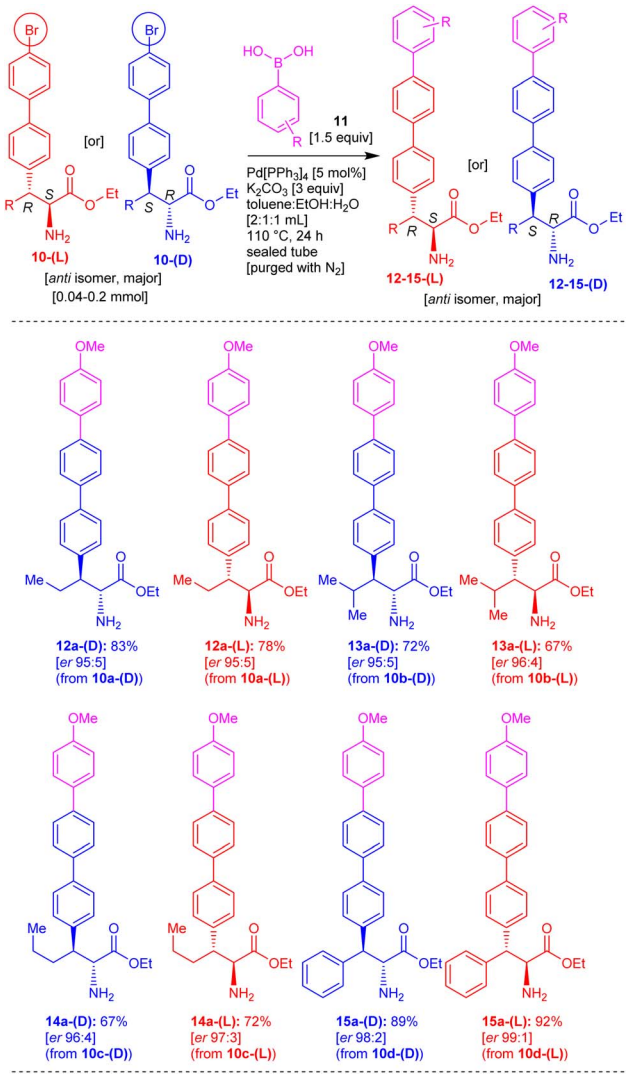


Scheme 9 Construction of terphenyl-based amino acid derivatives 12-15-(DL) *via* the Pd(II)-catalyzed Suzuki coupling reaction. (a) Substrates **10a,c,d-(DL)** were first treated with $(Boc)_2O$ (1.5 equiv) in $(CH_3)_2CO : H_2O$ (0.5 : 9 mL), DCM (2 mL), rt, 12 h and the corresponding *N*-Boc compounds (crude) obtained, which were used to synthesize the products **12b-(DL)**, **14d-(DL)** and **29-(DL)**.

a 4-bromobiphenyl moiety with (4-methoxyphenyl)boronic acid. These reactions afforded the corresponding targeted teraryl-based leucine **13a-(DL)**, norleucine **14a-(DL)**, and phenylalanine **15a-(DL)** in 67–92% yields (*anti* isomers) (Scheme 9).



Scheme 10 Construction of terphenyl-based amino acid derivatives 12-(D), 13-(D), 14-(D), 15-(D), 12-(L), 13-(L), 14-(L), and 15-(L) *via* the Pd(II)-catalyzed Suzuki coupling reaction.

Additionally, we carried out the Pd-catalyzed Suzuki coupling reaction on leucine **10b-(DL)** or norleucine **10c-(DL)** or phenylalanine **10d-(DL)** containing a 4-bromobiphenyl moiety using different arylboronic acids. These attempts afforded the corresponding targeted teraryl-based leucines **13b-(DL)**, **13c-(DL)**, norleucines **14b-(DL)**, **14c-(DL)**, and phenylalanines **15b-(DL)**, **15c-(DL)** in 57–82% yields (Scheme 9). While the Suzuki coupling reactions were successful in amino acid ester derivatives **10-(DL)**, having a free amino group. To prepare the orthogonally protected teraryl amino acid motifs, the free amino group in norvaline **10a-(DL)** or norleucine **10c-(DL)** or phenylalanine **10d-(DL)** was protected as an *N*-Boc group. Then, we carried out the Pd-catalyzed Suzuki coupling reaction on *N*-Boc norvaline **10a-(DL)** or *N*-Boc norleucine **10c-(DL)**, or *N*-Boc phenylalanine **10d-(DL)** containing a 4-bromobiphenyl moiety with different arylboronic acids. These reactions afforded the corresponding targeted teraryl-based *N*-Boc norvaline **12b-(DL)**

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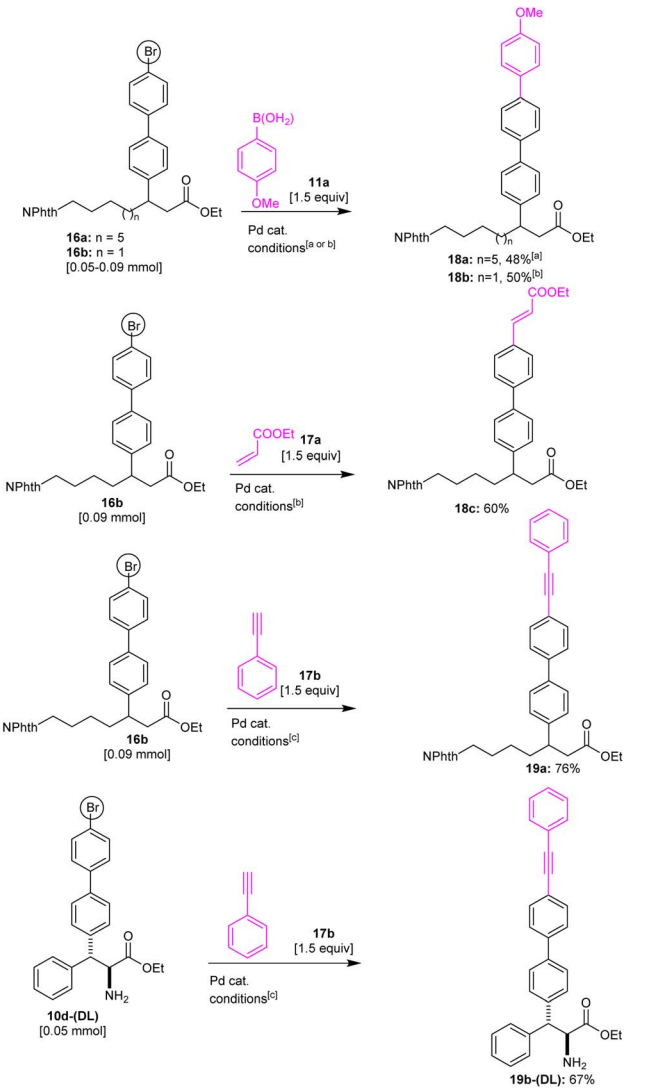
or *N*-Boc norleucine **14d-(DL)** and *N*-Boc phenylalanine **29-(DL)** (Scheme 9).

Next, we carried out the Pd-catalyzed Suzuki coupling reaction on enantioenriched L-amino acid substrates, leucine **10b-(L)**, norleucine **10c-(L)**, and phenylalanine **10d-(L)** containing a 4-bromobiphenyl moiety with (4-methoxyphenyl) boronic acid. These reactions afforded the corresponding targeted enantioenriched teraryl-based leucine **13a-(L)**, norleucine **14a-(L)**, and phenylalanine **15a-(L)** (*anti* isomers) with good enantiopurity (Scheme 10). Subsequently, we carried out the Pd-catalyzed Suzuki coupling reaction on enantioenriched D-amino acid substrates, including leucine **10b-(D)**, norleucine **10c-(D)**, and phenylalanine **10d-(D)** containing a 4-bromobiphenyl moiety with (4-methoxyphenyl)boronic acid. These reactions afforded the corresponding targeted enantioenriched teraryl-based leucine **13a-(D)**, norleucine **14a-(D)**, and phenylalanine **15a-(D)** (*anti*-isomers) with good enantiopurity (Scheme 10).

Having synthesized teraryl-based α-amino acids (Schemes 9 and 10), next to extend the substrate scope and generality of this protocol, we performed the Suzuki coupling on the long chain unnatural amino acid derivatives **16a**, **16b** containing the 4-bromobiaryl moiety (Scheme 11).[18a] We heated 11-aminoundecanoic acid ester substrate **16a** with boronic acid **11a** in the presence of $Pd(PPh_3)_4$ and K_3PO_4 in DMF at 110 °C for 24 h. This reaction afforded teraryl-based 11-aminoundecanoic acid motif **18a** in 48% yield (Scheme 11). Similarly, teraryl-based 7-aminoheptanoic acid motif **18b** was obtained from **16b**. Next, we attempted the Heck coupling reaction on **16b** with ethyl acrylate **17a** in the presence of $Pd(OAc)_2$, P(*o*-tolyl)$_3$, and Et_3N in MeCN at 85 °C for 17 h. This reaction afforded the olefin-unit appended, biaryl-based 7-aminoheptanoic acid ester substrate **18c** in 60% yield (Scheme 11). We continued to attempt the Sonogashira cross-coupling reaction on the 4-bromobiphenyl moiety in substrate **16b** and 4-phenylalanine derivative **10d-(DL)** containing the 4-bromobiphenyl moiety with phenylacetylene **17b**. Accordingly, treatment of **16b** or **10d-(DL)** in the presence of $Pd(PPh_3)_2Cl_2$, CuI and Et_3N in DMF for 110 °C for 17 h afforded the corresponding terphenyl-based compounds 7-aminoheptanoic acid motif **19a** and phenylalanine motif **19b-(DL)** possessing an alkyne unit (Scheme 11).

After having constructed a library of racemic and enantioenriched teraryl-based amino acid motifs, we shifted our attention towards the synthesis of quarteraryl-based amino acid scaffolds. Firstly, we attempted the Suzuki coupling reaction on norvaline **10a-(DL)** containing a 4-bromobiphenyl moiety with [1,1′-biphenyl]-4-ylboronic acid in the presence of $Pd(PPh_3)_4$, (5 mol%) and K_2CO_3 in toluene : EtOH : H_2O (2 : 1 : 1 mL) at 110 °C for 24 h. This reaction afforded the targeted quateraryl-based norvaline **26a-(DL)** in 71% yield (Scheme 12). Along this line,[18a] the Pd-catalyzed Suzuki coupling reaction on norvaline **10aa-(DL)** containing a 4-bromobiphenyl moiety (and 8-aminoquinoline directing group) with (6-methoxynaphthalen-2-yl) boronic acid afforded the targeted quateraryl-based norvaline **26b-(DL)** in 69% yield.

Next, we conducted the Pd-catalyzed Suzuki coupling reaction on leucine **10b-(DL)** with [1,1′-biphenyl]-4-ylboronic acid or



Scheme 11 Substrate scope extension. Construction of amino acid derivatives **18/19** *via* the Pd(II)-catalyzed Suzuki (or) Heck (or) Sonogashira coupling reactions. (a) $Pd(PPh_3)_4$ (2 mol%), K_3PO_4 (2.5 equiv.), DMF (1 mL), 110 °C, 24 h, sealed tube (purged with N_2). (b) $Pd(OAc)_2$ (10 mol%), P(*o*-tolyl)$_3$ (25 mol%), Et_3N (0.2 mL), MeCN (3 mL), 85 °C, 17 h, sealed tube (purged with N_2). (c) $Pd(PPh_3)_2Cl_2$ (5 mol%), CuI (3 mol%), Et_3N (0.12–0.25 mL), DMF (1 mL), 110 °C, 17 h, sealed tube (purged with N_2).

[1,1′-biphenyl]-3-ylboronic acid. These reactions afforded the corresponding targeted quateraryl-based leucine **27a-(DL)** and leucine **27b-(DL)** in 65–78% yields. Then, the Pd-catalyzed Suzuki coupling reaction on enantioenriched leucine **10b-(D)** with [1,1′-biphenyl]-4-ylboronic acid afforded the targeted quateraryl-based enantioenriched leucine **27a-(D)** in 74% yield with good enantiopurity.

Subsequently, we carried out the Pd-catalyzed Suzuki coupling reaction on *N*-Phth norleucine **8c-(DL)** with [1,1′-biphenyl]-4-ylboronic acid, which afforded the targeted quateraryl-based *N*-Phth norleucine **28a-(DL)** in 47% yield. Along this line, the Pd-catalyzed Suzuki coupling reaction on norleucine **10c-(DL)** with [1,1′-biphenyl]-4-ylboronic acid gave

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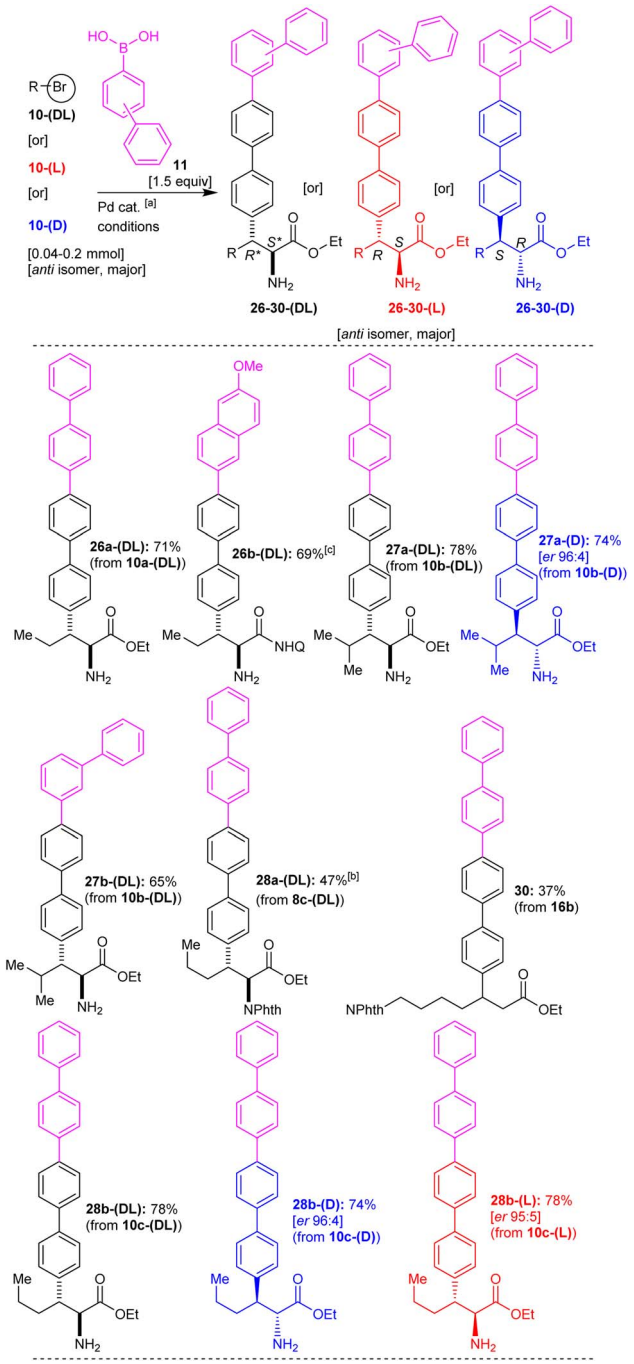
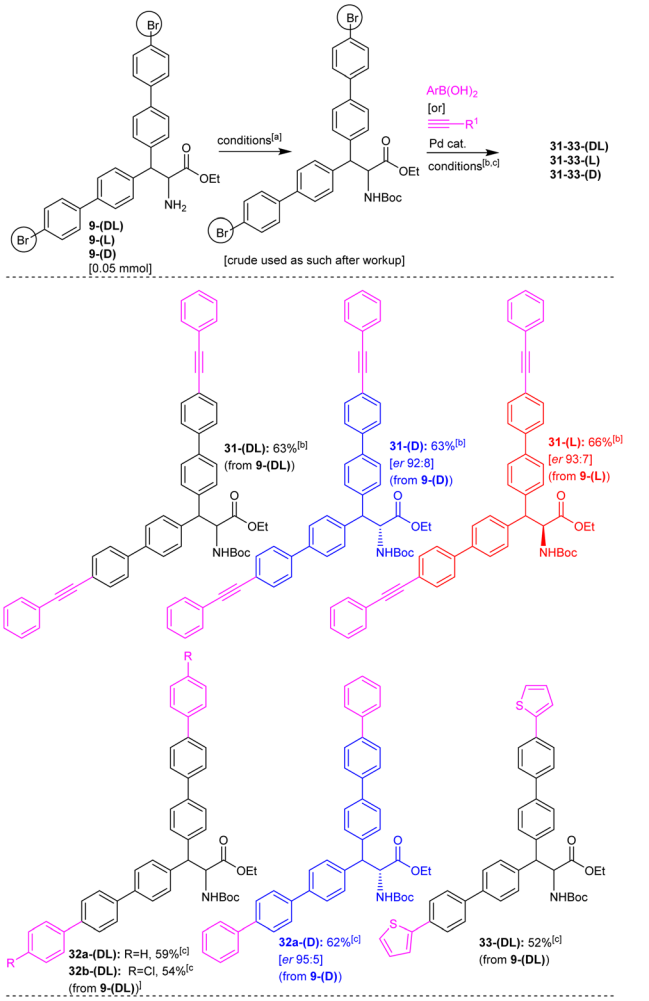


Scheme 12 Construction of quaternaryl-based amino acid derivatives **26–30** *via* the Pd(II)-catalyzed Suzuki coupling reaction. Conditions: (a) $Pd(PPh_3)_4$ (5 mol%), K_2CO_3 (3 equiv.), toluene : EtOH : H_2O (2 : 1 : 1 mL), 110 °C, 24 h, sealed tube (purged with N_2). (b) Compounds **28a-(DL)** and **30** are obtained from **8c-(DL)** and **16b** using reaction conditions, $Pd(OAc)_2$ (10 mol%), P(*o*-tolyl)$_3$ (25 mol%), Et_3N (0.2 mL), MeCN (3 mL), 85 °C, 17 h, sealed tube (purged with N_2). (c) Substrate **26b-(DL)** was obtained from **10aa-(DL)**.[18a]

the targeted quaternaryl-based norleucine **28b-(DL)** in 78% yield. Furthermore, the Pd-catalyzed Suzuki coupling reaction on enantioenriched norleucine **10c-(D)** or **10c-(L)** with [1,1′-biphenyl]-4-ylboronic acid gave the corresponding targeted enantioenriched quaternaryl-based norleucine **28b-(D)** and norleucine **28b-(L)** in 74–78% yields with good enantiopurity (Scheme 12). Additionally, the Pd-catalyzed Suzuki reaction of 7-aminooctanoic acid ester substrate **16b** with [1,1′-biphenyl]-4-ylboronic acid gave the teraryl-based 7-aminooctanoic acid motif **30** in 37% yield (Scheme 12).

Having obtained a series of teraryl- and quaternaryl-based amino acid derivatives, we shifted our attention toward the synthesis of hexaaryl-based amino acids (Scheme 13). Towards this end, we attempted the Sonogashira reaction on the 4-bromobiphenyl moiety present in alanine ethyl ester derivatives **9-(DL)**, **9-(D)**, and **9-(L)**. At first, the free amino group in alanine substrates **9-(DL)**, **9-(D)** and **9-(L)** was protected as *N*-Boc and then, we subjected the *N*-Boc **9-(DL)**, **9-(D)** and **9-(L)** to the Pd-



Scheme 13 Construction of hexaaryl-based alanine derivatives **31–33** *via* the Pd(II)-catalyzed Suzuki and Sonogashira coupling reactions. (a) Substrates **9-(DL)**, **9-(D)** and **9-(L)** were first treated with $(Boc)_2O$ (1.5 equiv.) in $(CH_3)_2CO$: H_2O (0.5 : 9 mL), DCM (2 mL), rt, 12 h, and the crude *N*-Boc compound obtained after workup was used for the next step. (b) Conditions: phenylacetylene (3 equiv.), $Pd(PPh_3)_2Cl_2$ (10 mol%), CuI (5 mol%), Et_3N (0.25 mL), DMF (2 mL), 110 °C, 17 h, sealed tube (purged with N_2). (c) Conditions: boronic acid (3 equiv.), $Pd(PPh_3)_4$ (10 mol%), K_3CO_3 (5 equiv), toluene:EtOH : H_2O (2 : 1:1 mL), 110 °C, 24 h, sealed tube (purged with N_2).

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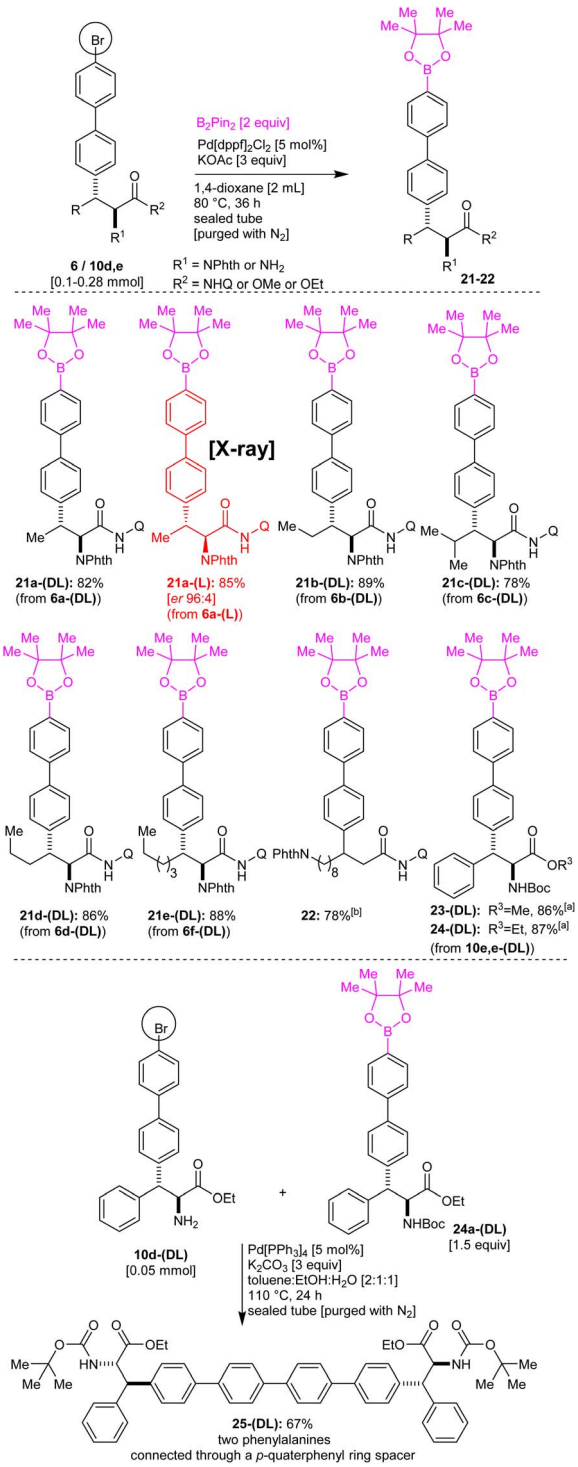
catalyzed Sonogashira reaction conditions. The corresponding *N*-Boc protected alanine **9a-(DL)**, having two 4-bromobiphenyl moieties, was heated with phenylacetylene **17b** in the presence of $Pd(PPh_3)_2Cl_2$, CuI, Et_3N in DMF at 110 °C for 17 h. This reaction afforded the dialkyne-unit incorporated, hexaaryl-based alanine ester derivative **31-(DL)** in 63% yield (Scheme 13). Along this line, the Pd-catalyzed Sonogashira reactions of corresponding *N*-Boc protected, enantioenriched alanines **9-(D)** and **9-(L)** having two 4-bromobiphenyl moieties with phenylacetylene **17b** were carried out. These reactions afforded the dialkyne-unit incorporated, enantioenriched hexaaryl-based alanine derivatives **31-(D)** and **31-(L)** in 63–66% yields with good enantiopurity (Scheme 13). Similarly, the corresponding *N*-Boc protected alanine **9a-(DL)**, having two 4-bromobiphenyl moieties, was subjected to the Pd-catalyzed Suzuki coupling reaction with phenylboronic acid or (4-chlorophenyl)boronic acid or thiophen-2-ylboronic acid. These reactions afforded the corresponding hexaaryl-based alanine ester derivatives **32a-(DL)**, **32b-(DL)**, and **33-(DL)** in 52–59% yields (Scheme 13). Additionally, the *N*-Boc protected enantioenriched alanine **9a-(D)**, having two 4-bromobiphenyl moieties, was subjected to the Pd-catalyzed Suzuki coupling reactions with phenylboronic acid. This reaction gave the targeted enantioenriched hexaaryl-based alanine ester derivative **32a-(D)** in 62% yield with good enantiopurity (Scheme 13).

After performing the cross-coupling reactions on amino acids and the synthesis of teraryl or tetraaryl, or hexaaryl-based amino acids, to expand the synthetic utility and scope of this work, we intended to perform the Miyaura borylation reaction on the 4-bromobiphenyl moiety present in amino acid motifs (Scheme 14). This approach would enable the synthesis of various biaryl-based amino acid motifs possessing boronate ester units, which may be used as coupling partners in the cross-coupling reactions. At the outset, carboxamide of 2-aminobutyric acid containing a 4-bromobiphenyl moiety **6a-(DL)** was subjected to the standard Miyaura borylation conditions involving B_2Pin_2 (2 equiv.) in the presence of $Pd(dppf)_2Cl_2$ and KOAc in 1,4-dioxane at 80 °C for 36 h. This reaction afforded the biaryl-based 2-aminobutyric acid motif possessing boronate ester unit **21a-(DL)** in 82% yield (Scheme 14). Along this line, the enantioenriched carboxamide of 2-aminobutyric acid containing a 4-bromobiphenyl moiety **6a-(L)** was subjected to the Pd-catalyzed reaction with B_2Pin_2. This reaction afforded the enantioenriched biaryl-based 2-aminobutyric acid motif possessing boronate ester unit **21a-(L)** in 85% yield with good enantiopurity (Scheme 14). The structure and *anti*-stereochemistry of the compound **21a-(L)** were confirmed by the X-ray structure analysis (Fig. 2).[21]

Similarly, carboxamides of norvaline **6b-(DL)**, leucine **6c-(DL)**, and norleucine **6d-(DL)** containing a 4-bromobiphenyl moiety were subjected to the Pd-catalyzed reaction with B_2Pin_2. The corresponding norvaline **21b-(DL)**, leucine **21c-(DL)**, and norleucine **21d-(DL)** compounds possessing boronate ester units were obtained in 78–89% yields (Scheme 14). Additionally, carboxamide of 2-aminooctanoic acid **6f-(DL)** and 11-aminoundecanoic acid **16c** containing a 4-bromobiphenyl moiety,[18a] was subjected to the Pd-catalyzed reaction with B_2Pin_2. The corresponding 2-aminooctanoic acid **21e-(DL)**, and 11-aminoundecanoic acid **22** compounds possessing boronate ester unit were obtained in 78–88% yields. Finally, phenylalanines **23-(DL)**



Scheme 14 Construction of biaryl-based amino acid motifs possessing boronate ester unit **21–24** and construction of quateraryl-based amino acid motif **25-(DL)**. (a) Substrate **10d,e-(DL)** were first treated with $(Boc)_2O$ (1.5 equiv.), $(CH_3)_2CO : H_2O$ (0.5 : 9 mL), DCM (2 mL), rt, 12 h, and the corresponding crude compound of *N*-Boc compound obtained after workup was used in the next step. (b) Product **22** was obtained from substrate **16c**.[18a]

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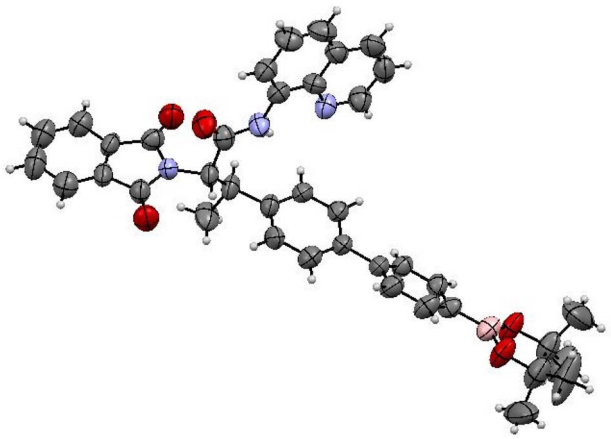


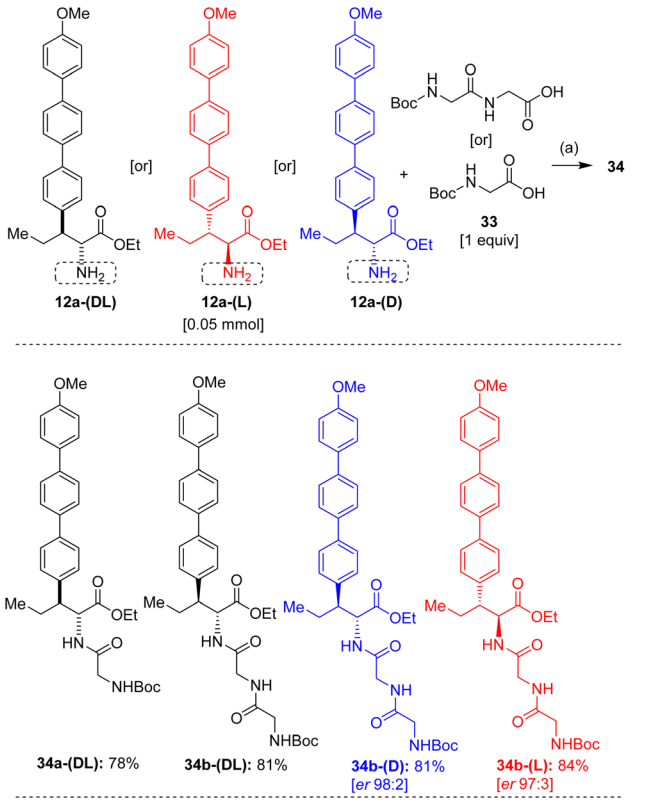
Fig. 2 Single-crystal X-ray structure (ORTEP diagram) of **21a-(L)**.

and **24-(DL)** possessing boronate ester unit were obtained from their corresponding *N*-Boc phenylalanines **10d-(DL)** and **10e-(DL)** containing the 4-bromobiphenyl moiety. Furthermore, to show the utility, the synthesized *N*-Boc phenylalanine **24-(DL)** possessing boronate ester unit was subjected to the Pd-catalyzed Suzuki coupling reaction with *N*-Boc phenylalanine **10d-(DL)** containing the 4-bromobiphenyl moiety. This reaction afforded the quateraryl-based compound **25-(DL)** appended with two phenylalanine units in 67% (Scheme 14).

Having prepared a variety of teraryl-, quarteraryl-, and hexaaryl amino acid scaffolds, we wished to expand the synthetic utility of these compounds by assembling representative examples of teraryl-based peptides (Scheme 15). Initially, we subjected teraryl-based norvaline **12a-(DL)** possessing a free amino group to the standard peptide coupling with *N*-Boc glycine. This reaction afforded the corresponding teraryl-based dipeptide norvaline-Gly **34a-(DL)** in 78% yield (Scheme 15). Similarly, the teraryl-based tripeptide norvaline-Gly-Gly **34b-(DL)** was prepared by treating **12a-(DL)** with *N*-Boc-Gly-Gly-OH under standard peptide coupling conditions (Scheme 15). Furthermore, enantioenriched teraryl-based norvalines **12a-(D)** or **12a-(L)** possessing free amino groups were subjected to peptide coupling with *N*-Boc-Gly-Gly-OH. These reactions afforded the corresponding enantioenriched teraryl-based tripeptides, norvaline-Gly-Gly **34b-(D)** and **34b-(L)** in 81–84% yields (Scheme 15).

We have performed the HPLC analysis of the substrates used and polyaryl-based α-amino acid motifs synthesized in this work (see the ESI†). The HPLC analysis patterns of the racemic unnatural amino acid starting materials **3a-f-(DL)** were determined. Subsequently, enantiopurity of starting material substrates,[18] such as *N*-phthaloyl 8-aminoquinoline carboxamides of alanine **3a-(D)** (*er* 97 : 3), alanine **3a-(L)** (*er* 97 : 3), 2-aminobutyric acid **3b-(L)** (*er* 95 : 5), norvaline **3c-(D)** (*er* 98 : 2), norvaline **3c-(L)** (*er* 98 : 2), leucine **3d-(D)** (*er* 98 : 2), leucine **3d-(L)** (*er* 98 : 2), norleucine **3e-(D)** (*er* 96 : 4), norleucine **3e-(L)** (*er* 96 : 4), phenylalanine **3f-(D)** (*er* 96 : 4), phenylalanine **3f-(L)** (*er* 97 : 3) were ascertained from HPLC analysis.

Next, the HPLC analysis patterns of the racemic 4-bromobiphenyl-based unnatural amino acid motifs including



Scheme 15 Synthetic transformations. Construction of representative examples of teraryl-based peptides. Reaction conditions: (a) EDC-HCl (1.1 equiv.), HOBt (1.1 equiv.), 0 °C to rt, 24 h.

alanine **5-(DL)**, 2-aminobutyric acid **6a-(DL)**, norvaline **6b-(DL)**, leucine **6c-(DL)**, norleucine **6d-(DL)** and phenylalanine **6e-(DL)** were ascertained. Then, the HPLC analysis patterns of the enantioenriched 4-bromobiphenyl-based unnatural amino acid motifs such as alanine **5-(D)**, alanine **5-(L)**, 2-aminobutyric acid **6a-(L)**, norvaline **6b-(D)**, norvaline **6b-(L)**, leucine **6c-(D)**, leucine **6c-(L)**, norleucine **6d-(D)**, norleucine **6d-(L)**, and phenylalanine **6e-(D)** phenylalanine **6e-(L)** were ascertained.

Along this line, the HPLC patterns of 8-aminoquinoline DG-free 4-bromobiphenyl-based amino acid esters such as alanine **7-(DL)**, norvaline **8a-(DL)**, leucine **8b-(DL)**, norleucine **8c-(DL)**, and phenylalanine **8d-(DL)** were obtained. Then, the HPLC analysis of their corresponding enantioenriched 8-aminoquinoline directing group-free 4-bromobiphenyl-based amino acid esters such as alanine **7-(D)**, alanine **7-(L)**, norvaline **8a-(D)**, norvaline **8a-(L)**, leucine **8b-(D)**, leucine **8b-(L)**, norleucine **8c-(D)**, norleucine **8c-(L)**, phenylalanine **8d-(D)** and phenylalanine **8d-(L)** was obtained.

Similarly, the HPLC patterns of 8-aminoquinoline directing group-free and phthalimide group-deprotected 4-bromobiphenyl-based amino acid derivatives such as alanine **9-(DL)**, norvaline **10a-(DL)**, leucine **10b-(DL)**, norleucine **10c-(DL)**, and phenylalanine **10d-(DL)** have been obtained. Subsequently, the HPLC patterns of their corresponding enantioenriched derivatives such as alanine **9-(D)**, alanine **9-(L)**, norvaline **10a-(D)**, norvaline **10a-(L)**, leucine **10b-(D)**, leucine **10b-(L)**,

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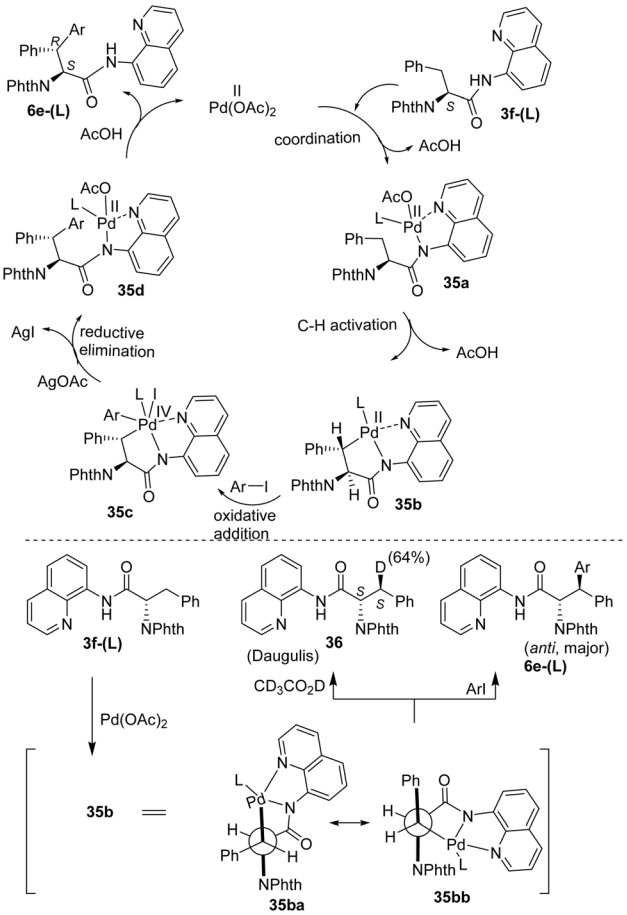
norleucine **10c-(D)**, norleucine **10c-(L)**, phenylalanine **10d-(D)** and phenylalanine **10d-(L)** were also ascertained.

We next established the HPLC analysis patterns of racemic polyaryl-based products such as norvaline **12a-(DL)**, leucine **13a-(DL)**, norleucine **14a-(DL)**, phenylalanine **15a-(DL)**, 2-aminobutyric acid **21a-(DL)**, leucine **27a-(DL)**, norleucine **28b-(DL)**, alanine **31-(DL)** and alanine **32a-(DL)**. Subsequently, we obtained the HPLC analysis of corresponding enantioenriched polyaryl-based products such as norvaline **12a-(D)**, norvaline **12a-(L)**, leucine **13a-(D)**, leucine **13a-(L)**, norleucine **14a-(D)**, norleucine **14a-(L)**, phenylalanine **15a-(D)**, phenylalanine **15a-(L)**, 2-aminobutyric acid **21a-(L)**, leucine **27a-(D)**, norleucine **28b-(D)**, norleucine **28b-(L)**, alanine **31-(D)**, alanine **31-(L)** and alanine **32a-(D)**. Thereafter, the HPLC analysis pattern of tripeptide **34b-(DL)** and enantioenriched tripeptides **34b-(D)** and **34b-(L)** were ascertained.

The structures of all the products obtained in this work were established by their respective NMR spectra and HRMS data. In addition to this, the structure and *anti*-stereochemistry of a representative biaryl-based 2-aminobutyric acid motif possessing boronate ester unit **21a-(L)** was unambiguously ascertained by the single-crystal X-ray structure analysis (Fig. 2). This indirectly indicated Pd(II)-catalyzed 8-aminoquinoline bidentate directing group-aided arylation of prochiral β–C(sp^3)–H bonds of carboxamides of amino acids with 4-bromo-4′-iodo-1,1′-biphenyl is a diastereoselective reaction.[14d,16,18] This process afforded the corresponding amino acid motifs possessing 4-bromobiphenyl as the major diastereomer having the *anti*-stereochemistry (Schemes 3 and 4). This observation is in concurrence with the reported works and the mechanism of the Pd(II)-catalyzed 8-aminoquinoline bidentate directing group-aided arylation of prochiral β–C(sp^3)–H bonds carboxamides is well documented.[15–18]

In concurrence with the mechanism proposed in the literature,[14d,15-18] we divulge that the coordination of the 8-aminoquinoline directing group in the substrate **3f-(L)** to the Pd(II) metal center is followed by concerted metalation deprotonation (CMP), affording the five-membered Pd(II) species **35b**. Oxidative addition of **35b** with an aryl iodide then forms the Pd(IV) species **35c**, which experiences reductive elimination to afford the new C–C bond in intermediate **35d**. Halide abstraction by a halide ion scavenger (*e.g.*, Ag(I) salt) followed by proteolysis of **35d** generated the β–C–H arylated product **6e-(L)** and regenerates the active Pd(II) species in the catalytic cycle (Scheme 16). The formation of an *anti*-isomer as the major compound from the arylation of the prochiral C(sp^3)–H bond of amino acid can be corroborated with the participation of possible conformations **35ba** or **35bb** of the palladacycle intermediate (generated after the β-C–H activation of the corresponding substrate **3f-(L)**). This observation is defended with the Pd(II)-catalyzed 8-aminoquinoline-aided deuteration experiments performed by Daugulis's group.[17m] Daugulis detected[17m] a 64% and less than 10% of deuterium incorporation at the 3S and 3R positions in the product **36**, respectively (Scheme 16). Since the protonation likely transpires with retention of configuration, it is anticipated that **35b** has an *anti*-arrangement of the *N*-Phth and phenyl groups in the conformation **35bb** or Pd and *N*-Phth groups in the conformation **35ba**.[14d] Thus, it was envisioned that the diastereoselectivity of the arylation of substrate **3f-(L)** is established at the palladation step.[17m]



Scheme 16 Proposed mechanism for the diastereoselective C–H functionalization.[14d,15-18]

Literature reports revealed that the π-extended aryl systems, including teraryl-based motifs, have been found to exhibit fluorescent properties and have been used as analytical probes.[5h-l] Preliminary efforts were made to ascertain the UV-Vis absorption spectra (λ_{max} (absorption)) of representative teraryl-, quateraryl-, and hexaaryl-based unnatural amino acid motifs synthesized in this work (Fig. 3, Charts A to F). Further, we have conducted a preliminary examination of fluorescence emission of representative teraryl-, quateraryl-, and hexaaryl-based unnatural amino acid motifs obtained *via* the successive sp^3 C–H arylation and Suzuki coupling method (Fig. 3, Charts G to I). It was noted that teraryl-, quateraryl-, and hexaaryl-based unnatural amino acid motifs exhibit fluorescence. Further, a screening of the fluorescence emission of teraryl-based unnatural amino acid motif **13c-(DL)** and teraryl-based peptide **34a-(DL)** under different concentrations was conducted. Increasing the concentration of the solution of teraryl-based unnatural amino acid/peptide motif did not show any quenching of fluorescence emission. There were no intermolecular interactions, and it was noted that the fluorescence

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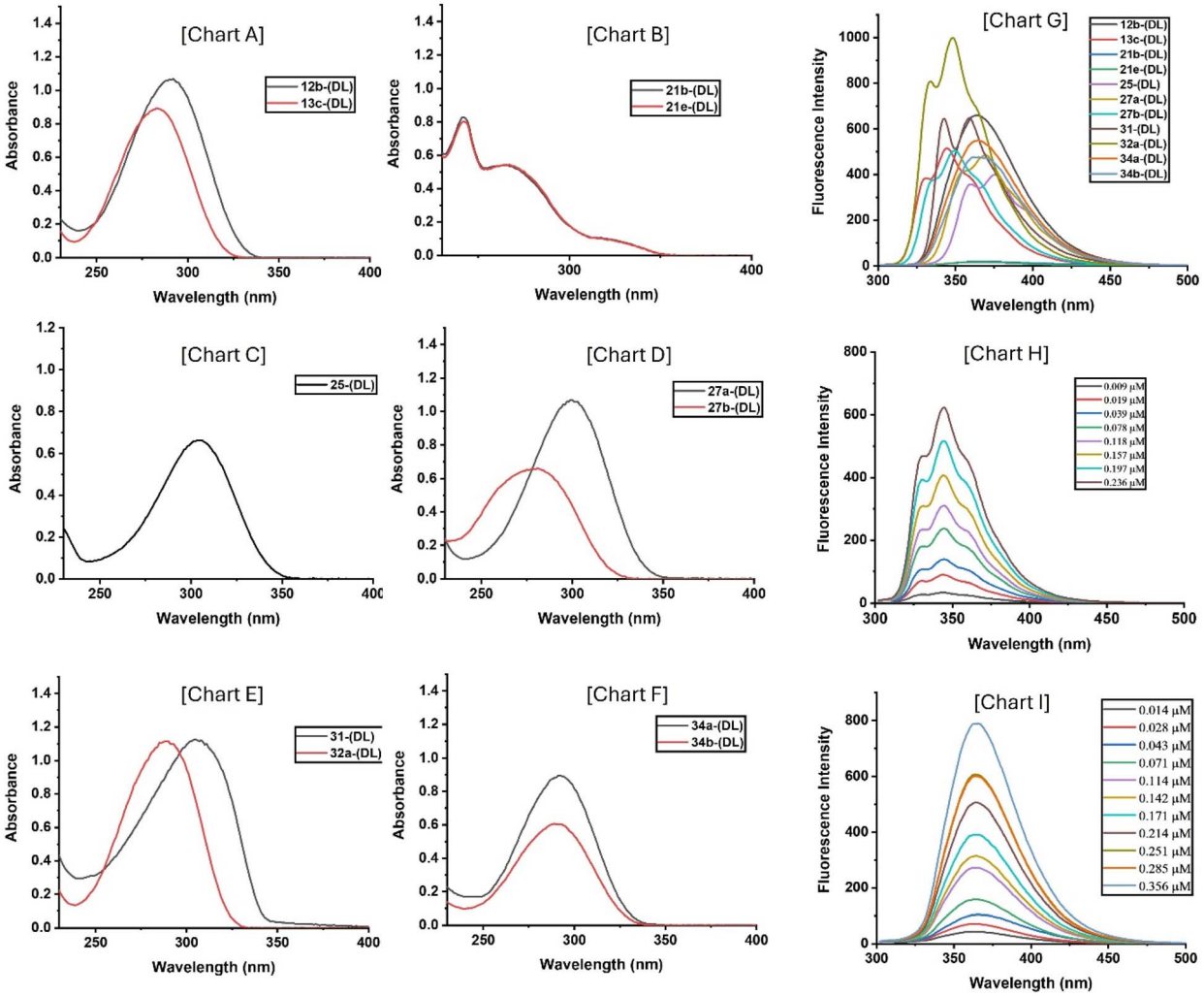

Fig. 3 [Charts A to F]: the UV-Vis absorption spectra of representative examples of teraryl-, quateraryl-hexaaryl unnatural amino acid motifs and teraryl peptides [recorded using concentration = 0.2 mg/10 mL in CH_3CN]. λ_{max} [nm] for the compounds: **12b-(DL)** = 292, **13c-(DL)** = 283, **21b-(DL)** = 240, **21e-(DL)** = 242, **25-(DL)** = 306, **27a-(DL)** = 299, **27b-(DL)** = 281, **31-(DL)** = 306, **32a-(DL)** = 289, **34a-(DL)** = 292, **34b-(DL)** = 289. [Charts G to I]: emission spectra of representative teraryl-, quateraryl-hexaaryl unnatural amino acid motifs and teraryl peptides [recorded using concentration = 0.23 mM in CH_3CN]. [Chart G] = λ_{max} [emission] [nm] at the excitation wavelength of 280 nm = **12b-(DL)**: 364, **13c-(DL)**: 344, **21b-(DL)**: 366, **21e-(DL)**: 361, **25-(DL)**: 376, **27a-(DL)**: 370, **27b-(DL)**: 350, **31-(DL)**: 359, **32a-(DL)**: 348, **34a-(DL)**: 365, **34b-(DL)**: 362. [Chart H] = Emission spectra of teraryl amino acid motif **13c-(DL)** in MeCN at the excitation wavelength of 280 nm with the different concentration of sample solution. [Chart I] = Emission spectra of teraryl peptide motif **34a-(DL)** in MeCN at the excitation wavelength of 280 nm with the different concentration of sample solution.

emission increased when the concentration of the solution **13c-(DL)** or **34a-(DL)** was increased. The potential of fluorescence properties is yet to be investigated and will be reported in the context of future work.

Conclusions

In summary, this work reports the preliminary efforts in generating racemic and enantioenriched teraryl-, quateraryl-, and hexaaryl-based unnatural amino acid motifs. The goal was accomplished *via* the chemo-, diastereoselective Pd(II)-catalyzed bidentate directing group-aided arylation of prochiral β–C(sp^3)–H bonds of carboxamides of amino acids with 4-bromo-4′-iodo-1,1′-biphenyl. As this process generated amino acids possessing the 4-bromobiphenyl units, subsequently, the Suzuki–Miyaura coupling reaction with the 4-bromobiphenyl unit present in amino acids has led to the assembling of teraryl-, quateraryl-, and hexaaryl-based unnatural amino acid motifs. Racemic and enantioenriched polyaryl-based unnatural amino acids comprising norvaline, leucine, norleucine, phenylalanine, 2-aminobutyric acid, 2-aminooctanoic acid, and alanine were synthesized. Pd-catalyzed C–H arylation and Suzuki or Sonogashira, or Heck coupling reactions were used as key steps to accomplish the synthesis of polyaryl-based unnatural amino acid derivatives. We also performed the Miyaura borylation reaction on the 4-bromobiphenyl moiety present in the biaryl-based amino acid motifs, and this process has led to the construction of biaryl-based amino acid motifs possessing

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a boronate ester unit. The substrate scope and generality of the protocol and synthesis of representative examples of teraryl-based peptides were shown. The yields of the C–H arylation, Suzuki coupling reactions affording the polyaryl-based unnatural amino acid derivatives are reasonably good. Accordingly, we believe that this process may be a scalable and practically useful route. It was noted that the representative teraryl-, quateraryl-, and hexaaryl-based unnatural amino acid derivatives synthesized in this work are fluorescent. In the literature, various non-peptidyl teraryl- and quateraryl-based α-helix mimetics have been reported as inhibitors of medicinally relevant protein–protein and protein-nucleic acid interactions. Thus, this work on the construction of teraryl-, quateraryl-, and hexaaryl-based unnatural amino acid motifs *via* the successive sp^3 C–H arylation and Suzuki coupling is a contribution towards strengthening the proteomimetic design and library of oligoaryl-based unnatural amino acids. Further works on establishing the photophysical properties and the application of this method for targeting unnatural amino acid-based α-helix mimetics will be carried out in the future.

Experimental section

General information

The reagents used are commercially available and used without purification. The TLC analyses were performed on silica gel 60 F254 pre-coated plates or preparative alumina TLC plates and visualized by observation under irradiation with a UV lamp or iodine vapor. Column chromatography separation of crude reaction mixtures/samples was conducted on silica gel (100–200 mesh). ^{1}H NMR and $^{13}C\{^1H\}$ NMR spectra were recorded on 400 and ∼101 MHz spectrometers, respectively (with TMS as an internal standard). The HRMS analysis data were obtained from the QTOF mass analyser using the electrospray ionization (ESI) method. The IR spectra were recorded either as neat samples/thin films or by using KBr for preparing pellets for solid samples, or in a solvent. The required anhydrous solvents were prepared under standard solvent drying procedures and reactions were conducted under a nitrogen atmosphere or in ambient air in an RB flask or the sealed tube as mentioned in the respective Schemes/Tables. Organic layers obtained from the work-up procedure were dried using anhydrous Na_2SO_4. Isolated yields of products were reported, and yields have not been optimized. The column chromatographic purification of the crude mixture of all the reactions comprising diastereomer formation gave only the major isomer, and we did not obtain the minor isomer in characterizable/detectable amounts from the fractions collected in the column purification process. In the case of reactions involving enantioenriched carboxamides, there is a minor gain or loss of *er* when compared to the starting substrates, and at this stage, we feel this may be due to handling/sampling error. The starting material amino acid carboxamides used for the construction of racemic and enantioenriched amino acid derivatives possessing a 4-bromobiphenyl moiety in the Pd(II)-catalyzed sp^3 C–H arylation are known compounds and prepared using the standard synthetic procedures[18]

General procedure for the synthesis of 4-bromobiaryl-based amino acid derivatives *via* the Pd(II)-catalyzed, 8-aminoquinoline-aided C–H arylation of amino acid carboxamides

A mixture of an appropriate amino acid carboxamide[18a] (0.25–4.6 mmol, 1 equiv.), 4-bromo-4′-iodobiphenyl (**4**, 4 equiv.), $Pd(OAc)_2$ (10 mol%) and AgOAc (2.5 equiv.) in anhydrous toluene (2–10 mL) was heated at 110 °C for 48 h under a nitrogen atm. After the reaction period, the reaction mixture was concentrated under reduced pressure, and the crude reaction mixture was purified by column chromatography on neutral alumina or silica gel (eluent = EtOAc:hexane) to afford the corresponding bromobiaryl-based amino acid derivatives **5**/**6** (see the corresponding scheme for specific entry).

General procedure for the removal of the 8-aminoquinoline directing group and synthesis of amino acid ester derivatives

A mixture of an appropriate 8-aminoquinoline-based carboxamide (0.10–0.38 mmol, 1 equiv.), $BF_3 \cdot Et_2O$ (15 equiv.), and anhydrous EtOH (3–4 mL) in a screw-capped sealed tube containing a magnetic bead was stirred, and the tube was heated at 130 °C for 36 h. Then, the reaction mixture was allowed to attain the rt and concentrated under reduced pressure to afford the corresponding crude reaction mixture. The crude reaction mixture was then purified by column chromatography to afford the corresponding amino acid ester derivatives **7**/**8** (see the corresponding Scheme for specific entry).

General procedure for the deprotection of phthalimide group and synthesis of Phth-free amino acid derivatives

To an appropriate Phth-protected amino acid derivative (0.2–0.35 mmol, 1 equiv.) in *t*-BuOH (1–3 mL), ethane-1,2-diamine (10 equiv.) was added. The reaction mixture was stirred at rt for 24 h, and then, the solvent was removed under reduced pressure. The resultant reaction mixture was diluted with EtOAc (5–7 mL) and washed with water. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resulting crude reaction mixture was then purified by column chromatography to afford the corresponding Phth-free amino acid derivatives **9**/**10** (see the corresponding scheme for specific entry).

General procedure for the Pd-catalyzed Suzuki–Miyaura cross-coupling reaction of *N*-Boc protected or free amino group-containing amino acid ester derivative

To a mixture of an appropriate free amino group or *N*-Boc protected amino acid derivative possessing 4-bromobiaryl moiety (0.054–0.2 mmol, 1 equiv.), arylboronic acid (1.5–3 equiv.), $Pd(PPh_3)_4$ (5–10 mol%), K_2CO_3 (3–5 equiv.) in toluene : EtOH : H_2O (2 : 1 : 1 mL) was heated at 110 °C for 24 h in a sealed tube (filled with N_2). After the reaction period was over, the crude reaction mixture was concentrated under vacuum and purified by column chromatography on silica gel (EtOAc : hexane) to afford the corresponding Suzuki–Miyaura cross-coupling products (see the corresponding Schemes for specific entry).

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General procedure for the Pd(II)-catalyzed Suzuki–Miyaura and Heck cross-coupling reaction of phthalimide-protected amino acid ester derivative

A solution of phthalimide-protected amino acid derivative possessing 4-bromobiaryl moiety (0.09 mmol, 1 equiv.), arylboronic acid (1.5 equiv.), or ethyl acrylate (1.5 equiv.), $Pd(OAc)_2$ (10 mol%), P(*o*-tolyl)$_3$ (40 mol%), Et_3N (0.2 mL) and CH_3CN (2 mL) were taken in a sealed tube under a nitrogen atm and the tube was then submerged in a silicon oil bath preheated at 85 °C. After 17 h, the reaction mixture was cooled down to rt and the solvent was removed under reduced pressure to provide the crude reaction mixture. Purification of the crude reaction mixture by column chromatography on silica gel (EtOAc/hexane) afforded the corresponding products (see the corresponding Schemes for specific entry).

General procedure for the Sonogashira cross-coupling reaction

A solution of the appropriate amino acid derivative possessing 4-bromobiaryl moiety (0.044–0.09 mmol, 1 equiv.), phenylacetylene (1.5–3 equiv.), Et_3N (0.12–0.25 mL), CuI (3–5 mol%), $Pd(PPh_3)_2Cl_2$ (5–10 mol%) and dry DMF (1–2 mL) was taken in a sealed tube under nitrogen atmosphere. The reaction tube was dipped in a silicon-containing oil bath preheated at 110 °C. After 17 h the reaction mixture was cooled down to rt and the reaction mixture was cooled down to rt and extracted with EtOAc (5–7 mL). The organic layer was washed with brine, dried over anhydrous Na_2SO_4, concentrated, and purified by column chromatography on silica gel (EtOAc/hexanes) to afford the cross-coupled products (see the corresponding Scheme for specific entry).

General procedure Pd-catalysed Miyaura borylation on 4-bromobiphenyl-based biaryl amino acid derivatives

A solution of an appropriate 4-bromobiphenyl-based biaryl amino acid derivative (0.1–0.25 mmol, 1 equiv.) was heated with B_2Pin_2 (2 equiv.) in $Pd(dppf)_2Cl_2$ (5 mol%), KOAc (3 equiv.), 1,4-dioxane (1–3 mL) at 80 °C for 36 h in a sealed tube purged with N_2 atmosphere. After the reaction time was over, the reaction mixture was concentrated and purified by column chromatography on silica gel (EtOAc/hexanes as eluent) to afford the corresponding biaryl amino acid derivative possessing boronate ester moiety (see the corresponding Scheme for specific entry).

3,3-Bis(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)propanamide (5-(DL))

For the data see ref. 18*a* the HPLC of the compound **5-(DL)** was determined using the Daicel Chiralpak IC column, hexane/*i*-PrOH (80 : 20), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 53.19 min, t_L = 63.38 min.

(*R*)-3,3-bis(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)propanamide (5-(D))

The compound **5-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 30 : 70) as a light yellow solid (209 mg, 92%, 0.28 mmol scale); R_f (30% EtOAc/hexane) 0.5; mp: 168–170 °C; IR (DCM): 3025, 1714, 769 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 10.22 (s, 1H), 8.72–8.68 (m, 1H), 8.59 (dd, J_1 = 4.2, J_2 = 1.6 Hz, 1H), 8.06 (dd, J_1 = 8.3, J_2 = 1.5 Hz, 1H), 7.79 (dd, J_1 = 5.4, J_2 = 3.0 Hz, 2H), 7.75 (d, J = 8.3 Hz, 2H), 7.63 (dd, J_1 = 5.4, J_2 = 3.0 Hz, 2H), 7.55–7.40 (m, 12H), 7.34–7.27 (m, 5H), 6.11 (d, J = 12.3 Hz, 1H), 5.82 (d, J = 12.4 Hz, 1H). ^{13}C{^{1}H} NMR (~101 MHz, $CDCl_3$): δ_C 167.9, 165.4, 148.0, 140.1, 139.9, 139.2, 139.1, 138.8, 138.3, 138.2, 135.9, 134.1, 133.8, 131.7, 131.6, 131.3, 128.6, 128.4, 128.3, 128.2, 127.7, 127.6, 127.1, 127.0, 123.4, 121.9, 121.4, 121.4, 116.8, 58.5, 49.6. HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{44}H_{30}Br_2N_3O_3$: 806.0654 found, 806.0653. $[\alpha]^{25}$ D = −40.00 (c = 0.05 g mL^{-1}, $CHCl_3$). The enantiomeric ratio (*er* = >95 : 5) of the compound **5-(D)** was determined by HPLC using the Daicel Chiralpak IC column, hexane/*i*-PrOH (80 : 20), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 54.08 min, t_L = 63.34 min.

(*S*)-3,3-bis(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)propanamide (5-(L))

The compound **5-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 30 : 70) as a light yellow solid (206 mg, 91%, 0.28 mmol scale); R_f (30% EtOAc/hexane) 0.5; mp: 169–171 °C; IR (DCM): 3026, 1713, 770 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 10.18 (s, 1H), 8.68–8.63 (m, 1H), 8.54 (dd, J_1 = 4.2, J_2 = 1.6 Hz, 1H), 8.00 (dd, J_1 = 8.3, J_2 = 1.6 Hz, 1H), 7.74 (dd, J_1 = 5.5, J_2 = 3.0 Hz, 2H), 7.71 (d, J = 8.3 Hz, 2H), 7.57 (dd, J_1 = 5.5, J_2 = 3.0 Hz, 2H), 7.50–7.35 (m, 12H), 7.28–7.22 (m, 5H), 6.07 (d, J = 12.4 Hz, 1H), 5.77 (d, J = 12.4 Hz, 1H). ^{13}C{^{1}H} NMR (~101 MHz, $CDCl_3$): δ_C 167.9, 165.4, 148.0, 140.0, 140.0, 139.2, 139.1, 138.8, 138.3, 138.2, 135.9, 134.1, 133.8, 131.7, 131.6, 131.3, 128.6, 128.4, 128.3, 128.2, 127.7, 127.6, 127.1, 127.0, 123.4, 121.9, 121.4, 121.4, 116.8, 58.5, 49.6. HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{44}H_{30}Br_2N_3O_3$: 806.0654 found, 806.0649. $[\alpha]^{25}$ $_D$ = +37.00 (c = 0.05 g mL^{-1}, $CHCl_3$). The enantiomeric ratio (*er* = 98 : 2) of the compound **5-(L)** was determined by HPLC using the Daicel Chiralpak IC column, hexane/*i*-PrOH (80 : 20), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 53.75 min, t_L = 64.97 min.

(2*S**,3*R**)-3-(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)butanamide (6a-(DL))

The compound **6a-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 30 : 70) as a colorless solid (149 mg, 90%, 0.28 mmol scale); R_f (30% EtOAc/hexane) 0.5; mp: 192–194 °C; IR (DCM): 2971, 1716, 771 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.93 (s, 1H), 8.59 (dd, J_1 = 6.4, J_2 = 2.6 Hz, 1H), 8.51 (dd, J_1 = 4.2, J_2 = 1.5 Hz, 1H), 8.03 (dd, J_1 = 8.3, J_2 = 1.4 Hz, 1H), 7.94 (dd, J_1 = 5.4, J_2 = 3.0 Hz, 2H), 7.77 (dd, J_1 = 5.4, J_2 = 3.1 Hz, 2H), 7.58 (d, J = 8.2 Hz, 2H), 7.52–7.50 (m, 4H), 7.41–7.40 (m, 2H), 7.33–7.26 (m, 3H), 5.33 (d, J = 11.6 Hz, 1H), 4.45–4.37 (m, 1H), 1.35 (d, J = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (~101 MHz, $CDCl_3$): δ_C 168.3, 165.9, 147.9, 142.2, 139.6, 138.8, 138.3, 135.9, 134.3, 133.9, 131.7, 131.7, 128.5, 128.4, 127.6, 127.6, 127.1, 123.7, 121.8, 121.4, 116.7, 61.4, 38.5, 20.3. HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{33}H_{25}BrN_3O_3$: 590.1079 found, 590.1083. The HPLC of the compound **6a-(DL)** was determined using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (90 : 10), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 33.32 min, t_D = 38.36 min.

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(2*S*,3*R*)-3-(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)butanamide (6a-(L))

The compound **6a-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 30 : 70) as a semi-solid (152 mg, 92%, 0.28 mmol scale); R_f (30% EtOAc/hexane) 0.5; mp: 191–193 °C; IR (DCM): 2972, 1716, 771 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.94 (s, 1H), 8.59 (dd, $J_1 = 5.9$, $J_2 = 3.1$ Hz, 1H), 8.51 (dd, $J_1 = 4.2$, $J_2 = 1.5$ Hz, 1H), 8.02 (dd, $J_1 = 8.3$, $J_2 = 1.4$ Hz, 1H), 7.95 (dd, $J_1 = 5.4$, $J_2 = 3.0$ Hz, 2H), 7.75 (dd, $J_1 = 5.4$, $J_2 = 3.0$ Hz, 2H), 7.58 (d, $J = 8.2$ Hz, 2H), 7.49 (d, $J = 8.1$ Hz, 4H), 7.40–7.39 (m, 2H), 7.32–7.5 (m, 3H), 5.33 (d, $J = 11.5$ Hz, 1H), 4.45–4.37 (m, 1H), 1.35 (d, $J = 6.9$ Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.1, 165.7, 147.8, 142.1, 139.3, 138.6, 138.1, 135.8, 134.2, 133.7, 131.6, 131.5, 128.3, 128.2, 127.4, 127.4, 126.9, 123.5, 121.7, 121.3, 121.3, 116.5, 61.2, 38.3, 20.2. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{33}H_{25}BrN_3O_3$: 590.1079 found, 590.1080. $[\alpha]^{25}$ $D = +38.00$ (c = 0.05 g mL^{-1}, $CHCl_3$). The enantiomeric ratio (*er* = 95 : 5) of the compound **6a-(L)** was determined by HPLC using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (90 : 10), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, $t_L = 35.88$ min, $t_D = 42.23$ min.

(2*S,3*R**)-3-(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)pentanamide (6b-(DL))**

For the data see ref. 18*a* The HPLC of the compound **6b-(DL)** was determined using the Daicel Chiralpak IC column, hexane/*i*-PrOH (50 : 50), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, $t_D = 14.93$ min, $t_L = 31.69$ min.

(2*R*,3*S*)-3-(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)pentanamide (6b-(D))

The compound **6b-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 30 : 70) as a light yellow solid (129 mg, 82%, 0.26 mmol scale); R_f (30% EtOAc/hexane) 0.5; mp: 181–183 °C; IR (DCM): 2967, 1713, 770 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.87 (s, 1H), 8.50–8.48 (m, 2H), 7.97 (dd, $J_1 = 8.2$, $J_2 = 1.2$ Hz, 1H), 7.86 (dd, $J_1 = 5.4$, $J_2 = 3.0$ Hz, 2H), 7.70 (dd, $J_1 = 5.4$, $J_2 = 3.0$ Hz, 2H), 7.48–7.42 (m, 6H), 7.35–7.22 (m, 5H), 5.30 (d, $J = 11.7$ Hz, 1H), 4.09 (td, $J_1 = 11.4$, $J_2 = 3.4$ Hz, 1H), 1.76–1.51 (m, 2H), 0.67 (t, $J = 7.3$ Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.1, 165.7, 147.8, 139.6, 139.2, 138.4, 138.0, 135.7, 134.1, 133.7, 131.5, 131.4, 129.0, 128.2, 127.4, 127.2, 126.8, 123.4, 121.6, 121.2, 121.1, 116.4, 60.7, 45.1, 25.9, 11.0; HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{34}H_{26}BrN_3NaO_3$: 626.1055 found, 626.1063. $[\alpha]^{25}{}_D = -39.00$ (c = 0.05 g mL^{-1}, $CHCl_3$). The enantiomeric ratio (*er* 99 : 1) of the compound **6b-(D)** was determined by HPLC using the Daicel Chiralpak IC column, hexane/*i*-PrOH (50 : 50), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, $t_D = 14.95$ min, $t_L = 31.83$ min.

(2*S*,3*R*)-3-(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)pentanamide (6b-(L))

The compound **6b-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 30 : 70) as a light yellow solid (129 mg, 82%, 0.26 mmol scale); R_f (30% EtOAc/hexane) 0.5; mp: 182–184 °C; IR (DCM): 2967, 1714, 769 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.94 (s, 1H), 8.58–8.55 (m, 2H), 8.04 (d, $J = 8.2$ Hz, 1H), 7.94 (dd, $J_1 = 5.4$, $J_2 = 3.0$ Hz, 2H), 7.77 (dd, $J_1 = 5.4$, $J_2 = 3.1$ Hz, 2H), 7.59–7.49 (m, 6H), 7.42–7.29 (m, 5H), 5.37 (d, $J = 11.7$ Hz, 1H), 4.17 (td, $J_1 = 11.4$, $J_2 = 3.6$ Hz, 1H), 1.83–1.57 (m, 2H), 0.74 (t, $J = 7.3$ Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.2, 165.8, 147.9, 139.7, 139.4, 138.6, 138.2, 135.9, 134.2, 133.9, 131.6, 131.6, 129.2, 128.4, 127.5, 127.3, 127.0, 123.6, 121.7, 121.3, 121.3, 116.6, 60.8, 45.2, 26.1, 11.6; HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{34}H_{26}BrN_3NaO_3$: 626.1055 found, 626.1059. $[\alpha]^{25}$ $D = +42.00$ (c = 0.05 g mL^{-1}, $CHCl_3$). The enantiomeric ratio (*er* = >98 : 2) of the compound **6b-(L)** was determined by HPLC using the Daicel Chiralpak IC column, hexane/*i*-PrOH (50 : 50), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, $t_D = 15.03$ min, $t_L = 31.52$ min.

(2*S,3*R**)-3-(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)-4-methyl-*N*-(quinolin-8-yl)pentanamide (6c-(DL))**

For the data see ref. 18*a* the HPLC of the compound **6c-(DL)** was determined using the Daicel Chiralpak IC column, hexane/*i*-PrOH (50 : 50), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, $t_D = 11.68$ min, $t_L = 17.68$ min.

(2*R*,3*S*)3-(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)-4-methyl-*N*-(quinolin-8-yl)pentanamide (6c-(D))

The compound **6c-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 30 : 70) as a colorless solid (148 mg, 96%, 0.25 mmol scale); R_f (30% EtOAc/hexane) 0.5; mp: 233–235 °C; IR (DCM): 2962, 1715, 771 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 10.11 (s, 1H), 8.60–8.56 (m, 2H), 8.04 (dd, $J_1 = 8.3$, $J_2 = 1.6$ Hz, 1H), 7.96 (dd, $J_1 = 5.5$, $J_2 = 3.0$ Hz, 2H), 7.76 (dd, $J_1 = 5.5$, $J_2 = 3.0$ Hz, 2H), 7.57–7.53 (m, 6H), 7.44–7.32 (m, 5H), 5.72 (d, $J = 12.4$ Hz, 1H), 4.35 (dd, $J_1 = 12.4$, $J_2 = 3.4$ Hz, 1H), 2.10–2.03 (m, 1H), 0.90 (d, $J = 6.8$ Hz, 3H), 0.85 (d, $J = 6.8$ Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.4, 166.1, 147.9, 139.5, 138.7, 138.4, 136.2, 135.9, 134.3, 134.1, 131.8, 131.8, 130.6, 128.5, 127.6, 127.0, 126.8, 123.7, 121.8, 121.4, 121.4, 116.8, 57.9, 48.1, 29.0, 21.5, 16.4; HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{35}H_{28}BrN_3NaO_3$: 640.1212 found, 640.1208. $[\alpha]^{25}{}_D = -46.00$ (c = 0.05 g mL^{-1}, $CHCl_3$). The enantiomeric ratio (*er* = 96 : 4) of the compound **6c-(D)** was determined by HPLC using the Daicel Chiralpak IC column, hexane/*i*-PrOH (50 : 50), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, $t_D = 11.25$ min, $t_L = 17.25$ min.

(2*S*,3*R*)-3-(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)-4-methyl-*N*-(quinolin-8-yl)pentanamide (6c-(L))

The compound **6c-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 30 : 70) as a colorless solid (147 mg, 95%, 0.25 mmol scale); R_f (30% EtOAc/hexane) 0.5; mp: 234–236 °C; IR (DCM): 2962, 1715, 771 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 10.09 (s, 1H), 8.57–8.53 (m, 2H), 8.02 (dd, $J_1 = 8.3$, $J_2 = 1.5$ Hz, 1H), 7.93 (dd, $J_1 = 5.4$, $J_2 = 3.0$ Hz, 2H), 7.76 (dd, $J_1 = 5.5$, $J_2 = 3.0$ Hz, 2H), 7.55–7.51 (m, 6H), 7.41–7.29 (m, 5H), 5.70 (d, $J = 12.4$ Hz, 1H), 4.32 (dd, $J_1 = 12.4$, $J_2 =$

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3.5 Hz, 1H), 2.07–2.00 (m, 1H), 0.87 (d, J = 6.9 Hz, 3H), 0.82 (d, J = 6.8 Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.4, 166.1, 147.9, 139.5, 138.6, 138.4, 136.2, 135.9, 134.3, 134.1, 131.8, 131.8, 130.5, 128.5, 127.6, 127.0, 126.8, 123.7, 121.8, 121.4, 121.4, 116.8, 57.9, 48.1, 29.0, 21.5, 16.3; HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{35}H_{29}BrN_3O_3$: 618.1392 found, 618.1404. $[\alpha]^{25}$ D = +49.00 (c = 0.05 g mL^{-1}, $CHCl_3$). The enantiomeric ratio (er = 97 : 3) of the compound **6c-(L)** was determined by HPLC using the Daicel Chiralpak IC column, hexane/*i*-PrOH (50 : 50), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 11.28 min, t_L = 17.16 min.

(2*S**,3*R**)-3-(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)hexanamide (6d-(DL))

For the data see ref. 18*a* the HPLC of the compound **6d-(DL)** was determined using the Daicel Chiralpak IC column, hexane/*i*-PrOH (50 : 50), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 13.38 min, t_L = 28.17 min.

(2*R*,3*S*)-3-(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)hexanamide (6d-(D))

The compound **6d-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 30 : 70) as a colorless solid (117 mg, 76%, 0.25 mmol scale); R_f (30% EtOAc/hexane) 0.5; mp: 187–189 °C; IR (DCM): 2959, 1714, 747 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.90 (s, 1H), 8.57–8.55 (m, 2H), 8.04–8.02 (m, 1H), 7.94 (dd, J_1 = 5.4, J_2 = 3.1 Hz, 2H), 7.77 (dd, J_1 = 5.4, J_2 = 3.1 Hz, 2H), 7.54 (d, J = 8.1 Hz, 2H), 7.50–7.47 (m, 4H), 7.41–7.36 (m, 2H), 7.31–7.26 (m, 3H), 5.34 (d, J = 11.6 Hz, 1H), 4.30–4.24 (m, 1H), 1.68–1.62 (m, 2H), 1.16–1.09 (m, 2H), 0.80 (t, J = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.1, 165.8, 147.8, 140.0, 139.2, 138.4, 138.0, 135.7, 134.1, 133.7, 131.5, 131.4, 129.0, 128.2, 127.4, 127.2, 126.8, 123.5, 121.6, 121.2, 121.2, 116.5, 61.0, 43.4, 35.0, 19.6, 13.7. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{35}H_{29}BrN_3O_3$: 618.1392 found, 618.1389. $[\alpha]^{25}$ D = −52.00 (c = 0.05 g mL^{-1}, $CHCl_3$). The enantiomeric ratio (er = 98 : 2) of the compound **6d-(D)** was determined by HPLC using the Daicel Chiralpak IC column, hexane/*i*-PrOH (50 : 50), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 14.39 min, t_L = 29.52 min.

(2*S*,3*R*)-3-(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)hexanamide (6d-(L))

The compound **6d-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 30 : 70) as a colorless solid (115 mg, 74%, 0.25 mmol scale); R_f (30% EtOAc/hexane) 0.5; mp: 185–187 °C; IR (DCM): 2958, 1714, 770 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.98 (s, 1H), 8.62–8.56 (m, 2H), 8.01–7.99 (m, 1H), 7.93 (dd, J_1 = 5.2, J_2 = 3.1 Hz, 2H), 7.74 (dd, J_1 = 5.4, J_2 = 3.0 Hz, 2H), 7.58 (d, J = 8.2 Hz, 2H), 7.51–7.47 (m, 4H), 7.38–7.37 (m, 2H), 7.31–7.26 (m, 3H), 5.41 (d, J = 11.6 Hz, 1H), 4.37–4.30 (m, 1H), 1.72–1.67 (m, 2H), 1.21–1.11 (m, 2H), 0.83 (t, J = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.2, 165.8, 147.9, 140.0, 139.4, 138.5, 138.1, 135.8, 134.2, 133.8, 131.6, 131.5, 129.0, 128.3, 127.5, 127.3, 126.9, 123.6, 121.7, 121.3, 121.2, 116.6, 61.1, 43.5, 35.0, 19.7, 13.8. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{35}H_{28}BrN_3NaO_3$: 640.1212 found, 640.1203. $[\alpha]^{25}$ D = +49.00 (c = 0.05 g mL^{-1}, $CHCl_3$). The enantiomeric ratio (er = 97 : 3) of the compound **6d-(L)** was determined by HPLC using the Daicel Chiralpak IC column, hexane/*i*-PrOH (50 : 50), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 13.90 min, t_L = 29.31 min.

(2*S**,3*R**)-3-(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)-3-phenyl-*N*-(quinolin-8-yl)propanamide (6e-(DL))

For the data see ref. 18*a* The HPLC of the compound **6e-(DL)** was determined using the Daicel Chiralpak IC column, hexane/*i*-PrOH (40 : 60), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 19.54 min, t_L = 28.87 min.

(2*R*,3*S*)-3-(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)-3-phenyl-*N*-(quinolin-8-yl)propanamide (6e-(D))

The compound **6e-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 30 : 70) as a colorless solid (2270 mg, 76%, 4.6 mmol scale); R_f (30% EtOAc/hexane) 0.5; mp: 233–235 °C; IR (DCM): 2924, 1715, 771 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 10.08 (s, 1H), 8.57 (dd, J_1 = 6.2, J_2 = 2.7 Hz, 1H), 8.49 (dd, J_1 = 4.2, J_2 = 1.4 Hz, 1H), 7.99 (dd, J_1 = 8.2, J_2 = 1.5 Hz, 1H), 7.69 (dd, J_1 = 5.4, J_2 = 3.0 Hz, 2H), 7.61 (d, J = 8.2 Hz, 2H), 7.57 (dd, J_1 = 5.4, J_2 = 3.0 Hz, 2H), 7.50–7.32 (m, 8H), 7.26–7.19 (m, 3H), 7.11 (t, J = 7.6 Hz, 2H), 6.98 (t, J = 7.4 Hz, 1H), 5.94 (d, J = 12.3 Hz, 1H), 5.61 (d, J = 12.3 Hz, 1H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 167.8, 165.5, 148.0, 140.6, 140.2, 139.4, 138.8, 138.4, 136.0, 134.0, 134.0, 131.8, 131.4, 128.7, 128.6, 128.5, 127.8, 127.7, 127.1, 127.0, 123.4, 121.9, 121.5, 121.4, 116.9, 58.5, 50.0. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{38}H_{27}BrN_3O_3$: 652.1236 found, 652.1234. $[\alpha]^{25}$ D = −52.00 (c = 0.05 g mL^{-1}, $CHCl_3$). The enantiomeric ratio (er = 97 : 3) of the compound **6e-(D)** was determined by HPLC using the Daicel Chiralpak IC column, hexane/*i*-PrOH (40 : 60), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 19.76 min, t_L = 29.84 min.

(2*S*,3*R*)-3-(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)-3-phenyl-*N*-(quinolin-8-yl)propanamide (6e-(L))

For the data see ref. 18*a* the enantiomeric ratio (er = 98 : 2) of the compound **6e-(L)** was determined by HPLC using the Daicel Chiralpak IC column, hexane/*i*-PrOH (40 : 60), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 19.86 min, t_L = 29.24 min.

Ethyl 3,3-bis(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)propanoate (7-(DL))

For the data see ref. 18*a* the HPLC of the compound **7-(DL)** was determined using the Daicel Chiralpak IA column, hexane/*i*-PrOH (80 : 20), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 31.48 min, t_D = 38.88 min.

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(*R*)-ethyl 3,3-bis(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)propanoate (7-(D))

The compound **7-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a colorless solid (109 mg, 51%, 0.3 mmol scale); R_f (50% EtOAc/hexane) 0.5; mp: 147–149 °C; IR (DCM): 2925, 1718, 757 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.75 (dd, $J_1 = 5.4$, $J_2 = 3.1$ Hz, 2H), 7.64 (dd, $J_1 = 5.4$, $J_2 = 3.0$ Hz, 2H), 7.59 (d, $J = 8.2$ Hz, 2H), 7.53 (d, $J = 7.9$ Hz, 4H), 7.43 (t, $J = 8.2$ Hz, 4H), 7.37–7.30 (m, 4H), 7.24 (d, $J = 9.0$ Hz, 2H), 5.79 (d, $J = 11.9$ Hz, 1H), 5.37 (d, $J = 11.9$ Hz, 1H), 4.09–4.03 (m, 2H), 1.02 (t, $J = 7.1$ Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.1, 167.4, 141.0, 139.8, 139.5, 139.2, 138.5, 138.3, 134.1, 131.8, 131.7, 131.2, 128.5, 128.4, 128.3, 128.2, 127.2, 127.0, 123.4, 121.4, 121.4, 61.8, 54.9, 50.0, 13.7. HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{37}H_{28}Br_2NO_4$: 708.0385 found, 708.0400. $[\alpha]^{25}$ $D = -102.00$ ($c = 0.05$ g mL^{-1}, $CHCl_3$). The enantiomeric ratio (*er* = 98 : 2) of the compound **7-(D)** was determined by HPLC using the Daicel Chiralpak IA column, hexane/*i*-PrOH (80 : 20), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, $t_L = 32.10$ min, $t_D = 38.46$ min.

(*S*)-Ethyl 3,3-bis(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)propanoate (7-(L))

The compound **7-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a semi-solid (112 mg, 53%, 0.3 mmol scale); R_f (50% EtOAc/hexane) 0.5; mp: 146–148 °C; IR (DCM): 2925, 1714, 752 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.75 (dd, $J_1 = 5.3$, $J_2 = 3.1$ Hz, 2H), 7.64 (dd, $J_1 = 5.3$, $J_2 = 3.0$ Hz, 2H), 7.60 (d, $J = 8.2$ Hz, 2H), 7.53 (d, $J = 7.9$ Hz, 4H), 7.43 (t, $J = 8.1$ Hz, 4H), 7.37–7.30 (m, 4H), 7.24 (d, $J = 8.9$ Hz, 2H), 5.79 (d, $J = 12.0$ Hz, 1H), 5.37 (d, $J = 12.0$ Hz, 1H), 4.09–4.03 (m, 2H), 1.02 (t, $J = 7.1$ Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.1, 167.4, 141.1, 139.9, 139.6, 139.2, 138.5, 138.4, 134.1, 131.8, 131.7, 131.3, 128.5, 128.4, 128.3, 128.2, 127.3, 127.0, 123.5, 121.5, 121.4, 61.8, 54.9, 50.0, 13.8. HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{37}H_{27}Br_2NNaO_4$: 730.0205 found, 730.0193. $[\alpha]^{25}$ $D = +100.00$ ($c = 0.05$ g mL^{-1}, $CHCl_3$). The enantiomeric ratio (*er* = 98 : 2) of the compound **7-(L)** was determined by HPLC using the Daicel Chiralpak IA column, hexane/*i*-PrOH (80 : 20), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, $t_L = 31.95$ min, $t_D = 40.50$ min.

(2*S,3*R**)-ethyl 3-(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)pentanoate (8a-(DL))**

For the data see ref. 18*a* The HPLC of the compound **8a-(DL)** was determined using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (95 : 05), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, $t_D = 15.00$ min, $t_L = 17.36$ min.

(2*R*,3*S*)-ethyl 3-(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)pentanoate (8a-(D))

The compound **8a-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a colorless solid (91 mg, 60%, 0.3 mmol scale); R_f (50% EtOAc/hexane) 0.5; mp: 130–132 °C; IR (DCM): 2932, 1718, 772 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.93 (dd, $J_1 = 5.4$, $J_2 = 3.0$ Hz, 2H), 7.79 (dd, $J_1 = 5.4$, $J_2 = 3.0$ Hz, 2H), 7.57–7.55 (m, 4H), 7.49 (d, $J = 8.5$ Hz, 2H), 7.44 (d, $J = 8.2$ Hz, 2H), 5.17 (d, $J = 10.4$ Hz, 1H), 4.09–3.98 (m, 2H), 3.79 (td, $J_1 = 11.1$, $J_2 = 3.8$ Hz, 1H), 1.71–1.52 (m, 2H), 1.02 (t, $J = 7.1$ Hz, 3H), 0.68 (t, $J = 7.3$ Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.3, 167.6, 141.1, 139.7, 138.2, 134.3, 131.7, 131.5, 129.0, 128.5, 126.7, 123.6, 121.2, 61.4, 56.9, 45.8, 25.3, 13.7, 11.3. HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{27}H_{24}BrNNaO_4$: 528.0786 found, 528.0786. $[\alpha]^{25}$ $D = -30.00$ ($c = 0.05$ g mL^{-1}, $CHCl_3$). The enantiomeric ratio (*er* = 98 : 2) of the compound **8a-(D)** was determined by HPLC using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (95 : 05), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, $t_D = 16.00$ min, $t_L = 18.76$ min.

(2*S*,3*R*)-ethyl 3-(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)pentanoate (8a-(L))

The compound **8a-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 20 : 80) as a colorless solid (90 mg, 59%, 0.3 mmol scale); R_f (20% EtOAc/hexane) 0.5; mp: 131–133 °C; IR (DCM): 2931, 1715, 771 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.92 (dd, $J_1 = 5.4$, $J_2 = 3.0$ Hz, 2H), 7.78 (dd, $J_1 = 5.4$, $J_2 = 3.0$ Hz, 2H), 7.56–7.53 (m, 4H), 7.47 (d, $J = 8.4$ Hz, 2H), 7.42 (d, $J = 8.1$ Hz, 2H), 5.14 (d, $J = 10.4$ Hz, 1H), 4.07–3.94 (m, 2H), 3.76 (td, $J_1 = 11.1$, $J_2 = 3.8$ Hz, 1H), 1.69–1.48 (m, 2H), 1.00 (t, $J = 7.1$ Hz, 3H), 0.67 (t, $J = 7.3$ Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.3, 167.7, 141.1, 139.7, 138.2, 134.3, 131.8, 131.6, 129.1, 128.5, 126.8, 123.6, 121.3, 61.4, 56.9, 45.8, 25.4, 13.7, 11.4. HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{27}H_{24}BrNNaO_4$: 528.0786 found, 528.0779. $[\alpha]^{25}$ $D = +33.00$ ($c = 0.05$ g mL^{-1}, $CHCl_3$). The enantiomeric ratio (*er* = 98 : 2) of the compound **8a-(L)** was determined by HPLC using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (95 : 05), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, $t_D = 16.41$ min, $t_L = 18.80$ min.

(2*S,3*R**)-ethyl 3-(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)-4-methylpentanoate (8b-(DL))**

The compound **8b-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 20 : 80) as a colorless solid (28 mg, 54%, 0.1 mmol scale); R_f (20% EtOAc/hexane) 0.5; mp: 150–152 °C; IR (DCM): 2926, 1714, 771 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.92 (dd, $J_1 = 5.4$, $J_2 = 3.0$ Hz, 2H), 7.78 (dd, $J_1 = 5.5$, $J_2 = 3.0$ Hz, 2H), 7.56–7.47 (m, 6H), 7.38 (d, $J = 8.2$ Hz, 2H), 5.42 (d, $J = 11.7$ Hz, 1H), 4.00–3.88 (m, 3H), 1.95–1.87 (m, 1H), 0.91 (t, $J = 7.1$ Hz, 3H), 0.80 (d, $J = 2.8$ Hz, 3H), 0.79 (d, $J = 2.8$ Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.5, 167.8, 139.7, 138.1, 137.7, 134.3, 131.8, 131.6, 130.2, 128.5, 126.1, 123.6, 121.3, 61.4, 54.4, 48.7, 28.6, 21.5, 16.7, 13.6. HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{28}H_{26}BrNNaO_4$: 542.0943 found, 542.0942. The HPLC of the compound **8b-(DL)** was determined using the Daicel Chiralpak AD column, hexane/*i*-PrOH (70 : 30), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, $t_L = 10.63$ min, $t_D = 15.62$ min.

(2*R*, 3*S*)-ethyl 3-(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)-4-methylpentanoate (8b-(D))

The compound **8b-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 20 : 80)

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as a colorless solid (29 mg, 56%, 0.1 mmol scale); R_f (20% EtOAc/hexane) 0.5; mp: 153–155 °C; IR (DCM): 2927, 1715, 770 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.94 (dd, $J_1 = 5.4, J_2 = 3.1$ Hz, 2H), 7.80 (dd, $J_1 = 5.4, J_2 = 3.0$ Hz, 2H), 7.58–7.49 (m, 6H), 7.40 (d, $J = 8.2$ Hz, 2H), 5.44 (d, $J = 11.7$ Hz, 1H), 3.99–3.93 (m, 3H), 1.97–1.90 (m, 1H), 0.93 (t, $J = 7.1$ Hz, 3H), 0.82 (d, $J = 3.0$ Hz, 3H), 0.80 (d, $J = 3.0$ Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.5, 167.8, 139.7, 138.1, 137.7, 134.3, 131.8, 131.7, 130.2, 128.5, 126.1, 123.6, 121.3, 61.4, 54.5, 48.7, 28.6, 21.5, 16.7, 13.6. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{28}H_{26}BrNNaO_4$: 542.0943 found, 542.0939. $[\alpha]^{25}$ $D = -20.00$ ($c = 0.05$ g mL^{-1}, $CHCl_3$). The enantiomeric ratio ($er = >95:5$) of the compound **8b-(D)** was determined by HPLC using the Daicel Chiralpak AD column, hexane/*i*-PrOH (70 : 30), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, $t_L = 10.36$ min, $t_D = 15.56$ min.

(2*S*,3*R*)-ethyl 3-(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)-4-methylpentanoate (8b-(L))

The compound **8b-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 20 : 80) as a colorless solid (28 mg, 53%, 0.1 mmol scale); R_f (20% EtOAc/hexane) 0.5; mp: 151–153 °C; IR (DCM): 2926, 1714, 771 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.84 (dd, $J_1 = 5.4, J_2 = 3.0$ Hz, 2H), 7.70 (dd, $J_1 = 5.4, J_2 = 3.0$ Hz, 2H), 7.48–7.39 (m, 6H), 7.30 (d, $J = 8.1$ Hz, 2H), 5.34 (d, $J = 11.7$ Hz, 1H), 3.88–3.83 (m, 3H), 1.87–1.79 (m, 1H), 0.83 (t, $J = 7.1$ Hz, 3H), 0.72 (d, $J = 2.7$ Hz, 3H), 0.70 (d, $J = 2.6$ Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.5, 167.8, 139.7, 138.1, 137.7, 134.3, 131.8, 131.7, 130.2, 128.5, 126.1, 123.6, 121.3, 61.4, 54.5, 48.7, 28.6, 21.5, 16.8, 13.6. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{28}H_{26}BrNNaO_4$: 542.0943 found, 542.0941. $[\alpha]^{25}$ $D = +18.00$ ($c = 0.05$ g mL^{-1}, $CHCl_3$). The enantiomeric ratio ($er = 98:2$) of the compound **8b-(L)** was determined by HPLC using the Daicel Chiralpak AD column, hexane/*i*-PrOH (70 : 30), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, $t_L = 10.68$ min, $t_D = 15.75$ min.

(2*S**,3*R**)-ethyl 3-(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)hexanoate (8c-(DL))

For the data see ref. 18*a* the HPLC of the compound **8c-(DL)** was determined using the Daicel Chiralpak AD column, hexane/*i*-PrOH (90 : 10), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, $t_L = 16.81$ min, $t_D = 21.55$ min.

(2*R*,3*S*)-ethyl 3-(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)hexanoate (8c-(D))

The compound **8c-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 20 : 80) as a colorless solid (93 mg, 58%, 0.31 mmol scale); R_f (20% EtOAc/hexane) 0.5; mp: 131–133 °C; IR (DCM): 2932, 1716, 772 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.92 (dd, $J_1 = 5.4, J_2 = 3.0$ Hz, 2H), 7.78 (dd, $J_1 = 5.5, J_2 = 3.0$ Hz, 2H), 7.56–7.41 (m, 8H), 5.11 (d, $J = 10.4$ Hz, 1H), 4.06–3.93 (m, 2H), 3.87 (td, $J_1 = 11.0, J_2 = 4.2$ Hz, 1H), 1.67–1.43 (m, 2H), 1.08–1.02 (m, 2H), 1.00 (t, $J = 7.1$ Hz, 3H), 0.75 (t, $J = 7.4$ Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.4, 167.7, 141.4, 139.7, 138.2, 134.3, 131.8, 131.6, 129.0, 128.5, 126.8, 123.7, 121.3, 61.5, 57.1, 44.0, 34.4, 19.9, 13.8, 13.8. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{28}H_{26}BrNNaO_4$: 542.0943 found, 542.0947.$[\alpha]^{25}$ $D = -45.00$ ($c = 0.05$ g mL^{-1}, $CHCl_3$). The enantiomeric ratio ($er = 97:3$) of the compound **8c-(D)** was determined by HPLC using the Daicel Chiralpak AD column, hexane/*i*-PrOH (90 : 10), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, $t_L = 17.14$ min, $t_D = 22.03$ min.

(2*S*,3*R*)-ethyl 3-(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)hexanoate (8c-(L))

The compound **8c-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 20 : 80) as a colorless solid (90 mg, 56%, 0.31 mmol scale); R_f (20% EtOAc/hexane) 0.5; mp: 133–135 °C; IR (DCM): 2932, 1716, 772 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.92 (dd, $J_1 = 5.4, J_2 = 3.0$ Hz, 2H), 7.79 (dd, $J_1 = 5.5, J_2 = 3.0$ Hz, 2H), 7.56–7.41 (m, 8H), 5.11 (d, $J = 10.4$ Hz, 1H), 4.06–3.93 (m, 2H), 3.87 (td, $J_1 = 11.0, J_2 = 4.2$ Hz, 1H), 1.64–1.43 (m, 2H), 1.09–1.04 (m, 2H), 1.00 (t, $J = 7.1$ Hz, 3H), 0.75 (t, $J = 7.4$ Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.4, 167.7, 141.4, 139.7, 138.2, 134.3, 131.8, 131.6, 129.0, 128.5, 126.8, 123.7, 121.3, 61.5, 57.1, 44.0, 34.4, 19.9, 13.8, 13.8. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{28}H_{26}BrNNaO_4$: 542.0943 found, 542.0937. $[\alpha]^{25}$ $D = +42.00$ ($c = 0.05$ g mL^{-1}, $CHCl_3$). The enantiomeric ratio ($er = 97:3$) of the compound **8c-(L)** was determined by HPLC using the Daicel Chiralpak AD column, hexane/*i*-PrOH (90 : 10), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, $t_L = 16.91$ min, $t_D = 21.92$ min.

(2*S**,3*R**)-ethyl 3-(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)-3-phenylpropanoate (8d-(DL))

For the data see ref. 18*a* the HPLC of the compound **8d-(DL)** was determined using the Daicel Chiralcel IC column, hexane/*i*-PrOH (50 : 50), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, $t_D = 9.37$ min, $t_L = 11.48$ min.

(2*R*,3*S*)-ethyl 3-(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)-3-phenylpropanoate (8d-(D))

The compound **8d-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 20 : 80) as a colorless solid (123 mg, 58%, 0.38 mmol scale); R_f (20% EtOAc/hexane) 0.5; mp: 168–170 °C; IR (DCM): 2930, 1715, 770 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.74 (dd, $J_1 = 5.4, J_2 = 3.1$ Hz, 2H), 7.64 (dd, $J_1 = 5.5, J_2 = 3.1$ Hz, 2H), 7.58–7.50 (m, 6H), 7.42 (d, $J = 8.4$ Hz, 2H), 7.29–7.26 (m, 2H), 7.11 (t, $J = 7.7$ Hz, 2H), 7.00 (t, $J = 7.4$ Hz, 1H), 5.76 (d, $J = 13.5$ Hz, 1H), 5.31 (d, $J = 11.8$ Hz, 1H), 4.10–4.02 (m, 2H), 1.02 (t, $J = 7.1$ Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.1, 167.2, 141.1, 140.2, 139.4, 138.2, 134.0, 131.7, 131.1, 128.5, 128.4, 128.1, 127.8, 127.0, 126.9, 123.2, 121.3, 61.6, 54.8, 50.2, 13.7. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{31}H_{24}BrNNaO_4$: 576.0786 found, 576.0789. $[\alpha]^{25}{}_D = -38.00$ ($c = 0.05$ g mL^{-1}, $CHCl_3$). The enantiomeric ratio ($er = 97:3$) of the compound **8d-(D)** was determined by HPLC using the Daicel Chiralcel IC column, hexane/*i*-PrOH (50 : 50), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, $t_D = 10.46$ min, $t_L = 13.00$ min.

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(2*S*,3*R*)-ethyl 3-(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)-3-phenylpropanoate (8d-(L))

For the data see ref. 18*a* the enantiomeric ratio (*er* = 97 : 3) of the compound **8d-(L)** was determined by HPLC using the Daicel Chiralcel IC column, hexane/*i*-PrOH (50 : 50), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 10.93 min, t_L = 13.16 min.

(2*S,3R*)-methyl 3-(4′-bromo-[1,1′-biphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)-3-phenylpropanoate (8e-(DL))**

The compound **8e-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 20 : 80) as a colorless semi-solid (123 mg, 60%, 0.38 mmol scale); R_f (20% EtOAc/hexane) 0.5; IR (DCM): 2925, 1715, 755 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.74 (dd, J_1 = 5.5, J_2 = 3.1 Hz, 2H), 7.65 (dd, J_1 = 5.4, J_2 = 3.1 Hz, 2H), 7.58–7.51 (m, 6H), 7.42 (d, J = 8.5 Hz, 2H), 7.27–7.26 (m, 2H), 7.11 (t, J = 7.7 Hz, 2H), 7.00 (t, J = 7.4 Hz, 1H), 5.78 (d, J = 11.9 Hz, 1H), 5.30 (d, J = 11.8 Hz, 1H), 3.61 (s, 3H). ^{13}C{^{1}H} NMR (~101 MHz, $CDCl_3$): δ_C 168.6, 167.2, 141.1, 140.1, 139.6, 138.4, 134.1, 131.8, 131.2, 128.6, 128.2, 127.9, 127.2, 127.0, 123.4, 121.4, 54.6, 52.7, 50.3. HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{30}H_{22}BrNNaO_4$: 562.0630 found, 562.0615.

Ethyl 2-amino-3,3-bis(4′-bromo-[1,1′-biphenyl]-4-yl) propanoate (9-(DL))

The compound **9-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a semi-solid (90 mg, 78%, 0.2 mmol scale); R_f (50% EtOAc/hexane) 0.5; IR (DCM): 2926, 1730, 771 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.53–7.23 (m, 16H), 4.32 (d, J = 8.8 Hz, 1H), 4.26 (d, J = 8.8 Hz, 1H), 3.99 (q, J = 7.1 Hz, 2H), 1.01 (t, J = 7.1 Hz, 3H). (the NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). ^{13}C{^{1}H} NMR (~101 MHz, $CDCl_3$): δ_C 174.3, 140.7, 139.8, 139.4, 139.4, 138.6, 138.4, 131.8, 129.1, 128.7, 128.5, 128.4, 127.2, 126.9, 121.4, 121.4, 60.8, 58.6, 55.6, 13.8. HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{29}H_{26}Br_2NO_2$: 578.0330 found, 578.0344. The HPLC of the compound **9-(DL)** was determined using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (90 : 10), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 17.23 min, t_L = 22.43 min.

(*R*)-ethyl 2-amino-3,3-bis(4′-bromo-[1,1′-biphenyl]-4-yl) propanoate (9-(D))

The compound **9-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a semi-solid (94 mg, 81%, 0.2 mmol scale); R_f (50% EtOAc/hexane) 0.5; IR (DCM): 2928, 1732, 772 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.54–7.38 (m, 16H), 4.32 (d, J = 8.7 Hz, 1H), 4.27 (d, J = 8.8 Hz, 1H), 4.01 (q, J = 7.1 Hz, 2H), 1.02 (t, J = 7.2 Hz, 3H). (the NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). ^{13}C{^{1}H} NMR (~101 MHz, $CDCl_3$): δ_C 174.3, 140.7, 139.9, 139.5, 139.4, 138.7, 138.4, 131.8, 129.2, 128.7, 128.5, 128.5, 127.3, 127.0, 121.5, 121.5, 60.9, 58.6, 55.7, 13.8. HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{29}H_{26}Br_2NO_2$: 578.0330 found, 578.0334. $[\alpha]^{25}$ D = −40.00 (c = 0.05 g mL^{-1}, $CHCl_3$). The enantiomeric ratio (*er* = 95 : 5) of the compound **9-(D)** was determined by HPLC using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (90 : 10), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 18.37 min, t_L = 22.53 min.

(*S*)-ethyl 2-amino-3,3-bis(4′-bromo-[1,1′-biphenyl]-4-yl) propanoate (9-(L))

The compound **9-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a semi-solid (91 mg, 79%, 0.2 mmol scale); R_f (50% EtOAc/hexane) 0.5; IR (DCM): 2927, 1730, 752 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.58–7.42 (m, 16H), 4.35 (d, J = 8.9 Hz, 1H), 4.30 (d, J = 8.8 Hz, 1H), 4.04 (q, J = 7.1 Hz, 2H), 1.05 (t, J = 7.1 Hz, 3H). (The NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). ^{13}C{^{1}H} NMR (~101 MHz, $CDCl_3$): δ_C 174.3, 140.7, 139.9, 139.5, 139.5, 138.7, 138.5, 131.8, 129.2, 128.8, 128.5, 128.5, 127.3, 127.0, 121.5, 121.5, 60.9, 58.6, 55.7, 13.8. HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{29}H_{26}Br_2NO_2$: 578.0330 found, 578.0329. $[\alpha]^{25}$ D = +45.00 (c = 0.05 g mL^{-1}, $CHCl_3$). The enantiomeric ratio (*er* = 95 : 5) of the compound **9-(L)** was determined by HPLC using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (90 : 10), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 18.96 min, t_L = 22.92 min.

(2*S,3*R**)-ethyl 2-amino-3-(4′-bromo-[1,1′-biphenyl]-4-yl) pentanoate (10a-(DL))**

The compound **10a-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a semi-solid (85 mg, 81%, 0.28 mmol scale); R_f (50% EtOAc/hexane) 0.5; IR (DCM): 2927, 1719, 772 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.56–7.43 (m, 6H), 7.29–7.26 (m, 2H), 4.09–3.98 (m, 2H), 3.59 (d, J = 6.3 Hz, 1H), 2.89–2.83 (m, 1H), 1.98–1.73 (m, 2H), 1.10 (t, J = 7.2 Hz, 3H), 0.83 (t, J = 7.4 Hz, 3H). (the NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). ^{13}C{^{1}H} NMR (~101 MHz, $CDCl_3$): δ_C 174.8, 140.6, 139.8, 138.4, 131.8, 129.1, 128.5, 126.8, 121.4, 60.7, 59.9, 51.7, 23.2, 14.0, 12.2. HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{23}BrNO_2$: 376.0912 found, 376.0903. The HPLC of the compound **10a-(DL)** was determined using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (90 : 10), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 6.66 min, t_D = 8.14 min.

(2*R*,3*S*)-ethyl 2-amino-3-(4′-bromo-[1,1′-biphenyl]-4-yl) pentanoate (10a-(D))

The compound **10a-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a semi-solid (86 mg, 82%, 0.28 mmol scale); R_f (50% EtOAc/hexane) 0.5; IR (DCM): 2927, 1719, 772 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.49–7.36 (m, 6H), 7.22–7.19 (m, 2H), 3.99–3.94 (m, 2H), 3.53 (d, J = 6.2 Hz, 1H), 2.82–2.77 (m, 1H), 1.89–1.70 (m, 2H), 1.03 (t, J = 7.1 Hz, 3H), 0.76 (t, J = 7.4 Hz, 3H). (the NH_2 signal could not be clearly assigned in the proton NMR

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spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 174.8, 140.5, 139.8, 138.4, 131.8, 129.1, 128.5, 126.7, 121.3, 60.7, 59.9, 51.7, 23.2, 14.0, 12.2. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{19}H_{23}BrNO_2$: 376.0912 found, 376.0919. $[\alpha]^{25}$ $D = -13.00$ ($c = 0.05$ g mL^{-1}, $CHCl_3$). The enantiomeric ratio (er = 98 : 2) of the compound **10a-(D)** was determined by HPLC using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (90 : 10), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 6.70 min, t_D = 7.79 min.

(2*S*,3*R*)-ethyl 2-amino-3-(4′-bromo-[1,1′-biphenyl]-4-yl) pentanoate (10a-(L))

The compound **10a-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a semi-solid (84 mg, 80%, 0.28 mmol scale); R_f (50% EtOAc/hexane) 0.5; IR (DCM): 2927, 1719, 772 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.55–7.42 (m, 6H), 7.28–7.26 (m, 2H), 4.09–3.97 (m, 2H), 3.59 (d, J = 6.3 Hz, 1H), 2.88–2.83 (m, 1H), 1.96–1.74 (m, 2H), 1.09 (t, J = 7.2 Hz, 3H), 0.82 (t, J = 7.4 Hz, 3H). (The NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 174.7, 140.5, 139.7, 138.3, 131.7, 129.0, 128.4, 126.7, 121.3, 60.6, 59.8, 51.7, 23.1, 13.9, 12.1. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{19}H_{23}BrNO_2$: 376.0912 found, 376.0923. $[\alpha]^{25}$ D = +10.00 ($c = 0.05$ g mL^{-1}, $CHCl_3$). The enantiomeric ratio (er = 98 : 2) of the compound **10a-(L)** was determined by HPLC using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (90 : 10), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 7.07 min, t_D = 8.13 min.

(2*S**,3*R**)-ethyl 2-amino-3-(4′-bromo-[1,1′-biphenyl]-4-yl)-4-methylpentanoate (10b-(DL))

The compound **10b-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a semi-solid (100 mg, 80%, 0.32 mmol scale); R_f (50% EtOAc/hexane) 0.5; IR (DCM): 2924, 1732, 772 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.55–7.43 (m, 6H), 7.20 (d, J = 8.2 Hz, 2H), 4.12–3.99 (m, 2H), 3.84 (d, J = 6.6 Hz, 1H), 2.72–2.68 (m, 1H), 2.45–2.37 (m, 1H), 1.13 (t, J = 7.2 Hz, 3H), 1.05 (d, J = 6.6 Hz, 3H), 0.79 (d, J = 6.7 Hz, 3H). (the NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 175.1, 139.7, 139.2, 138.2, 131.7, 129.8, 128.4, 126.3, 121.3, 60.5, 57.1, 56.5, 28.1, 21.4, 20.0, 13.9. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{20}H_{25}BrNO_2$: 390.1069 found, 390.1062. The HPLC of the compound **10b-(DL)** was determined using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (95 : 05), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 8.61 min, t_D = 11.40 min.

(2*R*,3*S*)-ethyl 2-amino-3-(4′-bromo-[1,1′-biphenyl]-4-yl)-4-methylpentanoate (10b-(D))

The compound **10b-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a semi-solid (102 mg, 82%, 0.32 mmol scale); R_f (50% EtOAc/hexane) 0.5; IR (DCM): 2924, 1732, 771 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.55–7.43 (m, 6H), 7.20 (d, J = 8.2 Hz, 2H), 4.11–4.00 (m, 2H), 3.86 (d, J = 6.5 Hz, 1H), 2.72–2.69 (m, 1H), 2.45–2.37 (m, 1H), 1.13 (t, J = 7.2 Hz, 3H), 1.05 (d, J = 6.6 Hz, 3H), 0.79 (d, J = 6.7 Hz, 3H). (The NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 175.0, 139.7, 139.2, 138.3, 131.8, 129.9, 128.5, 126.4, 121.3, 60.7, 57.1, 56.5, 28.2, 21.5, 20.1, 14.0. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{20}H_{25}BrNO_2$: 390.1069 found, 390.1065. $[\alpha]^{25}$ D = −38.00 ($c = 0.05$ g mL^{-1}, $CHCl_3$). The enantiomeric ratio (er = 98 : 2) of the compound **10b-(D)** was determined by HPLC using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (95 : 05), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 9.85 min, t_D = 12.71 min.

(2*S*,3*R*)-ethyl 2-amino-3-(4′-bromo-[1,1′-biphenyl]-4-yl)-4-methylpentanoate (10b-(L))

The compound **10b-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a semi-solid (104 mg, 83%, 0.32 mmol scale); R_f (50% EtOAc/hexane) 0.5; IR (DCM): 2924, 1732, 772 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.55–7.43 (m, 6H), 7.20 (d, J = 8.2 Hz, 2H), 4.11–4.01 (m, 2H), 3.85 (d, J = 6.6 Hz, 1H), 2.72–2.68 (m, 1H), 2.45–2.37 (m, 1H), 1.12 (t, J = 7.2 Hz, 3H), 1.04 (d, J = 6.6 Hz, 3H), 0.79 (d, J = 6.7 Hz, 3H). (The NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 175.1, 139.7, 139.2, 138.2, 131.8, 129.8, 128.5, 126.3, 121.3, 60.6, 57.1, 56.5, 28.2, 21.4, 20.0, 14.0. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{20}H_{25}BrNO_2$: 390.1069 found, 390.1060. $[\alpha]^{25}$ D = +40.00 ($c = 0.05$ g mL^{-1}, $CHCl_3$). The enantiomeric ratio (er = 90 : 10)* of the compound **10b-(L)** was determined by HPLC using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (95 : 05), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 9.76 min, t_D = 12.70 min. (*Ascertained using best peak integration. The peaks could not be clearly resolved).

(2*R**,3*S**)-ethyl 2-amino-3-(4′-bromo-[1,1′-biphenyl]-4-yl)-4-ylhexanoate (10c-(DL))

The compound **10c-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a semi-solid (100 mg, 74%, 0.35 mmol scale); R_f (50% EtOAc/hexane) 0.5; IR (DCM): 2930, 1729, 752 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.55–7.42 (m, 6H), 7.29–7.23 (m, 2H), 4.09–3.98 (m, 2H), 3.57 (d, J = 6.3 Hz, 1H), 3.00–2.94 (m, 1H), 1.82–1.76 (m, 2H), 1.30–1.14 (m, 2H), 1.10 (t, J = 7.2 Hz, 3H), 0.88 (t, J = 7.4 Hz, 3H). (The NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 174.8, 140.9, 139.7, 138.3, 131.8, 129.0, 128.5, 126.7, 121.3, 60.6, 60.0, 49.5, 32.2, 20.5, 14.0. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{20}H_{25}BrNO_2$: 390.1069 found, 390.1058. The HPLC of the compound **10c-(DL)** was determined using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (95 : 05), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 12.53 min, t_D = 14.10 min.

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(2*R*,3*S*)-ethyl 2-amino-3-(4′-bromo-[1,1′-biphenyl]-4-yl)-4-ylhexanoate (10c-(D))

The compound **10c-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a semi-solid (102 mg, 75%, 0.35 mmol scale); R_f (50% EtOAc/hexane) 0.5; IR (DCM): 2930, 1729, 751 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.56–7.42 (m, 6H), 7.29–7.26 (m, 2H), 4.09–4.00 (m, 2H), 3.62 (d, J = 6.2 Hz, 1H), 3.03–2.98 (m, 1H), 1.83–1.78 (m, 2H), 1.33–1.14 (m, 2H), 1.11 (t, J = 7.1 Hz, 3H), 0.88 (t, J = 7.3 Hz, 3H). (The NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 174.7, 140.8, 139.8, 138.4, 131.8, 129.0, 128.5, 126.7, 121.4, 60.7, 60.1, 49.5, 32.3, 20.6, 14.0. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{20}H_{25}BrNO_2$: 390.1069 found, 390.1065. $[\alpha]^{25}$ D = −25.00 (c = 0.05 g mL^{-1}, $CHCl_3$). The enantiomeric ratio (er = 97 : 3) of the compound **10c-(D)** was determined by HPLC using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (95 : 05), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 12.57 min, t_D = 14.10 min.

(2*S*,3*R*)-ethyl 2-amino-3-(4′-bromo-[1,1′-biphenyl]-4-yl)-4-ylhexanoate (10c-(L))

The compound **10c-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a semi-solid (105 mg, 77%, 0.35 mmol scale); R_f (50% EtOAc/hexane) 0.5; IR (DCM): 2930, 1729, 752 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.55–7.42 (m, 6H), 7.29–7.23 (m, 2H), 4.10–3.97 (m, 2H), 3.58 (d, J = 6.2 Hz, 1H), 3.00–2.94 (m, 1H), 1.82–1.77 (m, 2H), 1.34–1.14 (m, 2H), 1.10 (t, J = 7.1 Hz, 3H), 0.88 (t, J = 7.3 Hz, 3H). (The NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 174.8, 140.9, 139.8, 138.3, 131.8, 129.0, 128.5, 126.7, 121.3, 60.6, 60.1, 49.5, 32.2, 20.5, 14.0. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{20}H_{25}BrNO_2$: 390.1069 found, 390.1060. $[\alpha]^{25}$ D = +26.00 (c = 0.05 g mL^{-1}, $CHCl_3$). The enantiomeric ratio (er = 98 : 2) of the compound **10c-(L)** was determined by HPLC using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (95 : 05), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 12.57 min, t_D = 14.69 min.

(2*S,3*R**)-ethyl 2-amino-3-(4′-bromo-[1,1′-biphenyl]-4-yl)-3-phenylpropanoate (10d-(DL))**

The compound **10d-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a semi-solid (90 mg, 85%, 0.25 mmol scale); R_f (50% EtOAc/hexane) 0.5; IR (DCM): 2930, 1732, 771 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.52–7.23 (m, 13H), 4.27 (d, J = 8.8 Hz, 1H), 4.23 (d, J = 8.8 Hz, 1H), 3.99 (q, J = 7.1 Hz, 2H), 1.00 (t, J = 7.1 Hz, 3H). (the NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 174.2, 140.9, 140.2, 139.5, 138.2, 131.7, 128.7, 128.7, 128.6, 128.4, 127.0, 126.8, 121.3, 60.7, 58.6, 56.1, 13.8. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{23}H_{23}BrNO_2$: 424.0912 found, 424.0923. The HPLC of the compound **10d-(DL)** was determined using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (95 : 05), flow rate 0.5 mL min^{-1}, UV detection at 254 nm, t_L = 36.19 min, t_D = 37.94 min.

(2*R*,3*S*)-ethyl 2-amino-3-(4′-bromo-[1,1′-biphenyl]-4-yl)-3-phenylpropanoate (10d-(D))

The compound **10d-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a semi-solid (92 mg, 87%, 0.25 mmol scale); R_f (50% EtOAc/hexane) 0.5; IR (DCM): 2929, 1731, 771 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.54–7.24 (m, 13H), 4.27 (d, J = 9.0 Hz, 1H), 4.24 (d, J = 8.9 Hz, 1H), 4.00 (q, J = 7.1 Hz, 2H), 1.01 (t, J = 7.1 Hz, 3H). (The NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 174.3, 140.9, 140.3, 139.6, 138.4, 131.8, 128.8, 128.8, 128.7, 128.5, 127.1, 126.9, 121.4, 60.8, 58.7, 56.2, 13.8. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{23}H_{23}BrNO_2$: 424.0912 found, 424.0920. $[\alpha]^{25}$ D = −26.00 (c = 0.05 g mL^{-1}, $CHCl_3$). The enantiomeric ratio (er = 96 : 4) of the compound **10d-(D)** was determined by HPLC using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (95 : 05), flow rate 0.5 mL min^{-1}, UV detection at 254 nm, t_L = 34.80 min, t_D = 36.65 min.

(2*S*,3*R*)-ethyl 2-amino-3-(4′-bromo-[1,1′-biphenyl]-4-yl)-3-phenylpropanoate (10d-(L))

The compound **10d-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a semi-solid (92 mg, 87%, 0.25 mmol scale); R_f (50% EtOAc/hexane) 0.5; IR (DCM): 2920, 1732, 771 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.54–7.23 (m, 13H), 4.27 (d, J = 8.8 Hz, 1H), 4.24 (d, J = 8.8 Hz, 1H), 4.00 (q, J = 8.9 Hz, 2H), 1.01 (t, J = 7.1 Hz, 3H). (The NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). ^{13}C NMR (101 MHz, $CDCl_3$): δ_C 174.3, 141.0, 140.3, 139.6, 138.4, 131.8, 128.8, 128.8, 128.7, 128.5, 127.1, 126.9, 121.4, 60.8, 58.7, 56.2, 13.8. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{23}H_{23}BrNO_2$: 424.0912 found, 424.0922. $[\alpha]^{25}$ D = +28.00 (c = 0.05 g mL^{-1}, $CHCl_3$). The enantiomeric ratio (er = 95 : 5) of the compound **10d-(L)** was determined by HPLC using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (95 : 05), flow rate 0.5 mL min^{-1}, UV detection at 254 nm, t_L = 35.41 min, t_D = 37.19 min.

(2*S,3*R**)-methyl 2-amino-3-(4′-bromo-[1,1′-biphenyl]-4-yl)-3-phenylpropanoate (10e-(DL))**

The compound **10e-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 20 : 80) as a colorless semi-solid (69 mg, 84%, 0.2 mmol scale); R_f (20% EtOAc/hexane) 0.5; IR (DCM): 2925, 1734, 765 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.50–7.20 (m, 13H), 4.30 (d, J = 8.5 Hz, 1H), 4.24 (d, J = 8.5 Hz, 1H), 3.52 (s, 3H). (The NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 174.6, 140.8, 140.0, 139.3, 138.0, 131.6, 128.6, 128.6,

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128.5, 128.3, 126.9, 126.7, 121.3, 58.5, 55.6, 51.7. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{22}H_{21}BrNO_2$: 410.0756 found, 410.0771.

(2*S**,3*R**)-ethyl 2-amino-3-(4″-methoxy-[1,1′:4′,1″-terphenyl]-4-yl)pentanoate (12a-(DL))

The compound **12a-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a colorless solid (68 mg, 84%, 0.2 mmol scale); R_f (50% EtOAc/hexane) 0.5; mp: 167–169 °C; IR (DCM): 2934, 1730, 772 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.63–7.57 (m, 8H), 7.30–7.26 (m, 2H), 7.00 (d, J = 8.7 Hz, 2H), 4.06–4.01 (m, 2H), 3.86 (s, 3H), 3.61 (d, J = 6.3 Hz, 1H), 2.89–2.84 (m, 1H), 1.97–1.76 (m, 2H), 1.10 (t, J = 7.1 Hz, 3H), 0.84 (t, J = 7.4 Hz, 3H). (The NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~126 MHz, $CDCl_3$): δ_C 174.8, 159.2, 140.1, 139.6, 139.2, 133.2, 129.0, 128.0, 127.2, 127.0, 126.8, 114.2, 60.6, 60.0, 55.3, 51.8, 23.3, 14.0, 12.2. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{26}H_{30}NO_3$: 404.2226 found, 404.2239. The HPLC of the compound **12a-(DL)** was determined using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (80 : 20), flow rate 1.0 mL min^{-1}, UV detection at 291.7 nm, t_L = 12.12 min, t_D = 14.08 min.

(2*R*,3*S*)-ethyl 2-amino-3-(4″-methoxy-[1,1′:4′,1″-terphenyl]-4-yl) pentanoate (12a-(D))

The compound **12a-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a colorless solid (18 mg, 83%, 0.054 mmol scale); R_f (50% EtOAc/hexane) 0.5; mp: 165–167 °C; IR (DCM): 2934, 1730, 772 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.63–7.56 (m, 8H), 7.29–7.25 (m, 2H), 7.00 (d, J = 8.6 Hz, 2H), 4.07–4.00 (m, 2H), 3.85 (s, 3H), 3.61 (d, J = 6.4 Hz, 1H), 2.89–2.84 (m, 1H), 1.97–1.76 (m, 2H), 1.10 (t, J = 7.2 Hz, 3H), 0.84 (t, J = 7.3 Hz, 3H). (The NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 174.7, 159.1, 140.0, 139.5, 139.1, 139.1, 133.1, 129.0, 128.0, 127.2, 127.0, 126.8, 114.2, 60.7, 59.9, 55.3, 51.7, 23.2, 14.0, 12.2. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{26}H_{30}NO_3$: 404.2226 found, 404.2239. $[\alpha]^{25}$ D = −22.00 (c = 0.05 g mL^{-1}, $CHCl_3$). The enantiomeric ratio (er = 95 : 5) of the compound **12a-(D)** was determined by HPLC using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (80 : 20), flow rate 1.0 mL min^{-1}, UV detection at 291.7 nm, t_L = 12.15 min, t_D = 14.17 min.

(2*S*,3*R*)-ethyl 2-amino-3-(4″-methoxy-[1,1′:4′,1″-terphenyl]-4-yl) pentanoate (12a-(L))

The compound **12a-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a colorless solid (17 mg, 78%, 0.054 mmol scale); R_f (50% EtOAc/hexane) 0.5; mp: 167–169 °C; IR (DCM): 2934, 1730, 772 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.65–7.57 (m, 8H), 7.30–7.26 (m, 2H), 7.00 (d, J = 8.6 Hz, 2H), 4.06–4.01 (m, 2H), 3.86 (s, 3H), 3.61 (d, J = 6.3 Hz, 1H), 2.89–2.84 (m, 1H), 1.98–1.76 (m, 2H), 1.10 (t, J = 7.2 Hz, 3H), 0.84 (t, J = 7.3 Hz, 3H). (The NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 174.8, 159.1, 140.0, 139.5, 139.1, 139.1, 133.1, 129.0, 128.0, 127.2, 127.0, 126.8, 114.2, 60.7, 59.9, 55.3, 51.7, 23.2, 14.0, 12.2. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{26}H_{30}NO_3$: 404.2226 found, 404.2229. $[\alpha]^{25}$ D = +19.00 (c = 0.05 g mL^{-1}, $CHCl_3$). The enantiomeric ratio (er = 95 : 5) of the compound **12a-(L)** was determined by HPLC using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (80 : 20), flow rate 1.0 mL min^{-1}, UV detection at 291.7 nm, t_L = 12.05 min, t_D = 13.77 min.

(2*S**,3*R**)-ethyl 2-((*tert*-butoxycarbonyl)amino)-3-(4″-methoxy-[1,1′:4′,1″-terphenyl]-4-yl)pentanoate (12b-(DL))

The compound **12b-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 20 : 80) as a colorless solid (22 mg, 62%, 0.07 mmol scale); R_f (20% EtOAc/hexane) 0.5; mp: 201–203 °C; IR (DCM): 2933, 1742, 772 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.63–7.55 (m, 8H), 7.23 (d, J = 7.9 Hz, 2H), 6.99 (d, J = 8.7 Hz, 2H), 5.08 (d, J = 9.0 Hz, 1H), 4.51 (t, J = 8.2 Hz, 1H), 4.00 (q, J = 6.6 Hz, 2H), 3.86 (s, 3H), 2.90–2.84 (m, 1H), 1.96–1.77 (m, 2H), 1.45 (s, 9H), 1.04 (t, J = 6.9 Hz, 3H), 0.85 (t, J = 7.3 Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 171.8, 159.2, 155.2, 139.6, 139.4, 139.1, 138.7, 133.2, 129.0, 128.0, 127.3, 127.0, 126.8, 114.2, 79.9, 61.0, 58.3, 55.3, 51.0, 28.3, 24.3, 13.9, 12.1. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{31}H_{37}NNaO_5$: 526.2569 found, 526.2582.

(2*S**,3*R**)-ethyl 2-amino-3-(4″-methoxy-[1,1′:4′,1″-terphenyl]-4-yl)-4-methylpentanoate (13a-(DL))

The compound **13a-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a colorless solid (14 mg, 67%, 0.05 mmol scale); R_f (50% EtOAc/hexane) 0.5; mp: 129–131 °C; IR (DCM): 2924, 1729, 772 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.65–7.53 (m, 8H), 7.21 (d, J = 8.2 Hz, 2H), 7.00 (d, J = 8.7 Hz, 2H), 4.11–4.02 (m, 2H), 3.88 (d, J = 6.5 Hz, 1H), 3.86 (s, 3H), 2.72 (t, J = 7.8 Hz, 1H), 2.46–2.38 (m, 1H), 1.13 (t, J = 7.2 Hz, 3H), 1.06 (d, J = 6.6 Hz, 3H), 0.81 (d, J = 6.7 Hz, 3H). (the NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 175.1, 159.2, 139.5, 139.1, 138.6, 133.2, 129.8, 128.0, 127.2, 127.0, 126.4, 114.2, 60.7, 57.2, 56.6, 55.3, 28.2, 21.5, 20.1, 14.0. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{27}H_{32}NO_3$: 418.2382 found, 418.2398. The HPLC of the compound **13a-(DL)** was determined using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (80 : 20), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 9.18 min, t_D = 12.48 min.

(2*R*,3*S*)-ethyl 2-amino-3-(4″-methoxy-[1,1′:4′,1″-terphenyl]-4-yl)-4-methylpentanoate (13a-(D))

The compound **13a-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a colorless solid (15 mg, 72%, 0.05 mmol scale); R_f (50% EtOAc/hexane) 0.5; mp: 130–132 °C; IR (DCM): 2925, 1729, 772 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.65–7.53 (m, 8H), 7.21 (d, J = 8.2 Hz, 2H), 7.00 (d, J = 8.7 Hz, 2H), 4.12–4.01 (m, 2H), 3.88 (d, J = 6.6 Hz, 1H), 3.86 (s, 3H), 2.72 (t, J = 7.6 Hz, 1H), 2.46–

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2.38 (m, 1H), 1.13 (t, $J = 7.2$ Hz, 3H), 1.06 (d, $J = 6.6$ Hz, 3H), 0.81 (d, $J = 6.7$ Hz, 3H). (the NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 175.0, 159.2, 139.5, 139.1, 138.6, 133.2, 129.8, 128.0, 127.2, 127.0, 126.4, 114.2, 60.7, 57.1, 56.5, 55.3, 28.3, 21.5, 20.1, 14.0. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{27}H_{32}NO_3$: 418.2382 found, 418.2381. $[\alpha]^{25}$ $D = -16.00$ ($c = 0.05$ g mL^{-1}, $CHCl_3$). The enantiomeric ratio ($er = 95:5$) of the compound **13a-(D)** was determined by HPLC using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (80 : 20), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, $t_L = 10.87$ min, $t_D = 14.33$ min.

(2*S*,3*R*)-ethyl 2-amino-3-(4″-methoxy-[1,1′:4′,1″-terphenyl]-4-yl)-4-methylpentanoate (13a-(L))

The compound **13a-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a colorless solid (14 mg, 67%, 0.05 mmol scale); R_f (50% EtOAc/hexane) 0.5; mp: 128–130 °C; IR (DCM): 2925, 1729, 771 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.69–7.49 (m, 8H), 7.22 (d, $J = 8.1$ Hz, 2H), 6.99 (d, $J = 8.7$ Hz, 2H), 4.11–4.03 (m, 2H), 3.91 (d, $J = 6.4$ Hz, 1H), 3.86 (s, 3H), 2.73 (t, $J = 7.7$ Hz, 1H), 2.46–2.38 (m, 1H), 1.13 (t, $J = 7.2$ Hz, 3H), 1.07 (d, $J = 6.6$ Hz, 3H), 0.81 (d, $J = 6.6$ Hz, 3H). (The NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 175.0, 159.2, 139.5, 139.1, 138.6, 133.2, 129.8, 128.0, 127.2, 127.0, 126.4, 114.2, 60.7, 57.2, 56.6, 55.3, 28.3, 21.5, 20.1, 14.0. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{27}H_{32}NO_3$: 418.2382 found, 418.2384. $[\alpha]^{25}$ $D = +18.00$ ($c = 0.05$ g mL^{-1}, $CHCl_3$). The enantiomeric ratio ($er = 96:4$) of the compound **13a-(L)** was determined by HPLC using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (80 : 20), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, $t_L = 10.53$ min, $t_D = 14.41$ min.

(2*S**,3*R**)-ethyl 2-amino-3-(4″-chloro-[1,1′:4′,1″-terphenyl]-4-yl)-4-methylpentanoate (13b-(DL))

The compound **13b-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a colorless solid (12 mg, 57%, 0.05 mmol scale); R_f (50% EtOAc/hexane) 0.5; mp: 135–137 °C; IR (DCM): 2927, 1728, 749 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.74–7.37 (m, 10H), 7.22 (d, $J = 8.2$ Hz, 2H), 4.15–4.02 (m, 2H), 3.87 (d, $J = 6.5$ Hz, 1H), 2.73–2.69 (m, 1H), 2.46–2.38 (m, 1H), 1.13 (t, $J = 7.2$ Hz, 3H), 1.06 (d, $J = 6.6$ Hz, 3H), 0.81 (d, $J = 6.7$ Hz, 3H). (The NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 175.1, 140.1, 139.1, 138.9, 138.8, 138.7, 133.4, 129.8, 128.9, 128.2, 127.4, 127.3, 126.5, 60.7, 57.2, 56.6, 28.3, 21.5, 20.1, 14.0. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{26}H_{28}ClNNaO_2$: 444.1706 found, 444.1704.

(2*S**,3*R**)-ethyl 2-amino-3-(4″-fluoro-[1,1′:4′,1″-terphenyl]-4-yl)-4-methylpentanoate (13c-(DL))

The compound **13c-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a colorless solid (16 mg, 80%, 0.05 mmol scale); R_f (50% EtOAc/hexane) 0.5; mp: 153–155 °C; IR (DCM): 2928, 1728, 755 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.67–7.53 (m, 8H), 7.26–7.12 (m, 4H), 4.11–4.02 (m, 2H), 3.87 (d, $J = 6.5$ Hz, 1H), 2.72 (t, $J = 7.6$ Hz, 1H), 2.47–2.38 (m, 1H), 1.13 (t, $J = 7.2$ Hz, 3H), 1.06 (d, $J = 6.6$ Hz, 3H), 0.81 (d, $J = 6.7$ Hz, 3H). (The NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 175.1, 162.5 (d, $J_{C\text{-}F} = 247.3$ Hz), 139.7, 138.9 (d, $J_{C\text{-}F} = 5.2$ Hz), 136.8 (d, $J_{C\text{-}F} = 3.4$ Hz), 129.8, 128.6, 128.5, 127.3, 127.3, 126.5, 115.8 (d, $J_{C\text{-}F} = 21.4$ Hz), 60.7, 57.2, 56.6, 28.2, 21.5, 20.1, 14.0. $^{19}F\{1H\}$ NMR (~376 MHz, CDCl3): δ_F −115.64. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{26}H_{29}FNO_2$: 406.2182 found, 406.2189.

(2*S**,3*R**)-ethyl 2-amino-3-(4″-methoxy-[1,1′:4′,1″-terphenyl]-4-yl)hexanoate (14a-(DL))

The compound **14a-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a colorless solid (15 mg, 72%, 0.05 mmol scale); R_f (50% EtOAc/hexane) 0.5; mp: 160–162 °C; IR (DCM): 2933, 1724, 772 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.63–7.56 (m, 8H), 7.29 (d, $J = 8.2$ Hz, 2H), 7.00 (d, $J = 8.7$ Hz, 2H), 4.08–4.00 (m, 2H), 3.86 (s, 3H), 3.59 (d, $J = 6.3$ Hz, 1H), 2.98 (dd, $J_1 = 14.5$, $J_2 = 7.0$ Hz, 1H), 1.81 (q, $J = 7.8$ Hz, 2H), 1.33–1.16 (m, 2H), 1.10 (t, $J = 7.1$ Hz, 3H), 0.89 (t, $J = 7.3$ Hz, 3H). (The NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 174.9, 159.2, 140.3, 139.6, 139.2, 133.2, 128.9, 128.0, 127.2, 127.0, 126.8, 114.2, 60.7, 60.2, 55.3, 49.6, 32.3, 20.6, 14.0. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{27}H_{32}NO_3$: 418.2382 found, 418.2379. The HPLC of the compound **14a-(DL)** was determined using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (95 : 05), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, $t_L = 24.43$ min, $t_D = 34.81$ min.

(2*R*,3*S*)-ethyl 2-amino-3-(4″-methoxy-[1,1′:4′,1″-terphenyl]-4-yl) hexanoate (14a-(D))

The compound **14a-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a colorless solid (14 mg, 67%, 0.05 mmol scale); R_f (50% EtOAc/hexane) 0.5; mp: 163–165 °C; IR (DCM): 2933, 1724, 772 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.63–7.56 (m, 8H), 7.29 (d, $J = 8.1$ Hz, 2H), 6.99 (d, $J = 8.8$ Hz, 2H), 4.08–4.00 (m, 2H), 3.86 (s, 3H), 3.59 (d, $J = 6.3$ Hz, 1H), 2.98 (dd, $J_1 = 14.6$, $J_2 = 7.0$ Hz, 1H), 1.81 (q, $J = 8.0$ Hz, 2H), 1.33–1.16 (m, 2H), 1.10 (t, $J = 7.2$ Hz, 3H), 0.89 (t, $J = 7.4$ Hz, 3H). (The NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 174.9, 159.2, 140.4, 139.6, 139.1, 139.1, 133.2, 128.9, 128.0, 127.2, 127.0, 126.8, 114.2, 60.6, 60.2, 55.3, 49.6, 32.3, 20.6, 14.0. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{27}H_{32}NO_3$: 418.2382 found, 418.2378. $[\alpha]^{25}$ $D = -17.00$ ($c = 0.05$ g mL^{-1}, $CHCl_3$). The enantiomeric ratio ($er = 96:4$) of the compound **14a-(D)** was determined by HPLC using the Daicel Chiralcel ODH column,

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hexane/*i*-PrOH (95 : 05), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 25.01 min, t_D = 34.20 min.

(2*S*,3*R*)-ethyl 2-amino-3-(4″-methoxy-[1,1′:4′,1″-terphenyl]-4-yl) hexanoate (14a-(L))

The compound **14a-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a colorless solid (15 mg, 72%, 0.05 mmol scale); R_f (50% EtOAc/hexane) 0.5; mp: 161–163 °C; IR (DCM): 2933, 1724, 772 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.65–7.56 (m, 8H), 7.29 (d, J = 8.1 Hz, 2H), 6.99 (d, J = 8.7 Hz, 2H), 4.08–4.00 (m, 2H), 3.86 (s, 3H), 3.59 (d, J = 6.3 Hz, 1H), 2.97 (dd, J_1 = 14.5, J_2 = 6.8 Hz, 1H), 1.81 (q, J = 7.9 Hz, 2H), 1.31–1.14 (m, 2H), 1.10 (t, J = 7.2 Hz, 3H), 0.89 (t, J = 7.3 Hz, 3H). (The NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 174.9, 159.2, 140.4, 139.6, 139.1, 139.1, 133.2, 128.9, 128.0, 127.2, 127.0, 126.8, 114.2, 60.6, 60.2, 55.3, 49.6, 32.3, 20.6, 14.0. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{27}H_{32}NO_3$: 418.2382 found, 418.2390. $[\alpha]^{25}$ D = +14.00 (c = 0.05 g mL^{-1}, $CHCl_3$). The enantiomeric ratio (er = 97 : 3) of the compound **14a-(L)** was determined by HPLC using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (95 : 05), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 22.11 min, t_D = 31.86 min.

(2*S**,3*R**)-ethyl 2-amino-3-(4″-chloro-[1,1′:4′,1″-terphenyl]-4-yl)hexanoate (14b-(DL))

The compound **14b-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a colorless solid (12 mg, 57%, 0.05 mmol scale); R_f (50% EtOAc/hexane) 0.5; mp: 133–135 °C; IR (DCM): 2930, 1729, 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.79–7.55 (m, 8H), 7.43–7.41 (m, 2H), 7.31–7.25 (m, 2H), 4.10–3.97 (m, 2H), 3.64 (d, J = 6.1 Hz, 1H), 3.03–2.98 (m, 1H), 1.84–1.73 (m, 2H), 1.31–1.15 (m, 2H), 1.10 (t, J = 7.2 Hz, 3H), 0.88 (t, J = 7.4 Hz, 3H). (The NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 174.2, 140.0, 139.1, 138.7, 135.0, 133.4, 128.9, 128.9, 128.2, 127.7, 127.4, 127.3, 127.0, 60.9, 59.9, 49.1, 32.0, 20.5, 14.0. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{26}H_{29}ClNO_2$: 422.1887 found, 422.1885.

(2*S**,3*R**)-ethyl 2-amino-3-(4″-fluoro-[1,1′:4′,1″-terphenyl]-4-yl) hexanoate (14c-(DL))

The compound **14c-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a colorless solid (13 mg, 64%, 0.05 mmol scale); R_f (50% EtOAc/hexane) 0.5; mp: 167–169 °C; IR (DCM): 2928, 1727, 771 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.67–7.56 (m, 8H), 7.31–7.26 (m, 2H), 7.16–7.12 (m, 2H), 4.10–3.98 (m, 2H), 3.59 (d, J = 6.3 Hz, 1H), 2.98 (dd, J_1 = 14.9, J_2 = 6.6 Hz, 1H), 1.81 (q, J_1 = 15.1, J_2 = 7.9 Hz, 2H), 1.33–1.16 (m, 2H), 1.11 (t, J = 7.1 Hz, 3H), 0.89 (t, J = 7.4 Hz, 3H). (The NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 174.9, 162.5 (d, J_{C-F} = 247.3 Hz), 140.6, 139.8, 138.9 (d, J_{C-F} = 2.1 Hz), 136.8 (d, J_{C-F} = 3.0 Hz), 129.0, 128.6, 128.5, 127.3, 127.3, 126.8, 115.7 (d, J_{C-F} = 21.5 Hz), 60.6, 60.2, 49.6, 32.3, 20.6, 14.0. $^{19}F\{1H\}$ NMR (~376 MHz, CDCl3): δ_F −115.65. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{26}H_{29}FNO_2$: 406.2182 found, 406.2175.

(2*S**,3*R**)-ethyl 2-((*tert*-butoxycarbonyl)amino)-3-(3″-nitro-[1,1′:4′,1″-terphenyl]-4-yl)hexanoate (14d-(DL))

The compound **14d-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 20 : 80) as a colorless solid (22 mg, 59%, 0.07 mmol scale); R_f (20% EtOAc/hexane) 0.5; mp: 156–158 °C; IR (DCM): 2929, 1708, 755 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.51–8.50 (m, 1H), 8.23–8.20 (m, 1H), 7.98–7.96 (m, 1H), 7.71 (s, 4H), 7.65–7.57 (m, 3H), 7.27–7.25 (m, 2H), 5.10 (d, J = 9.3 Hz, 1H), 4.53–4.49 (m, 1H), 4.09–3.99 (m, 2H), 3.01 (dd, J_1 = 14.9, J_2 = 7.2 Hz, 1H), 1.81 (q, J = 8.8 Hz, 2H), 1.45 (s, 9H), 1.29–1.17 (m, 2H), 1.07 (t, J = 7.1 Hz, 3H), 0.89 (t, J = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 171.8, 155.2, 148.8, 142.3, 141.1, 139.6, 138.8, 137.3, 132.8, 129.8, 129.0, 127.7, 127.5, 126.9, 122.0, 121.8, 79.9, 61.0, 58.4, 48.8, 33.2, 28.3, 20.6, 13.9, 13.9. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{31}H_{36}N_2NaO_6$: 555.2471 found, 555.2471.

(2*S**,3*R**)-ethyl 2-amino-3-(4″-methoxy-[1,1′:4′,1″-terphenyl]-4-yl)-3-phenylpropanoate (15a-(DL))

The compound **15a-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a colorless solid (25 mg, 92%, 0.06 mmol scale); R_f (50% EtOAc/hexane) 0.5; mp: 186–188 °C; IR (DCM): 2924, 1731, 772 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.60–7.52 (m, 8H), 7.40–7.25 (m, 7H), 6.99 (d, J = 8.5 Hz, 2H), 4.26 (s, 2H), 3.98 (q, J = 6.8 Hz, 2H), 3.85 (s, 3H), 0.99 (t, J = 7.1 Hz, 3H). (The NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~126 MHz, $CDCl_3$): δ_C 174.4, 159.2, 140.4, 140.4, 139.7, 139.2, 139.0, 133.2, 128.8, 128.7, 128.0, 127.3, 127.2, 127.1, 127.0, 126.9, 114.3, 60.8, 58.8, 56.3, 55.3, 13.8. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{30}H_{30}NO_3$: 452.2226 found, 452.2238. The HPLC of the compound **15a-(DL)** was determined using the Daicel Chiralpak IA column, hexane/*i*-PrOH (85 : 15), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 24.25 min, t_L = 26.13 min.

(2*R*,3*S*)-ethyl 2-amino-3-(4″-methoxy-[1,1′:4′,1″-terphenyl]-4-yl)-3-phenylpropanoate (15a-(D))

The compound **15a-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a colorless solid (24 mg, 89%, 0.06 mmol scale); R_f (50% EtOAc/hexane) 0.5; mp: 185–187 °C; IR (DCM): 2923, 1730, 772 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.64–7.55 (m, 8H), 7.44–7.28 (m, 7H), 7.02 (d, J = 8.7 Hz, 2H), 4.30 (s, 2H), 4.02 (q, J = 7.1 Hz, 2H), 3.88 (s, 3H), 1.03 (t, J = 7.1 Hz, 3H). (The NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 174.4, 159.2, 140.4, 140.4, 139.7, 139.2, 139.0, 133.1, 128.8, 128.7, 128.0, 127.3, 127.2, 127.1, 127.0, 126.9, 114.2, 60.8, 58.8, 56.3, 55.3, 13.8. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{30}H_{30}NO_3$:

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452.2226 found, 452.2227. $[\alpha]^{25}$ $D = -36.00$ ($c = 0.05$ g mL^{-1}, $CHCl_3$). The enantiomeric ratio ($er = 98:2$) of the compound **15a-(D)** was determined by HPLC using the Daicel Chiralpak IA column, hexane/*i*-PrOH (85 : 15), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, $t_D = 24.55$ min, $t_L = 26.76$ min.

Ethyl (2*S*,3*R*)-2-amino-3-(4″-methoxy-[1,1′:4′,1″-terphenyl]-4-yl)-3-phenylpropanoate (15a-(L))

The compound **15a-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a colorless solid (25 mg, 92%, 0.06 mmol scale); R_f (50% EtOAc/hexane) 0.5; mp: 184–186 °C; IR (DCM): 2925, 1730, 770 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.57–7.53 (m, 8H), 7.41–7.25 (m, 7H), 6.99 (d, $J = 8.6$ Hz, 2H), 4.26 (s, 2H), 4.00 (q, $J = 7.1$ Hz, 2H), 3.85 (s, 3H), 1.00 (t, $J = 7.1$ Hz, 3H). (The NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). ^{13}C{^{1}H} NMR (~126 MHz, $CDCl_3$): δ_C 174.4, 159.2, 140.4, 139.7, 139.2, 139.0, 133.2, 128.8, 128.7, 128.7, 128.0, 127.3, 127.2, 127.1, 127.0, 126.9, 114.3, 60.8, 58.8, 56.3, 55.3, 13.8. HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{30}H_{30}NO_3$: 452.2226 found, 452.2220. $[\alpha]^{25}$ $D = +33.00$ ($c = 0.05$ g mL^{-1}, $CHCl_3$). The enantiomeric ratio ($er = 99:1$) of the compound **15a-(L)** was determined by HPLC using the Daicel Chiralpak IA column, hexane/*i*-PrOH (85 : 15), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, $t_D = 24.68$ min, $t_L = 26.01$ min.

(2*S**,3*R**)-ethyl 3-([1,1′:4′,1″-terphenyl]-4-yl)-2-amino-3-phenylpropanoate (15b-(DL))

The compound **15b-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a colorless solid (45 mg, 71%, 0.15 mmol scale); R_f (50% EtOAc/hexane) 0.5; mp: 140–142 °C; IR (DCM): 2928, 1731, 753 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.66–7.33 (m, 18H), 4.29–4.25 (m, 2H), 4.00 (q, $J = 7.0$ Hz, 2H), 1.01 (t, $J = 7.2$ Hz, 3H). (The NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). ^{13}C{^{1}H} NMR (~126 MHz, $CDCl_3$): δ_C 174.4, 140.6, 140.6, 140.4, 140.1, 139.6, 139.1, 128.8, 128.8, 128.7, 127.5, 127.3, 127.3, 127.1, 127.0, 60.8, 58.8, 56.3, 13.8. HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{29}H_{28}NO_2$: 422.2120 found, 422.2135.

(2*S**,3*R**)-ethyl 2-amino-3-(4″-chloro-[1,1′:4′,1″-terphenyl]-4-yl)-3-phenylpropanoate (15c-(DL))

The compound **15c-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a colorless solid (60 mg, 82%, 0.16 mmol scale); R_f (50% EtOAc/hexane) 0.5; mp: 140–142 °C; IR (DCM): 2929, 1731, 750 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.68–7.53 (m, 8H), 7.43–7.35 (m, 8H), 7.29–7.22 (m, 1H), 4.29–4.24 (m, 2H), 4.00 (q, $J = 7.1$ Hz, 2H), 1.01 (t, $J = 7.2$ Hz, 3H). (the NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). ^{13}C{^{1}H} NMR (~101 MHz, $CDCl_3$): δ_C 174.3, 140.6, 140.3, 139.9, 139.0, 138.8, 138.7, 133.4, 128.9, 128.8, 128.7, 128.6, 128.2, 127.3, 127.2, 127.1, 126.9, 60.8, 58.7, 56.2, 13.8. HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{29}H_{27}ClNO_2$: 456.1730 found, 456.1735.

Ethyl 11-(1,3-dioxoisoindolin-2-yl)-3-(4″-methoxy-[1,1′:4′,1″-terphenyl]-4-yl)undecanoate (18a)

The compound **18*a*** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 20 : 80) as a colorless solid (15 mg, 48%, 0.05 mmol scale); R_f (20% EtOAc/hexane) 0.5; mp: 115–117 °C; IR (DCM): 2929, 1710, 772 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.82 (dd, $J_1 = 5.4$, $J_2 = 3.1$ Hz, 2H), 7.69 (dd, $J_1 = 5.4$, $J_2 = 3.0$ Hz, 2H), 7.65–7.55 (m, 8H), 7.25 (d, $J = 6.4$ Hz, 2H), 6.99 (d, $J = 8.7$ Hz, 2H), 4.04 (q, $J = 7.1$ Hz, 2H), 3.86 (s, 3H), 3.65 (t, $J = 7.4$ Hz, 2H), 3.16–3.08 (m, 1H), 2.67–2.55 (m, 2H), 1.69–1.59 (m, 4H), 1.33–1.24 (m, 10H), 1.14 (t, $J = 7.1$ Hz, 3H). ^{13}C{^{1}H} NMR (~101 MHz, $CDCl_3$): δ_C 172.5, 168.4, 159.2, 143.3, 139.4, 139.2, 138.7, 133.8, 133.2, 132.2, 128.0, 127.9, 127.2, 126.9, 126.9, 123.1, 114.2, 60.2, 55.4, 41.9, 41.8, 38.0, 36.2, 29.4, 29.2, 29.1, 28.5, 27.3, 26.8, 14.1. HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{40}H_{44}NO_5$: 618.3219 found, 618.3221.

Ethyl 7-(1,3-dioxoisoindolin-2-yl)-3-(4″-methoxy-[1,1′:4′,1″-terphenyl]-4-yl)heptanoate (18b)

The compound **18b** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 20 : 80) as a colorless solid (25 mg, 50%, 0.09 mmol scale); R_f (20% EtOAc/hexane) 0.5; mp: 160–162 °C; IR (DCM): 2928, 1708, 750 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.80 (dd, $J_1 = 5.4$, $J_2 = 3.1$ Hz, 2H), 7.66 (dd, $J_1 = 5.4$, $J_2 = 3.0$ Hz, 2H), 7.67–7.50 (m, 8H), 7.23 (d, $J = 8.2$ Hz, 2H), 7.01–6.99 (m, 2H), 4.04 (q, $J = 7.1$ Hz, 2H), 3.86 (s, 3H), 3.62 (t, $J = 7.3$ Hz, 2H), 3.17–3.10 (m, 1H), 2.68–2.56 (m, 2H), 1.78–1.58 (m, 4H), 1.27–1.21 (m, 2H), 1.14 (t, $J = 7.1$ Hz, 3H). ^{13}C{^{1}H} NMR (~101 MHz, $CDCl_3$): δ_C 172.3, 168.4, 159.1, 142.7, 139.4, 139.1, 138.8, 133.8, 133.2, 132.0, 128.0, 127.9, 127.2, 126.9, 123.1, 114.2, 60.3, 55.3, 41.7, 41.6, 37.7, 35.5, 28.3, 24.5, 14.1. HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{36}H_{35}NNaO_5$: 584.2413 found, 584.2432.

(*E*)-ethyl 7-(1,3-dioxoisoindolin-2-yl)-3-(4′-(3-ethoxy-3-oxoprop-1-en-1-yl)-[1,1′-biphenyl]-4-yl)heptanoate (18c)

The compound **18c** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 20 : 80) as a colorless semi-solid (30 mg, 60%, 0.09 mmol scale); R_f (20% EtOAc/hexane) 0.5; IR (DCM): 2931, 1707, 770 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.83 (dd, $J_1 = 5.4$, $J_2 = 3.0$ Hz, 2H), 7.74 (d, $J = 16.0$ Hz, 1H), 7.68 (dd, $J_1 = 5.4$, $J_2 = 3.0$ Hz, 2H), 7.62–7.58 (m, 4H), 7.51 (d, $J = 8.2$ Hz, 2H), 7.26 (d, $J = 8.2$ Hz, 2H), 6.50 (d, $J = 16.0$ Hz, 1H), 4.30 (q, $J = 7.1$ Hz, 2H), 4.06 (q, $J = 7.1$ Hz, 2H), 3.63 (t, $J = 7.3$ Hz, 2H), 3.19–3.11 (m, 1H), 2.70–2.58 (m, 2H), 1.78–1.58 (m, 4H), 1.38 (t, $J = 7.1$ Hz, 3H), 1.31–1.22 (m, 2H), 1.16 (t, $J = 7.1$ Hz, 3H). ^{13}C{^{1}H} NMR (~101 MHz, $CDCl_3$): δ_C 172.2, 168.3, 167.1, 144.1, 143.5, 142.7, 138.2, 133.8, 133.2, 132.1, 128.5, 128.0, 127.3, 127.0, 123.1, 117.9, 60.5, 60.3, 41.6, 37.7, 35.5, 28.3, 24.5, 14.3, 14.1. HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{34}H_{35}NNaO_6$: 576.2362 found, 576.2380.

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Ethyl 7-(1,3-dioxoisoindolin-2-yl)-3-(4′-(phenylethynyl)-[1,1′-biphenyl]-4-yl)heptanoate (19a)

The compound **19a** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 20 : 80) as a colorless solid (38 mg, 76%, 0.09 mmol scale); R_f (20% EtOAc/hexane) 0.5; mp: 90–92 °C; IR (DCM): 2933, 1716, 771 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.80 (dd, $J_1 = 5.4$, $J_2 = 3.1$ Hz, 2H), 7.66 (dd, $J_1 = 5.4$, $J_2 = 3.0$ Hz, 2H), 7.59–7.47 (m, 8H), 7.36–7.35 (m, 3H), 7.26–7.22 (m, 2H), 4.04 (q, $J = 7.1$ Hz, 2H), 3.61 (t, $J = 7.2$ Hz, 2H), 3.17–3.09 (m, 1H), 2.67–2.55 (m, 2H), 1.75–1.58 (m, 4H), 1.29–1.13 (m, 2H), 1.15 (t, $J = 7.1$ Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 172.2, 168.4, 143.2, 140.6, 138.3, 133.8, 132.0, 131.9, 131.6, 128.3, 128.2, 127.9, 126.9, 126.8, 123.3, 123.1, 121.9, 90.0, 89.3, 60.3, 41.6, 41.6, 37.7, 35.5, 28.2, 24.4, 14.1. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{37}H_{34}NO_4$: 556.2488 found, 556.2512.

(2*S,3*R**)-ethyl 2-amino-3-phenyl-3-(4′-(phenylethynyl)-[1,1′-biphenyl]-4-yl)propanoate (19b-(DL))**

The compound **19b-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 30 : 70) as a colorless solid (15 mg, 67%, 0.05 mmol scale); R_f (30% EtOAc/hexane) 0.5; mp: 160–162 °C; IR (DCM): 2924, 1731, 755 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.58–7.50 (m, 9H), 7.41–7.39 (m, 2H), 7.36–7.34 (m, 7H), 4.28–4.23 (m, 2H), 4.00 (q, $J = 7.2$ Hz, 2H), 1.01 (t, $J = 7.2$ Hz, 3H). (The NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 174.3, 140.9, 140.4, 140.3, 138.7, 132.0, 131.6, 128.8, 128.7, 128.7, 128.3, 128.3, 127.1, 127.0, 126.8, 123.2, 122.1, 90.1, 89.2, 60.9, 58.8, 56.2, 13.9. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{31}H_{28}NO_2$: 446.2120 found, 446.2132.

(2*S,3*R**)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)-3-(4′-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-[1,1′-biphenyl]-4-yl)butanamide (21a-(DL))**

The compound **21a-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 30 : 70) as a brown colored semi-solid (52 mg, 82%, 0.1 mmol scale); R_f (30% EtOAc/hexane) 0.5; mp: 86–88 °C; IR (DCM): 2928, 1718, 758 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.89 (s, 1H), 8.60 (dd, $J_1 = 5.6$, $J_2 = 3.3$ Hz, 1H), 8.47 (dd, $J_1 = 4.0$, $J_2 = 1.2$ Hz, 1H), 8.02 (dd, $J_1 = 8.3$, $J_2 = 1.4$ Hz, 1H), 7.94 (dd, $J_1 = 5.4$, $J_2 = 3.0$ Hz, 2H), 7.84 (d, $J = 7.8$ Hz, 2H), 7.76 (dd, $J_1 = 5.4$, $J_2 = 3.0$ Hz, 2H), 7.59 (s, 4H), 7.49 (d, $J = 7.9$ Hz, 2H), 7.40–7.39 (m, 2H), 7.28–7.24 (m, 1H), 5.36 (d, $J = 11.6$ Hz, 1H), 4.44–4.36 (m, 1H), 1.43-1.36-1.35 (m, 15H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.3, 165.9, 148.0, 143.3, 142.1, 139.9, 138.3, 135.9, 135.2, 134.3, 133.9, 131.7, 128.3, 127.9, 127.6, 127.0, 126.2, 123.7, 121.8, 121.4, 116.7, 83.8, 61.3, 38.6, 24.8, 20.6. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{39}H_{37}BN_3O_5$: 638.2826 found, 638.2834. The HPLC of the compound **21a-(DL)** was determined using the Daicel Chiralpak IA column, hexane/*i*-PrOH (40 : 60), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, $t_L = 14.56$ min, $t_D = 19.86$ min.

(2*S*,3*R*)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)-3-(4′-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-[1,1′-biphenyl]-4-yl)butanamide (21a-(L))

The compound **21a-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 30 : 70) as a brown colored semi-solid (54 mg, 85%, 0.1 mmol scale); R_f (30% EtOAc/hexane) 0.5; mp: 85–87 °C; IR (DCM): 2928, 1718, 757 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.88 (s, 1H), 8.59 (dd, $J_1 = 5.8$, $J_2 = 3.1$ Hz, 1H), 8.47 (dd, $J_1 = 4.0$, $J_2 = 1.3$ Hz, 1H), 8.02 (dd, $J_1 = 8.3$, $J_2 = 1.4$ Hz, 1H), 7.94 (dd, $J_1 = 5.4$, $J_2 = 3.1$ Hz, 2H), 7.84 (d, $J = 7.8$ Hz, 2H), 7.77 (dd, $J_1 = 5.3$, $J_2 = 3.1$ Hz, 2H), 7.58 (s, 4H), 7.48 (d, $J = 7.8$ Hz, 2H), 7.41–7.39 (m, 2H), 7.28–7.25 (m, 1H), 5.36 (d, $J = 11.5$ Hz, 1H), 4.43–4.35 (m, 1H), 1.36–1.35 (m, 15H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.3, 165.9, 148.0, 143.3, 142.2, 139.9, 138.3, 135.9, 135.2, 134.3, 134.0, 131.8, 128.3, 128.0, 127.6, 127.1, 126.3, 123.7, 121.8, 121.4, 116.7, 83.8, 61.3, 38.6, 24.9, 24.9, 20.6. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{39}H_{37}BN_3O_5$: 638.2826 found, 638.2827. $[\alpha]^{25}$ D = +28.00 (c = 0.05 g mL^{-1}, $CHCl_3$). The enantiomeric ratio (er = 96 : 4) of the compound **21a-(L)** was determined by HPLC using the Daicel Chiralpak IA column, hexane/*i*-PrOH (40 : 60), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, $t_L = 13.00$ min, $t_D = 17.73$ min.

(2*S,3*R**)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)-3-(4′-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-[1,1′-biphenyl]-4-yl)pentanamide (21b-(DL))**

The compound **21b-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 30 : 70) as a colorless solid (145 mg, 89%, 0.25 mmol scale); R_f (30% EtOAc/hexane) 0.5; mp: 120–122 °C; IR (DCM): 2931, 1715, 753 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.93 (s, 1H), 8.59–8.57 (m, 1H), 8.51 (dd, $J_1 = 4.2$, $J_2 = 1.5$ Hz, 1H), 7.98 (d, $J = 8.3$ Hz, 1H), 7.91 (dd, $J_1 = 5.4$, $J_2 = 3.0$ Hz, 2H), 7.85 (d, $J = 7.9$ Hz, 2H), 7.72 (dd, $J_1 = 5.4$, $J_2 = 3.0$ Hz, 2H), 7.61–7.55 (m, 4H), 7.49 (d, $J = 8.0$ Hz, 2H), 7.36 (d, $J = 4.1$ Hz, 2H), 7.24 (dd, $J_1 = 8.2$, $J_2 = 4.2$ Hz, 1H), 5.42 (d, $J = 11.6$ Hz, 1H), 4.18 (td, $J_1 = 11.3$, $J_2 = 3.2$ Hz, 1H), 1.83–1.62 (m, 2H), 1.35 (s, 12H), 0.75 (t, $J = 7.2$ Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.3, 165.9, 147.9, 143.2, 139.7, 139.6, 138.2, 135.8, 135.1, 134.2, 133.9, 131.7, 129.1, 127.7, 127.5, 127.0, 126.1, 123.6, 121.7, 121.3, 116.6, 83.7, 60.8, 45.3, 26.3, 24.8, 11.2. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{40}H_{39}BN_3O_5$: 652.2983 found, 652.2993.

(2*S,3*R**)-2-(1,3-dioxoisoindolin-2-yl)-4-methyl-*N*-(quinolin-8-yl)-3-(4′-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-[1,1′-biphenyl]-4-yl)pentanamide (21c-(DL))**

The compound **21c-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 30 : 70) as a colorless solid (52 mg, 78%, 0.1 mmol scale); R_f (30% EtOAc/hexane) 0.5; mp: 140–142 °C; IR (DCM): 2927, 1716, 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 10.04 (s, 1H), 8.56–8.52 (m, 2H), 8.01–7.85 (m, 5H), 7.77–7.44 (s, 2H), 7.65–7.56 (m, 6H), 7.36–7.26 (m, 3H), 5.71 (d, $J = 12.2$ Hz, 1H), 4.31 (d, $J = 12.0$ Hz, 1H), 2.09–2.02 (m, 1H), 1.36 (s, 12H), 0.88 (d, $J = 6.1$ Hz, 3H), 0.82 (d, $J = 6.0$ Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.5, 166.2, 147.9,

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143.3, 139.8, 138.4, 136.1, 135.8, 135.2, 134.2, 134.2, 131.9, 130.5, 128.7, 127.6, 127.2, 127.0, 126.2, 123.7, 121.7, 121.4, 116.8, 83.8, 57.9, 48.3, 29.2, 24.9, 21.5, 16.3. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{41}H_{41}BN_3O_5$: 666.3139 found, 666.3145.

(2*S**,3*R**)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)-3-(4′-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-[1,1′-biphenyl]-4-yl)hexanamide (21d-DL)

The compound **21d-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 30 : 70) as a colorless solid (115 mg, 86%, 0.2 mmol scale); R_f (30% EtOAc/hexane) 0.5; mp: 123–125 °C; IR (DCM): 2928, 1716, 755 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.88 (s, 1H), 8.58 (dd, $J_1 = 5.6, J_2 = 3.4$ Hz, 1H), 8.51 (dd, $J_1 = 4.2, J_2 = 1.6$ Hz, 1H), 7.99 (dd, $J_1 = 8.3, J_2 = 1.4$ Hz, 1H), 7.93 (dd, $J_1 = 5.4, J_2 = 3.0$ Hz, 2H), 7.84 (d, $J = 8.0$ Hz, 2H), 7.74 (dd, $J_1 = 5.4, J_2 = 3.0$ Hz, 2H), 7.59–7.54 (m, 4H), 7.47 (d, $J = 8.1$ Hz, 2H), 7.39–7.34 (m, 2H), 7.25 (dd, $J_1 = 8.5, J_2 = 4.0$ Hz, 1H), 5.39 (d, $J = 11.7$ Hz, 1H), 4.32–4.24 (m, 1H), 1.71–1.62 (m, 2H), 1.36 (s, 12H), 1.20–1.06 (m, 2H), 0.80 (t, $J = 7.3$ Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.3, 166.0, 147.9, 143.2, 140.0, 139.7, 138.2, 135.8, 135.1, 134.2, 133.9, 131.7, 129.0, 127.7, 127.5, 126.9, 126.1, 123.6, 121.7, 121.3, 116.6, 83.7, 61.0, 43.6, 35.3, 24.8, 19.7, 13.8. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{41}H_{41}BN_3O_5$: 666.3139 found, 666.3140.

(2*S**,3*R**)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)-3-(4′-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-[1,1′-biphenyl]-4-yl)octanamide (21e-(DL))

The compound **21e-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 30 : 70) as a brown colored semi-solid (92 mg, 88%, 0.15 mmol scale); R_f (30% EtOAc/hexane) 0.5; mp: 184–186 °C; IR (DCM): 2928, 1715, 751 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.87 (s, 1H), 8.57 (dd, $J_1 = 6.9, J_2 = 3.4$ Hz, 1H), 8.51 (dd, $J_1 = 4.2, J_2 = 1.6$ Hz, 1H), 8.00 (dd, $J_1 = 8.3, J_2 = 1.6$ Hz, 1H), 7.93 (dd, $J_1 = 5.4, J_2 = 3.0$ Hz, 2H), 7.84 (d, $J = 8.1$ Hz, 2H), 7.75 (dd, $J_1 = 5.4, J_2 = 3.0$ Hz, 2H), 7.58–7.54 (m, 4H), 7.48 (d, $J = 8.1$ Hz, 2H), 7.38–7.37 (m, 2H), 7.27–7.23 (m, 1H), 5.38 (d, $J = 11.7$ Hz, 1H), 4.29–4.22 (m, 1H), 1.71–1.65 (m, 2H), 1.36 (s, 12H), 1.23–1.04 (m, 6H), 0.75 (t, $J = 6.5$ Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.3, 166.0, 147.9, 143.2, 140.0, 139.7, 138.2, 135.8, 135.1, 134.2, 133.9, 131.7, 129.0, 127.7, 127.5, 127.0, 126.1, 123.6, 121.7, 121.3, 116.6, 83.7, 61.1, 43.8, 33.1, 31.5, 26.2, 24.8, 22.4, 13.9. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{43}H_{45}BN_3O_5$: 694.3452 found, 694.3461.

11-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)-3-(4′-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-[1,1′-biphenyl]-4-yl) undecanamide (22)

The compound **22** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 30 : 70) as a brown colored semi-solid (115 mg, 78%, 0.20 mmol scale); R_f (30% EtOAc/hexane) 0.5; IR (DCM): 2928, 1711, 755 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.67 (s, 1H), 8.73 (d, $J = 7.4$ Hz, 1H), 8.68 (dd, $J_1 = 4.2, J_2 = 1.4$ Hz, 1H), 8.07 (d, $J = 8.2$ Hz, 1H), 7.82 (d, $J = 8.0$ Hz, 2H), 7.79 (dd, $J_1 = 5.4, J_2 = 3.1$ Hz, 2H), 7.65 (dd, $J_1 = 5.4, J_2 = 3.0$ Hz, 2H), 7.55–7.34 (m, 9H), 3.63 (t, $J = 7.4$ Hz, 2H), 3.37–3.30 (m, 1H), 2.88–2.85 (m, 2H), 1.86–1.60 (m, 4H), 1.35 (s, 12H), 1.25–1.17 (m, 10H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 170.2, 168.3, 147.9, 143.8, 143.5, 138.8, 138.1, 136.1, 135.1, 134.3, 133.7, 132.0, 128.5, 127.9, 127.7, 127.2, 126.8, 126.1, 123.0, 121.4, 121.3, 116.3, 83.7, 45.7, 42.2, 37.9, 36.1, 29.3, 29.2, 29.0, 28.4, 27.3, 26.7, 24.8. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{46}H_{51}BN_3O_5$: 736.3922 found, 736.3926.

(2*S**,3*R**)-methyl 2-((*tert*-butoxycarbonyl)amino)-3-phenyl-3-(4′-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-[1,1′-biphenyl]-4-yl)propanoate (23-(DL))

The compound **23-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 20 : 80) as a colorless semi-solid (48 mg, 86%, 0.1 mmol scale); R_f (20% EtOAc/hexane) 0.5; IR (DCM): 2927, 1712, 753 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.86 (d, $J = 7.9$ Hz, 2H), 7.57–7.52 (m, 4H), 7.35–7.22 (m, 7H), 5.12 (t, $J = 8.4$ Hz, 1H), 4.87 (d, $J = 8.8$ Hz, 1H), 4.44 (d, $J = 8.2$ Hz, 1H), 3.54 (s, 3H), 1.37 (s, 9H), 1.35 (s, 12H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 172.6, 155.2, 143.2, 139.6, 139.6, 139.5, 135.2, 129.0, 128.8, 128.7, 128.6, 128.3, 127.2, 126.2, 83.8, 80.2, 56.7, 53.3, 52.1, 28.2, 24.8. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{33}H_{40}BNNaO_6$: 580.2846 found, 580.2831.

(2*S**,3*R**)-ethyl 2-((*tert*-butoxycarbonyl)amino)-3-phenyl-3-(4′-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-[1,1′-biphenyl]-4-yl)propanoate (24-(DL))

The compound **24-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 20 : 80) as a colorless solid (50 mg, 87%, 0.1 mmol scale); R_f (20% EtOAc/hexane) 0.5; mp: 168–170 °C; IR (DCM): 2926, 1715, 758 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.88 (d, $J = 8.2$ Hz, 2H), 7.59–7.54 (m, 4H), 7.39–7.25 (m, 7H), 5.12 (t, $J = 9.0$ Hz, 1H), 4.91 (d, $J = 9.0$ Hz, 1H), 4.42 (d, $J = 8.8$ Hz, 1H), 4.04–3.96 (m, 2H), 1.39 (s, 9H), 1.38 (s, 12H), 0.99 (t, $J = 7.1$ Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 172.2, 155.2, 143.3, 139.7, 139.7, 139.6, 135.2, 128.8, 128.7, 128.6, 127.2, 126.2, 83.8, 80.1, 61.2, 56.8, 53.6, 28.2, 24.8, 13.7. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{34}H_{42}BNNaO_6$: 594.3003 found, 594.3008.

Diethyl 3,3′-([1,1′:4′,1″:4″,1‴-quaterphenyl]-4,4‴-diyl)(2*S**,2′*S**,3*R**,3′*R**)-bis(2-((tert-butoxycarbonyl)amino)-3-phenylpropanoate) (25-(DL))

The compound **25-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 20 : 80) as a colorless solid (30 mg, 67%, 0.05 mmol scale); R_f (20% EtOAc/hexane) 0.5; mp: 167–169 °C; IR (DCM): 2926, 1710, 752 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.72–7.70 (m, 4H), 7.67–7.65 (m, 4H), 7.60–7.57 (m, 4H), 7.41–7.33 (m, 12H), 7.30–7.26 (m, 2H), 5.13 (t, $J = 8.9$ Hz, 2H), 4.92 (d, $J = 9.1$ Hz, 2H), 4.43 (d, $J = 8.8$ Hz, 2H), 4.06–3.98 (m, 4H), 1.40 (br. s, 18H), 1.01 (t, $J = 7.1$ Hz, 6H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 172.2, 155.2, 139.6, 139.5, 139.3, 128.9, 128.7, 128.6, 127.3, 127.2, 127.0, 80.1, 61.2, 56.8, 53.6, 28.2, 13.7. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{56}H_{60}N_2NaO_8$: 911.4247 found, 911.4243.

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Ethyl (2*S,3*R**)-3-([1,1′:4′,1″:4″,1‴-quaterphenyl]-4-yl)-2-aminopentanoate (26a-(DL))**

The compound **26a-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a colorless solid (32 mg, 71%, 0.1 mmol scale); R_f (50% EtOAc/hexane) 0.5; mp: 130–132 °C; IR (DCM): 2928, 1732, 760 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.74–7.65 (m, 10H), 7.59 (d, J = 8.2 Hz, 2H), 7.47 (t, J = 7.8 Hz, 2H), 7.37 (t, J = 7.4 Hz, 1H), 7.31–7.26 (m, 2H), 4.07–4.01 (m, 2H), 3.61 (d, J = 6.4 Hz, 1H), 2.90–2.85 (m, 1H), 1.98–1.77 (m, 2H), 1.11 (t, J = 7.1 Hz, 3H), 0.85 (t, J = 7.3 Hz, 3H). (The NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 174.9, 140.6, 140.2, 140.1, 139.9, 139.5, 139.4, 139.0, 129.0, 128.8, 127.5, 127.3, 127.0, 126.8, 60.7, 60.0, 51.8, 23.2, 14.0, 12.2. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{31}H_{32}NO_2$: 450.2433 found, 450.2426.

(2*S,3*R**)-2-amino-3-(4′-(6-methoxynaphthalen-2-yl)-[1,1′-biphenyl]-4-yl)-*N*-(quinolin-8-yl)pentanamide (26b-(DL))**

The compound **26b-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 20 : 80) as a colorless solid (19 mg, 69%, 0.05 mmol scale); R_f (20% EtOAc/hexane) 0.5; mp: 165–167 °C; IR (DCM): 2927, 1525, 753 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 11.37 (s, 1H), 8.89 (dd, J_1 = 7.2, J_2 = 1.8 Hz, 1H), 8.85 (dd, J_1 = 4.1, J_2 = 1.6 Hz, 1H), 8.14 (dd, J_1 = 8.2, J_2 = 1.6 Hz, 1H), 8.08–8.02 (m, 1H), 7.83–7.75 (m, 5H), 7.67–7.51 (m, 6H), 7.44–7.41 (m, 2H), 7.20–7.17 (m, 2H), 3.94 (s, 3H), 3.80 (d, J = 4.0 Hz, 1H), 3.54–3.49 (m, 1H), 2.04–1.71 (m, 3H), 0.89 (t, J = 7.3 Hz, 3H). (The NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 172.6, 157.8, 148.5, 140.7, 139.9, 139.4, 139.1, 139.0, 136.2, 135.7, 134.3, 133.8, 129.7, 129.2, 128.9, 128.0, 127.5, 127.3, 127.3, 127.2, 126.1, 125.8, 125.4, 121.8, 121.5, 119.2, 116.4, 105.5, 62.2, 55.3, 49.9, 20.3, 12.4. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{37}H_{34}N_3O_2$: 552.2651 found, 552.2656.

(2*S,3*R**)-ethyl 3-([1,1′:4′,1″:4″,1‴-quaterphenyl]-4-yl)-2-amino-4-methylpentanoate (27a-(DL))**

The compound **27a-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a colorless solid (16 mg, 78%, 0.044 mmol scale); R_f (50% EtOAc/hexane) 0.5; mp: 230–232 °C; IR (DCM): 2929, 1727, 760 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.74–7.68 (m, 10H), 7.60 (d, J = 7.3 Hz, 2H), 7.50 (t, J = 7.0 Hz, 2H), 7.40 (t, J = 6.8 Hz, 1H), 7.27 (d, J = 7.5 Hz, 2H), 4.16–4.06 (m, 2H), 3.93 (d, J = 5.9 Hz, 1H), 2.77 (t, J = 6.8 Hz, 1H), 2.51–2.42 (m, 1H), 1.17 (t, J = 7.0 Hz, 3H), 1.11 (d, J = 6.0 Hz, 3H), 0.86 (d, J = 6.1 Hz, 3H). (The NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 175.1, 140.6, 140.2, 140.1, 139.8, 139.5, 139.4, 139.0, 138.8, 129.8, 128.8, 127.5, 127.3, 127.0, 126.5, 60.7, 57.2, 56.6, 28.3, 21.5, 20.1, 14.0.HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{32}H_{34}NO_2$: 464.2590 found, 464.2591. The HPLC of the compound **27a-(DL)** was determined using the Daicel Chiralpak IC column, hexane/*i*-PrOH (80 : 20), flow rate 1.0 mL min^{-1}, UV detection at 326.3 nm, t_L = 16.31 min, t_D = 19.30 min.

(2*R*,3*S*)-ethyl 3-([1,1′:4′,1″:4″,1‴-quaterphenyl]-4-yl)-2-amino-4-methylpentanoate (27a-(D))

The compound **27a-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a colorless solid (15 mg, 74%, 0.044 mmol scale); R_f (50% EtOAc/hexane) 0.5; mp: 231–233 °C; IR (DCM): 2929, 1728, 760 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.73–7.64 (m, 10H), 7.56 (d, J = 8.1 Hz, 2H), 7.46 (t, J = 7.8 Hz, 2H), 7.36 (t, J = 7.3 Hz, 1H), 7.25–7.21 (m, 2H), 4.13–4.00 (m, 2H), 3.88 (d, J = 6.6 Hz, 1H), 2.72 (t, J = 7.8 Hz, 1H), 2.47–2.38 (m, 1H), 1.13 (t, J = 7.1 Hz, 3H), 1.06 (d, J = 6.6 Hz, 3H), 0.82 (d, J = 6.7 Hz, 3H). (The NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 175.1, 140.6, 140.1, 139.8, 139.5, 139.4, 138.9, 138.8, 129.8, 128.8, 127.5, 127.3, 127.0, 126.4, 60.6, 57.2, 56.5, 28.2, 21.5, 20.1, 14.0. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{32}H_{34}NO_2$: 464.2590 found, 464.2587. $[\alpha]^{25}$ D = −21.00 (c = 0.05 g mL^{-1}, $CHCl_3$). The enantiomeric ratio (er = 96 : 4) of the compound **27a-(D)** was determined by HPLC using the Daicel Chiralpak IC column, hexane/*i*-PrOH (80 : 20), flow rate 1.0 mL min^{-1}, UV detection at 326.3 nm, t_L = 14.74 min, t_D = 18.49 min.

(2*S,3*R**)-ethyl 3-([1,1′:3′,1″:4″,1‴-quaterphenyl]-4‴-yl)-2-amino-4-methylpentanoate (27b-(DL))**

The compound **27b-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a colorless solid (15 mg, 65%, 0.05 mmol scale); R_f (50% EtOAc/hexane) 0.5; mp: 88–90 °C; IR (DCM): 2927, 1730, 758 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.85 (s, 1H), 7.73–7.36 (m, 14H), 7.25–7.21 (m, 2H), 4.13–4.01 (m, 2H), 3.88 (d, J = 6.5 Hz, 1H), 2.72 (t, J = 7.7 Hz, 1H), 2.47–2.38 (m, 1H), 1.13 (t, J = 7.1 Hz, 3H), 1.06 (d, J = 6.6 Hz, 3H), 0.82 (d, J = 6.7 Hz, 3H). (The NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 174.4, 141.8, 141.2, 141.2, 139.9, 139.8, 139.1, 138.5, 129.8, 129.2, 128.8, 127.5, 127.4, 127.3, 127.3, 126.6, 126.2, 126.0, 125.9, 60.8, 56.9, 56.4, 28.3, 21.5, 20.2, 14.0. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{32}H_{34}NO_2$: 464.2590 found, 464.2603.

(2*S,3*R**)-ethyl 3-([1,1′:4′,1″:4″,1‴-quaterphenyl]-4-yl)-2-(1,3-dioxoisoindolin-2-yl)hexanoate (28a-(DL))**

The compound **28a-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 20 : 80) as a colorless solid (25 mg, 47%, 0.09 mmol scale); R_f (20% EtOAc/hexane) 0.5; mp: 214–216 °C; IR (DCM): 2926, 1714, 769 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.94–7.92 (m, 2H), 7.79–7.78 (m, 2H), 7.75–7.62 (m, 12H), 7.49–7.43 (m, 4H), 7.37 (t, J = 7.5 Hz, 1H), 5.13 (d, J = 10.3 Hz, 1H), 4.07–3.86 (m, 2H), 1.59–1.50 (m, 2H), 3.92–3.86 (m, 1H), 1.13–1.05 (m, 2H), 1.00 (t, J

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= 7.1 Hz, 3H), 0.77 (t, J = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.5, 167.8, 141.0, 140.7, 140.1, 139.8, 139.6, 139.4, 138.9, 134.3, 131.7, 129.0, 128.8, 127.5, 127.4, 127.3, 127.3, 127.0, 126.9, 123.7, 61.5, 57.3, 44.0, 34.5, 19.9, 13.8. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{40}H_{35}NNaO_4$: 616.2464 found, 616.2438.

(2*S**,3*R**)-ethyl 3-([1,1′:4′,1″:4″,1‴-quaterphenyl]-4-yl)-2-aminohexanoate (28b-(DL))

The compound **28b-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a colorless solid (16 mg, 78%, 0.044 mmol scale); R_f (50% EtOAc/hexane) 0.5; mp: 240–242 °C; IR (DCM): 2928, 1730, 748 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.72–7.65 (m, 11H), 7.59 (d, J = 7.8 Hz, 2H), 7.47 (t, J = 7.4 Hz, 2H), 7.37 (t, J = 7.2 Hz, 1H), 7.31 (d, J = 7.9 Hz, 1H), 4.08–4.00 (m, 2H), 3.60 (d, J = 6.2 Hz, 1H), 3.01–2.96 (m, 1H), 1.84–1.79 (m, 2H), 1.33–1.26 (m, 2H), 1.11 (t, J = 7.1 Hz, 3H), 0.90 (t, J = 7.2 Hz, 3H). (the NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 174.9, 140.7, 140.6, 140.2, 139.9, 139.6, 139.4, 139.1, 129.0, 128.8, 127.5, 127.3, 127.0, 126.9, 60.7, 60.2, 49.6, 32.3, 20.6, 14.0. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{32}H_{34}NO_2$: 464.2590 found, 464.2589. The HPLC of the compound **28b-(DL)** was determined using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (50 : 50), flow rate 1.0 mL min^{-1}, UV detection at 291.9 nm, t_L = 6.94 min, t_D = 8.53 min.

(2*R*,3*S*)-ethyl 3-([1,1′:4′,1″:4″,1‴-quaterphenyl]-4-yl)-2-aminohexanoate (28b-(D))

The compound **28b-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a colorless solid (15 mg, 74%, 0.044 mmol scale); R_f (50% EtOAc/hexane) 0.5; mp: 242–244 °C; IR (DCM): 2929, 1730, 747 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.72–7.65 (m, 11H), 7.59 (d, J = 8.0 Hz, 2H), 7.47 (t, J = 7.6 Hz, 2H), 7.37 (t, J = 7.3 Hz, 1H), 7.31 (d, J = 8.0 Hz, 1H), 4.09–4.01 (m, 2H), 3.60 (d, J = 6.2 Hz, 1H), 3.01–2.96 (m, 1H), 1.82 (q, J = 7.8 Hz, 2H), 1.33–1.25 (m, 2H), 1.11 (t, J = 7.1 Hz, 3H), 0.90 (t, J = 7.3 Hz, 3H). (the NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 174.9, 140.7, 140.5, 140.2, 139.9, 139.6, 139.4, 139.1, 129.0, 128.8, 127.5, 127.3, 127.0, 126.9, 60.7, 60.2, 49.6, 32.3, 20.6, 14.0. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{32}H_{34}NO_2$: 464.2590 found, 464.2599. $[\alpha]^{25}$ D = −48.00 (c = 0.05 g mL^{-1}, $CHCl_3$). The enantiomeric ratio (er = 96 : 4) of the compound **28b-(D)** was determined by HPLC using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (50 : 50), flow rate 1.0 mL min^{-1}, UV detection at 291.9 nm, t_L = 6.87 min, t_D = 8.39 min.

(2*S*,3*R*)-ethyl 3-([1,1′:4′,1″:4″,1‴-quaterphenyl]-4-yl)-2-aminohexanoate (SB-1912, 28b-(L))

The compound **28b-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a colorless solid (16 mg, 78%, 0.044 mmol scale); R_f (50% EtOAc/hexane) 0.5; mp: 241–243 °C; IR (DCM): 2931, 1731, 745 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.72–7.65 (m, 11H), 7.59 (d, J = 8.1 Hz, 2H), 7.47 (t, J = 7.7 Hz, 2H), 7.37 (t, J = 7.2 Hz, 1H), 7.31 (d, J = 8.0 Hz, 1H), 4.09–4.01 (m, 2H), 3.61 (d, J = 6.3 Hz, 1H), 3.02–2.96 (m, 1H), 1.82 (q, J = 7.8 Hz, 2H), 1.33–1.25 (m, 2H), 1.11 (t, J = 7.1 Hz, 3H), 0.90 (t, J = 7.3 Hz, 3H). (the NH_2 signal could not be clearly assigned in the proton NMR spectrum as it may be merged with the residual water peak). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 174.9, 140.6, 140.5, 140.1, 139.9, 139.5, 139.4, 139.0, 129.0, 128.8, 127.5, 127.3, 127.0, 126.9, 60.7, 60.2, 49.6, 32.3, 20.6, 14.0. HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{32}H_{34}NO_2$: 464.2590 found, 464.2601. $[\alpha]^{25}$ D = +50.00 (c = 0.05 g mL^{-1}, $CHCl_3$). The enantiomeric ratio (er = 95 : 5) of the compound **28b-(L)** was determined by HPLC using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (50 : 50), flow rate 1.0 mL min^{-1}, UV detection at 291.9 nm, t_L = 6.89 min, t_D = 8.02 min.

(2*S**,3*R**)-ethyl 3-(4′-(benzo[*d*][1,3]dioxol-5-yl)-[1,1′-biphenyl]-4-yl)-2-((*tert*-butoxycarbonyl)amino)-3-phenylpropanoate (29-(DL))

The compound **29-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 20 : 80) as a colorless solid (40 mg, 71%, 0.1 mmol scale); R_f (20% EtOAc/hexane) 0.5; mp: 200–202 °C; IR (DCM): 2927, 1739, 754 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.60–7.53 (m, 6H), 7.37–7.30 (m, 6H), 7.27–7.23 (m, 1H), 7.10–7.08 (m, 2H), 6.90–6.88 (m, 1H), 6.00 (s, 2H), 5.10 (t, J = 8.9 Hz, 1H), 4.90 (d, J = 9.0 Hz, 1H), 4.40 (d, J = 8.7 Hz, 1H), 4.03–3.95 (m, 2H), 1.37 (s, 9H), 0.97 (t, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 172.2, 155.2, 148.1, 147.1, 139.8, 139.6, 139.4, 139.3, 139.2, 135.0, 128.8, 128.7, 128.6, 127.2, 127.2, 127.0, 120.5, 108.6, 107.5, 101.1, 80.1, 61.2, 56.8, 53.6, 28.2, 13.7. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{35}H_{35}NNaO_6$: 588.2362 found, 588.2364.

Ethyl 3-([1,1′:4′,1″:4″,1‴-quaterphenyl]-4-yl)-7-(1,3-dioxoisoindolin-2-yl)heptanoate (30)

The compound **30** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 20 : 80) as a colorless solid (20 mg, 37%, 0.09 mmol scale); R_f (20% EtOAc/hexane) 0.5; mp: 160–162 °C; IR (DCM): 2930, 1708, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.81 (dd, J_1 = 5.3, J_2 = 3.1 Hz, 2H), 7.75–7.63 (m, 12H), 7.53 (d, J = 8.0 Hz, 2H), 7.47 (t, J = 7.7 Hz, 2H), 7.37 (t, J = 7.3 Hz, 1H), 7.26–7.24 (m, 2H), 4.05 (q, J = 7.1 Hz, 2H), 3.62 (t, J = 7.2 Hz, 2H), 3.18–3.10 (m, 1H), 2.68–2.57 (m, 2H), 1.77–1.61 (m, 4H), 1.31–1.22 (m, 2H), 1.15 (t, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 172.3, 168.4, 142.9, 140.7, 140.1, 139.9, 139.6, 139.3, 138.7, 133.8, 132.1, 128.8, 127.9, 127.5, 127.4, 127.3, 127.3, 127.0, 127.0, 123.1, 60.3, 41.7, 41.7, 37.7, 35.6, 28.3, 24.5, 14.1. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{41}H_{37}NNaO_4$: 630.2620 found, 630.2607.

Ethyl 2-((*tert*-butoxycarbonyl)amino)-3,3-bis(4′-(phenylethynyl)-[1,1′-biphenyl]-4-yl)propanoate (31-(DL))

The compound **31-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 20 : 80) as a colorless solid (20 mg, 63%, 0.044 mmol scale); R_f (20% EtOAc/

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hexane) 0.5; mp: 109–111 °C; IR (DCM): 2924, 1713, 755 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.53–7.40 (m, 16H), 7.36–7.27 (m, 10H), 5.10–5.04 (m, 1H), 4.87–4.84 (m, 1H), 4.39–4.37 (m, 1H), 3.99–3.92 (m, 2H), 1.31 (s, 9H), 0.93 (t, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 172.0, 155.2, 140.3, 140.2, 139.7, 139.4, 139.1, 132.0, 131.8, 131.6, 129.1, 128.9, 128.5, 128.3, 128.2, 127.2, 127.1, 127.0, 126.8, 123.2, 122.2, 122.2, 90.1, 89.2, 80.2, 61.2, 56.7, 53.3, 28.2, 13.7. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{50}H_{43}NNaO_4$: 744.3090 found, 744.3063. The HPLC of the compound **31-(DL)** was determined using the Daicel Chiralpak IA column, hexane/*i*-PrOH (50 : 50), flow rate 1.0 mL min^{-1}, UV detection at 300 nm, t_L = 14.93 min, t_D = 28.67 min.

Ethyl (*R*)-2-((*tert*-butoxycarbonyl)amino)-3,3-bis(4′-(phenylethynyl)-[1,1′-biphenyl]-4-yl)propanoate (31-(D))

The compound **31-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 20 : 80) as a colorless solid (20 mg, 63%, 0.044 mmol scale); R_f (20% EtOAc/hexane) 0.5; mp: 108–110 °C; IR (DCM): 2925, 1715, 755 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.51–7.39 (m, 16H), 7.33–7.25 (m, 10H), 5.09–5.01 (m, 1H), 4.87–4.84 (m, 1H), 4.38–4.36 (m, 1H), 3.97–3.89 (m, 2H), 1.30 (s, 9H), 0.92 (t, J = 6.9 Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 172.0, 155.2, 140.3, 140.2, 139.6, 139.4, 139.1, 132.0, 131.8, 131.6, 129.1, 128.9, 128.5, 128.3, 128.3, 128.2, 127.3, 127.1, 126.8, 123.2, 122.2, 122.2, 90.1, 89.2, 80.2, 61.2, 56.7, 53.3, 28.2, 13.8. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{50}H_{43}NNaO_4$: 744.3090 found, 744.3087. $[\alpha]^{25}$ D = −39.00 (c = 0.05 g mL^{-1}, $CHCl_3$). The enantiomeric ratio (er = 92 : 8) of the compound **31-(D)** was determined by HPLC using the Daicel Chiralpak IA column, hexane/*i*-PrOH (50 : 50), flow rate 1.0 mL min^{-1}, UV detection at 300 nm, t_L = 14.74 min, t_D = 27.92 min.

Ethyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-3,3-bis(4′-(phenylethynyl)-[1,1′-biphenyl]-4-yl)propanoate (31-(L))

The compound **31-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 20 : 80) as a colorless solid (21 mg, 66%, 0.044 mmol scale); R_f (20% EtOAc/hexane) 0.5; mp: 107–109 °C; IR (DCM): 2925, 1714, 755 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.52–7.40 (m, 16H), 7.35–7.27 (m, 10H), 5.09–5.02 (m, 1H), 4.86–4.84 (m, 1H), 4.40–4.34 (m, 1H), 3.98–3.91 (m, 2H), 1.30 (s, 9H), 0.93 (t, J = 6.6 Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 172.0, 155.2, 140.3, 140.2, 139.5, 139.3, 139.2, 132.0, 132.0, 131.9, 131.6, 129.1, 129.1, 128.9, 128.9, 128.6, 128.5, 128.3, 128.3, 127.3, 127.2, 127.1, 127.0, 126.8, 123.2, 122.3, 90.2, 89.2, 80.2, 61.3, 56.7, 28.2, 13.8. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{50}H_{43}NNaO_4$: 744.3090 found, 744.3089. $[\alpha]^{25}$ D = +42.00 (c = 0.05 g mL^{-1}, $CHCl_3$). The enantiomeric ratio (er = 93 : 7) of the compound **31-(L)** was determined by HPLC using the Daicel Chiralpak IA column, hexane/*i*-PrOH (50 : 50), flow rate 1.0 mL min^{-1}, UV detection at 300 nm, t_L = 14.89 min, t_D = 28.52 min.

Ethyl 3,3-di([1,1′:4′,1″-terphenyl]-4-yl)-2-((*tert*-butoxycarbonyl)amino)propanoate (32a-(DL))

The compound **32a-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 20 : 80) as a colorless solid (20 mg, 59%, 0.05 mmol scale); R_f (20% EtOAc/hexane) 0.5; mp: 175–177 °C; IR (DCM): 2926, 1712, 761 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.71–7.37 (m, 26H), 5.18 (t, J = 9.0 Hz, 1H), 4.97 (d, J = 9.0 Hz, 1H), 4.48 (d, J = 8.7 Hz, 1H), 4.08–4.00 (m, 2H), 1.41 (s, 9H), 1.03 (t, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 172.2, 155.3, 140.6, 140.6, 140.2, 139.5, 139.5, 139.4, 138.8, 129.1, 128.9, 128.8, 127.5, 127.3, 127.1, 127.0, 80.2, 61.2, 56.8, 53.4, 28.2, 13.8. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{46}H_{43}NNaO_4$: 696.3090 found, 696.3088. The HPLC of the compound **32a-(DL)** was determined using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (50 : 50), flow rate 1.0 mL min^{-1}, UV detection at 296 nm, t_D = 8.66 min, t_L = 11.89 min.

(*R*)-ethyl 3,3-di([1,1′:4′,1″-terphenyl]-4-yl)-2-((*tert*-butoxycarbonyl)amino)propanoate (32a-(D))

The compound **32a-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 20 : 80) as a colorless solid (21 mg, 62%, 0.05 mmol scale); R_f (20% EtOAc/hexane) 0.5; mp: 176–178 °C; IR (DCM): 2926, 1712, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.68–7.33 (m, 26H), 5.16 (t, J = 8.9 Hz, 1H), 4.96 (d, J = 9.1 Hz, 1H), 4.46 (d, J = 8.8 Hz, 1H), 4.06–3.97 (m, 2H), 1.38 (s, 9H), 0.99 (t, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 172.2, 155.2, 140.6, 140.6, 140.1, 139.5, 139.4, 139.4, 138.8, 129.0, 128.9, 128.8, 127.5, 127.3, 127.1, 127.0, 80.2, 61.2, 56.8, 53.4, 28.2, 13.8. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{46}H_{43}NNaO_4$: 696.3090 found, 696.3092. $[\alpha]^{25}$ D = −25.00 (c = 0.05 g mL^{-1}, $CHCl_3$). The enantiomeric ratio (er = 95 : 5) of the compound **32a-(D)** was determined by HPLC using the Daicel Chiralcel ODH column, hexane/*i*-PrOH (50 : 50), flow rate 1.0 mL min^{-1}, UV detection at 296 nm, t_D = 7.98 min, t_L = 11.00 min.

Ethyl 2-((*tert*-butoxycarbonyl)amino)-3,3-bis(4″-chloro-[1,1′:4′,1″-terphenyl]-4-yl)propanoate (32b-(DL))

The compound **32b-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 20 : 80) as a colorless solid (20 mg, 54%, 0.05 mmol scale); R_f (20% EtOAc/hexane) 0.5; mp: 230–232 °C; IR (DCM): 2925, 1712, 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.65–7.41 (m, 24H), 5.20–5.16 (m, 1H), 4.97 (d, J = 8.1 Hz, 1H), 4.48 (d, J = 8.6 Hz, 1H), 4.10–3.99 (m, 2H), 1.41 (s, 9H), 1.03 (d, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 172.1, 155.2, 139.9, 139.8, 139.5, 139.5, 139.4, 139.3, 139.1, 138.9, 133.5, 131.9, 129.2, 129.1, 129.0, 128.9, 128.5, 128.2, 127.4, 127.4, 127.3, 127.2, 127.1, 127.0, 80.2, 61.2, 56.8, 53.5, 28.2, 13.8. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{46}H_{41}Cl_2NNaO_4$: 764.2310 found, 764.2323.

Ethyl 2-((*tert*-butoxycarbonyl)amino)-3,3-bis(4′-(thiophen-2-yl)-[1,1′-biphenyl]-4-yl)propanoate (33-(DL))

The compound **33-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 20 : 80) as a colorless solid (18 mg, 52%, 0.05 mmol scale); R_f (20% EtOAc/hexane) 0.5; mp: 166–168 °C; IR (DCM): 2925, 1711, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.69–7.08 (m, 22H), 5.13 (t, J = 8.8 Hz, 1H), 4.93 (d, J = 9.0 Hz, 1H), 4.43 (d, J = 8.7 Hz, 1H), 4.04–3.96 (m, 2H), 1.37 (s, 9H), 0.98 (t, J = 7.1 Hz,

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3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 172.2, 155.2, 143.9, 140.6, 140.6, 140.1, 140.0, 140.0, 139.5, 139.3, 138.7, 129.1, 129.0, 128.9, 128.8, 128.8, 128.1, 127.4, 127.3, 127.3, 127.3, 127.2, 127.0, 126.3, 124.9, 123.1, 80.1, 61.2, 56.8, 53.4, 28.2, 13.7. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{42}H_{39}NNaO_4S_2$: 708.2218 found, 708.2212.

(2*S**,3*R**)-ethyl 2-(2-((*tert*-butoxycarbonyl)amino)acetamido)-3-(4″-methoxy-[1,1′:4′,1″-terphenyl]-4-yl)pentanoate (34a-(DL))

The compound **34a-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 80 : 20) as a colorless solid (22 mg, 78%, 0.05 mmol scale); R_f (80% EtOAc/hexane) 0.5; mp: 190–192 °C; IR (DCM): 2932, 1660, 812 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.63–7.55 (m, 8H), 7.22 (d, J = 8.1 Hz, 2H), 6.99 (d, J = 8.7 Hz, 2H), 6.71 (d, J = 8.6 Hz, 1H), 5.20 (br. s, 1H), 4.83 (t, J = 7.9 Hz, 1H), 3.98 (q, J = 7.0 Hz, 2H), 3.90–3.76 (m, 5H), 2.92–2.86 (m, 1H), 1.97–1.78 (m, 2H), 1.46 (s, 9H), 1.03 (t, J = 7.0 Hz, 3H), 0.84 (t, J = 7.3 Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 171.2, 169.1, 159.2, 139.7, 139.6, 139.0, 138.3, 133.1, 128.9, 128.0, 127.2, 127.0, 126.9, 114.2, 80.3, 61.2, 56.8, 55.3, 50.8, 44.4, 28.2, 24.4, 13.8, 12.1. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{33}H_{40}N_2NaO_6$: 583.2784 found, 583.2789.

Ethyl (*S**)-12-((*R**)-1-(4″-methoxy-[1,1′:4′,1″-terphenyl]-4-yl) propyl)-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oate (34b-(DL))

The compound **34b-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 80 : 20) as a colorless solid (25 mg, 81%, 0.05 mmol scale); R_f (80% EtOAc/hexane) 0.5; mp: 168–170 °C; IR (DCM): 2932, 1655, 813 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.63–7.56 (m, 8H), 7.26–6.65 (m, 6H), 5.17 (s, 1H), 4.81 (t, J = 8.0 Hz, 1H), 4.05–3.94 (m, 4H), 3.86 (br. s, 5H), 2.96–2.90 (m, 1H), 1.96–1.70 (m, 2H), 1.47 (s, 9H), 1.04 (t, J = 7.1 Hz, 3H), 0.84 (t, J = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 171.1, 170.0, 168.2, 159.2, 156.1, 139.7, 139.6, 138.9, 138.2, 133.1, 129.0, 128.0, 127.2, 127.0, 126.9, 114.3, 80.6, 61.3, 57.1, 55.4, 50.5, 44.3, 43.0, 28.3, 24.4, 13.8, 12.1. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{35}H_{43}N_3NaO_7$: 640.2999 found, 640.2984. The HPLC of the compound **34b-(DL)** was determined using the Daicel Chiralpak IA column, hexane/*i*-PrOH (80 : 20), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 15.30 min, t_D = 17.91 min.

Ethyl (*R*)-12-((*S*)-1-(4″-methoxy-[1,1′:4′,1″-terphenyl]-4-yl) propyl)-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oate (34b-(D))

The compound **34b-(D)** was obtained after purification by column chromatography on silica gel (EtOAc:hexanes = 80 : 20) as a colorless solid (25 mg, 81%, 0.05 mmol scale); R_f (80% EtOAc/hexane) 0.5; mp: 167–169 °C; IR (DCM): 2932, 1655, 813 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.67–7.58 (m, 8H), 7.28–7.00 (m, 6H), 5.41 (s, 1H), 4.82 (t, J = 8.2 Hz, 1H), 4.11–3.96 (m, 4H), 3.88 (br. s, 5H), 2.97–2.91 (m, 1H), 2.21–1.79 (m, 2H), 1.48 (s, 9H), 1.03 (t, J = 7.1 Hz, 3H), 0.85 (t, J = 7.3 Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 171.1, 170.0, 168.2, 159.2, 156.1, 139.7, 139.6, 138.9, 138.2, 133.1, 129.0, 128.0, 127.2, 127.0, 126.9, 114.3, 80.6, 61.3, 57.1, 55.3, 50.4, 44.3, 42.9, 28.3, 24.4, 13.8, 12.1. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{35}H_{43}N_3NaO_7$: 640.2999 found, 640.2984. $[\alpha]^{25}$ D = −18.00 (c = 0.05 g mL^{-1}, $CHCl_3$).The enantiomeric ratio (er = 98 : 2) of the compound **34b-(D)** was determined by HPLC using the Daicel Chiralpak IA column, hexane/*i*-PrOH (80 : 20), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 15.50 min, t_D = 18.11 min.

Ethyl (*S*)-12-((*R*)-1-(4″-methoxy-[1,1′:4′,1″-terphenyl]-4-yl) propyl)-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oate (34b-(L))

The compound **34b-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 80 : 20) as a colorless solid (26 mg, 84%, 0.05 mmol scale); R_f (80% EtOAc/hexane) 0.5; mp: 169–171 °C; IR (DCM): 2932, 1655, 813 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.64–7.57 (m, 8H), 7.25–7.00 (m, 6H), 5.43 (br. s, 1H), 4.82 (t, J = 8.2 Hz, 1H), 4.11–3.96 (m, 4H), 3.88 (br. s, 5H), 2.97–2.91 (m, 1H), 1.95–1.80 (m, 2H), 1.48 (s, 9H), 1.02 (t, J = 7.2 Hz, 3H), 0.84 (t, J = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 171.3, 170.3, 168.6, 159.2, 156.2, 139.7, 139.5, 138.9, 138.2, 133.1, 128.9, 128.0, 127.2, 127.0, 126.8, 114.2, 80.4, 61.2, 57.2, 55.3, 55.3, 50.3, 42.9, 28.3, 24.4, 13.7, 12.0. HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{35}H_{43}N_3NaO_7$: 640.2999 found, 640.2984. $[\alpha]^{25}$ D = +14.00 (c = 0.05 g mL^{-1}, $CHCl_3$). The enantiomeric ratio (er = 97 : 3) of the compound **34b-(L)** was determined by HPLC using the Daicel Chiralpak IA column, hexane/*i*-PrOH (80 : 20), flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 15.04 min, t_D = 18.07 min.

Data availability

The data are available within the article or its ESI.† The crystallographic data for **21a(L)** have been deposited at the CCDC under number 2426927 and can be obtained from **https://www.ccdc.cam.ac.uk/structures/** (free of charge).

Conflicts of interest

There are no conflicts to declare.

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20 DL-Carboxamides of alanine **3a-(DL)**, 2-aminobutyric acid **3b-(DL)**, norvaline **3c-(DL)**, leucine **3d-(DL)**, norleucine **3e-(DL)**, phenylalanine, **3f-(DL)**, 2-aminooctanoic acid **3g-(DL)**, linked with 8-aminoquinoline directing group were assembled from their respective racemic amino acids and 8-aminoquinoline. Enantioenriched l-carboxamides of alanine **3a-(L)**, 2-aminobutyric acid **3b-(L)**, norvaline **3c-(L)**, leucine **3d-(L)**, norleucine **3e-(L)**, phenylalanine, **3f-(L)**, linked with 8-aminoquinoline directing group were assembled from their respective enantiopure L-amino acids and 8-aminoquinoline. Enantioenriched D-carboxamides of alanine **3a-(D)**, norvaline **3c-(D)**, leucine **3d-(D)**, norleucine **3e-(D)**, phenylalanine, **3f-(D)**, linked with 8-aminoquinoline directing group were assembled from their respective enantiopure D-amino acids and 8-aminoquinoline using standard methods, see ref. 18.

21 Single crystal of **21a-(L)** was recrystallized from dichloromethane/ diethyl ether. Crystal data. $C_{39}H_{36}BN_3O_5$, M = 637.52, Monoclinic, a = 14.619 (3), b = 6.8032 (17), c = 17.129 (3) Å, V = 1689.3 (6) Å^3, T = 293 K, space group = $P2_1$ (no. 4), Z = 2, 10152 reflections measured, 8670 unique (R^{int} = 0.066), which were used in all calculations. The final $wR(F^2)$ was 0.099 (all data).