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Construction of dansylated (fluorescent) amino acid motifs *via* C(sp^3)–H arylation

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We describe the construction of a library of novel dansylated (fluorescent) phenylalanine-type unnatural amino acid scaffolds using a Pd(II)-catalyzed C(sp^3)–H arylation method. A literature survey revealed that, in general, the dansyl moiety is introduced at the N-terminus of amino acids. Various dansylated amino acids and peptides have been used as fluorophores or probes and are known to show promising biological activities. Our strategy involved the introduction of dansylated anilines into the backbone of amino acids *via* a Pd(II)-catalyzed 8-aminoquinoline directing group-aided β-C(sp^3)–H arylation strategy. We have assembled novel racemic/enantioenriched dansylated α-amino acid scaffolds using norvaline, phenylalanine, leucine, norleucine, and non-α-amino acid derivatives. A preliminary study was conducted to show the application of representative dansylated phenylalanine-type molecules for detecting metal cations. We conducted screening of a library of 58 small molecules (10 μM), and identified compounds **18a-(L)** and **20b-(D)** as potent inhibitors of IAV infection in the human lung alveolar cell line A549.

Introduction

Transition metal-catalyzed functionalization of sp^3 C–H bonds in small molecules has emerged as a pivotal chemical transformation in organic synthesis.[1–3] Site-selective incorporation of functional groups into small molecules has been achieved with the aid of various types of directing groups (DGs).[2,3] In particular, Pd(II)-catalyzed bidentate directing group (8-aminoquinoline or picolinamide DG)-directed C–H functionalization is a well-known method for incorporating functional groups into the backbone of small molecules, including amino acids.[2–10] This route has enabled the diversification of amino acids and the construction of new and functionalized nonproteinogenic (unnatural/non-canonical) amino acid motifs.[3,6–10]

Unnatural amino acids, including D-amino acids, play a pivotal role in the ever-expanding areas of organic synthesis, chemical biology, and medicinal chemistry.[11,12] They have found applications as building blocks for synthesizing natural and bioactive molecules and as molecular tools for studying peptides, proteins, and enzymes. Incorporation of unnatural amino acids into proteins has been an intriguing topic of research in chemical biology.[11] Given their vast applications, there have been continuous efforts to develop new methods affording modified unnatural amino acid motifs.[11,12]

Fluorescent and fluorophore moiety-containing molecules are used as probes to study molecular functions and as sensors to detect metal ions and small or macromolecules.[13] The dansyl moiety is a widely employed fluorophore for labelling proteins, peptides, amino acids, and oligonucleotides and for detecting transition metal cations and imaging living systems (Fig. 1).[14–21] In particular, N-terminus dansylated amino acid motifs have been used as fluorescent probes for detecting metal ions and intracellular measurements, and as chiral molecular probes for apoptosis imaging and protein tyrosine phosphatase assays.[15–19] Furthermore, dansylated compounds have been explored as bio-active compounds, for example, as antagonists of human 5-HT$_4$ receptors and antagonists of neuropeptide FF,[20a,b] and some molecules have been found to exhibit cell-penetrating properties[20c] and strong micro-agonist potency *in vitro*.[20d] Hohsaka,[21a] Chamberlin[21b] and Schultz[21c] reported the incorporation of dansylated unnatural amino acid motifs into proteins.

Markedly, there have been continuous efforts to develop novel dansyl-based molecular architectures and explore their applications.[14–22]

Recently, we reported the incorporation of photo-responsive azobenzene or fluorene units into the backbone of amino acids *via* a Pd(II)-catalyzed bidentate DG-aided β-C(sp^3)–H arylation method.[6d,e] Along this line, we herein report the application of a Pd(II)-catalyzed DG-assisted C(sp^3)–H arylation

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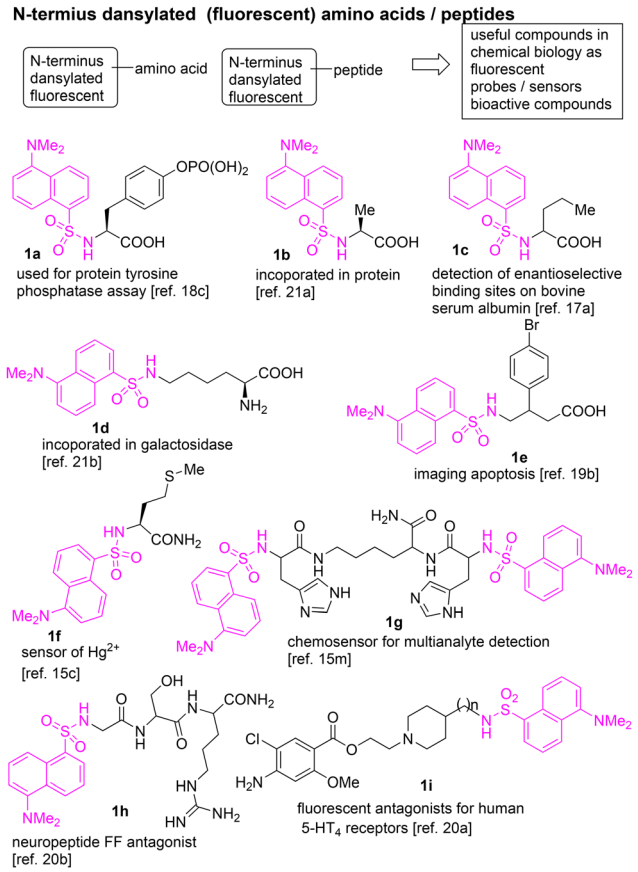
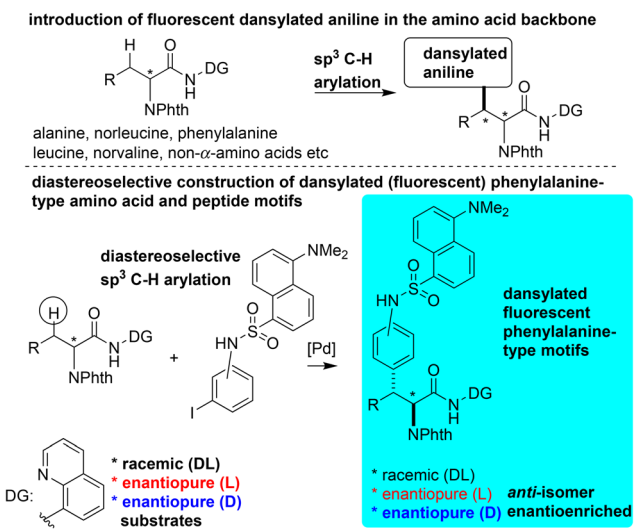


Fig. 1 Examples of N-terminus dansylated amino acid and peptide molecules and their applications.

route for the construction of dansylated (fluorescent) phenylalanine-type unnatural amino acid scaffolds (Scheme 1). We aimed to introduce fluorescent dansylated anilines into the backbone of amino acids *via* a Pd(II)-catalyzed 8-aminoquinoline DG-assisted β-C(sp^3)–H arylation strategy by using iodoanilines having a dansyl moiety as a coupling partner. This study aimed to synthesize racemic (DL)/enantioenriched (L and D) phenylalanine-type dansylated α-amino acid scaffolds using norvaline, phenylalanine, leucine, norleucine, 2-aminobutyric acid, 2-aminooctanoic acid, and non-α-amino acid derivatives.



Scheme 1 Introduction of dansylated anilines into the backbone of amino acids *via* β-C(sp^3)–H arylation and construction of dansylated phenylalanine motifs.

Results and discussion

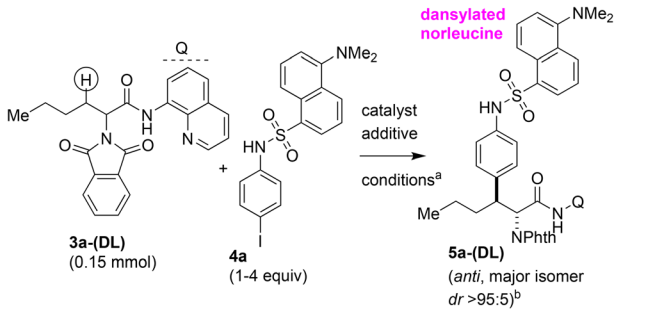
For the synthesis of dansyl-based unnatural amino acid derivatives *via* a Pd(II)-catalyzed directing group-assisted β-C(sp^3)–H arylation protocol, first, the *N*-phthaloyl norleucine derivative **3a-(DL)** possessing the bidentate directing group (DG) 8-aminoquinoline was synthesized from DL-norleucine. We then attempted the Pd(II)-catalyzed 8-aminoquinoline DG-assisted arylation of the prochiral β-C(sp^3)–H bond[6–9] of the norleucine derivative **3a-(DL)** with dansyl-linked 4-iodoaniline (**4a**, 5-(dimethylamino)-*N*-(4-iodophenyl)naphthalene-1-sulfonamide).

Optimization of the reaction conditions was carried out by using different metal catalysts and additives in different solvents. First, we heated a mixture of the norleucine derivative **3a-(DL)** possessing the bidentate directing group (DG) 8-aminoquinoline and dansyl-linked 4-iodoaniline (**4a**, 1 equiv.) in the presence of $Pd(OAc)_2$ (10 mol%) and AgOAc (as an iodide ion scavenger, 2.2 equiv.) in toluene (2 mL) at 110 °C for 24 h.[6d,e] This reaction afforded the expected dansyl-based norleucine unnatural amino acid **5a-(DL)** in 28% yield (entry 1, Table 1). Next, treatment of **3a-(DL)** with 2 and 3 equiv. of **4a** in the presence of $Pd(OAc)_2$ and AgOAc furnished product **5a-(DL)** in 45 and 68% yields, respectively (entries 2 and 3, Table 1). These trials indicated that when the equiv. of **4a** was increased, the yield of product **5a-(DL)** also increased.

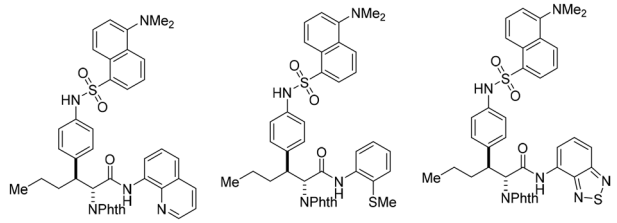
Subsequently, we treated **3a-(DL)** with 4 equiv. of **4a** in the presence of $Pd(OAc)_2$ and AgOAc in toluene at 110 °C for 24 h. The expected dansylated norleucine **5a-(DL)** was obtained in 80% yield (entry 4, Table 1). We then minimized the catalyst loading to 3–5 mol% under similar reaction conditions, and correspondingly, **5a-(DL)** was obtained in 15–55% yields (entries 5 and 6, Table 1). Furthermore, changing the catalyst from $Pd(OAc)_2$ to $Ni(OTf)_2$ failed to produce **5a-(DL)** (entry 7, Table 1). Next, we performed the reaction of **3a-(DL)** with **4a** using 1–2 equiv. of AgOAc, which resulted in a decreased yield of **5a-(DL)** (35 and 58% respectively, entries 8 and 9, Table 1).

We then attempted the reaction with various additives such as Ag_2CO_3 and K_2CO_3 instead of AgOAc. The Pd(II)-catalyzed 8-aminoquinoline DG-assisted β-C(sp^3)–H arylation of **3a-(DL)** with **4a** in the presence of Ag_2CO_3 in *t*-BuOH at 100 °C for 24 h afforded **5a-(DL)** in 30% yield (entry 10, Table 1). In contrast, a similar reaction with K_2CO_3 as the additive failed to give the expected product **5a-(DL)** (entry 11, Table 1). Finally, we heated a mixture of **3a-(DL)** with **4a** in the presence of $Pd(OAc)_2$ and AgOAc in *o*-xylene (instead of toluene) at 130 °C for 24 h, and product **5a-(DL)** was obtained in 74% yield (entry 12, Table 1). We also tested the Pd(II)-catalyzed arylation of **3a-(DL)** with **4a**

Table 1 Optimization of reaction conditions. Preparation of the dansylated norleucine motif **5a-(DL)** *via* the Pd(II)-catalyzed arylation of the C(sp^3)–H bond of **3a-(DL)** with **4a**



Entry	Catalyst (y mol%)	Additive (z equiv.)	Solvent (2 mL)	t (h)	T (°C)	**5a-(DL)**: yield (%)
1[c]	$Pd(OAc)_2$ (10)	AgOAc (2.2)	Toluene	24	110	28
2[d]	$Pd(OAc)_2$ (10)	AgOAc (2.2)	Toluene	24	110	45
3[e]	$Pd(OAc)_2$ (10)	AgOAc (2.2)	Toluene	24	110	68
4	$Pd(OAc)_2$ (10)	AgOAc (2.2)	Toluene	24	110	80
5	$Pd(OAc)_2$ (3)	AgOAc (2.2)	Toluene	24	110	15
6	$Pd(OAc)_2$ (5)	AgOAc (2.2)	Toluene	24	110	55
7	$Ni(OTf)_2$ (10)	$NaHCO_3$ (2)	Toluene	24	110	0
8	$Pd(OAc)_2$ (10)	AgOAc (1)	Toluene	24	110	35
9	$Pd(OAc)_2$ (10)	AgOAc (2)	Toluene	24	110	58
10	$Pd(OAc)_2$ (10)	Ag_2CO_3 (2)	*t*-BuOH	24	100	30
11	$Pd(OAc)_2$ (10)	K_2CO_3 (2)	Toluene	24	110	0
12	$Pd(OAc)_2$ (10)	AgOAc (2.2)	*o*-Xylene	24	130	74
13[f]	$Pd(OAc)_2$ (10)	AgOAc (2.2)	Toluene	1–6	110	0
14[f]	$Pd(OAc)_2$ (10)	AgOAc (2.2)	Toluene	10	110	<10



5a-(DL): 80%[g] **5aa-(DL)**: <5%[h] **5ab-(DL)**: <5%[i]

[a] All the reactions were conducted in a sealed tube (purged with N_2). [b] Isolated yields. In all the reactions, purification using column chromatography yielded the *anti*-isomer (major) **5a-(DL)** and the *syn*-isomer (minor) was not obtained in characterizable amounts. [c] 1 equiv. of **4a**. [d] 2 equiv. of **4a**. [e] 3 equiv. of **4a**. [f] The reaction was performed under microwave heating. [g] Substrate **3a-(DL)** with the 8-aminoquinoline DG was used. [h] Substrate **3f-(DL)** with the 2-(methylthio)aniline DG was used and the reaction was performed under the conditions shown in entry 4. [i] Substrate **3g-(DL)** with the 4-amino-2,1,3-benzothiadiazole DG was used and the reaction was performed under the conditions shown in entry 4.

under microwave heating for 1–10 h, but the reactions were not successful (entries 13 and 14, Table 1).

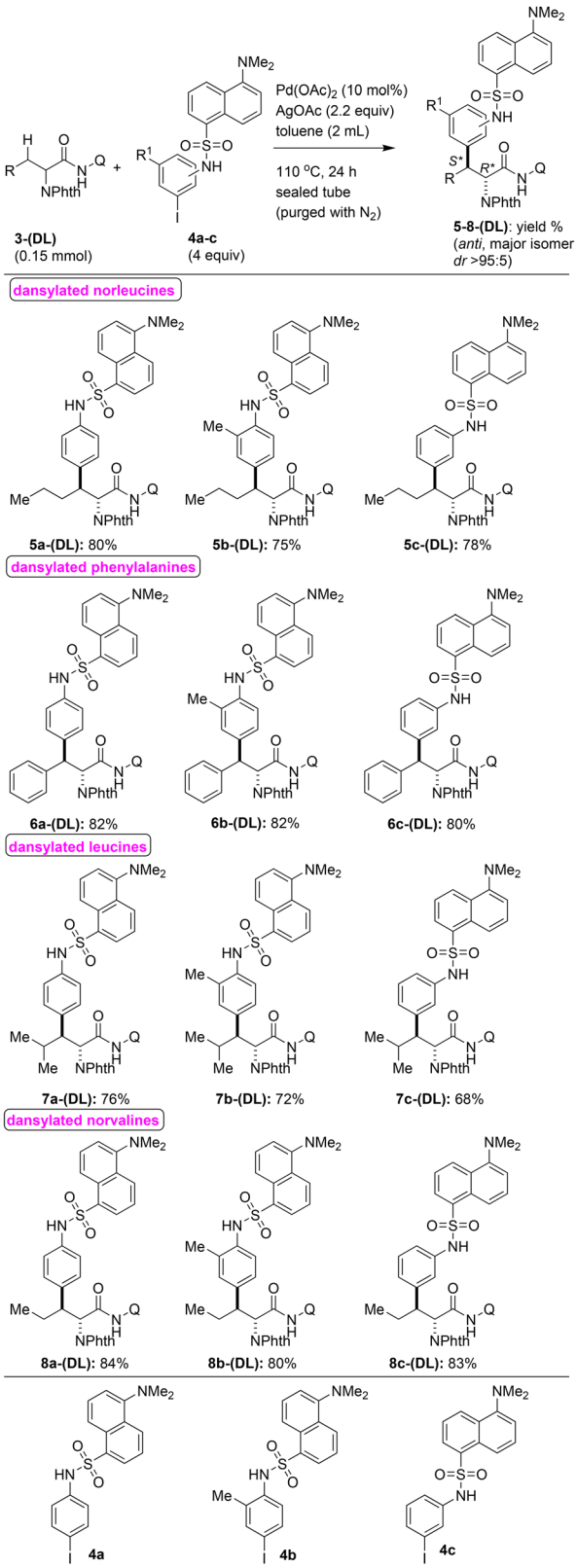
We then performed the Pd(II)-catalyzed β-C(sp^3)–H arylation of norleucine substrates **3f-(DL)** and **3g-(DL)** possessing other DGs such as 2-(methylthio)aniline (MTA) or 4-amino-2,1,3-benzothiadiazole (ABTD) with **4a**. These trials failed to afford the corresponding norleucine derivatives **5aa-(DL)** and **5ab-(DL)** (Table 1). Accordingly, 8-aminoquinoline was found to be a suitable directing group to conduct the Pd(II)-catalyzed β-C(sp^3)–H arylation of **3a-(DL)**, affording **5a-(DL)**.

In all these reactions, purification of the crude reaction mixture through column chromatography afforded the norleucine unnatural amino acid derivative **5a-(DL)** with *anti*-stereochemistry as the major compound. We did not obtain the corresponding *syn*-isomer in characterizable amounts. Consistent with previous reports, the Pd(II)-catalyzed 8-aminoquinoline DG-assisted arylation of the prochiral β-C(sp^3)–H bonds of the norleucine derivative **3a-(DL)** with **4a** was found to yield the *anti*-isomer.[6–10] Accordingly, the *anti*-stereochemistry of the major isomer **5a-(DL)** was assigned based on previous reports and our earlier experience.[6d,e]

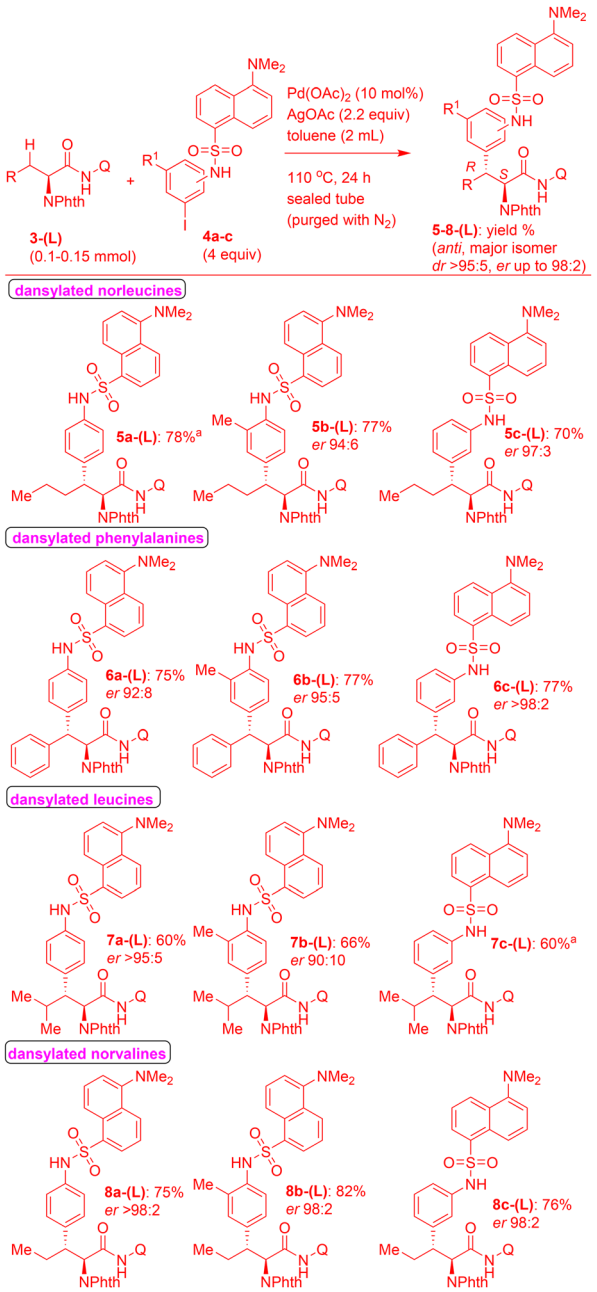
Having established the suitable reaction conditions (entry 4, Table 1), we then explored the substrate scope and synthesis of various dansylated phenylalanine-type unnatural amino acid scaffolds *via* a diastereoselective methylene β-C(sp^3)–H arylation protocol. We aspired to accomplish the diastereoselective construction of various dansylated aniline-linked unnatural amino acid scaffolds, including norleucine **5-(DL)**, phenylalanine **6-(DL)**, leucine **7-(DL)**, and norvaline **8-(DL)** (Scheme 2).

We assembled the required 8-aminoquinoline DG-containing *N*-phthaloyl protected (DL)-carboxamides such as phenylalanine **3b-(DL)**, leucine **3c-(DL)**, and norvaline **3d-(DL)** derivatives from their corresponding α-amino acids by using the standard amide coupling procedures.[6d,10] We treated norleucine carboxamide **3a-(DL)** with dansyl-linked 4-iodoaniline (**4a**), dansyl-linked 4-iodo-2-methylaniline (**4b**) or dansyl-linked 3-iodoaniline (**4c**) in the presence of $Pd(OAc)_2$ and AgOAc in toluene at 110 °C for 24 h. These attempts furnished the corresponding dansylated aniline-linked norleucine derivatives **5a-(DL)**, **5b-(DL)**, and **5c-(DL)** in 75–80% yields (*anti*-isomers, Scheme 2). Heating a mixture of phenylalanine carboxamide **3b-(DL)** with the dansyl-linked iodoanilines **4a**, **4b**, and **4c** under similar reaction conditions afforded the corresponding dansyl-based phenylalanine unnatural amino acid derivatives **6a-(DL)**, **6b-(DL)** and **6c-(DL)** in 80–82% yields (*anti*-isomers). Similarly, the Pd(II)-catalyzed 8-aminoquinoline-directed β-C(sp^3)–H arylation reaction of leucine carboxamide **3c-(DL)** with **4a**, **4b** and **4c** successfully afforded the corresponding dansyl-based leucine derivatives **7a-(DL)**, **7b-(DL)** and **7c-(DL)** in 68–76% yields (*anti*-isomers). Next, the treatment of norvaline carboxamide **3d-(DL)** with **4a**, **4b** and **4c** under similar reaction conditions produced the corresponding dansyl-linked norvaline derivatives **8a-(DL)**, **8b-(DL)** and **8c-(DL)** in 80–84% yields (*anti*-isomers, Scheme 2).

We then shifted our focus to the preparation of enantioenriched dansyl-based unnatural amino acid derivatives (Schemes 3 and 4). We prepared the required bidentate DG 8-aminoquinoline containing enantioenriched *N*-phthaloyl L- and D-carboxamides **3-(L)** and **3-(D)** from their respective enantioenriched α-amino acids. First, we conducted the Pd(II)-catalyzed 8-aminoquinoline-directed β-C(sp^3)–H arylation reaction of enantioenriched L-norleucine carboxamide **3a-(L)** with the dansyl-linked iodoanilines **4a**, **4b** and **4c** in the presence of

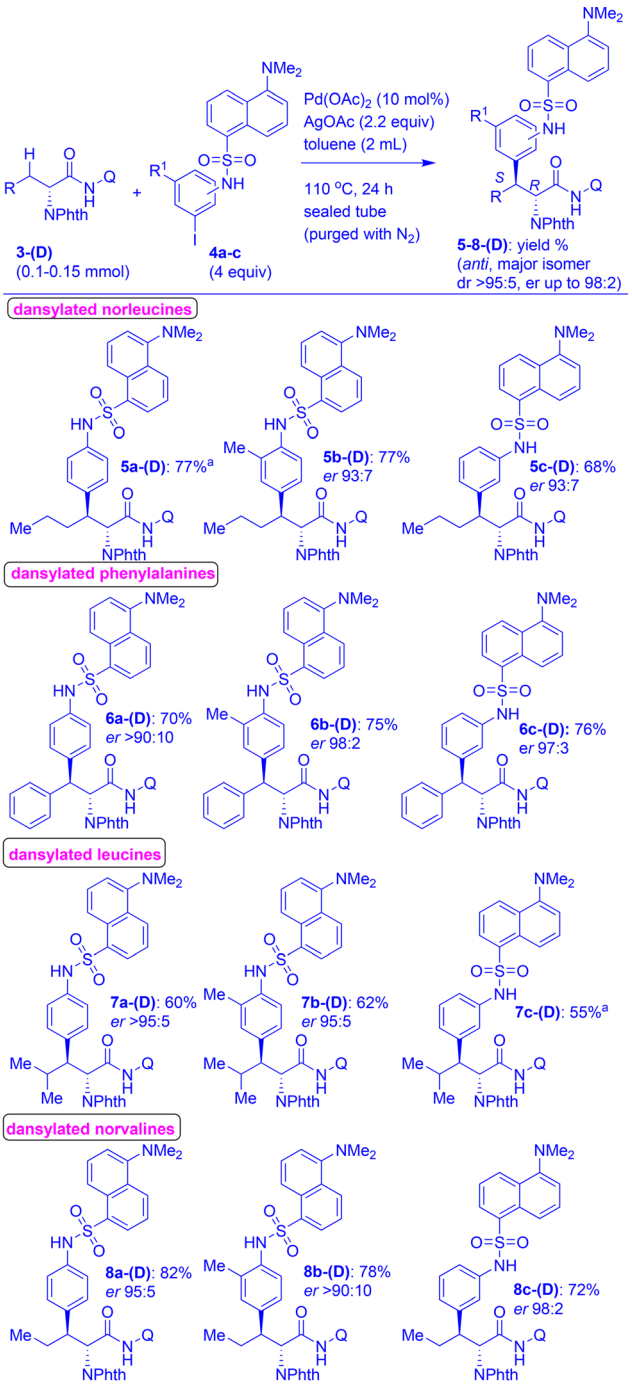


Scheme 2 Diastereoselective construction of dansyl-linked unnatural amino acid derivatives **5–8-(DL)** *via* Pd(II)-catalyzed methylene C(sp^3)–H functionalization.



Scheme 3 Diastereoselective construction of dansyl-linked enantioenriched L-unnatural amino acid derivatives **5–8-(L)** *via* Pd(II)-catalyzed methylene C(sp^3)–H functionalization. [a] For **5a-(L)** and **7c-(L)**, we could not get a clear HPLC pattern under different HPLC analyses using different chiral columns/methods. These compounds are believed to be enantioenriched in analogy to similar compounds described and based on specific rotation analysis.

$Pd(OAc)_2$ and AgOAc in toluene at 110 °C for 24 h. These attempts afforded the corresponding enantioenriched dansyl-based norleucine derivatives **5a-(L)**, **5b-(L)**, and **5c-(L)** in 70–78% yields (*anti*-isomers, Scheme 3). Treatment of enantioenriched L-phenylalanine carboxamide **3b-(L)** with **4a**, **4b**, and **4c** under similar reaction conditions furnished the corresponding enantioenriched dansyl-based phenylalanine deriva-



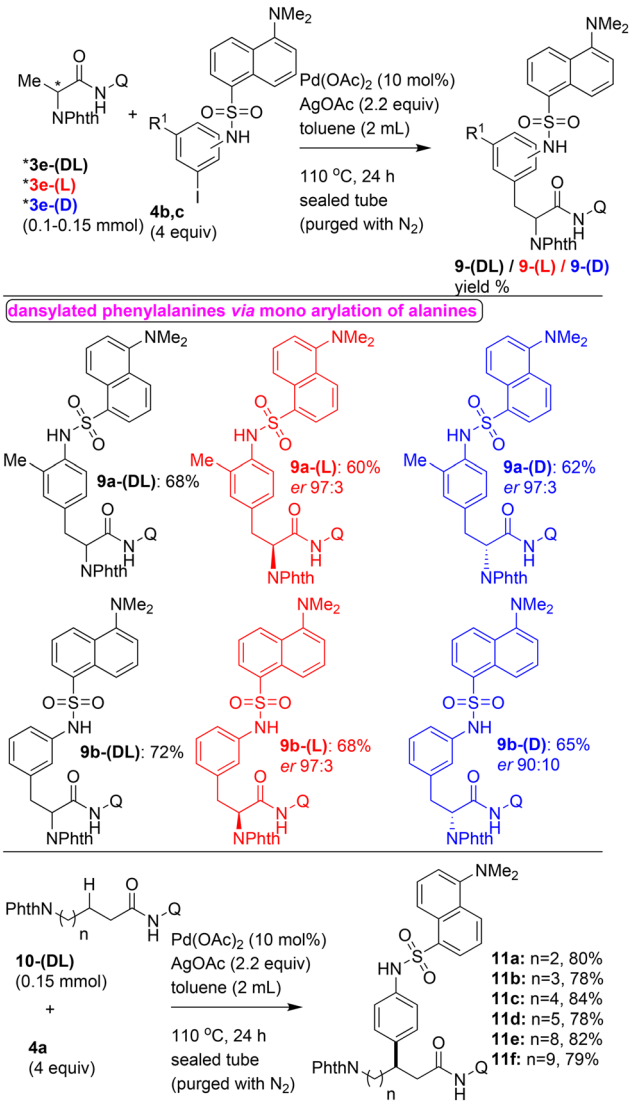
Scheme 4 Diastereoselective construction of dansyl-linked enantioenriched D-unnatural amino acid derivatives **5–8-(D)** *via* Pd(II)-catalyzed methylene C(sp^3)–H functionalization. [a] For **5a-(D)** and **7c-(D)**, we could not get a clear HPLC pattern under different HPLC analyses using different chiral columns/methods. These compounds are believed to be enantioenriched in analogy to similar compounds described and based on specific rotation analysis.

tives **6a-(L)**, **6b-(L)** and **6c-(L)** in 75–77% yields (*anti*-isomers, Scheme 3). Performing a similar reaction of enantioenriched L-leucine carboxamide **3c-(L)** with **4a**, **4b**, and **4c** gave the corresponding enantioenriched dansyl-based leucine derivatives **7a-(L)**, **7b-(L)** and **7c-(L)** in 60–66% yields (*anti*-isomers, Scheme 3). Heating a mixture of enantioenriched L-norvaline carboxamide **3d-(L)** with **4a**, **4b** and **4c** in the presence of Pd$(OAc)_2$ and AgOAc in toluene at 110 °C for 24 h furnished the corresponding enantioenriched dansyl-based norvaline derivatives **8a-(L)**, **8b-(L)** and **8c-(L)** in 75–82% yields (*anti*-isomers, Scheme 3).

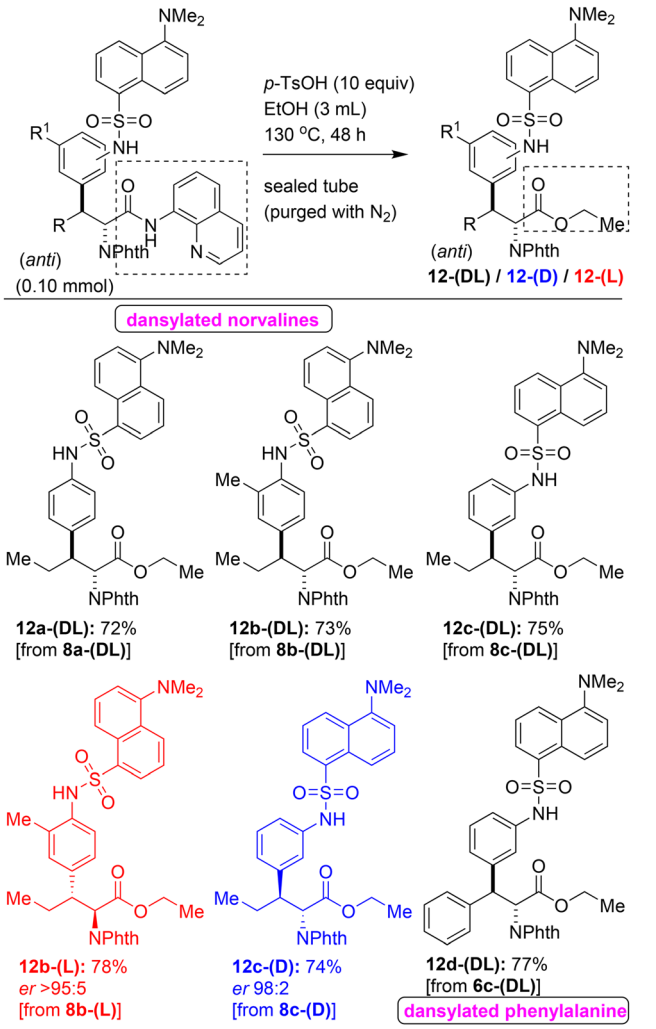
Next, enantioenriched D-norleucine carboxamide **3a-(D)** was treated with dansyl-linked iodoanilines **4a**, **4b**, and **4c** in the presence of Pd$(OAc)_2$ and AgOAc in toluene at 110 °C for 24 h. These reactions provided the corresponding enantioenriched dansyl-based norleucine derivatives **5a-(D)**, **5b-(D)**, and **5c-(D)** in 68–77% yields (*anti*-isomers). Next, we performed the Pd(II)-catalyzed β-C(sp^3)–H arylation of enantioenriched D-phenylalanine carboxamide **3b-(D)** with **4a**, **4b**, and **4c** under similar reaction conditions. These attempts afforded the corresponding enantioenriched dansyl-based phenylalanine derivatives **6a-(D)**, **6b-(D)** and **6c-(D)** in 70–76% yields (*anti*-isomers). The Pd(II)-catalyzed 8-aminoquinoline-directed β-C(sp^3)–H arylation of enantioenriched D-leucine carboxamide **3c-(D)** with **4a**, **4b** and **4c** in the presence of Pd$(OAc)_2$ and AgOAc in toluene at 110 °C for 24 h furnished the corresponding enantioenriched dansyl-based leucine derivatives **7a-(D)**, **7b-(D)** and **7c-(D)** in 55–62% yields (*anti*-isomers). We then subjected enantioenriched D-norvaline carboxamide **3d-(D)** to the Pd(II)-catalyzed β-C(sp^3)–H arylation with **4a**, **4b** and **4c**. The corresponding enantioenriched dansyl-based norvaline derivatives **8a-(D)**, **8b-(D)** and **8c-(D)** were obtained in 72–82% yields (*anti*-isomers, Scheme 4).

Next, we attempted the preparation of dansylated phenylalanines **9a-(DL)** and **9b-(DL)** *via* Pd(II)-catalyzed 8-aminoquinoline DG-aided methyl β-C(sp^3)–H arylation of alanine carboxamide (Scheme 5).[7–9] Accordingly, racemic *N*-phthaloyl alanine carboxamide **3e-(DL)** was treated with dansyl-linked iodoaniline **4b** or **4c** in the presence of Pd$(OAc)_2$ and AgOAc in toluene at 110 °C for 24 h. Notably, this reaction furnished the mono C(sp^3)–H arylated products dansylated phenylalanine derivatives **9a-(DL)** and **9b-(DL)** in 68–72% yields. Next, we performed similar reactions using enantioenriched L-alanine carboxamide **3e-(L)** with **4b** or **4c** and the corresponding enantioenriched dansylated phenylalanine derivatives **9a-(L)** and **9b-(L)** were obtained in 60–68% yields. Then, enantioenriched D-alanine carboxamide **3e-(D)** was treated with **4b** or **4c** in the presence of Pd$(OAc)_2$ and AgOAc, which provided the corresponding enantioenriched dansylated phenylalanine derivatives **9a-(D)** and **9b-(D)** in 62–65% yields (Scheme 5).

Subsequently, we aimed to construct dansyl-motif containing short, medium, and long chain-based non-α-amino acid derivatives *via* the Pd(II)-catalyzed β-C(sp^3)–H arylation method (Scheme 5). Towards this, we assembled the required carboxamides **10a–f** possessing the 8-aminoquinoline DG from their corresponding *N*-phthaloyl-protected aminoalkanoic acids. Then, substrates **10a–f** were subjected to the Pd(II)-catalyzed β-C(sp^3)–H arylation with dansyl-linked 4-iodoaniline **4a** in the presence of AgOAc in toluene at 110 °C for 24 h. These reactions furnished a library of the corresponding dansyl-linked



Scheme 5 Construction of dansylated phenylalanine derivatives **9-(DL)**, **9-(L)** and **9-(D)** and non-α-amino acid derivatives **11a–f** *via* Pd(II)-catalyzed C(sp^3)–H functionalization.

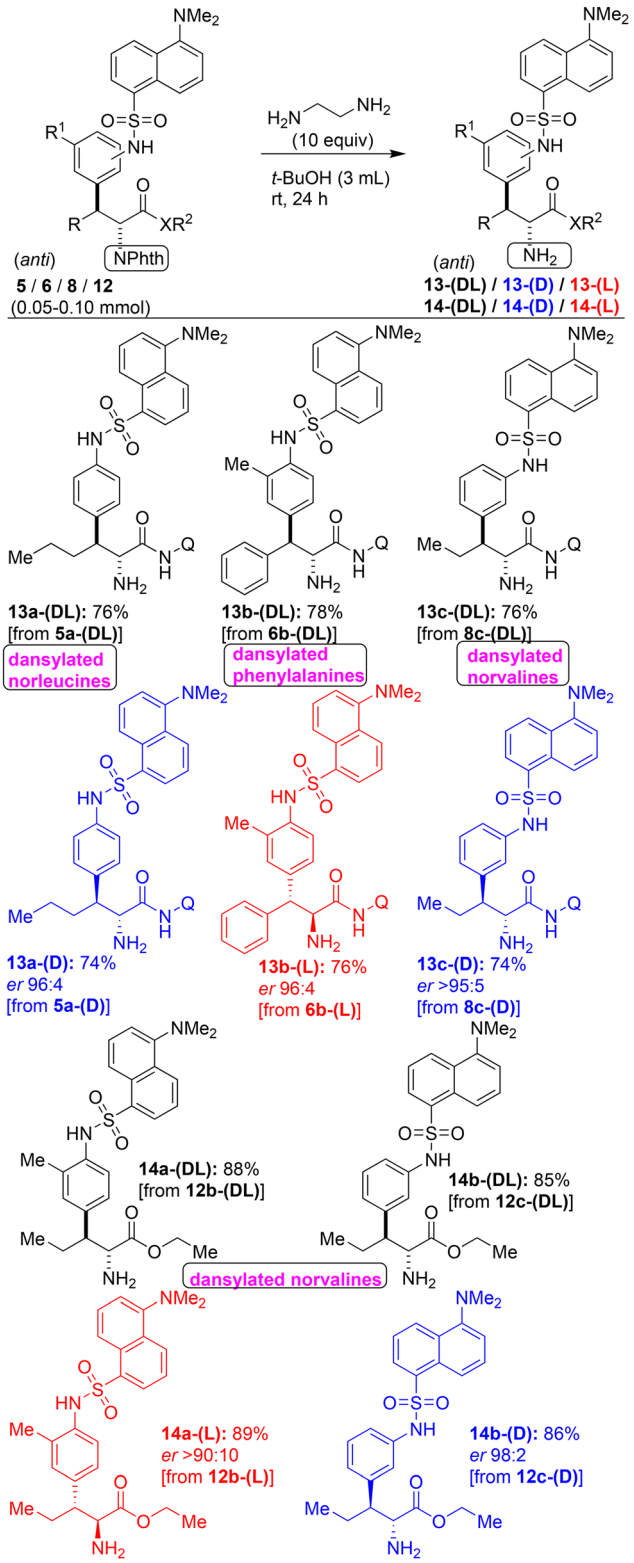


Scheme 6 Synthetic transformations. Removal of the 8-aminoquinoline DG and construction of dansyl-linked unnatural amino acid ester derivatives.

non-α-amino acid derivatives **11a–f** in 78–84% yields (Scheme 5).

Next, we shifted our focus towards the utility and synthetic transformations of dansyl-linked unnatural amino acid derivatives. We attempted the removal of the 8-aminoquinoline directing group *via* previously reported standard procedures.[4–6] We treated the dansyl-linked norvaline derivative **8a-(DL)** with PTSA (10 equiv.) in ethanol. This reaction afforded the DG-removed, dansyl-linked norvaline ethyl ester derivative **12a-(DL)** in 72% yield (*anti*-isomer, Scheme 6). Subsequently, we performed 8-aminoquinoline DG removal from substrates **8b-(DL)**, **8c-(DL)**, and **6c-(DL)** by using PTSA (10 equiv.) in ethanol. These attempts furnished the corresponding DG-removed, dansyl-linked norvaline, **12b-(DL)** and **12c-(DL)**, and phenylalanine, **12d-(DL)**, compounds in 73–77% yields (*anti*-isomers). Along this line, enantioenriched **8b-(L)** and **8c-(D)** were treated with PTSA (10 equiv.) in ethanol, which afforded the corresponding enantioenriched dansyl-linked L-norvaline **12b-(L)** and D-norvaline **12c-(D)** in 74–78% yields (*anti*-isomers, Scheme 6).

We then intended to obtain free amino group-containing dansyl-linked unnatural amino acid derivatives (Scheme 7). Accordingly, we attempted the *N*-Phth deprotection of the dansyl-linked amino acid derivative **5a-(DL)** with ethane-1,2-diamine,[6d–f] which afforded the free amino group-containing dansylated norleucine motif **13a-(DL)** in 76% yield (*anti*-isomer). Similarly, treatment of **6b-(DL)** and **8c-(DL)** with ethane-1,2-diamine furnished the corresponding free amino group-containing phenylalanine **13b-(DL)** and norvaline **13c-(DL)** derivatives in 76–78% yields (*anti*-isomers). Along this line, we treated enantioenriched derivatives **5a-(D)**, **6b-(L)** and **8c-(D)** with ethane-1,2-diamine. These reactions afforded the corresponding enantioenriched free amino group-containing D-norleucine **13a-(D)**, L-phenylalanine **13b-(L)**, and D-norvaline



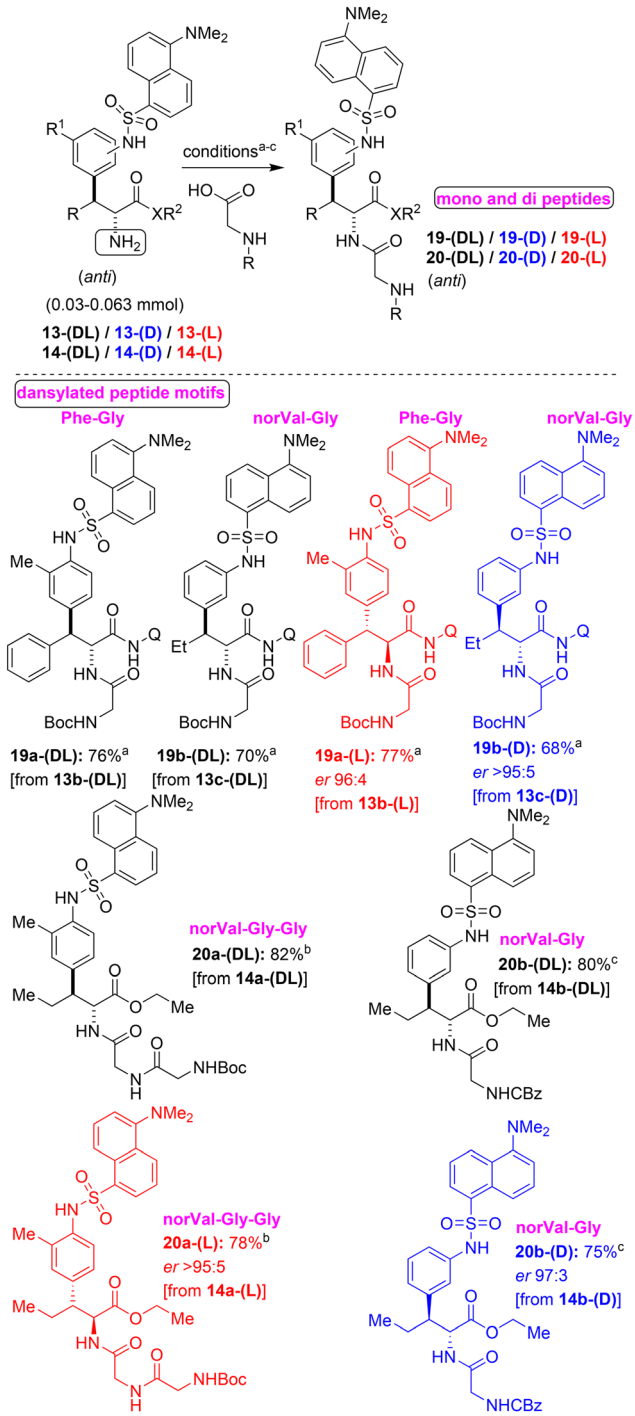
Scheme 7 Synthetic transformations. Construction of dansyl-linked free amino group-containing unnatural amino acid derivatives.

13c-(D) derivatives in 74–76% yields (*anti*-isomers). Additionally, compounds **12b-(DL)** and **12c-(DL)**, and enantioenriched **12b-(L)** and **12c-(D)** were subjected to the ethane-1,2-diamine-aided *N*-Phth deprotection conditions. These attempts furnished the corresponding DG-removed, phthalimide-deprotected, dansyl-linked norvaline motifs **14a-(DL)** and **14b-(DL)**, and enantioenriched L-norvaline **14a-(L)** and D-norvaline **14b-(D)** in 85–89% yields (*anti*-isomers, Scheme 7).

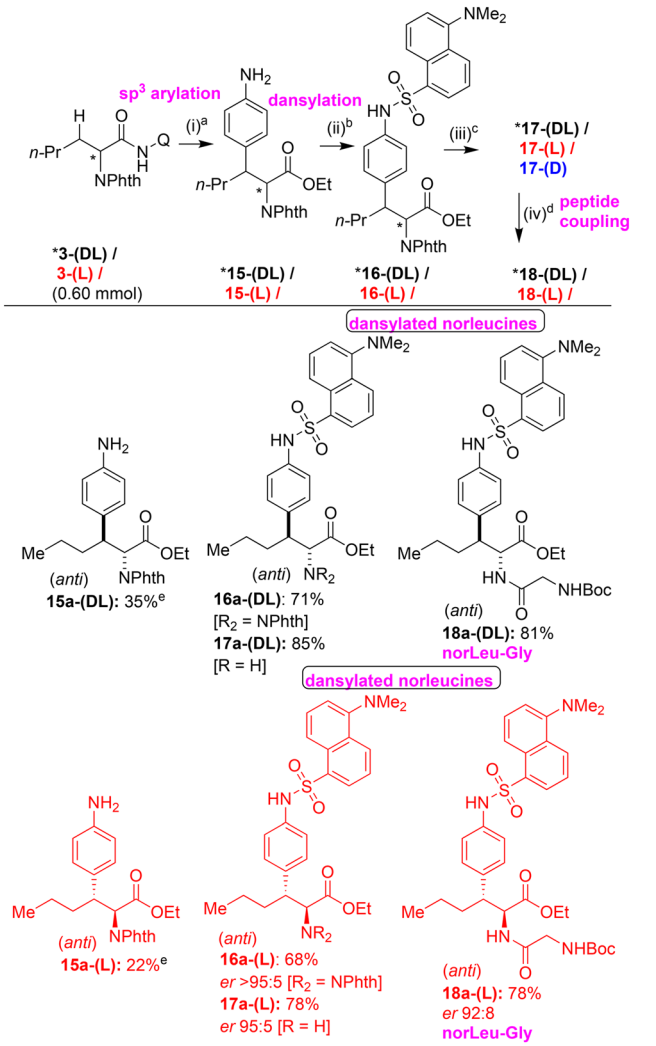
Subsequently, phenylalanine **13b-(DL)** and norvaline **13c-(DL)** derivatives containing the free amino ($-NH_2$) group were subjected to a standard peptide coupling reaction with *N*-Boc-glycine. These reactions provided the corresponding dansyl-based dipeptides Phe-Gly **19a-(DL)** and norVal-Gly **19b-(DL)** (*anti*-isomers). Similarly, the corresponding enantioenriched dansyl-based dipeptides Phe-Gly **19a-(L)** and norVal-Gly **19b-(D)** were obtained from their respective substrates **13b-(L)** and **13c-(D)** (*anti*-isomers). Along this line, dansyl-linked norvaline **14a-(DL)** and enantioenriched norvaline **14a-(L)** were subjected to peptide coupling with *N*-Boc-Gly-Gly-OH. These attempts provided the corresponding dansyl-based norVal-Gly-Gly tripeptides **20a-(DL)** and enantioenriched **20a-(L)** (*anti*-isomers). Similarly, dansyl-linked norvaline **14b-(DL)** and enantioenriched norvaline **14b-(D)** were subjected to peptide coupling with *N*-Boc-Gly-OH. These attempts provided the corresponding dansyl-based norVal-Gly dipeptide **20b-(DL)** and enantioenriched **20b-(D)** (*anti*-isomers, Scheme 8).

Furthermore, we also attempted the construction of dansyl-based unnatural amino acids and peptides *via* an alternative methodology. Toward this, we synthesized directing group-removed, aniline moiety-linked norleucine derivatives **15a-(DL)** and **15a-(L)** (*anti*-isomers) using a previously reported two-step procedure by our group.[6d] Accordingly, the synthesis of **15a-(DL)** and **15a-(L)** (*anti*-isomers)[6d] was accomplished *via* the Pd(II)-catalyzed 8-aminoquinoline directed β-C(sp^3)–H arylation reaction of norleucine carboxamides **3a-(DL)** and **3a-(L)** with 4-iodoacetanilide followed by treatment with ethanol in the presence of $BF_3{\cdot}OEt_2$ (Scheme 9). Next, norleucine derivatives **15a-(DL)** and enantioenriched **15a-(L)** (*anti*-isomers) were subjected to a conventional amide coupling reaction with dansyl chloride to successfully afford the directing group-removed, dansyl-linked norleucine derivatives **16a-(DL)** and enantioenriched **16a-(L)** (*anti*-isomers) in 68–71% yields. Subsequently, **16a-(DL)** and enantioenriched **16a-(L)** (*anti*-isomers) were treated with ethane-1,2-diamine to furnish the corresponding phthalimide group-deprotected norleucine derivatives **17a-(DL)** and enantioenriched **17a-(L)** (*anti*-isomers) in 78–85% yields. Finally, the conventional peptide coupling reaction of **17a-(DL)** and enantioenriched **17a-(L)** (*anti*-isomers) with *N*-Boc-glycine successfully afforded the corresponding dansyl-based peptides norLeu-Gly **18a-(DL)** and enantioenriched **18a-(L)** in 78–81% yields (Scheme 9).

It is well known that the Pd(II)-catalyzed bidentate directing group-directed arylation of β-C(sp^3)–H bonds in aliphatic carboxamide proceeds through a Pd(II)/Pd(IV) redox catalytic cycle.[4–6] Our attempts to obtain suitable crystals of products as shown in Schemes 2–4 and 9 for performing X-ray structure analysis were unsuccessful. Nevertheless, it is well documented that the diastereoselective arylation of the prochiral C(sp^3)–H bond of the aliphatic chains and amino acid chains

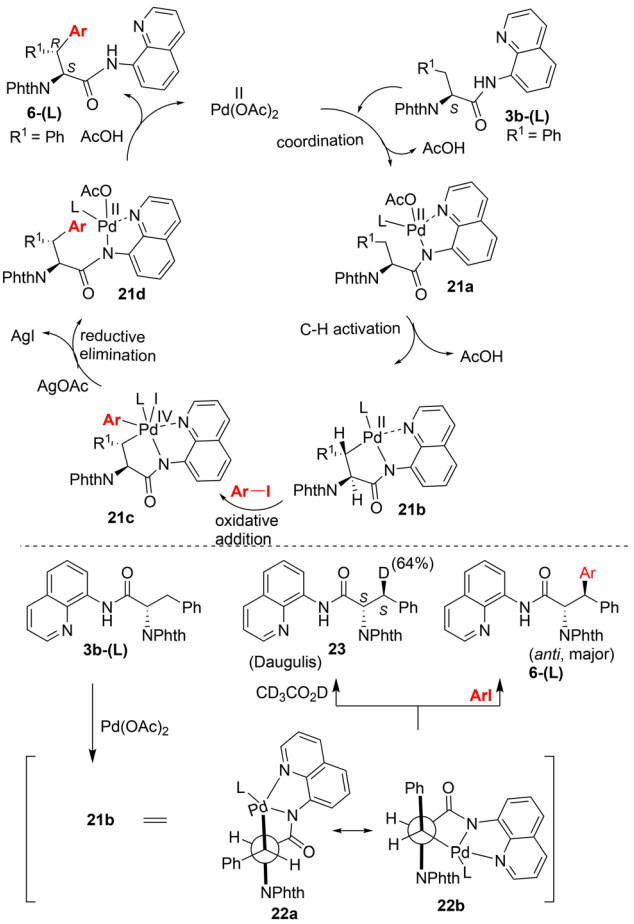


Scheme 8 Synthetic transformations. Construction of dansyl-based peptides. [a] *N*-Boc-glycine (1.1 equiv.), EDC·HCl (1.1 equiv.), HOBt (1.1 equiv.), 0 °C–rt, 24 h. [b] *N*-Boc-Gly-glycine (1.1 equiv.), EDC·HCl (1.1 equiv.), HOBt (1.1 equiv.), 0 °C–rt, 24 h. [c] *N*-Cbz-glycine (1.1 equiv.), EDC·HCl (1.1 equiv.), HOBt (1.1 equiv.), 0 °C–rt, 24 h.



Scheme 9 Construction of dansyl-linked amino acids and peptides *via* an alternative route (involving the initial introduction of an iodoaniline group into the amino acid backbone and then the introduction of the dansyl moiety). [a] (i) 4-Iodoacetanilide (4 equiv.), $Pd(OAc)_2$ (10 mol%), AgOAc (2.2 equiv.), toluene (2 mL), 110 °C, 24 h, sealed tube. Then, $BF_3{\cdot}OEt_2$ (20 equiv.), EtOH (3 mL), 130 °C, 96 h, sealed tube. [b] (ii) Dansyl chloride (1.1 equiv.), pyridine (3 equiv.), DCM (3 mL), 0 °C–rt, 24 h. [c] (iii) Ethane-1,2-diamine (3 equiv.), *t*-BuOH (3 mL), rt, 48 h. [d] (iv) *N*-Boc-glycine (1.1 equiv.), EDC·HCl (1.1 equiv.), HOBt (1.1 equiv.), 0 °C–rt, 24 h. [e] (v) Compounds **15a-(DL)** and **15a-(L)** are known compounds[6d] and compound **15-(L)** is believed to be enantioenriched based on compounds **16a-(L)** and **17a-(L)** and their HPLC analysis data.

afforded products possessing *anti*-stereochemistry as the major isomers.[5g,6a,d–f,l,n,r] Based on the mechanism proposed in the literature,[5,6] the coordination of the 8-aminoquinoline DG in **3b-(L)** to Pd(II) is followed by a concerted metalation–deprotonation (CMP) process, generating the five-membered Pd(II) species **21b.** Oxidative addition of species **21b** with aryl iodide then generates the Pd(IV) species **21c,** which undergoes reductive elimination to furnish a new C–C bond in species **21d.** Halide abstraction followed by proteolysis of species **21d** affords the β-C–H arylated product **6-(L)** and regenerates the Pd(II) species (Scheme 10). The formation of an *anti*-isomer as the major product[5–9] from the arylation of the prochiral $C(sp^3)$–H bond of the amino acid backbone aligns with the involvement of possible conformations **22a** or **22b** of the



Scheme 10 Proposed mechanism of diastereoselective arylation of the prochiral C(sp^3)–H bond of the aliphatic chains in concurrence with literature reports.[5g,6a,d–f,l,n,r]

palladacycle intermediate (formed after the β-C–H activation of **3b-(L)**). This observation is supported by the Pd(II)-catalyzed 8-aminoquinoline-assisted deuteration experiments reported by Daugulis *et al.*[6a] Daugulis observed 64% and less than 10% deuterium incorporation at the 3*S* and 3*R* positions in product **23**, respectively (Scheme 10). It is stated[6a] that since the protonation likely takes place with retention of configuration, it is anticipated that **21b** has an *anti* arrangement of the *N*-Phth and phenyl groups in the conformation **22b** or Pd and *N*-Phth groups in the conformation **22a**. Accordingly, it was proposed that the diastereoselectivity of the arylation in the backbone of the amino acid **3b-(L)** is established during the palladation step.[6a]

In concurrence with literature reports, our earlier studies and X-ray structure analysis of similar products,[2f,6d–f,l,n] the C–H arylation reactions described in this work (Schemes 2–4 and 9) have been shown to afford the corresponding products possessing *anti*-stereochemistry (major isomers). Accordingly, compounds **5-(DL)**, **6-(DL)**, **7-(DL)**, **8-(DL)**, and **15-(DL)**, and enantioenriched derivatives **5-(L)**, **6-(L)**, **7-(L)**, **8-(L)**, **5-(D)**, **6-(D)**, **7-(D)**, **8-(D)** and **15-(L)** possessing *anti*-stereochemistry were obtained as the major compounds. Similarly, compounds **12-(DL)**, **13-(DL)**, **14-(DL)**, **16-(DL)**, **17-(DL)**, **18-(DL)**, **19-(DL)**, and **20-(DL)** and enantioenriched motifs **12-(L)**, **12-(D)**, **13-(L)**, **13-(D)**, **14-(L)**, **14-(D)**, **16-(L)**, **17-(L)**, **18-(L)**, **19-(L)**, **19-(D)**, **20-(L)** and **20-(D)** possessing *anti*-stereochemistry were obtained from their corresponding enantioenriched compounds (Schemes 5–8 and 9). For all the chiral products shown in Schemes 3–9, the absolute stereochemistry was determined through extensive chiral HPLC studies (except for **5a-(L)**, **7c-(L)**, **5a-(D)** and **7c-(D)**).

Dansylated amino acid motifs and peptides have found applications as fluorescent reagents/probes for detecting transition metals and as bio-active substrates.[15,20] Inspired by previous literature reports, we recorded the UV-Vis absorption spectra (λ_{max} (absorption)) of representative compounds synthesized in this work (Fig. 2 and 3). We conducted a preliminary examination of the fluorescence emission of representative dansylated amino acid motifs obtained *via* the C–H arylation method (Fig. 3). A preliminary metal-binding study of the representative dansyl-based amino acid motifs prepared in this work was performed. The fluorescence response was examined in the presence of different metal ions. Emission spectra (Fig. 4 and 5) show the fluorescence response of dansyl-based amino acid motifs **8a-(DL)**, **5c-(DL)**, **12d-(DL)**, **20b-(DL)**, and **19a-(DL)**, respectively, in the presence of various metal ions (such as Sn^{2+}, Zn^{2+}, Cu^{2+}, Al^{3+}, and Fe^{2+} having chloride and Hg^{2+} having acetate as the counter anions) in DMSO/water (in all cases, at first, the initial emission spectra of compounds in DMSO were recorded. After this, the corresponding solution of the compound in DMSO and the metal salt in water were mixed (ratio = 2 : 1 v/v) and allowed to stand for 5 min, and then the emission spectra were recorded).

The dansylated amino acid motifs **8a-(DL)**, **5c-(DL)**, **12d-(DL)**, **20b-(DL)**, and **19a-(DL)** responded to Hg^{2+} ions predominantly and we noted a considerable decrease in the fluorescence intensity of these compounds in the presence of Hg^{2+} (charts D–F, Fig. 4 and charts G and H, Fig. 5). The dansylated amino acid motifs **8a-(DL)**, **5c-(DL)**, **12d-(DL)**, **20b-(DL)**, and **19a-(DL)** did not largely respond to metal ions including Sn^{2+}, Al^{3+}, and Zn^{2+} and there was no substantial change in the fluorescence intensity of these compounds in the presence of Sn^{2+}, Al^{3+}, and Zn^{2+} ions. It may be noted that, apart from Hg^{2+} ions, in some cases, we observed minor changes in the fluorescence intensity of compounds **8a-(DL)**, **5c-(DL)**, **12d-(DL)**, **20b-(DL)**,

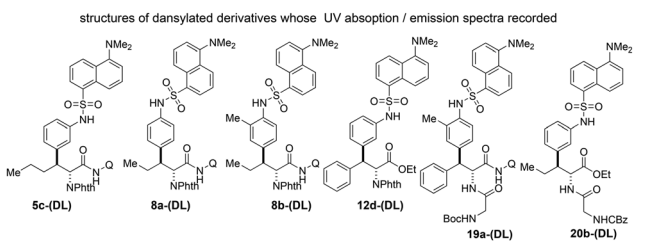
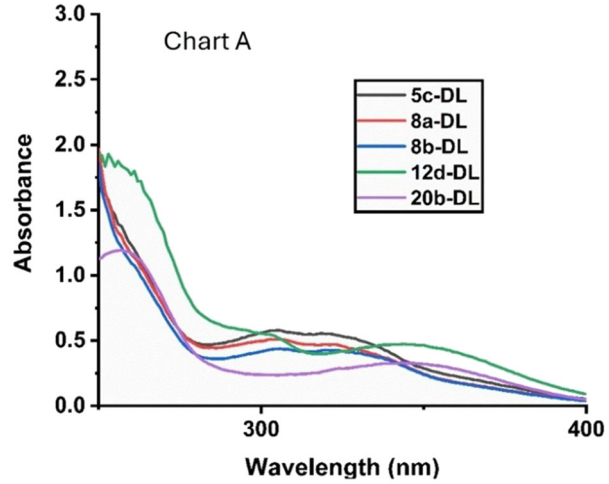
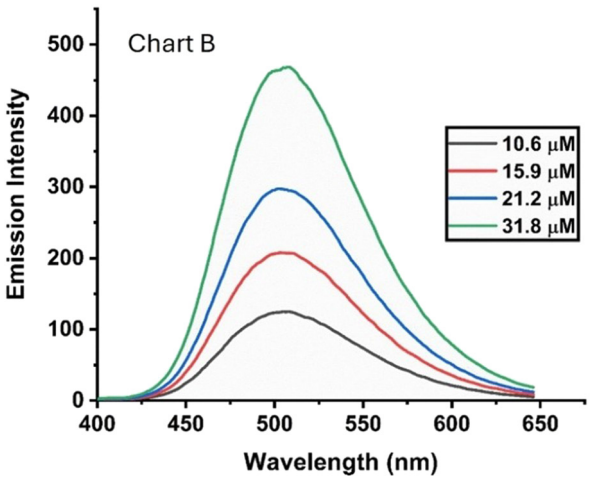


Fig. 2 Structures of dansylated derivatives whose UV absorption/emission spectra were recorded.





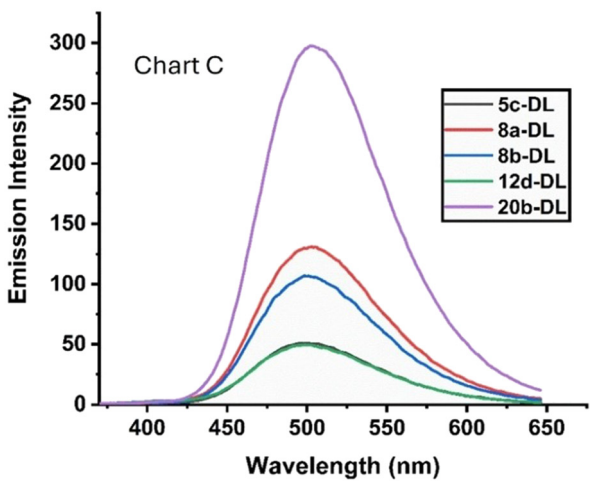
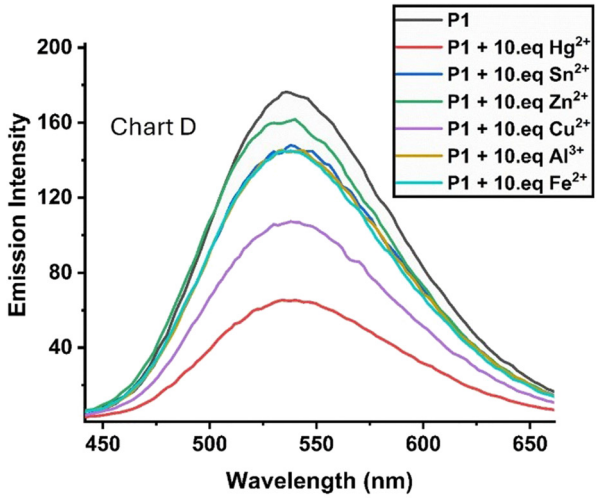
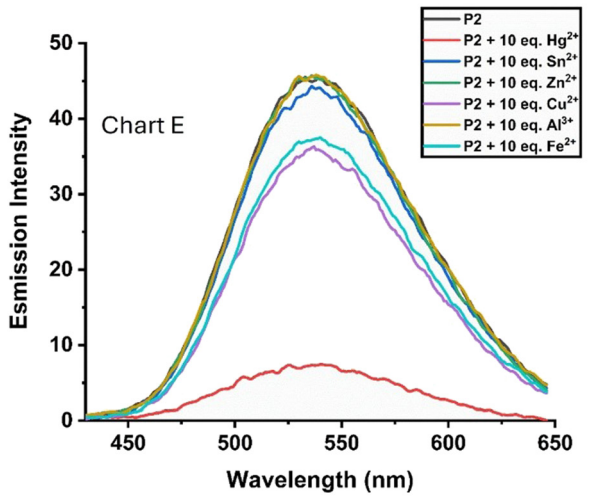


Fig. 3 (Chart A) Absorption spectra of **5c-(DL)**, **8a-(DL)**, **8b-(DL)**, **12d-(DL)**, and **20b-(DL)** in $CHCl_3$ (concentration of solution = 0.7 mg per 10 mL). Absorption (λ_{max} (nm)) value for the compounds, **5c-(DL)** = 318, **8a-(DL)** = 321, **8b-(DL)** = 320, **12d-(DL)** = 344, **20b-(DL)** = 343. (Chart B) Emission spectra of **20b-(DL)** in $CHCl_3$ at an excitation wavelength of 340 nm at different concentrations. (Chart C) Emission spectra of **5c-(DL)**, **8a-(DL)**, **8b-(DL)**, **12d-(DL)**, and **20b-(DL)** in $CHCl_3$ at an excitation wavelength of 340 nm (concentration of all the solutions was 21.2 mM). λ_{max} (emission) (nm) = **5c-(DL)**: 498, **8a-(DL)**: 502, **8b-(DL)**: 498, **12d-(DL)**: 498, **20b-(DL)**: 502 (at the excitation wavelength of 340 nm).





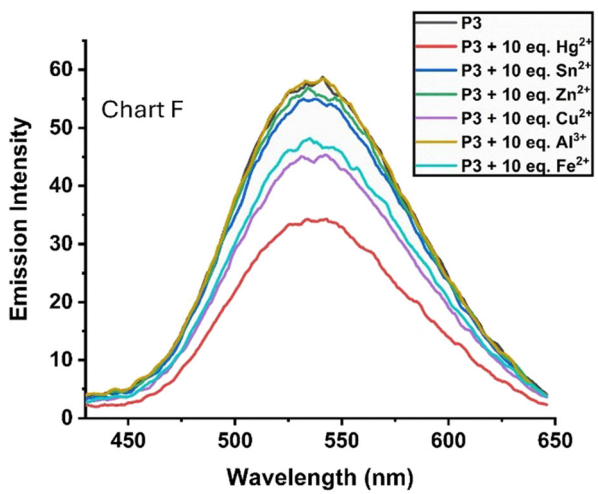


Fig. 4 (Chart D) Emission spectra of **P1** = **8a-(DL)** (concentration = 100 μM, at the excitation wavelength of 340 nm) in the presence of various metal ions (10 equiv.). (Chart E) Emission spectra of **P2** = **5c-(DL)** (concentration = 100 μM, at the excitation wavelength of 340 nm) in the presence of various metal ions (10 equiv.). (Chart F) Emission spectra of **P3** = **12d-(DL)** (concentration = 100 μM, at the excitation wavelength of 340 nm) in the presence of various metal ions (10 equiv.). **P** in **P1**/**P2**/**P3** refers to probe.

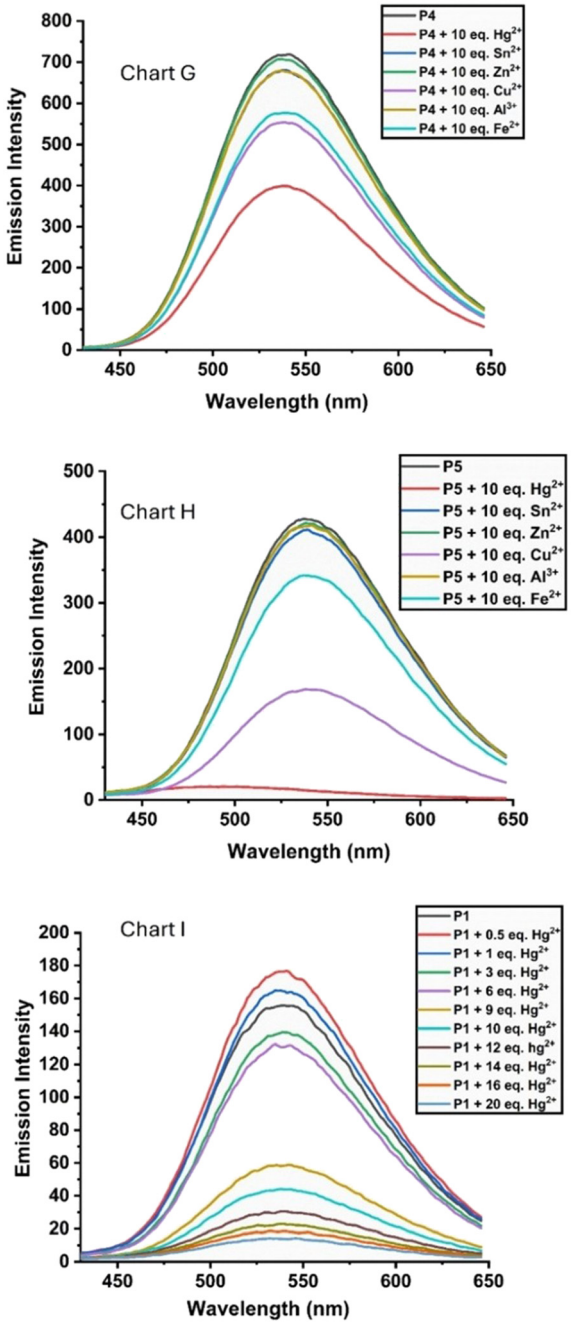


Fig. 5 (Chart G) Emission spectra of **P4** = **20b-(DL)** (concentration = 100 μM, at the excitation wavelength of 340 nm) in the presence of various metal ions (10 equiv.). (Chart H) Emission spectra of **P5** = **19a-(DL)** (concentration = 100 μM, at the excitation wavelength of 340 nm) in the presence of various metal ions (10 equiv.). λ_{max} (emission) (nm) = **19a-(DL)**: 537 (concentration = 100 μM, at the excitation wavelength of 340 nm). (Chart I) Emission spectra of **P1** = **8a-(DL)** (concentration = 100 μM, at the excitation wavelength of 340 nm) with increasing concentration of Hg^{2+} ions. **P** in **P1**/**P4**/**P5** stands for probe.

and **19a-(DL)** in the presence of Cu^{2+} and Fe^{2+} ions. Additionally, we recorded the fluorescence response of the dansyl-based amino acid motif **8a-(DL)** in the presence of different concentrations of Hg^{2+} ions (chart I, Fig. 5). In this titration attempt, we noted a gradual decrease in the fluorescence/emission intensity of **8a-(DL)** when the concentration of Hg^{2+} was increased gradually. These preliminary experiments revealed that compounds **8a-(DL)**, **5c-(DL)**, **12d-(DL)**, **20b-(DL)**, and **19a-(DL)** can predominantly detect Hg^{2+} ions and to some extent Cu^{2+} and Fe^{2+} ions.

Experiments were also performed to see the changes in emission intensity after adding mixtures of metal salts to the solution of **P1 8a-(DL)**. The addition of 10 equiv. of Zn^{2+} to the solution of **P1 8a-(DL)** did not result in any change in intensity (Fig. 6). Then, a mixture containing 10 equiv. each of the metal ions Zn^{2+} and Sn^{2+} did not result in any considerable change in emission intensity. Next, a mixture containing 10 equiv. each of the metal ions Zn^{2+}, Sn^{2+} and Fe^{2+} also did not result in any considerable change in emission intensity. But when a mixture containing 10 equiv. each of the metal ions Zn^{2+}, Sn^{2+}, Fe^{2+} and Hg^{2+} was added to the solution, we observed a drastic decrease in emission intensity, suggesting the detection of Hg^{2+} ions by compound **8a-(DL)**. When a mixture containing 10 equiv. each of the metal ions Zn^{2+}, Sn^{2+}, Fe^{2+}, Cu^{2+} and Hg^{2+} was added to the solution, there was a change in emission intensity, suggesting the detection of both Hg^{2+} and Cu^{2+} ions by compound **8a-(DL)**. However, the change in intensity was not as drastic as in the previous case, which involved the detection of only Hg^{2+}, suggesting that there seems to be a competition between Cu^{2+} and Hg^{2+} for interacting with compound **8a-(DL)**. These results confirm that the probe **P1 8a-(DL)** was successfully able to selectively detect Hg^{2+} and Cu^{2+} to some extent from the mixture of metal ions. While we have conducted a preliminary study, we are in the process of expanding the application of the synthesized dansylated amino acid motifs and peptides in detecting and monitoring metal ions (*e.g.*, Hg^{2+} or Cd^{2+}) in aqueous solution and live cells. Detailed analytical studies will be conducted and reported in our future work.

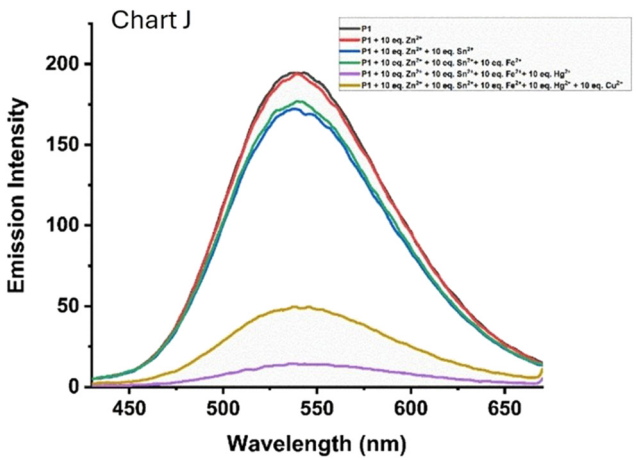


Fig. 6 (Chart J) Emission spectra of **P1** = **8a-(DL)** (concentration = 100 μM, at the excitation wavelength of 340 nm) after adding mixtures of metal ions. **P** in **P1** stands for probe.

High-content screening and identification of 18a-(L) and 20b-(D) as inhibitors of IAV infection

There is a precedence of dansylated molecules tested for antiviral activities.[22] Vermeire *et al.* examined the cellular kinetics of dansyl-labelled cyclotriazadisulfonamide (CADA) derivatives with anti-HIV and CD4 receptor downmodulating activities. Wojaczyńska *et al.* prepared chiral dansylated motifs and evaluated their antiviral activity. Bonora *et al.* reported the antiviral properties of dansyl thymidines. Using a previously described imaging-based high-content screening strategy,[23a,b] we conducted an initial screening of a library of 58 small molecules (10 μM) and identified **18a-(L)** and **20b-(D)** as potent inhibitors of IAV infection in the human lung alveolar cell line A549. In the screening, DMSO (solvent) was included as the negative control, while bafilomycin A1 (BafA1), a selective inhibitor of the vacuolar-type H^+-ATPase (v-ATPase) complex that prevents endosomal acidification, served as the positive control.

The screening was performed using the IAV X-31 (H3N2) strain at a multiplicity of infection (MOI) of 0.01, and the intensity of viral nucleoprotein (NP) per cell at 10 hours post-infection (h.p.i.), as detected by indirect immunofluorescence (IIF), was used as the infection readout (Fig. 8A). After hit identification in the initial screening (in duplicates), we performed focused validation of the hits and found that treatment of A549 cells with **18a-(L)** or **20b-(D)** (10 μM) reduced IAV infection by 79 and 81%, respectively (Fig. 8B and C). Next, we determined the half maximal inhibitory concentration (IC_{50}) of **18a-(L)** and **20b-(D)** against IAV X-31 in A549 cells, with DMSO and BafA1 serving as controls. The compounds were serially diluted from 50 μM to 0.5 μM and cells were infected with the virus in the presence of varying concentrations of these compounds. At 10 h.p.i., the cells were fixed and processed for IIF to detect NP. Using a non-linear regression function and plotting the compounds *vs.* normalised response-variable slope, we determined the IC_{50} values for **18a-(L)** and **20b-(D)** to be 1.56 μM and 2.01 μM, respectively (Fig. 8D). Together, these findings position **18a-(L)** and **20b-(D)** as promising lead compounds with strong potential as novel anti-influenza therapeutics.

After identifying **18a-(L)** and **20b-(D)** as potent inhibitors of IAV infection, we next sought to determine which step of the viral life cycle is blocked by these compounds. To this end, we monitored viral entry by high-content imaging as previously described.[23a–c] The multistep entry of IAV begins with virion attachment to the cell surface, followed by endocytosis. Once internalized, the virions are trafficked through early endosomes and are subsequently delivered to late endosomes. In the acidic lumen of the late endosome, viral hemagglutinin (HA) undergoes pH-dependent conformational rearrangements, rendering the virions fusion competent. As the virions fuse with the limiting membrane of the late endosome, the viral M1 capsid uncoats with the aid of distinct host factors,[23d] releasing viral nucleoprotein complexes (vRNPs). These vRNPs are subsequently imported into the nucleus for transcription and replication. We monitored IAV X-31 entry in the presence

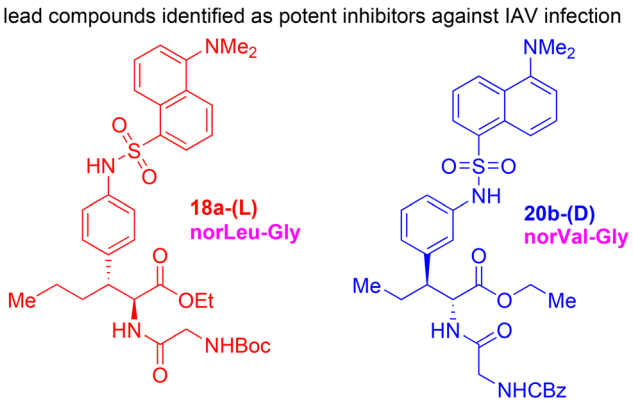


Fig. 7 Lead compounds **18a-(L)** and **20b-(D)** identified as inhibitors of IAV infection during the initial screening.

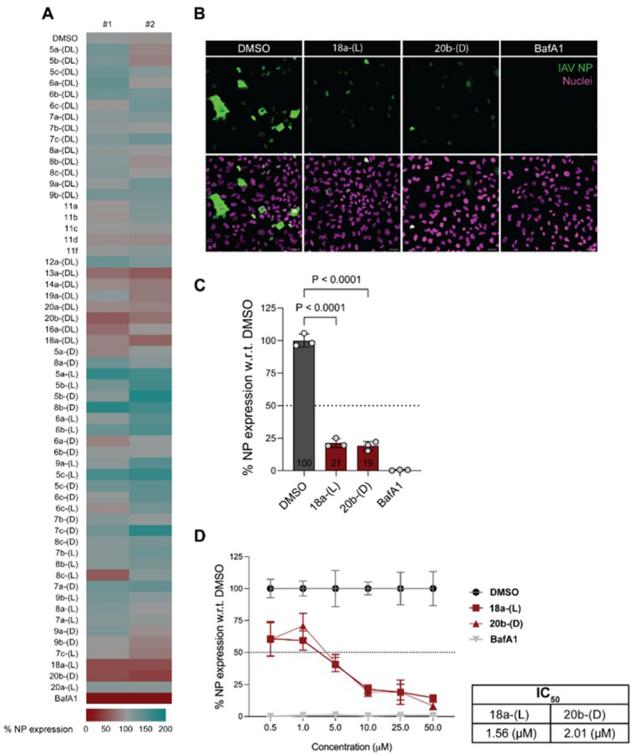


Fig. 8 High-content screening against IAV infection identified the antiviral properties of **18a-(L)** and **20b-(D)**. A: Heatmap showing percentage of NP intensity (in duplicate) in a high-content screening of 58 compounds (10 μM) against IAV X-31 (H3N2) infection for 10 h in A549 cells. BafA1 (50 nM) and DMSO served as positive and negative controls, respectively. B: High-content confocal microscopy images of IAV-infected cells in the presence of DMSO, **18a-(L)**, **20b-(D)**, or BafA1, respectively. Images showing cell nuclei stained with Hoechst (magenta) and IAV NP (green), visualised by IIF. C: Quantification of IAV infection assay. D: Graph showing concentration-dependent antiviral effects of **18a-(L)** and **20b-(D)** against IAV X-31 infection in A549 cells for 10 h. The half-maximal inhibitory concentrations (IC_{50}) for each compound were determined using a non-linear regression function. Scale bars, 50 μm. The *P* values were determined using one-way ANOVA with multiple comparisons w.r.t. DMSO. *P* values <0.05 were considered significant. The bar graphs show the mean of $n = 3 \pm$ SD, and all data except the high-content screening are representative of three biological replicates ($N = 3$).

of **18a-(L)** or **20b-(D)** (10 μM). To prevent the synthesis of new viral proteins, cycloheximide (1 mM) was added to the medium. Although we did not observe any significant difference in IAV endocytosis (Fig. 9A), HA acidification (Fig. 9B) or M1 uncoating (Fig. 9C) between **18a-(L)** or **20b-(D)** and DMSO-treated cells, vRNP nuclear import was significantly reduced in cells treated with **18a-(L)** or **20b-(D)**, compared to the control (Fig. 9D and E). Collectively, our data indicate that compounds **18a-(L)** and **20b-(D)** (Fig. 7) attenuate IAV infection by blocking the transport of vRNPs into the nucleus during viral entry. Further studies to profile the potential of these lead compounds will be carried out in our future work.

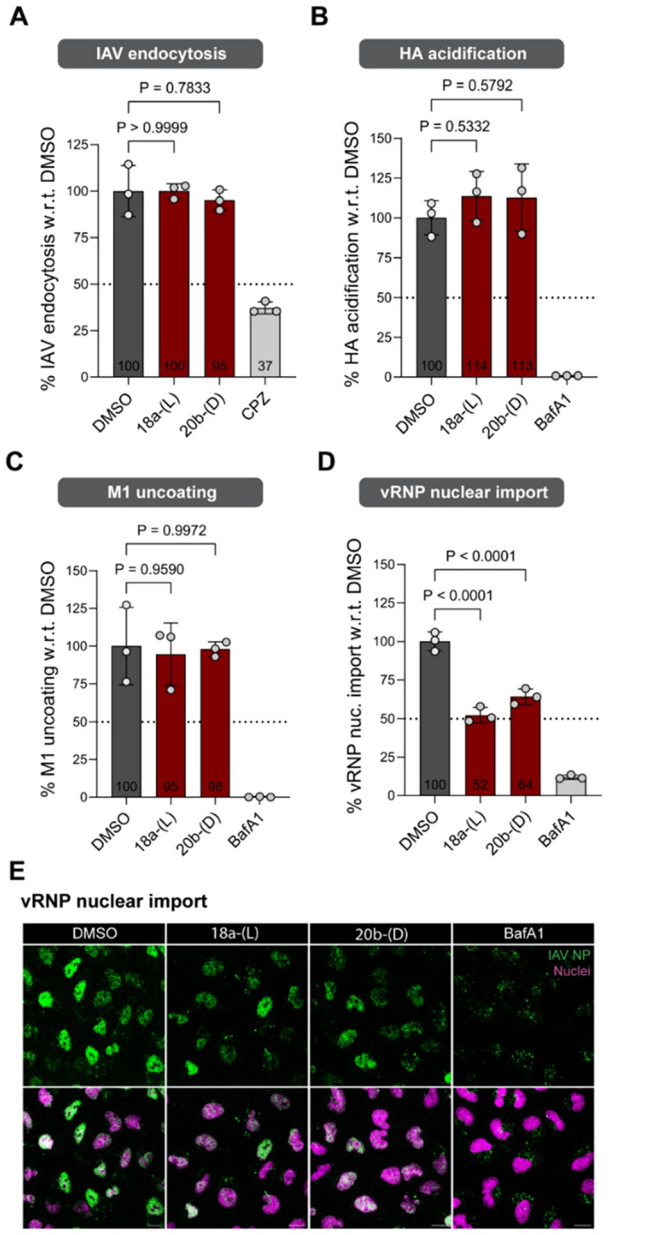


Fig. 9 Compounds **18a-(L)** and **20b-(D)** block IAV vRNP import during viral entry. Quantification of IAV endocytosis (A), HA acidification (B), M1 uncoating (C), and vRNP nuclear import (D). In IAV endocytosis, chlorpromazine (CPZ) was included as a positive control, whereas BafA1 served as the positive control in HA acidification, M1 uncoating, and vRNP nuclear import. E: High-content confocal images showing vRNP nuclear import in the presence of DMSO, **18a-(L)**, **20b-(D)** and BafA1. Cell nuclei were stained with Hoechst (magenta) and IAV NP (green) was detected by IIF. The *P* values were determined using one-way ANOVA with multiple comparisons w.r.t. DMSO. *P* values <0.05 were considered significant. The bar graphs show the mean of $n = 3 \pm$ SD, and all data are representative of three biological replicates ($N = 3$).

Conclusions

In summary, we have shown the construction of a library of novel dansylated phenylalanine-type unnatural amino acid motifs using the Pd(II)-catalyzed C(sp^3)–H arylation route. The β-C(sp^3)–H arylation is a well-regarded method for the functionalization of aliphatic chains.[2–6,24] Our strategy involved the introduction of dansylated anilines into the backbone of α-amino acids or non-α-amino acids *via* a Pd(II)-catalyzed 8-aminoquinoline DG-assisted C(sp^3)–H arylation strategy.[25] Various examples of racemic (DL) and enantioenriched (L and D) dansylated α-amino acid scaffolds, including norvaline, phenylalanine, leucine, norleucine, and non-α-amino acid derivatives, were synthesized. We performed the removal of the 8-aminoquinoline DG and the phthalimide moiety, and the subsequent assembly of dansylated phenylalanine derivatives possessing free amino and carboxylate groups. Then, we also showed the preparation of peptides using dansylated phenylalanine derivatives. We conducted a preliminary study of detecting metal cations using representative dansylated phenylalanines obtained in this work. Some dansylated phenylalanines were able to detect Hg^{2+} and Cu^{2+} ions. A high-content screening against IAV infection identified the antiviral properties of **18a-(L)** and **20b-(D)** (as potent inhibitors of IAV infection). Various dansylated amino acids and peptides are known in the literature and in general, the dansyl moiety has been introduced at the N-terminus of amino acids/peptides. This investigation deals with introducing dansylated anilines into the backbone of amino acids, generating dansylated phenylalanine-type amino acid motifs. It is well documented that dansylated amino acids and peptides are versatile fluorophores/probes in chemical biology and some compounds have biological activities. Accordingly, this work on constructing dansylated phenylalanine unnatural amino acid derivatives is expected to enrich the library of dansylated amino acid scaffolds.

Experimental

General

Reactions were performed in oven-dried round-bottom flasks/sealed tubes using anhydrous solvents under a nitrogen atmosphere. TLC analyses were performed on silica gel or silica gel 60 F_{254} pre-coated plates. The components were visualized with exposure to iodine vapour or by irradiation under a UV lamp. Column chromatography purification was performed

using silica gel (100–200 mesh) (eluent = ethyl acetate : hexane). ^{1}H NMR and ^{13}C{^{1}H} NMR spectra were recorded on 400 and ~101 MHz spectrometers (using TMS as an internal standard). HRMS data were obtained on a QTOF mass analyzer using the electrospray ionization (ESI) method. The IR spectra of samples were recorded either using neat samples or in an appropriate solvent. For finding the specific rotations of enantiopure samples, the solutions were prepared in $CHCl_3$. Polarimeter analysis data were recorded at 589 nm wavelength using a cell length of 100 mm; concentration (*c*) is expressed as g per 100 mL. All HPLC analysis patterns were determined using isolated compounds. Despite repeated trials and using different chiral columns, for some compounds, the HPLC profile was obtained with broad peaks and some other minor signals, presumably due to rotamers or solvent impurities. The HPLC analysis results are reported as obtained using the best possible conditions and chiral columns. All the yields reported are isolated yields and the yields are not optimized. Sometimes there were marginal/considerable variations in yields/enantiomeric ratios for the racemic/enantiopure pairs. This is perhaps due to inadvertent handling/processing errors and manual gathering of all possible pure fractions. While there seems to be partial racemization under the experimental conditions, the observed best er values in HPLC analysis are reported. The observed er values were checked for some selected pairs by repeating the reaction once again. The dansyl-based aryl iodides in this work were prepared *via* a standard amide coupling method using dansyl chloride and the corresponding anilines. For **5a-(L)**, **7c-(L)**, **5a-(D)** and **7c-(D)**, we could not get a clear HPLC pattern under different HPLC analyses using different chiral columns/methods. Compound **13a-(D)**, derived from **5a-(D)**, was successfully characterized *via* HPLC. By analogy, **5a-(D)** is believed to be enantioenriched. We measured the specific optical rotation of compounds **5a-(L)**, **7c-(L)**, **5a-(D)** and **7c-(D)**, which indicated their optical activities. Accordingly, compounds **5a-(L)**, **7c-(L)**, and **7c-(D)** are believed to be enantioenriched in analogy to other similar compounds described.

Biological activity studies: Materials and methods

Cells and viruses

The human alveolar lung epithelial cell line A549 was purchased from ATCC. A549 cells were cultured in Dulbecco's Modified Eagle's Medium (DMEM) (Gibco), supplemented with 10% fetal bovine serum (FBS) (Merck), 1% nonessential amino acid (NEAA) (Invitrogen), 1% penicillin–streptomycin, and glutamine (Invitrogen) at 37 °C in a 5% CO_2 incubator. The purified influenza A virus (IAV) X-31 (H3N2) strain was purchased from M/s Microbiologics, USA (formerly Virapur LLC).

High-content screening of compounds against IAV infection

A549 cells (8×10^4 cells per ml) were seeded in each well of a 96-well optical-bottom plate (Greiner). When the cells reached 75–80% confluency, they were washed once with the infection medium (DMEM, 50 mM HEPES pH 6.8, and 0.2% bovine serum albumin (BSA)). After washing, the cells were then infected with IAV X-31 (H3N2) at a multiplicity of infection (M.O.I.) of 0.001 in the presence of compounds (10 μM) diluted in infection medium. All compounds were previously dissolved in DMSO to generate 10 mM stock solutions. DMSO at equivalent volumes was used as a negative control. Bafilomycin A1 (BafA1) (50 nM) was used as the positive control for IAV infection. At 10 h post-infection (h.p.i.), the cells were washed twice with phosphate-buffered saline (PBS, pH 7.4) and fixed with 4% formaldehyde at room temperature (RT) for 20 min. Indirect immunofluorescence (IIF) against IAV NP was performed to detect infected cells. Briefly, the fixed cells were permeabilised with permeabilization solution (PS) (5% FBS, 1% BSA, 0.1% saponin in PBS) at RT for 30 min. The cells were then incubated with anti-NP (HB65) antibody diluted in PS (1 : 30) for 2 h at RT. After washing thrice with 1× PBS, the cells were incubated with anti-mouse Alexa Flour (AF) 488-conjugated secondary antibody (1 : 1000) and Hoechst (1 : 10 000) in PS for 1 h at RT. After staining, the cells were thoroughly washed with PBS and imaged using a high-content spinning-disk confocal quantitative image cytometer (CQ1, Yokogawa) with maximum intensity projection of five *Z*-stacked images. NP intensity was calculated using ImageJ and GraphPad Prism 9 was used to plot the data. The screening was performed in duplicate. Compounds inhibiting IAV infection by >50% were further validated in a follow-up infection assay, performed in triplicate.

Determination of IC_{50}

A549 cells were seeded at a density of 8×10^4 cells per mL in 96-well optical-bottom plates (Greiner). To calculate IC_{50} values, the respective compounds were serially diluted (50 μM to 500 nM) in the infection medium. IAV X-31 (H3N2) was added at an M.O.I. of 0.01 in the presence of serially diluted compounds when the cells were 75–80% confluent. At 10 h.p.i., the cells were fixed and IIF against NP was performed to detect infected cells, as previously described. IC_{50} values were calculated using a non-linear regression function. IC_{50} values have been plotted as (inhibitor) *vs.* normalised response-variable slope in GraphPad Prism 9.

IAV cellular entry assays

IAV cellular entry assays (IAV endocytosis, HA acidification, M1 uncoating, and vRNP nuclear import) were performed as previously described.[23a–c] Briefly, A549 cells (8×10^4 cells per ml) were seeded in each well of a 96-well optical-bottom plate (Greiner). When the cells reached 75–80% confluency, the IAV entry assays were performed. For all the assays, 0.25 μl of purified IAV X-31 was added to each well in the presence of 10 μM of the respective compounds diluted in infection media. DMSO was added as an equal volume of compounds and served as a negative control. Following viral addition, the cells were incubated to allow virus internalization for various time points and subsequently fixed with 4% formaldehyde. All the

IAV entry assays were performed in the presence of 1 mM cycloheximide to prevent the *de novo* synthesis of viral proteins. For the endocytosis assay, virus particles were allowed to internalise for 30 min. Chlorpromazine (CPZ) (25 μg ml^{-1}) was used as the positive control for the IAV endocytosis assay, and bafilomycin A1 (BafA1) (50 nM) was used as positive control in HA acidification, M1 uncoating and vRNP nuclear import assays. Virions were allowed to internalize for 1 h, 2.5 h and 4 h to detect HA acidification, M1 uncoating, and vRNP nuclear import, respectively. Following virus internalization, the cells were fixed with 4% formaldehyde at respective time points and processed for IIF. To detect endocytosed virus particles, first, the HA of surface-bound viruses was incubated with a saturating concentration of rabbit polyclonal anti-HA antibody (1 : 1000) diluted in blocking solution (BS) containing 5% FBS and 1% BSA in PBS in non-permeabilized cells to block all HA epitopes. Following blocking of HA epitopes, the cells were incubated with anti-rabbit Alexa Flour (AF) 647-conjugated secondary antibody (1 : 1000 in BS). Subsequently, the cells were re-fixed and permeabilised with PS at RT for 30 min. Next, the permeabilized cells were incubated with mouse monoclonal anti-HA1 antibody ((H3SKE) 1 : 100 in PS) for 1 h, and further incubated with anti-mouse Alexa Flour (AF) 488-conjugated secondary antibody (1 : 1000) and Hoechst (1 : 10 000) in PS for 1 h. Acidic pH-induced conformational changes in HA (HA acidification) were detected using mouse monoclonal antibody A1 (1 : 1000 in PS) that specifically reacts to the acid conformation of HA. M1 uncoating was detected using mouse monoclonal anti-M1 (HB64) antibody (1 : 10 in PS), and vRNP nuclear import was detected using mouse monoclonal anti-NP (HB65) antibody (1 : 30 in PS). Anti-mouse Alexa Flour (AF) 488-conjugated secondary antibody (1 : 1000) in PS was used to visualise acidified HA, M1, and NP. Imaging was performed in a high-content spinning-disk confocal quantitative image cytometer (CQ1, Yokogawa) with maximum intensity projection of five *Z*-stacked images. The intensity of HA (internalized) and HA (acid) per cell was calculated using ImageJ. Cytosolic M1 (dispersed) was used as a readout for M1 uncoating, and the percentage of cells displaying dispersed M1 was quantified. For vRNP nuclear import, the NP intensity within the nucleus was calculated. GraphPad Prism 9 was used to plot the data.

Statistical analysis

Statistical analysis was performed using Graphpad Prism 9. All data except for the high-content screening are represented as mean ± SD. All data are representative of three biological replicates (N = 3) and P values were determined using one-way ANOVA with multiple comparisons w.r.t. DMSO. P values <0.05 were considered statistically significant.

Procedure for the synthesis of dansylated unnatural amino derivatives 5a–c/6a–c/7a–c/8a–c/9a, 9b/11a–f *via* the Pd(II)-catalyzed 8-aminoquinoline-aided β-C–H arylation of amino acid carboxamides

A mixture of an appropriate amino acid carboxamide **3a–e** or **10a–f** (0.1–0.15 mmol), an appropriate dansyl-based aryl iodide **4a–c** (4 equiv.), $Pd(OAc)_2$ (10 mol%) and AgOAc[26] (2.2 equiv.) in anhydrous toluene (2 mL) was heated at 110 °C for 24 h under a nitrogen atmosphere. After the reaction period, the reaction mixture was concentrated under reduced pressure to afford a crude reaction mixture, which was purified by column chromatography on silica gel (eluent = EtOAc/hexane) to give the corresponding dansyl-based unnatural amino acid derivative (see the corresponding table/scheme for the specific entry).

Procedure for the removal of the 8-aminoquinoline directing group towards the preparation of dansylated amino acid ester derivatives 12a–d

Dansylated amino acid carboxamide **6c** or **8a–c** (0.1 mmol, 1 equiv.), *p*-TsOH·H_2O (10 equiv.) and anhydrous ethanol (3 mL) were added to a screw-cap sealed tube containing a magnetic bead. The tube containing the mixture was flushed with nitrogen and sealed before submerging into a silicon oil bath preheated to 130 °C. After 48 h, the reaction solution was cooled to rt and the excess solvent was removed under reduced pressure. Following this, the reaction mixture was poured into a separating funnel and diluted with water; then the aqueous phase was extracted with EtOAc (3 times). The collected organic layers were dried over anhydrous Na_2SO_4, and the solvent was evaporated under reduced pressure to afford a crude mixture, which was purified by column chromatography to afford the corresponding dansylated amino acid ester derivative (see the corresponding table/scheme for the specific entry).

Procedure for the synthesis of dansylated amino acid motif 16a

To the appropriate free-amine containing amino acid derivative (**15a**) were added anhydrous DCM and pyridine (3 equiv.). To this reaction mixture, dansyl chloride (1.1 equiv.) was added at 0 °C, and the reaction mixture was then stirred at room temperature for 24 h. After 24 h, the reaction mixture was washed with water and $NaHCO_3$. The collected organic layers were dried over anhydrous Na_2SO_4, and the solvent was evaporated under reduced pressure to afford a crude reaction mixture, which was purified by column chromatography to afford the corresponding dansylated amino acid derivative (see the corresponding table/scheme for the specific entry).

Procedure for the deprotection of the phthalimide group and synthesis of Phth-free amino acid derivatives 13a–c/14a, 14b/17a

To an appropriate Phth-protected amino acid derivative **5**/**6**/**8**/**12**/**16** (0.057–0.1 mmol, 1 equiv.) in *t*-BuOH (3 mL), ethylenediamine (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 purified by column chromatography to afford the corresponding phthalimide-free amino

acid derivatives **13a–c**/**14a, 14b**/**17a** (see the corresponding table/scheme for the specific entry).

Typical procedure for the synthesis of dansylated peptides (18a, 19a, 19b, 20a and 20b)

The appropriate free-amine containing dansylated amino acid derivative **13b, 13c**/**14a, 14b**/**17a** was dissolved in anhydrous DCM, and then EDCI (1.1 equiv.), HOBt (1.1 equiv.) and DMAP (0.1 equiv.) were added at 0 °C. After 30 min, glycine *N*-protected glycine (1 equiv.) or *N*-protected Gly–Gly (1 equiv.) was added and stirred at rt for 24 h. The reaction was monitored by TLC, and after completion, the crude product was extracted with DCM and water and washed thoroughly with $NaHCO_3$. The organic layers were collected and dried over anhydrous Na_2SO_4. The solvent was evaporated to afford a crude reaction mixture, which was purified by column chromatography to afford the corresponding dansyl-based peptide **18a**/**19a, 9b**/**20a, 20b** (see the corresponding table/scheme for the specific entry).

(2*R,3*S**)-3-(4-((5-(Dimethylamino)naphthalene)-1-sulfonamido) phenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)hexanamide (5a-(DL)).** Following the general procedure, **5a-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 70 : 30) as a brown coloured semi-solid (*anti* isomer, 80%, 85 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.40; IR (DCM): 3284, 2925, 1714, 1384, 721 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.90 (s, 1H), 8.60 (dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz, 1H), 8.49 (dd, J_1 = 7.3 Hz, J_2 = 1.6 Hz, 1H), 8.34 (d, J = 8.5 Hz, 1H), 8.29 (d, J = 8.6 Hz, 1H), 8.02 (dd, J_1 = 8.3 Hz, J_2 = 1.6 Hz, 1H), 7.98 (dd, J_1 = 7.4 Hz, J_2 = 1.0 Hz, 1H), 7.89 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2H), 7.73 (dd, J_1 = 5.5 Hz, J_2 = 3.0 Hz, 2H), 7.48 (t, J = 8.4 Hz, 1H), 7.40 (dd, J_1 = 8.2 Hz, J_2 = 1.6 Hz, 1H), 7.36 (t, J = 8.2 Hz, 1H), 7.28 (dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz, 1H), 7.23 (d, J = 8.4 Hz, 2H), 7.17–7.13 (m, 1H), 7.09 (d, J = 7.5 Hz, 1H), 7.00 (s, 1H), 6.90 (d, J = 8.4 Hz, 2H), 5.21 (d, J = 11.6 Hz, 1H), 3.96 (td, J_1 = 11.4 Hz, J_2 = 3.6 Hz, 1H), 2.82 (s, 6H), 1.66–1.59 (m, 1H), 1.46–1.40 (m, 1H), 0.93–0.82 (m, 2H), 0.53 (t, J = 7.3 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 168.2, 165.7, 148.2, 138.3, 137.6, 135.9, 135.5, 134.3, 134.0, 133.9, 131.6, 130.6, 130.1, 129.6, 129.6, 129.3, 128.5, 127.6, 127.0, 123.7, 122.9, 122.3, 121.8, 121.5, 118.5, 116.7, 115.1, 60.8, 45.3, 43.1, 35.1, 19.6, 13.7; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{41}H_{38}N_5O_5S$: 712.2594; found: 712.2573.

(2*S*,3*R*)-3-(4-((5-(Dimethylamino)naphthalene)-1-sulfonamido) phenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)hexanamide (5a-(L)). Following the general procedure, **5a-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 70 : 30) as a brown coloured semi-solid (*anti* isomer, 78%, 67 mg, 0.12 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.40; IR ($CHCl_3$): 3274, 2926, 1715, 1385, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.88 (s, 1H), 8.61 (dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz, 1H), 8.48 (dd, J_1 = 7.4 Hz, J_2 = 1.4 Hz, 1H), 8.34 (d, J = 8.5 Hz, 1H), 8.27 (d, J = 8.6 Hz, 1H), 8.04 (dd, J_1 = 8.3 Hz, J_2 = 1.4 Hz, 1H), 7.97 (dd, J_1 = 7.3 Hz, J_2 = 1.0 Hz, 1H), 7.90 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2H), 7.74 (dd, J_1 = 5.5 Hz, J_2 = 3.0 Hz, 2H), 7.48 (t, J = 8.4 Hz, 1H), 7.41 (dd, J_1 = 8.2 Hz, J_2 = 1.4 Hz, 1H), 7.39–7.35 (m,1H), 7.30 (dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz, 1H), 7.23 (d, J = 8.4 Hz, 2H), 7.17–7.09 (m, 2H), 6.92 (s, 1H) 6.87 (d, J = 8.4 Hz, 2H), 5.18 (d, J = 11.6 Hz, 1H), 4.06 (td, J_1 = 11.3 Hz, J_2 = 3.9 Hz, 1H), 2.82 (s, 6H), 1.51–1.41 (m, 2H), 0.89–0.82 (m, 2H), 0.69 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.2, 165.7, 151.9, 148.1, 138.2, 137.5, 135.9, 135.5, 134.3, 134.0, 133.8, 131.6, 130.6, 130.1, 129.6, 129.5, 129.3, 128.5, 127.6, 127.0 123.7, 122.8, 122.2, 121.8, 121.5, 118.4, 116.7, 115.1, 60.7, 45.3, 43.1, 35.1, 19.6, 13.7; $(\alpha)_D^{25}$ = −14.00 (c = 0.02 g per 100 mL, $CHCl_3$); HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{41}H_{38}N_5O_5S$: 712.2594; found: 712.2562.

(2*R*,3*S*)-3-(4-((5-(Dimethylamino)naphthalene)-1-sulfonamido) phenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)hexanamide (5a-(D)). Following the general procedure, **5a-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 70 : 30) as a brown coloured semi-solid (*anti* isomer, 77%, 55 mg, 0.1 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.40; IR ($CHCl_3$): 3279, 2927, 1715, 1387, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.88 (s, 1H), 8.61 (dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz, 1H), 8.48 (dd, J_1 = 7.4 Hz, J_2 = 1.4 Hz, 1H), 8.34 (d, J = 8.5 Hz, 1H), 8.27 (d, J = 8.6 Hz, 1H), 8.04 (dd, J_1 = 8.3 Hz, J_2 = 1.5 Hz, 1H), 7.96 (dd, J_1 = 7.3 Hz, J_2 = 1.0 Hz, 1H), 7.90 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2H), 7.74 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2H), 7.48 (t, J = 8.3 Hz, 1H), 7.41 (dd, J_1 = 8.2 Hz, J_2 = 1.4 Hz, 1H), 7.39–7.35 (m, 1H), 7.30 (dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz, 1H), 7.23 (d, J = 8.4 Hz, 2H), 7.17–7.10 (m, 2H), 6.88–6.86 (m, 3H), 5.18 (d, J = 11.6 Hz, 1H), 4.06 (td, J_1 = 11.4 Hz, J_2 = 3.9 Hz, 1H), 2.83 (s, 6H), 1.52–1.41 (m, 2H), 0.97–0.89 (m, 2H), 0.69 (t, J = 7.3 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.2, 165.7, 151.9, 148.2, 138.3, 137.6, 135.9, 135.5, 134.3, 134.0, 133.8, 131.6, 130.6, 130.1, 129.6, 129.5, 129.3, 128.5, 127.6, 127.0, 123.7, 122.8, 122.2, 121.8, 121.5, 118.4, 116.7, 115.1, 60.8, 45.3, 43.1, 35.1, 19.6, 13.7; $(\alpha)_D^{25}$ = +13.00 (c = 0.02 g per 100 mL, $CHCl_3$); HRMS (ESI): m/z $(M + Na)^+$ calcd for $C_{41}H_{37}N_5NaO_5S$: 734.2413; found: 734.2410.

(2*R,3*S**)-3-(4-((5-(Dimethylamino)naphthalene)-1-sulfonamido)-3-methylphenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl) hexanamide (5b-(DL)).** Following the general procedure, **5b-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 70 : 30) as a brown coloured semi-solid (*anti* isomer, 75%, 82 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.40; IR (DCM): 3289, 2926, 1712, 1381, 726 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.86 (s, 1H), 8.64 (dd, J_1 = 4.2 Hz, J_2 = 1.4 Hz, 1H), 8.51 (dd, J_1 = 7.2 Hz, J_2 = 1.6 Hz, 1H), 8.37 (d, J = 8.5 Hz, 1H), 8.28 (d, J = 8.6 Hz, 1H), 8.02 (dd, J_1 = 8.3 Hz, J_2 = 1.4 Hz, 1H), 7.90–7.87 (m, 3H), 7.72 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2H), 7.43–7.35 (m, 3H), 7.31 (dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz, 1H), 7.17–7.11 (m, 3H), 7.07–7.03 (m, 2H), 6.67 (s, 1H), 5.20 (d, J = 11.6 Hz, 1H), 4.07 (td, J_1 = 11.2 Hz, J_2 = 4.2 Hz, 1H), 2.82 (s, 6H), 1.86 (s, 3H), 1.56–1.43 (m, 2H), 1.02–0.88 (m, 2H), 0.72 (t, J = 7.3 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 168.2, 165.8, 151.8, 148.1, 138.2, 138.1, 135.9, 134.6, 134.2, 133.8, 133.6, 131.9, 131.6, 130.6, 130.5, 129.9, 129.6, 129.5, 128.2, 127.6, 126.9, 124.2, 123.6, 122.8, 121.7, 121.5, 118.6, 116.6, 115.0, 60.8, 45.3, 43.1, 35.0, 19.6, 17.6, 13.7. The enantiomeric ratio of compound **5b-(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_D = 45.25 min, t_L = 61.11 min; HRMS (ESI): *m*/*z* (M + H)$^+$ calcd for $C_{42}H_{40}N_5O_5S$: 726.2750; found: 726.2744.

(2*S*,3*R*)-3-(4-((5-(Dmethylamino)naphthalene)-1-sulfonamido)-3-methylphenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl) hexanamide (5b-(L)). Following the general procedure, **5b-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 70 : 30) as a brown coloured semi-solid (*anti* isomer, 77%, 56 mg, 0.1 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.4; IR ($CHCl_3$): 3293, 2927, 1713, 1382, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.87 (s, 1H), 8.66 (dd, J_1 = 4.2 Hz, J_2 = 1.4 Hz, 1H), 8.50 (dd, J_1 = 7.4 Hz, J_2 = 1.2 Hz, 1H), 8.38 (d, J = 8.5 Hz, 1H), 8.25 (d, J = 8.7 Hz, 1H), 8.08–8.06 (m, 1H), 7.91–7.86 (m, 3H), 7.74 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2H), 7.45–7.41 (m, 2H), 7.39–7.34 (m, 2H), 7.17–7.07 (m, 4H), 7.00 (d, J = 8.2 Hz, 1H), 6.39 (s, 1H), 5.18 (d, J = 11.6 Hz, 1H), 4.06 (td, J_1 = 11.2 Hz, J_2 = 4.5 Hz, 1H), 2.83 (s, 6H), 1.84 (s, 3H), 1.55–1.44 (m, 2H), 1.04–0.92 (m, 2H), 0.73 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.2, 165.8, 151.8, 148.2, 138.3, 138.2, 135.9, 134.6, 134.3, 133.9, 133.6, 131.8, 131.6, 130.7, 130.6, 130.0, 129.6, 129.5, 128.3, 127.6, 127.0, 124.2, 123.7, 122.9, 121.8, 121.6, 118.6, 116.7, 115.0, 60.9, 45.3, 43.2, 35.0, 19.7, 17.6, 13.8; $(\alpha)_D^{25}$ = −5.00 (*c* = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er 94 : 6) of compound **5b-(L)** 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_D = 46.71 min, t_L = 63.08 min; HRMS (ESI): *m*/*z* (M + H)$^+$ calcd for $C_{42}H_{40}N_5O_5S$: 726.2750; found: 726.2751.

(2*R*,3*S*)-3-(4-((5-(Dimethylamino)naphthalene)-1-sulfonamido)-3-methylphenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)hexanamide (5b-(D)). Following the general procedure, **5b-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 70 : 30) as a brown coloured semi-solid (*anti* isomer, 77%, 56 mg, 0.1 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.4; IR ($CHCl_3$): 3294, 2927, 1714, 1383, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.87 (s, 1H), 8.66 (d, J = 2.9 Hz, 1H), 8.50 (d, J = 7.2 Hz, 1H), 8.38 (d, J = 8.5 Hz, 1H), 8.25 (d, J = 8.6 Hz, 1H), 8.06 (d, J = 8.2 Hz, 1H), 7.90–7.86 (m, 3H), 7.74 (dd, J_1 = 5.1 Hz, J_2 = 3.0 Hz, 2H), 7.45–7.40 (m, 2H), 7.38–7.34 (m, 2H), 7.17–7.07 (m, 4H), 7.00 (d, J = 8.0 Hz, 1H), 6.43–6.40 (m, 1H), 5.18 (d, J = 11.5 Hz, 1H), 4.06 (td, J_1 = 11.4 Hz, J_2 = 3.6 Hz, 1H), 2.83 (s, 6H), 1.84 (s, 3H), 1.53–1.43 (m, 2H), 1.01–0.92 (m, 2H), 0.73 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.2, 165.8, 151.9, 148.2, 138.3, 138.2, 135.9, 134.6, 134.2, 133.9, 133.6, 131.9, 131.7, 130.7, 130.6, 130.0, 129.6, 129.5, 128.3, 127.6, 127.0, 127.0, 124.3, 123.7, 122.9, 121.8, 121.5, 118.6, 116.7, 115.0, 60.9, 45.3, 43.2, 35.1, 19.7, 17.6, 13.8; $(\alpha)_D^{25}$ = +6.25 (*c* = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er 93 : 7) of compound **5b-(D)** 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_D = 46.87 min, t_L = 64.15 min; HRMS (ESI): *m*/*z* (M + H)$^+$ calcd for $C_{42}H_{40}N_5O_5S$: 726.2750; found: 726.2744.

(2*R,3*S**)-3-(3-((5-(Dimethylamino)naphthalene)-1-sulfonamido) phenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)hexanamide (5c-(DL)).** Following the general procedure, **5c-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 70 : 30) as a brown coloured semi-solid (*anti* isomer, 78%, 83 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.40; IR (DCM): 3285, 2930, 1711, 1381, 723 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.53 (s, 1H), 8.40–8.39 (m, 2H), 8.28 (d, J = 8.4 Hz, 1H), 8.21 (d, J = 8.4 Hz, 1H), 8.03 (d, J = 7.2 Hz, 1H), 7.89 (d, J = 8.0 Hz, 1H), 7.82 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2H), 7.65 (dd, J_1 = 5.2 Hz, J_2 = 3.0 Hz, 2H), 7.44 (t, J = 8.0 Hz, 1H), 7.29–7.22 (m, 2H), 7.18–7.13 (m, 3H), 7.02–6.94 (m, 4H), 6.87 (d, J = 7.7 Hz, 1H), 5.10 (d, J = 11.6 Hz, 1H), 3.88 (td, J_1 = 11.4 Hz, J_2 = 3.3 Hz, 1H), 2.66 (s, 6H), 1.36–1.18 (m, 2H), 0.66–0.53 (m, 5H); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 168.2, 165.6, 151.8, 148.0, 141.8, 138.1, 137.2, 135.7, 134.2, 133.7, 133.5, 131.6, 130.6, 130.6, 129.8, 129.5, 129.5, 128.6, 127.5, 126.9, 125.7, 123.6, 122.8, 121.7, 121.4, 120.9, 120.6, 118.3, 116.6, 115.1, 60.3, 45.2, 43.6, 35.3, 19.4, 13.6. The enantiomeric ratio of compound **5c-(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 = 70.13 min, t_D = 94.53 min; HRMS (ESI): *m*/*z* (M + H)$^+$ calcd for $C_{41}H_{38}N_5O_5S$: 712.2594; found: 712.2596.

(2*S*,3*R*)-3-(3-((5-(Dimethylamino)naphthalene)-1-sulfonamido) phenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)hexanamide (5c-(L)). Following the general procedure, **5c-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 70 : 30) as a brown coloured semi-solid (*anti* isomer, 70%, 50 mg, 0.1 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.4; IR ($CHCl_3$): 3287, 2924, 1715, 1384, 754 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.62 (s, 1H), 8.51–8.49 (m, 2H), 8.37 (d, J = 8.6 Hz, 1H), 8.31 (d, J = 8.4 Hz, 1H), 8.13 (d, J = 7.2 Hz, 1H), 7.99 (dd, J_1 = 8.2 Hz, J_2 = 1.0 Hz, 1H), 7.92 (dd, J_1 = 5.5 Hz, J_2 = 3.0 Hz, 2H), 7.76 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2H), 7.55 (t, J = 8.4 Hz, 1H), 7.40–7.33 (m, 2H), 7.29–7.21 (m, 3H), 7.13–7.07 (m, 4H), 6.97 (d, J = 7.8 Hz, 1H), 5.20 (d, J = 11.6 Hz, 1H), 3.97 (td, J_1 = 12.4 Hz, J_2 = 4.0 Hz, 1H), 2.77 (s, 6H), 1.47–1.43 (m, 1H), 1.36–1.30 (m, 1H), 0.92–0.69 (m, 2H), 0.63 (t, J = 5.9 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.2, 165.6, 151.9, 148.0, 141.8, 138.1, 137.2, 135.7, 134.2, 133.7, 133.4, 131.6, 130.6, 130.6, 129.8, 129.5, 129.4, 128.6, 127.5, 126.9, 125.7, 123.7, 122.8, 121.7, 121.4, 120.9, 120.6, 118.3, 116.6, 115.1, 60.3, 45.2, 43.5, 35.3, 19.4, 13.6; $(\alpha)_D^{25}$ = −16.00 (*c* = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er 97 : 3) of compound **5c-(L)** 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 = 70.75 min, t_D = 96.86 min; HRMS (ESI): *m*/*z* (M + H)$^+$ calcd for $C_{41}H_{38}N_5O_5S$: 712.2594; found: 712.2592.

(2*R*,3*S*)-3-(3-((5-(Dimethylamino)naphthalene)-1-sulfonamido) phenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)hexanamide (5c-(D)). Following the general procedure, **5c-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 70 : 30) as a brown coloured semi-solid (*anti* isomer, 68%, 48 mg, 0.1 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.4; IR ($CHCl_3$): 3281, 2925, 1712, 1386, 753 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.62 (s, 1H), 8.51–8.49 (m, 2H),

8.38 (d, J = 8.6 Hz, 1H), 8.31 (d, J = 8.4 Hz, 1H), 8.13 (d, J = 7.2 Hz, 1H), 8.00 (d, J = 8.2 Hz, 1H), 7.92 (dd, J_1 = 5.5 Hz, J_2 = 3.0 Hz, 2H), 7.76 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2H), 7.55 (t, J = 8.2 Hz, 1H), 7.40–7.33 (m, 2H), 7.27–7.23 (m, 3H), 7.12–7.05 (m, 4H), 6.97 (d, J = 7.8 Hz, 1H), 5.20 (d, J = 11.6 Hz, 1H), 3.97 (td, J_1 = 11.5 Hz, J_2 = 3.8 Hz, 1H), 2.77 (s, 6H), 1.46–1.42 (m, 1H), 1.36–1.30 (m, 1H), 0.90–0.85 (m, 1H), 0.74–0.69 (m, 1H), 0.63 (t, J = 5.9 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.2, 165.6, 151.8, 148.0, 141.8, 138.1, 137.2, 135.7, 134.2, 133.7, 133.4, 131.6, 130.6, 130.6, 129.8, 129.5, 129.4, 128.6, 127.5, 126.9, 125.7, 123.7, 122.8, 121.7, 121.4, 120.9, 120.6, 118.3, 116.6, 115.1, 60.3, 45.2, 43.5, 35.3, 19.4, 13.6; $(\alpha)_D^{25}$ = +20.00 (c = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er 93 : 7) of compound **5c-(D)** 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 = 68.35 min, t_D = 93.73 min; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{41}H_{38}N_5O_5S$: 712.2594; found: 712.2595.

(2*R,3*S**)-3-(4-((5-(Dimethylamino)naphthalene)-1-sulfonamido) phenyl)-2-(1,3-dioxoisoindolin-2-yl)-3-phenyl-*N*-(quinolin-8-yl) propanamide (6a-(DL)).** Following the general procedure, **6a-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 60 : 40) as a brown coloured semi-solid (*anti* isomer, 82%, 92 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.40; IR (DCM): 3283, 2925, 1710, 1383, 725 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 10.08 (s, 1H), 8.57–8.55 (m, 2H), 8.33 (d, J = 8.5 Hz, 1H), 8.23 (d, J = 8.6 Hz, 1H), 8.03 (d, J = 7.4 Hz, 1H), 8.00 (dd, J_1 = 8.3 Hz, J_2 = 1.0 Hz, 1H), 7.69 (dd, J_1 = 5.5 Hz, J_2 = 3.1 Hz, 2H), 7.57–7.55 (m, 2H), 7.42–7.35 (m, 5H), 7.25–7.22 (m, 4H), 7.18–7.14 (m, 1H), 7.10–7.03 (m, 3H), 6.98 (t, J = 7.4 Hz, 1H), 6.91 (d, J = 7.6 Hz, 2H), 5.83 (d, J = 12.3 Hz, 1H), 5.48 (d, J = 12.3 Hz, 1H), 2.79 (s, 6H); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 167.8, 165.3, 151.8, 148.2, 140.4, 138.2, 137.0, 135.8, 134.2, 134.0, 133.8, 131.2, 130.7, 130.0, 129.6, 129.4, 128.9, 128.6, 128.4, 127.6, 127.6, 126.9, 126.9, 123.4, 122.9, 122.0, 121.6, 121.4, 118.4, 116.7, 115.1, 58.3, 49.5, 45.3. The enantiomeric ratio of compound **6a-(DL)** was determined using the Daicel Chiralpak IA column, hexane/i-PrOH 20 : 30, flow rate 0.5 mL min^{-1}, UV detection at 254 nm, t_L = 39.62 min, t_D = 48.22 min; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{44}H_{36}N_5O_5S$: 746.2437; found: 746.2430.

(2*S*,3*R*)-3-(4-((5-(Dimethylamino)naphthalene)-1-sulfonamido) phenyl)-2-(1,3-dioxoisoindolin-2-yl)-3-phenyl-*N*-(quinolin-8-yl) propanamide (6a-(L)). Following the general procedure, **6a-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 60 : 40) as a brown coloured semi-solid (*anti* isomer, 75%, 62 mg, 0.11 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.4; IR ($CHCl_3$): 3282, 2929, 1712, 1384, 749 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 10.09 (s, 1H), 8.55 (d, J = 5.1 Hz, 2H), 8.32 (d, J = 8.5 Hz, 1H), 8.26–8.24 (m, 1H), 8.03 (d, J = 7.3 Hz, 1H), 7.98 (m, 1H), 7.68 (dd, J_1 = 5.4 Hz, J_2 = 3.1 Hz, 2H), 7.54 (dd, J_1 = 5.3 Hz, J_2 = 2.9 Hz, 2H), 7.44–7.34 (m, 6H), 7.25–7.22 (m, 3H), 7.15 (t, J = 8.1 Hz, 1H), 7.08 (t, J = 7.6 Hz, 2H), 7.02 (d, J = 7.5 Hz, 1H), 6.99–6.96 (m, 1H), 6.93–6.91 (m, 2H), 5.84 (d, J = 12.3 Hz, 1H), 5.47 (d, J = 12.3 Hz, 1H), 2.78 (s, 6H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 167.8, 165.3, 151.8, 148.2, 140.4, 138.2, 136.9, 135.9, 135.8, 134.3, 134.3, 134.0, 133.8, 131.2, 130.6, 129.9, 129.6, 129.5, 128.9, 128.5, 128.4, 127.6, 127.5, 126.9, 126.9, 123.3, 122.9, 121.9, 121.5, 121.4, 118.5, 116.7, 115.1, 58.3, 49.5, 45.3; $(\alpha)_D^{25}$ = +10.00 (c = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er 92 : 8) of compound **6a-(L)** was determined using the Daicel Chiralpak IA column, hexane/i-PrOH 20 : 30, flow rate 0.5 mL min^{-1}, UV detection at 254 nm, t_L = 39.78 min, t_D = 47.46 min; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{44}H_{36}N_5O_5S$: 746.2437 found: 746.2435.

(2*R*,3*S*)-3-(4-((5-(Dimethylamino)naphthalene)-1-sulfonamido) phenyl)-2-(1,3-dioxoisoindolin-2-yl)-3-phenyl-*N*-(quinolin-8-yl) propanamide (6a-(D)). Following the general procedure, **6a-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 60 : 40) as a brown coloured semi-solid (*anti* isomer, 70%, 52 mg, 0.1 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.4; IR ($CHCl_3$): 3283, 2925, 1717, 1385, 755 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 10.09 (s, 1H), 8.57–8.55 (m, 2H), 8.33 (d, J = 8.5 Hz, 1H), 8.24 (d, J = 8.5 Hz, 1H), 8.04–7.99 (m, 2H), 7.69 (dd, J_1 = 5.4 Hz, J_2 = 3.1 Hz, 2H), 7.56 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2H), 7.41–7.35 (m, 5H), 7.28–7.22 (m, 4H), 7.16 (m, 1H), 7.08 (t, J = 7.6 Hz, 2H), 7.04 (d, J = 7.6 Hz, 1H), 7.00–6.97 (m, 1H), 6.91 (d, J = 8.4 Hz, 2H), 5.83 (d, J = 12.3 Hz, 1H), 5.48 (d, J = 12.3 Hz, 1H), 2.79 (s, 6H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 167.8, 165.3, 151.8, 148.2, 140.4, 138.2, 137.0, 135.9, 135.8, 134.3, 134.0 133.8, 131.2, 130.7, 129.9, 129.6, 129.5, 128.9, 128.6, 128.4, 127.6, 127.6, 126.9, 126.9, 123.4, 122.9, 121.9, 121.6, 121.5, 118.5, 116.8, 115.1, 58.3, 49.5, 45.3; $(\alpha)_D^{25}$ = −9.00 (c = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er >90 : 10) of compound **6a-(D)** was determined using the Daicel Chiralpak IA column, hexane/i-PrOH 20 : 30, flow rate 0.5 mL min^{-1}, UV detection at 254 nm, t_L = 40.17 min, t_D = 47.48 min; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{44}H_{36}N_5O_5S$: 746.2437; found: 746.2439.

(2*R,3*S**)-3-(4-((5-(Dimethylamino)naphthalene)-1-sulfonamido)-3-methylphenyl)-2-(1,3-dioxoisoindolin-2-yl)-3-phenyl-*N*-(quinolin-8-yl)propanamide (6b-(DL)).** Following the general procedure, **6b-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 70 : 30) as a brown coloured semi-solid (*anti* isomer, 82%, 94 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.40; IR (DCM): 3288, 2925, 1711, 1380, 726 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 10.07 (s, 1H), 8.64–8.63 (m, 1H), 8.58 (dd, J_1 = 7.0 Hz, J_2 = 1.5 Hz, 1H), 8.37 (d, J = 8.5 Hz, 1H), 8.17 (d, J = 8.6 Hz, 1H), 8.05 (d, J = 8.2 Hz, 1H), 7.93 (d, J = 7.3 Hz, 1H), 7.70 (dd, J_1 = 5.2 Hz, J_2 = 3.1 Hz, 2H), 7.59–7.57 (m, 2H), 7.45–7.40 (m, 2H), 7.35–7.30 (m, 2H), 7.28–7.25 (m, 4H), 7.18–7.10 (m, 3H), 7.05–7.00 (m, 3H), 6.57–6.53 (m, 1H), 5.84 (d, J = 12.3 Hz, 1H), 5.48 (d, J = 12.3 Hz, 1H), 2.81 (s, 6H), 1.86 (s, 3H); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 167.7, 165.4, 151.8, 148.3, 140.4, 138.3, 137.9, 135.9, 134.6, 134.0, 133.9, 131.6, 131.3, 130.6, 130.4, 129.9, 129.6, 129.5, 128.8, 128.6, 128.2, 127.7, 127.6, 127.0, 126.9, 126.3, 123.7, 123.4, 123.0, 121.9, 121.6, 118.5, 116.8, 115.1, 58.4, 49.6, 45.3, 17.6. The enantiomeric ratio of compound **6b-(DL)** was determined using the Daicel Chiralpak IA column, hexane/

i-PrOH 50 : 50, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 23.19 min, t_L = 28.55 min; HRMS (ESI): *m*/*z* (M + H)$^+$ calcd for $C_{45}H_{38}N_5O_5S$: 760.2594; found: 760.2574.

(2*S*,3*R*)-3-(4-((5-(Dimethylamino)naphthalene)-1-sulfonamido)-3-methylphenyl)-2-(1,3-dioxoisoindolin-2-yl)-3-phenyl-*N*-(quinolin-8-yl)propenamide (6b-(L)). Following the general procedure, **6b-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 70 : 30) as a brown coloured semi-solid (*anti* isomer, 77%, 59 mg, 0.1 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.4; IR ($CHCl_3$): 3286, 2926, 1713, 1382, 751 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 10.07 (s, 1H), 8.65–8.64 (m, 1H), 8.58 (dd, J_1 = 7.2 Hz, J_2 = 1.5 Hz 1H), 8.37 (d, J = 8.5 Hz, 1H), 8.16 (d, J = 8.6 Hz, 1H), 8.07 (d, J = 8.2 Hz, 1H), 7.93 (d, J = 7.3 Hz, 1H), 7.71 (dd, J_1 = 5.4 Hz, J_2 = 3.1 Hz, 2H), 7.59 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2H), 7.46–7.40 (m, 2H), 7.37–7.25 (m, 6H), 7.19–7.11 (m, 3H), 7.04–7.00 (m, 3H), 6.47–6.45 (m, 1H), 5.83 (d, J = 12.3 Hz, 1H), 5.47 (d, J = 12.3 Hz, 1H), 2.81 (s, 6H), 1.86 (s, 3H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 167.7, 165.4, 148.2, 140.4, 138.2, 137.9, 135.9, 134.7, 134.0, 134.0, 133.8, 131.6, 131.2, 130.6, 130.5, 130.5, 130.4, 129.9, 129.4, 128.5, 128.1, 127.7, 127.6, 127.0, 126.9, 126.3, 123.7, 123.3, 123.1, 121.9, 121.6, 116.8, 115.2, 58.3, 49.5, 45.3, 17.7; $(\alpha)_D^{25}$ = −25.00 (*c* = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er 95 : 5) of compound **6b-(L)** was determined using the Daicel Chiralpak IA column, hexane/i-PrOH 50 : 50, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 22.88 min, t_L = 27.31 min; HRMS (ESI): *m*/*z* (M + H)$^+$ calcd for $C_{45}H_{38}N_5O_5S$: 760.2594; found: 760.2605.

(2*R*,3*S*)-3-(4-((5-(Dimethylamino)naphthalene)-1-sulfonamido)-3-methylphenyl)-2-(1,3-dioxoisoindolin-2-yl)-3-phenyl-*N*-(quinolin-8-yl)propanamide (6b-(D)). Following the general procedure, **6b-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 70 : 30) as a brown coloured semi-solid (*anti* isomer, 75%, 57 mg, 0.1 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.4; IR ($CHCl_3$): 3287, 2928, 1713, 1382, 750 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 10.07 (s, 1H), 8.65 (d, J = 3.7 Hz, 1H), 8.59 (d, J = 7.2 Hz, 1H), 8.37 (d, J = 8.5 Hz, 1H), 8.16 (d, J = 8.6 Hz, 1H), 8.07 (d, J = 7.4 Hz, 1H), 7.93 (d, J = 7.3 Hz, 1H), 7.71 (dd, J_1 = 5.2 Hz, J_2 = 3.1 Hz, 2H), 7.59 (dd, J_1 = 5.4 Hz, J_2 = 2.9 Hz, 2H), 7.46–7.42 (m, 2H), 7.37–7.25 (m, 6H), 7.19–7.11 (m, 3H), 7.04–7.00 (m, 3H), 6.49–6.44 (m, 1H), 5.84 (d, J = 12.2 Hz, 1H), 5.48 (d, J = 12.3 Hz, 1H), 2.81 (s, 6H), 1.86 (s, 3H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 167.7, 165.4, 151.4, 148.2, 140.4, 138.3, 137.9, 135.9, 134.7, 134.0, 133.8, 131.7, 131.2, 130.5, 130.4, 129.9, 129.5, 129.4, 128.5, 128.2, 127.7, 127.6, 127.0, 126.9, 126.3, 123.8, 123.4, 123.3, 123.1, 122.0, 121.6, 118.8, 116.8, 115.1, 58.4, 49.5, 45.3, 17.6; $(\alpha)_D^{25}$ = +30.00 (*c* = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er 98 : 2) of compound **6b-(D)** was determined using the Daicel Chiralpak IA column, hexane/i-PrOH 50 : 50, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 23.52 min, t_L = 28.38 min; HRMS (ESI): *m*/*z* (M + H)$^+$ calcd for $C_{45}H_{38}N_5O_5S$: 760.2594; found: 760.2596.

(2*R,3*S**)-3-(3-((5-(Dimethylamino)naphthalene)-1-sulfonamido)phenyl)-2-(1,3-dioxoisoindolin-2-yl)-3-phenyl-*N*-(quinolin-8-yl)propanamide (6c-(DL)).** Following the general procedure, **6c-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 80 : 20) as a brown coloured semi-solid (*anti* isomer, 80%, 90 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.30; IR (DCM): 3282, 2924, 1713, 1385, 712 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.90 (s, 1H), 8.56 (dd, J_1 = 7.0 Hz, J_2 = 1.9 Hz, 1H), 8.51–8.49 (m, 1H), 8.30 (d, J = 8.6 Hz, 1H), 8.26 (d, J = 8.5 Hz, 1H), 8.03–8.00 (m, 2H), 7.72 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2H), 7.61–7.59 (m, 2H), 7.50–7.46 (m, 1H), 7.43–7.36 (m, 2H), 7.29–7.24 (m, 3H), 7.15–6.98 (m, 9H), 6.83–6.81 (m, 1H), 5.79 (d, J = 12.2 Hz, 1H), 5.41 (d, J = 12.3 Hz, 1H), 2.77 (s, 6H); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 167.7, 165.2, 151.9, 148.1, 141.8, 140.2, 138.3, 137.3, 135.8, 134.0, 133.8, 133.6, 131.3, 130.7, 130.5, 130.0, 129.6, 129.4, 128.6, 127.6, 127.6, 127.0, 126.9, 125.0, 123.4, 122.9, 121.9, 121.5, 120.2, 120.2, 118.3, 116.8, 115.1, 58.0, 50.0, 45.3. The enantiomeric ratio of compound **6c-(DL)** was determined using the Daicel Chiralpak IA column, hexane/i-PrOH 50 : 50, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 38.79 min, t_D = 88.06 min; HRMS (ESI): *m*/*z* (M + H)$^+$ calcd for $C_{44}H_{36}N_5O_5S$: 746.2437; found: 746.2435.

(2*S*,3*R*)-3-(3-((5-(Dimethylamino)naphthalene)-1-sulfonamido)phenyl)-2-(1,3-dioxoisoindolin-2-yl)-3-phenyl-*N*-(quinolin-8-yl)propanamide (6c-(L)). Following the general procedure, **6c-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 80 : 20) as a brown coloured semi-solid (*anti* isomer, 77%, 69 mg, 0.12 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.3; IR ($CHCl_3$): 3279, 2926, 1713, 1386, 752 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.93 (s, 1H), 8.59 (dd, J_1 = 7.1 Hz, J_2 = 1.8 Hz, 1H), 8.53 (dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz, 1H), 8.32 (d, J = 8.7 Hz, 1H) 8.29 (d, J = 8.5 Hz, 1H), 8.05–8.03 (m, 2H), 7.75 (dd, J_1 = 5.5 Hz, J_2 = 3.1 Hz, 2H), 7.63 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2H), 7.51 (t, J = 8.4 Hz, 1H), 7.45–7.41 (m, 2H), 7.32–7.27 (m, 3H), 7.17–7.03 (m, 9H), 6.85 (d, J = 7.8 Hz, 1H), 5.82 (d, J = 12.3 Hz, 1H), 5.44 (d, J = 12.3 Hz, 1H), 2.80 (s, 6H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 167.7, 165.2, 151.9, 148.1, 141.8, 140.2, 138.2, 137.3, 135.8, 134.0, 133.8, 133.5, 131.3, 130.7, 130.5, 130.0, 129.5, 129.4, 128.6, 127.6, 127.6, 127.0, 126.9, 125.0, 123.4, 122.9, 121.9, 121.5, 120.1, 118.2, 116.8, 115.1, 58.0, 50.0, 45.2; $(\alpha)_D^{25}$ = −24.00 (*c* = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er >98 : 2) of compound **6c-(L)** was determined using the Daicel Chiralpak IA column, hexane/i-PrOH 50 : 50, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 38.18 min, t_D = 87.61 min; HRMS (ESI): *m*/*z* (M + H)$^+$ calcd for $C_{44}H_{36}N_5O_5S$: 746.2437; found: 746.2438.

(2*R*,3*S*)-3-(3-((5-(Dimethylamino)naphthalene)-1-sulfonamido)phenyl)-2-(1,3-dioxoisoindolin-2-yl)-3-phenyl-*N*-(quinolin-8-yl)propanamide (6c-(D)). Following the general procedure, **6c-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 80 : 20) as a brown coloured semi-solid (*anti* isomer, 76%, 57 mg, 0.1 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.3; IR ($CHCl_3$): 3281, 2925, 1713, 1385, 752 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.93 (s, 1H), 8.59 (dd, J_1 = 7.1 Hz, J_2 = 1.7 Hz, 1H), 8.53 (dd, J_1 = 4.2 Hz, J_2 = 1.4 Hz, 1H), 8.33–8.28 (m, 2H), 8.05–8.03 (m, 2H), 7.75 (dd, J_1 = 5.4 Hz, J_2 = 3.1 Hz, 2H), 7.63 (dd, J_1 = 5.5 Hz, J_2 = 3.1 Hz, 2H), 7.51 (t, J = 8.3 Hz, 1H), 7.46–7.41 (m, 2H), 7.32–7.27 (m, 3H),

7.17–7.03 (m, 9H), 6.85 (d, J = 8.3 Hz, 1H), 5.81 (d, J = 12.3 Hz, 1H), 5.44 (d, J = 12.3 Hz, 1H), 2.80 (s, 6H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 167.7, 165.2, 151.9, 148.1, 141.8, 140.2, 138.2, 137.3, 135.8, 134.0, 133.8, 133.5, 131.3, 130.7, 130.5, 130.0, 129.5, 129.4, 128.6, 127.6, 127.6, 127.0, 126.9, 125.0, 123.4, 122.9, 121.9, 121.5, 120.2, 118.2, 116.8, 115.1, 58.0, 50.0, 45.3; $(\alpha)_D^{25}$ = +25.00 (c = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er 97 : 3) of compound **6c-(D)** was determined using the Daicel Chiralpak IA column, hexane/i-PrOH 50 : 50, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 37.11 min, t_D = 89.41 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{44}H_{36}N_5O_5S$: 746.2437; found: 746.2432.

(2*R,3*S**)-3-(4-((5-(Dimethylamino)naphthalene)-1-sulfonamido) phenyl)-2-(1,3-dioxoisoindolin-2-yl)-4-methyl-*N*-(quinolin-8-yl)pentanamide (7a-(DL)).** Following the general procedure, **7a-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 70 : 30) as a brown coloured semi-solid (*anti* isomer, 76%, 81 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.40; IR (DCM): 3284, 2929, 1712, 1383, 723 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.95 (s, 1H), 8.55 (dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz, 1H), 8.46 (dd, J_1 = 7.4 Hz, J_2 = 1.4 Hz, 1H), 8.32 (d, J = 8.6 Hz, 2H), 7.99 (dd, J_1 = 8.3 Hz, J_2 = 1.6 Hz, 1H), 7.94 (d, J = 7.2 Hz, 1H), 7.89 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2H), 7.72 (dd, J_1 = 5.5 Hz, J_2 = 3.0 Hz, 2H), 7.47 (t, J = 8.4 Hz, 1H), 7.37 (dd, J_1 = 8.2 Hz, J_2 = 1.4 Hz, 1H), 7.33 (t, J = 8.1 Hz, 1H), 7.24–7.21 (m, 3H), 7.12–7.07 (m, 3H), 6.93 (d, J = 8.5 Hz, 2H), 5.49 (d, J = 12.4 Hz, 1H), 4.12 (dd, J_1 = 12.4 Hz, J_2 = 3.3 Hz, 1H), 2.81 (s, 6H), 1.94–1.86 (m, 1H), 0.67 (d, J = 6.8 Hz, 3H), 0.63 (d, J = 6.8 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 168.4, 165.9, 151.9, 148.1, 138.3, 135.8, 135.7, 134.3, 134.0, 133.9, 133.3, 131.7, 130.6, 130.1, 129.6, 129.5, 128.5, 127.5, 126.9, 123.7, 122.8, 121.8, 121.5, 121.4, 118.4, 116.7, 115.1, 57.6, 47.7, 45.3, 28.9, 21.3, 16.1. The enantiomeric ratio of compound **7a-(DL)** was determined using the Daicel Chiralpak IA column, hexane/i-PrOH 30 : 70, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 13.46 min, t_D = 17.73 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{41}H_{38}N_5O_5S$: 712.2594; found: 712.2583.

(2*S*,3*R*)-3-(4-((5-(Dimethylamino)naphthalene)-1-sulfonamido) phenyl)-2-(1,3-dioxoisoindolin-2-yl)-4-methyl-*N*-(quinolin-8-yl) pentanamide (7a-(L)). Following the general procedure, **7a-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 70 : 30) as a brown coloured semi-solid (*anti* isomer, 60%, 64 mg, 0.15 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.4; IR ($CHCl_3$): 3278, 2925, 1714, 1384, 754 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.96 (s, 1H), 8.59 (dd, J_1 = 4.2 Hz, J_2 = 1.4 Hz, 1H), 8.47 (d, J = 7.4 Hz, 1H), 8.33–8.28 (m, 2H), 8.02 (dd, J_1 = 8.2 Hz, J_2 = 1.2 Hz, 1H), 7.92–7.90 (m, 1H), 7.89 (dd, J_1 = 5.6 Hz, J_2 = 3.3 Hz, 2H), 7.73 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2H), 7.49 (t, J = 8.3 Hz, 1H), 7.41–7.33 (m, 2H), 7.29–7.22 (m, 3H), 7.12–7.06 (m, 2H), 6.91–6.87 (m, 3H), 5.49 (d, J = 12.3 Hz, 1H), 4.13 (dd, J_1 = 12.4 Hz, J_2 = 3.2 Hz, 1H), 2.82 (s, 6H), 1.92–1.86 (m, 1H), 0.68 (d, J = 6.8 Hz, 3H), 0.64 (d, J = 6.8 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.4, 165.9, 152.0, 148.1, 138.3, 135.8, 135.7, 134.3, 134.0, 134.0, 133.5, 131.7, 130.7, 130.2, 129.6, 129.6, 128.5, 127.6, 127.0, 123.7, 122.8, 121.8, 121.6, 121.5, 118.4, 116.7, 115.1, 57.6, 47.7, 45.3, 28.8, 21.4, 16.1; $(\alpha)_D^{25}$ = +17.00 (c = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er >95 : 5) of compound **7a-(L)** was determined using the Daicel Chiralpak IA column, hexane/i-PrOH 30 : 70, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 12.81 min, t_D = 16.30 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{41}H_{38}N_5O_5S$: 712.2594; found: 712.2590.

(2*R*,3*S*)-3-(4-((5-(Dimethylamino)naphthalene)-1-sulfonamido) phenyl)-2-(1,3-dioxoisoindolin-2-yl)-4-methyl-*N*-(quinolin-8-yl) pentanamide (7a-(D)). Following the general procedure, **7a-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 70 : 30) as a brown coloured semi-solid (*anti* isomer, 60%, 64 mg, 0.15 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.4; IR ($CHCl_3$): 3282, 2926, 1714, 1385, 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.96 (s, 1H), 8.59 (dd, J_1 = 4.1 Hz, J_2 = 1.4 Hz, 1H), 8.47 (dd, J_1 = 7.5 Hz, J_2 = 1.2 Hz, 1H), 8.33–8.28 (m, 2H), 8.02 (dd, J_1 = 8.3 Hz, J_2 = 1.4 Hz, 1H), 7.92–7.90 (m, 1H), 7.89 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2H), 7.73 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2H), 7.49 (t, J = 8.3 Hz, 1H), 7.41–7.33 (m, 2H), 7.29–7.22 (m, 3H), 7.12–7.05 (m, 2H), 6.90 (d, J = 8.3 Hz, 2H), 6.85 (s, 1H), 5.49 (d, J = 12.4 Hz, 1H), 4.13 (dd, J_1 = 12.4 Hz, J_2 = 3.2 Hz, 1H), 2.82 (s, 6H), 1.94–1.87 (m, 1H), 0.68 (d, J = 6.8 Hz, 3H), 0.64 (d, J = 6.8 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.4, 165.9, 152.0, 148.1, 138.4, 135.8, 135.7, 134.3, 134.0, 134.0, 133.6, 131.7, 130.7, 130.2, 129.6, 129.6, 128.5, 127.6, 127.0, 123.7, 122.8, 121.8, 121.7, 121.5, 118.4, 116.7, 115.1, 57.7, 47.7, 45.3, 28.8, 21.4, 16.1; $(\alpha)_D^{25}$ = −12.00 (c = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er >95 : 5) of compound **7a-(D)** was determined using the Daicel Chiralpak IA column, hexane/i-PrOH 30 : 70, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 13.47 min, t_D = 17.66 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{41}H_{38}N_5O_5S$: 712.2594; found: 712.2581.

(2*R,3*S**)-3-(4-((5-(Dimethylamino)naphthalene)-1-sulfonamido)-3-methylphenyl)-2-(1,3-dioxoisoindolin-2-yl)-4-methyl-*N*-(quinolin-8-yl)pentanamide (7b-(DL)).** Following the general procedure, **7b-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 70 : 30) as a brown coloured semi-solid (*anti* isomer, 72%, 79 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.40; IR (DCM): 3290, 2925, 1713, 1381, 725 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.97 (s, 1H), 8.65–8.64 (m, 1H), 8.49 (d, J = 7.4 Hz, 1H), 8.36 (d, J = 8.5 Hz, 1H), 8.27 (d, J = 8.6 Hz, 1H), 8.05 (d, J = 8.2 Hz, 1H), 7.89 (dd, J_1 = 5.3 Hz, J_2 = 3.0 Hz, 2H), 7.83 (d, J = 7.3 Hz, 1H), 7.73 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2H), 7.45–7.32 (m, 4H), 7.14–7.03 (m, 5H), 6.46 (s, 1H), 5.50 (d, J = 12.3 Hz, 1H), 4.12 (dd, J_1 = 12.3 Hz, J_2 = 3.1 Hz, 1H), 2.83 (s, 6H), 1.91 (s, 3H), 1.93–1.88 (m, 1H), 0.72 (d, J = 6.8 Hz, 3H), 0.68 (d, J = 6.7 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 168.3, 166.0, 151.9, 148.1, 138.4, 135.9, 134.5, 134.2, 134.0, 133.8, 131.7, 131.2, 130.6, 130.0, 129.6, 129.6, 128.4, 127.6, 127.0, 123.7, 122.8, 121.8, 121.5, 118.6, 116.7, 115.1, 57.7, 47.7, 45.3, 28.8, 21.4, 17.7, 16.3. The enantiomeric ratio of compound **7b-(DL)** was determined using the Daicel Chiralpak IA column, hexane/i-PrOH 70 : 30, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 17.72 min, t_D = 21.21 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{42}H_{40}N_5O_5S$: 726.2750; found: 726.2747.

(2*S*,3*R*)-3-(4-((5-(Dimethylamino)naphthalene)-1-sulfonamido)-3-methylphenyl)-2-(1,3-dioxoisoindolin-2-yl)-4-methyl-*N*-(quinolin-8-yl)pentanamide (7b-(L)). Following the general procedure, **7b-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 70 : 30) as a brown coloured semi-solid (*anti* isomer, 66%, 62 mg, 0.13 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.4; IR ($CHCl_3$): 3290, 2926, 1714, 1384, 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.97 (s, 1H), 8.64 (dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz, 1H), 8.49 (dd, J_1 = 7.5 Hz, J_2 = 1.5 Hz, 1H), 8.36 (d, J = 8.5 Hz, 1H), 8.27 (d, J = 8.6 Hz, 1H), 8.05 (dd, J_1 = 8.3 Hz, J_2 = 1.6 Hz, 1H), 7.89 (dd, J_1 = 5.5 Hz, J_2 = 3.0 Hz, 2H), 7.83 (dd, J_1 = 7.3 Hz, J_2 = 1.0 Hz, 1H), 7.74 (dd, J_1 = 5.5 Hz, J_2 = 3.0 Hz, 2H), 7.45–7.32 (m, 4H), 7.12–7.04 (m, 5H), 6.49 (s, 1H), 5.50 (d, J = 12.4 Hz, 1H), 4.15–4.10 (m, 1H), 2.83 (s, 6H), 1.93–1.92 (m, 1H), 1.92 (s, 3H), 0.72 (d, J = 6.8 Hz, 3H), 0.68 (d, J = 6.8 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.4, 166.0, 151.9, 148.1, 138.4, 135.9, 134.5, 134.3, 134.2, 134.0, 133.8, 131.7, 131.1, 130.6, 130.0, 129.6, 129.5, 128.4, 127.6, 127.0, 123.7, 123.6, 122.8, 121.8, 121.5, 118.5, 116.7, 115.0, 57.7, 47.7, 45.3, 28.8, 21.4, 17.7, 16.2; $(\alpha)_D^{25}$ = −9.00 (c = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er 90 : 10) of compound **7b-(L)** was determined using the Daicel Chiralpak IA column, hexane/i-PrOH 70 : 30, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 17.48 min, t_D = 21.00 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{42}H_{40}N_5O_5S$: 726.2750; found: 726.2762.

(2*R*,3*S*)-3-(4-((5-(Dimethylamino)naphthalene)-1-sulfonamido)-3-methylphenyl)-2-(1,3-dioxoisoindolin-2-yl)-4-methyl-*N*-(quinolin-8-yl)pentanamide (7b-(D)). Following the general procedure, **7b-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 70 : 30) as a brown coloured semi-solid (*anti* isomer, 62%, 58 mg, 0.128 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.4; IR ($CHCl_3$): 3288, 2926, 1714, 1384, 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.97 (s, 1H), 8.64 (d, J = 2.9 Hz, 1H), 8.50–8.48 (m, 1H), 8.36 (d, J = 8.5 Hz, 1H), 8.27 (d, J = 8.6 Hz, 1H), 8.06 (d, J = 8.2 Hz, 1H), 7.89 (dd, J_1 = 5.2 Hz, J_2 = 3.0 Hz, 2H), 7.83 (d, J = 7.2 Hz, 1H), 7.74 (dd, J_1 = 5.3 Hz, J_2 = 3.0 Hz, 2H), 7.45–7.32 (m, 4H), 7.14–7.03 (m, 5H), 6.43 (s, 1H), 5.50 (d, J = 12.3 Hz, 1H), 4.12 (dd, J_1 = 12.4 Hz, J_2 = 3.3 Hz, 1H), 2.83 (s, 6H), 1.93–1.91 (m, 1H), 1.91 (s, 3H), 0.72 (d, J = 6.8 Hz, 3H), 0.68 (d, J = 6.8 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.3, 166.0, 151.9, 148.1, 138.4, 135.9, 134.5, 134.3, 134.2, 134.0, 133.8, 131.7, 131.2, 130.6, 130.0, 129.6, 129.6, 128.4, 127.7, 127.0, 123.7, 122.8, 121.8, 121.5, 118.6, 116.7, 115.1, 57.7, 47.4, 45.3, 28.8, 21.4, 17.7, 16.3; $(\alpha)_D^{25}$ = +10.00 (c = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er 95 : 5) of compound **7b-(D)** was determined using the Daicel Chiralpak IA column, hexane/i-PrOH 70 : 30, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 17.27 min, t_D = 21.49 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{42}H_{40}N_5O_5S$: 726.2750; found: 726.2749.

(2*R,3*S**)-3-(3-((5-(Dimethylamino)naphthalene)-1-sulfonamido)phenyl)-2-(1,3-dioxoisoindolin-2-yl)-4-methyl-*N*-(quinolin-8-yl)pentanamide (7c-(DL)).** Following the general procedure, **7c-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 70 : 30) as a brown coloured semi-solid (*anti* isomer, 68%, 73 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.40; IR (DCM): 3284, 2926, 1710, 1380, 724 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.61 (s, 1H), 8.44 (d, J = 3.0 Hz, 1H), 8.38 (d, J = 7.4 Hz, 1H), 8.28 (d, J = 8.6 Hz, 1H), 8.19 (d, J = 8.5 Hz, 1H), 8.01 (d, J = 7.1 Hz, 1H), 7.89 (d, J = 8.2 Hz, 1H), 7.81 (dd, J_1 = 5.4 Hz, J_2 = 3.1 Hz, 2H), 7.65 (dd, J_1 = 5.4 Hz, J_2 = 3.1 Hz, 2H), 7.44 (t, J = 8.2 Hz, 1H), 7.29–7.23 (m, 2H), 7.21–7.09 (m, 3H), 7.05–6.98 (m, 4H), 6.89 (s, 1H), 5.36 (d, J = 12.2 Hz, 1H), 3.93 (dd, J_1 = 12.3 Hz, J_2 = 3.3 Hz, 1H), 2.67 (s, 6H), 1.75–1.70 (m, 1H), 0.38 (d, J = 6.4 Hz, 3H), 0.27 (d, J = 6.4 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 168.4, 165.9, 151.9, 148.0, 138.2, 137.7, 136.6, 135.7, 134.2, 133.8, 133.5, 131.7, 130.6, 130.6, 129.6, 129.4, 129.2, 128.6, 127.5, 126.9, 123.7, 122.9, 121.7, 121.4, 121.1, 118.3, 116.7, 115.1, 57.4, 48.1, 45.2, 28.8, 21.1, 15.8; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{41}H_{38}N_5O_5S$: 712.2594; found: 712.2597.

(2*S*,3*R*)-3-(3-((5-(Dimethylamino)naphthalene)-1-sulfonamido)phenyl)-2-(1,3-dioxoisoindolin-2-yl)-4-methyl-*N*-(quinolin-8-yl)pentanamide (7c-(L)). Following the general procedure, **7c-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 70 : 30) as a brown coloured semi-solid (*anti* isomer, 60%, 64 mg, 0.15 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.4; IR ($CHCl_3$): 3285, 2925, 1713, 1385, 754 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.71 (s, 1H), 8.57 (d, J = 3.2 Hz, 1H), 8.48 (dd, J_1 = 7.6 Hz, J_2 = 1.0 Hz, 1H), 8.35 (d, J = 8.6 Hz, 1H), 8.30 (d, J = 8.3 Hz, 1H), 8.08 (d, J = 7.0 Hz, 1H), 8.02 (dd, J_1 = 8.2 Hz, J_2 = 1.3 Hz, 1H), 7.92 (dd, J_1 = 5.4 Hz, J_2 = 3.1 Hz, 2H), 7.77 (dd, J_1 = 5.4 Hz, J_2 = 3.1 Hz, 2H), 7.56 (t, J = 8.2 Hz, 1H), 7.41–7.35 (m, 2H), 7.32 (dd, J_1 = 8.3 Hz, J_2 = 4.3 Hz, 1H), 7.21 (t, J = 8.0 Hz, 1H), 7.16–7.06 (m, 5H), 6.94 (s, 1H), 5.44 (d, J = 12.3 Hz, 1H), 4.02 (dd, J_1 = 12.4 Hz, J_2 = 3.4 Hz, 1H), 2.79 (s, 6H), 1.85–1.83 (m, 1H), 0.47 (d, J = 6.4 Hz, 3H), 0.36 (d, J = 6.3 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.4, 165.9, 151.9, 148.0, 138.2, 137.7, 136.5, 135.8, 134.3, 133.8, 133.5, 131.7, 130.7, 130.6, 129.6, 129.4, 129.4, 129.3, 128.7, 127.5, 126.9, 123.7, 122.9, 121.8, 121.5, 121.3, 118.2, 116.7, 115.1, 57.4, 48.1, 45.3, 28.8, 21.1, 15.8; $(\alpha)_D^{25}$ = −21.00 (c = 0.02 g per 100 mL, $CHCl_3$); HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{41}H_{38}N_5O_5S$: 712.2594; found: 712.2587.

(2*R*,3*S*)-3-(3-((5-(Dimethylamino)naphthalene)-1-sulfonamido)phenyl)-2-(1,3-dioxoisoindolin-2-yl)-4-methyl-*N*-(quinolin-8-yl)pentanamide (7c-(D)). Following the general procedure, **7c-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 70 : 30) as a brown coloured semi-solid (*anti* isomer, 55%, 50 mg, 0.128 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.4; IR ($CHCl_3$): 3287, 2926, 1714, 1385, 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.70 (s, 1H), 8.55 (d, J = 3.6 Hz, 1H), 8.46 (dd, J_1 = 7.5 Hz, J_2 = 1.4 Hz, 1H), 8.33 (d, J = 8.6 Hz, 1H), 8.28 (d, J = 8.4 Hz, 1H), 8.06 (d, J = 7.0 Hz, 1H), 8.00 (d, J = 8.0 Hz, 1H), 7.90 (dd, J_1 = 5.4 Hz, J_2 = 3.1 Hz, 2H), 7.74 (dd, J_1 = 5.5 Hz, J_2 = 3.1 Hz, 2H), 7.54 (t, J = 8.2 Hz, 1H), 7.39–7.33 (m, 2H), 7.30 (dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz, 1H) 7.21–7.18 (m, 1H), 7.14–7.08 (m, 5H), 6.93 (s, 1H), 5.42 (d, J = 12.3 Hz, 1H), 4.00 (dd, J_1 = 12.3 Hz, J_2 = 3.4 Hz, 1H), 2.77 (s, 6H), 1.83–1.77 (m, 1H), 0.45 (d, J = 6.4 Hz, 3H), 0.34 (d, J = 6.4 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.4, 165.9,

151.9, 148.0, 138.2, 137.7, 136.5, 135.8, 134.3, 133.8, 133.5, 131.7, 130.7, 130.6, 129.6, 129.4, 129.3, 128.6, 127.5, 126.9, 123.7, 122.9, 121.8, 121.5, 121.2, 118.2, 116.7, 115.1, 57.4, 48.1, 45.2, 28.8, 21.1, 15.8; $(\alpha)_D^{25}$ = +30.00 (c = 0.02 g per 100 mL, $CHCl_3$); HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{41}H_{38}N_5O_5S$: 712.2594; found: 712.2590.

(2*R,3*S**)-3-(4-((5-(Dimethylamino)naphthalene)-1-sulfonamido) phenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)pentanamide (8a-(DL)).** Following the general procedure, **8a-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 60 : 40) as a brown coloured semi-solid (*anti* isomer, 84%, 88 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.50; IR (DCM): 3284, 2925, 1712, 1383, 724 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.82 (s, 1H), 8.50–8.49 (m, 1H), 8.41 (dd, J_1 = 7.2 Hz, J_2 = 1.2 Hz, 1H), 8.27–8.23 (m, 2H), 7.91 (d, J = 7.2 Hz, 2H), 7.80 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2H), 7.64 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2H), 7.37 (t, J = 8.2 Hz, 1H), 7.31–7.25 (m, 2H), 7.18–7.14 (m, 4H), 7.07 (t, J = 8.1 Hz, 1H), 7.00 (d, J = 7.5 Hz, 1H), 6.84 (d, J = 8.3 Hz, 2H), 5.13 (d, J = 11.6 Hz, 1H), 3.87 (td, J_1 = 11.4 Hz, J_2 = 3.3 Hz, 1H), 2.73 (s, 6H), 1.60–1.52 (m, 1H), 1.39–1.29 (m, 1H), 0.45 (t, J = 7.3 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 168.2, 165.6, 148.1, 138.2, 137.0, 135.8, 135.7, 134.3, 134.2, 133.8, 131.6, 130.6, 130.1, 129.5, 129.4, 128.4, 127.6, 126.9, 123.7, 122.9, 122.0, 121.8, 121.5, 118.6, 116.6, 115.1, 60.5, 45.3, 44.8, 26.2, 10.9. The enantiomeric ratio of compound **8a-(DL)** was determined using the Daicel Chiralpak IA column, hexane/i-PrOH 50 : 50, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 21.37 min, t_D = 34.31 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{40}H_{36}N_5O_5S$: 698.2437; found: 698.2436.

(2*S*,3*R*)-3-(4-((5-(Dimethylamino)naphthalene)-1-sulfonamido) phenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)pentanamide (8a-(L)). Following the general procedure, **8a-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 60 : 40) as a brown coloured semi-solid (*anti* isomer, 75%, 79 mg, 0.15 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.5; IR ($CHCl_3$): 3283, 2929, 1712, 1383, 748 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.90 (s, 1H), 8.55 (dd, J_1 = 4.2 Hz, J_2 = 1.5 Hz, 1H), 8.47 (dd, J_1 = 7.3 Hz, J_2 = 1.6 Hz, 1H), 8.34–8.31 (m, 2H), 8.02 (d, J = 7.3 Hz, 1H), 7.96 (dd, J_1 = 8.3 Hz, J_2 = 1.3 Hz, 1H), 7.87 (dd, J_1 = 5.5 Hz, J_2 = 3.1 Hz, 2H), 7.69 (dd, J_1 = 5.5 Hz, J_2 = 3.0 Hz, 2H), 7.59 (s, 1H) 7.45–7.41 (m, 1H), 7.37–7.30 (m, 2H), 7.22 (d, J = 8.4 Hz, 2H), 7.20–7.13 (m, 2H), 7.05 (d, J = 7.6 Hz, 1H), 6.95 (d, J = 8.4 Hz, 2H), 5.23 (d, J = 11.6 Hz, 1H), 3.95 (td, J_1 = 11.6 Hz, J_2 = 3.5 Hz, 1H), 2.79 (s, 6H), 1.66–1.59 (m, 1H), 1.45–1.37 (m, 1H), 0.52 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.2, 165.7, 151.7, 148.1, 138.1, 136.7, 135.8, 135.7, 134.2, 134.2, 133.7, 131.5, 130.5, 129.9, 129.5, 129.5, 129.3, 128.4, 127.5, 126.8, 123.6, 122.8, 121.8, 121.7, 121.5, 118.5, 116.6, 115.0, 60.4, 45.2, 45.2, 44.7, 26.2, 10.9; $(\alpha)_D^{25}$ = +14.00 (c = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er >98 : 2) of compound **8a-(L)** was determined using the Daicel Chiralpak IA column, hexane/i-PrOH 50 : 50, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 20.22 min, t_D = 30.58 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{40}H_{36}N_5O_5S$: 698.2437; found: 698.2429.

(2*R*,3*S*)-3-(4-((5-(Dimethylamino)naphthalene)-1-sulfonamido) phenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)pentanamide (8a-(D)). Following the general procedure, **8a-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 60 : 40) as a brown coloured semi-solid (*anti* isomer, 82%, 57 mg, 0.1 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.5; IR ($CHCl_3$): 3280, 2927, 1713, 1387, 755 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.91 (s, 1H), 8.62 (d, J = 2.8 Hz, 1H), 8.49 (dd, J_1 = 7.4 Hz, J_2 = 1.2 Hz, 1H), 8.36 (d, J = 8.1 Hz, 1H), 8.29 (d, J = 8.6 Hz, 1H), 8.06–8.04 (m, 1H), 7.97 (d, J = 7.2 Hz, 1H), 7.89 (dd, J_1 = 5.4 Hz, J_2 = 3.1 Hz, 2H), 7.74 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2H), 7.49 (t, J = 8.3 Hz, 1H), 7.43–7.36 (m, 2H), 7.31 (dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz, 1H), 7.24 (d, J = 8.4 Hz, 2H), 7.17–7.11 (m, 2H), 6.88 (d, J = 8.3 Hz, 2H), 6.83 (s, 1H), 5.20 (d, J = 11.6 Hz, 1H), 3.96 (td, J_1 = 10.9 Hz, J_2 = 3.6 Hz, 1H), 2.84 (s, 6H), 1.65–1.39 (m, 2H), 0.54 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.2, 165.6, 148.2, 138.3, 137.3, 135.9, 135.5, 134.3, 134.1, 133.9, 131.6, 130.6, 130.2, 129.5, 129.4, 128.5, 127.6, 127.0, 123.7, 123.0, 122.3, 121.8, 121.5, 116.7, 115.2, 60.6, 45.4, 44.8, 26.1, 11.0; $(\alpha)_D^{25}$ = −12.00 (c = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er 95 : 5) of compound **8a-(D)** was determined using the Daicel Chiralpak IA column, hexane/i-PrOH 50 : 50, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 21.35 min, t_D = 33.59 min; HRMS (ESI): m/z $(M)^+$ calcd for $C_{40}H_{35}N_5O_5S$: 697.2359; found: 697.2350.

(2*R,3*S**)-3-(4-((5-(Dimethylamino)naphthalene)-1-sulfonamido)-3-methylphenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)pentanamide (8b-(DL)).** Following the general procedure, **8b-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 60 : 40) as a brown coloured semi-solid (*anti* isomer, 80%, 86 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.50; IR (DCM): 3291, 2926, 1711, 1380, 727 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.90 (s, 1H), 8.67–8.66 (m, 1H), 8.51 (d, J = 7.2 Hz, 1H), 8.38 (d, J = 8.4 Hz, 1H), 8.26 (d, J = 8.6 Hz, 1H), 8.07 (d, J = 8.2 Hz, 1H), 7.90–7.87 (m, 3H), 7.74 (dd, J_1 = 5.1 Hz, J_2 = 3.0 Hz, 2H), 7.46–7.35 (m, 4H), 7.17–7.08 (m, 4H), 7.02 (d, J = 8.1 Hz, 1H), 6.39 (s, 1H), 5.20 (d, J = 11.6 Hz, 1H), 3.96 (td, J_1 = 11.2 Hz, J_2 = 3.0 Hz, 1H), 2.83 (s, 6H), 1.86 (s, 3H), 1.68–1.63 (m, 1H), 1.50–1.44 (m, 1H), 0.60 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 168.2, 165.8, 151.8, 148.1, 138.3, 137.8, 135.9, 134.6, 134.2, 133.9, 133.7, 131.9, 131.6, 130.8, 130.6, 130.0, 129.6, 129.5, 128.3, 127.6, 127.1, 127.0, 124.2, 123.6, 122.9, 121.8, 121.5, 118.6, 116.6, 115.1, 60.6, 45.3, 44.9, 26.0, 17.6, 11.1. The enantiomeric ratio of compound **8b-(DL)** was determined using the Daicel Chiralpak ADH column, hexane/i-PrOH 80 : 20, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 77.64 min, t_L = 108.81 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{41}H_{38}N_5O_5S$: 712.2594; found: 712.2589.

(2*S*,3*R*)-3-(4-((5-(Dimethylamino)naphthalene)-1-sulfonamido)-3-methylphenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl) pentanamide (8b-(L)). Following the general procedure, **8b-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 60 : 40) as a brown coloured semi-solid (*anti* isomer, 82%, 58 mg, 0.1 mmol scale); R_f (EtOAc/

hexanes = 50 : 50) 0.5; IR ($CHCl_3$): 3294, 2927, 1713, 1382, 751 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.90 (s, 1H), 8.65 (d, J = 3.2 Hz, 1H), 8.50 (d, J = 7.1 Hz, 1H), 8.37 (d, J = 8.4 Hz, 1H), 8.28 (d, J = 8.4 Hz, 1H), 8.04 (d, J = 8.0 Hz, 1H), 7.89–7.87 (m, 3H), 7.73–7.71 (m, 2H), 7.44–7.37 (m, 3H), 7.34 (dd, J_1 = 8.0 Hz, J_2 = 4.2 Hz, 1H), 7.17–7.02 (m, 5H), 6.62 (s, 1H), 5.22 (d, J = 11.6 Hz, 1H), 3.96 (dd, J_1 = 11.9 Hz, J_2 = 3.9 Hz, 1H), 2.82 (s, 6H), 1.86 (s, 3H), 1.67–1.63 (m, 1H), 1.48–1.43 (m, 1H), 0.59 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.2, 165.8, 151.8, 148.1, 138.3, 137.8, 135.9, 134.6, 134.3, 134.2, 133.8, 133.7, 131.9, 131.6, 130.7, 130.6, 129.9, 129.6, 129.5, 128.3, 127.6, 127.0, 127.0, 127.0, 124.2, 123.6, 122.8, 121.8, 121.5, 118.6, 116.6, 115.0, 60.6, 45.3, 44.8, 26.0, 17.6, 11.1; $(\alpha)_D^{25}$ = −5.00 (c = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er 98 : 2) of compound **8b-(L)** was determined using the Daicel Chiralpak ADH column, hexane/i-PrOH 80 : 20, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 84.25 min, t_L = 114.02 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{41}H_{38}N_5O_5S$: 712.2594; found: 712.2595.

(2*R*,3*S*)-3-(4-((5-(Dimethylamino)naphthalene)-1-sulfonamido)-3-methylphenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)pentanamide (8b-(D)). Following the general procedure, **8b-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 60 : 40) as a brown coloured semi-solid (*anti* isomer, 78%, 55 mg, 0.1 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.5; IR ($CHCl_3$): 3291, 2930, 1712, 1383, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.91 (s, 1H), 8.65 (d, J = 2.8 Hz, 1H), 8.50 (d, J = 7.0 Hz, 1H), 8.37 (d, J = 8.4 Hz, 1H), 8.28 (d, J = 8.4 Hz, 1H), 8.05 (d, J = 7.9 Hz, 1H), 7.89–7.87 (m, 3H), 7.72 (dd, J_1 = 5.7 Hz, J_2 = 3.0 Hz, 2H), 7.45–7.37 (m, 3H), 7.34 (dd, J_1 = 7.7 Hz, J_2 = 3.8 Hz, 1H), 7.17–7.02 (m, 5H), 6.59 (s, 1H), 5.21 (d, J = 11.6 Hz, 1H), 3.96 (td, J_1 = 11.2 Hz, J_2 = 3.0 Hz, 1H), 2.82 (s, 6H), 1.86 (s, 3H), 1.68–1.62 (m, 1H), 1.48–1.43 (m, 1H), 0.59 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.2, 165.8, 151.8, 148.1, 138.3, 137.8, 135.9, 134.6, 134.2, 133.9, 133.7, 131.9, 131.6, 130.8, 130.6, 130.0, 129.6, 129.5, 128.3, 127.6, 127.1, 127.0, 124.2, 123.6, 122.9, 121.8, 121.5, 118.6, 116.7, 115.0, 60.6, 45.3, 44.9, 26.0, 17.6, 11.1; $(\alpha)_D^{25}$ = +3.66 (c = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er >90 : 10) of compound **8b-(D)** was determined using the Daicel Chiralpak ADH column, hexane/i-PrOH 80 : 20, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 80.49 min, t_L = 110.09 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{41}H_{38}N_5O_5S$: 712.2594; found: 712.2609.

(2*R,3*S**)-3-(3-((5-(Dimethylamino)naphthalene)-1-sulfonamido) phenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)pentanamide (8c-(DL)).** Following the general procedure, **8c-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 60 : 40) as a brown coloured semi-solid (*anti* isomer, 83%, 87 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.50; IR (DCM): 3285, 2924, 1712, 1383, 722 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.63 (s, 1H), 8.49–8.48 (m, 2H), 8.35 (dd, J_1 = 8.3 Hz, J_2 = 2.5 Hz, 1H), 8.28 (d, J = 8.6 Hz, 1H), 8.11–8.08 (m, 1H), 8.00–7.98 (m, 1H), 7.90 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2H), 7.74 (dd, J_1 = 5.3 Hz, J_2 = 3.1 Hz, 2H), 7.57–7.52 (m, 1H), 7.39–7.32 (m, 2H), 7.29–7.20 (m, 2H), 7.10–6.97 (m, 6H), 5.18 (dd, J_1 = 11.6 Hz, J_2 = 2.1 Hz, 1H), 3.84 (td, J_1 = 11.4 Hz, J_2 = 3.4 Hz, 1H), 2.75 (s, 6H), 1.59–1.50 (m, 1H), 1.30–1.19 (m, 1H), 0.30 (t, J = 7.3 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 168.2, 165.6, 151.8, 148.0, 141.4, 138.1, 137.2, 135.6, 134.2, 133.7, 133.4, 131.6, 130.6, 129.8, 129.5, 129.4, 128.6, 127.5, 126.8, 125.9, 123.6, 122.8, 121.7, 121.4, 121.0, 120.7, 118.3, 116.5, 115.1, 60.0, 45.3, 45.2, 26.3, 10.8. The enantiomeric ratio of compound **8c-(DL)** was determined using the Daicel Chiralpak IA column, hexane/i-PrOH 50 : 50, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 22.30 min, t_D = 30.63 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{40}H_{36}N_5O_5S$: 698.2437; found: 698.2432.

(2*S*,3*R*)-3-(3-((5-(Dimethylamino)naphthalene)-1-sulfonamido) phenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)pentanamide (8c-(L)). Following the general procedure, **8c-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 60 : 40) as a brown coloured semi-solid (*anti* isomer, 76%, 80 mg, 0.15 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.5; IR ($CHCl_3$): 3285, 2926, 1715, 1386, 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.64 (s, 1H), 8.48–8.46 (m, 2H), 8.38 (d, J = 8.5 Hz, 1H), 8.27 (d, J = 8.6 Hz, 1H), 8.12 (d, J = 7.2 Hz, 1H), 7.95 (d, J = 8.0 Hz, 1H), 7.89 (dd, J_1 = 5.2 Hz, J_2 = 3.1 Hz, 2H), 7.73 (dd, J_1 = 5.2 Hz, J_2 = 3.1 Hz, 2H), 7.51 (t, J = 8.1 Hz, 1H), 7.41 (s, 1H), 7.36–7.31 (m, 2H), 7.25–7.21 (m, 2H), 7.07–7.02 (m, 4H), 6.99–6.97 (m, 1H), 5.21 (d, J = 11.6 Hz, 1H), 3.85 (td, J_1 = 12.1 Hz, J_2 = 3.2 Hz, 1H), 2.73 (s, 6H), 1.59–1.50 (m, 1H), 0.89–0.81 (m, 1H), 0.30 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.2, 165.6, 151.9, 148.0, 141.5, 138.1, 137.2, 135.7, 134.3, 133.7, 133.4, 131.6, 130.7, 129.8, 129.6, 129.4, 128.6, 127.5, 126.9, 125.9, 123.7, 122.9, 121.8, 121.5, 121.2, 120.8, 118.2, 116.6, 115.1, 60.1, 45.2, 45.2, 26.3, 10.8; $(\alpha)_D^{25}$ = −10.00 (c = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er 98 : 2) of compound **8c-(L)** was determined using the Daicel Chiralpak IA column, hexane/i-PrOH 50 : 50, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 22.37 min, t_D = 28.99 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{40}H_{36}N_5O_5S$: 698.2437; found: 698.2445.

(2*R*,3*S*)-3-(3-((5-(Dimethylamino)naphthalene)-1-sulfonamido) phenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)pentanamide (8c-(D)). Following the general procedure, **8c-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 60 : 40) as a brown coloured semi-solid (*anti* isomer, 72%, 75 mg, 0.15 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.5; IR ($CHCl_3$): 3285, 2931, 1712, 1384, 752 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.64 (s, 1H), 8.49–8.47 (m, 2H), 8.35 (d, J = 8.6 Hz, 1H), 8.28 (d, J = 8.5 Hz, 1H), 8.10 (d, J = 7.3 Hz, 1H), 7.98 (dd, J_1 = 8.2 Hz, J_2 = 1.1 Hz, 1H), 7.89 (dd, J_1 = 5.3 Hz, J_2 = 3.0 Hz, 2H), 7.74 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2H), 7.54 (t, J = 8.3 Hz, 1H), 7.38–7.32 (m, 2H), 7.28–7.21 (m, 2H), 7.16 (s, 1H), 7.10–7.04 (m, 3H), 7.00–6.96 (m, 2H), 5.18 (d, J = 11.6 Hz, 1H), 3.84 (td, J_1 = 11.4 Hz, J_2 = 3.3 Hz, 1H), 2.74 (s, 6H), 1.58–1.52 (m, 1H), 1.28–1.21 (m, 1H), 0.30 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.2, 165.6, 151.9, 148.0, 141.5, 138.2, 137.2, 135.7, 134.3, 133.7, 133.4, 131.7, 130.7, 129.8, 129.6, 129.5, 128.6, 127.5, 126.9, 125.9, 123.6, 122.9, 121.8, 121.5, 121.2, 120.8, 118.3, 116.6, 115.1, 60.1, 45.3, 45.2,

26.3, 10.8; $(\alpha)_D^{25}$ = +12.00 (c = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er 98 : 2) of compound **8c-(D)** was determined using the Daicel Chiralpak IA column, hexane/i-PrOH 50 : 50, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 18.54 min, t_D = 25.39 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{40}H_{36}N_5O_5S$: 698.2437; found: 698.2442.

3-(4-((5-(Dimethylamino)naphthalene)-1-sulfonamido)-3-methylphenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)propanamide (9a-(DL)). Following the general procedure, **9a-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 80 : 20) as a brown coloured semi-solid (*anti* isomer, 68%, 70 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.30; IR (DCM): 3302, 2926, 1712, 1383, 724 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 10.17 (s, 1H), 8.62–8.60 (m, 1H), 8.50–8.49 (m, 1H), 8.39 (d, J = 8.4 Hz, 1H), 8.23 (d, J = 8.6 Hz, 1H), 8.03 (d, J = 8.2 Hz, 1H), 7.94 (d, J = 7.2 Hz, 1H), 7.73 (dd, J_1 = 5.3 Hz, J_2 = 3.2 Hz, 2H), 7.64 (dd, J_1 = 5.2 Hz, J_2 = 3.1 Hz, 2H), 7.44–7.41 (m, 3H), 7.31–7.23 (m, 2H), 7.06 (d, J = 7.5 Hz, 1H), 6.86–6.79 (m, 3H), 6.42 (s, 1H), 5.23 (dd, J_1 = 9.6 Hz, J_2 = 6.9 Hz, 1H), 3.57–3.54 (m, 2H), 2.79 (s, 6H), 1.79 (s, 3H); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 167.8, 166.2, 151.9, 148.3, 138.4, 136.2, 134.5, 134.4, 134.2, 133.7, 133.4, 131.9, 131.5, 131.4, 130.7, 130.2, 129.7, 129.5, 128.4, 127.8, 127.2, 124.0, 123.5, 123.0, 122.0, 121.6, 118.5, 116.7, 115.1, 56.0, 45.4, 34.0, 17.5. The enantiomeric ratio of compound **9a-(DL)** was determined using the Daicel Chiralpak IA column, hexane/i-PrOH 30 : 70, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 30.43 min, t_L = 40.21 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{39}H_{34}N_5O_5S$: 684.2281; found: 684.2275.

(*S*)-3-(4-((5-(Dimethylamino)naphthalene)-1-sulfonamido)-3-methylphenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)propanamide (9a-(L)). Following the general procedure, **9a-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 80 : 20) as a brown coloured semi-solid (*anti* isomer, 60%, 41 mg, 0.1 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.3; IR ($CHCl_3$): 3325, 2926, 1715, 1383, 753 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 10.25 (s, 1H), 8.70–8.68 (m, 1H), 8.58 (dd, J_1 = 4.1 Hz, J_2 = 1.4 Hz, 1H), 8.46 (d, J = 8.5 Hz, 1H), 8.30 (d, J = 8.7 Hz, 1H), 8.11 (dd, J_1 = 8.2 Hz, J_2 = 1.3 Hz, 1H), 8.02 (d, J = 7.3 Hz, 1H), 7.81 (dd, J_1 = 5.4 Hz, J_2 = 3.1 Hz, 2H), 7.72 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2H), 7.53–7.49 (m, 3H), 7.39–7.31 (m, 2H), 7.14 (d, J = 7.6 Hz, 1H), 6.94–6.86 (m, 3H), 6.43 (s, 1H), 5.30 (dd, J_1 = 9.7 Hz, J_2 = 6.9 Hz, 1H), 3.65–3.62 (m, 2H), 2.87 (s, 6H), 1.86 (s, 3H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 167.8, 166.2, 152.0, 148.3, 138.4, 136.2, 134.5, 134.4, 134.2, 133.7, 133.4, 131.8, 131.5, 131.4, 130.7, 130.2, 129.7, 129.5, 128.4, 127.8, 127.2, 124.0, 123.6, 123.0, 122.0, 121.6, 118.5, 116.7, 115.1, 56.0, 45.4, 34.0, 17.5; $(\alpha)_D^{25}$ = −65.00 (c = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er 97 : 3) of compound **9a-(L)** was determined using the Daicel Chiralpak IA column, hexane/i-PrOH 30 : 70, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 30.83 min, t_L = 38.97 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{39}H_{34}N_5O_5S$: 684.2281; found: 684.2280.

(*R*)-3-(4-((5-(Dimethylamino)naphthalene)-1-sulfonamido)-3-methylphenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)propanamide (9a-(D)). Following the general procedure, **9a-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 80 : 20) as a brown coloured semi-solid (*anti* isomer, 62%, 63 mg, 0.15 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.3; IR ($CHCl_3$): 3295, 2928, 1713, 1383, 752 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 10.24 (s, 1H), 8.69–8.67 (m, 1H), 8.57 (dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz, 1H), 8.45 (d, J = 8.5 Hz, 1H), 8.32 (d, J = 8.7 Hz, 1H), 8.09 (dd, J_1 = 8.3 Hz, J_2 = 1.6 Hz, 1H), 8.02 (dd, J_1 = 7.4 Hz, J_2 = 1.2 Hz, 1H), 7.80 (dd, J_1 = 5.6 Hz, J_2 = 3.1 Hz, 2H), 7.71 (dd, J_1 = 5.4 Hz, J_2 = 3.1 Hz, 2H), 7.51–7.47 (m, 3H), 7.37–7.31 (m, 2H), 7.13 (d, J = 7.5 Hz, 1H), 6.93–6.87 (m, 3H), 6.59 (s, 1H), 5.31 (dd, J_1 = 9.8 Hz, J_2 = 6.8 Hz, 1H), 3.65–3.62 (m, 2H), 2.86 (s, 6H), 1.86 (s, 3H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 167.8, 166.2, 151.9, 148.2, 138.3, 136.2, 134.4, 134.4, 134.2, 133.7, 133.3, 131.8, 131.5, 131.4, 130.7, 130.2, 129.7, 129.4, 128.4, 127.7, 127.2, 123.9, 123.5, 123.0, 122.0, 121.6, 118.5, 116.6, 115.1, 56.0, 45.3, 34.0, 17.5; $(\alpha)_D^{25}$ = +73.00 (c = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er 97 : 3) of compound **9a-(D)** was determined using the Daicel Chiralpak IA column, hexane/i-PrOH 30 : 70, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 28.93 min, t_L = 40.74 min; HRMS (ESI): m/z $(M + Na)^+$ calcd for $C_{39}H_{33}N_5NaO_5S$: 706.2100; found: 706.2083.

3-(3-((5-(Dimethylamino)naphthalene)-1-sulfonamido)phenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)propanamide (9b-(DL)). Following the general procedure, **9b-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 80 : 20) as a brown coloured semi-solid (*anti* isomer, 72%, 72 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.30; IR (DCM): 3279, 2924, 1712, 1383, 725 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 10.18 (s, 1H), 8.69–8.66 (m, 1H), 8.52 (dd, J_1 = 4.2 Hz, J_2 = 1.0 Hz, 1H), 8.42 (d, J = 8.5 Hz, 1H), 8.29 (d, J = 8.6 Hz, 1H), 8.10–8.06 (m, 2H), 7.81 (dd, J_1 = 5.4 Hz, J_2 = 3.2 Hz, 2H), 7.69 (dd, J_1 = 5.3 Hz, J_2 = 3.1 Hz, 2H), 7.53 (t, J = 8.2 Hz, 1H), 7.51–7.48 (m, 2H), 7.39–7.33 (m, 3H), 7.13 (d, J = 7.6 Hz, 1H), 6.96–6.95 (m, 3H), 6.76–6.74 (m, 1H), 5.30 (dd, J_1 = 9.6 Hz, J_2 = 7.0 Hz, 1H), 3.65–3.62 (m, 2H), 2.82 (s, 6H); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 167.8, 166.1, 151.9, 148.2, 138.3, 138.0, 136.9, 136.1, 134.2, 134.0, 133.6, 131.5, 130.7, 130.2, 129.7, 129.5, 129.5, 128.6, 127.7, 127.2, 125.7, 123.6, 123.1, 122.0, 121.8, 121.6, 119.5, 118.4, 116.7, 115.1, 55.8, 45.3, 29.7. The enantiomeric ratio of compound **9b-(DL)** was determined using the Daicel Chiralpak IA column, hexane/i-PrOH 50 : 50, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 23.35 min, t_L = 39.49 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{38}H_{32}N_5O_5S$: 670.2124; found: 670.2125.

(*S*)-3-(3-((5-(Dimethylamino)naphthalene)-1-sulfonamido)phenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)propanamide (9b-(L)). Following the general procedure, **9b-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 80 : 20) as a brown coloured semi-solid (*anti* isomer, 68%, 68 mg, 0.15 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.3; IR ($CHCl_3$): 3279, 2928, 1713, 1385, 751 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 10.19 (s, 1H), 8.70–8.68 (m, 1H), 8.52 (d, J = 3.7 Hz, 1H), 8.43 (d, J = 8.5 Hz, 1H), 8.33 (d, J = 8.7 Hz, 1H), 8.12–8.08 (m, 2H), 7.81 (dd, J_1 = 5.2 Hz, J_2 = 3.2 Hz, 2H), 7.69 (dd, J_1 = 5.2 Hz, J_2 = 3.2 Hz, 2H), 7.54–7.48 (m, 3H),

7.41–7.29 (m, 3H), 7.13 (d, J = 7.6 Hz, 1H), 7.00–6.96 (m, 3H), 6.79 (d, J = 6.7 Hz, 1H), 5.36–5.32 (m, 1H), 3.67–3.65 (m, 2H), 2.83 (s, 6H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 167.8, 166.1, 151.9, 148.2, 138.3, 138.0, 137.0, 136.1, 134.2, 134.1, 133.6, 131.4, 130.7, 130.1, 129.7, 129.5, 129.4, 128.5, 127.7, 127.1, 125.6, 123.5, 123.0, 122.0, 121.6, 121.6, 119.4, 118.4, 116.7, 115.1, 55.8, 45.3, 34.4; $(\alpha)_D^{25}$ = +68.00 (c = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er 97 : 3) of compound **9b-(L)** was determined using the Daicel Chiralpak IA column, hexane/i-PrOH 50 : 50, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 23.88 min, t_L = 39.49 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{38}H_{32}N_5O_5S$: 670.2124; found: 670.2122.

(*R*)-3-(3-((5-(Dimethylamino)naphthalene)-1-sulfonamido) phenyl)-2-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)propanamide (9b-(D)). Following the general procedure, **9b-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 80 : 20) as a brown coloured semi-solid (*anti* isomer, 65%, 65 mg, 0.15 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.3; IR ($CHCl_3$): 3280, 2926, 1713, 1385, 754 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 10.20 (s, 1H), 8.71–8.69 (m, 1H), 8.54 (d, J = 4.2 Hz, 1H), 8.45 (d, J = 8.5 Hz, 1H), 8.31 (d, J = 8.6 Hz, 1H), 8.12–8.08 (m, 2H), 7.83 (dd, J_1 = 5.1 Hz, J_2 = 3.2 Hz, 2H), 7.71 (dd, J_1 = 5.2 Hz, J_2 = 3.2 Hz, 2H), 7.55 (t, J = 8.2 Hz, 1H), 7.51–7.50 (m, 2H), 7.41–7.37 (m, 2H), 7.15 (d, J = 7.6 Hz, 1H), 7.01–6.97 (m, 4H), 6.78–6.76 (m, 1H), 5.32 (dd, J_1 = 9.4 Hz, J_2 = 7.1 Hz, 1H), 3.67–3.65 (m, 2H), 2.85 (s, 6H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 167.8, 166.1, 151.9, 148.2, 138.3, 138.0, 136.9, 136.1, 134.2, 134.0, 133.6, 131.5, 130.7, 130.2, 129.7, 129.5, 129.5, 128.6, 127.7, 127.2, 125.7, 123.6, 123.1, 122.0, 121.8, 121.6, 119.6, 118.4, 116.7, 115.1, 55.8, 45.3, 34.4; $(\alpha)_D^{25}$ = −70.00 (c = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er 90 : 10) of compound **9b-(D)** was determined using the Daicel Chiralpak IA column, hexane/i-PrOH 50 : 50, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 23.29 min, t_L = 40.09 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{38}H_{32}N_5O_5S$: 670.2124; found: 670.2122.

3-(4-((5-(Dimethylamino)naphthalene)-1-sulfonamido)phenyl)-5-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)pentanamide (11a). Following the general procedure, **11a** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 60 : 40) as a brown coloured semi-solid (80%, 84 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.50; IR (DCM): 2929, 1704, 1522, 1326, 723 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.51 (s, 1H), 8.63 (dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz, 1H), 8.54 (t, J = 4.5 Hz, 1H), 8.27 (d, J = 8.5 Hz, 1H), 8.20 (d, J = 8.6 Hz, 1H), 8.04 (dd, J_1 = 8.3 Hz, J_2 = 1.6 Hz, 1H), 7.95 (dd, J_1 = 7.3 Hz, J_2 = 1.0 Hz, 1H), 7.64 (dd, J_1 = 5.5 Hz, J_2 = 3.1 Hz, 2H), 7.52 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2H), 7.42–7.38 (m, 3H), 7.32 (dd, J_1 = 8.2 Hz, J_2 = 4.2 Hz, 1H), 7.15–7.11 (m, 1H), 7.02–6.96 (m, 2H), 7.01 (d, J = 8.3 Hz, 2H), 6.73 (d, J = 8.5 Hz, 2H), 3.52–3.36 (m, 2H), 3.23–3.16 (m, 1H), 2.74 (s, 6H), 2.74–2.68 (m, 1H), 2.01–1.96 (m, 1H), 2.02–1.97 (m, 2H); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 169.3, 168.2, 151.9, 148.1, 139.7, 138.1, 136.2, 135.0, 134.2, 134.1, 133.7, 131.9, 130.6, 130.0, 129.6, 129.5, 128.4, 128.2, 127.8, 127.2, 123.0, 121.9, 121.5, 121.5, 118.5, 116.4, 115.1, 45.5, 45.3, 39.7, 36.3, 33.8; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{40}H_{36}N_5O_5S$: 698.2437; found: 698.2452.

3-(4-((5-(Dimethylamino)naphthalene)-1-sulfonamido)phenyl)-6-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)hexanamide (11b). Following the general procedure, **11b** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 70 : 30) as a brown coloured semi-solid (78%, 83 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.40; IR (DCM): 2926, 1705, 1523, 1327, 722 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.51 (s, 1H), 8.65 (dd, J_1 = 4.1 Hz, J_2 = 1.4 Hz, 1H), 8.54–8.52 (m, 1H), 8.25 (d, J = 8.5 Hz, 1H), 8.20 (d, J = 8.6 Hz, 1H), 8.04 (dd, J_1 = 8.3 Hz, J_2 = 1.4 Hz, 1H), 7.92 (d, J = 7.3 Hz, 1H), 7.69 (dd, J_1 = 5.3 Hz, J_2 = 3.1 Hz, 2H), 7.59 (dd, J_1 = 5.5 Hz, J_2 = 3.1 Hz, 2H), 7.42–7.38 (m, 3H), 7.34 (dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz, 1H), 7.12 (t, J = 8.2 Hz, 1H), 7.01 (d, J = 7.5 Hz, 1H), 6.94 (d, J = 8.4 Hz, 2H), 6.89 (s, 1H), 6.73 (d, J = 8.3 Hz, 2H), 3.50 (t, J = 7.2 Hz, 2H), 3.15–3.08 (m, 1H), 2.77–2.50 (m, 2H), 2.74 (s, 6H), 1.73–1.65 (m, 1H), 1.58–1.42 (m, 2H), 1.35–1.28 (m, 1H); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 169.7, 168.3, 151.9, 148.1, 140.7, 138.1, 136.2, 134.9, 134.2, 134.2, 133.8, 132.0, 130.5, 130.1, 129.6, 129.6, 128.4, 128.2, 127.8, 127.3, 123.1, 122.9, 122.4, 121.6, 121.4, 118.5, 116.4, 115.0, 45.3, 45.2, 41.5, 37.7, 33.2, 26.4; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{41}H_{38}N_5O_5S$: 712.2594; found: 712.2615.

3-(4-((5-(Dimethylamino)naphthalene)-1-sulfonamido)phenyl)-7-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)heptanamide (11c). Following the general procedure, **11c** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 65 : 35) as a brown coloured semi-solid (84%, 92 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.40; IR (DCM): 2928, 1704, 1523, 1328, 723 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.60 (s, 1H), 8.72–8.71 (m, 1H), 8.65–8.63 (m, 1H), 8.35 (d, J = 8.6 Hz, 1H), 8.31 (d, J = 8.6 Hz, 1H), 8.10 (d, J = 8.3 Hz, 1H), 8.02 (d, J = 7.3 Hz, 1H), 7.78 (dd, J_1 = 5.4 Hz, J_2 = 3.1 Hz, 2H), 7.65 (dd, J_1 = 5.3 Hz, J_2 = 3.1 Hz, 2H), 7.47–7.44 (m, 3H), 7.38 (dd, J_1 = 8.2 Hz, J_2 = 4.2 Hz, 1H), 7.21 (t, J = 8.2 Hz, 1H), 7.13–7.07 (m, 2H), 6.99 (d, J = 8.2 Hz, 2H), 6.82 (d, J = 8.3 Hz, 2H), 3.54 (t, J = 7.3 Hz, 2H), 3.18–3.11 (m, 1H), 2.81 (s, 6H), 2.76–2.63 (m, 2H), 1.75–1.67 (m, 1H), 1.62–1.49 (m, 3H), 1.18–1.04 (m, 2H); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 169.9, 168.3, 151.8, 148.0, 140.9, 138.1, 136.2, 134.8, 134.3, 134.1, 133.8, 131.9, 130.5, 129.9, 129.6, 129.5, 129.5, 128.3, 128.1, 127.7, 127.2, 125.7, 123.0, 122.9, 122.0, 121.5, 121.4, 118.6, 116.4, 115.0, 45.3, 41.5, 37.6, 35.4, 28.2, 24.4, 19.6; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{42}H_{40}N_5O_5S$: 726.2750; found: 726.2803.

3-(4-((5-(Dimethylamino)naphthalene)-1-sulfonamido)phenyl)-8-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)octanamide (11d). Following the general procedure, **11d** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 70 : 30) as a brown coloured semi-solid (78%, 87 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.40; IR (DCM): 2930, 1706, 1524, 1328, 723 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.52 (s, 1H), 8.66 (dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz, 1H), 8.57 (dd, J_1 = 5.0 Hz, J_2 = 3.9 Hz, 1H), 8.27 (d, J = 8.5 Hz, 1H), 8.20 (d, J = 8.6 Hz, 1H), 8.05 (dd, J_1 = 8.2 Hz, J_2 = 1.5 Hz, 1H),

7.94 (dd, J_1 = 7.4 Hz, J_2 = 1.1 Hz, 1H), 7.73 (dd, J_1 = 5.4 Hz, J_2 = 3.1 Hz, 2H), 7.61 (dd, J_1 = 5.4 Hz, J_2 = 3.1 Hz, 2H), 7.42–7.39 (m, 3H), 7.34 (dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz, 1H), 7.15–7.11 (m, 1H), 7.02 (d, J = 7.6 Hz, 1H), 6.95–6.90 (m, 1H), 6.94 (d, J = 8.4 Hz, 2H), 6.74 (d, J = 8.4 Hz, 2H), 3.50 (t, J = 7.2 Hz, 2H), 3.09–3.02 (m, 1H), 2.74 (s, 6H), 2.69–2.55 (m, 2H), 1.63–1.57 (m, 1H), 1.50–1.43 (m, 3H), 1.28–1.05 (m, 4H); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 170.0, 168.4, 151.9, 148.1, 141.3, 138.1, 136.2, 134.6, 134.2, 133.8, 132.0, 130.5, 130.1, 129.6, 129.5, 128.4, 128.1, 127.8, 127.3, 123.1, 122.9, 122.2, 121.6, 121.4, 118.5, 116.4, 115.0, 45.5, 45.3, 41.8, 37.8, 35.9, 28.3, 26.8, 26.7; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{43}H_{42}N_5O_5S$: 740.2907; found: 740.2937.

3-(4-((5-(Dimethylamino)naphthalene)-1-sulfonamido)phenyl)-11-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)undecanamide (11e). Following the general procedure, **11e** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 80 : 20) as a brown coloured semi-solid (82%, 96 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.30; IR (DCM): 2923, 1708, 1526, 1397, 721 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.61 (s, 1H), 8.71 (dd, J_1 = 4.2 Hz, J_2 = 1.6 Hz, 1H), 8.65 (dd, J_1 = 5.6 Hz, J_2 = 3.4 Hz, 1H), 8.34 (d, J = 8.5 Hz, 1H), 8.33 (d, J = 8.6 Hz, 1H), 8.09 (dd, J_1 = 8.3 Hz, J_2 = 1.6 Hz, 1H), 8.05 (dd, J_1 = 7.3 Hz, J_2 = 1.0 Hz, 1H), 7.81 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2H), 7.66 (dd, J_1 = 5.5 Hz, J_2 = 3.1 Hz, 2H), 7.54 (s, 1H), 7.47–7.41 (m, 3H), 7.37 (dd, J_1 = 8.2 Hz, J_2 = 4.2 Hz, 1H), 7.21–7.17 (m, 1H), 7.06 (d, J = 7.5 Hz, 1H), 7.01 (d, J = 8.4 Hz, 2H), 6.88 (d, J = 8.4 Hz, 2H), 3.62 (t, J = 7.4 Hz, 2H), 3.17–3.10 (m, 1H), 2.80 (s, 6H), 2.76–2.63 (m, 2H), 1.68–1.55 (m, 3H), 1.52–1.48 (m, 1H), 1.31–1.11 (m, 10H); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 170.2, 168.4, 151.7, 148.0, 141.2, 138.0, 136.2, 134.7, 134.4, 134.1, 133.7, 132.0, 130.4, 129.9, 129.5, 128.2, 128.1, 127.7, 127.2, 123.0, 122.8, 121.9, 121.5, 121.4, 118.6, 116.4, 114.9, 45.4, 45.2, 41.7, 37.9, 35.9, 29.1, 29.0, 28.8, 28.4, 26.9, 26.6; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{46}H_{48}N_5O_5S$: 782.3376; found: 782.3395.

3-(4-((5-(Dimethylamino)naphthalene)-1-sulfonamido)phenyl)-12-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)dodecanamide (11f). Following the general procedure, **11f** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 80 : 20) as a brown coloured semi-solid (79%, 94 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.30; IR (DCM): 2926, 1705, 1523, 1328, 723 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.61 (s, 1H), 8.71–8.71 (m, 1H), 8.65–8.64 (m, 1H), 8.35–8.32 (m, 2H), 8.09 (d, J = 8.2 Hz, 1H), 8.05 (d, J = 7.2 Hz, 1H), 7.82–7.81 (m, 2H), 7.66 (dd, J_1 = 5.2 Hz, J_2 = 2.9 Hz, 2H), 7.53–7.42 (m, 4H), 7.38 (dd, J_1 = 8.2 Hz, J_2 = 4.2 Hz, 1H), 7.19 (t, J = 8.2 Hz, 1H), 7.07 (d, J = 7.6 Hz, 1H), 7.01 (d, J = 8.0 Hz, 2H), 6.87 (d, J = 8.0 Hz, 2H), 3.63 (t, J = 7.2 Hz, 2H), 3.17–3.12 (m, 1H), 2.81 (s, 6H), 2.76–2.63 (m, 2H), 1.68–1.49 (m, 5H), 1.25–1.22 (m, 11H); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 170.2, 168.4, 151.7, 148.0, 141.2, 138.1, 136.2, 134.7, 134.4, 134.2, 133.8, 132.0, 130.4, 129.9, 129.6, 128.2, 128.1, 127.7, 127.2, 123.1, 122.8, 121.9, 121.5, 121.4, 118.7, 116.4, 115.0, 45.5, 45.2, 41.7, 38.0, 36.0, 29.3, 29.1, 28.9, 28.5, 27.0, 26.7; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{47}H_{50}N_5O_5S$: 796.3533; found: 796.3541.

(2*R,3*S**)-Ethyl 3-(4-((5-(dimethylamino)naphthalene)-1-sulfonamido)phenyl)-2-(1,3-dioxoisoindolin-2-yl)pentanoate (12a-(DL)).** Following the general procedure, **12a-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 30 : 70) as a brown coloured semi-solid (*anti* isomer, 72%, 43 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.60; IR (DCM): 2924, 1718, 1386, 1157, 724 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.43 (d, J = 8.4 Hz, 1H), 8.28 (d, J = 8.6 Hz, 1H), 8.09 (d, J = 7.3 Hz, 1H), 7.80 (dd, J_1 = 5.4 Hz, J_2 = 3.1 Hz, 2H), 7.68 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2H), 7.49 (t, J = 8.3 Hz, 1H), 7.35 (t, J = 8.2 Hz, 1H), 7.12 (d, J = 7.5 Hz, 1H), 7.02 (d, J = 8.3 Hz, 2H), 6.82 (d, J = 8.3 Hz, 2H), 6.83–6.81 (m, 1H), 4.86 (d, J = 10.4 Hz, 1H), 3.86–3.78 (m, 2H), 3.49 (td, J_1 = 11.3 Hz, J_2 = 3.6 Hz, 1H), 2.81 (s, 6H), 1.47–1.41 (m, 1H), 1.31–1.25 (m, 1H), 0.80 (t, J = 7.1 Hz, 3H), 0.41 (t, J = 7.3 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 168.2, 167.6, 138.7, 135.0, 134.3, 134.2, 131.6, 130.7, 130.4, 129.7, 129.6, 129.2, 128.5, 123.6, 123.1, 121.8, 118.6, 115.2, 61.4, 56.9, 45.5, 45.4, 25.3, 13.7, 11.2; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{33}H_{34}N_3O_6S$: 600.2168; found: 600.2163.

(2*R,3*S**)-Ethyl 3-(4-((5-(dimethylamino)naphthalene)-1-sulfonamido)-3-methylphenyl)-2-(1,3-dioxoisoindolin-2-yl)pentanoate (12b-(DL)).** Following the general procedure, **12b-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 40 : 60) as a brown coloured semi-solid (*anti* isomer, 73%, 45 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.50; IR (DCM): 2923, 1715, 1385, 1149, 722 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.44 (d, J = 8.4 Hz, 1H), 8.29 (d, J = 8.6 Hz, 1H), 8.08 (d, J = 7.3 Hz, 1H), 7.79 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2H), 7.67 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2H), 7.45 (t, J = 8.2 Hz, 1H), 7.35 (t, J = 8.1 Hz, 1H), 7.10 (d, J = 7.6 Hz, 1H), 6.98–6.96 (m, 1H), 6.90–6.89 (m, 2H), 6.53 (s, 1H), 4.87 (d, J = 10.4 Hz, 1H), 3.88–3.79 (m, 2H), 3.47 (td, J_1 = 11.3 Hz, J_2 = 3.6 Hz, 1H), 2.80 (s, 6H), 1.91 (s, 3H), 1.47–1.39 (m, 1H), 1.32–1.24 (m, 1H), 0.82 (t, J = 7.1 Hz, 3H), 0.45 (t, J = 7.3 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 168.2, 167.6, 151.8, 139.2, 134.8, 134.3, 133.1, 131.6, 131.3, 130.8, 130.7, 130.2, 129.7, 129.6, 128.4, 126.7, 123.7, 123.6, 123.1, 118.8, 115.2, 61.3, 56.9, 45.4, 45.4, 25.2, 17.7, 13.7, 11.2. The enantiomeric ratio of compound **12b-(DL)** was determined using the Daicel Chiralpak ODH column, hexane/i-PrOH 90 : 10, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 34.90 min, t_D = 45.61 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{34}H_{36}N_3O_6S$: 614.2325; found: 614.2319.

(2*S*,3*R*)-Ethyl 3-(4-((5-(dimethylamino)naphthalene)-1-sulfonamido)-3-methylphenyl)-2-(1,3-dioxoisoindolin-2-yl)pentanoate (12b-(L)). Following the general procedure, **12b-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 40 : 60) as a brown coloured semi-solid (*anti* isomer, 78%, 48 mg, 0.1 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.5; IR ($CHCl_3$): 2921, 1717, 1379, 1161, 722 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.44 (d, J = 8.4 Hz, 1H), 8.28 (d, J = 8.6 Hz, 1H), 8.08 (d, J = 7.3 Hz, 1H), 7.80 (dd, J_1 = 5.4 Hz, J_2 = 3.1 Hz, 2H), 7.68 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2H), 7.46 (t, J = 8.4 Hz, 1H), 7.36 (t, J = 8.1 Hz, 1H), 7.10 (d, J = 7.5 Hz, 1H), 6.97–6.95 (m, 1H), 6.89 (s, 2H), 6.46 (s, 1H), 4.87

(d, J = 10.4 Hz, 1H), 3.85–3.82 (m, 2H), 3.47 (td, J_1 = 11.2 Hz, J_2 = 3.6 Hz, 1H), 2.81 (s, 6H), 1.91 (s, 3H), 1.47–1.41 (m, 1H), 1.32–1.26 (m, 1H), 0.82 (t, J = 7.1 Hz, 3H), 0.45 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.2, 167.6, 139.3, 134.8, 134.3, 133.1, 131.6, 131.3, 130.9, 130.7, 130.2, 129.7, 129.6, 128.4, 126.7, 123.7, 123.6, 123.1, 118.8, 115.2, 61.4, 56.9, 45.5, 45.4, 25.3, 17.7, 13.7, 11.3; $(\alpha)_D^{25}$ = −15.00 (c = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er >95 : 5) of compound **12b-(L)** was determined using the Daicel Chiralpak ODH column, hexane/i-PrOH 90 : 10, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_L = 35.69 min, t_D = 45.60 min; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{34}H_{36}N_3O_6S$: 614.2325; found: 614.2319.

(2*R,3*S**)-Ethyl 3-(3-((5-(dimethylamino)naphthalene)-1-sulfonamido)phenyl)-2-(1,3-dioxoisoindolin-2-yl)pentanoate (12c-(DL)).** Following the general procedure, **12c-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 35 : 65) as a brown coloured semi-solid (*anti* isomer, 75%, 45 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.60; IR (DCM): 2925, 1715, 1386, 1148, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.40 (d, J = 8.3 Hz, 1H), 8.29 (d, J = 8.6 Hz, 1H), 8.12 (d, J = 7.3 Hz, 1H), 7.81 (dd, J_1 = 5.4 Hz, J_2 = 3.1 Hz, 2H), 7.68 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2H), 7.52 (t, J = 8.3 Hz, 1H), 7.34 (t, J = 8.1 Hz, 1H), 7.11 (d, J = 7.5 Hz, 1H), 7.02 (t, J = 7.8 Hz, 1H), 6.92–6.83 (m, 3H), 6.72 (s, 1H), 4.79 (d, J = 10.4 Hz, 1H), 3.84–3.76 (m, 2H), 3.38 (td, J_1 = 11.5 Hz, J_2 = 3.6 Hz, 1H), 2.78 (s, 6H), 1.40–1.31 (m, 1H), 1.16–1.07 (m, 1H), 0.80 (t, J = 7.1 Hz, 3H), 0.21 (t, J = 7.3 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 168.1, 167.6, 142.8, 136.4, 134.3, 133.8, 131.6, 130.8, 130.6, 129.6, 129.6, 129.1, 128.6, 125.5, 123.6, 123.2, 121.6, 120.2, 118.6, 115.3, 61.4, 56.6, 45.8, 45.4, 25.2, 13.6, 11.1. The enantiomeric ratio of compound **12c-(DL)** was determined using the Daicel Chiralpak IA column, hexane/i-PrOH 50 : 50, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 12.39 min, t_L = 15.61 min; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{33}H_{34}N_3O_6S$: 600.2168; found: 600.2163.

(2*R*,3*S*)-Ethyl 3-(3-((5-(dimethylamino)naphthalene)-1-sulfonamido)phenyl)-2-(1,3-dioxoisoindolin-2-yl)pentanoate (12c-(D)). Following the general procedure, **12c-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 35 : 65) as a brown coloured semi-solid (*anti* isomer, 74%, 44 mg, 0.1 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.6; IR ($CHCl_3$): 2925, 1716, 1388, 1145, 719 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.40 (d, J = 8.1 Hz, 1H), 8.29 (d, J = 8.6 Hz, 1H), 8.11 (d, J = 7.2 Hz, 1H), 7.81 (dd, J_1 = 5.4 Hz, J_2 = 3.1 Hz, 2H), 7.69 (dd, J_1 = 5.3 Hz, J_2 = 3.0 Hz, 2H), 7.53 (t, J = 8.2 Hz, 1H), 7.34 (t, J = 8.0 Hz, 1H), 7.12 (d, J = 7.4 Hz, 1H), 7.03 (t, J = 7.8 Hz, 1H), 6.91 (d, J = 7.6 Hz, 1H), 6.83 (d, J = 8.2 Hz, 1H), 6.79 (s, 1H), 6.71 (s, 1H), 4.79 (d, J = 10.4 Hz, 1H), 3.83–3.77 (m, 2H), 3.38 (td, J_1 = 11.4 Hz, J_2 = 3.4 Hz, 1H), 2.79 (s, 6H), 1.37–1.33 (m, 1H), 1.12–1.07 (m, 1H), 0.80 (t, J = 7.1 Hz, 3H), 0.22 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.1, 167.6, 142.9, 136.4, 134.3, 134.3, 133.8, 131.6, 130.8, 130.6, 129.6, 129.6, 129.6, 129.1, 128.6, 125.6, 123.6, 123.2, 121.6, 120.3, 115.3, 61.4, 56.6, 45.8, 45.4, 25.2, 13.6, 11.1; $(\alpha)_D^{25}$ = +35.500 (c = 0.04 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er 98 : 2) of compound **12c-(D)** was determined using the Daicel Chiralpak IA column, hexane/i-PrOH 50 : 50, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 10.02 min, t_L = 13.51 min; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{33}H_{34}N_3O_6S$: 600.2168; found: 600.2172.

(2*R,3*S**)-Ethyl 3-(3-((5-(dimethylamino)naphthalene)-1-sulfonamido)phenyl)-2-(1,3-dioxoisoindolin-2-yl)-3-phenylpropanoate (12d-(DL)).** Following the general procedure, **12d-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 30 : 70) as a brown coloured semi-solid (*anti* isomer, 77%, 50 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.60; IR (DCM): 2922, 1713, 1385, 1146, 709 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.40 (d, J = 8.4 Hz, 1H), 8.26 (d, J = 8.6 Hz, 1H), 8.10 (d, J = 7.3 Hz, 1H), 7.64 (dd, J_1 = 5.2 Hz, J_2 = 3.1 Hz, 2H), 7.55 (dd, J_1 = 4.9 Hz, J_2 = 3.2 Hz, 2H), 7.47 (t, J = 8.2 Hz, 1H), 7.30 (t, J = 8.2 Hz, 1H), 7.11 (d, J = 7.4 Hz, 1H), 7.06–7.02 (m, 2H), 7.00–6.90 (m, 6H), 6.71 (d, J = 7.8 Hz, 1H), 5.44 (d, J = 11.9 Hz, 1H), 5.00 (d, J = 11.9 Hz, 1H), 3.87–3.81 (m, 2H), 2.79 (s, 6H), 0.79 (t, J = 7.0 Hz, 3H); (the signal corresponding to the NH group was not clearly located in the proton NMR); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 167.9, 167.2, 142.9, 139.8, 136.7, 134.0, 133.9, 131.2, 130.7, 130.6, 129.6, 129.5, 129.4, 128.6, 128.4, 127.8, 126.9, 124.6, 123.3, 123.2, 120.2, 119.6, 118.6, 115.3, 61.7, 54.7, 50.2, 45.4, 13.6; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{37}H_{34}N_3O_6S$: 648.2168; found: 648.2175.

(2*R,3*S**)-2-Amino-3-(4-((5-(dimethylamino)naphthalene)-1-sulfonamido)phenyl)-*N*-(quinolin-8-yl)hexanamide (13a-(DL)).** Following the general procedure, **13a-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 70 : 30) as a brown coloured semi-solid (*anti* isomer, 76%, 44 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.40; IR (DCM): 2925, 1666, 1522, 1327, 790 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 11.22 (s, 1H), 8.80–8.77 (m, 2H), 8.44 (d, J = 8.5 Hz, 1H), 8.34 (d, J = 8.6 Hz, 1H), 8.15–8.10 (m, 2H), 7.49–7.46 (m, 3H), 7.40 (dd, J_1 = 8.2 Hz, J_2 = 4.2 Hz, 1H), 7.35 (t, J = 7.9 Hz, 1H), 7.12 (d, J = 7.5 Hz, 1H), 7.06 (d, J = 8.2 Hz, 2H), 6.91 (d, J = 8.0 Hz, 2H), 3.61 (d, J = 3.3 Hz, 1H), 3.39–3.36 (m, 1H), 2.84 (s, 6H), 1.74–1.67 (m, 1H), 1.59–1.52 (m, 1H), 1.09–1.03 (m, 2H), 0.74 (t, J = 7.3 Hz, 3H); (the signal corresponding to the NH group was not clearly located in the proton NMR); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 172.2, 151.9, 148.5, 138.9, 138.4, 136.1, 135.2, 134.5, 134.1, 130.6, 130.0, 129.7, 129.6, 128.9, 128.4, 128.0, 127.2, 123.0, 121.8, 121.6, 121.5, 118.7, 116.4, 115.1, 61.8, 47.3, 45.3, 29.6, 20.5, 13.9. The enantiomeric ratio of compound **13a-(DL)** was determined using the Daicel Chiralpak ODH column, hexane/i-PrOH 50 : 50, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 11.02 min, t_L = 28.35 min; HRMS (ESI): m/z (M + H)$^+$ calcd for $C_{33}H_{36}N_5O_3S$: 582.2539; found: 582.2540.

(2*R*,3*S*)-2-Amino-3-(4-((5-(dimethylamino)naphthalene)-1-sulfonamido)phenyl)-*N*-(quinolin-8-yl)hexanamide (13a-(D)). Following the general procedure, **13a-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 70 : 30) as a brown coloured semi-solid (*anti* isomer, 74%, 43 mg, 0.1 mmol scale); R_f (EtOAc/hexanes =

50 : 50) 0.4; IR ($CHCl_3$): 2926, 1664, 1518, 1326, 751 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 11.25 (s, 1H), 8.81–8.78 (m, 2H), 8.45 (d, J = 8.5 Hz, 1H), 8.34 (d, J = 8.6 Hz, 1H), 8.16–8.12 (m, 2H), 7.51–7.47 (m, 3H), 7.41 (dd, J_1 = 8.2 Hz, J_2 = 4.3 Hz, 1H), 7.36 (t, J = 8.0 Hz, 1H), 7.13 (d, J = 7.4 Hz, 1H), 7.06 (d, J = 8.3 Hz, 2H), 6.91 (d, J = 8.2 Hz, 2H), 3.61 (d, J = 3.2 Hz, 1H), 3.40–3.38 (m, 1H), 2.84 (s, 6H), 1.75–1.68 (m, 1H), 1.57–1.52 (m, 1H), 1.08–1.05 (m, 2H), 0.74 (t, J = 7.3 Hz, 3H); (the signal corresponding to the NH group was not clearly located in the proton NMR); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 172.3, 151.9, 148.5, 138.9, 138.4, 136.2, 135.2, 134.4, 134.1, 130.6, 130.0, 129.7, 129.6, 128.9, 128.4, 128.0, 127.2, 123.0, 121.8, 121.6, 121.5, 118.6, 116.4, 115.1, 61.8, 47.3, 45.3, 29.5, 20.5, 13.9; $(\alpha)_D^{25}$ = +13.00 (c = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er 96 : 4) of compound **13a-(D)** was determined using the Daicel Chiralpak ODH column, hexane/i-PrOH 50 : 50, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 11.43 min, t_L = 28.25 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{33}H_{36}N_5O_3S$: 582.2539; found: 582. 2538.

(2*R,3*S**)-2-Amino-3-(4-((5-(dimethylamino)naphthalene)-1-sulfonamido)-3-methylphenyl)-3-phenyl-*N*-(quinolin-8-yl)propanamide (13b-(DL)).** Following the general procedure, **13b-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 70 : 30) as a brown coloured semi-solid (*anti* isomer, 78%, 49 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.40; IR (DCM): 2924, 1672, 1524, 1324, 735 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 10.71 (s, 1H), 8.70–8.69 (m, 1H), 8.58–8.56 (m, 1H), 8.35 (d, J = 8.5 Hz, 1H), 8.17 (d, J = 8.6 Hz, 1H), 8.05–8.02 (m, 1H), 7.91 (d, J = 7.3 Hz, 1H), 7.47–7.32 (m, 5H), 7.22–7.15 (m, 5H), 7.11–7.07 (m, 1H), 7.02 (d, J = 7.5 Hz, 1H), 6.92–6.84 (m, 3H), 4.46 (d, J = 7.0 Hz, 1H), 4.18 (d, J = 7.1 Hz, 1H), 2.76 (s, 6H), 1.76 (s, 3H); (the signal corresponding to the NH_2 group was not clearly located in the proton NMR); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 172.0, 151.8, 148.4, 139.9, 139.4, 138.7, 136.1, 134.7, 134.0, 133.1, 131.6, 130.7, 130.6, 130.0, 129.7, 129.5, 129.0, 128.7, 128.2, 127.9, 127.1, 126.9, 126.3, 123.8, 123.0, 121.7, 121.5, 118.6, 116.4, 115.1, 60.4, 54.5, 45.3, 17.6. The enantiomeric ratio of compound **13b-(DL)** was determined using the Daicel Chiralpak ODH column, hexane/i-PrOH 50 : 50, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 17.54 min, t_L = 25.96 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{37}H_{36}N_5O_3S$: 630.2539; found: 630.2556.

(2*S*,3*R*)-2-Amino-3-(4-((5-(dimethylamino)naphthalene)-1-sulfonamido)-3-methylphenyl)-3-phenyl-*N*-(quinolin-8-yl)propanamide (13b-(L)). Following the general procedure, **13b-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 70 : 30) as a brown coloured semi-solid (*anti* isomer, 76%, 48 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.40; IR (DCM): 2924, 1672, 1523, 1324, 734 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 10.78 (s, 1H), 8.76–8.75 (m, 1H), 8.65–8.63 (m, 1H), 8.42 (d, J = 8.5 Hz, 1H), 8.25 (d, J = 8.6 Hz, 1H), 8.09 (d, J = 8.2 Hz, 1H), 7.98 (d, J = 7.3 Hz, 1H), 7.46–7.37 (m, 5H), 7.28–7.21 (m, 5H), 7.17–7.15 (m, 1H), 7.08 (d, J = 7.4 Hz, 1H), 6.99–6.86 (m, 3H), 4.54 (d, J = 7.0 Hz, 1H), 4.25 (d, J = 7.0 Hz, 1H), 2.83 (s, 6H), 1.82 (s, 3H); (the signal corresponding to the NH_2 group was not clearly located in the proton NMR); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 172.0, 151.8, 148.4, 139.8, 139.3, 138.6, 136.1, 134.7, 134.0, 133.1, 131.7, 130.7, 130.5, 129.9, 129.6, 129.5, 128.9, 128.6, 128.2, 127.8, 127.1, 126.9, 126.3, 123.8, 123.0, 121.7, 121.5, 118.6, 116.4, 115.0, 60.3, 54.5, 45.3, 17.6; $(\alpha)_D^{25}$ = −12.00 (c = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er 96 : 4) of compound **13b-(L)** was determined using the Daicel Chiralpak ODH column, hexane/i-PrOH 50 : 50, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 17.95 min, t_L = 25.51 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{37}H_{36}N_5O_3S$: 630.2539; found: 630.2546.

(2*R,3*S**)-2-Amino-3-(3-((5-(dimethylamino)naphthalene)-1-sulfonamido)phenyl)-*N*-(quinolin-8-yl)pentanamide (13c-(DL)).** Following the general procedure, **13c-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 65 : 35) as a brown coloured semi-solid (*anti* isomer, 76%, 43 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.40; IR (DCM): 2925, 1664, 1524, 1323, 736 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 11.21 (s, 1H), 8.76–8.75 (m, 1H), 8.72 (dd, J_1 = 6.3 Hz, J_2 = 2.4 Hz, 1H), 8.37 (d, J = 8.4 Hz, 1H), 8.29 (d, J = 8.5 Hz, 1H), 8.10 (d, J = 7.2 Hz, 1H), 8.05 (d, J = 8.2 Hz, 1H), 7.46–7.41 (m, 3H), 7.34 (dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz, 1H), 7.30 (t, J = 8.2 Hz, 1H), 7.05 (d, J = 7.5 Hz, 1H), 6.99 (t, J = 7.8 Hz, 1H), 6.89–6.84 (m, 2H), 6.76 (s, 1H), 3.37 (d, J = 3.5 Hz, 1H), 3.18–3.14 (m, 1H), 2.75 (s, 6H), 1.54–1.44 (m, 2H), 0.46 (t, J = 7.2 Hz, 3H); (the signal corresponding to the NH group and NH_2 was not clearly located in the proton NMR); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 172.4, 151.9, 148.5, 142.8, 138.9, 136.8, 136.2, 134.1, 134.0, 130.7, 130.4, 129.6, 129.6, 129.3, 128.5, 128.0, 127.2, 125.5, 123.0, 121.8, 121.5, 121.2, 120.2, 118.5, 116.4, 115.2, 61.7, 49.5, 45.3, 20.0, 12.0. The enantiomeric ratio of compound **13c-(DL)** was determined using the Daicel Chiralpak ADH column, hexane/i-PrOH 50 : 50, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 18.98 min, t_L = 30.87 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{32}H_{34}N_5O_3S$: 568.2382; found: 568.2386.

(2*R*,3*S*)-2-Amino-3-(3-((5-(dimethylamino)naphthalene)-1-sulfonamido)phenyl)-*N*-(quinolin-8-yl)pentanamide (13c-(D)). Following the general procedure, **13c-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 65 : 35) as a brown coloured semi-solid (*anti* isomer, 74%, 42 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.40; IR (DCM): 2923, 1674, 1525, 1323, 736 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 11.26 (s, 1H), 8.83–8.82 (m, 1H), 8.79 (dd, J_1 = 6.2 Hz, J_2 = 2.4 Hz, 1H), 8.45 (d, J = 8.5 Hz, 1H), 8.37 (d, J = 8.5 Hz, 1H), 8.18 (d, J = 7.2 Hz, 1H), 8.12 (d, J = 8.2 Hz, 1H), 7.53–7.48 (m, 3H), 7.42 (dd, J_1 = 8.3 Hz, J_2 = 4.2 Hz, 1H), 7.38 (t, J = 8.2 Hz, 1H), 7.13 (d, J = 7.6 Hz, 1H), 7.07 (t, J = 7.8 Hz, 1H), 6.96–6.92 (m, 2H), 6.84 (s, 1H), 3.45 (d, J = 3.2 Hz, 1H), 3.25–3.20 (m, 1H), 2.82 (s, 6H), 1.62–1.54 (m, 2H), 0.54 (t, J = 7.2 Hz, 3H); (the signal corresponding to the NH group and NH_2 was not clearly located in the proton NMR); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 172.4, 151.9, 148.5, 142.8, 138.9, 136.8, 136.1, 134.1, 134.0, 130.7, 130.4, 129.6, 129.6, 129.3, 128.5, 128.0, 127.2, 125.5, 123.0, 121.8, 121.5, 121.1, 120.1, 118.6, 116.4, 115.2, 61.7, 49.5, 45.3, 20.0, 12.0; $(\alpha)_D^{25}$ = +17.00

(c = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er >95 : 5) of compound **13c-(D)** was determined using the Daicel Chiralpak ADH column, hexane/i-PrOH 50 : 50, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 18.77 min, t_L = 30.50 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{32}H_{34}N_5O_3S$: 568.2382; found: 568.2390.

(2*R,3*S**)-Ethyl 2-amino-3-(4-((5-(dimethylamino)naphthalene)-1-sulfonamido)-3-methylphenyl)pentanoate (14a-(DL)).** Following the general procedure, **14a-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 70 : 30) as a brown coloured semi-solid (*anti* isomer, 88%, 26 mg, 0.061 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.40; IR (DCM): 2929, 1726, 1323, 1149, 733 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.42 (d, J = 8.5 Hz, 1H), 8.27 (d, J = 8.6 Hz, 1H), 8.07 (d, J = 7.2 Hz, 1H), 7.43 (t, J = 8.2 Hz, 1H), 7.34 (t, J = 8.0 Hz, 1H), 7.08 (d, J = 7.5 Hz, 1H), 6.95–6.92 (m, 1H), 6.75–6.67 (m, 2H), 3.87–3.82 (m, 2H), 3.37 (d, J = 6.2 Hz, 1H), 2.79 (s, 6H), 2.60–2.54 (m, 1H), 1.88 (s, 3H), 1.76–1.66 (m, 1H), 1.58–1.49 (m, 1H), 0.92 (t, J = 7.1 Hz, 3H), 0.61 (t, J = 7.3 Hz, 3H); (the signal corresponding to the NH group and NH_2 was not clearly located in the proton NMR); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 174.5, 151.8, 138.6, 135.0, 133.2, 131.4, 130.8, 130.6, 130.0, 129.7, 129.6, 128.2, 126.5, 123.7, 123.0, 118.7, 115.1, 60.5, 59.6, 51.3, 45.3, 23.0, 17.6, 13.8, 12.0. The enantiomeric ratio of compound **14a-(DL)** was determined using the Daicel Chiralpak IC column, hexane/i-PrOH 30 : 70, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 10.33 min, t_L = 22.49 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{26}H_{34}N_3O_4S$: 484.2270; found: 484.2268.

(2*S*,3*R*)-Ethyl 2-amino-3-(4-((5-(dimethylamino)naphthalene)-1-sulfonamido)-3-methylphenyl)pentanoate (14a-(L)). Following the general procedure, **14a-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 70 : 30) as a brown coloured semi-solid (*anti* isomer, 89%, 27 mg, 0.063 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.4; IR ($CHCl_3$): 2925, 1732, 1327, 1147, 736 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.44 (d, J = 8.4 Hz, 1H), 8.25 (d, J = 8.6 Hz, 1H), 8.08 (d, J = 7.3 Hz, 1H), 7.45 (t, J = 8.2 Hz, 1H), 7.36 (t, J = 8.2 Hz, 1H), 7.09 (d, J = 7.5 Hz, 1H), 6.94–6.92 (m, 1H), 6.77 (s, 2H), 3.87 (q, J = 7.1 Hz, 2H), 3.41 (d, J = 6.2 Hz, 1H), 2.80 (s, 6H), 2.61–2.59 (m, 1H), 1.89 (s, 3H), 1.75–1.69 (m, 1H), 1.57–1.52 (m, 1H), 0.94 (t, J = 7.1 Hz, 3H), 0.62 (t, J = 7.3 Hz, 3H); (the signal corresponding to the NH group and NH_2 was not clearly located in the proton NMR); $^3C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 174.3, 152.0, 138.5, 134.9, 133.3, 131.1, 130.9, 130.7, 130.1, 129.8, 129.6, 128.4, 126.7, 123.6, 123.1, 118.7, 115.2, 60.6, 59.6, 51.2, 45.4, 23.2, 17.7, 13.9, 12.0; $(\alpha)_D^{25}$ = −12.00 (c = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er >90 : 10) of compound **14a-(L)** was determined using the Daicel Chiralpak IC column, hexane/i-PrOH 30 : 70, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 10.90 min, t_L = 22.51 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{26}H_{34}N_3O_4S$: 484.2270; found: 484.2265.

(2*R,3*S**)-Ethyl 2-amino-3-(3-((5-(dimethylamino)naphthalene)-1-sulfonamido)phenyl)pentanoate (14b-(DL)).** Following the general procedure, **14b-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 80 : 20) as a brown coloured semi-solid (*anti* isomer, 85%, 40 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.30; IR (DCM): 2928, 1729, 1318, 1148, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.39 (d, J = 8.5 Hz, 1H), 8.28 (d, J = 8.6 Hz, 1H), 8.09 (d, J = 7.4 Hz, 1H), 7.47 (t, J = 8.3 Hz, 1H), 7.33 (t, J = 8.2 Hz, 1H), 7.08 (d, J = 7.5 Hz, 1H), 6.97 (t, J = 7.8 Hz, 1H), 6.80–6.75 (m, 2H), 6.67 (s, 1H), 3.83 (q, J = 7.1 Hz, 2H), 3.30 (d, J = 6.1 Hz, 1H), 2.77 (s, 6H), 2.55–2.50 (m, 1H), 1.69–1.59 (m, 1H), 1.44–1.33 (m, 1H), 0.91 (t, J = 7.1 Hz, 3H), 0.44 (t, J = 7.3 Hz, 3H); (the signal corresponding to the NH group and NH_2 was not clearly located in the proton NMR); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 174.4, 152.0, 142.1, 136.5, 134.0, 130.7, 130.4, 129.7, 129.6, 129.0, 128.5, 125.4, 123.0, 121.4, 120.0, 118.5, 115.1, 60.6, 59.5, 51.6, 45.3, 23.0, 13.9, 11.8. The enantiomeric ratio of compound **14b-(DL)** was determined using the Daicel Chiralpak ODH column, hexane/i-PrOH 96 : 04, flow rate 0.5 mL min^{-1}, UV detection at 254 nm, t_L = 172.34 min, t_D = 193.02 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{25}H_{32}N_3O_4S$: 470.2113; found: 470.2108.

(2*R*,3*S*)-Ethyl 2-amino-3-(3-((5-(dimethylamino)naphthalene)-1-sulfonamido)phenyl)pentanoate (14b-(D)). Following the general procedure, **14b-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 80 : 20) as a brown coloured semi-solid (*anti* isomer, 86%, 23 mg, 0.057 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.3; IR ($CHCl_3$): 2923, 1730, 1325, 1143, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.39 (d, J = 8.5 Hz, 1H), 8.26 (d, J = 8.6 Hz, 1H), 8.08 (d, J = 7.3 Hz, 1H), 7.49 (t, J = 8.2 Hz, 1H), 7.33 (t, J = 8.1 Hz, 1H), 7.09 (d, J = 7.5 Hz, 1H), 6.97 (t, J = 7.8 Hz, 1H), 6.80–6.76 (m, 2H), 6.66 (s, 1H), 3.84 (q, J = 7.1 Hz, 2H), 3.30 (d, J = 6.0 Hz, 1H), 2.78 (s, 6H), 2.54–2.51 (m, 1H), 1.67–1.61 (m, 1H), 1.42–1.35 (m, 1H), 0.92 (t, J = 7.1 Hz, 3H), 0.45 (t, J = 7.3 Hz, 3H); (the signal corresponding to the NH group and NH_2 was not clearly located in the proton NMR); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 174.4, 152.0, 142.2, 136.4, 133.9, 130.7, 130.5, 129.7, 129.6, 129.0, 128.5, 125.6, 123.0, 121.6, 120.2, 118.5, 115.2, 60.6, 59.5, 51.6, 45.3, 23.0, 13.9, 11.9; $(\alpha)_D^{25}$ = +32.50 (c = 0.04 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er 98 : 2) of compound **14b-(D)** was determined using the Daicel Chiralpak ODH column, hexane/i-PrOH 96 : 04, flow rate 0.5 mL min^{-1}, UV detection at 254 nm, t_L = 172.47 min, t_D = 188.82 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{25}H_{32}N_3O_4S$: 470.2113; found: 470.2108.

(2*R,3*S**)-Ethyl 3-(4-((5-(dimethylamino)naphthalene)-1-sulfonamido)phenyl)-2-(1,3-dioxoisoindolin-2-yl)hexanoate (16a-(DL)).** Following the general procedure, **16a-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a brown coloured semi-solid (*anti* isomer, 71%, 65 mg, 0.15 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.60; IR (DCM): 3276, 2929, 1712, 1383, 725 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.49 (d, J = 8.5 Hz, 1H), 8.36 (d, J = 8.6 Hz, 1H), 8.19 (dd, J_1 = 7.3 Hz, J_2 = 1.1 Hz, 1H), 7.88 (dd, J_1 = 5.5 Hz, J_2 = 3.1 Hz, 2H), 7.75 (dd, J_1 = 5.4 Hz, J_2 = 3.0 Hz, 2H), 7.56–7.52 (m, 1H), 7.44–7.40 (m, 1H), 7.18–7.16 (m, 2H), 7.09 (d, J = 8.5 Hz, 2H), 6.91 (d, J = 8.5 Hz, 2H), 4.91 (d, J = 10.4 Hz,

1H), 3.91–3.83 (m, 2H), 3.70–3.64 (m, 1H), 2.86 (s, 6H), 1.39–1.34 (m, 2H), 0.89–0.79 (m, 2H), 0.85 (t, J = 7.2 Hz, 3H), 0.65 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 168.2, 167.7, 151.9, 138.7, 135.0, 134.3, 134.2, 131.5, 130.7, 130.3, 129.7, 129.6, 129.1, 128.5, 123.7, 123.0, 121.4, 118.5, 115.1, 61.4, 57.0, 45.3, 43.5, 34.2, 19.7, 13.6, 13.6. The enantiomeric ratio of compound **16a-(DL)** was determined using the Daicel Chiralpak AD column, hexane/i-PrOH 35 : 15, flow rate 0.5 mL min^{-1}, UV detection at 254 nm, t_L = 79.31 min, t_D = 110.84 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{34}H_{36}N_3O_6S$: 614.2325; found: 614.2324.

(2*S*,3*R*)-Ethyl 3-(4-((5-(dimethylamino)naphthalene)-1-sulfonamido)phenyl)-2-(1,3-dioxoisoindolin-2-yl)hexanoate (16a-(L)). Following the general procedure, **16a-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a brown coloured semi-solid (*anti* isomer, 68%, 42 mg, 0.1 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.6; IR ($CHCl_3$): 3278, 2931, 1712, 1386, 754 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.49 (d, J = 8.5 Hz, 1H), 8.34 (d, J = 8.6 Hz, 1H), 8.18 (dd, J_1 = 7.3 Hz, J_2 = 1.0 Hz, 1H), 7.88 (dd, J_1 = 5.4 Hz, J_2 = 3.1 Hz, 2H), 7.76 (dd, J_1 = 5.5 Hz, J_2 = 3.0 Hz, 2H), 7.57–7.53 (m, 1H), 7.44–7.40 (m, 1H), 7.17 (d, J = 7.6 Hz, 1H), 7.09 (d, J = 8.4 Hz, 2H), 7.02 (s, 1H), 6.90 (d, J = 8.4 Hz, 2H), 4.91 (d, J = 10.4 Hz, 1H), 3.92–3.83 (m, 2H), 3.70–3.64 (m, 1H), 2.87 (s, 6H), 1.39–1.34 (m, 2H), 0.89–0.81 (m, 2H), 0.85 (t, J = 7.2 Hz, 3H), 0.66 (t, J = 7.3 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 168.2, 167.6, 151.9, 138.7, 135.0, 134.3, 134.2, 131.5, 130.7, 130.3, 129.7, 129.6, 129.1, 128.5, 123.6, 122.9, 121.5, 118.6, 115.1, 61.4, 60.4, 57.0, 45.3, 43.5, 34.3, 19.7, 13.6; $(\alpha)_D^{25}$ = −15.00 (c = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er >95 : 5) of compound **16a-(L)** was determined using the Daicel Chiralpak AD column, hexane/i-PrOH 35 : 15, flow rate 0.5 mL min^{-1}, UV detection at 254 nm, t_L = 78.09 min, t_D = 109.80 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{34}H_{36}N_3O_6S$: 614.2325; found 614.2326.

(2*R,3*S**)-Ethyl 2-amino-3-(4-((5-(dimethylamino)naphthalene)-1-sulfonamido)phenyl)hexanoate (17a-(DL)).** Following the general procedure, **17a-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 80 : 20) as a brown coloured semi-solid (*anti* isomer, 85%, 41 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.30; IR (DCM): 2922, 1733, 1461, 1186, 751 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.48 (d, J = 8.5 Hz, 1H), 8.35 (d, J = 8.6 Hz, 1H), 8.19 (dd, J_1 = 7.4 Hz, J_2 = 1.1 Hz, 1H), 7.50 (t, J = 8.2 Hz, 1H), 7.43–7.39 (m, 1H), 7.14 (d, J = 7.5 Hz, 1H), 6.94 (d, J = 8.5 Hz, 2H), 6.88 (d, J = 8.6 Hz, 2H), 3.92–3.86 (m, 2H), 3.44 (d, J = 6.6 Hz, 1H), 2.85 (s, 6H), 2.79–2.74 (m, 1H), 1.71–1.53 (m, 2H), 1.05–0.89 (m, 2H), 0.93 (t, J = 7.1 Hz, 3H), 0.77 (t, J = 7.4 Hz, 3H); (the signal corresponding to the NH group and NH_2 was not clearly located in the proton NMR); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 174.6, 151.8, 137.6, 135.3, 134.5, 130.5, 130.0, 129.6, 129.6, 129.0, 128.3, 122.9, 120.9, 118.6, 115.1, 60.5, 59.8, 49.1, 45.3, 32.2, 20.3, 13.8. The enantiomeric ratio of compound **17a-(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_L = 17.83 min, t_D = 27.13 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{26}H_{34}N_3O_4S$: 484.2270; found: 484.2266.

(2*S*,3*R*)-Ethyl 2-amino-3-(4-((5-(dimethylamino)naphthalene)-1-sulfonamido)phenyl)hexanoate (17a-(L)). Following the general procedure, **17a-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 80 : 20) as a brown coloured semi-solid (*anti* isomer, 78%, 19 mg, 0.05 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.3; IR ($CHCl_3$): 2925, 1728, 1461, 1153, 758 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.49 (d, J = 8.5 Hz, 1H), 8.36 (d, J = 8.7 Hz, 1H), 8.20 (dd, J_1 = 7.4 Hz, J_2 = 1.1 Hz, 1H), 7.53 (t, J = 8.2 Hz, 1H), 7.43 (dd, J_1 = 8.4 Hz, J_2 = 7.5 Hz, 1H), 7.16 (d, J = 7.5 Hz, 1H), 6.96 (d, J = 8.5 Hz, 2H), 6.89 (d, J = 8.5 Hz, 2H), 3.92–3.89 (m, 2H), 3.45 (d, J = 6.3 Hz, 1H), 2.87 (s, 6H), 2.79–2.76 (m, 1H), 1.72–1.55 (m, 2H), 1.05–1.01 (m, 1H), 0.97 (t, J = 7.1 Hz, 3H), 0.92–0.85 (m, 1H) 0.78 (t, J = 7.4 Hz, 3H); (the signal corresponding to the NH group and NH_2 was not clearly located in the proton NMR); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 174.6, 151.8, 137.7, 135.2, 134.5, 130.6, 130.0, 129.7, 129.6, 129.0, 128.4, 122.9, 121.0, 118.6, 115.1, 60.6, 59.8, 49.1, 45.3, 32.2, 29.6, 20.3, 13.8; $(\alpha)_D^{25}$ = −14.00 (c = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er 95 : 5) of compound **17a-(L)** 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_L = 18.06 min, t_D = 27.24 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{26}H_{34}N_3O_4S$: 484.2270; found: 484.2268.

(2*R,3*S**)-Ethyl 2-(2-((*tert*-butoxycarbonyl)amino)acetamido)-3-(4-((5-(dimethylamino)naphthalene)-1-sulfonamido)phenyl)hexanoate (18a-(DL)).** Following the general procedure, **18a-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a brown coloured semi-solid (*anti* isomer, 81%, 52 mg, 0.10 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.60; IR (DCM): 3276, 2930, 1669, 1147, 789 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.41 (d, J = 8.5 Hz, 1H), 8.27 (d, J = 8.6 Hz, 1H), 8.12 (dd, J_1 = 7.3 Hz, J_2 = 1.0 Hz, 1H), 7.78–7.73 (m, 1H), 7.44 (t, J = 8.2 Hz, 1H), 7.37–7.33 (m, 1H), 7.08 (d, J = 7.6 Hz, 1H), 6.82 (s, 4H), 6.67–6.67 (m, 1H), 5.22–5.22 (m, 1H), 4.59–4.55 (m, 1H), 3.77–3.63 (m, 4H), 2.78 (s, 6H), 1.59–1.46 (m, 2H), 1.35 (s, 9H), 0.94–0.86 (m, 2H), 0.75 (t, J = 6.6 Hz, 3H), 0.66 (t, J = 7.3 Hz, 3H); (one signal corresponding to the NH group was not clearly located in the proton NMR); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 171.2, 169.4, 156.1, 151.8, 136.0, 135.7, 134.4, 130.6, 130.1, 129.7, 129.6, 129.0, 128.4, 123.0, 120.8, 118.6, 115.1, 80.2, 61.1, 56.9, 47.9, 45.3, 44.2, 33.0, 28.2, 20.2, 13.7, 13.6. The enantiomeric ratio of compound **18a-(DL)** was determined using the Daicel Chiralpak IC column, hexane/i-PrOH 20 : 80, flow rate 0.1 mL min^{-1}, UV detection at 323 nm, t_D = 80.73 min, t_L = 92.86 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{33}H_{45}N_4O_7S$: 641.3009; found: 641.3024.

(2*S*,3*R*)-Ethyl 2-(2-((*tert*-butoxycarbonyl)amino)acetamido)-3-(4-((5-(dimethylamino)naphthalene)-1-sulfonamido)phenyl)hexanoate (18a-(L)). Following the general procedure, **18a-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a brown coloured semi-solid (*anti* isomer, 78%, 15 mg, 0.03 mmol scale); R_f (EtOAc/

hexanes = 50 : 50) 0.6; IR ($CHCl_3$): 3345, 2932, 1667, 1142, 751 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.51 (d, J = 8.5 Hz, 1H), 8.33 (d, J = 8.6 Hz, 1H), 8.19 (dd, J_1 = 7.3 Hz, J_2 = 1.1 Hz, 1H), 7.57 (dd, J_1 = 8.5 Hz, J_2 = 7.9 Hz, 1H), 7.45 (dd, J_1 = 8.5 Hz, J_2 = 7.4 Hz, 1H), 7.19 (d, J = 7.5 Hz, 1H), 7.12 (s, 1H), 6.92 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 6.58 (d, J = 8.6 Hz, 1H), 5.15–5.13 (m, 1H), 4.67 (dd, J_1 = 8.8 Hz, J_2 = 7.4 Hz, 1H), 3.91–3.70 (m, 4H), 2.89 (s, 6H), 2.85–2.81 (m, 1H), 1.69–1.60 (m, 2H), 1.45 (s, 9H), 1.06–0.99 (m, 2H), 0.91 (t, J = 7.1 Hz, 3H), 0.78 (t, J = 7.4 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 171.0, 169.1, 151.9, 135.5, 134.3, 130.7, 130.2, 129.7, 129.6, 129.1, 128.9, 128.5, 123.0, 121.3, 118.5, 115.2, 80.4, 61.1, 56.7, 48.1, 45.4, 45.3, 33.1, 28.2, 20.3, 13.7, 13.7; $(\alpha)_D^{25}$ = −18.00 (c = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er 92 : 8) of compound **18a-(L)** was determined using the Daicel Chiralpak IC column, hexane/i-PrOH 20 : 80, flow rate 0.1 mL min^{-1}, UV detection at 323 nm, t_D = 78.65 min, t_L = 93.57 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{33}H_{45}N_4O_7S$: 641.3009; found: 641.3004.

(1*S,2*R**)-*tert*-Butyl (2-((1-(4-((5-(dimethylamino)naphthalene)-1-sulfonamido)-3-methylphenyl)-3-oxo-1-phenyl-3-(quinolin-8-ylamino)propan-2-yl)amino)-2-oxoethyl)carbamate (19a-(DL)).** Following the general procedure, **19a-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a brown coloured semi-solid (*anti* isomer, 76%, 30 mg, 0.05 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.60; IR (DCM): 3301, 2924, 1666, 1325, 735 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.82 (s, 1H), 8.64 (d, J = 3.0 Hz, 1H), 8.46 (d, J = 6.7 Hz, 1H), 8.29 (d, J = 8.1 Hz, 1H), 8.09 (d, J = 8.5 Hz, 1H), 8.03 (d, J = 8.0 Hz, 1H), 7.73 (d, J = 6.7 Hz, 1H), 7.41–7.26 (m, 4H), 7.19–7.18 (m, 4H), 7.14–7.11 (m, 1H), 7.04 (t, J = 7.8 Hz, 1H), 6.99–6.93 (m, 3H), 6.79 (d, J = 8.0 Hz, 1H), 6.69 (d, J = 8.6 Hz, 1H), 6.35 (s, 1H), 5.41–5.37 (m, 1H), 4.91 (s, 1H), 4.45 (d, J = 9.3 Hz, 1H), 3.64–3.53 (m, 2H), 2.75 (s, 6H), 1.69 (s, 3H), 1.28 (s, 9H); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 169.4, 168.6, 155.6, 151.5, 148.3, 139.5, 138.1, 137.9, 136.2, 134.6, 133.5, 133.5, 131.7, 130.5, 129.9, 129.5, 129.4, 128.7, 128.4, 128.2, 127.7, 127.2, 127.0, 126.3, 123.9, 123.0, 122.1, 121.7, 118.7, 116.7, 115.1, 80.2, 57.2, 52.7, 45.4, 44.1, 28.2, 17.5. The enantiomeric ratio of compound **19a-(DL)** was determined using the Daicel Chiralpak ADH column, hexane/i-PrOH 50 : 50, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 11.66 min, t_L = 21.35 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{44}H_{47}N_6O_6S$: 787.3278; found: 787.3276.

(1*R*,2*S*)-*tert*-Butyl (2-((-1-(4-((5-(dimethylamino)naphthalene)-1-sulfonamido)-3-methylphenyl)-3-oxo-1-phenyl-3-(quinolin-8-ylamino)propan-2-yl)amino)-2-oxoethyl)carbamate (19a-(L)). Following the general procedure, **19a-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a brown coloured semi-solid (*anti* isomer, 77%, 32 mg, 0.053 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.60; IR (DCM): 3299, 2923, 1664, 1324, 733 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.87 (s, 1H), 8.71–8.70 (m, 1H), 8.54 (d, J = 6.9 Hz, 1H), 8.33 (d, J = 8.5 Hz, 1H), 8.16 (d, J = 8.6 Hz, 1H), 8.09 (d, J = 8.2 Hz, 1H), 7.80 (d, J = 7.0 Hz, 1H), 7.49–7.33 (m, 4H), 7.26–7.25 (m, 4H), 7.21–7.19 (m, 1H), 7.10 (t, J = 7.8 Hz, 1H), 7.05–7.00 (m, 3H), 6.86 (d, J = 8.0 Hz, 1H), 6.71 (d, J = 8.8 Hz, 1H), 6.38 (s, 1H), 5.48–5.44 (m, 1H), 4.96–4.91 (m, 1H), 4.52 (d, J = 9.4 Hz, 1H), 3.73–3.60 (m, 2H), 2.81 (s, 6H), 1.76 (s, 3H), 1.35 (s, 9H); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 169.3, 168.6, 155.5, 151.8, 148.4, 139.5, 138.2, 137.9, 136.0, 134.6, 133.6, 133.5, 131.7, 130.6, 130.5, 129.9, 129.6, 129.4, 128.7, 128.4, 128.2, 127.7, 127.2, 127.0, 126.3, 123.9, 122.9, 122.1, 121.7, 118.5, 116.5, 115.0, 80.2, 57.2, 52.7, 45.3, 44.1, 28.2, 17.5; $(\alpha)_D^{25}$ = −16.00 (c = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er 96 : 4) of compound **19a-(L)** was determined using the Daicel Chiralpak ADH column, hexane/i-PrOH 50 : 50, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 12.01 min, t_L = 21.64 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{44}H_{47}N_6O_6S$: 787.3278; found: 787.3279.

(2*R,3*S**)-*tert*-Butyl (2-((3-(3-((5-(dimethylamino)naphthalene)-1-sulfonamido)phenyl)-1-oxo-1-(quinolin-8-ylamino)pentan-2-yl)amino)-2-oxoethyl)carbamate (19b-(DL)).** Compound **19b-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 80 : 20) as a brown colour semi-solid (70%, 15 mg, 0.03 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.3; IR ($CHCl_3$): 3310, 2924, 1673, 1530, 735 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.74 (s, 1H), 8.66–8.65 (m, 1H), 8.43 (d, J = 7.1 Hz, 1H), 8.38 (d, J = 8.5 Hz, 1H), 8.26 (d, J = 7.8 Hz, 1H), 8.06–8.02 (m, 2H), 7.42–7.25 (m, 6H), 7.05–7.03 (m, 1H), 6.92–6.90 (m, 2H), 6.82–6.80 (m, 2H), 6.66 (s, 1H), 5.28–5.22 (m, 1H), 4.83–4.79 (m, 1H), 3.81–3.68 (m, 2H), 2.78 (s, 6H), 1.80–1.68 (m, 2H), 1.41 (s, 9H), 0.39 (t, J = 7.1 Hz, 3H); (one signal corresponding to the NH group was not clearly located in the proton NMR); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ 169.5, 168.5, 156.2, 148.3, 140.7, 138.0, 137.0, 136.3, 136.0, 134.3, 133.2, 130.4, 130.2, 129.6, 129.3, 128.3, 127.8, 127.0, 125.2, 123.1, 122.2, 121.7, 121.4, 120.0, 115.2, 114.0, 113.4, 80.6, 58.5, 45.4, 31.9, 28.3, 22.7, 14.1, 11.7; (the carbon NMR of these compounds showed additional minor signals in the aliphatic region, which are attributed to the presence of rotamers); The enantiomeric ratio of compound **19b-(DL)** was determined using the Daicel Chiralpak IA column, hexane/i-PrOH 70 : 30, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 19.91 min, t_L = 28.35 min; HRMS (ESI): m/z $(M + H)^+$ calcd for $C_{39}H_{45}N_6O_6S$: 725.3121; found: 725.3126.

(2*R*,3*S*)-*tert*-Butyl (2-((3-(3-((5-(dimethylamino)naphthalene)-1-sulfonamido)phenyl)-1-oxo-1-(quinolin-8-ylamino)pentan-2-yl)amino)-2-oxoethyl)carbamate (19b-(D)). Compound **19b-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 80 : 20) as a brown coloured semi-solid (68%, 15.3 mg, 0.031 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.3; IR ($CHCl_3$): 3311, 2924, 1670, 1529, 737 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.75 (s, 1H), 8.68–8.67 (m, 1H), 8.44 (d, J = 6.3 Hz, 1H), 8.41–8.40 (m, 1H), 8.28 (d, J = 9.0 Hz, 1H), 8.10–8.03 (m, 2H), 7.46–7.27 (m, 6H), 7.09–7.07 (m, 1H), 6.94–6.80 (m, 4H), 6.63 (s, 1H), 5.28–5.23 (m, 1H), 4.81–4.77 (m, 1H), 3.81–3.67 (m, 2H), 2.80 (s, 6H), 1.76–1.70 (m, 2H), 1.42 (s, 9H), 0.40 (t, J = 7.4 Hz, 3H); (one signal corresponding to the NH group was not clearly located in the proton NMR); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ 169.5, 168.5, 156.2, 148.3, 140.7, 138.0, 137.0, 134.3, 133.2, 130.4, 130.2, 129.6, 129.6,

129.3, 128.3, 128.0, 127.8, 127.2, 127.1, 125.3, 123.2, 122.2, 121.7, 121.6, 120.1, 116.7, 115.3, 114.4, 80.7, 58.5, 45.4, 31.4, 28.3, 22.7, 14.1, 11.8; (the carbon NMR of these compounds showed additional minor signals in the aliphatic region, which are attributed to the presence of rotamers); $(\alpha)_D^{25}$ = +19.0 (*c* = 0.02 g per 100 mL, $CHCl_3$); The enantiomeric ratio (er >95 : 5) of compound **19b-(D)** was determined using the Daicel Chiralpak IA column, hexane/i-PrOH 70 : 30, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 20.02 min, t_L = 28.68 min; HRMS (ESI): *m*/*z* $(M + H)^+$ calcd for $C_{39}H_{45}N_6O_6S$: 725.3121; found: 725.3120.

Ethyl (*R)-12-((*S**)-1-(4-((5-(dimethylamino)naphthalene)-1-sulfonamido)-3-methylphenyl)propyl)-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oate (20a-(DL)).** Following the general procedure, **20a-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a brown coloured semi-solid (*anti* isomer, 82%, 36 mg, 0.063 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.50; IR (DCM): 3308, 2927, 1664, 1508, 735 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.44 (d, *J* = 8.4 Hz, 1H), 8.26 (d, *J* = 8.6 Hz, 1H), 8.06 (d, *J* = 7.3 Hz, 1H), 7.45 (t, *J* = 8.4 Hz, 1H), 7.36 (t, *J* = 8.1 Hz, 1H), 7.10 (d, *J* = 7.5 Hz, 1H), 6.93–6.85 (m, 3H), 6.78–6.68 (m, 3H), 5.30–5.29 (m, 1H), 4.57 (t, *J* = 8.1 Hz, 1H), 3.90–3.77 (m, 4H), 3.71 (d, *J* = 5.2 Hz, 2H), 2.80 (s, 6H), 2.68–2.63 (m, 1H), 1.87 (s, 3H), 1.71–1.65 (m, 1H), 1.58–1.50 (m, 1H), 1.37 (s, 9H), 0.84 (t, *J* = 7.1 Hz, 3H), 0.60 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 171.0, 170.2, 168.4, 156.2, 151.8, 136.9, 134.9, 133.6, 131.6, 130.8, 130.6, 130.1, 129.7, 129.6, 128.3, 126.6, 123.9, 123.1, 118.8, 115.2, 80.4, 61.1, 56.9, 49.8, 45.4, 44.2, 42.9, 28.3, 24.0, 17.6, 13.7, 11.9. The enantiomeric ratio of compound **20a-(DL)** was determined using the Daicel Chiralpak IC column, hexane/i-PrOH 70 : 30, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 172.50 min, t_L = 220.26 min; HRMS (ESI): *m*/*z* $(M + H)^+$ calcd for $C_{35}H_{48}N_5O_8S$: 698.3223; found:698.3218.

Ethyl (*S*)-12-((*R*)-1-(4-((5-(dimethylamino)naphthalene)-1-sulfonamido)-3-methylphenyl)propyl)-2,2-dimethyl-4,7,10-trioxo-3-oxa-5,8,11-triazatridecan-13-oate (20a-(L)). Following the general procedure, **20a-(L)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 50 : 50) as a brown coloured semi-solid (*anti* isomer, 78%, 26 mg, 0.048 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.5; IR ($CHCl_3$): 3308, 2926, 1661, 1503, 735 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.45 (d, *J* = 8.3 Hz, 1H), 8.26 (d, *J* = 8.6 Hz, 1H), 8.06 (d, *J* = 7.3 Hz, 1H), 7.45 (t, *J* = 8.3 Hz, 1H), 7.36 (t, *J* = 8.0 Hz, 1H), 7.10 (d, *J* = 7.4 Hz, 1H), 6.93–6.68 (m, 6H), 5.29 (s, 1H), 4.57 (1H, t, *J* = 8.2 Hz), 3.90–3.78 (m, 4H), 3.71 (d, *J* = 5.2 Hz, 2H), 2.81 (s, 6H), 2.68–2.63 (m, 1H), 1.87 (s, 3H), 1.71–1.65 (m, 1H), 1.58–1.52 (m, 1H), 1.37 (s, 9H), 0.85 (t, *J* = 7.1 Hz, 3H), 0.60 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 171.0, 170.2, 168.4, 156.2, 151.7, 136.9, 135.0, 133.6, 131.6, 130.8, 130.6, 130.1, 129.7, 129.6, 128.3, 126.6, 123.9, 123.1, 118.9, 115.2, 80.4, 61.1, 56.9, 49.8, 45.4, 44.2, 42.9, 28.3, 24.0, 17.6, 13.7, 11.9; $(\alpha)_D^{25}$ = −18.00 (*c* = 0.02 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er >95 : 5) of compound **20a-(L)** was determined using the Daicel Chiralpak IC column, hexane/i-PrOH 70 : 30, flow rate 1.0 mL min^{-1}, UV detection at 254 nm, t_D = 171.50 min, t_L = 222.26 min; HRMS (ESI): *m*/*z* $(M + H)^+$ calcd for $C_{35}H_{48}N_5O_8S$: 698.3223; found:698.3228.

(2*R,3*S**)-Ethyl 2-(2-(((benzyloxy)carbonyl)amino)acetamido)-3-(3-((5-(dimethylamino)naphthalene)-1-sulfonamido)phenyl)pentanoate (20b-(DL)).** Following the general procedure, **20b-(DL)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 40 : 60) as a brown coloured semi-solid (*anti* isomer, 80%, 33 mg, 0.062 mmol); R_f (EtOAc/hexanes = 50 : 50) 0.60; IR (DCM): 3273, 2925, 1672, 1519, 736 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.39 (d, *J* = 8.4 Hz, 1H), 8.28 (d, *J* = 8.6 Hz, 1H), 8.09 (d, *J* = 7.3 Hz, 1H), 7.83 (s, 1H), 7.42 (t, *J* = 8.1 Hz, 1H), 7.34–7.24 (m, 6H), 7.07 (d, *J* = 7.5 Hz, 1H), 6.97 (t, *J* = 7.8 Hz, 1H), 6.86 (d, *J* = 6.5 Hz, 1H), 6.68 (d, *J* = 7.3 Hz, 1H), 6.58 (s, 1H), 6.51 (d, *J* = 8.4 Hz, 1H), 5.56 (s, 1H), 5.14–5.07 (m, 2H), 4.64–4.60 (m, 1H), 3.94–3.88 (m, 2H), 3.73 (d, *J* = 5.9 Hz, 2H), 2.77 (s, 6H), 2.71–2.68 (m, 1H), 1.63–1.56 (m, 1H), 1.47–1.40 (m, 1H), 0.96 (t, *J* = 6.9 Hz, 3H), 0.46 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101.0 MHz, $CDCl_3$): δ_C 170.8, 168.6, 156.9, 151.7, 140.0, 136.8, 136.0, 134.4, 130.5, 130.2, 129.7, 129.6, 129.1, 128.5, 128.3, 128.2, 128.1, 124.7, 123.1, 121.7, 120.0, 118.9, 115.2, 67.4, 61.5, 56.4, 49.7, 45.4, 44.4, 23.4, 13.8, 11.9. The enantiomeric ratio of compound **20b-(DL)** was determined using the Daicel Chiralpak IA column, hexane/i-PrOH 70 : 30, flow rate 0.5 mL min^{-1}, UV detection at 254 nm, t_D = 31.30 min, t_L = 35.29 min; HRMS (ESI): *m*/*z* $(M + H)^+$ calcd for $C_{35}H_{41}N_4O_7S$: 661.2696; found: 661.2690.

(2*R*,3*S*)-Ethyl 2-(2-(((benzyloxy)carbonyl)amino)acetamido)-3-(3-((5-(dimethylamino)naphthalene)-1-sulfonamido)phenyl)pentanoate (20b-(D)). Following the general procedure, **20b-(D)** was obtained after purification by column chromatography on silica gel (EtOAc : hexanes = 40 : 60) as a brown coloured semi-solid (*anti* isomer, 75%, 23 mg, 0.046 mmol scale); R_f (EtOAc/hexanes = 50 : 50) 0.6; IR ($CHCl_3$): 3338, 2926, 1671, 1524, 737 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.40 (d, *J* = 8.3 Hz, 1H), 8.28 (d, *J* = 8.6 Hz, 1H), 8.09 (d, *J* = 7.3 Hz, 1H), 7.79–7.72 (m, 1H), 7.43 (t, *J* = 8.1 Hz, 1H), 7.34–7.22 (m, 6H), 7.08 (d, *J* = 7.4 Hz, 1H), 6.97 (t, *J* = 7.8 Hz, 1H), 6.86 (d, *J* = 7.2 Hz, 1H), 6.69 (d, *J* = 7.4 Hz, 1H), 6.58 (s, 1H), 6.49 (s, 1H), 5.54 (s, 1H), 5.15–5.07 (m, 2H), 4.64–4.60 (m, 1H), 3.94–3.89 (m, 2H), 3.73 (d, *J* = 6.0 Hz, 2H), 2.78 (s, 6H), 2.71–2.69 (m, 1H), 1.63–1.58 (m, 1H), 1.47–1.42 (m, 1H), 0.97 (t, *J* = 6.5 Hz, 3H), 0.47 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (~101 MHz, $CDCl_3$): δ_C 170.8, 168.6, 156.9, 140.0, 137.6, 136.8, 136.0, 134.4, 130.5, 130.2, 129.6, 129.1, 128.5, 128.3, 128.2, 128.1, 124.7, 123.2, 123.1, 121.8, 120.0, 120.0, 115.2, 67.4, 61.5, 56.4, 49.7, 45.4, 44.5, 23.3, 13.8, 11.9; $(\alpha)_D^{25}$ = +37.00 (*c* = 0.04 g per 100 mL, $CHCl_3$). The enantiomeric ratio (er 97 : 3) of compound **20b-(D)** was determined using the Daicel Chiralpak IA column, hexane/i-PrOH 70 : 30, flow rate 0.5 mL min^{-1}, UV detection at 254 nm, t_D = 31.40 min, t_L = 35.25 min; HRMS (ESI): *m*/*z* $(M + H)^+$ calcd for $C_{35}H_{41}N_4O_7S$: 661.2696; found: 661.2690.

Conflicts of interest

There are no conflicts to declare.

Data availability

The data are available within the article or its SI (Copies of proton and carbon NMRs, HPLC analyses, UV-Vis absorption and fluorescence emission plots). See DOI: **https://doi.org/10.1039/d5ob01017a**.

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References

1 For reviews on C–H functionalization, see: (*a*) F. Kakiuchi and S. Murai, *Acc. Chem. Res.*, 2002, **35**, 826; (*b*) X. Chen, K. M. Engle, D.-H. Wang and J.-Q. Yu, *Angew. Chem., Int. Ed.*, 2009, **48**, 5094; (*c*) P. B. Arockiam, C. Bruneau and P. H. Dixneuf, *Chem. Rev.*, 2012, **112**, 5879; (*d*) S. A. Girard, T. Knauber and C.-J. Li, *Angew. Chem., Int. Ed.*, 2014, **53**, 74; (*e*) F. Kakiuchi and N. Chatani, *Adv. Synth. Catal.*, 2003, **345**, 1077; (*f*) J. Wencel-Delord and F. Glorius, *Nat. Chem.*, 2013, **5**, 369; (*g*) Y. Yang, J. Lan and J. You, *Chem. Rev.*, 2017, **117**, 8787; (*h*) Y. Segawa, T. Maekawa and K. Itami, *Angew. Chem., Int. Ed.*, 2015, **54**, 66; (*i*) W. Ali, G. A. Oliver, D. B. Werz and D. Maiti, *Chem. Soc. Rev.*, 2024, **53**, 9904; (*j*) J. He, M. Wasa, K. S. L. Chan, Q. Shao and J.-Y. Yu, *Chem. Rev.*, 2017, **117**, 8754; (*k*) R. Manoharan and M. Jeganmohan, *Asian J. Org. Chem.*, 2019, **8**, 1949; (*l*) M. M. Mingo, N. Rodríguez, R. G. Arrayás and J. C. Carretero, *Chem. Commun.*, 2022, **58**, 2034; (*m*) S. A. Babu, R. Padmavathi, S. Suwasia, A. Dalal, D. Bhattacharya, P. Singh and R. Tomar, *Stud. Nat. Prod. Chem.*, 2021, **71**, 311; (*n*) T. Besset, T. Poisson and X. Pannecoucke, *Chem. – Eur. J.*, 2014, **20**, 16830; (*o*) T. W. Lyons and M. S. Sanford, *Chem. Rev.*, 2010, **110**, 1147; (*p*) A. Mandal, S. Dana, D. Choudhury and M. Baidya, *Chem. – Asian J.*, 2019, **14**, 4074; (*q*) L. Ackermann, *Chem. Rev.*, 2011, **111**, 1315; (*r*) M. Miura, T. Satoh and K. Hirano, *Bull. Chem. Soc. Jpn.*, 2014, **87**, 751; (*s*) M.-Z. Lu, J. Goh, M. Maraswami, Z. Jia, J.-S. Tian and T.-P. Loh, *Chem. Rev.*, 2022, **122**, 17479; (*t*) D. Y.-K. Chen and S. W. Youn, *Chem. – Asian J.*, 2012, **18**, 9452; (*u*) P. Subramanian, G. C. Rudolf and K. P. Kaliappan, *Chem. – Asian J.*, 2016, **11**, 168.

2 For reviews on bidentate directing group-aided C–H functionalization, see: (*a*) S. Rej, Y. Ano and N. Chatani, *Chem. Rev.*, 2020, **120**, 1788; (*b*) O. Daugulis, J. Roane and L. D. Tran, *Acc. Chem. Res.*, 2015, **48**, 1053; (*c*) C. Sambiagio, D. Schönbauer, R. Blieck, T. Dao-Huy, G. Pototschnig, P. Schaaf, T. Wiesinger, M. F. Zia, J. Wencel-Delord, T. Besset, B. U. W. Maes and M. Schnürch, *Chem. Soc. Rev.*, 2018, **47**, 6603; (*d*) B. Liu, A. M. Romine, C. Z. Rubel, K. M. Engle and B.-F. Shi, *Chem. Rev.*, 2021, **121**, 14957; (*e*) R. K. Rit, M. R. Yadav, K. Ghosh and A. K. Sahoo, *Tetrahedron*, 2015, **71**, 4450; (*f*) S. A. Babu, Y. Aggarwal, P. Patel and R. Tomar, *Chem. Commun.*, 2022, **58**, 2612; (*g*) X. Yang, G. Shan, L. Wang and Y. Rao, *Tetrahedron Lett.*, 2016, **57**, 819; (*h*) S.-F. Ni, G. Huang, Y. Chen, J. S. Wright, M. Li and L. Dang, *Coord. Chem. Rev.*, 2022, **455**, 214255.

3 For reviews on C–H functionalization of amino acid derivatives, see: (*a*) A. F. M. Noisier and M. A. Brimble, *Chem. Rev.*, 2014, **114**, 8775; (*b*) T. Brandhofer and O. G. Mancheño, *Eur. J. Org. Chem.*, 2018, 6050; (*c*) A. Correa, *Eur. J. Inorg. Chem.*, 2021, **2021**, 2928; (*d*) J. Jeon, C. Lee, I. Park and S. Hong, *Chem. Rec.*, 2021, **21**, 3613; (*e*) L. Ackermann, R. Vicente and A. R. Kapdi, *Angew. Chem., Int. Ed.*, 2009, **48**, 9792; (*f*) G. He, B. Wang, W. A. Nack and G. Chen, *Acc. Chem. Res.*, 2016, **49**, 635; (*g*) S. Shabani, Y. Wu, H. G. Ryan and C. A. Hutton, *Chem. Soc. Rev.*, 2021, **50**, 9278; (*h*) S. Mondal and S. Choudhury, *Adv. Synth. Catal.*, 2018, **360**, 1884; (*i*) B.-B. Zhan, M.-X. Jiang and B.-F. Shi, *Chem. Commun.*, 2020, **56**, 13950.

4 For bidentate directing group-aided C–H functionalization, see: (*a*) D. Shabashov and O. Daugulis, *J. Am. Chem. Soc.*, 2010, **132**, 3965; (*b*) S. Rej and N. Chatani, *ACS Catal.*, 2018, **8**, 6699; (*c*) Y. Huang, X. Lv, H.-R. Tong, W. He, Z. Bai, H. Wang, G. He and G. Chen, *Org. Lett.*, 2024, **26**, 94; (*d*) R. Padmavathi and S. A. Babu, *Org. Biomol. Chem.*, 2023, **21**, 2689; (*e*) S. Suwasia, S. Venkataramani and S. A. Babu, *Org. Biomol. Chem.*, 2023, **21**, 1793; (*f*) C. Reddy, N. Bisht, R. Parella and S. A. Babu, *J. Org. Chem.*, 2016, **81**, 12143; (*g*) R. Padmavathi, R. Sankar, B. Gopalakrishnan, R. Parella and S. A. Babu, *Eur. J. Org. Chem.*, 2015, 3727; (*h*) J. Han, P. Liu, C. Wang, Q. Wang, J. Zhang, Y. Zhao, D. Shi, Z. Huang and Y. Zhao, *Org. Lett.*, 2014, **16**, 5682; (*i*) R. Parella and S. A. Babu, *J. Org. Chem.*, 2017, **82**, 6550; (*j*) H.-Y. Xiong, T. Besset, D. Cahard and X. Pannecoucke, *J. Org. Chem.*, 2015, **80**, 4204; (*k*) Y.-F. Zhang, H.-W. Zhao, H. Wang, J.-B. Wei and Z.-J. Shi, *Angew. Chem., Int. Ed.*, 2015, **54**, 13686; (*l*) J. Bolsakova, L. Lukasevics and L. Grigorjeva, *J. Org. Chem.*, 2020, **85**, 4482; (*m*) Z.-K. Wang, Y.-J. Wu, Q.-J. Yao and B.-F. Shi, *Angew. Chem., Int. Ed.*, 2023, **62**, e202304706; (*n*) D. Santrač, S. Cella, W. Wang and L. Ackermann, *Eur. J. Org. Chem.*, 2016, 5429; (*o*) R. Tomar, D. Bhattacharya and S. A. Babu, *Asian J. Org. Chem.*, 2022, **11**, e202100736; (*p*) R. Parella and S. A. Babu, *J. Org. Chem.*, 2017, **82**, 7123; (*q*) R. Kaur and S. A. Babu, *Chem. – Asian J.*, 2024, e202401353; (*r*) A. Matsumura, Y. Usuki and T. Satoh, *Chemistry*, 2023, **5**, 1369.

5 For diastereoselective C(sp^3)–H functionalization, see: (*a*) S. Biswas, N. R. Bheemireddy, M. Bal, B. F. V. Steijvoort

and B. U. W. Maes, *J. Org. Chem.*, 2019, **84**, 13112; (*b*) W. R. Gutekunst and P. S. Baran, *J. Org. Chem.*, 2014, **79**, 2430; (*c*) J. Ghouilem, C. Tran, N. Grimblat, P. Retailleau, M. Alami, V. Gandon and S. Messaoudi, *ACS Catal.*, 2021, **11**, 1818; (*d*) G. Kang, D. A. Strassfeld, T. Sheng, C.-Y. Chen and J.-Q. Yu, *Nature*, 2023, **618**, 519; (*e*) A. Seki and Y. Takahashi, *Tetrahedron Lett.*, 2021, **74**, 153130; (*f*) D. Antermite, A. J. P. White, L. Casarrubios and J. A. Bull, *ACS Catal.*, 2017, **82**, 9597; (*g*) B. Gopalakrishnan, S. A. Babu and R. Padmavathi, *Tetrahedron*, 2015, **71**, 8333; (*h*) M. B. Calvert and J. Sperry, *Org. Biomol. Chem.*, 2016, **14**, 5728; (*i*) J. Mio, K. Yang, M. Kurek and H. Ge, *Org. Lett.*, 2015, **17**, 3738; (*j*) J. Kim, M. Sim, N. Kim and S. Hong, *Chem. Sci.*, 2015, **6**, 3611; (*k*) B. Gopalakrishnan, S. Mohan, R. Parella and S. A. Babu, *J. Org. Chem.*, 2016, **81**, 8988; (*l*) R. Parella and S. A. Babu, *J. Org. Chem.*, 2015, **80**, 2339; (*m*) W. Nack, B. Wang, X. Wu, R. Jio, G. He and G. Chen, *Org. Chem. Front.*, 2016, **3**, 561.

6 For C(sp^3)–H functionalization of amino acid derivatives, see: (*a*) L. D. Tran and O. Daugulis, *Angew. Chem., Int. Ed.*, 2012, **51**, 5188; (*b*) G. He and G. Chen, *Angew. Chem., Int. Ed.*, 2011, **50**, 5192; (*c*) J.-W. Xu, Z.-Z. Zhang, W.-H. Rao and B.-F. Shi, *J. Am. Chem. Soc.*, 2016, **138**, 10750; (*d*) R. Tomar, S. Suwasia, A. R. Choudhury, S. Venkataramani and S. A. Babu, *Chem. Commun.*, 2022, **58**, 12967; (*e*) S. Banga and S. A. Babu, *Eur. J. Org. Chem.*, 2024, e202400272; (*f*) R. Kaur, S. Banga and S. A. Babu, *Org. Biomol. Chem.*, 2022, **20**, 4391; (*g*) N. Kaplaneris, A. Puet, F. Kallert, J. Pöhlmann and L. Ackermann, *Angew. Chem., Int. Ed.*, 2023, **62**, e202216661; (*h*) A. Deb, S. Singh, K. Seth, S. Pimparkar, B. Bhaskararao, S. Guin, R. B. Sunoj and D. Maiti, *ACS Catal.*, 2017, **7**, 8171; (*i*) N. Bisht, S. A. Babu and R. Tomar, *Asian J. Org. Chem.*, 2022, **11**, e202200589; (*j*) D. P. Affron, O. A. Davis and J. A. Bull, *Org. Lett.*, 2014, **16**, 4956; (*k*) Z.-L. Hou, Y. Tang, Y. Lu and B. Yao, *ACS Catal.*, 2024, **14**, 11026; (*l*) P. Patel, S. A. Babu and R. Tomar, *Eur. J. Org. Chem.*, 2024, e202400190; (*m*) M. Borgini and P. Wipf, *Tetrahedron*, 2022, **120**, 132876; (*n*) S. Banga, R. Kaur and S. A. Babu, *Eur. J. Org. Chem.*, 2021, 3641; (*o*) Q.-Y. Yu, H.-M. Zhong, W.-W. Sun, S.-J. Zhang, P. Cao, X.-P. Dong, H.-B. Qin, J.-K. Liu and B. Wu, *Asian. J. Org. Chem.*, 2016, **5**, 608; (*p*) J. Mio, K. Yang, M. Kurek and H. Ge, *Org. Lett.*, 2015, **17**, 3738; (*q*) T. Kinsinger and U. Kazmaier, *Org. Biomol. Chem.*, 2019, **17**, 5595; (*r*) L. Nicke, P. Horx, K. Harms and A. Geyer, *Chem. Sci.*, 2019, **10**, 8641; (*s*) R. Feng, B. Wang, Y. Liu, Z. Liu and Y. Zhang, *Eur. J. Org. Chem.*, 2015, 142; (*t*) R. Tomar, A. Kumar, A. Dalal, D. Bhattacharya, P. Singh and S. A. Babu, *Asian J. Org. Chem.*, 2022, **11**, e202200311; (*u*) N. Bisht, S. A. Babu and R. Tomar, *Asian J. Org. Chem.*, 2020, **9**, 1225; (*v*) S. Banga and S. A. Babu, *RSC Adv.*, 2025, **15**, 21493.

7 B. Wang, W. A. Nack, G. He, S. Y. Zhang and G. Chen, *Chem. Sci.*, 2014, **5**, 3952.

8 G. Chen, T. Shigenari, P. Jain, Z. Zhang, Z. Jun, J. He, S. Li, C. Mapelli, M. M. Miller, M. A. Poss, P. M. Scola, K.-S. Yeung and J.-Q. Yu, *J. Am. Chem. Soc.*, 2015, **137**, 3338.

9 J. He, S. Li, Y. Deng, H. Fu, B. N. Laforteza, J. E. Spangler, A. Homs and J.-Q. Yu, *Science*, 2014, **343**, 1216.

10 For C(sp^2)–H functionalization of aromatic amino acid derivatives, see: (*a*) X. Wang, S. Niu, L. Xu, C. Zhang, L. Meng, X. Zhang and D. Ma, *Org. Lett.*, 2017, **19**, 246; (*b*) P. Singh and S. A. Babu, *Eur. J. Org. Chem.*, 2023, e202300440; (*c*) Y. Zeng and W. Song, *Org. Lett.*, 2019, **21**, 3257; (*d*) U. Narang, P. Singh and S. A. Babu, *Eur. J. Org. Chem.*, 2023, e202300463; (*e*) P. Andrade-Sampedro, J. M. Matxain and A. Correa, *Chem. – Eur. J.*, 2021, **27**, 5782; (*f*) S.-Y. Zhang, G. He, Y. Zhao, K. Wright, W. A. Nack and G. Chen, *J. Am. Chem. Soc.*, 2012, **134**, 7313; (*g*) S. Martínez-Flores, C. A. Mujica-Martinez and L. A. Polindara-García, *Eur. J. Org. Chem.*, 2022, e202101517; (*h*) W. Zeng, M. Nukeyeva, Q. Wang and C. Jiang, *Org. Biomol. Chem.*, 2018, **16**, 598; (*i*) A. García-Rubia, E. Laga, C. Cativiela, E. P. Urriolabeitia, R. Gomez-Arrayás and J. C. Carretero, *J. Org. Chem.*, 2015, **80**, 3321; (*j*) S.-Y. Zhang, G. He, W. A. Nack, Y. Zhao, Q. Li and G. Chen, *J. Am. Chem. Soc.*, 2013, **135**, 2124; (*k*) L. Zhang, C. Wang, J. Han, Z.-B. Huang and Y. Zhao, *J. Org. Chem.*, 2016, **81**, 5256; (*l*) A. Dalal, S. Bodak and S. A. Babu, *Org. Biomol. Chem.*, 2024, **22**, 1279; (*m*) Y. Zhu, M. Bauer and L. Ackermann, *Chem. – Eur. J.*, 2015, **21**, 9980; (*n*) A. J. Reay, T. J. Willams and I. J. S. Fairelamb, *Org. Biomol. Chem.*, 2015, **13**, 8298.

11 Unnatural (non-canonical amino acid derivatives: (*a*) A. B. Hughes, *Amino Acids, Peptides, Proteins in Organic Chemistry: Origins, Synthesis of Amino Acids*, Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, 2009, vol. 1–5; (*b*) T. S. Young and P. G. Schultz, *J. Biol. Chem.*, 2010, **285**, 11039; (*c*) S. Smolskaya and Y. A. Andreev, *Biomolecules*, 2019, **9**, 255; (*d*) A. Strømgaard, A. A. Jensen and K. Strømgaard, *ChemBioChem*, 2004, **5**, 909; (*e*) L. Pollegioni and S. Servi, *Unnatural Amino Acids: Methods, Protocols*, Humana Totowa, New Jersey, 2011; (*f*) L. Pollegioni, E. Rosini and G. Molla, *Int. J. Mol. Sci.*, 2020, **21**, 3206; (*g*) S. Martínez-Rodríguez, J. M. Torres, P. Sánchez and E. Ortega, *Front. Bioeng. Biotechnol.*, 2020, **8**, 887; (*h*) K. Lang and J. W. Chin, *Chem. Rev.*, 2014, **114**, 4764; (*i*) C. H. Kim, Y. Y. Axup and P. G. Schults, *Curr. Opin. Chem. Biol.*, 2013, **17**, 412; (*j*) J. M. Chalker, G. J. L. Bernardes and B. G. Davis, *Acc. Chem. Res.*, 2011, **44**, 730; (*k*) J.-E. Jung, S. Y. Lee, H. Park, H. Cha, W. Ko, K. Sachin, D. W. Kim, D. Y. Chi and H. S. Lee, *Chem. Sci.*, 2014, **5**, 1881; (*l*) D. A. Dougherty and E. B. V. Arnam, *ChemBioChem*, 2014, **15**, 1710.

12 Unnatural (non-canonical) amino acid derivatives: (*a*) R. Saladino, G. Botta and M. Crucianelli, *Mini-Rev. Med. Chem.*, 2012, **12**, 277; (*b*) J. Wang, X. Liu and X. Feng, *Chem. Rev.*, 2011, **111**, 6947; (*c*) B. Eftekhari-Sis and M. Zirak, *Chem. Rev.*, 2017, **117**, 8326; (*d*) K. Maruoka and T. Ooi, *Chem. Rev.*, 2003, **103**, 3013; (*e*) A. Stevenazzi, M. Marchini, G. Sandrone, B. Vergani and M. Lattanzio, *Bioorg. Med. Chem. Lett.*, 2014, **24**, 5349; (*f*) C. Nájera and M. Sansano, *Chem. Rev.*, 2007, **107**, 4584; (*g*) J. M. Seckler and S. J. Lewis, *Int. J. Mol. Sci.*, 2020, **21**, 7325;

(*h*) D. V. Grishin, D. D. Zhdanov, M. V. Pokrovskaya and N. N. Sokolov, *All Life*, 2019, **13**, 11; (*i*) S. Du, M. Wey and D. W. Armstrong, *Chirality*, 2023, **35**, 508.

13 (*a*) V. I. Martynov, A. A. Pakhomov, N. V. Popova, I. E. Deyev and A. G. Petrenko, *Acta Nat.*, 2016, **8**, 33; (*b*) M. Saleem, M. Rafiq and M. Hanif, *J. Fluoresc.*, 2017, **27**, 31; (*c*) P. Gao, W. Pan, N. Li and B. Tang, *Chem. Sci.*, 2019, **10**, 6035; (*d*) L. Wang, M. S. Frei, A. Salim and K. Johnsson, *J. Am. Chem. Soc.*, 2019, **141**, 2770; (*e*) K. P. Carter, A. M. Young and A. E. Palmer, *Chem. Rev.*, 2014, **141**, 4564; (*f*) H.-W. Liu, L. Chen, C. Xu, Z. Li, H. Zhang, X.-B. Zhang and W. Tan, *Chem. Rev.*, 2018, **47**, 7140; (*g*) L.-Y. Niu, Y.-Z. Chen, H.-R. Zheng, L.-Z. Wu, C.-H. Tung and Q.-Z. Yang, *Chem. Soc. Rev.*, 2015, **44**, 6143; (*h*) D.-B. Sunga and J. S. Lee, *RSC Med. Chem.*, 2023, **14**, 412; (*i*) Z. Guo, S. Park, J. Yoon and I. Shin, *Chem. Soc. Rev.*, 2014, **43**, 16.

14 Application of dansyl, dansyl-containing compounds: (*a*) T. Kinoshita, F. Iinuma and A. Tsuji, *Chem. Pharm. Bull.*, 1974, **22**, 24132; (*b*) J. M. Walker, in *Basic Protein, Peptide Protocols. Methods in Molecular Biology*™, Humana Press Inc. Totowa, NJ, 1994, vol. 32, DOI: 10.1385/0-89603-268-X:321; (*c*) A. Misra, S. Mishra and K. Misra, *Bioconjugate Chem.*, 2004, **15**, 638; (*d*) M. Suchý, A. Kirby, T. Sabloff, E. E. Mulvihill and A. J. Shuhendler, *New J. Chem.*, 2021, **45**, 13185; (*e*) B. Wang, Y. Gao, H.-W. Li, Z.-P. Hu and Y. Wu, *Org. Biomol. Chem.*, 2011, **9**, 4032; (*f*) P. Wang, L. Duan and Y. Liao, *Microchem. J.*, 2019, **146**, 818; (*g*) A. Aliberti, P. Vaiano, A. Caporale, M. Consales, M. Ruvo and A. Cusano, *Sens. Actuators, B*, 2017, **247**, 727; (*h*) C. Li, E. Henry, N. K. Mani, J. Tang, J.-C. Brochon, E. Deprez and J. Xie, *Eur. J. Org. Chem.*, 2010, 2395; (*i*) G. Hasegawa, M. Kikuchie, Y. Kobayashi and Y. Saito, *J. Biochem. Biophys. Methods*, 2005, **63**, 33; (*j*) Y. Shiose, H. Kuga, H. Ohki, M. Ikeda, F. Yamashita and M. Hashida, *Bioconjugate Chem.*, 2009, **20**, 60; (*k*) P. Srivastava, M. Shahid and A. Misra, *Org. Biomol. Chem.*, 2011, **9**, 5051; (*l*) H. Itoh, S. Matsuoka, M. Kreir and M. Inoue, *J. Am. Chem. Soc.*, 2012, **134**, 14018; (*m*) G. Angelici, R. T. Carrera, G. Luppi and C. Tomasini, *Eur. J. Org. Chem.*, 2008, 3552; (*n*) L. He, H. Tao, S. Koo, G. Chen, A. Sharma, Y. Chen, I.-T. Lim, Q.-Y. Cao and J. S. Kim, *ACS Appl. Bio Mater.*, 2018, **1**, 871.

15 Dansyl containing amino acids/peptides as probes: (*a*) L. N. Neupane, J. M. Kim, C. R. Lohani and K.-H. Lee, *J. Mater. Chem.*, 2012, **22**, 4003; (*b*) P. Wang, J. Wu, L. Liu, P. Zhou, Y. Ge, D. Liu, W. Liu and Y. Tang, *Dalton Trans.*, 2015, **44**, 18057; (*c*) M.-H. Yang, C. R. Lohani, H. Cho and K.-H. Lee, *Org. Biomol. Chem.*, 2011, **9**, 2350; (*d*) T. R. Young, C. J. K. Wijekoon, B. Spyrou, P. S. Donnelly, A. G. Wedd and Z. Xiao, *Metallomics*, 2015, **7**, 567; (*e*) L. Fu, J. Mei, J.-T. Zhang, Y. Liu and F.-L. Jiang, *Luminescence*, 2013, **28**, 602; (*f*) P. Wanga, K. Chen and Y. Ge, *J. Lumin.*, 2019, **208**, 495; (*g*) W. Deng, S. Li, M. Zhou, M. Zheng, P. Weng and Y. An, *Spectrochim. Acta, Part A*, 2024, **315**, 124306; (*h*) C. R. Lohani, L. N. Neupane, J.-m. Kim and K.-H. Lee, *Sens. Actuators, B*, 2012, **161**, 1088; (*i*) J. Song, Y. Liu, C. Wang, B. Xu and L. Zhao, *J. Fluoresc.*, 2023, **33**, 2515; (*j*) L. N. Neupane and K.-H. Lee, *Tetrahedron Lett.*, 2013, **54**, 5007; (*k*) B. R. White and J. A. Holcombe, *Talanta*, 2007, **71**, 2015; (*l*) K. H. Jung, E.-T. Oh, H. J. Park and K.-H. Lee, *Biosens. Bioelectron.*, 2016, **85**, 437; (*m*) P. Wang, L. Liu, P. Zhou, W. Wu, J. Wu, W. Liu and Y. Tang, *Biosens. Bioelectron.*, 2015, **72**, 80; (*n*) R. Nagarajan, H.-I. Ryoo, B. D. Vanjare, N. G. Choi and H. H. Lee, *J. Photochem. Photobiol., A*, 2021, **418**, 113435; (*o*) Y. Liu, B. Jiang, L. Zhao, L. Zhao, Q. Wang and C. W. B. Xu, *Spectrochim. Acta, Part A*, 2021, **261**, 120009.

16 Dansyl containing amino acids/peptides as probes: (*a*) C. R. Lohani, J. M. Kim and K.-H. Lee, *Tetrahedron*, 2011, **67**, 4130; (*b*) S. Xue, P. Wang and K. Chen, *Spectrochim. Acta, Part A*, 2020, **226**, 117616; (*c*) P. Wang, L. Duan and Y. Liao, *Microchem. J.*, 2019, **146**, 818; (*d*) A. V. Saura, M. J. Marín, M. I. Burguete, D. A. Russell, F. Galindo and S. V. Luis, *Org. Biomol. Chem.*, 2015, **13**, 7736.

17 Dansyl containing amino acids/peptides as probes: (*a*) Y. Abe, S. Fukui, Y. Koshiji, M. Kobayashi, T. Shoji, S. Sugata, H. Nishizawa, H. Suzuki and K. Iwata, *Biochim. Biophys. Acta*, 1999, **1433**, 188; (*b*) A. J. Ryan, J. Ghuman, P. A. Zunszain, C.-w. Chung and S. Curry, *J. Struct. Biol.*, 2011, **174**, 84.

18 Dansyl containing amino acids/peptides as probes: (*a*) B. P. Joshi, W.-M. Cho, J. Kim, J. Yoon and K.-H. Lee, *Bioorg. Med. Chem. Lett.*, 2007, **17**, 6425; (*b*) P. Wang, J. Wu, P. Zhou, W. Liu and Yu Tang, *J. Mater. Chem. B*, 2015, **3**, 3617; (*c*) T. Watanabe, M. Imoto, H. Taniguchi, K. Kinoshita and K. Umezawa Jr., *Bioorg. Med. Chem. Lett.*, 1998, **8**, 1301.

19 Dansyl containing amino acids/peptides as probes: (*a*) W. Zeng, W. Miao, M. L. Puil, G. Shi, J. Biggerstaff, G. Kabalka and D. Townsend, *Biochem. Biophys. Res. Commun.*, 2010, **398**, 571; (*b*) W. Zeng, W. Miao, G. Kabalka, M. L. Puil, J. Biggerstaff and D. Townsend, *Tetrahedron Lett.*, 2008, **49**, 6429; (*c*) M. Tang, J. Huang, X. Weng, L. Yang, M. Liu, M. Zhou, X. Wang, J. Gao, W. Yi, W. Zeng, L. Sun and Y. Cao, *Apoptosis*, 2015, **20**, 410; (*d*) W. Zeng, W. Miao, G. Kabalka, M. L. Puil, J. Biggerstaff and D. Townsend, *Tetrahedron Lett.*, 2008, **49**, 6429.

20 Dansylated bio-active compounds: (*a*) I. Berque-Bestel, J.-L. Soulier, M. Giner, L. Rivail, M. Langlois and S. Sicsic, *J. Med. Chem.*, 2003, **46**, 2606; (*b*) L. Prokai, K. Prokai-Tatrai, A. Zharikova, X. Li and J. R. Rocca, *J. Med. Chem.*, 2001, **44**, 1623; (*c*) C. D. Navo, A. Asín, E. Gómez-Orte, M. I. Gutiérrez-Jiménez, I. Compañón, B. Ezcurra, A. Avenoza, J. H. Busto, F. Corzana, M. M. Zurbano, G. Jiménez-Osés, J. Cabello and J. M. Peregrina, *Chem. – Eur. J.*, 2018, **24**, 7991; (*d*) I. Berezowska, C. Lemieux, N. N. Chung, B. Zelent and P. W. Schiller, *Acta Biochim. Pol.*, 2004, **51**, 107.

21 Incorporation of dansylated amino acids into proteins: (*a*) T. Hohsaka;, N. Muranaka, C. Komiyama, K. Matsui, S. Takaura, R. Abe, H. Murakami and M. Sisido, *FEBS Lett.*,

2004, **560**, 173; (*b*) L. E. Steward, C. S. Collins, M. A. Gilmore, J. E. Carlson, J. B. A. Ross and A. R. Chamberlin, *J. Am. Chem. Soc.*, 1997, **119**, 6; (*c*) D. Summerer, S. Chen, N. Wu, A. Deiters, J. W. Chin and P. G. Schultz, *Proc. Natl. Acad. Sci. U. S. A.*, 2006, **103**, 9785.

22 (*a*) K. Vermeire, A. Lisco, J.-C. Grivel, E. Scarbrough, K. Dey, N. Duffy, L. Margolis, T. W. Bell and D. Schols, *Biochem. Pharmacol.*, 2007, **74**, 566; (*b*) D. Iwan, K. Kamińska, M. Denel-Bobrowska, A. B. Olejniczak and E. Wojaczyńska, *Biomed. Pharmacother.*, 2022, **153**, 113473; (*c*) G. M. Bonora, G. Palu, C. D. Santos, M. A. Biasolo and G. A. Meloni, *Farmaco*, 1989, **44**, 951.

23 (*a*) I. Banerjee, Y. Yamauchi, A. Helenius and P. Horvath, *PLoS One*, 2013, **8**, e68450; (*b*) N. Kumar, I. M. Taily, C. Singh, S. Kumar, R. S. Rajmani, D. Chakraborty, A. Sharma, P. Singh, K. G. Thakur, R. Varadarajan, R. P. Ringe, P. Banerjee and I. Banerjee, *PLoS Pathog.*, 2023, **19**, e1011358; (*c*) T. Pathak, K. Gupta, N. Kumar and I. Banerjee, *Monitoring Influenza A Virus Entry Using Quantitative Fluorescence Microscopy*, Humana, New York, 2025, vol. 2890, DOI: 10.1007/978-1-0716-4326-6_5; (*d*) I. Banerjee, Y. Miyake, S. P. Nobs, C. Schneider, P. Horvath, M. Kopf, P. Matthias, A. Helenius and Y. Yamauchi, *Science*, 2014, **346**, 473.

24 J. Li, J. Xu, B. Chen, Q. Pang, J. Shen, K. Wang and P. Zhang, *J. Org. Chem.*, 2025, **90**, 1354 and references therein.

25 (*a*) A literature survey revealed that 8-aminoquinoline is an efficient and commonly used directing group for substrates involving aliphatic sp^3 C–H bond functionalization. Presumably, for substrates involving aliphatic sp^3 C–H bond functionalization, the palladacycle formation involving the 8-aminoquinoline directing group may be relatively quick when compared to the other directing groups such as 2-(methylthio)aniline and 4-amino-2,1,3-benzothiadiazole in the catalytic cycle.[2,4–6] The palladacycle formation involving 2-(methylthio)aniline and 4-amino-2,1,3-benzothiadiazole directing groups may be relatively slow/sluggish or gentle in the catalytic cycles. While the efficiency of 8-aminoquinoline sometime deters the selectivity, 2-(methylthio)aniline and 4-amino-2,1,3-benzothiadiazole were found to be somewhat useful. While a fully convincing study is not available, literature reports including our recent studies reveal the utility and efficiency of the 8-aminoquinoline directing group: (*b*) See ref. 4*p* and 6*i*,*t*,*u*.

26 (*a*) In all reactions, we used AgOAc as an additive; while its role is not fully understood, it is believed to function, among other possibilities, as an iodide ion scavenger in the proposed catalytic cycle. After the reaction, the solution appears to be brown/black; the solvent is evaporated, and the residue is generally subjected to column chromatography. The residual salts, including the generated AgI, are believed to remain trapped in the column. For papers revealing the role of silver salts, see: (*b*) M. D. Lotz, N. M. Camasso, A. J. Canty and M. S. Sanford, *Organometallics*, 2017, **36**, 165; (*c*) K. L. Bay, Y.-F. Yang and K. N. Houk, *J. Organomet. Chem.*, 2018, **864**, 19; (*d*) M. Anand, R. B. Sunoj and H. F. Schaefer III, *J. Am. Chem. Soc.*, 2014, **136**(15), 5535; (*e*) T. Bhattacharya, S. Dutta and D. Maiti, *ACS Catal.*, 2021, **11**, 9702.