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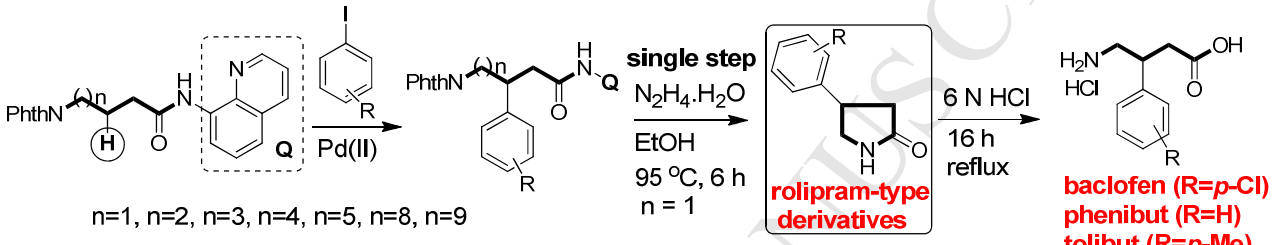

n=1, n=2, n=3, n=4, n=5, n=8, n=9

assembling of
-libraries of *β*-arylated aminoalkanoic acid (unnatural amino acid) derivatives
-rolipram-type derivatives & baclofen, phenibut and tolibut hydrochloride

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Assembling of medium/long chain-based β-arylated unnatural amino acid derivatives via the Pd(II)-catalyzed sp^3 β-C-H arylation and a short route for rolipram-type derivatives

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ABSTRACT

In this paper, we report the assembling of libraries of β-arylated short/medium/long chain-based non-α-amino acid (aminoalkanoic acid) derivatives via the Pd(II)-catalyzed, bidentate directing group 8-aminoquinoline-aided sp^3 β-C-H activation/arylation method. Short/medium chain-based unnatural amino acid derivatives containing an aryl group at the β-position are promising small molecules with therapeutic properties. Thus, it is necessary to enrich the libraries of short/medium/long chain-based unnatural amino acid derivatives containing an aryl group at the β-position. Considering the importance of β-arylated short/medium/long chain-based non-α-amino acid derivatives, an inclusive attention was paid to explore the Pd(II)-catalyzed sp^3 β-C-H arylation of short/medium/long chain-based non-α-amino acids. Representative synthetic transformations including a short route for the assembling of rolipram and related compounds and 3-arylated GABA derivatives such as, baclofen, phenibut and tolibut were shown using selected β-C-H arylated non-α-amino acid derivatives.

1. Introduction

Proteinogenic α-amino acids are indispensable small molecules of life[1] and non-proteinogenic or unnatural amino acids are those not encoded and discovered in any organism. Markedly, numerous unnatural amino acids and their derivatives have also received extensive attention in various fields. In particular, unnatural amino acids are sought after by the pharmaceutical industry for their promising biological properties.[2,3] Apart from natural and unnatural α-amino acid derivatives, some short/medium chain-based aminoalkanoic acids (non-α-amino acids) containing an amino group at the β- or γ- or δ-position have also been found in organisms.[4-7] For examples; (a) β-alanine (**1a**) is produced by aspartate 1-decarboxylase and a precursor to coenzyme A,[4] (b) γ-aminobutyric acid (**1d**, GABA) is an inhibitory neurotransmitter in animals,[5] (c) δ-aminolevulinic acid (**1b**) is an intermediate in the tetrapyrrole biosynthesis pathway[6] and (d) 4-aminobenzoic acid (**1c**, PABA) is an intermediate in the folate biosynthesis pathway[7] (Figure 1).

Various short/medium chain-based aminoalkanoic acids (non-α-amino acids) possessing an aryl group at the β-position are noteworthy small molecules and they display valuable pharmacological properties (Figure 1).[8-13] Firstly, γ-aminobutyric acid (**1d**, GABA) and especially, various β-arylated derivatives of GABA (e.g., **2a-d**) are used as drug molecules in treating various central nervous system (CNS) disorders. Some of them are used as anticonvulsant, sedative and anxiolytic, analgesic, tranquilizing agents (e.g., baclofen (**2a**),[9] phenibut (**2b**)[10] and tolibut (**2c**)[11]). Along this line, some piracetam-based GABA derivatives are also used as drug molecules. E.g., Phenotropil (phenylpiracetam)[12] is known to exhibit antidepressant, anticonvulsant, anxiolytic effects and similarly, rolipram (**2d**)[13] is an antidepressant agent. Next, some β-arylated δ-aminopentanoic acid derivatives (e.g., homobaclofen derivative **3**) have been found with pharmacological activity (e.g., $GABA_B$-agonistic activity).[14] Next, β-arylated ε-aminohexanoic acid derivative **4** was used as a starting material to assemble various bioactive benzazepinones.[15] Given their importance, various classical and multistep synthetic procedures have been used to construct short/medium chain-based aminoalkanoic acids (non-α-amino acids) possessing an aryl group at the β-position.[8-15]

The transition metal-catalyzed, bidentate directing group-aided sp^3 C-H activation/functionalization has emerged as a vital synthetic strategy in organic synthesis.[16,17] In particular, the Pd(II)-catalyzed, bidentate directing group (e.g. 8-aminoquinoline)-aided sp^3 C–H activation/functionalization was studied using a wide range of aliphatic and alicyclic carboxamides[18-20] and α-amino acid derivatives.[21] Considering the recent developments in the field of bidentate directing group-aided sp^3 C-H activation/functionalization

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involving α-amino acid derivatives, the direct introduction of different aryl groups at the β-position of short/medium/long chain-based aminoalkanoic acids (non-α-amino acids) via the C-H activation would afford an entry into libraries of β-arylated aminoalkanoic acid (unnatural amino acid) derivatives. A literature survey revealed that while C-H functionalization of various α-amino acid derivatives have been well studied, however, there have been only a few attempts pertaining to the Pd(II)-catalyzed, directing group-aided sp^3 β-C-H arylation of short/medium/long chain-based aminoalkanoic acids (non-α-amino acids).[22,23] Explicitly, the Pd(II)-catalyzed C-H functionalization was explored using only two short/medium chain-based aminoalkanoic acids (non-α-amino acids) and those two are, γ-aminobutyric acid (**1d**)[22] and ε-aminohexanoic acid (**1f**).[23]

Conversely, considerable attention was not paid towards the sp^3 β-C-H arylation of other medium/long chain-based aminoalkanoic acids (non-α-amino acids), such as **1e,g-j** (Figures 1 and 2). Given the importance of various short/medium/long chain-based aminoalkanoic acid (non-α-amino acid) derivatives, especially

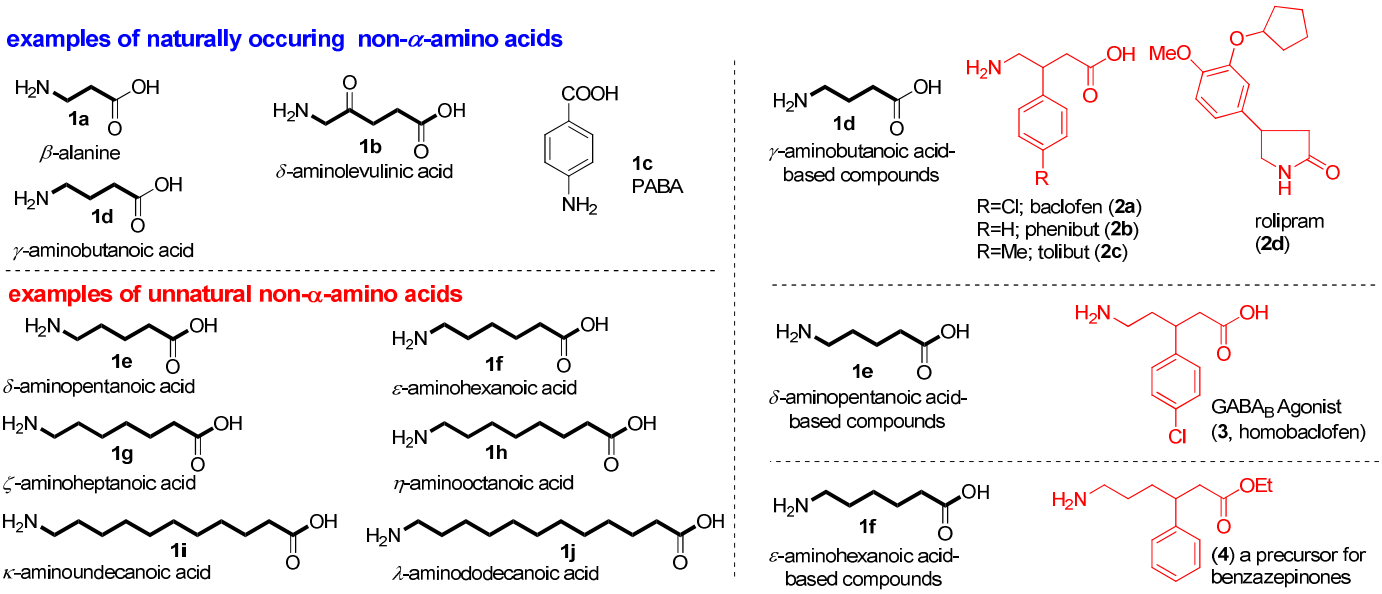


Figure 1. Short/medium/long chain-based non-α-amino acid derivatives.

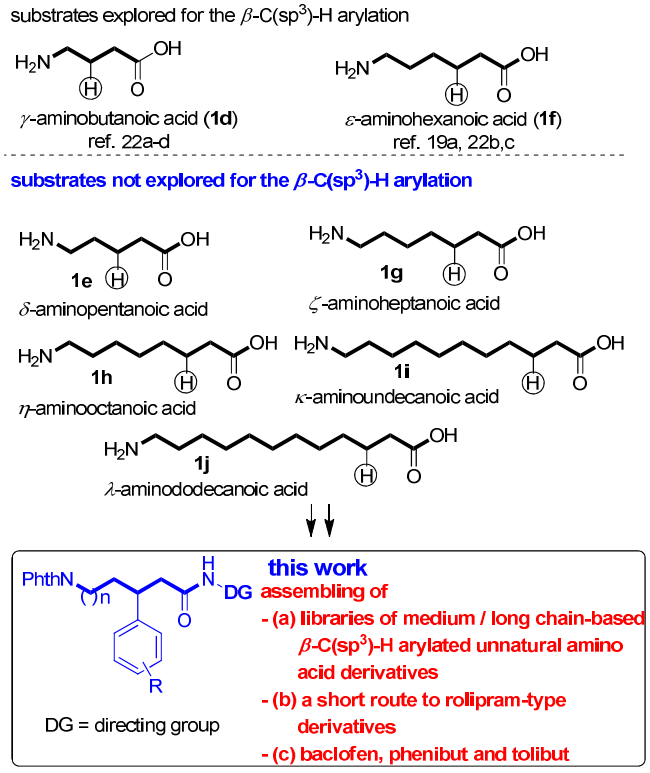


Figure 2. β-Arylated short/medium/long chain-based non-α-amino acid derivatives.

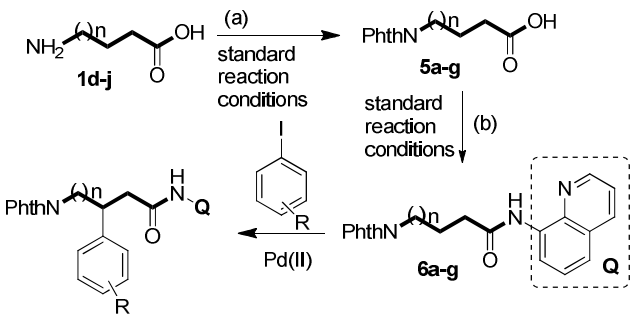
aminoalkanoic acids possessing an aryl group at the β-position with promising therapeutic properties, it will be useful to enrich the libraries of short/medium/long chain-based aminoalkanoic acid (non-α-amino acid) derivatives.

Accordingly, in continuation of our interest on the C-H activation reactions, herein we report the sp^3 β-C-H arylation of various aminoalkanoic acids (non-α-amino acids). We have paid an inclusive attention to assemble/enrich the libraries of different β-arylated aminoalkanoic acid (non-α-amino acid) and rolipram-type derivatives. While there have been a few attempts of synthesis of β-arylated γ-aminobutyric acid and ε-aminohexanoic acid derivatives via the β-C-H arylation, we have added some more examples to their corresponding libraries and it was necessary to prepare different examples of β-arylated γ-aminobutyric acid derivatives to attempt a short route for assembling rolipram and related derivatives.

2. Results and Discussion

To begin the assembling of β-C-H arylated medium/long chain-based aminoalkanoic acids (non-α-amino acids) derivatives via the Pd(II)-catalyzed, directing group-aided β-C-H arylation, initially we prepared the required starting materials **6a-g** possessing the directing group 8-aminoquinoline from their corresponding *N*-protected aminoalkanoic acids **5a-g** (Scheme 1). Though a few reaction conditions of sp^3 β-C-H arylation involving γ-aminobutyric acid and ε-aminohexanoic acid derivatives have been already reported under different reaction conditions,[22,23] in order to get the best reaction condition in our hand, we performed some optimization reactions using different Pd catalysts, additives and solvents (Table 1). At first, we heated a mixture of substrate **6a**, ArI (**7a**) and Pd(OAc)$_2$ catalyst (10 mol%) in the absence of any additive at 110 ^{o}C for 24 h and this

reaction did not afford the *β*-C-H arylated product **8a** (entry 1, Table 1). Next, the same reaction was carried out in the presence of only AgOAc without any Pd(II) catalyst and this reaction also did not afford the *β*-C-H arylated product **8a** (entry 2, Table 1). Typically, the bidentate directing group 8-aminoquinoline-aided *β*-C-H arylation of carboxamides have been performed using the Pd(II) catalyst and also an additive (e.g., AgOAc or Ag_2CO_3 or K_2CO_3), which will help as a halide ion scavenger and to regenerate the palladium(II) catalyst in the catalytic cycle.[18-20] Accordingly, next we heated a mixture of substrate **6a**, ArI (**7a**, 4-5 equiv), $Pd(OAc)_2$ catalyst (10 mol%) and AgOAc additive in toluene at 110 ^oC for 24 h. This reaction afforded the *β*-C-H arylated *γ*-aminobutyric acid (GABA) derivative **8a** in 70-89% yields (entries 3 and 4, Table 1). The Pd(II)-catalyzed arylation of **6a** with **7a** in the presence of AgOAc in ^{t}AmylOH instead of toluene also afforded the product **8a** in 83% yield (entry 5, Table 1). Then, we performed the arylation of **6a** using different palladium catalysts, which also afforded the *β*-C-H arylated derivative **8a** in 50-88% yields (entries 6-8, Table 1). The Pd(II)-catalyzed arylation of **6a** was also performed using different additives (entries 9-14, Table 1). The reactions involving Ag_2CO_3 or Na_2CO_3 as an additive only were fruitful and the product **8a** was obtained in 77 and 28% yields, respectively. We also performed the Pd(II)-catalyzed arylation of **6a** using 4-bromotoluene or 4-chlorotoluene, which were not fruitful (entries 15-18, Table 1).



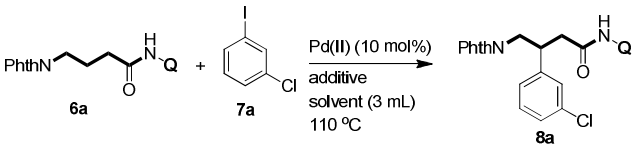
Reagents: (a) phthalic anhydride. (b) $SOCl_2$ and 8-aminoquinoline.

Scheme 1. Preparation of short/medium/long chain-based non-*α*-amino acid derivatives linked with the directing group.

Having the suitable reaction conditions in hand for the Pd(II)-catalyzed *β*-C-H arylation of *γ*-aminobutyric acid (GABA) substrate **6a** with **7a**, we next intended to enrich the library of *β*-C-H arylated *γ*-aminobutyric acid via the Pd(II)-catalyzed *β*-C-H arylation of substrate **6a**. Towards this, we performed the Pd(II)-catalyzed arylation of **6a** using a variety of aryl iodides (Scheme 2). The Pd(II)-catalyzed arylation of **6a** with aryl iodides containing different halogen substituents at the *meta* or *para* position afforded the corresponding *β*-C-H arylated *γ*-aminobutyric acid (GABA) derivatives **8a-f** in good to high yields (64-92%, Scheme 2). Next, the Pd(II)-catalyzed arylation of **6a** with different di- and trisubstituted aryl iodides afforded the corresponding *β*-C-H arylated *γ*-aminobutyric acid derivatives **8g-i** in 57-74% yields (Scheme 2). The Pd(II)-catalyzed arylation of **6a** with PhI and aryl iodides containing the electron-withdrawing and donating groups (e.g., alkoxy, alkyl, NO_2, Ac, CN, ester, CF_3) at the *para or meta* position afforded the corresponding *β*-C-H arylated *γ*-aminobutyric acid derivatives **8j-v** in good to high yields (54-92%, Scheme 2). Further, the Pd(II)-catalyzed arylation of **6a** with different heteroaryl iodides also afforded the corresponding *β*-C-H arylated *γ*-aminobutyric acid derivatives **8w,x** in 72-73% yields (Scheme 2).

After assembling various *β*-C-H arylated *γ*-aminobutyric acid (GABA) derivatives **8**, we then wished to expand the substrate scope of this work by assembling various *β*-arylated medium chain-based non-*α*-amino acid derivatives (Schemes 3-5). In this regard, initially we performed the Pd(II)-catalyzed *β*-C-H arylation of medium chain carboxamide **6b**, which was derived from *δ*-aminopentanoic acid. The arylation of **6b** with different aryl iodides and a heteroaryl iodide afforded the corresponding *β*-C-H arylated *δ*-aminopentanoic acid (homo GABA) derivatives **9a-e** in 70-85% yields (Scheme 3). Next, we performed the Pd(II)-catalyzed *β*-C-H arylation of medium chain carboxamide **6c**, which was derived from *ε*-aminohexanoic acid. The arylation of **6c** with different aryl iodides afforded the corresponding *β*-C-H arylated *ε*-aminohexanoic acid derivatives **10a-d** in 59-79% yields (Scheme 3). Then, the Pd(II)-catalyzed *β*-C-H arylation of medium chain carboxamide **6d** (which was derived from *ζ*-aminoheptanoic acid) using a heteroaryl iodide and different aryl iodides afforded the corresponding *β*-C-H arylated *ζ*-aminoheptanoic acid derivatives **11a-e** in 65-72% yields (Scheme 3).

Table 1. Optimization Reactions. Pd(II)-catalyzed arylation of **6a**.



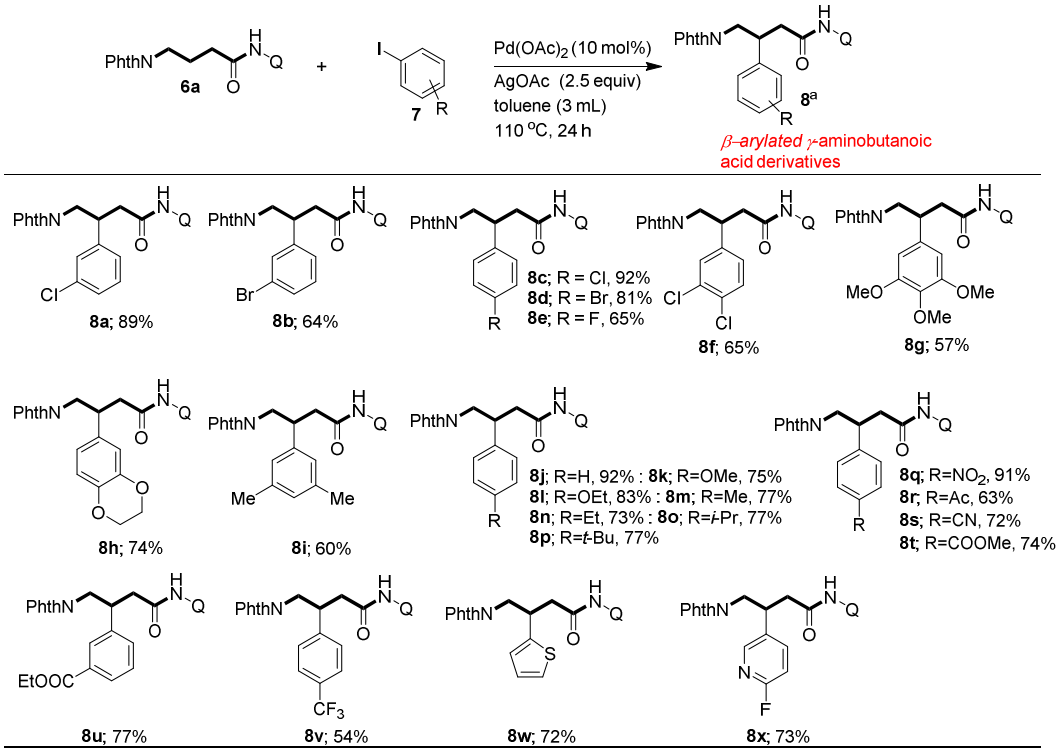
Entry[a]	**6a** (mmol)	Pd(II) cat.	Additive	**8a**: Yield (%)
1	0.15	$Pd(OAc)_2$	-	0
2	0.15	-	AgOAc	0
3[b]	0.2	$Pd(OAc)_2$	AgOAc	89
4[c]	0.2	$Pd(OAc)_2$	AgOAc	70
5[d]	0.2	$Pd(OAc)_2$	AgOAc	83
6	0.2	$PdCl_2$	AgOAc	88
7	0.2	$PdCl_2(MeCN)_2$	AgOAc	50
8	0.2	$Pd(TFA)_2$	AgOAc	85
9	0.15	$Pd(OAc)_2$	KOAc	0
10	0.15	$Pd(OAc)_2$	K_2CO_3	0
11	0.15	$Pd(OAc)_2$	Cs_2CO_3	0
12	0.2	$PdCl_2(MeCN)_2$	KOAc	0
13[b]	0.15	$Pd(OAc)_2$	Ag_2CO_3	77
14	0.15	$Pd(OAc)_2$	Na_2CO_3	28
15	0.2	$Pd(OAc)_2$	AgOAc	**8m**; (0)[e] (0)[f]
16	0.2	$PdCl_2$	AgOAc	**8m**; (0)[e] (0)[f]
17	0.2	$Pd(OAc)_2$	Ag_2CO_3	**8m**; (0)[e] (0)[f]
18[d]	0.2	$Pd(OAc)_2$	AgOAc	**8m**; (0)[e] (0)[f]

[a] Reactions were carried out using **6a** (0.15-0.2 mmol, 1 equiv), ArI (5 equiv), additive (2.5 equiv) for 24 h in toluene. Q = refers to the directing group. [b] Reaction time = 15 h. [c] 4 equiv of ArI. [d] ^{t}AmylOH was instead of toluene. [e] The reaction was done using 4-bromotoluene for 24/48 h. [f] The reaction was done using 4-chlorotoluene for 24/48 h.

Subsequently, we paid our attention to assemble various *β*-arylated long chain-based non-*α*-amino acid derivatives (Scheme 4). Towards this, we performed the Pd(II)-catalyzed *β*-C-H arylation of long chain carboxamide **6e**, which was derived from *η*-aminooctanoic acid. The reaction of **6e** with different aryl iodides and a heteroaryl iodide afforded the corresponding *β*-C-H arylated *η*-aminooctanoic acid derivatives **12a-e** in 61-74% yields (Scheme 4). Next, we carried out the Pd(II)-catalyzed *β*-C-H arylation of long chain carboxamide **6f**, which was derived from *κ*-aminoundecanoic acid. The reaction of **6f** with different aryl iodides and a heteroaryl iodide afforded the corresponding *β*-C-H arylated *κ*-aminoundecanoic acid derivatives **13a-e** in 55-77% yields (Scheme 4). Furthermore, the Pd(II)-catalyzed *β*-C-H arylation of long chain carboxamide **6g** (which was derived from *λ*-aminododecanoic acid)

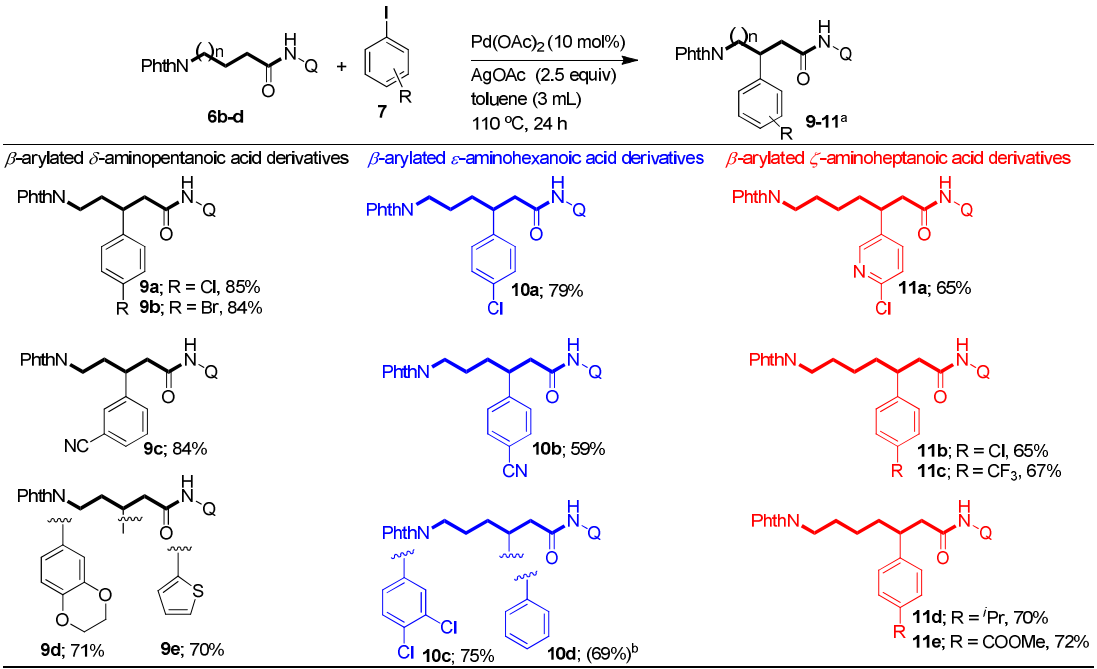
using different aryl iodides and a heteroaryl iodide afforded the corresponding *β*-C-H arylated *λ*-aminododecanoic acid derivatives **14a-e** in 70-76% yields (Scheme 4).

Subsequently, we were interested to expand the scope of this method and utility of the *β*-C-H arylated non-*α*-amino acid derivatives prepared in this work. In this regard, we intended to assemble rolipram (**2d**) and some 3-arylated piracetam derivatives similar to rolipram (**2d**). Towards this, it was necessary to assemble the *β*-C-H arylated *γ*-aminobutyric acid (GABA) derivative **16** (Scheme 5), which can be subjected to the lactamization to afford rolipram (**2d**). Initially, we performed the Pd(II)-catalyzed *β*-C-H arylation of **6a** with a desired aryl iodide **15**, which successfully afforded the product **16** in 69% yield (Scheme 5). Then, we also intended to assemble some *β*-C-H arylated long chain-based amino acid derivatives similar to the product **16** by using the ArI **15**.



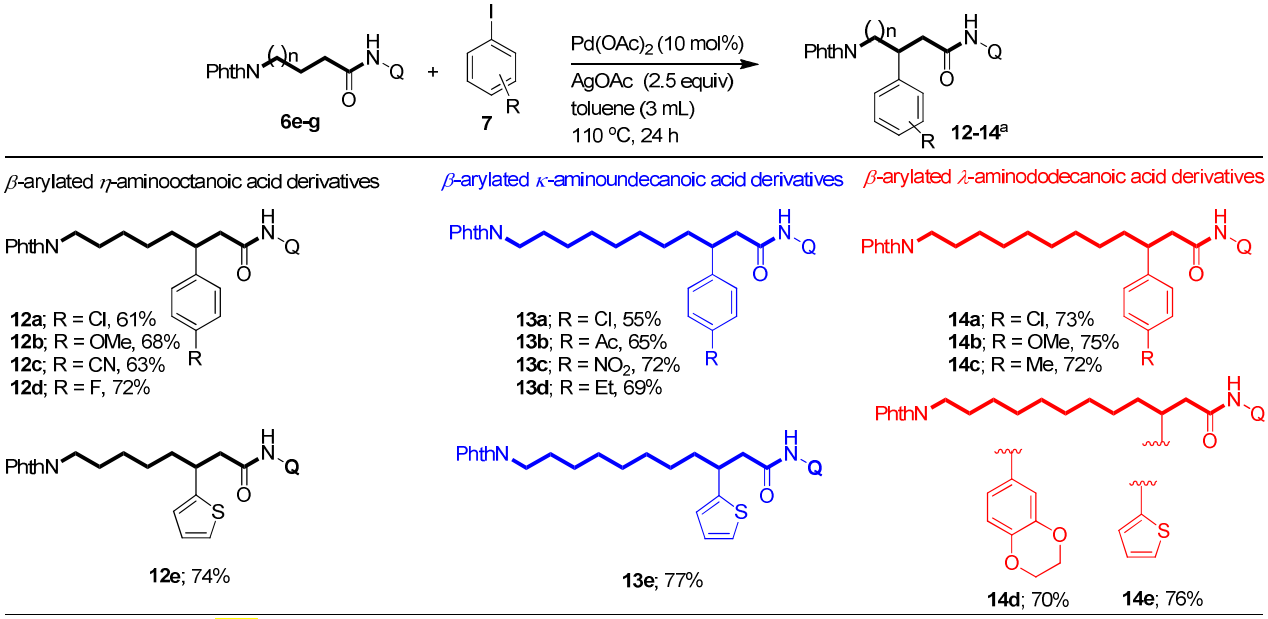
[a] Reactions are done using **6a** (0.15-0.2 mmol) and an appropriate aryl iodide (0.9-1 mmol).

Scheme 2. Enriching the library of *β*-C-H arylated *γ*-aminobutyric acid (GABA) derivatives with the Pd(II)-catalyzed arylation of **6a**.



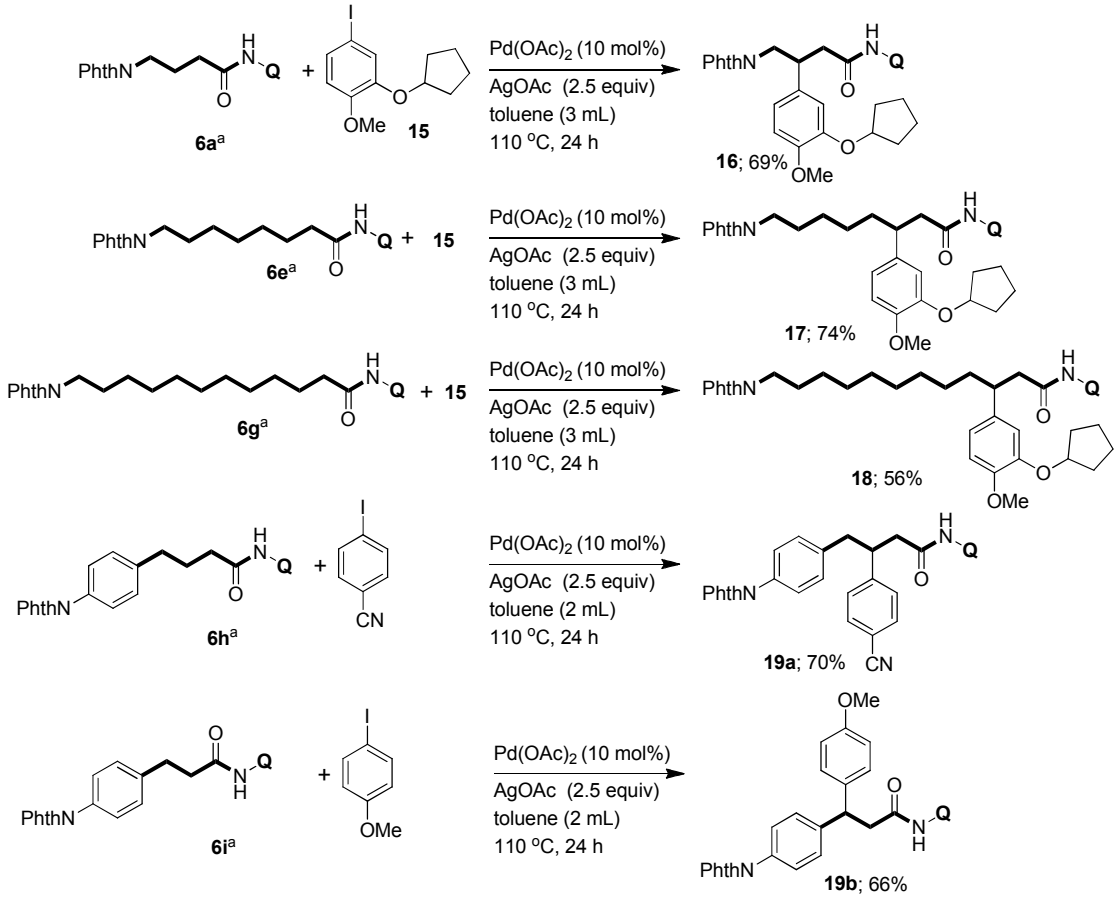
[a] Reactions are done using **6b-d** (0.15-0.2 mmol) and an appropriate aryl iodide (0.9-1 mmol). [b] **6c** (2 mmol), PhI (5 equiv) and toluene (15 mL).

Scheme 3. Enriching the library of *β*-C-H arylated medium/long chain-based amino acid derivatives via the Pd(II)-catalyzed *β*-C-H arylation.



[a] Reactions are done using **6e-g** (0.15-0.2 mmol) and an appropriate aryl iodide (0.9-1 mmol).

Scheme 4. Enriching the library of *β*-C-H arylated medium/long chain-based amino acid derivatives via the Pd(II)-catalyzed *β*-C-H arylation.



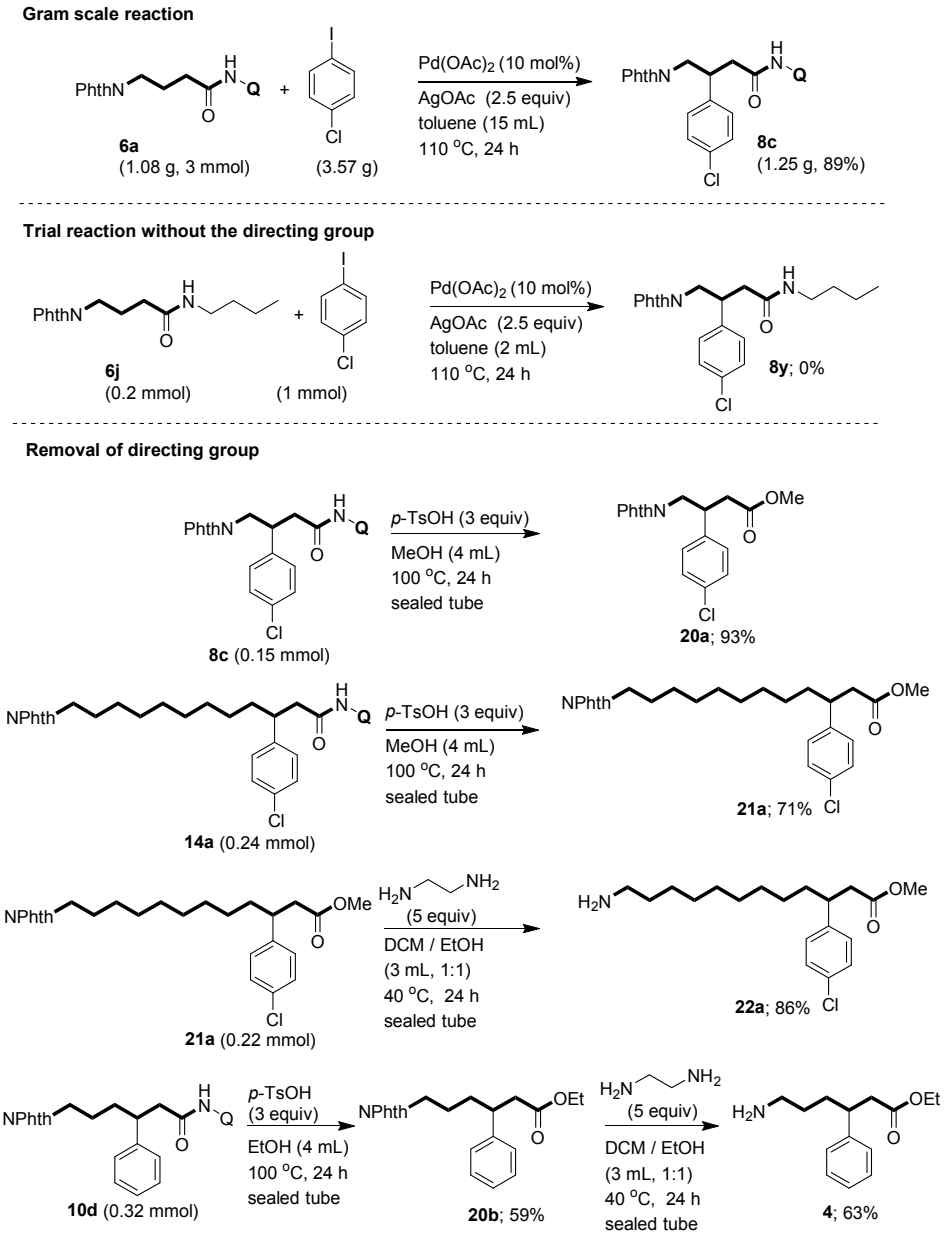
[a] Reactions are done using **6a,e,g-i** (0.15-0.2 mmol) and an appropriate aryl iodide (0.9-1 mmol).

Scheme 5. The Pd(II)-catalyzed *β*-C-H arylation of **6a,e,g-i**.

The Pd(II)-catalyzed β-C-H arylation of long chain carboxamides **6e** and **6g** with the **15** afforded the corresponding β-C-H arylated carboxamides **17** (74%) and **18** (56%) in moderate yields (Scheme 5). We then paid our attention towards the β-C-H arylation of aromatic amino acids and in this regard, we assembled the substrates **6h,i** (Scheme 5) possessing the directing group 8-aminoquinoline from their corresponding *N*-protected aromatic amino acids (**5h,i**). Then, we performed the Pd(II)-catalyzed β-C-H arylation of aromatic amino acid substrates **6h,i** with different aryl iodides, which afforded the corresponding β-C-H arylated aromatic amino acid derivatives **19a** (70%) and **19b** (66%) in moderate yields (Scheme 5).

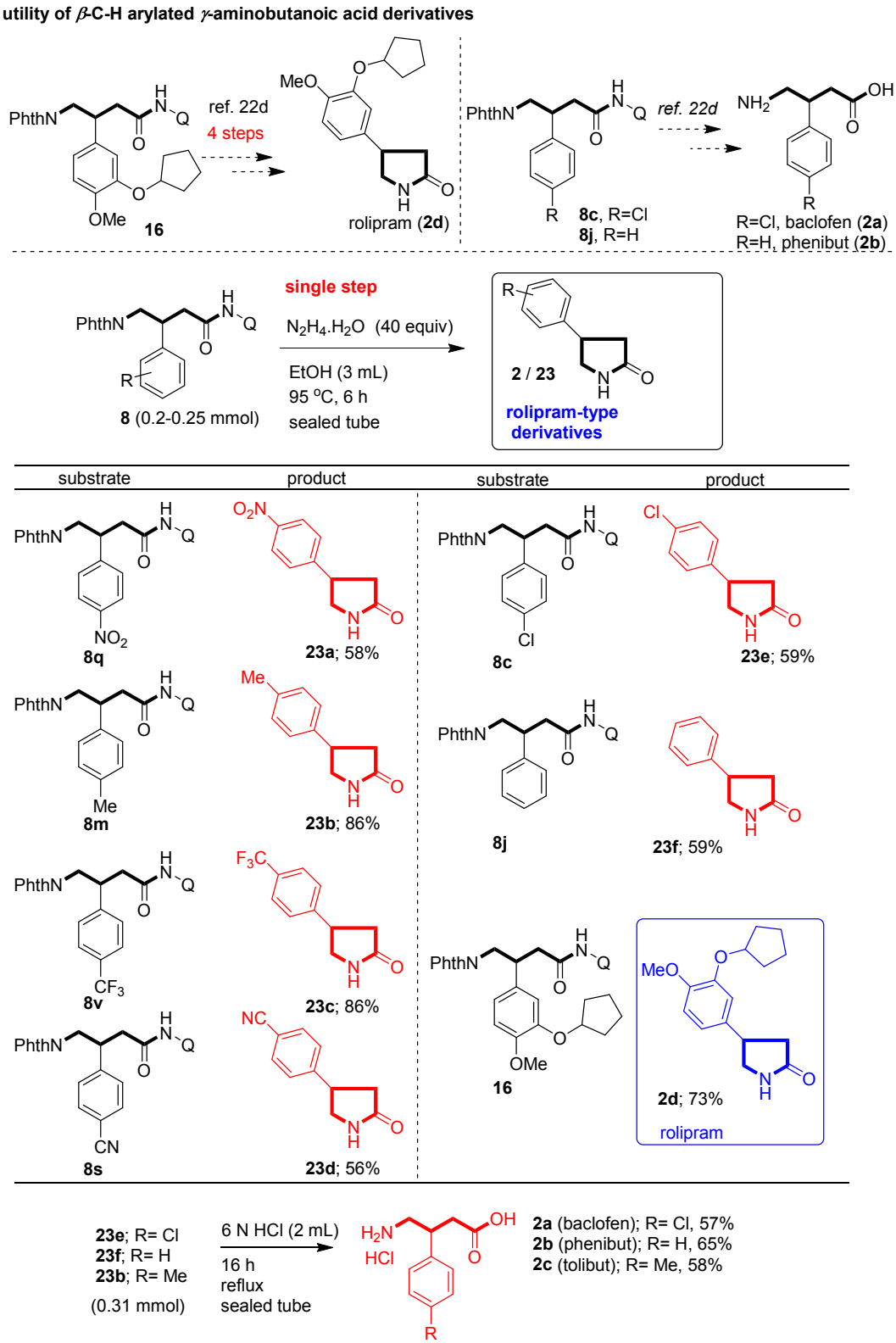
Interestingly, the Pd(II)-catalyzed arylation simple amide **6j** without the directing group 8-aminoquinoline failed to afford the β-C-H arylated γ-aminobutyric acid derivative **8y** (Scheme 6). Then, we focused our attention to remove the directing group 8-aminoquinoline from the representative β-C-H arylated products. In this regard, we treated the β-C-H arylated γ-aminobutyric acid derivative **8c** with *p*-TsOH in MeOH at 100 ^{o}C for 24 h, which afforded the γ-aminobutyric acid ester **20a** in 93% yield (Scheme 6).

Similarly, treatment of the β-C-H arylated λ-aminododecanoic acid derivative **14a** with *p*-TsOH in MeOH at 100 ^{o}C for 24 h afforded the λ-aminododecanoic acid ester **21a** in 71% yield (Scheme 6). The



Scheme 6. Gram scale Pd(II)-catalyzed β-C-H arylation of **6a** and removal of directing group.

We also tried the Pd(II)-catalyzed, β-C-H arylation reaction in a gram scale and towards this, we heated a mixture of substrate **6a** (1.08 g), 1-chloro-4-iodobenzene (3.57 g), $Pd(OAc)_2$ catalyst (10 mol%) and AgOAc (2.5 equiv) in toluene at 110 ^{o}C for 24 h. This reaction afforded the β-C-H arylated γ-aminobutyric acid derivative **8c** in 89% yield (Scheme 6). A trial reaction comprising the Pd(II)-removal of the phthalimide group was also achieved by treating the phthalimide protected λ-aminododecanoic acid ester **21a** with ethylenediamine in DCM/EtOH at 40 ^{o}C for 24 h and this reaction afforded the λ-aminododecanoic acid ester **22a** in 86% yield (Scheme 6). Additionally, removal of the directing group from **10d** gave the compound **20b**, which was further converted into the compound **4** (Scheme 6) and the compound **4** was used as a precursor for benzazepinones.[15]



Scheme 7. Conversion of *β*-C-H arylated *γ*-aminobutyric acid derivatives **8**/**16** into rolipram-type compounds in a single step with hydrazine monohydrate in EtOH and synthesis of GABA derivatives **2a-c**.

Furthermore, we were interested to reveal the utility of representative *β*-C-H arylated non-*α*-amino acid derivatives. A literature survey revealed that the utility of some of the *β*-C-H arylated *γ*-aminobutyric acid derivatives, e.g., **8c,j** and **16** have been already reported.[22d] Accordingly, baclofen (**2a**) and phenibut (**2b**) were synthesized from **8c,j**, respectively and rolipram (**2d**) was synthesized from **16** in four steps.[22d] While we were interested in enriching the library of rolipram-type compounds and at the same time we wished to attempt the conversion of *β*-C-H arylated *γ*-aminobutyric acid derivatives **8**/**16** into rolipram-type compounds using minimum synthetic steps. With our efforts we found that the treatment of *β*-C-H arylated *γ*-aminobutyric acid derivatives **8**/**16** with hydrazine monohydrate in EtOH at 95 °C for 6 h afforded the

corresponding 3-arylated pyrrolidone derivatives **2d**/**23** in a single step (Scheme 7). Accordingly, various rolipram-type compounds were obtained in 56-86% yields from the corresponding substrates **8q,m,v,s,c,j**. Rolipram (**2d**) was obtained in 73% yield from the corresponding *β*-C-H arylated *γ*-aminobutyric acid derivative **16** in a single step (Scheme 7). Treatment of 3-arylated pyrrolidone derivatives **23b,e,f** with 6 N HCl at reflux for 16 h in sealed tube[24h] led to the construction of the corresponding 3-arylated GABA derivatives such as, baclofen (**2a**), phenibut (**2b**) and tolibut (**2c**) in 57-65% yields (Scheme 7).

In summary, we have shown the assembling of libraries of *β*-arylated short/medium/long chain-based aminoalkanoic acid (non-*α*-amino acid) derivatives via the Pd(II)-catalyzed, bidentate directing group 8-aminoquinoline-aided sp^3 *β*-C-H activation/arylation method. Given the promising therapeutic properties of short/medium chain-based aminoalkanoic acids (non-*α*-amino acids) containing an aryl group at the *β*-position, it is important to enrich the libraries of the *β*-arylated aminoalkanoic acids (non-*α*-amino acids). Accordingly, we paid an inclusive attention to study the Pd(II)-catalyzed sp^3 *β*-C-H arylation of various short/medium/long chain-based non-*α*-amino acids. Though there have been a few attempts on the Pd-catalyzed, bidentate directing group-aided sp^3 *β*-C-H arylation involving *γ*-aminobutyric acid (**1d**) and *ε*-aminohexanoic acid (**1f**), we have also enriched the library of *β*-arylated *γ*-aminobutyric acid and *ε*-aminohexanoic acid derivatives with further examples. We have shown a gram scale Pd(II)-catalyzed reaction and also removal of the directing group after the sp^3 *β*-C-H arylation. We have shown a short route for assembling rolipram and related compounds and also 3-arylated GABA derivatives such as, baclofen, phenibut and tolibut from their corresponding *β*-C-H arylated *γ*-aminobutyric acid derivatives **8**/**16**.

3. Experimental Section

3.1. General information. The ^{1}H and ^{13}C{H} NMR spectra of all compounds have been recorded in 400 and ~101 MHz spectrometers by using TMS as an internal standard, respectively. The HRMS analysis data of samples reported here were obtained from QTOF mass analyzer by ESI method. The IR spectra of samples reported here were recorded as neat or thin films. Column chromatography purification of crude reaction mixtures/samples was carried out on silica gel (100−200 mesh). Thin layer chromatography (TLC) analyses were carried out on alumina or silica gel plates. The components of TLC analysis were visualized by observation under iodine vapor. Reactions were performed in dry solvents (prepared using standard drying methods) under a nitrogen atm wherever required. Isolated yields of all the *β*-C-H arylated products are reported and yields were not optimized. The compounds **2a**,[22d,24h] **2b**,[22d,24h] **2c**,[24h] **2d**,[22d,24i] **4**,[15] **5a**,[24a] **5b**,[24b] **5c**,[24c] **5e**,[24d] **5f**,[24e] **5i**,[24f] **6a**,[24g] **6c**,[19b] **8c**,[22d] **8j**,[22d] **8k**,[22d] **8w**,[22d] **8x**,[22d] **10d**,[22b] **16**,[22d] **23b**,[24h] **23c**,[24i] **23e**,[24h] and **23f**[24h] are known compounds and their characterization data are reported in the literature and we have also included their corresponding NMR spectra in the supplementary data section. The preparation of **15** was carried out using the literature method from 2-methoxyphenol (via acetylation, iodination followed by deacetylation and alkylation) and the NMR of **15** was compared with the literature.[24j] The synthesis of compounds **2a-c** from the corresponding starting compounds **23b,e,f** was carried out using the procedure reported in the literature.[24h]

3.2. General procedure for the phthalimide protection of amino acids (1): A dry RB flask containing a mixture of amino acid (1 mmol), phthalic anhydride (1 mmol) and triethylamine (20 mol% mmol) in toluene (5 mL) was heated for 12 h. Then, the reaction mixture was cooled to rt and concentrated under reduced pressure. The residue was dissolved in dichloromethane (5 mL), washed with 10% hydrochloric acid solution (7-10 mL), followed by water. The combined organic layers were dried over anhydrous Na_2SO_4 and then, the solvent was evaporated under reduced pressure to afford the phthalimide protected amino acid (**1**).

3.2.1. 7-(1,3-Dioxoisoindolin-2-yl)heptanoic acid (5d)*:* The compound **5d** was obtained by following the general procedure as a colourless solid (210 mg, 76%); mp: 116-118 ^{o}C; IR (DCM): 2930, 1718, 1395, 1360, 721 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.86 (2H, dd, J_1 = 5.4, J_2 = 3.1 Hz), 7.73 (2H, dd, J_1 = 5.4, J_2 = 3.1 Hz), 3.69 (2H, t, J = 7.2 Hz), 2.36 (2H, t, J = 7.4 Hz), 1.72-1.63 (4H, m), 1.40-1.38 (4H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 179.9, 168.5, 133.9, 132.1, 123.2, 37.9, 33.9, 28.6, 28.4, 26.5, 24.5; HRMS (ESI) calcd for $C_{15}H_{16}NO_4$ $[M-H]^+$ 274.1079 found, 274.1087. The carboxylic acid proton could not be detected in the ^{1}H NMR.

3.2.2. 12-(1,3-Dioxoisoindolin-2-yl)dodecanoic acid (5g): The compound **5g** was obtained by following the general procedure as a colourless solid (564 mg, 80%); mp: 90-92 ^{o}C; IR (DCM): 3055, 2987, 1713, 1265, 747 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.85 (2H, dd, J_1 = 5.4, J_2 = 3.2 Hz), 7.72 (2H, dd, J_1 = 5.4, J_2 = 3.2 Hz), 3.68 (2H, t, J = 7.4 Hz), 2.35 (2H, t, J = 7.6 Hz), 1.71-1.59 (4H, m), 1.33-1.26 (14H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 180.1, 168.5, 133.9, 132.2, 123.2, 38.1, 34.1, 29.4, 29.4, 29.4, 29.2, 29.2, 29.0, 28.6, 26.8, 24.7; HRMS (ESI) calcd for $C_{20}H_{27}NNaO_4$ $[M+Na]^+$ 368.1838 found 368.1820. The carboxylic acid proton could not be detected in the ^{1}H NMR.

3.2.3. 4-(4-(1,3-Dioxoisoindolin-2-yl)phenyl)butanoic acid (5h): The compound **5h** was obtained by following the general procedure as a colourless solid (537 mg, 87%); mp: 138-140 ^{o}C; IR (DCM): 3041, 1703, 1234, 1112, 714 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.98 (2H, dd, J_1 = 5.4, J_2 = 3.1 Hz), 7.81 (2H, dd, J_1 = 5.4, J_2 = 3.0 Hz), 7.40-7.34 (4H,m), 2.78 (2H, t, J = 7.9 Hz), 2.45 (2H, t, J = 7.4 Hz), 2.03 (2H, quint, J = 7.6 Hz); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 179.4, 167.4, 141.4, 134.4, 131.8, 129.6, 129.2, 126.6, 123.8, 34.7, 33.3, 26.1; HRMS (ESI) calcd for $C_{18}H_{15}NNaO_4$ $[M+Na]^+$ 332.0899 found, 332.0887. The carboxylic acid proton could not be detected in the ^{1}H NMR.

3.3. General procedure for the synthesis of carboxamides (6): A dry RB flask containing the corresponding carboxylic acid **5** (1-5 mmol) and $SOCl_2$ (9 equiv) was stirred for 24 h at rt under a nitrogen atmosphere. Then, the reaction mixture was concentrated under reduced pressure to remove the volatiles and the resultant crude reaction mixture was diluted with anhydrous DCM (2-10 mL). The DCM solution of corresponding acid chloride was slowly added to another RB flask containing the 8-aminoquinoline (0.9 equiv), Et_3N (1.2 equiv) and DCM (5-12 mL) under a nitrogen atmosphere. The resulting crude mixture was stirred at rt for 24 h. After this period, the reaction mixture was diluted with DCM (2-10 mL, if needed) and washed with water and saturated aqueous $NaHCO_3$ solution. The combined organic layers were dried over anhydrous Na_2SO_4, and then, the solvent was evaporated under reduced pressure to afford a crude mixture, which was purified by column chromatography on silica gel to afford the corresponding carboxamide (**6**).

3.3.1. 5-(1,3-Dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)pentanamide (6b): The compound **6b** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a brown color solid (228 mg, 61%); R_f (40% EtOAc/hexane) = 0.5; mp: 110-112 ^{o}C; IR (DCM): 3055, 2986, 1711, 1265, 743 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.78 (1H, br. s), 8.75-8.72 (2H, m), 8.10 (1H, dd, J_1 = 8.2, J_2 = 1.4 Hz), 7.79 (2H, dd, J_1 = 5.4, J_2 = 3.1 Hz), 7.65 (2H, dd, J_1 = 5.4, J_2 = 3.1 Hz), 7.50-7.43 (2H, m), 7.40 (1H, dd, J_1 = 8.3, J_2 = 4.2 Hz), 3.74 (2H, t, J = 6.4 Hz), 2.61 (2H, t, J = 7.1 Hz), 1.87-1.83 (4H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 171.1, 168.4, 148.1, 138.2, 136.3, 134.4, 133.9, 132.0, 127.9, 127.4, 123.2, 121.6, 121.4,

116.4, 37.5, 37.4, 28.2, 22.8; HRMS (ESI) calcd for $C_{22}H_{20}N_3O_3$ $[M+H]^+$ 374.1505 found 374.1519.

3.3.2. 7-(1,3-Dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)heptanamide (6d): The compound **6d** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a brown color solid (1.2 g, 64%); R_f (40% EtOAc/hexane) = 0.4; mp: 124-126 ^oC; IR (DCM): 2936, 1710, 1525, 1396, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.81 (1H, br. s), 8.82 (1H, dd, J_1 = 4.2, J_2 = 1.6 Hz), 8.79 (1H, dd, J_1 = 7.3, J_2 = 1.4 Hz), 8.17 (1H, dd, J_1 = 8.2, J_2 = 1.6 Hz), 7.85 (2H, dd, J_1 = 5.4, J_2 = 3.1 Hz), 7.72 (2H, dd, J_1 = 5.5, J_2 = 3.0 Hz), 7.57-7.50 (2H, m), 7.47 (1H, dd, J_1 = 8.3, J_2 = 4.2 Hz), 3.71 (2H, t, J = 7.3 Hz), 2.58 (2H, t, J = 7.6 Hz), 1.88-1.80 (2H, m) 1.73 (2H, quint, J = 7.4 Hz),) 1.53-1.40 (4H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 171.7, 168.4, 148.1, 138.3, 136.3, 134.5, 133.8, 132.1, 127.9, 127.4, 123.1, 121.6, 121.3, 116.4, 38.0, 37.9, 28.8, 28.5, 26.7, 25.5; HRMS (ESI) calcd for $C_{24}H_{24}N_3O_3$ $[M+H]^+$ 402.1818, found 402.1834.

3.3.3. 8-(1,3-Dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)octanamide (6e): The compound **6e** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a grey color solid (329 mg, 66%); R_f (40% EtOAc/hexane) = 0.4; mp: 86-88 ^oC; IR (DCM): 3353, 3055, 1721, 1265, 743 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.78 (1H, br. s), 8.76-8.74 (2H, m), 8.10 (1H, dd, J_1 = 8.3, J_2 = 1.6 Hz), 7.77 (2H, dd, J_1 = 5.4, J_2 = 2.0 Hz), 7.64 (2H, dd, J_1 = 5.6, J_2 = 3.0 Hz), 7.50-7.38 (3H, m), 3.64 (2H, t, J = 7.4 Hz), 2.53 (2H, t, J = 7.6 Hz), 1.82-1.75 (2H, m) 1.69-1.62 (2H, m) 1.38 (6H, br. s); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 171.8, 168.4, 148.0, 138.2, 136.4, 134.5, 133.8, 132.1, 127.9, 127.4, 123.1, 121.6, 121.3, 116.4, 38.1, 37.9, 29.1, 28.9, 28.5, 26.7, 25.5; HRMS (ESI) calcd for $C_{25}H_{26}N_3O_3$ $[M+H]^+$ 416.1974 found 416.1989.

3.3.4. 11-(1,3-Dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)undecanamide (6f): The compound **6f** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a colourless solid (419 mg, 59%); R_f (40% EtOAc/hexane) = 0.6; mp: 70-72 ^oC; IR (DCM): 3055, 2928, 1709, 1265, 741 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.72 (1H, br. s), 8.72-8.68 (2H, m), 8.03 (1H, dd, J_1 = 6.7, J_2 = 1.7 Hz), 7.71 (2H, dd, J_1 = 5.3, J_2 = 2.4 Hz), 7.57 (2H, dd, J_1 = 5.2, J_2 = 2.9 Hz), 7.44-7.31 (3H, m), 3.58 (2H, t, J = 6.7 Hz), 2.47 (2H, t, J = 6.6 Hz), 1.75-1.71 (2H, m) 1.58 (2H, br. s), 1.33-1.20 (12H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 171.8, 168.3, 148.0, 138.2, 136.2, 134.5, 133.7, 132.0, 127.8, 127.3, 123.0, 121.5, 121.3, 116.3, 38.1, 37.9, 29.4, 29.3, 29.3, 29.2, 29.1, 28.5, 26.8, 25.6; HRMS (ESI) calcd for $C_{28}H_{32}N_3O_3$ $[M+H]^+$ 458.2444 found 458.2426.

3.3.5. 12-(1,3-Dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)dodecanamide (6g): The compound **6g** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a brown color solid (262 mg, 55%); R_f (40% EtOAc/hexane) = 0.6; mp: 48-50 ^oC; IR (DCM): 3055, 2987, 1709, 1265, 744 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.77 (1H, br. s), 8.76-8.75 (2H, m), 8.09 (1H, d, J = 8.2 Hz), 7.79 (2H, dd, J_1 = 5.3, J_2 = 3.1 Hz), 7.64 (2H, dd, J_1 = 5.3, J_2 = 3.1 Hz), 7.50-7.42 (2H, m), 7.40 (1H, dd, J_1 = 8.2, J_2 = 4.2 Hz), 3.63 (2H, t, J = 7.3 Hz), 2.53 (2H, t, J = 7.6 Hz), 1.82-1.77 (2H, m), 1.65-1.62 (2H, m), 1.42-1.35 (2H, m), 1.28-1.23 (12H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 171.9, 168.4, 148.1, 138.3, 136.3, 134.5, 133.8, 132.1, 127.9, 127.4, 123.1, 121.5, 121.3, 116.4, 38.2, 38.0, 29.5, 29.4, 29.3, 29.3, 29.1, 28.6, 26.8, 25.7; HRMS (ESI) calcd for $C_{29}H_{34}N_3O_3$ $[M+H]^+$ 472.2600 found 472.2584.

3.3.6. 4-(4-(1,3-Dioxoisoindolin-2-yl)phenyl)-*N*-(quinolin-8-yl)butanamide (6h): The compound **6h** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a colourless solid (611 mg, 88%); R_f (40% EtOAc/hexane) = 0.5; mp: 162-164 ^oC; IR (DCM): 2923, 1716, 1524, 1381, 717 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.85 (1H, br. s), 8.84-8.81 (2H, m), 8.18 (1H, dd, J_1 = 8.3, J_2 = 1.6 Hz), 7.97 (2H, dd, J_1 = 5.5, J_2 = 3.0 Hz), 7.80 (2H, dd, J_1 = 5.4, J_2 = 3.0 Hz), 7.59-7.55 (1H, m), 7.52 (1H, dd, J_1 = 8.3, J_2 = 1.6 Hz), 7.48 (1H, dd, J_1 = 8.3, J_2 = 4.2 Hz), 7.43-7.38 (4H, m), 2.85 (2H, t, J = 7.8 Hz), 2.65 (2H, t, J = 7.4 Hz), 2.22 (2H, quint, J = 7.6 Hz); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 171.3, 167.4, 148.2, 141.7, 138.3, 136.4, 134.5, 134.4, 131.8, 129.6, 129.3, 127.9, 127.4, 126.6, 123.7, 121.6, 121.5, 116.5, 37.2, 34.9, 26.9; HRMS (ESI) calcd for $C_{27}H_{22}N_3O_3$ $[M+H]^+$ 436.1661 found 436.1646.

3.3.7. 3-(4-(1,3-Dioxoisoindolin-2-yl)phenyl)-*N*-(quinolin-8-yl)propanamide (6i): The compound **6i** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a brown color solid (258 mg, 76%); R_f (40% EtOAc/hexane) = 0.5; mp: 182-184 ^oC; IR (DCM): 2927, 1718, 1523, 1382, 739 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.86 (1H, br. s), 8.81 (2H, d, J = 5.0 Hz), 8.17 (1H, d, J = 8.2 Hz), 7.96 (2H, dd, J_1 = 5.4, J_2 = 3.2 Hz), 7.79 (2H, dd, J_1 = 5.4, J_2 = 3.2 Hz), 7.59-7.51 (2H, m), 7.48-7.39 (5H, m), 2.23 (2H, t, J = 8.1 Hz), 2.95 (2H, t, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 170.5, 167.3, 148.1, 141.0, 138.2, 136.5, 134.4, 131.8, 129.8, 129.2, 128.0, 127.4, 126.7, 123.7, 121.6, 121.6, 116.7, 39.4, 31.1; HRMS (ESI) calcd for $C_{26}H_{20}N_3O_3$ $[M+H]^+$ 422.1505 found 422.1484.

3.3.8. *N*-Butyl-4-(1,3-dioxoisoindolin-2-yl)butanamide (6j): The compound **6j** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a colourless solid (355 mg, 62%); R_f (40% EtOAc/hexane) = 0.6; mp: 108-110 ^oC; IR (DCM): 3305, 2935, 1713, 1399, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.86 (2H, dd, J_1 = 5.4, J_2 = 3.0 Hz), 7.74 (2H, dd, J_1 = 5.4, J_2 = 3.0 Hz), 6.04 (1H, br. s), 3.76 (2H, t, J = 6.4 Hz), 3.27-3.22 (2H, m), 2.21 (2H, t, J = 7.0 Hz), 2.08-2.01 (2H, m), 1.54-1.47 (2H, m), 1.42-1.34 (2H, m), 0.93 (3H, t, J = 7.3 Hz); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 171.9, 168.7, 134.1, 132.0, 123.3, 39.4, 37.2, 33.9, 31.6, 25.1, 20.1, 13.8; HRMS (ESI) calcd for $C_{16}H_{21}N_2O_3$ $[M+H]^+$ 289.1552 found 289.1540.

3.4. General procedure for the Pd(II)-catalyzed, 8-aminoquinoline-aided *β*-C-H arylation of short/medium/long chain-based unnatural amino acid carboxamides (6): A mixture of an appropriate unnatural amino acid carboxamide **6** (0.15-0.2 mmol, 1 equiv), an appropriate aryl iodide (5 equiv), $Pd(OAc)_2$ (10 mol%) and AgOAc (2.5 equiv) in anhydrous toluene (2-3 mL) was heated at 110 ^oC for 15-24 h under a nitrogen atm or in a sealed tube. 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 neutral alumina or silica gel (eluent = EtOAc:hexane) to give the corresponding arylated amino acid (see the respective Schemes/Tables for the specific entries).

3.4.1. 3-(3-Chlorophenyl)-4-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)butanamide (8a): The compound **8a** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a brown color solid (84 mg, 89%); R_f (40% EtOAc/hexane) = 0.6; mp: 170-172 ^oC; IR (DCM): 3055, 2986, 1713, 1265, 739 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.72 (1H, br. s), 8.82 (1H, dd, J_1 = 4.2, J_2 = 1.6 Hz), 8.46 (1H, dd, J_1 = 7.6, J_2 = 1.1 Hz), 8.13 (1H, dd, J_1 = 8.2, J_2 = 1.6 Hz), 7.67 (2H, dd, J_1 = 5.5, J_2 = 3.1 Hz), 7.57 (2H, dd, J_1 = 5.4, J_2 = 3.1 Hz), 7.48-7.42 (3H, m), 7.36 (1H, t, J = 8.0), 7.32 (1H, dt, J_1 = 7.5, J_2 = 1.5 Hz), 7.25 (1H, t, J = 7.8 Hz), 7.20 (1H, dt, J_1 = 8.0, J_2 = 1.6 Hz), 4.05-3.95 (3H, m), 3.04-2.93 (2H, m), ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 168.7, 168.3, 148.1, 143.0, 138.1, 136.2, 134.6, 134.1, 133.8, 131.7, 130.1, 128.0, 127.7, 127.5, 127.2, 126.1, 123.2, 121.6, 121.4, 116.2, 43.1, 41.8, 40.7; HRMS (ESI) calcd for $C_{27}H_{21}ClN_3O_3$ $[M+H]^+$ 470.1271 found 470.1252.

3.4.2. 3-(3-Bromophenyl)-4-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)butanamidebutanamide (8b): The compound **8b** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a yellow color solid (87 mg, 64%); R_f (40% EtOAc/hexane) = 0.6; mp: 146-148 ^oC; IR (DCM): 3055, 2987, 1712, 1265, 742 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.72 (1H, br. s), 8.82 (1H, dd, J_1 = 4.2, J_2 = 1.6 Hz), 8.45 (1H, dd, J_1 = 7.6, J_2 = 1.0 Hz), 8.13 (1H, dd, J_1 = 8.2, J_2 = 1.5 Hz), 7.67 (2H, dd, J_1 = 5.4, J_2 = 3.1 Hz), 7.59-7.56 (3H, m), 7.46 (1H, dd, J_1 = 8.3, J_2 = 4.3 Hz), 7.43 (1H, dd, J_1 = 8.4, J_2 = 1.3 Hz), 7.38- 7.34 (3H, m), 7.18 (1H, t, J = 7.8 Hz), 4.07-3.93 (3H, m), 3.03-2.92 (2H, m), ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 168.7, 168.3, 148.2, 143.2, 138.1, 136.2, 134.0, 133.8, 131.7, 130.8, 130.5, 130.4, 127.7, 127.2, 126.6, 123.2, 122.8, 121.6, 121.4, 116.2, 43.1, 41.8, 40.6; HRMS (ESI) calcd for $C_{27}H_{21}BrN_3O_3$ $[M+H]^+$ 514.0766 found 514.0745.

3.4.3. 3-(4-Bromophenyl)-4-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)butanamide (8d): The compound **8d** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a colourless solid (84 mg, 81%); R_f (40% EtOAc/hexane) = 0.6; mp: 174-176 ^oC; IR (DCM): 3055, 2987, 1710, 1265, 741 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.72 (1H, br. s), 8.80 (1H, dd, J_1 = 4.3, J_2 = 1.6 Hz), 8.49 (1H, dd, J_1 = 7.6, J_2 = 1.2 Hz), 8.13 (1H, dd, J_1 = 8.3, J_2 = 1.5 Hz), 7.68 (2H, dd, J_1 = 5.5, J_2 = 3.0 Hz), 7.58 (2H, dd, J_1 = 5.4, J_2 = 3.0 Hz), 7.47-7.42 (4H, m), 7.38 (1H, t, J = 8.1 Hz), 7.30 (2H, d, J = 8.5 Hz), 4.03-3.96 (3H, m), 3.03-2.91 (2H, m), ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 169.0, 168.2, 147.6, 139.8, 137.3, 137.3, 133.9, 133.7, 131.9, 131.7, 129.6, 127.9, 127.6, 123.2, 121.6, 121.5, 121.1, 117.3, 43.0, 41.9, 40.5; HRMS (ESI) calcd for $C_{27}H_{21}BrN_3O_3$ $[M+H]^+$ 514.0766 found 514.0778.

3.4.4. 4-(1,3-Dioxoisoindolin-2-yl)-3-(4-fluorophenyl)-*N*-(quinolin-8-yl)butanamide (8e): The compound **8e** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a colourless solid (59 mg, 65%); R_f (40% EtOAc/hexane) = 0.6; mp: 200-202 ^oC; IR (DCM): 3055, 2987, 1424, 1265, 745 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.71 (1H, br. s), 8.81 (1H, d, J = 3.9 Hz), 8.50 (1H, d, J = 7.4 Hz), 8.10 (1H, d, J = 8.2 Hz), 7.69 (2H, dd, J_1 = 4.6, J_2 = 3.2 Hz), 7.59 (2H, dd, J_1 = 5.6, J_2 = 3.0 Hz), 7.48-7.37 (5H, m), 7.00 (2H, t, J = 8.3 Hz), 4.04-3.96 (3H, m), 3.02-2.91 (2H, m), ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 168.9, 168.3, 162.0 (d, J = 243.7 Hz), 148.1, 138.2, 136.4 (d, J = 3.0 Hz), 136.2, 134.1, 133.8, 131.8, 129.3 (d, J = 8.0 Hz), 127.8, 127.2, 123.2, 121.6, 121.4, 116.3, 115.6 (d, J = 21.1 Hz), 43.2, 42.2, 40.3; HRMS (ESI) calcd for $C_{27}H_{21}FN_3O_3$ $[M+H]^+$ 454.1567, found 454.1547.

3.4.5. 3-(3,4-Dichlorophenyl)-4-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)butanamide (8f): The compound **8f** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a colourless solid (65 mg, 65%); R_f (40% EtOAc/hexane) = 0.6; mp: 186-188 ^oC; IR (DCM): 3055, 2985, 1711, 1265, 746 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.70 (1H, br. s), 8.81 (1H, dd, J_1 = 4.2, J_2 = 1.6 Hz), 8.47 (1H, dd, J_1 = 7.5, J_2 = 1.0Hz), 8.14 (1H, dd, J_1 = 8.3, J_2 = 1.5 Hz), 7.70 (2H, dd, J_1 = 5.4, J_2 = 3.1 Hz), 7.60 (2H, dd, J_1 = 5.5, J_2 = 3.0 Hz), 7.53 (1H, d, J = 2.0 Hz), 7.48-7.44 (2H, m), 7.41-7.36 (2H, m), 7.28–7.26 (1H, m), 4.03-3.95 (3H, m), 3.03-2.90 (2H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 168.4, 168.2, 148.2, 141.1, 138.1, 136.2, 134.0, 133.9, 132.8, 131.7, 131.3, 130.7, 129.8, 127.8, 127.3, 127.2, 123.3, 121.6, 121.5, 116.3, 42.8, 41.8, 40.3; HRMS (ESI) calcd for $C_{27}H_{20}Cl_2N_3O_3$ $[M+H]^+$ 504.0882 found 504.0901.

3.4.6. 4-(1,3-Dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)-3-(3,4,5-trimethoxyphenyl)butanamide (8g): The compound **8g** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a colourless solid (60 mg, 57%); R_f (40% EtOAc/hexane) = 0.4; mp: 168-170 ^oC; IR (DCM): 3345, 3055, 1709, 1264, 737 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.69 (1H, br. s), 8.79 (1H, d, J = 3.5 Hz), 8.49 (1H, d, J = 7.4 Hz), 8.13 (1H, d, J = 8.2 Hz), 7.67 (2H, dd, J_1 = 5.2, J_2 = 3.2 Hz), 7.58 (2H, dd, J_1 = 5.2, J_2 = 3.3 Hz), 7.47-7.43 (2H, m), 7.38 (1H, t, J = 8.0), 6.61 (2H, s), 4.04-3.97 (3H, m), 3.84 (6H, s), 3.72 (3H, s), 2.95 (2H, d, J = 6.8); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 169.2, 168.3, 153.3, 148.1, 138.1, 137.0, 136.3, 136.2, 134.1, 133.8, 131.8, 127.7, 127.2, 123.1, 121.6, 121.4, 116.2, 104.6, 60.7, 56.1, 43.1, 42.6, 41.3; HRMS (ESI) calcd for $C_{30}H_{28}N_3O_6$ $[M+H]^+$ 526.1978 found 526.1965.

3.4.7. 3-(2,3-Dihydrobenzo[*b*][1,4]dioxin-6-yl)-4-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)butanamide (8h): The compound **8h** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a colourless solid (55 mg, 74%); R_f (40% EtOAc/hexane) = 0.3; mp: 190-192 ^oC; IR (DCM): 3347, 2929, 1711, 1286, 724 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.69 (1H, br. s), 8.79 (1H, dd, J_1 = 4.2, J_2 = 1.5 Hz), 8.46 (1H, dd, J_1 = 7.6, J_2 = 1.2 Hz), 8.10 (1H, dd, J_1 = 8.2, J_2 = 1.5 Hz), 7.64 (2H, dd, J_1 = 5.4, J_2 = 3.0 Hz), 7.54 (2H, dd, J_1 = 5.4, J_2 = 3.1 Hz), 7.43 (1H, dd, J_1 = 8.2, J_2 = 4.2 Hz), 7.39 (1H, dd, J_1 = 8.3, J_2 = 1.3 Hz), 7.33 (1H, t, J = 8.0), 6.93 (1H, d, J = 2.0 Hz), 6.70 (1H, dd, J_1 = 8.3, J_2 = 2.1 Hz), 6.80 (1H, d, J = 8.2 Hz), 4.19 (4H, s), 4.03-3.89 (3H, m), 2.97-2.88 (2H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 169.3, 168.3, 148.1, 143.6, 142.6, 138.1, 136.2, 134.2, 134.1, 133.7, 131.8, 127.7, 127.2, 123.1, 121.5, 121.3, 120.7, 117.5, 116.5, 116.2, 64.3, 43.4, 42.2, 40.2; HRMS (ESI) calcd for $C_{29}H_{24}N_3O_5$ $[M+H]^+$ 494.1716 found 494.1696.

3.4.8. 3-(3,5-Dimethylphenyl)-4-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)butanamide (8i): The compound **8i** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a colourless solid (37 mg, 60%); R_f (40% EtOAc/hexane) = 0.6; mp: 104-106 ^oC; IR (DCM): 3055, 2986, 1714, 1265, 743 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.70 (1H, br. s), 8.81 (1H, dd, J_1 = 4.2, J_2 = 1.6 Hz), 8.43 (1H, dd, J_1 = 7.6, J_2 = 1.2 Hz), 8.12 (1H, dd, J_1 = 8.3, J_2 = 1.6 Hz), 7.64 (2H, dd, J_1 = 5.5, J_2 = 3.1 Hz), 7.54 (2H, dd, J_1 = 5.5, J_2 = 3.1 Hz), 7.46 (1H, dd, J_1 = 8.3, J_2 = 4.2 Hz), 7.41 (1H, dd, J_1 = 8.2, J_2 = 1.2 Hz), 7.33 (1H, t, J = 8.0 Hz), 7.05 (2H, s), 6.86 (1H, s), 4.05-3.89 (3H, m), 2.97 (2H, d, J = 6.8 Hz), 2.29 (6H, s); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 169.4, 168.4, 148.0, 140.8, 138.3, 138.2, 136.2, 134.2, 133.7, 131.9, 128.9, 127.7, 127.2, 125.5, 123.0, 121.5, 121.2, 116.1, 43.6, 42.1, 40.7, 21.3; HRMS (ESI) calcd for $C_{29}H_{26}N_3O_3$ $[M+H]^+$ 464.1974 found 464.1996.

3.4.9. 4-(1,3-Dioxoisoindolin-2-yl)-3-(4-ethoxyphenyl)-*N*-(quinolin-8-yl)butanamide (8l): The compound **8l** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a colourless solid (60 mg, 83%); R_f (40% EtOAc/hexane) = 0.4; mp: 129-131 ^oC; IR (DCM): 3348, 2980, 1712, 1245, 722 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.69 (1H, br. s), 8.78 (1H, dd, J_1 = 4.2, J_2 = 1.6 Hz), 8.48 (1H, dd, J_1 = 7.5, J_2 = 1.0 Hz), 8.10 (1H, dd, J_1 = 8.4, J_2 = 1.5 Hz), 7.65 (2H, dd, J_1 = 5.4, J_2 = 3.0 Hz), 7.54 (2H, dd, J_1 = 5.5, J_2 = 3.1 Hz), 7.44-7.35 (3H, m), 7.32 (2H, d, J = 8.5 Hz), 6.82 (2H, d, J = 8.6 Hz), 4.04-3.92 (5H, m), 3.00-2.91 (2H, m), 1.36 (3H, t, J = 7.0 Hz);^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 169.3, 168.3, 158.0, 148.1, 138.1, 136.2, 134.2, 133.7, 132.6, 131.8, 128.7, 127.7, 127.2, 123.1, 121.5, 121.3, 116.2, 114.7, 63.3, 43.4, 42.4, 40.1, 14.8; HRMS (ESI) calcd for $C_{29}H_{26}N_3O_4$ $[M+H]^+$ 480.1923 found 480.1902.

3.4.10. 4-(1,3-Dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)-3-(*p*-tolyl)butanamide (8m): The compound **8m** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a yellow color solid (70 mg, 77%); R_f (40% EtOAc/hexane) = 0.7; mp: 158-160 ^oC; IR (DCM): 3055, 2986, 1708, 1265, 743cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.71 (1H, br. s), 8.80 (1H, dd, J_1 = 4.3, J_2 = 1.4 Hz), 8.47 (1H, dd, J_1 = 7.5, J_2 = 0.7 Hz), 8.12 (1H, dd, J_1 = 8.2, J_2 = 0.9 Hz), 7.65 (2H, dd, J_1 = 5.3, J_2 = 3.1 Hz), 7.55 (2H, dd, J_1 = 5.3, J_2 = 3.1 Hz), 7.45 (1H, dd, J_1 =

8.3, J_2 = 4.3 Hz), 7.41-7.32 (2H, m), 7.32 (2H, d, J = 8.0), 7.13 (2H, d, J = 7.8, Hz), 4.05-3.95 (3H, m), 2.99-2.96 (2H, m), 2.29 (3H, s); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 169.3, 168.4, 148.1, 138.1, 137.8, 136.8, 136.2, 134.2, 133.7, 131.8, 129.5, 127.7, 127.6, 127.2, 123.1, 121.5, 121.3, 116.2, 43.4, 42.2, 40.5, 21.1; HRMS (ESI) calcd for $C_{28}H_{24}N_3O_3$ $[M+H]^+$ 450.1818 found 450.1833.

3.4.11. 4-(1,3-Dioxoisoindolin-2-yl)-3-(4-ethylphenyl)-*N*-(quinolin-8-yl)butanamide (8n): The compound **8n** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a yellow color solid (68 mg, 73%); R_f (40% EtOAc/hexane) = 0.75; mp: 138-140 ^{o}C; IR (DCM): 3348, 2965, 1713, 1326, 721 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.81 (1H, br. s), 8.80 (1H, dd, J_1 = 4.2, J_2 = 1.4 Hz), 8.47 (1H, d, J = 7.4 Hz), 8.15 (1H, d, J = 8.0 Hz), 7.64 (2H, dd, J_1 = 5.4, J_2 = 3.1 Hz), 7.53 (2H, dd, J_1 = 5.4, J_2 = 3.0 Hz), 7.46 (1H, dd, J_1 = 8.2, J_2 = 4.2 Hz), 7.42-7.38 (1H, m), 7.34 (2H, d, J = 8.0 Hz), 7.14 (2H, d, J = 7.9 Hz), 4.08-3.95 (3H, m), 3.00 (2H, d, J = 5.7 Hz), 2.58 (2H, q, J = 7.6), 1.16 (3H, t, J = 7.6); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 169.4, 168.4, 148.0, 143.1, 138.1, 136.3, 134.2, 133.7, 131.9, 128.2, 127.7, 127.7, 127.3, 123.0, 121.5, 121.3, 116.3, 43.4, 42.2, 40.5, 28.4, 15.4; HRMS (ESI) calcd for $C_{29}H_{26}N_3O_3$ $[M+H]^+$ 464.1974 found 464.1994.

3.4.12. 4-(1,3-Dioxoisoindolin-2-yl)-3-(4-isopropylphenyl)-*N*-(quinolin-8-yl)butanamide (8o): The compound **8o** was obtained after purification by column chromatography on silica gel (EtOAc:hexane =40:60) as a brown color solid (55 mg, 77%); R_f (40% EtOAc/hexane) = 0.6; mp: 90-92 ^{o}C; IR (DCM): 3054, 2961, 1713, 1265, 740 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.70 (1H, br. s), 8.81-8.80 (1H, m), 8.43 (1H, dd, J_1 = 7.6, J_2 = 1.0 Hz), 8.11 (1H, d, J = 8.2 Hz), 7.62 (2H, dd, J_1 = 5.1, J_2 = 3.6 Hz), 7.53-7.51 (2H, m), 7.44 (1H, dd, J_1 = 8.2, J_2 = 4.3 Hz), 7.41-7.31 (4H, m), 7.18 (2H, d, J = 8.1 Hz), 4.09-3.93 (3H, m), 3.01-2.97 (2H, m), 2.88-2.81 (1H, m), 1.19 (6H, d, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 169.4, 168.4, 148.0, 147.7, 138.3, 138.1, 136.2, 134.2, 133.6, 131.9, 127.7, 127.6, 127.2, 126.8, 123.0, 121.5, 121.2, 116.1, 43.4, 42.2, 40.4, 33.7, 23.9; HRMS (ESI) calcd for $C_{30}H_{28}N_3O_3$ $[M+H]^+$ 478.2131 found 478.2109.

3.4.13. 3-(4-(*Tert*-butyl)phenyl)-4-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)butanamide (8p): The compound **8p** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a yellow color solid (57 mg, 77%); R_f (40% EtOAc/hexane) = 0.6; mp: 120-122 ^{o}C; IR (DCM): 3054, 2963, 1714, 1265, 737 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.70 (1H, br. s), 8.80 (1H, dd, J_1 = 4.2, J_2 = 1.9 Hz), 8.42 (1H, dd, J_1 = 7.6, J_2 = 0.9 Hz), 8.09 (1H, dd, J_1 = 8.3, J_2 = 1.6 Hz), 7.61 (2H, dd, J_1 = 5.5, J_2 = 3.1 Hz), 7.51 (2H, dd, J_1 = 5.4, J_2 = 3.2 Hz), 7.43 (1H, dd, J_1 = 8.2, J_2 = 4.2 Hz), 7.40-7.29 (6H, m), 4.09-3.93 (3H, m), 3.01-2.95 (2H, m), 1.26 (9H, s); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 169.4, 168.4, 150.0, 148.1, 138.1, 137.9, 136.2, 134.2, 133.7, 131.8, 127.7, 127.3, 127.2, 125.7, 123.0, 121.5, 121.2, 116.1, 43.4, 42.2, 40.3, 34.4, 31.3; HRMS (ESI) calcd for $C_{31}H_{30}N_3O_3$ $[M+H]^+$ 492.2287 found 492.2267.

3.4.14. 4-(1,3-Dioxoisoindolin-2-yl)-3-(4-nitrophenyl)-*N*-(quinolin-8-yl)butanamide (8q): The compound **8q** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a brown color solid (88 mg, 91%); R_f (40% EtOAc/hexane) = 0.3; mp: 148-150 ^{o}C; IR (DCM): 3343, 3057, 1714, 1348, 724 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.73 (1H, br. s), 8.79 (1H, dd, J_1 = 4.2, J_2 = 1.4 Hz), 8.51-8.49 (1H, m), 8.18-8.14 (3H, m), 7.72 (2H, dd, J_1 = 5.4, J_2 = 3.1 Hz), 7.63 (2H, dd, J_1 = 5.4, J_2 = 3.0 Hz), 7.59 (2H, d, J = 8.7 Hz), 7.48-7.45 (2H, m), 7.42-7.38 (1H, m), 4.20-4.10 (1H, m), 4.09-4.01 (2H, m), 3.09 (1H, dd, J_1 = 15.4, J_2 = 6.2 Hz), 3.00 (1H, dd, J_1 = 15.3, J_2 = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 168.2, 168.1, 148.4, 148.2, 147.2, 138.1, 136.3, 134.1, 133.9, 131.6, 128.9, 127.8, 127.2, 124.0, 123.3, 121.7, 116.4, 42.6, 41.6, 40.9; HRMS (ESI) calcd for $C_{27}H_{21}N_4O_5$ $[M+H]^+$ 481.1512 found 481.1534.

3.4.15. 3-(4-Acetylphenyl)-4-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)butanamide (8r): The compound **8r** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a brown color solid (60 mg, 63%); R_f (40% EtOAc/hexane) = 0.3; mp: 178-180 ^{o}C; IR (DCM): 3343, 1715, 1527, 1267, 724 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.72 (1H, br. s), 8.79 (1H, dd, J_1 = 4.2, J_2 = 1.4 Hz), 8.48 (1H, dd, J_1 = 7.7, J_2 = 0.8 Hz), 8.13 (1H, dd, J_1 = 8.3, J_2 = 1.4 Hz), 7.90 (2H, d, J = 8.2 Hz), 7.69 (2H, dd, J_1 = 5.4, J_2 = 3.1 Hz), 7.59 (2H, dd, J_1 = 5.4, J_2 = 3.1 Hz), 7.52 (2H, d, J = 8.2 Hz), 7.47-7.43 (2H, m), 7.38 (1H, t, J = 8.0 Hz), 4.13-4.0 (3H, m), 3.09-2.96 (2H, m), 2.55 (3H, s); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 197.7, 168.7, 168.2, 148.1, 146.4, 138.1, 136.2, 136.1, 134.0, 133.9, 131.7, 128.9, 128.1, 127.7, 127.2, 123.2, 121.6, 121.5, 116.3, 42.8, 41.7, 40.9, 26.6; HRMS (ESI) calcd for $C_{29}H_{24}N_3O_4$ $[M+H]^+$ 478.1767 found 478.1789.

3.4.16. 3-(4-Cyanophenyl)-4-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)butanamide (8s): The compound **8s** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a yellow color solid (50 mg, 72%); R_f (40% EtOAc/hexane) = 0.4; mp: 156-158 ^{o}C; IR (DCM): 3344, 3057, 2229, 1526, 727 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.72 (1H, br. s), 8.79 (1H, dd, J_1 = 4.2, J_2 = 1.6 Hz), 8.48 (1H, dd, J_1 = 7.5, J_2 = 1.3 Hz), 8.14 (1H, dd, J_1 = 8.3, J_2 = 1.6 Hz), 7.70 (2H, dd, J_1 = 5.5, J_2 = 3.1 Hz), 7.63-7.59 (4H, m), 7.53 (2H, d, J = 8.3), 7.48-7.44 (2H, m), 7.39 (1H, t, J = 8.1 Hz), 4.12-3.97 (3H, m), 3.06 (1H, dd, J_1 = 15.4, J_2 = 6.2 Hz), 2.97 (1H, dd, J_1 = 15.4, J_2 = 7.8 Hz); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 168.3, 168.2, 148.2, 146.3, 138.1, 136.3, 134.0, 133.9, 132.6, 131.6, 128.8, 127.8, 127.2, 123.3, 121.7, 121.6, 118.7, 116.4, 111.2, 42.6, 41.5, 41.1; HRMS (ESI) calcd for $C_{28}H_{21}N_4O_3$ $[M+H]^+$ 461.1614 found 461.1595.

3.4.17. Methyl 4-(1-(1,3-dioxoisoindolin-2-yl)-4-oxo-4-(quinolin-8-ylamino)butan-2-yl)benzoate (8t): The compound **8t** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a colourless solid (55 mg, 74%); R_f (40% EtOAc/hexane) = 0.3; mp: 194-196 ^{o}C; IR (DCM):3056, 2922, 1716, 1269, 740 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.72 (1H, br. s), 8.80 (1H, dd, J_1 = 4.2, J_2 = 1.6 Hz), 8.48 (1H, dd, J_1 = 7.6, J_2 = 1.2 Hz), 8.13 (1H, dd, J_1 = 8.3, J_2 = 1.6 Hz), 7.98 (2H, d, J = 8.3 Hz), 7.68 (2H, dd, J_1 = 5.5, J_2 = 3.1 Hz), 7.58 (2H, dd, J_1 = 5.5, J_2 = 3.0 Hz), 7.50 (2H, d, J = 8.3 Hz), 7.47-7.42 (2H, m), 7.37 (1H, t, J = 8.1 Hz), 4.13-3.98 (3H, m), 3.88 (3H, s), 3.08-2.96 (2H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 168.7, 168.2, 166.9, 148.1, 146.1, 138.1, 136.2, 134.0, 133.9, 131.7, 130.1, 129.2, 127.9, 127.7, 127.2, 123.2, 121.6, 121.5, 116.3, 52.1, 42.9, 41.8, 40.9; HRMS (ESI) calcd for $C_{29}H_{24}N_3O_5$ $[M+H]^+$ 494.1716 found 494.1696.

3.4.18. Ethyl 3-(1-(1,3-dioxoisoindolin-2-yl)-4-oxo-4-(quinolin-8-ylamino)butan-2-yl)benzoate (8u): The compound **8u** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a colourless solid (59 mg, 77%); R_f (40% EtOAc/hexane) = 0.3; mp: 142-144 ^{o}C; IR (DCM):3054, 2986, 1713, 1266, 743 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.72 (1H, br. s), 8.80-8.79 (1H, m), 8.45 (1H, d, J = 7.5 Hz), 8.12-8.10 (2H, m), 7.92 (2H, d, J = 7.6 Hz), 7.67-7.62 (3H, m), 7.56 (2H, dd, J_1 = 5.6, J_2 = 3.0 Hz), 7.46-7.33 (4H, m), 4.37 (2H, q, J = 7.1 Hz), 4.10-3.97 (3H, m), 3.08-2.97 (2H, m), 1.39 (3H, t, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 168.9, 168.3, 166.4, 148.1, 141.3, 138.1, 136.2, 134.1, 133.8, 132.6, 131.8, 131.0, 128.8, 128.6, 127.7, 127.2, 123.1, 121.6, 121.4, 116.2, 61.0, 43.1, 41.8, 40.8, 14.4; HRMS (ESI) calcd for $C_{30}H_{26}N_3O_5$ $[M+H]^+$ 508.1872 found 508.1847.

3.4.19. 4-(1,3-Dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)-3-(4-(trifluoromethyl)phenyl)butanamide (8v): The compound **8v** was obtained after purification by column chromatography on silica gel

(EtOAc:hexane = 40:60) as a colourless solid (41 mg, 54%); R_f (40% EtOAc/hexane) = 0.6; mp: 168-170 °C; IR (DCM): 3351, 2935, 1711, 1326, 721 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.71 (1H, br. s), 8.79 (1H, dd, J_1 = 4.1, J_2 = 1.4 Hz), 8.48 (1H, d, J = 7.5 Hz), 8.13 (1H, dd, J_1 = 8.2, J_2 = 1.3 Hz), 7.69 (2H, dd, J_1 = 5.4, J_2 = 3.1 Hz), 7.60-7.54 (6H, m), 7.47-7.43 (2H, m), 7.38 (1H, t, J = 8.0 Hz), 4.14-3.97 (3H, m), 3.08-2.95 (2H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 168.6, 168.2, 148.1, 145.0, 138.1, 136.3, 134.0, 133.9, 131.7, 129.5 (q, J_{C-F} = 32.4 Hz), 128.2, 127.8, 127.2, 125.8 (q, J_{C-F} = 3.7 Hz), 124.1 (q, J_{C-F} = 271 Hz), 123.2, 121.6, 121.5, 116.3, 42.9, 41.8, 40.8; HRMS (ESI) calcd for $C_{28}H_{21}F_3N_3O_3$ $[M+H]^+$ 504.1535 found 504.1521.

3.4.20. 3-(4-Chlorophenyl)-5-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)pentanamide (9a): The compound **9a** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a yellow color solid (83 mg, 85%); R_f (40% EtOAc/hexane) = 0.6; mp: 91-93 °C; IR (DCM): 3055, 1704, 1422, 1265, 742 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.62 (1H, br. s), 8.74 (1H, dd, J_1 = 4.2, J_2 = 1.6 Hz), 8.67 (1H, dd, J_1 = 6.2, J_2 = 2.7 Hz), 8.13 (1H, dd, J_1 = 8.2, J_2 = 1.5 Hz), 7.76 (2H, dd, J_1 = 5.5, J_2 = 3.1 Hz), 7.67 (2H, dd, J_1 = 5.4, J_2 = 3.1 Hz), 7.51-7.46 (2H, m), 7.43 (1H, dd, J_1 = 8.3, J_2 = 4.2 Hz), 7.27 (2H, d, J = 8.4 Hz), 7.20 (2H, d, J = 8.4 Hz), 3.70-3.62 (2H, m), 3.44-3.37 (1H, m), 2.91-2.77 (2H, m), 2.28-2.15 (2H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 169.2, 168.2, 148.1, 141.2, 138.1, 136.3, 134.1, 133.8, 132.4, 131.9, 128.9, 128.8, 127.8, 127.3, 123.0, 121.6, 121.6, 116.5, 45.8, 40.0, 36.4, 33.7; HRMS (ESI) calcd for $C_{28}H_{23}ClN_3O_3$ $[M+H]^+$ 484.1428 found 484.1444.

3.4.21. 3-(4-Bromophenyl)-5-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)pentanamide (9b): The compound **9b** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a green color viscous liquid (67 mg, 84%); R_f (40% EtOAc/hexane) = 0.5; IR (DCM): 2929, 17014, 1530, 1326, 719 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.62 (1H, br. s) 8.75 (1H, dd, J_1 = 4.2, J_2 = 1.5 Hz), 8.67 (1H, dd, J_1 = 6.2, J_2 = 2.7 Hz), 8.13 (1H, dd, J_1 = 8.2, J_2 = 1.5 Hz), 7.76 (2H, dd, J_1 = 5.4, J_2 = 3.1 Hz), 7.67 (2H, dd, J_1 = 5.4, J_2 = 3.1 Hz), 7.52-7.47 (2H, m), 7.44 (1H, dd, J_1 = 8.2, J_2 = 4.2 Hz), 7.32 (2H, d, J = 8.4 Hz), 7.21 (2H, d, J = 8.4 Hz), 3.66 (2H, t, J = 7.4 Hz), 3.43-3.36 (1H, m), 2.87 (1H, dd, J_1 = 14.7, J_2 = 6.7 Hz), 2.79 (1H, dd, J_1 = 14.7, J_2 = 8.0 Hz), 2.31-2.15 (2H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 169.2, 168.2, 148.1, 141.8, 138.2, 136.3, 134.1, 133.9, 132.0, 131.8, 129.3, 127.8, 127.3, 123.0, 121.6, 120.5, 116.5, 45.8, 40.2, 36.4, 33.6; HRMS (ESI) calcd for $C_{28}H_{23}BrN_3O_3$ $[M+H]^+$ 528.0923, found 528.0906.

3.4.22. 3-(3-Cyanophenyl)-5-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)pentanamide (9c): The compound **9c** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a brown color solid (60 mg, 84%); R_f (40% EtOAc/hexane) = 0.3; mp: 132-134 °C; IR (DCM): 3055, 2987, 1710, 1265, 743 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.65 (1H, br. s), 8.76 (1H, dd, J_1 = 4.2, J_2 = 1.7 Hz), 8.66-8.61 (1H, m), 8.14 (1H, dd, J_1 = 8.3, J_2 = 1.7 Hz), 7.78 (2H, dd, J_1 = 5.6, J_2 = 3.1 Hz), 7.69 (2H, dd, J_1 = 5.4, J_2 = 3.2 Hz), 7.65 (1H, s), 7.61-7.58 (1H, m), 7.49-7.48 (2H, m), 7.44 (1H, dd, J_1 = 8.2, J_2 = 4.2 Hz), 7.33-7.32 (2H, m), 3.68 (2H, t, J = 7.0 Hz), 3.51-3.44 (1H, m), 2.95 (1H, dd, J_1 = 14.9, J_2 = 6.4 Hz), 2.82 (1H, dd, J_1 = 14.9, J_2 = 8.3 Hz), 2.30-2.17 (2H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 168.7, 168.2, 148.2, 144.4, 138.1, 136.4, 133.9, 132.5, 131.9, 131.1, 130.4, 129.4, 127.8, 127.3, 123.1, 121.7, 121.7, 118.7, 116.5, 112.6, 45.2, 40.1, 36.2, 33.7, 29.7; HRMS (ESI) calcd for $C_{29}H_{23}N_4O_3$ $[M+H]^+$ 475.1770 found 475.1790.

3.4.23. 3-(2,3-Dihydrobenzo[*b*][1,4]dioxin-6-yl)-5-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)pentanamide (9d): The compound **9d** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a colourless solid (54 mg, 71%); R_f (40% EtOAc/hexane) = 0.3; mp: 142-144 °C; IR (DCM): 3055, 2986, 1709, 1265, 743 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.65 (1H, br. s), 8.76 (1H, dd, J_1 = 4.4, J_2 = 1.6 Hz), 8.70 (1H, dd, J_1 = 7.2, J_2 = 2.0 Hz), 8.13 (1H, dd, J_1 = 8.2, J_2 = 1.4 Hz), 7.77 (2H, dd, J_1 = 5.6, J_2 = 3.2 Hz), 7.67 (2H, dd, J_1 = 5.4, J_2 = 3.0 Hz), 7.52-7.47 (2H, m), 7.44 (1H, dd, J_1 = 8.2, J_2 = 4.0 Hz), 6.83-6.81 (2H, m), 6.73 (1H, d, J = 8.0 Hz), 4.16-4.12 (4H, m), 3.67 (2H, t, J = 7.2 Hz), 3.33-3.28 (1H, m), 2.87-2.77 (2H, m), 2.24-2.12 (2H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 169.7, 168.2, 148.0, 143.4, 142.2, 138.2, 136.3, 136.0, 134.3, 133.7, 132.1, 127.8, 127.4, 123.0, 121.5, 121.4, 120.5, 117.4, 116.5, 116.1, 64.2, 64.2, 46.1, 40.1, 36.6, 33.8; HRMS (ESI) calcd for $C_{30}H_{26}N_3O_5$ $[M+H]^+$ 508.1872 found 508.1846.

3.4.24. 5-(1,3-Dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)-3-(thiophen-2-yl)pentanamide (9e): The compound **9e** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a green color viscous liquid (48 mg, 70%); R_f (40% EtOAc/hexane) = 0.5; IR (DCM): 2929, 1707, 1526, 1264, 733 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.72 (1H, br. s), 8.76 (1H, dd, J_1 = 4.2, J_2 = 1.6 Hz), 8.72 (1H, dd, J_1 = 6.8, J_2 = 2.2 Hz), 8.14 (1H, dd, J_1 = 8.2, J_2 = 1.6 Hz), 7.80 (2H, dd, J_1 = 5.5, J_2 = 3.1 Hz), 7.68 (2H, dd, J_1 = 5.4, J_2 = 3.1 Hz), 7.53-7.47 (2H, m), 7.44 (1H, dd, J_1 = 8.3, J_2 = 4.2 Hz), 7.11 (1H, d, J = 5.1 Hz), 7.03 (1H, d, J = 3.4 Hz), 6.86 (1H, dd, J_1 = 5.0, J_2 = 3.5 Hz), 3.82-3.69 (3H, m), 2.99-2.88 (2H, m), 2.31-2.17 (2H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 169.1, 168.3, 148.1, 146.5, 138.2, 136.3, 134.3, 133.8, 132.1, 127.8, 127.3, 126.7, 125.0, 123.7, 123.1, 121.6, 121.5, 116.5, 46.5, 36.3, 35.9, 35.4; HRMS (ESI) calcd for $C_{26}H_{22}N_3O_3S$ $[M+H]^+$ 456.1382 found 456.1399.

3.4.25. 3-(4-Chlorophenyl)-6-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)hexanamide (10a): The compound **10a** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a yellow color viscous liquid (59 mg, 79%); R_f (40% EtOAc/hexane) = 0.5; IR (DCM): 3054, 2939, 1711, 1527, 722 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.64 (1H, br. s), 8.75 (1H, dd, J_1 = 2.9, J_2 = 1.7 Hz), 8.66 (1H, dd, J_1 = 5.7, J_2 = 3.3 Hz), 8.14-8.11 (1H, m), 7.80-7.78 (2H, m), 7.69-7.67 (2H, m), 7.48-7.42 (3H, m), 7.25-7.20 (4H, m), 3.67-3.63 (2H, m), 3.37-3.29 (1H, m), 2.89-2.77 (2H, m), 1.91-1.83 (1H, m), 1.78-1.61 (2H, m), 1.57-1.50 (1H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 169.6, 168.3, 148.1, 142.0, 138.2, 136.3, 134.2, 133.9, 132.3, 132.0, 128.9, 128.9, 127.8, 127.3, 123.2, 121.6, 121.5, 116.4, 45.4, 41.7, 37.8, 33.3, 26.5; HRMS (ESI) calcd for $C_{29}H_{25}ClN_3O_3$ $[M+H]^+$ 498.1584, found 498.1567.

3.4.26. 3-(4-Cyanophenyl)-6-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)hexanamide (10b): The compound **10b** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a green color viscous liquid (43 mg, 59%); R_f (40% EtOAc/hexane) = 0.4; IR (DCM): 3056, 2938, 1701, 1327, 724 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.65 (1H, br. s), 8.77 (1H, dd, J_1 = 4.2, J_2 = 1.6 Hz), 8.65-8.63 (1H, m), 8.16 (1H, dd, J_1 = 8.3, J_2 = 1.5 Hz), 7.82 (2H, dd, J_1 = 5.4, J_2 = 3.1 Hz), 7.71 (2H, dd, J_1 = 5.5, J_2 = 3.0 Hz), 7.57 (2H, d, J = 8.2 Hz), 7.51-7.46 (3H, m), 7.42 (2H, d, J = 8.2 Hz), 3.73-3.64 (2H, m), 3.48-3.41 (1H, m), 2.93 (1H, dd, J_1 = 14.9, J_2 = 6.3 Hz), 2.83 (1H, dd, J_1 = 14.9, J_2 = 8.4 Hz), 1.95-1.87 (1H, m), 1.83-1.67 (2H, m), 1.59-1.50 (1H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 169.1, 168.3, 149.3, 148.1, 138.1, 136.4, 134.0, 134.0, 132.5, 132.0, 128.5, 127.9, 127.3, 123.2, 121.7, 118.9, 116.5, 110.5, 44.8, 42.2, 37.6, 33.0, 26.5; HRMS (ESI) calcd for $C_{30}H_{25}N_4O_3$ $[M+H]^+$ 489.1927, found 489.1940.

3.4.27. 3-(3,4-Dichlorophenyl)-6-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)hexanamide (10c): The compound **10c** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a green color solid (60 mg, 75%); R_f (40% EtOAc/hexane) = 0.7; mp: 110-112 °C; IR (DCM): 3346,

2937, 1771, 1394, 723 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.64 (1H, br. s), 8.78 (1H, d, J = 3.2 Hz), 8.65 (1H, t, J = 4.5 Hz), 8.15 (1H, d, J = 7.7 Hz), 7.81 (2H, dd, J_1 = 5.2, J_2 = 3.1 Hz), 7.70 (2H, dd, J_1 = 5.4, J_2 = 3.1 Hz), 7.49 (2H, d, J = 4.6 Hz), 7.46 (1H, dd, J_1 = 8.3, J_2 = 4.2 Hz), 7.39 (1H, d, J = 1.4 Hz), 7.32 (1H, d, J = 8.2 Hz), 7.13 (1H, dd, J_1 = 8.2, J_2 = 1.5 Hz), 3.67 (2H, t, J = 7.3 Hz), 3.36–3.29 (1H, m), 2.87 (1H, dd, J_1 = 14.8, J_2 = 6.4 Hz), 2.80 (1H, dd, J_1 = 14.8, J_2 = 8.3 Hz), 1.92-1.82 (1H, m), 1.78-1.65 (2H, m), 1.60-1.52 (1H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 169.2, 168.3, 148.1, 143.9, 138.2, 136.3, 134.1, 133.9, 132.7, 132.0, 130.6, 130.6, 129.4, 127.9, 127.3, 127.2, 123.2, 121.6, 121.6, 116.5, 45.1, 41.6, 37.7, 33.2, 26.5; HRMS (ESI) calcd for $C_{29}H_{24}Cl_2N_3O_3$ $[M+H]^+$ 532.1195 found 532.1177.

3.4.28. 3-(6-Chloropyridin-3-yl)-7-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)heptanamide (11a): The compound **11a** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a colourless solid (50 mg, 65%); R_f (40% EtOAc/hexane) = 0.4; mp: 92-94 ^oC; IR (DCM): 2936, 1708, 1524, 1396, 721 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.69 (1H, br. s), 8.78 (1H, d, J = 3.8 Hz), 8.67 (1H, t, J = 4.4 Hz), 8.33 (1H, s), 8.15 (1H, d, J = 8.2 Hz), 7.82 (2H, dd, J_1 = 5.0, J_2 = 3.2 Hz), 7.70 (2H, dd, J_1 = 5.2, J_2 = 3.3 Hz), 7.59 (1H, dd, J_1 = 8.2, J_2 = 1.9 Hz), 7.53-7.49 (2H, m), 7.45 (1H, dd, J_1 = 8.2, J_2 = 4.2 Hz), 7.23 (1H, d, J = 8.2 Hz), 3.64 (2H, t, J = 7.2 Hz), 3.37-3.32 (1H, m), 2.92 (1H, dd, J_1 = 15.0, J_2 = 6.6 Hz), 2.80 (1H, dd, J_1 = 14.9, J_2 = 8.2 Hz), 1.92-1.83 (1H, m), 1.81-1.70 (2H, m), 1.68-1.61 (1H, m), 1.36-1.29 (1H, m), 1.25-1.21 (1H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 169.1, 168.3, 149.6, 149.2, 148.2, 138.2, 138.2, 138.0, 136.4, 134.0, 133.9, 132.0, 127.9, 127.3, 124.2, 123.2, 121.7, 121.7, 116.5, 44.8, 39.2, 37.5, 35.2, 28.2, 24.4; HRMS (ESI) calcd for $C_{29}H_{26}ClN_4O_3$ $[M+H]^+$ 513.1693, found 513.1667.

3.4.29. 3-(4-Chlorophenyl)-7-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)heptanamide (11b): The compound **11b** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a green color viscous liquid (50 mg, 65%); R_f (40% EtOAc/hexane) = 0.5; IR (DCM): 2938, 1712, 1526, 1326, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.65 (1H, br. s), 8.77 (1H, d, J = 4.1 Hz), 8.70 (1H, dd, J_1 = 6.6, J_2 = 1.4 Hz), 8.14 (1H, dd, J_1 = 8.2, J_2 = 0.2 Hz), 7.82 (2H, dd, J_1 = 5.0, J_2 = 3.3 Hz), 7.70 (2H, dd, J_1 = 5.9, J_2 = 3.2 Hz), 7.53-7.47 (2H, m), 7.44 (1H, dd, J_1 = 8.2, J_2 = 4.2 Hz), 7.21 (4H, s), 3.62 (2H, t, J = 7.2 Hz), 3.33-3.26 (1H, m), 2.89-2.77 (2H, m), 1.88-1.81 (1H, m), 1.75-1.68 (2H, m), 1.66-1.59 (1H, m), 1.32-1.20 (2H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 169.8, 168.4, 148.1, 142.3, 138.2, 136.3, 134.3, 133.9, 132.1, 132.1, 128.9, 128.7, 127.9, 127.3, 123.1, 121.6, 121.5, 116.5, 45.5, 41.8, 37.7, 35.5, 28.3, 24.5; HRMS (ESI) calcd for $C_{30}H_{27}ClN_3O_3$ $[M+H]^+$ 512.1741, found 512.1765.

3.4.30. 7-(1,3-Dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)-3-(4-(trifluoromethyl)phenyl)heptanamide (11c): The compound **11c** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a yellow color viscous liquid (55 mg, 67%); R_f (40% EtOAc/hexane) = 0.5; IR (DCM): 2936, 1710, 1524, 1326, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.66 (1H, br. s), 8.76 (1H, d, J = 2.8 Hz), 8.70 (1H, dd, J_1 = 6.4, J_2 = 2.2 Hz), 8.14 (1H, d, J = 7.1 Hz), 7.81 (2H, dd, J_1 = 5.4, J_2 = 3.1 Hz), 7.70 (2H, dd, J_1 = 5.3, J_2 = 3.1 Hz), 7.51-7.48 (4H, m), 7.45 (1H, dd, J_1 = 8.2, J_2 = 4.2 Hz), 7.40 (2H, d, J = 8.0 Hz), 3.63 (2H, t, J = 6.9 Hz), 3.41-3.38 (1H, m), 2.93-2.81 (2H, m), 1.93-1.84 (1H, m), 1.82-1.75 (2H, m), 1.67-1.58 (1H, m), 1.31-1.30 (1H, m), 1.25-1.20 (1H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 169.6, 168.4, 148.1, 138.2, 136.3, 134.2, 133.9, 132.0, 128.7 (q, J_{C-F} = 32.2 Hz), 127.9, 127.9, 127.3, 125.5 (q, J_{C-F} = 3.6 Hz), 124.2 (q, J_{C-F} = 271 Hz), 123.1, 122.8, 121.6, 121.6, 116.5, 45.2, 42.2, 37.6, 35.4, 28.2, 24.5; HRMS (ESI) calcd for $C_{31}H_{27}F_3N_3O_3$ $[M+H]^+$ 546.2005, found 546.2027.

3.4.31. 7-(1,3-Dioxoisoindolin-2-yl)-3-(4-isopropylphenyl)-*N*-(quinolin-8-yl)heptanamide (11d): The compound **11d** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a green color viscous liquid (55 mg, 70%); R_f (40% EtOAc/hexane) = 0.7; IR (DCM): 2933, 1711, 1525, 1326, 736 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.69 (1H, br. s), 8.77 (1H, d, J = 4.0 Hz), 8.74 (1H, d, J = 7.2 Hz), 8.14 (1H, d, J = 8.2 Hz), 7.81 (2H, dd, J_1 = 5.0, J_2 = 3.2 Hz), 7.69 (2H, dd, J_1 = 5.1, J_2 = 3.2 Hz), 7.53-7.47 (2H, m), 7.43 (1H, dd, J_1 = 8.2, J_2 = 4.2 Hz), 7.20 (2H, d, J = 7.8 Hz), 7.12 (2H, d, J = 7.8 Hz), 3.62 (2H, t, J = 7.2 Hz), 3.32-3.25 (1H, m), 2.85-2.78 (3H, m), 1.89-1.82 (1H, m), 1.78-1.70 (2H, m), 1.65-1.56 (1H, m), 1.35-1.31 (1H, m), 1.26-1.24 (1H, m), 1.17 (6H, d, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 170.4, 168.4, 148.0, 146.8, 141.2, 138.3, 136.3, 134.4, 133.8, 132.1, 127.9, 127.4, 127.3, 126.6, 123.1, 121.5, 121.3, 116.4, 45.7, 42.0, 37.8, 35.7, 33.6, 28.4, 24.7, 24.0, 23.9; HRMS (ESI) calcd for $C_{33}H_{34}N_3O_3$ $[M+H]^+$ 520.2600, found 520.2623.

3.4.32. Methyl 4-(7-(1,3-dioxoisoindolin-2-yl)-1-oxo-1-(quinolin-8-ylamino)heptan-3-yl)benzoate (11e): The compound **11e** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a yellow color viscous liquid (58 mg, 72%); R_f (40% EtOAc/hexane) = 0.3; IR (DCM): 2939, 1712, 1525, 1282, 735 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.67 (1H, br. s), 8.76 (1H, d, J = 3.8 Hz), 8.69 (1H, dd, J_1 = 6.9, J_2 = 2.0 Hz), 8.14 (1H, d, J = 8.2 Hz), 7.93 (2H, d, J = 8.0 Hz), 7.81 (2H, dd, J_1 = 5.2, J_2 = 3.1 Hz), 7.69 (2H, dd, J_1 = 5.3, J_2 = 3.2 Hz), 7.52-7.47 (2H, m), 7.44 (1H, dd, J_1 = 8.2, J_2 = 4.2 Hz), 7.36 (2H, d, J = 8.0 Hz), 3.88 (3H, s), 3.62 (2H, t, J = 7.2 Hz), 3.43-3.36 (1H, m), 2.93-2.81 (2H, m), 1.92-1.85 (1H, m), 1.82-1.74 (2H, m), 1.66-1.59 (1H, m), 1.34-1.29 (1H, m), 1.24-1.17 (1H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 169.7, 168.3, 166.9, 149.4, 148.1, 138.2, 136.3, 134.2, 133.8, 132.0, 130.0, 128.4, 127.8, 127.6, 127.3, 123.1, 121.6, 121.5, 116.5, 51.9, 45.2, 42.4, 37.6, 35.4, 28.3, 24.5; HRMS (ESI) calcd for $C_{32}H_{30}N_3O_5$ $[M+H]^+$ 536.2185, found 536.2204.

3.4.33. 3-(4-Chlorophenyl)-8-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)octanamide (12a): The compound **12a** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a yellow color viscous liquid (64 mg, 61%); R_f (40% EtOAc/hexane) = 0.5; IR (DCM): 3351, 2933, 1709, 1531, 721 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.65 (1H, br. s), 8.75 (1H, dd, J_1 = 4.1, J_2 = 1.2 Hz), 8.70 (1H, dd, J_1 = 6.8, J_2 = 2.0 Hz), 8.13 (1H, dd, J_1 = 8.2, J_2 = 1.0 Hz), 7.81 (2H, dd, J_1 = 5.3, J_2 = 3.1 Hz), 7.68 (2H, dd, J_1 = 5.3, J_2 = 3.1 Hz), 7.51–7.46 (2H, m), 7.43 (1H, dd, J_1 = 8.2, J_2 = 4.2 Hz), 7.25-7.20 (4H, m), 3.62 (2H, t, J = 7.2 Hz), 3.31-3.24 (1H, m), 2.87-2.75 (2H, m), 1.83-1.76 (1H, m), 1.71-1.58 (3H, m), 1.38-1.18 (4H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 169.9, 168.4, 148.1, 142.6, 138.1, 136.4, 134.2, 133.8, 132.1, 132.0, 128.9, 128.7, 127.9, 127.3, 123.1, 121.6, 121.5, 116.5, 45.7, 42.0, 37.9, 36.0, 28.4, 27.0, 26.8; HRMS (ESI) calculated for $C_{31}H_{29}ClN_3O_3$ $[M+H]^+$ 526.1897 found 526.1876.

3.4.34. 8-(1,3-Dioxoisoindolin-2-yl)-3-(4-methoxyphenyl)-*N*-(quinolin-8-yl)octanamide (12b): The compound **12b** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a green color viscous liquid (53 mg, 68%); R_f (40% EtOAc/hexane) = 0.5; IR (DCM): 2930, 1708, 1523, 1246, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.66 (1H, br. s), 8.77 (1H, d, J = 4.1 Hz), 8.72 (1H, d, J = 7.0 Hz), 8.14 (1H, d, J = 8.2 Hz), 7.83 (2H, dd, J_1 = 5.1, J_2 = 3.1 Hz), 7.70 (2H, dd, J_1 = 5.2, J_2 = 3.2 Hz), 7.53–7.47 (2H, m), 7.44 (1H, dd, J_1 = 8.3, J_2 = 4.3 Hz), 7.20 (2H, d, J = 8.4 Hz), 6.82 (2H, d, J = 8.4 Hz), 3.75 (3H, s), 3.63 (2H, t, J = 7.3 Hz), 3.28-3.21 (1H, m), 2.86-2.76 (2H, m), 1.82-1.76 (1H, m), 1.63-1.58 (3H, m), 1.40-1.32 (3H, m), 1.24-1.18 (1H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 170.4, 168.4, 158.1, 148.0, 138.3, 136.2, 136.1, 134.4, 133.8, 132.2, 128.4, 127.9, 127.4, 123.1, 121.5, 121.3, 116.4, 114.0, 55.2, 46.1, 41.8, 38.0, 36.2, 28.5, 27.0, 26.9; HRMS (ESI) calculated for $C_{32}H_{32}N_3O_4$ $[M+H]^+$ 522.2393 found 522.2418.

3.4.35. 3-(4-Cyanophenyl)-8-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)octanamide (12c): The compound **12c** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a green color solid (49 mg, 63%); R_f (40% EtOAc/hexane) = 0.4; mp: 48-50 ^oC; IR (DCM): 2934, 2227, 1710, 1524, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.64 (1H, br. s), 8.77 (1H, dd, J_1 = 4.2, J_2 = 1.6 Hz), 8.67 (1H, dd, J_1 = 5.3, J_2 = 3.7 Hz), 8.15 (1H, dd, J_1 = 8.3, J_2 = 1.6 Hz), 7.83 (2H, dd, J_1 = 5.5, J_2 = 3.0 Hz), 7.71 (2H, dd, J_1 = 5.4, J_2 = 3.1 Hz), 7.57 (2H, d, J = 8.2 Hz), 7.53-7.48 (2H, m), 7.46 (1H, dd, J_1 = 8.2, J_2 = 4.2 Hz), 7.40 (2H, d, J = 8.2 Hz), 3.63 (2H, t, J = 7.2 Hz), 3.40-3.36 (1H, m), 2.90 (1H, dd, J_1 = 14.8, J_2 = 6.4 Hz), 2.80 (1H, dd, J_1 = 14.8, J_2 = 8.3 Hz), 1.86-1.79 (1H, m), 1.76-1.69 (1H, m), 1.66-1.59 (2H, m), 1.39-1.29 (3H, m), 1.22-1.13 (1H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 169.4, 168.4, 149.9, 148.1, 138.2, 136.4, 134.1, 133.9, 132.4, 132.1, 128.4, 127.9, 127.3, 123.2, 121.7, 119.0, 116.5, 110.3, 45.1, 42.6, 37.8, 35.7, 28.3, 26.9, 26.7; HRMS (ESI) calculated for $C_{32}H_{29}N_4O_3$ $[M+H]^+$ 517.2240 found 517.2217.

3.4.36. 8-(1,3-Dioxoisoindolin-2-yl)-3-(4-fluorophenyl)-*N*-(quinolin-8-yl)octanamide (12d): The compound **12d** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a colourless viscous liquid (50 mg, 72%); R_f (40% EtOAc/hexane) = 0.5; IR (DCM): 2934, 1713, 1525, 1222, 721 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.64 (1H, br. s), 8.77 (1H, d, J = 3.8 Hz), 8.71 (1H, d, J = 6.6 Hz), 8.14 (1H, d, J = 8.2 Hz), 7.83 (2H, dd, J_1 = 5.2, J_2 = 3.3 Hz), 7.71 (2H, dd, J_1 = 5.2, J_2 = 3.1 Hz), 7.53–7.47 (2H, m), 7.45 (1H, dd, J_1 = 8.3, J_2 = 4.2 Hz), 7.26-7.23 (2H, m), 6.97 (2H, t, J = 8.6 Hz), 3.63 (2H, t, J = 7.2 Hz), 3.30-3.27 (1H, m), 2.88-2.75 (2H, m), 1.83-1.77 (1H, m), 1.66-1.59 (3H, m), 1.44-1.30 (3H, m) 1.22-1.16 (1H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 170.0, 168.4, 161.4 (d, J_{C-F} = 242.6 Hz), 148.0, 139.7 (d, J_{C-F} = 2.9 Hz), 138.2, 136.3, 134.3, 133.8, 132.1, 128.9 (d, J_{C-F} = 7.9 Hz), 127.9, 127.3, 123.1, 121.6, 121.4, 116.4, 115.3 (d, J_{C-F} = 21.0 Hz), 41.2, 37.1, 33.2, 31.4, 23.7, 22.2, 22.0; HRMS (ESI) calcd for $C_{31}H_{29}FN_3O_3$ $[M+H]^+$ 510.2193 found 510.2219.

3.4.37. 8-(1,3-Dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)-3-(thiophen-2-yl)octanamideoctanamide (12e): The compound **12e** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a yellow color viscous liquid (55 mg, 74%); R_f (40% EtOAc/hexane) = 0.5; IR (DCM): 2935, 1712, 1525, 1325, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.74 (1H, br. s), 8.79 (1H, d, J = 4.0 Hz), 8.75 (1H, d, J = 7.0 Hz), 8.15 (1H, d, J = 8.2 Hz), 7.83 (2H, dd, J_1 = 5.1, J_2 = 3.3 Hz), 7.70 (2H, dd, J_1 = 5.2, J_2 = 3.1 Hz), 7.55–7.48 (2H, m), 7.45 (1H, dd, J_1 = 8.2, J_2 = 4.2 Hz), 7.13 (1H, d, J = 4.9 Hz), 6.91-6.88 (2H, m), 3.68-3.63 (3H, m), 2.88 (2H, d, J = 7.2 Hz), 1.87-1.81 (1H, m), 1.76-1.61 (3H, m), 1.44-1.31 (4H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 169.8, 168.4, 148.1, 148.1, 138.3, 136.3, 134.4, 133.8, 132.1, 127.9, 127.4, 126.6, 124.3, 123.2, 123.1, 121.6, 121.5, 116.5, 46.7, 38.0, 37.2, 28.5, 26.9, 26.8; HRMS (ESI) calcd for $C_{29}H_{28}N_3O_3S$ $[M+H]^+$ 498.1851, found 498.1830.

3.4.38. 3-(4-Chlorophenyl)-11-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)undecanamide (13a): The compound **13a** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a pale yellow color semisolid (47 mg, 55%); R_f (40% EtOAc/hexane) = 0.6; IR (DCM): 3351, 2933, 1709, 1531, 721 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.65 (1H, br. s), 8.77 (1H, d, J = 3.1 Hz), 8.71 (1H, dd, J_1 = 6.9, J_2 = 1.2 Hz), 8.14 (1H, dd, J_1 = 8.2, J_2 = 0.6 Hz), 7.84 (2H, dd, J_1 = 5.2, J_2 = 3.1 Hz), 7.70 (2H, dd, J_1 = 5.3, J_2 = 3.1 Hz), 7.53-7.47 (2H, m), 7.45 (1H, dd, J_1 = 8.3, J_2 = 4.3 Hz), 7.27-7.22 (4H, m), 3.66 (2H, t, J = 7.3 Hz), 3.32-3.24 (1H, m), 2.89-2.76 (2H, m), 1.82-1.75 (1H, m), 1.70-1.58 (3H, m), 1.27-1.13 (10H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 170.0, 168.5, 148.1, 142.8, 138.2, 136.3, 134.3, 133.8, 132.2, 132.0, 128.9, 128.7, 127.9, 127.4, 123.1, 121.6, 121.5, 116.4, 45.7, 42.1, 38.0, 36.2, 29.4, 29.3, 29.1, 28.6, 27.3, 26.8; HRMS (ESI) calcd for $C_{34}H_{35}ClN_3O_3$ $[M+H]^+$ 568.2367 found 568.2390.

3.4.39. 3-(4-Acetylphenyl)-11-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)undecanamide (13b): The compound **13b** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a pale yellow color viscous liquid (56 mg, 65%); R_f (40% EtOAc/hexane) = 0.3; IR (DCM): 2929, 1710, 1528, 1267, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.68 (1H, br. s), 8.74–8.69 (2H, m), 8.12 (1H, dd, J_1 = 8.2, J_2 = 1.2 Hz), 7.89 (2H, d, J = 7.9 Hz), 7.83-7.82 (2H, m), 7.70-7.68 (2H, m), 7.51-7.38 (5H, m), 3.64 (2H, t, J = 7.3 Hz), 3.42-3.35 (1H, m), 2.94-2.81 (2H, m), 2.54, (3H, s), 1.84-1.59 (4H, m), 1.26-1.12 (10H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 197.9, 169.9, 168.5, 150.2, 148.1, 138.2, 136.3, 135.5, 134.2, 133.9, 132.2, 128.7, 127.8, 127.3, 123.1, 121.6, 121.5, 116.4, 45.3, 42.6, 38.0, 36.0, 29.4, 29.3, 29.0, 28.5, 27.3, 26.8, 26.8; HRMS (ESI) calcd for $C_{36}H_{38}N_3O_4$ $[M+H]^+$ 576.2862 found 576.2882.

3.4.40. 11-(1,3-Dioxoisoindolin-2-yl)-3-(4-nitrophenyl)-*N*-(quinolin-8-yl)undecanamide (13c): The compound **13c** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a yellow color viscous liquid (63 mg, 72%); R_f (40% EtOAc/hexane) = 0.4; IR (DCM): 2927, 1711, 1523, 1395, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.66 (1H, br. s), 8.76 (1H, d, J = 3.3 Hz), 8.62 (1H, dd, J_1 = 5.6, J_2 = 3.1 Hz), 8.17-8.15 (3H, m), 7.85 (2H, dd, J_1 = 5.2, J_2 = 3.2 Hz), 7.72 (2H, dd, J_1 = 5.2, J_2 = 3.1 Hz), 7.53-7.44 (5H, m), 3.66 (2H, t, J = 7.3 Hz), 3.49-3.42 (1H, m), 2.95 (1H, dd, J_1 = 14.8, J_2 = 6.2 Hz), 2.84 (1H, dd, J_1 = 14.8, J_2 = 8.5 Hz), 1.84-1.68 (4H, m), 1.24-1.13 (10H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 169.4, 168.5, 152.4, 148.1, 146.7, 138.2, 136.4, 134.1, 133.8, 132.1, 128.5, 127.9, 127.3, 123.9, 123.1, 121.7, 116.5, 45.1, 42.5, 38.0, 36.0, 29.3, 29.2, 29.0, 28.5, 27.3, 26.7; HRMS (ESI) calcd for $C_{34}H_{35}N_4O_5$ $[M+H]^+$ 579.2607 found 579.2584.

3.4.41. 11-(1,3-Dioxoisoindolin-2-yl)-3-(4-ethylphenyl)-*N*-(quinolin-8-yl)undecanamide (13d): The compound **13d** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a yellow color liquid (58 mg, 69%); R_f (40% EtOAc/hexane) = 0.5; IR (DCM): 2927, 1710, 1523, 1395, 719 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.69 (1H, br. s), 8.78-8.74 (2H, m), 8.15 (1H, d, J = 8.2 Hz), 7.85 (2H, dd, J_1 = 5.3, J_2 = 3.0 Hz), 7.71 (2H, dd, J_1 = 5.4, J_2 = 3.1 Hz), 7.54-7.43 (3H, m), 7.21 (2H, d, J = 7.8 Hz), 7.13 (2H, d, J = 7.8 Hz), 3.66 (2H, t, J = 7.3 Hz), 3.29-3.25 (1H, m), 2.84 (2H, d, J = 7.4 Hz), 2.60 (2H, q, J = 7.6 Hz), 1.81-1.58 (4H, m), 1.32-1.17 (13H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 170.6, 168.4, 148.0, 142.1, 141.6, 138.2, 136.3, 134.5, 133.8, 132.2, 128.0, 127.9, 127.9, 127.4, 123.1, 121.5, 121.3, 116.4, 45.9, 42.2, 38.0, 36.2, 29.5, 29.3, 29.1, 28.6, 28.4, 27.4, 26.8, 15.4; HRMS (ESI) calcd for $C_{36}H_{40}N_3O_3$ $[M+H]^+$ 562.3070 found 562.3087.

3.4.42. 11-(1,3-Dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)-3-(thiophen-2-yl)undecanamide (13e): The compound **13e** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a green color viscous liquid (62 mg, 77%); R_f (40% EtOAc/hexane) = 0.3; IR (DCM): 2928, 1712, 1525, 1325, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.75 (1H, br. s), 8.80-8.76 (2H, m), 8.15 (1H, d, J = 8.2 Hz),), 7.85 (2H, dd, J_1 = 5.3, J_2 = 3.1 Hz), 7.71 (2H, dd, J_1 = 5.3, J_2 = 3.1 Hz), 7.55-7.48 (2H, m), 7.45 (1H, dd, J_1 = 8.2, J_2 = 4.2 Hz), 7.14 (1H, d, J = 4.8 Hz), 6.92-6.89 (2H, m) 3.70-3.63 (3H, m), 2.89 (2H, d, J = 7.3 Hz), 1.86-1.80 (1H, m), 1.74-1.63 (3H, m), 1.31-1.28 (10H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 169.9, 168.5, 148.3, 148.1, 138.3, 136.3, 134.4, 133.8, 132.2, 127.9, 127.4, 126.6, 124.2, 123.1, 123.1, 121.6, 121.4, 116.5, 46.7, 38.0, 38.0, 37.3, 29.3, 29.3, 29.1, 28.6, 27.2, 26.8; HRMS (ESI) calcd for $C_{32}H_{34}N_3O_3S$ $[M+H]^+$ 540.2321 found 540.2296.

3.4.43. 3-(4-Chlorophenyl)-12-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)dodecanamide (14a): The compound **14a** was obtained after purification by column chromatography on silica gel

(EtOAc:hexane = 40:60) as a pale yellow color viscous liquid (64 mg, 73%); R_f (40% EtOAc/hexane) = 0.6; IR (DCM): 3352, 2928, 1698, 1530, 722 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.65 (1H, br. s), 8.75 (1H, dd, J_1 = 4.2, J_2 = 1.7 Hz), 8.71 (1H, dd, J_1 = 7.0, J_2 = 2.1 Hz), 8.13 (1H, dd, J_1 = 8.3, J_2 = 1.7 Hz), 7.83 (2H, dd, J_1 = 5.5, J_2 = 3.1 Hz), 7.69 (2H, dd, J_1 = 5.5, J_2 = 3.1 Hz), 7.52-7.45 (2H, m), 7.43 (1H, dd, J_1 = 8.2, J_2 = 4.2 Hz), 7.27-7.21 (4H, m), 3.66 (2H, t, J = 7.4 Hz), 3.32-3.24 (1H, m), 2.89-2.75 (2H, m), 1.80-1.73 (1H, m), 1.70-1.61 (3H, m), 1.31-1.12 (12H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 170.1, 168.5, 148.1, 142.9, 138.2, 136.3, 134.3, 133.8, 132.1, 132.0, 129.0, 128.7, 127.8, 127.3, 123.1, 121.6, 121.5, 116.4, 45.7, 42.1, 38.0, 36.2, 29.5, 29.4, 29.4, 29.1, 28.6, 27.3, 26.8; HRMS (ESI) calcd for $C_{35}H_{37}ClN_3O_3$ $[M+H]^+$ 582.2523 found 582.2496.

3.4.44. 12-(1,3-Dioxoisoindolin-2-yl)-3-(4-methoxyphenyl)-*N*-(quinolin-8-yl)dodecanamide (14b): The compound **14b** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a pale green color viscous liquid (65 mg, 75%); R_f (40% EtOAc/hexane) = 0.5; IR (DCM): 2928, 1731, 1527, 1247, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.67 (1H, br. s), 8.77-8.73 (2H, m), 8.15 (1H, d, J = 7.8 Hz), 7.84 (2H, dd, J_1 = 5.2, J_2 = 3.1 Hz), 7.71 (2H, dd, J_1 = 5.3, J_2 = 3.1 Hz), 7.53-7.47 (2H, m), 7.44 (1H, dd, J_1 = 8.3, J_2 = 4.3 Hz), 7.22 (2H, d, J = 8.4 Hz), 6.84 (2H, d, J = 8.5 Hz), 3.75 (3H, s), 3.67 (2H, t, J = 7.3 Hz), 3.26-3.23 (1H, m), 2.88-2.77 (2H, m), 1.80-1.74 (1H, m), 1.66-1.61 (3H, m), 1.31-1.20 (12H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 170.6, 168.5, 158.0, 147.9, 138.1, 136.5, 136.4, 134.3, 133.8, 132.2, 128.4, 127.9, 127.4, 123.1, 121.5, 121.4, 116.7, 113.9, 55.1, 46.1, 41.9, 38.1, 36.4, 29.7, 29.5, 29.4, 29.1, 28.6, 27.4, 26.8; HRMS (ESI) calcd for $C_{36}H_{40}N_3O_4$ $[M+H]^+$ 578.3019 found 578.3033.

3.4.45. 12-(1,3-Dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)-3-(*p*-tolyl)dodecanamide (14c): The compound **14c** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a colourless viscous liquid (61 mg, 72%); R_f (40% EtOAc/hexane) = 0.5; IR (DCM): 2926, 1711, 1524, 1395, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.69 (1H, br. s), 8.78-8.74 (2H, m), 8.14 (1H, d, J = 8.2 Hz), 7.84 (2H, dd, J_1 = 5.4, J_2 = 3.0 Hz), 7.70 (2H, dd, J_1 = 5.4, J_2 = 3.1 Hz), 7.53-7.46 (2H, m), 7.44 (1H, dd, J_1 = 8.3, J_2 = 4.3 Hz), 7.19 (2H, d, J = 8.0 Hz), 7.11 (2H, d, J = 7.9 Hz), 3.67 (2H, t, J = 7.3 Hz), 3.28-3.23 (1H, m), 2.87-2.79 (2H, m), 2.29 (3H, s), 1.82-1.75 (1H, m), 1.71-1.61 (3H, m), 1.32-1.20 (12H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 170.5, 168.4, 148.0, 141.3, 138.3, 136.3, 135.7, 134.5, 133.8, 132.2, 129.2, 127.8, 127.4, 127.4, 123.1, 121.5, 121.3, 116.4, 46.0, 42.2, 38.1, 36.3, 29.5, 29.4, 29.4, 29.1, 28.6, 27.4 26.8, 21.0; HRMS (ESI) calcd for $C_{36}H_{40}N_3O_3$ $[M+H]^+$ 562.3070 found 562.3097.

3.4.46. 3-(2,3-Dihydrobenzo[*b*][1,4]dioxin-6-yl)-12-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)dodecanamide (14d): The compound **14d** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a pale yellow color liquid (64 mg, 70%); R_f (40% EtOAc/hexane) = 0.3; IR (DCM): 2928, 1708, 1526, 1286, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.68 (1H, br. s), 8.79-8.74 (2H, m), 8.15 (1H, d, J = 8.2 Hz), 7.85 (2H, dd, J_1 = 5.0, J_2 = 3.0 Hz), 7.71 (2H, dd, J_1 = 4.8, J_2 = 3.0 Hz), 7.54-7.49 (2H, m), 7.45 (1H, dd, J_1 = 8.3, J_2 = 4.3 Hz), 6.80-6.78 (3H, m), 4.20 (4H, s), 3.67 (2H, t, J = 7.2 Hz), 3.20-3.16 (1H, m), 2.80 (2H, d, J = 7.2 Hz), 1.75-1.72 (1H, m), 1.67-1.64 (3H, m), 1.31-1.21 (12H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 170.5, 168.5, 148.0, 143.4, 141.9, 138.3, 137.8, 136.3, 134.5, 133.8, 132.2, 127.9, 127.4, 123.1, 121.5, 121.3, 120.6, 117.2, 116.4, 116.0, 64.3, 64.3, 46.0, 42.0, 38.1, 36.3, 29.5, 29.4, 29.1, 29.1, 28.6, 27.4, 26.8; HRMS (ESI) calcd for $C_{37}H_{40}N_3O_5$ $[M+H]^+$ 606.2968 found 606.2943.

3.4.47. 12-(1,3-Dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)-3-(thiophen-2-yl)dodecanamide (14e): The compound **14e** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a yellow color viscous liquid (60 mg, 76%); R_f (40% EtOAc/hexane) = 0.5; IR (DCM): 2927, 1711, 1527, 1393, 718 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.75 (1H, br. s), 8.79-8.76 (2H, m), 8.15 (1H, d, J = 8.3 Hz), 7.85 (2H, dd, J_1 = 5.4, J_2 = 3.1 Hz), 7.71 (2H, dd, J_1 = 5.3, J_2 = 3.2 Hz), 7.55-7.49 (2H, m), 7.45 (1H, dd, J_1 = 8.2, J_2 = 4.2 Hz), 7.15-7.14 (1H, m), 6.93-6.89 (2H, m), 3.68-3.65 (3H, m), 2.89 (2H, d, J = 7.2 Hz), 1.85-1.81 (1H, m), 1.75-1.62 (3H, m), 1.31-1.23 (12H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 169.9, 168.5, 148.4, 148.1, 138.3, 136.3, 134.4, 133.8, 132.2, 127.9, 127.4, 126.6, 124.2, 123.2, 123.1, 121.6, 121.5, 116.5, 46.7, 38.1, 38.0, 37.3, 29.7, 29.7, 29.4, 29.1, 28.6, 27.3, 26.8; HRMS (ESI) calcd for $C_{33}H_{36}N_3O_3S$ $[M+H]^+$ 554.2477 found 554.2497.

3.4.48. 3-(3-(Cyclopentyloxy)-4-methoxyphenyl)-8-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)octanamide (17): The compound **17** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a yellow color viscous liquid (67 mg, 74%); R_f (40% EtOAc/hexane) = 0.2; IR (DCM): 3353, 2936, 1711, 1260, 724 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.62 (1H, br. s), 8.75-8.72 (2H, m), 8.14 (1H, d, J = 8.2 Hz), 7.83 (2H, dd, J_1 = 5.3, J_2 = 3.2 Hz), 7.71-7.69 (2H, m), 7.52-7.42 (3H, m), 6.81-6.76 (3H, m), 4.72 (1H, br. s), 3.76 (3H, s), 3.63 (2H, t, J = 7.2 Hz), 3.23-3.16 (1H, m), 2.85-2.74 (2H, m), 1.88-1.54 (11H, m), 1.35-1.27 (5H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 170.5, 168.4, 148.6, 148.0, 147.6, 138.2, 136.5, 136.3, 134.4, 133.8, 132.2, 127.9, 127.4, 123.1, 121.5, 121.3, 119.4, 116.5, 114.6, 112.2, 80.2, 56.0, 46.3, 42.4, 38.0, 36.2, 32.8, 28.5, 271, 26.9, 24.1, 24.0; HRMS (ESI) calcd for $C_{37}H_{40}N_3O_5$ $[M+H]^+$ 606.2968 found 606.2938.

3.4.49. 3-(3-(Cyclopentyloxy)-4-methoxyphenyl)-12-(1,3-dioxoisoindolin-2-yl)-*N*-(quinolin-8-yl)dodecanamide (18): The compound **18** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a yellow color viscous liquid (56 mg, 56%); R_f (40% EtOAc/hexane) = 0.2; IR (DCM): 3354, 2929, 1693, 1259, 724 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 9.64 (1H, br. s), 8.75-8.74 (2H, m), 8.14 (1H, d, J = 8.2 Hz), 7.84 (2H, dd, J_1 = 5.4, J_2 = 3.0 Hz), 7.70 (2H, dd, J_1 = 5.4, J_2 = 3.1 Hz), 7.52-7.46 (2H, m), 7.43 (1H, dd, J_1 = 8.3, J_2 = 4.2 Hz), 6.82-6.77 (3H, m), 4.75-4.71 (1H, m), 3.77 (3H, s), 3.66 (2H, t, J = 7.3 Hz), 3.23-3.16 (1H, m), 2.86-2.75 (2H, m), 1.89-1.85 (2H, m), 1.83-1.74 (5H, m), 1.70-1.63 (3H, m), 1.60-1.50 (2H, m), 1.31-1.21 (12H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 170.7, 168.5, 148.5, 147.9, 147.5, 138.1, 136.7, 136.4, 134.4, 133.8, 132.2, 127.9, 127.4, 123.1, 121.5, 121.3, 119.4, 116.5, 114.6, 112.1, 80.2, 56.0, 46.4, 42.4, 38.1, 36.3, 32.8, 32.7, 29.5, 29.4, 29.2, 28.6, 27.4, 26.8, 24.1, 24.0; HRMS (ESI) calcd for $C_{41}H_{48}N_3O_5$ $[M+H]^+$ 662.3594 found 662.3562.

3.4.50. 3-(4-Cyanophenyl)-4-(4-(1,3-dioxoisoindolin-2-yl)phenyl)-*N*-(quinolin-8-yl)butanamide (19a): The compound **19a** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a colourless solid (52 mg, 70%); R_f (40% EtOAc/hexane) = 0.4; mp: 140-142 ^oC; IR (DCM): 2968, 1701, 1485, 1382, 826 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.71 (1H, br. s), 8.79 (1H, dd, J_1 = 4.2, J_2 = 1.6 Hz), 8.68 (1H, dd, J_1 = 5.5, J_2 = 3.4 Hz), 8.16 (1H, dd, J_1 = 8.3, J_2 = 1.6 Hz), 7.95 (2H, dd, J_1 = 5.4, J_2 = 3.0 Hz), 7.79 (2H, dd, J_1 = 5.5, J_2 = 3.1 Hz), 7.56 (2H, d, J = 8.3Hz), 7.54-7.49 (2H, m), 7.47 (1H, dd, J_1 = 8.2, J_2 = 4.2 Hz), 7.39 (2H, d, J = 8.2 Hz), 7.34 (2H, d, J = 8.4 Hz), 7.22 (2H, d, J = 8.4 Hz), 3.83-3.76 (1H, m), 3.18 (1H, dd, J_1 = 13.6, J_2 = 6.7 Hz), 3.08-3.01 (2H, m), 2.92 (1H, dd, J_1 = 15.2, J_2 = 8.4 Hz); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 169.0, 167.3, 148.9, 148.2, 138.7, 138.2, 136.4, 134.4, 134.1, 132.4, 131.7, 130.1, 129.8, 128.6, 127.9, 127.3, 126.4, 123.7, 121.7, 121.7, 118.9, 116.5, 110.6, 44.0, 43.3, 41.9; MS *m/z* (ASAP) 537 $(M+H)^+$.

3.4.51. 3-(4-(1,3-Dioxoisoindolin-2-yl)phenyl)-3-(4-methoxyphenyl)-*N*-(quinolin-8-yl)propanamide (19b): The compound **19b** was obtained after purification by column

chromatography on silica gel (EtOAc:hexane = 40:60) as a green color solid (52 mg, 66%); R_f (40% EtOAc/hexane) = 0.4; mp: 70-72 °C; IR (DCM): 2923, 1717, 1523, 1382, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.81 (1H, br. s), 8.80-8.78 (1H, m), 8.73 (1H, dd, J_1 = 6.6, J_2 = 1.5 Hz), 8.14 (1H, d, J = 8.2 Hz), 7.95 (2H, dd, J_1 = 5.4, J_2 = 3.1 Hz), 7.78 (2H, dd, J_1 = 5.4, J_2 = 3.0 Hz), 7.54-7.43 (5H, m), 7.39 (2H, d, J = 8.3 Hz), 7.30 (2H, d, J = 8.6 Hz), 6.85 (2H, d, J = 8.5 Hz), 4.84 (1H, t, J = 7.6 Hz), 3.76 (3H, s), 3.33 (2H, d, J = 7.6 Hz); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 169.4, 167.3, 158.3, 148.1, 144.2, 138.3, 136.3, 135.3, 134.4, 134.3, 131.7, 129.9, 128.9, 128.4, 127.9, 127.4, 126.5, 123.7, 121.6, 121.5, 116.6, 114.1, 55.2, 46.0, 44.5. MS *m/z* (ASAP) 528 $(M+H)^+$.

3.5. Procedure for the removal of the directing group 8-aminoquinoline and preparation of the carboxylate derivatives 20a,b and 21a: Arylated carboxamide **8c**/**14a/10d** (0.15-0.25 mmol, 1 equiv), *p*-TsOH.H_2O (3 equiv) and methanol/ethanol (3-4 mL) were added to screw-cap seal tube. The vial containing the mixture was sealed and submerged into a silicon oil bath pre-heated to 100 °C. After 24 h, the dark brown solution was cooled to rt. After the reaction period, the solvent was evaporated under reduced pressure to afford a crude reaction mixture, which was purified by column chromatography to afford the corresponding carboxylate derivatives **20a,b**/**21a**.

3.5.1. Methyl 3-(4-chlorophenyl)-4-(1,3-dioxoisoindolin-2-yl)butanoate (20a): The compound **20a** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 40:60) as a colourless solid (50 mg, 93%); R_f (40% EtOAc:hexane) 0.7; mp: 104-106 °C; IR (DCM): 2949, 1714, 1397, 1171, 722 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 7.82 (2H, d, J = 4.0 Hz), 7.72 (2H, d, J = 4.0 Hz), 7.28-7.22 (4H, m), 3.94-3.84 (2H, m), 3.75 (1H, quint, J = 7.6 Hz), 3.52 (3H, m), 2.79-2.67 (2H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 171.7, 168.1, 138.8, 134.1, 133.1, 131.7, 129.1, 128.8, 123.4, 51.7, 42.9, 40.2, 38.3; HRMS (ESI) calcd for $C_{19}H_{16}ClNNaO_4$ $[M+Na]^+$ 380.0666 found 380.0650.

3.5.2. Ethyl 6-(1,3-dioxoisoindolin-2-yl)-3-phenylhexanoate (20b): The compound **20b** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 30:70) as a colourless liquid (69 mg, 59%); R_f (30% EtOAc/hexane) = 0.6; IR (DCM): 2920, 1711, 1396, 1031, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.83-7.81 (2H, m), 7.71-7.70 (2H, m), 7.29-7.26 (2H, m), 7.20-7.17 (3H, m), 4.01 (2H, q, J = 7.1 Hz), 3.64 (2H, t, J = 7.2 Hz), 3.16-3.09 (1H, m), 2.66-2.54 (2H, m), 1.78-1.56 (3H, m), 1.52-1.43 (1H, m), 1.12 (3H, t, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 172.1, 168.3, 143.3, 133.9, 132.1, 128.5, 127.5, 126.6, 123.2, 60.3, 41.9, 41.8, 37.8, 33.3, 26.5, 14.1; HRMS (ESI) calcd for $C_{22}H_{23}NNaO_4$ $[M+Na]^+$ 388.1525 found 388.1514.

3.5.3. Methyl 3-(4-chlorophenyl)-12-(1,3-dioxoisoindolin-2-yl)dodecanoate (21a): The compound **21a** was obtained after purification by column chromatography on silica gel (EtOAc:hexane = 30:70) as a colourless liquid (80 mg, 71%); R_f (30% EtOAc/hexane) = 0.6; IR (DCM): 2928, 2855, 1713, 1397, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.85 (2H, dd, J_1 = 5.5, J_2 = 3.1 Hz), 7.72 (2H, dd, J_1 = 5.4, J_2 = 3.1 Hz), 7.29 (2H, d, J = 8.4 Hz), 7.11 (2H, d, J = 8.4 Hz), 3.67 (2H, t, J = 7.3 Hz), 3.59 (3H, s), 3.10-3.03 (1H, m), 2.65-2.50 (2H, m), 1.70-1.54 (4H, m), 1.30-1.29 (4H, m), 1.20-1.08 (8H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 172.6, 168.4, 142.6, 133.8, 132.2, 132.0, 128.8, 128.5, 123.1, 51.5, 41.6, 41.5, 38.0, 36.1, 29.4, 29.3, 29.3, 29.1, 28.6, 27.2, 26.8; HRMS (ESI) calcd for $C_{27}H_{32}ClNaNO_4$ $[M+Na]^+$ 492.1918 found 492.1924.

3.6. Procedure for deprotection of phthalimide group from substrate 21a/20b:[211] A RB flask containing substrate **21a/20b** (0.19-0.22 mmol) in DCM (1-1.5 mL), EtOH (1-1.5 mL) and ethylenediamine (5 equiv) was heated to 40 °C for 24 h with vigorous stirring. Then, the solvents were removed under reduced pressure. $CuCl_2$ (2.5 equiv.) and deionized water (10 mL) were added into the resulting mixture. The aqueous solution was extracted with EtOAc (3 × 10 mL). The organic layers was washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford the corresponding products.

3.6.1. Methyl 12-amino-3-(4-chlorophenyl)dodecanoate (22a): The compound **22a** was obtained by following the above procedure as a pale green color liquid (73 mg, 86%); IR (DCM): 2928, 2855, 1735, 1261, 752 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.27 (2H, d, J = 7.8 Hz), 7.12 (2H, d, J = 7.5 Hz), 3.59 (3H, s), 3.07 (1H, br. s), 2.65-2.51 (2H, m), 1.61-1.09 (18H, m); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 172.6, 142.6, 132.0, 128.8, 128.6, 51.5, 41.6, 41.5, 36.1, 30.2, 29.4, 27.2; HRMS (ESI) calcd for $C_{19}H_{31}ClNO_2$ $[M+H]^+$ 340.2043 found 340.2054.

3.6.2. Ethyl 6-amino-3-phenylhexanoate (4): The compound **4** was obtained by following the above procedure as a brown color liquid (28 mg, 63%, the purity of this sample around 85-90%); IR (DCM): 2928, 1730, 1643, 1163 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ_H 7.32-7.27 (2H, m), 7.19-7.17 (3H, m), 4.01 (2H, q, J = 6.8 Hz), 3.10-3.08 (1H, m), 2.67-2.54 (2H, m), 1.79-1.42 (4H, m), 1.30-1.27 (2H, m), 1.13 (3H, t, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 172.3, 143.2, 128.6, 127.5, 126.7, 60.4, 41.7, 29.7, 14.1; HRMS (ESI) calcd for $C_{14}H_{22}NO_2$ $[M+H]^+$ 236.1651 found 236.1656. The NH protons could not be clearly identified in the proton NMR.

3.7. General procedure preparation of the pyrrolidone derivatives (2d/23): *β*-C-H Arylated *γ*-aminobutyric acid derivatives **8**/**16** (0.2-0.25 mmol, 1 equiv), $N_2H_4.H_2O$ (40 equiv) and ethanol (3 mL) were added to screw-cap seal tube. Then, the resulting mixture was sealed and the tube was submerged into a silicon oil bath pre-heated to 95 °C. After 6 h, the solution was cooled to rt. After the reaction period, the reaction mixture was diluted with EtOAc (7-10 mL) and transferred into a separating funnel, the organic layers were washed with water and then the organic layers were collected and dried over anhydrous Na_2SO_4. Next, the solvent was evaporated to afford a crude reaction mixture, which was purified by column chromatography to afford the corresponding pyrrolidone derivatives (**2d**/**23**).

3.7.1. 4-(4-Nitrophenyl)pyrrolidin-2-one (23a): The compound **23a** was obtained after purification by column chromatography on silica gel (EtOAc:MeOH = 90:10) as a brown color solid (24 mg, 58%); R_f (90% EtOAc:MeOH) 0.2; mp: 166-168 °C; IR (DCM): 3256, 1690, 1513, 1254, 744 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 8.22 (2H, d, J = 8.7 Hz), 7.45 (2H, d, J = 8.6 Hz), 6.96 (1H, br. s), 3.91-3.81 (2H, m), 3.47 (1H, dd, J_1 = 9.1, J_2 = 6.2 Hz), 2.83 (1H, dd, J_1 = 17.0, J_2 = 8.8 Hz), 2.51 (1H, dd, J_1 = 17.1, J_2 = 7.9 Hz); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 177.1, 149.8, 147.1, 127.7, 124.2, 49.0, 39.9, 37.8; HRMS (ESI) calcd for $C_{10}H_{11}N_2O_3$ $[M+H]^+$ 207.0770 found 207.0761.

3.7.2. 4-(5-Oxopyrrolidin-3-yl)benzonitrile (23d): The compound **23d** was obtained after purification by column chromatography on silica gel (EtOAc:MeOH = 90:10) as a brown color solid (21 mg, 56%); R_f (90% EtOAc:MeOH) 0.3; mp: 166-168 °C; IR (DCM): 3270, 2905, 1686, 1255, 734 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ_H 7.66 (2H, d, J = 8.3 Hz), 7.39 (2H, d, J = 8.2 Hz), 6.90 (1H, br. s), 3.88-3.75 (2H, m), 3.43 (1H, dd, J_1 = 9.4, J_2 = 6.6 Hz), 2.80 (1H, dd, J_1 = 17.0, J_2 = 8.9 Hz), 2.48 (1H, dd, J_1 = 17.0, J_2 = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 101 MHz): δ_C 177.1, 147.7, 132.8, 127.7, 118.6, 111.2, 49.0, 40.1, 37.6; HRMS (ESI) calcd for $C_{11}H_{11}N_2O$ $[M+H]^+$ 187.0871 found 187.0866.

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Supplementary data

Supplementary data (copy of ^{1}H, ^{13}C NMR Charts of compounds) associated with this article can be found, in the online version.