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Regioselective β-Csp^3-Arylation of β-Alanine: An Approach for the Exclusive Synthesis of Diverse β-Aryl-β-Amino Acids

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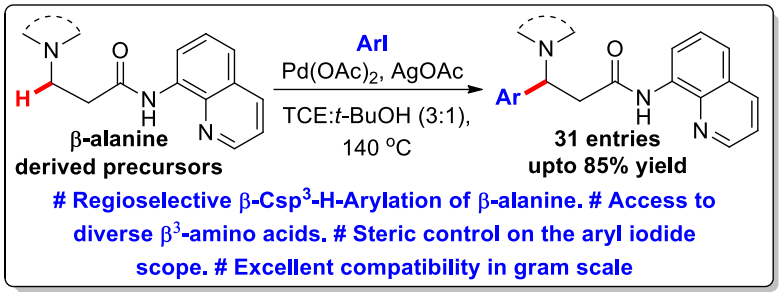
Abstract. An approach for the synthesis of a variety of new β-aryl-β-amino acids has been developed *via* a palladium catalyzed auxiliary directed regioselective Csp^3-H arylation of unactivated β-methylene bond of β-alanine. The use of 8-aminoquinoline amide as an auxiliary efficiently directs the desired regioselective β-Csp^3-H functionalization. The developed protocol enables the easy and straight-forward access to the several high value β-aryl-β-amino acids useful for peptide engineering starting from inexpensive and readily available β-alanine precursors in moderate to excellent yields.



Introduction:

The importance of natural as well as the nonproteinogenic β-amino acids and non-natural linkages consisting of those units are widely acknowledged.[1] Several important drugs and drug like molecules, structural motifs presented in biological systems consist of β-amino acids e.g. β-alanine and its derivatives (Figure 1).[2,3] It has been observed that incorporation of β-amino acids into peptide chains induces new secondary and tertiary structures leading to their unique biological activity in different cases. The change in the helical pitch of the peptide arising due to the incorporation of β-amino acids can lead to their different interaction with DNA and makes them biologically active.[4,5]

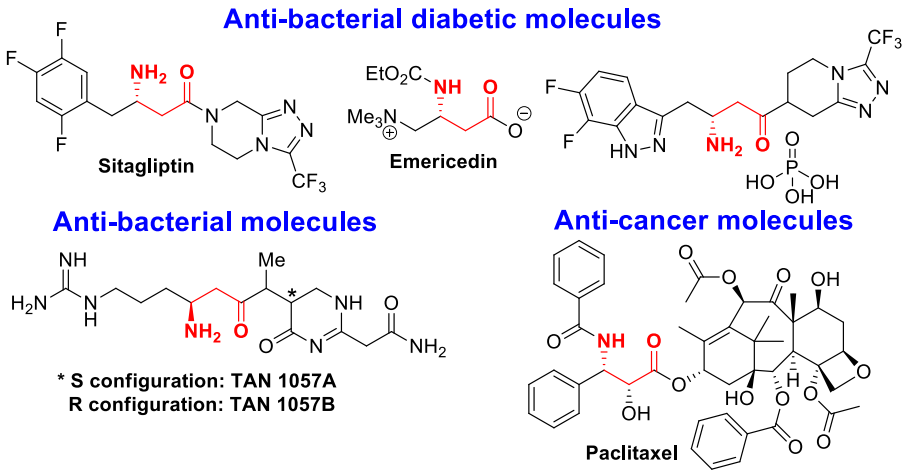


Figure 1: Examples of bioactive molecules with β-amino acid.

Owing to their importance several synthetic methods have been derived to access natural as well as non-natural β-amino acids e.g. Mannich reactions, Kowalsky rearrangements, radical reactions, isoxazoline intermediates, organocatalysis, enzymatic hydrolysis of β-lactams, and metal catalysis etc.[6-9] The other routes include the step up modification of α-amino acids using Arndt-Eistert protocol, oxazoline carbonylation/hydrolysis approach but unfortunately they came up with the limitations of using hazardous components like diazomethane or carbon monoxide, multiple steps and the lack of substrate versatility.[1,10-11] Thus a precise method like straightforward functionalization of the simple, inexpensive and readily available β-alanine can be a highly desirable alternative choice to access diverse β-amino acids.

Apart from the initial works of Daugulis and Corey *et al*. a lot of advancement has been observed over the last few years in the field of auxiliary directed regioselective Csp^3-/Csp^2-H functionalization of amino acids. But interestingly the major attention was centred on the synthetic modifications of α-amino acids and related derivatives.[10,11] The probable reasons are the high natural abundancy of a variety of enantiopure α-amino acids affording a range of excellent substrates to study and the relative ease in their desired Csp^3-H functionalization. More advantageously in most of the cases the desired functionalization ends up with predefined stereochemistry induced by the neighbouring chiral environment of the α-amino acid substrates (Figure 2). In this regard the β-amino acids with their flat structures and remote positioning of the respective amino and carboxyl groups are comparatively tough targets for the regioselctive Csp^3-H functionalization (Figure 2) and thus are considerably less studied although there exists immense synthetic and application scope of the β-amino acids and related structures.

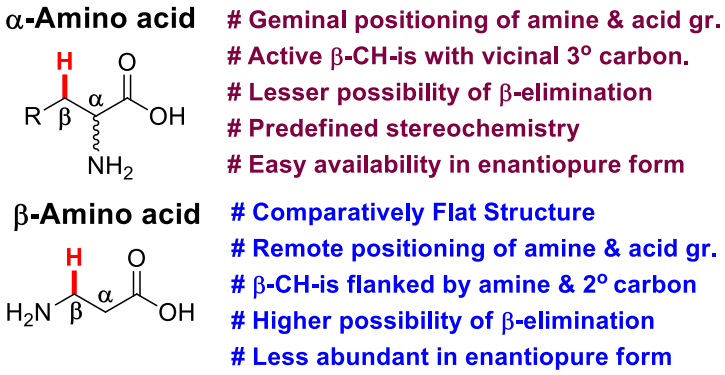
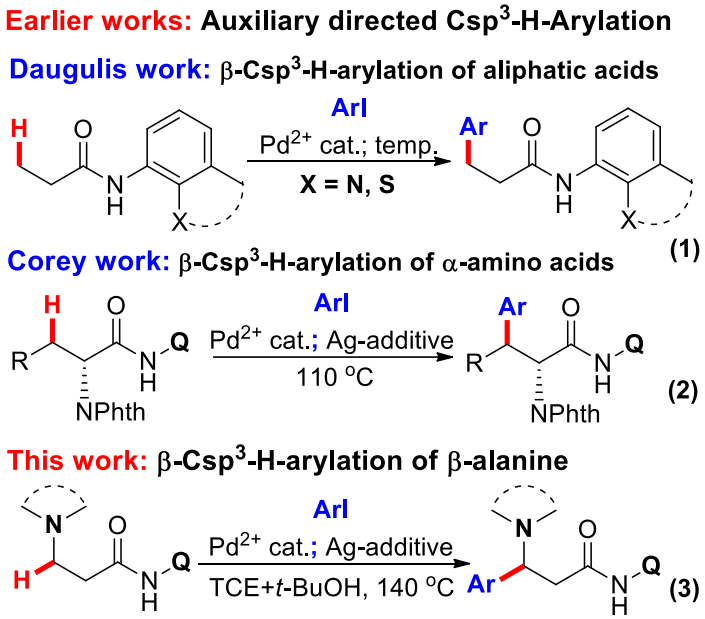


Figure 2. Structure-reactivity comparison of α- and β-amino acids.

Taking into account the importance and challenges of the issue we focused on the development of a straightforward protocol for the synthesis of β-amino acids and related structures. To our delight we report here our recently developed method for the auxiliary directed, palladium catalyzed regioselective β-functionalization of inexpensive and readily available β-alanine *via* the activation of comparatively unactivated β-Csp^3-H-bond to directly generate a wide range of important natural as well as nonproteinogenic β-aryl-β-amino acids with diverse architectural scope (Scheme 1, eq. 3).

Scheme 1. Directing group assisted Pd-catalyzed arylation of unactivated β-C(sp^3)−H bonds.



In earlier reports Daugulis *et al*. demonstrated the auxiliary directed Pd(II)/Pd(IV)-catalyzed arylation of comparatively unactivated β-Csp^3-H-bonds of carboxylic acid amides (Scheme 1, eq. 1).[12] Gradually, the concept has been utilized for β-Csp^3-H functionalization of different α-amino acids

(Scheme 1, eq. 2).[10-11,13] Later the similar concept was also used for β-Csp^3-H arylation of alkanoic amides with very limited and specific aryl scope.[14] We anticipated that this might be a potential route to achieve our desired β-Csp^3-H functionalization of β-alanine.

Results and Discussion:

In order to achieve the regioselective β-Csp^3-H functionalization, an auxiliary directed Pd(II)/Pd(IV) catalytic pathway was attempted on N-protected β-alanine (**I**) using its suitable amide as the directing group. The chelating ability of the amide auxiliary is important to direct the regioselective functionalization of β-Csp^3-H as it actively involves in the cyclometalation and promotes oxidative addition by stabilizing the high energy Pd(IV) intermediate (**III**). Additionally it can also decrease the possibility of β-hydride elimination by saturating the coordination sites on palladium through the formation of a preferred five-membered fused palladacycle (**II/III**) (Figure 3).[10,12] Unlike α-amino acids the sp^3-carbon to be activated in this case will be α-to the amine with a possibility to impart its effect on the proceeding catalytic sequence.

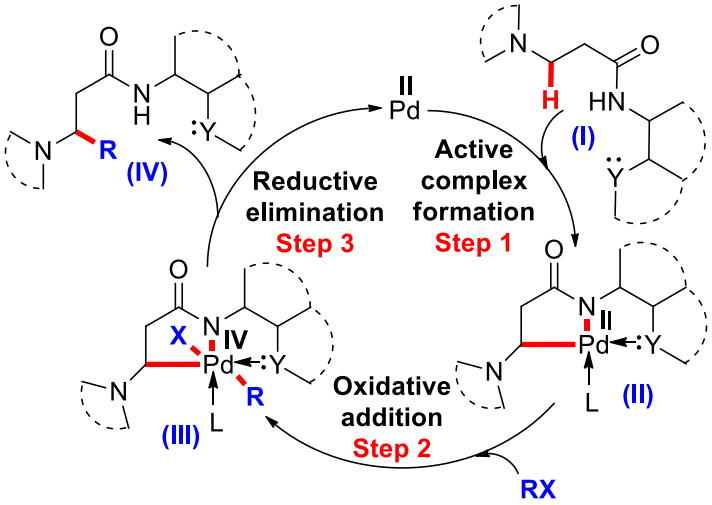


Figure 3: Proposed Pd(II)/Pd(IV)-catalytic pathway for the β-Csp^3-H-functionalization.

A close review of the recent literature reveals that generally nitrogenous specifically amine based auxiliaries are used for the Palladium catalysed functionalization of unactivated Csp^3-H bonds of amino acids and related derivatives (Figure 4).[10a] Out of the mentioned directing groups we opted N-phthalimido protected β-alanine using 8-amino quinoline and thiomethyl aniline amide as the auxiliaries for the initial screening.

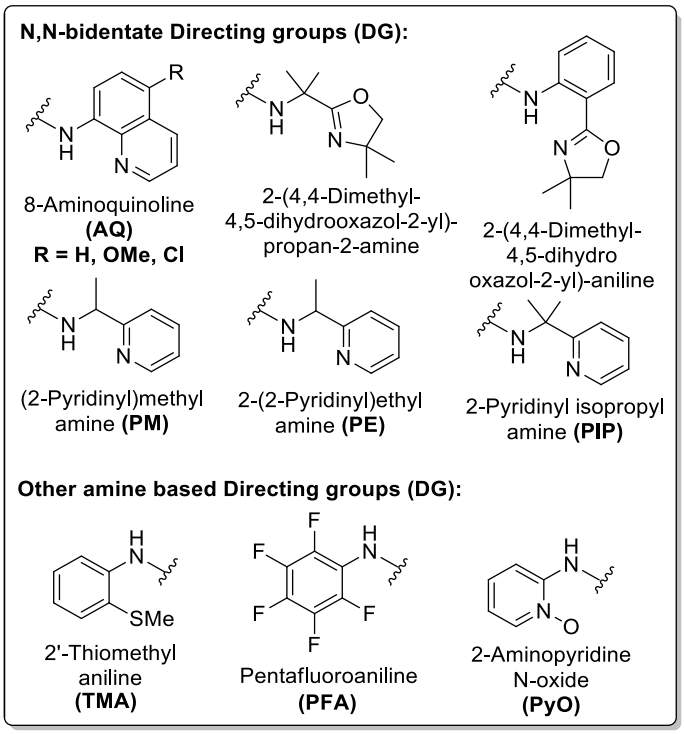


Figure 4: Directing groups used for Csp^3-H-functionalization of amino acid derivatives.

The initial trial prompted us to opt the former one (8-amino quinoline amide of β-alanine) **1a** as the preferred substrate to screen for the standardization of the protocol. A mixture of β-alanine substrate **1a** (0.25 mmol) and phenyl iodide **2a** (4.0 equiv., 1.0 mmol) was heated at 110 ^{o}C in presence of $Pd(OAc)_2$ (10 mol%) and AgOAc (1.5 equiv.) which led to the formation of the desired product in 30% yield (Table 1, Entry 1). Consequently we screened the reaction in different solvents (0.5 M) under heating condition and an increased yield of the desired β-arylated product **3a** (65%) was observed in 3:1 mixture of TCE and ^{t}-BuOH which was set to be the optimized solvent system for the protocol (Table 1, Entries 2-12). Different silver additives were also tested but 1.5 equiv. of AgOAc was found to be optimum (Table 1, Entries 13-17). The use of other additives could not lead to any more increment in the yield (Table 1, Entries 18-21). Since 10 mol% $Pd(OAc)_2$ led to the 65% of the product (Table 1, Entry 11), it can be realized that grossly 5 mol% of the catalyst might be needed for ~30% product formation (Table 1, Entry 22) and thus another 5 mol% increment in the catalyst loading may increase the product yield to the desired extent. To our delight the assumption worked well and a descent yield (86%) of the desired β-arylated product was achieved with 15 mol% $Pd(OAc)_2$ (Table 1, Entry 22).

A drastic decrease in the yield of the reaction was observed when the reaction was performed in absence of AgOAc or using NaOAc instead of silver (Table 1, Entry 23, 24). It indicates the importance

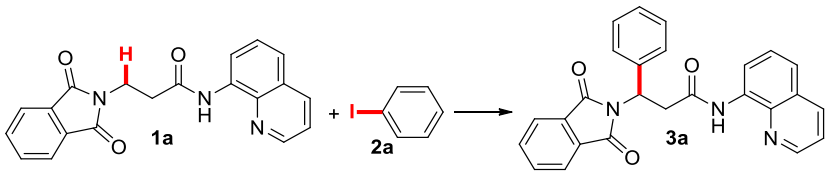
of silver in the reaction. It is also evident from the literature review that silver plays a crucial role to initiate/promote/complete the catalytic cycle.[15a] Since the yield of the product in absence of silver shows the catalyst turn over number>2 it is clear that silver does not necessarily take part in the regeneration of catalyst.

Two critical roles of silver can be understood in case of our reaction. In the initial step silver salt helps in the deprotonation to form the initial cylometallated complex which is also facilitated to some extent by the use of external base. It is also evident from our trial reaction with base like NaOAc in absence of silver salt which slightly improved the yield (Table 1, Entry 24). Silver plays another crucial role in the final step of reductive elimination by scavenging the iodide generated after each catalytic cycle.

Moreover, it is apparent from our screening reactions that the common counter acetate anion of silver is particularly helpful in our case than other silver additives probably because it shares common acetate counterpart with palladium catalyst. In this context the contribution of silver in the regeneration of catalyst cannot be completely ruled out.

The amount of aryl iodide was fixed solely on the basis of the best yield of the product with the full consumption of starting amino acid precursor which is the limiting component here. When 1.5 equiv. Phenyliodide was used, only 55% yield of the desired product was observed with the remaining of the unreacted starting amino acid precursor. It is evident from the well-established Pd(II)/Pd(IV) catalytic cycle that the key step here is the formation of Pd(IV)-intermediate through the oxidative addition of aryl iodide. So excess aryl iodide is needed to push the key step forward and the amount of excess aryl iodide varies from one reaction to another depending on the substrate and conditions.[15b,c] It is worth to mention during work up a satisfactory portion of the excess aryl iodide can be recovered.

Table 1. Optimization of the 8-aminoquinoline amide directed β-Csp^3-H arylation of β-alanine.[a]



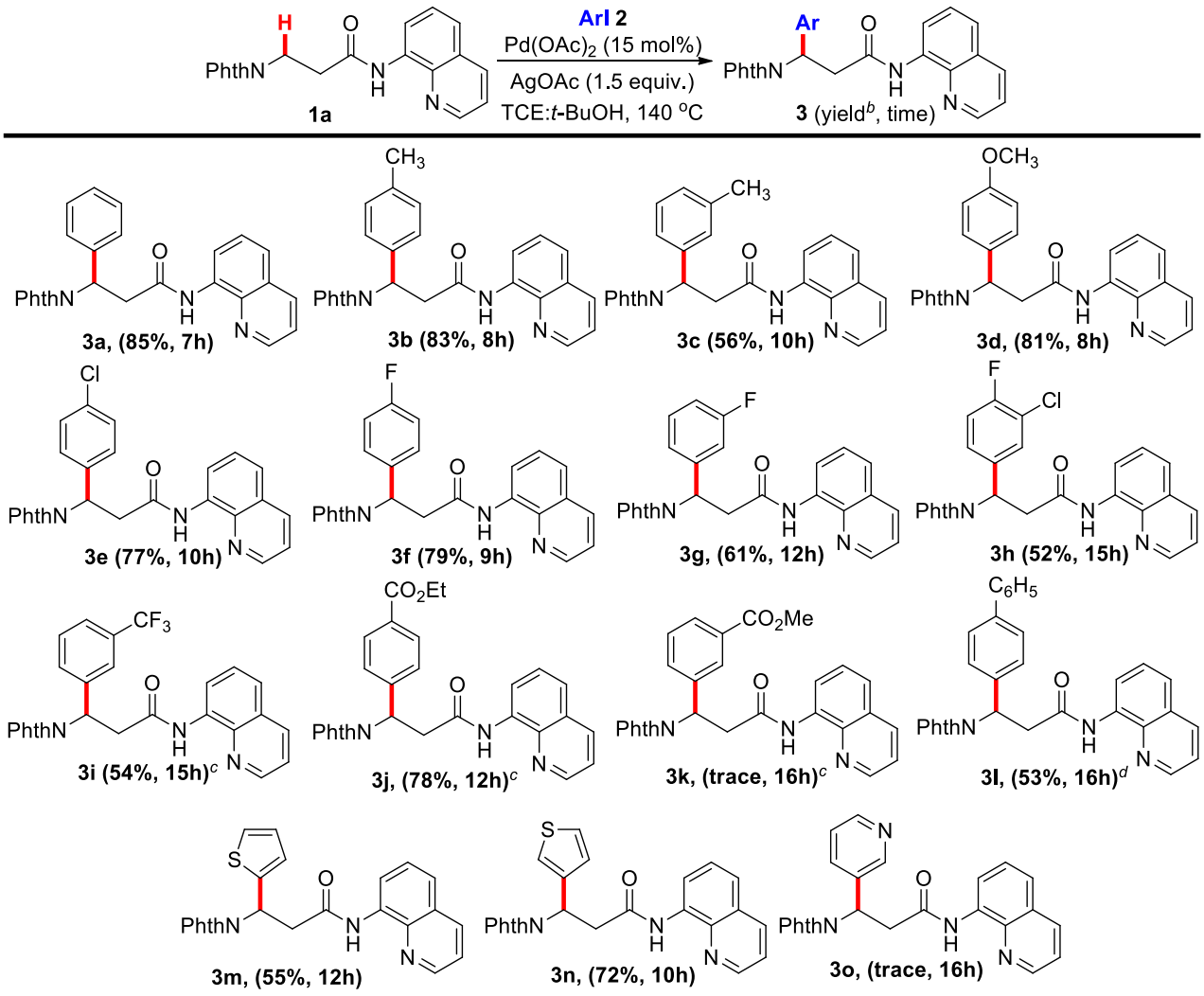
Entry	Catalyst (mol%)	Additives (equiv.)	Solvent	Temp (°C)	Time (h)	Yield[b] (%)
1	$Pd(OAc)_2$ (10)	AgOAc (1.5)	-	110	15	30
2	$Pd(OAc)_2$ (10)	AgOAc (1.5)	Toluene	110	15	Trace
3	$Pd(OAc)_2$ (10)	AgOAc (1.5)	Dioxane	110	15	-
4	$Pd(OAc)_2$ (10)	AgOAc (1.5)	Xylene	140	15	Trace

5	$Pd(OAc)_2$ (10)	AgOAc (1.5)	ACN	80	15	-
6	$Pd(OAc)_2$ (10)	AgOAc (1.5)	DMF	140	15	-
7	$Pd(OAc)_2$ (10)	AgOAc (1.5)	DMSO	140	15	-
8	$Pd(OAc)_2$ (10)	AgOAc (1.5)	DCE	reflux	15	30
9	$Pd(OAc)_2$ (10)	AgOAc (1.5)	TCE	140	15	50
10	$Pd(OAc)_2$ (10)	AgOAc (1.5)	*t*-BuOH	110	15	-
11	$Pd(OAc)_2$ (10)	AgOAc (1.5)	TCE+ *t*-BuOH (3:1)	140	10	65
12	$Pd(OAc)_2$ (10)	AgOAc (1.5)	TCE+ H_2O (3:1)	140	10	52
13	$Pd(OAc)_2$ (10)	AgOAc (2.0)	TCE+ *t*-BuOH (3:1)	140	15	63
14	$Pd(OAc)_2$ (10)	Ag_2CO_3 (1.5)	TCE+ *t*-BuOH (3:1)	140	15	48
15	$Pd(OAc)_2$ (10)	Ag_3PO_4 (1.5)	TCE+ *t*-BuOH (3:1)	140	15	52
16	$Pd(OAc)_2$ (10)	AgOTf (1.5)	TCE+ *t*-BuOH (3:1)	140	15	38
17	$Pd(OAc)_2$ (10)	AgTFA (1.5)	TCE+ *t*-BuOH (3:1)	140	15	42
18	$Pd(OAc)_2$ (10)	AgOAc (1.5), PivOH (0.2)	TCE+ *t*-BuOH (3:1)	140	15	51
19	$Pd(OAc)_2$ (10)	AgOAc (1.5), TFA (1.0)	TCE+ *t*-BuOH (3:1)	140	15	57
20	$Pd(OAc)_2$ (10)	AgOAc (1.5), Oxone (1.0)	TCE+ *t*-BuOH (3:1)	140	15	58
21	$Pd(OAc)_2$ (10)	AgOAc (1.5), NaOAc (1.5)	TCE+ *t*-BuOH (3:1)	140	15	64
22	**$Pd(OAc)_2$ (15)**	**AgOAc (1.5)**	**TCE+ *t*-BuOH (3:1)**	**140**	**7**	**86**
23	$Pd(OAc)_2$ (15)	-	TCE+ *t*-BuOH (3:1)	140	15	36
24	$Pd(OAc)_2$ (15)	NaOAc (1.5)	TCE+ *t*-BuOH (3:1)	140	15	45

[a] All the reactions were performed in 0.25 mmol scale with 1:4 substrate **1** to aryl iodide **2** ratio under stipulated temperature and time. [b] Isolated yields are given.

With the optimization condition in hand we attempted to explore the substrate tolerance of the developed protocol. As evident from Table 2, aryl iodides bearing electron donating or electron neutral substituents react faster than those bearing electron withdrawing substituents. *Para*-substituted aryl iodides are the best tolerated under the developed condition with the formation of the desired products in excellent yields. The reaction is sluggish in case of *meta*-substituted aryl iodides affording the corresponding β-arylated products in moderate yields while the *ortho*-substituted aryl iodides failed to generate the desired β-arylated products (Table 2). Heteroaryl iodides e.g. 2- and 3-iodothiophene worked well under the optimized condition giving moderate to good yields of the corresponding products whereas 3-iodopyridine ended up with trace amount of product (Table 2).

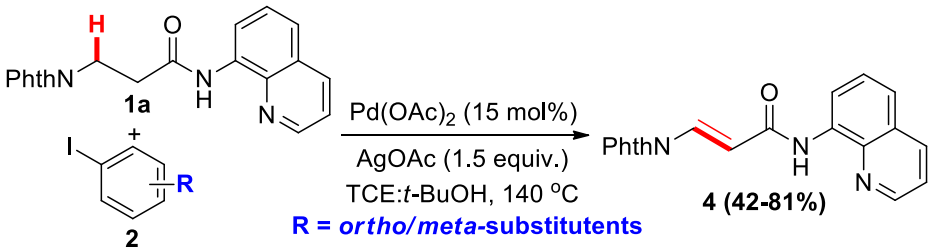
Table 2. Substrate scope for the auxilary directed β-Csp^3-H-Arylation of β-amino acids.[a]



[a] Unless mentioned all the reactions were performed in 0.5 mmol scale with 1:4 substrate **1** to aryl iodide **2** ratio under 140 °C for stipulated time. [b] Isolated yields are given. [c] 1:3 substrate **1** to aryl iodide **2** ratio. [d] 1:1.5 substrate **1** to aryl iodide **2** ratio.

In case of *meta*- and *ortho*-substituted aryl iodides β-hydride elimination of the substrate appeared to be the major competitive side reaction decreasing the yield of the desired product (Scheme 2).

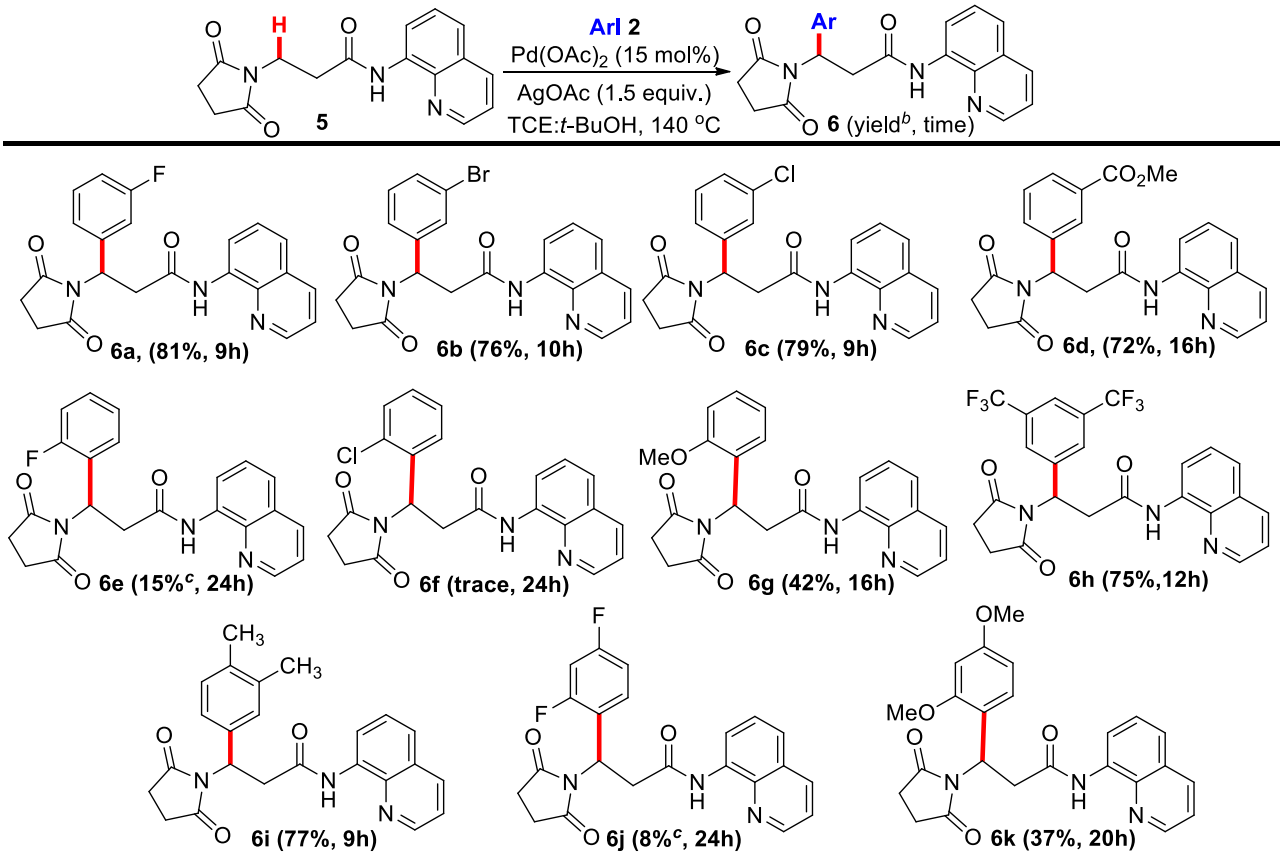
Scheme 2: Predominant β-hydride elimination in case of *ortho/meta*-substituted aryl iodides.



The β-elimination is often a common problem for the developed protocols using this DG-mediated palladium catalyzed functionalization strategy. Except in discrete cases[16] often the problem remained

unresolved and ended up with decreased yields of the desired products limiting the scope of the developed protocols. Since in case of β-alanine the problem is quite severe, so in our next attempt we tried to resolve the problem of β-elimination in case of reactions with the sterically hindered *meta*- and *ortho*-substituted aryl iodides.

Table 3: Steric modification of the precursor to minimize β-elimination for *ortho*-and *meta*-substituted aryl iodides.

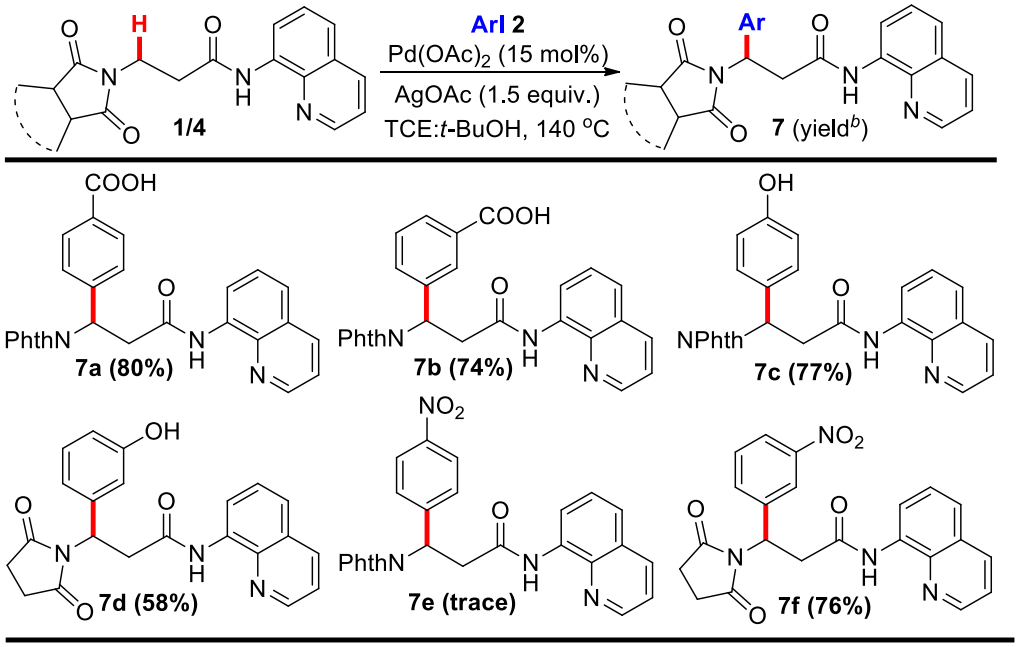


[a] Unless mentioned all the reactions were performed in 0.5 mmol scale with 1:4 substrate **1** to aryl iodide **2** ratio under 140 °C for stipulated time. [b] Isolated yields are given. [c] NMR yield using mesitylene as the internal standard.

We anticipated that the hindrance will be more from the phthalimide protected amine side since it is vicinal to the site of activation. Therefore we tried to reduce the bulkiness of the palladium intermediate by replacing the phthalimide protecting group with the succinimide of the corresponding substrate. To our delight the strategy solved the problem to a good extent yielding the desired β-arylated products in good yields for *meta*-substituted aryl iodides with full consumption of starting material and low to moderate yield for *ortho*-substituted aryl iodides keeping rest of the starting material unreacted (Table 3). Interestingly the β-elimination side product was observed only in few cases in negligible amount.

We extended the scope of the protocol by screening its compatibility with aryl iodides bearing chemically susceptible groups. Notably, the protocol was found to be highly compatible with aryl iodides bearing hydroxyl (-OH), carboxyl (-COOH) and nitro (-NO_2) substituents yielding the corresponding β-arylated products in good to excellent yields. Since reaction is sluggish for aryl iodides bearing electron withdrawing groups, it did not proceed at all for aryl iodides bearing nitro (-NO_2) group at *para*- and *ortho*-position where it is highly electron withdrawing by both of its –I and strongest –R effects. In case of *meta*-NO_2 only weak –I effect operates and thus makes the corresponding reaction feasible. However none of the iodoanilines worked well under this condition giving the corresponding product in trace amount (Table 4).

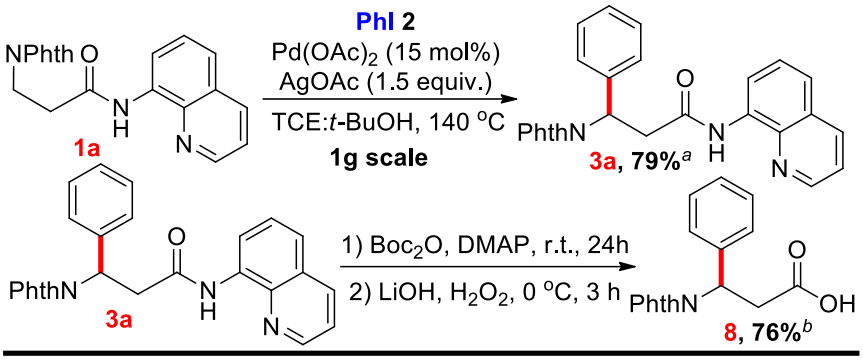
Table 4. Scopes of the protocol for aryl iodides bearing chemically susceptible substituents.[a]



[a] All the reactions were performed in 0.5 mmol scale with 1:4 substrate **1** to aryl iodide **2** ratio under heating at the optimized temperature of 140 °C for 10 h. [b] Isolated yields.

We further explored the compatibility of the protocol in gram scale synthesis. To our delight the protocol worked well in gram scale with the substrate **1a** giving **3a** in good yield (79%). Finally, the AQ-auxiliary was successfully removed from the β-arylated product **3a** in sequential steps following initially reported Chen's protocol to get back the corresponding native β-aryl-β-amino acids **8** in satisfactory yield (76%) (Scheme 3).[17]

Scheme 3: Gram scale compatibility of the protocol and removal of directing group (DG).



[a]Isolated yield with 1g scale (2.90 mmol) of the substrate**1a**; [b]Isolated overall yield with 0.3 mmol scale.

Conclusion:

In conclusion we have developed an efficient, generalized straightforward approach for the regioselctive β-functionalization of β-alanine. Notably, the directing group mediated palladium catalyzed protocol is compatible to a wide variety of aryl iodides leading to the corresponding β-aryl-β-amino acids in satisfactory yields. The predominant problem of β-elimination is also solved reasonably by reducing the steric effect in the palladium intermediate by choosing less bulky N-protecting group. Thus the protocol offers straightforward access to a variety of protected non-proteinogenic β-aryl-β-amino acids starting from simple, inexpensive β-alanine precursors enabling their further transformation to the native β-amino acids suitable for peptide and drug research.

Experimental Section:

General information:

All reactions were carried out in oven or flame dried glassware with magnetic stirring. The chemicals were purchased from Sigma-Aldrich, Alfa-Aesar, TCI-chemicals and Spectrochem Pvt. Ltd. Solvents were procured from Merck, CDH, Finar Ltd. and QUALIGENS. Unless noted all the chemicals and the solvents were used as received. Reactions were monitored by thin layer chromatography (TLC) on readymade TLC silica gel $60F_{254}$ plates (Merck, Dermstadt, Germany). The TLC plates were either seen directly under UV light or developed under iodine vapors, Dragendorff's stain or by charring with HBr/Ninhydrin solution. Silica gel of 100-200 mesh was used for column chromatography. High resolution mass spectrometry (HRMS) data for all new products were obtained under ESI model apparatus equipped with TOF analyzer (Available models are Waters Agilent 6520-Q-TofMS/MS system and JEOL-AccuTOF JMST100LC). ^{1}H NMR spectra were recorded on 300,400 and 500MHz spectrometers at room temperature in appropriate solvents using TMS as internal standard

or the solvent signals as secondary standards and the chemical shifts (δ) are shown in ppm scales. ^{13}C spectra were recorded at 75, 100 and 125MHz with complete proton decoupling. ^{19}F spectra were recorded at 376 MHz.

Synthesis of β-alanine precursors:

Synthesis of 3-(1,3-Dioxoisoindolin-2-yl)-N-(quinolin-8-yl)propanamide 1a:[14a]

Step 1: Synthesis of 3-(1,3-dioxoisoindolin-2-yl)propanoic acid: A mixture of β-alanine ($C_3H_7NO_2$) (40.0 mmol, 3.563 g) and phthalic anhydride ($C_8H_4O_3$) (40.0 mmol, 5.924 g) were taken in a 250 mL round bottom flask fitted with a guard tube. The mixture was stirred at 160℃ for 5 h. After the stipulated time period the mixture was cooled down to room temperature, dissolved in minimum amount of boiling methanol. Upon diluting the solution with ice-water the phthalimide protected β-alanine was crushed out as white solid. The precipitate was filtered through sintered funnel, dried and used for the next step.

Step 2a: Synthesis of acid chloride: 10.0 mmol (2.19 g) of phthalimide protected β-alanine was suspended in 20.0 mL of dry DCM in a round bottom flask. To it 1.8 mL (2.5 equiv.) of oxalyl chloride $(COCl)_2$ was added at 0℃ followed by few drops of N,N-dimethylformamide (DMF). The mixture was allowed to come to r.t. and stirred for 6 h. After the stipulated time corresponding acid chloride thus formed was dried in rotary evaporator to get a muddy residue.

Step 2b: Synthesis of 8-aminoquinoline amide precursor: 8-aminoquinoline (11.0 mmol, 1.6 g) was taken in a 250 mL 2-neck round bottom flask. To it 20.0 mL of dry DCM was added and the solution was stirred for 10 min. in a ice bath. The acid chloride obtained in the previous step was dissolved in 20.0 mL dry DCM and added to it dropwise followed by the dropwise addition of 1.5 equiv. (2.0 mL) of triethylamine (Et_3N) at 0℃ under nitrogen atmosphere and the whole mixture was stirred for overnight. After the completion of reaction as monitored by TLC, the mixture was diluted with 20.0 mL DCM and washed with saturated solution of ammonium chloride (NH_4Cl) followed by 2 times washing with the saturated solution of sodiumbicarbonate ($NaHCO_3$). The organic layer was collected, dried over anhydrous sodium sulfate (Na_2SO_4) and concentrated on rotary evaporator. The crude product was purified by column chromatography on silica gel with increasing amount of ethyl acetate in hexane to afford the desired compound as off white solid.

Synthesis of 3-(1,3-dioxoisoindolin-2-yl)-N-(2-(methylthio)phenyl)propanamide 1b:

Step 1: Synthesis of 3-(1,3-dioxoisoindolin-2-yl)propanoic acid: A mixture of β-alanine ($C_3H_7NO_2$) (40.0 mmol, 3.563 g) and phthalic anhydride ($C_8H_4O_3$) (40.0 mmol, 5.924 g) were taken in a 250 mL round bottom flask fitted with a guard tube. The mixture was stirred at 160℃ for 5 h. After the stipulated time period the mixture was cooled down to room temperature, dissolved in minimum amount of boiling methanol. Upon diluting the solution with ice-water the phthalimide protected β-alanine was crushed out as white solid. The precipitate was filtered through sintered funnel, dried and used for the next step.

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Step 2b: Synthesis of 2-thiomethyl anilineamide precursor:[13b] 11.0 mmol (1.38 mL) of 2-(methylthio)aniline in 20.0 mL of DCM was taken in a 250 mL round bottom flask and the solution was stirred for 10 min. in a ice bath. The acid chloride obtained in the previous step was dissolved in 20.0 mL dry DCM and added to it dropwise followed by the dropwise addition of 1.5 equiv. (2.0 mL) of triethylamine (Et_3N) at 0℃ under nitrogen atmosphere and the whole mixture was stirred for overnight. After the completion of reaction as monitored by TLC, the mixture was diluted with 20.0 mL DCM and washed with saturated solution of ammonium chloride (NH_4Cl) followed by washing with the saturated solution of sodiumbicarbonate ($NaHCO_3$). The organic layer was collected, dried over anhydrous sodium sulfate (Na_2SO_4) and concentrated on rotary evaporator. The crude product was purified by column chromatography on silica gel with increasing amount of ethyl acetate in hexane to afford the desired compound as yellowish white solid.

Synthesis of 3-(2,5-dioxopyrrolidin-1-yl)-N-(quinolin-8-yl)propanamide 5:

Step 1: Synthesis of 3-(2,5-dioxopyrrolidin-1-yl)propanoic acid:[15a] A mixture of 20.0 mmol (1.80 g) of β-alanine($C_3H_7NO_2$) and 20.0 mmol (2.00 g) of succinic anhydride ($C_4H_2O_3$) were taken in a 100 mL round bottom flask fitted with a guard tube. The above mixture was stirred at 160℃ for 8h. After the stipulated time period the reaction mixture was cooled down to room temperature. The pasty material was suspended in 20.0 mL of boiling chlroform and the turbid solution was filtered. The flask and filter cake were rinsed with the additional of 5.0 mL chloroform. The combined filterates were cooled down to room temperature and then placed in referigerator for overnight. The resulting beige

coloured prcipitate thus formed was collected by vaccum filtration and further dried in rotary evaporator.

Step 2a: Synthesis of acid chloride: 10.0 mmol (1.71 g) of succinamide protected β- alanine in 20.0 mL of dry DCM was taken in a round bottom flask. To it 1.8 mL (2.5 equiv.) of oxalyl chloride $(COCl)_2$ was added at 0℃ followed by few drops of N,N-dimethylformamide (DMF). The mixture was allowed to come at r.t. and stirred for 6 h. After the stipulated time corresponding acid chloride thus formed was dried in rotary evaporator to get a muddy residue.

Step 2b: Synthesis of final 8-aminoquinoline amide precursor: 8-aminoquinoline (11.0 mmol, 1.6 g) was taken in a 250 mL 2-neck round bottom flask. To it 20.0 mL of dry DCM was added and the solution was stirred for 10 min. in a ice bath. The acid chloride obtained in the previous step was dissolved in 20.0 mL dry DCM and added to it dropwise followed by the dropwise addition of 1.5 equiv. (2.0 mL) of triethylamine (Et_3N) at 0℃ under nitrogen atmosphere and the whole mixture was stirred for overnight. After the completion of reaction as monitored by TLC, the mixture was diluted with 20.0 mL DCM and washed with water. The organic layer was collected, dried over anhydrous sodium sulfate (Na_2SO_4) and concentrated on rotary evaporator. The crude product was purified by column chromatography on silica gel with increasing amount of ethyl acetate in hexane to afford the desired compound as off white solid.

General Procedure for the Synthesis of β-aryl-β-amino acids:

A screw-capped reaction tube with a magnetic bead was charged with 0.5 mmol of the β-alanine precursor. To it 1.0 mL solvent (TCE+*t*-BuOH in 3:1 ratio) was added followed by the addition of aryl iodide (1.5-4.0 equiv.), $Pd(OAc)_2$ (15 mol%) and AgOAc (1.5 equiv.). The resultant mixture was heated at requisite temperature for the required period of time with checking TLC at a regular time interval to monitor the maximum consumption of the starting material. After the stipulated period of time the crude reaction mixture was diluted with 10 mL DCM and filtered through G3 sintered glass funnel. The residue was further washed with DCM (2x5 mL). For carboxylic acid and phenolic compounds ethyl acetate was used for dilution of the reaction mixture. All the portions of the filtrate was collected together, reduced to minimum volume under vacuo and directly charged into column. The product was purified by column chromatography over silica gel with increasing amount of ethyl acetate in hexane or toluene. In case of acidic and phenolic compounds acetic was used with the eluting solvent.

Deprotection of 8-amino quinoline amide directing group:[16]

Step 1: A reaction tube was charged with a solution of compound **3a** (0.3 mmol, 1 equiv) in dry acetonitrile (4.0 mL). To it 4-(dimethylamino)pyridine (0.4 mmol, 1.3 equiv) and Boc anhydride (0.4 mmol, 1.3 equiv) was added subsequently. The whole reaction mixture was stirred at room temperature for 24 hours and then concentrated under reduced pressure. The crude mixture was purified by column chromatography over silica gel in 40% ethylacetate in hexane to give the N-Boc intermediate as white foam in 92% yield.

Step 2: The N-Boc intermediate obtained in previous step was dissolved totally (0.27 mmol, 1 equiv) in THF and water (3.0 mL+1.0 mL) and taken in a 25 mL round bottom flask. The solution was cooled to 0 ^{o}C followed by the addition of 30% hydrogen peroxide (2.4 mmol, 9 equiv) and lithium hydroxide monohydrate (0.3 mmol, 1.1 equiv). The reaction mixture was stirred at 0 ^{o}C for 3 hours. After the time period the reaction was quenched at 0 ^{o}C with 1.5 M aqueous sodium thiosulfate and the solvent was concentrated under reduced pressure. The residue solution was was acidified to pH 2 with 10% HCl solution and extracted with ethyl acetate (10 mL) twice. The organic extracts were dried over anhydrous sodium sulfate, concentrated under reduced pressure and purified by column chromatography over silica gel using increasing amount of methanol in DCM to afford the pure compound as sticky white solid in 83% yield.

Characterization data of the isolated compounds:

3-(1,3-Dioxoisoindolin-2-yl)propanoic acid:[14a] Yield: 82% (7.2 g), Texture: white solid, ^{1}H NMR (501 MHz, DMSO-d6) δ 12.34 (s, 1H), 7.87 – 7.82 (m, 4H), 3.80 (t, *J* = 7.4 Hz, 2H), 2.61 (t, *J* = 7.4 Hz, 2H); ^{13}C{^{1}H} NMR (126 MHz, DMSO-d6) δ 172.5, 168.1, 134.8, 132.1, 123.5, 34.1, 32.8.

3-(1,3-Dioxoisoindolin-2-yl)-N-(quinolin-8-yl)propanamide 1a: Yield: 75% (2.8 g), Texture: off white solid, Rf = 0.4 (30% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 8.74 – 8.69 (m, 2H), 8.13 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.85 – 7.81 (m, 2H), 7.72 – 7.67 (m, 2H), 7.53 – 7.46 (m, 2H), 7.41 (dd, *J* = 8.3, 4.2 Hz, 1H), 4.19 (t, *J* = 7.3 Hz, 2H), 3.02 (t, *J* = 7.3 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.3, 168.1, 148.1, 138.2, 136.3, 134.2, 133.9, 132.1, 127.9, 127.3, 123.3, 121.6,

121.6, 116.7, 36.0, 34.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{20}H_{16}N_3O_3^+$=346.1186; Found=346.1181.

3-(1,3-Dioxoisoindolin-2-yl)-N-(2-(methylthio)phenyl)propanamide 1b: Yield: 81% (2.7 g), Texture: Yellowish white solid, Rf = 0.5 (30% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 – 8.24 (m, 2H), 7.86 – 7.82 (m, 2H), 7.73 – 7.69 (m, 2H), 7.44 (d, *J* = 7.5 Hz, 1H), 7.26 (dd, *J* = 8.9, 5.8 Hz, 1H), 7.06 (t, *J* = 7.4 Hz, 1H), 4.13 (t, *J* = 7.3 Hz, 2H), 2.89 (t, *J* = 7.1 Hz, 2H), 2.33 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 168.1, 137.9, 134.0, 132.7, 132.1, 129.0, 128.8, 125.5, 124.6, 123.3, 120.9, 35.8, 34.2, 18.9; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{18}H_{17}N_2O_3S^+$= 341.0954; Found=341.0957.

3-(2,5-Dioxopyrrolidin-1-yl)propanoic acid:[15a] Yield: 87% (3.0 g), Texture: beige coloured solid, ^{1}H NMR (400 MHz, DMSO-d6) δ 3.57 (t, *J* = 7.6 Hz, 2H), 2.60 (s, 4H), 2.4 (t, *J* = 7.6 Hz, 2H); $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d6) δ 177.6, 172.4, 34.3, 32.0, 28.4.

3-(2,5-Dioxopyrrolidin-1-yl)-N-(quinolin-8-yl)propanamide 5: Yield: 72% (2.1 g), Texture: off white solid, Rf = 0.1 (50% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.75 (s, 1H), 8.74 (ddd, *J* = 8.7, 5.5, 1.8 Hz, 2H), 8.14 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.58 – 7.40 (m, 3H), 4.00 (t, *J* = 7.3 Hz, 2H), 2.90 (t, *J* = 7.3 Hz, 2H), 2.71 (s, 4H).; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 177.0, 168.2, 148.1, 138.2, 136.4, 134.1, 127.9, 127.4, 121.7, 121.6, 116.6, 35.1, 28.2; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{16}H_{16}N_3O_3^+$= 298.1186; Found=298.1181.

3-(1,3-Dioxoisoindolin-2-yl)-3-phenyl-N-(quinolin-8-yl)propanamide 3a: Yield: 85% (178 mg), Texture: White solid; Rf = 0.45 (30% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.90 (s, 1H), 8.74 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.70 – 8.65 (m, 1H), 8.09 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.79 – 7.75 (m, 2H), 7.64 – 7.60 (m, 4H), 7.44 – 7.26 (m, 6H), 6.09 (dd, *J* = 10.0, 5.6 Hz, 1H), 4.12 (dd, *J* = 15.8, 10.0 Hz, 1H), 3.49 (dd, *J* = 15.7, 5.7 Hz, 1H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 168.3, 168.1, 148.2, 139.1, 138.2, 136.2, 134.2, 133.9, 131.9, 128.8, 128.1, 127.9, 127.8, 127.3, 123.3, 121.6, 116.6, 51.4, 39.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{26}H_{20}N_3O_3^+$=422.1499; Found=422.1502.

3-(1,3-Dioxoisoindolin-2-yl)-N-(quinolin-8-yl)-3-(p-tolyl)propanamide 3b: Yield: 83% (180 mg), Texture: White solid; Rf = 0.5 (30% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.89 (s, 1H), 8.74 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.69 – 8.65 (m, 1H), 8.09 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.78 – 7.74 (m, 2H), 7.63 – 7.59 (m, 2H), 7.52 (d, *J* = 8.1 Hz, 2H), 7.42 (dq, *J* = 12.5, 4.0 Hz, 3H), 7.14 (d, *J* = 7.9 Hz, 2H), 6.05 (dd, *J* = 10.0, 5.7 Hz, 1H), 4.08 (dd, *J* = 15.7, 10.0 Hz, 1H), 3.47 (dd, *J* = 15.7, 5.7 Hz, 1H), 2.29 (s,

3H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 168.3, 168.7, 148.1, 138.2, 137.9, 136.2, 136.1, 134.2, 133.8, 131.9, 129.4, 127.8, 127.3, 123.3, 121.6, 116.6, 51.1, 39.4, 21.1; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{27}H_{22}N_3O_3^+$ =436.1656; Found-436.1656.

3-(1,3-Dioxoisoindolin-2-yl)-N-(quinolin-8-yl)-3-(m-tolyl)propanamide 3c: Yield: 56% (122 mg), Texture: white solid; Rf = 0.5 (30% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.90 (s, 1H), 8.75 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.72 – 8.64 (m, 1H), 8.10 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.83 – 7.73 (m, 2H), 7.68 – 7.59 (m, 2H), 7.49 – 7.36 (m, 5H), 7.23 (dd, *J* = 11.6, 5.0 Hz, 1H), 7.09 (d, *J* = 7.4 Hz, 1H), 6.05 (dd, *J* = 10.1, 5.6 Hz, 1H), 4.12 (dd, *J* = 15.7, 10.1 Hz, 1H), 3.47 (dd, *J* = 15.7, 5.6 Hz, 1H), 2.34 (s, 3H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 168.3, 168.1, 148.1, 139.0, 138.5, 138.2, 136.2, 134.2, 133.8, 131.9, 128.9, 128.7, 128.6, 127.8, 127.3, 124.9, 123.3, 121.6, 116.6, 51.4, 39.4, 21.5; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{27}H_{22}N_3O_3^+$=436.1656; Found=436.1642.

3-(1,3-Dioxoisoindolin-2-yl)-3-(4-methoxyphenyl)-N-(quinolin-8-yl)propanamide 3d: Yield: 81% (182 mg), Texture: Off white solid; Rf = 0.5 (30% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.91 (s, 1H), 8.72 (d, *J* = 32.2 Hz, 2H), 8.13 (d, *J* = 8.2 Hz, 1H), 7.78 (dd, *J* = 5.0, 2.7 Hz, 2H), 7.64 – 7.57 (m, 4H), 7.46-7.43 (m, 3H), 6.87 (d, *J* = 8.4 Hz, 2H), 6.06 – 6.02 (m, 1H), 4.07 (dd, *J* = 15.5, 9.9 Hz, 1H), 3.77 (s, 3H), 3.49 (dd, *J* = 15.4, 5.3 Hz, 1H).; $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 168.3, 168.2, 159.3, 148.0, 138.1, 136.4, 134.2, 133.8, 132.0, 131.3, 129.3, 127.9, 127.3, 123.3, 121.6, 121.5, 116.8, 114.1, 55.2, 50.9, 39.5; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{27}H_{22}N_3O_4^+$=452.1605; Found=452.1613.

3-(4-Chlorophenyl)-3-(1,3-dioxoisoindolin-2-yl)-N-(quinolin-8-yl)propanamide 3e: Yield: 77% (175 mg), Texture: White solid; Rf = 0.4 (30% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.89 (s, 1H), 8.74 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.68 – 8.64 (m, 1H), 8.10 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.81 – 7.76 (m, 2H), 7.66 – 7.63 (m, 2H), 7.58 (dd, *J* = 8.9, 2.1 Hz, 2H), 7.46 – 7.39 (m, 3H), 7.32 – 7.29 (m, 2H), 6.07 (dd, *J* = 9.5, 6.1 Hz, 1H), 4.03 (dd, *J* = 15.7, 9.5 Hz, 1H), 3.52 (dd, *J* = 15.7, 6.1 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 168.2, 167.7, 148.2, 138.2, 137.5, 136.3, 134.1, 134.0, 131.8, 129.4, 128.9, 127.8, 127.2, 123.4, 121.7, 121.6, 116.7, 50.7, 39.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{26}H_{19}ClN_3O_3^+$=456.1109; Found=456.1108.

3-(1,3-Dioxoisoindolin-2-yl)-3-(4-fluorophenyl)-N-(quinolin-8-yl)propanamide 3f: Yield: 79% (173 mg), Texture: White solid; Rf = 0.5 (30% EtOAc/hexane). ^{1}H NMR (501 MHz, $CDCl_3$) δ 9.89 (s, 1H), 8.71 (d, *J* = 44.6 Hz, 2H), 8.11 (d, *J* = 8.1 Hz, 1H), 7.79 (s, 2H), 7.64-7.62 (m, 4H), 7.45 – 7.41

(m, 3H), 7.02 (t, *J* = 8.4 Hz, 2H), 6.07 (dd, *J* = 8.7, 6.6 Hz, 1H), 4.04 (dd, *J* = 15.5, 9.7 Hz, 1H), 3.51 (dd, *J* = 15.6, 5.8 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 168.2, 167.8, 162.4 (d, *J* = 247.0 Hz), 148.2, 138.2, 136.3, 134.9 (d, *J* = 3.2 Hz), 134.1, 133.9, 131.8, 129.8 (d, *J* = 8.2 Hz), 127.8, 127.2, 123.4, 121.7, 121.6, 116.7, 115.6 (d, *J* = 21.5 Hz), 50.7, 39.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.80; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{26}H_{19}FN_3O_3^+$=440.1405; Found=440.1397.

3-(1,3-Dioxoisoindolin-2-yl)-3-(3-fluorophenyl)-N-(quinolin-8-yl)propanamide 3g: Yield: 61% (133 mg), Texture: White solid; Rf = 0.5 (30% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.90 (s, 1H), 8.76 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.69 – 8.64 (m, 1H), 8.11 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.81-7.78 (m, 2H), 7.67 – 7.64 (m, 2H), 7.47-7.28 (m, 6H), 6.97 (td, *J* = 8.4, 1.7 Hz, 1H), 6.08 (dd, *J* = 9.7, 5.9 Hz, 1H), 4.06 (dd, *J* = 15.8, 9.7 Hz, 1H), 3.50 (dd, *J* = 15.8, 5.9 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 168.2, 167.7, 162.9 (d, *J* = 246.8 Hz) 148.2, 141.4 (d, *J* = 6.9 Hz), 138.2, 136.3, 134.1, 134.0, 131.8, 130.3 (d, *J* = 8.2 Hz), 127.8, 127.2, 123.6 (d, *J* = 2.2 Hz), 123.4, 121.7 (d, *J* = 6.3 Hz), 116.7, 115.3, 115.05, 115.00 (d, *J* = 22.2 Hz), 50.8, 39.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.02; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{26}H_{19}FN_3O_3^+$=440.1405; Found=440.1396.

3-(3-Chloro-4-fluorophenyl)-3-(1,3-dioxoisoindolin-2-yl)-N-(quinolin-8-yl)propanamide 3h: Yield: 52% (123 mg), Texture: White solid; Rf = 0.45 (30% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.99 (s, 1H), 8.78 (dd, *J* = 4.1, 1.3 Hz, 1H), 8.70 – 8.65 (m, 1H), 8.17 – 8.15 (m, 1H), 7.83 – 7.79 (m, 2H), 7.74 (dd, *J* = 6.9, 2.2 Hz, 1H), 7.69 – 7.64 (m, 2H), 7.55 (ddd, *J* = 8.5, 4.4, 2.3 Hz, 1H), 7.49 – 7.44 (m, 3H), 7.11 (t, *J* = 8.7 Hz, 1H), 6.06 (dd, *J* = 9.4, 6.2 Hz, 1H), 4.03 (dd, *J* = 15.8, 9.4 Hz, 1H), 3.57 (dd, *J* = 15.8, 6.2 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 168.1, 167.6, 157.8 (d, *J* = 247.0 Hz), 147.9, 137.8, 136.7, 136.2 (d, *J* = 3.7 Hz), 134.1, 133.9, 131.7, 130.4, 128.0 (d, *J* = 7.3 Hz), 127.9, 127.4, 123.5, 121.7 (d, *J* = 23.2 Hz), 121.2 (d, *J* = 17.8 Hz), 117.1, 116.8 (d, *J* = 21.2 Hz), 50.3, 39.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -115.88; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{26}H_{18}ClFN_3O_3^+$=474.1015; Found=474.1018.

3-(1,3-Dioxoisoindolin-2-yl)-N-(quinolin-8-yl)-3-(3-(trifluoromethyl)phenyl)propanamide 3i: Yield: 54% (132 mg), Texture: White solid; Rf = 0.5 (30% EtOAc/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.91 (s, 1H), 8.75 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.68 – 8.63 (m, 1H), 8.10 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.92 – 7.77 (m, 4H), 7.67 – 7.62 (m, 2H), 7.56 – 7.39 (m, 5H), 6.15 (dd, *J* = 9.8, 5.8 Hz, 1H), 4.11 (dd, *J* = 15.8, 9.8 Hz, 1H), 3.52 (dd, *J* = 15.8, 5.8 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 168.2, 167.5, 148.2, 140.0, 138.2, 136.3, 134.1, 131.8, 131.5, 131.2 (q, *J* = 32.4 Hz), 129.4, 127.8, 127.2,

125.1 (q, *J* = 3.6 Hz), 124.8 (d, *J* = 3.7 Hz), 123.9 (q, *J* = 272.6 Hz), 123.5, 121.7, 121.6, 116.7, 50.9, 39.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.48; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{27}H_{19}F_3N_3O_3^+$= 490.1373; Found=490.1379.

Ethyl-4-(1-(1,3-dioxoisoindolin-2-yl)-3-oxo-3-(quinolin-8-ylamino)propyl)benzoate 3j: Yield: 78% (192 mg), Texture: White solid; Rf = 0.4 (10% EtOAc/Toluene). ^{1}H NMR (501 MHz, $CDCl_3$) δ 9.90 (s, 1H), 8.74 – 8.66 (m, 2H), 8.10 (d, *J* = 7.6 Hz, 1H), 8.02 (d, *J* = 8.1 Hz, 2H), 7.79 (d, *J* = 1.9 Hz, 2H), 7.67 (dd, *J* = 24.8, 5.0 Hz, 4H), 7.45 – 7.40 (m, 3H), 6.15 (dd, *J* = 8.6, 6.6 Hz, 1H), 4.35 (q, *J* = 7.0 Hz, 2H), 4.07 (dd, *J* = 15.6, 9.7 Hz, 1H), 3.54 (dd, *J* = 15.7, 5.8 Hz, 1H), 1.36 (t, *J* = 7.0 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.2, 167.7, 166.1, 148.2, 143.7, 138.2, 136.2, 134.1, 134.0, 131.8, 130.3, 130.1, 127.8, 127.8, 127.2, 123.4, 121.7, 121.6, 116.6, 60.9, 51.0, 39.1, 14.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{29}H_{24}N_3O_5^+$= 494.1710; Found=494.1712.

3-([1,1'-Biphenyl]-4-yl)-3-(1,3-dioxoisoindolin-2-yl)-N-(quinolin-8-yl)propanamide 3l: Yield: 53% (131 mg), Texture: White solid; Rf = 0.5 (30% EtOAc/Hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.92 (s, 1H), 8.75 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.72 – 8.64 (m, 1H), 8.10 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.84 – 7.75 (m, 2H), 7.71 (d, *J* = 8.2 Hz, 2H), 7.67 – 7.60 (m, 2H), 7.59 – 7.50 (m, 4H), 7.47 – 7.36 (m, 5H), 7.33 (dd, *J* = 4.9, 3.7 Hz, 1H), 6.14 (dd, *J* = 9.8, 5.8 Hz, 1H), 4.13 (dd, *J* = 15.7, 9.8 Hz, 1H), 3.55 (dd, *J* = 15.7, 5.8 Hz, 1H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 168.3, 168.0, 148.2, 141.1, 140.6, 138.3, 138.1, 136.2, 134.2, 133.9, 131.9, 128.8, 128.4, 127.9, 127.5, 127.4, 127.3, 127.1, 123.4, 121.6, 121.6, 116.7, 51.1, 39.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{32}H_{24}N_3O_3^+$=498.1812; Found=498.1809.

3-(1,3-Dioxoisoindolin-2-yl)-N-(quinolin-8-yl)-3-(thiophen-2-yl)propanamide 3m: Yield: 55% (117 mg), Texture: Pale yellow solid; Rf = 0.55 (10% EtOAc/Toluene). ^{1}H NMR (501 MHz, $CDCl_3$) δ 9.89 (s, 2H), 8.77 – 8.68 (m, 4H), 8.11 (d, *J* = 8.2 Hz, 2H), 7.80 (d, *J* = 3.0 Hz, 4H), 7.65 (d, *J* = 1.8 Hz, 4H), 7.46 – 7.22 (m, 6H), 6.95 (s, 2H), 6.36 (dd, *J* = 9.2, 6.1 Hz, 2H), 4.06 (dd, *J* = 15.6, 9.7 Hz, 2H), 3.56 (dd, *J* = 15.6, 5.7 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 167.7, 167.4, 148.2, 141.5, 138.2, 136.2, 134.1, 133.9, 131.9, 127.8, 127.2, 126.7, 126.6, 125.5, 123.4, 121.7, 121.6, 116.7, 46.5, 40.8; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{24}H_{18}N_3O_3S^+$=428.1063; Found=428.1051.

3-(1,3-Dioxoisoindolin-2-yl)-N-(quinolin-8-yl)-3-(thiophen-3-yl)propanamide 3n: Yield: 72% (153 mg), Texture: Pale yellow solid; Rf = 0.6 (10% EtOAc/Toluene). ^{1}H NMR (501 MHz, $CDCl_3$) δ

9.88 (s, 1H), 8.77 – 8.68 (m, 2H), 8.12 (d, *J* = 8.2 Hz, 1H), 7.80 – 7.79 (m, 2H), 7.66 – 7.65 (m, 2H), 7.47 – 7.26 (m, 6H), 6.18 (dd, *J* = 9.3, 6.0 Hz, 1H), 4.02 (dd, *J* = 15.5, 9.8 Hz, 1H), 3.49 (dd, *J* = 15.5, 5.6 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 168.1, 167.9, 148.1, 139.6, 138.2, 136.3, 134.2, 133.9, 131.9, 127.8, 127.3, 127.2, 126.2, 123.5, 123.3, 121.6, 121.6, 116.7, 46.7, 39.9; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{24}H_{18}N_3O_3S^+$=428.1063; Found=428.1061.

3-(1,3-Dioxoisoindolin-2-yl)-N-(quinolin-8-yl)acrylamide 4: Texture: Off white sticky solid; Rf = 0.45 (10% EtOAc/Toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.99 (s, 1H), 8.90 (dd, *J* = 7.4, 1.4 Hz, 1H), 8.86 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.18 (dd, *J* = 8.3, 1.6 Hz, 1H), 8.13 (d, *J* = 14.2 Hz, 1H), 8.00 – 7.96 (m, 2H), 7.88 – 7.75 (m, 3H), 7.60 – 7.52 (m, 2H), 7.48 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.42 (d, *J* = 14.2 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 165.7, 164.1, 148.2, 138.4, 136.4, 135.1, 134.7, 131.5, 129.3, 127.9, 127.5, 124.2, 121.7, 116.9, 111.8; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{20}H_{14}N_3O_3^+$ = 344.1030; Found=344.1024.

3-(2,5-Dioxopyrrolidin-1-yl)-3-(3-fluorophenyl)-N-(quinolin-8-yl)propanamide 6a: Yield: 81% (158 mg), Texture: Pale yellow sticky solid; Rf = 0.3 (50% EtOAc/Hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.85 (s, 1H), 8.74 (ddd, *J* = 13.3, 6.6, 3.1 Hz, 2H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.52 – 7.46 (m, 2H), 7.44 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.35 – 7.25 (m, 3H), 7.01 – 6.96 (m, 1H), 5.89 (dd, *J* = 10.1, 5.6 Hz, 1H), 4.00 (dd, *J* = 15.7, 10.2 Hz, 1H), 3.34 (dd, *J* = 15.7, 5.6 Hz, 1H), 2.65 (s, 4H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 177.2, 167.8, 162.8 (d, *J* = 246.4 Hz), 148.3, 140.8 (d, *J* = 7.1 Hz), 138.2, 136.3, 134.1, 130.3 (d, *J* = 8.2 Hz), 127.9, 127.3, 123.7 (d, *J* = 2.3 Hz), 121.7 (d, *J* = 10.1 Hz), 116.7, 115.4, 115.2, 115.1 (d, *J* = 22.2), 51.5, 38.2, 28.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.04; HRMS (ESI-TOF) m/z: $[M+H]^+$calculated for $C_{22}H_{19}FN_3O_3^+$= 392.1405; Found=392.1406.

3-(3-Bromophenyl)-3-(2,5-dioxopyrrolidin-1-yl)-N-(quinolin-8-yl)propanamide 6b: Yield: 76% (170 mg), Texture: Pale yellow sticky solid; Rf = 0.25 (50% EtOAc/Hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.84 (s, 1H), 8.76 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.66 (p, *J* = 4.4 Hz, 1H), 8.10 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.73 (t, *J* = 1.7 Hz, 1H), 7.51 – 7.39 (m, 5H), 7.18 (t, *J* = 7.9 Hz, 1H), 5.85 (dd, *J* = 10.1, 5.6 Hz, 1H), 3.98 (dd, *J* = 15.7, 10.1 Hz, 1H), 3.32 (dd, *J* = 15.7, 5.6 Hz, 1H), 2.63 (s, 4H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 177.2, 167.7, 148.2, 140.6, 138.2, 136.3, 134.0, 131.4, 131.1, 130.3, 127.8, 127.2, 126.8, 122.7, 121.8, 121.7, 116.6, 51.4, 38.1, 28.1; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{22}H_{19}BrN_3O_3^+$= 452.0604; Found=452.0603.

3-(3-Chlorophenyl)-3-(2,5-dioxopyrrolidin-1-yl)-N-(quinolin-8-yl)propanamide 6c: Yield: 79% (161 mg), Texture: Pale yellow sticky solid; Rf = 0.2 (50% EtOAc/Hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.85 (s, 1H), 8.80 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.71 – 8.66 (m, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.59 (s, 1H), 7.52 – 7.43 (m, 4H), 7.30-7.26 (m, 2H), 5.87 (dd, *J* = 10.2, 5.6 Hz, 1H), 4.01 (dd, *J* = 15.7, 10.2 Hz, 1H), 3.33 (dd, *J* = 15.7, 5.6 Hz, 1H), 2.66 (s, 4H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 177.1, 167.7, 148.3, 140.3, 138.2, 136.3, 134.6, 134.1, 130.0, 128.5, 128.2, 127.9, 127.3, 126.3, 121.8, 121.7, 116.7, 51.5, 38.2, 28.1; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{22}H_{19}ClN_3O_3^+$= 408.1109; Found=408.1100.

Methyl-3-(1-(2,5-dioxopyrrolidin-1-yl)-3-oxo-3-(quinolin-8-ylamino)propyl)benzoate 6d: Yield: 72% (155 mg), Texture: Pale yellow sticky solid; Rf = 0.2 (50% EtOAc/Hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.86 (s, 1H), 8.79 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.69 (t, *J* = 4.5 Hz, 1H), 8.23 (s, 1H), 8.14 (dd, *J* = 8.3, 1.6 Hz, 1H), 8.02 – 7.94 (m, 1H), 7.77 (d, *J* = 7.8 Hz, 1H), 7.49 (d, *J* = 4.5 Hz, 2H), 7.46 – 7.40 (m, 2H), 5.96 (dd, *J* = 10.3, 5.5 Hz, 1H), 4.06 (dd, *J* = 15.6, 10.3 Hz, 1H), 3.91 (s, 3H), 3.37 (dd, *J* = 15.6, 5.5 Hz, 1H), 2.66 (s, 4H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 177.2, 167.8, 166.7, 148.3, 138.8, 138.2, 136.3, 134.1, 132.6, 130.7, 129.6, 129.0, 128.9, 127.9, 127.3, 121.8, 121.7, 116.7, 52.2, 51.6, 38.2, 28.1; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{24}H_{22}N_3O_5^+$= 432.1554; Found=432.1555.

3-(2,5-Dioxopyrrolidin-1-yl)-3-(2-methoxyphenyl)-N-(quinolin-8-yl)propanamide 6g: Yield: 42% (85 mg)%, Texture: Pale yellow sticky solid; Rf = 0.3 (50% EtOAc/Hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.84 (s, 1H), 8.79 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.71 (dd, *J* = 6.2, 2.8 Hz, 1H), 8.15 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.53 – 7.43 (m, 4H), 7.30 – 7.25 (m, 1H), 6.95 (td, *J* = 7.6, 0.9 Hz, 1H), 6.89 (d, *J* = 8.2 Hz, 1H), 6.24 (dd, *J* = 11.0, 4.6 Hz, 1H), 3.96 – 3.87 (m, 4H), 3.24 (dd, *J* = 15.4, 4.6 Hz, 1H), 2.67 (s, 4H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 177.4, 168.7, 156.6, 148.2, 138.3, 136.3, 134.3, 129.2, 128.1, 127.9, 127.4, 126.4, 121.6, 121.5, 120.4, 116.6, 110.7, 55.6, 46.8, 38.0, 28.1; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{23}H_{22}N_3O_4^+$=404.1605; Found=404.1606.

3-(3,5-Bis(trifluoromethyl)phenyl)-3-(2,5-dioxopyrrolidin-1-yl)-N-(quinolin-8-yl)propan amide 6h: Yield: 75% (190 mg), Texture: White solid; Rf = 0.3 (50% EtOAc/Hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.88 (s, 1H), 8.79 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.68 – 8.64 (m, 1H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 8.07 (s, 2H), 7.83 (s, 1H), 7.51 – 7.43 (m, 3H), 6.02 (dd, *J* = 10.0, 5.7 Hz, 1H), 4.04 (dd, *J* = 15.7, 10.0 Hz, 1H), 3.39 (dd, *J* = 15.7, 5.7 Hz, 1H), 2.70 (s, 4H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 177.0, 167.0, 148.3, 140.8, 138.2, 136.3, 133.9, 132.1 (q, *J* = 33.5 Hz), 128.6 (d, *J* = 2.8 Hz), 127.9, 127.2,

123.1 (q, *J* = 272.9 Hz), 122.4 (p, *J* = 3.8 Hz), 121.9, 121.7, 116.7, 51.1, 37.8, 28.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.77; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{24}H_{18}F_6N_3O_3^+$= 510.1247; Found=510.1245.

3-(3,4-Dimethylphenyl)-3-(2,5-dioxopyrrolidin-1-yl)-N-(quinolin-8-yl)propanamide 6i: Yield: 77% (155 mg), Texture: Pale yellow gelly; Rf = 0.2 (50% EtOAc/Hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.85 (s, 1H), 8.80 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.73 – 8.68 (m, 1H), 8.14 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.52 – 7.42 (m, 3H), 7.33 (d, *J* = 8.1 Hz, 2H), 7.10 (d, *J* = 7.5 Hz, 1H), 5.84 (dd, *J* = 10.4, 5.4 Hz, 1H), 4.05 (dd, *J* = 15.6, 10.5 Hz, 1H), 3.30 (dd, *J* = 15.5, 5.4 Hz, 1H), 2.61 (s, 4H), 2.25 (s, 3H), 2.23 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 177.3, 168.3, 148.2, 138.3, 136.9, 136.8, 136.3, 135.9, 134.2, 129.9, 129.3, 127.9, 127.3, 125.4, 121.6, 116.6, 51.9, 38.5, 28.1, 19.8, 19.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{24}H_{24}N_3O_3^+$=402.1812; Found=402.1812.

3-(2,4-Dimethoxyphenyl)-3-(2,5-dioxopyrrolidin-1-yl)-N-(quinolin-8-yl)propanamide 6k: Yield: 37% (80 mg), Texture: White solid; Rf = 0.25 (50% EtOAc/Hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.82 (s, 1H), 8.78 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.73 – 8.68 (m, 1H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.52 – 7.42 (m, 4H), 6.48 – 6.43 (m, 2H), 6.17 (dd, *J* = 10.8, 4.9 Hz, 1H), 3.90 – 3.79 (m, 7H), 3.22 (dd, *J* = 15.3, 4.9 Hz, 1H), 2.64 (s, 4H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 177.3, 168.6, 160.6, 157.8, 148.1, 138.3, 136.3, 134.3, 129.0, 127.9, 127.3, 121.6, 121.5, 118.8, 116.6, 104.1, 98.5, 55.6, 55.3, 46.3, 38.3, 28.1; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{24}H_{24}N_3O_5^+$=434.1710; Found=434.1708.

4-(1-(1,3-Dioxoisoindolin-2-yl)-3-oxo-3-(quinolin-8-ylamino)propyl)benzoic acid 7a: Yield: 80% (186 mg), Texture: White solid; Rf = 0.45 (EtOAc/Toluene/Acetic acid in 10:88:2 ratio). ^{1}H NMR (400 MHz, DMSO-d6) δ 10.39 (s, 1H), 8.90 (d, *J* = 3.8 Hz, 1H), 8.46 (d, *J* = 7.6 Hz, 1H), 8.36 (d, *J* = 8.2 Hz, 1H), 8.05 – 7.54 (m, 10H), 7.49 (t, *J* = 7.9 Hz, 1H), 5.96 (t, *J* = 7.7 Hz, 1H), 3.80 (d, *J* = 8.2 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, DMSO-d6) δ 169.1, 168.1, 167.4, 149.2, 144.3, 138.7, 136.9, 135.1, 134.8, 131.7, 130.6, 130.0, 128.3, 127.8, 127.5, 123.7, 122.5, 122.4, 117.6, 50.6, 38.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{27}H_{20}N_3O_5^+$= 466.1397; Found=466.1398.

3-(1-(1,3-Dioxoisoindolin-2-yl)-3-oxo-3-(quinolin-8-ylamino)propyl)benzoic acid 7b: Yield: 74% (172 mg), Texture: White solid; Rf = 0.45 (EtOAc/Toluene/Acetic acid in 10:88:2 ratio). ^{1}H NMR (501 MHz, DMSO-d6) δ 10.43 (s, 1H), 8.90 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.46 (d, *J* = 7.6 Hz, 1H), 8.35 (dd, *J* = 8.3, 1.5 Hz, 1H), 8.13 (s, 1H), 7.94 – 7.73 (m, 6H), 7.67 – 7.56 (m, 2H), 7.50 (dt, *J* = 14.4, 7.9 Hz, 2H), 5.96 (t, *J* = 7.8 Hz, 1H), 3.83 (d, *J* = 7.8 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, DMSO-d6) δ 169.3,

168.2, 167.5, 149.3, 140.1, 138.7, 136.9, 135.1, 134.8, 132.3, 131.6, 129.4, 129.1, 128.6, 128.3, 127.3, 123.7, 122.6, 122.5, 117.6, 50.7, 38.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{27}H_{20}N_3O_5^+$= 466.1397; Found=466.1395.

3-(1,3-Dioxoisoindolin-2-yl)-3-(4-hydroxyphenyl)-N-(quinolin-8-yl)propanamide 7c: Yield: 77% (170 mg), Texture: Off white solid; Rf = 0.5 (EtOAc/Toluene/Acetic acid in 10:88:2 ratio). ^{1}H NMR (501 MHz, DMSO-d6) δ 10.28 (s, 1H), 9.56 (s, 1H), 8.88 (s, 1H), 8.42 (d, *J* = 7.5 Hz, 1H), 8.35 (d, *J* = 8.2 Hz, 1H), 7.82 (d, *J* = 5.5 Hz, 4H), 7.60 (dd, *J* = 15.4, 6.4 Hz, 2H), 7.49 (t, *J* = 7.9 Hz, 1H), 7.32 (d, *J* = 8.2 Hz, 2H), 6.73 (d, *J* = 8.2 Hz, 2H), 5.77 (t, *J* = 7.7 Hz, 1H), 3.76 (dd, *J* = 15.3, 9.6 Hz, 2H); ^{13}C{^{1}H} NMR (101 MHz, DMSO-d6) δ 169.4, 168.3, 157.2, 149.3, 138.6, 136.9, 135.1, 134.7, 131.6, 129.9, 128.9, 128.2, 127.3, 123.6, 122.6, 122.5, 117.5, 115.7, 50.6, 38.8; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{26}H_{20}N_3O_4^+$= 438.1448; Found=438.1449.

3-(2,5-Dioxopyrrolidin-1-yl)-3-(3-hydroxyphenyl)-N-(quinolin-8-yl)propanamide 7d: Yield: 58% (110 mg), Texture: Off white solid; Rf = 0.3 (EtOAc/Hexane/Acetic acid in 50:48:2 ratio). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.85 (s, 1H), 8.76 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.66 (p, *J* = 4.4 Hz, 1H), 8.12 (dd, *J* = 8.3, 1.6 Hz, 1H), 7.50 – 7.40 (m, 3H), 7.20-7.08 (m, 3H), 6.79 (dd, *J* = 8.0, 1.7 Hz, 1H), 5.83 (dd, *J* = 10.4, 5.3 Hz, 1H), 4.03 (dd, *J* = 15.6, 10.5 Hz, 1H), 3.32 (dd, *J* = 15.6, 5.4 Hz, 1H), 2.62 (s, 4H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 177.7, 168.4, 156.6, 148.3, 139.8, 138.2, 136.4, 134.0, 130.0, 127.9, 127.3, 121.9, 121.7, 119.7, 116.9, 115.6, 115.1, 52.1, 38.3, 28.1; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{22}H_{20}N_3O_4^+$= 390.1448; Found=390.1440.

3-(2,5-Dioxopyrrolidin-1-yl)-3-(3-nitrophenyl)-N-(quinolin-8-yl)propanamide 7f: Yield: 76% (160 mg), Texture: Off white solid; Rf = 0.35 (60% EtOAc/Hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.88 (s, 1H), 8.79 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.68 – 8.63 (m, 1H), 8.45 (t, *J* = 1.9 Hz, 1H), 8.14 (dd, *J* = 8.3, 1.7 Hz, 2H), 7.91 (d, *J* = 7.8 Hz, 1H), 7.54 – 7.43 (m, 4H), 6.01 (dd, *J* = 9.6, 6.1 Hz, 1H), 3.98 (dd, *J* = 15.7, 9.6 Hz, 1H), 3.47 (dd, *J* = 15.7, 6.1 Hz, 1H), 2.70 (s, 4H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 177.1, 167.3, 148.4, 148.3, 140.3, 138.2, 136.3, 134.4, 133.9, 129.8, 127.9, 127.2, 123.3, 123.1, 121.9, 121.7, 116.7, 51.1, 37.9, 28.1; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{22}H_{19}N_4O_5^+$= 419.1350; Found=419.1352.

3-(1,3-Dioxoisoindolin-2-yl)-3-phenylpropanoic acid 8: Yield: Yield: 76% (70 mg), Texture: White solid; Rf = 0.6 (10% MeOH in DCM). ^{1}H NMR (501 MHz, $CDCl_3$) δ 7.81 – 7.78 (m, 2H), 7.69 – 7.67 (m, 2H), 7.51 (d, *J* = 7.4 Hz, 2H), 7.33 – 7.25 (m, 3H), 5.80 (dd, *J* = 9.9, 5.8 Hz, 1H), 3.84 (dd, *J* =

17.0, 9.9 Hz, 1H), 3.28 (dd, *J* = 17.0, 5.8 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 175.5, 168.1, 138.4, 134.1, 131.8, 128.8, 128.3, 127.8, 123.4, 50.6, 29.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ calculated for $C_{17}H_{14}NO_4^+$= 296.0917; Found=296.0912.

Supporting Information:

The Supporting Information is available free of charge on the ACS Publications website.

Copies of ^{1}H NMR, $^{13}C\{^{1}H\}$ NMR, ^{19}F NMR of the synthesized compounds.

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Notes

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