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Transamidation

Synthesis of 3-Substituted 2-Indolinones by a Multicomponent Coupling Isocyanide-Dependent Microwave-Assisted Intramolecular Transamidation Process

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Abstract: A small-molecule library synthesis of 3-substituted 2-indolinones using methyl isocyanide and a microwave-assisted intramolecular transamidation process with 10 % TFA in dichloroethane has been achieved in 3 steps. A modified Fe^0 Bechamp-type reduction of a substituted bifunctional substrate, *o*-nitrobenzaldehyde, renders 3-substituted 2-indolinones in yields ranging from 76–91 % (21 examples). Furthermore, it has been determined that symmetrical 2° *N*-alkyl or aryl substituents, as a component of the amine starting material, suppresses 3-substituted 2-indolinone rotameric mixtures and allows for facile compound ^{1}H NMR characterization. In the absence of methyl isocyanide, 3,4-dihydroquinazolines or transamidation products predominate under both Brønsted or Lewis acid conditions in reasonable yields.

Introduction

Recent developments in diversity-oriented synthesis (DOS)[1] have led to reaction transformations that allow synthetic chemists to impart post-reaction modifications leading to molecular complexity in core scaffolds allowing for the construction of regio- and stereo-specific frameworks.[2] Many of these processes are conducive towards the syntheses of libraries containing useful building blocks and biologically validated motifs of pharmaceutical and medicinal chemistry importance.[3] Within the concept of DOS, multicomponent reactions (MCRs)[4] followed by chemical modifications such as nucleophilic addition,[5] aromatic substitution,[6] metal catalyzed transformations,[7] and Lewis/Brønsted acid[8] mediated intra-/intermolecular additions have allowed for the preparation of natural products,[9] diverse library sets of small molecule motifs and derivatives thereof.[10] Through the combination of three or more reaction-compatible reagents employed in a one-pot or multistep process, new types of hetero/aromatic and macromolecular connectivities[11] can be achieved in a cost effective and highly atom economical process. The validation of these approaches is confirmed by numerous examples found in the literature,[2c,12] where an increased interest towards the development of chemical libraries aimed at producing cost effective drugs with rationalized biologically validated scaffolds predominates. One particularly interesting motif containing a fused ring system is the 2-indolinone core found abundantly in natural products[13] as well as in a wide range of biologically validated compounds such as antidepressants,[14] anticancer (Sutent®),[15,16] antiinflammatory,[17] and anti-HIV.[18]

Not surprisingly, synthetic strategies for diversifying the indolinone scaffold have increased likely due to the aforementioned importances. Over the past 10 years, several versatile synthetic methods for indolinone preparation have been reported including those utilizing C–H bond activation,[19] C–N coupling reactions,[20] and modifications of natural products amongst others.[21] Although these approaches have worked well, the need for more efficient and effective syntheses leading to structurally diverse indolinones remains significant. More recent efforts from the groups of Kalinski[22] and Zhu[20a,23,24] have focused on the preparation of 1,3-substituted 2-indolinones via palladium catalyzed *N*-aryl amidation methodology derived from peptide-based coupling.[25] Their chemistry allows for facile 1,3-substitution, however, limitations include the formation of *N*-alkylated products, and the use of expensive metal catalysts and ligands. Herein, we report on the synthesis of 3-substituted 2-indolinones (**1**) utilizing an intramolecular transamidation[26] reaction arising from multicomponent condensation products generated through microwave irradiation. Selective intramolecular acyl transfer[27] (i.e., preponderance for an acyl group transfer from a 2° amide over a 3° amide bond) is important in synthetic transformations and our approach selects for the migration to occur on an *ortho*-substituted aniline scaffold **2**. The reaction sequence (Scheme 1) involves an *ortho*-aniline intermediate (**2**), which is derived from a Bechamp-type reduction[28] of an α-acylamino-2-nitrophenylacetamide (**3**). A MCR reaction from the exclusive use of cost effective and readily available 2-nitrobenzaldehydes **4** [2-(BOC-amino] benzaldehydes not used, due to additional synthetic steps[29]), methyl isocyanide **5**, as well as amine derivatives **6** and carboxylic acids **7** gives rise to acyclic intermediate **3** which ultimately leads to the desired final compounds.

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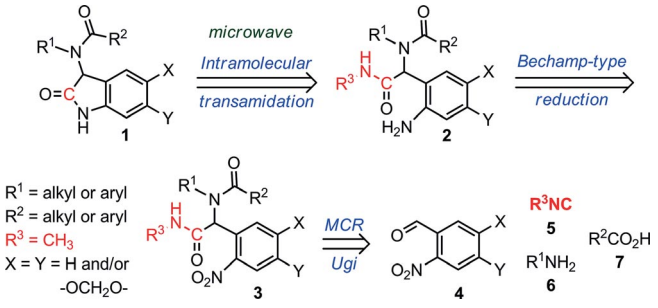


Scheme 1. Retrosynthetic analysis for 2-indolinones **1** arising from an intramolecular Ugi transamidation process following Bechamp-type reduction **2** made possible from α-acylamino-2nitrophenylacetamide precursors **3**.

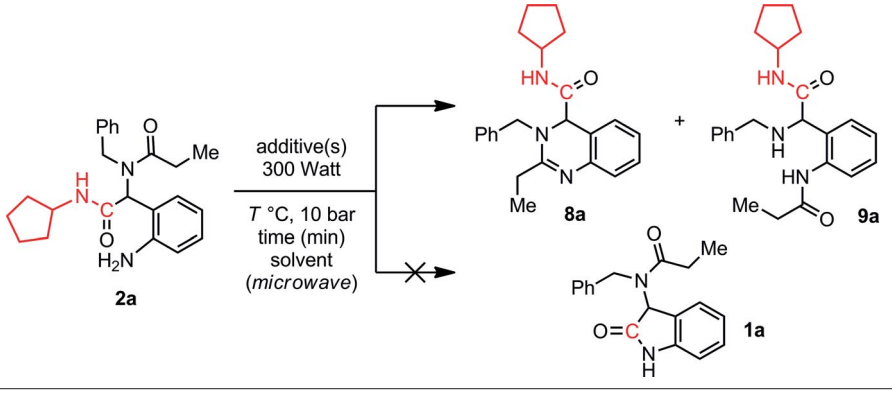
Results and Discussion

Initial attempts towards the synthesis of 3-substituted 2-indolinones began with the formation and optimization of acyclic dipeptide compounds **2**. As previous work emanating from our lab has demonstrated,[30] using Fe/NH_4Cl (10:1) in a 3:1 → EtOH/H_2O solution for *ortho*-nitro group reduction of compounds **3** to **2** gave acyclic anilines in excellent yields. However, efforts towards the synthesis of **1a** required some finesse as we initially observed 3,4-dihydroquinazolines[31] compounds **8a** and/or transamidation products **9a**, both of which most likely resulted from initial amine condensation on the 3° amide. In these early efforts, the cyclization attempts of compounds **2** to **1** were conducted with the cyclopentyl-substituted aniline **2a** (Table 1).

Efforts to delineate pathway selectivity for either **8a** or **9a** mostly yielded reaction mixtures, however, favorable outcomes occurred when 2 equiv. of Et_2O•HCl (2 M solution) or $Sc(OTf)_3$ in DCE was used leading to the major product **8a** (Table 1; entries 9 and 10). Although we examined a number of reaction conditions, pathway selectivity for transamidation leading to major product **9a** was elusive. We rationalized that the formation of **8a** and **9a** were the direct result of amine condensation and acyl group transfer, respectfully, on the 3° amide carbonyl and not the 2° amide because of steric bulk imposed by the cyclopentyl ring and also due to a high energy barrier for the generation of a cyclopentylamine by-product.[32]

Although we were pleased to obtain compounds **8a** and **9a**, our attention did not deviate from synthesizing 3-substituted 2-indolinones. Upon reading the literature for alternative conditions, we came across microwave-irradiation reports based on TFA-catalyzed reactions[26a,27a,33] designed to synthesize heterocyclic ring structures.[34] Using modified procedures, we conducted cyclization experiments with compounds **2b**–**2g** that contained various substituted 2° amides to probe reactivity and confirm sterically-controlled selectivity. Substituents (2,6-dimethyl phenyl (**2b**), cyclohexyl (**2c**), *p*-anisyl (**2d**), *tert*-butyl (**2e**), isopropyl (**2f**), *n*-pentyl (**2g**) were used. In all instances, the microwave-assisted reactions were run in DCE with 10 % TFA at

Table 1. Reaction conditions leading to the formation of **8a** and **9a**.



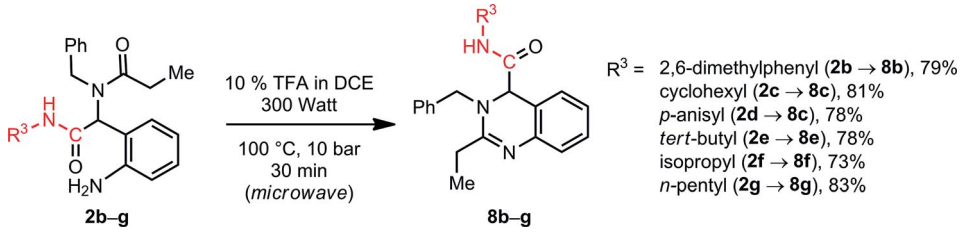
Entry[a]	Additive (equiv.)	Solvent	*T* [°C][a]	Time	**8a** (% yield)[b]	**9a** (% yield)[b]
1	BF_3•OEt_2 (2)	DCM	50	10 min	70	20
2	BF_3•OEt_2 (2)	MeCN	100	10 min	75	20
3	$ZnCl_2$ (2)	DCM	50	10 min	n.a.	n.a.
4	BEt_3 (1 M in hexanes) (2.5)	DCE	100	10 min	n.a.	n.a.
5	$TiCl_4$ (2)	DCM	45	30 min	n.a.	n.a.
6	$TiBr_4$ (2)	DCM	50	30 min	57	40
7	$AlCl_3$ (1)	DCM	40	20 min	n.a.	n.a.
8	*p*TsA (0.5)	DCM	50	10 min	50	40
9	Et_2O•HCl (2 M) (2)	Et_2O	50	10 min	80	<5
10	$Sc(OTf)_3$ (2)	DCE	100	30 min	67	3
11	$Sc(OTf)_3$ (2)	toluene	110	30 min	n.a.	n.a.
12	$Y(OTf)_3$ (2)	DCM	50	20 min	40	35
13	(*S*)-CSA (0.5)	DCM	50	10 min	45	30

[a] Microwave conditions (CEM® Discover microwave reactor): 300 W and 10 bar. [b] Isolated yield; n.a.: not available/not observed.

100 °C but the only observable products were of type **8** (**8b-g**) obtained in good to excellent yields (compounds of type **9** were not detected) (Scheme 2). Based on these results we concluded that the bulky 2° amide substituents, from isocyanide starting reagents, play an important role in selecting for products of type **8** directing amine condensation toward the 3° amide and forming 3,4-dihydroquinazoline products (**8b-g**).

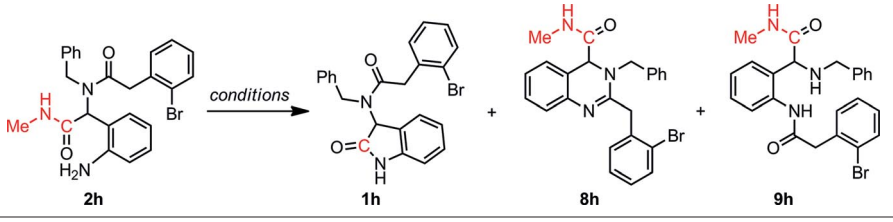
In an attempt to lower the steric demands of the 2° amides found in substrates **2b-g** and encourage transamidation for the desired 2-indolinones, we turned our attention to methyl isocyanide[35a] and the preparation of aniline precursor **2h** (Table 2). Methyl isocyanide was synthesized on a 50 g quantity using a dehydratative distillation procedure.[35b] With **2h** in hand, the cyclization for 2-indolinones using Lewis/Brønsted acids and a variety of solvents under the influence of microwave irradiation was attempted (Table 2). In many instances we observed the formation of the desired product **1h** along with products **8a** and **9a** when BF_3•OEt_2 in DCM or DCE at 40 °C was used (Table 2; entries 1 and 2). Taking these results into consideration we decided to use Lewis acids $InCl_3$, $AlCl_3$, $ZnCl_2$, $CeCl_3$, $TiCl_4$, $Sc(OTf)_3$, $Y(OTf)_3$ with solvents such as DCM, THF, toluene and DCE (Table 2; entries 3–10). Unfortunately, these conditions did not lead to any appreciable improvements in product ratios or yields.

It is known that Lewis acid complexes will form with 3° amide carbonyls over 2° amide nitrogens increasing the electrophilic potential.[36] In our case this leads to a general preponderance for compounds **8h** and **9h**. We decided to move forward to study the effects of Brønsted acids such as camphorsufonic acid, *p*-toluenesulfonic acid and trifluoroacetic acid in solvents DCM, DCE, $CHCl_3$ toluene, and diethyl ether (Table 2; entries 11–17). In many of these experiments we observed an



Scheme 2. Bulky isocyanides and 10 % TFA lead to the formation of 3,4-dihydroquinazolines.

Table 2. Scope of reaction conditions for compounds **1h**, **8h** and **9h** when methyl isocyanide is incorporated into **2h**.



Entry[a]	Additive	Solvent	*T* [°C]	Time	**1h** (% yield)[b]	**8h** (% yield)[b]	**9h** (% yield)[b]
1	BF_3•OEt_2 (2)	DCM	40	10 min	<5	60	20
2	BF_3•OEt_2 (2)	DCE	70	10 min	<5	40	20
3	$InCl_3$ (2)	DCM	45	1 h	<5	20	20
4	$AlCl_3$ (2)	DCE	100	10 min	<5	35	35
5	$ZnCl_2$ (2)	toluene	80	10 min	10	35	30
6	$ZnCl_2$ (2)	DCE	80	1 h	15	40	20
7	$CeCl_3$ (4)	THF	120	1 h	30	20	20
8	$TiCl_4$ (2)	DCE	80	1 h	<5	60	20
9	$Sc(OTf)_3$ (2)	MeCN	80	20 min	<5	40	5
10	$Y(OTf)_3$ (1)	DCE	120	30 min	10	40	35
11	(*S*)-CSA (1)	DCE	50	10 min	30	20	35
12	*p*TsA (1)	DCE	60	20 min	35	30	25
13	10 % TFA	DCM	30	10 min	80	10	10
14	10 % TFA	DCM	45	10 min	80	10	10
15	10 % TFA	toluene	100	10 min	50	30	20
16	10 % TFA	$CHCl_3$	45	10 min	40	20	10
17	10 % TFA	Et_2O	45	30 min	38	25	10
18	10 % TFA	DCE	120	10 min	90	n.a.	n.a.
19	5 % TFA	DCE	120	10 min	80	n.a.	n.a.
20	20 % TFA	DCE	120	10 min	90	n.a.	n.a.
21	40 % TFA	DCE	120	10 min	85	traces	n.a.

[a] Microwave conditions (CEM® Discover microwave reactor): 300 Watt, 10 bar. [b] Isolated yields; n.a.: not available/not observed.

increase in yields of the desired product **1h**, especially when 10 % TFA in DCE was employed. Encouraged with the use of TFA, several more conditions were screened including 5, 20, and 40 % TFA in DCE (Table 2; entries 18–21). The results indicated that 10 % TFA in DCE proved superior in product yield and pathway selectivity for **1h**. One plausible explanation might be that the highly acidic TFA acts to increase the electrophilicity of the more polarizable 2° amide carbonyl through protonation and hence promote lactamization. The characterization of **1h** was verified using NMR and MS and unequivocally confirmed through X-ray crystal structure analysis (Figure 1). Combined with previous data, these results indicate that the steric environment of the 2° amide is critical for product selectivity and we believe that the formation of methylamine gas is a driving force for the formation of 2-indolinones via our intramolecular transamidation.[37]

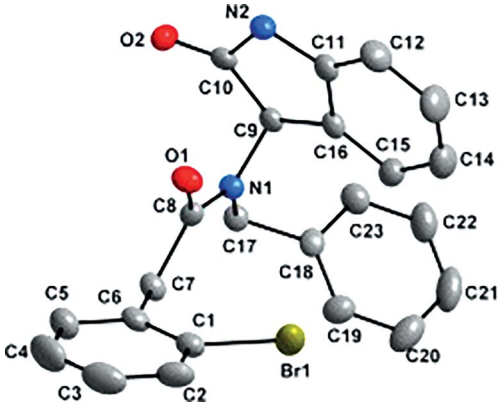


Figure 1. ORTEP structure of 2-indolinone **1h**.

In light of the structure of 2-indolinone **1h** being directly confirmed using X-ray diffraction (Figure 1), it must be noted that substantial difficulty in interpreting ^{1}H NMR for this compound was encountered (Figure 2).[38] We attributed this challenge to the formation of amide rotomers which were also noted and apparent in a previous report.[20a] In good practice, we attempted to resolve spectral complexity by screening NMR solvents under variable temperature (VT) NMR,[39] however this did not provide a viable solution to our problem as we continued to observe peak broadening and further complexity.[40] To resolve the rotameric issue, we elected to study nitrogen substituents on the 3° amide of the 3-substituted 2-indolinones, where symmetrical and sterically demanding groups could be utilized to favor a single conformer.[41] To this end, we synthesized compound **1i** containing an isopropyl substituent (isopropylamine was the starting reagent) on the 3° amide and observed clean, highly resolved peak splitting patterns in ^{1}H NMR analysis (Figure 2; **1i**). Based on these observations, we turned our attention to utilizing straight chain **1h**, and **1o**–**r** and branched symmetrical substituents **1j**–**n** for the synthesis of 2-indolinone derivatives (Figure 3). The ^{1}H NMR spectra of compounds **1j**–**n** provided sharp well-defined peaks and splitting patterns at room temperature while the spectroscopic data for **1o**–**r** was similar to that observed for compound **1h**.

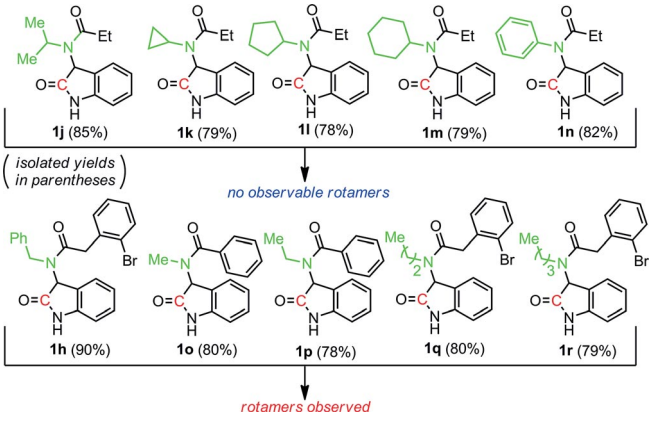


Figure 3. Differences in amine starting reagents lead to 3-substituted 2-indolinone (analogues for library - 1) amide rotameric mixtures.

To further examine the scope of the transamidation process and to determine if carboxylic acid components would influence rotamer formation, compounds **1s-bb** (Figure 4) were prepared in good isolated yields. The 3-step sequence was well tolerated by aliphatic, aromatic, and unsaturated carboxylic acids. Compounds **1s**–**1bb** gave well-defined ^{1}H NMR spectroscopic data suggesting that in the presence of branched amide substitution a major conformation is preferred. This trend also

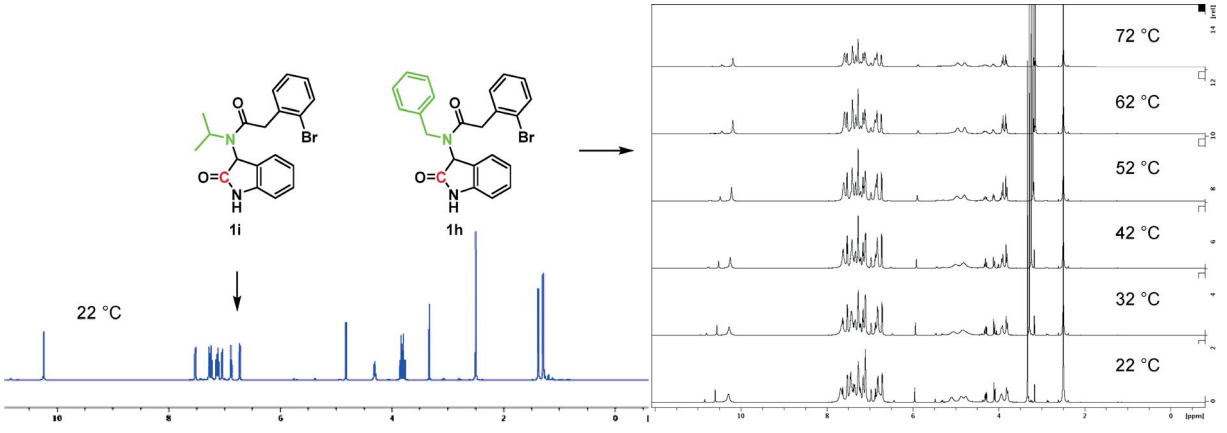


Figure 2. Temperature-dependent ^{1}H NMR ([D$_6$]DMSO) spectra showing rotameric mixtures of **1h** at ca. 10.5–10.1 ppm (NH) when benzylamine is used as a starting reagent vs. ^{1}H NMR ([D$_6$]DMSO) spectra of **1i** at 22 °C at ca. 10.3 ppm (NH) where isopropylamine is a starting reagent and rotamers are not observed.

suggests that branched symmetrical *N*-substitution on the amide bond forces the 2-indolinone products **1i**–**n** into a single conformation avoiding the complex ^{1}H NMR peak patterns observed from rotamers of compounds **1h**, **1o**–**r**.

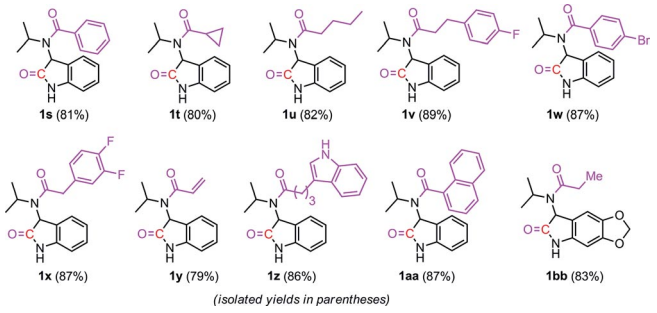


Figure 4. Carboxylic acids as starting reagents do not influence the formation of rotamers when the *N*-isopropyl substituent is a component of the 3° amide (2-indolinone analogues for library - 2).

Conclusions

In conclusion, we have developed a selective intramolecular transamidation strategy for the synthesis of 3-substituted 2-indolinones, 3,4-dihydroquinazolines and other transamidation products. The strategy takes advantage of an atom economical cascade coupling reaction, a Bechamp-type reduction and microwave assisted cyclization. Through this process we have learned that when varying alkyl- or aryl isocyanides are used, with the exception of methyl isocyanide (**5**), 3,4-dihydroquinazolines **8** and/or 3° amide transamidation products **9** are obtained in reasonable yields. Although the process is efficient and leads to good compound yields, we encountered rotameric issues with 3-substituted 2-indolinone compounds. To overcome this challenge and for legible ^{1}H NMR spectroscopic data, we discovered that the use of symmetrical branched 2° *N*-amide or *N*-aryl substituents diminished rotameric conformers and simplified NMR characterization. This work is currently being extended toward the synthesis of spiro-indolinones and other bio-relevant scaffolds.

Experimental Section

All reagents and solvents were commercially available and used without purification unless otherwise stated. Reaction progress was monitored using thin layer chromatography (TLC) on pre-coated silica gel (particle size 0.03–0.07 mm). TLC was visualized using UV followed by staining with ninhydrin or PMA solutions. Column chromatography was performed using Whatman Purasil 60 Å (230–400 mesh ASTM) silica gel, yields refer to chromatographically and spectroscopically pure compounds. ^{1}H and ^{13}C NMR were recorded using a Bruker Avance 600 MHz spectrometer at 22 °C (default) unless otherwise noted. The residual $CDCl_3$ ^{1}H singlet at δ = 7.27 ppm and ^{13}C triplet at δ = 77.23 ppm, CD_2Cl_2 ^{1}H triplet at δ = 5.32 ppm and ^{13}C quintet at δ = 54.00, and [D_6]DMSO ^{1}H quintet at δ = 2.50 ppm and residual ^{13}C septet at δ = 39.51 ppm, CD_3OD ^{1}H singlet at δ = 4.87 ppm and ^{13}C triplet at δ = 49.15 ppm, CD_3CN ^{1}H quintet at δ = 1.94 ppm and ^{13}C singlet at δ = 118.69, and [D_6]Acetone ^{1}H quintet at δ = 2.05 ppm and residual ^{13}C heptet at δ = 29.92 ppm, were used as the standards for ^{1}H NMR and ^{13}C NMR spectra respectively. Signal patterns are indicated as s: singlet; d: doublet; t: triplet; q: quartet; m: multiplet; dd: doublet of doublets; br: broad and coupling constants are reported in Hertz (Hz). Low resolution mass spectra (LRMS) were acquired on an Esquire-LC electrospray ionization (ESI) mass spectrometer. High resolution mass spectra (HRMS) were obtained with a Bruker Maxis 4G mass spectrometer. Melting points were recorded on a MEL-TEMP® electro thermal apparatus. A CEM Discovery® microwave system (ESP 1500 Plus model) was used for all microwave reactions. X-ray crystallographic analysis was performed on an Apex Duo.

General Procedure for Ugi Products 3a–3bb: Amine **6** (1 equiv.) was added to a clear solution of 2-nitrobenzaldehyde (**4**) (1 equiv.) in methanol (5 mL) and allowed to stir for 10 minutes at room temperature and then carboxylic acid **7** (1 equiv.), and isocyanide **5** (1 equiv.) were subsequently added. The reaction was continually stirred until no noticeable starting reagents were visualized using TLC. Upon completion of the reaction, methanol was evaporated under reduced pressure. After obtaining the mass of unpurified product(s) the material was dissolved in CH_2Cl_2. The organic layer was washed with a saturated $NaHCO_3$ solution (2 × 5 mL) followed by brine (5 mL) and then the organic layer was dried with anhydrous Na_2SO_4 (1–2 g). Complete removal of solvent was carried out under reduced pressure on a rotoevaporator. The crude product was subjected to flash column chromatography (EtOAc/hexanes – isocratic or gradient depending on measured R_f from TLC) to yield pure compound.

***N*-Benzyl-*N*-[2-(cyclopentylamino)-1-(2-nitrophenyl)-2-oxoethyl]propionamide (3a):** The compound was obtained as an off-white solid; m.p. 102–104 °C; yield 90 %. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.03–7.85 (m, 1 H), 7.66–7.08 (m, 8 H), 6.46–5.99 (m, 1 H), 5.37–4.65 (m, 2 H), 4.29–3.93 (m, 1 H), 2.47–2.24 (m, 2 H), 1.85–1.65 (m, 2 H), 1.56–0.90 (m, 11 H) (rotamers) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 175.75, 167.83, 149.68, 137.02, 133.22, 131.18, 129.94, 129.16, 128.81, 128.62, 127.51, 126.35, 125.20, 59.82, 51.79, 50.83, 33.04, 32.54, 27.29, 23.83, 9.63 ppm. EIMS $[M + Na]^+$ calcd. for $C_{23}H_{27}N_3O_4$: 432.2 found 432.3.

***N*-Benzyl-*N*-[2-(2,6-dimethylphenyl)amino-1-(2-nitrophenyl)-2-oxoethyl]propionamide (3b):** The compound was obtained as a light brown solid; m.p. 101–103 °C; yield 80 %. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.92–7.91 (d, J = 7.0 Hz, 1 H), 7.82–7.81 (d, J = 7.3 Hz, 1 H), 7.56 (s, 1 H), 7.44–7.40 (t, J = 6.8 Hz, 1 H), 7.23–7.01 (m, 9 H), 6.48 (s, 1 H), 4.86–4.83 (d, J = 16.9 Hz, 1 H), 4.61–4.58 (d, J = 16.9 Hz, 1 H), 2.51 (s, 2 H), 2.38 (s, 6 H), 1.61 (s, 3 H), 1.22–1.20 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 175.47, 166.83, 149.91, 136.61, 135.42, 133.27, 133.07, 131.05, 129.85, 129.57, 128.83, 128.36, 128.19, 127.57, 127.31, 126.51, 124.94, 58.93, 51.16, 27.28, 18.42, 9.50 ppm. EIMS $[M + Na]^+$ calcd. for $C_{26}H_{27}N_3O_4$: 468.2 found 468.5.

***N*-Benzyl-*N*-[2-(cyclohexylamino)-1-(2-nitrophenyl)-2-oxoethyl]propionamide (3c):** The compound was obtained as a pale yellow solid; m.p. 123–125 °C; yield 87 %. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.03–7.84 (m, 2 H), 7.66–7.29 (m, 8 H), 6.42–6.25 (d, 1 H), 5.87–5.86 (d, J = 3.6 Hz, 1 H), 5.28–5.05 (m, 1 H), 4.80–4.77 (d, J = 17.2 Hz, 1 H), 4.65–4.63 (d, J = 17.2 Hz, 1 H), 4.26–4.25 (d, J = 11.64 Hz, 1 H), 3.57–3.49 (m, 2 H), 2.49–2.27 (m, 3 H), 1.82–0.74 (m, 13 H) (rotamers) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 175.85, 167.44, 149.74, 137.03, 133.52, 133.22, 131.10, 130.10, 129.64, 129.23, 128.84, 128.68, 128.07, 127.55, 126.42, 125.79, 125.18, 62.47, 51.02, 49.68, 48.94, 32.84, 32.52, 27.33, 25.63, 24.85, 24.79, 9.63 (rotamers) ppm. EIMS $[M + Na]^+$ calcd. for $C_{24}H_{29}N_3O_4$: 446.2 found 446.6.

***N*-Benzyl-*N*-[2-(4-methoxyphenyl)amino-1-(2-nitrophenyl)-2-oxoethyl]propionamide (3d):** The compound was obtained as a dark brown solid; m.p. 179–181 °C; yield 79 %. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.10–7.85 (m, 2 H), 7.65–7.33 (m, 5 H), 7.09–6.46 (m, 10 H), 5.18–4.29 (m, 2 H), 3.76 (s, 3 H), 2.50–2.29 (m, 2 H), 1.17 (s, 3 H) (rotamers) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 176.19, 166.76, 156.84, 149.71, 136.62, 133.33, 130.49, 130.31, 129.51, 128.96, 127.68, 126.45, 125.27, 122.21, 60.78, 55.66, 51.40, 27.36, 9.62 ppm. EIMS [M + Na]$^+$ calcd. for $C_{25}H_{25}N_3O_5$: 470.2 found 470.5.

***N*-Benzyl-*N*-[(2-(*tert*-butylamino)-1-(2-nitrophenyl)-2-oxoethyl]propionamide (3e):** The compound was obtained as a yellow solid; m.p. 142–144 °C; yield 85 %. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.04–7.88 (m, 1 H), 7.87–7.49 (m, 3 H), 7.32–7.25 (m, 4 H), 7.09–7.08 (d, J = 5.6 Hz, 1 H), 6.48–6.21 (m, 1 H), 5.78–5.23 (m, 1 H), 1.36–1.07 (m, 12 H) (rotamers) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 175.78, 167.45, 149.84, 137.15, 133.50, 133.40, 133.23, 132.56, 131.58, 129.64, 129.49, 129.37, 129.08, 128.89, 128.84, 128.81, 128.57, 128.44, 128.09, 127.66, 127.51, 126.31, 125.65, 125.26, 124.72, 60.55, 52.07, 50.65, 28.86, 28.37, 27.27, 9.66 (rotamers) ppm. EIMS [M + Na]$^+$ calcd. for $C_{25}H_{27}N_3O_4$: 420.2 found 420.5.

***N*-Benzyl-*N*-[2-(isopropylamino)-1-(2-nitrophenyl)-2-oxoethyl]propionamide (3f):** The compound was obtained as a pale brown solid; m.p. 166–1168 °C; yield 83 %. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.03–7.99 (m, 1 H), 7.86–7.09 (m, 8 H), 6.46 (m, 1 H), 5.79–4.99 (m, 1 H), 4.80–4.32 (m, 2 H), 3.86–3.78 (m, 1 H), 2.47–2.27 (m, 2 H), 1.18–1.15 (t, J = 7.3 Hz, 3 H), 1.06–0.79 (m, 6 H) (rotamers) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 175.77, 167.46, 149.72, 137.03, 133.54, 133.23, 131.15, 130.01, 129.62, 129.20, 128.98, 128.82, 128.63, 128.45, 128.04, 127.67, 127.53, 126.36, 125.80, 125.65, 125.21, 27.29, 22.57, 22.21, 9.63 ppm. EIMS [M + Na]$^+$ calcd. for $C_{21}H_{25}N_3O_4$: 406.2 found 406.6.

***N*-Benzyl-*N*-[1-(2-nitrophenyl)-2-oxo-2-(pentylamino)ethyl]-propionamide (3g):** The compound was obtained as an off-white solid; m.p. 90–92 °C; yield 79 %. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.02–7.83 (m, 1 H), 7.65–7.40 (m, 4 H), 7.23–7.07 (m, 4 H), 6.43–6.31 (m, 1 H), 5.92–5.38 (m, 1 H), 4.97–4.37 (m, 2 H), 3.13–2.79 (m, 2 H), 2.46–2.30 (m, 2 H), 1.37–1.16 (m, 8 H), 0.86 (s, 3 H) (rotamers) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 175.77, 168.35, 149.74, 136.93, 133.22, 130.30, 129.30, 129.09, 128.83, 128.44, 127.56, 126.39, 125.17, 59.76, 51.00, 39.99, 29.16, 28.96, 27.30, 22.44, 14.16, 9.60(rotamers) ppm. EIMS [M + Na]$^+$ calcd. for $C_{23}H_{29}N_3O_4$: 434.2 found 434.6.

***N*-Benzyl-2-(2-bromophenyl)-*N*-[2-(methylamino)-1-(2-nitrophenyl)-2-oxoethyl]acetamide (3h):** The compound was obtained as a white solid; m.p. 156–158 °C; yield 95 %. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.49–7.48 (d, J = 7.9 Hz, 1 H), 7.23–7.21 (t, J = 7.3 Hz, 1 H), 7.17–7.12 (m, 5 H), 7.09–7.07 (t, J = 7.6 Hz, 2 H), 6.95–6.94 (d, J = 7.1 Hz, 2 H), 6.67–6.66 (d, J = 7.3 Hz, 1 H), 6.63–6.60 (t, J = 7.2 Hz, 1 H), 6.50 (s, 1 H), 4.95–4.92 (d, J = 17.7 Hz, 1 H), 4.84–4.81 (d, J = 17.7 Hz, 1 H), 3.82–3.79 (d, J = 16.7 Hz, 1 H), 3.52–3.49 (d, J = 16.7 Hz, 1 H), 2.79–2.78 (d, J = 4.7 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 173.32, 170.34, 146.17, 137.94, 135.43, 132.69, 131.73, 130.22, 128.77, 128.60, 127.65, 127.11, 126.40, 125.16, 119.06, 118.60, 116.34, 57.42, 50.25, 42.07, 26.55 (rotamers) ppm. EIMS [M + Na]$^+$ calcd. for $C_{23}H_{29}BrN_3O_4$: 518.1 found 518.3.

2-(2-Bromophenyl)-*N*-isopropyl-*N*-[2-(methylamino)-1-(2-nitrophenyl)-2-oxoethyl]acetamide (3i): The compound was obtained as a white solid; m.p. 168–170 °C; yield 90 %. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.01–8.00 (d, J = 6.4 Hz, 1 H), 7.75–7.74 (d, J = 6.2 Hz, 1 H), 7.59 (s, 2 H), 7.49–7.16 (m, 4 H), 5.74 (s, 1 H), 4.37 (s, 1 H), 4.12–4.09 (d, J = 15.8 Hz, 1 H), 3.89–3.86 (d, J = 15.8 Hz, 1 H), 2.68 (s, 3 H), 1.43 (s, 3 H), 1.00 (s, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.99, 168.69, 149.16, 134.96, 133.67, 132.88, 131.86, 131.59, 130.74, 129.27, 129.09, 127.96, 125.24, 124.74, 57.30, 50.65, 41.58, 27.01, 21.66, 21.10 ppm. EIMS [M + Na]$^+$ calcd. for $C_{20}H_{22}N_3O_4$: 470.1 found 472.3.

***N*-Isopropyl-*N*-[2-(methylamino)-1-(2-nitrophenyl)-2-oxoethyl]propionamide (3j):** The compound was obtained as a light yellow solid; m.p. 122–124 °C; yield 86 %. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.01–8.00 (d, J = 7.1 Hz, 1 H), 7.62–7.59 (t, J = 7.4 Hz, 2 H), 7.51–7.50 (d, J = 6.0 Hz, 1 H), 5.67 (s, 1 H), 5.21 (s, 1 H), 4.24 (s, 1 H), 2.58–2.57 (d, J = 7.9 Hz, 3 H), 2.50–2.46 (m, 2 H), 1.45–1.44 (d, J = 5.0 Hz, 3 H), 1.21 (s, 3 H), 0.96–0.95 (d, J = 5.1 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 177.66, 169.06, 149.16, 133.70, 131.96, 130.46, 129.25, 125.26, 57.05, 49.79, 27.50, 27.03, 21.51, 21.14, 9.51 ppm. EIMS [M + Na]$^+$ calcd. for $C_{15}H_{21}N_3O_4$: 330.1 found 330.3.

***N*-Cyclopropyl-*N*-[2-(methylamino)-1-(2-nitrophenyl)-2-oxoethyl]propionamide (3k):** The compound was obtained as an off-white solid; m.p. 176–178 °C; yield 81 %. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.08–8.07 (d, J = 4.2 Hz, 1 H), 7.98–7.97 (d, J = 7.9 Hz, 1 H), 7.65–7.63 (t, J = 7.6 Hz, 1 H), 7.55–7.53 (t, J = 7.7 Hz, 1 H), 7.15–7.13 (d, J = 7.8 Hz, 1 H), 6.24 (s, 1 H), 2.66–2.62 (m, 2 H), 2.61–2.60 (d, J = 4.5 Hz, 3 H), 1.04–1.02 (t, J = 7.3 Hz, 3 H), 0.98–0.96 (m, 1 H), 0.63–0.55 (m, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 176.25, 167.70. 149.39, 132.92, 131.80, 129.15, 128.62, 124.39, 61.31, 29.45, 26.85, 26.02, 9.10, 8.66, 8.51 ppm. EIMS [M + Na]$^+$ calcd. for $C_{15}H_{19}N_3O_4$: 328.1 found 328.3.

***N*-Cyclopentyl-*N*-[2-(methylamino)-1-(2-nitrophenyl)-2-oxoethyl]propionamide (3l):** The compound was obtained as a light yellow solid; m.p. 101–103 °C; yield 84 %. ^{1}H NMR (600 MHz, [D_6]DMSO): δ = 8.06–8.05 (d, J = 4.0 Hz, 1 H), 7.96–7.95 (d, J = 8.0 Hz, 1 H), 7.63–7.61 (t, J = 7.5 Hz, 1 H), 7.54–7.51 (d, J = 7.7 Hz, 1 H), 7.13–7.11 (d, J = 7.8 Hz, 1 H), 6.22 (s, 1 H), 2.64–2.58 (m, 6 H), 1.02–0.93 (m, 4 H), 0.60–0.54 (m, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 178.26, 170.08, 149.55, 132.83, 130.95, 130.73, 129.20, 124.76, 63.66, 31.69, 27.99, 26.82, 9.96, 9.93, 9.20 ppm. EIMS [M + Na]$^+$ calcd. for $C_{17}H_{23}N_3O_4$: 356.2 found 356.6.

***N*-Cyclohexyl-*N*-[2-(methylamino)-1-(2-nitrophenyl)-2-oxoethyl]propionamide (3m):** The compound was obtained as an off-white solid; m.p. 168–170 °C; yield 89 %. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.02 (s, 1 H), 7.59–7.50 (m, 3 H), 5.75 (s, 1 H), 5.23 (s, 1 H), 3.76–3.48 (m, 1 H), 2.84–2.73 (m, 3 H), 2.59–1.94 (m, 4 H), 1.81–1.65 (m, 3 H), 1.48–1.11 (m, 8 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 174.73, 169.11, 149.14, 133.58, 131.95, 130.39, 129.16, 125.28, 58.65, 58.13, 32.22, 31.75, 27.59, 27.06, 26.21, 25.92, 25.24, 9.59 ppm. EIMS [M + Na]$^+$ calcd. for $C_{18}H_{25}N_3O_4$: 370.2 found 370.6.

***N*-[2-(Methylamino)-1-(2-nitrophenyl)-2-oxoethyl]-*N*-phenylpropionamide (3n):** The compound was obtained as a light yellow solid; m.p. 204–206 °C; yield 85 %. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.82–7.80 (d, J = 7.9 Hz, 1 H), 7.35–7.32 (t, J = 7.8 Hz, 2 H), 7.29–7.27 (m, 1 H), 7.18 (s, 4 H), 6.50 (s, 1 H), 5.96 (s, 1 H), 2.87–2.86 (d, J = 2.7 Hz, 3 H), 2.09–2.07 (m, 2 H), 1.07–1.05 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 174.68, 170.01, 150.17, 139.88, 132.64, 132.51, 130.27, 129.53, 129.27, 128.91, 128.52, 124.47, 59.84, 28.47, 26.83, 9.45 ppm. EIMS [M + Na]$^+$ calcd. for $C_{18}H_{19}N_3O_4$: 364.1 found 364.3.

***N*-Methyl-*N*-[2-(methylamino)-1-(2-nitrophenyl)-2-oxoethyl]benzamide (3o):** The compound was obtained as a white solid; m.p. 178–180 °C; yield 75 %. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.98 (s, 1 H), 7.65–7.45 (m, 8 H), 6.66 (s, 1 H), 3.03–2.84 (m, 6 H). ^{13}C NMR (150 MHz, $CDCl_3$): δ = 173.16, 168.96, 150.07, 135.23, 133.15, 130.69, 129.93, 129.42, 128.82, 127.61, 125.37, 59.19, 36.15, 26.68. EIMS [M + Na]$^+$ calcd. for $C_{17}H_{17}N_3O_4$: 350.1 found 350.3.

***N*-Ethyl-*N*-[2-(methylamino)-1-(2-nitrophenyl)-2-oxoethyl]benzamide (3p):** The compound was obtained as a white solid; m.p. 190–192 °C; yield 76 %. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.97 (s, 1 H), 7.67–7.44 (m, 8 H), 6.65 (s,1 H), 6.28 (s, 1 H), 3.53–3.40 (m, 2 H), 2.89 (s, 3 H), 0.96 (s, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 173.46, 169.61, 149.72, 135.92, 133.24, 130.21, 129.37, 128.81, 126.93, 125.34, 66.05, 60.37, 44.90, 26.68, 15.47, 14.86 ppm. EIMS $[M + Na]^+$ calcd. for $C_{18}H_{19}N_3O_4$: 350.1364.1 found 364.3.

2-(2-Bromophenyl)-*N*-[2-(methylamino)-1-(2-nitrophenyl)-2-oxoethyl]-*N*-propylacetamide (3q): The compound was obtained as a white solid; m.p. 193–195 °C; yield 87 %. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.94–7.93 (d, J = 7.9 Hz, 1 H), 7.59–7.56 (m, 3 H), 7.50–7.47 (t, J = 7.5 Hz, 1 H), 7.33–7.28 (m, 3 H), 7.17–7.14 (t, J = 7.1 Hz, 1 H), 6.41–6.40 (d, J = 2.9 Hz, 1 H), 6.33 (s, 1 H), 4.00–3.98 (d, J = 16.1 Hz, 1 H), 3.88–3.85 (d, J = 16.1 Hz, 1 H), 3.42–3.38 (m, 2 H), 2.78–2.77 (d, J = 4.6 Hz, 3 H), 1.62–1.58 (m, 1 H), 1.52–1.48 (m, 1 H), 0.86–0.83 (t, J = 57.3 Hz, 3 H) (rotamers) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 171.50, 169.35, 149.73, 135.01, 133.09, 132.85, 131.75, 130.16, 129.18, 129.06, 127.88, 125.13, 124.90, 60.69, 50.52, 41.16, 26.65, 23.10, 11.56 (rotamers) ppm. EIMS $[M + Na]^+$ calcd. for $C_{20}H_{22}N_3O_4$: 470.1 found 470.3.

2-(2-Bromophenyl)-*N*-butyl-*N*-[2-(methylamino)-1-(2-nitrophenyl)-2-oxoethyl]acetamide (3r): The compound was obtained as a light brown solid; m.p. 101–103 °C; yield 83 %. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.93–7.92 (d, J = 8.0 Hz, 1 H), 7.58–7.56 (m, 3 H), 7.49–7.47 (m, 1 H), 7.33–7.29 (m, 2 H), 7.17–7.14 (m, 1 H), 6.27 (s, 1 H), 6.22–6.21 (d, J = 4.1 Hz, 1 H), 3.98–3.95 (d, J = 16.0 Hz, 1 H), 3.88–3.85 (d, J = 16.0 Hz, 1 H), 3.44–3.41 (t, J = 8.3 Hz, 3 H), 2.82–2.81 (d, J = 4.9 Hz, 3 H), 1.53–1.44 (m, 2 H), 1.28–1.22 (m, 2 H), 0.87–0.84 (t, J = 7.4 Hz, 3 H) (rotamers) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 171.51, 169.39, 149.77, 135.00, 133.12, 132.90, 131.81, 130.24, 129.23, 121.12, 127.93, 125.14, 124.92, 61.03, 48.93, 41.22, 31.78, 26.73, 20.37, 13.84(rotamers) ppm. EIMS $[M + Na]^+$ calcd. for $C_{21}H_{24}N_3O_4$: 484.1 found 484.3 and 486.3.

***N*-Isopropyl-*N*-[2-(methylamino)-1-(2-nitrophenyl)-2-oxoethyl]benzamide (3s):** The compound was obtained as a white solid; m.p. 131–133 °C; yield 85 %. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.03–8.02 (d, J = 7.7 Hz, 1 H), 7.85–7.84 (d, J = 7.5 Hz, 1 H), 7.69–7.67 (t, J = 7.1 Hz, 1 H), 7.55–7.53 (t, J = 7.4 Hz, 1 H),7.45 (s, 5 H), 5.81 (s, 1 H), 5.43 (s, 1 H), 4.15 (s, 1 H), 2.79–2.78 (d, J = 2.1 Hz, 3 H), 1.40–1.39 (d, J = 5.1 Hz, 3 H), 0.91 (s, 3 H) ppm; ^{13}CNMR (150MHz,$CDCl_3$): δ = 172.85, 168.82, 149.46, 136.59, 133.81, 131.87, 130.54, 130.01, 129.53, 128.90, 126.31, 125.44, 52.07, 27.13, 21.62, 21.24 ppm. EIMS $[M + Na]^+$ calcd. for $C_{19}H_{21}N_3O_4$: 378.1 found 378.3.

***N*-Isopropyl-*N*-[2-(methylamino)-1-(2-nitrophenyl)-2-oxoethyl]cyclopropanecarboxamide (3t):** The compound was obtained as a light yellow solid; m.p. 133–135 °C; yield 78 %. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.05–7.45 (m, 4 H), 7.17 (s, 1 H), 6.27–5.89 (m, 1 H), 4.55 (s, 2 H), 1.42 (s, 3 H), 1.31–0.59 (m, 7 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 172.90, 167.73, 149.56, 132.98, 132.65, 131.26, 129.29, 129.10, 128.77, 128.38, 124.84, 124.29, 79.12, 55.95, 48.39, 26.48, 22.05, 21.81, 21.05, 20.39, 20.11, 13.36, 12.46, 8.40, 7.74, 6.84 ppm. EIMS $[M + Na]^+$ calcd. for $C_{16}H_{21}N_3O_4$: 342.1 found 350.3.

***N*-Isopropyl-*N*-[2-(methylamino)-1-(2-nitrophenyl)-2-oxoethyl]pentanamide (3u):** The compound was obtained as a white solid; m.p. 110–112 °C; yield 82 %. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.01–7.99 (d, J = 6.3 Hz, 1 H), 7.60–7.57 (t, J = 7.4 Hz, 2 H), 7.50–7.49 (d, J = 5.5 Hz, 1 H), 5.67 (s, 1 H), 5.21 (s, 1 H), 4.24 (s, 1 H), 2.71 (s, 3 H), 2.53–2.52 (d, J = 6.5 Hz, 1 H), 2.45–2.44 (d, J = 6.5 Hz, 1 H), 1.68–1.67 (d, J = 5.8 Hz, 2 H), 1.45–1.44 (d, J = 4.3 Hz, 3 H), 1.41 (s, 2 H), 0.96–0.95 (d, J = 4.3 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 174.37, 169.24, 149.41, 133.86, 132.20, 130.68, 129.44, 125.47, 57.27, 50.15, 34.27, 27.62, 27.23, 22.98, 21.77, 21.44, 14.33 ppm. EIMS $[M + Na]^+$ calcd. for $C_{17}H_{25}N_3O_4$: 358.2 found 358.3.

3-(4-fluorophenyl)-*N*-isopropyl-*N*-[2-(methylamino)-1-(2-nitrophenyl)-2-oxoethyl]propanamide (3v): The compound was obtained as a cream white solid; m.p. 67–69 °C; yield 85 %. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.02–8.00 (d, J = 7.0 Hz, 1 H), 7.56–6.99 (m, 8 H), 5.69 (s, 1 H), 5.19 (s, 1 H), 4.23–4.21 (m, 1 H), 3.03–3.00 (m, 2 H), 2.88–2.83 (m, 2 H), 2.76–2.72 (t, J = 7.3 Hz, 3 H), 1.42–1.41 (d, J = 6.0 Hz, 3 H), 0.91–0.90 (d, J = 6.0 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 172.80, 168.83, 162.44, 160.82, 149.15, 136.80, 133.62, 131.64, 130.42, 130.17, 130.12, 129.31, 125.29, 115.52, 115.38, 57.10, 49.95, 35.97, 30.42, 27.04, 21.49, 21.16 ppm. EIMS $[M + Na]^+$ calcd. for $C_{21}H_{24}N_3O_4$: 424.2 found 424.3.

4-Bromo-*N*-isopropyl-*N*-[2-(methylamino)-1-(2-nitrophenyl)-2-oxoethyl]benzamide (3w): The compound was obtained as a white solid; m.p. 176–178 °C; yield 89 %. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.03–7.34 (m, 8 H), 5.79 (s, 1 H), 5.38 (s, 1 H), 4.07 (s, 1 H), 2.77 (s, 3 H), 1.38 (s, 3 H), 0.91–0.90 (d, J = 4.1 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 171.82, 168.53, 149.20, 135.51, 133.84, 132.07, 130.47, 129.63, 127.95, 125.43, 124.43, 52.11, 31.73, 27.06, 21.56 ppm. EIMS $[M + Na]^+$ calcd. for $C_{19}H_{20}BrN_3O_4$:456.1 found 456.1 and 458.1.

2-(3,4-Difluorophenyl)-*N*-isopropyl-*N*-[2-(methylamino)-1-(2-nitrophenyl)-2-oxoethyl]acetamide (3 ×): The compound was obtained as a white solid; m.p. 137–139 °C; yield 89 %. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.01–8.00 (d, J = 7.5 Hz, 1 H), 7.57–7.50 (m, 3 H), 7.15 (s, 1 H), 7.04 (s, 1 H), 5.68 (s, 1 H), 5.15 (s, 1 H), 4.42 (s, 1 H), 3.86–3.83 (d, J = 15.3 Hz, 1 H), 3.80–3.77 (d, J = 15.3 Hz, 1 H), 2.71 (s, 3 H), 1.37–1.36 (d, J = 5.0 Hz, 3 H), 0.91–0.90 (d, J = 5.0 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 171.40, 168.60, 149.25, 133.90, 131.74, 130.42, 129.63, 125.52, 118.46, 118.36, 117.88, 117.78, 57.21, 50.91, 40.78, 27.19, 21.72, 21.12 ppm. EIMS $[M + Na]^+$ calcd. for $C_{20}H_{21}N_3O_4$: 428.1 found 428.2.

***N*-Isopropyl-*N*-[2-(methylamino)-1-(2-nitrophenyl)-2-oxoethyl]acrylamide (3y):** The compound was obtained as a white solid; m.p. 130–132 °C; yield 79 %. ^{1}H NMR (600 MHz, $CDCl_3$, 55 °C): δ = 8.01–8.00 (d, J = 7.6 Hz, 3 H), 7.70–7.58 (m, 3 H), 6.90–6.77 (m, 2 H), 6.90–5.68 (m, 3 H), 4.38–4.24 (m, 1 H), 2.58–2.57 (d, J = 3.7 Hz, 3 H), 7.21–7.18 (t, J = 7.3 Hz, 1 H), 7.13–7.10 (t, J = 7.4 Hz, 1 H), 7.06 (s, 1 H), 5.67 (s, 1 H), 5.24–5.23 (d, J = 4.3 Hz, 1 H), 1.38–1.37 (d, J = 6.6 Hz, 3 H), 0.69–0.95 (d, J = 6.6 Hz, 3 H) (rotamers) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 167.47, 166.34, 149.62, 132.65, 130.85, 129.61, 129.51, 128.56, 128.28, 127.64, 124.43, 56.00, 48.88, 26.49, 21.91, 21.04 ppm. EIMS $[M + Na]^+$ calcd. for $C_{15}H_{19}N_3O_4$: 328.1 found 328.3.

4-(1*H*-indol-3-yl)-*N*-isopropyl-*N*-[2-(methylamino)-1-(2-nitrophenyl)-2-oxoethyl]butanamide (3z): The compound was obtained as a yellow solid; m.p. 86–88 °C; yield 85 %. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.07–8.01 (m, 2 H), 7.63–7.59 (m, 3 H), 7.51–7.48 (m, 1 H), 7.38–7.37 (d, J = 8.1 Hz, 1 H), 7.21–7.18 (t, J = 7.3 Hz, 1 H), 7.13–7.10 (t, J = 7.4 Hz, 1 H), 7.06 (s, 1 H), 5.67 (s, 1 H), 5.24–5.23 (d, J = 4.3 Hz, 1 H), 4.14–4.10 (m, 1 H), 2.94–2.84 (m, 2 H), 2.61–2.47 (m, 2 H), 2.19–2.07 (m, 2 H), 1.37–1.36 (d, J = 6.5 Hz, 3 H), 0.89–0.88 (d, J = 6.5 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 174.03, 169.08, 149.17, 136.60, 133.73, 131.98, 130.55, 129.29, 127.65, 125.29, 122.15, 121.99, 119.38, 119.09, 115.74, 111.35, 57.13, 49.88, 33.56, 27.09, 25.44, 24.69, 21.52, 21.12. EIMS $[M + Na]^+$ calcd. for $C_{24}H_{28}N_4O_4$: 459.2 found 459.5.

***N*-Isopropyl-*N*-[2-(methylamino)-1-(2-nitrophenyl)-2-oxoethyl]-1-naphthalenecarboxamide (3aa):** The compound was obtained

as a light yellow solid; m.p. 108–110 °C; yield 80 %. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.43–8.42 (d, J = 7.7 Hz, 1 H), 8.26–8.24 (d, J = 8.2 Hz, 1 H), 8.10–8.08 (d, J = 7.9 Hz, 1 H), 7.91–7.84 (m, 3 H), 7.78–7.50 (m, 5 H), 7.44–7.43 (d, J = 6.8 Hz, 1 H), 5.89–5.81 (m, 1 H), 5.36–5.35 (m,1 H), 3.98–3.82 (m, 1 H), 2.85–2.83 (t, J = 4.8 Hz, 3 H),1.31–1.25 (dd, J = 6.5 Hz, 3 H), 0.82–0.80 (t, J = 6.6 Hz, 3 H) (rotamers) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 172.61 172.43, 168.72, 168.37, 149.45, 149.28, 134.64, 134.47, 134.32, 134.24, 133.72, 133.65, 132.71, 132.09, 131.43, 130.64, 130.07, 129.86, 129.80, 129.76, 129.43, 129.36, 128.99, 128.19, 127.69, 127.29, 127.08, 126.57, 125.94, 125.61, 125.59, 125.52, 125.03, 124.19, 124.19, 123.93, 122.60, 56.97, 56.36, 52.37, 52.05, 27.28, 21.98, 21.90, 21.10, 20.43 (rotamers) ppm. EIMS [M + Na]$^+$ calcd. for $C_{23}H_{23}N_3O_4$: 428.2 found 428.2.

***N*-Benzyl-*N*-[2-(methylamino)-1-(2-nitrophenyl)-2-oxoethyl]-pivalamide (3bb):** The compound was obtained as a yellow solid; m.p. 209–211 °C; yield 83 %. ^{1}H NMR (600 MHz, $CDCl_3$, 55 °C): δ = 7.58 (s, 1 H), 7.09 (s, 1 H), 6.15–6.14 (d, J = 1.2 Hz, 1 H), 6.134–6.132 (d, J = 1.2 Hz, 1 H), 5.64 (s, 1 H), 5.24 (m, 1 H), 4.23–4.19 (m, 1 H), 4.23–4.22 (d, J = 4.6 Hz, 3 H), 2.59–2.52 (m, 1 H), 2.49–2.43 (m, 1 H), 1.43–1.42 (d, J = 6.5 Hz, 3 H), 1.21–1.20 (t, J = 7.3 Hz, 3 H), 0.95–0.94 (d, J = 6.6 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 174.80, 169.01, 152.51, 147.99, 143.17, 129.87, 109.57, 106.22, 103.42, 57.37, 49.84, 27.54, 27.09, 21.58, 21.01, 9.52 ppm. EIMS [M + Na]$^+$ calcd. for $C_{21}H_{25}N_3O_4$: 406.2 found 406.3.

General Procedure for the Synthesis of Aniline Intermediates 2a–2bb: Into a mixture of product **3** (1 equiv.) in a 25 % water in ethanol (3.2 mL) solution was added iron powder (10 equiv.) and ammonium chloride (1 equiv.). The reaction mixture was allowed to stir at 60–70 °C for 1–2 hours. The reaction progress was monitored by TLC. Upon completion of the reaction the mixture was cooled to room temperature and subsequently filtered through a pad of Celite®. The filtrate was collected and evaporated under reduced pressure to obtain a crude mass. The material was then diluted with CH_2Cl_2 and the organic layer was washed with saturated $NaHCO_3$ solution (3 mL) followed by washing with a brine solution (5 mL). The organic layer was then dried with anhydrous Na_2SO_4 (1–2 g). Complete removal of solvent was carried out under reduced pressure and the reaction mixture was then purified using flash column chromatography (EtOAc/hexanes) to yield pure product **2**.

***N*-[1-(2-Aminophenyl)-2-(cyclopentylamino)-2-oxoethyl]-*N*-benzylpropionamide (2a):** The compound was obtained as a white solid; m.p. 128–130 °C; yield 90 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 8.07–8.06 (d, J = 5.3 Hz,1 H), 7.11–6.93 (m, 7 H), 6.64–6.63(d, J = 7.08Hz,1 H), 6.42 (s, 1 H), 6.26 (s, 1 H), 5.44 (s, 1 H), 5.04 (s, 2 H, D_2O exchangeable), 4.70–4.60 (dd, J = 17.34 Hz, 2 H),4.03–4.02 (d, J = 8.88 Hz, 2.25–2.22 (m, 1 H), 1.91–1.87 (m, 1 H), 1.58–1.28 (m, 6 H), 0.84(s, 3 H) (rotamers) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 175.23, 169.33, 147.46, 139.27, 128.92, 128.81, 127.98, 126.28, 125.88, 119.18, 115.98, 114.89, 55.89, 50.41, 48.68, 32.16, 31.66, 26.73, 23.45, 23.42, 9.27 ppm. EIMS [M + Na]$^+$ calcd. for $C_{23}H_{29}N_3O_2$: 402.2 found 402.3.

***N*-(1-(2-Aminophenyl)-2-[(2,6-dimethylphenyl)amino)-2-oxoethyl]-*N*-benzylpropionamide (2b):** The compound was obtained as a yellow solid; m.p. 118–120 °C; yield 85 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 9.48 (s, 1 H), 7.17–6.98 (m, 10 H), 6.70–6.68 (d, J = 7.7 Hz, 1 H), 6.49–6.41 (m, 2 H), 5.15 (s, 2 H, D_2O exchangeable), 4.71–4.68 (d, J = 17.8 Hz, 1 H), 4.60–4.57 (d, J = 17.8 Hz, 1 H), 2.33–2.29 (m, 1 H), 2.14 (s, 3 H), 2.00–1.96 (m, 1 H), 0.90–0.88 (t, J = 6.8 Hz, 1 H)(rotamers) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 175.02, 168.46, 147.20, 138.88, 135.18, 134.59, 129.68, 128.82, 127.55, 127.30, 126.11, 125.92, 118.29, 115.89, 115.30, 57.40, 48.09, 30.57, 26.42, 17.76, 8.96 ppm. EIMS [M + Na]$^+$ calcd. for $C_{25}H_{26}N_3O_4$: 423.2 found 423.5.

***N*-(1-(2-Aminophenyl)-2-(cyclohexylamino)-2-oxoethyl]-*N*-benzylpropionamide (2c):** The compound was obtained as a white solid; m.p. 132–134 °C; yield 87 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 7.98–7.96 (d, J = 7.3 Hz, 1 H), 7.11–6.92 (m, 7 H), 6.64–6.4 (m, 1 H), 6.42 (s, 1 H), 6.26 (s, 1 H), 5.03 (s, 2 H, D_2O exchangeable), 4.68–4.59 (dd, J = 17.52 Hz, 2 H), 3.33–2.119 (m, 1 H), 1.92–1.87 (m, 1 H), 1.71–1.69 (m, 1 H), 1.51–1.21 (m, 5 H), 1.191.00 (m, 5 H), 0.85–0.83 (t, J = 7.1 Hz, 3 H)(rotamers) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 175.24, 168.85, 147.28, 139.27, 128.99, 128.81, 127.98, 127.33, 126.28, 125.90, 119.20, 115.99, 114.88, 55.86, 48.69, 32.22, 32.05, 26.74, 25.17, 24.65, 24.51, 9.28 ppm. EIMS [M + Na]$^+$ calcd. for $C_{24}H_{31}N_3O_2$: 416.2 found 416.7.

***N*-[1-(2-Aminophenyl)-2-((4-methoxyphenyl)amino)-2-oxoethyl]-*N*-benzylpropionamide (2d):** The compound was obtained as a brown solid; m.p. 103–105 °C; yield 83 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO, 65 °C): δ = 9.88 (s, 1 H), 7.49–7.47 (d, J = 8.3 Hz, 2 H), 7.14–6.95 (m, 9 H), 6.68–6.67 (d, J = 7.0 Hz, 1 H), 6.47 (s, 1 H), 6.38 (s, 1 H), 4.96 (s, 2 H, D_2O exchangeable), 4.74–4.62 (m, 2 H), 2.38–2.32 (m, 1 H), 2.05 (s, 1 H), 0.93 (s, 3 H) (rotamers) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 175.49, 168.66, 155.22, 147.41, 139.14, 132.09, 129.14, 128.03, 126.37, 125.94, 120.72, 118.40, 116.21, 115.17, 113.85, 57.19, 55.16, 48.59, 26.79, 9.25 ppm. EIMS [M + Na]$^+$ calcd. for $C_{25}H_{27}N_3O_2$: 440.2 found 440.5.

***N*-[1-(2-Aminophenyl)-2-(*tert*-butylamino)-2-oxoethyl]-*N*-benzylpropionamide (2e):** The compound was obtained as an off-white solid; m.p. 98–100 °C; yield 85 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 7.73 (s, 1 H), 7.10–6.85 (m, 9 H), 6.64–6.62 (d, J = 7.5 Hz, 1 H), 6.44–6.43 (m, 1 H), 6.28 (s, 1 H), 5.01 (s, 2 H, D_2O exchangeable), 4.70–4.64 (m, 2 H), 2.24–2.20 (m, 1 H), 1.90–1.86 (m, 1 H), 1.23 (s, 9 H), 0.84–0.83 (d, J = 6.6 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 175.11, 169.50, 147.29, 139.38, 128.78, 128.68, 127.95, 127.30, 126.23, 125.87, 119.62, 115.94, 114.86, 55.77, 50.35, 48.71, 28.40, 26.73, 9.73 ppm. EIMS [M + Na]$^+$ calcd. for $C_{22}H_{29}N_3O_2$: 390.2 found 390.6.

***N*-[1-(2-Aminophenyl)-2-(isopropylamino)-2-oxoethyl]-*N*-benzylpropionamide (2f):** The compound was obtained as a white solid; m.p. 118–120 °C; yield 85 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 7.30–7.03 (m, 5 H), 6.81–6.80 (d, J = 6.7 Hz, 2 H), 6.64–6.63 (d, J = 7.9 Hz, 1 H), 6.57–6.52 (m, 2 H), 5.36–5.35 (d, J = 7.2 Hz, 1 H), 4.83–4.80 (d, J = 17.8 Hz, 1 H), 6.64–6.63 (d, J = 17.8 Hz, 1 H), 4.41 (s, 2 H, D_2O exchangeable), 4.16–4.12 (m, 1 H), 2.42–2.37 (m,1 H), 2.08–2.04 (m, 1 H), 1.13 (s, 3 H), 1.12–1.03 (m, 9 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 175.24, 168.85, 147.29, 139.25, 128.98, 128.83, 127.98, 126.29, 125.86, 119.13, 116.00, 114.89, 55.81, 54.94, 48.68, 40.54, 26.73, 22.16, 22.08, 9.27 ppm. EIMS [M + Na]$^+$ calcd. for $C_{21}H_{27}N_3O_2$: 376.2 found 376.6.

***N*-[1-(2-Aminophenyl)-2-oxo-2-(pentylamino)ethyl]-*N*-benzylpropionamide (2g):** The compound was obtained as a light yellow solid; m.p. 80–82 °C; yield 87 %; %. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 7.12–7.03 (m, 5 H), 6.81–6.80 (d, J = 6.7 Hz, 2 H), 6.64–6.6 (d, J = 7.9 Hz, 1 H), 6.57–6.53 (m, 2 H), 5.5 (s, 1 H), 4.83–4.80 (d, J = 17.8 Hz, 1 H), 4.69–4.67 (d, J = 17.8 Hz, 1 H), 4.41 (s, 2 H, D_2O exchangeable), 3.33–3.23 (m, 2 H), 2.43–2.38 (m, 1 H), 2.09–2.05 (m, 1 H), 1.56–1.29 (m, 2 H), 1.28–1.23 (m, 6 H), 1.05–1.03 (t, J = 7.3 Hz, 3 H), 0.89–0.84 (m, 4 H) (rotamers) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 175.72, 170.14, 147.77, 139.64, 129.67, 129.34, 129.25, 128.44, 127.72, 127.29, 126.76, 126.31, 119.45, 116.40, 115.37, 56.54, 49.09, 39.00, 29.01, 28.97, 28.90, 27.18, 22.25, 22.22, 14.39, 9.71 ppm. EIMS [M + Na]$^+$ calcd. for $C_{23}H_{31}N_3O_2$: 404.2 found 404.3.

2-(2-Aminophenyl)-2-[*N*-benzyl-2-(2-bromophenyl)acetamido]-*N*-methylacetamide (2h): The compound was obtained as a white solid; m.p. 194–196 °C; yield 97 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 8.01–8.00 (d, J = 4.5 Hz, 1 H), 7.52–7.50 (d, J = 7.6 Hz, 1 H), 7.29–7.05 (m, 8 H), 6.97–6.95 (t, J = 7.5 Hz, 2 H), 6.67–6.66 (d, J = 7.9 Hz, 1 H), 6.45–6.42 (t, J = 7.3 Hz, 1 H), 6.21 (s, 1 H), 5.06 (s, 2 H, D2O exchangeable), 4.83–4.80 (d, J = 17.9 Hz, 1 H), 4.74–4.71 (d, J = 17.9 Hz, 1 H), 3.82–3.79 (d, J = 16.8 Hz, 1 H), 3.39–3.36 (m, 1 H), 2.60–2.59 (d, J = 4.4 Hz, 3 H) (rotamers) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 173.34, 170.27, 135.42, 132.75, 131.76, 130.33, 130.27, 128.83, 128.66, 127.74, 127.18, 125.18, 57.40, 50.33, 42.10, 29.91, 26.63 (rotamers) ppm. EIMS [M + Na]$^+$ calcd. for $C_{24}H_{24}BrN_3O_2$: 488.1 found 488.3 and 490.3.

2-[2-Aminophenyl)-2-[2-(2-bromophenyl)-*N*-isopropylacetamido]-*N*-methylacetamide (2i): The compound was obtained as a white solid; m.p. 171–173 °C; yield 94 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO, 65 °C): δ = 7.58–7.57 (d, J = 7.9 Hz, 1 H), 7.37–7.04 (m, 5 H), 6.74–6.72 (d, J = 7.0 Hz, 1 H), 6.61–6.59 (t, J = 6.8 Hz, 1 H), 5.65 (s, 1 H), 4.75 (s, 2 H, D$_2$O exchangeable), 3.96–3.80 (m, 3 H), 2.62 (s, 3 H), 1.43 (s, 3 H), 0.91 (s, 3 H). ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 170.18, 169.96, 169.69, 169.01, 146.82, 136.48, 132.49,132.29, 132.08, 129.27, 128.56, 127.43, 124.68, 116.14, 115.96, 114.98, 56.62, 49.23, 48.15, 42.29, 41.95, 25.82, 21.85, 20.95, 19.92, 19.66 ppm. EIMS [M + Na]$^+$ calcd. for $C_{20}H_{24}BrN_3O_2$: 440.1 found 440.1 and 442.1.

***N*-[1-(2-Aminophenyl)-2-(methylamino)-2-oxoethyl]-*N*-isopropylpropionamide (2j):** The compound was obtained as a cream-white solid; m.p. 148–150 °C; yield 90 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO, 65 °C): δ = 7.51 (s, 1 H), 7.03–6.99 (m, 2 H), 6.71–6.70 (d, J = 6.84 Hz, 1 H), 6.57 (s, 1 H),7.70–5.66 (m, 1 H), 4.69 (s, 2 H, D$_2$O exchangeable), 3.79 (s, 1 H), 2.61 (s, 3 H), 2.43–2.22 (m, 2 H),1.38–1.37 (d, J = 6.18 Hz, 1 H), 1.05 (s, 3 H), 0.18(s, 3 H) (rotamers) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO, 65 °C): δ = 173.53, 169.76, 146.50, 128.81, 128.24, 119.89, 116.15, 115.61, 47.53, 27.40, 25.38, 20.45, 9.54 (rotamers) ppm. EIMS [M + Na]$^+$ calcd. for $C_{15}H_{23}N_3O_2$: 300.2 found 300.3.

***N*-[1-(2-Aminophenyl)-2-(methylamino)-2-oxoethyl]-*N*-cyclopropylpropionamide (2k):** The compound was obtained as a light-yellow solid; m.p. 160–162 °C; yield 89 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 7.79–7.78 (d, J = 3.6 Hz, 1 H), 7.02–7.00 (t, J = 7.3 Hz, 1 H), 6.91–6.90 (d, J = 7.5 Hz, 1 H), 6.69–6.67 (d, J = 7.9 Hz, 1 H), 6.57–6.54 (t, J = 7.3 Hz, 1 H), 5.77 (s, 1 H), 4.57 (s, 2 H, D$_2$O exchangeable), 2.60–2.59 (d, J = 4.6 Hz, 3 H), 2.57–2.53 (m, 2 H), 2.14–2.13 (m, 1 H), 1.04–1.01 (t, J = 7.3 Hz, 3 H), 0.61–0.59 (m, 2 H), 0.21–0.19 (m, 1 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 176.76, 170.53, 146.57, 130.19, 128.25, 119.70, 115.99, 114.93, 59.03, 27.40, 26.76, 25.80, 9.40, 8.59. EIMS [M + Na]$^+$ calcd. for $C_{15}H_{21}N_3O_2$: 298.2 found 298.3.

***N*-[1-(2-Aminophenyl)-2-(methylamino)-2-oxoethyl]-*N*-cyclopentylpropionamide (2l):** The compound was obtained as a light-yellow solid; m.p. 132–134 °C; yield 85 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO, 65 °C): δ = 7.53 (s, 1 H), 7.04–7.02 (t, J = 7.4 Hz, 1 H), 6.98–6.97 (d, J = 7.6 Hz, 1 H), 6.72–6.71 (d, J = 7.8 Hz, 1 H), 6.60–6.57 (t, J = 7.3 Hz, 1 H), 5.56 (s, 1 H), 4.62 (s, 2 H, D$_2$O exchangeable), 3.84 (s, 1 H), 2.64–2.63 (d, J = 4.3 Hz, 3 H), 2.44–2.33 (m, 1 H), 2.29–2.25 (m, 1 H), 1.91 (s, 1 H), 1.66–1.56 (m, 3 H), 1.37–1.20 (m, 2 H), 1.05–1.03 (m, 4 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO, 65 °C): δ = 173.18, 169.57, 146.39, 128.59, 128.16, 120.37, 116.24, 115.35, 57.51, 29.36, 27.13, 25.41, 24.10, 23.89, 9.44 ppm. EIMS [M + Na]$^+$ calcd. for $C_{17}H_{25}N_3O_2$: 326.2 found 326.3.

***N*-[1-(2-Aminophenyl)-2-(methylamino)-2-oxoethyl]-*N*-cyclohexylpropionamide (2m):** The compound was obtained as a cream-white solid; m.p. 174–176 °C; yield 85 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO, 65 °C): δ = 7.38 (s, 1 H), 7.03–7.01 (s, 2 H), 6.69–6.68 (d, J = 7.1 Hz, 1 H), 6.59–6.56 (t, J = 7.3 Hz, 1 H), (m, 2 H), 5.59 (s, 1 H), 4.68 (s, 2 H, D$_2$O exchangeable), 3.42 (s, 1 H), 2.61–2.60 (d, J = 4.5 Hz, 1 H), 2.46–2.2.09 (m, 3 H), 1.73–1.71 (m, 2 H), 1.47–0.82 (m, 10 H) (rotamers) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO, 65 °C): δ = 173.50, 169.64, 146.38, 128.73, 128.13, 120.23, 116.06, 115.23, 56.23, 30.56, 27.39, 25.98, 25.71, 25.46, 24.78, 9.64 (rotamers) ppm. EIMS [M + Na]$^+$ calcd. for $C_{18}H_{27}N_3O_2$: 340.2 found 340.4.

***N*-[1-(2-Aminophenyl)-2-(methylamino)-2-oxoethyl]-*N*-phenylpropionamide (2n):** The compound was obtained as an off-white solid; m.p. 170–172 °C; yield 91 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO, 65 °C): δ = 7.92 (s, 1 H), 7.09–6.54 (m, 4 H), 6.53–6.47 (m, 2 H), 6.22–6.19 (s, 1 H), 6.00 (s, 1 H), 4.87 (s, 2 H, D$_2$O exchangeable), 2.62 (s, 3 H), 2.03–1.82 (m, 2 H), 0.89–0.88 (d, J = 6.9 Hz, 3 H), (s, 3 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO, 65 °C): δ = 173.23, 170.68, 146.76, 139.69, 129.79, 128.40, 128.01, 127.42, 118.80, 115.84, 114.95, 59.01, 27.84, 25.75, 9.30 ppm. EIMS [M + Na]$^+$ calcd. for $C_{18}H_{21}N_3O_2$: 334.2 found 334.4.

***N*-[1-(2-Aminophenyl)-2-(methylamino)-2-oxoethyl]-*N*-methylbenzamide (2o):** The compound was obtained as a light yellow solid; m.p. 110–112 °C; yield 86 %; %. ^{1}H NMR (600 MHz, [D$_6$]DMSO, 65 °C): δ = 7.90 (s, 1 H), 7.44–7.40 (m, 5 H),7.08–7.06 (m, 2 H), 6.76–6.75 (d, J = 7.9 Hz, 1 H), 6.61–6.59 (t, J = 7.2 Hz, 1 H), 6.10 (s, 1 H), 4.94 (s, 2 H, D$_2$O exchangeable), 2.67–2.66 (d, 6 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 171.43, 169.39, 147.04, 136.32, 129.60, 129.41, 128.99, 128.39, 126.84, 118.26, 116.16, 115.12, 56.67, 34.60, 25.63 ppm. EIMS [M + Na]$^+$ calcd. for $C_{17}H_{19}N_3O_2$: 320.1 found 320.8.

***N*-[1-(2-Aminophenyl)-2-(methylamino)-2-oxoethyl]-*N*-ethylbenzamide (2p):** The compound was obtained as a white solid; m.p. 178–180 °C; yield 84 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 7.78 (s, 1 H), 7.46–7.38 (m, 5 H), 7.08–7.01 (m, 2 H), 6.74–6.72 (m, 1 H), 6.61–6.58 (m, 1 H), 6.01–5.87 (m, 1 H),4.83(s, 2 H, D$_2$O exchangeable), 3.28–3.27 (d, 2 H), 2.66–2.65 (d, J = 4.5 Hz, 3 H), 0.94 (s, 3 H) (rotamers) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 172.10, 170.06, 147.44, 137.19, 129.33, 129.19, 129.06, 128.37, 126.28, 118.56, 116.19, 114.92, 56.87, 41.14, 30.96, 25.69, 14.75 ppm. EIMS [M + Na]$^+$ calcd. for $C_{18}H_{21}N_3O_2$: 334.2 found 334.7.

2-(2-Aminophenyl)-2-[2-(2-bromophenyl)-*N*-propylacetamido]-*N*-methylacetamide (2q): The compound was obtained as a white solid; m.p. 145–147 °C; yield 92 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO, 65 °C): δ = 7.74 (s, 1 H), 7.59–7.58 (d, J = 6.3 Hz, 1 H), 7.37–7.33 (m, 2 H), 7.19 (s, 1 H), 7.07–7.02 (m, 2 H), 6.01 (s, 1 H), 4.72 (s, 2 H, D$_2$O exchangeable), 3.96–3.84 (m, 2 H), 3.31 (s, 2 H), 2.62 (s, 3 H), 1.43 (s, 1 H), 0.79 (s, 1 H), 0.54 (s, 3 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO, 65 °C): δ = 170.34, 169.69, 147.25, 136.19, 132.16, 132.13, 129.04, 128.98, 128.66, 127.54, 124.74, 119.08, 116.08, 114.72, 55.97, 47.39, 40.50, 25.64, 2.31, 11.21 ppm. EIMS [M + Na]$^+$ calcd. for $C_{15}H_{21}N_3O_2$: 440.1 found 440.1 and 442.1.

2-(2-Aminophenyl)-2-[2-(2-bromophenyl)-*N*-butylacetamido]-*N*-methylacetamide (2r): The compound was obtained as a cream white solid; m.p. 154–156 °C; yield 95 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 7.94–7.93 (d, J = 4.3 Hz, 1 H), 7.60–7.59 (d, J = 7.9 Hz, 1 H), 7.38–7.32 (m, 2 H), 7.22–7.19 (m, 1 H), 6.97–6.96 (d, J = 7.5 Hz, 1 H), 6.69–6.67 (d, J = 7.9 Hz, 1 H), 6.59–6.56 (m, 2 H, D$_2$O exchangeable), 3.97–3.94 (d, J = 16.5 Hz, 1 H), 3.82–3.79 (d, 16.5 Hz, 1 H), 2.60–2.59 (d, J = 4.3 Hz, 3 H), 1.44–1.42 (m, 1 H), 1.02–0.84 (m, 2 H), 0.64–0.61 (m, 1 H), 0.59–0.57 (t, J = 7.3 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 170.31, 170.00, 147.28, 136.16, 132.16, 132.12, 129.14, 128.94, 128.67, 127.54, 124.73, 119.03, 116.14, 114.71, 56.03, 45.039, 40.50, 30.90, 25.64, 19.54, 13.38 ppm. EIMS [M + Na]$^+$ calcd. for $C_{21}H_{26}BrN_3O_2$: 454.1 found 454.1 and 456.1.

***N*-[1-(2-Aminophenyl)-2-(methylamino)-2-oxoethyl]-*N*-isopropylbenzamide (2s):** The compound was obtained as a light-yellow solid; m.p. 198–200 °C; yield 92 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO, 65 °C): δ = 7.45–7.24 (m, 6 H), 7.06–7.04 (d, *J* = 7.1 Hz, 2 H), 6.73–6.72 (d, *J* = 7.9 Hz, 1 H), 6.63–6.60 (t, *J* = 7.5 Hz, 1 H), 5.17 (s, 1 H), 4.56 (s, 2 H, D$_2$O exchangeable), 2.63–2.62 (d, *J* = 4.6 Hz, 3 H), 1.38 (s, 3 H), 0.80–0.79 (d, *J* = 6.6 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 170.71, 169.65, 146.39, 137.96, 128.95, 128.84, 128.44, 128.05, 125.73, 119.96, 116.60, 115.60, 49.44, 25.49, 20.11, 19.91 ppm. EIMS [M + Na]$^+$ calcd. for $C_{19}H_{23}N_3O_2$: 348.2 found 348.3.

***N*-[1-(2-Aminophenyl)-2-(methylamino)-2-oxoethyl]-*N*-isopropylcyclopropanecarboxamide (2t):** The compound was obtained as a light-yellow solid; m.p. 149–151 °C; yield 86 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO, 65 °C): δ = 7.65 (s,1 H), 7.05–7.01 (m, 2 H), 6.70–6.68 (d, *J* = 7.3 Hz, 1 H), 6.59–6.58 (d, *J* = 6.4 Hz, 1 H), 5.96 (s, 1 H), 4.69 (s, 2 H, D$_2$O exchangeable), 3.91 (s, 1 H), 2.61 (s, 3 H), 1.83 (s, 1 H), 1.48 (s, 3 H), 0.88 (m, 1 H), 0.85–0.84 (d, *J* = 6.5 Hz, 3 H), 0.79–0.74 (m, 3 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO, 65 °C): δ = 173.24, 169.81, 146.59, 128.78, 128.32, 119.54, 115.96, 114.83, 57.22, 47.28, 25.29, 21.65, 21.37, 20.65, 13.24, 7.58, 7.40 ppm. EIMS [M + Na]$^+$ calcd. for $C_{16}H_{23}N_3O_2$: 312.2 found 312.3.

***N*-[1-(2-Aminophenyl)-2-(methylamino)-2-oxoethyl]-*N*-isopropylpentanamide (2u):** The compound was obtained as a yellow solid; m.p. 130–132 °C; yield 90 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO, 65 °C): δ = 7.50 (s, 1 H), 7.03–7.00 (m, 2 H), 6.71–6.71 (d, *J* = 6.6 Hz, 1 H), 6.59 (s, 1 H), 5.69 (s, 1 H), 4.69 (s, 2 H, D$_2$O exchangeable), 3.80 (s, 1 H), 2.61 (s, 3 H), 2.41–2.29 (m, 2 H), 1.55 (s, 2 H), 1.39–1.38 (d, *J* = 6.4 Hz, 3 H), 1.33–1.32 (d, *J* = 6.7 Hz, 2 H), 0.90–0.88 (d, *J* = 7.0 Hz, 3 H), 0.87–0.81 (d, *J* = 6.4 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO, 65 °C): δ = 172.84, 169.76, 146.48, 128.82, 128.25, 119.87, 116.11, 115.10, 47.58, 33.96, 27.13, 25.37, 21.58, 20.55, 13.43 ppm. EIMS [M + Na]$^+$ calcd. for $C_{17}H_{27}N_3O_2$: 328.2 found 328.4.

***N*-[1-(2-Aminophenyl)-2-(methylamino)-2-oxoethyl]-3-(4-fluorophenyl)-*N*-isopropylpropanamide (2v):** The compound was obtained as a light-yellow solid; m.p. 122–124 °C; yield 94 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO, 65 °C): δ = 7.29 (s, 1 H), 7.26 (s, 2 H), 7.07–7.04 (m, 4 H), 6.72–6.71 (d, *J* = 5.8 Hz, 3 H), 6.56 (s, 1 H), 5.63 (s, 1 H), 4.66 (s, 2 H, D$_2$O exchangeable), 2.89–2.88 (d, *J* = 5.9 Hz, 2 H), 2.74–2.71 (m, 1 H), 2.62–2.61 (m, 4 H), 1.37–1.36 (d, *J* = 6.5 Hz, 3 H), 0.79 (s, 3 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO @ 65 °C): δ = 171.83, 169.66, 161.22, 159.62, 146.45, 137.24, 129.78, 129.73, 128.85, 128.27, 119.76, 116.17, 115.20, 114.58, 114.44, 47.68, 40.05, 35.93, 29.96, 25.40 ppm. EIMS [M + Na]$^+$ calcd. for $C_{21}H_{26}FN_3O_2$: 394.2 found 494.6.

***N*-[1-(2-Aminophenyl)-2-(methylamino)-2-oxoethyl]-4-bromo-*N*-isopropylbenzamide (2w):** The compound was obtained as a light-yellow solid; m.p. 160–162 °C; yield 87 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO, 65 °C): δ = 7.65–7.63 (d, *J* = 8.3 Hz, 2 H), 7.29–7.28 (d, *J* = 8.2 Hz, 3 H), 7.06–7.04 (m, 2 H), 6.74–6.73 (d, *J* = 8.0 Hz, 1 H), 6.62–6.60 (t, *J* = 7.3 Hz, 1 H), 5.14 (s, 1 H), 4.54 (s, 2 H, D$_2$O exchangeable), 3.68 (s, 1 H), 2.63 (s, 3 H), 1.38 (s, 3 H), 0.80–079 (d, *J* = 6.0 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO, 65 °C): δ = 169.76, 169.41, 146.40, 137.08, 131.10, 128.64, 128.50, 127.91, 122.17, 119.85, 116.69, 115.73, 49.47, 40.04, 25.45. 19.98, 19.84 ppm. EIMS [M + Na]$^+$ calcd. for $C_{19}H_{22}BrN_3O_2$: 426.1 found 426.1 and 428.1.

2-(2-Aminophenyl)-2-[2-(3,4-difluorophenyl)-*N*-isopropylacetamido]-*N*-methylacetamide (2x): The compound was obtained as a cream-white solid; m.p. 100–102 °C, yield 87 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO, 65 °C): δ = 7.59 (s, 1 H), 7.34–7.27 (m, 3 H), 7.09–7.01 (m, 3 H), 6.73–6.71 (d, *J* = 7.9 Hz, 1 H), 6.60–6.57 (t, *J* = 7.3 Hz, 1 H), 5.58 (s, 1 H), 4.69 (s, 2 H, D$_2$O exchangeable), 3.80–3.77 (d, *J* = 15.5 Hz, 2 H), 3.72–3.70 (d, *J* = 13.7 Hz, 1 H), 2.62–2.61(d, *J* = 4.5 Hz, 3 H), 1.40–1.39 (d, *J* = 6.8 Hz, 3 H), 0.87–0.86 (d, *J* = 6.2 Hz, 1 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO, 65 °C): δ = 170.27, 169.50, 149.61146.48, 133.55, 128.91, 128.40, 125.78, 15.76, 125.74, 125.72, 119.62, 118.06, 117.95, 116.57, 11.46, 116.29, 115.38, 48.20, 25.43, 20.49 ppm. EIMS [M + Na]$^+$ calcd. for $C_{20}H_{23}F_2N_3O_2$: 398.2 found 398.3.

***N*-[1-(2-Aminophenyl)-2-(methylamino)-2-oxoethyl]-*N*-isopropylacrylamide (2y):** The compound was obtained as a light-yellow solid; m.p. 126–128 °C; yield 85 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO, 65 °C): δ = 7.69 (s, 1 H), 7.05–7.01 (m, 2 H), 6.70–6.58 (m, 3 H),6.16–6.13 (d, *J* = 16.0 Hz, 1 H), 5.93–5.91(d, *J* = 9.8 Hz,1 H), 5.68–5.66 (d, *J* = 8.5 Hz,1 H), 4.69 (s, 2 H, D$_2$O exchangeable), 3.85 (s, 1 H), 2.63–2.62 (s, *J* = 4.3 Hz, 3 H), 1.43–1.42 (s, *J* = 6.8 Hz, 3 H), 0.82–0.81 (s, *J* = 6.2 Hz, 3 H). ^{13}C NMR (150 MHz, [D$_6$]DMSO, 65 °C): δ = 169.58, 166.04, 146.58, 130.54, 128.84, 128.44, 126.29, 119.23, 116.08, 114.99, 47.79, 40.04, 25.31ppm. EIMS [M + Na]$^+$ calcd. for $C_{15}H_{21}N_3O_2$: 298.2 found 298.3.

***N*-[1-(2-Aminophenyl)-2-(methylamino)-2-oxoethyl]-4-(1*H*-indol-3-yl)-*N*-isopropylbutanamide (2z):** The compound was obtained as a yellow solid; m.p. 109–111 °C; yield 91 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO, 65 °C): δ = 10.59 (s, 1 H), 7.53–7.52 (d, *J* = 7.8 Hz, 1 H), 7.33–7.32 (d, *J* = 8.0 Hz, 1 H), 7.08–6.56 (m, 7 H), 5.72–5.62 (m, 1 H), 4.70 (s, 2 H, D$_2$O exchangeable), 3.79 (s, 1 H), 2.73 (s, 2 H), 2.61–2.60 (d, *J* = 4.3 Hz, 3 H), 1.86–1.85 (m, 2 H), 1.35–1.26 (m, 3 H), 0.88–0.76 (m, 3 H). ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 173.46, 169.90, 146.72, 136.29, 129.04, 128.58, 127.17, 122.33, 120.80, 118.37, 118.08, 116.01, 114.88, 111.30, 56.09, 47.64, 40.04, 34.37, 31.33, 26.62, 25.76, 24.29, 22.08, 21.08 ppm. EIMS [M + Na]$^+$ calcd. for $C_{24}H_{30}N_4O_2$: 429.2 found 429.3.

***N*-[1-(2-Aminophenyl)-2-(methylamino)-2-oxoethyl]-*N*-isopropyl-1-naphthalenecarboxamide (2aa):** The compound was obtained as a white solid; m.p. 110–112 °C; yield 85 %. ^{1}H NMR (600 MHz, CD_2Cl_2): δ = 8.07–8.06 (d, *J* = 5.3 Hz, 1 H), 7.11–6.93 (m, 9 H), 6.64–6.42 (m, 2 H), 6.26 (s, 1 H), 5.44–5.04 (m, 2 H), 4.70–4.60 (m, 2 H, D$_2$O exchangeable), 4.25–4.02 (m, 1 H), 2.25–2.21 (m, 1 H), 1.91–1.87 (m, 1 H), 1.76–1.28 (m, 8 H), 1.00–0.84 (m, 3 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 171.57, 171.48, 169.34, 169.19, 144.52, 135.50, 135.25, 133.62, 133.48, 130.07, 129.91, 129.44, 129.26, 129.08, 128.80, 128.72, 128.47, 128.05, 127.10, 127.04, 126.66, 126.44, 125.78, 125.30, 125.13, 124.79, 123.33, 122.59, 122.01, 119.60, 119.39, 117.43, 117.23, 57.62, 56.89, 51.97, 51.69, 26.66, 26.59, 22.71, 21.30, 21.16, 20.28, 13.94 ppm. EIMS [M + Na]$^+$ calcd. for $C_{23}H_{25}N_3O_2$: 398.2 found 398.4.

***N*-[1-(2-Aminophenyl)-2-(methylamino)-2-oxoethyl]-*N*-benzylpivalamide (2bb):** The compound was obtained as a light-brown solid; m.p. 113–115 °C; yield 90 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO, 65 °C): δ = 7.36–7.31 (m, 1 H), 6.57 (s, 1 H), 6.37 (s,1 H), 5.85–5.83 (d, *J* = 10.0 Hz, 2 H), 5.44 (s, 1 H), 4.46 (s, 2 H, D$_2$O exchangeable), 3.81 (s, 1 H), 2.601–2.60 (d, *J* = 4.1 Hz, 3 H), 2.45–2.27 (m, 2 H), 1.37–1.36 (d, *J* = 6.7 Hz, 3 H), 1.05–1.03 (t, *J* = 7.1 Hz, 3 H), 0.87–0.86 (d, *J* = 5.9 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO, 65 °C): δ = 173.25, 169.68, 147.09, 141.76, 138.44, 111.96, 108.29, 99.98, 97.13, 47.57, 40.04, 27.22, 25.47, 20.49, 9.47 ppm. EIMS [M + Na]$^+$ calcd. for $C_{21}H_{27}N_3O_2$: 344.3 found 344.5.

General Procedure for Synthesis of 3-Substituted 2-Indolinones 1h–1bb and 8a–8g: Compound **2** (100 mg, 1 equiv.) and 10 % TFA were taken up in dichloroethane (1 mL) in a Discovery® microwave reactor-based test-tube and subjected to microwave irradiation at 300 W, 10 bar pressure, 120 °C, for 10 minutes. After the allotted microwave time, the reaction was cooled to room temperature and

then diluted with CH_2Cl_2 (5 mL). Saturated $NaHCO_3$ (5 mL) was then slowly added while the test-tube sat on an ice bath. The organic layer was washed with a brine solution (5 mL) and dried with anhydrous Na_2SO_4. The contents were concentrated under reduced pressure and the mixture was then purified using flash column chromatography (CH_3OH/CH_2Cl_2) to yield pure compounds **1h–1bb** and **8a–8g**.

***N*-Benzyl-2-(2-bromophenyl)-*N*-(2-oxoindolin-3-yl)acetamide (1h):** The compound was obtained as a white solid; m.p. 194–196 °C; yield 90 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO, 52 °C): δ = 10.48–10.21 (m, 1 H), 7.60–6.72 (m, 13 H), 5.89–4.80 (m, 1 H), 4.34–4.10 (m, 2 H), 3.97–3.81 (m, 2 H) (rotamers) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 174.63, 174.53, 170.94, 142.30, 142.25, 137.49, 136.26, 135.66, 132.31, 132.22, 132.11, 131.98, 129.30, 128.75, 128.70, 127.75, 127.61, 127.44, 126.59, 125.37, 124.93, 124.54, 124.22, 121.58, 120.94, 110.01, 109.13, 60.13, 46.94 (rotamers) ppm. HRMS: EIMS [M + Na]$^+$ calcd. for $C_{23}H_{19}BrN_2O_2$: 457.0528 found 457.0549.

2-(2-Bromophenyl)-*N*-isopropyl-*N*-(2-oxoindolin-3-yl)acetamide (1i): The compound was obtained as a white solid; m.p. 196–198 °C; yield 90 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 10.23 (s, 1 H), 7.52–7.51 (d, J = 7.9 Hz, 1 H), 7.28–7.22 (m, 2 H), 7.15–7.10 (m, 2 H), 7.04–7.03 (d, J = 7.3 Hz, 1 H), 6.89–6.87 (t, J = 7.4 Hz, 1 H), 6.73–6.71 (d, J = 7.7 Hz, 1 H), 4.82 (s, 1 H), 4.32–4.30 (m, 1 H), 3.85–3.76 (q, J = 16.3 Hz, 2 H), 1.38–1.37 (d, J = 6.5 Hz, 3 H), 1.29–1.28 (d, J = 6.5 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 175.31, 167.09, 142.40, 135.67, 132.00, 131.43, 128.48, 127.95, 127.41, 127.28, 124.37, 122.21, 120.71, 54.76, 48.16, 40.00, 21.84, 21.12 ppm. HRMS: EIMS [M + Na]$^+$ calcd. for $C_{19}H_{19}N_2O_2Br$: 386.0630 found 386.0649.

***N*-Isopropyl-*N*-(2-oxoindolin-3-yl)propionamide (1j):** The compound was obtained as an off-white solid; m.p. 136–138 °C; yield 85 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 10.24 (s, 1 H), 7.12–7.10 (t, J = 7.62 Hz, 1 H), 6.98–6.97 (d, J = 7.32 Hz, 1 H), 6.85–6.84 (m, 1 H), 4.70 (s, 1 H), 4.22–4.20 (d, J = 12.5 Hz, 3 H), 2.33–2.31 (sep, 2 H), 1.34–1.33 (d, J = 6.6 Hz, 3 H), 1.24–1.23 (d, J = 6.5 Hz, 3 H), 0.86–0.84 (t, J = 7.4 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 175.78, 170.69, 142.55, 128.50, 127.48, 122.19, 120.88, 108.96, 54.72, 47.49, 25.76, 22.08, 21.28, 9.15 ppm. HRMS: EIMS [M + H]$^+$ calcd. for $C_{14}H_{19}N_2O_2$: 247.1447 found 247.1443.

***N*-Cyclopropyl-*N*-(2-oxoindolin-3-yl)propionamide (1k):** The compound was obtained as a white solid; m.p. 142–144 °C; yield 79 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO, 52 °C): δ = 10.25 (s, 1 H), 7.13–6.74 (m, 5 H), 4.71 (s, 1 H), 3.20–3.07 (m, 1 H), 2.68–2.2.48 (m, 2 H), 1.27–0.86 (m, 4 H), 0.84–0.82 (t, J = 9.0 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 175.26, 175.11, 142.18, 127.89, 122.21, 121.24, 109.07, 62.32, 39.93, 32.29, 26.39, 10.38, 8.76 ppm. HRMS: EIMS [M + Na]$^+$ calcd. for $C_{14}H_{16}N_2O_2$: 267.1109 found 267.1098.

***N*-Cyclopentyl-*N*-(2-oxoindolin-3-yl)propionamide (1l):** The compound was obtained as a white solid; m.p. 168–170 °C; yield 78 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 10.27 (s, 1 H), 70.14–7.12 (t, J = 5.0 Hz, 1 H), 6.97–6.96 (d, J = 7.2 Hz,1 H), 6.89–6.86 (t, J = 7.4 Hz, 1 H), 7.14–7.12 (t, J = 7.5 Hz, 1 H), 6.97–6.96 (d, J = 7.2 Hz,1 H), 6.89–6.86 (t, J = 7.4 Hz, 1 H), 6.76–6.75 (d, J = 7.6 Hz, 1 H), 4.71–4.70 (d, J = 8.3 Hz,1 H), 4.42–4.36 (m, 1 H), 2.41–2.32 (m, 2 H), 2.10–2.08 (t, J = 3.6 Hz, 1 H), 1.94–1.91 (t, J = 8.5 Hz, 1 H),1.70–1.56 (m, 6 H), 0.88–0.86 (t, J = 7.4 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 175.67, 171.15, 142.51, 128.33, 127.57, 121.99, 120.89, 109.00, 57.74, 55.63, 30.92, 29.51, 25.85, 23.67, 23.41, 9.21 ppm. HRMS: EIMS [M + H]$^+$ calcd. for $C_{16}H_{20}N_2O_2$: 273.1603 found 273.1611.

***N*-Cyclohexyl-*N*-(2-oxoindolin-3-yl)propionamide (1m):** The compound was obtained as a white solid; m.p. 140–142 °C; yield 79 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 10.22 (s, 1 H), 7.13–7.11 (t, J = 7.6 Hz, 1 H), 6.98–6.97 (d, J = 7.3 Hz, 1 H), 6.87–6.84 (dd, J = 7.0 Hz, 1 H), 6.74–6.73 (d, J = 7.7 Hz, 1 H), 4.73 (s, 1 H), 3.76–3.71 (m, 1 H), 2.38–2.30 (m, 2 H), 1.98–1.97 (d, J = 11.52 Hz, 1 H), 1.83–1.36 (m, 8 H), 1.13–1.08 (m, 1 H), 0.87–0.85 (t, J = 7.4 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 175.67, 170.84, 142.45, 128.51, 127.44, 122.14, 120.82, 108.92, 55.60, 55.55, 32.15, 31.42, 25.81, 25.44, 25.25, 24.57, 9.13 ppm. HRMS: EIMS [M + Na]$^+$ calcd. for $C_{17}H_{22}N_2O_2$: 309.1579 found 309.1589.

***N*-(2-Oxoindolin-3-yl)-*N*-phenylpropionamide (1n):** The compound was obtained as a yellow solid; m.p. 65–69 °C; yield 82 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 10.29 (s, 1 H), 7.39–7.32 (m, 7 H), 7.127–7.14 (t, J = 7.6 Hz, 1 H), 6.96–6.94 (t, J = 7.5 Hz, 1 H), 6.73–6.72 (d, J = 7.1 Hz, 1 H), 2.05 (m, 2 H), 0.96–0.92 (t, J = 6.7 Hz, 2 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 174.07, 142.09, 129.08, 128.53, 128.15, 127.77, 121.08, 109.23, 26.51, 8.92 ppm. HRMS: EIMS [M + H]$^+$ calcd. for $C_{17}H_{16}N_2O_2$: 281.1285 found 281.1273.

***N*-Methyl-*N*-(2-oxoindolin-3-yl)benzamide (1o):** The compound was obtained as a creamy-white solid; m.p. 142–144 °C; yield 80 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 10.70–10.61 (m, 1 H), 7.60–7.26 (m, 7 H), 7.04–7.01 (dd, J = 7.3 Hz, 1 H), 6.86–6.85 (d, J = 5.9 Hz, 1 H), 5.26 (s, 1 H), 2.76–2.56 (m, 3 H) (rotamers) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): 174.36, 174.27, 171.78, 142.88, 142.32, 135.40, 135.20, 129.96, 129.83, 129.67, 128.93, 128.69, 128.49, 127.10, 124.38, 124.11, 123.85, 122.12, 121.79, 110.26, 109.77, 61.82, 28.91(rotamers) ppm. HRMS: EIMS [M + Na]$^+$ calcd. for $C_{16}H_{14}N_2O_2$: 289.0953 found 289.0941.

***N*-Ethyl-*N*-(2-oxoindolin-3-yl)benzamide (1p):** The compound was obtained as a yellow solid; m.p. 121–123 °C; yield 78 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO, 67 °C): δ = 10.32 (s, 1 H), 7.45–7.21 (m, 7 H), 6.98 (s, 1 H), 6.84–6.83 (d, J = 6.7 Hz, 1 H), 5.22 (s, 1 H), 3.35 (m, 2 H), 1.09 (s, 3 H) (rotamers) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 174.98, 174.73, 142.48, 135.80, 129.67, 128.67, 128.54, 126.98, 126.37, 121.97, 121.30, 110.25, 109.32, 61.91, 14.86, 13.67 (rotamers) ppm. HRMS: EIMS [M + Na]$^+$ calcd. for $C_{17}H_{16}N_2O_2$: 303.1109 found 303.1116.

2-(2-Bromophenyl)-*N*-(2-oxoindolin-3-yl)-*N*-propylacetamide (1q): The compound was obtained as a misty rose solid; m.p. 141–143 °C; yield 80 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO, 52 °C): δ = 10.60–10.22 (m, 1 H), 7.60–6.76 (m, 8 H), 5.76–4.81 (m, 1 H), 4.17–3.86 (m, 2 H), 3.50–3.38 (m, 2 H), 1.69–1.09 (m, 2 H), 0.94–0.61 (m, 3 H) (rotamers) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO @ 32 °C): δ = 174.60, 174.38, 142.09, 135.49, 131.86, 131.40, 128.30, 127.14, 124.16, 122.61, 120.83, 109.04, 64.52, 59.93, 22.34, 10.64 (rotamers) ppm. HRMS: EIMS [M + Na]$^+$ calcd. for $C_{19}H_{19}BrN_2O_2$: 409.0528 found 409.0547.

***N*-Butyl-*N*-(2-oxoindolin-3-yl)-2-phenylacetamide (1r):** The compound was obtained as a light pink solid; m.p. 108–110 °C; yield 79 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO, 65 °C): δ = 10.54–10.18 (m, 1 H), 7.61–7.20 (m, 1 H), 7.17–7.04 (m, 6 H), 6.93–6.77 (m, 2 H), 5.73–4.92 (m, 1 H), 4.17–3.83 (m, 2 H), 3.50 (s, 2 H), 1.64–0.82 (m, 4 H), 0.66 (s, 3 H) (rotamers) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 174.82, 170.35, 142.28, 135.79, 132.13, 131.78, 128.67, 127.47, 125.03, 124.50, 122.40, 121.94, 120.98, 110.53, 109.58, 31.52, 30.19, 29.90, 19.57, 19.32, 13.67, 13.13 (rotamers) ppm. HRMS: EIMS [M + Na]$^+$ calcd. for $C_{20}H_{21}N_2O_3Br$: 423.0684 found 247.1447.

***N*-Isopropyl-*N*-(2-oxoindolin-3-yl)benzamide (1s):** The compound was obtained as a white solid; m.p. 238–240 °C; yield 81 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 10.37 (s,1 H), 7.45–7.43 (t, J = 2.8 Hz, 3 H), 7.30–7.29 (dd, J = 2.4 Hz, 2 H), 7.19–7.15 (dd, J = 7.9 Hz, 2 H), 6.94–6.92 (t, J = 7.4 Hz, 1 H), 6.79–6.78 (d, J = 7.6 Hz, 1 H),

7.45–7.43 (t, *J* = 2.8 Hz, H), 7.30–7.29 (q, *J* = 2.4 Hz, 2 H), 7.19–7.15 (q, *J* = 7.9 Hz, 2 H), 6.94–6.92 (t, *J* = 7.4 Hz, 1 H), 6.79–6.78 (d, *J* = 7.6 Hz, 1 H),4.95(s,1 H), 3.96–3.94 (t, *J* = 6.0 Hz, 1 H), 1.36–1.35 (d, *J* = 6.6 Hz, 3 H), 1.21–1.20 (d, *J* = 6.5 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): *δ* = 175.37, 168.72, 142.74, 136.20, 129.45, 128.62, 127.94, 127.81, 125.97, 122.35, 121.12, 109.10, 54.65, 50.02, 21.58, 21.20 ppm. HRMS: EIMS [M + Na]$^+$ calcd. for $C_{18}H_{18}N_2O_2$: 317.1266 found 317.1279.

N-Isopropyl-N-(2-oxoindolin-3-yl)cyclopropanecarboxamide (1t): The compound was obtained as a cream white solid; m.p. 76–78 °C, yield 80 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO): *δ* = 10.20 (s, 1 H), 7.12–7.10 (t, *J* = 7.6 Hz, 1 H), 7.00–6.99 (d, *J* = 7.3 Hz, 1 H), 6.87–6.85 (t, *J* = 7.4 Hz, 1 H), 6.73–6.72 (d, *J* = 7.7 Hz, 1 H), 4.75 (s, 1 H), 4.67–4.62 (m, 1 H), 2.00–1.96 (m, 1 H), 1.40–1.39 (d, *J* = 6.5 Hz, 3 H), 1.31–1.30 (d, *J* = 6.5 Hz, 3 H), 0.72–0.60 (m, 2 H), 0.54–0.53 (m, 2 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): *δ* = 175.66, 170.33, 142.50, 128.50, 127.46, 122.12, 120.88, 108.94, 55.01, 47.49, 22.27, 21.52, 10.89, 6.94, 6.57 ppm. HRMS: EIMS [M + Na]$^+$ calcd. for $C_{19}H_{19}N_2O_3$: 258.1390 found 258.1368.

N-Isopropyl-N-(2-oxoindolin-3-yl)pentanamide (1u): The compound was obtained as a yellow solid; m.p. 59–61 °C; yield 82 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO): *δ* = 10.24 (s, 1 H), 7.13–7.10 (t, *J* = 7.9 Hz, 1 H), 6.98–6.96 (d, *J* = 7.3 Hz, 1 H), 6.87–6.85 (t, *J* = 7.4 Hz, 1 H), 6.74–6.73 (d, *J* = 7.6 Hz, 1 H), 4.70 (s, 1 H), 4.25–4.23 (m, 1 H), 2.31–2.27 (m, 2 H), 1.35–1.33 (d, *J* = 6.2 Hz, 5 H), 1.25–1.24 (d, *J* = 6.4 Hz, 3 H), 1.22–0.90 (m, 6 H), 0.83–0.80 (t, *J* = 7.3 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): *δ* = 175.65, 169.97, 142.41, 128.40, 127.34, 121.98, 120.74, 108.85, 54.61, 47.57, 32.10, 26.74, 22.02, 21.58, 21.23, 13.72 ppm. HRMS: EIMS [M + H]$^+$ calcd. for $C_{16}H_{23}N_2O_2$: 275.1760 found 275.1767.

3-(4-Fluorophenyl)-N-isopropyl-N-(2-oxoindolin-3-yl)propanamide (1v): The compound was obtained as a white solid; m.p. 166–168 °C; yield 85 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO): *δ* = 10.28 (s, 1 H), 7.22–7.20 (m, 2 H), 7.14–7.12 (t, *J* = 7.6 Hz, 1 H), 7.07–7.04 (t, *J* = 8.9 Hz, 2 H), 6.97–6.96 (d, *J* = 7.3 Hz, 1 H), 6.90–6.87 (t, *J* = 7.4 Hz, 1 H), 6.76–6.75 (d, *J* = 7.7 Hz, 1 H), 4.73 (s, 1 H), 4.26–4.21 (m, 1 H), 2.68–2.57 (m, 4 H), 1.30–1.29 (d, *J* = 6.5 Hz, 3 H), 1.23–1.22 (d, *J* = 6.5 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): *δ* = 175.69, 169.31, 161.47, 159.87, 142.54, 137.31, 137.29, 130.22, 130.16, 128.33, 127.51, 122.27, 120.84, 114.87, 114.74, 108.97, 54.77, 47.65, 34.20, 29.70, 22.00, 21.26 ppm. ^{19}F NMR (188 MHz, CDCl$_3$): *δ* = –117.58 (s, 1F) ppm. HRMS: EIMS [M + Na]$^+$ calcd. for $C_{20}H_{21}FN_2O_2$: 363.1485 found 363.1498.

4-Bromo-N-isopropyl-N-(2-oxoindolin-3-yl)benzamide (1w): The compound was obtained as a cream white solid; m.p. 218–220 °C; yield 87 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO): *δ* = 10.39 (s, 1 H), 7.65–7.64 (d, *J* = 8.3 Hz, 2 H), 7.27–7.26 (d, *J* = 8.3 Hz, 2 H), 7.19–7.15 (q, *J* = 7.0 Hz, 2 H), 6.94–6.91 (t, *J* = 7.4 Hz, 1 H), 6.79–6.78 (d, *J* = 7.6 Hz, 1 H), 4.97 (s, 1 H), 3.93–3.89 (m, 1 H), 1.36–1.35 (d, *J* = 6.6 Hz, 3 H), 1.21–1.20 (d, *J* = 6.5 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): *δ* = 175.23, 167.77, 142.72, 135.26, 131.68, 128.23, 127.74, 122.81, 122.39, 121.14, 109.12, 54.70, 50.18, 21.52, 21.16 ppm. HRMS: EIMS [M + Na]$^+$ calcd. for $C_{18}H_{17}BrN_2O_2$: 395.0371 found 395.0353.

2-(3,4-Difluorophenyl)-N-isopropyl-N-(2-oxoindolin-3-yl)acetamide (1x): The compound was obtained as a white solid; m.p. 178–180 °C; yield 87 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO): *δ* = 10.27 (s, 1 H),7.36–7.31 (m, 1 H), 7.18–7.11 (m, 2 H), 6.99–6.95 (m, 2 H), 6.89–6.86 (t, *J* = 7.2 Hz, 1 H), 6.75–6.74 (d, *J* = 7.7 Hz, 1 H), 4.77 (s, 1 H), 4.28–4.23 (m, 1 H), 3.76–3.70 (q, *J* = 15.8 Hz, 2 H), 1.26–1.25 (d, *J* = 6.5 Hz, 3 H), 1.17–1.16 (d, *J* = 6.5 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): *δ* = 175.52, 167.89, 142.57, 128.08, 127.62, 125.79, 125.77, 125.73, 122.13, 120.92, 117.94, 117.82, 117.14, 117.03, 109.07, 54.86, 38.56, 21.91, 21.09 ppm. ^{19}F NMR (188 MHz, CDCl$_3$): *δ* = –137.50 to –137.71 (m, 1F), –140.47 to –140.64 (m, 1F) ppm. HRMS: EIMS [M + Na]$^+$ calcd. for $C_{19}H_{18}N_2O_2F_2$: 367.1234 found 367.1245.

N-Isopropyl-N-(2-oxoindolin-3-yl)acrylamide (1y): The compound was obtained as a light-yellow solid; m.p. 144–146 °C; yield 79 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO): *δ* = 10.32 (s, 1 H), 7.16–7.13 (t, *J* = 7.6 Hz, 1 H), 7.02–7.01 (d, *J* = 7.2 Hz, 1 H), 6.89–6.88 (t, *J* = 7.4 Hz, 1 H), 6.83–6.76 (m, 2 H), 5.96–5.92 (dd, *J* = 2.0 Hz, 1 H), 5.65–5.63 (dd, *J* = 2.0 Hz, 1 H), 4.48 (s, 1 H), 4.46–4.41 (m, 1 H), 1.38–1.37 (d, *J* = 6.5 Hz, 3 H), 1.28–1.27 (d, *J* = 6.5 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): *δ* = 175.44, 163.78, 142.61, 128.29, 127.65, 127.62, 122.27, 120.94, 109.02, 54.99, 47.92, 22.13, 21.49 ppm. HRMS: EIMS [M + Na]$^+$ calcd. for $C_{14}H_{17}N_2O_2$: 245.1290 found 245.1301.

4-(1H-Indol-3-yl)-N-isopropyl-N-(2-oxoindolin-3-yl)butanamide (1z): The compound was obtained as a light-yellow solid; m.p. 138–140 °C; yield 86 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO): *δ* = 10.74 (s, 1 H), 10.26 (s, 1 H), 7.45–7.44 (d, *J* = 7.9 Hz, 1 H), 7.30–7.29 (d, *J* = 8.0 Hz, 1 H), 7.13–7.10 (t, *J* = 7.7 Hz, 1 H), 7.05–6.99 (m, 3 H), 6.94–6.92 (t, *J* = 7.1 Hz, 1 H), 6.87–6.85 (t, *J* = 7.4 Hz, 1 H), 6.75–6.74 (d, *J* = 7.6 Hz, 1 H), 4.71 (s, 1 H), 4.18–4.14 (m, 1 H), 2.63–2.60 (t, *J* = 7.4 Hz, 2 H), 2.38–2.33 (m, 1 H), 1.30–1.29 (d, *J* = 6.5 Hz, 3 H), 1.23–1.21 (dd, *J* = 6.5 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): 175.79, 170.07, 142.53, 136.25, 128.57, 127.47, 122.29, 122.14, 120.85, 120.80, 118.06, 114.08, 111.30, 108.98, 54.74, 47.66, 32.09, 25.61, 23.90, 22.08, 21.25 ppm. HRMS: EIMS [M + Na]$^+$ calcd. for $C_{20}H_{21}N_2O_2$: 363.1485 found 363.1501.

N-Isopropyl-N-(2-oxoindolin-3-yl)-1-naphthalenecarboxamide (1aa): The compound was obtained as an off-white solid; m.p. 284–286 °C; yield 87 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO): *δ* = 10.50 (s, 1 H), 8.03–7.97 (m, 3 H), 7.60–7.53 (m, 3 H), 7.36–7.20 (m, 3 H), 7.09–6.99 (m, 1 H), 9.88–6.85 (t, *J* = 9.8 Hz, 1 H), 5.11–5.10 (d, *J* = 9.6 Hz, 1 H), 3.73–3.62 (m, 1 H), 1.32–1.23 (dd, *J* = 6.6 Hz, 3 H), 1.21–1.13 (dd, *J* = 6.6 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): *δ* = 175.73, 168.19, 142.71, 133.99, 133.05, 129.42, 128.68, 128.22, 127.98, 127.88, 126.80, 126.65, 125.35, 124.88, 122.44, 122.38, 121.28. 109.31, 54.83, 50.16, 21.64, 21.06 (rotomers) ppm. HRMS: EIMS [M + Na]$^+$ calcd. for $C_{22}H_{20}N_2O_2$: 367.1422 found 367.1440.

N-Benzyl-N-(2-oxoindolin-3-yl)pivalamide (1bb): The compound was obtained as a yellow solid; m.p. 106–108 °C; yield 83 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO): *δ* = 10.08 (s, 1 H), 6.59 (s, 1 H), 6.41 (s, 1 H), 5.90–5.89 (q, *J* = 0.8 Hz, 2 H), 4.60 (s, 1 H), 4.21–4.17 (m, 1 H), 2.38–2.26 (m, 2 H), 1.32–1.31 (d, *J* = 6.6 Hz, 3 H), 1.23–1.22 (d, *J* = 6.5 Hz, 3 H), 0.88–0.86 (t, *J* = 7.4 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): *δ* = 175.08, 170.70, 146.23, 141.59, 136.68, 120.04, 104.20, 104.18, 100.46, 92.75, 92.73, 54.89, 47.50, 47.47, 25.80, 21.97, 21.32, 9.16 ppm. HRMS: EIMS [M + Na]$^+$ calcd. for $C_{15}H_{18}N_2O_4$: 3313.1159 found 313.1170.

3-Benzyl-N-cyclopentyl-2-ethyl-3,4-dihydroquinazoline-4-carboxamide (8a): The compound was obtained as a white solid; m.p. 122–124 °C, yield 61 %. ^{1}H NMR (600 MHz, CDCl$_3$): *δ* = 7.31–6.96 (m, 9 H), 5.55–5.54 (d, *J* = 6.00 Hz, 1 H), 4.97–4.94 (d, *J* = 16.2 Hz, 1 H), 4.78 (s, 1 H), 4.50–4.48 (d, *J* = 16.2 Hz, 1 H), 4.08–4.06 (m, 1 H), 2.64–2.61 (q,1 H), 2.53–2.49 (m, 1 H), 1.89–1.83 (m, 2 H) 1.52–1.50 (m, 4 H), 1.32–1.29 (t, *J* = 7.2 Hz, 3 H), 1.25–1.15 (m, 2 H) ppm. ^{13}C NMR (150 MHz, CDCl$_3$): *δ* = 169.97, 160.23, 142.55, 135.96, 129.45, 128.98, 128.64, 128.20, 127.86, 126.80, 125.73, 124.91, 124.38, 120.19, 62.01, 60.02, 53.25, 51.35, 33.08, 32.82, 28.25, 23.57,

23.54, 23.47, 11.63 ppm. HRMS (EIMS) calcd. for $C_{23}H_{28}N_3O[M + H]^+$: 362.2232, found 362.2222.

3-Benzyl-*N*-(2,6-dimethylphenyl)-2-ethyl-3,4-dihydroquinazoline-4-carboxamide (8b): The compound was obtained as a pale yellow solid; m.p. 91–93 °C; yield 79 %. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.37–7.01 (m, 12 H), 6.91 (s, 1 H), 5.10–5.08 (d, J = 16.2 Hz, 1 H), 5.02 (s, 1 H), 4.71–4.68 (d, J = 16.2 Hz, 1 H), 2.70–2.64 (m, 1 H), 2.60–2.54 (m, 1 H), 2.01 (s, 6 H), 1.35–1.33 (t, J = 7.5 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 169.10, 160.39, 141.92,135.94, 135.06, 132.91, 129.389, 129.07, 128.24, 127.96, 127.56, 126.93, 125.81, 125.05, 124.81, 120.24, 62.19, 53.29, 28.36, 18.08, 11.68 ppm. HRMS (EIMS) calcd. for $C_{26}H_{28}N_3O[M + H]^+$: 398.2232, found 398.2243.

3-Benzyl-*N*-cyclohexyl-2-ethyl-3,4-dihydroquinazoline-4-carboxamide (8c): The compound was obtained as an off-white solid; m.p. 159–161 °C; yield 81 %. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.32 (t, 2 H),7.26 (m, 3 H), 7.22–7.19 (m,4 H), 7.03–6.99 (m, 2 H), 5.52 (s, 1 H), 4.99 (d, J = 16.0 Hz, 1 H), 4.80–4.79 (d, J = 4.38 Hz, 1 H), 4.52–4.49 (d, J = 16.0 Hz, 1 H), 3.68 (s, 1 H), 2.64–2.52 (m, 2 H), 1.80–1.72 (m, 2 H),1.62–1.55(m, 6 H),1.33–1.32 (m, 6 H), 1.12–0.98 (m,3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 169.65, 160.20, 141.72, 136.11, 129.49, 129.05, 127.92, 126.89, 125.81, 124.92, 124.57, 120.38, 62.17, 53.24, 48.34, 32.88, 32.61, 28.43, 25.41, 24.59, 24.54, 11.74 ppm. HRMS (EIMS) calcd. for $C_{24}H_{30}N_3O$ [M + H]$^+$: 376.2398, found 376.2401.

3-Benzyl-2-ethyl-*N*-(4-methoxyphenyl)-3,4-dihydroquinazoline-4-carboxamide (8d): The compound was obtained as a brown solid; m.p. 187–189 °C; yield 78 %. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.35–7.23 (m, 9 H), 7.09–7.08 (t, J = 5.94Hz, 2 H), 6.82–6.81 (dd, 2 H),5.05–5.02 (d, J = 16.2 Hz, 1 H), 4.96 (s, 1 H), 4.62–4.60 (d, J = 16.2 Hz, 1 H), 3.77 (s, 3 H), 2.72–2.66 (m, 1 H), 2.61–2.55 (m, 1 H), 1.38–1.35 (t, J = 7.62 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 168.71, 160.46, 157.12, 136.23, 130.47, 129.99, 129.29, 128.20, 126.06, 125.38, 125.13, 121.93, 114.47, 63.10, 55.74, 53.73, 28.50, 11.84 ppm. HRMS (EIMS) calcd. for $C_{25}H_{26}N_3O_2$ [M + H]$^+$: 400.2025, found 400.2038.

3-Benzyl-*N*-(*tert*-butyl)-2-ethyl-3,4-dihydroquinazoline-4-carboxamide (8e): The compound was obtained as a yellow solid; m.p. 150–152 °C; yield 78 %. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 7.70 (s,1 H), 7.36–7.35 (d, J = 6.9 Hz,2 H), 7.29–7.28 (d, J = 5.5 Hz, 1 H), 7.25–7.24 (d, J = 6.9 Hz, 2 H),7.10–7.08 (t, J = 8.1 Hz, 2 H), 4.92–4.89 (d, J = 16.5 Hz, 1 H), 4.86 (s, 1 H), 3.91–3.88 (d, J = 16.2 Hz, 1 H), 2.37–2.34 (q, 1 H),1.18 (s, 9 H), 1.12–1.10 (t, 3 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 169.26, 159.42, 137.24, 128.69, 128.10, 127.34, 126.70, 125.15, 123.51, 121.57, 61.44, 51.43, 50.27, 28.27, 26.75, 11.05 ppm. HRMS (EIMS) calcd. for $C_{25}H_{26}N_3O_2$ [M + H]$^+$: 350.2232, found 350.2254.

3-Benzyl-2-ethyl-*N*-isopropyl-3,4-dihydroquinazoline-4-carboxamide (8f): The compound was obtained as an off-white solid; m.p. 120–122 °C; yield 73 %. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.79–7.78 (d, J = 5.5 Hz, 1 H), 7.38–7.11 (m, 6 H), 6.91–6.90 (d, J = 5.4 Hz, 2 H), 4.93–4.90 (d, J = 16.6 Hz, 1 H), 4.85 (s, 1 H), 4.00–3.98 (d, J = 16.3 Hz, 1 H), 3.84–3.74 (m, 1 H), 2.60–2.53 (m, 1 H), 2.42–2.38 (m, 1 H), 1.17–1.15 (t, J = 7.0 Hz, 3 H), 1.07–1.06 (d, J = 5.5 Hz, 3 H), 0.96–0.95 (t, J = 5.5 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 169.66, 160.64, 136.04, 129.73, 129.24, 128.15, 127.06, 125.96, 125.25, 124.44, 120.25, 62.29, 53.46, 41.97, 29.92, 22.78, 22.57, 11.86 ppm. HRMS (EIMS) calcd. for $C_{21}H_{26}N_3O$ [M + H]$^+$: 336.2076, found 336.2081.

3-Benzyl-2-ethyl-*N*-pentyl-3,4-dihydroquinazoline-4-carboxamide (8g): The compound was obtained as a colorless syrup; Yield 83 %. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.38–7.22 (m, 8 H), 7.08–7.06 (t, J = 7.50 Hz, 1 H), 5.26 (s, 1 H), 4.98–4.96 (d, J = 19.1 Hz, 1 H), 4.54–4.52 (d, J = 16.1 Hz, 1 H), 3.24–3.11 (m, 2 H), 2.80–2.77 (q, 2 H), 1.44–1.39 (m, 2 H), 1.38–1.36 (t, J = 7.5 Hz, 3 H), 1.25–1.14 (m, 4 H), 0.83–0.81 (t, J = 7.14 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 169.01, 162.61, 134.35, 129.90, 129.43, 128.69, 127.31, 126.42, 121.35, 119.23, 62.27, 53.95, 39.99, 29.91, 29.12, 29.09, 26.82, 22.41, 14.17, 11.74 ppm. HRMS (EIMS) calcd. for $C_{23}H_{30}N_3O$ [M + H]$^+$: 382.2495, found 382.2495.

3-Benzyl-2-(2-bromobenzyl)-*N*-methyl-3,4-dihydroquinazoline-4-carboxamide (8h): The compound was obtained as a brown solid; m.p. 98–100 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.11–8.10 (d, J = 4.6 Hz, 8 H), 7.81–7.80 (dd, J = 1.2 Hz, 1 H), 7.61–7.59 (dd, J = 1.0 Hz, 1 H), 7.38–7.10 (m, 11 H), 4.90 (s, 1 H), 4.65–4.62 (d, J = 16.56 Hz, 1 H), 3.94–3.91 (d, J = 16.4 Hz, 2 H), 3.84–3.81 (d, J = 16.6 Hz, 1 H), 2.59–2.58 (d, J = 4.6 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.80, 156.95, 135.91, 135.56, 133.51, 129.80, 129.57, 129.57, 129.51, 128.15, 128.04, 127.25, 126.46, 125.71, 124.92, 124.75, 120.32, 61.86, 53.85, 41.65, 29.92, 26.49 ppm. HRMS (EIMS) calcd. for $C_{24}H_{24}BrN_3O$ [M + H]$^+$: 448.1025, found 448.1030.

***N*-(2-[1-(Benzylamino)-2-(cyclopentylamino)-2-oxoethyl]phenyl)propionamide (9a):** The compound was obtained as a white solid; m.p. 116–118 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 10.27 (s,1 H), 8.07–8.06 (d, J = 8.4 Hz,1 H), 7.36–7.09 (m, 9 H), 5.32 (s, 1 H), 4.27 (s, 1 H), 4.07–4.05 (m, 1 H), 3.75–3.73 (d, J = 13.2 Hz, 1 H), 3.62–3.60 (d, J = 13.2 Hz, 1 H), 2.38–2.34 (q, 2 H), 1.87–1.58 (m, 2 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 172.45, 171.03,170.95, 138.71, 137.55, 137.42, 129.23, 128.73, 128.65, 128.20, 127.45, 127.03, 124.25, 123.79, 123.73, 64.03, 60.04, 60.02, 51.62, 51.62, 51.30, 51.17, 32.99, 32.96, 32.52, 32.49, 30.90, 30.86, 29.68, 23.47, 9.79 ppm. HRMS: EIMS [M + H]$^+$ calcd. for $C_{23}H_{30}N_3O_2$: 380.2338, found 380.2345.

2-(Benzylamino)-2-{2-[2-(2-bromophenyl)acetamido]phenyl}-*N*-methylacetamide (9h): The compound was obtained as a light brown solid; m.p. 99–101 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 10.54 (s, 1 H), 7.90–7.89 (d, J = 4.4 Hz, 1 H), 7.83–7.82 (d, J = 8.0 Hz, 1 H), 7.60–7.58 (d, J = 7.8 Hz, 1 H), 7.42–7.40 (d, J = 6.78 Hz, 1 H), 7.34–7.19 (m, 10 H), 7.11–7.08 (t, J = 7.44 Hz, 1 H), 4.32 (s, 1 H), 3.757–753 (d, J = 2.0 Hz, 2 H), 3.53 (s, 2 H), 3.05 (s, 1 H), 2.60–2.59 (d, J = 4.6 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.64, 156.80,135.40, 133.35, 129.65, 129.41, 128.99, 127.99, 127.88, 127.09, 126.30, 125.55, 124.76, 124.59, 61.71, 53.70, 41.49, 29.76, 26.33 ppm. HRMS: EIMS [M + H]$^+$ calcd. for $C_{24}H_{25}BrN_3O_2$: 466.1130, found 466.1154.

Supporting Information (see footnote on the first page of this article): ^{1}H and ^{13}C NMR spectra for all new compounds and X-ray crystallography data for **1h**.

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