JOC The Journal of Organic Chemistry

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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.9b02127 • Publication Date (Web): 19 Nov 2019

Just Accepted

is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

BF_3·OEt_2 Catalyzed Vinyl Azides Addition to *in situ* Generated *N*-Acyl Iminium Salts: Synthesis of 3-Oxoisoindoline-1-acetamides

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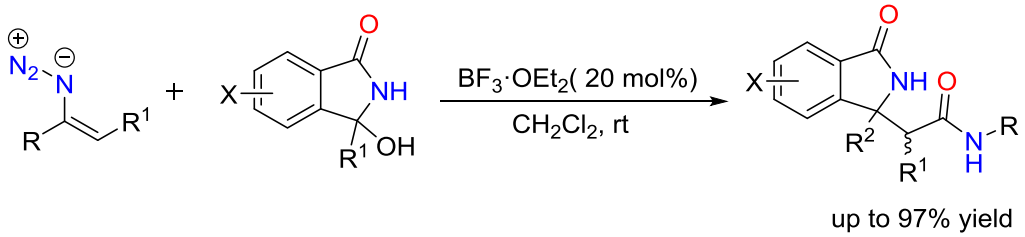


Abstract

BF_3·OEt_2 catalyzed nucleophilic addition of vinyl azide towards *in situ* generated *N*-acyl iminium salts obtained from 3-hydroxyisoindolinones has been described in this manuscript. The procedure is operationally simple, mild, additive and metal free. The reaction proceeds smoothly at ambient temperature with a wide range of 3-hydroxyisoindol-1-ones and vinyl azides, to afford 3-oxoisoindoline-1-acetamides (32 examples) in high yields (up to 97%). Furthermore, the synthetic utility of this methodology has been depicted by exploiting the reactivity of an amide functionality in the products.

Introduction

The amide functionality is omnipresent in many modern pharmaceuticals and biologically active compounds.[1] It has also been found that small organic molecules containing methylene amide linkages exist in numerous bio-active compounds, chemical probes and drug leads.[2] Significant properties of amides, such as high polarity, stability and conformational diversity, make them of

great importance in contemporary chemistry. Amide functional group can serve as an important surrogate for the synthesis of various nitrogen-containing heterocycles.[3] Thus, installation of the amide functionality into organic molecule is highly desirable.[4]

On the other hand, isoindolinones have been found as key structural unit present in many naturally or synthetically useful bio-active compounds as shown in Figure 1.[5] In particular, 3-substituted isoindolinones bearing methylene amide linkage have received considerable attention since they represent the core unit of a broad range of medicinally important compounds.[6] For examples, JM-1232[6a] (sedative and hypnotic drug) and Pazinaclone[6b] (sedative and anxiolytic drug) consist of the similar core in their structures. Therefore, the synthesis of 3-substituted isoindolinones bearing methylene amide linkage is interesting in the context of drug discovery. Towards this, our group has already developed a number of novel and efficient methodologies for the synthesis of 3-substituted isoindolinones.[6c-f]

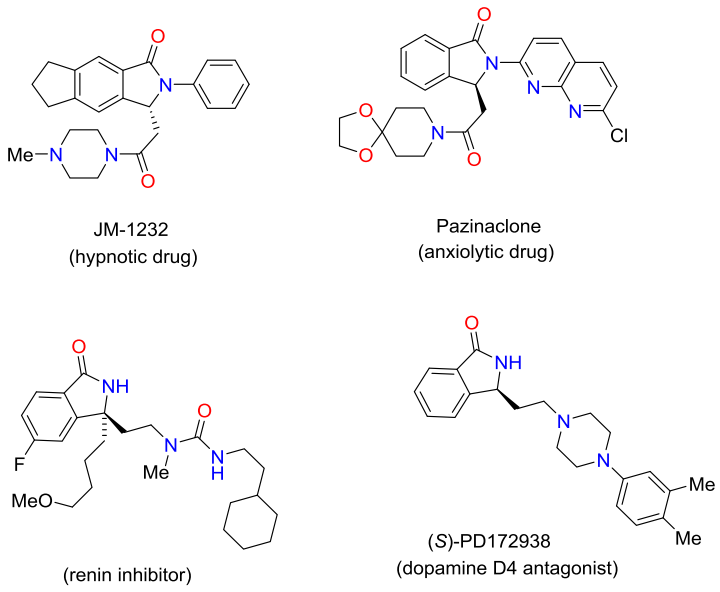
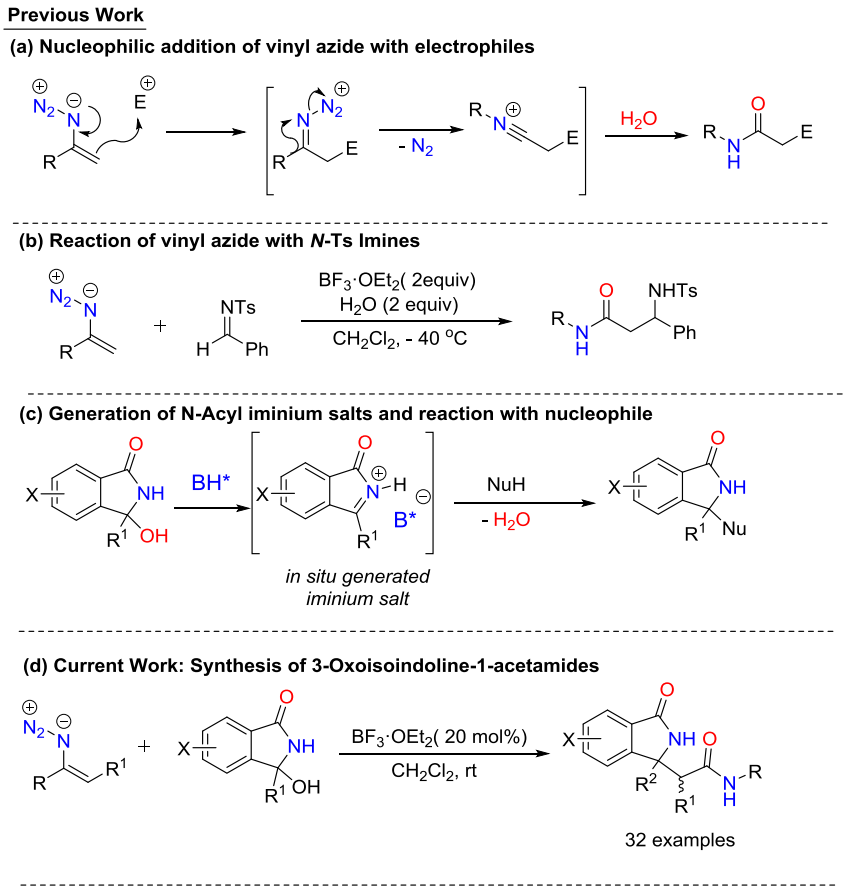


Figure 1. Some biologically active isoindolinone derivatives.

Amide moiety could be installed in organic molecules by nucleophilic addition of amide enolates to appropriate carbon electrophiles *via* carbon-carbon bond formation.[7] In recent times, vinyl azides have attracted a great deal of interest among synthetic chemists for being used as an alternative to amide enolates.[8] Vinyl azides display similar nucleophilic reactivity like enamines.[8] These have been successfully employed as nucleophiles with a variety of electrophiles such as

aldehydes, imines, and carbocations obtained from alcohols to provide amides (Scheme **1a** and **1b**).[9] Cui's group has reported nucleophilic addition reaction of vinyl azides with *p*-quinone methides (p-QMs) to furnish amides and nitriles.[10] Later on, this strategy was applied for the reaction of glycols with vinyl azides to access α-C-glycosyl amides.[11] These reports reveal that these can serve as good amide precursors under various reaction conditions.

3-Aryl-3-hydroxyisoindolinones can be readily dehydrated to generate cyclic *N*-acyl iminium salts in the presence of Brønsted acids (Scheme 1c).[12] This reactive *N*-acyl iminium salt intermediate has been successfully used in various asymmetric reactions such as arylation,[13] annulation reactions,[14] hydrogenolysis,[15] hydrophosphonylation,[16] nucleophilic addition of *N*-tert-butyl hydrazones,[17] indoles,[18] thiols[19] and alcohols.[20] Very recently our group has used this substrate for enantioselective Mannich-type reaction of α-diazo esters catalyzed by chiral Brønsted acid.[21] Inspired by these aforementioned strategies, we envisaged that under Lewis acid activation, i*n situ* generated *N*-acyl iminium salts resulting from 3-aryl-3-hydroxyisoindolinone might act as an electrophile which can be trapped by vinyl azide. This would provide 3-oxoisoindoline tethered imino diazonium ion intermediate, which might further undergo a Schmidt-type 1,2-migration to furnish nitrilium ion intermediate. Finally, hydrolysis of this intermediate will generate 3-oxoisoindoline-1-acetamide derivative bearing methylene amide linkages. Herein, we have reported a $BF_3{\cdot}OEt_2$ catalyzed reaction of vinyl azides with a variety of 3-hydroxyisoindolinones for the synthesis of 3-oxoisoindoline-1-acetamides comprising of a quaternary carbon center as shown in Scheme **1d**.



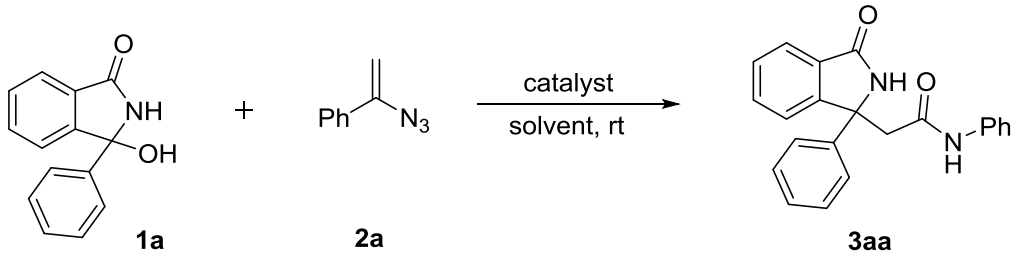
Scheme 1. Synthesis of Amide Functionality by Nucleophilic Addition of Vinyl Azides

Result and discussion

To determine the optimized conditions, a model reaction was carried out using 3-hydroxy-3-phenylisoindolin-1-one (**1a**) and (1-azidovinyl)benzene (**2a**) in the presence of 20 mol % of $Cu(OTf)_2$ in dichloromethane at room temperature. Delightfully, the desired product 2-(3-oxo-1-phenylisoindolin-1-yl)-*N*-phenylacetamide (**3aa)** was obtained in 46% yield (entry 1, Table 1). Encouraged by this initial result, efforts were given to further improve the yield of **3aa**. A series of Lewis acid catalysts such as $(CuOTf)_2{\cdot}C_6H_6$, $Sc(OTf)_3$, $InCl_3$, $In(OTf)_3$ were investigated in our reaction (entries 2-5, Table 1). Among all, $In(OTf)_3$ was found to be effective catalyst providing the desired product **3aa** in 69% yield. To our delight, when the reaction was conducted by employing $BF_3{\cdot}OEt_2$ as a catalyst, the reaction proceeded well, affording the desired product **3aa** in an excellent level of yield (92%, Table 1, entry 6) in a shorter reaction time (3 h). Brønsted acid catalysts such as CF_3CO_2H, CF_3SO_3H and *p*-toluenesulfonic acid monohydrate (*p*-$TsOH{\cdot}H_2O$) also afforded the isoindolinone derivative **3aa** in moderate to good yields (up to

74% yield). Notably, it was found that there was no product formation in the absence of catalyst even after 3 days and only the starting materials were recovered (Table 1, entry 10). Subsequently, the effect of solvents on the product formation was screened (Table 1, entries 6 and 11-15). It was observed that dichloromethane was the best solvent to furnish the desired product **3aa** in excellent yields (Table 1, entry 6). In contrast, comparatively lower yields were obtained when the reaction was performed in other solvents such as acetonitrile and toluene (Table 1, entries 13-14). THF turned out to be ineffective as a solvent for this reaction, and only a trace amount of **3aa** was observed (Table 1, entry 15). Afterward, the effect of catalyst loading was investigated. It was found that decreasing the amount of $BF_3{\cdot}OEt_2$ from 20 mol % to 10 mol % showed little impact on the outcome of the reaction (Table 1, entry 16) whereas increasing the amount of catalyst loading to 50 mol % gave 3-oxoisoindoline-1-acetamides product in lower yield (78% yield, Table 1, entry 17). This drop in the yield of the product was attributed to the fact that phenyl vinyl azide (**2a**) was decomposed to acetanilide (isolated as a by-product), when higher concentration of $BF_3{\cdot}OEt_2$ was used. Extensive optimization of the reaction conditions revealed that 20 mol % of $BF_3{\cdot}OEt_2$ as catalyst and CH_2Cl_2 as a solvent were optimal for the addition reaction of vinyl azides to 3-aryl-3-hydroxyisoindolinones at ambient temperature.

Table 1. Optimization of the reaction conditions[a]



1a **2a** **3aa**

entry	catalyst	amount (equiv.)	solvent	time (h)	yield[b](%)
1	$Cu(OTf)_2$	0.2	CH_2Cl_2	12	46
2	$(CuOTf)_2.C_6H_6$	0.2	CH_2Cl_2	12	40
3	$Sc(OTf)_3$	0.2	CH_2Cl_2	12	33
4	$InCl_3$	0.2	CH_2Cl_2	12	64
5	$In(OTf)_3$	0.2	CH_2Cl_2	12	69
6	**$BF_3{\cdot}OEt_2$**	**0.2**	**CH_2Cl_2**	**3**	**92**

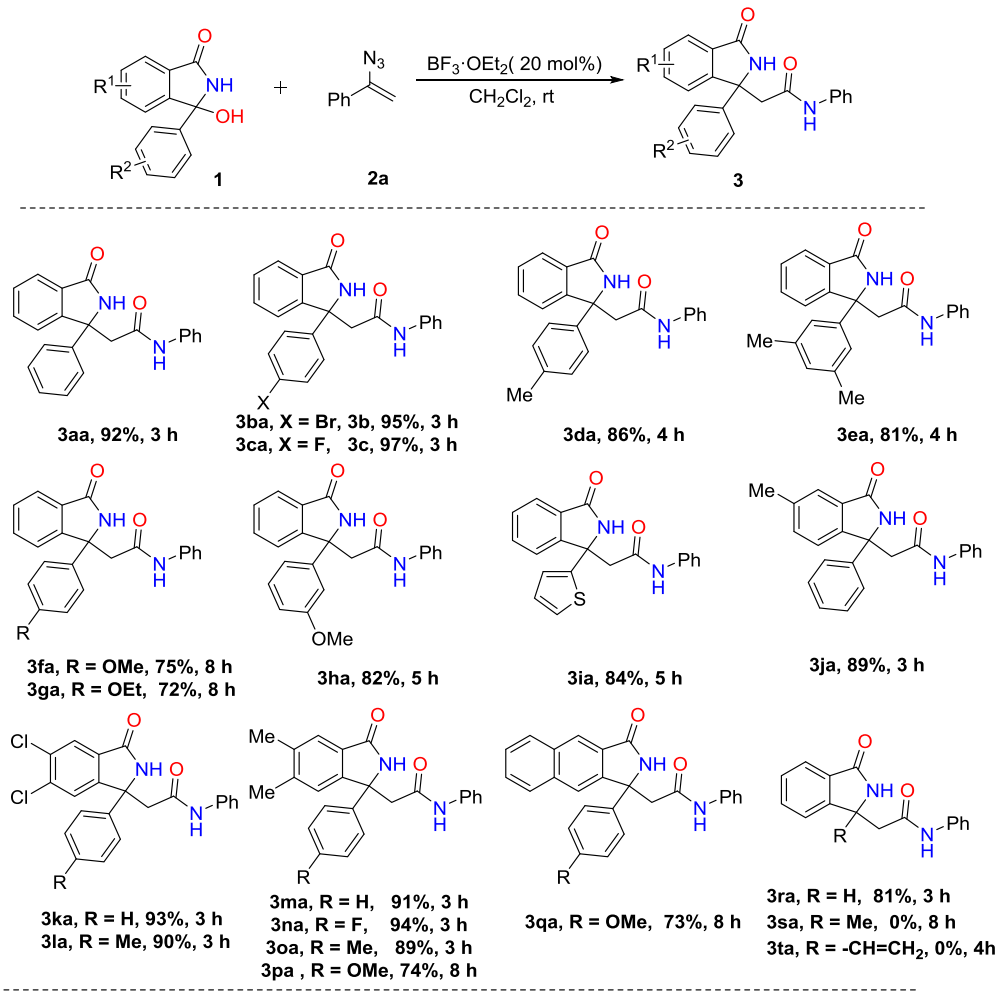
7	CF_3CO_2H	0.2	CH_2Cl_2	12	66
8	CF_3SO_3H	0.2	CH_2Cl_2	12	74
9	*p*-TsOH, H_2O	0.2	CH_2Cl_2	12	38
10	none	-	CH_2Cl_2	72	n.r
11	$BF_3{\cdot}OEt_2$	0.2	DCE	3	81
12	$BF_3{\cdot}OEt_2$	0.2	$CHCl_3$	3	76
13	$BF_3{\cdot}OEt_2$	0.2	CH_3CN	12	52
14	$BF_3{\cdot}OEt_2$	0.2	toluene	12	32
15	$BF_3{\cdot}OEt_2$	0.2	THF	24	Trace
16	$BF_3{\cdot}OEt_2$	0.1	CH_2Cl_2	3	89
17	$BF_3{\cdot}OEt_2$	0.5	CH_2Cl_2	3	78

[a]In all cases, reactions were performed using **1a** (1.0 equiv , 0.20 mmol, 45.0 mg) and vinyl azide **2a** (1.1 equiv , 0.22 mmol, 32.0 mg) in 2.0 mL of CH_2Cl_2 at room temperature. [b]Isolated yield, n.r = no reaction.

Having identified the optimal reaction conditions for this transformation, the substrate scope and reaction limitations were explored. At first, a variety of differently substituted 3-aryl 3-hydroxyisoindolinones were screened with the reaction of (1-azidovinyl)benzene (**2a**), affording an array of functionalized 3-oxoisoindoline-1-acetamides in good to excellent level of yields. The results are summarized in Table 2. Substrates (**1b** and **1c**) bearing halogen as a substituent on the *para*-position of the aromatic ring at the C-3 position of 3-aryl-3-hydroxyisoindolinones smoothly reacted to afford the corresponding 3-oxoisoindoline-1-acetamide (**3ba** and **3ca**) with 95% and 97% yields, respectively. Substrates (**1d-1h**) having electron rich alkyl or alkoxy group as substituent on the aromatic ring at C-3 position reacted well and furnished products **3da-3ha** in good yields (up to 86%). Noticeably, 3-hydoxy-isoindolinones having electron donating substituents on the 3-aryl ring took comparably a longer reaction time for completion of the reaction and also gave lower yield than 3-hydoxy-isoindolines bearing electron withdrawing substituents on the 3-aryl ring (**3da-ha** *vs*. **3ba-ca**). Substrate **1i** containing a heteroaryl moiety (thiophene) at C-3 position, affording the desired product **3ia** in 84% yield. Isoindolinones with different substituents on the phthalimide aromatic ring were also examined. The reaction of 3-hydroxy-isoindolinone derivative **1j** with vinyl azide (**2a**) provided 3-oxoisoindoline-1-acetamide **3ja** in 89% yield (Table 2). Phthalimide aromatic moiety bearing a 5,6-dimethyl or 5,6-dichloro substituents were compatible under the present reaction conditions and furnished

products **3ka**-**3pa** in good yields. In addition, substrates **1q** tethered with a naphthyl ring took a longer time for completion of the reaction to afford the corresponding product **3qa** in 73% yield. The protocol was successful in producing 3-oxoisoindoline-1-acetamide **3ra** in 81% yield when 3-hydroxyisoindolin-1-one **1r** was used.

Table 2. Scope of various 3-hydroxy-3-arylisoindolinones for the synthesis of 3-oxoisoindoline-1-acetamides[a,b]



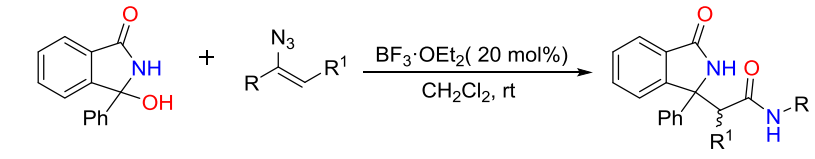
[a]In all cases, reactions were performed using **1** (1.0 equiv, 0.20 mmol), vinyl azide **2** (1.1 equiv, 0.22 mmol) and $BF_3{\cdot}Et_2O$ (0.20 equiv, 0.04 mmol) in 2 mL of CH_2Cl_2 at room temperature. [b]Isolated yield

However, 3-hydroxyisoindolinone **1s** and **1t** bearing a methyl and vinyl group respectively at the C-3 position failed to give the desired 3-oxoisoindoline-1-acetamide **3sa** and **3ta** under the current protocol. The reaction of 3-hydroxy-2,3-diphenylisoindolin-1-one **1u** with vinyl azide **2a** did not proceed at all under standard conditions. This control experiment clearly suggests that the

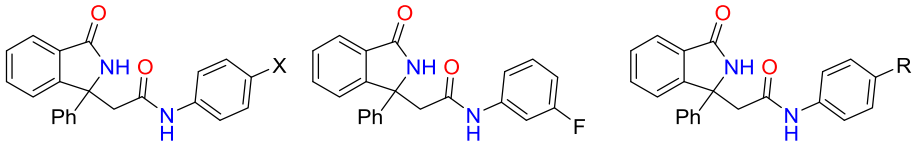
free NH group in 3-hydroxy isoindolinones is essential for the present transformation. An X-ray crystal structure analysis of compound **3ba** (CCDC No. 1919472) unambiguously confirmed the proposed structure (please see SI for more details).

Subsequently, the substrate generality of this reaction was further explored by the reaction of 3-hydroxy-3-phenylisoindolin-1-one (**1a**) with a broad range of vinyl azides (**2b-n**) under optimized conditions. A variety of vinyl azides having functionalized aromatic ring as substituents were tested, affording corresponding 3-oxoisoindoline-1-acetamides derivative **3ab-am** in synthetically viable yields (67% - 94% yields).

Table 3. Scope of various vinyl azides for the synthesis of 3-Oxoisoindoline-1-acetamides[a,b]



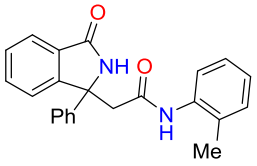
1a **2b-n** **3**



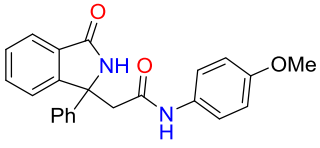
3ab, X = Cl, 90%, 3 h
3ac, X = F, 88%, 3 h

3ad, 91%, 3 h

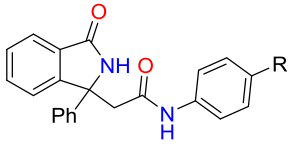
3ae, R = Me, 94%, 3 h
3af, R = ^{t}Bu, 89%, 3 h



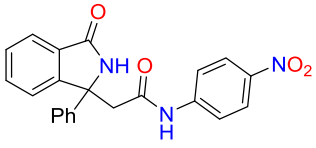
3ag, 67%, 5 h



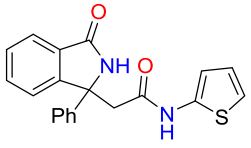
3ah, 90%, 3 h



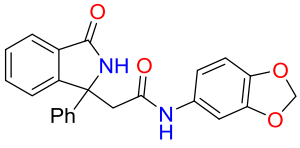
3ai, R = CN, 76%, 8 h
3aj, R = CF_3, 74%, 8 h



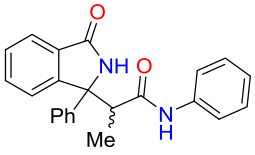
3ak, 71%, 8 h



3al, 81%, 3 h



3am, 90%, 3 h



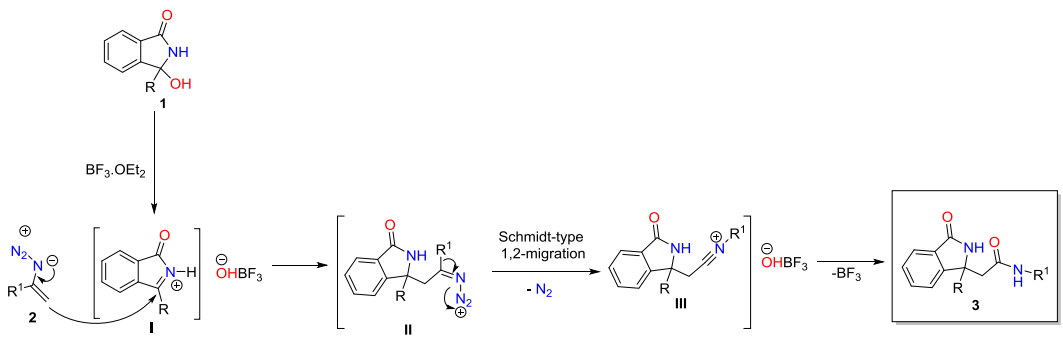
(1:1)

3an, 88%, 3 h

[a]In all cases, reactions were performed using **1** (1.0 equiv, 0.20 mmol), vinyl azide **2** (1.1 equiv, 0.22 mmol) and $BF_3{\cdot}Et_2O$ (0.20 equiv, 0.04 mmol) in 2 mL of CH_2Cl_2 at room temperature. [b]Isolated yield

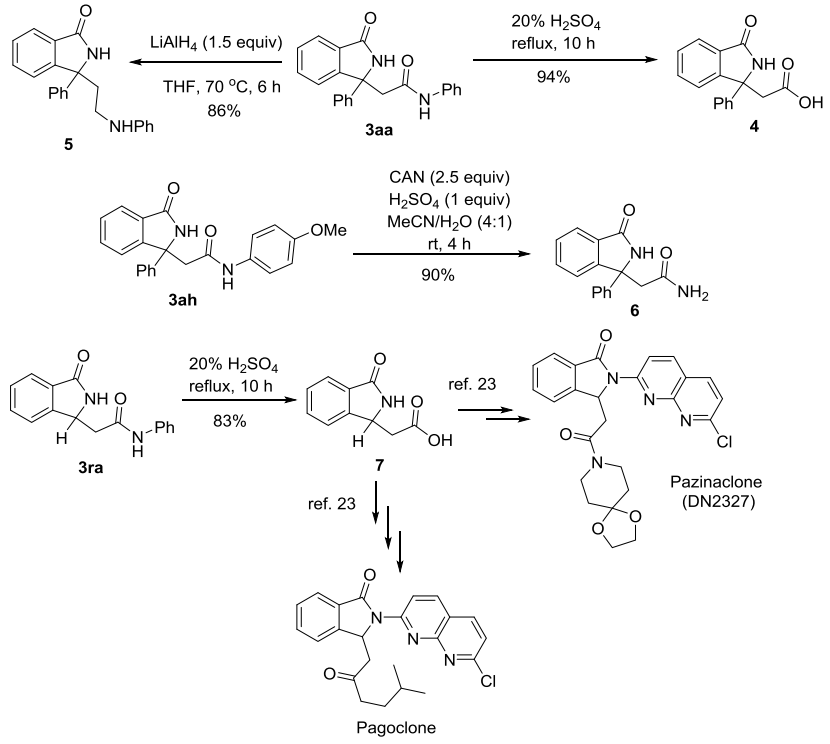
The halide-containing vinyl azides (**2b-d**) were well tolerated, generating the halo-substituted 3-oxoisoindoline-1-acetamides (entries **3ab-ad**, Table 3) in good yields. The intact halogen atom in the products offers an opportunity for further cross-coupling reactions. The reaction efficiencies remain the same when meta-substituted aromatic vinyl azide **2d** was used. Vinyl azides **2e** and **2f** bearing an electron-rich alkyl substituent (Me, ^{t}Bu) readily reacts with 3-hydroxyisoindolinone **1a** to afford the corresponding oxoisoindoline-1-acetamide (**3ae** and **3af**) with excellent yields (up to 94%). The reaction with sterically hindered 1-(1-azidovinyl)-2-methylbenzene **2g** was comparatively slow, resulting 3-oxoisoindoline-1-acetamide **3ag** in a moderate yield (67%). The slow reactivity of sterically hindered vinyl azide is might be due to the increased steric barrier for Schmidt-type 1,2-migration to furnish nitrilium ion intermediate (See reaction mechanism in Scheme 3). *Para*-methoxy substituted vinyl azide (**2h)** reacted well with 3-hydroxy-isoindolinone **1a** to produce **3ah** in 90% yield. The reactions of aryl vinyl azides (**2i-k**) bearing strong electron-deficient substituents (CN, CF_3, NO_2) were sluggish, requiring a longer reaction time to afford the products (**3ai-ak**) in moderate yields. Aryl rings having electron-donating groups provided the desired products in comparatively better yields than the substrates having electron-withdrawing groups for the present protocol. Furthermore, vinyl azide **2l** tethered with thiophene moiety was amenable to this protocol, affording product **3al** in 81% yield. The fused aryl vinyl azide (**2m**) also worked smoothly to furnish **3am** in excellent yield. Interestingly, when methyl substitution was introduced at β-position of the vinyl azide **2n** (R = Ph, R^1 = Me), the reaction proceeded smoothly and provided **3an** in 88% yield with 1:1 dr. To validate the practical usefulness of this methodology, a gram scale reaction of **1a** (5 mmol, 1.12 g) with 1-(1-azidovinyl)-4-methoxybenzene **2h** (5.5 mmol, 0.96 g) was performed under optimized conditions, furnishing the desired product **3ah** in 84% yield (1.56 g)

This transformation may be rationalized with a plausible mechanism as shown in Scheme 2.[11, 22] Initially, *N*-acyl iminium salt intermediate **I** will be generated from 3-aryl-3-hydroxyisoindolinones **1** in the presence of $BF_3{\cdot}Et_2O$. The nucleophilic addition of vinyl azide **2** to intermediate **I** will provide iminodiazonium intermediate **II**. Next, this iminodiazonium intermediate (**II**) will undergo Schmidt-type 1,2-migration (migratory aptitude aryl>alkyl), with extrusion of dinitrogen (N_2) to furnish the nitrilium ion intermediate **III**. Finally, hydrolysis of this intermediate **III** will provide oxoisoindoline-1-acetamides **3** (Scheme 2).



Scheme 2. Possible reaction mechanism for the synthesis of oxoisoindoline-1-acetamides **3**

To unravel the potential utility of this method in organic synthesis, a variety of synthetic transformations were carried out using oxoisoindoline-1-acetamides **3** (Scheme 3).



Scheme 3. Synthetic transformation of functionalized 3-Oxoisoindoline-1-acetamides **3**.

Compound **3aa** was effectively hydrolyzed with 20% H_2SO_4 to furnish acid derivative **4** under reflux condition. The primary amide bond in compound **3aa** was selectively reduced with lithium aluminum hydride to afford secondary amine derivative **5** in good yields. PMP group of **3ah** was oxidatively cleaved using ceric ammonium nitrate (CAN) to furnish amide derivative **6** in 90%

yield. In addition, compound **3ra** was hydrolyzed with 20% H_2SO_4 to afford 2-(3-oxoisoindolin-1-yl)acetic acid **7** which could be easily transformed into bioactive compounds Pazinaclone and Pagoclone by literature know procedure.[23] These results demonstrate the usefulness of 3-Oxoisoindoline-1-acetamides as synthetic intermediates.

Conclusion

In summary, we have reported $BF_3.OEt_2$ catalyzed vinyl azides addition to *in situ* generated *N*-acyl iminium salt derived from 3-aryl-3-hydroxyisoindolinones, enabling the straightforward synthesis of 3-oxoisoindoline-1-acetamides derivatives. A variety of vinyl azides were used to access biologically interesting 3-oxoisoindoline-1-acetamides derivatives with remarkable high yields (up to 97%). This methodology is equally efficient in gram-scale. The synthetic utility of this protocol was demonstrated by transforming oxoisoindoline-1-acetamides derivatives into a variety of advanced synthetic intermediates. Salient features of this protocol are (i) metal and additive free, (ii) mild reaction conditions (iii) generation of a quaternary carbon centre having methylene amide linkage, (iv) broad substrates scope.

Experimental Section

Materials and Methods

All reactions were carried out in oven-dried glassware with magnetic stirring. All solvents were purified and dried according to standard methods prior to use. ^{1}H NMR spectra were recorded on 400 MHz or 500 MHz in $CDCl_3$ and DMSO-d_6. $^{13}C\{^1H\}$NMR spectra were recorded on 100 or 125 MHz in $CDCl_3$ and DMSO-d_6 using TMS or residual solvent signals as internal standard. Data for ^{1}H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet or unresolved, coupling constant (s) in Hz, integration). Data for $^{13}C\{^1H\}$NMR are reported in terms of chemical shift (δ, ppm). High resolution mass spectra (HRMS) were obtained by the ESI (Q-TOF) ionization sources. IR spectra were measured with FT/IR Vector22 spectrometer. Routine monitoring of reactions was performed using precoated silica gel TLC plates. All the chromatographic separations were carried out by using silica gel (100-200 mesh). Melting points were recorded by using a melting point apparatus and are uncorrected.

Ethyl acetate (EA), petroleum ether (PE), $BF_3{\cdot}OEt_2$, and dichloromethane (DCM) are commercially available. All 3-aryl-3-hydroxyisoindolinones and vinyl azides were known compounds and prepared according to reported procedures.[16, 23, 24] Organic azides are potentially explosive. Proper safety precautions were utilized while performing the reactions.

General Procedure and characterization data for the Synthesis of 3-hydroxy-3-aryl isoindolin-1-one:

Characterization data for compounds (**1b,**[16] **1f,**[24a] **1g,**[16] **1p,**[16] **1q**[16]) Compounds (**1a, 1c, 1d, 1h, 1i, 1k**, **1s**) [24a] and compound (**1e**,[24b] **1l**,[24c] **1r**[24d-e] and **1u** [24f]) are reported in literature.

3-hydroxy-3-aryl isoindolin-1-one **1j, 1m, 1n, 1o, 1t** were synthesized according to modified literature procedure[16].

To a solution of aryl bromide/vinyl bromide (4.0 equiv) in THF (20 mL) cooled at –78 °C temperature, *n*-butyllithium solution (4.0 equiv, 1.6 M in hexane) was slowly added and stirred for 30 min at the same temperature. Further, a solution of phthalimide (1.0 equiv, 3.4 mmol) in THF (15 mL) was added in one portion and stirred for another 30 min at –78 °C. The reaction mixture was brought to room temperature and stirred until the completion of the reaction (monitored by TLC) the reaction mixture was then quenched with saturated NH_4Cl solution and acidified with 1N HCl till it reached pH 5.0. The aqueous solution was extracted with ethyl acetate (thrice). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The pure product was obtained after washing the crude product with CH_2Cl_2/hexane (1:2, v/v) as a solvent.

3-hydroxy-6-methyl-3-phenylisoindolin-1-one (1j): White solid, 617.76 mg, 76% yield. R_f= 0.38 (50% EtOAc in hexanes). **MP**: 151−153 °C. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.13 (s, 1H), 7.53 (d, *J* = 7.7 Hz, 1H), 7.49 (d, *J* = 7.2 Hz, 2H), 7.35 (dd, *J* = 8.4, 6.7 Hz, 2H), 7.31 – 7.27 (m, 2H), 7.11 (s, 1H), 6.86 (s, 1H), 2.34 (s, 3H). **^{13}C{^{1}H}NMR**(125 MHz, DMSO-d_6) δ 168.9, 151.8, 143.0, 142.8, 130.1, 128.7, 128.6, 128.2, 125.9, 123.5, 122.9, 87.6, 21.8. **IR** (film) ν_{max} 2079, 1655, 1445, 1344, 1180, 1050 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{15}H_{13}NO_2Na$, $[M+Na]^+$: 262.0838; Found 262.0837.

3-hydroxy-5,6-dimethyl-3-phenylisoindolin-1-one (1m): White solid, 689.18 mg, 80% yield. R_f= 0.40 (50% EtOAc in hexanes). **MP**: 158−160 °C.**^{1}H NMR** (500 MHz, $CDCl_3$+DMSO-d_6)δ 8.91 (s, 1H), 7.48 (d, *J* = 7.2 Hz, 2H), 7.38 (s, 1H), 7.28 (s, 2H), 7.23 (d, *J* = 7.0 Hz, 1H), 7.02 (s, 1H), 6.64 (d, *J* = 14.4 Hz, 1H), 2.27 (s, 3H), 2.23 (s, 3H). **^{13}C{^{1}H}NMR**(125 MHz, $CDCl_3$+DMSO-d_6) δ 169.3, 149.3, 142.7, 141.4, 137.5, 128.9, 128.3, 127.8, 125.8, 123.8, 123.5, 87.5, 20.5, 20.0. **IR** (film) ν_{max} 2840, 2127, 1660, 1450, 1402, 1203, 1111, 1015 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{16}H_{15}NO_2Na$ $[M+Na]^+$: 276.0995; Found 276.1013.

3-(4-fluorophenyl)-3-hydroxy-5,6-dimethylisoindolin-1-one (1n): White solid, 691.25 mg, 75% yield. R_f= 0.36 (50% EtOAc in hexanes). **MP**: 142−146 °C.**^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.08 (s, 1H), 7.49 (dd, *J* = 8.7, 5.6 Hz, 2H), 7.42 (s, 1H), 7.16 (t, *J* = 8.7 Hz, 2H), 7.08 (s, 1H), 6.85 (s, 1H), 2.28 (s, 3H), 2.24 (s, 3H). **^{13}C{^{1}H}NMR** (125 MHz, DMSO-d_6) δ 169.0, 162.1 (d, *J* = 243.5 Hz), 149.2, 141.9, 139.2 (d, *J* = 2.8 Hz), 137.9, 128.9, 128.1 (d, *J* = 8.6 Hz), 123.9, 123.6, 115.3 (d, *J* = 21.4 Hz), 87.2, 20.4, 19.9. **IR** (film) ν_{max} 2132,1710,1649,1511,1339,1222,1020 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{16}H_{15}FNO_2$, $[M+H]^+$: 272.1081; Found 272.1096.

3-hydroxy-5,6-dimethyl-3-(p-tolyl)isoindolin-1-one (1o): White solid, 763.69 mg, 84% yield. R_f= 0.40 (50% EtOAc in hexanes). **MP**: 156−158 °C**. ^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.99 (s, 1H), 7.38 (s, 1H), 7.35 – 7.29 (m, 2H), 7.12 (d, *J* = 7.9 Hz, 2H), 7.03 (s, 1H), 6.69 (s, 1H), 2.26 (s, 6H), 2.22 (s, 3H). **^{13}C{^{1}H}NMR** (125 MHz, DMSO-d_6) δ 168.6, 149.1, 141.2, 139.5, 137.2, 136.7, 128.6, 128.5, 125.4, 123.4, 123.0, 87.0, 20.6, 19.9, 19.4. **IR** (film) ν_{max} 2909, 1673, 1625, 1426, 1331, 1201, 1050 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{17}H_{17}NO_2Na$ $[M+Na]^+$: 290.1151; Found 290.1176.

3-hydroxy-3-vinylisoindolin-1-one (1t): White solid, 476 mg, 80% yield. R_f= 0.38 (60% EtOAc in hexanes). **MP**: 96-98 °C**. ^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.00 (d, *J* = 3.0 Hz, 1H), 7.66 – 7.56 (m, 2H), 7.56 – 7.43 (m, 2H), 6.52 (d, *J* = 3.1 Hz, 1H), 6.03 (dd, *J* = 17.1, 10.4 Hz, 1H), 5.47 (d, *J* = 17.1 Hz, 1H), 5.17 (d, *J* = 10.4 Hz, 1H). **^{13}C{^{1}H}NMR** (100 MHz, Chloroform-*d*) δ 170.0, 148.3, 136.5, 133.1, 130.0, 129.7, 123.7, 122.8, 116.5, 87.0. **IR** (film) ν_{max} 2918, 1711, 1665, 1466, 1352, 1206,1066, 995,755,609,694 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{10}H_9NO_2Na$ $[M+Na]^+$: 198.0525; Found 198.0520.

General Procedure and characterization data for the Synthesis of Vinyl azide:

Characterization data for compounds (**2a, 2b, 2c, 2e, 2f** and **2g**)[25a], Compounds (**2h** and **2i**)[25b] and compounds (**2j,**[25c] **2n**[25c] and **2k**[25d]) are reported in literature.

Vinyl azide derivatives **2d**, **2l** and **2m** were synthesized according to the modified literature procedure[25d]

A mixture of aryl acetylene (1.0 equiv, 2.0 mmol), TMS-N_3 (2.0 equiv, 4.0 mmol) and H_2O (1.5 equiv, 3.0 mmol) was taken in 10 mL DMSO solvent. Then Ag_2CO_3 (0.1 equiv, 0.2 mmol) was added to the reaction mixture and heated at 80 ºC in oil bath. The mixture was then stirred at the same temperature for 2 h until the starting material consumed (monitored by TLC). The reaction mixture was cooled down to room temperature then concentrated and extracted with dichloromethane (3 × 30 mL). The combined organic layer was washed with brine (2 × 60 mL) and dried over anhydrous Na_2SO_4. The solvent was evaporated in *vacuo* and the crude product was purified over silica gel by column chromatography (5-10% EtOAc in Hexane) to afford vinyl azide.

Note: Proper safety precautions were utilized while performing the reactions as explosive AgN_3 was precipitated as by-product.

1-(1-azidovinyl)-3-fluorobenzene (2d): Colorless viscous liquid, 189.25 mg, 58% yield. R_f= 0.46 (10% EtOAc in hexanes).**^{1}H** (500 MHz, $CDCl_3$) δ 7.40 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.37 – 7.30 (m, 2H), 7.11 – 7.05 (m, 1H), 5.51 (d, *J* = 2.8 Hz, 1H), 5.04 (d, *J* = 2.7 Hz, 1H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 162.9 (d, *J* = 245.7 Hz), 144.0 (d, *J* = 2.8 Hz), 136.5 (d, *J* = 8.0 Hz), 129.9 (d, *J* = 8.3 Hz), 121.1 (d, *J* = 2.8 Hz), 115.9 (d, *J* = 21.3 Hz), 112.6 (d, *J* = 23.5 Hz), 98.6. **IR** (film) ν_{max} 2925, 2106, 1583, 1490, 1310, 1180, 922 cm^{-1}; **HRMS** (ESI-TOF) m/z: Exact mass calcd for $C_8H_7FN_3$ $[M+H]^+$: 164.0619; Found 164.0631.

2-(1-azidovinyl)thiophene (2l): Yellow viscous liquid, 160.06 mg, 53% yield. R_f= 0.40 (10% EtOAc in hexanes). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.49 (dd, *J* = 3.1, 1.4 Hz, 1H), 7.33 (dd, *J* = 5.1, 3.0 Hz, 1H), 7.29 (dd, *J* = 5.1, 1.4 Hz, 1H), 5.39 (d, *J* = 2.5 Hz, 1H), 4.96 (d, *J* = 2.5 Hz, 1H). **^{13}C{^{1}H}NMR**(125 MHz, $CDCl_3$) δ 141.0, 136.6, 126.5, 125.0, 122.8, 96.9. **IR** (film) ν_{max} 3117, 2930, 2111, 1604, 1400, 1288, 935 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_6H_6N_3S$, $[M+H]^+$: 152.0277; Found 152.0284.

5-(1-azidovinyl)benzo[d][1,3]dioxole (2m): colorless viscous liquid, 241.92 mg, 64% yield. R_f= 0.38 (10% EtOAc in hexanes). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.12 (dd, *J* = 8.2, 1.9 Hz, 1H), 7.07 (d, *J* = 1.9 Hz, 1H), 6.81 (d, *J* = 8.2 Hz, 1H), 5.98 (s, 2H), 5.33 (d, *J* = 2.5 Hz, 1H), 4.89 (d, *J* = 2.5 Hz, 1H). **^{13}C{^{1}H}NMR**(125 MHz, $CDCl_3$) δ 148.4, 147.9, 144.6, 128.5, 119.7, 108.0, 106.1, 101.4, 96.6. **IR** (film) ν_{max} 3297, 2893, 2111, 1737, 1445, 1209, 930 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_9H_8N_3O_2$, $[M+H]^+$: 190.0611; Found 190.0633.

General Procedure and characterization data for the Synthesis of 3-Oxoisoindoline-1-acetamides, 3.

In a round bottomed flask, 3-aryl-3-hydroxyisoindolinones **1** (0.2 mmol, 1 equiv) and BF_3-Et_2O (2.4 μL, 0.02 mmol) were taken in 2.0 mL CH_2Cl_2 solvent. The mixture was stirred at room temperature (25 °C) for 10 minutes under nitrogen atmosphere. Then vinyl azide **2** (0.22 mmol, 1.1 equiv) was added dropwise. The reaction mixture was allowed to stir at room temperature. After completion of reaction as indicated by TLC, the reaction was quenched with saturated $NaHCO_3$ (aq) and warmed to room temperature. The resulting mixture was extracted three times with CH_2Cl_2. The combined organic layer was washed with brine, dried over Na_2SO_4 and concentrated under vacuum. The resulting crude mixture was purified over silica gel by chromatography using petroleum ether/ethyl acetate (PE/EA = 4/1 to 1/1) as the eluent to give the corresponding products **3**.

2-(3-oxo-1-phenylisoindolin-1-yl)-N-phenylacetamide (3aa): White solid, 62.92 mg, 92% yield. R_f= 0.32 (30% EtOAc in hexanes).**MP**: 107−109 °C.**^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.92 (s, 1H), 8.95 (s, 1H), 7.64 (t, *J* = 5.6 Hz, 2H), 7.61 – 7.52 (m, 3H), 7.45 – 7.38 (m, 3H), 7.35 (t, *J* = 7.7 Hz, 2H), 7.27 – 7.21 (m, 3H), 7.00 (t, *J* = 7.2 Hz, 1H), 3.57 (d, *J* = 14.8 Hz, 1H), 3.40 (s, 1H). **^{13}C{^{1}H}NMR**(125 MHz, DMSO-d_6) δ 168.8, 167.2, 150.7, 142.5, 138.7, 131.8, 130.8, 128.6, 128.5, 128.1, 127.3, 125.1, 123.3, 123.0, 123.0, 119.2, 64.7, 44.9. **IR** (film) ν_{max} 3377, 3280, 2129, 1010, 1654, 817 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{22}H_{18}N_2O_2Na$ $[M+Na]^+$: 365.1260; Found 365.1262.

N-(4-bromophenyl)-2-(3-oxo-1-phenylisoindolin-1-yl)acetamide (3ba): White solid,80.04 mg, 95% yield. R_f= 0.33 (30% EtOAc in hexanes). **MP**: 228-230 °C. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.92 (s, 1H), 9.00 (s, 1H), 7.64 (dd, *J* = 7.6, 4.7 Hz, 2H), 7.54 (s, 5H), 7.43 (dd, *J* = 13.4, 7.5 Hz, 3H), 7.24 (t, *J* = 7.9 Hz, 2H), 7.00 (t, *J* = 7.4 Hz, 1H), 3.56 (d, *J* = 15.6 Hz, 1H), 3.28 (d,

J = 15.1 Hz, 1H).**^{13}C{^{1}H}NMR**(125 MHz, DMSO-d_6) δ 168.8, 167.1, 150.3, 142.0, 138.7, 132.0, 131.4, 130.7, 128.7, 128.3, 127.6, 123.3, 123.1, 123.0, 120.6, 119.2, 64.4, 44.7. **IR** (film) ν_{max} 3368, 3220, 2241, 1655, 827 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{22}H_{17}BrN_2O_2Na$ $[M+Na]^+$: 443.0366. Found: 443.0339.

N-(4-fluorophenyl)-2-(3-oxo-1-phenylisoindolin-1-yl)acetamide (3ca): White solid, 69.91 mg, 97% yield. ***R*$_f$** = 0.32 (30% EtOAc in hexanes).**MP**: 238-240 °C. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.92 (s, 1H), 9.00 (s, 1H), 7.65 (d, *J* = 7.7 Hz, 2H), 7.61 (d, *J* = 5.2 Hz, 2H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.42 (d, *J* = 8.3 Hz, 3H), 7.24 (t, *J* = 7.7 Hz, 2H), 7.18 (t, *J* = 8.6 Hz, 2H), 7.00 (t, *J* = 7.4 Hz, 1H), 3.55 (d, *J* = 15.1 Hz, 1H), 3.31 (d, *J* = 15.1 Hz, 1H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 168.8, 167.1, 161.4 (d, *J* = 243.9 Hz), 150.6, 138.7, 138.7 (d, *J* = 3.1 Hz), 132.0, 130.8, 128.7, 128.2, 127.4 (d, *J* = 8.0 Hz), 123.3, 123.0, 119.2, 115.2 (d, *J* = 21.4 Hz), 64.4, 45.0. **IR** (film) ν_{max} 3412, 3368, 2130, 1646, 1006 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{22}H_{18}FN_2O_2$ $[M+H]^+$: 361.1347. Found: 361.1326.

2-(3-oxo-1-(p-tolyl)isoindolin-1-yl)-N-phenylacetamide (3da): White solid, 61.23 mg, 86% yield. ***R*$_f$**= 0.38 (30% EtOAc in hexanes). **MP**: 118-120 °C.**^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.03 (s, 1H), 7.99 (s, 1H), 6.77 – 6.72 (m, 2H), 6.66 (t, *J* = 6.9 Hz, 1H), 6.58 (d, *J* = 8.3 Hz, 2H), 6.55 (dd, *J* = 7.3, 3.1 Hz, 3H), 6.38 – 6.34 (m, 2H), 6.27 (d, *J* = 8.1 Hz, 2H), 6.12 (t, *J* = 7.4 Hz, 1H), 2.66 (d, *J* = 15.0 Hz, 1H), 2.40 (d, *J* = 15.0 Hz, 1H), 1.37 (s, 3H).**^{13}C{^{1}H}NMR**(125 MHz, DMSO-d_6) δ 168.8, 167.3, 150.9, 139.4, 138.8, 136.5, 131.8, 130.8, 129.1, 128.6, 128.0, 125.1, 123.3, 122.9, 119.2, 64.5, 44.8, 20.5. **IR** (film) ν_{max} 3278, 3266, 2132, 1659, 1022, 822 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{23}H_{20}N_2O_2Na$ $[M+Na]^+$: 379.1417. Found: 379.1423.

2-(1-(3,5-dimethylphenyl)-3-oxoisoindolin-1-yl)-N-phenylacetamide (3ea): White solid, 59.94 mg, 81% yield. ***R*$_f$**= 0.40 (40% EtOAc in hexanes).**MP**: 204-206 °C. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.89 (s, 1H), 8.81 (s, 1H), 7.62 (d, *J* = 7.8 Hz, 2H), 7.54 (t, *J* = 8.0 Hz, 1H), 7.41 (dd, *J* = 7.4, 5.2 Hz, 3H), 7.23 (t, *J* = 7.8 Hz, 2H), 7.20 (s, 2H), 6.99 (t, *J* = 7.4 Hz, 1H), 6.87 (s, 1H), 3.51 (d, *J* = 15.0 Hz, 1H), 3.28 (d, *J* = 15.0 Hz, 1H), 2.24 (s, 6H). **^{13}C{^{1}H}NMR** (125 MHz, DMSO-d_6) δ 168.8, 167.2, 150.8, 142.4, 138.7, 137.5, 131.7, 130.8, 128.7, 128.6, 128.0, 123.2, 122.9, 122.9, 122.8, 119.2, 64.6, 44.8, 21.1. **IR** (film) ν_{max} 3404, 2936, 2261, 1655, 1022, 828

cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{24}H_{23}N_2O_2$ $[M+H]^+$: 371.1754. Found: 371.1746

2-(1-(4-methoxyphenyl)-3-oxoisoindolin-1-yl)-N-phenylacetamide (3fa): White solid, 55.80 mg, 75% yield. R_f= 0.20 (30% EtOAc in hexanes). **MP**: 64-66 °C. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.88 (s, 1H), 8.86 (s, 1H), 7.61 (t, *J* = 7.7 Hz, 2H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.46 (d, *J* = 8.9 Hz, 2H), 7.41 (t, *J* = 7.8 Hz, 3H), 7.26 – 7.21 (m, 2H), 6.99 (t, *J* = 7.3 Hz, 1H), 6.90 (d, *J* = 8.9 Hz, 2H), 3.71 (s, 3H), 3.49 (d, *J* = 15.0 Hz, 1H), 3.27 (d, *J* = 14.9 Hz, 1H). **^{13}C{^{1}H}NMR** (125 MHz, DMSO-d_6) δ 168.7, 167.2, 158.4, 151.1, 138.7, 134.3, 131.8, 130.8, 128.6, 127.9, 126.4, 123.2, 122.9, 122.9, 119.2, 113.8, 64.3, 55.1, 44.9. **IR** (film) ν_{max} 3382, 2944, 1659, 1015, 828 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{23}H_{21}N_2O_3$ $[M+H]^+$: 373.1547. Found: 373.1543.

2-(1-(4-ethoxyphenyl)-3-oxoisoindolin-1-yl)-N-phenylacetamide (3ga): White solid, 55.58 mg, 72% yield. R_f= 0.22 (30% EtOAc in hexanes).**MP**: 170-172 °C. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.88 (s, 1H), 8.86 (s, 1H), 7.61 (t, *J* = 7.4 Hz, 2H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.45 (d, *J* = 8.9 Hz, 2H), 7.42 (dd, *J* = 7.3, 5.7 Hz, 3H), 7.26 – 7.21 (m, 2H), 6.99 (t, *J* = 7.3 Hz, 1H), 6.88 (d, *J* = 8.9 Hz, 2H), 3.97 (q, *J* = 7.0 Hz, 2H), 3.49 (d, *J* = 14.9 Hz, 1H), 3.27 (d, *J* = 14.9 Hz, 1H), 1.28 (t, *J* = 7.0 Hz, 3H).**^{13}C{^{1}H}NMR** (125 MHz, DMSO-d_6) δ 168.7, 167.3, 157.7, 151.1, 138.8, 134.1, 131.8, 130.8, 128.6, 127.9, 126.4, 123.3, 122.9, 122.9, 119.2, 114.3, 64.3, 63.0, 44.9, 14.6. **IR** (film) ν_{max} 3359, 3357, 2126, 1646, 1001, 819 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{24}H_{23}N_2O_3$ $[M+H]^+$: 387.1703. Found: 387.1692.

2-(1-(3-methoxyphenyl)-3-oxoisoindolin-1-yl)-N-phenylacetamide(3ha): White solid, 61.01 mg, 82% yield. R_f= 0.31 (30% EtOAc in hexanes).**MP**: 180-182 °C. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.17 (s, 1H), 8.16 (s, 1H), 6.89 (t, *J* = 7.7 Hz, 2H), 6.78 (t, *J* = 6.9 Hz, 1H), 6.66 (dd, *J* = 7.5, 4.5 Hz, 3H), 6.52 – 6.45 (m, 3H), 6.38 (d, *J* = 6.0 Hz, 2H), 6.23 (t, *J* = 7.3 Hz, 1H), 6.06 (d, *J* = 7.0 Hz, 1H), 2.96 (s, 3H), 2.80 (d, *J* = 15.1 Hz, 1H), 2.51 (d, *J* = 15.0 Hz, 1H).**^{13}C{^{1}H}NMR**(125 MHz, DMSO-d_6) δ 169.3, 167.7, 159.8, 151.1, 144.5, 139.2, 132.3, 131.2, 130.2, 129.1, 128.6, 123.8, 123.5, 119.6, 117.8, 112.7, 111.9, 65.2, 55.6, 45.3. **IR** (film) ν_{max} 3412, 3396, 2126, 1659, 1006, 828 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{23}H_{21}N_2O_3$ $[M+H]^+$: 373.1547. Found: 373.1537.

2-(3-oxo-1-(thiophen-2-yl)isoindolin-1-yl)-N-phenylacetamide (3ia): Yellow solid, 58.54 mg, 84% yield. R_f = 0.40 (30% EtOAc in hexanes).**MP**: 208-210 °C. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.91 (s, 1H), 9.06 (s, 1H), 7.65 – 7.62 (m, 2H), 7.60 – 7.56 (m, 1H), 7.45 (t, *J* = 7.5 Hz, 1H), 7.40 (d, *J* = 8.7 Hz, 2H), 7.36 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.31 (dd, *J* = 3.6, 1.3 Hz, 1H), 7.26 – 7.22 (m, 2H), 7.02 – 6.99 (m, 2H), 3.48 (d, *J* = 14.9 Hz, 1H), 3.40 (s, 1H).**^{13}C{^{1}H}NMR**(125 MHz, DMSO-d_6) δ 168.5, 166.6, 150.3, 147.6, 138.7, 132.0, 130.5, 128.7, 128.4, 127.5, 124.8, 124.0, 123.3, 123.0, 122.9, 119.2, 62.9, 45.3. **IR** (film) ν_{max} 3375,3102,2128,1652,1015,822 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{20}H_{17}N_2O_2S$ $[M+H]^+$: 349.1005. Found: 349.0981.

2-(5-methyl-3-oxo-1-phenylisoindolin-1-yl)-N-phenylacetamide (3ja): White solid, 63.44 mg, 89% yield. R_f= 0.32 (20% EtOAc in hexanes).**MP**: 220-222 °C. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.90 (s, 1H), 8.80 (s, 1H), 7.57 (t, *J* = 6.7 Hz, 2H), 7.52 (d, *J* = 7.7 Hz, 1H), 7.43 (d, *J* = 7.4 Hz, 3H), 7.35 (t, *J* = 7.8 Hz, 2H), 7.24 (t, *J* = 8.0 Hz, 4H), 7.00 (t, *J* = 7.3 Hz, 1H), 3.56 (d, *J* = 15.0 Hz, 1H), 3.28 (d, *J* = 15.0 Hz, 1H), 2.35 (s, 3H).**^{13}C{^{1}H}NMR**(125 MHz, DMSO-d_6) δ 168.9, 167.3, 151.3, 148.1, 142.6, 142.0, 138.8, 137.7, 132.7, 128.9, 128.6, 127.2, 125.2, 123.3, 122.8, 119.2, 64.5, 44.9, 21.5. **IR** (film) ν_{max} 3391, 2940, 2129, 1652, 1014, 760 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{23}H_{21}N_2O_2$ $[M+H]^+$: 357.1598. Found: 357.1574.

2-(5,6-dichloro-3-oxo-1-phenylisoindolin-1-yl)-N-phenylacetamide (3ka): Yellow solid, 75.44 mg, 93% yield. R_f = 0.36 (30% EtOAc in hexanes).**MP**: 246-248°C. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.9 (s, 1H), 9.4 (s, 1H), 8.0 (s, 1H), 7.8 (s, 1H), 7.6 (d, *J* = 7.8 Hz, 2H), 7.4 (d, *J* = 8.0 Hz, 2H), 7.4 (t, *J* = 7.6 Hz, 2H), 7.3 (t, *J* = 7.3 Hz, 1H), 7.2 (t, *J* = 7.8 Hz, 2H), 7.0 (t, *J* = 7.3 Hz, 1H), 3.7 (d, *J* = 15.0 Hz, 1H), 3.4 (s, 1H). **^{13}C{^{1}H}NMR**(125 MHz, DMSO-d_6) δ 167.4, 167.2, 151.3, 142.2, 139.1, 134.9, 132.3, 131.7, 129.2, 129.1, 128.2, 126.0, 125.6, 125.1, 123.8, 119.6, 64.9, 44.6. **IR** (film) ν_{max} 3399, 3262, 2121, 1648, 1014, 821 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{22}H_{16}Cl_2N_2O_2Na$ $[M+Na]^+$: 433.0481. Found: 433.0477.

2-(5,6-dichloro-3-oxo-1-(p-tolyl)isoindolin-1-yl)-N-phenylacetamide (3la): White solid, 76.50 mg, 90% yield.R_f= 0.30 (30% EtOAc in hexanes).**MP**: 238-240 °C. **^{1}HNMR** (500 MHz, DMSO-d_6) δ 9.92 (s, 1H), 9.29 (s, 1H), 7.99 (s, 1H), 7.80 (s, 1H), 7.43 (dd, *J* = 14.8, 7.9 Hz, 4H), 7.24 (t, *J* = 7.8 Hz, 2H), 7.17 (d, *J* = 7.9 Hz, 2H), 7.00 (t, *J* = 7.3 Hz, 1H), 3.64 (d, *J* = 15.0 Hz, 1H), 3.34 (d, *J* = 6.2 Hz, 1H), 2.25 (s, 3H). **^{13}C{^{1}H}NMR**(125 MHz, DMSO-d_6) δ 166.9,

166.8, 151.0, 138.8, 138.7, 137.0, 134.4, 131.8, 131.1, 129.3, 128.7, 125.5, 125.1, 124.6, 123.3, 119.2, 64.3, 44.1, 20.5. **IR** (film) ν_{max} 3388, 3218, 2126, 1651, 1030, 824 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{23}H_{19}Cl_2N_2O_2$ $[M+H]^+$: 425.0818. Found: 425.0831.

2-(5,6-dimethyl-3-oxo-1-phenylisoindolin-1-yl)-N-phenylacetamide (3ma): White solid, 67.42 mg, 91% yield.R_f= 0.26 (30% EtOAc in hexanes).**MP**: 240-242 °C. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.95 (s, 1H), 8.69 (s, 1H), 7.52 (d, *J* = 7.3 Hz, 2H), 7.39 (d, *J* = 6.6 Hz, 3H), 7.33 (dd, *J* = 15.0, 7.3 Hz, 3H), 7.25 – 7.20 (m, 3H), 6.99 (t, *J* = 7.4 Hz, 1H), 3.53 (s, 1H), 3.17 (d, *J* = 15.1 Hz, 1H), 2.24 (s, 3H), 2.22 (s, 3H). **^{13}C{^{1}H}NMR**(125 MHz, DMSO-d_6) δ 169.7, 167.8, 149.2, 142.7, 141.5, 138.9, 137.0, 129.0, 128.9, 128.6, 127.6, 125.3, 123.9, 123.8, 123.8, 119.6, 64.7, 45.1, 20.5, 19.7. **IR** (film) ν_{max} 3418, 3329, 2121, 1648, 821 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{24}H_{23}N_2O_2$ $[M+H]^+$: 371.1754. Found: 371.1726.

2-(1-(4-fluorophenyl)-5,6-dimethyl-3-oxoisoindolin-1-yl)-N-phenylacetamide (3na): White solid, 73.02 mg, 94% yield. R_f= 0.22 (30% EtOAc in hexanes).**MP**: 238-240 °C. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.88 (s, 1H), 8.76 (s, 1H), 7.58 (dd, *J* = 8.9, 5.4 Hz, 2H), 7.40 (dd, *J* = 15.8, 7.7 Hz, 4H), 7.27 – 7.21 (m, 2H), 7.16 (t, *J* = 8.9 Hz, 2H), 7.00 (t, *J* = 7.3 Hz, 1H), 3.52 (d, *J* = 15.0 Hz, 1H), 3.21 (d, *J* = 15.1 Hz, 1H), 2.26 (d, *J* = 6.4 Hz, 6H). **^{13}C{^{1}H}NMR** (125 MHz, DMSO-d_6) δ 168.9, 167.2, 161.3 (d, *J* = 243.8 Hz), 148.8, 141.0, 138.9 (d, *J* = 3.2 Hz), 138.7, 136.6, 128.6, 128.6, 127.3 (d, *J* = 8.1 Hz), 123.6, 123.5, 123.3, 119.2, 115.1 (d, *J* = 21.2 Hz), 63.9, 45.1, 20.2, 19.4. **IR** (film) ν_{max} 3432, 3312, 2127, 1647, 1004, 821 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{24}H_{22}FN_2O_2$ $[M+H]^+$: 389.1660. Found: 389.1653.

2-(5,6-dimethyl-3-oxo-1-(p-tolyl)isoindolin-1-yl)-N-phenylacetamide (3oa): White solid, 67.40 mg, 89% yield. R_f= 0.36 (30% EtOAc in hexanes).**MP**: 212-214 °C. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.92 (s, 1H), 8.64 (s, 1H), 7.45 – 7.41 (m, 4H), 7.39 (s, 1H), 7.33 (s, 1H), 7.24 (t, *J* = 7.9 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 7.00 (t, *J* = 7.4 Hz, 1H), 3.54 (d, *J* = 15.0 Hz, 1H), 3.17 (d, *J* = 14.9 Hz, 1H), 2.25 (s, 3H), 2.23 (d, *J* = 3.1 Hz, 6H).**^{13}C{^{1}H}NMR**(125 MHz, DMSO-d_6) δ 169.1, 167.5, 149.2, 140.9, 139.7, 138.8, 136.5, 136.4, 129.1, 128.7, 128.6, 125.0, 123.6, 123.5, 123.3, 119.2, 64.2, 45.0, 20.5, 20.2, 19.4. **IR** (film) ν_{max} 3345, 2948, 2886, 1652, 1022, 760 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{25}H_{24}N_2O_2Na$ $[M+Na]^+$: 407.1730. Found: 407.1748

2-(1-(4-methoxyphenyl)-5,6-dimethyl-3-oxoisoindolin-1-yl)-N-phenylacetamide (3pa): White solid, 59.20 mg, 74% yield. R_f= 0.22 (30% EtOAc in hexanes). **MP**: 264-266 °C. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.88 (s, 1H), 8.63 (s, 1H), 7.45 – 7.41 (m, 4H), 7.38 (s, 1H), 7.33 (s, 1H), 7.26 – 7.22 (m, 2H), 7.00 (t, *J* = 7.3 Hz, 1H), 6.88 (d, *J* = 8.9 Hz, 2H), 3.70 (s, 3H), 3.50 (d, *J* = 15.0 Hz, 1H), 3.17 (d, *J* = 14.9 Hz, 1H), 2.25 (d, *J* = 6.0 Hz, 6H).**^{13}C{^{1}H}NMR**(125 MHz, DMSO-d_6) δ 169.0, 167.5, 158.3, 149.3, 140.8, 138.8, 136.4, 134.5, 128.7, 128.6, 126.4, 123.5, 123.5, 123.3, 119.2, 113.8, 64.0, 55.1, 45.1, 20.2, 19.4. **IR** (film) ν_{max} 3408, 3375, 2126, 1656, 1024, 824 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{25}H_{25}N_2O_3$ $[M+H]^+$: 401.1860. Found: 401.1846.

2-(1-(4-methoxyphenyl)-3-oxo-2,3-dihydro-1H-benzo[f]isoindol-1-yl)-N-phenylacetamide(3qa): White solid, 61.61 mg, 73% yield. R_f = 0.23 (30% EtOAc in hexanes).**MP**: 256-258 °C. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.92 (s, 1H), 9.01 (s, 1H), 8.26 (s, 1H), 8.11 (d, *J* = 8.1 Hz, 1H), 8.07 (s, 1H), 7.98 (d, *J* = 8.1 Hz, 1H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.54 (d, *J* = 8.8 Hz, 3H), 7.40 (d, *J* = 7.4 Hz, 2H), 7.23 – 7.18 (m, 2H), 6.98 (t, *J* = 7.4 Hz, 1H), 6.92 (d, *J* = 8.9 Hz, 2H), 3.71 (s, 3H), 3.56 (d, *J* = 15.1 Hz, 1H), 3.47 (d, *J* = 15.1 Hz, 1H). **^{13}C{^{1}H}NMR** (125 MHz, DMSO-d_6) δ 168.4, 167.3, 158.4, 146.6, 138.8, 135.1, 134.8, 132.4, 129.6, 129.3, 128.6, 128.1, 127.6, 126.4, 126.2, 123.2, 123.0, 121.5, 119.1, 113.9, 64.1, 55.1, 45.4. **IR** (film) ν_{max} 3406, 3396, 2126, 1659, 1006, 828, 764 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{27}H_{22}N_2O_3Na$ $[M+Na]^+$: 445.1523. Found: 445.1528.

2-(3-oxoisoindolin-1-yl)-N-phenylacetamide (3ra): White solid, 43.09 mg, 81% yield. R_f = 0.42 (30% EtOAc in hexanes)**MP**: 146-148 °C.**^{1}H NMR** (500 MHz, DMSO-d_6) δ 10.03 (s, 1H), 8.68 (s, 1H), 7.67 (d, *J* = 7.5 Hz, 1H), 7.63 – 7.57 (m, 4H), 7.49 (td, *J* = 7.0, 6.6, 1.9 Hz, 1H), 7.35 – 7.30 (m, 2H), 7.09 – 7.04 (m, 1H), 5.00 (t, *J* = 6.9 Hz, 1H), 2.83 (dd, *J* = 15.0, 6.3 Hz, 1H), 2.66 (dd, *J* = 15.0, 7.7 Hz, 1H).**^{13}C{^{1}H}NMR**(125 MHz, DMSO-d_6) δ 169.0, 168.2, 147.2, 138.9, 132.2, 131.6, 128.7, 128.2, 123.4, 123.1, 122.9, 119.4, 53.1, 41.8. **IR** (film) ν_{max} 3380, 3308, 2126, 1664, 824 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{16}H_{15}N_2O_2$ $[M+H]^+$: 267.1128. Found: 267.1125

N-(4-chlorophenyl)-2-(3-oxo-1-phenylisoindolin-1-yl)acetamide (3ab): White solid, 67.68 mg, 90% yield. R_f= 0.26 (30% EtOAc in hexanes). **MP**: 217-219 °C. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 10.06 (s, 1H), 8.98 (s, 1H), 7.65 (d, *J* = 7.6 Hz, 2H), 7.58 (d, *J* = 7.8 Hz, 2H), 7.54

(t, *J* = 7.7 Hz, 1H), 7.46 (d, *J* = 8.9 Hz, 2H), 7.42 (t, *J* = 7.4 Hz, 1H), 7.34 (t, *J* = 7.8 Hz, 2H), 7.29 (d, *J* = 8.7 Hz, 2H), 7.24 (t, *J* = 7.3 Hz, 1H), 3.55 (d, *J* = 15.1 Hz, 1H), 3.35 (d, *J* = 15.0 Hz, 1H).**^{13}C{^{1}H}NMR**(125 MHz, DMSO-d_6) δ 168.9, 167.3, 150.7, 142.4, 137.7, 131.8, 130.9, 128.6, 128.1, 127.3, 126.8, 125.2, 123.0, 120.7, 64.7, 44.9. **IR** (film) ν_{max} 3411, 3380, 2124, 1657, 1018, 824cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{22}H_{17}ClN_2O_2Na$ $[M+Na]^+$: 399.0871. Found: 399.0879.

N-(4-fluorophenyl)-2-(3-oxo-1-phenylisoindolin-1-yl)acetamide (3ac): White solid, 63.36 mg, 88% yield. R_f= 0.32 (30% EtOAc in hexanes).**MP**: 178-180 °C. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.99 (s, 1H), 8.96 (s, 1H), 7.65 (d, *J* = 8.5 Hz, 2H), 7.58 (d, *J* = 7.2 Hz, 2H), 7.54 (t, *J* = 7.8 Hz, 1H), 7.45 – 7.40 (m, 3H), 7.34 (t, *J* = 7.8 Hz, 2H), 7.24 (t, *J* = 7.3 Hz, 1H), 7.08 (t, *J* = 8.9 Hz, 2H), 3.54 (d, *J* = 15.0 Hz, 1H), 3.32 (d, *J* = 15.0 Hz, 1H). **^{13}C{^{1}H}NMR** (125 MHz, DMSO-d_6) δ 168.9, 167.2, 158.0 (d, *J* = 239.9 Hz), 150.8, 142.4, 135.1 (d, *J* = 2.6 Hz), 131.9, 130.9, 128.6, 128.1, 127.4, 125.2, 123.1, 123.0, 121.0 (d, *J* = 7.8 Hz), 115.2 (d, *J* = 22.2 Hz), 64.8, 44.8. **IR** (film) ν_{max} 3354, 3276, 2120, 1647, 987, 822 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{22}H_{18}FN_2O_2$ $[M+H]^+$: 361.1347. Found: 361.1324.

N-(3-fluorophenyl)-2-(3-oxo-1-phenylisoindolin-1-yl)acetamide (3ad): White solid, 65.52 mg, 91% yield. R_f = 0.38 (30% EtOAc in hexanes).**MP**: 118-120 °C. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 10.14 (s, 1H), 8.99 (s, 1H), 7.65 (d, *J* = 8.3 Hz, 2H), 7.59 (d, *J* = 7.8 Hz, 2H), 7.55 (t, *J* = 7.7 Hz, 1H), 7.42 (dd, *J* = 9.2, 5.5 Hz, 2H), 7.35 (t, *J* = 7.7 Hz, 2H), 7.31 – 7.23 (m, 2H), 7.14 (d, *J* = 9.9 Hz, 1H), 6.83 (td, *J* = 8.5, 2.6 Hz, 1H), 3.56 (d, *J* = 15.1 Hz, 1H), 3.36 (d, *J* = 15.1 Hz, 1H). **^{13}C{^{1}H}NMR** (125 MHz, DMSO-d_6) δ 168.9, 167.6, 162.1 (d, *J* = 241.2 Hz), 150.7, 142.4, 140.5 (d, *J* = 11.1 Hz), 131.9, 130.8, 130.3 (d, *J* = 9.5 Hz), 128.6, 128.1, 127.3, 125.1, 123.0, 114.8 (d, *J* = 2.6 Hz), 109.7 (d, *J* = 21.1 Hz), 106.0, 105.8, 64.6, 44.9. **IR** (film) ν_{max} 3425, 3318, 2120, 1657, 1006, 825 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{22}H_{18}FN_2O_2$ $[M+H]^+$: 361.1347. Found: 361.1328.

2-(3-oxo-1-phenylisoindolin-1-yl)-N-(p-tolyl)acetamide (3ae): White solid, 66.93 mg, 94% yield. R_f= 0.32 (30% EtOAc in hexanes). **MP**: 106-108 °C. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.83 (s, 1H), 8.93 (s, 1H), 7.64 (d, *J* = 7.9 Hz, 2H), 7.58 (d, *J* = 7.3 Hz, 2H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.44 – 7.40 (m, 1H), 7.34 (t, *J* = 7.8 Hz, 2H), 7.30 (d, *J* = 8.5 Hz, 2H), 7.24 (t, *J* = 7.4 Hz, 1H), 7.04 (d, *J* = 8.2 Hz, 2H), 3.54 (d, *J* = 15.1 Hz, 1H), 3.30 (d, *J* = 15.0 Hz, 1H), 2.20 (s,

3H).**^{13}C{^{1}H}NMR** (125 MHz, DMSO-d_6) δ 168.8, 167.0, 150.8, 142.5, 136.2, 132.2, 131.8, 130.9, 129.0, 128.5, 128.1, 127.3, 125.2, 123.0, 123.0, 119.2, 64.7, 44.8, 20.4. **IR** (film) ν_{max} 3382, 3279, 2124, 1646, 944, 821 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{23}H_{21}N_2O_2$ $[M+H]^+$: 357.1598. Found: 357.1573.

N-(4-(tert-butyl)phenyl)-2-(3-oxo-1-phenylisoindolin-1-yl)acetamide (3af): White solid, 70.94mg, 89% yield. R_f = 0.42 (30% EtOAc in hexanes).**MP**: 186-188 °C. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.84 (s, 1H), 8.91 (s, 1H), 7.64 (d, *J* = 8.6 Hz, 2H), 7.58 (d, *J* = 7.2 Hz, 2H), 7.57 – 7.52 (m, 1H), 7.45 – 7.40 (m, 1H), 7.37 – 7.31 (m, 4H), 7.27 – 7.22 (m, 3H), 3.54 (d, *J* = 14.9 Hz, 1H), 3.28 (d, *J* = 14.9 Hz, 1H), 1.22 (s, 9H). **^{13}C{^{1}H}NMR** (125 MHz, DMSO-d_6) δ 168.7, 167.0, 150.7, 145.6, 142.4, 136.2, 131.8, 130.8, 128.5, 128.1, 127.3, 125.2, 125.2, 123.0, 123.0, 119.0, 64.7, 44.9, 34.0, 31.2. **IR** (film) ν_{max} 3418, 3308, 2259, 1656, 1014, 824 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{26}H_{26}N_2O_2Na$ $[M+Na]^+$: 421.1886. Found: 421.1874.

2-(3-oxo-1-phenylisoindolin-1-yl)-N-(o-tolyl)acetamide (3ag): White solid, 47.76 mg, 67% yield. R_f= 0.32 (30% EtOAc in hexanes).**MP**: 210-212 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.25 (s, 1H), 8.90 (s, 1H), 7.70 – 7.60 (m, 4H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.44 (t, *J* = 7.4 Hz, 1H), 7.37 (t, *J* = 7.8 Hz, 2H), 7.27 (t, *J* = 7.3 Hz, 1H), 7.14 (t, *J* = 8.0 Hz, 2H), 7.07 (t, *J* = 6.7 Hz, 1H), 7.04 – 6.99 (m, 1H), 3.60 (d, *J* = 14.5 Hz, 1H), 3.34 (d, *J* = 14.5 Hz, 1H), 2.00 (s, 3H).**^{13}C{^{1}H}NMR**(125 MHz, DMSO-d_6) δ 168.7, 167.2, 150.5, 142.5, 135.9, 131.8, 131.6, 130.9, 130.2, 128.6, 128.1, 127.3, 125.8, 125.2, 125.1, 124.7, 123.2, 123.0, 64.8, 44.5, 17.6. **IR** (film) ν_{max} 3378, 3352, 2126, 1648, 998 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{23}H_{21}N_2O_2$ $[M+H]^+$: 357.1598. Found: 357.1588.

N-(4-methoxyphenyl)-2-(3-oxo-1-phenylisoindolin-1-yl)acetamide (3ah): White solid, 66.96 mg, 90% yield. R_f= 0.26 (30% EtOAc in hexanes).**MP**: 188-190 °C. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.77 (s, 1H), 8.91 (s, 1H), 7.66 – 7.62 (m, 2H), 7.58 (d, *J* = 7.3 Hz, 2H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.42 (t, *J* = 7.4 Hz, 1H), 7.36 – 7.30 (m, 4H), 7.25 (t, *J* = 7.3 Hz, 1H), 6.81 (d, *J* = 9.0 Hz, 2H), 3.68 (s, 3H), 3.52 (d, *J* = 14.9 Hz, 1H), 3.27 (d, *J* = 14.9 Hz, 1H).**^{13}C{^{1}H}NMR** (125 MHz, DMSO-d_6) δ 168.8, 166.8, 155.3, 150.8, 142.5, 131.9, 131.8, 130.9, 128.5, 128.1, 127.3, 125.2, 123.0, 123.0, 120.8, 113.8, 64.8, 55.1, 44.8. **IR** (film) ν_{max} 3389, 3216, 2134, 1640, 1027 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{23}H_{20}N_2O_3Na$ $[M+Na]^+$: 395.1366. Found: 395.1337.

N-(4-cyanophenyl)-2-(3-oxo-1-phenylisoindolin-1-yl)acetamide (3ai): White solid, 55.74 mg, 76% yield. R_f = 0.20 (30% EtOAc in hexanes).**MP**: 144−145 °C.**^{1}H NMR** (500 MHz, DMSO-d_6) δ 10.35 (s, 1H), 9.00 (s, 1H), 7.70 (d, *J* = 8.4 Hz, 2H), 7.66 – 7.59 (m, 4H), 7.58 – 7.52 (m, 3H), 7.42 (t, *J* = 7.4 Hz, 1H), 7.35 (t, *J* = 7.6 Hz, 2H), 7.25 (t, *J* = 7.4 Hz, 1H), 3.56 (d, *J* = 15.0 Hz, 1H), 3.42 (d, *J* = 15.3 Hz, 1H).**^{13}C{^{1}H}NMR**(125 MHz, DMSO-d_6) δ 168.9, 167.9, 150.6, 142.9, 142.4, 133.2, 131.8, 130.9, 128.6, 128.1, 127.3, 125.1, 123.0, 123.0, 119.1, 119.0, 105.0, 64.6, 45.0. **IR** (film) ν_{max} 3416, 3380, 2234, 2128, 1655, 1020, 818 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{23}H_{18}N_3O_2$ [M+H] $^+$: 368.1394. Found: 368.1403.

2-(3-oxo-1-phenylisoindolin-1-yl)-N-(4-(trifluoromethyl)phenyl)acetamide (3aj): White solid, 60.68 mg, 74% yield. R_f = 0.21 (30% EtOAc in hexanes). **MP**: 254-256 °C. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 10.28 (s, 1H), 8.99 (s, 1H), 7.66 – 7.59 (m, 6H), 7.58 – 7.52 (m, 3H), 7.42 (t, *J* = 7.9 Hz, 1H), 7.35 (t, *J* = 7.8 Hz, 2H), 7.25 (t, *J* = 7.3 Hz, 1H), 3.56 (d, *J* = 15.1 Hz, 1H), 3.37 (d, *J* = 10.5 Hz, 1H). **^{13}C{^{1}H}NMR** (125 MHz, DMSO-d_6) δ 169.0, 167.8, 150.6, 142.4, 142.3, 131.9, 130.9, 128.6, 128.2, 127.4, 126.1, 126.0, 126.0, 125.2, 123.1, 123.0, 119.0, 64.7, 45.0. **IR** (film) ν_{max} 3368, 3221, 2252, 1659, 1031, 824 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{23}H_{17}F_3N_2O_2Na$[M+Na]$^+$: 433.1134. Found: 433.1120.

N-(4-nitrophenyl)-2-(3-oxo-1-phenylisoindolin-1-yl)acetamide(3ak): Yellow solid, 54.95 mg, 71% yield. R_f = 0.20 (30% EtOAc in hexanes).**MP**: 252-254 °C. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 10.54 (s, 1H), 9.05 (s, 1H), 8.16 (d, *J* = 8.7 Hz, 2H), 7.72 – 7.63 (m, 4H), 7.59 (d, *J* = 7.6 Hz, 2H), 7.54 (t, *J* = 7.7 Hz, 1H), 7.42 (t, *J* = 7.7 Hz, 1H), 7.35 (t, *J* = 7.9 Hz, 2H), 7.26 (d, *J* = 7.6 Hz, 1H), 3.61 (d, *J* = 15.5 Hz, 1H), 3.39 (d, *J* = 16.6 Hz, 1H).**^{13}C{^{1}H}NMR**(125 MHz, DMSO-d_6) δ 169.0, 168.1, 150.6, 144.9, 142.4, 142.2, 131.9, 130.9, 128.6, 128.1, 127.4, 125.1, 124.9, 123.0, 118.7, 64.6, 45.0. **IR** (film) ν_{max} 3396, 3361, 2119, 1648, 2246, 759 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{22}H_{17}N_3O_4Na$ [M+Na]$^+$: 410.1111. Found: 410.1134.

2-(3-oxo-1-phenylisoindolin-1-yl)-N-(thiophen-2-yl)acetamide (3al): Yellow solid, 56.44 mg, 81% yield. R_f = 0.32 (20% EtOAc in hexanes).**MP**: 82-84 °C. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 10.33 (s, 1H), 8.92 (s, 1H), 7.66 – 7.61 (m, 2H), 7.55 (dd, *J* = 13.4, 7.4 Hz, 3H), 7.43 (t, *J* = 7.4 Hz, 1H), 7.39 (dd, *J* = 5.1, 3.2 Hz, 1H), 7.37 (dd, *J* = 3.3, 1.4 Hz, 1H), 7.34 (t, *J* = 7.8 Hz, 2H), 7.24 (t, *J* = 7.3 Hz, 1H), 6.97 (dd, *J* = 5.1, 1.4 Hz, 1H), 3.52 (d, *J* = 15.1 Hz, 1H), 3.28 (d, *J* = 15.2 Hz, 1H). **^{13}C{^{1}H}NMR** (125 MHz, DMSO-d_6) δ 168.8, 166.3, 150.8, 142.4, 136.4, 131.9,

130.8, 128.5, 128.1, 127.3, 125.1, 124.6, 123.0, 123.0, 121.2, 108.6, 64.6, 44.3. **IR** (film) ν_{max} 3375, 3318, 2117, 1654, 1006, 824,762 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{20}H_{17}N_2O_2S$ $[M+H]^+$: 349.1005. Found: 349.0996.

N-(benzo[d][1,3]dioxol-5-yl)-2-(3-oxo-1-phenylisoindolin-1-yl)acetamide (3am): White solid, 69.55 mg, 90% yield.R_f= 0.34 (30% EtOAc in hexanes).**MP**: 218-220 °C. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 9.82 (s, 1H), 8.92 (s, 1H), 7.63 (d, *J* = 9.0 Hz, 2H), 7.55 (dd, *J* = 17.3, 8.1 Hz, 3H), 7.43 (t, *J* = 6.9 Hz, 1H), 7.35 (t, *J* = 7.8 Hz, 2H), 7.25 (t, *J* = 7.4 Hz, 1H), 7.09 (d, *J* = 1.8 Hz, 1H), 6.82 – 6.73 (m, 2H), 5.94 (s, 2H), 3.50 (d, *J* = 14.9 Hz, 1H), 3.27 (d, *J* = 14.9 Hz, 1H). **^{13}C{^{1}H}NMR** (125 MHz, DMSO-d_6) δ 168.8, 166.8, 150.7, 146.9, 142.9, 142.4, 133.1, 131.8, 130.8, 128.5, 128.1, 127.3, 125.2, 123.0, 123.0, 112.1, 107.9, 101.4, 100.9, 64.7, 44.8. **IR** (film) ν_{max} 3405, 2939, 2245, 1652, 1014, 821 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{23}H_{19}N_2O_4$ $[M+H]^+$: 387.1339. Found: 387.1335.

2-(3-oxo-1-phenylisoindolin-1-yl)-N-phenylpropanamide (3an-upper spot): White solid, 31.32 mg, 88% overall yield. R_f = 0.32 (30% EtOAc in hexanes).**MP**: 146−148 °C.**^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.81 (s, 1H), 7.99 (s, 1H), 7.72 (d, *J* = 7.5 Hz, 1H), 7.60 (d, *J* = 7.6 Hz, 2H), 7.39 – 7.34 (m, 2H), 7.32 – 7.27 (m, 3H), 7.21 – 7.17 (m, 2H), 7.16 – 7.09 (m, 3H), 6.96 (t, *J* = 7.4 Hz, 1H), 3.90 (q, *J* = 6.8 Hz, 1H), 0.95 (d, *J* = 6.9 Hz, 3H).**^{13}C{^{1}H}NMR**(125 MHz, Chloroform-*d*) δ 173.1, 170.9, 149.9, 141.3, 137.7, 132.9, 131.0, 129.1, 129.0, 128.7, 128.0, 124.9, 124.7, 124.1, 122.2, 120.6, 68.8, 47.9, 13.4. **IR** (film) ν_{max} 3306, 3138, 2354, 1664, 1041, 696 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{23}H_{20}N_2O_2Na$ $[M+Na]^+$: 379.1417. Found: 379.1426.

2-(3-oxo-1-phenylisoindolin-1-yl)-N-phenylpropanamide (3an-lower spot): White solid, 31.32 mg, 88% overall yield. R_f= 0.42 (20% EtOAc in hexanes). **MP**: 196−198 °C. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.86 (s, 1H), 7.78 – 7.75 (m, 2H), 7.64 (d, *J* = 7.2 Hz, 3H), 7.57 (t, *J* = 7.6 Hz, 1H), 7.42 (d, *J* = 7.2 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 2H), 7.30 (t, *J* = 7.3 Hz, 1H), 7.14 – 7.09 (m, 2H), 7.03 (d, *J* = 7.3 Hz, 2H), 6.99 (t, *J* = 7.3 Hz, 1H), 3.72 (q, *J* = 7.1 Hz, 1H), 1.33 (d, *J* = 7.1 Hz, 3H).**^{13}C{^{1}H}NMR**(125 MHz, DMSO-d_6) δ 170.0, 169.0, 148.6, 141.9, 138.4, 131.5, 131.1, 128.6, 128.4, 128.1, 127.4, 125.5, 124.2, 123.2, 122.5, 119.4, 68.7, 47.2, 13.5. **IR** (film) ν_{max} 3391, 3328, 2256, 1658, 991, 828 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{23}H_{21}N_2O_2$ $[M+H]^+$: 357.1598. Found: 357.1571.

General Procedure for the Synthesis of 2-(3-oxoisoindolin-1-yl)acetic acid (4/7):

A solution of 3-Oxoisoindoline-1-acetamide **3aa**(1.0 equiv, 0.2 mmol, 68.48 mg) or **3ra** (1.0 equiv, 0.2 mmol, 53.26 mg) in 4 mL 20% H_2SO_4 were reflux at 110°C in oil bath for 10 h. Upon completion of reaction (monitored by TLC) the reaction was quenched with a saturated aqueous solution of $NaHCO_3$ and extracted with EtOAc (3x10 mL). The organic was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography using EtOAc/Hexane as eluent to afford the product **4/7**.

2-(3-oxo-1-phenylisoindolin-1-yl)acetic acid (4): Yellow solid, 50.2 mg, 94% yield. $\boldsymbol{R_f}$ = 0.24 (50% EtOAc in hexanes). **MP**: 158−160 °C.**^{1}H NMR** (500 MHz, Chloroform-*d*) δ 10.68 (s, 1H), 8.91 (s, 1H), 7.72 (d, *J* = 7.6 Hz, 1H), 7.42 (t, *J* = 7.0 Hz, 1H), 7.36 – 7.31 (m, 3H), 7.26 (d, *J* = 7.7 Hz, 1H), 7.20 – 7.12 (m, 3H), 3.75 (d, *J* = 17.1 Hz, 1H), 2.69 (d, *J* = 17.1 Hz, 1H).**^{13}C{^{1}H}NMR**(125 MHz, Chloroform-*d*) δ 173.7, 171.8, 151.2, 139.7, 133.2, 129.3, 129.1, 128.8, 128.0, 124.9, 124.5, 122.3, 65.6, 43.4.**IR** (film) ν_{max} 3398, 2932, 1678, 1029 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{16}H_{14}NO_3$ $[M+H]^+$: 268.0968. Found: 268.0948.

2-(3-oxoisoindolin-1-yl)acetic acid (7): White solid, 31.70 mg, 83% yield. $\boldsymbol{R_f}$ = 0.20 (50% EtOAc in hexanes).**MP**: 148−152 °C. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.6 (s, 1H), 7.6 (d, *J* = 7.5 Hz, 1H), 7.6 (d, *J* = 5.9 Hz, 2H), 7.5 (t, *J* = 7.9 Hz, 1H), 4.8 (t, *J* = 6.6 Hz, 1H), 3.4 (s, 1H), 2.8 (dd, *J* = 16.4, 5.7 Hz, 1H), 2.5 (dd, *J* = 16.3, 7.5 Hz, 1H).**^{13}C{^{1}H}NMR**(125 MHz, Chloroform-*d*) δ 174.9, 172.2, 146.1, 132.5, 131.4, 128.8, 124.2, 122.4, 53.9, 39.1.**IR** (film) ν_{max} 3351, 2925, 1761, 1283, 1066, 750 cm^{-1};**HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{10}H_{10}NO_3$, $[M+H]^+$:192.0655. Found: 192.0637.

General Procedure for the Synthesis of 3-phenyl-3-(2-(phenylamino)ethyl)isoindolin-1-one (5): $LiAlH_4$ (1.5 equiv, 0.3 mmol, 11.38 mg) was added to a solution of 2-(3-oxo-1-phenylisoindolin-1-yl)-N-phenylacetamide **3aa** (1.0 equiv, 0.2 mmol, 68.48 mg) in dry THF (4 mL) at room temperature. The reaction mixture was heated at 70°C in sealed tube in oil bath for 10 h, upon completion of reaction (monitored by TLC), the reaction mixture was quenched with a saturated aqueous solution of NH_4Cl and extracted with EtOAc (3x10 mL). The organic was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography using EtOAc/Hexane as eluent to afford the product **5**.

3-phenyl-3-(2-(phenylamino)ethyl)isoindolin-1-one (5): White solid, 56.41 mg, 86% yield.R_f= 0.40 (20% EtOAc in hexanes).**MP**: 109−111 °C. **^{1}H NMR** (500 MHz, Chloroform-*d*)δ 7.88 (d, *J* = 7.5 Hz, 1H), 7.56 (td, *J* = 7.5, 1.2 Hz, 2H), 7.52 (dd, *J* = 8.4, 1.3 Hz, 2H), 7.48 (td, *J* = 7.5, 0.9 Hz, 1H), 7.43 (d, *J* = 7.7 Hz, 1H), 7.39 – 7.36 (m, 2H), 7.33 – 7.29 (m, 1H), 7.13 (dd, *J* = 8.6, 7.2 Hz, 2H), 6.74 – 6.67 (m, 1H), 6.48 (d, *J* = 7.4 Hz, 2H), 3.61 (bs, 1H), 3.24 (td, *J* = 8.1, 4.0 Hz, 1H), 3.04 (dt, *J* = 13.2, 7.4 Hz, 1H), 2.80 (ddd, *J* = 13.4, 7.9, 5.0 Hz, 1H), 2.54 (ddd, *J* = 14.5, 8.0, 6.9 Hz, 1H). **^{13}C{^{1}H}NMR** (125 MHz, Chloroform-*d*) δ 170.5, 151.1, 147.5, 141.2, 132.6, 130.3, 129.3, 129.1, 128.5, 127.9, 125.2, 124.2, 122.2, 117.9, 113.1, 66.3, 39.9, 38.4. **IR** (film) ν_{max} 3212, 2920, 1692, 1318, 1182, 747 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{22}H_{21}N_2O$, $[M+H]^+$: 329.1648. Found: 329.1638.

General Procedure for the Synthesis of (3-oxo-1-phenylisoindolin-1-yl)acetamide(6):

A solution of N-(4-methoxyphenyl)-2-(3-oxo-1-phenylisoindolin-1-yl)acetamide **3ah** (1.0 equiv, , 0.2 mmol, 74.48 mg) in CH_3CN (4 mL) was cooled at -5 °C using ice-salt water bath. An aqueous solution of CAN (2.5 equiv, 0.5 mmol, 274.11 mg dissolved in 1.0 mL H_2O) and H_2SO_4 (1.0 equiv, 0.2 mmol) were added dropwise sequentially. The mixture was stirred at room temperature for 2 h, upon completion of reaction (monitored by TLC), the reaction was quenched with a saturated aqueous solution of $NaHCO_3$ and extracted with EtOAc (3x10 mL). The organic was dried over anhydrous $Na_2SO_4$and concentrated under reduced pressure. The crude product was purified by column chromatography using EtOAc/Hexane as eluent to afford the product **6**.

2-(3-oxo-1-phenylisoindolin-1-yl)acetamide (6): White solid, 74.80 mg, 90% yield.R_f = 0.32 (50% EtOAc in hexanes). **MP**: 182−184 °C. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.69 (s, 1H), 7.63 (d, *J* = 7.5 Hz, 1H), 7.56 – 7.50 (m, 4H), 7.45 – 7.40 (m, 1H), 7.35 – 7.30 (m, 3H), 7.24 (t, *J* = 7.3 Hz, 1H), 6.89 (s, 1H), 3.39 (d, *J* = 15.0 Hz, 1H), 2.89 (d, *J* = 15.0 Hz, 1H).**^{13}C{^{1}H}NMR**(125 MHz, DMSO-d_6) δ 170.7, 168.6, 151.0, 142.4, 131.9, 130.7, 128.5, 128.0, 127.2, 125.1, 123.0, 122.9, 64.5, 43.5. **IR** (film) ν_{max} 2927, 2095, 1694, 1301 cm^{-1}; **HRMS** (ESI-TOF) m/z : Exact mass calcd for $C_{16}H_{15}N_2O_2$ $[M+H]^+$: 267.1128. Found: 267.1106.

Associated Content

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Notes

The authors declare no competing financial interest.

Supporting Information

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Crystallographic data for compound **3ba**.

^{1}H, $^{13}C\{^{1}H\}$NMR spectra for all isolated compounds.

ACKNOWLEDGMENT

V.K.S. acknowledges DST/SERB, India for a J. C. Bose fellowship (SR/S2/JCB-17/2008) and SERB (CRG/2018/ 000552) for the financial support. D. K. D. thanks to IISERB for Institute postdoctoral fellowship. V. K. K. is thankful to IISERB for Project fellowship. S. K. R. thanks DST for an INSPIRE Faculty award (DST/INSPIRE/04/2016001704). M. M. S. thanks DST-Inspire for fellowship. Facilities from the Department of Chemistry, IISER Bhopal are gratefully acknowledged. We thank CIF, XRD facility, IISER Bhopal and Dr. Syed Meheboob Elahi from Nanjing University, Department of Chemistry for the help in structure determination and data analysis.

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