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# Synthesis of Functionalized Isoindolinones via Calcium Catalyzed Generation and Trapping of N-Acyliminium Ions

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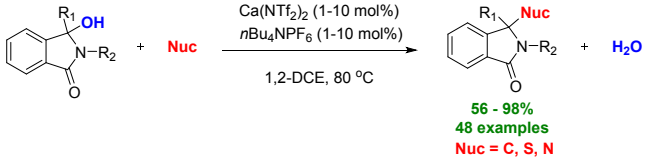



**ABSTRACT:** Herein we report our full investigation into the calcium catalyzed generation and trapping of N-acyliminium ions from readily available 3-hydroxyisoindolinones. We have successfully employed a range of traditional nucleophiles including carbon, nitrogen and sulfur containing reactive partners. The reaction is tolerant to a wide range of functionalities and provides high value scaffolds in good to excellent yields.

## INTRODUCTION

*N*-acyliminium ions represent a highly useful reactive intermediate that has found use in a plethora of synthetic methodologies and total synthesis alike.[1-2] Over the course of several decades, these reactive intermediates have been employed to form new carbon-carbon and carbon-heteroatom bonds with great success. In particular, *N*-acyliminium ions have shown utility in the synthesis of fused ring systems through intramolecular trapping of the generated reactive intermediate.[3-6] This strategy has been thoroughly explored over the last two decades with noted examples such as in the total syntheses of stemoamide,[7] crispine A,[8] and minfiensine (**Fig 1**).[9]

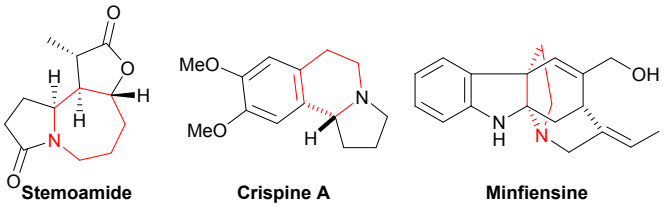
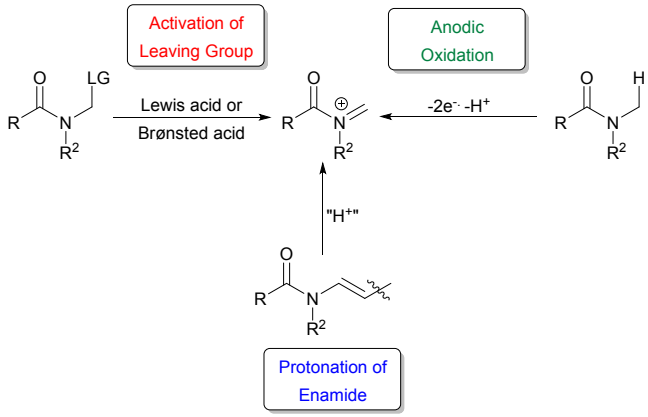



**Figure 1. Synthesis of complex natural products employing N-acyliminium ions**

Traditionally, *N*-acyliminium ions are generated via the activation and release of a suitable leaving group under acidic conditions. There is a wide range of these suitable leaving groups including hydroxyl,[10] alkyl- and aryloxy,[11] acetoxy[12-13] and carbamate,[14-15] however sulfur containing and sulfoxide based groups have also found use.[16] As the synthetic utility of these intermediates becomes more obvious, the need to generate them using more functionally tolerant reagents remains high. Success using stoichiometric Lewis acids such as $BF_3.OEt_2$,[17] $Sc(OTf)_3$,[18] $TiCl_4$,[19] and $AlCl_3$[20] have all recently been reported. Furthermore, organic acids such as *p*-TsOH and TFA have also been shown to generate *N*-acyliminium ions efficiently under notably milder conditions.[21] Although great successes have been described employing stoichiometric reagents, there is a clear need to develop catalytic processes by which these important intermediates can be generated. This need is twofold; firstly, catalytic generation inherently produces less waste, with the byproducts using hydroxyl or akyloxy leaving groups being water or innocuous alcohols. Secondly, from a reactivity point of view, catalytic generation will result in a more controlled reaction profile, with a much-reduced propensity for side reactions. Unsurprisingly, there has been noted successes in this endeavor (**Scheme 1**), with elegant examples using Brønsted

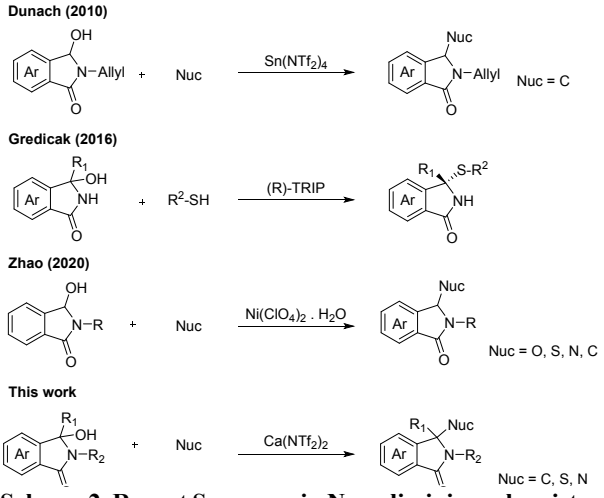



acids,[22-24] thiourea organocatalysts[25-28] and Lewis acids.[29-33]

**Scheme 1 .Strategies towards N-acyliminium Ions**

Other methods including protonation of enamides[34] and anodic (Shono)oxidation[35] have also been described with varying success

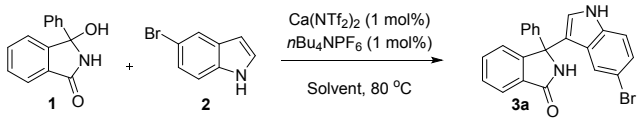
Our group has a growing interest in developing methodology to catalytically generate reactive intermediates,[36] and in particular using calcium complexes to mediate these processes.[37-38] Calcium represents a relatively underexplored metal in catalysis,[39] however over the past decade there has been an icrease in interest in exploring the reactivity of calcium, which has resulted in a wealth of innovative uses for this abundant element.[40-60] We,[37] and others,[61] have recently reported the use of $Ca(NTf_2)_2$ as an excellent catalyst to produce *N*-acyliminium ions from readily available 3-hydroxyisoindolinones. Due to the importance of these scaffolds in both total synthesis[62-64] and medicinal chemistry,[65] we wanted to explore this reaction further. In particular, we set out to probe the limits of the reaction towards traditional carbon, amine and sulfur nucleophiles. In particular, we wanted to focus our attention on the synthesis of functionalized isoindolinones, due to their importance in an ongoing medicinal chemistry campaign within our group. Unsurprisingly, due to their range of interesting biological activities,[66-68] the synthesis of these scaffolds has attracted much attention in the literature (**Scheme 2**). In particular, the use of Brønsted and Lewis acids catalysts have been shown to be well tolerated. Although these examples provide the desired products in typically good yields, the use of tertiary hydroxyisoindolinones remains underexplored. This somewhat limits the use of the more complex catalytic systems, as it results in less than optimum substrate availability. Thus we wanted to explore these tertiary alcohols, and to probe the limits of the reactions.




**Scheme 2. Recent Successes in N-acyliminium chemistry**

## RESULTS AND DISCUSSION

We began our investigation employing indoles as nucleophiles. We rationalized that due to its importance in medicinal chemistry, paired with the availability of the motif, we could provide high value scaffolds bearing pendant functional groups in a controlled and high yielding manner. Furthermore, due to the ubiquitous nature of functionalized indoles in natural products, functionally tolerant catalytic methods to afford these types of compounds are constantly required. Indeed, upon treating 3-hydroxyisoindolinone with 10 mol% $Ca(NTf_2)_2$ . /$nBu_4NPF_6$ in the presence of 5-bromoindole, the desired product was formed in high yield (83%). Reducing the catalyst loading to 1 mol% had little effect on the reaction, providing the product in identical yield. Further optimization including varying the solvent, temperature and concentration had a deleterious effect on the yield of the reaction (**Table 1**). Finally, lowering the catalyst loading to below 1 mol% resulted in a noticeably more sluggish reaction, and we decided that in the interest between balancing catalyst loading and reaction time, 1 mol% was optimum. Importantly, we also performed a series of control experiments, most notable of which was using 2,6-ditertbutylpyridine (**entry 9**), a known inhibitor of Brønsted acid catalysis. The reaction proceeded unhindered, and proves that the reaction is indeed calcium catalyzed.

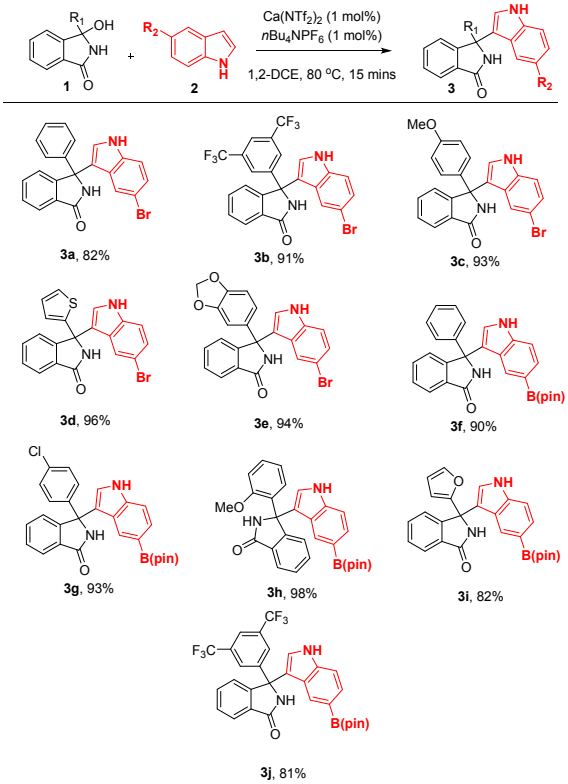



| Entry | Calcium source | Additive | Solvent | Yield[a] |
|---|---|---|---|---|
| 1 | $Ca(NTf_2)_2$ | $nBu_4NPF_6$ | THF | 15% |
| 2 | $Ca(NTf_2)_2$ | $nBu_4NPF_6$ | MeCN | 66% |
| 3 | $Ca(NTf_2)_2$ | $nBu_4NPF_6$ | Toluene | n.r. |
| 4 | $Ca(NTf_2)_2$ | $nBu_4NPF_6$ | $CH_2Cl_2$ | 79% |
| **5** | **$Ca(NTf_2)_2$** | **$nBu_4NPF_6$** | **1,2-DCE** | **82%** |
| 6 | $Ca(NTf_2)_2$ | - | 1,2-DCE | 39% |
| 7 | - | $nBu_4NPF_6$ | DCE:DME | n.r. |
| 8 | $Ca(NTf_2)_2$ | $nBu_4NPF_6$ | HFIP | decomp. |
| 9 | $Ca(NTf_2)_2$ | $nBu_4NPF_6$ | 1,2-DCE | 82%[b] |

a Isolated Yield b 2,6-ditertbutylpyridine added

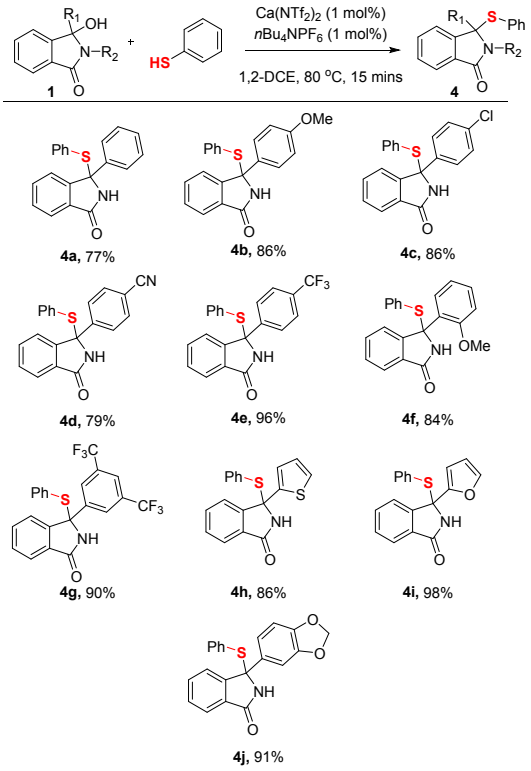
**Table 1. Optimization study**

With these conditions in hand we probed the substrate scope of the reaction (**Scheme 3**). We observed excellent conversion to the products in all cases, providing a wide variety of complex scaffolds quickly. As shown, the reaction is tolerant to 5-bromo and 5-pinacolboronate indoles, affording a range of highly useful building blocks, including electron electron-withdrawing (**3b**) and donating groups (**3c, 3h**) as well as further heterocyclic substrates (**3d, 3e, 3i**).



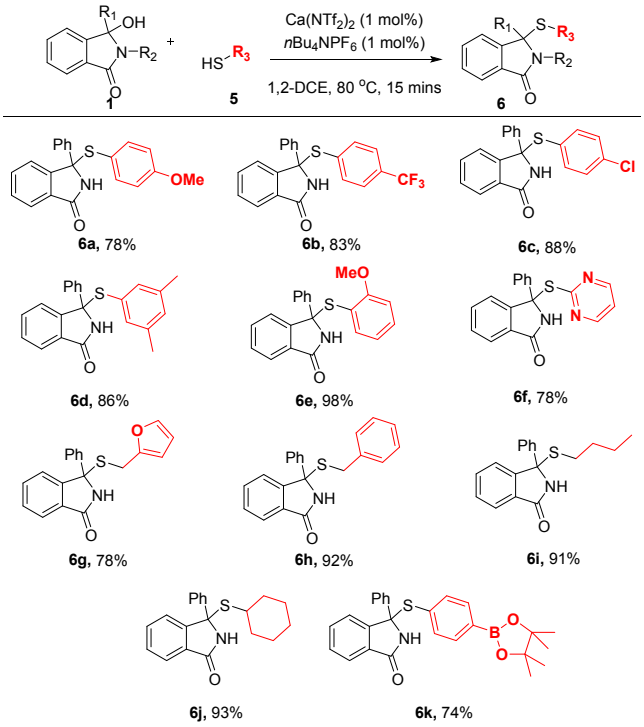

**Scheme 3. Indole Substituted Isoindolinones**

As many catalytic processes are tolerant to carbon based functional groups, but show limited reactivity when heterocyclic reaction partners are used, we wanted explore the limits of the calcium system to these coupling partners. We decided to therefore move onto sulfur containing fragments, and in particular, aromatic and aliphatic thiols. *N*(acyl),*S*-acetals are found in numerous pharmacologically relevant natural products and APIs alike. The most well-known of these being β-lactam antibiotics[69] and HIV-1 Reverse Transcriptase inhibitors.[67] Several methods have been developed for their synthesis, including a range of Brønsted acid catalyzed transformations,[70] however they typically require long reaction times and showed a limited scope towards certain functional groups. We reasoned that the use of calcium to mediate these reactions would have several advantages including much shorter reaction times, a wider functional group tolerance and overall easier reaction set up i.e. no requirement for anhydrous or air free condition. Traditionally, it would be expected that that the nucleophilic nature of these species would poison the catalyst, or at the very least, drastically hinder the catalytic turnover. However, to our delight, we found that the reaction using thiophenol proceeded well, with the reaction complete in under 15 minutes. Once again, we probed the substrate scope of the reaction, and a range of substituted hydroxyisoindolinones were subjected to our reaction conditions, resulting in a library of 3,3-disubstituted lactams (**Scheme 4**). As shown, the reaction was again tolerant of a range of functional groups with electron donating (**4a-b**) and withdrawing groups (**4c-e**) providing the desired products in high yields. Phenyl ring substituents was also well tolerated, with *ortho* and *meta* substituents proceeding smoothly (**4f-g**). Finally, heterocyclic substrates also worked well, providing the lactam products in high yields (**4h-j**).



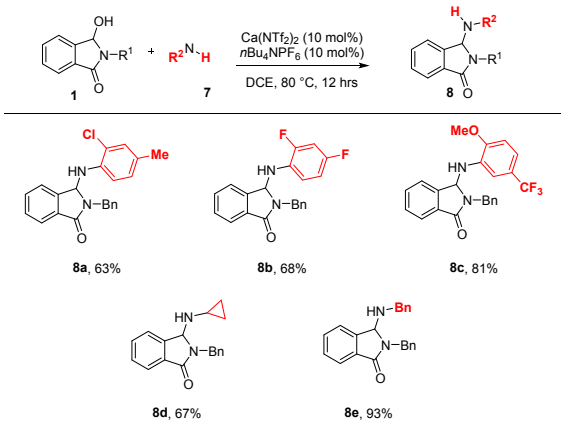

**Scheme 4. Thiophenol substrate scope**

As these examples all employed thiophenol as a nucleophile, we wanted to explore the tolerance of other sulfur derivatives. Once again, the reaction proceeded well, providing a wide range of medicinally relevant scaffolds (**Scheme 5**). In addition to the traditional electron donating (**6a, 6d, 6e)** and withdrawing (**6b, 6c)** groups, heteroaryl (**6f, 6g**), benzyl (**6h**) and alkyl (**6i, 6j**) substituents all worked well. Furthermore, boronate esters (**6k**) are also well tolerated, providing avenues for the modular synthesis of bioactive small molecules.



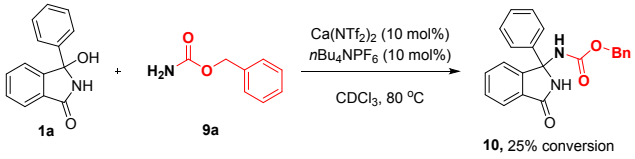

**Scheme 5. Scope of Sulfur Nucleophiles**

We next turned our attention to amine nucleophiles, as we envisaged that they would be more problematic in the reaction, mainly through direct Lewis acid-Lewis base interactions. Additionally, in contrast to their sulfur counterparts, 3-aminoisoindolinones are relatively underexplored in synthesis, with very few reports focusing on the synthesis of carbamate and sulfonamide derivatives. This is somewhat surprising, given the fact that many isoindolinones have exhibited marked activity against a range of bacterial infections[71-72] as well as interesting anticancer properties.[68] Due to this, we initially focused on delivering a robust method to produce these potentially high value molecules from readily available starting materials. We started our investigation employing our optimized conditions and simple amine nucleophiles (**Scheme 6**). We observed a clear trend in reactivity, in which only electron withdrawing anilines were tolerated, however we could never manage to isolate the products in useful yields. Additionally, the reaction was highly variable, and in our hands, remained unreproducible. On the small amount of material we did isolate, we observed a rapid degradation profile, with complete degradation after 2 hours, regardless of storage temperature. After some investigation, that the reaction employing N-Bn substituted hydroxyisoindolinones were much more user friendly, reproducibly providing the desired product in good yield. As shown, the reaction proceeded well, with substrates bearing contrasting electronics (**8a-c**) being tolerated. Furthermore, unsaturated (**8d**) and benzyl amines (**8e**) also worked well



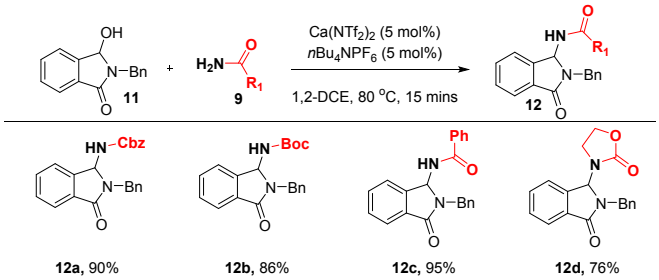

**Scheme 6. 3-Amino substituted isoindolinones**

Once complete, we probed the applicability of using less nucleophilic amine sources, such as the previously mentioned amide and sulfonamide moieties. Once again employing our optimized conditions, and using **1a** as our model substrate, we screened a range of carbamate nucleophiles. Unfortunately, all of these proved unsuccessful, with the reactions plateauing at 25% conversion (**Scheme 7**).



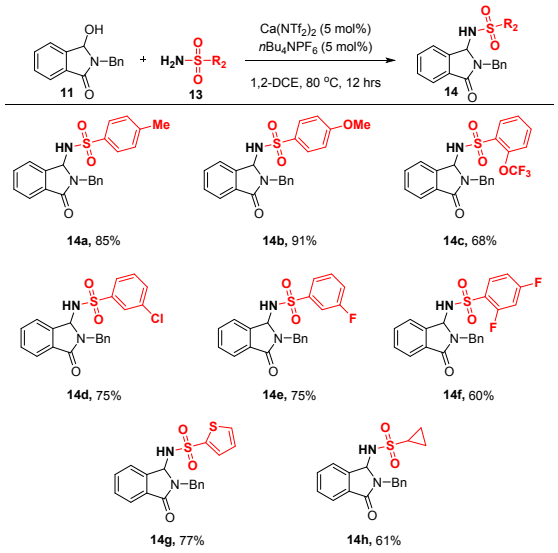

**Scheme 7. Reaction with Benzylcarbamate**

After extensive experimentation in which we screened a wide range of conditions including solvent, temperature, time and nucleophile, we were unsuccessful in delivering a reliable reaction that produced these compounds in synthetically useful yields. Although unsuccessful for compounds such as **1a**, we were successful in performing the reaction on **11** using a small range of carbamate and amide nucleophiles, as shown (**Scheme 8**). This provides a range of differentially protected amines (**12a-12c**), which has the potential to find use in target synthesis.




**Scheme 8. Carbamate and amide substitution reactions**

Due to the limited scope of these carbamates, we moved our attention to the more useful sulfonamides. Once again these have been seemingly ignored by the synthetic community, and therefore provides potentially new avenues of biological activities to be uncovered. The reactivity pattern remained, with only unsubstituted **11,** providing reproducible reactivity and good yields throughout. Probing the variability of the sulfonamides produced a range of useful scaffolds using 5 mol% of the catalyst system. As shown above (**Scheme9**), the reaction was once again tolerant to a range of synthetically useful functional groups including electron donating (**14a**, **14b**) withdrawing (**14c**) halides (**14d-f**) thiophene (**14g**). Furthermore, saturated groups (**14h**) also worked well, providing access to 3-dimensional scaffolds.




**Scheme 9. Functionalized isoindolinones bearing pendant sulfonamides**

As observed, the reaction is generally tolerant to a wide range of functional groups and nucleophiles. However, during the course of this work, we noted some limitations which we believe the community will find useful when deciding to use this methodology. Firstly, when employing amine nucleophiles, the reactions were very sluggish with tertiary alcohols such as **1a**, with many reactions not going to completion. This was consistent across all amine nucleophiles used in this study. In a similar vein, we also observed that the choice of amine was important, with secondary amines such as piperidine and morpholine providing variable reactivity patterns, with irreproducible results being obtained. Secondly, carbon based nucleophiles (outside indole and allylsilane) were unreactive towards the conditions described here. We are currently working on this, and hope to report on it soon.

A proposed general mechanism is provided below (**Fig. 2**). The postulated active catalyst, $[CaPF_6NTf_2]$ **A**, is formed between $Ca(NTf_2)_2$ and $nBu_4NPF_6$ which in turn produces N-acyliminium ion **B** and complex **C** via loss of the non-coordinating $PF_6$ ligand**.** Following nucleophilic attack, the aforementioned displaced $PF_6$ re-enters the cycle, providing the product, water byproduct and reforming the active catalyst.

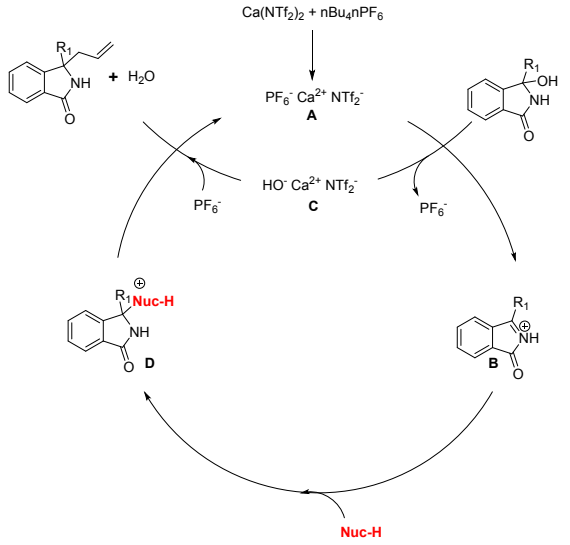



**Figure 2. Proposed general catalytic cycle**

In conclusion, we have developed a robust and high yield methodology to afford a range of substituted isoindolinones. Using low loadings of catalyst, the reaction proceeded smoothly, with reaction times ranging from 15 minutes to 12 hours. The reaction is tolerant towards a series of traditional nucleophiles including carbon, nitrogen and sulfur containing moieties. We envisage that this methodology will find use within medicinal chemistry campaigns due to the range of biological activities these scaffolds have shown.

## EXPERIMENTAL SECTION

**Solvents and Reagents.** All solvents were purchased from commercial sources and used without purification (HPLC or analytical grade). Anhydrous solvent was obtained from a The Solv™ Solvent Purification System. Standard vacuum line techniques were used and glassware was oven dried prior to use. Organic solvents were dried during workup using anhydrous $Na_2SO_4$. All calcium catalyzed reactions where done without the need for anhydrous or air free conditions. All reaction were performed using DrySyn™ heating mantles and pressure regulated vials.

**Purification and chromatography.** Thin Layer Chromatography (TLC) was carried out using aluminum plates coated with 60 F254 silica gel. Plates were visualized using UV light (254 or 365 nm) or staining with 1% aq. $KMnO_4$, vanillin or ninhydrin. Normal-phase silica gel chromatography was carried out using either a Biotage Isolera One flash column chromatography system (LPLC) or traditional flash column chromatography using Geduran® Silica gel 60, 40–63 microns RE.

**Characterization.** Infrared spectroscopy was carried out with a Nicolet® 380 FT/IR – Fourier Transform Infrared Spectrometer. Only the most significant frequencies have been considered during the characterization and selected absorption maxima (vmax) recorded in wavenumbers ($cm^{-1}$). NMR spectra were recorded using a JEOL® ECS-400 MHz spectrometer using the deuterated solvent stated. Chemical shifts (δ) quoted in parts per million (ppm) and referenced to the residual solvent peak. Multiplicities are denoted as s- singlet, d- doublet, t- triplet, q- quartet and quin- quintet and derivatives thereof (br denotes a broad resonance peak). Coupling constants recorded as Hz and round to the nearest 0.1 Hz. High Resolution Mass Spectrometry (HRMS) was recorded using an Agilent Technologies® 6540 Ultra-High-Definition (UHD) AccurateMass equipped with a time of flight (Q-TOF) analyzer and the samples were ionized by ESI techniques and introduced through a high pressure liquid chromatography (HPLC) model Agilent Technologies® 1260 Infinity Quaternary LC system.

*3-(5-bromo-1H-indol-3-yl)-3-phenyl-2,3-dihydro-1H-isoindol-1-one (**3a**)*. To a 4 mL vial was added 3-hydroxy-3-phenylisoindolin-1-one (50 mg, 0.22 mmol), $Ca(NTf_2)_2$ (1.3 mg, 0.0022 mmol) and $n$$Bu_4NPF_6$ (1 mg, 0.0022 mmol) in DCE (1 mL) at 80 ºC. The reaction was stirred for 1 minute and 5-bromoindole (65 mg, 0.33 mmol) was added in a single portion and stirred at 80 ºC for 15 minutes. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (3:1 EtOAc:Hex) to afford a cream solid (73 mg, 82%). RF (3:1 EtOAc/Hex) = 0.37. IR $\nu_{max}$ ($cm^{-1}$): 3209, 3058, 1978, 1671, 1491, 1314. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{16}BrN_2O$ 403.0446; found 403.0441.. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 11.30 (s, 1H), 9.73 (s, 1H), 7.74 (d, $J$ = 7.4 Hz, 1H), 7.64 – 7.57 (m, 2H), 7.53 (dq, $J$ = 4.7, 4.1 Hz, 1H), 7.45 (d, $J$ = 7.2 Hz, 2H), 7.40 – 7.25 (m, 4H), 7.16 (dd, $J$ = 8.6, 1.6 Hz, 1H), 6.94 (dd, $J$ = 15.7, 1.8 Hz, 2H). $^{13}$C {$^1$H} (101 MHz, DMSO-$d_6$): δ 168.6, 150.6, 142.5, 135.8, 132.1, 130.9, 128.5, 127.6, 126.9, 126.3, 125.9, 124.2, 123.9, 123.3, 122.1, 116.5, 113.8, 111.4, 65.9.

Reaction also performed on a 2.2 mmol from 3-hydroxy-3-phenylisoindolin-1-one (500 mg, 2.20 mmol), $Ca(NTf_2)_2$ (13 mg, 0.02 mmol) and $n$$Bu_4NPF_6$ (9 mg, 0.02 mmol) with 5-bromoindole (653 mg, 3.33 mmol) in DCE (10 mL) for 2.5 h. Purification (3:1 EtOAc:Hex) afforded the product as a cream solid (880 mg, 98%)

*3-[3,5-bis(trifluoromethyl)phenyl]-3-(5-bromo-1H-indol-3-yl)-2,3-dihydro-1H-isoindol-1-one (**3b**)*. To a 4 mL vial was added 3-hydroxy-3-(3,5-bis(trifluoromethyl))isoindolin-1-one (50 mg, 0.14 mmol), $Ca(NTf_2)_2$ (4 mg, 0.0069 mmol) and $n$$Bu_4NPF_6$ (3 mg, 0.0069 mmol) in DCE (1 mL) at 80 ºC. The reaction was stirred for 1 minute and 5-bromoindole (41 mg, 0.21 mmol) was added in a single portion and stirred at 80 ºC for 30 minutes. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (1:1, EtOAC:Hex) to afford a cream solid (68 mg, 91%). RF (1:1 EtOAc/Hex) = 0.33 . IR $\nu_{max}$ ($cm^{-1}$): 3333, 3185, 3052, 1978, 1669, 1368. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{24}H_{14}BrF_6N_2O$ 539.0194; found 539.0188. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 11.44 (s, 1H), 9.91 (s, 1H), 8.16 (s,1H), 8.11 (s, 2H), 7.79 (dd, $J$ = 15.3, 7.5 Hz, 2H), 7.67 (t, $J$ = 7.4 Hz, 1H), 7.60 (t, $J$ = 7.4 Hz, 1H), 7.38 (d, $J$ = 8.6 Hz, 1H), 7.19 (dd, $J$ = 8.7, 1.3 Hz, 1H), 6.98 (d, $J$ = 2.4 Hz, 1H), 6.83 (s, 1H). $^{13}$C{$^1$H} NMR (101 MHz, DMSO-$d_6$):δ 168.4, 149.0, 145.9, 135.8, 132.8, 130.8, 130.5(q, $J_F$ = 32.3 Hz), 129.3, 127.0, 126.9, 126.3, 124.6, 124.3, 124.2, 123.6, 122.1, 121.8, 121.4, 115.1, 114.1, 111.7, 65.5.

*3-(5-bromo-1H-indol-3-yl)-3-(4-methoxyphenyl)-2,3-dihydro-1H-isoindol-1-one (**3c**)*. To a 4 mL vial was added 3-(4-methoxyphenyl)-3-hydroxyisoindolin-1-one (50 mg, 0.20 mmol mmol), $Ca(NTf_2)_2$ (1.1 mg, 0.002 mmol) and $n$$Bu_4NPF_6$ (0.8 mg, 0.002 mmol) in DCE (1 mL) at 80 ºC. The reaction was stirred for 1 minute and 5-bromoindole (58 mg, 0.29 mmol)

was added in a single portion and stirred at 80 ºC for 30 minutes. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (1:1, EtOAc:Hex) to afford a cream solid (79 mg, 93%). RF (1:1 EtOAc/DCM) = 0.41. IR $\nu_{max}$ ($cm^{-1}$): 3169, 3040, 2838, 1668, 1608, 1255. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{23}H_{18}BrN_2O_2$ 433.0552; ; found 433.0549.. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 11.28 (s, 1H), 9.67 (s, 1H), 7.73 (d, *J* = 7.3 Hz, 1H), 7.65 – 7.46 (m, 3H), 7.34 (t, *J* = 8.6 Hz, 3H), 7.16 (d, *J* = 8.5 Hz, 1H), 7.01 (s, 1H), 6.99 – 6.79 (m, 3H), 3.72 (s, 3H). $^{13}$C{$^1$H}NMR (101 MHz, DMSO-$d_6$): δ 168.5, 158.6, 150.9, 135.8, 134.4, 132.0, 130.9, 128.4, 127.6, 126.9, 125.9, 124.1, 123.9, 123.2, 122.2, 116.7, 113.8, 113.7, 111.4, 65.50, 55.11.

*3-(5-bromo-1H-indol-3-yl)-3-(thiophen-2-yl)-2,3-dihydro-1H-isoindol-1-one (**3d**)*. To a 4 mL vial was added 3-hydroxy-3-(thiophen-2-yl)isoindolin-1-one (50 mg, 0.22 mmol), $Ca(NTf_2)_2$ (1.3 mg, 0.0022 mmol) and $n$Bu$_4$NPF$_6$ (0.9 mg, 0.0022 mmol) in DCE (1 mL) at 80 ºC. The reaction was stirred for 1 minute and 5-bromoindole (64 mg, 0.32 mmol) was added in a single portion and stirred at 80 ºC for 30 minutes. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (1:1 EtOAc:DCM) to afford a light brown solid (85 mg, 96%). RF (1:1 EtOAc/DCM) = 0.38. IR $\nu_{max}$ ($cm^{-1}$): 3172, 3041, 2851, 1667, 1466, 1356. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{14}BrN_2OS$ 409.0010 ; found 409.0007. Cald. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 11.36 (m, 1H), 9.85 (s, 1H), 7.76 (d, *J* = 7.4 Hz, 1H), 7.68 – 7.51 (m, 3H), 7.45 (d, *J* = 5.0 Hz, 1H), 7.35 (d, *J* = 8.6 Hz, 1H), 7.17 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.08 (m, 2H), 7.05 – 6.92 (m, 2H). $^{13}$C{$^1$H} NMR (101 MHz, DMSO-$d_6$): δ 168.3, 150.6, 147.3, 135.7, 132.3, 130.5, 128.8, 127.2, 126.7, 126.0, 125.7, 125.5, 124.0, 123.9, 123.2, 121.9, 115.4, 113.9, 111.6, 63.53.

*3-(2H-1,3-benzodioxol-5-yl)-3-(5-bromo-3a,7a-dihydro-1H-indol-2-yl)-2,3-dihydro-1H-isoindol-1-one (**3e**)*. To a 4 mL vial was added 3-(benzo[d][1,3]dioxol-5-yl)isoindolin-1-one (50 mg, 0.19 mmol), $Ca(NTf_2)_2$ (1.1 mg, 0.0019 mmol) and $n$Bu$_4$NPF$_6$ (0.7 mg, 0.0019 mmol) in DCE (1 mL) at 80 ºC. The reaction was stirred for 1 minute and 5-bromoindole (64 mg, 0.32 mmol) was added in a single portion and stirred at 80 ºC for 30 minutes. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (2:1, EtOAc:Hex) to afford a cream solid (78 mg, 94%). RF (2:1 EtOAc/Hex) = 0.17. IR $\nu_{max}$ ($cm^{-1}$): 3219, 2896, 1674, 1611, 1485, 1237. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{23}H_{16}BrN_2O_3$ 447.0344 ; found 447.0350. $^1$H NMR (400 MHz, $CDCl_3$): δ 8.25 (s, 1H), 7.89 (d, *J* = 7.4 Hz, 1H), 7.63 – 7.40 (m, 3H), 7.31 – 7.21 (m, 2H), 7.16 (s, 1H), 6.96 – 6.85 (m, 3H), 6.82 (d, *J* = 1.8 Hz, 1H), 6.72 (d, *J* = 8.2 Hz, 1H), 5.95 (dd, *J* = 6.6, 1.1 Hz, 2H). $^{13}$C{$^1$H} NMR (101 MHz, $CDCl_3$): δ 169.9, 150.9, 148.3, 147.7, 135.9, 135.3, 132.6, 128.8, 127.3, 125.9, 124.6, 124.3, 123.7, 122.7, 119.9, 117.7, 113.7, 113.3, 108.5, 107.2, 101.5, 66.5.

*3-phenyl-3-[5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3a,7a-dihydro-1H-indol-2-yl]-2,3-dihydro-1H-isoindol-1-one (**3f**)*. To a 4 mL vial was added 3-hydroxy-3-phenylisoindolin-1-one (50 mg, 0.22 mmol), $Ca(NTf_2)_2$ (1.3 mg, 0.0022 mmol) and $n$Bu$_4$NPF$_6$ (0.9 mg, 0.0022 mmol) in DCE (1 mL) at 80 ºC. The reaction was stirred for 1 minute and 5-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indole (81 mg, 0.33 mmol) was added in a single portion and stirred at 80 ºC for 1h. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (2:1, EtOAc:Hex) to afford a white solid (90 mg, 90%). RF (3:1 EtOAc/Hex) = 0.48. IR $\nu_{max}$ ($cm^{-1}$): 3257, 2976, 1683, 1613, 1352, 1142. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{28}H_{28}BN_2O_3$ 451.2193; found 451.2204. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 11.20 (s, 1H), 9.73 (s, 1H), 7.74 (d, *J* = 7.3 Hz, 1H), 7.65 – 7.44 (m, 4H), 7.44 – 7.22 (m, 7H), 6.88 (d, *J* = 2.2 Hz, 1H), 1.22 (s, 12H). $^{13}$C{$^1$H} NMR (101 MHz, DMSO-$d_6$): δ 168.6, 151.1, 142.9, 139.2, 131.9, 131.0, 128.4, 128.3, 127.7, 127.5, 127.5, 126.5, 124.8, 124.3, 124.2, 123.2, 117.2, 111.2, 83.0, 66.2, 24.8, 24.6.

*3-(4-chlorophenyl)-3-[5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3a,7a-dihydro-1H-indol-2-yl]-2,3-dihydro-1H-isoindol-1-one (**3g**)*. To a 4 mL vial was added 3-(4-chlorophenyl)-3-hydroxyisoindolin-1-one (50 mg, 0.19 mmol), $Ca(NTf_2)_2$ (1mg, 0.0019 mmol) and $n$Bu$_4$NPF$_6$ (0.8 mg, 0.0019 mmol) in DCE (1 mL) at 80 ºC. The reaction was stirred for 1 minute and 5-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indole (70 mg, 0.29 mmol) was added in a single portion and stirred at 80 ºC for 30 mins. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (1:1, EtOAc:Hex) to afford a white solid (87 mg, 93%). RF (1:1 EtOAc/Hex) = 0.19. IR $\nu_{max}$ ($cm^{-1}$): 3237, 2977, 1673, 1613, 1469, 1352. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{28}H_{27}BClN_2O_3$ 485.1803; found 485.1815. . $^1$H NMR (400 MHz, DMSO-$d_6$): δ 11.24 (d, *J* = 1.9 Hz, 1H), 9.77 (s, 1H), 7.74 (d, *J* = 7.3 Hz, 1H), 7.64 – 7.49 (m, 3H), 7.46 – 7.29 (m, 7H), 6.89 (d, *J* = 2.1 Hz, 1H), 1.23 (s, 12H). $^{13}$C{$^1$H}NMR (101 MHz, DMSO-$d_6$): δ 168.6, 150.7, 142.0, 139.2, 132.2, 132.2, 131.0, 128.5, 128.4, 127.6, 127.6, 124.9, 124.7, 124.1, 123.3, 116.7, 111.3, 83.03, 65.8, 24.8, 24.7.

*3-(2-methoxyphenyl)-3-[5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3a,7a-dihydro-1H-indol-2-yl]-2,3-dihydro-1H-isoindol-1-one (**3h**)*. To a 4 mL vial was added 3-hydroxy-3-(2-methoxyphenyl)isoindolin-1-one (50 mg, 0.20 mmol), $Ca(NTf_2)_2$ (1.2 mg, 0.0020 mmol) and $n$Bu$_4$NPF$_6$ (0.8 mg, 0.0020 mmol) in DCE (1 mL) at 80 ºC. The reaction was stirred for 1 minute and 5-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indole (71 mg, 0.29 mmol) was added in a single portion and stirred at 80 ºC for 30 mins. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (2:1, EtOAc:Hex) to afford an off white solid (92 mg, 98%). RF (2:1 EtOAc/Hex) = 0.17. IR $\nu_{max}$ ($cm^{-1}$): 3414, 3264, 3008, 1680, 1612, 1351. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{29}H_{30}BN_2O_4$ 481.2299; found 481.2314. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 11.06 (d, *J* = 1.9 Hz, 1H), 9.16 (s, 1H), 7.79 – 7.69 (m, 1H), 7.58 – 7.46 (m, 4H), 7.40 – 7.28 (m, 3H), 7.21 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.04 (d, *J* = 7.7 Hz, 1H), 6.93 – 6.85 (m, 1H), 6.82 (d, *J* = 2.4 Hz, 1H), 3.51 (s, 3H), 1.23 (s, 12H). $^{13}$C{$^1$H} NMR (101 MHz, DMSO-$d_6$): δ 168.6, 157.9, 150.7, 139.0, 131.6, 131.4, 129.7, 129.5, 128.1, 127.7, 127.4, 127.2, 124.7, 124.6, 123.5, 123.1, 119.9, 117.1, 112.6, 111.1, 83.0, 79.2, 65.4, 55.4, 24.1, 24.7.

*3-(furan-2-yl)-3-[5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3a,7a-dihydro-1H-indol-2-yl]-2,3-dihydro-1H-isoindol-1-one (**3i**)*. To a 4 mL vial was added 3-hydroxy-3-(furan-2-yl)isoindolin-1-one (50 mg, 0.23 mmol), $Ca(NTf_2)_2$ (1.4 mg, 0.0023 mmol) and $n$Bu$_4$NPF$_6$ (0.9 mg, 0.0023 mmol) in DCE (1 mL) at 80 ºC. The reaction was stirred for 1 minute and 5-

(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indole (85 mg, 0.35 mmol) was added in a single portion and stirred at 80 ºC for 30 mins. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (1:1 EtOAc:Hex) to afford a pale orange solid (84 mg, 82%). RF (2:1 EtOAc/Hex) = 0.35. IR $\nu_{max}$ ($cm^{-1}$): 3295, 3059, 2869, 1679, 1614, 1377. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{26}H_{26}BN_2O_4$ 441.1989; found 441.1993.. $^1H$ NMR (400 MHz, DMSO-$d_6$): δ 11.25 (d, $J$ = 2.1 Hz, 1H), 9.70 (s, 1H), 7.80 – 7.73 (m, 1H), 7.70 – 7.65 (m, 1H), 7.63 – 7.50 (m, 3H), 7.41 – 7.30 (m, 3H), 6.97 (d, $J$ = 2.5 Hz, 1H), 6.45 (dd, $J$ = 3.2, 1.8 Hz, 1H), 6.30 (dd, $J$ = 3.2, 0.6 Hz, 1H), 1.25 (s, 12H). $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-$d_6$): δ 169.0, 155.3, 149.5, 143.7, 139.4, 132.6, 131.6, 129.2, 127.9, 127.5, 125.0, 124.4, 123.6, 115.5, 111.8, 110.9, 107.5, 83.5, 62.6, 25.3, 25.2.

*3-[3,5-bis(trifluoromethyl)phenyl]-3-[5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3a,7a-dihydro-1H-indol-2-yl]-2,3-dihydro-1H-isoindol-1-one (**3j**)*. To a 4 mL vial was added 3-hydroxy-3-(3,5-bis(trifluoromethyl))isoindolin-1-one (50 mg, 0.14 mmol), $Ca(NTf_2)_2$ (0.8 mg, 0.0014 mmol) and $n$$Bu_4NPF_6$ (0.5 mg, 0.0014 mmol) in DCE (1 mL) at 80 ºC. The reaction was stirred for 1 minute and 5-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indole (51 mg, 0.21 mmol) was added in a single portion and stirred at 80 ºC for 30 mins. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (1:1, EtOAc:Hex) to afford an off white solid (66 mg, 81%). RF (1:1 EtOAc/Hex) = 0.30. IR $\nu_{max}$ ($cm^{-1}$): 3273, 2980, 1695, 1355, 1275, 1131. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{30}H_{26}BF_6N_2O_3$ 587.1941; found 587.1947.. $^1H$ NMR (400 MHz, $CDCl_3$): δ 8.56 (s, 1H), 7.99 – 7.88 (m, 3H), 7.81 (s, 1H), 7.69 – 7.57 (m, 2H), 7.57 – 7.48 (m, 1H), 7.43 (d, $J$ = 7.6 Hz, 1H), 7.41 – 7.29 (m, 2H), 7.18 (s, 1H), 1.28 (s, 12H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 170.2, 149.6, 145.3, 139.4, 133.2 (q, $J_F$ = 33.4 *Hz*), 132.0, 130.1, 129.3, 129.3, 126.8, 126.8, 125.0, 124.7, 124.6, 123.8, 123.6, 122.2, 121.9, 116.3, 111.6, 83.75, 66.24, 24.9, 24.8.

*3-phenyl-3-phenylsulfanyl-2,3-dihydro-isoindol-1-one (**4a**)*. To a 4 mL vial was added 3-hydroxy-3-phenylisoindolin-1-one (50 mg, 0.22 mmol), $Ca(NTf_2)_2$ (3 mg, 0.0022 mmol) and $n$$Bu_4NPF_6$ (1.7 mg, 0.0022 mmol) in DCE (1 mL) at 80 ºC. The reaction was stirred for 5 minutes and thiophenol (29 mg, 0.27 mmol) was added in a single portion and stirred at 80 ºC for 15 minutes. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (1:1, EtOAc:Hex) to afford a white solid (54 mg, 77%). RF (1:1 EtOAc/Hex) = 0.43. IR $\nu_{max}$ ($cm^{-1}$): 3062, 2848, 1696, 1494, 1345, 742. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{16}NOS$ 318.0953; found 318.0947. $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.84 – 7.75 (m, 2H), 7.73 – 7.67 (m, 1H), 7.56 (td, $J$ = 7.5, 1.1 Hz, 1H), 7.51 – 7.29 (m, 6H), 7.24 – 7.18 (m, 1H), 7.14 (dt, $J$ = 8.2, 1.7 Hz, 1H), 7.08 – 7.02 (m, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 169.2, 148.7, 139.1, 137.1, 132.6, 129.9, 129.8, 129.4, 129.2, 129.0, 128.7, 128.6, 126.1, 123.9, 123.4, 75.79.

Reaction also performed on a 2.0 mmol from 3-hydroxy-3-phenylisoindolin-1-one (450 mg, 2.0 mmol), $Ca(NTf_2)_2$ (12 mg, 0.02 mmol) and $n$$Bu_4NPF_6$ (8 mg, 0.02 mmol) with thiophenol (265 mg, 2.40 mmol) in DCE (9 mL) for 30 min. Purification (1:1 EtOAc:Hex) afforded the product as a white solid (608 mg, 96%)

*3-(4-methoxyphenyl)-3-(phenylthio)isoindolin-1-one (**4b**)*. To a 4 mL vial was added 3-(4-methoxyphenyl)-3-hydroxyisoindolin-1-one (60 mg, 0.24 mmol), $Ca(NTf_2)_2$ (1.5 mg, 0.0024 mmol) and $n$$Bu_4NPF_6$ (1 mg, 0.0024 mmol) in DCE (1 mL) at 80 ºC. The reaction was stirred for 5 minutes and thiophenol (39 mg, 0.353 mmol) was added in a single portion and stirred at 80 ºC for 15 minutes. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (1:1 EtOAc:Hex) to afford a white solid (70 mg, 86%). RF (1:1 EtOAc/CycHex) = 0.53. IR $\nu_{max}$ ($cm^{-1}$): 3057, 2930, 2849, 1700, 1606, 1509. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{21}H_{18}NO_2S$ 348.1058; found 348.1053. $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.74 – 7.64 (m, 3H), 7.61 – 7.51 (m, 1H), 7.46 (d, $J$ = 7.5 Hz, 1H), 7.35 – 7.28 (m, 1H), 7.24 – 7.18 (m, 1H), 7.17 – 7.11 (m, 3H), 7.11 – 7.01 (m, 2H), 6.97 – 6.88 (m, 2H), 3.81 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): 169.1, 160.0, 148.9, 137.1, 132.5, 131.1, 131.04, 129.9, 129.8, 129.6, 128.6, 127.5, 123.8, 123.4, 114.4, 75.5, 55.5..

*3-(4-chlorophenyl)-3-(phenylthio)isoindolin-1-one (**4c**)*. To a 4 mL vial was added 3-(4-chlorophenyl)-3-hydroxyisoindolin-1-one (100 mg, 0.39 mmol), $Ca(NTf_2)_2$ (2 mg, 0.0039 mmol) and $n$$Bu_4NPF_6$ (1.5 mg, 0.0039 mmol) in DCE (2 mL) at 80 ºC. The reaction was stirred for 5 minutes and thiophenol (64 mg, 0.578 mmol) was added in a single portion and stirred at 80 ºC for 15 minutes. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (1:1, EtOAC:Hex) to afford a white solid (116 mg, 86%). RF (1:1 EtOAc/CycHex) = 0.6. IR $\nu_{max}$ ($cm^{-1}$): 3130, 3062, 2851, 1702, 1470, 1096. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{15}ClNOS$ 352.0563; found 352.0559. $^1H$ NMR (400 MHz, DMSO-$d_6$): 9.84 (s, 1H), 7.98 – 7.72 (m, 3H), 7.72 – 7.59 (m, 1H),7.58-7.56 (m, 2H), 7.45 – 7.20 (m, 3H), 7.20 – 6.90 (m, 4H). $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-$d_6$): δ167.7, 147.5, 138.5, 136.71, 133.4, 132.4, 130.3, 129.7, 129.1, 128.9, 128.8, 128.4, 128.0, 124.0, 122.4, 74.9.

*4-(1-Hydroxy-3-oxoisoindolin-1-yl)benzonitrile (**4d**)*. To a 4 mL vial was added 4-(1-hydroxy-3-oxoisoindolin-1-yl)benzonitrile (50 mg, 0.20 mmol), $Ca(NTf_2)_2$ (1.2 mg, 0.002 mmol) and $n$$Bu_4NPF_6$ (0.8 mg, 0.002 mmol) in DCE (1 mL) at 80 ºC. The reaction was stirred for 5 minutes and thiophenol (33 mg, 0.3 mmol) was added in a single portion and stirred at 80 ºC for 15 minutes. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (1:1, EtOAc:Hex) to afford a cream solid (54 mg, 79%). RF (1:1 EtOAc/CycHex) = 0.50. IR $\nu_{max}$ ($cm^{-1}$): 3215, 3075, 2229, 1714, 1679, 1497. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{21}H_{15}N_2OS$ 343.0905; found 343.0907. $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.93 (d, $J$ = 8.5 Hz, 2H), 7.71 (d, $J$ = 8.5 Hz, 2H), 7.68 – 7.57 (m, 2H), 7.54 – 7.46 (m, 2H), 7.38 (t, $J$ = 7.3 Hz, 1H), 7.25 – 7.21 (m, 1H), 7.14 (d, $J$ = 6.9 Hz, 2H), 7.11 – 7.04 (m, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 169.3, 147.7, 144.5, 137.1, 133.0, 132.9, 130.2, 129.3, 128.9, 128.7, 127.2, 123.8, 123.7, 118.4, 112.9, 75.1.

*3-(4-trifluoromethylphenyl)-3-(phenylthio)isoindolin-1-one (**4e**)*. To a 4 mL vial was added 3-hydroxy-3-(4-(trifluoromethyl)phenyl)isoindolin-1-one (60 mg, 0.21 mmol), $Ca(NTf_2)_2$ (1.2 mg, 0.0021 mmol) and $n$$Bu_4NPF_6$ (0.8 mg,

0.0021 mmol) in DCE (1 mL) at 80 ºC. The reaction was stirred for 5 minutes and thiophenol (34 mg, 0.307 mmol) was added in a single portion and stirred at 80 ºC for 15 minutes. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (1:1, EtOAc:Hex) to afford a white solid (76 mg, 96%). RF (1:1 EtOAc/CycHex) = 0.60. IR $\nu_{max}$ ($cm^{-1}$): 3126, 3071, 1699, 1496, 1392. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{21}H_{15}F_3NOS$ 386.0826; found 386.0823.. $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.93 (d, *J* = 8.3 Hz, 1H), 7.73 – 7.62 (m, 2H), 7.59 (t, *J* = 7.0 Hz, 1H), 7.50 (d, *J* = 7.5 Hz, 1H), 7.36 (t, *J* = 7.3 Hz, 1H), 7.24 - 7.23 (m, 3.6 Hz, 1H), 7.15 – 7.07 (m, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 169.1, 148.1, 143.3, 137.1, 132.9, 130.1, 129.7, 129.2, 128.9, 128.8, 126.7, 126.2, 126.2, 123.7, 75.2.

*3-(2-methoxyphenyl)-3-(phenylthio)isoindolin-1-one (**4f**)*. To a 4 mL vial was added 3-(2-methoxyphenyl)-3-hydroxyisoindolin-1-one (100 mg, 0.39 mmol), $Ca(NTf_2)_2$ (2.4 mg, 0.0039 mmol) and $n$$Bu_4NPF_6$ (1.5 mg, 0.0039 mmol) in DCE (2 mL) at 80 ºC. The reaction was stirred for 5 minutes and thiophenol (65 mg, 0.353 mmol) was added in a single portion and stirred at 80 ºC for 15 minutes. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (1:1, EtOAc:Hex) to afford a white solid (115 mg, 84%). RF (1:1 EtOAc/CycHex) = 0.40. IR $\nu_{max}$ ($cm^{-1}$): 3283, 3051, 2932, 1692, 1489, 1249. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{21}H_{18}NO_2S$ 348.1058; found 348.1050. $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.95 – 7.80 (m, 2H), 7.64 (td, *J* = 7.6, 1.1 Hz, 1H), 7.59 – 7.47 (m, 2H), 7.44 – 7.32 (m, 2H), 7.21 – 7.14 (m, 1H), 7.14 – 7.09 (m, 2H), 7.08 – 7.01 (m, 3H), 6.92 (td, *J* = 7.7, 1.1 Hz, 1H), 4.02 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 168.0, 157.8, 146.4, 136.8, 131.5, 131.4, 130.5, 129.4, 128.7, 128.4, 127.4, 126.5, 125.6, 123.5, 120.8, 112.8, 74.5, 56.2.

*3-(3,5-bis(trifluoromethyl))-3-(phenylthio)isoindolin-1-one (**4g**)*. To a 4 mL vial was added 3-hydroxy-3-(3,5-bis(trifluoromethyl))isoindolin-1-one (100 mg, 0.28 mmol), $Ca(NTf_2)_2$ (1.7 mg, 0.0028 mmol) and $n$$Bu_4NPF_6$ (1 mg, 0.0028 mmol) in DCE (2 mL) at 80 ºC. The reaction was stirred for 5 minutes and thiophenol (46 mg, 0.42 mmol) was added in a single portion and stirred at 80 ºC for 15 minutes. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (2:3, EtOAc:Hex) to afford a white solid (113 mg, 90%). RF (2:3 EtOAc/CycHex) = 0.56. IR $\nu_{max}$ ($cm^{-1}$): 3208, 3094, 1715, 1469, 1312, 1280. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{14}F_6NOS$ 454.0700; found 454.0699. $^1H$ NMR (400 MHz, $CDCl_3$): δ 8.26 (s, 2H), 7.89 (s, 1H), 7.64 – 7.62 (m, 2H), 7.53 (d, *J* = 7.7 Hz, 1H), 7.47 – 7.36 (m, 1H), 7.28 – 7.24 (m, 2H), 7.20 – 7.05 (m, 4H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 167.6, 146.1, 142.6, 136.7, , 131.6 (d, *J* = 238 Hz), 131.1, 130.8, , 130.1, 129.4, 128.6, 128.6, 126.8, , 124.2, 123.1 (d, *J* = 275 Hz), 123.0, 122.8, , 74.5.

*3-(thiophen-2-yl)-3-(phenylthio)isoindolin-1-one (**4h**)*. To a 4 mL vial was added 3-hydroxy-3-(thiophen-2-yl)isoindolin-1-one (100 mg, 0.43 mM), $Ca(NTf_2)_2$ (2.4 mg, 0.0043 mmol) and $n$$Bu_4NPF_6$ (1.5 mg, 0.0043 mmol) in DCE (2 mL) at 80 ºC. The reaction was stirred for 5 minutes and thiophenol (72 mg, 0.65 mmol) was added in a single portion and stirred at 80 ºC for 15 minutes. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (1:1, EtOAc:Hex) to afford a light brown solid (120 mg, 86%). RF (1:1 EtOAc/CycHex) = 0.60. IR $\nu_{max}$ ($cm^{-1}$): 3155, 3060, 2836, 1691, 1470, 1354. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{14}NOS_2$ 324.0517; found 324.0516. $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.75 (d, *J* = 7.8 Hz, 1H), 7.59 (td, *J* = 7.5, 0.9 Hz, 1H), 7.50 (d, *J* = 7.5 Hz, 1H), 7.39 – 7.29 (m, 3H), 7.24 – 7.23 (m, 1H), 7.18 – 7.16 (m, 2H), 7.13 – 7.05 (m, 2H), 7.01 (dd, *J* = 5.0, 3.7 Hz, 1H), 6.92 – 6.91 (m, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 168.8, 148.2, 143.0, 136.9, 132.7, 130.0, 129.5, 129.5, 129.1, 128.7, 127.6, 126.4, 125.7, 123.8, 123.4, 72.8.

*3-(furan-2-yl)-3-(phenylthio)isoindolin-1-one (**4i**)*. To a 4 mL vial was added 3-hydroxy-3-(furan-2-yl)isoindolin-1-one (50 mg, 0.23 mmol), $Ca(NTf_2)_2$ (1.4 mg, 0.0023 mmol) and $n$$Bu_4NPF_6$ (1 mg, 0.0023 mmol) in DCE (1 mL) at 80 ºC. The reaction was stirred for 5 minutes and thiophenol (38 mg, 0.35 mmol) was added in a single portion and stirred at 80 ºC for 15 minutes. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (1:1, EtOAc:Hex) to afford a light brown solid (70 mg, 98%). RF (1:1 EtOAc/CycHex) = 0.6. IR $\nu_{max}$ ($cm^{-1}$): 3153, 3060, 1689, 1500, 1307, 1154. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{14}NO_2S$ 308.0745; found 308.0748. $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.86 (t, *J* = 10.3 Hz, 1H), 7.65 – 7.57 (m, 2H), 7.51 (d, *J* = 0.9 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.31 – 7.20 (m, 2H), 7.18 – 7.10 (m, 4H), 6.94 (s, 1H), 6.37 – 6.28 (m, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, DMSOd-$_6$): δ 167.6, 150.7, 145.8, 144.0, 136.7, 132.4, 130.4, 129.7, 129.2, 128.6, 128.5, 124.1, 122.4, 110.9, 108.2, 70.6.

*3-(benzo[d][1,3]dioxol-5-yl)-3-(phenylthio)isoindolin-1-one (**4j**)*. To a 4 mL vial was added 3-(benzo[d][1,3]dioxol-5-yl)isoindolin-1-one (80 mg, 0.30 mmol), $Ca(NTf_2)_2$ (1.8 mg, 0.003 mmol) and $n$$Bu_4NPF_6$ (1.2 mg, 0.003 mmol) in DCE (1 mL) at 80 ºC. The reaction was stirred for 5 minutes and thiophenol (33 mg, 0.3 mmol) was added in a single portion and stirred at 80 ºC for 15 minutes. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (1:1, EtOAc:Hex) to afford a peach solid (98 mg, 91%). RF (1:1 EtOAc/CycHex) = 0.56. IR $\nu_{max}$ ($cm^{-1}$): 3209, 2902, 1706, 1671, 1485, 1246. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{21}H_{16}NO_3S$ 362.0851; found 362.0852. $^1H$ NMR (400 MHz, $CDCl_3$): δ 9.74 (s, 1H), 7.88 (d, *J* = 7.7 Hz, 1H), 7.62 (t, *J* = 7.4 Hz, 1H), 7.38 – 7.30 (m, 2H), 7.29 – 7.18 (m, 4H), 7.10 (d, *J* = 4.3 Hz, 5H), 6.96 (d, *J* = 8.2 Hz, 1H), 6.06 (s, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$):δ 167.6, 147.7, 147.4, 136.6, 133.2, 132.1, 130.4, 129.7, 129.5, 128.6, 128.3, 124.2, 122.3, 119.3, 108.2, 106.8, 101.6, 75.30.

*3-((4-methoxyphenyl)thio)-3-phenylisoindolin-1-one (**6a**)*. To a 4 mL vial was added 3-hydroxy-3-phenylisoindolin-1-one (100 mg, 0.44 mmol), $Ca(NTf_2)_2$ (3 mg, 0.0044 mmol) and $n$$Bu_4NPF_6$ (1.7 mg, 0.0044 mmol) in DCE (2 mL) at 80 ºC. The reaction was stirred for 5 minutes and 4-methoxythiophenol (75 mg, 0.533 mmol) was added in a single portion and stirred at 80 ºC for 15 minutes. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (1:1, EtOAc:Hex) to afford a cream solid (121 mg, 78%). RF (1:1 EtOAc/Hex) = 0.26. IR $\nu_{max}$ ($cm^{-}$

$^{-1}$): 3198, 3078, 2840, 1698, 1589, 1243. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{21}H_{18}NO_2S$ 348.1058; found 348.1059. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 9.73 (s, 1H), 7.86 (d, *J* = 7.8 Hz, 1H), 7.78 (d, *J* = 7.6 Hz, 2H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 2H), 7.41 – 7.23 (m, 3H), 7.02 (d, *J* = 8.7 Hz, 2H), 6.67 (d, *J* = 8.7 Hz, 2H), 3.66 (s, 3H). $^{13}$C{$^1$H} NMR (101 MHz, DMSO-$d_6$): δ 167.8, 160.4, 148.0, 139.5, 138.4, 132.1, 130.5, 128.8, 128.6, 128.5, 126.0, 124.0, 122.3, 120.1, 113.9, 75.4, 55.2.

*3-((4-(trifluoromethyl)phenyl)thio)-3-phenylisoindolin-1-one **(6b)***. To a 4 mL vial was added 3-hydroxy-3-phenylisoindolin-1-one (100 mg, 0.44 mmol), $Ca(NTf_2)_2$ (2.7 mg, 0.0044 mmol) and $n$Bu$_4$NPF$_6$ (1.7 mg, 0.0044 mmol) in DCE (2 mL) at 80 ºC. The reaction was stirred for 5 minutes and 4-(trifluoromethyl)thiophenol (95 mg, 0.533 mmol) was added in a single portion and stirred at 80 ºC for 15 minutes. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (1:1, EtOAc:Hex) to afford a cream solid (142 mg, 83%). RF (1:1 EtOAc/Hex) = 0.54. IR $\nu_{max}$ (cm$^{-1}$): 3160, 3062, 2850, 1694, 1319, 1124. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{21}H_{15}F_3NOS$ 386.0826; found 386.0828. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 9.96 (s, 1H), 7.90 (d, *J* = 7.8 Hz, 1H), 7.80 (d, *J* = 7.5 Hz, 2H), 7.65 (t, *J* = 7.2 Hz, 1H), 7.54 – 7.45 (m, 4H), 7.45 – 7.35 (m, 2H), 7.35 – 7.27 (m, 3H). $^{13}$C{$^1$H} NMR (101 MHz, DMSO-$d_6$): δ 167.7, 147.5, 139.1, 137.0, 134.9, 132.5, 130.2, 129.8, 129.4, 129.0, 128.8, 126.0, 125.1, 125.1, 124.1, 122.4, 75.8.

*3-((4-chlorophenyl)thio)-3-phenylisoindolin-1-one **(6c)***. To a 4 mL vial was added 3-hydroxy-3-phenylisoindolin-1-one (100 mg, 0.44 mmol), $Ca(NTf_2)_2$ (2.67 mg, 0.0044 mmol) and $n$Bu$_4$NPF$_6$ (1.72 mg, 0.0044 mmol) in DCE (2 mL) at 80 ºC. The reaction was stirred for 5 minutes and 4-chlorothiophenol (77 mg, 0.533 mmol) was added in a single portion and stirred at 80 ºC for 15 minutes. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (1:1, EtOAc:Hex) to afford a cream solid (136 mg, 88%). RF (1:1 EtOAc/Hex) = 0.50. IR $\nu_{max}$ (cm$^{-1}$): 3162, 3060, 2828, 1694, 1469, 1312. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{15}ClNOS$ 352.0563; found 352.0562. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 9.86 (s, 1H), 7.88 (d, *J* = 7.7 Hz, 1H), 7.78 (d, *J* = 7.6 Hz, 2H), 7.63 (dd, *J* = 10.8, 4.2 Hz, 1H), 7.52 – 7.42 (m, *J* = 7.3 Hz, 2H), 7.42 – 7.29 (m, *J* = 15.2, 7.3Z Hz, 3H), 7.21 (d, *J* = 8.5 Hz, 2H), 7.11 (d, *J* = 8.5 Hz, 2H). $^{13}$C{$^1$H} NMR (101 MHz, DMSO-$d_6$): δ 167.8, 147.6, 139.2, 138.4, 134.9, 132.4, 130.3, 129.0, 128.9, 128.7, 128.5, 126.0, 124.0, 122.4, 75.6.

*3-((3,5-dimethylphenyl)thio)-3-phenylisoindolin-1-one **(6d)***. To a 4 mL vial was added 3-hydroxy-3-phenylisoindolin-1-one (100 mg, 0.44 mmol), $Ca(NTf_2)_2$ (3 mg, 0.0044 mmol) and $n$Bu$_4$NPF$_6$ (1.7 mg, 0.0044 mmol) in DCE (2 mL) at 80 ºC. The reaction was stirred for 5 minutes and 3,5-dimethylthiophenol (74 mg, 0.533 mmol) was added in a single portion and stirred at 80 ºC for 15 minutes. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (1:1, EtOAc:Hex) to afford a cream solid (132 mg, 86%). RF (1:1 EtOAc/Hex) = 0.75. IR $\nu_{max}$ (cm$^{-1}$): 3173, 3062, 2920, 2855, 1699, 1312. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{20}NOS$ 346.1266; found 346.1263. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 9.74 (s, 1H), 7.86 (d, *J* = 7.7 Hz, 1H), 7.78 (d, *J* = 7.7 Hz, 2H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.5 Hz, 2H), 7.42 – 7.27 (m, 2H), 6.87 (s, 1H), 6.68 (s, 2H), 2.04 (s, 6H). $^{13}$C{$^1$H} NMR (101 MHz, DMSO-$d_6$): δ 167.8, 148.0, 139.5, 137.2, 134.2, 132.0, 130.8, 130.6, 129.0, 128.9, 128.5, 126.0, 124.2, 122.2, 75.5, 20.6.

*3-((2-methoxyphenyl)thio)-3-phenylisoindolin-1-one **(6e)***. To a 4 mL vial was added 3-hydroxy-3-phenylisoindolin-1-one (100 mg, 0.44 mmol), $Ca(NTf_2)_2$ (3 mg, 0.0044 mmol) and $n$Bu$_4$NPF$_6$ (1.7 mg, 0.0044 mmol) in DCE (2 mL) at 80 ºC. The reaction was stirred for 5 minutes and 2-methoxythiophenol (93 mg, 0.666 mmol) was added in a single portion and stirred at 80 ºC for 15 minutes. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (1:1, EtOAC:Hex) to afford a cream solid (151 mg, 98%). RF (1:1 EtOAc/Hex) = 0.25. IR $\nu_{max}$ (cm$^{-1}$): 3190, 3065, 2925, 2830, 1695, 1471. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{21}H_{18}NO_2S$ 348.1058; found 348.1060. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, *J* = 7.5 Hz, 2H), 7.69 (d, *J* = 7.7 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.45 (d, *J* = 7.4 Hz, 1H), 7.44 – 7.19 (m, 5H), 6.91 (d, *J* = 7.3 Hz, 1H), 6.81 – 6.73 (m, 2H), 6.59 (t, *J* = 7.4 Hz, 1H), 3.80 (s, 3H). $^{13}$C{$^1$H} NMR (101 MHz, $CDCl_3$): δ 160.9, 148.9, 139.5, 139.3, 132.3, 132.2, 129.0, 128.8, 128.6, 126.0, 124.0, 123.0, 120.7, 117.2, 111.3, 76.3, 55.9.

*3-(2-pyrimidinethio)-3-phenylisoindolin-1-one **(6f)***. To a 4 mL vial was added 3-hydroxy-3-phenylisoindolin-1-one (100 mg, 0.44 mmol), $Ca(NTf_2)_2$ (3 mg, 0.0044 mmol) and $n$Bu$_4$NPF$_6$ (1.7 mg, 0.0044 mmol) in DCE (2 mL) at 80 ºC. The reaction was stirred for 5 minutes and 2-mercaptopyrimidine (75 mg, 0.666 mmol) was added in a single portion and stirred at 80 ºC for 15 minutes. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (3:1, EtOAC:Hex) to afford a white solid (111 mg, 78%). RF (3:1 EtOAc/Hex) = 0.6. IR $\nu_{max}$ (cm$^{-1}$): 3288, 3057, 2924, 1693, 1609, 1377. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{13}N_3OSNa$ 342.0672; found 342.0671. $^1$H NMR (400 MHz, $CDCl_3$): δ.81 (s, 1H), 8.42 (d, *J* = 4.9 Hz, 2H), 7.90 (d, *J* = 7.1 Hz, 1H), 7.86 – 7.81 (m, 2H), 7.62 – 7.42 (m, 3H), 7.32 – 7.26 (m, 2H), 7.26 – 7.19 (m, 1H), 6.96 (t, *J* = 4.9 Hz, 1H). $^{13}$C{$^1$H} NMR (101 MHz, $CDCl_3$): δ 171.4, 169.4, 157.5, 147.7, 140.2, 133.1, 130.2, 129.7, 128.8, 128.3, 126.2, 124.6, 123.2, 117.7, 74.3.

*3-(2-furfurylthio)-3-phenylisoindolin-1-one **(6g)***. To a 4 mL vial was added 3-hydroxy-3-phenylisoindolin-1-one (100 mg, 0.44 mmol), $Ca(NTf_2)_2$ (3 mg, 0.0044 mmol) and $n$Bu$_4$NPF$_6$ (1.7 mg, 0.0044 mmol) in DCE (2 mL) at 80 ºC. The reaction was stirred for 5 minutes and 2-furfurylthiol (76 mg, 0.666 mmol) was added in a single portion and stirred at 80 ºC for 15 minutes. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (1:1, EtOAc:Hex) to afford a cream solid (143 mg, 78%). RF (1:1 EtOAc/Hex) = 0.39. IR $\nu_{max}$ (cm$^{-1}$): 3170, 3061, 2926, 1692, 1467, 1148. HRMS (ESI) m/z: Calcd for $C_{19}H_{16}NO_2S$ 322.0902; found 322.0901. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 9.90 (s, 1H), 7.78 – 7.66 (m, *J* = 7.2 Hz, 4H), 7.61 (t, *J* = 7.3 Hz, 1H), 7.56 – 7.48 (m, *J* = 7.3 Hz, 1H), 7.46 (s, 1H), 7.43 – 7.36 (m, *J* = 7.1 Hz, 2H), 7.36 – 7.26 (m, 1H), 6.25 (s, 1H), 5.92 (s, 1H), 3.50 (d, *J* = 14.0 Hz, 1H), 3.42 (d, *J* = 14.0 Hz, 1H). $^{13}$C{$^1$H} NMR (101 MHz, DMSO-$d_6$): δ 168.1, 149.7, 148.0, 142.5, 139.7, 132.8, 130.5, 129.2, 128.9, 128.5, 125.9, 123.8, 123.0, 110.7, 107.8, 72.9, 26.4.

*3-(benzylthio)-3-phenylisoindolin-1-one (**6h**)*. To a 4 mL vial was added 3-hydroxy-3-phenylisoindolin-1-one (100 mg, 0.44 mmol), $Ca(NTf_2)_2$ (3 mg, 0.0044 mmol) and $nBu_4NPF_6$ (1.7 mg, 0.0044 mmol) in DCE (2 mL) at 80 ºC. The reaction was stirred for 5 minutes and benzylmercaptan (66 mg, 0.53 mmol) was added in a single portion and stirred at 80 ºC for 15 minutes. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (1:1, EtOAC:Hex) to afford a cream solid (135 mg, 92%). RF (1:1 EtOAc/Hex) = 0.46. IR $\nu_{max}$ ($cm^{-1}$): 3127, 3056, 2843, 1694, 1609, 1491. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{21}H_{18}NOS$ 332.1109; found 332.1104. $^1H$ NMR (400 MHz, DMSO-$d_6$): δ 9.92 (s, 1H), 7.84 – 7.66 (m, 4H), 7.61 (t, *J* = 7.1 Hz, 1H), 7.51 (t, *J* = 7.3 Hz, 1H), 7.46 – 7.38 (m, 2H), 7.38 – 7.27 (m, 1H), 7.26 – 7.12 (m, 3H), 7.11 – 7.03 (m, 2H), 3.45 (d, *J* = 12.2 Hz, 1H), 3.30 (d, *J* = 12.2 Hz, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-$d_6$): δ 168.1, 148.2, 139.9, 136.5, 132.8, 130.6, 129.1, 128.9, 128.8, 128.4, 127.0, 125.9, 123.8, 123.0, 73.1, 34.1.

*3-(butanethio)-3-phenylisoindolin-1-one (**6i**)*. To a 4 mL vial was added 3-hydroxy-3-phenylisoindolin-1-one (100 mg, 0.44 mmol), $Ca(NTf_2)_2$ (3 mg, 0.0044 mmol) and $nBu_4NPF_6$ (1.7 mg, 0.0044 mmol) in DCE (2 mL) at 80 ºC. The reaction was stirred for 5 minutes and butanethiol (48 mg, 0.53 mmol) was added in a single portion and stirred at 80 ºC for 15 minutes. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (1:1, EtOAc:Hex) to afford a yellow oil which solidified upon standing (120 mg, 91%). RF (1:1 EtOAc/Hex) = 0.70. IR $\nu_{max}$ ($cm^{-1}$): 3185, 3066, 2956, 1698, 1310. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{20}NOS$ 298.1266; found 298.1259. $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.98 (s, 1H), 7.83 (d, *J* = 7.5 Hz, 1H), 7.77 – 7.67 (m, 2H), 7.67 – 7.53 (m, 2H), 7.45 (td, *J* = 7.4, 0.8 Hz, 1H), 7.40 – 7.27 (m, 3H), 2.35 – 2.25 (m, 1H), 2.11 – 1.98 (m, 1H), 1.45 – 1.12 (m, 4H), 0.74 (t, *J* = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 169.7, 149.3, 140.0, 132.9, 130.3, 129.0, 128.9, 128.6, 125.8, 123.8, 123.7, 73.2, 30.7, 29.3, 22.1, 13.6.

*3-(cyclohexanethio)-3-phenylisoindolin-1-one (**6j**)*. To a 4 mL vial was added 3-hydroxy-3-phenylisoindolin-1-one (100 mg, 0.44 mmol), $Ca(NTf_2)_2$ (3 mg, 0.0044 mmol) and $nBu_4NPF_6$ (1.7 mg, 0.0044 mmol) in DCE (2 mL) at 80 ºC. The reaction was stirred for 5 minutes and cyclohexanethiol (77 mg, 0.66 mmol) was added in a single portion and stirred at 80 ºC for 15 minutes. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (1:1, EtOAc:Hex) to afford a yellow oil which solidified upon standing (134 mg, 93%). RF (1:1 EtOAc/Hex) = 0.52. IR $\nu_{max}$ ($cm^{-1}$): 3156, 3061, 2926, 1690, 1464, 1312. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{22}NOS$ 324.1422; found 324.1418. $^1H$ NMR (400 MHz, $CDCl_3$): δ 7.83 (d, *J* = 7.5 Hz, 1H), 7.75 – 7.68 (m, 3H), 7.63 (d, *J* = 7.7 Hz, 1H), 7.56 (td, *J* = 7.6, 1.0 Hz, 1H), 7.45 (td, *J* = 7.5, 0.9 Hz, 1H), 7.39 – 7.24 (m, 3H), 2.35 – 2.20 (m, 1H), 1.91 – 1.75 (m, 1H), 1.68 – 1.55 (m, 1H), 1.55 – 1.44 (m, 1H), 1.44 – 1.28 (m, 3H), 1.28 – 0.97 (m, 4H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 169.5, 149.6, 140.3, 132.8, 130.1, 128.9, 128.6, 125.8, 124.0, 123.8, 77.5, 43.3, 35.1, 34.6, 26.0, 25.9, 25.5.

*3-(4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)benzenethiol)-3-phenylisoindolin-1-one (**6k**)*. To a 4 mL vial was added 3-hydroxy-3-phenylisoindolin-1-one (50 mg, 0.22 mmol), $Ca(NTf_2)_2$ (3 mg, 0.0022 mmol) and $nBu_4NPF_6$ (1.7 mg, 0.0022 mmol) in DCE (1 mL) at 80 ºC. The reaction was stirred for 5 minutes and 4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)benzenethiol (79 mg, 0.33 mmol) was added in a single portion and stirred at 80 ºC for 15 minutes. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (1:1, EtOAc:Hex) to afford a peach solid (73 mg, 74%). RF (1:1 EtOAc/CycHex) = 0.60. IR $\nu_{max}$ ($cm^{-1}$): 3502, 3162, 3067, 2989, 1697, 1358. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{26}H_{27}BNO_3S$ 444.1805; found 444.1813. $^1H$ NMR (400 MHz, DMSO-$d_6$): δ 9.88 (s, 1H), 7.89 (d, *J* = 7.8 Hz, 1H), 7.78 (d, *J* = 7.4 Hz, 2H), 7.68 – 7.61 (m, 1H), 7.46 (t, *J* = 7.5 Hz, 2H), 7.38 (q, *J* = 8.1 Hz, 4H), 7.30 (d, *J* = 7.4 Hz, 1H), 7.14 (d, *J* = 8.0 Hz, 2H), 1.25 (s, 12H). $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-$d_6$): δ 167.8, 147.8, 139.4, 135.9, 134.1, 133.1, 132.3, 130.3, 128.9, 128.8, 128.7, 126.0, 124.1, 122.4, 84.0, 75.5, 25.0, 24.7, 24.7.

*2-benzyl-3-(2-chloro-4-methylanilino)-2,3-dihydro-1H-isoindol-1-one (**8a**)*. To a 4 mL vial was added 2-benzyl-3-hydroxy-2,3-dihydro-isoindol-1-one (50 mg, 0.21 mmol), $Ca(NTf_2)_2$ (13 mg, 0.021 mmol) and $nBu_4NPF_6$ (8 mg, 0.021 mmol) in DCE (1 mL) at room temperature. 2-chloro-4-methylaniline (45 mg, 0.31 mmol) was added in a single portion and the reaction was stirred at 80 ºC overnight. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (0 to 2% EtOAc:DCM) to afford the desired product as a cream solid (48 mg, 63%). RF (1:1 EtOAc/Hex) = 0.71. IR $\nu_{max}$ ($cm^{-1}$): 3361, 3031, 2924, 1683, 1615, 1520. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{20}ClN_2O$ 363.1264; found. 363.1265. $^1H$ NMR (400 MHz, DMSO-$d_6$): δ 7.86 – 7.78 (m, 1H), 7.69 – 7.53 (m, 2H), 7.46 (d, *J* = 7.1 Hz, 1H), 7.33 – 7.22 (m, 2H), 7.22 – 7.17 (m, 2H), 7.09 (d, *J* = 1.5 Hz, 1H), 6.68 (dd, *J* = 8.4, 1.5 Hz, 1H), 6.25 (d, *J* = 8.2 Hz, 1H), 6.12 (d, *J* = 8.3 Hz, 1H), 6.04 (d, *J* = 8.2 Hz, 1H), 4.87 (d, *J* = 15.4 Hz, 1H), 4.21 (d, *J* = 15.5 Hz, 1H), 2.10 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-$d_6$): δ 166.6, 143.9, 139.1, 137.5, 132.3, 132.1, 129.7, 129.3, 128.4, 128.1, 128.0, 127.6, 127.1, 123.3, 122.9, 119.3, 113.8, 68.5, 42.4, 19.6.

*2-benzyl-3-(2,4-difluoroanilino)-2,3-dihydro-1H-isoindol-1-one (**8b**)*. To a 4 mL vial was added 2-benzyl-3-hydroxy-2,3-dihydro-isoindol-1-one (50 mg, 0.21 mmol), $Ca(NTf_2)_2$ (13 mg, 0.021 mmol) and $nBu_4NPF_6$ (8 mg, 0.021 mmol) in DCE (1 mL) at room temperature. 2,4-difluoroaniline (41 mg, 0.31 mmol) was added in a single portion and the reaction was stirred at 80 ºC overnight. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (1:10 EtOAc:Hex) to afford the desired product as a colorless oil (48 mg, 68%). RF (1:1 EtOAc/Hex) = 0.58. IR $\nu_{max}$ ($cm^{-1}$): 3415, 2917, 1694, 1497, 1113. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{21}H_{17}F_2N_2O$ 351.1309; found 351.1315. . $^1H$ NMR (400 MHz, DMSO-$d_6$): δ 7.94 – 7.92 (m, 1H), 7.57 – 7.53 (m, 2H), 7.47 – 7.43 (m, 1H), 7.32 – 7.24 (m, 3H), 7.21 – 7.19 (m, 2H), 6.79 (ddd, *J* = 11.3, 8.4, 2.8 Hz, 1H), 6.56 (ddd, *J* = 4.3, 3.5, 1.6 Hz, 1H), 6.27 (td, *J* = 9.3, 5.4 Hz, 1H), 5.71 (s, 1H), 5.26 (d, *J* = 15.1 Hz, 1H), 4.29 – 4.11 (m, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-$d_6$): δ 167.7, 143.2, 137.0, 132.4, 132.1, 129.8, 129.6 (dd, *J* = 11.4,

2.9 Hz), 128.9, 128.2, 127.8, 124.00, 123.1, 115.3 (dd, $J$ = 8.9, 3.4 Hz), 111.2 (d, $J$ = 3.7 Hz), 111.0 (d, $J$ = 3.7 Hz), 104.0 (dd, $J$ = 26.4, 23.5 Hz), 68.9, 43.2.

*2-benzyl-3-[2-methoxy-5-(trifluoromethyl)anilino]-2,3-dihydro-1H-isoindol-1-one (**8c**)*. To a 4 mL vial was added 2-benzyl-3-hydroxy-2,3-dihydro-isoindol-1-one (50 mg, 0.21 mmol), $Ca(NTf_2)_2$ (13 mg, 0.021 mmol) and $n$Bu$_4$NPF$_6$ (8 mg, 0.021 mmol) in DCE (1 mL) at room temperature. 2-methoxy-5-(trifluoromethyl)aniline (60 mg, 0.31 mmol) was added in a single portion and the reaction was stirred at 80 ºC overnight. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (0 to 5% EtOAc:DCM) to afford the desired product as a light brown solid (70 mg, 81%). RF (1:20 EtOAc/DCM) = 0.33. IR $\nu_{max}$ (cm$^{-1}$): 3415, 2917, 1694, 1497, 1113. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{23}H_{19}F_3N_2O_2$ 413.1477; found 413.1497. $^1$H NMR (400 MHz, DMSO-d$_6$): δ 7.81 (d, $J$ = 6.5 Hz, 1H), 7.70 – 7.52 (m, 2H), 7.48 (d, $J$ = 6.8 Hz, 1H), 7.28 – 7.05 (m, 5H), 6.95 – 6.82 (m, 2H), 6.44 (d, $J$ = 8.1 Hz, 1H), 6.21 (s, 1H), 6.12 (d, $J$ = 8.3 Hz, 1H), 4.79 (d, $J$ = 15.4 Hz, 1H), 4.28 (d, $J$ = 15.5 Hz, 1H), 3.81 (s, 3H). $^{13}$C{$^1$H} NMR (101 MHz, DMSO-d$_6$): δ 166.6, 149.6, 143.7, 137.4, 135.2, 132.3, 132.1, 129.4, 128.2, 127.4, 126.9, 123.4, 122.9, 114.6, 110.0, 107.5, 68.2, 55.8, 42.7.

*2-benzyl-3-(cyclopropylamino)-2,3-dihydro-1H-isoindol-1-one (**8d**)*. To a 4 mL vial was added 2-benzyl-3-hydroxy-2,3-dihydro-isoindol-1-one (50 mg, 0.21 mmol), $Ca(NTf_2)_2$ (13 mg, 0.021 mmol) and $n$Bu$_4$NPF$_6$ (8 mg, 0.021 mmol) in DCE (1 mL) at room temperature. cyclopropylamine (18 mg, 0.31 mmol) was added in a single portion and the reaction was stirred at 80 ºC overnight. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (1:5 EtOAc:Hex, 1% $NEt_3$) to afford the desired product as a colorless oil (39 mg, 67%). RF (1:5 EtOAc/Hex) = 0.48. IR $\nu_{max}$ (cm$^{-1}$): 3415, 2917, 1694, 1497, 1113. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{19}N_2O$ 279.1497; found 279.1492. $^1$H NMR (400 MHz, DMSO-d$_6$): δ 7.88 – 7.86 (m, 1H), 7.55 – 7.46 (m, 3H), 7.33 – 7.24 (m, 5H), 5.30 (d, $J$ = 15.0 Hz, 1H), 5.16 (s, 1H), 4.27 (d, $J$ = 15.0 Hz, 1H), 2.05 – 2.00 (m, 1H), 0.39 – 0.30 (m, 2H), 0.22 – 0.08 (m, 2H). $^{13}$C{$^1$H}NMR (101 MHz, DMSO-d$_6$):δ 167.8, 144.6, 137.6, 132.5, 131.6, 129.0, 128.9, 128.3, 127.6, 123.6, 123.5, 72.4, 43.1, 24.7, 7.6, 6.0.

*2-benzyl-3-(benzylamino)-2,3-dihydro-1H-isoindol-1-one (**8e**)*. To a 4 mL vial was added 2-benzyl-3-hydroxy-2,3-dihydro-isoindol-1-one (50 mg, 0.21 mmol), $Ca(NTf_2)_2$ (12.5 mg, 0.021 mmol) and $n$Bu$_4$NPF$_6$ (8.1 mg, 0.021 mmol) in DCE (1 mL) at room temperature. benzylamine (34 mg, 0.31 mmol) was added in a single portion and the reaction was stirred at 80 ºC overnight. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (1:5 EtOAc:Hex, 1% $NEt_3$) to afford the desired product as a colorless oil (64 mg, 93%). RF (1:1 EtOAc/Hex) = 0.61. IR $\nu_{max}$ (cm$^{-1}$): 3320, 3029, 2850, 1678, 1454, 1219. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{21}N_2O$ 329.1654; found 329.1652. $^1$H NMR (400 MHz, DMSO-d$_6$): δ 7.89 (d, $J$ = 7.3 Hz, 1H), 7.57 – 7.48 (m, 3H), 7.34 – 7.21 (m, 8H), 7.16 (d, $J$ = 6.8 Hz, 2H), 5.34 (s, 1H), 5.19 (d, $J$ = 15.0 Hz, 1H), 4.34 (d, $J$ = 15.0 Hz, 1H), 3.36 (d, $J$ = 13.0 Hz, 1H), 3.25 (d, $J$ = 13.0 Hz, 1H). $^{13}$C{$^1$H} NMR (101 MHz, DMSO-d$_6$): δ 168.2, 143.6, 140.0, 137.8, 133.2, 132.3, 129.6, 129.3, 128.8, 128.7, 128.5, 128.1, 127.6, 124.0, 123.6, 72.7, 45.9, 43.6.

*Benzyl (2-benzyl-3-oxo-2,3-dihydro-1H-isoindol-1-yl)carbamate (**12a**)*. To a 4 mL vial was added 2-benzyl-3-hydroxy-2,3-dihydro-isoindol-1-one (50 mg, 0.21 mM), $Ca(NTf_2)_2$ (1.3 mg, 0.0021 mmol) and $n$Bu$_4$NPF$_6$ (0.8 mg, 0.0021 mmol) in DCE (1 mL) at 80 ºC. The reaction was stirred for 1 minute and benzylcarbamate (35 mg, 0.23 mmol) was added in a single portion and stirred at 80 ºC for 15 minutes. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (1:1, EtOAc:Hex) followed by trituration with $Et_2O$ to afford the product as a white solid (70 mg, 90%). RF (1:5 EtOAc/DCM) = 0.74. IR $\nu_{max}$ (cm$^{-1}$): 3306, 3034, 2925, 1687, 1528, 1425. . HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{23}H_{21}N_2O_3$ 373.1552 found 373.1552. $^1$H NMR (400 MHz, DMSO-d$_6$): δ 8.23 (d, $J$ = 9.2 Hz, 1H), 7.73 (d, $J$ = 7.4 Hz, 1H), 7.64 (t, $J$ = 7.3 Hz, 1H), 7.55 (dd, $J$ = 13.5, 7.3 Hz, 2H), 7.46 – 7.20 (m, 10H), 6.09 (d, $J$ = 9.1 Hz, 1H), 5.20 – 4.98 (m, 2H), 4.80 (d, $J$ = 15.4 Hz, 1H), 4.32 (d, $J$ = 15.4 Hz, 1H). $^{13}$C{$^1$H} NMR (101 MHz, DMSO-d$_6$): δ 166.5, 156.3, 143.0, 137.6, 136.7, 132.3, 131.7, 129.4, 128.4, 128.0, 127.8, 127.7, 127.2, 123.5, 122.7, 65.9, 65.8, 43.1

*tert-butyl (2-benzyl-3-oxo-2,3-dihydro-1H-isoindol-1-yl)carbamate (**12b**)*. To a 4 mL vial was added 2-benzyl-3-hydroxy-2,3-dihydro-isoindol-1-one (50 mg, 0.21 mmol), $Ca(NTf_2)_2$ (1.3 mg, 0.0021 mmol) and $n$Bu$_4$NPF$_6$ (0.8 mg, 0.0021 mmol) in DCE (1 mL) at 80 ºC. The reaction was stirred for 1 minute and tert-butylcarbamate (29 mg, 0.25 mmol) was added in a single portion and stirred at 80 ºC for 15 minutes. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (1:1 EtOAC:Hex) followed by trituration with $Et_2O$ to afford the product as a white solid (61 mg, 86%). RF (1:1 EtOAc/Hex) = 0.50. IR $\nu_{max}$ (cm$^{-1}$): 3270, 2985, 2929, 1712, 1684, 1519. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{23}N_2O_2$ 339.1709; found 339.1696. $^1$H NMR (400 MHz, DMSO-d$_6$): δ 7.81 (d, $J$ = 9.1 Hz, 1H), 7.71 (d, $J$ = 7.4 Hz, 1H), 7.63 (t, $J$ = 7.2 Hz, 1H), 7.58 – 7.46 (m, 1H), 7.39 – 7.18 (m, 1H), 6.03 (d, $J$ = 9.0 Hz, 1H), 4.83 (d, $J$ = 15.3 Hz, 1H), 4.28 (d, $J$ = 15.5 Hz, 1H), 1.39 (s, 1H). $^{13}$C{$^1$H} NMR (101 MHz, DMSO-d$_6$): δ 166.6, 155.6, 143.3, 137.8, 132.2, 131.7, 129.3, 128.5, 127.6, 127.1, 123.5, 122.6, 79.0, 65.5, 43.1, 28.1.

*N-(2-benzyl-3-oxo-2,3-dihydro-1H-isoindol-1-yl)benzamide (**12c**)*. To a 4 mL vial was added 2-benzyl-3-hydroxy-2,3-dihydro-isoindol-1-one (50 mg, 0.21 mmol) $Ca(NTf_2)_2$ (6.3 mg, 0.0104 mmol) and $n$Bu$_4$NPF$_6$ (4 mg, 0.0104 mmol) in DCE (1 mL) at 80 ºC. The reaction was stirred for 1 minute and benzamide (38 mg, 0.3 mmol) was added in a single portion and stirred at 80 ºC for 15 minutes. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (1:1, EtOAc:Hex) to afford a white solid (68 mg, 95%). RF (1:1 EtOAc/Hex) = 0.41. IR $\nu_{max}$ (cm$^{-1}$): 3548, 3278, 3031, 2933, 1705, 1270. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{19}N_2O_2$ 343.1447; found 343.1441. $^1$H NMR (400 MHz, DMSO-d$_6$): δ 9.20 (d, $J$ = 8.9 Hz, 1H), 7.82 (d, $J$ = 7.6 Hz, 2H), 7.78 (d, $J$ = 7.3 Hz, 1H), 7.71 – 7.51 (m, 4H), 7.45 (t, $J$ = 7.6 Hz, 2H), 7.38 – 7.14 (m, 5H), 6.61 (d, $J$ = 8.9 Hz, 1H), 4.85 (d, $J$ = 15.4 Hz, 1H), 4.37 (d, $J$ = 15.4 Hz, 1H). $^{13}$C{$^1$H} NMR (101 MHz, DMSO-d$_6$): δ 167.3,

166.9, 143, 137.7, 133.3, 132.3, 131.9, 131.9, 129.4, 128.5, 128.3, 127.7, 127.6, 127.2, 123.6, 122.8, 63.8, 43.2.

*2-benzyl-3-(2-oxo-1,3-oxazolidin-3-yl)-2,3-dihydro-1H-isoindol-1-one (**12d**)*. To a 4 mL vial was added 2-benzyl-3-hydroxy-2,3-dihydro-isoindol-1-one (50 mg, 0.21 mmol), $Ca(NTf_2)_2$ (1.3 mg, 0.0021 mmol) and $n$$Bu_4NPF_6$ (1 mg, 0.0021 mmol) in DCE (1 mL) at 80 ºC. The reaction was stirred for 1 minute and 2-oxazolidinone (27 mg, 0.31 mmol) was added in a single portion and stirred at 80 ºC for 15 minutes. Once TLC analysis indicated conversion to the product, the product was concentrated and purified by flash column chromatography (1:9, EtOAc:DCM) to afford a white semi-solid (49 mg, 76%). RF (1:5 EtOAc/DCM) = 0.64. IR $\nu_{max}$ ($cm^{-1}$): 2972, 1755, 1701, 1404, 1215. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{17}N_2O_3$ 309.1239; found 309.1246. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.91 (d, $J$ = 6.9 Hz, 1H), 7.64 – 7.53 (m, 2H), 7.46 (d, $J$ = 6.9 Hz, 2H), 7.41 (d, $J$ = 7.2 Hz, 1H), 7.38 – 7.27 (m, 3H), 6.42 (s, 1H), 4.96 (d, $J$ = 14.7 Hz, 1H), 4.47 (d, $J$ = 14.7 Hz, 1H), 4.06 (td, $J$ = 9.0, 6.5 Hz, 1H), 3.53 (td, $J$ = 9.0, 7.2 Hz, 1H), 2.75 (dd, $J$ = 15.9, 8.8 Hz, 1H), 2.54 (td, $J$ = 9.0, 6.5 Hz, 1H). $^{13}$C{$^1$H} NMR (101 MHz, $CDCl_3$): δ 167.5, 158.2, 139.7, 137.4, 132.7, 132.4, 130.3, 128.9, 128.8, 128.0, 124.3, 123.0, 68.7, 62.2, 45.1, 38.8.

*N-(2-benzyl-3-oxo-2,3-dihydro-1H-isoindol-1-yl)-4-methylbenzene-1-sulfonamide (**14a**)*. To a 4 mL vial was added 2-benzyl-3-hydroxy-2,3-dihydro-isoindol-1-one (50 mg, 0.21 mmol), $Ca(NTf_2)_2$ (6.3 mg, 0.0104 mmol) and $n$$Bu_4NPF_6$ (4 mg, 0.0104 mmol) in DCE (1 mL) at 80 ºC. The reaction was stirred for 1 minute and $p$-toluenesulfonamide (36 mg, 0.21 mmol) was added in a single portion and stirred at 80 ºC overnight. Once TLC analysis indicated conversion to the product, hexane (2 mL) was added and the product was collected by filtration as a white solid (68 mg, 85%). RF (1:5 EtOAc/DCM) = 0.57. IR $\nu_{max}$ ($cm^{-1}$): 3125, 2935, 2884, 1674, 1495, 1162. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{21}N_2O_3S$ 393.1273; found 393.1276. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 8.94 (d, $J$ = 8.8 Hz, 1H), 7.72 (dd, $J$ = 25.2, 6.9 Hz, 3H), 7.58 – 7.46 (m, 2H), 7.43 (d, $J$ = 7.9 Hz, 2H), 7.35 – 7.20 (m, 3H), 7.16 (d, $J$ = 7.2 Hz, 2H), 6.73 (d, $J$ = 6.2 Hz, 1H), 5.78 (d, $J$ = 8.7 Hz, 1H), 4.82 (d, $J$ = 15.6 Hz, 1H), 4.22 (d, $J$ = 15.5 Hz, 1H), 2.44 (s, 3H). $^{13}$C{$^1$H} NMR (101 MHz, DMSO-$d_6$): δ 166.3, 143.3, 142.7, 139.0, 137.3, 132.3, 131.2, 123.0, 129.7, 128.4, 127.50, 127.1, 126.4, 123.1, 122.8, 67.6, 42.3, 21.1.

*N-(2-benzyl-3-oxo-2,3-dihydro-1H-isoindol-1-yl)-4-methoxybenzene-1-sulfonamide (**14b**)*. To a 4 mL vial was added 2-benzyl-3-hydroxy-2,3-dihydro-isoindol-1-one (50 mg, 0.21 mmol), $Ca(NTf_2)_2$ (6.27 mg, 0.0104 mmol) and $n$$Bu_4NPF_6$ (4.05 mg, 0.0104 mmol) in DCE (1 mL) at 80 ºC. The reaction was stirred for 1 minute and 4-methoxybenezenesulfonamide (39 mg, 0.21 mmol) was added in a single portion and stirred at 80 ºC overnight. Once TLC analysis indicated conversion to the product, hexane (2 mL) was added and the product was collected by filtration as a white solid (78 mg, 91%). RF (1:5 EtOAc/DCM) = 0.30. IR $\nu_{max}$ ($cm^{-1}$): 3130, 2929, 2843, 1677, 1594, 1495. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{21}N_2O_4S$ 409.1222; found 409.1227. $^1$H NMR (400 MHz, DMSO-$d_6$):δ 8.97 – 8.76 (m, 1H), 7.80 (d, $J$ = 8.5 Hz, 2H), 7.70 (s, 1H), 7.57 – 7.47 (m, 2H), 7.35 – 7.09 (m, 7H), 6.77 (s, 1H), 5.86 – 5.65 (m, 1H), 4.82 (d, $J$ = 15.6 Hz, 1H), 4.24 (d, $J$ = 15.5 Hz, 1H), 3.87 (s, 3H). $^{13}$C{$^1$H} NMR (101 MHz, DMSO-$d_6$): δ 166.3, 162.5, 142.8, 137.4, 133.5, 132.3, 131.2, 129.7, 128.6, 128.4, 127.5, 127.1, 123.2, 122.8, 114.6, 67.5, 55.8, 42.3.

*N-(2-benzyl-3-oxo-2,3-dihydro-1H-isoindol-1-yl)-2-(trifluoromethoxy)benzene-1-sulfonamide (**14c**)*. To a 4 mL vial was added 2-benzyl-3-hydroxy-2,3-dihydro-isoindol-1-one (50 mg, 0.21 mmol), $Ca(NTf_2)_2$ (6.2 mg, 0.0104 mmol) and $n$$Bu_4NPF_6$ (4 mg, 0.0104 mmol) in DCE (1 mL) at 80 ºC. The reaction was stirred for 1 minute and 2-(trifluoromethoxy)benezenesulfonamide (55 mg, 0.23 mmol) was added in a single portion and stirred at 80 ºC overnight. Once TLC analysis indicated conversion to the product, hexane (2 mL) was added and the product was collected by filtration as a white solid (75 mg, 78%). RF (1:5 EtOAc/DCM) = 0.56. IR $\nu_{max}$ ($cm^{-1}$): 3106, 3063, 1687, 1592, 1444, 1163. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{18}F_3N_2O_4S$ 463.0939; found 463.0930. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 9.28 (d, $J$ = 8.8 Hz, 1H), 8.03 – 7.81 (m, 2H), 7.80 – 7.61 (m, 2H), 7.61 – 7.46 (m, 3H), 7.42 – 7.19 (m, 3H), 7.12 (d, $J$ = 6.8 Hz, 2H), 7.06 – 6.88 (m, 1H), 5.79 (d, $J$ = 8.7 Hz, 1H), 4.90 (d, $J$ = 15.6 Hz, 1H), 4.17 (d, $J$ = 15.6 Hz, 1H). $^{13}$C{$^1$H} NMR (101 MHz, DMSO-$d_6$): δ 166.4, 144.9, 142.5, 137.1, 135.5, 133.6, 132.4, 131.3, 130.1, 129.8, 128.5, 127.8, 127.3, 127.2, 123.0, 122.9, 121.1, 67.5, 42.2.

*N-(2-benzyl-3-oxo-2,3-dihydro-1H-isoindol-1-yl)-3-chlorobenzene-1-sulfonamide (**14d**)*. To a 4 mL vial was added 2-benzyl-3-hydroxy-2,3-dihydro-isoindol-1-one (50 mg, 0.21 mmol), $Ca(NTf_2)_2$ (6.3 mg, 0.0104 mmol) and $n$$Bu_4NPF_6$ (4 mg, 0.0104 mmol) in DCE (1 mL) at 80 ºC. The reaction was stirred for 1 minute and 3-chloro-benezenesulfonamide (44 mg, 0.23 mmol) was added in a single portion and stirred at 80 ºC for 2h. Once TLC analysis indicated conversion to the product, hexane (2 mL) was added and the product was collected by filtration as a white solid (65 mg, 75%). RF (1:5 EtOAc/DCM) = 0.60. IR $\nu_{max}$ ($cm^{-1}$): 3181, 3056, 1687, 1494, 1468, 1157. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{21}H_{18}ClN_2O_3S$ 413.0727; found 413.0727. $^1$H NMR (400 MHz, DMSO-$d_6$): δ 9.19 (d, $J$ = 8.7 Hz, 1H), 7.89 – 7.78 (m, 3H), 7.76 – 7.64 (m, 2H), 7.53 (p, $J$ = 8.1 Hz, 2H), 7.36 – 7.22 (m, 3H), 7.18 (d, $J$ = 7.3 Hz, 2H), 6.76 (d, $J$ = 6.2 Hz, 1H), 5.90 (d, $J$ = 8.7 Hz, 1H), 4.83 (d, $J$ = 15.6 Hz, 1H), 4.24 (d, $J$ = 15.6 Hz, 1H). $^{13}$C{$^1$H} NMR (101 MHz, DMSO-$d_6$): δ 166.3, 143.7, 142.4, 137.2, 134.1, 133.0, 132.3, 131.9, 131.2, 129.8, 128.5, 127.5, 127.2, 126.1, 125.0, 123.2, 122.9, 67.7, 42.7.

*N-(2-benzyl-3-oxo-2,3-dihydro-1H-isoindol-1-yl)-3-fluorobenzene-1-sulfonamide (**14e**)*. To a 4 mL vial was added 2-benzyl-3-hydroxy-2,3-dihydro-isoindol-1-one (50 mg, 0.21 mmol), $Ca(NTf_2)_2$ (6.3 mg, 0.0104 mmol) and $n$$Bu_4NPF_6$ (4 mg, 0.0104 mmol) in DCE (1 mL) at 80 ºC. The reaction was stirred for 1 minute and 3-fluorobenezenesulfonamide (40 mg, 0.23 mmol) was added in a single portion and stirred at 80 ºC overnight. Once TLC analysis indicated conversion to the product, hexane (2 mL) was added and the product was collected by filtration as a white solid (65 mg, 68%). RF (1:5 EtOAc/DCM) = 0.60. IR $\nu_{max}$ ($cm^{-1}$): 3197, 3072, 2936, 1685, 1494, 1345. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{21}H_{18}FN_2O_3S$ 397.1022; found 397.1023. $^1$H NMR (400 MHz,

DMSO-$d_6$): δ 9.17 (d, *J* = 8.8 Hz, 1H), 7.80 – 7.57 (m, 5H), 7.52 (p, *J* = 7.7 Hz, 2H), 7.35 – 7.14 (m, 5H), 6.73 (d, *J* = 6.0 Hz, 1H), 5.90 (d, *J* = 8.8 Hz, 1H), 4.83 (d, *J* = 15.6 Hz, 1H), 4.25 (d, *J* = 15.6 Hz, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-$d_6$): δ 166.3, 163.1, 160.6, 143.9 (d, *J* = 6.6 Hz), 142.5, 137.3, 132.4, 132.1 (d, *J* = 7.9 Hz), 131.2, 129.8, 128.5, 127.5, 127.1, 123.1, 122.9, 122.6, 120.2 (d, *J* = 21.1 Hz), 113.6 (d, *J* = 24.5 Hz), 67.7, 42.5

*N-(2-benzyl-3-oxo-2,3-dihydro-1H-isoindol-1-yl)-2,4-difluorobenzene-1-sulfonamide (**14f**)*. To a 4 mL vial was added 2-benzyl-3-hydroxy-2,3-dihydro-isoindol-1-one (43 mg, 0.18 mmol), $Ca(NTf_2)_2$ (6 mg, 0.00906 mmol) and $n$$Bu_4NPF_6$ (4 mg, 0.0906 mmol) in DCE (1 mL) at 80 ºC. The reaction was stirred for 1 minute and 2,4-difluorobenezenesulfonamide (35 mg, 0.18 mmol) was added in a single portion and stirred at 80 ºC overnight. Once TLC analysis indicated conversion to the product, hexane (2 mL) was added and the product was collected by filtration as a white solid (45 mg, 60%). RF (1:5 EtOAc/DCM) = 0.69. IR $\nu_{max}$ ($cm^{-1}$): 3541, 3265, 3091, 1681, 1601, 1418. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{21}H_{17}F_2N_2O_3S$ 415.0928; found 415.0924. $^1H$ NMR (400 MHz, DMSO-$d_6$): δ 9.43 (d, *J* = 8.7 Hz, 1H), 7.80 (dd, *J* = 14.9, 8.5 Hz, 1H), 7.76 – 7.67 (m, 1H), 7.66 – 7.50 (m, 3H), 7.35 – 7.20 (m, 5H), 7.15 (d, *J* = 6.9 Hz, 2H), 7.06 (d, *J* = 6.9 Hz, 1H), 5.79 (d, *J* = 8.6 Hz, 1H), 4.89 (d, *J* = 15.8 Hz, 1H), 4.23 (d, *J* = 15.8 Hz, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-$d_6$): δ 166.5, 166.5, 164.0 (d, *J* = 11.6 Hz), 160.1 (d, *J* = 13.6 Hz), 157.5 (d, *J* = 13.5 Hz), 142.4, 137.1, 132.5, 131.4 (d, *J* = 10.8 Hz), 131.3, 129.8, 128.5, 127.2, 127.2, 126.2 (dd, *J* = 13.9, 3.4 Hz), 123.0 (d, *J* = 24.2 Hz), 112.4 (d, *J* = 22.7 Hz), 67.5, 42.3.

*N-(2-benzyl-3-oxo-2,3-dihydro-1H-isoindol-1-yl)thiophene-2-sulfonamide (**14g**)*. To a 4 mL vial was added 2-benzyl-3-hydroxy-2,3-dihydro-isoindol-1-one (50 mg, 0.21 mmol), $Ca(NTf_2)_2$ (6.3 mg, 0.0104 mmol) and $n$$Bu_4NPF_6$ (4 mg, 0.0104 mmol) in DCE (1 mL) at 80 ºC. The reaction was stirred for 1 minute and 2-thiophenesulfonamide (38 mg, 0.23 mmol) was added in a single portion and stirred at 80 ºC overnight. Once TLC analysis indicated conversion to the product, hexane (2 mL) was added and the product was collected by filtration as a white solid (62 mg, 77%). RF (1:5 EtOAc/DCM) = 0.58. IR $\nu_{max}$ ($cm^{-1}$): 3345, 3105, 2894, 1664, 1467, 1198. . HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{19}H_{17}N_2O_3S_2$ 385.0681; found 385.0680. $^1H$ NMR (400 MHz, DMSO-$d_6$): δ 9.25 (d, *J* = 8.8 Hz, 1H), 8.04 (d, *J* = 4.8 Hz, 1H), 7.75 – 7.60 (m, 2H), 7.56 – 7.45 (m, 2H), 7.37 – 7.17 (m, 6H), 6.83 – 6.61 (m, 1H), 5.84 (d, *J* = 8.8 Hz, 1H), 4.85 (d, *J* = 15.5 Hz, 1H), 4.29 (d, *J* = 15.6 Hz, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-$d_6$): δ 166.3, 142.7, 142.5, 137.4, 133.4, 132.4, 132.4, 131.2, 129.8, 128.5, 128.1, 127.6, 127.1, 123.1, 122.9, 67.7, 42.5.

*N-(2-benzyl-3-oxo-2,3-dihydro-1H-isoindol-1-yl)cyclopropanesulfonamide (**14h**)*. To a 4 mL vial was added 2-benzyl-3-hydroxy-2,3-dihydro-isoindol-1-one (50 mg, 0.21 mmol), $Ca(NTf_2)_2$ (6.3 mg, 0.0104 mmol) and $n$$Bu_4NPF_6$ (4 mg, 0.0104 mmol) in DCE (1 mL) at 80 ºC. The reaction was stirred for 1 minute and cyclopropanesulfonamide (28 mg, 0.23 mmol) was added in a single portion and stirred at 80 ºC overnight. Once TLC analysis indicated conversion to the product, hexane (2 mL) was added and the product was collected by filtration as a white solid (44 mg, 61%). RF (1:5 EtOAc/DCM) = 0.35. IR $\nu_{max}$ ($cm^{-1}$): 3387, 3277, 3125, 1671, 1470, 1295. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{19}N_2O_3S$ 343.1116; found 343.1118.. $^1H$ NMR (400 MHz, DMSO-$d_6$):δ 8.48 (s, 1H), 7.80 – 7.65 (m, 3H), 7.65 – 7.54 (m, 1H), 7.42 – 7.28 (m, 4H), 7.28 – 7.17 (m, 1H), 5.88 (s, 1H), 4.92 (d, *J* = 15.5 Hz, 1H), 4.42 (d, *J* = 15.6 Hz, 1H), 3.08 – 2.80 (m, 1H), 1.13 – 0.97 (m, 2H), 0.96 – 0.83 (m, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-$d_6$): δ 166.3, 143.2, 137.7, 132.4, 131.3, 129.7, 128.5, 127.7, 127.1, 124.0, 122.7, 67.7, 42.2, 31.6, 5.6, 5.3.

**Supporting Information**

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

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